ALAGAPPA UNIVERSITY

[Accredited with 'A+' Grade by NAAC (CGPA:3.64) in the Third Cycle and Graded as Category–I University by MHRD-UGC]

KARAIKUDI – 630 003

DIRECTORATE OF DISTANCE EDUCATION

M.Sc. [Home Science – Nutrition and Dietetics]

365 22

FUNCTIONAL FOODS AND NUTRACEUTICALS

II - Semester

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SYLLABI-BOOK MAPPING TABLE

Functional Foods and Nutraceuticals

Syllabi	Mapping in Book
BLOCK - I: FUNCTIONAL FOODS, PROBIOTICS AND PREBIOTICS	
Unit 1: Definition, History, Classification of Functional Foods: Probiotics, Prebiotics and Synbiotics; Nutrient vs. Non-nutrient.	**Unit 1:** Functional Food **(Pages 1-26);**
Unit 2: Probiotics - Taxonomy and Important Features of Probiotic Micro-Organisms. Health Effects of Probiotics Including Mechanism of Action.	**Unit 2:** Probiotics **(Pages 27-40);**
Unit 3: Probiotic Micro- Organisms in Fermented Milk Products And non-Milk Products. Quality Assurance of Probiotics and Safety.	**Unit 3:** Probiotic Microorganisms in Fermented Products and Quality Assurance **(Pages 41-56);**
Unit 4: Prebiotics - Chemistry, Sources and Bioavailability, Effect of Processing, Effects on Human Health and Potential Applications in Risk Reduction of Diseases, Perspective for Food Applications for the Following: Non-Digestible Carbohydrates/Oligosaccharides: Dietary Fibre, Resistant Starch, Gums.	**Unit 4:** Prebiotics: Chemistry, Sources and Effect **(Pages 57-75)**
BLOCK-II: PLANT METABOLITES AND NON- NUTRIENT EFFECT OF SPECIFIC NUTRIENTS	
Unit 5: Alkaloids, Glucosinolates, Terpenoides and Phenolics- Chemistry, Classes, Sources, Bioavailability and Effects on Human Health	**Unit 5:** Alkaloids, Glucosinolates, Terpenoides and Phenolics **(Pages 76-106);**
Unit 6: Antinutrients Present in Food: Phytate, Saponin, Haemagglutinins, Protease, Amylase and Lipase Inhibitors. Spices and Condiments- Nutritive Value and Uses in Cooking.	**Unit 6:** Antinutrients Present in Food **(Pages 107-136);**
Unit 7: Non- Nutrient Effect of Specific Nutrients: Proteins, Peptides and Nucleotides, Conjugated Linoleic Acid and n-3 Fatty Acids, Vitamins and Minerals.	**Unit 7:** Non-Nutrient Effect of Specific Nutrients **(Pages 137-148)**
BLOCK-III: PROPERTIES, STRUCTURE AND FUNCTIONS OF NUTRACEUTICALS	
Unit 8: Introduction to Nutraceuticals as Science - Historical Perspective, Classification, Scope & Future Prospects.	**Unit 8:** Nutraceuticals **(Pages 149-168);**
Unit 9: Applied Aspects of the Nutraceutical Science: Sources of Nutraceuticals. Relation of Nutraceutical Science with Other Sciences: Medicine, Human Physiology, Genetics, Food Technology, Chemistry and Nutrition.	**Unit 9:** Nutraceutical: Applied Aspects and Relation with Science **(Pages 169-187);**
Unit 10: Properties, Structure and Functions of Various Nutraceuticals - Glucosamine, Octacosanol, Lycopene, Carnitine, Melatonin and Ornithine Alpha Ketoglutarate. Use of Proanthocyanidins, Grape Products, Flaxseed Oil as Nutraceuticals.	**Unit 10:** Nutraceuticals: Properties, Structure and Functions **(Pages 188-199)**

BLOCK-IV: NUTRACEUTICAL SUPPLEMENTS AND REMEDIES

CONTENTS

INTRODUCTION

NOTES

The word 'nutraceutical' is a combination of two words 'Nutrition' and 'Pharmaceutical', coined in 1989 by Stephen L. De Felice, founder and chairman of the Foundation of Innovation Medicine. In contrast to the natural herbs and spices used as folk medicine for centuries throughout Asia, the nutraceutical industry has grown alongside the expansion and exploration of modern technology. A nutraceutical or bioceutical is a pharmaceutical alternative which provides physiological benefits. According to the authority of the Federal Food, Drug, and Cosmetic Act (FFDCA), the Food and Drug Administration (FDA) states that 'nutraceuticals' are basically unregulated as they exist in the same category or group of dietary supplements and food additives. Nutraceuticals are special products derived from food sources to provide extra health benefits in addition to the basic nutritional value found in foods, hence also considered as functional foods. Depending on the jurisdiction, these nutraceutical or bioceutical products can prevent chronic diseases, improve health, delay the aging process, increase life expectancy, or support the structure or function of the body. Functional foods are fortified or enriched during processing providing some benefit to consumers. Sometimes, additional complementary nutrients are added, such as Vitamin D to milk.

Fundamentally, the large numbers of plant preparations and extracts as well as a few from animal sources are used as 'traditional' or 'herbal' medicines and many of these are also marketed as dietary supplements. Nutraceuticals, functional food ingredients and dietary supplements are important for health promotion and disease risk reduction. Over the past few years, various types of dietary supplements are available in supermarkets, health food shops and also in chemist shops or pharmacies. Nutraceuticals, are also termed as medical foods, exclusive health foods, phytochemicals, functional foods and nutritional supplements, include the everyday products, such as 'bio' yoghurts and fortified breakfast cereals, as well as vitamins, herbal remedies and even genetically modified foods and supplements. Processing of by-products from plant sources are particularly rich in a number of bioactives at much higher concentration than those present in the main products and these can be used as value-added ingredients for application in food or as supplements for alleviating certain health problems.

Functional foods can be considered to be those whole, fortified, enriched or enhanced foods that provide health benefits beyond the provision of essential nutrients, for example vitamins and minerals, when they are consumed at efficacious levels as part of a varied diet on a regular basis. However, nutraceuticals are commodities derived from foods, but are used in the medicinal form of pills, capsules or liquids and again render demonstrated physiological benefits. This category includes both nutraceuticals and herbal as well as other natural products. In some countries, however, functional foods and nutraceuticals are used interchangeably.

NOTES

Linking the consumption of functional foods or food ingredients with health claims should be based on sound scientific evidence, with the 'gold standard' being replicated, randomized, placebo-controlled, intervention trials in human subjects. Functional foods represent one of the most intensively investigated and widely promoted areas in the food and nutrition sciences today.

This book, *Functional Foods and Nutraceuticals,* is divided into four block, which is further divided into fourteen units which will help you understand the basics, history, classification of functional foods (probiotics, prebiotics and synbiotics), probiotics, taxonomy and important features of probiotic micro-organisms, probiotic microorganisms in fermented milk products and non-milk products, quality assurance of probiotics and safety, prebiotics, chemistry, sources and bioavailability, effect of processing, effects on human health and potential applications in risk reduction of diseases, alkaloids, glucosinolates, terpenoides and phenolics, classes, sources, bioavailability and effects on human health, antinutrients present in food, spices and condiments, non- nutrient effect of specific nutrients, introduction to nutraceuticals as science, applied aspects of the nutraceutical science, relation of nutraceutical science with other sciences, properties, structure and functions of various nutraceuticals, use of proanthocyanidins, grape products, flaxseed oil as nutraceuticals, nutraceutical rich supplements, food as remedies, nutraceuticals in treatment for cognitive disorders, nutraceutical remedies for arthritis, bronchitis, circulatory problems, hypoglycemia, nutraceutical remedies for nephrological disorders.

The book follows the self-instruction mode or the SIM format wherein each unit begins with an 'Introduction' to the topic followed by an outline of the 'Objectives'. The content is presented in a simple and structured form interspersed with 'Check Your Progress' questions and answers for better understanding. A list of 'Key Words' along with a 'Summary' and a set of 'Self Assessment Questions and Exercises' is provided at the end of the each unit for effective recapitulation.

BLOCK - I
FUNCTIONAL FOODS, PROBIOTICS AND PREBIOTICS

NOTES

UNIT 1 FUNCTIONAL FOOD

Structure

1.0 INTRODUCTION

A functional food is a food claimed to have an additional function by adding new ingredients or more of existing ingredients. The term may also apply to traits purposely bred into existing edible plants, such as purple or gold potatoes having enriched anthocyanin or carotenoid contents, respectively. As per the definition, 'Functional foods may be specifically designed to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions, and may be similar in appearance to conventional food and consumed as part of a regular diet'. The term was first used in Japan in the 1980s where there is a government approval process for functional foods called Foods for Specified Health Use (FOSHU).

Fundamentally, the functional foods are foods that have a potentially positive effect on health beyond basic nutrition. Proponents of functional foods say they promote optimal health and help reduce the risk of disease. A familiar example of a functional food is 'Oatmeal' because it contains soluble fiber that can help lower cholesterol levels. The Food and Drug Administration regulates the claims that manufacturers can make about functional food nutrient contents that effects on disease, health or body function.

In this unit, you will study about the functional food - definition and history, classification of functional foods, probiotics, prebiotics and synbiotics, nutrient and non-nutrient functional foods.

NOTES

1.1 OBJECTIVES

After going through this unit, you will be able to:

- Understand the significance of the functional foods
- Provide various definitions and history of the functional foods
- Classify the functional foods
- Explain probiotics, prebiotics and synbiotics types of functional foods
- Discuss nutrient and non-nutrient functional foods

1.2 FUNCTIONAL FOOD: DEFINITION AND HISTORY

A functional food is a food claimed to have an additional function by adding new ingredients or more of existing ingredients. The term may also apply to traits purposely bred into existing edible plants, such as purple or gold potatoes having enriched anthocyanin or carotenoid contents, respectively. As per the definition, 'Functional foods may be specifically designed to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions, and may be similar in appearance to conventional food and consumed as part of a regular diet'. The term was first used in Japan in the 1980s where there is a government approval process for functional foods called Foods for Specified Health Use (FOSHU).

Fundamentally, the functional foods are foods that have a potentially positive effect on health beyond basic nutrition. Proponents of functional foods say they promote optimal health and help reduce the risk of disease. A familiar example of a functional food is 'Oatmeal' because it contains soluble fiber that can help lower cholesterol levels. The Food and Drug Administration regulates the claims that manufacturers can make about functional food nutrient contents that effects on disease, health or body function.

Definitions of Functional Food

Following are some standard definitions of functional foods:

1. A modified food that claims to improve health or well-being by providing benefit beyond that of the traditional nutrients it contains. Functional foods may include such items as cereals, breads, beverages that are fortified with vitamins, some herbs and nutraceuticals.
2. Functional food are foods that have a potentially positive effect on health beyond basic nutrition. Proponents of functional foods say they promote optional optimal health and help in reducing the risk of disease. The physiological benefits show that it can reduce the risk factors of chronic diseases as it contains bioactive components.

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3. Functional foods can be considered to be those whole, fortified, enriched or enhanced foods that provide health benefits when they are consumed with diet on a regular basis. All foods are functional, as they provide taste, aroma or nutritive value.
4. Functional foods deliver additional or enhanced benefits over and above their basic nutritional values. Some functional foods are generated around a particular functional ingredient, for example foods containing probiotics, prebiotics a plant Stanols and Sterols. Other functional foods or drinks can be foods fortified with a nutrient that would not usually be present to any great extent, for example, Folic Acid Fortified Bread or Breakfast Cereals. The functional foods should not be seen as an alternative to a varied and balanced diet and a healthy lifestyle.

   Stanols and Sterols occur naturally in small amounts in plants and fruits and are considered that it has cholesterol lowering effect and are added to products, such as reduced/low fat spreads.
5. Functional foods are foods that have health promoting properties over and above their nutritional values. The functional foods can be viewed as encompassing a very broad range of products ranging from foods generated around a particular ingredient, for example Stanols (sterol-enriched reduced), Low Fat Spreads and Dairy Products containing Probiotic Bacteria, through to staple everyday foods fortified with a nutrient that would not usually be present to any great extent.

   Figure 1.1 illustrates the various features of functional foods.

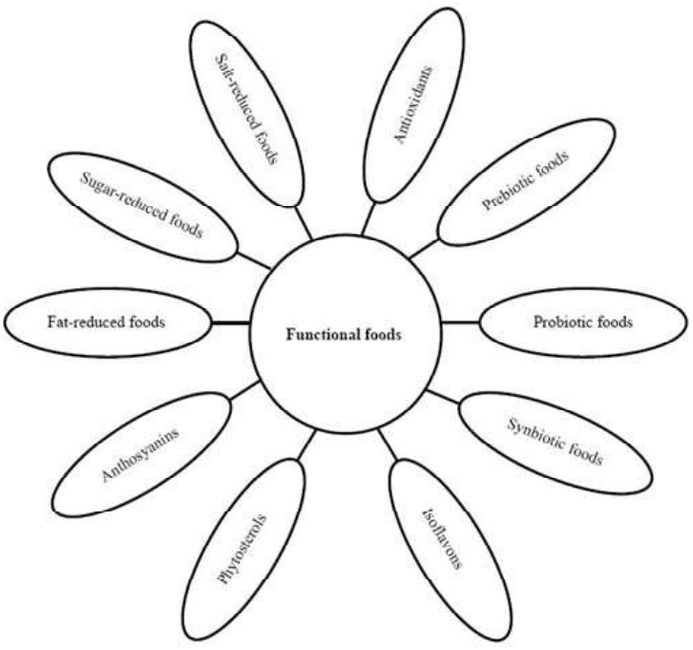

Fig. 1.1 *Features of Functional Foods*

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The level of consumption of the food that is required to achieve a beneficial effect on health is an important consideration in particular, it should be possible to achieve the required level of intake of the functional food within normal dietary pattern.

A possible disadvantage of functional foods from a health point of view is that they may obscure the boundaries between food groups, normally defined by the specific selection of nutrients that foods in each group provide.

History

The term functional foods was introduced in Japan in the mid-1980s and refers to processed food containing ingredients that aid specific bodily functions in addition to being nutritious. Over two thousand years ago Hippocrates said, 'Let food be thy medicine'. Although the concept of functional foods is not entirely new, it has evolved considerably over the years. In the early 1900s food manufacturers in the United States started adding 'Iodine to Salt' in an effort to prevent Goiter, representing one of the first attempts at creating a functional food through fortification.

Other twentieth-century examples include Vitamin A and D fortification of Milk and Niacin, and Folic Acid fortification of Grains. These early fortification examples, however, focused on reducing the risk of diseases of deficiency. In the latter part of the twentieth century, consumers began to focus on wellness and the reduction of chronic disease. Research now focuses frequently on the promotion of health through many lifestyle factors, including the consumption of an optimal diet. As of 2002, researchers have identified hundreds of food components with functional qualities, and they continue to make new discoveries surrounding the complex benefits of phytochemicals in foods.

Benefits of Functional Foods

A functional food may be a traditional food which we consume as part of our usual diets. It is shown to have physiological benefits and reduce that risk of chronic disease is it contains bioactive compounds.

A functional food is a typical food that have specific nutrients added to it, like vitamins or minerals, fiber or probiotics or prebiotics. In general, this includes anything for a specific function purpose.

Functional foods can be considered be those whole, fortified, enriched or enhanced foods that provide health benefits beyond the provision of essential nutrients, for example vitamins and minerals, when they are consumed at efficacious levels as part of a varied diet on a regular basis. Linking the consumption of functional foods or food ingredients with health claims should be based on sound scientific evidence, with the 'gold standard' being replicated, randomized, placebo-controlled, intervention trials in human subjects. However, not all foods on the market today that are claimed to be functional foods. This review categorizes a variety of functional foods according to the type of evidences supporting their

functionality, the strength of that evidence and the recommended intakes. Functional foods represent one of the most intensively investigated and widely promoted areas in the food and nutrition sciences today. However, it must be emphasized that these foods and ingredients are not magic bullets or panaceas for poor health habits. Diet is only one aspect of a comprehensive approach to good health.

NOTES

1.2.1 Types of Functional Foods

1. **Whole Food:** It includes Oats, Soya, Fish, Garlic, Flaxseeds and Nuts, Grapes, Fruits and Vegetable.
2. **Fortified Foods:** It includes the following;
   - Fortified foods are natural foods fortified with other nutrients.
   - Cereal and Cereals-Based products fortified with Folic Acid.
   - Milk and Milk products are fortified with Vitamin B.
   - Fats and Oils are fortified with Vitamin D and E.
3. Enhanced foods are foods that have more of a functional component through traditional breeding, genetic engineering, etc., for example dairy product with probiotics.

   The benefits derived by these foods are as follows:
   - Reduce risk of Colon Cancer.
   - Treatment of Respiratory Allergies.
   - Control of Diarrhea and Dysentery Disorders.
   - Decreases the Cholesterol level thus reducing the risk of Heart Disease.

Classification of Functional Foods

The functional foods are classified as follows:

1. Cereals: Wheat Bran, Oats, Corn
2. Legumes: Soya Bean and Soya-Based products
3. Oilseeds: Flaxseed Oil
4. Vegetables: Carrots, Psyllium, Green Leafy Vegetables, Tomatoes, Onion, Garlic
5. Fruits: Citrus Fruits
6. Dairy Products: Yoghurt and Other Dairy Products
7. Beverages: Green Tea
8. Fishes: Tuna, Salmon, Mackerel
9. Herbs and Spices: Turmeric, Gingers, Fenugreek

Grouping of Functional Foods

The functional foods are grouped as follows.

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Basic Foods

- Tomatoes having the natural level of the antioxidant Lycopene.
- Processed food includes Oat Bran Cereal having the natural level of Beta Glucan.

Fortified Foods

- Tea, Beverages and Fruit Juices are fortified with Calcium.
- Milk is fortified with Vitamin D.
- Grains are fortified with Added Fibers.
- Fats and Oils are fortified with Vitamin D and E.

Enhanced Foods

Enhanced foods have more of a functional component through traditional breeding, genetic, engineering, etc.

- Dairy products with probiotics.
- Eggs with Omega-3 isolated. Purified preparations of active food ingredients, such as herbal products.
- Curcumin from Turmeric.
- Isoflavones from Soy.
- Omega-3 from Fish Oils.

Oats

Oat products are dietary source of the cholesterol lowering, such as the soluble fibers of Beta Glucan. It is now significant that tomatoes can reduce and Low Density Lipoprotein (LDL) cholesterol thereby reducing the risk of Coronary Hearts Disease (CHD).

Soy

As we are aware that Soy has the highest protein content. It is now thought to play preventive and therapeutic roles in Cardio Vascular Disease (CVD), Cancer, Osteoporosis and the alleviation of Menopausal symptoms.

Flaxseed

Amongst the major seed oils, flaxseed oil contains the most (57%) of the Omega-3 Fatty Acid, a-Linoleic Acid. Consumption of flaxseed has also been shown to reduce total and LDL cholesterol as well as platelet aggregation.

Tomatoes

Those who consume tomato products 10 or more times per meal had less than one half the risk of developing Prostate Cancer. Lycopene is the most abundant

Carotenoid in the prostate gland and Lycopene is the most efficient quencher of singlet oxygen in biological systems.

Garlic

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As we all know that Garlic is known for its medicinal properties. The health benefits of garlic are numerous, including Cancer, Antibiotic, Antihypertensive, and Cholesterol-Lowering properties. The flavor and pungency of garlic are due to an abundance of oil and water soluble, sulfur containing elements, which are responsible for the medicinal effects ascribed to this plant. The intact garlic bulb contains an odour less Amino Acid, Alliin which is converted enzymatically by Alliance into Allicin when the garlic cloves are crushed. Allicin then spontaneously decomposes to form numerous Sulphur containing compounds some of which have been investigated for their chemo-preventive activity.

Citrus Fruits

Some studies have shown that citrus fruits are protective against a variety of human Cancer. Although Oranges, Lemons, Grape Fruits are sources of important nutrients, such as Vitamin C and fibers. Citrus fruits are particularly high in a class of phytochemicals known as the Limonoids.

Table 1.1 illustrates the diet-disease relationship and their possible effects.

Table 1.1 *Diet-Disease Relationship and Possible Effects*

Diet-Disease Relationship	Effects
Calcium - Osteoporosis	Regular exercise and a healthy diet with enough Calcium help the teenagers and young adults to maintain good bone health and may reduce their risk of Osteoporosis.
Sodium - Hypertension	Diets low in Sodium may reduce the risk of High Blood Pressure, a disease associated with many factors.
Dietary Fat - Cancer	Development of Cancer depends on many factors. A diet low in total fat may reduce the risk of some cancers.
Dietary Saturated Fat and Cholesterol - Coronary Heart Disease (CHD)	While many factors affect Heart Disease, diets low in Saturated Fat and Cholesterol may reduce the risk of this disease.
Fiber containing Grain Products, Fruits and Vegetables - Cancer	Low fat diets rich in fiber containing grain products, fruits, and vegetables may reduce the risk of some types of Cancer, a disease associated with many factors.
Fruits, Vegetables and Grain Products that contain Fiber, particularly Soluble Fibers - Coronary Heart Disease (CHD)	Diets low in Saturated Fat and Cholesterol, and rich in fruits, vegetables and grain products that contain some types of dietary fiber, particularly soluble fiber, may reduce the risk of Heart Disease, a disease associated with many factors.

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Fruits and Vegetables - Cancer	Low fat diets rich in fruits and vegetables may reduce the risk of some types of Cancer, a disease associated with many factors.
Folate - Neural Tube Birth Defects	Healthful diets with adequate daily Folate may reduce a woman's risk of having a child with a Brain or Spinal Cord Birth Defect.
Potassium - Blood Pressure and Stroke	Diets containing foods that are good sources of Potassium and low in Sodium may reduce the risk of High Blood Pressure and Stroke.
Whole Grains - Heart Disease and Cancer	Diets rich in Whole Grain Foods and other plant foods and low in Total Fat, Saturated Fat, and Cholesterol may reduce the risk of Heart Disease and certain Cancers.

Cranberry

Cranberry juice is recognized as efficacious in the treatment of Urinary Tract Injections (UTIs). The Benzoic Acid rich fruit causes acidification of the urine investigation have focuses on the ability of Cranberry juice to inhibit the adherence of *Escherichia coli* to uro-epithelial cells. This phenomenon has been attributed to two compounds, Fructose and a Non-Dialyzable Polymeric compound.

Dairy Products

There is no doubt that dairy products are functional foods. They are one of the best sources of Calcium, an essential nutrient which can prevent Osteoporosis and possibly Colon Cancer. In addition to Calcium, other components which recent researches have focused in dairy products are known as probiotics.

A comprehensive list of herbal nutraceuticals from plant origin are given in Table 1.2.

Table 1.2 *Herbal Nutraceuticals with Anti-Diabetic Potential*

Plant	Family	Plant Part
Artocarpus integrifolia Linn	Moraceae	Root Barks
Abelmoschus esculentus Unn	Malvaceae	Fruits
Acacia arabica	Leguminosae	Seeds
Acacia modesta Wall	Fabaceae	Leaves
Adhatoda zeylanica Nees	Acanthaceae	Leaves and Fruits
Aegle marmelos	Rutaceae	Root Bark, Fruits and Leaves
Allium cepa	Liliaceae	Bulbs
Aloe vera Linn	Liliaceae	Leaves
Alpinia calcarata Rose	Zingiberaceae	Rhizomes
Alpinia galangal Wild	Zingiberaceae	Rhizomes
Alternanthera sessilis Unn	Amaranthaceae	Whole Plant
Amaranthus esculentus	Amaranthaceae	Whole Plant, Oil
Ampelodesmos mauritanica Durand	Poaceae	Roots
Andrographis paniculata Nees	Acanthaceae	Roots

Annona squamosa	Annonaceae	Leaves
Artemisia pallens	Compositae	Aerial Parts
Biophytum sensitivum Unn	Oxalidaceae	Leaves
Boerhaavia diffusa Linn	Nyctaginaceae	Aerial Parts
Bridelia retusa Spreng	Euphorbiaceae	Stem Barks
Caesalpinia bonducella Roxb	Caesalpiniaceae	Seeds
Camellia sinensis	Theaceae	Leaves
Casearia esculenta	Flacourtiaceae	Roots
Cassia auriculata Linn	Leguminosae	Flowers
Catharanthus roseus	Apocynaceae	Aerial Parts
Chamaemelum nobile	Asteraceae	Leaves
Chrysanthellum indicum Linn	Compositae	Aerial Parts
Citrullus colocynthis Unn	Cucurbitaceae	Fruits
Cinnamomum zylanicum Nees	Lauraceae	Stem Barks
Coccinia indica	Cucurbitaceae	Leaves
Coscinium fenestratum	Menispermaceae	Stem Barks
Cucurbita maxima Duch	Cucurbitaceae	Aerial Parts
Dioscorea bulbifera Linn	Dioscoreaceae	Bulbs
Diospyros cordifolia Roxb	Ebenaceae	Stems
Dodonaea viscosa Inn	Sapindaceae	Leaves
Egyptian morus	Moraceae	Root Barks
Elaeodendron glaucum Pers	Celastraceae	Stem Barks
Enicostemma littorale	Gentlease	Whole Plant
Eugenia jambolana Lam	Myrtaceae	Seeds
Ficus benghalensis	Moraceae	Berries
Ficus glomerata	Moraceae	Leaves
Ficus racemosa Linn	Moraceae	Fruits
Foeniculum vulgare Mill	Apiaceae	Volatile Oil
Glycyrrhiza glabra Linn	Leguminosae	Roots
Gnidia glauca Linn	Thymelaeaceae	Whole Plant
Helicteres isora	Sterculiaceae	Roots
Hibiscus rasa	Malvaceae	Whole Plant
Lycium shawii Roem	Solanaceae	Aerial Parts
Madhuca longifolia	Sapotaceae	Berries
Mangifera indica Linn	Anacardiaceae	Leaves
Melia azadirachta Unn	Meliaceae	Leaves
Michelia champaca Linn	Magnoliaceae	Leaves
Mirabilis jalapa Linn	Nyctaginaceae	Roots
Momordica charantia	Cucurbitaceae	Fruits
Momordica cymbalaria	Cucurbitaceae	Fruits
Morinda tinctoria Roxb	Rubiaceae	Fruits
Morus alba	Moraceae	Leaves
Morus indica	Moraceae	Leaves

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Mucuna pruriens	Leguminosae	Whole Plant
Murraya koenigii	Rutaceae	Leaves
Neolamarckia cadamba Roxb	Rubiaceae	Leaves
Ocimum sanctum Linn	Labiatae	Leaves
Orthosiphon stamineus Benth	Lamiaceae	Leaves
Ougeinia oojeinensis Roxb	Fabaceae	Berries
Piper betle	Piperaceae	Leaves
Psyllium guajava	Myrtaceae	Whole Plant
Pterocarpus marsupium Roxb	Fabaceae	Wood and Barks
Punica granatum	Punicaceae	Whole Plants
Rubus ellipticus Smith	Rosaceae	Fruits
Salacia reticulata	Celastraceae	Leaves
Sesbania sesban Linn	Fabaceae	Leaves
Shorea tumbuggaia Roxb	Dipterocarpaceae	Leaves
Sida acuta Burm	Malvaceae	Leaves
Sida cordifolia	Malvaceae	Roots
Sorbus decora	Rosaceae	Inner Barks
Strychnos potatorum Linn	Loganiaceae	Ripened Fruits
Swertia chirayita	Gentianaceae	Berries
Tabernaemontana divaricata Linn	Apocynaceae	Flowers
Terminalia chebula	Combretaceae	Seeds
Tinospora cordifolia	Menispermaceae	Roots
Trigonella foenum graceum	Leguminosae	Seeds
Triumfetta rhomboidea	Liliaceae	Whole Plant
Viscum album	Loranthaceae	Whole Plant
Withania somnifera	Solanaceae	Roots

Figure 1.2 illustrates the dietary/nutrient based nutraceuticals.

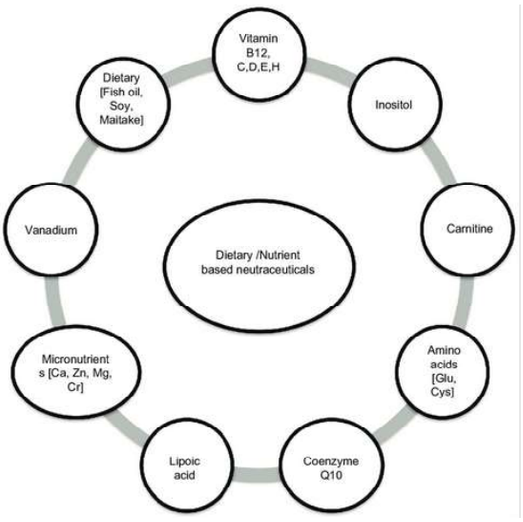

Fig. 1.2 *Dietary/Nutrient Based Nutraceuticals*

Following are the various vitamins and micronutrients used as nutraceuticals in treatment of diabetes and other diseases/disorders.

1.2.2 Prebiotics

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Prebiotics are compounds in food that induce the growth or activity of beneficial microorganisms, such as Bacteria and Fungi. The most important example is in the gastrointestinal tract, where prebiotics can alter the composition of organism in the gut micro-biome.

Definition of Prebiotics: According to International Scientific Association Probiotics and Prebiotics (ISAPP), 'the prebiotics are a substrate that is selectively used by a host microorganism to produce a health benefit'.

Dietary prebiotics are typically non-digestible fiber compounds that pass indigested through the upper part of the gastrointestinal tract and stimulate the growth or activity of advantageous bacteria that are colonial in the large bowel by acting as substrate for them.

Compounds that can be classified as prebiotics must also meet the following criteria:

- Non-digestible and resistant to breakdown by stomach acid and enzymes in the human gastrointestinal tract.
- Selectively fermented by intestinal microorganisms.
- Selectively target and stimulate the growth and activity of beneficial bacteria.

Prebiotics are classified as the non-digestible food ingredients that probiotics can feed. They are used in the gut to increase populations of healthy bacteria and digestion and enhance the production of valuable vitamins. Good bacteria play a significant role in regulating your immune system, inhibiting the growth of pathogens and digesting food. Galacto-Oligo-Saccharides (GOS) are the most advanced form of prebiotics which belong to a group of particular nutrient fibers that feed and encourage the growth of good bacteria in the gut.

Fermentation is the main mechanism of action by which prebiotics are used by beneficial in the colon. Both 'Bifidobacterium' and 'Lactobacillus' are bacterial populations which use Saccharolytic metabolism to breakdown substrates. Bifidobacterium genome includes many genes that encode for Carbohydrate-modifying enzymes as well as genes that encode for Carbohydrate update Proteins. Presence of these genes indicates that Bifidobacterium contains specific metabolic pathways specialized for the fermentation and metabolism of plant derided Oligosaccharides or Prebiotics. These pathways are Bifidobacterium and ultimately produce short chain Fatty Acids, which have diverse physiological roles in body functions.

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Sources

Sources can be classified into two forms as (a) Endogenous and (b) Exogenous. Prebiotic sources must be proven to confer a benefit to the host in order to be classified as a prebiotic. Fermentable carbohydrates derived from Fructans and Xylans are the most well documented example of prebiotics, and Galacto-oligosaccharides are enzymatically synthesized from Lactose. However, there are additional endogenous prebiotics and exogenous food sources that can be classified as prebiotic sources. Additionally, functional foods containing prebiotic food ingredients serve as an additional prebiotic food source. However, the FOS and inulin content in food sources is very low, meaning it is difficult to consume sufficient prebiotics from food alone.

The major source of prebiotics is dietary fiber. They occur naturally in fruits and vegetables. Though all dietary fibers cannot be classified as a prebiotic source. The common forms of dietary fibre present in the majority of plant-based foods and grains are less selectively fermented by the bacteria in the gut and lack of some of the health benefits demonstrated by prebiotics.

Endogenous: An endogenous source of prebiotics in humans is human breast milk, which contains oligosaccharides structurally similar to GOS, referred to as Human Milk Oligosaccharides (HMOs). These HMOs were found to increase the Bifidobacterium bacterial population in breastfed infants, and to strengthen the infant immune system. Furthermore, HMOs play a role in the establishment of a healthy intestinal microbiota composition of newborns.

Exogenous: Indigestible carbohydrate compounds classified as prebiotics are a type of fermentable fiber, and thus can be classified as dietary fiber. However, not all dietary fiber can be classified as a prebiotic source. In addition to the food sources highlighted in the following Table 1.3, raw oats, unrefined barley, yacon, and whole grain breakfast cereals are also classified as prebiotic fiber sources. The predominant type of prebiotic fiber may vary according to the food. For instance, oats and barley have high amounts of beta-glucan, fruit and berries contain pectin, seeds contain gums, onions and Jerusalem artichokes are rich in inulin and oligofructose, and bananas and legumes contain resistant starch.

Table 1.3 *Top 10 Foods Containing Prebiotics*

Food	Prebiotic Fiber Content by Weight
Raw, Dry Chicory Root	64.6%
Raw, Dry Jerusalem Artichoke	31.5%
Raw, Dry Dandelion Greens	24.3%
Raw, Dry Garlic	17.5%
Raw, Dry Leek	11.7%
Raw, Dry Onion	8.6%

Raw Asparagus	5%
Raw Wheat Bran	5%
Whole Wheat Flour Cooked	4.8%
Raw Banana	1%

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Natural Sources of Prebiotics

- Bananas
- Raw Leeks
- Raw Onions
- Artichokes
- Raw Garlic Cloves
- Chicory Root Powder
- Cooked Onions
- Raw Asparagus
- Whole Wheat Flour

While have is no broad consensus on an ideal daily serving of prebiotics, recommendations typically range from 4 to 8 grams (0.14-0.28) for general digestive health support to 15 grams (0.53 oz) or more for those with active digestive disorders.

One of the biggest advantages of prebiotic supplements is that they all highly stable being unaffected either by temperature or long term storage.

Prebiotics are also resistant to the body's enzymes and gastric acids which means that they are not destroyed, digested or absorbed as they bowel through your digestive system. Prebiotics reach the colon intact and unaltered.

1.2.3 Probiotics

Probiotics are good bacteria that are either the same as or very similar to the bacteria that are already in your body. Your similar digestive tract teams with a complex and diverse community of these bacteria. In fact there are greater humble of bacteria in your intestines than there are cells in your body.

We take antibiotics to kill harmful bacterial infections and use antibacterial soaps and lotions. The wrong bacteria in the wrong place can cause problems, but the right bacteria in the right place can have benefits. There the role of probiotics comes, which are live microorganisms that can help and treat some illnesses. Probiotics can be supplied through food, beverages and dietary supplements.

Health Benefits of Probiotics

Most of the bacteria reside in your gut and the majority are quite harmless. Having the right gut bacteria have various health benefits including weight loss, improved digestion, reduce depression and promote heart health.

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When digestive tract is healthy, it eliminates all harmful bacteria, toxins, chemicals and other waste products. The healthy balance of bacteria assists with the regulation of gastrointestinal motility and maintenance of gut barrier function. Probiotics are also helpful in infections diarrhoea, gut transmit diarrhoea, IBS, abdominal pain and bloating, ulcerative colitis, etc.

Probiotics helps to improve immune system also and promote the production of natural antibodies in the body. They may also boost immune cells like the IgA-producing cells, t-Lymphocytes and natural killer cells.

Taking probiotic supplement for 8 weeks decreased depression levels and reduced levels and reduced levels of C-reactive protein (a marker of inflammation) and hormones, such as Insulin, compared to people who did not take a probiotic.

Probiotics may help protect the heats by reducing bad LDL cholesterol levels and modestly lowering blood pressure.

It may reduce the risk and severity of certain allergies, such as eczema in infants.

Different Types of Probiotics

There are several different kinds of probiotics, and their health benefits are determined by the job that they do in the gut. There are the different types of probiotics and their health benefits.

1. Lactobacillus

There are more than 50 species of Lactobacilli. They are naturally found in the digestive, urinary and genital systems. It is the most common probiotic and you will find in yoghurt and other fermented foods. Lactobacillus has been used for treating and preventing a wide variety of diseases and conditions. According to some studies the Lactobacillus help in treating/preventing yeast infections, bacterial vaginosis, urinary tract infections, irritable bowels syndrome, traveler's diarrhoea, lactose intolerances, skin disorders, eczema and acne and prevention of respiratory infections.

2. Bifidobacteria

There are approximately 30 species of Bifidobacteria. They make up most of the healthy bacteria in the colon. It is present in some dairy products. It may help ease the symptoms of Irritable Bowel Syndrome (IBS) and some other conditions. They can help on improving Blood Lipids and Glucose Tolerance.

3. Saccharomyces Boulardii

Saccharomyces Boulardii is a yeast found in probiotics. It appears to help tight diarrhoea and other digestive problems.

4. Streptococcus Thermophilus

Lactase enzyme is produced by Streptococcus Thermophilus probiotic making it effective, according to some reports, in prevention of Lactose Intolerance.

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5. Leuconostoc

Leuconostoc has been used extensively in food processing throughout human history, and ingestion of foods containing live bacteria, dead bacteria and metabolites of these microorganisms has taken for a long time.

Sources of Probiotics

1. Yoghurt

It is one of the best probiotics, which are friendly bacteria that can improve your health. It is made from milk that has been fermented by friendly bacteria, mainly Lactic Acid bacteria and Bifidobacteria. Yoghurt improves Bone Health, Blood Pressure (BP), can help in delivering the symptoms of Irritable Bowel Syndrome (IBS). Suitable for people with Lactose Intolerance, this is because bacteria turn some of the Lactose into Lactic Acid, which makes yoghurt tastes sour.

2. Kefir

Kefir is the most important ideal probiotic dairy product because it contains both bacteria and yeast working together to provide the numerous health benefits. It is combination of goat milk and fermented kefir grains. It is rich is bacteria and lactobacilli. It is also rich in antioxidants. Kefir contains several major strains of friendly bacteria and yeast, making it a diverse and potent probiotic.

3. Sauerkraut

Sauerkraut is finely shredded Cabbage that has been fermented by lactic acid bacteria. It has a sour and salty taste. It is rich in antioxidants Lutein and Zeaxanthin which are important for eye health also. It is rich in fiber as well as Vitamins C, B and K.

4. Dark Chocolates

Chocolates always comes very usefully as a probiotic. Probiotic helps in getting extreme pH, so that digestion becomes proper.

5. Microalgae

Microalgae are also very good probiotic. Other foods which are rich sources of probiotics are Miso Soup, Tempeh, Pickles and Kimchi.

Probiotics foods and supplements are thought to be safe for most people, though some people with immune system problems or other serious conditions should not take them. In some cases, mild side effects might include, such as stomach upset, diarrhoea, gas, etc.

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1.2.4 Synbiotics

Synbiotics refer to dietary supplements combining probiotics and prebiotics in a form a synergism, hence Synbiotics. Synbiotic can help support gut health by increasing the amount of beneficial bacteria in the digestive tract while also providing these bacterial cells with the full they need to function and thrive. Synbiotics can be found in supplement form which often combine nutritious plant based prebiotic fibers with specific health promoting strains of probiotics.

Benefits of Synbiotics

1. Support Digestive Health

Synbiotics pack a double punch when it comes to gut health by supplying a stream of both pre and probiotics to the body. Probiotics are form of beneficial bacteria that help promote proper digestion. In fact probiotics have shown improvement in several digestive ailments and are helpful in the treatment of uncreative colitis and Irritable Bowel Syndrome (IBS).

2. Enhance Immune Functions

Studies have shown that 70 per cent to 80 per cent of the body's immune cells are right in digestive tract. Synbiotics can help enhance immune function by increasing the amount of good bacteria in the gut while simultaneously decreasing inflammation.

Studies have found that supplements with probiotic can improve immunity. In one study consuming milk with probiotics decreased the incidence and severity of respiratory infections by about 17 per cent among children.

3. Improve Mental Health

Adding synbiotics to your diet may improve cognitive function and protect mental health by delivering a healthy dose of probiotics and prebiotics in each serving certain types of bacteria, such as Lactobacillus and Bifidobacterium enhance memory and improve symptom of Anxiety, Depression, Autism, Spectrum Disorder and Obsessive Compulsive Disorder.

4. Boost Weight Loss

Most interesting benefits of Synbiotics is their ability to boost weight loss and grant up fat burning. Probiotics may help block fat absorption to cut calories consumption. Prebiotics are found in high fibre which have been linked to a lower body weight and decreased body fat.

5. Promote Heart Health

Heart problem is increasing day by day around the world. Synbiotics can help keep your heart healthy and strong by reducing several heart disease risk factors. Studies showed that supplementing with Synbiotics for 12 weeks improved both Insulin Metabolism and good HDL cholesterol levels in people with diabetes and

Coronary Heart Disease (CHD). HDL cholesterol travels through the blood stream, removing fatty plaque build up to help keep arteries clear. Some studies suggested that probiotics may reduce blood pressure levels.

6. Decrease Inflammation

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Acute inflammation is a normal part of immune system that can help protect the body against infection and disease. Chronic inflammation on the other hand is thought to play an important part in health and disease. It may be involved in the development of chronic conditions like Heart Disease, Diabetes and Cancer as well. Synbiotics can provide a concentrated dose of probiotics and prebiotics both of which can optimize gut health to lower levels of inflammation.

Synbiotics can be used by those looking to enhance digestion, boost immunity or simply improve overall health. Synbiotics foods can be made by combining prebiotic-rich foods with several good source of probiotics to bring a concentrated dose of both to your diet. Prebiotic foods include Green Bananas, Chicory Root, Onions, Oats, Acacia Gum, Garlic and Asparagus. You can make your own synbiotics by combining this nutrition ingredients. You can cook up a tasty stir fry with Asparagus, Garlic and Onions with other Veggies. When opt for synbiotics supplement, look for a product with high CFU count and has a good amount of probiotic strain.

Synbiotics are categorized as either complementary synbiotics or synergistic synbiotics. Complementary synbiotics contain both prebiotics and probiotics that are independently selected for their beneficial effects on health. Conversely, synergistic synbiotics contain prebiotics that are chosen specifically to support the effects of probiotics.

Prebiotics are fermented in the gut and can cause adverse digestive symptoms when consumed in high amount. Probiotics may also contribute to side effects, such as diarrhoea, abdominal pain especially when it is initiated for the first time. Try to start with low amount of synbiotics and increase gradually. Increase water intake when you are consuming prebiotic foods as they are high in fibre, which absorbs water in colon, but can also cause side effects like dehydration and constipation.

1.2.5 Nutrient and Non-Nutrient

Nutrient density is the measure of the nutrients in a food relation to the calories. Foods containing different combinations of nutrients but a food that provides more key nutrients than calories is considered nutrient-dense of key nutrients. List of key nutrients used to factor nutrient density as Protein, Fiber, Vitamins A, C, E and B-12, Thiamine, Ribophorin, Folate, Calcium, Iron, Potassium and Zinc.

Nutrient Density and Energy Density

Nutrient dense foods contain a lot of essential nutrients per serving, while energy dense foods are those that have a lot of calories in serving. Foods that are very high in fat or sugar are energy dense. Some foods are both nutrient-dense and energy-dense, such as Cheese, Meat and Nuts.

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Non-Nutrient Dense Foods

Now-a-days family lifestyle often interferes with making smart food choices. Busy families spend more time in the car, which leads to eating more meals on the run. Because of this you may find yourself choosing convenient foods at mealtime over nutritious foods unfortunately these foods provides calories but lack nutrients like Vitamins, Mineral and Fiber.

Benefits of Nutrient-Dense Foods

People with metabolic syndrome, which consists of high blood pressure, high blood sugar, high triglycerides, and low HDL cholesterol have an increased risk for stroke, diabetes and heart disease. Foods that are nutrient dense may help to lower your risk for metabolic syndrome. This is due at least in part to the high fiber content of many nutrient dense foods. People who eat a more nutrient dense diet also tend to fell less hunger than those who eat a diet that does not contain a lot of nutrients. The Vitamins, Minerals, Antioxidants and Phytochemicals in a nutrient-dense diet help the body to get rid of free radicals and other damaging waste products, which can sometimes cause oxidative stress or inflammatory reactions with symptoms people sometimes mistakes for hunger. Table 1.4 illustrates the macrominerals and microminerals, their sources and role in health maintenance.

Table 1.4 Macrominerals and Microminerals, Their Sources and Role in Health Maintenance

Minerals	Best Food Sources	Role in Health
Macrominerals		
Calcium	Milk and Dairy Products, Tinned Sardines with Bones, Green Leafy Vegetables, Sesame Seeds.	Builds Bones and Teeth and keeps them strong, vital to Nerve Transmission, Blood Clotting and Muscle Functions.
Chloride	Table Salt (Sodium Chloride) and Foods containing it.	Maintains the Fluid and Electrolyte Balanced in the Body. Vital for Stomach Acid Formation.
Magnesium	Wholegrain Cereals, Wheat Germ, Pulses, Nuts, Sesame Seeds, Dried Figs and Green Vegetables.	Important constituent of Bones and Teeth, assists in Nerve Impulses, important for Muscle Contraction.
Phosphorus	Present in all Plants and Animal Proteins, such as Milk, Cheese, Red Meat and Poultry, Fish and Seafood, Nuts, Seeds and Whole Grains.	Helps to form and maintain healthy Bones and Teeth; needed to release energy in cells, essentials for absorption of many nutrients.

Potassium	Avocados, Fresh and Dried Fruit, Seeds and Nuts, Bananas, Citrus Fruit, Potatoes and Pulses.	Works with Sodium to maintain the Fluid and Electrolyte Balance within cells, to keep Hear Beat Regular and to maintain normal Blood Pressure. Essentials for the transmission of all Nerve Impulses.
Sodium	Table Salt (Sodium Chloride), Tinned Anchovies, Processed Meats and Yeast Extracts.	Works with Potassium to regulate Fluid Balance; essential for Nerve and Muscle Function.
	Microminerals	
Aluminum	Ingestion of Aluminium should be avoided where possible.	No known biological function in the body.
Chromium	Red Meat and Liver, Egg Yolk, Seafood, Wholegrain Cereals, Molasses and Cheese.	Important for regulation of Blood Sugar Levels; helps to regulate Blood Cholesterol Levels.
Copper	Offal, Shellfish, such as Oysters, Nuts and Seeds, Mushrooms and Cocoa.	Needed for Growth and Connective Tissue Formation. Helps the body to absorb Iron from food. Present in many enzymes which protect against free radicals.
Fluoride	Toothpaste, Tap Water and Tea.	Protects against Tooth Decay.
Iodine	Seaweed, Seafood and Iodised Table Salt.	Vital part of Hormones secreted by the Thyroid Gland.
Iron	Offal, Lean Meat, Sardines, Egg Yolk, Dark Green Leafy Vegetables and Iron-Fortified Cereals.	Essential component of Haemoglobin and many Enzymes involved in Energy Metabolism.
Manganese	Nuts, Cereals, Brown Rice, Pulses and Wholegrain Bread.	Vital component of various Enzymes involved in Energy Production; helps to form Bone and Connective Tissue.
Molybdenum	Offal (especially Liver), Yeast and Pulses, Whole Grains and Leafy Vegetables, depending on soil.	Essential component of Enzymes involved in the production of DNA and RNA; may fight Tooth Decay.

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Selenium	Meat and Fish, Dairy Foods, such as Butter, Brazil Nuts, Avocados and Lentils.	Antioxidant Mineral; protects cells against free radical damage. Vital for normal sexual development.
Sulphur	Protein from Animal and Vegetable sources.	Component of two essential Amino Acids which help to form many Proteins in the body. Present in every cells.
Zinc	Oysters, Red Meat, Peanuts and Sunflower Seeds.	Essential for normal Growth, Reproduction and Immunity. Aids the action of many Enzymes.

Check Your Progress

1. What is functional food?
2. Give definition for functional food.
3. What is the role of functional food?
4. Explain the types of functional foods.
5. Why dairy products are considered as functional foods?
6. What are prebiotics?
7. Explain the role of probiotics.
8. What is synbiotics?
9. Explain the term nutrient density.

1.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. A functional food is a food claimed to have an additional function by adding new ingredients or more of existing ingredients. The term may also apply to traits purposely bred into existing edible plants, such as purple or gold potatoes having enriched anthocyanin or carotenoid contents, respectively.
2. As per the definition, 'Functional foods may be specifically designed to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions, and may be similar in appearance to conventional food and consumed as part of a regular diet'. The term was first used in Japan in the 1980s where there is a government approval process for functional foods called Foods for Specified Health Use (FOSHU).
3. Fundamentally, the functional foods are foods that have a potentially positive effect on health beyond basic nutrition. Proponents of functional foods say

they promote optimal health and help reduce the risk of disease. A familiar example of a functional food is 'Oatmeal' because it contains soluble fiber that can help lower cholesterol levels. The Food and Drug Administration regulates the claims that manufacturers can make about functional food nutrient contents that effects on disease, health or body function.

4. Following are the types of functional foods:
   - Whole food: It includes Oats, Soya, Fish, Garlic, Flaxseeds and Nuts, Grapes, Fruits and Vegetable.
   - Fortified foods: It includes Natural foods fortified with other Nutrients, Cereal and Cereals-Based products fortified with Folic Acid, Milk and Milk products are fortified with Vitamin B, Fats and Oils are fortified with Vitamin D and E.
   - Enhanced foods: These are foods that have more of a functional component through traditional breeding, genetic engineering, etc., for example dairy product with probiotics.
5. The dairy products are functional foods. They are one of the best sources of Calcium, an essential nutrient which can prevent Osteoporosis and possibly Colon Cancer. In addition to Calcium, other components which recent researches have focused in dairy products are known as probiotics.
6. Prebiotics are compounds in food that induce the growth or activity of beneficial microorganisms, such as Bacteria and Fungi. The most important example is in the gastrointestinal tract, where prebiotics can alter the composition of organism in the gut micro-biome.

   According to International Scientific Association Probiotics and Prebiotics (ISAPP), 'the prebiotics are a substrate that is selectively used by a host microorganism to produce a health benefit'.

   Dietary prebiotics are typically non-digestible fiber compounds that pass indigested through the upper part of the gastrointestinal tract and stimulate the growth or activity of advantageous bacteria that are colonial in the large bowel by acting as substrate for them.
7. Probiotics are good bacteria that are either the same as or very similar to the bacteria that are already in your body. Your similar digestive tract teams with a complex and diverse community of these bacteria. In fact there are greater humble of bacteria in your intestines than there are cells in your body.

   Most of the bacteria reside in your gut and the majority are quite harmless. Having the right gut bacteria have various health benefits including weight loss, improved digestion, reduce depression and promote heart health.

   Probiotics helps to improve immune system also and promote the production of natural antibodies in the body.

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8. Synbiotics refer to dietary supplements combining probiotics and prebiotics in a form a synergism, hence Synbiotics. Synbiotic can help support gut health by increasing the amount of beneficial bacteria in the digestive tract while also providing these bacterial cells with the full they need to function and thrive. Synbiotics can be found in supplement form which often combine nutritious plant based prebiotic fibers with specific health promoting strains of probiotics.
9. Nutrient density is the measure of the nutrients in a food relation to the calories. Foods containing different combinations of nutrients but a food that provides more key nutrients than calories is considered nutrient-dense of key nutrients. List of key nutrients used to factor nutrient density as Protein, Fiber, Vitamins A, C, E and B-12, Thiamine, Ribophorin, Folate, Calcium, Iron, Potassium and Zinc.

1.4 SUMMARY

- A functional food is a food claimed to have an additional function by adding new ingredients or more of existing ingredients. The term may also apply to traits purposely bred into existing edible plants, such as purple or gold potatoes having enriched anthocyanin or carotenoid contents, respectively.
- As per the definition, 'Functional foods may be specifically designed to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions, and may be similar in appearance to conventional food and consumed as part of a regular diet'.
- The term was first used in Japan in the 1980s where there is a government approval process for functional foods called Foods for Specified Health Use (FOSHU).
- Fundamentally, the functional foods are foods that have a potentially positive effect on health beyond basic nutrition. Proponents of functional foods say they promote optimal health and help reduce the risk of disease.
- A familiar example of a functional food is 'Oatmeal' because it contains soluble fiber that can help lower cholesterol levels. The Food and Drug Administration regulates the claims that manufacturers can make about functional food nutrient contents that effects on disease, health or body function.
- Functional food is a modified food that claims to improve health or well-being by providing benefit beyond that of the traditional nutrients it contains. Functional foods may include such items as cereals, breads, beverages that are fortified with vitamins, some herbs and nutraceuticals.
- Functional food are foods that have a potentially positive effect on health beyond basic nutrition. Proponents of functional foods say they promote optional optimal health and help in reducing the risk of disease. The

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physiological benefits show that it can reduce the risk factors of chronic diseases as it contains bioactive components.

- Functional foods can be considered to be those whole, fortified, enriched or enhanced foods that provide health benefits when they are consumed with diet on a regular basis. All foods are functional, as they provide taste, aroma or nutritive value.
- Functional foods deliver additional or enhanced benefits over and above their basic nutritional values.
- Some functional foods are generated around a particular functional ingredient, for example foods containing probiotics, prebiotics a plant Stanols and Sterols.
- Stanols and Sterols occur naturally in small amounts in plants and fruits and are considered that it has cholesterol lowering effect and are added to products, such as reduced/low fat spreads.
- The level of consumption of the food that is required to achieve a beneficial effect on health is an important consideration in particular, it should be possible to achieve the required level of intake of the functional food within normal dietary pattern.
- The term functional foods was introduced in Japan in the mid-1980s and refers to processed food containing ingredients that aid specific bodily functions in addition to being nutritious.
- A functional food may be a traditional food which we consume as part of our usual diets. It is shown to have physiological benefits and reduce that risk of chronic disease is it contains bioactive compounds.
- A functional food is a typical food that have specific nutrients added to it, like vitamins or minerals, fiber or probiotics or prebiotics. In general, this includes anything for a specific function purpose.
- Whole food includes Oats, Soya, Fish, Garlic, Flaxseeds and Nuts, Grapes, Fruits and Vegetable.
- Fortified foods includes Natural foods fortified with other Nutrients, Cereal and Cereals-Based products fortified with Folic Acid, Milk and Milk products are fortified with Vitamin B, Fats and Oils are fortified with Vitamin D and E.
- Enhanced foods are foods that have more of a functional component through traditional breeding, genetic engineering, etc., for example dairy product with probiotics.
- Oat products are dietary source of the cholesterol lowering, such as the soluble fibers of Beta Glucan. It is now significant that tomatoes can reduce and Low Density Lipoprotein (LDL) cholesterol thereby reducing the risk of Coronary Hearts Disease (CHD).

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- Soy has the highest protein content. It is now thought to play preventive and therapeutic roles in Cardio Vascular Disease (CVD), Cancer, Osteoporosis and the alleviation of Menopausal symptoms.
- Amongst the major seed oils, flaxseed oil contains the most (57%) of the Omega-3 Fatty Acid, a-Linoleic Acid. Consumption of flaxseed has also been shown to reduce total and LDL cholesterol as well as platelet aggregation.
- Dairy products are functional foods. They are one of the best sources of Calcium, an essential nutrient which can prevent Osteoporosis and possibly Colon Cancer. In addition to Calcium, other components which recent researches have focused in dairy products are known as probiotics.
- Prebiotics are compounds in food that induce the growth or activity of beneficial microorganisms, such as Bacteria and Fungi. The most important example is in the gastrointestinal tract, where prebiotics can alter the composition of organism in the gut micro-biome.
- According to International Scientific Association Probiotics and Prebiotics (ISAPP), 'the prebiotics are a substrate that is selectively used by a host microorganism to produce a health benefit'.
- Dietary prebiotics are typically non-digestible fiber compounds that pass indigested through the upper part of the gastrointestinal tract and stimulate the growth or activity of advantageous bacteria that are colonial in the large bowel by acting as substrate for them.
- An endogenous source of prebiotics in humans is human breast milk, which contains oligosaccharides structurally similar to GOS, referred to as Human Milk Oligosaccharides (HMOs). These HMOs were found to increase the Bifidobacterium bacterial population in breastfed infants, and to strengthen the infant immune system.
- Exogenous are the indigestible carbohydrate compounds classified as prebiotics are a type of fermentable fiber, and thus can be classified as dietary fiber. However, not all dietary fiber can be classified as a prebiotic source.
- Probiotics are good bacteria that are either the same as or very similar to the bacteria that are already in your body. Your similar digestive tract teams with a complex and diverse community of these bacteria. In fact there are greater humble of bacteria in your intestines than there are cells in your body.
- Probiotics helps to improve immune system also and promote the production of natural antibodies in the body.
- Synbiotics refer to dietary supplements combining probiotics and prebiotics in a form a synergism, hence Synbiotics.
- Synbiotic can help support gut health by increasing the amount of beneficial bacteria in the digestive tract while also providing these bacterial cells with the full they need to function and thrive.

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- Synbiotics can be found in supplement form which often combine nutritious plant based prebiotic fibers with specific health promoting strains of probiotics.
- Nutrient density is the measure of the nutrients in a food relation to the calories.
- Foods containing different combinations of nutrients but a food that provides more key nutrients than calories is considered nutrient-dense of key nutrients.
- List of key nutrients used to factor nutrient-density as Protein, Fiber, Vitamins A, C, E and B-12, Thiamine, Ribophorin, Folate, Calcium, Iron, Potassium and Zinc.
- Nutrient dense foods contain a lot of essential nutrients per serving, while energy dense foods are those that have a lot of calories in serving. Foods that are very high in fat or sugar are energy dense. Some foods are both nutrient-dense and energy-dense, such as Cheese, Meat and Nuts.

1.5 KEY WORDS

- **Functional foods:** These may be specifically designed to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions, and may be similar in appearance to conventional food and consumed as part of a regular diet.
- **Whole food:** It includes Oats, Soya, Fish, Garlic, Flaxseeds and Nuts, Grapes, Fruits and Vegetable.
- **Fortified foods:** It includes Natural foods fortified with other Nutrients, Cereal and Cereals-Based products fortified with Folic Acid, Milk and Milk products are fortified with Vitamin B, Fats and Oils are fortified with Vitamin D and E.
- **Enhanced foods:** These are foods that have more of a functional component through traditional breeding, genetic engineering, etc., for example dairy product with probiotics.
- **Prebiotics:** These are compounds in food that induce the growth or activity of beneficial microorganisms, such as Bacteria, Fungi and the most important is gastrointestinal tract, where prebiotics can alter the composition of organism in the gut micro-biome.
- **Probiotics:** These are good bacteria that are either the same as or very similar to the bacteria that are already in your body, it helps to improve immune system also and promote the production of natural antibodies in the body.
- **Synbiotics:** It refer to dietary supplements combining probiotics and prebiotics in a form a synergism, hence Synbiotics.
- **Nutrient density:** It is the measure of the nutrients in a food relation to the calories.

1.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

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Short Answer Questions

1. What are functional foods?
2. Distinguish between whole foods and fortified foods.
3. Write in brief about garlic.
4. What are dairy products?
5. List the criteria that is used to classify compounds as probiotics.
6. Name some of the natural sources of prebiotics.
7. What is Lactobacillus?
8. Explain about synbiotics, nutrient and non-nutrient functional foods.

Long Answer Questions

1. Explain with the help of diagram different types of functional foods.
2. How are functional foods beneficial?
3. Write a detailed note on enhanced foods.
4. Explain with the help of table diet-disease relationship.
5. Discuss in detail about prebiotics.
6. Distinguish between endogenous and exogenous.
7. What are probiotics? Give the health benefits of probiotics.
8. Briefly discuss the features and benefits of synbiotics.
9. Explain in detail about nutrient and non-nutrient functional foods.

1.7 FURTHER READINGS

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UNIT 2 PROBIOTICS

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Structure

2.0 INTRODUCTION

Probiotics are live microorganisms intended to provide health benefits when consumed, generally by improving or restoring the gut flora. Probiotics are considered generally safe to consume, but may cause bacteria-host interactions and unwanted side effects in rare cases. The original theory, similar to the modern concept, but not the term, is generally attributed to Nobel laureate Élie Metchnikoff, who postulated that yoghurt-consuming Bulgarian peasants lived longer lives because of that custom.

A growing probiotics market has led to the need for stricter requirements for scientific substantiation of putative benefits conferred by microorganisms claimed to be probiotic. Although numerous claimed benefits are marketed towards using consumer probiotic products, such as reducing gastrointestinal discomfort, improving immune health, relieving constipation, or avoiding the common cold, such claims are not supported by scientific evidence, and are prohibited as deceptive advertising in the United States by the Federal Trade Commission. As of 2019, numerous applications for approval of health claims by European manufacturers of probiotic dietary supplements have been rejected by the European Food Safety Authority for insufficient evidence of beneficial mechanism or efficacy. In a clinical setting, some probiotics have been found to be useful in treating antibiotic-associated diarrhea in children and Clostridium difficile infection in adults.

In this unit, you will study about probiotics, its taxonomy and important features of probiotic microorganisms and health effects of probiotics including mechanism of action in detail.

2.1 OBJECTIVES

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After going through this unit, you will be able to:

- Explain probiotics its taxonomy
- Discuss the important features of probiotic microorganisms
- Understand the health effects of probiotics including mechanism of action

2.2 PROBIOTICS

Probiotics are usually defined as microbial food supplements with beneficial effects on the consumers. Most probiotics fall into the group of organisms' known as lactic acid-producing bacteria and are normally consumed in the form of yogurt, fermented milks or other fermented foods. Some of the beneficial effect of lactic acid bacteria consumption include:

- Improving intestinal tract health.
- Enhancing the immune system, synthesizing and enhancing the bioavailability of nutrients.
- Reducing symptoms of lactose intolerance, decreasing the prevalence of allergy in susceptible individuals.
- Reducing risk of certain cancers.

The mechanisms by which probiotics exert their effects are largely unknown, but may involve modifying gut pH, antagonizing pathogens through production of antimicrobial compounds, competing for pathogen binding and receptor sites as well as for available nutrients and growth factors, stimulating immunomodulatory cells, and producing lactase. Selection criteria, efficacy, food and supplement sources and safety issues around probiotics are reviewed. Recent scientific investigation has supported the important role of probiotics as a part of a healthy diet for human as well as for animals and may be an avenue to provide a safe, cost effective, and 'natural' approach that adds a barrier against microbial infection.

Definitions of Probiotics

In Europe in 1999, probiotics accounted for more than two-thirds of the total market for functional foods. They are live cultures of microorganisms, usually bacteria that survive passage through the upper parts of the gut, particularly the acid environment of the stomach, and adhere to and colonise the bowel where they favourably alter the microbial balance. When they colonise the bowel they displace other potentially pathogenic bacteria and create an environment that is unfavourable for pathogen multiplication. Most of the organisms used as probiotics are lactic acid bacteria which are a large group of bacteria that produce lactic acid as the end products of their fermentation of carbohydrate. The Lactic Acid Bacteria

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include the lactobacilli, the bifidobacteria and some streptococci and other gram-positive cocci: a few yeasts have also been used as probiotics. Over twenty different species are listed by Fuller and Gibson (1999) as having been used as probiotics and others have been added since they compiled this list. Probiotics have been mainly consumed as fermented milk drinks or yoghurts although other foods and drinks are now being used as vehicles for probiotic bacteria and they are also available in powders or pills that contain live freeze dried bacteria.

Table 2.1 *Examples of Probiotics*

Class/Component	Source	Potential Benefit
Probiotics		
Certain species and strains of *Lactobacilli*, *Bifidobacteria*, Yeast	Certain yogurts, other cultured dairy products, and non-dairy applications	May improve gastrointestinal health and systemic immunity

The Lactic Acid Bacteria

Lactic Acid Bacteria (LAB) are an order of Gram-Positive, low-GC, acid-tolerant, generally non-sporulating, non-respiring, either rod-shaped (*bacilli*) or spherical (cocci) bacteria that share common metabolic and physiological characteristics. These bacteria, usually found in decomposing plants and milk products, produce lactic acid as the major metabolic end product of carbohydrate fermentation. This trait has, throughout history, linked LAB with food fermentations, as acidification inhibits the growth of spoilage agents. Proteinaceous bacteriocins are produced by several LAB strains and provide an additional hurdle for spoilage and pathogenic microorganisms. Furthermore, lactic acid and other metabolic products contribute to the organoleptic and textural profile of a food item. The industrial importance of the LAB is further evidenced by their Generally Recognized As Safe (GRAS) status, due to their ubiquitous appearance in food and their contribution to the healthy microbiota of animal and human mucosal surfaces.

Yogurt also spelled yoghurt, is a food produced by bacterial fermentation of milk. The bacteria used to make yogurt are known as *yogurtcultures*. Yoghurt is usually made by fermenting milk with a mixed culture of *Lactobacillus bulgaricus* and *Streptococcus thermophilus*; in the USA, the FDA requires that these two species must have been used if the food is to be called yoghurt. Even if 'live natural yoghurt' is eaten, it has limited value as a probiotic unless organisms other than the traditional ones have been added because these particular bacterial strains have low survival in the acid environment of the stomach and so other more resistant lactobacilli and bifidobacteria are used in probiotic preparations.

Breast Milk and the 'Bifidus Factor'

Up to 99% of the bacteria in the stools of breastfed babies are bifidobacteria whereas in formula-fed babies there is a much more diverse gut microflora. Breast milk contains oligosaccharides and perhaps other substances that stimulate the

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growth of bifidobacteria and this has been dubbed the 'bifidus factor'; nature's prebiotic? Breastfed babies have many fewer gut and respiratory infections than bottle-fed babies; in developing countries hygiene problems with bottle feeds is a major reason for this difference. However, this difference is still seen in developing countries where the anti-infective properties of breast milk are thought to be the main reason for it (Filteau and Tomkins 1994); this 'bifidus factor' in breast milk is one of several agents in breast milk that may directly or indirectly have anti-infective properties. Anything that might contribute to reduced rates of diarrhoea in babies is of great significance: diarrhoeal disease is by far the greatest cause of infant mortality in the world and mortality rates in bottle-fed babies in developing countries are much higher than those in breastfed babies.

What Makes a Good Probiotic?

The following are the ideal characteristics of a good probiotic and thus as criteria for the selection of new probiotic organisms.

- Species compatibility (Ideally probiotic organisms intended for humans should be isolated from human intestines because those isolated from different species are generally less effective).
- The ability to survive passage through the gut and reach the intestines in a viable state.
- Good ability to adhere to the intestinal epithelium.
- A short generation time so that they can colonise the bowel rapidly (Some bacteria with poor adherence to the intestinal epithelium are still able to temporarily colonise the bowel because of their short generation time).
- Production of antimicrobial agents that will kill or inhibit the growth of pathogens.
- Good survival in foods or powdered supplements so that the product has a reasonable shelf life.
- No pathogenicity itself (Current probiotics are generally recognised as safe and are nonpathogenic and non-toxin-producing organisms although on rare occasions they might be a source of infection in people whose immune systems have been compromised).
- Antigenotoxic properties (the ability to reduce mutation and carcinogenesis for example by reducing the production of mutagenic substances by other organisms in the intestine).

Benefits of Probiotics

Listed below are some of the many claims for health benefits of probiotics.

- They increase the nutrient content or nutrient availability in fermented food or even produce nutrients within the gut. Fermentation by Lactic Acid

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Bacteria can increase the B vitamin content of dairy foods including the folic acid content; it can also partially digest proteins and fats. It is difficult to establish the contribution to the host of intestinal production of vitamins by the gut microflora. The improved nutrient availability, together with reduced infection rates, may account for the increased weight gain reported in several studies when probiotics have been added to the food of young animals and bottle-fed babies.

- They reduce the symptoms of lactose intolerance. Milk is the only natural source of lactose and in around 70% of the world population the ability to digest lactose declines markedly after about four years of age, and lactase production is not re-induced by lactose consumption. High consumption of lactose in people with this 'primary lactase non-persistence' can precipitate unpleasant symptoms such as diarrhoea, bloating and flatulence caused by the osmotic effects of lactose in the large bowel and its fermentation by colonic bacteria. If lactose is administered in yoghurt containing live bacteria, it is well established that this improves its digestibility in those who are normally intolerant to it. The most likely explanation from the available evidence is that lactase of bacterial origin increases the digestion of lactose in the small intestine. Bacteria do not need to be alive when they reach the small intestine to produce this effect but the cells must remain intact to protect their lactase as it passes through the stomach.
- They reduce the rates or severity of intestinal infections. Claims have been made that probiotics can help to prevent or treat a number of different categories of diarrhoeal disease, including infectious diarrhoea in children and adults, traveller's diarrhoea and diarrhoea associated with antibiotic treatment. This suggested benefit of probiotics is discussed in more detail later in the chapter.
- They may reduce blood cholesterol concentrations and thus reduce atherosclerotic changes in arteries and ultimately reduce the risk of coronary heart disease. The Masai of East Africa eat a diet rich in saturated fat and cholesterol but have low rates of coronary heart disease. Observational and experimental studies of the Masai in the 1970s led to the suggestion that live fermented milk might contain a factor which lowered blood cholesterol. More recent human experimental studies that have used more reasonable quantities of fermented milk have produced no consistent evidence that probiotics significantly lower either total or LDL-cholesterol. In a review of several such studies, Taylor and Williams (1998) concluded that if probiotics do have any cholesterol-lowering effect it is weak. It would require large samples to get sufficient statistical power to detect such small changes against the background of wide intra-individual variation in serum cholesterol and significant technical errors in measurement.

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- They have been claimed to reduce the incidence of vaginal infections particularly vaginal candidiasis (thrush) caused by the yeast Candida albicans which is the most common vaginal infection. Lactic Acid Bacteria, particularly Lactobacillus acidophilus, predominate in the normal microflora of the vagina as they do in the intestine. *L. acidophilus* generates an acid, pH 4, which inhibits the growth of other organisms which can cause vaginal infections. A number of factors predispose to changes in the gut microflora that favour colonisation by candida or one of the other organisms that cause vaginal infections, for example, pregnancy, oral contraceptive use, diabetes, antibiotic use. The theoretical case for consuming probiotic preparations (especially *L. acidophilus*) to treat or prevent vaginal infections is essentially very similar to their use to treat or prevent intestinal infections: that they restore or maintain a healthy balance to the vaginal microflora that reduces the risk of colonisation by pathogenic organisms. There is, as yet, only limited evidence to support their effectiveness (Elmer *et al.* 1996) although several studies have shown that oral consumption of probiotics can alter the vaginal microflora (Reid *et al.* 2004). Preparations containing probiotic bacteria are sometimes applied directly to the vaginal area.
- It is suggested that long-term consumption of probiotics might afford some protection against bowel cancer.

Effect of Probiotics upon Incidence and Severity of Diarrhoea

Diarrhoea is not only a common, incapacitating and unpleasant condition of adults and children, but diarrhoeal diseases are also the most common cause of infant mortality in the world. Whilst diarrhoea-associated mortality is most common in developing countries it also causes the deaths of many babies in developed countries. Mortality rates from diarrhoea are much higher in developing countries in those babies who are bottle-fed compared with those who are breastfed. The normal gut microflora provides protection against infection by pathogenic organisms and it is suggested that probiotics alter the balance of the gut microflora so as to maximise this effect. This idea is given general support by observations on breastfed and bottle-fed babies mentioned earlier. There are major differences between the gut microflora in breastfed and bottle-fed babies. Up to 99% of the bacterial population in the gut of a breastfed baby are bifidobacteria and most of the rest are other lactic acid bacteria. Bottle-fed babies have a much more diverse flora with higher levels of Bacteroides, Clostridia and Escherichia coli, some of which are potentially pathogenic and may have other adverse effects such as production of potential carcinogens and intestinal putrefaction. The faeces of bottle-fed babies are similar in colour and odour to those of adults whereas those of breastfed babies are paler, looser and have a cheese-like odour. This unique microflora associated with breastfeeding is considered to be generally beneficial and is thought to contribute to the lower infection rates of breastfed babies which is apparent even in countries where hygiene standards are good. It is suggested that a number of different mechanisms could contribute to the reduced risk of pathogen infection

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that results from the presence of high levels of lactic acid and other 'good bacteria' in the gut; several of these are listed below:

- They may compete with other bacteria for key nutrients even though one would expect the gut to be a nutrient-rich environment.
- They produce an acidic environment that inhibits the growth and survival of pathogens. The pH of the stools of breastfed babies is acidic with a pH of 5–5.5 whereas that of bottle-fed babies is close to neutral (pH 7).
- They secrete antimicrobial substances that kill or inhibit the growth of other bacteria. Many lactic acid bacteria produce peptides or bacteriocins that inhibit the growth of other bacteria but these tend to be active against other lactic acid bacteria.
- They compete with pathogens for adhesion sites on the intestinal epithelium and thus speed up their elimination and reduce the chances of them colonising the gut.
- They may break down toxins that are responsible for the adverse symptoms that a pathogen produces.
- It is suggested that lactic acid bacteria bind strongly to epithelial membranes and may provoke an immune response. This could enhance the host's ability to combat both enteric and systemic infections.

From simple observational comparisons of the infection rates of breastfed and bottlefed babies one can only speculate on the contribution made by the unique gut microflora of breastfed babies to the overall reduction in infection risk. Differences in hygiene risks and other anti-infective agents in breast milk also contribute to this reduced risk. Use of probiotics in bottle-fed babies is one way of trying to make their gut microflora more like that of 'naturally' fed babies. Probiotic manufacturers also advocate use of probiotic supplements even in breastfed babies. Diarrhoea is a frequent side-effect of antibiotic therapy. The antibiotic not only kills the targeted bacteria but also kills many of those that make up the normal gut microflora. This distorts the gut microflora and increases the chances of pathogenic bacteria colonising the gut and producing diarrhoea. The organism Clostridium difficile is now known to be a major cause of antibiotic associated diarrhoea. This diarrhoea can be treated with other antibiotics but there are obvious grounds for believing that probiotics might offer an alternative or an adjunct to this further antibiotic use. Many people experience a bout of 'traveller's diarrhoea' when they travel abroad on holiday or business. This susceptibility seems to occur even in people who travel from traditional summer holiday destinations to colder climes. A high proportion of these cases of diarrhoea are caused by strains of *E. colito* which the visitor has less immunity than the local population. A large number of other organisms can, of course, cause any particular outbreak or case of diarrhoea in travellers. Several studies have looked at the potential of probiotics taken before and/or during a foreign visit to reduce the risk of suffering a bout of diarrhoea. There have been some studies that have reported significant, even substantial,

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reductions in diarrhoea risk associated with use of probiotics but there have also been others which have not shown any beneficial effect. Conflicting results are perhaps inevitable given the variety of probiotics and the range of potential organisms capable of causing traveller's diarrhoea: a variety of preventatives have been tested on their ability to prevent a variety of different infections. When looking at individual causes and types of diarrhoea, much of the evidence is inconclusive. However, taken overall there does seem to be support on both theoretical and experimental grounds for expecting that some probiotics could be helpful in the treatment and/or prevention of some types of diarrhoea. There are almost no reports of significant adverse effects of using probiotics in a normal population.

Possible Effects of Probiotics upon Risk of Developing Bowel Cancer

In the UK and USA, bowel cancer is the second most common cancer site for both men and women. Internationally, rates of bowel cancer vary by as much as fifteen-fold and evidence from studies with migrants as well as recent large and rapid increases in bowel cancer rates in some genetically stable populations (for example, Japan) suggest that most of this international variation is due to environmental factors including diet. Populations or groups who eat diets that are low in meat and fat but high in starch, fibre, fruits and vegetables have low rates whereas those who eat typical western diets that are high in meat and fat but low in starch, fibre, fruit and vegetables have high bowel cancer rates. It is suggested that diet could alter susceptibility to bowel cancer by a number of mechanisms such as those listed below:

- Substances present in food and food degradation products could have mutagenic effects.
- Substances produced from the breakdown of bile acids could be mutagenic.
- Some products of bacterial fermentation in the colon could have a protective effect, for example butyrate is known to have an anti-proliferative effect which may inhibit tumour development.
- An acid pH in the colon generated by bacterial fermentation may prevent the production of mutagenic substances from bile acids or prevent the growth of mutagen-generating bacterial species.
- Increases in stool bulk and more rapid clearance of waste might reduce the exposure of colonic epithelium to mutagens that are demonstrably present in faeces.

At least two observations have encouraged nutritionists to speculate that regular probiotic consumption might afford some protection against developing bowel cancer:

- The growing evidential support for the protective effect of probiotics against acute pathogen colonisation by the bowel and thus against intestinal infections.

- That several of the mechanisms proposed above by which diet might alter bowel cancer risk would be affected by differences in the gut microflora and differences in the end products of bacterial fermentation in the gut.

It has proved difficult to find consistent evidence for the ability of probiotics to produce significant short-term benefits on infection rates and blood cholesterol. It is therefore likely to be some years before a substantial body of consistent direct evidence is able to provide a convincing case for or against a protective effect of probiotics upon bowel cancer risk. Reddy (1998) reviews evidence to suggest that probiotics can reduce rates of chemically induced bowel cancers in animal models of human cancer but there is no direct evidence that fermented food consumption prevents cancer in people.

Probiotics and the Prevention of Childhood Eczema

There has been considerable media and scientific attention devoted to the apparent large and rapid increases in the incidence of atopic (allergic) diseases in recent years – asthma, allergic rhinitis (hay fever) and eczema. In some developed countries it is estimated that half of all children may develop one or more of these conditions. There has been much speculation about why these increases have occurred and many factors have been blamed including those listed below:

- Reduced breastfeeding of infants
- Maternal smoking
- Atmospheric pollution
- High number of immunisations
- An over-hygienic home environment.

Check Your Progress

1. How is the consumption of Lactic Acid Bacteria beneficial?
2. What are the areas where LAB's are used?
3. What does normal gut microflora provides?
4. List the major causes for rapid increases in the incidence of atopic diseases in recent years.

2.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Some of the beneficial effect of lactic acid bacteria consumption include:
   - Improving intestinal tract health.
   - Enhancing the immune system, synthesizing and enhancing the bioavailability of nutrients.

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- Reducing symptoms of lactose intolerance, decreasing the prevalence of allergy in susceptible individuals.
- Reducing risk of certain cancers.

2. Lactic Acid Bacteria are widely used in the production of traditional fermented foods such as yoghurt, cheese, kefir, koumiss, sauerkraut, sourdough bread, salami and some sausages. The resulting acidity of the food and other products of the fermentation help to preserve the food by inhibiting the growth of spoilage organisms and also reduce the risk of food poisoning by inhibiting the growth of potential pathogens. The fermentation process also adds distinctive flavours to the food and in the case of milk alters its texture by curdling the milk protein.
3. The normal gut microflora provides protection against infection by pathogenic organisms and it is suggested that probiotics alter the balance of the gut microflora so as to maximise this effect.
4. The main cause for rapid increases in the incidence of atopic (allergic) diseases in recent years – asthma, allergic rhinitis (hay fever) and eczema are as follows:
   - Reduced breastfeeding of infants
   - Maternal smoking
   - Atmospheric pollution
   - High number of immunisations
   - An over-hygienic home environment

2.4 SUMMARY

- Probiotics are usually defined as microbial food supplements with beneficial effects on the consumers.
- Most probiotics fall into the group of organisms' known as lactic acid-producing bacteria and are normally consumed in the form of yogurt, fermented milks or other fermented foods.
- The mechanisms by which probiotics exert their effects are largely unknown, but may involve modifying gut pH, antagonizing pathogens through production of antimicrobial compounds, competing for pathogen binding and receptor sites as well as for available nutrients and growth factors, stimulating immunomodulatory cells, and producing lactase.
- Recent scientific investigation has supported the important role of probiotics as a part of a healthy diet for human as well as for animals and may be an avenue to provide a safe, cost effective, and 'natural' approach that adds a barrier against microbial infection.

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- In Europe in 1999, probiotics accounted for more than two-thirds of the total market for functional foods.
- Most of the organisms used as probiotics are lactic acid bacteria which are a large group of bacteria that produce lactic acid as the end products of their fermentation of carbohydrate.
- The lactic acid bacteria include the lactobacilli, the bifidobacteria and some streptococci and other Gram-Positive cocci: a few yeasts have also been used as probiotics.
- Over twenty different species are listed by Fuller and Gibson (1999) as having been used as probiotics and others have been added since they compiled this list.
- Probiotics have been mainly consumed as fermented milk drinks or yoghurts although other foods and drinks are now being used as vehicles for probiotic bacteria and they are also available in powders or pills that contain live freeze dried bacteria.
- Lactic Acid Bacteria are widely used in the production of traditional fermented foods such as yoghurt, cheese, kefir, koumiss, sauerkraut, sourdough bread, salami and some sausages.
- The resulting acidity of the food and other products of the fermentation help to preserve the food by inhibiting the growth of spoilage organisms and also reduce the risk of food poisoning by inhibiting the growth of potential pathogens.
- The fermentation process also adds distinctive flavours to the food and in the case of milk alters its texture by curdling the milk protein.
- Yoghurt is usually made by fermenting milk with a mixed culture of *Lactobacillus bulgaricus* and *Streptococcus thermophilus*; in the USA, the FDA requires that these two species must have been used if the food is to be called yoghurt.
- Even if 'live natural yoghurt' is eaten, it has limited value as a probiotic unless organisms other than the traditional ones have been added because these particular bacterial strains have low survival in the acid environment of the stomach and so other more resistant lactobacilli and bifidobacteria are used in probiotic preparations.
- Breast milk contains oligosaccharides and perhaps other substances that stimulate the growth of bifidobacteria and this has been dubbed the 'bifidus factor'; nature's prebiotic.
- Breastfed babies have many fewer gut and respiratory infections than bottle-fed babies; in developing countries hygiene problems with bottle feeds is a major reason for this difference.

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- Diarrhoea is not only a common, incapacitating and unpleasant condition of adults and children, but diarrhoeal diseases are also the most common cause of infant mortality in the world.
- Whilst diarrhoea-associated mortality is most common in developing countries it also causes the deaths of many babies in developed countries.
- Mortality rates from diarrhoea are much higher in developing countries in those babies who are bottle-fed compared with those who are breastfed.
- The normal gut microflora provides protection against infection by pathogenic organisms and it is suggested that probiotics alter the balance of the gut microflora so as to maximise this effect.
- Up to 99% of the bacterial population in the gut of a breastfed baby are bifidobacteria and most of the rest are other Lactic acid Bacteria.
- Bottle-fed babies have a much more diverse flora with higher levels of *Bacteroides*, *Clostridia* and *Escherichia coli*, some of which are potentially pathogenic and may have other adverse effects such as production of potential carcinogens and intestinal putrefaction.
- The faeces of bottle-fed babies are similar in colour and odour to those of adults whereas those of breastfed babies are paler, looser and have a cheese-like odour.
- Differences in hygiene risks and other anti-infective agents in breast milk also contribute to this reduced risk.
- Use of probiotics in bottle-fed babies is one way of trying to make their gut microflora more like that of 'naturally' fed babies.
- Probiotic manufacturers also advocate use of probiotic supplements even in breastfed babies.
- Diarrhoea is a frequent side-effect of antibiotic therapy. The antibiotic not only kills the targeted bacteria but also kills many of those that make up the normal gut microflora.
- The organism Clostridium difficile is now known to be a major cause of antibiotic associated diarrhoea.
- It has proved difficult to find consistent evidence for the ability of probiotics to produce significant short-term benefits on infection rates and blood cholesterol.
- It is therefore likely to be some years before a substantial body of consistent direct evidence is able to provide a convincing case for or against a protective effect of probiotics upon bowel cancer risk.

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- Reddy (1998) reviews evidence to suggest that probiotics can reduce rates of chemically induced bowel cancers in animal models of human cancer but there is no direct evidence that fermented food consumption prevents cancer in people.
- There has been considerable media and scientific attention devoted to the apparent large and rapid increases in the incidence of atopic (allergic) diseases in recent years – asthma, allergic rhinitis (hay fever) and eczema.
- In some developed countries it is estimated that half of all children may develop one or more of these conditions.

2.5 KEY WORDS

- **Probiotics**: Probiotics are usually defined as microbial food supplements with beneficial effects on the consumers.
- **Yoghurt**: Yogurt also spelled yoghurt, is a food produced by bacterial fermentation of milk.
- **Yogurt cultures**: The bacteria used to make yogurt are known as yogurt cultures.

2.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. What are probiotics?
2. How are probiotics useful?
3. Give few examples of probiotics.
4. What are LAB's?

Long Answer Questions

1. Write a detailed note on breast milk and the 'bifidus factor'
2. What makes a good probiotic?
3. List the benefits of probiotics.
4. What are the effect of probiotics upon incidence and severity of diarrhoea?
5. Give the possible effects of probiotics upon risk of developing bowel cancer.
6. Discuss about probiotics and the prevention of childhood eczema.

2.7 FURTHER READINGS

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UNIT 3 PROBIOTIC MICROORGANISMS IN FERMENTED PRODUCTS AND QUALITY ASSURANCE

Structure

3.0 INTRODUCTION

Probiotics are defined as live microorganisms, which when administered in adequate amounts, confer a health benefit on the host. Health benefits have mainly been demonstrated for specific probiotic strains of the following genera: *Lactobacillus, Bifidobacterium, Saccharomyces, Enterococcus, Streptococcus, Pediococcus, Leuconostoc, Bacillus* and *Escherichia coli*. The human microbiota is getting a lot of attention today and research has already demonstrated that alteration of this microbiota may have far-reaching consequences. One of the possible routes for correcting dysbiosis is by consuming probiotics. The credibility of specific health claims of probiotics and their safety must be established through science-based clinical studies. This overview summarizes the most commonly used probiotic microorganisms and their demonstrated health claims. As probiotic properties have been shown to be strain specific, accurate identification of particular strains is also very important. On the other hand, it is also demonstrated that the use of various probiotics for immunocompromised patients or patients with a leaky gut has also yielded infections, sepsis, fungemia, bacteraemia. Although the vast majority of probiotics that are used today are generally regarded as safe and beneficial for healthy individuals, caution in selecting and monitoring of probiotics for patients is needed and complete consideration of risk-benefit ratio before prescribing is recommended.

Probiotic bacteria, when administered in sufficient quantity, confer several physiological benefits to their host. The bacteria, however, are sensitive to moisture,

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temperature, oxygen, and acid environments and therefore require protection against the detrimental conditions encountered during food processing, storage, and in vivo until their release at the desired site in the body. Protein gels offer protection to probiotics during processing and storage and extend the food applications of probiotics. Additionally, proteins have a nutritional advantage over polysaccharide-based systems. Milk proteins, in particular, are well known for their nutritional and bioactive properties.

In this unit, you will study about probiotic microorganisms in fermented milk products and non-milk products and quality assurance of probiotics and safety in detail.

3.1 OBJECTIVES

After going through this unit, you will be able to:

- Discuss about the probiotic microorganisms in fermented milk products and non-milk products
- Analyse the quality assurance of probiotics and safety

3.2 PROBIOTIC PRODUCTS

Probiotics are live microorganisms intended to provide health benefits when consumed, generally by improving or restoring the gut flora. Probiotics are considered generally safe to consume, but may cause bacteria-host interactions and unwanted side effects in rare cases.

The original theory, similar to the modern concept, but not the term, is generally attributed to Nobel laureate Élie Metchnikoff, who postulated that yoghurt-consuming Bulgarian peasants lived longer lives because of that custom

A growing probiotics market has led to the need for stricter requirements for scientific substantiation of putative benefits conferred by microorganisms claimed to be probiotic. Although numerous claimed benefits are marketed towards using consumer probiotic products, such as reducing gastrointestinal discomfort, improving immune health, relieving constipation, or avoiding the common cold, such claims are not supported by scientific evidence, and are prohibited as deceptive advertising in the United States by the Federal Trade Commission. As of 2019, numerous applications for approval of health claims by European manufacturers of probiotic dietary supplements have been rejected by the European Food Safety Authority for insufficient evidence of beneficial mechanism or efficacy.

In a clinical setting, some probiotics have been found to be useful in treating antibiotic-associated diarrhea in children and Clostridium difficile infection in adults.

Yogurt

Yogurt is defined as a fermented milk obtained by specific lactic acid fermentation, brought about by *Lb. bulgaricus* and *S. thermophilus*. Other bacteria may be added to enhance organoleptic properties, or, more recently, to increase the probiotic properties. Yogurt can now be found on the market that contains *Lactobacillus*, *Streptococcus*, *Leuconostoc*, and *Bifidobacterium* bacteria.

The amount of research on yogurt far surpasses any other probiotic product. Yogurt has been studied to determine its effects on lactase deficiency, cholesterol metabolism, immunity, infantile diarrhea, and certain cancers with varying levels of success.

Lactase Deficiency

Yogurt has been shown to be a dairy product that may be tolerated by people with a lactase (β- galactosidase) deficiency. It is more accurate to refer to a lactase deficiency as opposed to a lactose intolerance. Lactase is the digestive enzyme found in the intestinal brush border responsible for the hydrolysis of milk sugar lactose into glucose and galactose. A Lactase deficiency results in the buildup of unabsorbed lactose which acts osmotically to retain water. The deficiency is characterized by diarrhea, excessive flatulence, bloating, and abdominal pain after the ingestion of milk or milk products.

Yogurt, but not heat-treated yogurt, improves lactose digestion indicating that the live bacteria in yogurt are responsible, and long-term ingestion (8 days) does not seem to change this. The bacteria in yogurt survive passage through the stomach due to the enhanced protective (buffering) properties of the yogurt compared with milk. However, the buffering capacity of yogurt may also slow hydrolysis until the digest passes to a point in the intestinal tract where the pH favours β-galactosidase activity. The β-galactosidase activity in commercial yogurts has been found to vary depending on the manufacturer, whether fruit is added and whether the yogurt is frozen or not. Frozen yogurt that is pasteurized before freezing has no β-galactosidase activity. To overcome this, some manufacturers add starter culture to the pasteurized yogurt before freezing, but this does not necessarily increase enzyme activity.

Cholesterol Metabolism

The research into the effects of yogurt consumption on blood cholesterol has been difficult to understand because of the contradictory results that have been reported over the years. It is now clear that in many cases, results and conclusions from one experiment cannot be compared with others because of differences in experimental protocol. The sex, age, general health status, initial cholesterol level, and level of activity of subjects all influence cholesterol metabolism. The diet before and during the experiment can also influence results, as can the time of day the yogurt is consumed, whether it is consumed with other food or not, and the position in the

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meal (beginning or end of meal). One of the most important details of many yogurt-blood cholesterol experiments, namely, the type of yogurt fed (including details of the levels and types of bacteria in the test yogurt or fermented milk), are often not described. This, together with the fact that proper controls for such feeding trials were often not included, reduces the scientific validity of many studies.

Immune Function

The organs of the immune system are varied and within this system the leukocytes or white blood cells provide specific or nonspecific immunity. A wide variety of parameters including levels of specific immunoglobulins, numbers of different cell types, and measurement of specific metabolite concentrations are used to measure immune function. At the present time several hypotheses have been put forward regarding how yogurt might improve the immune system. Interaction of the yogurt bacteria with intestinal bacteria could produce indirect effects or the gut associated or systemic immune system might be affected by metabolites of the bacteria themselves or fermentation products in the yogurt.

Diarrhea

Diarrhea, particularly in young children, can be problematic because of the need to rehydrate the patient as quickly as possible, combined with the problems associated with decreased nutrient intake. The detrimental consequences of complete withdrawal of food from infants as a treatment have been defined, but withholding food during early stages of diarrhoea is still widespread. Fermented milk or yogurt can supply liquid and at the same time may supply natural antibiotics produced by the lactic acid bacteria to prevent or reduce the severity of infantile diarrhea. However, these positive results appear only to be applicable in infants who are otherwise well nourished.

Cancer

The beneficial effects of yogurt consumption on reduced cancer incidence is not established. The article published by van't Veer and colleagues is often quoted as proof of a link between yogurt consumption and a low incidence of breast cancer. Based on a daily food consumption questionnaire of newly diagnosed breast cancer patients or a group of healthy women (control), they concluded that fermented milk products (yogurt, buttermilk, Gouda cheese) may have a protective effect against breast cancer.

A Vehicle for Other Nutrients

The popularity of yogurt has prompted several studies that have investigated the feasibility of using yogurt as a vehicle for other important nutrients that normally would not be of importance in yogurt. Plant sterols have been added to yogurt producing a product that significantly lowers serum cholesterol after only 3 weeks

of consumption. In spite of the potential problems of off-flavour and encouragement of growth of contaminating bacteria, Hekmat and McMahon' were able to produce a yogurt with up to 40 mg/kg of added iron that was acceptable particularly to untrained consumers.

Kefir

Kefir is a fermented milk drink that has its origins in the Caucasus Mountains of the former U.S.S.R. Traditionally, it was made from goat's or cow's milk that was stored in skin bags. Over time a mass of bacteria, yeasts, proteins, carbohydrates precipitated out from the drink and was used to inoculate new milk. This mass is called kefir grains, and it is the grains that give kefir its texture, taste, and possible health benefits. Kefir has a long oral tradition for its health-promotion properties in Eastern Europe and has only recently been produced in North America on a commercial scale. A product of the fermentation process is CO_2 gas, which continues to be produced after packaging and results in a thick drink with a 'sparkling' mouth-feel when consumed. This has prompted some to refer to kefir as the 'champagne of dairy products'. Unlike yogurt, which requires only two well-defined bacteria for production, the microbiology of kefir is much more complex and has been shown to vary from country to country, thus making a comparison of its properties difficult. Changes that occur during fermentation promote the growth of certain microorganisms, while reducing the growth of others.

Fabrication

Three different types of kefir drink are produced - traditional kefir, Russian-type kefir, and industrial kefir - depending on whether the grains or a mother culture from the grains is used to inoculate pasteurized milk. No studies have been published that compare the properties (health benefits or otherwise) of kefir produced by different processes. Incubation is carried out at 20 to 22°C for 18 to 20 hours until a specific pH is reached, and then packaged, or a maturation period can be introduced. The grains themselves have a strong yeasty taste, and, therefore, using a mother culture or sieving out the grains may be ways of making a product closer to buttermilk in taste.

Health Benefits

The (Western) scientific literature to support the beneficial health claims for kefir is not extensive and few human feeding trials using kefir have been carried out. The Russian literature lists peptic ulcers, biliary tract diseases, chronic enteritis, bronchitis, and pneumonia as all being treated with kefir. Kefir is included as a regular part of hospital diets, is a recommended food for nursing mothers, and is often used as a first weaning food for babies in Russia. Both kefir grains and the drink itself have been shown to have antitumoral, antibacterial, and antifungal properties that may explain the diverse list of diseases and infections it is used to treat.

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Fermented Vegetables and Other Foods

Fermented vegetables are known throughout the world. Fermentation is often viewed as an effective method to preserve vegetables, without regard to any health benefits. Reddy and colleagues list 23 legume-based fermented foods, the majority of which are soybean products. Only *natto*, a popular fermented soybean product from Japan, is mentioned as encouraging the growth of Bifidobacterium in animals. Most reports of fermented vegetables have centered on the organism(s) used to produce the fermentation and on any increases in the protein, amino acid, and vitamin concentrations of the final product, not any possible probiotic effects.

Various other foods have been tested as possible vectors to carry probiotic bacteria. The verification of the efficacy of these products has not been the focus to date, but, rather, investigation of whether the bacteria will survive in the food matrix and during processing and storage. Cheddar cheese containing *Enterococcus faecium*, *B. longum* in frozen yogurt, and *B. longum*, *B. infantis*, and *B. brevis, L. acidophilus*, and *B. bifidum* in ice cream are examples. It has been predicted that probiotic infant formulae, baby food, fermented fruit juices, fermented soy products, cereal-based products, as well as disease-specific products, are products of the future.

Safety Concerns of Probiotic Use

Probiotics are be defined as 'An oral supplement or a food product that contains a sufficient number of viable microorganisms to alter the microflora of the host & has the potential for beneficial health effects'. It is also defined as 'Live microorganisms that when administered in adequate amounts confer a health benefit on the host'. Most of the commercially available probiotics belong to the *Lactobacillus* and *Bifidobacterium* species that are part of normal heathy gastrointestinal micro biota. Probiotic effects are strain specific, thus each individual bacterial strain must be tested separately for health benefit in question, and the effects described for one strain cannot be directly applied to others. Lactobacilli fall into the category of organisms classified as 'generally regarded as safe'. Organisms that are regarded as safe along with *lactobacilli*, are *Lactococci, Bifidobacterium* and yeast. There are other probiotic organisms, such as enterococcus, bacillus, and other spore forming bacteria, as well as streptococci, that are not generally regarded as safe but have been used as probiotics. Finally, there are concerns about product quality, since products that do not contain the probiotic on the label, or that contain contaminants may also place the consumer at risk. Probiotics are generally considered safe when ingested orally or used vaginally and are well tolerated. One safety concern associated with probiotics is the potential for these organisms to cause systemic infections. Although rare, probiotic related bacteremia and fungemia have been reported. It is estimated that the risk of developing bacteremia from ingested Lactobacillus probiotics is less than 1 per 1million users, and the risk of developing fungemia from *Saccharomyces*

boulardii is estimated at 1 per 5.6 million users, and is estimated to be lower in healthy individuals.

3.3 QUALITY ASSURANCE OF PREBIOTICS AND SAFETY

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Criteria for functional quality assurance and analytical approaches for characterization and validation of probiotic products. The criteria currently used to select probiotics define the optimal quality control of probiotic strains in industrial practice. Important quality-control properties that must be constantly controlled and optimized are the following: adhesive properties; bile and acid stability; viability and survival throughout the manufacturing process; effects on carbohydrate, protein, and fat utilization; and, especially, colonization properties and immunogenicity. Most of these properties are related to the physiologic properties of the strain, but long-term industrial processing and storage conditions may influence probiotic properties. Thus, in addition to technologic properties, functional properties should be considered in quality-control measures.

The methods available for detection, enumeration and identification of microorganisms could be also applied to probiotic microorganisms.

Molecular Methods

Identification of probiotic species, including their differentiation in different strains by culture-dependent or culture-independent techniques, the study of microbial community composition, and assessment of its different populations and interactions in food products are some of the main achievements of molecular techniques. With the use of molecular methods, the ability to detect and to identify food microbes, including probiotic bacteria, has made tremendous advances in recent years, especially after the introduction of PCR (Polymerase Chain Reaction) in the 1980s. Several detection techniques have been developed based on PCR, namely Denaturing Gradient Gel Electrophoresis (DGGE), real-time PCR (qPCR), Terminal Restriction Fragment Length Polymorphism (T-RFLP), Random Amplified Polymorphic DNA (RAPD). To rapidly detect multiple microorganisms in a single reaction, simultaneous amplification of more than one locus is required; a methodology referred to as Multiplex PCR (MPCR) in which several specific primer sets are combined into a single PCR assay. Hence, MPCR is undoubtedly useful to rapidly identify several isolates and, with respect to DGGE, it enables the selection of various species and represents the fastest culture-independent approach for strain specific detection in complex matrices. At a certain level, MPCR might be considered a quantitative (or better yet, a semi-quantitative) technique, since, once it has been established, the detection limit can be retrieved and used as the minimal microbial concentration detectable.

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Non-Molecular Methods

The non-molecular approach to detect, to enumerate and to identify probiotic strains includes those methods considered conventional, based on the growth of the microorganism in culture media, and those not requiring this step. The basis of the conventional methods relies on standard procedures encompassing isolation, counting and identification of the probiotic strains at the genus and species levels based on cell ability to reproduce and to form colonies on selective/differential agar media plates.

Alternative methodologies have been applied to quantify probiotic bacteria in a more accurate way able to reduce the underestimation of viable bacteria obtained by plate-count methods. Fluorescence methods have been applied in bacterial viability studies; Fluorescence methods are able to detect and to differentiate between viable, injured, stressed and dead bacterial cells through fluorescent dyes, which, in turn, can be detected by fluorescence microscopy, fluorometry, flow cytometry, or Fluorescence In Situ Hybridization (FISH).

An alternative method is Fourier Transform Infrared (FT-IR) spectroscopy that has been applied for detection, discrimination, identification and classification of Lactic Acid Bacteria (LAB) and probiotics and also provides information about cell metabolism from cultures and foods. FT-IR is able to discriminate viable, injured and dead bacteria and is used in the analysis of structural components of bacteria. FT-IR is a relatively fast, simple, sensitive technique, requiring very little sample, and the biological cell remains intact during analysis. It is possible to make qualitative and quantitative analysis and the sample can be in the form of liquid, gas, powder, solid, or film. If the sample is complex, then it can produce overlapping spectra, and so previous separation or purification steps may be needed or may require standardization, rigorous data collection, and expertise in the chemometric analyses of spectra.

Applications and Dosage Forms

As discussed above the most common species of probiotics used in foods are *Lactobacilli* and *Bifidobacteria*. The same Lactobacilli and Bifidobacteria are used in both foods and food supplements. In addition some Enterococcus species, Bacillus species, *Escherichia coli*, *Saccharomyces boulardii* (a yeast), and other species are used in food supplements. A wider variety of probiotic strains, either singly or in combination, is used in supplements rather than in foods. Several product formulations exist, like: hard gelatin or vegetable capsules, tablets with or without enteric coating (for example, those that dissolve in neutral conditions), chewable tablets, and sachets. Supplement formulations may also contain other active components, including vitamins and prebiotics. Probiotics are also found as sold in oil suspensions, which makes them easy to administer to infants. Furthermore, probiotics are combined with oral rehydration salts for the treatment of acute diarrhea, whereas some of these products are registered as drugs.

Probiotics are worldwide available, as supplements consisting of freeze-dried bacteria, secondly in fermented foods, such as yoghurts, and thirdly in products aimed at enhancing specific aspects of health, such as bowel cleansers. In some countries probiotics are also sold as remedies for specific medical conditions, such as diarrhea.

Not surprisingly, in some late experiments of probiotic products have been found that about 70 to 80 percent of the samples tested do not measure up to their label claims. In these experiments is also established, that about half of the tested samples did not have even 10 percent of the claimed number of live microorganisms as listed on their labels. In some products tested have even been determined a presence of undesirable microorganisms not listed on the label. Keeping this in mind, in order to obtain well produced product is essential to follow the following steps, when producing: eliminating oxygen from and including nitrogen in probiotic supplement bottles to enhance the stability of probiotics; probiotic supplements should be refrigerated to maintain their potency and viability; any new bacterial culture that has no history of prior safe use in humans should be subject to toxicological studies prior to incorporation in any probiotic supplement and also selecting acid resistant strains of is the key to the success of the probiotic supplement.

In order to assure the qualities of the probiotic product, it is important to know that the supplement is tested for viable microorganisms at the time of manufacturing and at the expiration date. This quality control procedure is important to the manufacturer as well as the consumer. The viable cells are guaranteed as CFU (Colony Forming Units) per gram at the time of probiotic supplement packaging. If the supplement does not list viable cells, or does not list the amount in CFU form, it may not be a quality supplement. Consumption of probiotic supplements with two to five billion CFU per day is necessary to have any chance of offering significant beneficial effects.

In conclusion in order for a consumer to be sure of the quality and safety of the probiotic product, the following tips should be considered:

- All probiotic supplements lose their potency when they exposed to oxygen, moisture, and heat.
- The probiotic strain must also be proven to survive stomach acids in live human subjects. The bacteria strain should be able to adhere to the intestinal walls and proliferate.
- Many probiotic combinations lack research. No studies exist showing their compatiblity and experts agree too many different bacteria may be antagonistic to each other.
- The selection of bacteria for incorporation in probiotic supplements that are on the federal GRAS (Generally Recognized as Safe) list is imperative for the products safety.

- Fortification of probiotics with prebiotic FructoOligoSaccharides (FOS) enhances the value of the probiotic supplement by providing a nutrient that selectively enhances the growth of friendly cultures.

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The Future for Probiotics and Prebiotics

The market for probiotic and prebiotic products will continue to grow as our knowledge of the intestinal microflora and its role in the maintenance of health and disease resistance advances. Food manufacturers will have to be able to produce products that maintain viable bacteria up until the time of consumption and in many cases will also have to provide encapsulation or other protective mechanisms for the live microorganisms in their products to be able to deliver bacteria to the correct site of action in the GI tract.

Check Your Progress

1. What are prebiotics?
2. Define the term yogurt.
3. To what does lactase deficiency results into?
4. What are the main achievements of molecular techniques?
5. Name the various detection techniques have been developed based on PCR.
6. What are the non-molecular approach to detect probiotic strains?

3.4 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Probiotics are live microorganisms intended to provide health benefits when consumed, generally by improving or restoring the gut flora. Probiotics are considered generally safe to consume, but may cause bacteria-host interactions and unwanted side effects in rare cases.
2. Yogurt is defined as a fermented milk obtained by specific lactic acid fermentation, brought about by *Lb. bulgaricus* and *S. thermophilus*. Other bacteria may be added to enhance organoleptic properties, or, more recently, to increase the probiotic properties. Yogurt can now be found on the market that contains *Lactobacillus*, *Streptococcus*, *Leuconostoc*, and *Bifidobacterium* bacteria.
3. A Lactase deficiency results in the buildup of unabsorbed lactose which acts osmotically to retain water. The deficiency is characterized by diarrhea, excessive flatulence, bloating, and abdominal pain after the ingestion of milk or milk products.

4. Identification of probiotic species, including their differentiation in different strains by culture-dependent or culture-independent techniques, the study of microbial community composition, and assessment of its different populations and interactions in food products are some of the main achievements of molecular techniques.
5. Several detection techniques have been developed based on PCR, namely Denaturing Gradient Gel Electrophoresis (DGGE), real-time PCR (qPCR), Terminal Restriction Fragment Length Polymorphism (T-RFLP), Random Amplified Polymorphic DNA (RAPD). To rapidly detect multiple microorganisms in a single reaction, simultaneous amplification of more than one locus is required; a methodology referred to as Multiplex PCR (MPCR) in which several specific primer sets are combined into a single PCR assay.
6. The non-molecular approach to detect, to enumerate and to identify probiotic strains includes those methods considered conventional, based on the growth of the microorganism in culture media, and those not requiring this step. The basis of the conventional methods relies on standard procedures encompassing isolation, counting and identification of the probiotic strains at the genus and species levels based on cell ability to reproduce and to form colonies on selective/differential agar media plates.

3.5 SUMMARY

- Probiotics are live microorganisms intended to provide health benefits when consumed, generally by improving or restoring the gut flora.
- Probiotics are considered generally safe to consume, but may cause bacteria-host interactions and unwanted side effects in rare cases.
- The original theory, similar to the modern concept, but not the term, is generally attributed to Nobel laureate Élie Metchnikoff, who postulated that yoghurt-consuming Bulgarian peasants lived longer lives because of that custom.
- A growing probiotics market has led to the need for stricter requirements for scientific substantiation of putative benefits conferred by microorganisms claimed to be probiotic.
- Although numerous claimed benefits are marketed towards using consumer probiotic products, such as reducing gastrointestinal discomfort, improving immune health, relieving constipation, or avoiding the common cold, such claims are not supported by scientific evidence, and are prohibited as deceptive advertising in the United States by the Federal Trade Commission.

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- In a clinical setting, some probiotics have been found to be useful in treating antibiotic-associated diarrhea in children and Clostridium difficile infection in adults.
- Yogurt is defined as a fermented milk obtained by specific lactic acid fermentation, brought about by *Lb. bulgaricus* and *S. thermophilus*.
- Other bacteria may be added to enhance organoleptic properties, or, more recently, to increase the probiotic properties.
- Yogurt can now be found on the market that contains *Lactobacillus*, *Streptococcus*, *Leuconostoc*, and *Bifidobacterium* bacteria.
- Yogurt has been studied to determine its effects on lactase deficiency, cholesterol metabolism, immunity, infantile diarrhea, and certain cancers with varying levels of success.
- Yogurt has been shown to be a dairy product that may be tolerated by people with a lactase (β- galactosidase) deficiency. It is more accurate to refer to a lactase deficiency as opposed to a lactose intolerance.
- Lactase is the digestive enzyme found in the intestinal brush border responsible for the hydrolysis of milk sugar lactose into glucose and galactose.
- A Lactase deficiency results in the buildup of unabsorbed lactose which acts osmotically to retain water.
- The deficiency is characterized by diarrhea, excessive flatulence, bloating, and abdominal pain after the ingestion of milk or milk products.
- Yogurt, but not heat-treated yogurt, improves lactose digestion indicating that the live bacteria in yogurt are responsible, and long-term ingestion (8 days) does not seem to change this.
- The bacteria in yogurt survive passage through the stomach due to the enhanced protective (buffering) properties of the yogurt compared with milk. However, the buffering capacity of yogurt may also slow hydrolysis until the digest passes to a point in the intestinal tract where the pH favours β-galactosidase activity.
- The β-galactosidase activity in commercial yogurts has been found to vary depending on the manufacturer, whether fruit is added and whether the yogurt is frozen or not.
- Frozen yogurt that is pasteurized before freezing has no β-galactosidase activity. To overcome this, some manufacturers add starter culture to the pasteurized yogurt before freezing, but this does not necessarily increase enzyme activity.
- The research into the effects of yogurt consumption on blood cholesterol has been difficult to understand because of the contradictory results that have been reported over the years.

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- The sex, age, general health status, initial cholesterol level, and level of activity of subjects all influence cholesterol metabolism.
- The diet before and during the experiment can also influence results, as can the time of day the yogurt is consumed, whether it is consumed with other food or not, and the position in the meal (beginning or end of meal).
- One of the most important details of many yogurt-blood cholesterol experiments, namely, the type of yogurt fed (including details of the levels and types of bacteria in the test yogurt or fermented milk), are often not described.
- The organs of the immune system are varied and within this system the leukocytes or white blood cells provide specific or nonspecific immunity.
- A wide variety of parameters including levels of specific immunoglobulins, numbers of different cell types, and measurement of specific metabolite concentrations are used to measure immune function.
- At the present time several hypotheses have been put forward regarding how yogurt might improve the immune system.
- Interaction of the yogurt bacteria with intestinal bacteria could produce indirect effects or the gut associated or systemic immune system might be affected by metabolites of the bacteria themselves or fermentation products in the yogurt.
- Diarrhea, particularly in young children, can be problematic because of the need to rehydrate the patient as quickly as possible, combined with the problems associated with decreased nutrient intake.
- The detrimental consequences of complete withdrawal of food from infants as a treatment have been defined, but withholding food during early stages of diarrhoea is still widespread.
- Fermented milk or yogurt can supply liquid and at the same time may supply natural antibiotics produced by the lactic acid bacteria to prevent or reduce the severity of infantile diarrhea. However, these positive results appear only to be applicable in infants who are otherwise well nourished.
- The beneficial effects of yogurt consumption on reduced cancer incidence is not established.
- Kefir is a fermented milk drink that has its origins in the Caucasus Mountains of the former U.S.S.R. Traditionally, it was made from goat's or cow's milk that was stored in skin bags.
- Over time a mass of bacteria, yeasts, proteins, carbohydrates precipitated out from the drink and was used to inoculate new milk. This mass is called kefir grains, and it is the grains that give kefir its texture, taste, and possible health benefits. Kefir has a long oral tradition for its health-promotion

properties in Eastern Europe and has only recently been produced in North America on a commercial scale.

- A product of the fermentation process is CO_2 gas, which continues to be produced after packaging and results in a thick drink with a 'sparkling' mouth-feel when consumed. This has prompted some to refer to kefir as the 'champagne of dairy products'.
- Unlike yogurt, which requires only two well-defined bacteria for production, the microbiology of kefir is much more complex and has been shown to vary from country to country, thus making a comparison of its properties difficult.
- Changes that occur during fermentation promote the growth of certain microorganisms, while reducing the growth of others.
- Criteria for functional quality assurance and analytical approaches for characterization and validation of probiotic products.
- The criteria currently used to select probiotics define the optimal quality control of probiotic strains in industrial practice.
- Important quality-control properties that must be constantly controlled and optimized are the following: adhesive properties; bile and acid stability; viability and survival throughout the manufacturing process; effects on carbohydrate, protein, and fat utilization; and, especially, colonization properties and immunogenicity.
- Most of these properties are related to the physiologic properties of the strain, but long-term industrial processing and storage conditions may influence probiotic properties.
- Identification of probiotic species, including their differentiation in different strains by culture-dependent or culture-independent techniques, the study of microbial community composition, and assessment of its different populations and interactions in food products are some of the main achievements of molecular techniques.
- With the use of molecular methods, the ability to detect and to identify food microbes, including probiotic bacteria, has made tremendous advances in recent years, especially after the introduction of PCR (Polymerase Chain Reaction) in the 1980s.
- Several detection techniques have been developed based on PCR, namely Denaturing Gradient Gel Electrophoresis (DGGE), real-time PCR (qPCR), Terminal Restriction Fragment Length Polymorphism (T-RFLP), Random Amplified Polymorphic DNA (RAPD).

- To rapidly detect multiple microorganisms in a single reaction, simultaneous amplification of more than one locus is required; a methodology referred to as Multiplex PCR (MPCR) in which several specific primer sets are combined into a single PCR assay.
- At a certain level, MPCR might be considered a quantitative (or better yet, a semi-quantitative) technique, since, once it has been established, the detection limit can be retrieved and used as the minimal microbial concentration detectable.
- Alternative methodologies have been applied to quantify probiotic bacteria in a more accurate way able to reduce the underestimation of viable bacteria obtained by plate-count methods.
- Fluorescence methods have been applied in bacterial viability studies; Fluorescence methods are able to detect and to differentiate between viable, injured, stressed and dead bacterial cells through fluorescent dyes, which, in turn, can be detected by fluorescence microscopy, fluorometry, flow cytometry, or Fluorescence In Situ Hybridization (FISH).
- The same Lactobacilli and Bifidobacteria are used in both foods and food supplements.
- In addition some Enterococcus species, Bacillus species, *Escherichia coli*, *Saccharomyces boulardii* (a yeast), and other species are used in food supplements.
- A wider variety of probiotic strains, either singly or in combination, is used in supplements rather than in foods.
- Several product formulations exist, like: hard gelatin or vegetable capsules, tablets with or without enteric coating (for example, those that dissolve in neutral conditions), chewable tablets, and sachets.
- Supplement formulations may also contain other active components, including vitamins and prebiotics. Probiotics are also found as sold in oil suspensions, which makes them easy to administer to infants.
- Furthermore, probiotics are combined with oral rehydration salts for the treatment of acute diarrhea, whereas some of these products are registered as drugs.

3.6 KEY WORDS

- **Probiotics**: Probiotics are live microorganisms intended to provide health benefits when consumed, generally by improving or restoring the gut flora.
- **Yogurt**: Yogurt is defined as a fermented milk obtained by specific lactic acid fermentation, brought about by *Lb. bulgaricus* and *S. thermophilus*.

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3.7 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. What are prebiotics?
2. What is yogurt?
3. How does immune function?
4. Write a short note on fermented vegetables and other foods?
5. What are the different molecular methods used in identification of probiotic species?
6. Write the future for probiotics and prebiotics.

Long Answer Questions

1. What are the various probiotic products?
2. How is lactase deficiency caused?
3. What is cholesterol metabolism?
4. Write about diarrhea and cancer.
5. What is Kefir? Explain briefly.
6. What are the various safety concerns of probiotic use?
7. Elaborate a note on quality assurance of prebiotics and safety.

3.8 FURTHER READINGS

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UNIT 4 PREBIOTICS: CHEMISTRY, SOURCES AND EFFECT

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Structure

4.0 INTRODUCTION

Prebiotics are defined as 'non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species already resident in the colon and thus attempt to improve host health'. Dietary prebiotics are typically non-digestible fiber compounds that pass undigested through the upper part of the gastrointestinal tract and stimulate the growth or activity of advantageous bacteria that colonize the large bowel by acting as substrate for them. They were first identified and named by Marcel Roberfroid in 1995. As a functional food component, prebiotics, like probiotics, are a conceptual intermediary between foods and drugs. Depending on the jurisdiction, they typically receive an intermediate level of regulatory scrutiny, in particular of the health claims made concerning them for marketing purposes.

Most prebiotic research has focused on the effects that prebiotics confer on Bifidobacteria and Lactobacillus. These bacteria have been highlighted as key probiotics and beneficial gut bacteria as they may have several beneficial effects on the host in terms of improving digestion (including but not limited to enhancing mineral absorption) and the effectiveness and intrinsic strength of the immune system. Both Bifidobacteria and Lactobacillus have been shown to have differing prebiotic specificity and selectively to ferment prebiotic fiber based on the enzymes characteristic of the bacterial population. Thus, Lactobacilli prefers inulin and fructooligosaccharides, while Bifidobacteria displays specificity for inulin, fructooligosaccharides, xylooligosaccahrides and galactooligosaccharides. A product that stimulates bifidobacteria is described as a bifidogenic factor, a concept that overlaps, but is not identical with, being prebiotic. Studies have also shown that prebiotics, besides stimulating the growth of beneficial gut bacteria, can also

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inhibit the growth of detrimental and potentially pathogenic microbes in the gut, such as clostridia.

In this unit, you will study about prebiotics, its chemistry, sources and bioavailability, effect of processing, effects on human health and potential applications in risk reduction of diseases, perspective for food applications for non-digestible carbohydrates/ oligosaccharides: dietary fibre, resistant starch, gums, in detail.

4.1 OBJECTIVES

After going through this unit, you will be able to:

- Discuss about prebiotics, its chemistry, sources and bioavailability, effect of processing
- Explain the effects of prebiotics on human health and potential applications in risk reduction of diseases
- Discuss the perspective for food applications for non-digestible carbohydrates/ oligosaccharides: dietary fibre, resistant starch, gums

4.2 PREBIOTICS: CHEMISTRY, SOURCES AND EFFECT

Prebiotics are supplements or foods that contain non digestible food ingredients that selectively stimulate the favourable growth and/or enhance the activities of indigenous probiotic bacteria. Prebiotic therapies have been found to cure gut related diseases such as constipation relief, suppression of diarrhoea, reduction of the risks of osteoporosis, atherosclerotic cardiovascular disease associated with dyslipidemia, insulin resistance, obesity, and possibly type 2 diabetes. Fast life style of humans has changed the regular diets which were sufficiently enriched with fibers needed for proper gut work. Prebiotics are special fibers having selective fermenting ingredients that are needed by microbiota of human gut. Human colon is one of the body's most metabolically active organs because of the presence of microbiota.

The **prebiotic** word was first introduced by Gibson and Roberfroid in 1995 and is defined as 'a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and improve host health'. In common terms, bacterial species that are believed to be beneficial for health and well-being of humans use prebiotics as food. The word prebiotic should be specific always: defined substances that exhibit a particular scientifically observed effect as stated by the prebiotic definition. Fermentable fibers in particular to other fibers are crucial for good health. But prebiotics are specified ingredients which are aimed to affect the specific bacteria,

end- products of their fermentation, and possible health benefits on the host. So, prebiotics are typically oligosaccharides or more complex saccharides that are selectively used by commensal bacteria, including species considered to be beneficial for the human host.

Prebiotics must resist host digestion, absorption, and adsorption before fermentation by one species of the resident microbiota. The most common prebiotics are inulin, its derivatives FructoOligoSaccharides (FOSs) and GalactoOligoSaccharides (GOSs), however, other complex saccharides and fibers have been recently considered as prebiotics. Poly- and oligosaccharides are commonly available in the usually taken diets. They are mainly found in vegetables, as a reserve of energy to be used during germination. In the milk of other mammals some oligosaccharides with prebiotic activity are also found. The most commonly used prebiotics to develop the foodstuffs, including baby foods, are fructans (inulin and FructoOligoSaccharides, FOS) and Galacto-OligoSaccharides (GOS). They are believed as GRAS and their health-benefiting effects have been widely studied. For example, Inulin is a mixture of polymers composed of fructose units forming linear chains having variable degrees of polymerization, bound to a single glucose moiety. Chicory is the source of inulin which is isolated and purified from it after energy density. On the other hand, various new prebiotics are having either natural origin (soy oligosaccharides, resistant starch, etc.) or synthetic origin (xylooligosaccharides, pyrodextrin, isomalte-oligosaccharides, lactosucrose, polydextrose, lactulose) are entering in the world market.

In Japan many of these new products have been developed and some of them have been currently commercialized. However, these new compounds have been studied mainly in vitro and animal models. It is important to note that more clinical trials are needed to confirm their safety as well as their healthy effects in humans. It is becoming more and more acceptable that the specific health effects are due to specific bacterial strains, thanks to double blind placebo controlled clinical studies for providing an increasing number of citations.

It is now well-known that specific prebiotics encourage specific colon microbial populations both in vitro and in vivo. For example, it has been found that amylomaize starch selectively stimulates the growth of (bifidobacteria) at the cost of (bacteroides and coliforms). Likewise, lactulose has been reported to support the growth of bifidobacteria and decrease the number of bacteroides in a continuous culture model as well as in the human colon. Additionally it has been found that the faecal levels of *B. lactis* increases by oral administration of galactooligosaccharides. On the contrary, beta-glucans support the growth of lactobacilli more than the bifidobacteria. So prebiotics support a specific microorganism for specific function.

4.2.1 Effect of Prebiotics on Human Health

Prebiotics reach the colon without being digested because of their chemical nature. A part of the material is not digested by pancreatic and small-bowel enzymes in

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the human gut and therefore, reaches the large bowel. The whole length of human gut is occupied by microorganisms with population numbers and species distribution characteristics of specific region of guts. In the gut the relatively more stable colonies are in large intestines than smaller intestines because the transit time in small intestines is faster (4-6 h) than large intestines (48-70 h) in adults. The pH and relatively low absorptive state of colon further supports large microbial colonisation and growth. Due to this microflora, the colon has the ability to undertake complex hydrolytic digestive functions. This involves breakdown of dietary components, complex carbohydrates and some proteins that are not hydrolysed or absorbed in the upper digestion tract. The colonic microflora derives their food from the undigested food for example, non-digestible oligosaccharides, dietary fibre, and undigested protein. They also get their substrates from the mucin: the main glycoprotein constituent of the mucus. Therefore, any undigested food that reaches the colon for example, non-digested carbohydrates, some peptides and proteins, certain lipids is a source of prebiotics. Prebiotics have been suggested of having various health benefits on humans. It acts as a substrate for the useful gut microorganisms. The various benefits are:

- **Gastroenteritis:** Gastroenteritis is a common disease usually occurs due to ingestion of food or water contaminated with pathogenic microorganisms and/or their toxins. The main pathogenic organisms responsible for gastroenteritis are *Shigellae, Salmonellae, Yersina enterocolitica, Campylobacter jejuni, Escherichia coli, Vibro cholera* and *Clostridus perfringens.* These pathogens grow and colonise within the gastrointestinal tract and invade the host tissue or they secrete toxins in the foods before ingestion. These toxins disrupt the functions of the intestinal mucosa, causing nausea, vomiting and diarrhoea. Therefore, prebiotics help to increase the population of useful organisms in large intestines that may possibly help in preventing gastroenteritis.
- **Inflammatory Bowel Disease:** Inflammatory bowel disease has been related to the intestinal microbiota pathogenesis. One of the understandable ways for therapeutic intervention is probiotic treatment. Administration of prebiotics is an additional treatment. Germinated barley foods are high in glutamine rich protein and hemicelluloses rich dietary fibre showing the prebiotic characteristics in the dextran sulphate sodium model of rat colitis as it has reduced the incidence of bloody diarrhoea and mucosal injury. Germinated barley foods also displayed a greater ability to decrease the symptoms of dextran sulphate sodium colitis than that of a probiotic mixture of lactobacilli and *C. butyricum.* A mixture of long chain inulin and oligosaccharide has shown the ability to decrease the inflammatory histological and gross cecal scores in the cecum and colon. It also decreased the levels of the pro-inflammatory cytokine IL-1β and increased the anti-inflammatory TGF-β, at the same time it increases cecal lactobacillus and bifidobacterium levels. Two other prebiotics lactulose and goat's milk

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oligosaccharides have shown an ability to reduce dextran sulphate sodium colitis in rats. Despite having definitive proof on the therapeutic value of prebiotic in the treatment of inflammatory bowel disease from animal models. However, all prebiotics are not beneficial. As in the case of probiotics, not every prebiotics have anti-inflammatory effects in curing of inflammatory bowel disease, instead of that the severity of damage increases by some prebiotics. For example, FructoOligoSaccharides (FOS) has demonstrated antagonistic effects in the intestine. Administering of FOS as a dietary supplement (6% w/w of total diet), stimulate lactobacilli and bifidobacteria, and increase SCFAs in the large intestines (a result that has been repeated in humans with ulcerative colitis. Due to the rapid fermentation of elevated FOS levels in the cecum by cecal bacteria causing elevated levels of organic acids, which damage the mucosa of the cecum and colon. Interestingly, however, oral gavage of FOS in the TriNitroBenzene Sulfonic Acid (TNBS) rat model of colitis showed the decrease of severity of damage, which means by increasing lactic acid bacteria, lactate and butyrate causes to decrease inflammation scores and myeloperoxidase activity. On the contrary, the effects of FOS in dextran sulfate sodium colitis showed that FOS treated rats had no shield from inflammation. These contradictory conclusions may be due to differences in the model of colitis or may be a result of change in the delivery of FOS, leading to change the rates of fermentation, and consecutively SCFA production.

- **Reduction of Cancer Risk:** Upon the administration of prebiotics it has been found that the activity of genotoxic enzyme decreases. A study carried on feeding galactooligosaccharides to humans showed decrease in nitro reductase (a mutagenic/carcinogenic substances) and also decreased levels of indole and isovaleric acid (produced due to proteolysis and deamination and markers of putrefaction). It has been shown that genotoxic enzymes beta-glucosidase, beta-glucuronidase, and arylsulphatase were strongly inhibited when galacto oligosaccharides was applied on model system of the human gut. As these effects happened quickly upon the addition of GOS to the system, changes attributable to population levels can be ruled out and it is more possible that direct inhibition by GOS or the production of repressors by bacteria was responsible. However, the proportion of bifidobacteria and lactobacilli increasing at the expense of bacteroides and clostridia may too decrease genotoxic enzyme production, as the former produces lower levels of such enzymes than the latter. Further study was carried to see the effects of resistant starch administration to human flora-associated rats. Even though β-glucosidase increased while as beta-glucuronidase and ammonia levels got decreased. Another observation a high level of caecal butyrate important to the reduction of cancer is not only the major source of energy for colonocytes but also helps to maintain a healthy epithelium. It can also play an important role in preventing cancer. These interactions include apoptosis induction, a process which is inactivated

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in cancer cells which would generally lead to their elimination and an increase in the immunogenicity of cancer cells due to an increase in cell surface proteins expression. However, the usual target bacteria for prebiotic use are bifidobacteria and lactobacilli but not butyrate producers. Therefore, other gut flora components (for example Eubacteria) should be fortified.

- **Prevention and Treatment of Allergy:** The series of bacterial intestinal colonization is possibly important for the development of the immune response of neonates and young infants. In pregnancy, the cell mediated immunity (T-helper 1 [Th1] type) is side tracked away towards the humoral immunity (Th2 type) due to the cytokine inflammatory response profile of the fetus. Therefore, the general type of immune response in early babyhood is Th2. The lack or delay in the eventual shift of the main Th2 type of response to more of a balance between Th1 and Th2 type responses could well be the result of the risk of allergic disease. In a review it was concluded that there was no firm conclusive evidence for giving prebiotics to prevent allergic disorders in infants. However, a report showed that 132 infants were at risk of atopy because of parental atopy, based on the 2 year follow-up of randomized controlled trials. FOS and GOS or maltodextrin placebo were fed to infants with partially hydrolyzed formula in first 6 months of life. There was a reduced incidence of atopic disease in those which was given the prebiotic mixture of FOS and GOS. Increasing rates of atopic eczema, recurrent wheezing, and allergic urticaria were higher in the maltodextrin placebo group (27.9%, 20.6%, and 10.3%, respectively) than in the intervention group (13.6%, 7.6%, and 1.5%) (P=.05). After analyzed the relevant publications it was concluded that there is no sufficient proof currently available to support the use of probiotics, prebiotics, or synbiotics for the prevention or treatment of allergic dermatitis in children. Studies supporting the benefits of prebiotics, particularly for children fed formula either partially hydrolyzed or not partially hydrolyzed formula, which are previously being promoted to decrease the prevalence of atopic disease, are needed to continue till other recommendations can be made for the use of prebiotics in infants and toddlers to stop infection or atopic disease.
- **Effects of Prebiotics on Bone Mineralization:** Bone mass of an adult is dependent on supply as well as bioavailability of calcium. In either cases of deficiency osteoporosis is prone to occur and in addition to this it is highly associated with increasing age and postmenopausal conditions. Presently, osteoporosis treatment and prevention is restricted to increasing calcium uptake, or by stimulating bone formation. Even though, a lot of studies have been carried out on calcium metabolism using rats, results depicted that prebiotics play a role in escalating the bioavailability of calcium. But so far, only a few human trials have been translated from these results. Prebiotic consumption increasing calcium absorption has the majority supporting data from the rat studies where as human trials have had diverse results.

- **Cardiovascular Effects of Prebiotics:** Obesity and diet have direct link with atherosclerosis, cardiovascular disease and type 2 diabetes, and there are number of animal experiments signifying the ability of prebiotics to influence the serum lipid levels. Double-blind randomized controlled trials were carried on 12 humans using inulin, FOS and GalactoOligoSaccharides (GOS) of the dosage of 15g per day. It was shown that higher concentrations of faecal acetate in inulin and GOS treatment periods (P combination of inulin when used for 4 weeks on normal lipidaemic persons showed significant reduction in triacylglycerol.

4.2.2 Food Applications of Prebiotics

Both important technological characteristics and interesting nutritional properties have been shown by Prebiotics. Some of them are found in fruits and vegetables and some can be processed industrially from renewable materials. In foods they affect considerably by improving organoleptic characteristics, enhancing both taste and mouth feel. As functional food ingredients prebiotics must be chemically stable to processing treatments of food, such as high temperature, low pH, and Maillard reaction conditions. Therefore, if the prebiotic was degraded to its component mono- and disaccharides or chemically altered, a prebiotic would no longer provide selective stimulation of beneficial microorganisms and it was unavailable for bacterial metabolism. A study ascertained the effect on the prebiotic activity by processing conditions of commercial prebiotics using a prebiotic activity assay. The results showed that a significant decrease in prebiotic activity was only seen when heating at low pH, with one of the FructoOligoSaccharides (FOS) products being the least stable. Little change in activity was caused by other conditions. These results help us in selecting of prebiotics as functional food ingredients and predicting the extent to which processing affects prebiotic activity. Presently known prebiotics and prebiotic candidates are non-digestible oligosaccharides. They are acquired either by extraction from plants (for example, chicory inulin), enzymatic hydrolysis (for example, oligofructose from inulin) or by synthesis (by trans-glycosylation reactions) from monoor disaccharides such as sucrose (fructooligosaccharides) or lactose (trans-galactosylated oligosaccharides or galactooligosaccharides). Among these prebiotics, inulin and oligosaccharides have been most studied prebiotics and recognized as dietary fibers in most countries. Prebiotics can be used to offer a double benefit such as an improved organoleptic quality and a better-balanced nutritional composition. As fiber ingredients the use of inulin and non-digestible oligosaccharides is simple and often leads to enhance taste and texture. Specific colonic bacteria, such as bifidobacteria and lactobacilli species readily ferment these particular forms of dietary fibre and by raising their cell population with the parallel production of short-chain fatty acids. These acids, mainly butyrate, acetate, and propionate provide acidification of the bowel as well as metabolic energy for the host. Lactose occurs wholly in the milk of mammals

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and one might observe from a teleological point of view that lactose ingestion provides specific health benefits beyond just being a source of energy to the suckling animal. In fact, it is used in different foods such as in baby foods, cakes, biscuits, chocolates, sugar confectionary, and soups and sauces and the global demand has grown considerably over the previous 10 years to amount to approximately 500,000 t per annum. Currently, more and more prebiotics are used in different foods as an ingredient which helps in the growth of health promoting colon microorganisms particularly probiotics and offer additional health benefits. Some of the recent works done in the development of prebiotic foods are as follows:

- **Prebiotics in Infant Formula:** There are number of prebiotic substances present in human milk, the most abundant of which are oligosaccharides. Many commercially available dietary food supplements are also added with oligosaccharide prebiotics. Concerning to their addition to infant food, the European Commission's Scientific Committee on Food concluded in 2003 that the addition of oligosaccharides to infant formulas had no major worry and including the studied infant formulas (formulas adapted especially for 6- to 12-month-old infants), up to a total concentration of 0.8 g/dL in ready-to-feed formula products. Few randomized controlled trials have been examined to see the effects of fortifying prebiotic oligosaccharides to infant foods. A study showed the effect of the addition of oligosaccharides having a concentration of 1 g/dL to newly born infant formula for 1 month having 90% of GOSs and 10% of FOSs. In the oligosaccharide supplemented group the faecal bifidobacteria counts increased significantly when compared with the non-supplemented group and the counts of bifidobacteria reached the range of a breastfed reference group. In another study, it was shown that the infants fed with the same oligosaccharide fortified formula. These infants had higher bifidobacteria counts as well as lactobacilli in their faecal matter. A multicenter trial was conducted that examined the efficiency of the fortification of prebiotics to infant foods. They stated the good overall tolerance and no undesirable effects during the study period of 12 weeks. Also a large multicenter trials have been evaluated by United States in 2004 on the safety of FOS supplemented infant formula. The study demonstrated the effect of FOS supplemented infant formula for 12 week study period and was seen that the infant growth was maintained without having any adverse effects. In weaning infant food formulas the fortification of prebiotics to solid foods shows to have a bifidogenic effect, as revealed by the results of recently published randomized controlled trials. Infant food formulas containing either GOS or FOS are now marketed in the United States. On the other hand more information, including data from randomized controlled trials, is required before the efficacy of adding prebiotics to infant food formulas can be determined.
- **Prebiotics in Cheese:** Dairy products are considered a potential vehicle for prebiotics and probiotics and are increasingly being used to produce

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synbiotic foods. A research conducted to evaluate the potential of prebiotic in novel petit-suisse cheeses using an in vitro fermentation model. Prebiotics candidate (inulin, oligofructose, honey) and probiotics (Lactobacillus acidophilus, Bifidobacterium lactis) were combined in five petitsuisse cheese formulations and were tested in vitro with human faecal slurry. It was seen that with addition of prebiotics to a probiotic cheese (made using starter + probiotics) fastest fermentation and high lactic acid production, promoting increased growth rates of bifidobacteria and lactobacilli, were achieved. Addition of probiotics as starter culture to control cheese also resulted in high lactic acid production. In vitro conditions, cheese made from the combination of different prebiotics and probiotics shows potential functional petitsuisse cheese. An investigation conducted to see the influence of prebiotic compounds (FOS and inulin), probiotic bacteria (Lactobacillus casei-01, Bifidobacterium lactis B94) and ripening time (0-60 days) on the Free Fatty Acid (FFA) profile of cheese, with special prominence on the Conjugated Linoleic Acid (CLA) content. 109-1010 cfu g-1 cheese were recorded in both probiotic and synbiotic cheeses after 60 days of ripening, in spite of harsh conditions of low pH values (4.1-5.1) and low moisture content (of 4.0 ± 0.1ºC and 6.0 ± 0.1ºC. The total solid content of the prebiotic fermented milk increased with the addition of inulin, also increased its acidity. The Power Law and Mizhari and Berk models described the flow of the fermented milks as shear thinning and non-Newtonian fluid behaviour. The apparent viscosity of the product added with inulin increased with storage time. The prebiotic fermented milk showed greater thixotropy and the hysteresis got lowered with an increase in the temperature. Debon *et al*. used permeate obtained from the best microfiltration process for the preparation of fermented milks, with and without of inulin (5 g 100 g-1), stored at 5 ± 1ºC for 28 days. It has been seen that the storage period and addition of inulin increased the total solids and carbohydrate contents, the caloric value and the acidity but decreased the pH. Lower syneresis index resulted with the addition of inulin in a fermented product also with greater firmness and cohesiveness. The inulin addition in a product resulted with a greater tendency toward a greenish coloration. Cruz *et al.* evaluated the effect of addition on physicochemical, rheological and microbiological characteristics of non-flavoured yogurt. There was no influence on the pH, proteolysis or the viability of Streptococcus thermophilus or Lactobacillus bulgaricus during 28 days of refrigerated storage with the addition of oligofructose. Yogurt added with oligofructose was characterized as a weak gel, showing thixotropic and pseudoplastic behaviour as per the rheological measurements. As per the survival analysis 25% of the consumers rejected the yogurt added with different levels of oligofructose, and the level of oligofructose that can be added to the yogurt was shown to be 2.58% wt. V-1.

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- **Prebiotics in Dairy Fruit Beverages:** Guergoletto *et al.* evaluated the survival of Lactobacillus Casei (LC1) when adhered to dehydrated prebiotic fibers. After vacuum drying in oat bran with 9% β-glucan and green banana flour, viability of LC-1 was 79% and 76%, respectively. Images revealed by scanning electron microscopy showed no morphological changes in the cells adhered to these fibers and the cell protectant trehalose addition had a positive and significant effect on the survival of LC-1. Greater viability of LC-1 has been seen when adhered to the oat bran (7.1 log CFU g–1) than in the free form (2.4 log CFU g–1). Sensory evaluation showed that the probiotic oat bran added to a dairy fruit beverage was well accepted by consumers.
- **Prebiotics in Cereals:** Several studies have publicized the prebiotic activity of cereal derived ArabinoXylan OligoSaccharides (AXOS). A study investigated the in situ AXOS production during bread making process. Firstly AXOS producing ability of different xylanases was compared in whole meal bread making. Different dosages of xylanase were used originating from *Bacillus subtilis*, *Aspergillus niger* and *Hypocrea jecorina*, and *thermophilic xylanase* from *H. jecorina* (HjXynA). Dosages which do not impair dough manageability, arabinoxylan fraction are solubilised and cleaved to the largest extent by HjXynA, resulting in an AXOS content of 2.1% on dry basis and an average degree of polymerisation of 9. Secondly the HjXynA effect on the AXOS levels in dietary fibre enriched breads was studied. Breads fortified with rye or wheat bran treated with HjXynA yielded high-quality breads with AXOS levels above 2.0% with an average degree of polymerization of 26 and 19, respectively. Due to wide occurrence of celiac disease and wheat allergy has led to an increasing demand for gluten-free foods that present an appropriate sensory acceptance. A consumer test was performed with 65 celiac people. Additionally, 15 trained assessors were used in the sensory profiling by using Quantitative Descriptive Analysis (QDA). By using QDA, the samples differed significantly with respect to all parameters, and Partial Least Squares (PLS) regression was used to recognize the factors of liking of gluten-free breads. The results show that the softness, traditional bread aroma, sweetness and crumb colour are the most desired sensory properties of such products which can be considered as drivers of liking of prebiotic gluten free breads. In a clinical study Partially Hydrolysed Guar Gum (PHGG) and FructoOligoSaccharides (FOS) were incorporated in biscuit and was assessed in human volunteers. The study showed consumption of biscuits added with FOS and PHGG gave a significant increase in faecal bifidobacterial numbers ($P=2.15\times10\text{-}5$). Bifidobacteria increased from 9.18 log10 cells/g faeces to 9.59 log10 cells/g faeces after the experimental treatment. There was small change in the total numbers of bacteria, *Bacteroides* spp., *Clostridium* spp. or *Lactobacillus-Enterococcus* spp. present in faecal samples collected over

the course of the trial. No changes were observed in bacterial populations on eating of the placebo biscuits.

- **Prebiotics in Salad Dressing:** A study conducted by Mantzouridou *et al*. to develop a low-in oil salad dressing emulsion, based on oat flour, that has both health promoting effect as well as provides growth to probiotic *Lactobacillus paracasei* subsp. *paracasei* DC412 with the functional properties also for example emulsion stabilization and thickening ability. Probiotic viability, following emulsion storage and enzymatic treatment, was persistent in oat flour presence at the levels near to those found for inulin. The dressing emulsion was further investigated by applying response surface methodology and the optimum formulation (g/100 g) was as: oil (20), xanthan (0.475) and oat flour (3.0); viable cell counts of emulsions reached levels as high as 108 cfu/g after the refrigerated storage period of 7.5 weeks and treatment with simulated gastric and intestinal juices. In addition to enhancing cell viability, appreciable improvement of the emulsion rheological properties and physical stability of salad dressing occur by oat flour incorporation. Prebiotic as thermoprotector *Bifidobacterium bifidum* viability to spray-drying and with storage time can be considerably improved by adding aguamiel as a thermoprotector prebiotic offering resistance to oxygen diffusion. *B. bifidum* harvested in the late log phase were mixed with three different protective colloids blends exhibiting relatively high, medium and low activation energies with or without aguamiel were spray dried at 130, 140 and 155ºC, and stored at 4ºC at a water activity of 0.32. The blend exhibiting highest activation energy (40.7 kJ mol-1), with aguamiel, and dried at 140ºC showed best viability when microencapsulating the microorganism. After 5 weeks storage time at 4ºC the viability ranged from 1.26×108 cfu g-1 immediately after drying to 6.0×106 cfu g-1. Prebiotics in edible coating. The idea for encapsulating probiotic living cells by prebiotic edible films was investigated. In combination of gelatine based matrices and plasticizer glycerol, four soluble fibres (inulin, polydextrose, glucose oligosaccharides and wheat dextrin) were selected as prebiotic cocomponents for the immobilisation of *L. Rhamnosus* GG. Glucoseoligosaccharides and polydextrose considerably improved the viability of *L. rhamnosus* GG during air drying (by 300% and 75% respectively), whereas a 33 and 80% decrease in viable counts was seen for inulin and wheat dextrin. On the other hand it was seen that inulin was the most effective at controlling the sub-lethal effects on *L. rhamnosus* GG during storage. Yet in all cases the prebiotics supplementation of edible films increased the storage stability of *L. Rhamnosus* GG.
- **Prebiotics in Custard:** Rheological and sensory properties were studied for low-fat custards added with (7.5 g/100 g) of long-chain inulin (TEX) and short-chain inulin (CLR) combined in different proportions (25:75,

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50:50, and 75:25). Low-fat samples added with inulin blends did not cope to fully imitate the rheological behaviour of full-fat custard. However, inulin blends in the ratio of 50:50 of TEX: CLR added to the low-fat samples perceived to have the same creaminess and thickness as the full-fat sample. When this blend was used in combined with carrageenan gave thicker, creamier custard, which was preferred over the full-fat custard. A seven-day period of refrigerated storage was studied for the changes in rheological properties and microstructure of inulin-enriched custard desserts. The comparison in desserts prepared with 7.5% short-chain inulin (CLR), long-chain inulin (TEX), native inulin (IQ), and a mixture of short and long-chain inulin (MIX) were carried out. During the seven-day storage period of CLR samples the rheological changes and inulin aggregates formation were not observed. Conversely TEX, MIX and IQ samples formed inulin aggregates and as a result became more thixotropic, consistent and elastic. The order of the rate of the inulin aggregates formation and the percentage of volume occupied by them was TEX > MIX > IQ. Although for both skimmed milk and whole-milk samples the same trend was observed and the effects of inulin type and storage time on rheology and microstructure were less prominent in the whole-milk samples. Thus, Prebiotics have a noteworthy effect on human health and have greater potential for incorporation into a broader range of common foodproducts as they have both technical as well as nutritional properties. They act as substrate for the growth of probiotic bacteria (bifidobacteria and Lactic Acid Bacteria), thus enhance the gastrointestinal functions and immune system. Prebiotics also increase the absorption of calcium and magnesium, influence blood glucose levels and improve plasma lipids. To confirm the health benefits of prebiotics by incorporating in formulated foods a long term clinical trials are needed, hence a lot of work is yet to be done.

The functional foods market promises a very bright future, both in developed as well as developing country. This is because of the fact that consumers are now becoming more and more health conscious. They have understood the importance of diet on one's health. But still the need of the hour is that consumers should be given more and more information about the functional foods, their health benefits by the use of various advertising sources. The biggest problem with this market is that there are no strict regulations for functional foods, especially in India. However, Integrated Food Law promises a better regulation over these functional foods. Almost all food companies are progressing towards these functional foods and beverages sector. So, there are tremendous opportunities in this field of industry. The conclusion is that this sector is growing at a fast pace even if some flaws are there. However, these flaws need to be overcome if further growth is required. And innovations are very important if we want to be on the top in this sector.

India is an untapped market of functional foods. We, Indians, are taking herbs and spices as a part of our diet from centuries. These herbs and spices are

full of health beneficial ingredients. Turmeric, for example, has so many health benefits starting from anti-inflammatory, anti-mutagenic to anti-carcinogenic and anti-microbial. So, our current food market strategy should be based on functional foods, if, we want to be on the top. This is because India is the richest source of spices and herbs which can be incorporated in various foods and beverages to get health benefits.

Many functional foods and beverages are available in the market. As a consumer, there are some questions which need to be kept in mind before buying any functional food or beverage:

Does It Work?

The calcium in calcium-fortified orange juice helps build bone. The folate in enriched flour helps prevent birth defects. Those are the easy ones. It is much tougher to figure out whether the claims for other ingredients added to functional foods are backed by solid evidence. Even if there appears to be good research, the results may be inconclusive or may not apply to everyone.

How Much Does It Contain?

If a food is fortified with vitamins or minerals, the label has to tell you exactly how much or how little have been added. That's not the case with herbs or other added ingredients. Snapple, for example, refuses to divulge the amount of ginseng it puts into its Ginseng Tea. And even when labels say how much is in each serving, most shoppers have no idea whether that is a lot or a little. For example, according to its label, each cup of Peace Cereal Vanilla Almond Crisp with Ginkgo and Gotu Kola ('an Herbal Brain Power Cereal') contains two milligrams of ginkgo leaf extract. What it doesn't say is that two milligrams is just one or two percent of the 120 to 320 milligrams that were used as a daily dose in studies of people with Alzheimer's.

Labels should also clearly describe the population for whom the product is intended for (for example, elderly, diabetics), the length of time within the product must be used, the minimum and maximum amounts to be consumed on a daily basis, whether particular cooking methods (for example, microwave, boiling) enhance or destroy the potency of the product, whether the product should be consumed in conjunction with another product for best performance, and whether certain other products should be avoided while the functional food is consumed. The consumer should also be informed of any side effects and provided with guidance as to warning signs that use of the product should be discontinued and that an expert should be consulted.

Is It Safe?

The safety of functional foods is also a very important aspect. Since the functional ingredient will be added to food, it must first be approved for use in food either via

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a food additive petition or obtaining GRAS (Generally Recognized As Safe) status. However, functional ingredients are biologically active and may therefore produce a range of outcomes in the body, at various levels of intake, from suboptimal physiologic action to therapeutic effect to frank toxicity. It is seen that functional foods manufacturers are not putting warning labels on the foods. For example, most echinachea supplement labels caution users not to take the herb for extended periods of time. Others warn people with compromised immune systems (like those with HIV or who have undergone organ transplants) or autoimmune diseases to steer clear of it. You won't find those cautions on Fresh Samantha Super Juice with Echinacea...or on most other foods that contain the herb. So, these things should be worked upon so as to prevent consumers from detrimental effects of these ingredients.

Is It Healthy?

It is observed that even if a food contains one of the nutraceutical factors even then it is labelled as functional food. But it should not be like this. Foods containing functional ingredients with significant amounts of fat, saturated fat, cholesterol, sodium, or added sugars should not be labelled as functional. As good health depends on a diet low in such nutrients, it makes little sense to encourage the consumption of foods high in those nutrients, by allowing manufacturers to promote such foods on the basis of added functional ingredients. The task of raising awareness and educating consumers is vitally important if functional foods are to fulfil their potential.

All these questions needs to be answered to ensure that a particular food product has beneficial effect on health and has is safe for human consumption.

There are various sources of functional food ingredients. They are present in almost all fruits and vegetables and various animal and marine sources, however, quantities vary. Hence what is required is a proper extraction method so that we can incorporate beneficial ingredients in foods of our choice like pizza, soft drinks, toffees, ice creams, etc. Also, it is important for companies to remember that people are not willing to give up taste and flavour for health—especially for long-term use. Another aspect to flavouring fortified and functional foods is that consumers sometimes expect them to have a certain level of off-taste, or they may not feel they are 'getting the real thing'. So, a proper balance is required for satisfying consumers.

Future research will focus on mechanisms by which food components such as phytochemicals positively affect health, and whether these components work independently or synergistically, so that if two functional ingredients are added what will be the effect on the health. Further research is required in the area of functional fats which are new to this market. Various opportunities are there for new product development in this market. Try making new products using various combinations and who knows may be we will be able to make a product which will give us so much of energy and power that we will become super human beings.

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1. What are the cardiovascular effects of prebiotics?
2. Give the effects of prebiotics on bone mineralization.
3. Explain the prebiotics in dairy fruit beverages.
4. How are prebiotics present in cereals?

4.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Obesity and diet have direct link with atherosclerosis, cardiovascular disease and type 2 diabetes, and there are number of animal experiments signifying the ability of prebiotics to influence the serum lipid levels. Double-blind randomized controlled trials were carried on 12 humans using inulin, FOS and Galacto-OligoSaccharides (GOS) of the dosage of 15g per day. It was shown that higher concentrations of faecal acetate in inulin and GOS treatment periods (P combination of inulin when used for 4 weeks on normal lipidaemic persons showed significant reduction in triacylglycerol.
2. Bone mass of an adult is dependent on supply as well as bioavailability of calcium. In either cases of deficiency osteoporosis is prone to occur and in addition to this it is highly associated with increasing age and postmenopausal conditions. Presently, osteoporosis treatment and prevention is restricted to increasing calcium uptake, or by stimulating bone formation. Even though, a lot of studies have been carried out on calcium metabolism using rats, results depicted that prebiotics play a role in escalating the bioavailability of calcium. But so far, only a few human trials have been translated from these results. Prebiotic consumption increasing calcium absorption has the majority supporting data from the rat studies where as human trials have had diverse results.
3. Guergoletto *et al.* evaluated the survival of Lactobacillus Casei (LC1) when adhered to dehydrated prebiotic fibers. After vacuum drying in oat bran with 9% β-glucan and green banana flour, viability of LC-1 was 79% and 76%, respectively. Images revealed by scanning electron microscopy showed no morphological changes in the cells adhered to these fibers and the cell protectant trehalose addition had a positive and significant effect on the survival of LC-1. Greater viability of LC-1 has been seen when adhered to the oat bran (7.1 log CFU g–1) than in the free form (2.4 log CFU g–1). Sensory evaluation showed that the probiotic oat bran added to a dairy fruit beverage was well accepted by consumers.
4. Several studies have publicized the prebiotic activity of cereal derived ArabinoXylan OligoSaccharides (AXOS). A study investigated the in situ AXOS production during bread making process. Firstly AXOS producing

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ability of different xylanases was compared in whole meal bread making. Different dosages of xylanase were used originating from *Bacillus subtilis*, *Aspergillus niger* and *Hypocrea jecorina*, and *thermophilic xylanase* from *H. jecorina* (HjXynA). Dosages which do not impair dough manageability, arabinoxylan fraction are solubilised and cleaved to the largest extent by HjXynA, resulting in an AXOS content of 2.1% on dry basis and an average degree of polymerisation of 9.

4.4 SUMMARY

- Prebiotics are supplements or foods that contain non digestible food ingredients that selectively stimulate the favourable growth and/or enhance the activities of indigenous probiotic bacteria.
- Prebiotic therapies have been found to cure gut related diseases such as constipation relief, suppression of diarrhoea, reduction of the risks of osteoporosis, atherosclerotic cardiovascular disease associated with dyslipidemia, insulin resistance, obesity, and possibly type 2 diabetes.
- Prebiotics are special fibers having selective fermenting ingredients that are needed by microbiota of human gut.
- Human colon is one of the body's most metabolically active organs because of the presence of microbiota.
- The prebiotic word was first introduced by Gibson and Roberfroid in 1995 and is defined as 'a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and improve host health'.
- Prebiotics must resist host digestion, absorption, and adsorption before fermentation by one species of the resident microbiota.
- Chicory is the source of inulin which is isolated and purified from it after energy density.
- Prebiotics reach the colon without being digested because of their chemical nature. A part of the material is not digested by pancreatic and small-bowel enzymes in the human gut and therefore, reaches the large bowel.
- The pH and relatively low absorptive state of colon further supports large microbial colonisation and growth.
- Gastroenteritis is a common disease usually occurs due to ingestion of food or water contaminated with pathogenic microorganisms and/or their toxins.
- The main pathogenic organisms responsible for gastroenteritis are *Shigellae, Salmonellae, Yersina enterocolitica, Campylobacter jejuni, Escherichia coli, Vibro cholera and Clostridus perfringens*.

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- Inflammatory bowel disease has been related to the intestinal microbiota pathogenesis.
- Germinated barley foods also displayed a greater ability to decrease the symptoms of dextran sulphate sodium colitis than that of a probiotic mixture of lactobacilli and *C. butyricum.*
- A mixture of long chain inulin and oligosaccharide has shown the ability to decrease the inflammatory histological and gross cecal scores in the cecum and colon.
- Administering of FOS as a dietary supplement (6% w/w of total diet), stimulate lactobacilli and bifidobacteria, and increase SCFAs in the large intestines (a result that has been repeated in humans with ulcerative colitis.
- Due to the rapid fermentation of elevated FOS levels in the cecum by cecal bacteria causing elevated levels of organic acids, which damage the mucosa of the cecum and colon.
- As these effects happened quickly upon the addition of GOS to the system, changes attributable to population levels can be ruled out and it is more possible that direct inhibition by GOS or the production of repressors by bacteria was responsible.
- Another observation a high level of caecal butyrate important to the reduction of cancer is not only the major source of energy for colonocytes but also helps to maintain a healthy epithelium. It can also play an important role in preventing cancer.
- The series of bacterial intestinal colonization is possibly important for the development of the immune response of neonates and young infants.
- After analyzed the relevant publications it was concluded that there is no sufficient proof currently available to support the use of probiotics, prebiotics, or synbiotics for the prevention or treatment of allergic dermatitis in children.
- Obesity and diet have direct link with atherosclerosis, cardiovascular disease and type 2 diabetes, and there are number of animal experiments signifying the ability of prebiotics to influence the serum lipid levels.
- Double-blind randomized controlled trials were carried on 12 humans using inulin, FOS and Galacto-OligoSaccharides (GOS) of the dosage of 15g per day.
- Prebiotics can be used to offer a double benefit such as an improved organoleptic quality and a better-balanced nutritional composition.
- As fiber ingredients the use of inulin and non-digestible oligosaccharides is simple and often leads to enhance taste and texture.

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- Specific colonic bacteria, such as bifidobacteria and lactobacilli species readily ferment these particular forms of dietary fibre and by raising their cell population with the parallel production of short-chain fatty acids.
- Lactose occurs wholly in the milk of mammals and one might observe from a teleological point of view that lactose ingestion provides specific health benefits beyond just being a source of energy to the suckling animal.
- Dairy products are considered a potential vehicle for prebiotics and probiotics and are increasingly being used to produce synbiotic foods.
- A research conducted to evaluate the potential of prebiotic in novel petit-suisse cheeses using an in vitro fermentation model.
- Prebiotics candidate (inulin, oligofructose, honey) and probiotics (Lactobacillus acidophilus, Bifidobacterium lactis) were combined in five petit-suisse cheese formulations and were tested in vitro with human faecal slurry.
- Addition of probiotics as starter culture to control cheese also resulted in high lactic acid production.
- In vitro conditions, cheese made from the combination of different prebiotics and probiotics shows potential functional petit-suisse cheese.
- Lower syneresis index resulted with the addition of inulin in a fermented product also with greater firmness and cohesiveness.
- Yogurt added with oligofructose was characterized as a weak gel, showing thixotropic and pseudoplastic behaviour as per the rheological measurements.
- Prebiotics have a noteworthy effect on human health and have greater potential for incorporation into a broader range of common food products as they have both technical as well as nutritional properties.
- Prebiotics also increase the absorption of calcium and magnesium, influence blood glucose levels and improve plasma lipids.

4.5 KEY WORDS

- **Prebiotics**: Prebiotics are supplements or foods that contain non digestible food ingredients that selectively stimulate the favourable growth and/or enhance the activities of indigenous probiotic bacteria.
- **Gastroenteritis**: Gastroenteritis is a common disease usually occurs due to ingestion of food or water contaminated with pathogenic microorganisms and/or their toxins.

4.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

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Short Answer Questions

1. Write a short note on prebiotics and its chemistry.
2. What is inflammatory bowel disease?
3. How do prebiotics help in reduction of cancer risk?
4. Briefly explain prebiotics in infant formula.

Long Answer Questions

1. What are the sources and bioavailability of prebiotics?
2. What are the effect of processing?
3. Explain the effects of prebiotics on human health.
4. Explain the potential applications in risk reduction of diseases.
5. What are the perspective for food applications for non-digestible carbohydrates/ oligosaccharides: dietary fibre, resistant starch, gums.

4.7 FURTHER READINGS

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BLOCK - II
PLANT METABOLITES AND NON-NUTRIENT
EFFECT OF SPECIFIC NUTRIENTS

UNIT 5 ALKALOIDS, GLUCOSINOLATES, TERPENOIDES AND PHENOLICS

Structure

5.0 INTRODUCTION

Alkaloid, any of a class of naturally occurring organic nitrogen-containing bases. Alkaloids have diverse and important physiological effects on humans and other animals. Well-known alkaloids include morphine, strychnine, quinine, ephedrine, and nicotine. Alkaloids are found primarily in plants and are especially common in certain families of flowering plants. More than 3,000 different types of alkaloids have been identified in a total of more than 4,000 plant species. In general, a given species contains only a few kinds of alkaloids, though both the opium poppy (*Papaver somniferum*) and the ergot fungus (*Claviceps*) each contain about 30 different types.

Glucosinolates are biologically active compounds found in the Brassicaceae family of plants, including broccoli, cabbage, cauliflower, rapeseed, mustard, and horseradish. Recent studies have shown beneficial effects of glucosinolates,

including regulatory functions in inflammation, stress response, phase I metabolism, and antioxidant activities, as well as direct antimicrobial properties. However, livestock species fed rations with high glucosinolates may exhibit adverse effects, including reduced feed intake and growth, gastrointestinal irritation, goiter, anemia, and hepatic and renal lesions. High sulfur can be associated with trace mineral deficiencies and polioencephalomalacia.

The terpenoids, sometimes called isoprenoids, are a large and diverse class of naturally occurring organic chemicals derived from terpenes. Most are multicyclic structures with oxygen-containing functional groups. About 60% of known natural products are terpenoids. Although sometimes used interchangeably with 'terpenes', terpenoids contain additional functional groups, usually O-containing. Terpenes are hydrocarbons.

Phenolic compounds are a group of small molecules characterized by their structures having at least one phenol unit. Based on their chemical structures, phenolic compounds can be divided into different subgroups, such as phenolic acids, flavonoids, tannins, coumarins, lignans, quinones, stilbens, and curcuminoids.

In this unit, you will study about Alkaloids, Glucosinolates, Terpenoides and Phenolics- chemistry, classes, sources, bioavailability and effects on human health.

5.1 OBJECTIVES

After going through this unit, you will be able to:

- Discuss what Alkaloid, Glucosinolates, Terpenoides and Phenolics are
- Explain the chemistry, classes, sources, bioavailability of Alkaloid, Glucosinolates, Terpenoides and Phenolics
- Understand how Alkaloid, Glucosinolates, Terpenoides and Phenolics effects human health

5.2 ALKALOIDS

Alkaloids are secondary metabolites originally outlined as pharmacologically active compounds, primarily composed of N. They are synthesized from the following amino acids: essential amino acid, amino alkanoic acid and tryptophan. There are more than 12,000 alkaloids, together with over a hundred and fifty families, known in plants. In plants, alkaloids typically exist as salts of organic acids like carboxylic acid, malic, lactic, citric, oxalic, tartaric, phenolic acids, etc. Some weak basic alkaloids (such as nicotine) occur freely in nature. Some alkaloids conjointly occur as glycosides of sugar like aldohexose, rhamnose and saccharose, for instance, alkaloids of the Solanum cluster (solanine), as amides (piperine) and as esters (atropine, cocaine) of organic acids (Refer Figure 5.1).

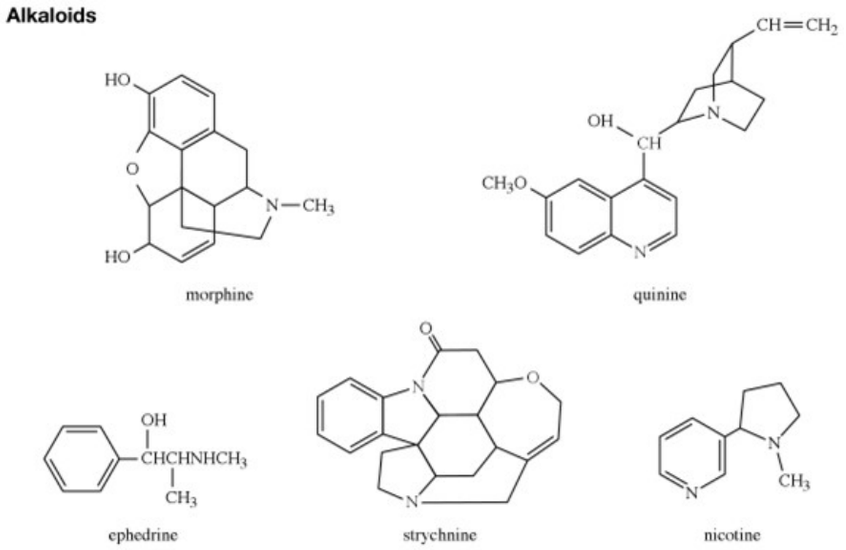


Fig. 5.1 *Alkaloids*

The term organic compound comes from the Arabic word 'al-qali' that refers to K carbonate-containing ashes from material.

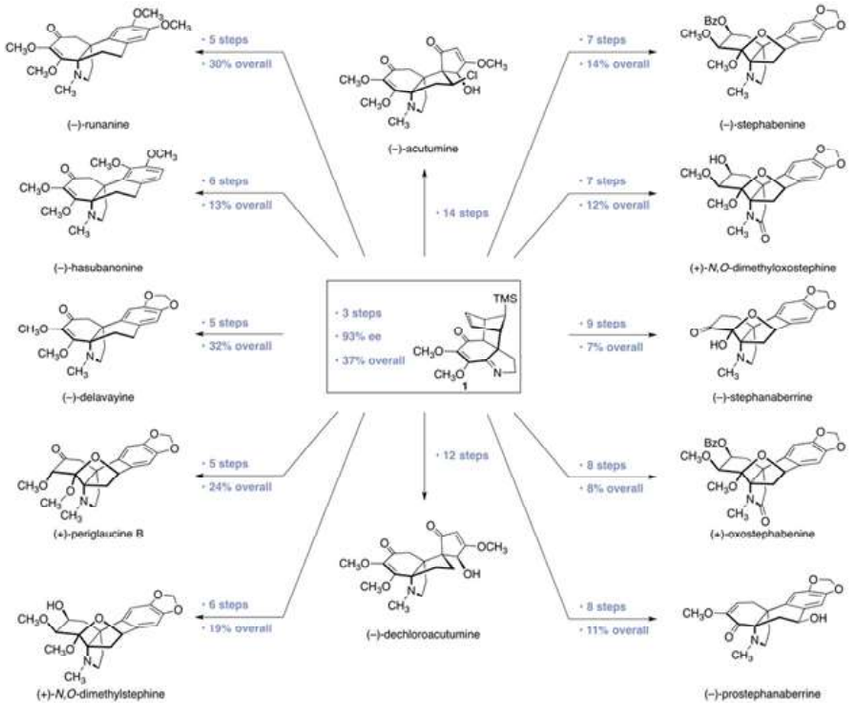
Table 5.1 *Alkaloid Classification according to Structure of Derivatives*

Group	Representatives
Tropane derivatives	Atropine, cocaine, ecgonine, scopolamine
Isoquinoline derivatives	Opium alkaloids: morphine, codeine, thebaine, papaverine, narcotine, sanguinarine, narceine, hydrastiane, berberine
Quinoline derivatives	Quinine, quinidine, dihydroquinone, dihyrdoqunidine, strychnine, brucine, veratrine, cevadine
Pyridine derivatives	Piperine, coniine, trigonelline, arecaidine, guvacine, pilocarpine, cytosine, nicotine, sparteine, pelletierine
Pyrolidine derivatives	Hygrine, cuschygrine, nicotine
Terpeness	From aconite: aconitine Sterols: solanine, samandarine
Betaine derivatives (with quaternary azoth)	muscarine, choline, neurine
Phenethylamine derivatives	Mescalime, ephedrine
Indole derivatives	Tryptamie derivatives: dimethyltryptamine (DMT), NMT, psilocybin, serotonin, melatonin Ergolines: alkaloids originating from ergot: ergine, ergotamine, lyseric acid, and so on.; derivatives of lysergic acid (LSD) Beta-carbolines: harmine, yohimbine, reserpină, emetine
Purine derivatives	Xanthine derivatives: caffeine, theobromine, theophylline

Traditionally, alkaloids are outlined as heterocyclic element compounds biosynthesized from amino acids. Several different substances, however, that do not precisely match this rule are classified as alkaloids, either for historical reasons or due to their biological potential and activities.

- Purine alkaloids are element containing compounds derived from glycoside metabolism. Alkaloid could be a central stimulant and usually consumed in beverages like tea, and carbonated beverages. It is also consumed in medicines and analgesics.

- Tropane alkaloids originate from the amino acids amino acid and/or essential amino acid, containing cyclic tropane skeleton that consists of a 7-membered ring with associate N -bridge between C-1 and C-5, the element being alkyl. They occur in plants of C*onvolvulaceae, Solanaceae, Euphorbiaceae, Proteaceae*, and dicot family.
- (S)-Hyoscyamine and (S)-scopolamine are esters of the amino alcohols tropine and scopine with (S)-tropic acid, that comes from essential amino acid. They are used as antispasmodics for treatment of spasms in biliary intestinal colic, as antidote against intoxication with organophosphorus pesticides, and as pre-medication before surgery to decrease secretion and metabolism secretion.
- Cocaine is the carboxylic acid organic compound of the tropane base methylecgonine. They are found in Erythroxylon coca and Erythroxylum novogranatense, shrubs or tiny trees native to the mountain range, contain substantial amounts of cocaine in their leaves, i.e., up to fifteen of their dry mass.
- Quinolizidine alkaloids are biosynthesized from essential amino acid via ptomain. The amino acid amino alkanoic acid would be a precursor of diverse alkaloids.
- The biggest cluster is created by the benzylisoquinoline alkaloids. Additionally, many different organic compound categories originate from amino alkanoic acid, for instance, the emetic alkaloids and also the Amaryllidaceae alkaloids.



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Alkaloids can be divided into three large groups on the basis of their relation to the innovations in the fields of both chemistry and technology:

- Natural Alkaloids
- Biomimic and Bionic Alkaloids
- Synthetic Alkaloids
  - **Natural Alkaloids:** Alkaloids existing in nature, presently known or still unknown by the science. They are molecules naturally synthesized and novelized in time by living organisms as a result of the evolution of life on Earth.
  - **Biomimic Alkaloids:** Natural alkaloids copied artificially by chemists in the laboratories. They are identical in structure to natural alkaloids. Bionic alkaloids are those biomimic molecules being novelized by the chemists and engineers using natural models and high-level technology. Bionic alkaloids are not identical analogues to natural alkaloids.
  - **Synthetic Alkaloids:** Molecules totally modeled by chemists and engineers using high-level technology, planned models, and artificial synthesis. Synthetic alkaloids are not produced naturally by the living organisms.

5.2.1 Sources and Effect of Alkaloids

Alkaloids have been known for several centuries and have been mainly obtained from natural sources that presented important properties with biochemical, pharmacological, and medical effects in living organisms. Alkaloids are derived from amino acids like other important molecules in the functioning of life in our body. Hence, alkaloids are considered as pharmacologically important. Alkaloids are secondary metabolites widely distributed in leaves, stem, root, and fruits of plants which synthesize them. However, administration and consumption of them at right doses are beneficial in terms of health; excess doses will be definitely poisonous and may cause even death. The pharmacological activities of alkaloids are quite diverse. They are important natural products with a wide range of medicinal properties including relief of pain (for example, morphine), analgesic (for example, codeine), antiarrhythmic (for example, quinidine), antibacterial (for example, chelerythrine), antiasthma (for example, ephedrine), cholinomimetic (for example, galantamine), and vasodilatory (for example, vincamine).

Plants as a Source of Alkaloids

There is an enormous range of chemical compounds present in plants where alkaloids take place as a content of secondary metabolites. Alkaloid content is inhomogeneous and usually within a few percent over the plant tissues. Further, most plants produce a few types of closely related alkaloids, whereas some of them may contain several alkaloids in different tissues of the same plants. Therefore,

firstly there is a need on the extraction of their mixture and then separation of individual alkaloids. Medicinal bioactive compounds from raw extracts of the plants can be isolated by acid-base extraction. Pure alkaloids are not readily soluble in water, but found to be fairly soluble in organic solvents (ether, chloroform, alcohol, and oils), relatively nonpolar solvents (hexane, benzene, petroleum ether). On the contrary, alkaloids are mostly present in the corresponding salt form in the plant and almost freely soluble in water, mostly insoluble or relatively less soluble in many of organic solvents. As a group, alkaloids are easily extracted in acidic forms because of their basic and lipid properties and separated from other water-soluble materials.

Usually, the dried and powdered plant source is extracted with lipophilic or nonpolar organic solvents, such as 1, 2-dichloroethane, chloroform, diethyl ether, benzene, or petroleum ether. Since the alkaloids present in the plant sources as the salt of acids, they are exposed to an alkaline medium to convert the alkaloid salts to the corresponding alkaloid bases. The extraction of the alkaloid bases from the bulk of the crude alkaloid solution is achieved again with a nonpolar solvent. The impurities from the plant in solution are dissolved by dilute aqueous acid and are washed away with water. Alkaloids have different solubilities in certain solvents and different reactivities with certain reagents because of the structural diversity.

The alkaloid-based drugs used today are of plant origin, and screening of plant extracts for alkaloids and other pharmacologically active compounds is still in progress for new drug discoveries. Chemists extensively investigated production of alkaloids in plants on a large scale, to make many derivatives of these natural compounds and improve technologies correlated to chemical preparation. The discoveries of high-value chemical compounds in plants serve as model structures for synthetic drugs and allow the large-scale production of them with improved properties. Recently, the deep sea bioenvironment is considered an extremely rich source of novel bioactive alkaloids since marine natural products represent a fascinating example of the large variety of secondary metabolites.

Effects of Alkaloids on Human Health

Alkaloids have many effects on humans and other animals, some of the known effects on mammals are as follows:

- Inhibit /Activate Enzymes: ADH (Alcohol DeHydrogenase), phosphatases

  Inhibit phosphodiesters which normally destroy cAMP which is involved in breakdown of fats and carbohydrates. Net result - it alters storage of carbohydrates and fats, for example smokers stay thinner as it impacts on their cAMP system and only gain weight after quitting.

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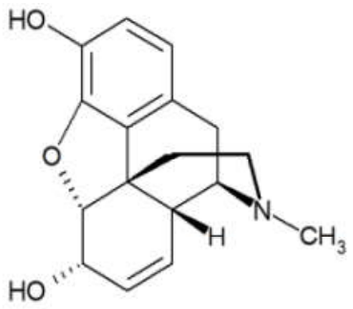
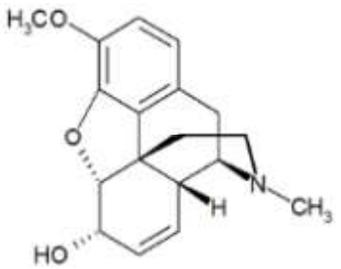
- Effects nucleic acid and protein synthesis:
  - Certain alkaloids bind to nucleic acids, intercalates with DNA that makes DNA susceptible to UV damage, effects binding of regulators, effects repair. These effects are congenital defects in offspring, such as skeletal or palate damage or impact in adults with increased cancer rates as with smokers.
  - Binds with RNA: affects transcription, r-RNA formation, can cause chain terminations.
- Affects membrane structure and cytoskeletal structure- cellular weakening or collapse as well as production of leaky membranes.
- Can affect nerve transmission / induction, for example first cup of coffee in the morning can be the cause of effect.
- It may alter energy dynamics- use of energy from detoxification with MFO (NADPH-dependent) / conjugation systems reduces energy for growth and can also alter acid balance with release of glucuronic acid used in conjugation. Our body normally defends itself from the 'toxins' you take in daily (by toxins anything it can readily use for metabolism and nutrition, such as drugs you take for health or whatever) by breaking them down. Your body also treats the alkaloids in the foods you eat as toxins and oxidizes them to make them water soluble using your MFO or mixed function oxidases thus allowing them to be easily eliminated from the body as quickly as possible. If you take in too much of these compounds by smoking, drinking coffee and eating alit of foods with alkaloids, it costs the body quite a bit of energy. Energy it could better use for growth and repair.

Some other alkaloids and the description of their role on the human body is as follows:

Morphine: Morphine and Codeineare extracted from opium. Morphine leads to an insensitivity to pain due to its actions on the central nervous system. Morphine is a complete opioid agonist, whose action is localized at a central level, with affinity for the arcuate nucleus. The term is derived from Morpheus, the god of dreams Greek mythology. It is the main active agent in opium (as meconate), its concentration in opium extracts varying from 8 to 14%, with an average of 10%. It is a powerful analgesic. It is a part of the true morphinic alkaloid group, alongside codeine and tebaine. The better part of its effects (supraspinal analgesia, euphoria, significant respiratory depression, inhibition of the coughing centre, myosis, physical addiction, inhibition of digestive motility – responsible for constipation) are explained by the fact that its links with μ receptors. Morphine is used to treat acute and chronic pain. Morphine is usually administered parentally, as morphine chlorhydrate. Oral administration of morphine is not beneficial, because its bio-availability in this case is very small. Morphine sulphate has a slightly better bio-availability with oral administration. It can also be administered rectally, as suppository or enema.



Codeine: Codeine, or metylmorphine, is a natural alkaloid derived from opium. Its concentration in opium extracts varies between 0.7% and 2.5%. Industrial synthesis of codeine is performed through morphine metylation. It has less significant analgesic properties in comparison to morphine, but it is more advantageous in what regards anti-coughing and anti-diarrheic properties. It is metabolized at hepatic level into 6-glucuronidecodeine through conjugation with glucuronic acid in a percentage of 80%.



Papaverine: Papaverine is extracted from the milky juice of raw poppy capsules (opium). Its effect is exerted directly on smooth muscles. It is an opium alkaloid antispasmodic drug, used primarily in the treatment of visceral spasm, vasospasm (especially those involving the heart and the brain), and occasionally in the treatment of erectile dysfunction. While it is found in the opium poppy, papaverine differs in both structure and pharmacological action from the analgesic (morphine-related) opium alkaloids (opiates). Papaverine is used as an erectile dysfunction drug, alone or sometimes in combination. Papaverine, when injected in penile tissue causes direct smooth muscle relaxation and consequent filling of the corpus cavernosum with blood resulting in erection. A topical gel is also available for ED treatment. Papaverine is also present in combinations of opium alkaloid salts, such as papaveretum (*Omnopon, Pantopon*) and others, along with morphine, codeine, and in some cases noscapine and others in a percentage similar to that in opium, or modified for a given application.

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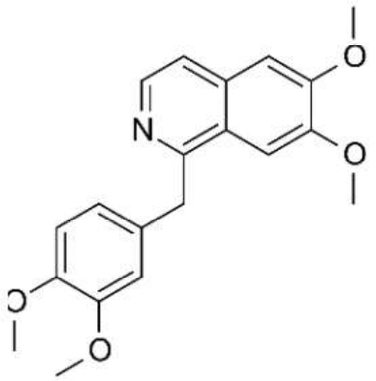
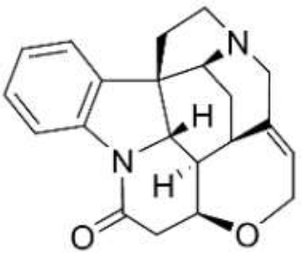
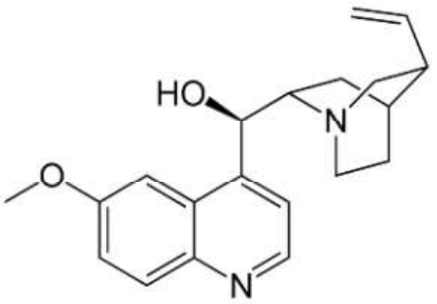


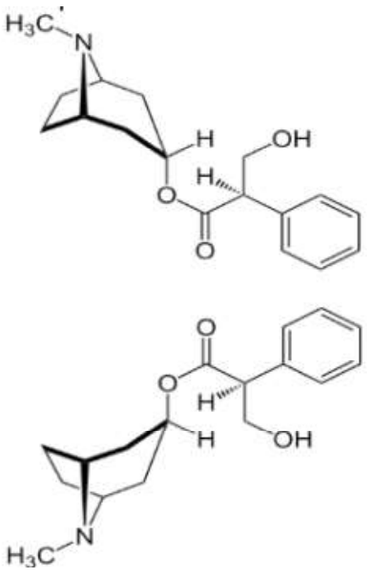
Strychnine: Strychnine is a very toxic alkaloid, extracted from the seed of the tropical tree – Strychnos nux vomica. Strychnine presents itself as crystals, which are little soluble in water, colourless, odourless, and with bitter taste. The lethal dose for an adult is usually between 60 and100 mg. Symptoms of intoxication appear 60-90 from ingestion: bitter taste, anxiety, respiratory discomfort, hyperreflexia, convulsions accompanied by the forced extension of the limbs, death.



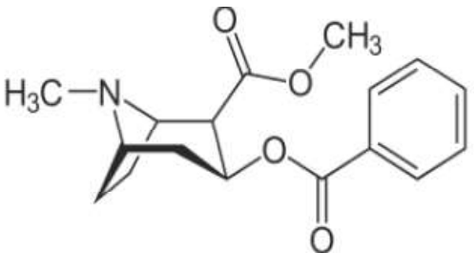
Quinine: It is extracted from the chinona tree. It is used in malaria treatment. It regulated body temperature. Quinine contains in its molecule a quinolinic heterocyclic atom. It presents itself as fine crystalline powder, odourless, with very bitter taste, little soluble in water, very soluble in alcohol. In therapy, it is used as salts: sulphate, chlorhydrate. Quinine has an anti-malaria action, anti-pyretic, and slight analgesic. It also desensitizes the pregnant uterus. Indications: malaria, persistent febrile states, migraine Contraindications: pregnancy, breast-feeding, cardiac insufficiency, myasthenia, atrial fibrillation, sensitivity to quinine, haemolytic anaemia, optic neuritis.



Atropine: Atropine is a part of the group of alkaloids with a tropanic nucleus, representing a racemic mixture of hyoscyamine. Atropine is used as an antidote in muscarine intoxications due to its role as an excessive blocker of the parasympathetic system, stimulated by an excess of acetylcholine. Atropine can also be used during narcosis, in case of reduced cardiac frequency. It is no longer used as an anti-asthma agent, due to the fact that its derivatives are easier to tolerate. In ophthalmology, it is used for pupil dilation (mydriasis) in ocular examinations. Currently, it has yet to be replaced for its role in cardio-pulmonary resuscitation, such as asystole.



Cocaine: Cocaine is a crystalline tropanic alkaloid, which is obtained from the coca tree (Eritroxylon coca). It is a drug with a potent stimulatory effect on the central nervous system and it is one of the most spreaded drugs that lead to consumer addiction.



Check Your Progress

1. What are alkaloids?
2. How are alkaloids synthesized?
3. How does alkaloids exist in plants?

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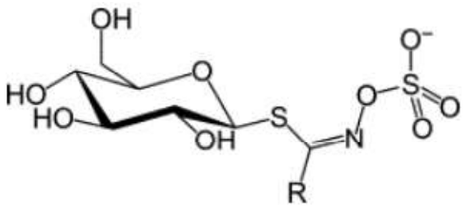
5.3 GLUCOSINOLATES

Glucosinolates are biologically active compounds found within the Cruciferae family of plants, together with broccoli, cabbage, cauliflower, rapeseed, mustard, and horseradish. Recent studies have shown helpful effects of glucosinolates, together with restrictive functions in inflammation, stress response, clinical trial metabolism, and inhibitor activities, in addition as direct antimicrobial properties. However, stock species fed rations with high glucosinolates might exhibit adverse effects, together with reduced feed intake and growth, channel irritation, goiter, anemia, and internal organ and urinary organ lesions. High sulfur may be related to trace mineral deficiencies and PolioEncephaloMalacia (PEM). Therefore, though a decent supply of nutrition, it is best to avoid feeding Cruciferae.



Basic Glucosinolate Structure, R = Aliphatic, Aromatic or Indolic Side Chain

Chemistry of Glucosinolates

Glucosinolates constitute a natural class of organic compounds that contain sulphur and nitrogen and are derived from glucose and an amino acid. They are water-soluble anions and belong to the glucosides. Every glucosinolate contains a central carbon atom, which is bound via a sulfur atom to the thioglucose group and via a nitrogen atom to a sulfate group (making a sulfated aldoxime). In addition, the central carbon is bound to a side group; different glucosinolates have different side groups, and it is variation in the side group that is responsible for the variation in the biological activities of these plant compounds. The semisystematic naming of glucosinolates consists of the chemical name of that side chain followed by 'glucosinolate'. Spelling glucosinolate names in one or two words (for example, allylglucosinolate versus allyl glucosinolate) are both in use and has equivalent meaning. Isothiocyanates must be spelled in two words.

The essence of glucosinolate chemistry is the ability of a glucosinolate to convert into an isothiocyanate (a 'mustard oil') upon hydrolysis of the thioglucoside bond by the enzyme myrosinase.

Some Glucosinolates

- Allylglucosinolate (sinigrin) is the precursor of allyl isothiocyanate.
- Benzylglucosinolate (Glucotropaeolin) is the precursor of benzyl isothiocyanate.

- Phenethylglucosinolate (Gluconasturtiin) is the precursor of phenethyl isothiocyanate.
- (R)-4-(methylsulfinyl) butylglucosinolate (Glucoraphanin) is the precursor of (R)-4-(methylsulfinyl) butyl isothiocyanate (sulforaphane).
- (R)-2-hydroxybut-3-enylglucosinolate (progoitrin) is probably the precursor of (S)-2-hydroxybut-3-enyl isothiocyanate, which is expected to be unstable and immediately cyclize to form (S)-5-vinyloxazolidine-2-thione (goitrin).

Chemical Structure

Glucosinolates represent thioglucosidic secondary metabolites occurring in the angiosperm plant families, mainly in the order Brassicales. To date, more than ca 130 structurally different GLs have been reported GLs are water-soluble organic anions that share a common basic structural features and bear a side chain which constitution, depending on plant species, is the sole structural variant:

- β-D-Glucopyrano unit.
- A O-sulfated anomeric (Z)-thiohydroximate function.
- A variable aglycone side chain.

The aglycone can originate from one of eight natural amino acids according to which GLs can be classified into: aliphatic (derived from Ala, Leu, Ile, Val, and Met), arylaliphatic (derived from Phe or Tyr), and indolyl GLs (derived from Trp). Many GLs are biosynthesized via extensive changes in the aglycone side chains which is due to a wide variety of chemical modifications, such as elongation, hydroxylation, O-methylation, desaturation, further glycosylation, oxidation, and acylation.

Many GLs are derived from chain-elongated derivatives of Met and Phe. The structures of the several known aliphatic GLs are derived from the elongated and modified side chains of Met homologues (Refer Figure 5.2).

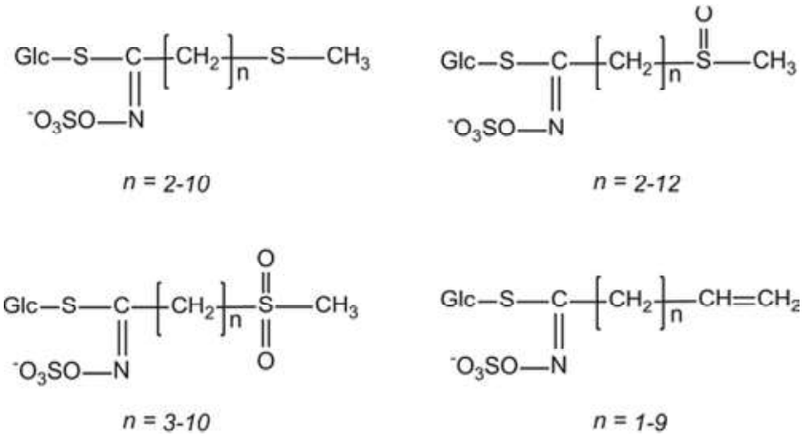
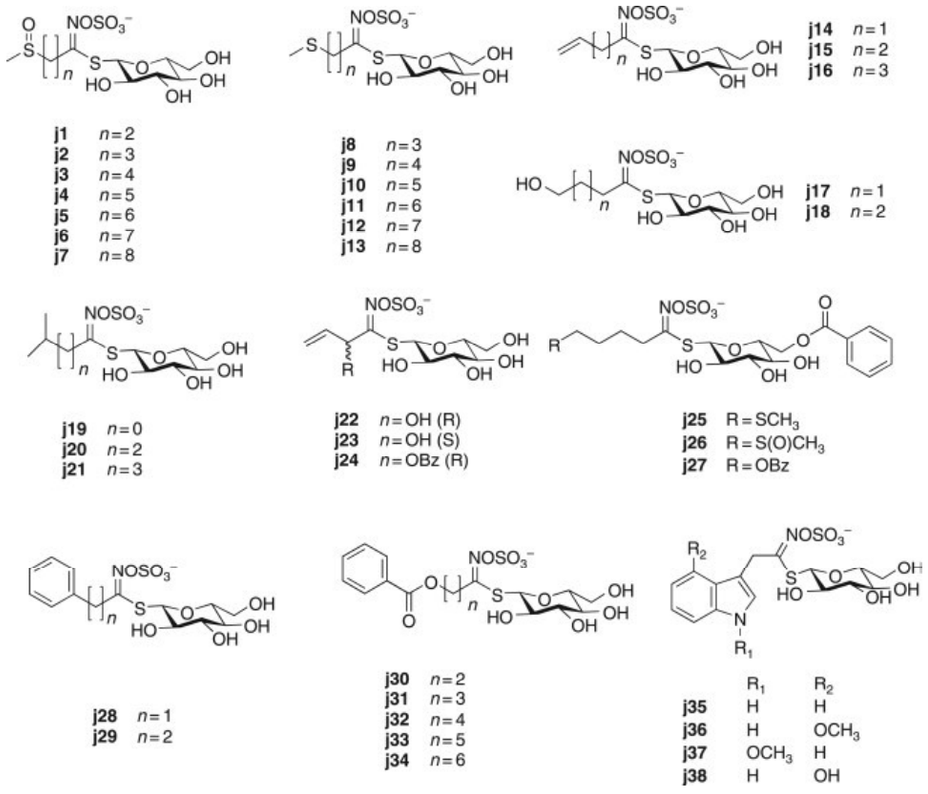


Fig. 5.2 *General Structure of Chain-Elongated Aliphatic GLs*

Glucosinolates are found in the order Capparales, which includes the economically important Brassicaceae. Glucosinolates are secondary metabolites derived from a variety of amino acids, several of which are not part of protein ribosomal biosynthetic pathways. They occur naturally as salts of sulfate and are therefore very polar compounds classified as aliphatic, aromatic, and indolic, depending on the amino acid from which they are derived (Refer Figure 5.3). A protein amino acid can undergo a series of chain elongations prior to assembly into a glucosinolates that in turn can be subjected to additional metabolic transformations, such as hydroxylations, methylations, and oxidations. The glucosinolates found in *A. thaliana* ecotype Columbia are derived from tryptophan, several chain-elongated methionine homologues, chain-elongated phenylalanine, and phenylalanine. The bishom methionine-derived glucosinolates 4-methylthio butyl glucosinolate (j9) and 4-methylsulfinyl-butyl-glucosinolate (j3) account for more than 50% of the total glucosinolate content in the rosette leaves of *A. thaliana.*



In the Figure given below Glucosinolates are shown, in which. A shows the examples of the three classes of glucosinolates: aliphatic; indole; and aromatic glucosinolates, here represented by 3-methyl sulfony propyl glucosinolate; indol-3-ylmethyl glucosinolate; and benzyl glucosinolate. B shows simplified biosynthesis of glucosinolates in three steps, illustrated here with the biosynthesis of methionine-derived glucosinolates, the largest and most diverse group of glucosinolates in

Arabidopsis. The three steps are indicated in blue: amino acid elongation (optional); glucosinolate synthesis; and glucosinolate modification (optional). The optional steps are not required for every glucosinolate. Five major loci controlling much of the variation in glucosinolate composition are indicated in red. GS-ELONG is involved in side-chain elongation (n indicates number of elongation cycles); GS-OX converts methylthioalkyl glucosinolates to methyl sulfonyl alkyl glucosinolates; GS-OHP and GS-ALK represent two different alleles from the GS-AOP locus, GS-OHP only acts on 3 carbon side-chain glucosinolates (n=1) and produces hydroxypropyl glucosinolates and GS-AOP produces alkenyl glucosinolates; GS-OH hydroxylates alkenyl glucosinolates and only acts on 4 carbon side-chain glucosinolates. C shows degradation of glucosinolates leading either to isothiocyanate or nitrile production depending on activity of EthioSpecifier Protein (ESP) and/or EthioSpecifier Modifier1 (ESM1) (Refer Figure 5.3).

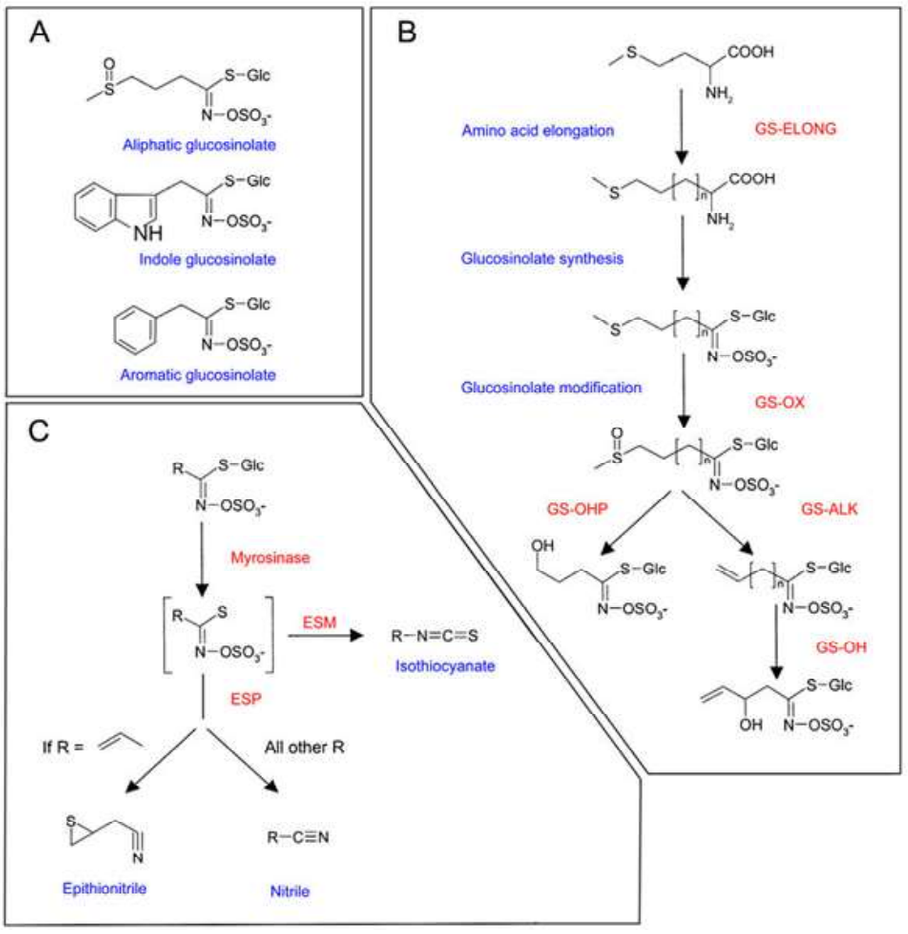


Fig. 5.3 *Glucosinolates Types*

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Table 5.2 *Commonly Consumed Dietary Glucosinolates and their Sources*

Glucosinolate	Chemical Name	Occurrence
Glucoiberverin	3-(Methylthio) Propyl	Cabbage, Broccoli, Brussels Sprouts, Sauerkraut, Turnip.
Glucoiberin	3-(Methyl-Sulfinyl) Propyl	Brussels Sprouts, Cauliflower, Broccoli, Turnip, Sauerkraut.
Glucoraphanin	4-Methylsulfinyl-3-Butenyl	Broccoli, Horseradish, Cabbage.
Sinigrin	2-Propenyl	Brussels Sprouts, Cabbage, Cauliflower, Mustard.
Gluconapin	3-Butenyl	Cabbage, Brussels Sprouts, Turnip.
Progoitrin	2-Hydroxy-3-Butenyl	Brussels Sprouts, Cabbage, Turnip.
Glucotropaeolin	Benzyl	Garden Cress, Horseradish, Mustard.
Gluconasturtiin	Phenylethyl	Watercress, Turnip, Horseradish.
[Glu]sinalbin	2-Hydroxy-3-Butenyl	White Mustard.
Glucobrassicin	Indol-3-Ylmethyl	Brussels Sprouts, Broccoli, Cabbage, Mustard, Cauliflower, Kohlrabi, Horseradish.
Neoglucobraassicin	1-Methoxyindol-3-Ylmethyl	Brussels Sprouts, Broccoli, Cabbage, Horseradish, Kohlrabi, Cauliflower.

Effect on Humans and Other Mammals

Toxicity

The use of glucosinolate-containing crops as primary food source for animals can have negative effects if the concentration of glucosinolate is higher than what is acceptable for the animal in question, because some glucosinolates have been shown to have toxic effects (mainly as goitrogens and anti-thyroid agents) in both humans and animals at high doses. However, tolerance level to glucosinolates varies even within the same genus (for example, *Acomys cahirinus* and *Acomys russatus*).

Taste and Eating Behavior

The glucosinolate sinigrin, among others, was shown to be responsible for the bitterness of cooked cauliflower and Brussels sprouts. Glucosinolates may alter animal eating behavior.

Table 5.3 shows some of the plants that cause glucosinolate poisoning.

Table 5.3 *Plants Causing Glucosinolate Poisoning*

Goitrogenic Effect	
Pasture and Forage Plants	
Rape (syn. Canola)	*Brassica napus*
Kale, Kohlrabi, Chou Moellier	*Brassica oleracea*
Cabbage, Cauliflower, Broccoli	
Brussels Sprouts, Calabrese	
Chinese Cabbage	*Brassica chinensis*
Turnip Rape, Cole	*Brassica campestris*
Swede, Rutabaga	*Brassica napobrassica*
Turnip	*Brassica rapa*
Radish	*Raphanus sativus*
Plant By-Products	
Rapeseed Oil Cake	
Weeds:	
Turnip Weed	*Rapistrum rugosum*
Diarrhea, Unpalatability, Taint Effects (Caused by Mustard Oil Glucosinolates)	
Culinary Plants	
Horse Radish	*Armoracia rusticana*
Cress, Mustard Greens	*Lepidium, Nasturtium, Tropaeolum* spp.
Wild Radish	*Raphanus raphanistrum*
White Mustard	*Sinapis alba*
Black Mustard	*Sinapis nigra*
Oriental Mustard	*Brassica juncea*
Weeds	
Fanweed	*Thlaspi arvense*
Charlock	*Sinapis arvensis*
Wormseed or Treacle Mustard	*Erysimum cheiranthoides*

Note: The taxonomy of the Brassica spp. varies between countries.

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Check Your Progress

4. What are glucosinolates?
5. What does glucosinolates constitute?
6. Name some glucosinolates.

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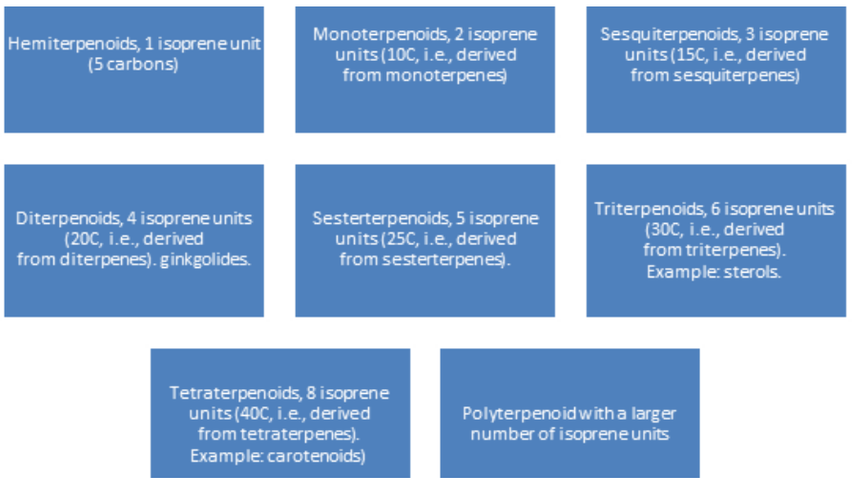
5.4 TERPENOIDS

The terpenoids, generally referred to as isoprenoids, are an outsized and numerous category of present organic chemicals derived from terpenes. Most are multicyclic structures with oxygen-containing compounds. Though generally used interchangeably with 'terpenes', terpenoids usually contain Oxygen and their functional group. Terpenes are hydrocarbons.

Plant terpenoids are used for aromatic traits and play a job in ancient seasoning remedies. Terpenoids contribute to the fragrance of eucalyptus, the flavors of cinnamon, cloves, and ginger, the yellow sunflowers, and the red colour in tomatoes. Well-known terpenoids embody citral, menthol, camphor, hallucinogen A within the plant salvia, the cannabinoids found in *cannabis, ginkgolide* and *bilobalide* found in *Ginkgo biloba*, and the curcuminoids found in turmeric and mustard seed.

The steroids and sterols in animals are biologically created from terpenoid precursors. Generally terpenoids are of great significance to proteins, for example to reinforce their attachment to the cell membrane; this is often referred to as isoprenylation.

Terpenoids are modified terpenes, wherein methyl groups have been moved or removed, or oxygen atoms added.



Classification of Terpenoids (Refer Table 5.4). Most natural terpenoid hydrocarbon have the general formula $(C_5H_8)n$. They can be classified on the basis of value of n or number of carbon atoms present in the structure.

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Table 5.4 *Classification of Terpenoids*

S.No.	Number of carbon atoms	Value of n	Class
1.	10	2	Monoterpenoids($C_{10}H_{16}$)
2.	15	3	Sesquiterpenoinds($C_{15}H_{24}$)
3.	20	4	Diterpenoids($C_{20}H_{32}$)
4.	25	5	Sesterpenoids($C_{25}H_{40}$)
5.	30	6	Troterpenoids($C_{30}H_{48}$)
6.	40	8	Tetraterpenoids($C_{40}H_{64}$)
7.	>40	>8	Polyterpenoids(C_5H_8)n

Each class can be further subdivided into subclasses according to the number of rings present in the structure.

- Acyclic Terpenoids: They contain open structure.
- Monocyclic Terpenoids: They contain one ring in the structure.
- Bicyclic Terpenoids: They contain two rings in the structure.
- Tricyclic Terpenoids: They contain three rings in the structure.
- Tetracyclic Terpenoids: They contain four rings in the structure.

General Properties of Terpenoids

- Most of the terpenoids are colourless, fragrant liquids which are lighter than water and volatile with steam. A few of them are solids, for example camphor. All are soluble in organic solvent and usually insoluble in water. Most of them are optically active.
- They are open chain or cyclic unsaturated compounds having one or more double bonds. Consequently they undergo addition reaction with hydrogen, halogen, acids, etc. A number of addition products have antiseptic properties.
- They undergo polymerization and dehydrogenation.
- They are easily oxidized nearly by all the oxidizing agents. On thermal decomposition, most of the terpenoids yields isoprene as one of the product.

Effect on Human Health

- Plant antioxidants are composed of a broad form of completely different substances like vitamin C and tocopherols, polyphenolic compounds, or terpenoids. They perform many necessary functions in plants and humans (for example carotenoids operate as accent pigments for light-weight gather and supply photoprotection and pigmentation in plants).
- Monoterpenes and diterpenes that are the most elements of essential oils, act as allelopathic agents, attractants in plant-plant or plant-pathogen/

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herbivore interactions or repellants. For humans, carotenoids play a very important role for health, carotenoids with carotene activity are necessary for vision; alternative carotenoids influence the human immune operate and Gap-Junctional Communication (GJC).

- Due to their antioxidative capability they areliable for the health promoting properties of fruits and vegetables.
- The antioxidant properties of carotenoids are attributed to the terpenoids
- The monoterpenes and perillyl alcohol is also promising substances in cancer medical aid.
- Many investigations have studied the inhibitor activity of monoterpenes and diterpenes or essential oils in vitro. Results further because the action of a recently discovered, terribly effective inhibitor (i.e., gamma-terpinene) are mentioned.
- A very important purpose once assessing the inhibitor activity of plant antioxidants is being studied for example, mixtures of hydrophilic and lipotropic antioxidants could exert synergistic effects, as has been shown for rutin together with gamma-terpinene, lutein, or carotenoid.

Check Your Progress

7. What are terpenoids?
8. How are plant terpenoids used?
9. Give some general features of terpenoids.

5.5 PHENOLS

Phenols, sometimes called phenolics, are a class of chemical compounds consisting of a hydroxyl group (—OH) bonded directly to an aromatic hydrocarbon group. The simplest of the class is phenol, C_6H_5OH. Phenolic compounds are classified as simple phenols or polyphenols based on the number of phenol units in the molecule.

5.5.1 Classification of Phenolics

Phenolic and polyphenolic compounds can be classified into several classes, namely phenolic acids, flavonoids, stilbenes, coumarins, lignins, and tannins. Phenolic acids constitute a primary phenolic class of compounds in natural sources, such as cereals, legumes, and other seeds, in which they act as the building material of cell wall matrices by forming bridges with macromolecules, such as cellulose, hemicellulose, and pectin, thus supporting the construction of compact cell wall structures. Thus, they generally occur in various conjugated forms other than the free type. Phenolic acids are divided into two groups, hydroxycinnamic acids and hydroxybenzoic

acids. Hydroxycinnamic acids include p-coumaric, caffeic, ferulic and sinapic acids, while hydroxybenzoic acids encompass p-hydroxybenzoic, protocatechuic, vanillic, syringic and gallic acids (Refer Figure 5.4). The differentiation is in the substitution and functional groups, namely hydroxyl and methoxy groups, which decide the individual differences of each phenolic acid. The ingested phenolic acids are absorbed in the gastrointestinal tract and then circulate in the blood system after methylation, sulfation, and glucuronidation in the liver. For example, hydroxycinnamic acids in wines are absorbed in the gastrointestinal tract after ingestion and transformed into glucuronide and sulfate conjugates, followed by circulation in the blood. This conjugation process increases the hydrophilicity of the phenolic compounds and helps remove them via the biliary or the urinary route. Figure 5.5 illustrates some main classes of phenolics.

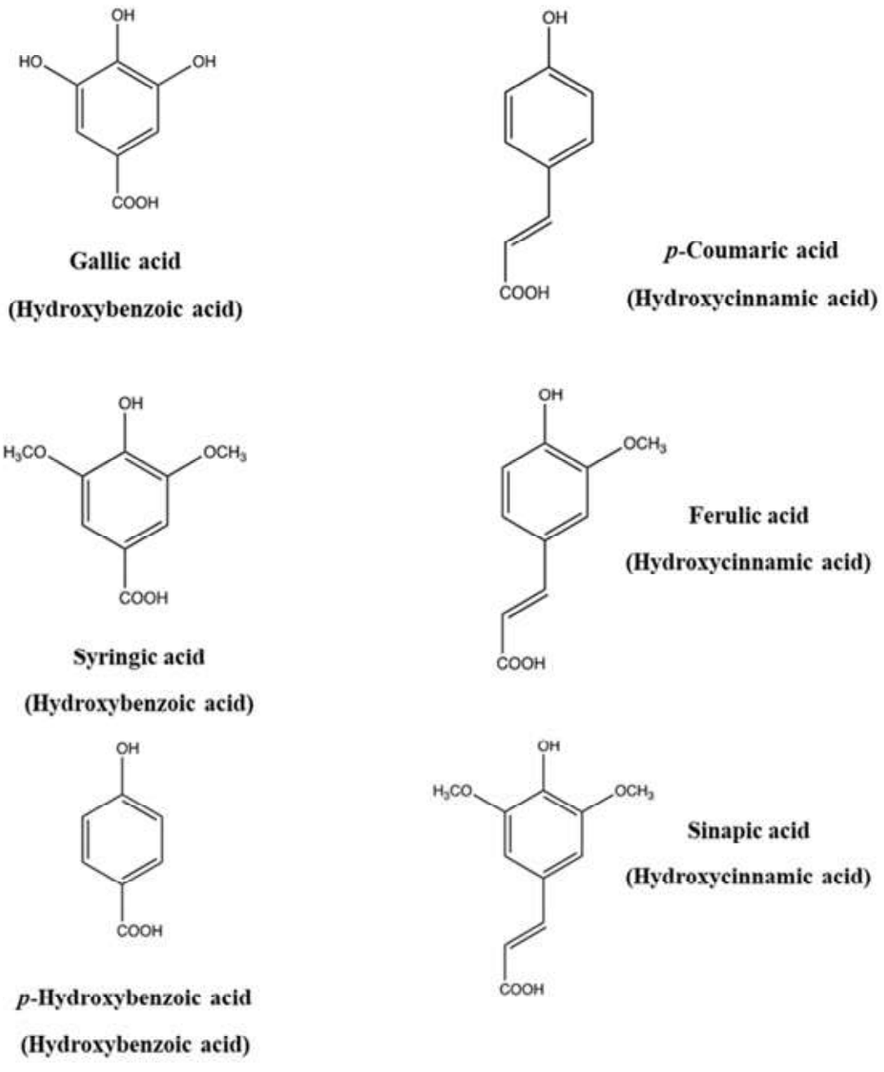

Fig. 5.4 *Chemical Structures of Representative Phenolic Acids*

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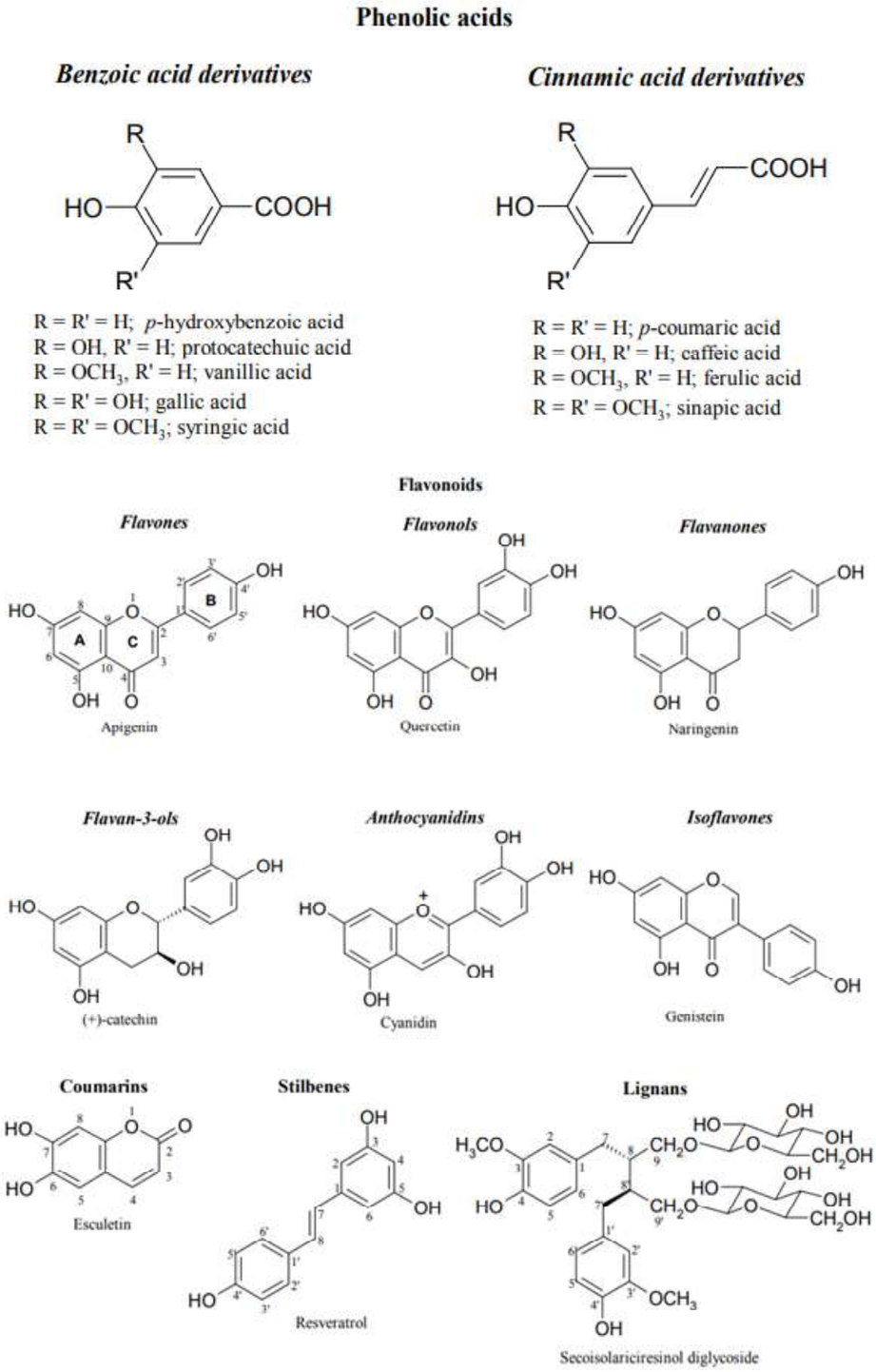

Fig. 5.5 *Main Classes of Phenolics*

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5.5.2 Solubility, Glycosylation and Acetylation and Methylation of Phenols

- The chemical structure of a molecule defines the degree of solubility.
- It is been ascertained in each in-vivo and in-vitro studies, victimization phenoplast compounds with totally different solubility, that there's variation in condition to digestion, fermentation, and absorption from the alimentary canal.
- There is a classification of phenoplast compounds that distinguishes between removable and non-extractable phenols.
- Extractable polyphenols have low-intermediate molecular mass.
- Some hydrolysable tannins and proanthocyanidins have high relative molecular mass compounds that are largely guaranteed to dietary fiber or macromolecule that is still insoluble within the usual solvent and needs an additional step of reaction throughout extraction to create them soluble and bioavailable.
- Also, it's been ascertained that the particular absorption of various removable phenolics, depends on their extractability with totally different solvents.

Glycosylation

- Free aglycones and organic compound forms as O-glycosides or as C-glycosides, usually occur as Phenolic compounds with variety of sugars, aldohexose is that the most typically encountered, followed by brain sugar, rhamnose, sugar and arabinose, whereas mannose, fructose, glucuronic and galacturonic acids are uncommon.
- Aglycones and polyphenols guaranteed to glucose, galactose or sugar are absorbed within the bowel when deglycosylation by β-glucosidase and Lactaid phlorizin hydrolase.
- It has been observed that the phenolic compound, rhamnose, reaches the colon and gets hydrolysed by microorganism rhamnosidase prior to its absorption.

Acetylation and Methylation

- Few acylated phenols/flavonoids are absorbed without previous chemical reaction or deconjugation for example epicatechin and epicatechin gallate
- Elimination of (–)-epicatechin has been observed as:
  - It that reaches the enteric cells for absorption, and a percentage of metabolites (especially sulphate conjugates) eliminated by flow into the enteric lumen.
  - It is also eliminated by bile.
  - It has been determined as a possible absorption of (–)-epicatechin and elimination by flow in another part of the gut lumen.

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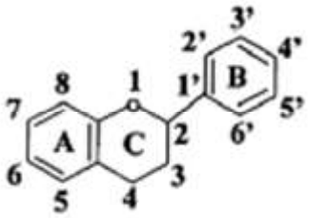
Graphic representation of the common structure of phenolic acids:



A diet provides many various phenolic compounds. Therefore, their bioavailability might vary, besides the diet changes in every country and each season. To contemplate phenolic compounds nutraceutical potential it is vital to understand what quantity of a phenolic is present in specific food along with its bioavailability.

Bioavailability is outlined as that fraction of an ingested nutrient or compound that reaches the circulation and also the specific sites wherever it will exert its biological action. Bioavailability depends metabolic processes, the discharge of an indefinite quantity type and presystemic elimination. Therefore, bioavailability additionally depends on the route of administration and dose type used, however will vary from one individual to a different, particularly dependent on the factors that alter the absorption.

Bioavailability is connected to 2 concepts: bioaccessibility and bioactivity. During this sense, availability if the phenolics are represented because the quantity of any food constituent that is discharged from the food matrix, detectable within the gut, which could also be able to withstand the intestinal obstruction? This can be crucial as a result of solely the compounds that discharged from the matrix or absorbed within the gut are doubtless bioavailable and bioactive.

Furthermore, recently it had been planned that when a compound is absorbed it's inevitably bioactive, due to this was instructed that the idea of bioavailability includes bioactivity. Notwithstanding, it is vital to notice that the very fact that a compound being bioavailable does not invariably imply it is bioactive.

Phenolic bioavailability varies over a good vary from 0.3% calculable for anthocyanins to forty three within the case of isoflavones. During this sense, bioavailability is influenced by phenolic structure, food process and matrix, host, among others; besides of these factors will move with one another and influence phenolic com pounds bioavailability.

- Epidemiological studies have connected dietary intake of phenolic-rich food with lower incidence within the look of many chronic diseases
- Phenolic compounds are among the health-promoting phytochemicals gift in cereals. phenolic compounds are receiving a lot of attention due to their inhibitor properties. Phenolic acids and flavonoids are the foremost common styles of phenolic compounds found in whole grains.
- In cereals, phenolic compounds are often gift within the free or finite

form; certain phenolics are principally hooked up to arabinosyl chains of plasma membrane arabinoxylans. phenolic acids like coumaric, ferulic, gallic, hydroxybenzoic, syringic, and sinapic acid are found in each, free and finite type in hard wheat, bread wheat, barley, oat, rye, rice, corn, and triticale.

- In cereals, the free phenolic acids represent a tiny low portion of the whole phenolic content whereas certain phenolic acids are the foremost predominant.
- Twenty varieties of cereals, have been identified for total phenolic and flavonoid content. The very best content of those phytochemicals was found in hulless barley, followed by hulless oat, rye, hard wheat, and bread wheat. Notwithstanding, monomeric phenolic compounds like catechin and epicate chin were solely detected in hulless barley genotypes. Phenolic compounds play a major role within the hindrance of the many chronic diseases because of their inhibitor, medicine and anti-carcinogenic properties.
- The medicine action of ferulic, caffeic, ρ-coumaric and sinapic acids found in extracts of free and certain phenolic acids from oat, barley, and flour by finding out the modulation of NF-κB activity.
- NF-κB could be a transcription issue concerned within the regulation of pro-inflammatory genes that plays a vital role in the management of resistance procedures and whose hyperbolic activation has been detected in many human cancers.
- Modulation of NF-κB activity exposed to cereal extracts containing phenolic acids is that the results of phenolic acids synergic action. Moreover, a combination of ferulic, caffeic, ρ-coumaric and sinapic acid in low concentrations had a major synergistic outcome on NF-κB activity; whereas higher concentrations had higher impact suppressing NF-κB activity.
- Apples are one amongst the foremost standard fruits whose health edges are attributed to phenolic compounds. The four polyphenol teams predominant in apples are flavan-3-ols, phenolic acids, dihydrochalcones and flavonols.
- Mango fruits contain many bioactive compounds, like vitamins, carotenoids, terpenoids and phenolic compounds. Phenolic acids like gallic, protocatechuic, chlorogenic and vanillic acids are predominant in mango pulp.
- Citrus fruits are wealthy in numerous nutrients, like vitamins A and C, vitamin Bc and dietary fiber. Further- a lot of, these fruits are a supply of bioactive compounds, being cinnamic acid derivatives, coumarins, and

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flavonoids the most important teams of phenolic compounds. Flavan-3-ols, phloretin glycosides, quercetin glycosides, cyanidin organic compound and hydroxycinnamic acids were among the phenolic compounds in apple phenolic extracts.

- Phenolic compounds from apples verified to assist to decrease polymer injury in HT29 cells considerably, to enhance the colonic barrier operate of $CaCO_2$ cells and to cut back the invasive potential of HT115 cells. Apple consumption might serve to safeguard against carcinoma by protective gut cells against polymer injury and abnormal animate thing behavior. In addition, some studies relate apple consumption to lower plasma sterol and reduction of risk of disorder. Among the foremost common phenolic compounds found in vegetables are flavonoids, phenolic acids and isocoumarins. As an example, most of the compounds detected in black carrot roots and black juice are composed of ρ-coumaric, caffeic and ferulic acids; 5-caffeoylquinic acid was the predominant phenolic acid. Besides, some phenolic glycosides like dihydroxybenzoic acid hexoside and quercetin-3-O-galactoside were detected. Onions, spinach and pepper fruits are a chic supply of flavonoids.
- Among the variability of phenolic compounds found, flavonols were the foremost exuberant. a complete of twenty eight compounds were known that belong to the dihydrochalcones, flavones, flavonols, hydroxycinnamic acids, lignans and glucosinolate groups.

5.5.3 Effect of Phenolic Compounds on Humans and Animals Health

The chemical constituents extracted from plants, phenolic compounds, can inhibit the absorption of amylase in the treatment of carbohydrate absorption, such as diabetes. There are many fruits and vegetables that contain phenolic compounds, especially, grapes, berries and tomatoes. Phenolic compounds, for instance phenolic acids and flavonoids, could promote health benefits by reducing the risk of metabolic syndrome and the related complications of type 2 diabetes. However, different groups of phenolic compounds have different biological characteristics, and very little is known about the mechanisms by which they could contribute to the prevention of disease; there still is the need for further studies.

Reactive Oxygen (ROS) and Reactive Nitrogen Species (RNS) are highly reactive oxidized molecules, which are generated constantly by normal cellular conditions, for instance the activity of the mitochondrial respiratory chain and inflammation, which could lead to damage in other biological molecules, like proteins and DNA. The antioxidant enzymes include SuperOxide Dismutase (SOD), Glutathione Peroxidase (GPx) and Catalase (CAT), all of them will play a vital role in getting rid of these oxidants and preventing cellular injury.

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How can Phenol Affect the Health?

Studies concerning potential health effects in animal and human studies:

Workers

- **Inhalation/ Dermal:** Long-term exposure to phenol at work can be the cause of cardiovascular disease, but the workers may also get exposed to other chemicals at the same time.

General population

- **Oral:** Ingestion of liquid products containing concentrated phenol causes serious gastrointestinal damage which can be fatal that may be the reason for death.
- **Dermal:** Application of concentrated phenol to the skin can cause severe skin damage.

Laboratory Animals

- **Inhalation:** Short-term exposure to high levels of phenol can cause irritation of the respiratory tract and muscle twitching in animals, while longterm exposure to high levels of phenol caused damaged to the heart, kidneys, liver, and lungs in animals.
- **Oral:** Drinking water with extremely high concentrations of phenol has causes muscle tremors, difficulty walking, and death in animals.
- **Dermal:** Short-term application of phenol to the skin has produces blisters and burns in animals.

How can Phenol affect Children?

Health effects in humans from exposures during the period from conception to maturity at 18 years of age.

Effects in Children: Vomiting and lethargy are the main symptoms that can be observed in children following accidental ingestion of a disinfectant containing phenol. Children might be more sensitive than adults to the effects of phenol.

Birth Defects: Two studies of women exposed to phenol and other chemicals during pregnancy did not provide evidence of birth defects.

Some birth defects have been observed in animals born to females exposed to phenol during pregnancy. This generally occurred at exposure levels that were also toxic to the mothers.

How Phenol Enter and Leave the Body?

Enter

- **Inhalation:** When you breathe air containing phenol, most of the phenol will rapidly enter your body through your lungs.

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- **Ingestion:** Phenol in food or water may also rapidly enter your body through the digestive tract.
- **Dermal Contact:** A significant amount may enter through your skin when you come into contact with phenol vapor, liquid phenol or liquids containing phenol.

Leave the Body

Once in your body, phenol is transformed into other chemicals called metabolites. Most of these other chemicals leave your body in the urine within few days.

Check Your Progress

10. What are phenols?
11. On what basis phenolic compounds classified?
12. Name the classes of phenolic compounds.
13. In how many groups phenolic acids are divided into?

5.6 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Alkaloids are secondary metabolites originally outlined as pharmacologically active compounds, primarily composed of N.
2. Alkaloids are synthesized from the following amino acids: essential amino acid, amino alkanoic acid and tryptophan.
3. In plants, alkaloids typically exist as salts of organic acids like carboxylic acid, malic, lactic, citric, oxalic, tartaric, phenolic acids, etc.
4. Glucosinolates are biologically active compounds found within the Cruciferae family of plants, together with broccoli, cabbage, cauliflower, rapeseed, mustard, and horseradish.
5. Glucosinolates constitute a natural class of organic compounds that contain sulphur and nitrogen and are derived from glucose and an amino acid.
6. Some Glucosinolates are as follows:
   - Allylglucosinolate (sinigrin) is the precursor of allyl isothiocyanate.
   - Benzylglucosinolate (Glucotropaeolin) is the precursor of benzyl isothiocyanate.
   - Phenethylglucosinolate (Gluconasturtiin) is the precursor of phenethyl isothiocyanate.
7. The terpenoids, generally referred to as isoprenoids, are an outsized and numerous category of present organic chemicals derived from terpenes.

8. Plant terpenoids are used for aromatic traits and play a job in ancient seasoning remedies.
9. General properties of terpenoids are as follows:
   - Most of the terpenoids are colourless, fragrant liquids which are lighter than water and volatile with steam. A few of them are solids, for example camphor. All are soluble in organic solvent and usually insoluble in water. Most of them are optically active.
   - They are open chain or cyclic unsaturated compounds having one or more double bonds. Consequently they undergo addition reaction with hydrogen, halogen, acids, etc. A number of addition products have antiseptic properties.
   - They undergo polymerization and dehydrogenation.
10. Phenols, sometimes called phenolics, are a class of chemical compounds consisting of a hydroxyl group (—OH) bonded directly to an aromatic hydrocarbon group. The simplest of the class is phenol, C_6H_5OH.
11. Phenolic compounds are classified as simple phenols or polyphenols based on the number of phenol units in the molecule.
12. Phenolic and polyphenolic compounds can be classified into several classes, namely phenolic acids, flavonoids, stilbenes, coumarins, lignins, and tannins.
13. Phenolic acids are divided into two groups, hydroxycinnamic acids and hydroxybenzoic acids.

5.7 SUMMARY

- Alkaloids are secondary metabolites originally outlined as pharmacologically active compounds, primarily composed of N.
- Alkaloids are synthesized from the following amino acids: essential amino acid, amino alkanoic acid and tryptophan. There are more than 12,000 alkaloids, together with over a hundred and fifty families, known in plants.
- In plants, alkaloids typically exist as salts of organic acids like carboxylic acid, malic, lactic, citric, oxalic, tartaric, phenolic acids, etc.
- Some alkaloids conjointly occur as glycosides of sugar like aldohexose, rhamnose and saccharose, for instance, alkaloids of the Solanum cluster, as amides and as esters of organic acids.
- Alkaloids are outlined as heterocyclic element compounds biosynthesized from amino acids.
- Several different substances, however, that do not precisely match this rule are classified as alkaloids, either for historical reasons or due to their biological potential and activities.

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- Purine alkaloids are element containing compounds derived from glycoside metabolism.
- Alkaloid could be a central stimulant and usually consumed in beverages like tea, and carbonated beverages. It is also consumed in medicines and analgesics.
- Cocaine is the carboxylic acid organic compound of the tropane base methylecgonine. They are found in Erythroxylon coca and Erythroxylum novogranatense, shrubs or tiny trees native to the mountain range, contain substantial amounts of cocaine in their leaves, i.e., up to fifteen of their dry mass.
- Quinolizidine alkaloids are biosynthesized from essential amino acid via ptomain. The amino acid amino alkanoic acid would be a precursor of diverse alkaloids.
- The extraction of the alkaloid bases from the bulk of the crude alkaloid solution is achieved again with a nonpolar solvent.
- The impurities from the plant in solution are dissolved by dilute aqueous acid and are washed away with water.
- Alkaloids have different solubilities in certain solvents and different reactivities with certain reagents because of the structural diversity.
- Morphine and Codeineare extracted from opium. Morphine leads to an insensitivity to pain due to its actions on the central nervous system.
- Morphine is a complete opioid agonist, whose action is localized at a central level, with affinity for the arcuate nucleus.
- Morphine sulphate has a slightly better bio-availability with oral administration. It can also be administered rectally, as suppository or enema.
- Papaverine is extracted from the milky juice of raw poppy capsules (opium). Its effect is exerted directly on smooth muscles. It is an opium alkaloid antispasmodic drug, used primarily in the treatment of visceral spasm, vasospasm, and occasionally in the treatment of erectile dysfunction.
- Quinine is extracted from the chinona tree. It is used in malaria treatment. It regulated body temperature.
- Quinine contains in its molecule a quinolinic heterocyclic atom. It presents itself as fine crystalline powder, odourless, with very bitter taste, little soluble in water, very soluble in alcohol. In therapy, it is used as salts: sulphate, chlorhydrate.
- Glucosinolates are biologically active compounds found within the Cruciferae family of plants, together with broccoli, cabbage, cauliflower, rapeseed, mustard, and horseradish.
- Glucosinolates constitute a natural class of organic compounds that contain sulphur and nitrogen and are derived from glucose and an amino acid. They are water-soluble anions and belong to the glucosides.

- The terpenoids, generally referred to as isoprenoids, are an outsized and numerous category of present organic chemicals derived from terpenes.
- Most terpenoids are multicyclic structures with oxygen-containing compounds. Though generally used interchangeably with 'terpenes', terpenoids usually contain Oxygen and their functional group.
- Phenols, sometimes called phenolics, are a class of chemical compounds consisting of a hydroxyl group (—OH) bonded directly to an aromatic hydrocarbon group. The simplest of the class is phenol, C_6H_5OH.
- Phenolic compounds are classified as simple phenols or polyphenols based on the number of phenol units in the molecule.
- Phenolic and polyphenolic compounds can be classified into several classes, namely phenolic acids, flavonoids, stilbenes, coumarins, lignins, and tannins.
- Phenolic acids constitute a primary phenolic class of compounds in natural sources, such as cereals, legumes, and other seeds, in which they act as the building material of cell wall matrices by forming bridges with macromolecules, such as cellulose, hemicellulose, and pectin, thus supporting the construction of compact cell wall structures.
- Bioavailability is outlined as that fraction of an ingested nutrient or compound that reaches the circulation and also the specific sites wherever it will exert its biological action.

5.8 KEY WORDS

- **Alkaloids**: Alkaloids are secondary metabolites originally outlined as pharmacologically active compounds, primarily composed of N.
- **Terpenoids**: The terpenoids, generally referred to as isoprenoids, are an outsized and numerous category of present organic chemicals derived from terpenes.
- **Phenols**: Phenols, sometimes called phenolics, are a class of chemical compounds consisting of a hydroxyl group (—OH) bonded directly to an aromatic hydrocarbon group.

5.9 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. What are alkaloids?
2. What are the sources of alkaloids?
3. How does glucosinolates effect human health?

4. What are terpenoides and what are its sources?
5. How does phenolics effect the health of humans?

Long Answer Questions

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1. Write a detailed note on alkaloids explaining its chemistry, classes, sources and effect on human health.
2. Discuss about glucosinolates in detail. Also give its basic structure, chemistry and effect on human health.
3. Explain with the help of diagram biosynthesis of glucosinolates and degradation of glucosinolates.
4. What are terpenoids? Give its classification and general properties.
5. Explain phenols. Also give its classification.
6. Elaborate a note on how phenols can effect humans and animals. Also explain how they can enter and exit from the body.
7. Draw a well labelled diagram of main classes of phenolics.

5.10 FURTHER READINGS

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UNIT 6 ANTINUTRIENTS PRESENT IN FOOD

NOTES

Structure

6.0 INTRODUCTION

Antinutrients are natural or synthetic compounds that interfere with the absorption of nutrients. Nutrition studies focus on these antinutrients commonly found in food sources and beverages. In nature, plants use antinutrients to protect themselves from predators. In other words, these substances prevent plants from being eaten by animals or humans. Raw potatoes have high amounts of these natural components that help them defend against pests and pathogens. However, they are toxic for humans and only cooking potatoes lowers their concentration to reduce their toxicity. Unlike nutrients that provide nourishment, antinutrients block the absorption of individual proteins, vitamins and minerals, and they can punch holes in your intestinal walls. That leads to increased intestinal permeability, which is a fancy term for a leaky gut. The consumption of antinutrients can also lead to mineral deficiencies particularly if you have a diet low in wholesome foods.

Spices and condiments are known as one of the most remarkable ingredients of the many styles of cuisine in the world. Generally, spices are food ingredients mainly used to season a food dish during its preparation. In contrast, condiments are mainly used at the dining table to enhance the dish. This is the main difference between spices and condiments. Spices share some similarities with condiments, but they do have some key differences as well. The purpose of this article is to highlight the difference between condiments and spices. Biologically, spice is a fruit, leave, seed, root, bark, berry, bud, flower or vegetable substance principally used as a flavoring, coloring or preserving agent in food. In addition, many spices have antimicrobial and antioxidant properties. As a result, spices are also used in meat curries to produce safe food for human consumption. Also, they are sometimes

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used in medicine, religious rituals, cosmetics or perfume production, or as a vegetable due to their unique sensory attributes. A condiment is a spice, sauce, or spice mixture that is mainly added to different food dishes to contribute a specific flavor, to improve its flavor, or in some nations, to supplement the dish. It is mainly added to food immediately before consumption. Food items such as pickles, sauces, mustards, etc. are considered to be condiments.

In this unit, you will study about antinutrients present in food: phytate, saponin, haemagglutinins, protease, amylase and lipase inhibitors, spices and condiments nutritive value and uses in cooking in detail.

6.1 OBJECTIVES

After going through this unit, you will be able to:

- Explain the role of antinutrients present in food
- Discuss about spices and condiments

6.2 ANTINUTRIENTS PRESENT IN FOOD

Antinutritional factors are compounds that cut back the nutrient utilization and/or food intake of plants or plant products used as human foods and they play a significant role in deciding the employment of plants for humans. This unit is aimed to review the updated scientific information concerning the potential health edges and adverse effects associated with major antinutritional factors found in plant foods. Antinutrients in plant foods are accountable for injurious effects related to the absorption of nutrients and micronutrients. However, some antinutrients may exert useful health effects at low concentrations. For example, phytic acid, lectins, tannins, saponins, amylase inhibitors and peptidase inhibitors have been shown to reduce the supply of nutrients and cause growth inhibition. However, when used at low levels, phytate, lectins, tannins, amylase inhibitors and saponins have conjointly been shown to cut back the glucose and hypoglycaemic agent responses to starchy foods and/or the plasma cholesterol and triglycerides. In addition, phytates, tannins, saponins, protease inhibitors, goetrogens and oxalates have been associated with reduce cancer risks. This implies that antinutrients may not be always harmful even though lack of wholesome value. Despite of this, the balance between beneficial and dangerous effects of plant bioactives and anti-nutrients rely on their concentration, chemical structure, time of exposure and interaction with other dietary components. Due to this, they can be thought-about as anti-nutritional factors with negative effects or non-nutritive compounds with positive effects on health.

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Antinutrients are chemicals which have been produced by plants for their defense in the biological functions and decrease the utmost utilization of nutrients especially proteins, vitamins, and minerals, hence preventing optimal misuse of the supplements display in a nourishment and decreasing the nutritive value. A few of these plant chemicals have been appeared to be pernicious to wellbeing or evidently profitable to human and creature wellbeing if consumed at suitable amounts.

Antinutrients in plant foods reported to reduce the bioavailability of iron, zinc, or both.

Table 6.1 *Antinutrients and Their Major Sources*

Antinutrient	Major dietary sources
Phytic acid or phytin	Whole legume seeds and cereal grains
Fibre (for example, cellulose, hemicellulose, lignin, cutin, suberin)	Whole cereal grain products (for example, wheat, rice, maize, oats, barley)
Tannins and polyphenols	Tea, coffee, beans, sorghum
Oxalic acid	Spinach leaves, rhubarb
Hemagglutinins (for example, lectins)	Most legumes and wheat
Heavy metals (for example, cadmium, mercury, lead, gold)	Plant foods obtained from crops grown on metal-polluted soils (for example, cdmium in rice)

Tannins

The word tannin is exceptionally ancient and reflects a traditional technology. Tanning was the word utilized within the scientific literature to depict the method of changing raw animal covers up or skins into tough, non-putrescible leathers by utilizing plant extricates from distinctive plant parts. Tannin is an astringent, bitter plant polyphenolic compound that either binds or precipitates proteins and various other organic compounds including amino acids and alkaloids. Tannins are the most widely occurring antinutritional factors found in plants. These compounds are present in numerous tree and shrub foliages, seeds and agro-industrial by-products. Tannin is an astringent, biting plant polyphenolic compound that either ties or accelerates proteins and different other organic compounds counting amino acids and alkaloids. The term tannin alludes to the utilize of tannins in tanning animal stows away into calfskin; be that as it may, the term is widely applied to any huge polyphenolic compound containing sufficient hydroxyls and other appropriate classes to form strong complexes with proteins and other macromolecules. Tannins have atomic weights extending from 500 to over 3000 (Refer Figure 6.1).

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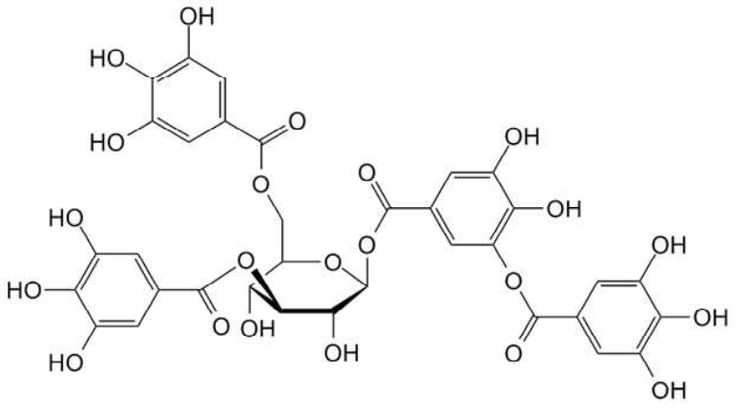

Fig. 6.1 Structure of Tannin

Tannins are heat stable and they decreased protein digestibility in animals and humans, probably by either making protein partially unavailable or inhibiting digestive enzymes and increasing fecal nitrogen. Tannins are known to be present in food products and to inhibit the activities of trypsin, chemotrypsin, amylase and lipase, decrease the protein quality of foods and interfere with dietary iron absorption. Tannins are known to be responsible for decreased feed intake, growth rate, feed efficiency and protein digestibility in experimental animals. If tannin concentration in the diet becomes too high, microbial enzyme activities including cellulose and intestinal digestion may be depressed. Tannins also form insoluble complexes with proteins and the tanninprotein complexes may be responsible for the anti-nutritional effects of tannin containing foods.

Phytate

Phytate, which is also known as inositol hexakisphosphate, is a phosphorus containing compound that binds with minerals and inhibits mineral absorption. The cause of mineral deficiency is commonly due to its low bioavailability in the diet. The presence of phytate in feeds has been associated with reduced mineral absorption due to the structure of phyate which has high density of negatively charged phosphate groups which form very stable complexes with mineral ions causing non-availability for intestinal absorption. Phytates are generally found in feed high in fibre especially in wheat bran, whole grains and legumes (Refer Figure 6.2).

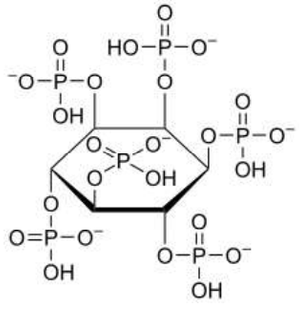

Fig. 6.2 Structure of Phytic Acid

Phytate, additionally known as Inositol hexakisphosphate (InsP6) is the salt frame of phytic corrosive, are found in plants, animals and soil. It is basically show as a salt of the mono- and divalent cations K^+, Mg^{2+}, and Ca^{2+} and accumulates within the seeds amid the aging period. Phytate is respected as the essential capacity frame of both phosphate and inositol in plant seeds and grains. In addition, phytate has been recommended to serve as a store of cations, of high vitality phosphoryl bunches, and, by chelating free iron, as a powerful normal anti-oxidant. Phytate works in a broad pH-region as a highly negatively charged ion, and so its nearness in the diet includes a negative influence on the bioavailability of divalent, and trivalent mineral particles such as Zn^{2+}, $Fe^{2+/3+}$, Ca^{2+}, Mg^{2+} , Mn^{2+}, and Cu^{2+}.

Oxalate

A salt shaped from oxalic corrosive is known as an Oxalate: for case, Calcium oxalate, which has been found to be widely disseminated in plants. Solid bonds are formed between oxalic corrosive, and different other minerals, such as Calcium, Magnesium, Sodium, and Potassium. This chemical combination comes about within the arrangement of oxalate salts. A few oxalate salts, such as sodium and potassium, are dissolvable, though calcium oxalate salts are basically insoluble. The insoluble calcium oxalate has the tendency to precipitate (or set) within the Kidneys or within the Urinary tract, hence shaping sharp-edged calcium oxalate crystals when the levels are tall enough. These precious stones play a role to the arrangement of kidney stones arrangement within the urinary tract when the corrosive is excreted within the urine (Refer Figure 6.3).

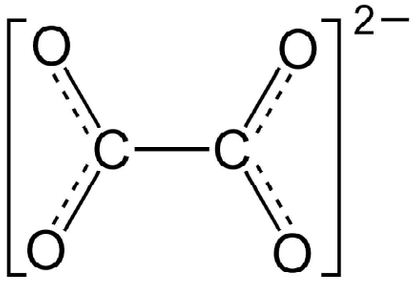

Fig. 6.3 *Structure of Oxalate*

Oxalic corrosive shapes water solvent salts with Na^+, K^+, and NH_4^+ particles, it moreover ties with Ca^{2+}, Fe^{2+}, and Mg^{2+} rendering these minerals inaccessible to creatures. However Zn^{2+} shows up to be moderately unaffected. In plants with a cell sap of roughly pH 2, such as a few species of Oxalis and rumex oxalate exists as the corrosive oxalate (HC_2O_4), essentially as corrosive potassium oxalate. In plants with a cell sap of around pH 6, such as a few plants of goosefoot family it exists as oxalate $(C_2O_4)_2^-$ ion usually as solvent sodium oxalate and insoluble calcium and magnesium oxalates. Calcium oxalate is insoluble at a neutral or soluble pH, but unreservedly breaks down in acids.

Saponins

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Saponins are auxiliary compounds that are generally known as non-volatile, surface dynamic compounds which are widely disseminated in nature, happening fundamentally in the plant kingdom. The title 'saponin' is determined from the Latin word sapo which suggests 'soap', since saponin molecules shape soap-like froths when shaken with water. They are fundamentally different atoms that are chemically referred to as triterpene and steroid glycosides. They consist of non-polar aglycones coupled with one or more monosaccharide moieties. This combination of polar and non-polar basic components in their atoms explains their soap-like conduct in watery solutions. The auxiliary complexity of saponins comes about in a number of physical, chemical, and organic properties, which incorporate sweetness and intensity, frothing and emulsifying properties, pharmacological and medicinal properties, haemolytic properties, as well as antimicrobial, insecticidal, and molluscicidal exercises (Refer Figure 6.4).

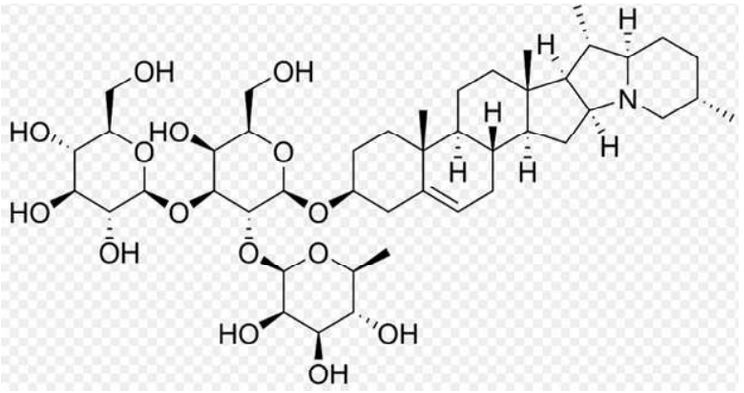

Fig. 6.4 *Structure of Saponin*

Saponins are drawing in significant intrigued as a result of their useful impacts in people. Later evidence suggests that saponins have hypocholesterolemic, immune stimulatory, and anti-carcinogenic properties. In addition, they decrease the chance of heart maladies in humans consuming a count calories wealthy in nourishment vegetables containing saponins. Saponin rich nourishments are imperative in human diets to control plasma cholesterol, anticipating peptic ulcer, osteoporosis and to diminish the hazard of heart illness. Saponins are utilized as adjuvants in viral and bacterial applications.

The amphiphilic behavior of a saponin could be a result of the contradicting lyophilic and lyophobic characteristics of the carbohydrate and aglycone moieties; hence the structure affects its chemical behavior and leads to the expression of numerous of its biological properties. Changes in saponin structure, maybe as a result of fractional hydrolysis during processing, will hence have noteworthy impacts on the quality of the processed produce.

Lectin/Haemagglutinins

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Lectin comes from the Latin word 'legere', which means 'to select'. Lectins have the capacity to bind carbohydrates. These days, proteins that can agglutinate red blood cells with known sugar specificity are alluded to as 'lectins'. The title 'hemagglutinins' is utilized when the sugar specificity is obscure. Lectins and hemagglutinins are proteins/glycoproteins, which have at least one non-catalytic space that shows reversible binding to particular monosaccharides or oligosaccharides.

Lectins are glycoproteins broadly dispersed in legumes and a few certain oil seeds (counting soybean) which possess a liking for particular sugar atoms and are characterized by their capacity to combine with carbohydrate membrane receptors. Lectins have the capability to directly bind to the intestinal muscosa, collaboration with the enterocytes and interferometer with the retention and transportation of 0.01% free gossypol inside a few lowgossypol cotton supplements (especially carbohydrates) during absorption and causing epithelial injuries inside the intestine.

Numerous lectins are poisonous and/or fiery, safe to cooking and stomach related enzymes/stomach acids within the body. They can harm intestine divider permitting other proteins to cross undigested causing unfavorably susceptible reactions. When lectins are within the blood stream, they can tie to cell layers in supply routes and organs such as joints, kidney, pancreas and brain, causing antigen-antibody responses driving to immune system disarranges. Lectins can be blocked by straightforward sugars and oligosaccharides within the body. Soybean lectins have been appeared to discourage nitrogen maintenance and increment nitrogen excretion by means of the pee, showing impedances with protein digestion system. Lectins have been found in wheat, rye, grain, oats, corn and rice, but not in sorghum or millet. The lectins in grains show up to have to some degree comparable natural action. The carbohydrates and proteins that are undigested and unabsorbed within the little insides reach the colon where they are matured by the bacterial greenery to brief chain greasy acids and gasses. The lectin actuated disturbance of the intestinal mucosa may permit entrance of the microscopic organisms and their endotoxins to the blood stream and cause harmful reaction. Lectins may moreover be internalized specifically and cause precise impacts such as expanded protein catabolism and breakdown of put away fat and glycogen, and unsettling influence in mineral digestion system.

Protease Inhibitors

Protease inhibitors are broadly disseminated inside the plant kingdom, counting the seeds of most developed legumes and cereals. Protease inhibitors are the foremost commonly encountered lesson of antinutritional variables of plant origin. Protease inhibitors have the capacity to restrain the action of proteolytic proteins inside the gastrointestinal tract of animals. Due to their specific protein nature,

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protease inhibitors may be effectively denatured by warm processing although a few leftover action may still stay in the commercially created items. The antinutrient activity of protease inhibitors is related with development inhibition and pancreatic hypertrophy. Potential useful impacts of protease inhibitors stay hazy, in spite of the fact that lower incidences of pancreatic cancer have been watched in populations where the admissions of soybean and its items is high.

Trypsin Inhibitor

Trypsin inhibitor and chymotrypsin inhibitor are protease inhibitors happening in crude vegetable seeds. Trypsin inhibitors that hinder the movement of the chemicals trypsin and chymotrypsin within the intestine, in this way anticipating protein digestion, are found in many plant species basically in numerous grain legumes. Trypsin inhibitors are an interesting lesson of proteins found in crude soybeans that hinder protease chemicals in the digestive tract by shaping inedible complexes with dietary protein. These complexes are toxic indeed in the nearness of tall sums of stomach related enzymes. Protease inhibitors decrease trypsin movement and to a lesser extent chymotrypsin; hence disabling protein digestion by monogastric creatures and a few youthful ruminant creatures.

Amylase Inhibitors

Restraint of α-amylase, protein that plays a part in absorption of starch and glycogen, is considered a procedure for the treatment of clutters in carbohydrate take-up, such as diabetes and weight, as well as, dental caries and periodontal infections. Plants are an imperative source of chemical constituents with potential for restraint of α-amylase and can be utilized as restorative or useful nourishment sources. A survey approximately unrefined extricates and separated compounds from plant source that have been tried for α-amylase inhibitory action has been done. The examination of the comes about appears an assortment of unrefined extricates that display α-amylase inhibitory action and a few of them had pertinent action when compared with controls utilized within the considers. Among the phyto-constituents that have been explored, flavonoids are one of them that illustrated the most elevated inhibitory exercises with the potential of hindrance related to number of hydroxyl bunches within the atom of the compound.

Overweight, weight, and diabetes are the foremost common disarranges within the world. In most diets, carbohydrates are the most prominent source of calories. Restraint of carbohydrate absorption or retention can diminish calorie admissions to promote weight misfortune and combat weight. It is additionally an instrument for diminishing hyperglycemia in diabetic subjects. Sometime recently being ingested by the body, carbohydrates must be broken down into monosaccharides. α-Amylase catalyzes the hydrolysis of α-(1,4)-d-glycosidic linkages of starch and other glucose polymers. Inhibitors of this protein can be utilized in treatment of weight and diabetes. In diabetic patients, restraint of α-amylase leads to forbiddance starch breaking and comes about in lower levels of

blood glucose. The impacts of pseudosaccharides, proteinaceous, and polyphenolic inhibitors have been already detailed. Polyphenolic compounds are broadly disseminated in plants and natural products and are show in typical diets. These compounds have been appeared to have useful impacts in diabetes, cardiovascular infections, atherosclerosis, hypersensitivity, aggravation, and osteoporosis. Among polyphenolic compounds, flavonoids are of specific noteworthiness: They have been appeared to diminish cholesterol blend through coordinate activity on HMG-CoA reductase and hydrolyze lipids through hindrance of PhosphoDiEsterase (PDE) and reduction of cAMP breakdown. In later a long time, numerous lines of investigate have been done on those plants which are being utilized customarily as medicate plants, and their impacts have been studied on weight misfortune and control of blood glucose levels in diabetic patients.

Check Your Progress

1. What are antinutients?
2. Writs a short note on phytate.
3. What are saponins?

6.3 SPICES AND CONDIMENTS

Spices and condiments are known as one of the most remarkable ingredients of the many styles of cuisine in the world. Generally, spices are food ingredients mainly used to season a food dish during its preparation. In contrast, condiments are mainly used at the dining table to enhance the dish. This is the main difference between spices and condiments. Spices share some similarities with condiments, but they do have some key differences as well. Biologically, spice is a fruit, leave, seed, root, bark, berry, bud, flower or vegetable substance principally used as a flavoring, coloring or preserving agent in food. In addition, many spices have antimicrobial and antioxidant properties. As a result, spices are also used in meat curries to produce safe food for human consumption. Also, they are sometimes used in medicine, religious rituals, cosmetics or perfume production, or as a vegetable due to their unique sensory attributes. A condiment is a spice, sauce, or spice mixture that is mainly added to different food dishes to contribute a specific flavor, to improve its flavor, or in some nations, to supplement the dish. It is mainly added to food immediately before consumption. Food items such as pickles, sauces, mustards, etc. are considered to be condiments.

6.3.1 Spices

A spice is a seed, fruit, root, bark, or other plant substance primarily used for flavoring, coloring or preserving food. Spices are distinguished from herbs, which are the leaves, flowers, or stems of plants used for flavoring or as a garnish.

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Many spices have antimicrobial properties. This is the reason taht spices are more commonly used in warmer climates, which have more infectious diseases, and why the use of spices is prominent in meat, which is particularly susceptible to spoiling. Spices are sometimes used in medicine, religious rituals, cosmetics or perfume production.

Spices are in tall request to meet extraordinary flavors required for home cooking and by nourishment processors. The new and dried shapes are found within the open markets or general stores. Flavors are utilized for enhancing either in their entirety or ground frame or as extractives (Refer Figure 6.5).

Fig. 6.5 *Some Commonly Used Spices*

Flavor Profile of Spices

Bitter

- Bitter spices are believed to have an acquired taste.
- Spices that are considered bitter are bay leaves, fenugreek seeds, horseradish, mace, cloves, cumin seeds, etc.

Earthy

- These spices have an earthy flavor, which comes from geosmin.
- Cumin and saffron are spices that have an earthy flavor.

Hot

- Hot spices are those that add a strong flavor to the food and make it spicier.
- Pepper, chilis, mustard seeds, garlic are all hot spices.

Sweet

- These spices are slightly sweet in taste and can be used with sour and bitter flavors.
- Allspice, caraway, fennel, cardamom, nutmeg, poppy seeds, sesame seeds, star anise seeds are all considered as sweet spices.

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Spices by Cuisine

Some of the spices used in popular cuisines across the world are as follows:

- **Indian Spices:** Indian spices apart from being famous for culinary aspects have long been used to treat various health issues that include improving heart health. The following spices are included in a variety of Indian dishes: Cardamom, black pepper, curry leaves, fenugreek, ginger, fennel, ajwain, tamarind, bay leaves, cayenne pepper, cumin, coriander seed, turmeric, clove, ginger, nutmeg, paprika, garam masala, curry powder, and cinnamon.
- **Middle Eastern Spices:** Middle Eastern cuisines include the following spices: Cumin, nutmeg, cardamom, turmeric, sumac, Baharat, caraway, anise seeds, allspice, cinnamon.
- **Mediterranean Spices:** Majority of Mediterranean dishes include these common spices: Cinnamon, oregano, bay leaves, cardamom, cinnamon, allspice, pepper, nutmeg.
- **Other Spices:** Sichuan pepper, ginseng, and chipotle are other spices that are used in many cuisines.

In industries, ground flavors are normally utilized to supply visual offer and are regularly supplemented with fundamental oils or oleoresins. Zest extractives (essential oil and oleoresins) serve as elective to whole and ground flavors and give the soundness required in item definition. The essential oils are fragrant unstable components show in most flavors giving the characteristic flavour of spices and these are blends of hydrocarbons (terpenes) and oxygenated compounds (liquor, esters, aldehydes).

Spices from seeds are rich wellsprings of fat protein and starches. Spices play a key job in nourishment as great wellsprings of miniaturized scale and macronutrients. Numerous Spices have rich wellsprings of calcium, phosphorus, magnesium and micronutrients, for example, zinc. Nutraceuticals are substances considered as nourishments or part of nourishment that gives restorative or wellbeing benefits, notwithstanding their standard capacities. A sustenance that has parts or fixings that give a potential advantage to wellbeing, prosperity, physical wellness, or disease resistance well beyond the advantage anticipated from its primary wholesome segments of sugars, lipids, proteins, minerals, and nutrients are alluded to as practical nourishment. Spices are likewise rich wellsprings of phenolic mixes with cell reinforcement movement which impact sustenance through numerous pathways.

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Rancidity is the oxidative or hydrolytic decay of fats in charge of the loss of the regular flavor, surface, appearance just as loss of healthy benefit of fat. Component of lipid oxidation includes three particular advances: commencement or arrangement of free radical, engendering or free-chain response and end step which is the development of non-radical items. In the commencement stage or acceptance period, on introduction of an unsaturated hydrocarbon to warmth or light, there is lost hydrogen to shape a radical. The response continues when the fat free radical responds with oxygen to shape peroxide radical. The peroxide radical at that point remove hydrogen from another fat atom shaping a hydroperoxide and another fat free radical. Amid the spread advance, the anchor response is proceeded to from a hydroperoxide and another fat free radical. Amid the spread advance, the chain response is proceeded to from peroxy radicals, hydroperoxides and new hydrocarbon radicals. Hydroperoxides are promptly deteriorated by warmth, radiations, metals and catalysts. They deteriorate to frame extra radicals which add to chain response. At the point when two radicals cooperate, end jumps out at structure decompositional items. Ginger rhizomes averted lipid oxidation in creature fat. Rosemary, wise, inlet and thyme have been utilized for heated items. Cancer prevention agent property of *Aframomum danielli* in lessening rate of peroxidation in oils had been accounted for. The phenolic structures of numerous flavors enable them to work as essential cancer prevention agents. These empower them to frame vitality free radicals through reverberation half and half. A few flavors works as auxiliary cancer prevention agents, such as chelators or synergists. A few capacities better within the sight of different chelators or synergists. As corrosive or metal chelators, they work by restricting metals or metalloproteins that advance oxidation in this way enabling the essential cancer prevention agents to play out its capacity and catch free radicals. As synergists, they work better within the sight of at least one cancer prevention agents. Synergism is that occasions when the consolidated impact from at least two cell reinforcements is more prominent than the total of the individual impact acquired when utilized alone. Corrosive synergists enhance essential cell reinforcements by giving acidic medium to enhance the cancer prevention agents. They can likewise recover cancer prevention agents by chelating or deactivating ace oxidant. Cancer prevention agents, for example, allicin in garlic restrain free extreme action. Flavors like garlic likewise which have capacity to rummage free radicals contains vitamin C, thus they can be utilized to avert skin pigmentation issues and aggravations. The antimicrobial properties of flavors can be assembled into bactericidal, bacteriostatic, fungicidal and fungistatic properties. Unstable parts of cardamom showed inhibitory impact on Gram negative microscopic organisms. Onion extricates showed antimicrobial properties. The fundamental oils of oregano and thyme hindered the development of mycelia of *Aspergillus* spp. Garlic has been viewed as a characteristic anti-infection which significant movement has been ascribed to the allicin.

Health Benefits of Spices

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According to a study published in the Critical Reviews in Food Science and Nutrition journal, various spices that are used to add flavour to recipes also provide many health benefits. It highlighted how spices and herbs improve public health through flavourful eating.

Allspice: Allspice is a soothing, anti-inflammatory, and carminative spice. Its benefits include reducing cancer, improving oral health, stimulating digestion, facilitating bone growth, and boosting the immune system. It also helps in reducing blood pressure and acts as an analgesic substance (Refer Figure 6.6).

Fig. 6.6 *Raw and Dry Allspice Berries*

Anise Seed: This powerful spice has an antioxidant as well as a stomachic, anti-spasmodic, carminative, antiseptic, digestive, expectorant, and stimulant properties. It is a great source of vitamins and minerals like iron, potassium, copper, and manganese. These seeds help increase the circulation and oxygenation of body parts while boosting the immune system and improving the quality of your skin (Refer Figure 6.7).

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Fig. 6.7 *Star Anise and Anise Seed*

Arrowroot: Arrowroot helps in growth and development, reducing blood pressure, increasing circulation, and improving the health of the digestive system (Refer Figure 6.8).

Fig. 6.8 *Arrowroot Root*

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***Asafoetida* (Hing):** This is sap from stem and root of a plant, dried into a hard resin. The smell of this spice in the raw uncooked form is strong and pungent; so unpleasant that it is often called as the *devils dung*, or the *stinking gum*. However this initial funky pungent smell mellows and almost disappears, replaced by a smooth pleasant flavour when it is added to hot oil or ghee. The flavour is not the spicy fiery kind, but more like Leek or Onion. Hing is definitely a gem in the kitchen. In its raw form, the strong aroma will contaminate other spices, so it is better stored in an air tight container (Refer Figure 6.9).

Fig. 6.9 *Asafoetida*

The resin form is hard and deep amber in colour. It has to be powdered before it is used for cooking or medicinal purposes.

Bay Leaf: Bay leaf is a very popular spice throughout the world and is praised for its ability to prevent cancer, boost immunity, reduce neural tube defects, protect oral health, skin care, and hair care. It also helps improve nervous system function, regulate body metabolism, and prevent blood-related conditions like anemia (Refer Figure 6.10).

Fig. 6.10 *Bay Leaves*

Black Pepper: Black pepper is one of the most common spices in the world packed with many health benefits. It has an ability to reduce inflammation and excess gas, optimize gastrointestinal action, and regulate enzymatic

reactions. Black pepper helps control heart rate and blood pressure and prevent cancer due to its antioxidant properties (Refer Figure 6.11).

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Fig. 6.11 *Black Pepper*

Cayenne Pepper: Cayenne pepper has the ability to clear the sinuses, increase urination, eliminate toxins from the body, help manage diabetes, prevent cancer, and lower blood pressure. Use of cayenne pepper helps speed up weight loss, optimize the metabolism, regulate hormonal activity, and fight toxins and potential infections, due to its powerful antioxidant properties.

Capers: Capers prevent cancer, reduce illness, boost immunity, strengthen blood vessels, reduce clotting, lower cholesterol levels, and increase circulation. They also provide a huge wealth of vitamins like vitamin A, vitamin K, niacin, riboflavin, and minerals like iron and copper (Refer Figure 6.12).

Fig. 6.12 *Capers*

Caraway Seeds: Caraway seeds can improve digestion, reduce constipation, lower blood cholesterol levels, reduce excess gas, neutralize free radicals, and prevent various diseases like cancer. They also regulate blood pressure and eliminate atherosclerosis. These seeds provide vitamins like thiamin, pyridoxine, riboflavin, and niacin. Not only that, they also provide minerals like iron, copper, calcium, potassium, manganese, selenium, zinc, and magnesium (Refer Figure 6.13).

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Fig. 6.13 *Caraway Seeds*

Cardamom: The health benefits of cardamom include its ability to aid digestion, reduce spasms, lower blood pressure, increase the metabolism, improve circulation, and increase frequency and volume of urination. It also provides the essential vitamins like riboflavin, niacin, vitamin C, and minerals like iron, manganese, and potassium (Refer Figure 6.14).

Fig. 6.14 *Cardamom*

Cinnamon: Cinnamon is praised for its ability to reduce inflammation, eliminate pain, manage diabetes, eliminate infections, reduce excess gas, and improve heart health. It also helps in increasing cognitive function, building strong bones, preventing cancer, and improving the health of the eyes and skin (Refer Figure 6.15).

Fig. 6.15 *Cinnamon*

Cloves: Cloves have antimicrobial properties, which help in fighting oral diseases. They also are good for boosting the immune system, preventing cancer, and preserving bone health (Refer Figure 6.16).

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Fig. 6.16 *Cloves*

Cumin: Cumin seeds are antioxidant, anti-inflammatory, and carminative by nature. They improve digestion, increase sperm count, build strong bones, improve eyesight, and prevent macular degeneration. Other benefits of cumin seeds include their ability to manage heart rate, lower blood pressure, act as a co-factor in many enzymatic reactions, increase red blood cell count, and prevent various types of cancer.

Carom Seeds /Ajwain (*Trachyspermum copticum*): These are pungent, tiny seeds grayish in colour and often mistaken to be the 'Bishop's Weed'. Ajwain has very strong flavours and the smell and the taste bears close similarity to Thyme. They have a sharp and slightly bitter taste on the tongue. In Indian cooking, the Ajwain is rarely used raw. They are usually dry roasted lightly or tempered in hot oil or ghee and used for seasoning a dish. Other than using the seeds for curries, the flavour of this spice works really well with breads and are very popularly used in 'Paratha' (griddle fried flatbreads) in the northern regions of the country. Besides culinary uses, it is used for medicinal purposes to aid in digestion and also as an antiseptic (Refer Figure 6.17).

Fig. 6.17 *Carom Seeds*

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Coriander Seeds (Dhania): These seeds are the dry seeds of the regularly used fresh cilantro/coriander. Light brown or golden in colour, the seeds are kind of hollow and crunchy and has a nice earthy, nutty flavour. The seeds are used whole for tempering, but more often they are ground into a powder to flavour food. Do yourselves a favour and stop yourself from buying store bought coriander powder. They lose the flavour fairly quick when stored, so you will end up with a sawdust kind of powder with no flavour in it. The best way go about it, is to grind the seeds when you use them or store them in an airtight container only for a few days. I use the coffee grinder or the spice grinder to powder the seeds (Refer Figure 6.18).

Fig. 6.18 *Coriander Seeds and Powder*

The seeds are powdered either by roasting them first in a dry skillet or without roasting them. The roasted seeds powdered have a darker shade and a different flavour than the other. Both are used in Indian cuisine.

The seeds are usually used in the ground form to be a part of various spice mixes, like Garam Masala**,** Sambar Powder, etc.

Coriander Powder: Coriander seeds are ground to make coriander powder. The powder is used in Indian cooking for flavour. Avoid store bought packaged coriander powder. They sit on the shelves too long and lose all its freshness. Grind up coriander seeds at home in a spice or coffee grinder and store in airtight containers for a couple of months.

Fennel Seeds: According to Michigan Medicine, fennel has raditionally been used to cure upset stomach, prevent gas, and treat colic and cough in infants.Fennel has also been known for its ability to regulate bowel movements, prevent cancer, delay aging through antioxidant activity, and increase enzymatic activity. Fennel seeds act as a great source of many minerals, including copper, iron, calcium, potassium, manganese, selenium, zinc, and magnesium. They are also rich in organic compounds and acids like pinene, myrcene, fenchone, chavicol, cineole, anethole, limonene, and anisic aldehyde.

Fenugreek Seeds: Fenugreek seeds are a very popular and effective spice in certain Asian cultures that add a powerful nutrient boost to the body. They have the ability to improve digestion and reduce constipation, lower cholesterol levels, regulate insulin levels, and manage fluid levels in the body (Refer Figure 6.19).

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Fig. 6.19 *Fenugreek Seeds*

Garlic: Garlic is a great spice used to add a unique flavour to the food. It helps fight heart disorders, high blood pressure, and cold and cough, says a study published in the Avicenna Journal of Phytomedicine (Refer Figure 6.20).

Fig. 6.20 *Garlic*

Ginger: Largely known for aiding in digestion, ginger is a spice that exerts many benefits like preventing cancer, boosting the appetite, and improving respiratory conditions, among others.

Horseradish: Horseradish has the ability to increase urination, reduce inflammation, and soothe the nerves. It also helps in preventing cancer, stimulating healthy digestion, and boosting the immune system due to its antioxidant compounds. According to the Michigan Medicine, horseradish has been traditionally used as a digestive stimulant and to treat worms, coughs, and sore throats.

Kala Namak or Rock Salt: A culinary salt, with unique flavors. This is the common name for the mineral 'halite'. Rock salt is a form of NaCl or the common table salt with some impurities in them. The slightly pungent smell in the salt comes from the presence of the sulphate. This salt is used as a final garnish by sprinkling on the fresh fruits and vegetables, salads and fried savories most of the time, though it is used during the cooking process in some dishes. The salt comes in the form of different hued crystals and are usually ground to a powder before used for culinary purposes.

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Mace: Mace has the ability to boost the immune system, build strong bones, reduce depression, increase sexual libido, stimulate digestion, and reduce excess gas and insomnia. It also helps keep the skin healthy, boost hair health, and increase circulation to all parts of the body (Refer Figure 6.21).

Fig. 6.21 *Mace*

Mustard Seeds: Mustard seeds are packed with organic compounds and volatile oils that can boost your overall health. They are also a wonderful source of B-complex vitamins, which are essential for the normal functioning of your organs.

Nutmeg: Nutmeg is a great source of antioxidants, vitamins, and minerals necessary for human health. It can fight fungal infections, work as an aphrodisiac, improve digestion, reduce excess gas, improve hair and skin health. It also helps prevent macular degeneration, and reduce the chances of developing cancer (Refer Figure 6.22).

Fig. 6.22 *Nutmeg*

Nigella (Kalonji/Kalo Jeera): These are tiny black seeds mostly forming a part of the Panch Foron (recipe below). Nigella is also referred to as Onion Seeds. They are mostly used in breads – like naan, tandoori rotis, parathas, and also sometimes to season stir fries and curries. In the Eastern India this is extensively used to season fish.

Red Dry Chilli: This is the hot peppers dried up, esp. the cayenne pepper type. They have different flavour then the green hot peppers are usually sizzled in oil and

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cooked up with the vegetables or meat. These dried peppers may be ground up to make Red Chili Powder.

Red Chilli/Chile Powder: This is ground up dried red chili peppers (as shown below). There are different varieties of Chili Powder available in the Indian groceries. They are made from different kind of peppers with different colours, aroma and also the spice/heat level.

The Kashmiri Chili Red Chili Powder is a mild chili powder but with very vibrant colours and usually used in kitchen. Another one which is used is the Reshmapati Red Chilli Powder; which adds a beautiful colour too.

Saffron: Saffron contains many carotenoids and boosts immune system health in a big way. It also fights infections in wounds, elevates mood, induces sleep, stimulates red blood cell formation, eliminates spasms, and modulates hormonal activity. Saffron can reduce blood pressure through the vasodilating properties of potassium found in it (Refer Figure 6.23).

Fig. 6.23 *Saffron*

Turmeric: Turmeric rich in curcumin is best known for its anti-inflammatory properties. It aids in skin care, prevents cancer, eases menstruation, and detoxifies the body.

Tamarind: Tamarind is a South Asian spice is very popular because it has the ability to improve blood vessels and artery strength, regulate digestion and excretion in a healthy way, prevent cancer, lower blood cholesterol, and build strong bones. It also helps increase blood circulation and oxygenation, regulate enzymatic activity in the body and improve the mucous membranes throughout the body as well (Refer Figure 6.24).

Fig. 6.24 *Tamarind*

Vanilla Beans: Vanilla contains a wide array of chemical compounds and volatile oils, all of which have their own health benefits. However, the studies done on vanilla beans have shown that they help control blood pressure, reduce heart rate, soothe nerves, regulate the body metabolism, induce sleep, and build strong bones.

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6.3.2 Condiments

A condiment or table sauce is a spice, sauce, or preparation (such as onions) that is added to food to impart a specific flavor, to enhance the flavor, or, in some cultures, to complement the dish. The term originally described pickled or preserved foods, but its meaning has changed over time.

Many condiments, such as mustard or ketchup, are available in single-serving packets, commonly when supplied with take-out or fast-food meals. The diner usually applies them, but they are sometimes added prior to serving, for example, in a sandwich made with ketchup, mustard or mayonnaise. Some condiments are used during cooking to add flavor or texture; barbecue sauce, compound butter, teriyaki sauce, soy sauce, and marmite and sour cream are examples.

The term condiment comes from the Latin condimentum, meaning 'spice, seasoning, sauce' and from the Latin condere, meaning 'preserve, pickle, season' (Refer Figure 6.25).

Fig. 6.25 *Various Kinds of Condiments*

Condiments were known in Ancient Rome, Ancient India, Ancient Greece and Ancient China. There is a myth that before food preservation techniques were widespread, pungent spices and condiments were used to make the food more palatable, but this claim is not supported by any evidence or historical record.

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The Romans made the condiments garum and liquamen by crushing the innards of various fish and then ferment it in salt, resulting in a liquid containing glutamic acid, suitable for enhancing the flavor of food. This process would lead to a flourishing condiment industry. Apicius, a cookbook based on fourth and fifth century cuisine, contains a section based solely on condiments.

Aioli was mentioned as a condiment in the writings of 1st-century historian Pliny the Elder.

Condiments fall into five nonexclusive categories. The first is salt, the earliest and most important condiment employed by humans. In addition to its ubiquitous presence on tables around the world, salt is often a constituent ingredient in many other condiments. It is employed on a wide range of foods, including vegetables, meats, fish, and poultry. Salt is also occasionally shaken on beer and sprinkled on watermelons. Salt is a major preservative and today is commonly found in most processed foods.

The second most common condiment is sugar or other sweeteners, such as honey or maple syrup. Sugar and honey are used directly in everything from bitter beverages, such as tea, coffee, and chocolate, to a topping for breakfast cereals. Sugar and honey are also employed in making other condiments such as jams, jellies, preserves, and marmalades, and are used extensively on bread, rolls, scones, and in pastries. Maple syrup is commonly used on pancakes.

A third category of condiments is pickled foods, which date back to the ancient world in Europe as well as Asia. Common pickled foods used as condiments today include ginger (Japan), chutney (South Asia), and cucumbers (dill, butter, and gherkins). Almost all vegetables have been pickled and used as condiments in some form. They are served whole, in slices, or diced in a relish. Sliced and diced pickles are frequently used on sandwiches.

Common condiments include salt, pepper, butter, ketchup, vinegar and dried herbs. Different cultures have their own condiments that help to enhance or improve the flavour of local dishes. What may be a very common table seasoning in one place might be completely unfamiliar to diners in other countries.

Some condiments are best suited to vegetable dishes, others to fried foods, and still others are best on fruits, pasta sauces, soups or meat dishes.

Popular condiments from around the world include:

- Mayonnaise (United States)
- Salsa (Latin America)
- Brown sauce (UK)
- Banana sauce (Philippines)
- Vegemite (Australia)
- Harissa (North Africa)
- Wasabi (Japan)

- Chutney (India)
- Sriracha (Thailand)
- Hoisin sauce (China)

NOTES

Most condiments can be purchased in the supermarket, but many condiments can be made at home from a few simple ingredients.

Check Your Progress

4. What is a spice?
5. How is flavor profile of spices defined?
6. How Anise Seed are helpful?
7. What are the benefits of garlic?
8. Briefly explain condiment.

6.4 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Antinutrients are chemicals which have been produced by plants for their defense in the biological functions and decrease the utmost utilization of nutrients especially proteins, vitamins, and minerals, hence preventing optimal misuse of the supplements display in a nourishment and decreasing the nutritive value. A few of these plant chemicals have been appeared to be pernicious to wellbeing or evidently profitable to human and creature wellbeing if consumed at suitable amounts.
2. Phytate, which is also known as inositol hexakisphosphate, is a phosphorus containing compound that binds with minerals and inhibits mineral absorption. The cause of mineral deficiency is commonly due to its low bioavailability in the diet. The presence of phytate in feeds has been associated with reduced mineral absorption due to the structure of phyate which has high density of negatively charged phosphate groups which form very stable complexes with mineral ions causing non-availability for intestinal absorption. Phytates are generally found in feed high in fibre especially in wheat bran, whole grains and legumes.
3. Saponins are auxiliary compounds that are generally known as non-volatile, surface dynamic compounds which are widely disseminated in nature, happening fundamentally in the plant kingdom. The title 'saponin' is determined from the Latin word sapo which suggests 'soap', since saponin molecules shape soap-like froths when shaken with water. They are fundamentally different atoms that are chemically referred to as triterpene and steroid glycosides. They consist of nonpolar aglycones coupled with one or more monosaccharide moieties.

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4. A spice is a seed, fruit, root, bark, or other plant substance primarily used for flavoring, coloring or preserving food. Spices are distinguished from herbs, which are the leaves, flowers, or stems of plants used for flavoring or as a garnish. Many spices have antimicrobial properties. This may explain why spices are more commonly used in warmer climates, which have more infectious diseases, and why the use of spices is prominent in meat, which is particularly susceptible to spoiling. Spices are sometimes used in medicine, religious rituals, cosmetics or perfume production.
5. Flavor Profile of Spices
   - Bitter
     - Bitter spices are believed to have an acquired taste.
     - Spices that are considered bitter are bay leaves, fenugreek seeds, horseradish, mace, cloves, cumin seeds, etc.
   - Earthy
     - These spices have an earthy flavor, which comes from geosmin.
     - Cumin and saffron are spices that have an earthy flavor.
   - Hot
     - Hot spices are those that add a strong flavor to the food and make it spicier.
     - Pepper, chilis, mustard seeds, garlic are all hot spices.
   - Sweet
     - These spices are slightly sweet in taste and can be used with sour and bitter flavors.
     - Allspice, caraway, fennel, cardamom, nutmeg, poppy seeds, sesame seeds, star anise seeds are all considered as sweet spices.
6. Anise seed is powerful spice has an antioxidant as well as a stomachic, anti-spasmodic, carminative, antiseptic, digestive, expectorant, and stimulant properties. It is a great source of vitamins and minerals like iron, potassium, copper, and manganese. These seeds help increase the circulation and oxygenation of body parts while boosting the immune system and improving the quality of your skin.
7. Garlic is a great spice used to add a unique flavour to the food. It helps fight heart disorders, high blood pressure, and cold and cough, says a study published in the Avicenna Journal of Phytomedicine.
8. A condiment or table sauce is a spice, sauce, or preparation (such as onions) that is added to food to impart a specific flavor, to enhance the flavor, or, in some cultures, to complement the dish. The term originally described pickled or preserved foods, but its meaning has changed over time.

6.5 SUMMARY

NOTES

- Antinutritional factors are compounds that cut back the nutrient utilization and/or food intake of plants or plant products used as human foods and they play a significant role in deciding the employment of plants for humans.
- Antinutrients in plant foods are accountable for injurious effects related to the absorption of nutrients and micronutrients.
- The word tannin is exceptionally ancient and reflects a traditional technology.
- Tannin is an astringent, bitter plant polyphenolic compound that either binds or precipitates proteins and various other organic compounds including amino acids and alkaloids.
- Tannin is an astringent, biting plant polyphenolic compound that either ties or accelerates proteins and different other organic compounds counting amino acids and alkaloids.
- Phytate, which is also known as inositol hexakisphosphate, is a phosphorus containing compound that binds with minerals and inhibits mineral absorption.
- The presence of phytate in feeds has been associated with reduced mineral absorption due to the structure of phyate which has high density of negatively charged phosphate groups which form very stable complexes with mineral ions causing non-availability for intestinal absorption.
- A salt shaped from oxalic corrosive is known as an Oxalate: for case, Calcium oxalate, which has been found to be widely disseminated in plants.
- Solid bonds are formed between oxalic corrosive, and different other minerals, such as Calcium, Magnesium, Sodium, and Potassium.
- The insoluble calcium oxalate has the tendency to precipitate (or set) within the Kidneys or within the Urinary tract, hence shaping sharp-edged calcium oxalate crystals when the levels are tall enough.
- Saponins are auxiliary compounds that are generally known as non-volatile, surface dynamic compounds which are widely disseminated in nature, happening fundamentally in the plant kingdom.
- Lectins are glycoproteins broadly dispersed in legumes and a few certain oil seeds (counting soybean) which possess a liking for particular sugar atoms and are characterized by their capacity to combine with carbohydrate membrane receptors.
- Protease inhibitors are broadly disseminated inside the plant kingdom, counting the seeds of most developed legumes and cereals. Protease inhibitors are the foremost commonly encountered lesson of antinutritional variables of plant origin.

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- Protease inhibitors have the capacity to restrain the action of proteolytic proteins inside the gastrointestinal tract of animals.
- Trypsin inhibitor and chymotrypsin inhibitor are protease inhibitors happening in crude vegetable seeds.
- Trypsin inhibitors that hinder the movement of the chemicals trypsin and chymotrypsin within the intestine, in this way anticipating protein digestion, are found in many plant species basically in numerous grain legumes.
- A spice is a seed, fruit, root, bark, or other plant substance primarily used for flavoring, coloring or preserving food. Spices are distinguished from herbs, which are the leaves, flowers, or stems of plants used for flavoring or as a garnish.
- Spices are sometimes used in medicine, religious rituals, cosmetics or perfume production.
- Allspice is a soothing, anti-inflammatory, and carminative spice. Its benefits include reducing cancer, improving oral health, stimulating digestion, facilitating bone growth, and boosting the immune system.
- Anise seed is a powerful spice has an antioxidant as well as a stomachic, anti-spasmodic, carminative, antiseptic, digestive, expectorant, and stimulant properties.
- Arrowroot helps in growth and development, reducing blood pressure, increasing circulation, and improving the health of the digestive system.
- Bay leaf is a very popular spice throughout the world and is praised for its ability to prevent cancer, boost immunity, reduce neural tube defects, protect oral health, skin care, and hair care.
- Black pepper is one of the most common spices in the world packed with many health benefits. It has an ability to reduce inflammation and excess gas, optimize gastrointestinal action, and regulate enzymatic reactions.
- Black pepper helps control heart rate and blood pressure and prevent cancer due to its antioxidant properties.
- Capers prevent cancer, reduce illness, boost immunity, strengthen blood vessels, reduce clotting, lower cholesterol levels, and increase circulation.
- Caraway seeds can improve digestion, reduce constipation, lower blood cholesterol levels, reduce excess gas, neutralize free radicals, and prevent various diseases like cancer.
- A condiment or table sauce is a spice, sauce, or preparation (such as onions) that is added to food to impart a specific flavor, to enhance the flavor, or, in some cultures, to complement the dish.
- Condiments fall into five nonexclusive categories. The first is salt, the earliest and most important condiment employed by humans.

- The second most common condiment is sugar or other sweeteners, such as honey or maple syrup.
- A third category of condiments is pickled foods, which date back to the ancient world in Europe as well as Asia.
- Common pickled foods used as condiments today include ginger (Japan), chutney (South Asia), and cucumbers (dill, butter, and gherkins).

NOTES

6.6 KEY WORDS

- **Antinutrients**: Antinutrients are chemicals which have been produced by plants for their defense in the biological functions and decrease the utmost utilization of nutrients especially proteins, vitamins, and minerals, hence preventing optimal misuse of the supplements display in a nourishment and decreasing the nutritive value.
- **Spice:** A spice is a seed, fruit, root, bark, or other plant substance primarily used for flavoring, coloring or preserving food.
- **Condiment**: A condiment or table sauce is a spice, sauce, or preparation (such as onions) that is added to food to impart a specific flavor, to enhance the flavor, or, in some cultures, to complement the dish.

6.7 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. What are antinutients?
2. What is the function of phytate?
3. Write a short note on lipase inhibitor.
4. What are spices?
5. How do spices add taste to food?
6. What are condiments and how are they used?

Long Answer Questions

1. Explain antinutients and their functions in detail.
2. What are haemagglutinins? Give its structure.
3. Give the structures of phytate, saponin, protease and amylase.
4. Discuss about spices in detail. Also explain how spices are used in foods and what nutritive value they support.
5. Elaborate a note on condiments.

6.8 FURTHER READINGS

NOTES

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UNIT 7 NON-NUTRIENT EFFECT OF SPECIFIC NUTRIENTS

NOTES

Structure

7.0 INTRODUCTION

Nutrients are generally conceived as dietary substances which the body requires more-or-less continuously, within a particular dosage range, to protect against developing the characteristic syndromes that occur when they are deficient. However some nutrients - when given apart from their usual food sources or at higher doses than those obtained from the diet - can also exercise pharmacologic effects, particularly on the CNS. Some, like folic acid, can promote neuronal development; others, like the neurotransmitter precursors tryptophan, choline, and histidine, can modulate the rates at which their products are synthesized; yet others, like uridine and omega-3 fatty acids, can increase the production of synaptic membrane, and thus promote synaptogenesis. In order for the nutrient to produce such effects, its plasma levels must be allowed to increase substantially when larger amounts are consumed; an unsaturated or competitive system must exist for transporting the nutrient across the blood-brain barrier; and the enzymes that convert the nutrient to its pharmacologically-active form must also be unsaturated with substrate. Nutrient mixtures chosen for their pharmacologic effects are presently used for ameliorating several conditions, and more such uses can be anticipated.

Vitamin means 'vital for life'. Vitamins and minerals are compounds necessary for the healthy functioning of our bodies. We need vitamins and minerals to help us grow, to see correctly, to form bones, muscles, skin and organs, as well as to help us battle infections. Deficiencies in certain vitamins and minerals can lead to severe problems. The best way to ensure your child receives enough vitamins and minerals for healthy growth and development is to provide a wide variety of fresh foods from the five food groups including whole grain bread and cereals, vegetables, fruit, meat, fish, poultry, eggs, nuts and legumes, and dairy products such as milk, cheese and yoghurt.

In this unit, you will study about non- nutrient effect of specific nutrients: proteins, peptides and nucleotides, conjugated linoleic acid and n-3 fatty acids, Vitamins and Minerals.

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7.1 OBJECTIVES

After going through this unit, you will be able to:

- Explain non-nutrient effect of specific nutrients
- Discuss about conjugated linoleic acid and n-3 fatty acids
- Understand what vitamins and minerals are

7.2 NON-NUTRIENT EFFECT OF SPECIFIC NUTRIENTS

A nutrient is a substance used by an organism to survive, grow, and reproduce. The requirement for dietary nutrient intake applies to animals, plants, fungi, and protists. Nutrients can be incorporated into cells for metabolic purposes or excreted by cells to create non-cellular structures, such as hair, scales, feathers, or exoskeletons. Some nutrients can be metabolically converted to smaller molecules in the process of releasing energy, such as for carbohydrates, lipids, proteins, and fermentation products (ethanol or vinegar), leading to end-products of water and carbon dioxide. All organisms require water. Essential nutrients for animals are the energy sources, some of the amino acids that are combined to create proteins, a subset of fatty acids, vitamins and certain minerals. Plants require more diverse minerals absorbed through roots, plus carbon dioxide and oxygen absorbed through leaves. Fungi live on dead or living organic matter and meet nutrient needs from their host.

Different types of organism have different essential nutrients. Ascorbic acid (vitamin C) is essential, meaning it must be consumed in sufficient amounts, to humans and some other animal species, but not to all animals and not to plants, which are able to synthesize it. Nutrients may be organic or inorganic: organic compounds include most compounds containing carbon, while all other chemicals are inorganic. Inorganic nutrients include nutrients such as iron, selenium, and zinc, while organic nutrients include, among many others, energy-providing compounds and vitamins.

Disease or stress shatters the immune capability. We can believe that a nutritional involvement could boost up the immune system with the purpose of resistance and even prevention of disease or stress. Both macronutrients and micronutrients affect the resistance against viruses, bacteria, parasites and fungi. Proteo-energetic malnutrition is a major cause of immune depression, leading to a

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modification in cellular immunity and more exclusively exhaustion in lymphocytes and change of their functions.

Major nutrients like proteins (including amino acids and nucleotides), fatty acids, beta-glucans, carrageenans, peptidoglycan and chitosan), vitamins, carotenoids and minerals are recognized to play a part, in different ways, in the immune responses of an individual (Refer Figure 7.1).

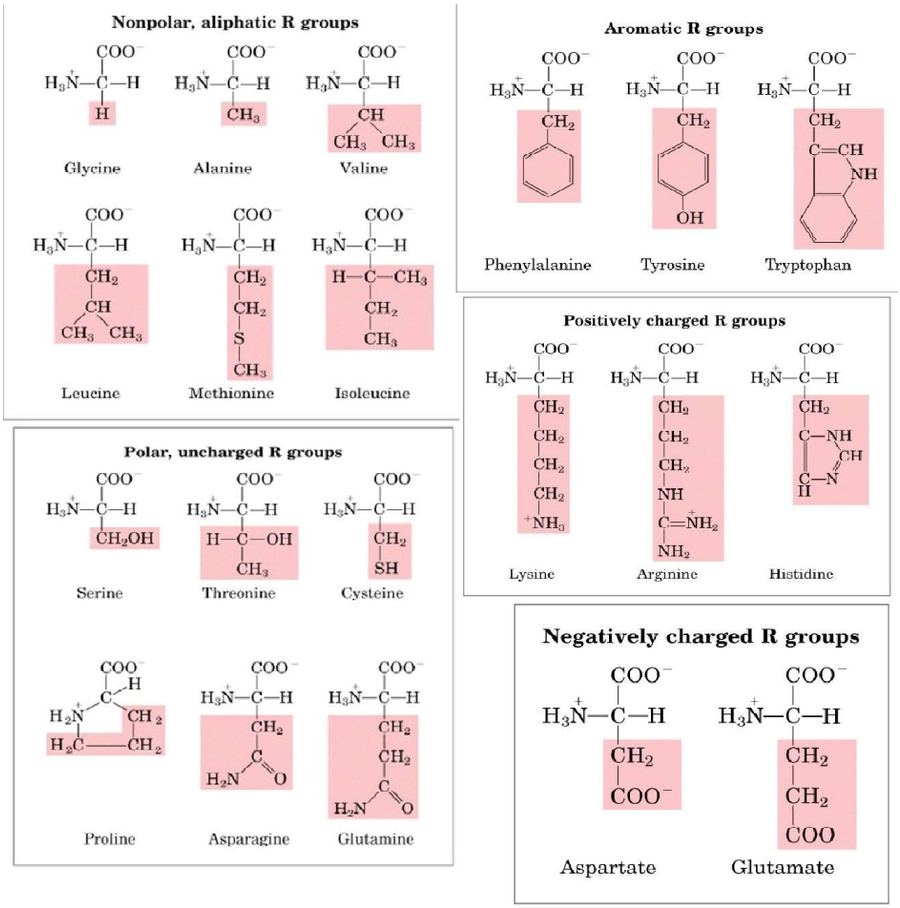

Fig. 7.1 *20 Standard Amino Acids of Proteins, Shown with their Amino And Carboxyl Groups Ionized, as they Would Occur at pH 7.0.*

Protein, Amino Acids and Nucleotides

Animals need to produce new proteins to protect themselves. The impact of distinct nutrients on protein synthesis is consequently a significant component of every facet of immunity. Proteins as such are antigenic. Animals and humans cope with this uncertainty by having immune tolerance mechanisms at the level of the intestinal mucosa. That is why, not all proteins are well thought-out to be a foreign agent that has to be eliminated. Figure 7.2 shows the single strand of DNA.

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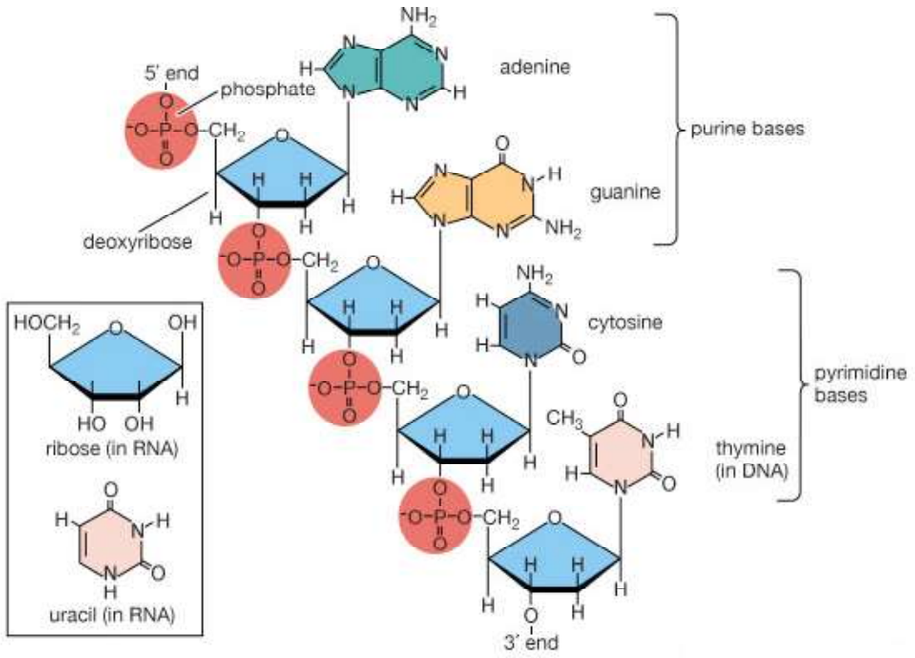

Fig. 7.2 *Single Strand of DNA*

It is found that process of a number of the vegetable macromolecule sources into macromolecule concentrates can solve the matter by eliminating many of the anti-nutritional factors they originally contain. Amino acids area unit essential elements of the cells associate degreed tissues of a functional and optimal system. Their role in immunity has been extensively studied in mammals. Many papers trot out the link between human nutrition and immunity, particularly using amino acid as a dietary supplement for patients in essential conditions.

Nucleotides area unit low-molecular-weight compounds that area unit vital for several biological processes. They are preponderantly important in new cell production as they're a part of the building blocks of nucleic acids. Nucleotides have 2 synthesis pathways, either; they are created from tiny precursors or through rescue pathway victimization merchandise from ester breakdown. Immune cells like lymphocytes, monocytes/macrophages and granulocytes likewise as viscus cells are not able to synthesize them. Associate degree exogenous supply of nucleotides not solely provides nucleotides to those cells however it conjointly accumulates energy expenses for his or her synthesis. The speed of ester generation by the living being is sort of never enough to satisfy the need at bound life stages and through times of stress and illness.

The dietary provides of nucleotides is maybe essential. Studies have shown that even if some suppressing effects are discovered within the case of polymer or polymer, all ester sources give helpful effects on growth reckoning on the viscous cell line investigated. This conjointly tends to point out that free nucleotides can be additional helpful as a result of they are additional simply obtainable. The nucleotide

nutrition together with the modulation of the innate and adaptive immune responses. Several studies in animals have shown the following results:

- Improved immune resistance and on disease resistance were visible due to nucleotide nutrition.
- Positive effect of dietary nucleotides on immune response, vaccination and disease resistance in Atlantic salmon.
- The dietary nucleotides from yeast RNA affect the immune responses and resistance of hybrid striped bass to Streptococcus infection.
- The expression of immune genes in nucleotide-supplemented diet increase particularly in case of immunoglobulin, transferrin, lysozyme and cytokine genes, etc. It is moreover imperative to reveal that nucleotides involved in the nutritional modulation of immunity as exogenous sources are mainly of yeast origin and are not same s that from the synthetic CpG OligoDeoxyNucleotides (CpG ODN) that have been identified by stimulation of type I IFN activity.

Conjugated Linoleic Acid

Conjugated Linoleic Acids (CLA) are a family of at least 28 isomers of linoleic acid found mostly in the meat and dairy products derived from ruminants. CLAs can be either cis- or trans-fats and the double bonds of CLAs are conjugated and separated by a single bond between them.

CLA is marketed as a dietary supplement on the basis of its supposed health benefits. CLA isomers are produced from the biohydrogenation of linoleic acid by rumen bacteria of animals. The isomers that contain a double bond in the trans configuration are biologically active. CLA has been shown to offer numerous health benefits with respect to cardiovascular disease, cancer, obesity, osteoporosis and the immune system.

CLA is marketed in dietary supplement form for its supposed anti-cancer benefit and as a bodybuilding aid. A 2004 review of the evidence said that while CLA seemed to benefit non-human animals, there was a lack of good evidence of human health benefits, despite the many claims made for it.

Likewise, there is insufficient evidence that CLA has a useful benefit for overweight or obese people as it has no long-term effect on body composition. CLA has shown an effect on insulin response in diabetic rats but there is no evidence of this effect in humans.

A 2017 study found CLA supplementation has been associated with increased plasma C-reactive protein concentrations and a reduction in serum adiponectin concentrations, which indicates that CLA supplements have a pro-inflammatory effect.

Food products from grass-fed ruminants are good sources of CLA, and contain much more of it than those from grain-fed animals. Eggs from chickens

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that have been fed CLA are also rich in CLA, and CLA in eggs has been shown to survive the temperatures encountered during frying. Some mushrooms, such as *Agaricus bisporus* and *Agaricus subrufescens*, are rare non-animal sources of CLA.

Fatty Acids

Fats have the highest energy density among dietary components. Fatty acids are basic chemical units of fat. The fatty acids most commonly found in primates and in primate diets have 16 and 18 carbon atoms; those found less commonly have 12, 14, 20, and 22 carbon atoms. All are straight carbon chains that have zero to six double bonds in the *cis* conformation. Fatty acids with double bonds in the *trans*conformation are rare in nature and are unlikely to have an important presence in natural foods of primates. Multiples of double bonds typically occur in series, with a double bond beginning every fourth carbon. Essential fatty acids are those which cannot be made by the body; and for primates, these include the n-3 and n-6 fatty acids (Innis, 1991).

The designations n-3 and n-6 (sometimes written ω-3 and ω-6) refer to the number of carbons from the methyl end of the fatty acyl chain to the first double bond. The fatty acid that is the building block for the n-6 series is linoleic acid, an 18-carbon fatty acid containing two double bonds, the first between the sixth and seventh carbons. The building block for the n-3 fatty acids is α-linolenic acid, an 18-carbon fatty acid with three double bonds, the first between the third and fourth carbons. A short-form designation for fatty acids lists the number of carbons, a colon, the number of double bonds, and identity of the n series, for example, C18:2 n-6 for linoleic acid. The liver and, to a lesser extent, other tissues have enzymes needed to elongate and further desaturate linoleic and α-linolenic acid to make other fatty acids in these series. However, the primates that have been studied have no enzymes that can desaturate fatty acids at the third or sixth carbon. Thus, the basic fatty acids with these double bonds are termed essential and must be consumed in the diet.

Most dietary fats of animal or vegetable origin are triacylglycerols (TAGs; formerly called triglycerides); they have three fatty acids esterified to a glycerol molecule in one of three stereochemically distinct bonding positions: sn-1, sn-2, and sn-3. To a lesser extent, phospholipids also are parts of primate diets, typically with two fatty acids esterified to a glycerol phosphate molecule and an acidic or basic adduct attached to the phosphate residue.

They are distinctive amongst the key macronutrients in this they endure digestion intact, remodelling as an example the composition of the cell membranes.

Fatty acids assist energy production for the cells. The fatty acids that comprehend the membrane phospholipids contribute to the physical and practical properties of the membrane. Fatty acids might additionally act as valency modelers of macromolecule structure, touching the position and also the role of proteins. They will additionally management organic phenomenon through effects on receptor, living thing signal transduction mechanisms or transcription issue activation, with subsequence alteration of organic phenomenon.

Fatty acids additionally play a job as precursors of PG and leukotrienes. Studies have shown that Associate in Nursing altered provide of fatty acids might have an effect on the immune responses. In mammals, many studies have incontestable roles of fatty acids in immune responses just like the modulation of T-cell signalling by non-esterified fatty acids. A group of fatty acids modify the membrane composition, particularly dynamics of transportation across the membrane.

The positive effects of Unsaturated Fatty Acids (PUFA) significantly of the n-3 series are recognized in fish and alternative animals. However, PUFA are extraordinarily vulnerable to oxidization. At the cellular level, many nutrients act in performance to thwart aerobic injury.

Vitamins and Minerals

Antioxidant vitamins and carotenoids are mainly important. The Antioxidant vitamins, carotenoids and minerals Vitamin E plays an imperative role in shielding lipid from peroxidation.

Dietary vitamin E is to a certain extent used to protect the cellular lipids (including those of the immune cells) from peroxidation. The vitamin E concentration in the immune cells is furthermore associated to its dietary intake. It is also reliant on the lipid level in the diet. Vitamin E is present in the membranes in addition to its role in fluidity and the receptor-based functioning of the immune response. There exists a positive association in nearly all immune responses investigated in relation to increasing dietary dose of vitamin E.

Ascorbic acid plays a foremost role by protecting the cells from oxidative damage. High concentrations of ascorbic acid were measured in phagocytes and lymphocytes. Ascorbic acid is absorbed by the cells and stored in the cytoplasm. A positive association between the cellular ascorbic acid concentration and the activity of phagocytes has also been recognized. It has been found that a modulation of phagocyte functions as well as ultrastructural changes distinctive of cell activation in the existence of the two vitamins.

Carotenoid pigments are potent antioxidants. They also play a key role in intercellular communication, which is vital for the harmonization of all organic activities in tissues.

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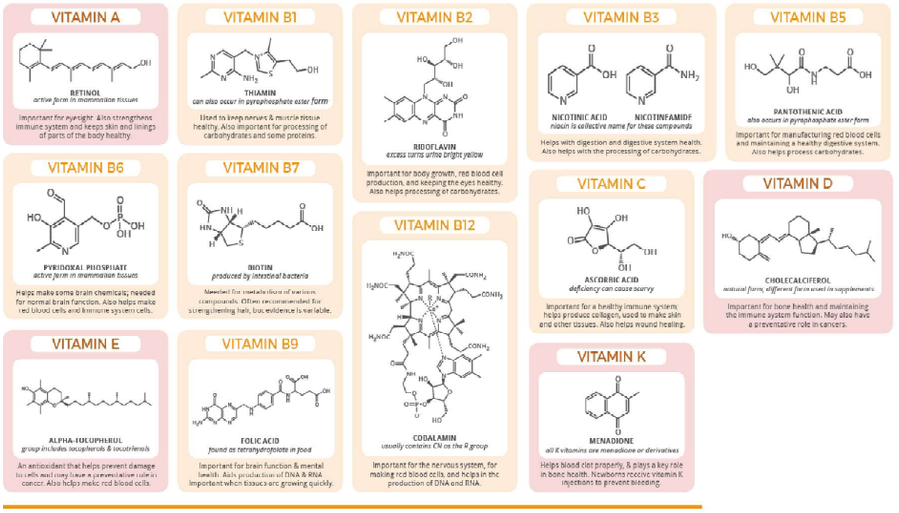

Fig. 7.3 *Chemical Structure of Vitamins*

Check Your Progress

1. Define the term nutrient.
2. What are essential nutrients for animals?
3. Give a short on CLA.
4. How is ascorbic acid helpful?

7.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. A nutrient is a substance used by an organism to survive, grow, and reproduce. The requirement for dietary nutrient intake applies to animals, plants, fungi, and protists. Nutrients can be incorporated into cells for metabolic purposes or excreted by cells to create non-cellular structures, such as hair, scales, feathers, or exoskeletons.
2. Essential nutrients for animals are the energy sources, some of the amino acids that are combined to create proteins, a subset of fatty acids, vitamins and certain minerals.
3. Conjugated Linoleic Acids (CLA) are a family of at least 28 isomers of linoleic acid found mostly in the meat and dairy products derived from ruminants. CLAs can be either cis- or trans-fats and the double bonds of CLAs are conjugated and separated by a single bond between them.
4. Ascorbic acid plays a foremost role by protecting the cells from oxidative damage. High concentrations of ascorbic acid were measured in phagocytes and lymphocytes. Ascorbic acid is absorbed by the cells and stored in the cytoplasm.

7.4 SUMMARY

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- A nutrient is a substance used by an organism to survive, grow, and reproduce. The requirement for dietary nutrient intake applies to animals, plants, fungi, and protists.
- Nutrients can be incorporated into cells for metabolic purposes or excreted by cells to create non-cellular structures, such as hair, scales, feathers, or exoskeletons.
- Some nutrients can be metabolically converted to smaller molecules in the process of releasing energy, such as for carbohydrates, lipids, proteins, and fermentation products (ethanol or vinegar), leading to end-products of water and carbon dioxide.
- Plants require more diverse minerals absorbed through roots, plus carbon dioxide and oxygen absorbed through leaves.
- Nutrients may be organic or inorganic: organic compounds include most compounds containing carbon, while all other chemicals are inorganic. Inorganic nutrients include nutrients such as iron, selenium, and zinc, while organic nutrients include, among many others, energy-providing compounds and vitamins.
- Disease or stress shatters the immune capability. We can believe that a nutritional involvement could boost up the immune system with the purpose of resistance and even prevention of disease or stress.
- Proteo-energetic malnutrition is a major cause of immune depression, leading to a modification in cellular immunity and more exclusively exhaustion in lymphocytes and change of their functions.
- Major nutrients like proteins (including amino acids and nucleotides), fatty acids, beta-glucans, carrageenans, peptidoglycan and chitosan), vitamins, carotenoids and minerals are recognized to play a part, in different ways, in the immune responses of an individual.
- Animals need to produce new proteins to protect themselves. The impact of distinct nutrients on protein synthesis is consequently a significant component of every facet of immunity.
- Animals and humans cope with this uncertainty by having immune tolerance mechanisms at the level of the intestinal mucosa.
- Nucleotides area unit low-molecular-weight compounds that area unit vital for several biological processes. They are preponderantly important in new cell production as they are a part of the building blocks of nucleic acids.
- Nucleotides have 2 synthesis pathways, either; they are created from tiny precursors or through rescue pathway victimization merchandise from ester breakdown. Immune cells like lymphocytes, monocytes/ macrophages and granulocytes likewise as viscus cells are not able to synthesize them.

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- Associate degree exogenous supply of nucleotides not solely provides nucleotides to those cells however it conjointly accumulates energy expenses for his or her synthesis.
- The speed of ester generation by the living being is sort of never enough to satisfy the need at bound life stages and through times of stress and illness.
- The dietary provides of nucleotides is maybe essential. Studies have shown that even if some suppressing effects are discovered within the case of polymer or polymer, all ester sources give helpful effects on growth reckoning on the viscous cell line investigated.
- Conjugated Linoleic Acids (CLA) are a family of at least 28 isomers of linoleic acid found mostly in the meat and dairy products derived from ruminants. CLAs can be either cis- or trans-fats and the double bonds of CLAs are conjugated and separated by a single bond between them.
- CLA is marketed as a dietary supplement on the basis of its supposed health benefits. CLA isomers are produced from the biohydrogenation of linoleic acid by rumen bacteria of animals.
- The isomers that contain a double bond in the trans configuration are biologically active. CLA has been shown to offer numerous health benefits with respect to cardiovascular disease, cancer, obesity, osteoporosis and the immune system.
- CLA is marketed in dietary supplement form for its supposed anti-cancer benefit and as a bodybuilding aid. A 2004 review of the evidence said that while CLA seemed to benefit non-human animals, there was a lack of good evidence of human health benefits, despite the many claims made for it.
- CLA has shown an effect on insulin response in diabetic rats but there is no evidence of this effect in humans.
- Food products from grass-fed ruminants are good sources of CLA, and contain much more of it than those from grain-fed animals.
- Eggs from chickens that have been fed CLA are also rich in CLA, and CLA in eggs has been shown to survive the temperatures encountered during frying.
- Fats have the highest energy density among dietary components. Fatty acids are basic chemical units of fat.
- The fatty acids most commonly found in primates and in primate diets have 16 and 18 carbon atoms; those found less commonly have 12, 14, 20, and 22 carbon atoms.
- Multiples of double bonds typically occur in series, with a double bond beginning every fourth carbon.

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- The designations n-3 and n-6 (sometimes written ω-3 and ω-6) refer to the number of carbons from the methyl end of the fatty acyl chain to the first double bond.
- The fatty acid that is the building block for the n-6 series is linoleic acid, an 18-carbon fatty acid containing two double bonds, the first between the sixth and seventh carbons.
- A short-form designation for fatty acids lists the number of carbons, a colon, the number of double bonds, and identity of the n series, for example, C18:2 n-6 for linoleic acid.
- The liver and, to a lesser extent, other tissues have enzymes needed to elongate and further desaturate linoleic and α-linolenic acid to make other fatty acids in these series.
- The primates that have been studied have no enzymes that can desaturate fatty acids at the third or sixth carbon. Thus, the basic fatty acids with these double bonds are termed essential and must be consumed in the diet.
- Antioxidant vitamins and carotenoids are mainly important. The Antioxidant vitamins, carotenoids and minerals Vitamin E plays an imperative role in shielding lipid from peroxidation.
- Dietary vitamin E is to a certain extent used to protect the cellular lipids (including those of the immune cells) from peroxidation. The vitamin E concentration in the immune cells is furthermore associated to its dietary intake. It is also reliant on the lipid level in the diet.
- Vitamin E is present in the membranes in addition to its role in fluidity and the receptor-based functioning of the immune response.
- Ascorbic acid plays a foremost role by protecting the cells from oxidative damage. High concentrations of ascorbic acid were measured in phagocytes and lymphocytes.
- Ascorbic acid is absorbed by the cells and stored in the cytoplasm. A positive association between the cellular ascorbic acid concentration and the activity of phagocytes has also been recognized.

7.5 KEY WORDS

- **Nutrient:** A nutrient is a substance used by an organism to survive, grow, and reproduce.
- **Essential fatty acids**: Essential fatty acids are those which cannot be made by the body; and for primates, these include the n-3 and n-6 fatty acids.

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7.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. Write a short note on proteins.
2. How is fatty acid helpful?
3. Give a short note on CLA.
4. What are vitamins?
5. Give the non-nutrient effect of minerals.

Long Answer Questions

1. Discuss in detail non-nutrient effects of some nutrients.
2. Explain the role of proteins, amino acids and nucleotides**.**
3. Discuss about Conjugated Linoleic Acid in detail.
4. How are fatty acids helpful? Explain.
5. Give the role of vitamins and minerals. Also give the chemical structures of some of the vitamins.

7.7 FURTHER READINGS

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BLOCK - III
PROPERTIES, STRUCTURE AND FUNCTIONS OF NUTRACEUTICALS

NOTES

UNIT 8 NUTRACEUTICALS

Structure

8.0 INTRODUCTION

Nutraceutical is a type of food substance that helps to maintain health and prevent illness. The term nutraceutical was introduced in 1989 by American medical doctor Stephen L. De Felice. Nutraceutical is sometimes used interchangeably with the terms functional food and dietary supplement, though there are distinctions. Functional foods are foods normally consumed in the diet that have scientifically assessed health benefits. Dietary supplements are ingestible preparations purposefully added to the diet to benefit health but are not necessarily derived from foods. Nutraceuticals, on the other hand, are products with biological functions that are derived only from foods. Similar to dietary supplements, they generally are consumed in a form that resembles a medicinal product, and they usually are sold Over-The-Counter (OTC). These distinctions, however, are complicated by the fact that many substances fall within all three categories. For example, beta-carotene occurs naturally in fruits, vegetables, and grains but is also manufactured and sold as a dietary supplement and as a nutraceutical.

Nutraceuticals are often sold with remarkable health claims, such as being able to slow the aging process. However, these claims are problematic and difficult to substantiate. Since foods are not used in the treatment of diseases, the claim that nutraceuticals can treat disease is deemed inappropriate for a food substance.

In this unit, you will study about nutraceuticals as science, historical perspective, classification, scope and future prospects in detail.

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8.1 OBJECTIVES

After going through this unit, you will be able to:

- Explain nutraceuticals as science
- Discuss the historical perspective of nutraceuticals
- Classify nutraceuticals
- Understand the scope and future prospects of nutraceuticals

8.2 NUTRACEUTICALS AS SCIENCE

Nutraceuticals and Functional Foods in the recent years have witnessed a tremendous increase in the interest among the consumers due to their potential of providing health benefits. In 2006, the Indian government passed Food Safety and Standard Act to integrate and streamline the many regulations covering food industry including nutraceuticals, functional foods and dietary supplements. The nutraceuticals have been defined under Clause 22 of the Food Safety and Standards Act (FSSA), 2006. Over the last 7 years, the nutraceuticals market in India has been growing rapidly. An increase in health consciousness, increasing awareness about the various types of nutraceuticals available in the market, and willingness of people to spend on health foods are the factors propelling the market.

Defining Nutraceuticals and Functional Foods

Nutraceutical, is a term combining the words 'nutrition' and 'pharmaceutical', are diet supplements that deliver a concentrated form of a presumed bioactive agent from a food, presented in a non-food matrix, and used with the purpose of enhancing health in dosages that exceed those that could be obtained from normal foods. Nutraceuticals are sold in presentations similar to drugs: pills, extracts, tablets, capsules, solutions, gels, liquors, powders, granulate, etc. The major nutraceuticals have a number of origins, being either endogenous human metabolites, dietary constituents, animal or plant constituents normally not present in the diet in therapeutic levels, or synthetic compounds; whereas Functional Foods are those that when consumed regularly exert a specific health-beneficial effect beyond their nutritional properties (i.e., a healthier status or a lower risk of disease) and this effect must be scientifically proven. The boundary between nutraceuticals and functional foods is not always clear. For example, when a phytochemical or phytochemical extract is included in a food formulation, i.e., 300 mg of extract dissolved in 1 L of juice, we have a new potential functional food. The same amount of phytochemical or phytochemical extract included in a capsule will constitute a new nutraceutical. The consumption of one litre of this functional juice would provide the same dose of bioactive compounds as one capsule of the nutraceutical.

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8.2.1 Historical Perspective of Nutraceuticals

Hippocrates (460–377 BC), the father of modern medicine, almost 2500 years back established the relation of food and its importance for the treatment of various ailments in a very classical way optimizing various benefits. Nutraceutical is composed of two words: **nutrient** and **pharmaceutical**. It is a food supplement that has a vital role in maintaining the healthy body and provides necessary supplements required for various metabolic processes to regulate body functions and thus prevents the body from diseases.

Since long time, even before the development of 'Nutrition' as a distinct scientific discipline, physicians paid close attention to the role of the daily diet in health maintenance. During the 16th, 17th and 18th centuries, many crewmen on long voyages across the Seas often died because of scurvy. The 18th century sea captains (under the direction of the British Admiralty) explored the role of various foods and food practices in maintaining the health of seamen. Some foods provided the missing vitamins B and C, whereas others reduced the antiscorbutic effects of the seamen's diet. Biomedical research during the past 20 years has revealed that diet plays an important role in the prevention and progression of many of the major chronic diseases, such as atherosclerosis and cancer.

The term 'nutraceutical' was coined in 1989 by the Foundation for Innovation in Medicine, to provide a name for this rapidly growing area of biomedical research. A nutraceutical was defined as any substance that may be considered a food or part of a food and provides medical or health benefits including the prevention and treatment of disease. Nutraceuticals may range from isolated nutrients, dietary supplements and diets to genetically engineered 'designer' foods, herbal products and processed products such as cereals, soups and beverages. Doubtlessly, many of these products possess pertinent physiological functions and valuable biological activities. The ongoing research will lead to a new generation of foods, which will certainly cause the interface between food and drug to become increasingly permeable. The present accumulated knowledge about nutraceuticals represents undoubtedly a great challenge for nutritionists, physicians, food technologists and food chemists. Public health authorities consider prevention and treatment with nutraceuticals as a powerful instrument in maintaining health and to act against nutritionally induced acute and chronic diseases, thereby promoting optimal health, longevity and quality of life.

Since ancient period the mankind made medicines from the extracts of natural materials and has been used for various purposes. In 1989 Dr. Stephen coined the term 'Nutraceuticals', which is combination of nutrition and pharmaceutical. Nutraceuticals have a come long way since a new trend in the care of companion animals emerged in the 1990s and the similar trends in the human sector as well. With the passage of the dietary supplement health and education act of 1994, the definition of nutraceuticals has been expanded to include vitamins, minerals, herbs and other botanicals, amino acids, and dietary substance for human use as a

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supplement diet. The term nutraceutical is not well accepted on global, regulatory systems while the dietary supplements are considered to be more prominent. Currently over 470 nutraceutical and functional food products are available with documented health benefits.

The success of traditional therapies is essentially due to the art of balancing the effect of one variety of food with other so that all complimented each other. Currently, the medical practitioners are considered as magic wand to cure disease. A recent study reports that 70% of patients typically consult a medical practitioner before or during the traditional therapy, indicates the disapproval of the natural therapy. However, the patients are much aware of the side effects, contraindications caused due to the chemical agents in short and long term therapy. Thus the interest to prevent medicine from every small disease came into trend and consequently led to new research on alternative therapies preferably with the help of nutritional approaches. This review gives highlights of some important facts regarding therapeutic use of nutraceuticals as the commercial and traditional remedies.

8.2.2 Classification of Nutraceuticals

The number of claimed nutraceutical substances is in the hundreds, and some of the more recognizable substances include isoflavones, tocotrienols, allyl sulphur compounds, fibre, and carotenoids. In light of a long and growing list of nutraceutical substances, organization systems are needed to allow for easier understanding and application. This is particularly true for academic instruction, as well as product formulation by food companies. Depending upon one's interest and/or background, the appropriate organizational scheme for nutraceuticals can vary. For example, cardiologists may be most interested in those nutraceutical substances that are associated with reducing the risk factors of heart disease. Specifically, their interest may lie in substances supposed to positively influence hypertension and hypercholesterolemia and to reduce free radical- or platelet-dependent thrombotic activity. Nutraceutical factors such as n-3 fatty acids, phytosterols, quercetin, and grape flavonoids would be of particular interest to them. Meanwhile, oncologists may be more interested in those substances that target anti-carcinogenic activities. These substances may be associated with augmentations of microsomal detoxification systems and antioxidant defences, or they may slow the progression of existing cancer. Thus, their interest may lie in both chemo preventive or potential adjunctive therapy. On the other hand, the nutraceutical interest of food scientists working on the development of a functional food product will not only include physiological properties, but also stability and sensory properties, as well as issues of cost efficiency. To demonstrate this point, the anti-carcinogenic triterpene-limonin is lipid-soluble and intensely bitter, somewhat limiting its commercial use as a functional food ingredient (Miller *et. al.,* 1994). However, the glucoside derivative of limonin, which shares some of the ant carcinogenic activity of limonin, is water soluble and virtually tasteless, thereby enhancing its potential use as an ingredient. Whether it is for academic instruction, clinical trial design, functional food

development, or dietary recommendations, nutraceutical factors can be organized in several ways.

There are several ways of classifying Nutraceuticals. One way is according to the food source, other on the basis of mechanism of action and third on the basis of chemical nature of the functional components.

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Classification on the Basis of Food Source

One of the broader models of organization for nutraceuticals is based upon their potential as a food source to humans. Here nutraceuticals may be separated into plant, animal, and microbial (i.e., bacteria and yeast) groups (Refer Table 8.1).

Table 8.1 *Classifcation of Nutraceuticals Grouped by Food Source*

Plants	Animal	Microbial
β-Glucan	Conjugated Linoleic Acid (CLA)	*Lactobacillus acidophilus*
Ascorbic Acid	EicosaPentaenoic Acid (EPA)	*Saccharomyces boulurdii* (Yeast)
y-Tocotrienol	DocosaHexenoic Acid (DHA)	*Bifidobacterium bifidum*
Quercetin	Spingolipids	*B.longum*
Cellulose	Choline	*B.infantis*
Lutein	Lecithin	*L. acidophilus (NCFB 1748)*
Gallic Acid	Calcium	*Streptococcus salvarius (subs. Thermophilus)*
Pectin	Ubiquinone (Coenzyme Q 10)	
Lutein	Selenium	
Gallic Acid	Zinc	
Pectin		

Classification on the Basis of Mechanism of Action

Another means of classifying nutraceuticals is by their mechanism of action. This system groups nutraceutical factors together, regardless of food source, based upon their proven or purported physiological properties (Refer Table 8.2).

Table 8.2 *Classification on the Basis of Mechanism of Action*

Anticancer	Positive Influence on Blood Lipid Profile	Antioxidant Activity	Anti-inflammatory	Osteogenetic or Bone Protective
Capsaicin	Beta-glucan	CLA	Linolenic Acid	CLA
Genestein	Tocotrienols	Ascorbic Acid	EPA	Soy Protein
Daidzein	Resveratrol	Carotene	DHA	Genestein
Tocotrienol	Tannins	Tocopherols	GLA	Daidzein
CLA	Quercetin	Tocotrienols	gamma-linolenic Acid	FOS

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Lactobacillus Acidophilus	Pectin	Ellagic acid	Capsaicin	Calcium
Sphingolipids	Guar	Glutathione Gingerol	Quercetin	Casein phosphopeptides
Liminene	Saponins	Hydroxytyrosol Polyphenols	Curcumin	Inulin
Dialllyl sulphide	Sitosterol	Luteolin		Fructo oligosaccharides
Ajoene , Equol	MUFA	Lycopene		
Tocopherol	Omega-3-Fatty Acids	Tannins		
Glycyrrhizin		Chlorogenic Acid		

Among the classes are included antioxidants, antibacterial, antihypertensive, anti-hypercholesterolemic, anti-aggregate, anti-inflammatory, anti-carcinogenic, osteoprotective, and so on. This model would be helpful to an individual who is genetically predisposed to a particular medical condition or to scientists trying to develop powerful functional foods for just such a person. This developer might consider the ingredients listed in several categories to develop a product that would reduce blood pressure, LDL cholesterol level, and inflammation.

Classification on the Basis of Chemical Nature

Another method of grouping nutraceuticals is based upon their chemical nature. This approach allows nutraceuticals to be categorized under molecular/ elemental groups. This preliminary model includes several large groups, which then provide a basis for sub classification or subgroups, and so on. One way to group nutraceuticals grossly is as shown in Table 8.3.

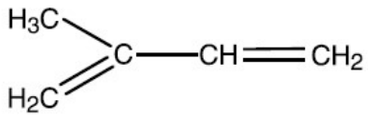
Table 8.3 *Classification of Nutraceutical Factors based on Chemical Nature*

Isoprenoid (Terpenoids)	Phenolic Compounds	Fatty Acids and Structural Lipids	Carbohydrate and Derivatives	Protein/ Amino Acid Based	Microbes	Minerals
Carotenoids	Coumarinns	n-3 PUFA	Ascorbic Acid	Amino Acids	Ca	Pro- biotics
Saponins	Tannins	CLA	Oligo saccharides	Allyl-S comps.	Se	Pre- biotics
Tocotrienols	Lignins	MUFA	Non-Starch PS	Capsaicinoid	K	
Tocopherols	Flavonols	Sphingo-lipids		Isothioc-yanates	Cu	
Simple Terpenes	Flavonones	Lecithin		Indoles	Zn	
	Isoflavones			Folate, Choline		
	Anthro-cyanins			Choline		

Isoprenoid Derivatives (Terpenoids) - Based

NOTES

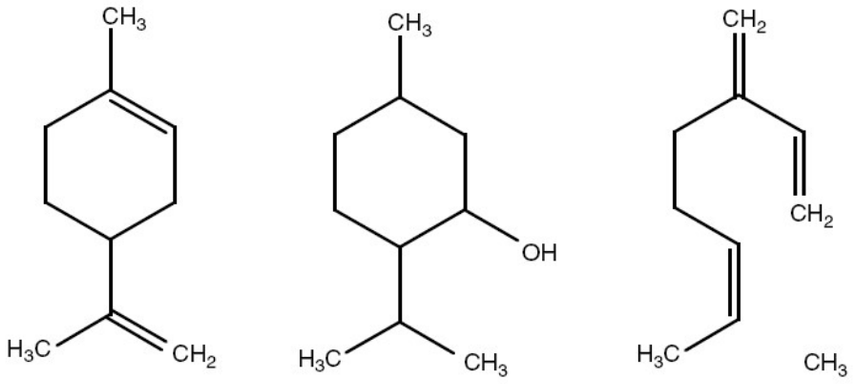
Isoprenoids and *terpenoids* are terms used to refer to the same class of molecules. These substances are one of the largest groups of plant secondary metabolites and are basis of many plant-derived nutraceuticals. Under this large umbrella are many popular nutraceutical families such as carotenoids, tocopherols, tocotrienols, and saponins. This group is also referred to as isoprenoid derivatives because the principal building block molecule is isoprene.



Isoprene

Isoprene itself is synthesized from acetyl Coenzyme A (CoA), in the well-researched mevalonic acid pathway, and the glycolysis-associated molecules pyruvate and 3-phosphoglycerate in a lesser-understood metabolic pathway (Taiz and Zeiger, 1998). This series of reactions result in the formation of monoterpenes, diterpenes, sesquiterpenes, triterpenes, etc.

Most plants contain so-called essential oils, which contain a mixture of volatile monterpenes and sesquiterpenes. Limonene is found in the essential oils of citrus peels, whereas menthol is the chief monoterpene in peppermint essential oil (Refer Figure 8.1). Two potentially nutraceutical diterpenes in coffee beans are kahweol and cafestol (Wattenberg and Lam, 1984 and Miller *et. al.*, 1991). Both of these diterpenes contain a furan ring. As discussed by Miller and colleagues (Miller *et. al*., 1994), the furan ring component might be very important in yielding some of the potential antineoplastic activity of these compounds.



Limonene Menthol Myrcene

Fig. 8.1 *Structure of Some Monoterpenes*

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Several triterpenes have been reported to have nutraceutical properties. These compounds include plant sterols; however, some of these structures may have been modified to contain fewer than 30 carbons. One of the most recognizable triterpene families is the limonoids. These triterpenes are found in citrus fruit and impart most of their bitter flavour. Limonin and nomilin are two triterpenoids that may have nutraceutical application, limonin more so than nomilin. Both of these molecules contain a furan component. In citrus fruit limonoids can also be found with an attached glucose, forming a limonoids glycoside (Hasegawa, 1989). Saponins are also triterpene derivatives, and their nutraceutical potential is attracting interest (Lee *et. al.*, 1999 and Craig, 1999).

Phenolic Compounds – Based

Like the terpenoids, phenolic compounds are also considered secondary metabolites. The base for this very diverse family of molecules is a phenol structure. From this structure, larger and interesting molecules are formed such as anthocyanins, coumarins, phenylpropamides flavonoids, tannins, and lignin. Phenolic compounds perform a variety of functions for plants including defending against herbivores and pathogens, absorbing light, attracting pollinators, reducing the growth of competitive plants, and promoting symbiotic relationships with nitrogen-fixing bacteria. The flavonoids are one of the largest classes of phenolic compounds in plants. The basic carbon structure of flavonoids contains 15 carbons and is endowed with 2 aromatic rings linked by a 3- carbon bridge.

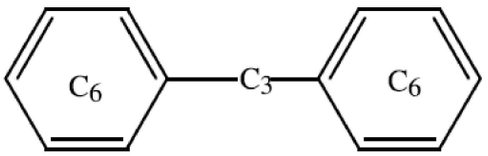

Fig. 8.2 *Basic Flavonoid Structure*

There are a couple of biosynthetic pathways that form phenolic compounds. The predominant pathways are the shikimic acid pathway and the malonic acid pathway (Taiz and Zeiger, 1998). The malonic acid pathway begins with acetyl CoA. Meanwhile, in the shikimic pathway, simple carbohydrate intermediates of glycolysis and the Pentose Phosphate Pathway (PPP) are used to form the aromatic amino acids phenylalanine and tyrosine. A third aromatic amino acid, tryptophan, is also a derivative of this pathway. As animals do not possess the shikimic acid pathway, these aromatic amino acids are diet essentials. These amino acids are considered primary metabolites or products. Thus, it is the reactions beyond the formation of these amino acids that are of greater importance to the production of secondary metabolites. Once formed, phenylalanine can be used to generate flavonoids. Figure 8.3 shows the image for some phenolic compounds.

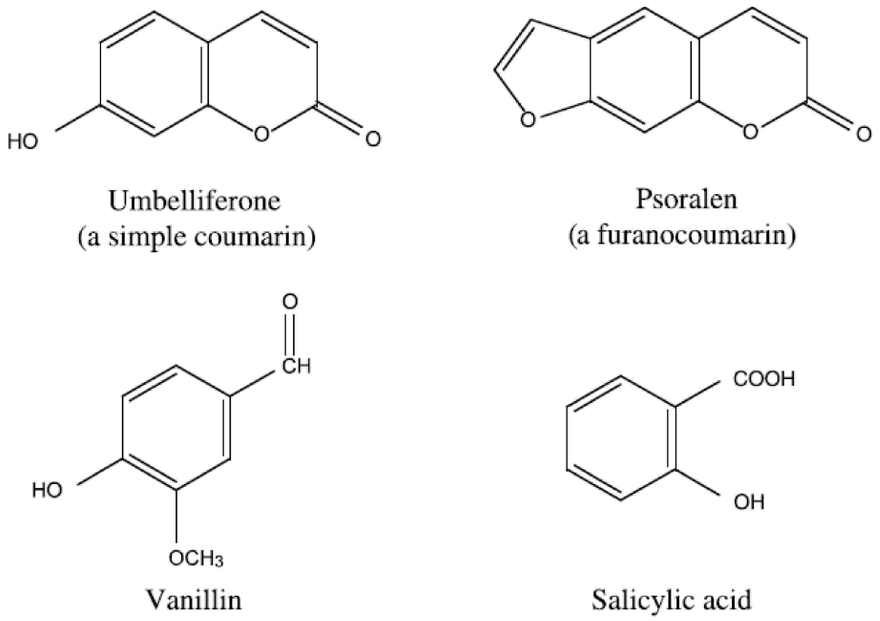

Fig. 8.3 *Some Phenolic Compounds*

Whereas the simpler phenolic compounds and lignin-building blocks result from the shikimic pathway and are phenylalanine derivatives, formation of the flavonoids requires some assistance from both the shikimic pathway and the malonic acid pathway. The majority of naturally occurring flavonoids are actually glycosides, meaning a sugar moiety is attached. The attachment of hydroxyl groups and sugars will increase the hydrophilic properties of the flavonoid molecule, while attachment of methyl esters or modified isopentyl units will increase the lipophilic character.

Carbohydrates – Based

The glucose derivative ascorbic acid (vitamin C) is perhaps one of the most recognizable nutraceutical substances and is a very popular supplement. Ascorbic acid functions as a nutraceutical compound, primarily as an antioxidant. Meanwhile, plants produce some oligosaccharides that appear to function as Prebiotics substances. Several plant polysaccharide families are not readily available energy sources for humans as they are resistant to secreted digestive enzymes. These polysaccharides are grouped together along with the phenolic polymer compound lignin to form one of the most recognizable nutraceutical families - fibres. By and large the role of fibres is structural for plants. For example, cellulose and hemicellulose are major structural polysaccharides found within plant cell walls. Beyond providing structural characteristics to plant tissue, another interesting role of certain fibers is in tissue repair after trauma, somewhat analogous to scar tissue in animals. The non-starch polysaccharides can be divided into homogeneous and heterogeneous polysaccharides, as well as into soluble and insoluble substances. Cellulose is a homogeneous non-starch polysaccharide as it consists of repeating

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units of glucose monomers. The links between the glucose monomers is β 1-4 in nature. These polysaccharides are found in plant cell walls as micro-fibril bundles. Hemicellulose is found in association with cellulose within plant-cell walls and is composed of a mixture of both straight-chain and highly branched polysaccharides containing pentoses, hexoses, and uronic acids. Pentoses such as xylans, mannans, galactans, and arabicans are found in relatively higher abundance. Hemicelluloses are somewhat different from cellulose in that they are not limited to glucose, and they are also vulnerable to hydrolysis by bacterial degradation. Another homo-polysaccharide is pectin where the repeating subunits are largely methyl-galacturonic acid units. It is a jelly-like material that acts as the cellular cement in plants. The linkage between the subunits is also β 1-4 bonds. The carboxyl groups become methylated in a seemingly random manner as fruit ripen. Chemically related to pectin is chitin. Chitin is not a plant polysaccharide but is found within the animal kingdom, although not necessarily in humans. It is a β 1-4 homo-polymer of N-acetyl-glucosamine found in shells or exoskeletons of insects and crustacean. Chitin has recently surfaced as a dietary supplement for weight loss.

Another family of polysaccharides that is worthy of discussion is GlycosAminoGlycans (GAGs). While these compounds are found in animal connective tissue, they are important to this discussion as they are potential components of functional foods. At present, GAG and chondroitin sulphate are popular nutrition supplements being used by individuals recovering from joint injuries and suffering joint inflammatory disorders. Glycosaminoglycans are often referred to as mucopolysaccharides. They are characterized by their content of amino sugars and uronic acids, which occur in combination with proteins in secretions and structures. These polysaccharides are responsible for the viscosity of body-mucus secretions and are components of extracellular amorphous ground substances surrounding collagen and elastin fibers, and cells of connective tissues and bone. Some examples of glycosaminoglycans are hyaluronic acid and chondroitin sulphate. Hyaluronic acid is a component of the ground substance found in most connective tissue including the synovial fluid of joints. It is a jelly-like substance composed of repeating disaccharides of beta-glucuronic acid and N-acetyl-D-glucosamine. Hyaluronic acid can contain several thousand disaccharide residues and is unique from the other glycosaminoglycans in that it will not interact with proteins to form proteoglycans. Chondroitin sulphate is composed of beta-glucuronic acid and N-acetylgalactosamine sulphate. This molecule has a relatively high viscosity and ability to bind water. It is the major organic component of the ground substance of cartilage and bone. Both of these polysaccharides have beta 1-3 linkage between uronic acid and acetylated amino sugars but are linked by beta 1-4 covalent bonds to other polysaccharide units. Unlike hyaluronic acid, chondroitin sulphate will bind to proteins to form proteoglycans.

Fatty Acids and Structural Lipids - Based

At present, there are several fatty acids and their derivatives that have received the interests of researchers for their functional potential. These include the

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omega -3 PUFA found in higher concentrations in plants, fish, and other marine animals, and Conjugated Linoleic Acid (CLA) produced by bacteria in the rumen of grazing animals such as cattle. The formation of CLA probably serves to help control the vitality of the released bacterial population in the rumen, whereas plants and fish use omega-3 fatty acids for their properties in membranes. Some plants also use omega-3 PUFA in a second messenger system to form jasmonic acid when plant tissue is under attack, i.e., by insect feeding. Fish oil n-3 polyunsaturated fatty acids (fish oil PUFAs) comprise EPA, DPA, and DHA. Numerous studies have shown beneficial effects in CHD, in particular a reduction in the risk of fatal CHD, and in inflammatory and immunological diseases (Oliver, 1997).

The CLA precursor, linoleic acid, and omega-3 PUFA are produced largely in plants. In processes very similar to those found in humans, plants construct fatty acids using two-carbon units derived from acetyl CoA. Some of the major fatty acids produced by plants include palmitic acid (16:0), oleic acid (18:1 omega-9), linoleic acid (18:2 omega-6), and linolenic acid (18:3 omega-3). Grazing animals ingest linoleic acid, which is then metabolized to CLA by rumen bacteria. Herbivorous fish also ingest these fatty acids when they consume algae and other seaweeds and phytoplankton. Carnivorous fish and marine animals then acquire these PUFA and derivatives from the tissue of other fish and marine life. Fish will further metabolize the PUFA to produce longer and more unsaturated fatty acids such as DHA and EPA.

Two other types of lipids in food products are structured lipids and diglycerides. Structured lipids are triglycerides that have undergone hydrolysis and re-esterification under conditions that resulted in triglycerides with new combinations of fatty acids (Babayan, 1987). For example, a mixture of medium chain triglycerides and fish oil taken through this process results in triglycerides that can contain medium-chain fatty acids and EPA, and DHA. The basic process results in the free fatty acids being randomly re-esterified to the glycerol backbones. However, the process can be manipulated to place specific fatty acids in preferred positions on the glycerol molecule. This option is quite expensive and thus has not been adopted by the food industry to any degree. However, the random re-esterification process has been used to produce structured triglycerides designed to facilitate the absorption of both medium-chain and long-chain omega-3 fatty acids (Tso *et. al.*, 1999). Diglycerides have been used as emulsifying agents in manufactured food products for many years.

Amino Acid - Based

This group include intact protein (i.e., soy protein), polypeptides, amino acids, and nitrogenous and sulphur amino acid derivatives. Nowadays, a few amino acids are also being investigated for their nutraceutical potential like arginine, ornithine, taurine, and aspartic acid. Arginine has been speculated to be cardio protective in that it is a precursor molecule for the vasodilating substance Nitric Oxide (NO) (Nittynen, 1999). Also, arginine may reduce atherogenesis. The non-

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protein amino acid taurine may also have blood pressure-lowering properties as well as antioxidant roles. However, the research in these areas is still inconclusive, and the effect of supplementation of these amino acids on other aspects of human physiology is unclear. Several plant molecules are formed via amino acids. A few of the most striking examples are isothiocyanates, indole-3-carbinol, allyl sulphur compounds, and capsaicinoids. Another nutraceutical amino acid-derived molecule is folic acid, which is believed to be cardio protective in its role of minimizing homocysteine levels (Wildman and Medeiros, 2000). Other members of this group would include the tripeptide glutathione and choline.

Microbes (Probiotics) – Based

Where the other groupings of nutraceuticals involve molecules or elements, probiotics involves intact micro-organisms. This group largely includes bacteria, and its criteria are that a microbe must be resistant to: acid conditions of the stomach, bile, and digestive enzymes normally found in the human gastrointestinal tract; able to colonize the human intestine; be safe for human consumption; and, lastly, have scientifically proven efficacy. Among the bacterial species recognized as having functional food potential are *Lactobacillus acidophilus, L. plantarum, L. casei, Bifidobacterium bifidum, B. infantis*, and *Streptococcus salvarius* subspecies *thermophilus*. Some yeasts were noted as well, including *Saccharomyces boulardii*.

Minerals – Based

Several minerals have been recognized for their nutraceutical potential and thus become components for functional food recipes. Among the most obvious is calcium with relation to bone health, colon cancer, hypertension and cardiovascular disease. Potassium has also been reported to reduce hypertension and thus improve cardiovascular health. A couple of trace minerals have also been found to have nutraceutical properties. These include copper, selenium, manganese, and zinc. Their nutraceutical potential is usually discussed in relation to antioxidation. Copper, zinc, and manganese are components of Superoxide Dismutase (SOD) enzymes, whereas selenium is a component of glutathione peroxidase. Certainly more investigation is required in the area of trace elements in light of their metabolic relationships to other nutrients and the potential for toxicity.

8.2.3 Scope and Future Prospects

The global nutraceutical industry, valued at US$ 182.6 bn in 2015, is one of the fastest growing industries today and expected to expand at a CAGR of 7.3% from 2015 to 2021.

Currently, the United States, Europe and Japan account for most (93%) of the total global nutraceutical market. The market, however, seems to have attained maturity in all the three regions. Therefore, the nutraceutical industries across the world are now turning their attention to emerging markets like India.

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Tapping India's Market Potential

The nutraceuticals industry in India is one of the rapid growing markets in the Asia-Pacific region. According to a recent report, the nutraceuticals industry in India is worth about $ 2.2 billion and is projected to grow at 20% to $6.1 billion by 2019-2020.

Why India?

The popularity and growth of this industry can be attributed to consumers' increased inclination towards health and nutrition. Over the past decade, there has been a radical change in lifestyles of Indians. Adoption of fast foods and packaged foods and sedentary lifestyle, has led to an increase in the incidences of lifestyle diseases, such as diabetes, cardiovascular diseases and obesity. As a result, Indian consumers, predominantly the higher socio-economic and upper middle class, are perceiving nutraceuticals as alternatives to prescription drugs. The usage of dietary supplements is not limited to fulfilment of the daily requirement of particular required nutrients, but consumers are also considering the functional health benefits of these supplements for prevention of diseases. Furthermore, they have been showing a keen interest in products for boosting energy and improving their physical endurance and mental alertness.

As a result, dietary supplements hold the largest share in the market. The Indian dietary supplement market is composed of over 500 participants. Vitamins and minerals supplement market is the most competitive with over 100 participants. Further, India is opening up its market to foreign players. This could lead to healthy competition in this sector.

To keep up with the growing competition, nutraceutical companies are focusing their energies in developing new product and innovative formulations and using proper advertising techniques to help consumers choose the right products.

Latest Trends in Nutraceutical Formulations in India

Changing Trends Dosage Forms

Nutraceutical ingredients have typically been positioned as natural and healthy alternatives to allopathic medicines. However, one of the primary challenges being faced by these products is the difficulty in formulating these products using the right dosage form. Besides, flavour and fragrance masking, the dosage forms also need to increase the stability of ingredients in the final product. But lately consumers are seeking more variety and benefits from delivery methods beyond those possible through traditional (tablet and capsule) technologies. As a result, the formulator needs to work far harder to cater to increasing consumer demands. As the nutraceutical industries look to carve a niche of their own and create a differentiated product, an important trend is the growth and diversity of new dosage formulations. As a result, traditional tablets and chewable are slowly being replaced by capsules, particularly liquid-filled capsules.

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Capsules: A suitable Choice for Consumers and Manufacturers

The shift toward capsule formulation is consumer driven. Consumers prefer dosage forms like capsules as they are easier to swallow. Capsules, especially liquid-filled capsules, are also considered to work faster and better. For nutraceutical companies, capsules make for an ideal formulation as it requires fewer excipients and manufacturing steps, enables faster development, and offers more formulation flexibility. In addition, capsule formulations offer brand recognition in a crowded nutraceutical products market.

Liquid Encapsulation Technology: The Future of Capsule Technologies

Capsule technologies are also advancing with designs that provide superior protection of the ingredients through moisture protection, enhancing and preserving bioavailability and stability, and offering timed or targeted release of ingredients for maximum effect. One of the hottest trends in nutraceutical industry is use of innovative formulation for capsules. Encapsulation technology has made a lot of progress allowing multiple ingredients to be encapsulated in a single capsule. The novel formulations allow nutraceutical companies to incorporate liquids, pellets, tablets and powders in capsules.

Advantages of Novel Liquid-Filled Capsules

- **Patient-Friendly Dosage form:** As mentioned earlier, liquid-filled capsules have high acceptance amongst consumers, as they perceive them as being easy and familiar dosage forms.
- **Convenience:** Clean and convenient option for many inherently liquid products in nutraceutical and dietary supplement industry, such as mineral extracts and essential oils.
- **Ideal for Lipophilic Compounds:** Nutraceutical compounds, viz. omega-3 fatty acids, phytosterols, carotenoids, have poor aqueous solubility. This is one of biggest challenges concerning nutraceutical companies, who need to invest in developing methodologies to formulate these lipid based nutraceuticals. Liquid-fill encapsulation is therefore ideal for molecules that exhibit poor aqueous solubility.
- **Protection and Taste Masking of Ingredients:** Through these multiple encapsulation offerings, the formulation can provide enhanced protection to multiple ingredients from degradation. These capsules are also ideal for taste and fragrance masking, an important consideration for some nutraceuticals like fish oils.
- **Aids Bioavailability:** Liquid encapsulation can aid in improving bio-availability of certain ingredients.

- **Product Differentiation:** These features create distinct brand differentiation in line with latest trends in health and wellness. Moreover, the products are also visually attractive—an added benefits that guarantees instant consumer appeal.
- **Brand Life-Cycle Extension:** Due to the novel and aesthetic dosage format, existing formulation can be re-introduced in a new attractive format that revitalizes the brand and helps extending the brand life.
- **Stronger Anti-Counterfeiting:** The high product differentiation also makes counterfeiting difficult.

Thus, the latest trend of capsule innovation and manufacturing technologies will undoubtedly help nutraceutical companies develop brands that boast of a differentiated dosage form that is preferred by nutritional supplement consumers.

Check Your Progress

1. What are nutraceuticals? Give any two examples.
2. Define functional foods and give examples.
3. What are the different ways in which nutraceuticals can be classified?
4. Give two examples of nutraceuticals of plant origin and animal origin each.
5. Where are limonene found?

8.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Nutraceutical, a term combining the words 'nutrition' and 'pharmaceutical', are diet supplements that deliver a concentrated form of a presumed bioactive agent from a food, presented in a non-food matrix. Example includes Vitamin C capsule, lycopene tablet.
2. Functional foods are those foods which when consumed regularly exert a specific health-beneficial effect beyond their nutritional properties (i.e., a healthier status or a lower risk of disease) and this effect must be scientifically proven. For example: fortified wheat flour, fibre enriched biscuits.
3. There are three ways of classifying Nutraceuticals. One way is according to the food source, other on the basis of mechanism of action and third on the basis of chemical nature of the functional components.
4. Nutraceuticals from plant origin: Lycopene, Ascorbic Acid
   Nutraceuticals from animal origin: Conjugated Linoleic Acid (CLA), Lecithin.
5. Limonene is found in the essential oils of citrus peels, whereas menthol is the chief monoterpene in peppermint essential oil.

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8.4 SUMMARY

- Nutraceuticals and functional foods in the recent years have witnessed a tremendous increase in the interest among the consumers due to their potential of providing health benefits.
- In 2006, the Indian government passed Food Safety and Standard Act to integrate and streamline the many regulations covering food industry including nutraceuticals, functional foods and dietary supplements.
- The nutraceuticals have been defined under Clause 22 of the Food Safety and Standards Act (FSSA), 2006.
- Over the last 7 years, the nutraceuticals market in India has been growing rapidly.
- An increase in health consciousness, increasing awareness about the various types of nutraceuticals available in the market, and willingness of people to spend on health foods are the factors propelling the market.
- Nutraceutical, is a term combining the words 'nutrition' and 'pharmaceutical', are diet supplements that deliver a concentrated form of a presumed bioactive agent from a food, presented in a non-food matrix, and used with the purpose of enhancing health in dosages that exceed those that could be obtained from normal foods.
- Nutraceuticals are sold in presentations similar to drugs: pills, extracts, tablets, capsules, solutions, gels, liquors, powders, granulate, etc.
- The same amount of phytochemical or phytochemical extract included in a capsule will constitute a new nutraceutical.
- The consumption of one litre of this functional juice would provide the same dose of bioactive compounds as one capsule of the nutraceutical.
- Hippocrates (460–377 BC), the father of modern medicine, almost 2500 years back established the relation of food and its importance for the treatment of various ailments in a very classical way optimizing various benefits.
- Nutraceutical is composed of two words: nutrient and pharmaceutical.
- Since long time, even before the development of 'Nutrition' as a distinct scientific discipline, physicians paid close attention to the role of the daily diet in health maintenance.
- During the 16th, 17th and 18th centuries, many crewmen on long voyages across the Seas often died because of scurvy.
- The 18th century sea captains (under the direction of the British Admiralty) explored the role of various foods and food practices in maintaining the health of seamen.

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- Some foods provided the missing vitamins B and C, whereas others reduced the antiscorbutic effects of the seamen's diet.
- Biomedical research during the past 20 years has revealed that diet plays an important role in the prevention and progression of many of the major chronic diseases, such as atherosclerosis and cancer.
- The term 'nutraceutical' was coined in 1989 by the Foundation for Innovation in Medicine, to provide a name for this rapidly growing area of biomedical research.
- A nutraceutical was defined as any substance that may be considered a food or part of a food and provides medical or health benefits including the prevention and treatment of disease.
- Nutraceuticals may range from isolated nutrients, dietary supplements and diets to genetically engineered 'designer' foods, herbal products and processed products, such as cereals, soups and beverages.
- The ongoing research will lead to a new generation of foods, which will certainly cause the interface between food and drug to become increasingly permeable.
- The present accumulated knowledge about nutraceuticals represents undoubtedly a great challenge for nutritionists, physicians, food technologists and food chemists.
- Public health authorities consider prevention and treatment with nutraceuticals as a powerful instrument in maintaining health and to act against nutritionally induced acute and chronic diseases, thereby promoting optimal health, longevity and quality of life.
- The number of claimed nutraceutical substances is in the hundreds, and some of the more recognizable substances include isoflavones, tocotrienols, allyl sulphur compounds, fibre, and carotenoids.
- Depending upon one's interest and/or background, the appropriate organizational scheme for nutraceuticals can vary.
- Specifically, their interest may lie in substances supposed to positively influence hypertension and hypercholesterolemia and to reduce free radical- or platelet-dependent thrombotic activity.
- Nutraceutical factors, such as n-3 fatty acids, phytosterols, quercetin, and grape flavonoids would be of particular interest to them.
- Whether it is for academic instruction, clinical trial design, functional food development, or dietary recommendations, nutraceutical factors can be organized in several ways.
- *Isoprenoids* and *terpenoids* are terms used to refer to the same class of molecules. These substances are one of the largest groups of plant secondary metabolites and are basis of many plant-derived nutraceuticals.

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- The glucose derivative ascorbic acid (vitamin C) is perhaps one of the most recognizable nutraceutical substances and is a very popular supplement.
- Ascorbic acid functions as a nutraceutical compound, primarily as an antioxidant.
- The non-starch polysaccharides can be divided into homogeneous and heterogeneous polysaccharides, as well as into soluble and insoluble substances.
- Cellulose is a homogeneous non-starch polysaccharide as it consists of repeating units of glucose monomers.
- The links between the glucose monomers is β 1-4 in nature. These polysaccharides are found in plant cell walls as micro-fibril bundles.
- Hemicellulose is found in association with cellulose within plant-cell walls and is composed of a mixture of both straight-chain and highly branched polysaccharides containing pentoses, hexoses, and uronic acids.
- Pentoses, such as xylans, mannans, galactans, and arabicans are found in relatively higher abundance.
- Hemicelluloses are somewhat different from cellulose in that they are not limited to glucose, and they are also vulnerable to hydrolysis by bacterial degradation.
- Another homo-polysaccharide is pectin where the repeating subunits are largely methyl-galacturonic acid units. It is a jelly-like material that acts as the cellular cement in plants.
- The linkage between the subunits is also β 1-4 bonds. The carboxyl groups become methylated in a seemingly random manner as fruit ripen.
- Chitin is not a plant polysaccharide but is found within the animal kingdom, although not necessarily in humans.
- At present, there are several fatty acids and their derivatives that have received the interests of researchers for their functional potential.
- The formation of CLA probably serves to help control the vitality of the released bacterial population in the rumen, whereas plants and fish use omega-3 fatty acids for their properties in membranes.
- Fish oil n-3 polyunsaturated fatty acids (fish oil PUFAs) comprise EPA, DPA, and DHA.
- Numerous studies have shown beneficial effects in CHD, in particular a reduction in the risk of fatal CHD, and in inflammatory and immunological diseases (Oliver, 1997).
- Several minerals have been recognized for their nutraceutical potential and thus become components for functional food recipes.
- Potassium has also been reported to reduce hypertension and thus improve cardiovascular health.

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- A couple of trace minerals have also been found to have nutraceutical properties.
- Copper, zinc, and manganese are components of Superoxide Dismutase (SOD) enzymes, whereas selenium is a component of glutathione peroxidase.
- Nutraceutical ingredients have typically been positioned as natural and healthy alternatives to allopathic medicines.
- As the nutraceutical industries look to carve a niche of their own and create a differentiated product, an important trend is the growth and diversity of new dosage formulations.
- The shift toward capsule formulation is consumer driven. Consumers prefer dosage forms like capsules as they are easier to swallow.
- Capsules, especially liquid-filled capsules, are also considered to work faster and better.
- For nutraceutical companies, capsules make for an ideal formulation as it requires fewer excipients and manufacturing steps, enables faster development, and offers more formulation flexibility.
- Capsule technologies are also advancing with designs that provide superior protection of the ingredients through moisture protection, enhancing and preserving bioavailability and stability, and offering timed or targeted release of ingredients for maximum effect.
- Encapsulation technology has made a lot of progress allowing multiple ingredients to be encapsulated in a single capsule.

8.5 KEY WORDS

- **Nutraceutical:** Nutraceutical, a term combining the words 'nutrition' and 'pharmaceutical', are diet supplements that deliver a concentrated form of a presumed bioactive agent from a food, presented in a non-food matrix.
- **Functional foods**: Functional foods are those foods which when consumed regularly exert a specific health-beneficial effect beyond their nutritional properties and this effect must be scientifically proven.

8.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. Define the term nutraceuticals.
2. What are functional foods?

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3. Give the classification of nutraceuticals based on food sources.
4. Draw the structure of flavonoid.
5. What is the scope and future prospects of nutraceuticals?
6. How are non-liquid filled capsules more useful?

Long Answer Questions

1. What is the difference between Nutraceuticals & Functional Foods?
2. Explain the Nutraceuticals from 'Microbial Origin' in detail.
3. How are the nutraceuticals divided on the basis of their 'Mechanism of Action'?
4. Explain the classification of nutraceuticals based on their chemical nature.
5. What is the current status of nutraceutical Industry in India? Explain in detail.

8.7 FURTHER READINGS

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UNIT 9 NUTRACEUTICAL: APPLIED ASPECTS AND RELATION WITH SCIENCE

Structure

9.0 INTRODUCTION

Nutraceutical is a food or part of a food that allegedly provides medicinal or health benefits, including the prevention and treatment of disease. A nutraceutical may be a naturally nutrient-rich or medicinally active food, such as garlic or soybeans, or it may be a specific component of a food, such as the omega-3 fish oil that can be derived from salmon and other cold-water fish. The body requires carbohydrates, fats, proteins, vitamins, and minerals to maintain healthy organs, bones, muscles, and nerves, and to produce hormones and chemicals that are necessary for the proper function of organs. Vitamins and minerals are naturally occurring substances that are essential for the growth and function of the body. Vitamins and minerals are both necessary (in small amounts) for normal chemical reactions (metabolism) in the body.

Obesity and heart attacks are major public-health problems in the United States and other countries. Therefore, most dietary recommendations are aimed at preventing these two diseases. Obesity comes over time by eating more calories than the body burns. Obesity, in turn, can contribute to the development of many diseases such as heart disease, diabetes, sleep apnea, liver disease, arthritis, high blood pressure, gout, gallstones, and certain cancers.

To lose weight or maintain a healthy weight, it helps to eat more low-energy-dense foods. Low-energy-dense foods (such as vegetables and fruits) contain few calories per unit volume of food so that one can eat a large volume of it (for example, lettuce) without taking in many calories. One should also eat less of the high-energy-dense foods such as fats, egg yolks, fried foods, sweets, and high-fat

salad dressings. Foods with a high energy density also often have high cholesterol and saturated fat content. One should also eat less of those foods that provide calories but little other nutrients, such as alcohol and many packaged snack foods. MyPyramid is an online animated program to help a person customize his/her diet by choosing proper foods and portion sizes based on the individual's age, sex, and activity level. The key objectives of the MyPyramid Plan are to help a person get the most nutrition (proteins, vitamins, and minerals) out of the recommended number of daily calories and to achieve a balance between food intake and physical activity to maintain a healthy weight.

In this unit, you will study about applied aspects of the nutraceutical science: sources of nutraceuticals, relation of nutraceutical science with other sciences: medicine, human physiology, genetics, food technology, chemistry and nutrition in detail.

9.1 OBJECTIVES

After going through this unit, you will be able to:

- Discuss about applied aspects of the nutraceutical science
- Analyse the sources of nutraceuticals
- Explain the relation of nutraceutical science with other sciences like medicine, human physiology

9.2 APPLIED ASPECTS OF THE NUTRACEUTICAL SCIENCE

A nutraceutical or 'bioceutical' is a pharmaceutical alternative which claims physiological benefits. In the US, 'nutraceuticals' are largely unregulated, as they exist in the same category as dietary supplements and food additives by the FDA, under the authority of the Federal Food, Drug, and Cosmetic Act.

Nutraceuticals are products derived from food sources that are purported to provide extra health benefits, in addition to the basic nutritional value found in foods. Depending on the jurisdiction, products may claim to prevent chronic diseases, improve health, delay the aging process, increase life expectancy, or support the structure or function of the body.

The word 'nutraceutical' is a portmanteau of the words 'nutrition' and 'pharmaceutical', coined in 1989 by Stephen L. DeFelice, founder and chairman of the Foundation of Innovation Medicine. Indians, Egyptians, Chinese, and Sumerians are just a few civilizations that have used food as medicine. 'Let food

be thy medicine'' is a common misquotation attributed to Hippocrates, who is considered by some to be the father of Western medicine.

The modern nutraceutical market began to develop in Japan during the 1980s. In contrast to the natural herbs and spices used as folk medicine for centuries throughout Asia, the nutraceutical industry has grown alongside the expansion and exploration of modern technology.

Sources of Nutraceuticals

The health-promoting products are getting more popular amongst health-conscious consumers and, thus, a large list of nutraceuticals containing phytochemicals from foods is now available in the market. For example, the carotenoid lycopene, Alliaceae (garlic, onion) extracts containing sulphur derivatives (i.e., alliin and allicin), glucosinolate extracts, and phytosterol extracts are widely commercialized products.

The most common phytochemicals found in the nutraceutical market are from three major classes of plant chemicals termed as terpenoids, phenolic metabolites, alkaloids and other nitrogen-containing plant constituents.

Terpenoids (Terpenes): The terpenes, also known as isoprenoids, are the largest class of phytonutrients in green foods, soy plants and grains. Terpenes have a unique antioxidant activity in their interaction with free radicals. Perhaps the most studied of the terpene antioxidants are the tocotrienols and tocopherols. Tocotrienols and tocopherols are terpenes that occur naturally in grains. The tocotrienols *(*α*,* δ and γ*)* and RRR- δ**-**tocopherol have been found to be effective apoptotic inducers for human breast cancer cells. The impact of a diet of fruits, vegetables and grains on reduction of cancer risk in part may be explained by the actions of terpenes.

The carotenoid terpenes have been extensively studied as antioxidants. These compounds are highly pigmented, being yellow, orange and red, are present in fruits and vegetables. Carotenoids comprise two types of molecules, carotenes and xanthophylls. Carotenes are tissue specific in their biological activity. β carotene, α-carotene and ε-carotene have vitamin A activity. As reviewed by Bendich, the carotenes, including with γ-carotene, lycopene and lutein, protect against uterine, prostate, breast, colorectal and lung cancers. They may also protect against risk of digestive tract cancer. The xanthophyll type of carotenoids offers protection to other antioxidants, and they may exhibit tissue specific protection. Zeaxanthin, cryptoxanthin and astaxanthin are members of the xanthophyll group.

Limonoids are terpenes present in citrus fruit. Limonoids appear to provide chemotherapeutic activity (Hertog *et al*., 1993). D-Limonene, the commonest monocyclic monoterpene, found within orange peel oil, inhibits pancreatic carcinogenesis. Limonoids may also provide protection to lung tissue (Dorow *et al*., 1987).

Phytosterols are another important terpene subclass. Two sterol molecules that are synthesized by plants are β-sitosterol and its glycoside. In the body, phytosterols can compete with cholesterol in the intestine for uptake, and aid in the elimination of cholesterol from the body.

Phenolic Constituents: Several groups of polyphenols such as anthocyanins, proanthocyanidins, flavones, isoflavones, resveratrol and ellagic acid are currently used in the nutraceutical industry. Reports suggest that anthocyanins, and anthocyanin-rich berries or derived extracts, exhibit a wide range of protective effects with potential benefits for human and animal health. It has been recognized that some of these effects may be related to the chemical characteristics and inherent associated antioxidant capacity of these compounds.

Proanthocyanidins are the second most abundant natural phenolics. They are widespread throughout the plant kingdom, and become part of the human diet upon consumption of fruits (grapes, apples, strawberries, etc.), beans, nuts, cocoa, and wine (Santos-Buelga and Scalbert, 2000). Proanthocyanidins have been extensively investigated (more than 2700 bibliographic entries from 1945 to early 2007) and they have mainly attracted attention due to their effects on the vascular system, including increase in the antioxidant activity of plasma, decrease of LDL-cholesterol fraction and oxidative stress-derived substances, improvement of endothelium vasodilatation, decrease of blood pressure, maintenance of endothelium function, etc. (Williamson and Manach, 2005). These activities have been mainly reported in grape seed extracts and cocoa derived products.

The most representative and investigated flavanones are the aglycones naringenin and hesperetin, and their corresponding glycosides, naringin and hesperidin, abundant in grapefruits and oranges respectively. As reported in numerous animal experiments and in vitro studies, these compounds exhibit a wide range of biological and pharmacological activities including antioxidant, hypocholesterolemic, hypoglycemic, prevention of bone losses, and anti-tumor, which indicates they may have potential beneficial effects in humans against diseases such as cardiovascular diseases, diabetes, osteoporosis, or cancer.

The major sources of catechins are grapes, berries, cocoa and green tea. Tea contains considerable amounts of gallic acid esters, such as epicatechin, epicatechin gallate and epigallocatechin gallate. Numerous studies have suggested that these components provide protective benefits by their free radical scavenging ability (Hanasaki, *et al.,* 1994) and their inhibition of eicosanoid synthesis (Moroney, *et al*., 1988), and platelet aggregation (Pace-Asciak, *et al.,* 1995). Experimental evidence in cell culture systems (Gupta *et al*., 1999) supports the possible use of tea, especially green tea, for prevention of prostate cancer. Catechin is one of the major phenolics in grapes and red wines, and it is considered to be

responsible for part of the protective effect of red wine against atherosclerotic cardiovascular disease (Kinsella, *et al*., 1993: Frankel, *et al.,* 1993: Kanner, *et al.,* 1994).

Isoflavonoids are another subclass of the phenolic phytonutrients. Soybeans are an unusually concentrated source of isoflavones, including genistein and daidzein, and soy is the major source of dietary isoflavones. The isoflavones of soy have received considerable attention owing to their binding to the estrogen receptor class of compounds, thus representing an activity of a number of phytochemicals termed phytoestrogens. Genistein inhibits the growth of most hormone-dependent and independent cancer cells in vitro, including colonic cancer cells.

Alkaloids and other Nitrogen-Containing Metabolites

Glucosinolates, which are present in cruciferous vegetables, are activators of liver detoxification enzymes. Consumption of cruciferous vegetables offers a phytochemical strategy for providing protection against carcinogenesis, mutagenesis and other forms of toxicity of electrophiles and reactive forms of oxygen. Crucifer sprouts may protect against the risk of cancer more effectively than the same quantity of mature vegetables of the same variety (Fahey, *et al*., 1997).

To conclude most nutraceuticals are natural products, being derived roughly equally from plants and animals. Some are endogenous human metabolites, while others are common dietary constituents that appear in human metabolism, for example lycopene. A number of entities exist in higher plants, and are commercially extracted from them, although some are present in insufficient levels for commercial exploitation, such as MethylSulfonylMethane (MSM) and DeHydro EpiAndrosterone (DHEA), and consequently are produced commercially by chemical synthesis. Similarly, those of animal origin may be produced by chemical synthesis, such as carnitine, creatine and the carotenoids, but may also be produced by fermentation, such as coenzyme Q10 (Co Q10) and *S*-Adenosyl Methionine (SAMe). Soy isoflavones which occur naturally in the glycoside form are available as both glycosides and their aglycones, and are invariably complex mixtures, as are green tea extracts, Grape Seed Proanthocyanidin Extract (GSPE) and pycnogenol. The *n*-3 fatty acids such as DocosaHexaenoic Acid (DHA)/ EicosaPentaenoic Acid (EPA) and linolenic acid are usually available as complex mixtures, containing supradietary levels of the active constituents, and often partial purification from the other fatty acids is not carried out. However, enrichment of these entities is increasingly being carried out using sophisticated techniques. Microalgal fermentation is also an option for production of DHA/EPA.

Table 9.1 and 9.2 summarize information on the key nutraceuticals, sources and their medicinal properties.

Table 9.1 *Nutraceuticals from Plant Origin*

Chemical Groups	Nutraceutical	Sources	Medicinal Property
Alkaloids	Quinine	Cinchona	Anti-Malarial
	Tropane Alkaloids	Solanaceous Members: Deadly Night Shade, Datura	In Treatment of Heart Ailments
	Morphine	Opium poppy	Antidepressant, Pain Killer
	Ergot Alkaloids	Fungus: Claviceps purpurea	Abortifacients
	Vincristine	Periwinkle	Antineoplastic
	Vinblastine	Periwinkle	Antineoplastic
	Coumarin,	Fenugreek	Hypoglycaemic
	Scopoletin	Fenugreek	Hypoglycaemic
	Fenugreekine	Fenugreek	Hypoglycaemic
	Trigonelliine	Fenugreek	Hypoglycaemic
Carotenoid Terpenoids/ Isoprenoids	α-Carotene	Carrots	Antioxidants, Anticarcinogenic
	β-Carotene	Fruits and Vegetables	Antioxidants
	β-Cryptoxanthin	Oranges and Tangerines	Antioxidants, Anticancer
	Lutein	Vegetables (Kale, Spinach, Watercress, Parsley)	Reduce risk of macular degeneration protect against colon cancer
	Zeaxanthin	Corn, Avocado	Protects eye from macular degeneration and cataracts
	Lycopene	Tomatoes, Pink Grapefruit, Watermelon, Guava, Papaya	Reduces Risk of Prostate Cancer in Males
Non-Carotenoid Terpenoids	Perillyl Alcohol	Cherries and Mints	Anticancer
	Saponins	Legumes (Chicks, Peas, Fenugreek, all Pulse Crops)	Reduces Cholesterol Levels in Blood
	Terpenol	Carrots	Anticancer
	Terpene	limonoids Peels and Membranes of Citrus Fruits	Anticarcinogenic
Flavonoid Polyphenolics	Anthocyanins	Stawberries, Raspberries, Cherries, Cranberries, Pomegranate, Apples, Red Grapes	Antioxidants
	Betacyanins	Beet Root	Antioxidant
	Catechins	Tea	Antioxidant
	Flavonones	Citrus Fruits	Antioxidant
	Flavones	Fruits and Vegetables	Anticancer
	Isoflavones	Soybean	Anticancer
	Hesperetin	Citrus Fruits	Antioxidant
	Naringin	Grapefruit	Reduces Cholesterol
	Rutin	Asparagus, Buckwheat and Citrus Fruits	Protects against Cardio Vascular Ailments

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	Rutin	Asparagus, Buckwheat and Citrus Fruits	Protects against Cardio Vascular Ailments
	Quercitin	Red Onions, Buckwheat, Red Grapes, Green Tea, Apple Skins	Anti-sitaminic, antioxidant
	Silymarin	Artichoke and Milk Thistle	Anti-atherosclerotic
	Tangeretin	Tangerines	Anticancer
	Tannins	Cranberries, Pomegranate, Cocoa and Tea ,	Reduces blood cholesterol
Phenolic Acids	Ellagic Acids	Strawberries and Raspberries Blueberries, Tomatoes, Grapes and Bell Peppers	Prevents colon cancer
	Chlorogenic Acids	Red and Green Bell Peppers, Legumes	Antioxidant
	p-Coumaric Acids	Legumes and Whole Seed Grains	Antioxidant, anticancer
	Phytic Acids	Seeds of Brown Rice, Whole Wheat and Oats,	Lowers blood glucose
	Ferulic Acids	Apple, Artichoke, Orange, Peanut and Pine Apple	Antioxidant, anticancer
	Vanillin	Vanilla Bean Antioxidant,	anticancer
	Cinnamic Acid	Cinnamon, Balsam Tree Resins	Antibacterial, antifungal
	Hydroxycinnamic Acid	Grapes, Blueberries and Blackberries	Antioxidant, anticancer
Non-Flavonoid Polyphenolics	Resveratrol	Grapes	Anti-microbial, anticancer, antioxidant
	Curcumin	Turmeric	Anti-inflammatory, anticancer
	Lignans	Plant Cell Walls	Reduces skin cancer
Glucosinolates	Isothiocyanates	Horseradish, Radish and Mustard	Anticancer
	Phenethyl isothiocyanate	Watercress	Anticancer
	Sulforaphene	Broccoli	Anticancer
	Indoles	Broccoli	Anticancer
	Thiosulfonates	Garlic and Onions	Anticancer, Antimicrobial, Reduces Blood Pressure and Blood Cholesterol

	Phytosterols (Plant Sterols)	Peanuts, Cashews, Almonds, Peas, Kidney Beans and Avocado	Anticancer, Blocks Cholesterol Absorption
Anthraquinones	Senna	Legumes and Pulses	Purgative
	Barbaloin	Aloe	Laxative, Anti-Helminthic
	Hypericin	St. John's Wort	Analgesic
	Capsaicin	Capsicum (Hot Peppers)	Anticancer, Anti-Inflammatory, Anti-Apoptotic
	Piperine	Black Peppers, Jalapeno Peppers	Helps in digestion
Terpenes	Menthol (Monoterpene)	Plants of Mint Family	Topical Pain Reliever and Anti-Pyretic
	Borneol (Monoterpene)	Pine Oil	Disinfectant
	Santonin (Sesquiterpene)	Wormwood	Photosensitizer
	Gossypol (Sesquiterpene)	Cotton	Contraceptive

Table 9.2 *Nutraceuticals from Animal Origin*

Nutraceutical	**Sources**	**Benefits**
Chondroitin	Bovine Trachea/Cartilage	Osteoarthritis
Methylsulfonylmethane	Meat, Milk	Joint health, Skin Health
Melatonin	Bovine Pineal Glands	Sleap Enhancer, Antioxidant
Acetyl-L-Carnitine	Brain, Liver, Kidney	Alzheimer's/Dementia
Docosahexaenoic Acid/Eicosapentaenoic Acid	Fish, Algae, Plankton,	Visual Acuity, Reduction in Blood Pressure
Conjugated Linoleic Acid	Beef, Dairy Products	Weight Loss
Astaxanthin	Fish, Shellfish	Antioxidant
Lipoic Acid	Meat, Liver	Diabetic Polyneuropathy
Glucosamine	Bovine Trachea, Shellfish	Analgesic, Anti-Inflammatory, Joint Health

Check Your Progress

1. What are nutraceuticals?
2. What are the most common phytochemicals found in the nutraceutical market?
3. Define isoflavonoids.

9.3 RELATION OF NUTRACEUTICAL SCIENCE WITH OTHER SCIENCES: NUTRACEUTICALS IN MEDICINE

With the modernised, competitive lifestyle and ever increasing stressful conditions, all types of diseases are having a field day. Allopathic cure is available for most of the disorders but it comes at a price. First, the cost of medicine is increasing day by day as for all other commodities. Second, allopathic medicines are associated with a variety of side effects. Therefore, more and more people are inclining towards lifestyle modification and use of Nutraceuticals. This helps in keeping various diseases at bay and boosting the overall health of the person.

In recent years, a new diet health paradigm is evolving which places more emphasis on the positive aspects of diet. The new lifestyle adopted by people today has changed the basic food habits of the latter. Consumption of the junk food has increased manifold leading to a number of diseases caused due to improper nutrition. Obesity is now recognized as a global issue.

Nutraceuticals for Cardiovascular Diseases

CardioVascular Disease (CVD) is now the leading cause of death globally. Nutraceuticals have the potential to significantly reduce the risk of side effects associated with chemotherapy along with reducing the global health care cost. It has been proposed that CVD can be prevented by lifestyle changes, including diet. Certain nutraceuticals affect chronic disease and are claimed to have a favourable impact on cardiovascular diseases such as heart attack/ischemia, stroke, coronary artery disease, corpulmonale, hypertension, deep vein thrombosis and/or atherosclerosis. Nutraceuticals tend to reduce circulating levels of LDL-cholesterol by modulating cholesterol production in the liver (i.e., monacolin, policosanol, red yeast, rice etc.), binding cholesterol within the intestines and/or increasing LDL-c receptor uptake in the liver (i.e., berberina, phytosterols, etc.). Excessive consumption of foods that are calorie dense, nutritionally poor, highly processed, and rapidly absorbable can lead to systemic inflammation, reduced insulin sensitivity, and a cluster of metabolic abnormalities, including obesity, hypertension, dyslipidemia, and glucose intolerance. Polyphenols found in grapes and grape derivatives, cocoa and tea are of interest in the prevention of CVD. Phenolic compounds are found in grapes and these include anthocyanins, flavanols, flavonols, stilbenes and phenolic acids. Anti-oxidants, Dietary fibres, Omega-3 poly unsaturated fatty acids, Vitamins, minerals for prevention and treatment of CVD.

Nutraceuticals against Alzheimer's Disease

Alzheimer's Disease (AD) is the most common and feared form of dementia representing circa 70% of all dementia cases and displaying a dramatic epidemics

due to the enormous growth of the aged population worldwide. Advanced age is often characterized by a decline in a large spectrum of cognitive abilities including reasoning, memory, perceptual speed, and language. Botanical extracts with anti-amyloidogenic activity, including green tea catechins, turmeric, Salvia miltiorrhiza, berry anthocyanins, and Panax ginseng have demonstrated significant efficacy in Alzheimer's Diseases. Bacopa monnieri has been demonstrated as an Ayurvedic nerve tonic, indicating a potential role in helping prevent dementia and serving as a novel memory enhancer. Also, astaxanthin-rich algal biomass, fish oil including omega-3 fatty acids (PUFAs) and krill oil have demonstrated a potential role in preserving memory, sustaining cognitive functions and preventing neuro-inflammatory, neuromotor and neurodegenerative disorders in humans and animals.

Nutraceuticals for Diabetes

Diabetes is a chronic metabolic disorder, where the body is unable to utilize carbohydrate due to absolute or relative lack of insulin, a hormone naturally produced by the â cell of the islets of langerhans in pancreas. Isoflavones are phytoestrogens have a structural/functional similarity to human estrogen and have been consumed by humans worldwide. Cinnamon tea and green tea can help people suffering with diabetes. Dietary fibers from psyllium have been used for glucose control in diabetic patients and to reduce lipid levels in hyperlipidemia Omega-3 fatty acids supplementation in type 2 diabetes has a favourable impact in lowering triglycerides and VLDL cholesterol, and reducing blood pressure and inflammatory markers.

Nutraceuticals in Parkinson's disease

Parkinson's Disease (PD) is characterized by the progressive loss of dopaminergic neurons in the substantia nigra pars compacta and other parts of the brain, leading to motor impairment, cognitive impairment, and dementia. Nutraceuticals can provide neuroprotection via a wide range of proposed mechanisms, such as scavenging of free radicals and ROS, chelation of iron, modulation of cell-signaling pathways, and inhibition of inflammation. These nutraceuticals include vitamins C, D, E, coenzyme Q10, creatine, unsaturated fatty acids, sulphur-containing compounds, polyphenols, stilbenes, and phytoestrogens. Researchers found that curcumin decreases synuclein toxicity and the generation of Reactive Oxygen Species (ROS), which are found to be involved in the programmed cell death. It also increases neuronal survival in the substantia nigra that is present in the midbrain and have a function in movement. Zingerone is an extract obtained from the ginger root.

Nutraceuticals in Hypertension

Hypertension as 'a common condition in which the force of the blood against artery walls is high enough that it may eventually cause health problems, such as heart disease'. Many natural compounds in food, as well as certain nutraceutical supplements, vitamins, antioxidants, or minerals, can mimic drugs, functioning in a

similar fashion to a specific class of antihypertensive medications. Melatonin, Hesperidin, pomegranate juice and grape seed extract have shown to be helpful in reducing BP. Flavonoids are the natural substances found to reduce stroke and enable smooth cardiac functions. Lycopene present in the carotenoid family, it helps reduce BP and oxidative stress. Use of garlic helps reduce BP and is also useful in treating patients already on drugs. Clinical studies show that seaweed lower BP within 4 weeks of administration. Sesame reduces BP, arterial stiffness, and improves oxidative defence. Beverages: Tea, coffee, and coco. These help to reduce BP and improve endothelial function.

Nutraceuticals with Anti-Inflammatory Activities

Inflammation is a process by which the body's white blood cells and substances they produce protect us from infection with foreign organisms, such as bacteria and viruses. It is the response of body tissues to injury or irritation, characterized by pain and swelling and redness and heat. Rheumatoid Arthritis (RA) is a chronic inflammatory disease characterized by elevated oxidative stress and inflammatory biomarkers28. Various studies were conducted by many researchers on fish oil, primrose oil, curcumin, fenugreek, liquorice, coriander, tomato, carrot, sweet potato, broccoli, green tea, rosemary, hazelnut, walnut, wheat germ, beet roots, cucumber fruits, spinach leaves and date for anti-inflammatory properties. During these studies, changes in inflammatory biomarkers, Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), seromucoid, fibrinogen, Tumor Necrosis Factor-á (TNF-á), prostaglandin E2, oxidative stress (malondialdehyde), antioxidant status (total antioxidant capacity, vitamin C, vitamin E, retinol, â-carotene), the level of Copper (Cu) and Zinc (Zn) and colonic microflora in response to the administration of nutraceuticals have been assessed. Studies concluded that the majority of nutraceuticals studied possess beneficial effect toward chronic inflammatory diseases, which might be due to the presence of one or more of the above-mentioned phytochemicals.

Nutraceuticals in Obesity

Obesity leads to chronic, excessive adipose tissue expansion resulting in an increase in the risk for cardiovascular disease, type 2 diabetes mellitus, and other metabolic abnormalities. Herbal stimulants, such as ephedrine, caffeine, ma huang-guarana, chitosan and green tea help in body weight loss. Capsaicin, a biologically active ingredient found in red chili peppers leads to alteration of thermogenesis and lipid metabolism-related proteins in white adipose tissue and skeletal muscle. Thereby it induces thermogenesis and fat oxidation. A blend of glucomannan, chitosan, fenugreek, G sylvestre, and vitamin C in the dietary supplement significantly reduced body weight.

Nutraceuticals in Cancer

As concluded by many researchers nutraceuticals, mostly phytochemicals derived from dietary or medicinal plants such as soya bean, garlic, ginger, tea, honey and

others, may have chemopreventive activities. Soyfoods source of isoflavones, curcumin from curry and soya isoflavones possess cancer chemopreventive properties. People using large amount of lutein-rich foods such as chicken eggs, spinach, tomatoes, oranges and leafy greens experienced the lowest incidence of colon cancer. Lycopene prevents cancer, cardiovascular disease, and gastrointestinal tract. It concentrates in the skin, testes, adrenal and prostate where it protects against cancer. Flavonoids which block the enzymes that produce estrogen reduce of estrogen induced cancers. Isoflavones are a group of phytochemicals that are predominant constituents of a soy-based diet. Among isoflavones, the three major constituents that have been shown to have remarkable influences in cancer prevention and therapy are genistein, daidzein, and glycitein.

Nutraceuticals and Gene Interactions

Since nutrient and nutraceuticals have interactions with genes, it poses the possibility that a genetic cause may explain the continued appearance of nutritional disease in the population by nutritional silencing of phenotype expression. Nutraceuticals which can influence genes are given in (Refer Table 9.3). Nutrients, which can modulate concerned genes or genetic determinants. Polyunsaturated fatty acids (w-6 and w-3), milk, calcium, vitamin, iron, ascorbate and saturated fat have been found to modulate gene expression in various experimental studies.

Table 9.3 *Nutraceuticals Having Possible Influence on Genes Nutrient Effects*

Refined Carbohydrates (Sugar and Refined Starches)	**Adverse**
Trans Fatty Acids	Adverse
Excess of Saturated Fat	Adverse
Excess of Linoleic Acid	Adverse
Omega-3 Fatty Acids	Beneficial
Monounsaturated Fatty Acids	Beneficial
Calcium, Magnesium, Potassium, Iron	Beneficial
Zinc, Copper, Selenium, Chromium Manganese, Molybdenum, Cobalt	Beneficial
Coenzyme Q10, Carnitine	Beneficial
Lead, Mercury, Arsenic, Cadmium, Fluoride	Adverse
Excess of Iron	Adverse
Vitamin A and beta-Carotene	Beneficial
Pyridoxine, Thiamin, Riboflavin, Cyanocobalamin, Nicotinic Acid, Folic Acid	Beneficial
Vitamin E	Beneficial
Vitamin C	Beneficial
Vitamin D	Beneficial
Vitamin K	Beneficial
Fibre, (Polysaccharides)	Beneficial
Amino Acids; Arginine, Taurine, Cysteine	Beneficial

Nutraceuticals in Food Processing Technology, Chemistry & Nutrition

For several years, the food industry has been interested in identifying components in foods which have health benefits to be used in the development of functional food and nutraceutical products. Examples of these ingredients include fibre, phytosterols, peptides, proteins, isoflavones, saponins, phytic acid, probiotics, prebiotics and functional enzymes. Although much progress has been made in the identification, extraction and characterisation of these ingredients, there remains a need for ready and near-market platform technologies for processing these ingredients into marketable value-added functional food and nutraceutical products.

Biotechnology in the Product Development of Nutraceuticals

Biotechnology has a key role to play in nutraceutical industry. Traditionally, the application of biotechnology techniques in the food industry focused on the major energy-providing foods, such as bread, alcohol, fermented starch, yogurt, cheese, vinegar, and others. More recently, there has been increased interest in biologically active non-nutritive ingredients (or components) from natural products or foods. Major breakthroughs have occurred and enormous progress has been made during the past decade in all aspects of genetic engineering and biotechnology. It has been given high priority by researchers in the extraction of bioactive components by enzyme /fermentation technology as well as genetic engineering technology. Changing values in society, for instance with respect to recombinant DNA, and the growing need to explore all the alternative food sources has made the use of this technique in the production of enzymes and of recombinant microorganisms attractive to the food industry.

Recombinant DNA methods are having a significant impact on enzyme technology applied to the food industry. Some of the benefits include increased enzyme production yields, improvement of thermo-stability and the ability to tolerate large pH ranges. Genetic engineering has made it possible to isolate particular genes coding for enzymes, from organisms whose genetics are unknown. Using in vitro recombination, these genes can be introduced into microorganisms that have been used in food preparation for centuries. Genetic engineering methods provide the opportunity to increase gene expression and so affect product yield. Information on how biotechnology can affect traditional methods of producing foods and beverages and the production of nutraceuticals is thus desirable.

Nanotechnology for Enhancing the Bioavailability and Delivery of Nutraceuticals

Nanotechnology is an enable technology that has the potential to revolutionize agriculture and food systems. Driven by increasing consumer demand for healthy food products, researchers have been applying tools and knowledge in nanotechnology to address the issues relevant to food and nutrition. Owing to the greater surface area of nanoparticles per mass unit, they are expected to be more

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biologically active than larger sized particles of the same chemical composition. This offers several perspectives for food applications. Nanoparticles can, for instance, be used as bioactive compounds in functional foods.

By reducing particle size, nanotechnology can contribute to improve the properties of bioactive compounds, such as delivery properties, solubility, prolonged residence time in the gastrointestinal tract and efficient absorption through cells. Omega 3 and omega 6 fatty acids, probiotics, prebiotics, vitamins and minerals have found their applications in food nanotechnology as bioactive compounds. Nanoemulsions and polymer micelles-based delivery systems show enhanced oral bioavailability and biological efficacies (that is, anti-inflammation, anti-cancer, and so on) of different phytochemicals. Nanoemulsions are a class of extremely small droplets that appear to be transparent or translucent with a bluish coloration. They are usually in the range 50 to 200 nm but much smaller than the range (from 1 to 100 ìm) for conventional emulsions. Curcumin nanoemulsions showed 85% inhibition of TPA-induced mouse ear inflammation as well as the inhibition of cyclin D1 expression, while DiBenzoylMethane (DBM) nanoemulsion showed about 3-fold increase in oral bioavailability compared to the conventional DBM emulsion. Biopolymer micelles show significantly improved water solubility/dispersibility and in vitro anti-cancer activity of phytochemicals. More research efforts are still needed for the understanding of the potential impacts of nanoencapsulated phytochemicals on the human body and environment to address the public concerns.

Spray Drying for the Production of Nutraceutical Ingredients

Contributions of spray drying to food processing applications are increasing as compared to other conventional drying methods. Spray drying has not only contributed in drying of fluids but also has played a vital role in encapsulation and microencapsulation of valuable foods and functional–nutraceutical ingredients. Microencapsulation by spray drying is a cost-effective one-step process as compared to other encapsulation methods. Encapsulation using spray drying is mainly used in the food sector to protect bioactive compounds or functional foods from light, temperature, oxidation, etc. Hence, spray drying plays an important role in encapsulation of vitamins, minerals, flavouring substances, antioxidant compounds and fatty acids.

Check Your Progress

4. What is Alzheimer's Disease (AD)?
5. How does diabetes occur?
6. What is Parkinson's Disease (PD)?

9.4 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

NOTES

1. Nutraceuticals are products derived from food sources that are purported to provide extra health benefits, in addition to the basic nutritional value found in foods. Depending on the jurisdiction, products may claim to prevent chronic diseases, improve health, delay the aging process, increase life expectancy, or support the structure or function of the body.
2. The most common phytochemicals found in the nutraceutical market are from three major classes of plant chemicals termed as terpenoids, phenolic metabolites, alkaloids and other nitrogen-containing plant constituents.
3. Isoflavonoids are another subclass of the phenolic phytonutrients. Soybeans are an unusually concentrated source of isoflavones, including genistein and daidzein, and soy is the major source of dietary isoflavones.
4. Alzheimer's Disease (AD) is the most common and feared form of dementia representing circa 70% of all dementia cases and displaying a dramatic epidemics due to the enormous growth of the aged population worldwide.
5. Diabetes is a chronic metabolic disorder, where the body is unable to utilize carbohydrate due to absolute or relative lack of insulin, a hormone naturally produced by the â cell of the islets of langerhans in pancreas.
6. Parkinson's Disease (PD) is characterized by the progressive loss of dopaminergic neurons in the substantia nigra pars compacta and other parts of the brain, leading to motor impairment, cognitive impairment, and dementia.

9.5 SUMMARY

- A nutraceutical or 'bioceutical' is a pharmaceutical alternative which claims physiological benefits.
- Nutraceuticals are products derived from food sources that are purported to provide extra health benefits, in addition to the basic nutritional value found in foods.
- Depending on the jurisdiction, products may claim to prevent chronic diseases, improve health, delay the aging process, increase life expectancy, or support the structure or function of the body.
- The health-promoting products are getting more popular amongst health-conscious consumers and, thus, a large list of nutraceuticals containing phytochemicals from foods is now available in the market.
- The most common phytochemicals found in the nutraceutical market are from three major classes of plant chemicals termed as terpenoids, phenolic metabolites, alkaloids and other nitrogen-containing plant constituents.

- The terpenes, also known as isoprenoids, are the largest class of phytonutrients in green foods, soy plants and grains.
- Terpenes have a unique antioxidant activity in their interaction with free radicals.
- The impact of a diet of fruits, vegetables and grains on reduction of cancer risk in part may be explained by the actions of terpenes.
- The carotenoid terpenes have been extensively studied as antioxidants.
- Carotenoids comprise two types of molecules, carotenes and xanthophylls. Carotenes are tissue specific in their biological activity. β-carotene, α-carotene and ε-carotene have vitamin A activity.
- The xanthophyll type of carotenoids offers protection to other antioxidants, and they may exhibit tissue specific protection.
- Zeaxanthin, cryptoxanthin and astaxanthin are members of the xanthophyll group.
- The most representative and investigated flavanones are the aglycones naringenin and hesperetin, and their corresponding glycosides, naringin and hesperidin, abundant in grapefruits and oranges respectively.
- The major sources of catechins are grapes, berries, cocoa and green tea. Tea contains considerable amounts of gallic acid esters, such as epicatechin, epicatechin gallate and epigallocatechin gallate.
- Catechin is one of the major phenolics in grapes and red wines, and it is considered to be responsible for part of the protective effect of red wine against atherosclerotic cardiovascular disease (Kinsella, *et al*., 1993: Frankel, *et al.,* 1993: Kanner, *et al.,* 1994).
- Isoflavonoids are another subclass of the phenolic phytonutrients. Soybeans are an unusually concentrated source of isoflavones, including genistein and daidzein, and soy is the major source of dietary isoflavones.
- Genistein inhibits the growth of most hormone-dependent and independent cancer cells in vitro, including colonic cancer cells.
- Glucosinolates, which are present in cruciferous vegetables, are activators of liver detoxification enzymes.
- Soy isoflavones which occur naturally in the glycoside form are available as both glycosides and their aglycones, and are invariably complex mixtures, as are green tea extracts, Grape Seed Proanthocyanidin Extract (GSPE) and pycnogenol.
- Allopathic cure is available for most of the disorders but it comes at a price.
- CardioVascular Disease (CVD) is now the leading cause of death globally.
- Nutraceuticals have the potential to significantly reduce the risk of side effects associated with chemotherapy along with reducing the global health care cost.

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- Certain nutraceuticals affect chronic disease and are claimed to have a favourable impact on cardiovascular diseases such as heart attack/ischemia, stroke, coronary artery disease, corpulmonale, hypertension, deep vein thrombosis and/or atherosclerosis.
- Excessive consumption of foods that are calorie dense, nutritionally poor, highly processed, and rapidly absorbable can lead to systemic inflammation, reduced insulin sensitivity, and a cluster of metabolic abnormalities, including obesity, hypertension, dyslipidemia, and glucose intolerance.
- Alzheimer's Disease (AD) is the most common and feared form of dementia representing circa 70% of all dementia cases and displaying a dramatic epidemics due to the enormous growth of the aged population worldwide.
- Advanced age is often characterized by a decline in a large spectrum of cognitive abilities including reasoning, memory, perceptual speed, and language.
- Botanical extracts with anti-amyloidogenic activity, including green tea catechins, turmeric, Salvia miltiorrhiza, berry anthocyanins, and Panax ginseng have demonstrated significant efficacy in Alzheimer's Diseases.
- Bacopa monnieri has been demonstrated as an Ayurvedic nerve tonic, indicating a potential role in helping prevent dementia and serving as a novel memory enhancer.
- Diabetes is a chronic metabolic disorder, where the body is unable to utilize carbohydrate due to absolute or relative lack of insulin, a hormone naturally produced by the β cell of the islets of langerhans in pancreas.
- Isoflavones are phytoestrogens have a structural/functional similarity to human estrogen and have been consumed by humans worldwide.
- Cinnamon tea and green tea can help people suffering with diabetes. Dietary fibers from psyllium have been used for glucose control in diabetic patients and to reduce lipid levels in hyperlipidemia.
- Omega-3 fatty acids supplementation in type 2 diabetes has a favourable impact in lowering triglycerides and VLDL cholesterol, and reducing blood pressure and inflammatory markers.
- Nutraceuticals can provide neuroprotection via a wide range of proposed mechanisms, such as scavenging of free radicals and ROS, chelation of iron, modulation of cell-signaling pathways, and inhibition of inflammation.
- Researchers found that curcumin decreases synuclein toxicity and the generation of Reactive Oxygen Species (ROS), which are found to be involved in the programmed cell death.
- Flavonoids are the natural substances found to reduce stroke and enable smooth cardiac functions.
- Lycopene present in the carotenoid family, it helps reduce BP and oxidative stress.

- Inflammation is a process by which the body's white blood cells and substances they produce protect us from infection with foreign organisms, such as bacteria and viruses.
- Various studies were conducted by many researchers on fish oil, primrose oil, curcumin, fenugreek, liquorice, coriander, tomato, carrot, sweet potato, broccoli, green tea, rosemary, hazelnut, walnut, wheat germ, beet roots, cucumber fruits, spinach leaves and date for anti-inflammatory properties.
- Obesity leads to chronic, excessive adipose tissue expansion resulting in an increase in the risk for cardiovascular disease, type 2 diabetes mellitus, and other metabolic abnormalities.
- Herbal stimulants, such as ephedrine, caffeine, ma huang-guarana, chitosan and green tea help in body weight loss.
- Capsaicin, a biologically active ingredient found in red chili peppers leads to alteration of thermogenesis and lipid metabolism-related proteins in white adipose tissue and skeletal muscle.
- Since nutrient and nutraceuticals have interactions with genes, it poses the possibility that a genetic cause may explain the continued appearance of nutritional disease in the population by nutritional silencing of phenotype expression.
- Traditionally, the application of biotechnology techniques in the food industry focused on the major energy-providing foods, such as bread, alcohol, fermented starch, yogurt, cheese, vinegar, and others.
- Changing values in society, for instance with respect to recombinant DNA, and the growing need to explore all the alternative food sources has made the use of this technique in the production of enzymes and of recombinant microorganisms attractive to the food industry.
- Recombinant DNA methods are having a significant impact on enzyme technology applied to the food industry.
- Genetic engineering has made it possible to isolate particular genes coding for enzymes, from organisms whose genetics are unknown.
- Genetic engineering methods provide the opportunity to increase gene expression and so affect product yield.
- Information on how biotechnology can affect traditional methods of producing foods and beverages and the production of nutraceuticals is thus desirable.

9.6 KEY WORDS

- **Nutraceutical:** A nutraceutical or 'bioceutical' is a pharmaceutical alternative which claims physiological benefits.

- **Terpenes**: The terpenes, also known as isoprenoids, are the largest class of phytonutrients in green foods, soy plants and grains.

9.7 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. What is nutraceuticals?
2. Give the sources of nutraceuticals.
3. Write in brief about alkaloids and other nitrogen-containing metabolites.
4. 'Nutraceuticals against Alzheimer's Disease'. Explain.
5. How is nutraceuticals used with anti-inflammatory activities?

Long Answer Questions

1. Write in detail about the applied aspects of the nutraceutical science.
2. What are the sources of nutraceuticals? Discuss in detail.
3. Explain the relation of nutraceutical science with other sciences.
4. How is nutraceuticals used in medicine, human physiology, genetics, food technology, chemistry and nutrition? Explain.

9.8 FURTHER READINGS

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NOTES

UNIT 10 NUTRACEUTICALS: PROPERTIES, STRUCTURE AND FUNCTIONS

Structure

10.0 INTRODUCTION

Nutraceuticals is a broad umbrella term that is used to describe any product derived from food sources with extra health benefits in addition to the basic nutritional value found in foods. They can be considered non-specific biological therapies used to promote general well-being, control symptoms and prevent malignant processes. The term 'nutraceutical' combines two words – 'nutrient' and 'pharmaceutical'. The name was coined in 1989 by Stephen DeFelice, founder and chairman of the Foundation for Innovation in Medicine, an American organization located in Cranford, New Jersey. The philosophy behind nutraceuticals is to focus on prevention, according to the saying by a Greek physician Hippocrates (known as the father of medicine) who said 'let food be your medicine'. Their role in human nutrition is one of the most important areas of investigation, with wide-raging implications for consumers, health-care providers, regulators, food producers and distributors.

The definition of nutraceuticals and related products generally depends on the source. They can be classified on the basis of their natural sources, pharmacological conditions, as well as chemical constitution of the products. Most often they are grouped in the following categories: dietary supplements, functional food, medicinal food, farmaceuticals. A dietary supplement represents a product that contains nutrients derived from food products, and is often concentrated in liquid, capsule, powder or pill form. Although dietary supplements are regulated by the FDA as foods, their regulation differs from drugs and other foods.

According to their generally accepted definition, functional food is a category which includes whole foods and fortified, enriched or enhanced dietary components that may reduce the risk of chronic disease and provide a health-benefit beyond

the traditional nutrients it contains. Medical food is formulated to be consumed or administered internally, under the supervision of a qualified physician. Its intended use is a specific dietary management of a disease or condition for which distinctive nutritional requirements are established by the medical evaluation.

Farmaceuticals are medically valuable components produced from modified agricultural crops or animals. The term is a combining of the words 'farm' and 'pharmaceuticals'. Proponents of this concept are convinced that using crops as pharmaceutical factories is much more cost effective than conventional methods, with higher revenue for agricultural producers.

In this unit, you will study about the properties, structure and functions of various nutraceuticals, Glucosamine, Octacosanol, Lycopene, Carnitine, Melatonin and Ornithine alpha ketoglutarate and the use of proanthocyanidins, grape products, flax seed oil as Nutraceuticals in detail.

10.1 OBJECTIVES

After going through this unit, you will be able to:

- Discuss the properties, structure and functions of various nutraceuticals
- Explain the use of proanthocyanidins, grape products, flax seed oil as nutraceuticals

10.2 PROPERTIES, STRUCTURE AND FUNCTIONS OF NUTRACEUTICALS

Glucosamine

Structure and Properties

Glucosamine is an amino monosaccharide, consisting of glucose and the amino acid glutamic acid. It is found naturally in the body and is present in almost all human tissue, especially in cartilage, tendons and ligament tissues. It is a precursor of the disaccharide units of articular cartilage GlycoAminoGlycan (GAG), which forms most of the cartilage tissue. The sulphate, hydrochloride and N-acetyl forms are usually used for therapeutic purposes.

Glucosamine is not found in significant amounts in the usual diet and must be synthesised by the body. This ability declines with age and predisposes the body to degenerative joint disease or arthritis.

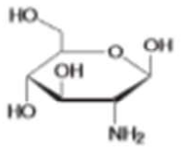

Fig. 10.1 *The Structure of Glucosamine*

NOTES

Therapeutic Areas: Joint, skin and animal health.

Recommended Oral Dose: 1500 mg/day.

Formulations Available: Tablet, capsule, patch, gel, effervescent tablet, sustained release tablet.

Lycopene

Structure and Properties

Lycopene is a natural red pigment synthesised by plants and microorganisms, but not by animals. It is found in red fruits and vegetables, particularly the tomato, and is one of over 600 carotenoids found in nature which function as pigments in photosynthesis and in photoprotection. Of these, about 24 are present in foods. Examples include β-carotene found in carrots, broccoli and other green-leafed vegetables and lutein found in spinach, peas and watercress. Unlike many of the other carotenoids, however, lycopene is not a precursor of vitamin A.

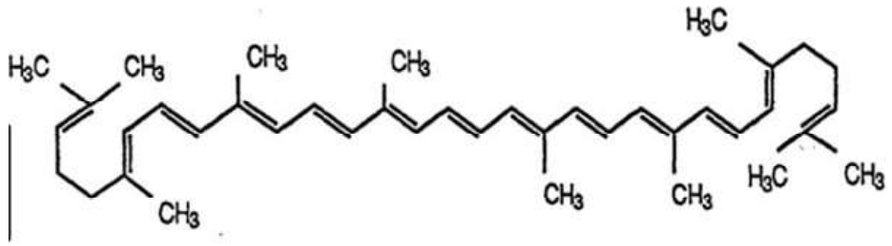

Fig. 10.2 *The Structure of Lycopene*

As humans are unable to synthesise carotenoids such as lycopene, they must be obtained from dietary intake. One group has estimated the processed tomato products such as tomato ketchup, tomato paste and tomato juice are all good sources of lycopene and, unlike some other nutrients, lycopene is not lost through cooking or food processing. Indeed, the lycopene bioavailability increases with heat processing and therefore tomato-based products are a better source than raw tomatoes (Refer Table 10.1). Studies have shown that heat processing causes isomerisation of the ingested trans-lycopene to the cis-form, which may be responsible for the increased absorption.

Therapeutic Areas: Cardiovascular and respiratory health, cancer prevention (antioxidant).

Recommended Dose: 10–40 mg/day.

Formulations Available: Tablet, capsule, oral gel.

Melatonin

Structure and Properties

Melatonin is the primary hormone secreted by the pineal gland. It is biosynthesised from the amino acid trytophan, via the intermediate serotonin. This biosynthesis

and the subsequent release of melatonin is usually inhibited by exposure to light and stimulated by darkness, via a multi synaptic neural pathway connecting the pineal gland to the retina. However, the 24-hour cycle (or circadian rhythm) of melatonin secretion is observed even when subjects are kept in darkness, so it is thought that light adjusts this rhythm rather than primarily causing it. Melatonin secretion usually starts as soon as darkness falls and usually peaks between 2 and 4 am.

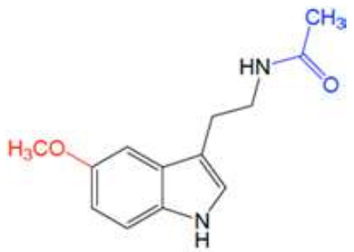

Fig. 10.3 *The Structure of Melatonin*

The amount of melatonin produced varies with age. Babies secrete low levels, but from the age of about three months, melatonin concentrations begin to increase, reaching a maximum between one and three years of age. Young adults secrete 5–25 μg of melatonin daily and this decreases markedly with advancing age.

As it is a hormone, melatonin has been called a drug, however it is also a nutrient. The consumption of plant materials containing high levels of melatonin could alter serum concentrations. Melatonin has been identified in bananas, tomatoes, cucumbers and beetroots, but unrealistically large amounts of these foods would have to be eaten to achieve pharmacological doses.

Therapeutic Areas: Cardiovascular health, cancer prevention, sport enhancement, sleep improvement, and bone health (antioxidant).

Recommended Dose: 0.3–25 mg/day.

Formulations Available: Tablet, patch, liquid.

Carnitine

Structure and Properties

Carnitine is an essential cellular component, synthesised from lysine and methionine in the liver and kidney, from where it is released into the systemic circulation, and is also synthesised in the brain. Carnitine exists in two isomeric forms, the D- and L-forms, which have different biochemical and pharmacological properties. Naturally occurring carnitine is almost always the L-isomer, whereas the D-isomer is usually obtained from chemical synthesis. The L-isomer is a substrate for carnitine-acetyltransferase and is the only isomer with biological activity, but the D-isomer acts as a competitive inhibitor, interfering with fatty acid oxidation and energy production.

Some people do not excrete the D-isomer efficiently and it has also been reported that administration of the D-isomer causes a depletion of L-carnitine in the heart muscle, leading to abnormalities.

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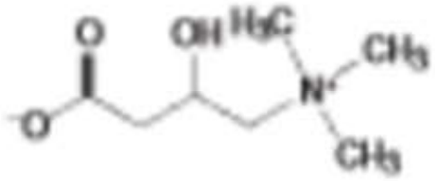

Fig. 10.4 *The Structure of Carnitine*

The main function of carnitine is in fatty acid metabolism. The biochemical reactions of this nutrient are based on the reversible reaction between carnitine and long-chain fatty acyl groups:

Carnitine + Acyl-CoA → Acyl-L-carnitine + Coenzyme A

Carnitine is therefore involved with many coenzyme A-dependent pathways.

Therapeutic areas: Sport enhancement, cardiovascular and bone health, weight optimisation, veterinary health

Recommended dose: 2–4 g/day

Formulations available: Tablet

Octacosanol/ Policosanol

Structure and Properties

Octacosanol is a 28-carbon aliphatic primary alcohol (CH_3 (CH_2)26CH_2OH), which is present in the superficial waxy layers of fruit, leaves and epidermis of many plants, as well as whole grains. The main commercial source is a by-product from the sugarcane industry, but it is also found in the leaves of alfalfa and wheat, in wheat germ and also in various animal sources. It is also a component of paraffin. As only very small amounts are available in the diet, to gain any health benefits from octacosanol it must be ingested as a supplement. Most studies assessing these benefits have been carried out using either a wheatgerm oil extract or policosanol, which is a natural mixture of primary alcohols purified from sugarcane wax, whose main component is octacosanol. Both wheatgerm extract and policosanol are reported to contain 8% hexacosanol, 67% octacosanol, 12% triacosanol and 13% other long-chain alcohols.

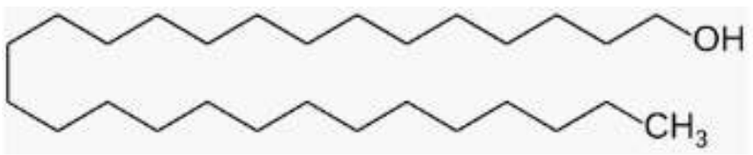

Fig. 10.5 *The Structure of Octacosanol*

There is limited data available in this area.

Therapeutic Areas: Cardiovascular health, sport enhancement.

Recommended Dose: 100 mg/day.

Formulations Available: Tablet, capsule.

NOTES

Flaxseed/ α Linolenic Acid

Structure and Properties

Flaxseed, also known as linseed, is produced from the flax plant (*Linum usitatissimum*), and has traditionally been used for a number of medical and non-medical applications. Over recent years flaxseed applications have been 'rediscovered' in the area of health and are often promoted by producers.

Flaxseed oil contains more than 50% ALA, which is an essential n-3 fatty acid. Other sources of ALA include candlenut, hemp seed, pumpkin seed, canola, walnut and soybean. Because ALA is an essential fatty acid humans need to make sure there is enough in the diet. Health recommendations to replace saturated fats with unsaturated fats have often resulted in replacement by n-6 rather than n-3 PUFAs. This has led to the modern, Western diet including far more n-6 fatty acids than n-3, in a ratio of approximately 20–30:1. Ideally the ratio should be almost equal. Moreover, fish consumption, which was a source of n-3 oils, has decreased in recent years. Due to modern food industry and agricultural methods, the n-3 content of many foods, including meat, fish, eggs and vegetables is much lower than it used to be. As a result many people are deficient in the n3 essential fatty acid ALA.

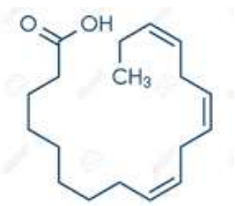

Fig. 10.6 *The Structure of α Linolenic Acid (ALA)*

Both n-6 and n-3 fatty acids are precursors of longer chain eicosanoids, such as prostaglandins, thromboxanes and leukotrienes.

Therapeutic Areas: Cancer prevention, respiratory health (antioxidant).

Recommended Dose: 1–2 g/day.

Formulations Available: Soft capsule.

Resveratrol

Structure and Properties

Resveratrol has been identified in the leaves, skins and petals of *Vitis vinifera*, and also in wines and grape juice, but is also in other foods, such as peanut butter.

NOTES

In grape products, levels are higher after infection of the vine with Botrytis cinerea, and in red wines manufactured with extended time in contact with the skins. In addition to resveratrol, a number of closely related stilbene analogues are also present.

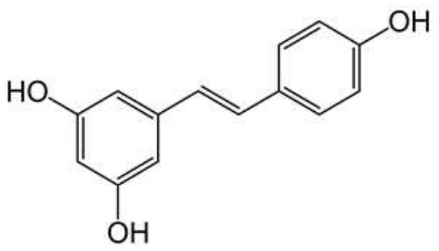

Fig. 10.7 *The Structure of Resveratrol*

A number of degradation products have been identified. After oral administration of 25 mg resveratrol to humans, the highest plasma concentrations were detected after 30 minutes, which returned to baseline after 2 hours. Most work has been carried out in rats, and it appears to be well absorbed after oral administration; plasma values peaked at about 60 minutes.

Therapeutic Areas: Cardiovascular health, cancer prevention, women's health (antioxidant and weakly oestrogenic).

Recommended Dose: 15–200 mg/day.

Formulations Available: Tablet, capsule.

Grape Seed Proanthocyanidin Extract

Structure and Properties

Proanthocyanidins occur naturally in many fruits, vegetables, nuts, seeds, flowers and bark. It is thought that protection from diseases results from the increase of antioxidants in the body. Grape Seed Proanthocyanidin Extract (GSPE) contains proanthocyanidins based on either catechin or epicatechin. The monomers join together to form dimers, trimers and other oligomers, and many different structures are formed due to changes in stereochemistry. Dimeric procyanidins have been classified as procyanidins B1, B2, B3 and B4 depending on the configuration of catechin and epicatechin subunits. A number of these catechin derivatives are present as their gallates in addition to the free form.

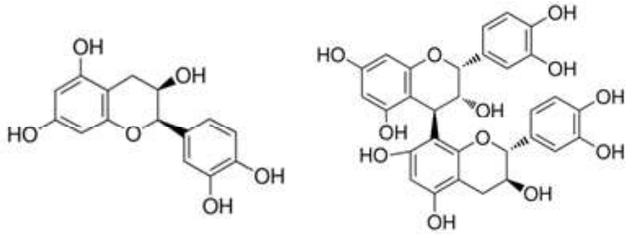

Fig. 10.8 *The Structures of Epicatechin and Procyanidin*

The proanthocyanidins are poorly absorbed in the small intestine, and it is thought that ingestion results in metabolism by colonic bacteria. Hydroxyphenyl Propionic acid has been identified as the major metabolite.

Therapeutic Areas: Cardiovascular and skin health (antioxidant).

Recommended Oral Dose: 1500 mg/day.

Formulations Available: Tablet, capsule, patch, gel, effervescent tablet, sustained release tablet.

Check Your Progress

1. What is glucosamine?
2. Write in brief about lycopene.
3. Define carnitine, and explain briefly.
4. What is octacosanol.

10.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Glucosamine is an amino monosaccharide, consisting of glucose and the amino acid glutamic acid. It is found naturally in the body and is present in almost all human tissue, especially in cartilage, tendons and ligament tissues. It is a precursor of the disaccharide units of articular cartilage GlycoAminoGlycan (GAG), which forms most of the cartilage tissue. The sulphate, hydrochloride and N-acetyl forms are usually used for therapeutic purposes.
2. Lycopene is a natural red pigment synthesised by plants and microorganisms, but not by animals. It is found in red fruits and vegetables, particularly the tomato, and is one of over 600 carotenoids found in nature which function as pigments in photosynthesis and in photoprotection. Of these, about 24 are present in foods. Examples include β-carotene found in carrots, broccoli and other green-leafed vegetables and lutein found in spinach, peas and watercress. Unlike many of the other carotenoids, however, lycopene is not a precursor of vitamin A.
3. Carnitine is an essential cellular component, synthesised from lysine and methionine in the liver and kidney, from where it is released into the systemic circulation, and is also synthesised in the brain. Carnitine exists in two isomeric forms, the D- and L-forms, which have different biochemical and pharmacological properties. Naturally occurring carnitine is almost always the L-isomer, whereas the D-isomer is usually obtained from chemical synthesis. The L-isomer is a substrate for carnitine-acetyltransferase and is the only isomer with biological activity, but the D-isomer acts as a competitive inhibitor, interfering with fatty acid oxidation and energy production.

NOTES

4. Octacosanol is a 28-carbon aliphatic primary alcohol ($CH_3(CH_2)26CH_2OH$), which is present in the superficial waxy layers of fruit, leaves and epidermis of many plants, as well as whole grains. The main commercial source is a by-product from the sugarcane industry, but it is also found in the leaves of alfalfa and wheat, in wheat germ and also in various animal sources. It is also a component of paraffin. As only very small amounts are available in the diet, to gain any health benefits from octacosanol it must be ingested as a supplement. Most studies assessing these benefits have been carried out using either a wheatgerm oil extract or policosanol, which is a natural mixture of primary alcohols purified from sugarcane wax, whose main component is octacosanol. Both wheatgerm extract and policosanol are reported to contain 8% hexacosanol, 67% octacosanol, 12% triacosanol and 13% other long-chain alcohols.

10.4 SUMMARY

- Glucosamine is an amino monosaccharide, consisting of glucose and the amino acid glutamic acid.
- Glucosamine is found naturally in the body and is present in almost all human tissue, especially in cartilage, tendons and ligament tissues.
- It is a precursor of the disaccharide units of articular cartilage GlycoAminoGlycan (GAG), which forms most of the cartilage tissue.
- The sulphate, hydrochloride and N-acetyl forms are usually used for therapeutic purposes.
- Glucosamine is not found in significant amounts in the usual diet and must be synthesised by the body. This ability declines with age and predisposes the body to degenerative joint disease or arthritis.
- Lycopene is a natural red pigment synthesised by plants and microorganisms, but not by animals.
- Lycopene is found in red fruits and vegetables, particularly the tomato, and is one of over 600 carotenoids found in nature which function as pigments in photosynthesis and in photoprotection.
- Unlike many of the other carotenoids, however, lycopene is not a precursor of vitamin A.
- Melatonin is the primary hormone secreted by the pineal gland. It is biosynthesised from the amino acid trytophan, via the intermediate serotonin. This biosynthesis and the subsequent release of melatonin is usually inhibited by exposure to light and stimulated by darkness, via a multi synaptic neural pathway connecting the pineal gland to the retina.
- Melatonin secretion usually starts as soon as darkness falls and usually peaks between 2 and 4 am.

- The amount of melatonin produced varies with age. Babies secrete low levels, but from the age of about three months, melatonin concentrations begin to increase, reaching a maximum between one and three years of age.
- Young adults secrete 5–25 μg of melatonin daily and this decreases markedly with advancing age.
- As it is a hormone, melatonin has been called a drug, however it is also a nutrient.
- The consumption of plant materials containing high levels of melatonin could alter serum concentrations.
- Melatonin has been identified in bananas, tomatoes, cucumbers and beetroots, but unrealistically large amounts of these foods would have to be eaten to achieve pharmacological doses.
- Carnitine is an essential cellular component, synthesised from lysine and methionine in the liver and kidney, from where it is released into the systemic circulation, and is also synthesised in the brain.
- Carnitine exists in two isomeric forms, the D- and L-forms, which have different biochemical and pharmacological properties.
- Naturally occurring carnitine is almost always the L-isomer, whereas the D-isomer is usually obtained from chemical synthesis.
- The L-isomer is a substrate for carnitine-acetyltransferase and is the only isomer with biological activity, but the D-isomer acts as a competitive inhibitor, interfering with fatty acid oxidation and energy production.
- Some people do not excrete the D-isomer efficiently and it has also been reported that administration of the D-isomer causes a depletion of L-carnitine in the heart muscle, leading to abnormalities.
- Octacosanol is a 28-carbon aliphatic primary alcohol ($CH_3(CH_2)26CH_2OH$), which is present in the superficial waxy layers of fruit, leaves and epidermis of many plants, as well as whole grains.
- The main commercial source is a by-product from the sugarcane industry, but it is also found in the leaves of alfalfa and wheat, in wheat germ and also in various animal sources. It is also a component of paraffin.
- Most studies assessing these benefits have been carried out using either a wheatgerm oil extract or policosanol, which is a natural mixture of primary alcohols purified from sugarcane wax, whose main component is octacosanol.
- Both wheatgerm extract and policosanol are reported to contain 8% hexacosanol, 67% octacosanol, 12% triacosanol and 13% other long-chain alcohols.

- Flaxseed, also known as linseed, is produced from the flax plant (*Linum usitatissimum*), and has traditionally been used for a number of medical and non-medical applications.
- Over recent years flaxseed applications have been 'rediscovered' in the area of health and are often promoted by producers.
- Flaxseed oil contains more than 50% ALA, which is an essential n-3 fatty acid. Other sources of ALA include candlenut, hemp seed, pumpkin seed, canola, walnut and soybean.
- Health recommendations to replace saturated fats with unsaturated fats have often resulted in replacement by n-6 rather than n-3 PUFAs. This has led to the modern,
- Western diet including far more n-6 fatty acids than n-3, in a ratio of approximately 20–30:1.
- Fish consumption, which was a source of n-3 oils, has decreased in recent years.
- Due to modern food industry and agricultural methods, the n-3 content of many foods, including meat, fish, eggs and vegetables is much lower than it used to be.
- Resveratrol has been identified in the leaves, skins and petals of *Vitis vinifera*, and also in wines and grape juice, but is also in other foods, such as peanut butter.
- In grape products, levels are higher after infection of the vine with *Botrytis cinerea*, and in red wines manufactured with extended time in contact with the skins.

10.5 KEY WORDS

- **Glucosamine**: Glucosamine is an amino monosaccharide, consisting of glucose and the amino acid glutamic acid.
- **Lycopene**: Lycopene is a natural red pigment synthesised by plants and microorganisms, but not by animals.
- **Melatonin**: Melatonin is the primary hormone secreted by the pineal gland.

10.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. Define glucosamine.
2. Write in brief about lycopene.

3. Give the structure of carnitine, and explain briefly.
4. What is octacosanol? Draw its structure.

Long Answer Questions

1. Write in detail about the properties, structure and functions of various nutraceuticals.
2. Give a detailed note on glucosamine and octacosanol. Also, draw their structures.
3. Explain about melatonin and ornithine alpha ketoglutarate.
4. Discuss the uses of proanthocyanidins, grape products, flaxseed oil as nutraceuticals.

NOTES

10.7 FURTHER READINGS

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BLOCK - IV
NUTRACEUTICAL SUPPLEMENTS AND REMEDIES

NOTES

UNIT 11 NUTRACEUTICAL SUPPLEMENTS

Structure

11.0 INTRODUCTION

The word 'nutraceutical' is a combination of two words 'Nutrition' and 'Pharmaceutical', coined in 1989 by Stephen L. DeFelice, founder and chairman of the Foundation of Innovation Medicine. In contrast to the natural herbs and spices used as folk medicine for centuries throughout Asia, the nutraceutical industry has grown alongside the expansion and exploration of modern technology. A nutraceutical or bioceutical is a pharmaceutical alternative which provides physiological benefits. According to the authority of the Federal Food, Drug, and Cosmetic Act (FFDCA), the Food and Drug Administration (FDA) states that 'nutraceuticals' are basically unregulated as they exist in the same category or group of dietary supplements and food additives. Nutraceuticals are special products derived from food sources to provide extra health benefits in addition to the basic nutritional value found in foods, hence also considered as functional foods. Depending on the jurisdiction, these nutraceutical or bioceutical products can prevent chronic diseases, improve health, delay the aging process, increase life expectancy, or support the structure or function of the body. Functional foods are fortified or enriched during processing providing some benefit to consumers. Sometimes, additional complementary nutrients are added, such as vitamin D to milk.

Fundamentally, the large numbers of plant preparations and extracts as well as a few from animal sources are used as 'traditional' or 'herbal' medicines and many of these are also marketed as dietary supplements. There are a number of advantages for companies to market such products as dietary supplements so that they are subject to regulations relating to foods rather than medicines.

In this unit, you will study about the nutraceutical rich supplements specifically the bee pollen, caffeine, green tea, grape tea, wheat grass, lecithin, mushroom extract, chlorophyll, kelp and spirulina, Garcinia Cambogia, Aloe Vera and Blue Tea.

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11.1 OBJECTIVES

After going through this unit, you will be able to;

- Understand what nutraceutical supplements are
- Explain the significance of spirulina, kelp, caffeine, green tea and grape tea as nutraceutical supplements
- Describe the importance of spices, whole grains, broccoli and other cruciferous vegetables
- Analyse the special nutraceutical features of Aloe Vera, bee pollen, wheat grass, lecithin, mushroom extract, chlorophyll, Garcinia Cambogia and Blue Tea

11.2 NUTRACEUTICAL SUPPLEMENTS FROM PLANT SOURCES

The word 'Nutraceutical' is a combination of two words 'Nutrition' and 'Pharmaceutical', coined in 1989 by Stephen L. DeFelice, founder and chairman of the Foundation of Innovation Medicine. In contrast to the natural herbs and spices used as folk medicine for centuries throughout Asia, the nutraceutical industry has grown alongside the expansion and exploration of modern technology. A nutraceutical or bioceutical is a pharmaceutical alternative which provides physiological benefits. According to the authority of the Federal Food, Drug, and Cosmetic Act (FFDCA), the Food and Drug Administration (FDA) states that 'nutraceuticals' are basically unregulated as they exist in the same category or group of dietary supplements and food additives. Nutraceuticals are special products derived from food sources to provide extra health benefits in addition to the basic nutritional value found in foods, hence also considered as functional foods. Depending on the jurisdiction, these nutraceutical or bioceutical products can prevent chronic diseases, improve health, delay the aging process, increase life expectancy, or support the structure or function of the body. Functional foods are fortified or enriched during processing providing some benefit to consumers. Sometimes, additional complementary nutrients are added, such as Vitamin D to milk.

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many of these are also marketed as dietary supplements. There are a number of advantages for companies to market such products as dietary supplements so that they are subject to regulations relating to foods rather than medicines.

Overwhelming evidence indicates that a plant-based diet can reduce the risk of chronic disease, particularly cancer. In 1992, a review of 200 epidemiological studies showed that cancer risk in people consuming diets high in fruits and vegetables was only one-half that in those consuming few of these foods. Steinmetz and Potter identified more than a dozen classes of these biologically active plant chemicals, now known as 'phytochemicals'.

Health professionals are gradually recognizing the role of phytochemicals in health enhancement (ADA, 1995), aided in part by the Nutrition Labelling and Education Act of 1990 (NLEA). The NLEA required nutrition labelling for most foods and allowed disease-related or health-related messages on food labels which enable the consumers to know about the health benefits provided by the product.

Spirulina and Kelp

Spirulina and Kelp are the two significant discoveries of algae as nutraceutical supplements. Spirulina is a small, single-celled microorganism which is rich in chlorophyll, a plant pigment that provides their dark Blue-Green colour to so many lakes and ponds. In contrast, the Kelp is a Brown Algae that grows only in the sea. The name refers to any of the numerous long-stemmed seaweeds that belong to the order Laminariales or Fucales.

In the United States, the 'rockweed' is the type of 'Kelp' which is specifically cultivated to prepare dietary supplements and health drinks. This kelp is olive green in colour and measures 3 to 6 feet long.

Health Benefits: Both spirulina and kelp have been characterized as miracle cures, since it is capable to reduce arthritis pain, increases energy, boosts immunity, improves liver function, prevents from heart disease and cancer, suppresses AIDS, controls appetite, and guards against cell damage from exposure to X-rays or heavy metals.

Both these seaweeds spirulina and kelp contribute to health benefits by providing essential nutrients, such as carotenoids, protein and minerals, and thus constitute a nutritious part of a vegetarian or macrobiotic diet.

Specifically, spirulina and kelp help to:

Control Bad Breath: The high chlorophyll content present in spirulina makes it an exceptional remedy for bad breath providing the problem is caused by something other than gum disease or chronic sinusitis. It is often the key ingredient in chlorophyll breath fresheners.

Treat Thyroid Problems: Kelp is rich in iodine and hence the best supplement for an underactive thyroid condition that is caused by a lack of iodine mineral. The

use of iodized salt is now so common. Since suspected thyroid problems are diagnosed with blood tests and can be successfully treated with medication, hence consult your doctor if you believe you have a problem with your thyroid gland before trying kelp or any other dietary supplement.

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Spirulina is Extremely High in Many Nutrients: Spirulina is an organism that grows in both fresh and salt water.

It is a type of cyanobacteria, which is a family of single-celled microbes that are often referred to as blue-green algae.

Just like plants, cyanobacteria can produce energy from sunlight via a process called photosynthesis.

Spirulina was consumed by the ancient Aztecs but became popular again when NASA proposed that it could be grown in space for use by astronauts. This tiny alga is packed with nutrients. A single tablespoon (7 grams) of dried spirulina powder contains:

- **Protein:** 4 grams
- **Vitamin B1 (Thiamine):** 11% of the RDA
- **Vitamin B2 (Riboflavin):** 15% of the RDA
- **Vitamin B3 (Niacin):** 4% of the RDA
- **Copper:** 21% of the RDA
- **Iron:** 11% of the RDA
- It also contains decent amounts of magnesium, potassium and manganese and small amounts of almost every other nutrient that you need.

Caffeine

Caffeine is a Central Nervous System (CNS) stimulant of the methylxanthine class. There are several known mechanisms of action to explain the effects of caffeine. The most significant is that it reversibly blocks the action of adenosine on its receptor and consequently prevents the onset of drowsiness induced by adenosine. Caffeine also stimulates certain portions of the Autonomic Nervous System (ANS).

Fundamentally, the caffeine acts as a CNS stimulant, hence when it reaches the brain, then the most noticeable effect is alertness. The person will feel more conscious and less tired, so it is a common ingredient in medications to treat or manage drowsiness, headaches, and migraines. It is also revealed by various studies that people who regularly drink coffee have a lower risk of developing Alzheimer's and Dementia. These benefits are limited to people who drink only high-octane coffee and not decaf. It has adverse effects also. Too much caffeine can be the cause of headaches and is principally linked to caffeine withdrawal.

Caffeine provides no nutritional value on its own. Some medications may also contain caffeine.

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Green Tea

Green tea is a type of tea that is made from ***Camellia sinensis*** leaves and buds that have not undergone the same withering and oxidation process used to make oolong teas and black teas. Green tea originated in China, but its production and manufacture has spread to many other countries in Asia.

Several varieties of green tea exist, which differ substantially based on the variety of *Camellia sinensis* used, growing conditions, horticultural methods, production processing, and time of harvest. Although there has been considerable research on the possible health effects of consuming green tea regularly, there is little evidence that drinking green tea has any effects on health.

All types of tea, except herbal tea, are brewed from the dried leaves of the *Camellia sinensis* bush. The level of oxidation of the leaves determines the type of tea. Green tea is made from unoxidized leaves and is one of the less processed types of tea. It therefore contains the most antioxidants and beneficial polyphenols.

Health Effects: Regular green tea is 99.9% water, provides 1 Calorie per 100 mL serving, is devoid of significant nutrient content and contains phytochemicals, such as polyphenols and caffeine. Although numerous claims have been made for the health benefits of green tea, human clinical research has not provided conclusive evidence of any effects. In 2011, a panel of scientists published a report on the claims for health effects at the request of the European Commission: in general they found that the claims made for green tea were not supported by sufficient scientific evidence. The green tea has been used in traditional Indian and Chinese medicines.

According to the National Cancer Institute, the polyphenols in tea have been shown to decrease tumour growth in laboratory and may protect against damage caused by ultraviolet UVB radiation. Some studies have shown the positive impacts of green tea on the types of cancer, namely breast, bladder, ovarian, colorectal (bowel), esophageal (throat), lung, prostate, skin, stomach, etc.

Grape Tea

Grapes are the fruit of grapevines. *Vitis vinifera* and *Vitis labrusca* are two common grapevine species. *Vitis labrusca* is commonly known as Concord grapes. The whole fruit, skin, leaves and seed of the grape plant are used as medicine. Extracts from grape leaves and grape seeds may help patients with swelling in the legs due to poor blood flow (Chronic Venous Insufficiency). Grape products are also commonly used for diseases of the heart and blood vessels, high blood pressure, high cholesterol, and many other conditions. The grape tea has many health benefits.

Grape contains flavonoids, which can have antioxidant effects, lowers the levels of Low Density Lipoproteins (LDLs or bad cholesterol), relaxes blood vessels, and reduces the risk of Coronary Heart Disease (CHD). The antioxidants

in grape might help to prevent heart disease and have other potentially beneficial effects. Red grape varieties provide more antioxidants than white or blush grape varieties.

Grape leaf might reduce inflammation and have astringent effects. In other words, grape leaf seems to be able to draw tissue together, which could help stop bleeding and diarrhoea. These properties appear to be greatest in the red leaves.

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Wheat Grass

Wheatgrass is the freshly sprouted first leaves of the common wheat plant, used as a food, drink, or dietary supplement. Wheatgrass is served freeze dried or fresh, and so it differs from wheat malt, which is convectively dried. Wheatgrass is allowed to grow longer and taller than wheat malt. Like most plants, wheatgrass contains chlorophyll, amino acids, minerals, vitamins and enzymes. The health benefits of wheatgrass ranges from providing supplemental nutrition to having unique curative properties.

Wheatgrass juice is often available at juice bars, and some people grow and juice their own in their homes. It is available fresh as produce, in tablets, frozen juice, and powder. Wheatgrass is also sold commercially as a spray, cream, gel, massage lotion, and liquid herbal supplement. Because it is extracted from wheatgrass sprouts, i.e., before the 'wheat seed' or 'berry' used in flour begins to form. The wheatgrass juice is gluten-free.

Wheatgrass is a food made from the ***Triticum aestivum*** plant. It is regarded as a super potent health food with amazing benefits and is usually consumed as a fresh juice, but it also comes in powdered form.

Wheatgrass is packed with a powerful combination of nutrients that make it extremely useful for the health. It has many therapeutic benefits and is known as 'Complete Nourishment'. The extensive combination of Vitamins and Nutrients may make wheatgrass an exceptional choice to enhance your well-being. Wheatgrass has antioxidant, antibacterial, and anti-inflammatory properties. It contains iron, calcium, enzymes, magnesium, phytonutrients, 17 amino acids, vitamins A, C, E, K, and B complex, chlorophyll and proteins.

Lecithin

Lecithin is a generic term to designate any group of yellow-brownish fatty substances occurring in animal and plant tissues which are amphiphilic – they attract both water and fatty substances (and so are both hydrophilic and lipophilic), and are used for smoothing food textures, emulsifying, homogenizing liquid mixtures, and repelling sticking materials.

Lecithins are mixtures of glycerophospholipids including phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol, phosphatidylserine, and phosphatidic acid.

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Lecithin can easily be extracted chemically using solvents, such as hexane, ethanol, acetone, petroleum ether or benzene; or extraction can be done mechanically. It is usually available from sources, such as soybeans, egg yolk, milk, marine sources, rapeseed, cottonseed, and sunflower oil. It has low solubility in water, but is an excellent emulsifier. In aqueous solution, its phospholipids can form either liposomes, bilayer sheets, micelles, or lamellar structures, depending on hydration and temperature. This results in a type of surfactant that usually is classified as amphipathic. Lecithin is sold as a food additive and dietary supplement. In cooking, it is sometimes used as an emulsifier and to prevent sticking, for example in non-stick cooking spray.

Lecithin is a fat that is essential in the cells of the body. It can be found in many foods, including Soybeans and Egg Yolks. Lecithin is taken as a medicine and is also used in the manufacturing of medicines. Lecithin is used for treating memory disorders, such as Dementia and Alzheimer's disease.

Mushroom Extract

'Reishi Mushroom' is a fungus that some people describe as 'tough' and 'woody' with a bitter taste. The fruiting body (above-ground part) and mycelium (filaments connecting a group of mushrooms) are used as medicine.

Reishi mushroom is specifically used for boosting the immune system; viral infections, such as the flu (influenza), swine flu, and avian flu; lung conditions including asthma and bronchitis; heart diseases and contributing conditions, such as high blood pressure and high cholesterol; kidney disease; cancer; and liver diseases. It is also used for HIV/AIDS, altitude sickness, Chronic Fatigue Syndrome (CFS), trouble sleeping (insomnia), stomach ulcers, poisoning, and herpes pain. Other uses include reducing stress and preventing fatigue. In combination with other herbs, Reishi mushroom is used to treat prostate cancer.

Chlorophyll

Chlorophyll is a green pigment found in plants. People use chlorophyll as medicine. Common sources of chlorophyll used for medicine include Alfalfa (***Medicago sativa***) and Silkworm Droppings. Chlorophyll is used for bad breath and reducing colostomy odour. A colostomy is a surgical opening made in the abdomen that allows intestinal waste to be collected in a bag. Chlorophyll is also used for constipation, 'detoxification', and wound healing. Chlorophyll is found in virtually all photosynthetic organisms, including green plants, prokaryotic Blue-Green Algae (Cyanobacteria), and Eukaryotic Algae. The chlorophyll is intravenously used for treating a pancreas problem called Chronic Relapsing Pancreatitis.

Garcinia Cambogia

Garcinia is a genus of flowering plants in the family Clusiaceae native to Asia, America, Australia, tropical and southern Africa, and Polynesia. The Garcinia

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Cambogia fruit has been a focus for many people looking for natural ways to lose weight. The small fruit, which resembles a cross between a pumpkin and a tomato, is native to India and Southeast Asia and is exported all over the world.

Garcinia Cambogia contains an ingredient called HydroxyCitric Acid (HCA), which has been used to aid weight loss. The extract of HCA is available in powdered form or pill form and can be purchased online or in health stores.

Blue Tea

Blue Tea or Butterfly Pea Flower Tea, is a caffeine-free herbal concoction, made by seeping dried or fresh leaves of the ***Clitoria ternatea*** plant. The Butterfly Pea is also known as Blue Pea or Pigeon Wings and it is a plant common to most South East Asian countries. The deep blue colour of the flower's petals has traditionally been used to make dye. The 'Blue Tea' is popular in Thailand and Vietnam, where it is served post dinner, usually with lemon and honey added to it. Adding lemon juice to the tea changes the pH of the drink, making it change colour from deep blue to purple. The blue tea leaves are now available in stores and supermarkets around the world. The tea leaves are also used to change colour in cocktails or soft drinks as well.

Aloe Vera

Aloe Vera is a gelatinous substance that is obtained from the thick leaves of the cactus-like Aloe Vera plant. The most popular and most familiar use of this extract is for topical use in cosmetic preparations and after-sun lotions. Aloe Vera is also used as an ingredient of ointments to treat skin conditions because it is claimed to have anti-inflammatory, itch relieving, painkilling and healing properties. It has also been promoted more recently as an oral supplement with claims that it may reduce blood lipid levels and reduce blood glucose levels in Type 2 Diabetes. The leaves of this plant also exude a bitter yellow substance called Aloe Latex or Aloe Juice and this contains Anthraquinone which is a harsh laxative, on drying the juice yields dark brown granules that are approved by the Food and Drug Administration (FDA) as a counter laxative. Kiple and Ornelas (2000) give no dietary use for this plant, unsurprisingly given the bitter taste and laxative effects of Aloe Latex. Aloe Vera gel as a dietary supplement should contain no juice and should not have laxative effects.

The Aloe Gel contains polysaccharides that would be classed as components of the Soluble Dietary fibre as well as Vitamins, Minerals, Saponins (Triterpenoids with surfactant properties) and essential Fatty Acids. Despite the exaggerated claims made by suppliers and advocates of Aloe Vera supplements, there is little evidence in the scientific literature to support the claims that these oral supplements have beneficial effects upon Blood Lipoprotein Profiles or are useful in the management of Type 2 Diabetes. One systematic review published in 1999 suggested that the clinical effectiveness of neither oral nor topical Aloe Vera was

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sufficiently defined at that time, very few controlled clinical trials of oral Aloe Vera were found (Vogler and Ernst 1999). In the UK, Aloe Vera is usually taken as tablets or capsules (one or two per day) that contain the concentrated Aloe Vera gel extract. There seems no significant evidence to justify the oral consumption of Aloe Vera supplements although there is also no evidence of any harmful effects.

Aloe Vera is a popular medicinal plant that has been used for thousands of years. The gel contains most of the bioactive compounds in the plant, including Vitamins, Minerals, Amino Acids and Antioxidants.

Oats

Oat products are a dietary source of the cholesterol-lowering soluble fibre beta-glucan. There is now significant scientific agreement that consumption of this particular plant food can reduce total and Low Density Lipoprotein (LDL) cholesterol, thereby reducing the risk of Coronary Heart Disease (CHD). For this, the Food and Drug Administration (FDA) awarded the first food-specific health claim in January 1997 (DHHS/FDA, 1997), in response to a petition submitted by the Quaker Oats Company (Chicago).

Quaker Oats determined that 3 g of beta-glucan would be required to achieve a 5% reduction in serum cholesterol, an amount equivalent to approximately 60 g of Oatmeal or 40 g of Oat Bran (dry weight). Thus, a food bearing the health claim must contain 13 g of Oat Bran or 20 g Oatmeal, and provide, without fortification, at least 1.0 g of β-glucan per serving.

Soy

Not only is soy a high quality protein, as assessed by the FDA's, 'Protein Digestibility Corrected Amino Acid Score' method, bit it is now thought to play preventive and therapeutic roles in Cardio-Vascular Disease (CVD), cancer, osteoporosis, and the alleviation of menopausal symptoms.

A study shows that the consumption of 'Soy Protein' results in significant reductions in total cholesterol (9.3%), LDL cholesterol (12.9%), and triglycerides (10.5%), with a small but insignificant increase (2.4%) in High Density Lipoprotein (HDL) cholesterol. Regarding the specific component responsible for the cholesterol-lowering effect of soy, recent attention has focused on the isoflavones.

On May 4, 1998, Protein Technologies International (PTI, St. Louis, Mo.) petitioned the FDA for a health claim on soy protein containing products pertaining to reduced risk of CHD. Based on an effective daily level of 25 g soy protein, PTI proposed that the amount of soy protein required to qualify an individual food to bear the health claim is 6.25 g with a minimum of 12.5 mg of total isoflavones per reference amount customarily consumed.

Several classes of anti-carcinogens have been identified in soybeans, including protease inhibitors, phytosterols, saponins, phenolic acids, phytic acid, and

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isoflavones. Of these, isoflavones (Genestein and Daidzein) are particularly noteworthy because soybeans are the only significant dietary source of these compounds. Isoflavones are heterocyclic phenols structurally similar to the estrogenic steroids. Because they are weak estrogens, isoflavones may act as anti-estrogens by competing with the more potent, naturally-occurring endogenous estrogens (for example, 17-b-estradiol) for binding to the estrogen receptor. This may explain why populations that consume significant amounts of soy (for example, Southeast Asia) have reduced risk of estrogen-dependent cancer.

Soy may also benefit bone health. A recent clinical study involving 66 post-menopausal women conducted at the University of Illinois found that 40 g Isolated Soy Protein (ISP) per day (containing 90 mg total isoflavones) significantly increased (approximately 2%) both bone mineral content and density in the lumbar spine after 6 months.

Flaxseed

Among the major seed oils, Flaxseed Oil contains the most (57%) of the omega-3 fatty acid, β-linolenic acid. Recent research, however, has focused more specifically on fibre associated compounds known as lignans. The two primary mammalian lignans, enterodiol and its oxidation product, enterolactone, are formed in the intestinal tract by bacterial action on plant lignan precursors. Flaxseed is the richest source of mammalian lignan precursors. Because enterodiol and enterolactone are structurally similar to both naturally-occurring and synthetic estrogens, and have been shown to possess weakly estrogenic and antiestrogenic activities, they may play a role in the prevention of estrogen-dependent cancers.

Fewer studies have evaluated the effects of flaxseed feeding on risk markers for cancer in humans. Phipps *et al.* (1993) demonstrated that the ingestion of 10 g of flaxseed per day elicited several hormonal changes associated with reduced breast cancer risk. Consumption of flaxseed has also been shown to reduce total and LDL cholesterol, as well as platelet aggregation.

Fundamentally, the flaxseeds are one of the oldest crops. There are two types, brown and golden, which are equally nutritious.

A typical serving size for ground flax seeds is 1 tablespoon (7 grams).

Just one tablespoon provides a good amount of protein, fiber and omega-3 fatty acids, in addition to being a rich source of some vitamins and minerals.

One tablespoon of ground flax seeds contains:

- **Calories:** 37
- **Protein:** 1.3 grams
- **Carbs:** 2 grams
- **Fiber:** 1.9 grams
- **Total Fat:** 3 grams

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- **Saturated Fat:** 0.3 grams
- **Monounsaturated Fat:** 0.5 grams
- **Polyunsaturated Fat:** 2.0 grams
- **Omega-3 Fatty Acids:** 1,597 mg
- **Vitamin B1:** 8% of the RDI
- **Vitamin B6:** 2% of the RDI
- **Folate:** 2% of the RDI
- **Calcium:** 2% of the RDI
- **Iron:** 2% of the RDI
- **Magnesium:** 7% of the RDI
- **Phosphorus:** 4% of the RDI
- **Potassium:** 2% of the RDI

Therefore the health benefits of flaxseeds are mainly attributed to the omega-3 fatty acids, lignans and fiber that they contain.

Tomatoes

Lycopene, the primary carotenoid found in Tomato fruit has a significant role in cancer risk reduction.

In a study of more than 47,000 men, those who consumed tomato products 10 or more times per week had less than one-half the risk of developing advanced prostate cancer. Interestingly, lycopene is the most abundant carotenoid in the prostate gland. Other cancers whose risks have been inversely associated with serum or tissue levels of lycopene include breast, digestive tract, cervix, bladder, and skin and possibly lung. Proposed mechanisms by which lycopene could influence cancer risk are related to its antioxidant function. Lycopene is the most efficient quencher of singlet oxygen in biological systems.

Spices

Spices are a group of esoteric food adjuncts that have been in use for thousands of years to enhance the sensory quality of foods, the quantity and variety consumed in tropical countries is particularly extensive. These spice ingredients impart characteristic flavour, aroma, or piquancy and colour to foods. Some spices, like fenugreek, can also modify the texture of food. It is a common experience that their distinct aroma stimulates the appetite. Not only are spices used as flavourings and seasonings, but many are also used in perfumery, cosmetics, and toiletries. In addition, several spices have long been recognized to possess medicinal properties, such as tonic, carminative, stomachic antispasmodic, and anti-helminthic, as listed in Table 11.1.

Table 11.1 *Medicinal Properties of Spices*

Spice	Medicinal Properties
Coriander (*Coriandrum sativum*)	Anti-Dyspeptic, Flavourant
Cumin (*Cuminum cymminum*)	Antispasmodic, Carminative, Digestive Stimulant
Fenugreek (*Trigonella foenumgraecum*)	Diuretic, Emmenagogue, Emollient, useful in Heart Diseases
Garlic (*Allium sativum*)	Anti-Dyspeptic, Anti-Flatulent, for Ear Infection, Duodenal Ulcers, as Rubefacient in Skin Diseases
Ginger (*Zingiber officinale*)	Sialagogue, Useful in Diseases of Heart and Blood
Onion (*Allium cepa*)	Diuretic, Emmenagogue, Expectorant, for Bleeding Piles
Pepper (*Piper nigrum*)	Antipyretic, Rubefacient
Red Pepper (*Capsicum annuum*)	Anti-Inflammatory, for Pain Relief (Rheumatism/Neuralgia), Useful in Indigestion, Rubefacient
Turmeric (*Curcuma longa*)	Anti-Inflammatory, Diuretic, Laxative, Good for the Liver, Jaundice, Diseases of Blood

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Broccoli and Other Cruciferous Vegetables

Epidemiological evidence has associated the frequent consumption of cruciferous vegetables with decreased cancer risk. Glucosinolates are a group of glycosides stored within cell vacuoles of all cruciferous vegetables. Myrosinase, an enzyme found in plant cells, catalyzes these compounds to a variety of hydrolysis products, including isothiocyanates and indoles. Indole-3 Carbinol (I3C) is currently under investigation for its cancer chemo preventive properties, particularly of the mammary gland. In addition to the induction of Phase I and II detoxification reactions, I3C may reduce cancer risk by modulating estrogen metabolism. In humans, I3C administered at 500 mg daily (equivalent to 350-500 g cabbage/day) for 1 week significantly increased the extent of estradiol 2-hydroxylation in women (Michnovicz and Bradlow, 1991), suggesting that this compound may be a novel approach for reducing the risk of breast cancer.

Although a wide variety of naturally occurring and synthetic isothiocyanates have been shown to prevent cancer in animals, attention has been focused on a particular isothiocyanates isolated from broccoli, known as sulforaphane which are shown to be the principal inducer of a particular type of Phase II enzyme, quinone reductase.

Citrus Fruits

Several epidemiological studies have shown that citrus fruits are protective against a variety of human cancers. Although Oranges, Lemons, Limes, and Grapefruits are a principal source of such important nutrients as Vitamin C, Folate, and Fibre. Citrus fruits are particularly high in a class of phytochemicals known as the Limonoids.

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Over the last decade, evidence has been accumulating in support of the cancer preventative effect of Limonene (Gould, 1997). Crowell (1997) showed this compound to be effective against a variety of both spontaneous and chemically induced rodent tumours.

Cranberry

Recent investigations have focused on the ability of cranberry juice to inhibit the adherence of *Escherichia coli* to uro-epithelial cells (Schmidt and Sobota, 1988). This phenomenon has been attributed to two compounds: Fructose and a Non-Dialyzable Polymeric Compound. The latter compound, subsequently isolated from Cranberry and Blueberry juices was found to inhibit adhesins present on the pili of the surface of certain pathogenic *Escherichia coli*.

Wine and Grapes

There is growing evidence that wine, particularly red wine, can reduce the risk of CVD. The link between wine intake and CVD first became apparent in 1979 when St. Leger *et. al*. (1979) found a strong negative correlation between wine intake and death from ischemic heart disease in both men and women from 18 countries. France, in particular, has a relatively low rate of CVD despite diets high in dairy fat (Renaud and de Lorgeril, 1992). Although this 'French Paradox' can be partly explained by the ability of alcohol to increase HDL cholesterol, more recent investigations have focused on the non-alcohol components of wine, in particular, the Flavonoids.

The high phenolic content of red wine, which is about 20-50 times higher than white wine, is due to the incorporation of the grape skins into the fermenting grape juice during production. The Black Seedless Grapes and Red Wines contain high concentrations of Phenolic: 920, 1800, and 3200 mg/L, respectively, while Green Thomson Grapes contain only 260 mg/kg Phenolic. Frankel and co-workers (1993) attributed the positive benefits of red wine to the ability of phenolic substances to prevent the oxidation of LDL, a critical event in the process of Atherogenesis, a disorder of the artery wall that involves adhesion of monocytes and lymphocytes to the endothelial cell surface, migration of monocytes into the sub-endothelial space, ingestion of low density lipoproteins, etc.

Those who desire health benefits of wine without potential risk may wish to consider alcohol-free wine, which has been shown to increase total plasma antioxidant capacity (Serafini *et. al*., 1998). Red wine is also a significant source of trans-resveratrol, a phytoalexin found in grape skins. Resveratrol have estrogenic properties which may explain in part the cardiovascular benefits of wine drinking, and it has been shown to inhibit carcinogenesis in vivo (Jang *et. al*., 1997).

Table 11.2 shows the various functional components present in different fruits and vegetables and also tells about the expected potential benefit of them on health.

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Table 11.2 *Examples of Functional Components*

Class/Components	Source	Potential Benefit
Carotenoids		
Beta-Carotene	Carrots, Various Fruits	Neutralizes Free Radicals, Bolsters Cellular Antioxidant Defences
Lutein, Zeaxanthin	Kale, Collards, Spinach, Corn, Eggs, Citrus Foods	Contribute to Maintenance of Healthy Vision
Lycopene	Tomatoes and Processed Tomato Products	Contribute to Maintenance of Prostate Health
Flavonoids		
Anthocyanidins	Berries, Cherries, Red Grapes	Bolster Cellular Antioxidant Defences, Contribute to Maintenance of Brain Function
Flavanols — Catechins, Epicatechins, Procyanidins	Tea, Cocoa, Chocolate, Apples, Grapes	Contribute to Maintenance of Heart Health
Flavanones	Citrus Foods	Neutralize Free Radicals, Bolster Cellular Antioxidant Defences
Flavonols	Onions, Apples, Tea, Broccoli	Neutralize Free Radicals, Bolster Cellular Antioxidant Defences
Proanthocyanidins	Cranberries, Cocoa, Apples, Strawberries, Grapes, Wine, Peanuts, Cinnamon	Contribute to Maintenance of Urinary Tract Health and Heart Health
Isothiocyanates		
Sulforaphane	Cauliflower, Broccoli, Broccoli Sprouts, Cabbage, Kale, Horseradish	Enhances Detoxification of Undesirable Compounds and Bolster Cellular Antioxidant Defences
Phenols		
Caffeic Acid, Ferulic Acid	Apples, Pears, Citrus Fruits, Some Vegetables	Bolster Cellular Antioxidant Defences, May Contribute to Maintenance of Healthy Vision and Heart Health

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Sulphides/Thiols		
Diallyl Sulphide, Allyl Methyl Trisulphide	Garlic, Onions, Leeks, Scallions	Enhances Detoxification of Undesirable Compounds, Contribute to Maintenance of Heart Health and Healthy Immune Function
Dithiolethiones	Cruciferous Vegetables—Broccoli, Cabbage, Bok Choy or Bok Choi, Collards	Contributes to Maintenance of Healthy Immune Function
Whole Grains		
Whole Grains	Cereal Grains	Reduce Risk Of Coronary Heart Diseases, Cancer and Diabetes

Bee Products

Bees and their pollination facilities contribute to maintain the biological balance in nature and enable various animals and plant species, including humans, to thrive. The bees provide the bee products that are an entirely natural food source. People are using these bee products since time immemorial, and even today these products are a predominantly appropriate source of food.

Together with honey, which is definitely the most widespread bee product, bees also provide us with Pollen, Propolis, Royal Jelly and Wax. Bee venom is another product from which people can be benefitted. Honey is the most used of the products derived from beekeeping and is the naturally obtained food. Three by-products of beekeeping include Royal Jelly, Bee Pollen and Bee Propolis – are used as dietary supplements.

Honey: Honey is a sweet liquid made by bees using the nectar from flowers. The flavour of a particular type of honey will vary based on the types of flower from which the nectar was harvested. Both raw and pasteurized forms of honey are available. Raw honey is removed from the hive and bottled directly, and as such will contain trace amounts of yeast, wax, and pollen.

Consuming local raw honey is believed to help with seasonal allergies, due to repeated exposure to the pollen in the area. Pasteurized honey has been heated and processed to remove impurities. Honey has high levels of Monosaccharaides, Fructose, and Glucose, and it contains about 70 to 80 percent Sugar, which provides its sweetness. Honey also has antiseptic and antibacterial properties. Modern medical science has managed to find uses for honey in chronic wound management and combating infection.

Royal Jelly: Royal jelly is a substance secreted by young worker bees and used to feed the young larvae and the queen bee throughout her life. Royal jelly is not normally

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stored in the hive because it is fed directly to the larvae or queen as it is secreted. However, some accumulates around the larval queen in the 'queen cell' in the early stages of development. In order to produce royal jelly commercially the hive must be stimulated to produce queens at inappropriate times and that one hive has the potential to produce about 500 g of royal jelly during the course of a summer.

Fresh royal jelly varies in composition but a typical composition might be:

- 70% Water
- 12% Carbohydrate (mainly as Glucose and Fructose)
- 12% Protein
- 5% Lipids

Given that a typical daily dose in supplements is 250–500 mg, these amounts of macronutrients are nutritionally insignificant. Royal jelly is practically devoid of Fat-Soluble Vitamins and Vitamin C. The 'Royal Jelly' contains 'B Vitamins' and several Minerals but the amounts present in a typical supplement dose are nutritionally insignificant and would probably not reach 1% of the Reference Nutrient Intake (RNI) for any Vitamin or Mineral. Royal jelly also contains an assortment of other chemically diverse substances, which from a human perspective are present in minute amounts (free nucleotide bases, acetylcholine and two heterocyclic compounds, biopterine and neopterine). There are huge numbers of claims for the beneficial effects of taking royal jelly supplements and some for its topical use. According to Krell (1996) there is almost no scientific substantiation for these claims. Prominent amongst these claims for royal jelly is that it acts as a General Tonic, Reducing Fatigue, Improving Mental and Physical Performance and leading to a General Health Improvement. There are reports that in vitro it has antibacterial activity and that it has anti-tumour activity in animal studies but their significance for human consumption is impossible to say.

Bee Pollen: Bee pollen is a mixture of pollens collected by bees from flowers mixed with nectar and regurgitated honey and thus containing digestive enzymes of the bees. It is collected from bees, as they enter the hive, by a wire mesh that brushes the pollen off into a collecting vessel. The exact composition of bee pollen will depend upon the types of flower that it has been collected from. Typically bee pollen contains about 20% protein and 30–40% carbohydrate mainly in the form of simple sugars. It contains smaller amounts of lipids including essential fatty acids. It does not contain fat-soluble vitamins, except carotenoids, but does contain water-soluble vitamins and essential minerals. As typical doses in supplements are in the range 0.5–1.5 g, this will make little contribution to the human requirements for either macronutrients or micronutrients.

Bee pollen contains flavonoids, carotenoids, free amino acids, nucleic acids and many enzymes (although these will be inactivated and digested in the human gut). Several of these constituents are known to have antioxidant activity and so bee pollen probably has some antioxidant activity, it is also claimed to have anti-inflammatory activity.

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As with royal jelly, there are numerous claimed beneficial effects of bee pollen supplements, including a general increase in vitality, improved athletic performance, reduced atherosclerosis and lowered blood pressure. It is also claimed to be beneficial in the treatment of benign hypertrophy of the prostate gland in men but no clinical trials were found in the English language literature to support this. Some trials of its effects upon athletic performance were carried out in the 1970s and 1980s (for example, Maughan and Evans 1982 in swimmers) but none of these found it to be effective.

There are several reports of allergic reactions to bee pollen, some of which have resulted in life-threatening anaphylaxis. Anyone with a known allergy to pollen should avoid bee pollen and it should probably be avoided by anyone with a history of atopic diseases, such as eczema, asthma or allergic rhinitis. Claims that it may be helpful in curing allergies are based upon false logic. Pure pollens collected directly from the plant to which a person is allergic can be used to desensitise people to particular pollens when injected in controlled doses. Eating bee pollen with its unpredictable content is likely to provoke allergic reactions rather than to desensitise. Given the risk of allergic reactions and the lack of any substantial evidence for benefit, bee pollen is not recommended as a dietary supplement.

11.2.1 Nutraceutical Components from Animal Sources

Functional foods fall into two broad categories - plant origin and animal origin. The plant based foods have some components that act against lethal diseases, such as cancer. A vast number of components, such as fish oil and dairy products naturally present in animal sources are potentially beneficial to health. Nutraceuticals deliver a concentrated form of a biologically active component from a food to enhance health. The use of probiotics in combination with prebiotic has been very effective against several chronic diseases. Probiotics and prebiotics provide an alternate source for the management of different intestinal disorders. The major contributions associated with the work of probiotics on human health are proper colonic function and increased metabolism.

Fish

Omega-3 fatty acids or omega-3s have a Carbon–Carbon double bond located three carbons from the Methyl end of the chain. Omega-3s, sometimes referred to as ‘n-3s’, are present in certain foods, such as Flaxseed and Fish, as well as dietary supplements, such as Fish Oil. Omega-3 (n-3) fatty acids are basically an essential class of Polyunsaturated Fatty Acids (PUFAs) derived primarily from fish oil. The n-3 fatty acids play significant role in CVD was first brought to light in the 1970s when Bang and Dyerberg (1972) reported that Eskimos had low rates of this disease despite consuming a diet which was high in fat. The cardio-protective effect of fish consumption has been observed in some prospective investigations.

Although eating large amounts of fish has not unequivocally been shown to reduce CVD risk in healthy men, consumption of 35 g or more of fish daily has been

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shown to reduce the risk of death from non-sudden myocardial infarction in the Chicago Western Electric Study (Daviglus *et. al.,* 1997), and as little as one serving of fish per week was associated with a significantly reduced risk of total cardiovascular mortality after 11 years in more than 20,000 males (Albert *et. al*., 1998).

Fish contains high levels of nutrients and protein, particularly oily fish, such as salmon and tuna. Fish often has less cholesterol and saturated fat than meat, and it is a staple of the healthful Mediterranean diet. Fish also provides Vitamins and Minerals, including B Vitamins, Zinc, and Iron.

Oily fish contains omega-3 fatty acids, which are beneficial fats that humans must obtain from their diet. Omega-3 fatty acids have potential health benefits, such as helping prevent cardiovascular disease. As fish is a low-fat protein source, incorporating it into the diet can also potentially lead to weight loss.

Fish oil is one of the most commonly consumed dietary supplements. It is rich in Omega-3 fatty acids, which are vital and essential for the health.

Fish oil is the fat or oil that is extracted from fish tissues. It usually comes from oily fish, such as herring, tuna, anchovies, and mackerel. Yet it is sometimes produced from the livers of other fish, as is the case with Cod Liver Oil. The World Health Organization (WHO) recommends eating 1–2 portions of fish per week. This is because the omega-3 fatty acids in fish provides many health benefits, including protection against a number of diseases.

In case a person is not eating a lot of oily fish, he/she can take a fish oil supplement that will help to get enough omega-3 fatty acids.

Dairy Products

There is no doubt that dairy products are functional foods. They are one of the best sources of Calcium, an essential nutrient which can prevent Osteoporosis and possibly Colon Cancer. In addition to Calcium, recent research has focused specifically on other components in dairy products, particularly fermented dairy products known as 'Probiotics'. Probiotics are defined as, 'live microbial feed supplements which beneficially affect the host animal by improving its intestinal microbial balance' (Fuller, 1994).

Although a variety of health benefits have been attributed to probiotics, their anti-carcinogenic, hypocholesterolemic and antagonistic actions against enteric pathogens and other intestinal organisms have received the most attention (Mital and Garg, 1995).

The hypocholesterolemic effect of fermented milk was discovered more than 30 years ago during studies conducted in Maasai tribesmen in Africa (Mann *et. al.,* 1964). The Maasai have low levels of serum cholesterol and clinical coronary heart disease despite a high meat diet. However, they consume daily 4 to 5 L of fermented whole milk.

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More evidence supports the role of probiotics in cancer risk reduction, particularly colon cancer (Mital and Garg, 1995). This observation may be due to the fact that lactic acid cultures can alter the activity of faecal enzymes (for example., b-Glucuronidase, Azoreductase, Nitroreductase) because they play a role in the development of colon cancer.

In addition to probiotics, there is growing interest in fermentable carbohydrates that feed the good micro flora of the gut. These prebiotics, defined by Gibson and Roberfroid (1995) as, 'non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thus improves host health', may include starches, dietary fibers, other non-absorbable sugars, sugar alcohols, and oligosaccharides. Of these, oligosaccharides have received the most attention, and numerous health benefits have been attributed to them (Tomomatsu, 1994). Oligosaccharides consist of short chain polysaccharides composed of three and 10 simple sugars linked together. They are found naturally in many fruits and vegetables (including Banana, Garlic, Onions, Milk, Honey, Artichokes). The prebiotic concept has been further extended to encompass the concept of synbiotics, a mixture of probiotic and prebiotics. Many synbiotic products are currently on the market in Europe.

Marine Sources as Nutraceutical Rich Supplements

Marine ecosystems have a high diversity of living organisms compared to terrestrial ecosystems providing numerous resources for human nutrition and health. Marine invertebrates are a diverse group with habitats in the ocean ecosystems are composed of different taxonomic groups classified as, Porifera (Sponges), Cnidaria (Corals, Sea Anemones, Hydrozoans, Jellyfish), Annelida (Polychaetes, Marine Worms), Bryozoa (Moss Animals or Sea Mats), Mollusca (Oysters, Abalone, Clams, Mussels, Squid, Cuttlefish, Octopuses), Arthropoda (Lobsters, Crabs, Shrimps, Prawns, Crayfish), and Echinodermata (Sea Stars, Sea Cucumbers, Sea Urchins). This diverse group also includes Macroalgae, Microalgae, Bacteria, Cyanobacteria, certain Fish species and Crustaceans that produce secondary metabolites as an adaptation to their hostile marine environment. A diverse range of marine natural products containing medicinally useful nutritional substances, i.e., marine nutraceuticals that are beneficial for mankind. Carbohydrates, present in considerable amount of many marine organisms have several nutraceutical and pharmaceutical features that defend from various diseases. Furthermore, the carbohydrates from algae in addition to from shellfish wastes, like chitosan and its derivatives, have remarkable applications in biology and biomedicine. The marine carbohydrates from various marine flora and fauna have applications in the development of nutraceuticals and pharmaceuticals. The various bioactive compounds present in the marine sources are shown in the Table 11.3. These bioactive compounds are an untapped source of functional food ingredients.

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Table 11.3 *Bioactive Substances Isolated from Marine Sources*

Activity	Substance	Origin	Specific Bioactivity
Antimicrobial	Macrolactin A Onnamide A Squalamine	Deep Sea Bacteria, *Theonella* sp., *Squalus acanthias guts*	HIV Herpex Simplex Antivirus Activity
Antitumour	Tedanolide Pungalandin 3	*Tedania ignis*, *Telesto riisie*	P388 and L1210 Leukemia Cell
Anti-Inflammatory	Monalide	*Luffariella variabilis*	Anti-Inflammation
Cardiac Activity	Xestosongin A	*Xestospongia exigua*	Cardiac Activity

Check Your Progress

1. What is nutraceutical?
2. What are nutraceutical products?
3. Explain about Spirulina and Kelp.
4. What is Wheatgrass?
5. Explain about the functional foods.
6. Why fish is considered significant nutritional food? What is fish oil?

11.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. The word 'Nutraceutical' is a combination of two words 'Nutrition' and 'Pharmaceutical', coined in 1989 by Stephen L. DeFelice, founder and chairman of the Foundation of Innovation Medicine. A nutraceutical or bioceutical is a pharmaceutical alternative which provides physiological benefits. According to the authority of the Federal Food, Drug, and Cosmetic Act (FFDCA), the Food and Drug Administration (FDA) states that 'nutraceuticals' are basically unregulated as they exist in the same category or group of dietary supplements and food additives.
2. Nutraceuticals are special products derived from food sources to provide extra health benefits in addition to the basic nutritional value found in foods, hence also considered as functional foods. Depending on the jurisdiction, these nutraceutical or bioceutical products can prevent chronic diseases, improve health, delay the aging process, increase life expectancy, or support the structure or function of the body. Functional foods are fortified or enriched during processing providing some benefit to consumers. Sometimes, additional complementary nutrients are added, such as Vitamin D to milk. Fundamentally, the large numbers of plant preparations and extracts as well as a few from animal sources are used as 'traditional' or 'herbal' medicines and many of these are also marketed as dietary supplements.

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3. Spirulina and Kelp are the two significant discoveries of algae as nutraceutical supplements. Spirulina is a small, single-celled microorganism which is rich in chlorophyll, a plant pigment that provides their dark Blue-Green colour to so many lakes and ponds. In contrast, the Kelp is a Brown Algae that grows only in the sea. The name refers to any of the numerous long-stemmed seaweeds that belong to the order Laminariales or Fucales.

   Both these seaweeds spirulina and kelp contribute to health benefits by providing essential nutrients, such as carotenoids, protein and minerals, and thus constitute a nutritious part of a vegetarian or macrobiotic diet.

4. Wheatgrass is the freshly sprouted first leaves of the common wheat plant, used as a food, drink, or dietary supplement. Like most plants, wheatgrass contains chlorophyll, amino acids, minerals, vitamins and enzymes. The health benefits of wheatgrass ranges from providing supplemental nutrition to having unique curative properties. Because it is extracted from wheatgrass sprouts, i.e., before the 'wheat seed' or 'berry' used in flour begins to form. The wheatgrass juice is gluten-free. Wheatgrass is a food made from the *Triticum aestivum* plant. It has many therapeutic benefits and is known as 'Complete Nourishment'. Wheatgrass has antioxidant, antibacterial, and anti-inflammatory properties. It contains iron, calcium, enzymes, magnesium, phytonutrients, 17 amino acids, vitamins A, C, E, K, and B complex, chlorophyll and proteins.

5. Functional foods fall into two broad categories - plant origin and animal origin. The plant based foods have some components that act against lethal diseases, such as cancer. A vast number of components, such as fish oil and dairy products naturally present in animal sources are potentially beneficial to health. Nutraceuticals deliver a concentrated form of a biologically active component from a food to enhance health. The use of probiotics in combination with prebiotic has been very effective against several chronic diseases. Probiotics and prebiotics provide an alternate source for the management of different intestinal disorders. The major contributions associated with the work of probiotics on human health are proper colonic function and increased metabolism.

6. Fish contains high levels of nutrients and protein, particularly oily fish, such as salmon and tuna. Fish often has less cholesterol and saturated fat than meat, and it is a staple of the healthful Mediterranean diet. Fish also provides Vitamins and Minerals, including B Vitamins, Zinc, and Iron.

   Oily fish contains omega-3 fatty acids, which are beneficial fats that humans must obtain from their diet. Omega-3 fatty acids have potential health benefits, such as helping prevent cardiovascular disease. As fish is a low-fat protein source, incorporating it into the diet can also potentially lead to weight loss.

   Fish oil is the fat or oil that is extracted from fish tissues. It usually comes from oily fish, such as herring, tuna, anchovies, and mackerel. Yet it is

sometimes produced from the livers of other fish, as is the case with Cod Liver Oil. The World Health Organization (WHO) recommends eating 1–2 portions of fish per week. This is because the omega-3 fatty acids in fish provides many health benefits, including protection against a number of diseases.

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11.4 SUMMARY

- The word 'Nutraceutical' is a combination of two words 'Nutrition' and 'Pharmaceutical', coined in 1989 by Stephen L. DeFelice, founder and chairman of the Foundation of Innovation Medicine. I
- In contrast to the natural herbs and spices used as folk medicine for centuries throughout Asia, the nutraceutical industry has grown alongside the expansion and exploration of modern technology.
- A nutraceutical or bioceutical is a pharmaceutical alternative which provides physiological benefits.
- According to the authority of the Federal Food, Drug, and Cosmetic Act (FFDCA), the Food and Drug Administration (FDA) states that 'nutraceuticals' are basically unregulated as they exist in the same category or group of dietary supplements and food additives.
- Nutraceuticals are special products derived from food sources to provide extra health benefits in addition to the basic nutritional value found in foods, hence also considered as functional foods.
- Functional foods are fortified or enriched during processing providing some benefit to consumers. Sometimes, additional complementary nutrients are added, such as Vitamin D to milk.
- Spirulina and Kelp are the two significant discoveries of algae as nutraceutical supplements.
- Spirulina is a small, single-celled microorganism which is rich in chlorophyll, a plant pigment that provides their dark Blue-Green colour to so many lakes and ponds.
- The Kelp is a Brown Algae that grows only in the sea. The name refers to any of the numerous long-stemmed seaweeds that belong to the order Laminariales or Fucales.
- Caffeine is a Central Nervous System (CNS) stimulant of the methylxanthine class. There are several known mechanisms of action to explain the effects of caffeine. The most significant is that it reversibly blocks the action of adenosine on its receptor and consequently prevents the onset of drowsiness induced by adenosine.
- Caffeine also stimulates certain portions of the Autonomic Nervous System (ANS).

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- Green tea is a type of tea that is made from *Camellia sinensis* leaves and buds that have not undergone the same withering and oxidation process used to make oolong teas and black teas.
- Studies have shown the positive impacts of green tea on the types of cancer, namely breast, bladder, ovarian, colorectal (bowel), esophageal (throat), lung, prostate, skin, stomach, etc.
- Grape contains flavonoids, which can have antioxidant effects, lowers the levels of Low Density Lipoproteins (LDLs or bad cholesterol), relaxes blood vessels, and reduces the risk of Coronary Heart Disease (CHD). The antioxidants in grape might help to prevent heart disease and have other potentially beneficial effects.
- Wheatgrass is the freshly sprouted first leaves of the common wheat plant, used as a food, drink, or dietary supplement. Like most plants, wheatgrass contains chlorophyll, amino acids, minerals, vitamins and enzymes.
- The health benefits of wheatgrass ranges from providing supplemental nutrition to having unique curative properties. Because it is extracted from wheatgrass sprouts, i.e., before the 'wheat seed' or 'berry' used in flour begins to form. The wheatgrass juice is gluten-free.
- Wheatgrass is a food made from the *Triticum aestivum* plant. It has many therapeutic benefits and is known as 'Complete Nourishment'. Wheatgrass has antioxidant, antibacterial, and anti-inflammatory properties. It contains iron, calcium, enzymes, magnesium, phytonutrients, 17 amino acids, vitamins A, C, E, K, and B complex, chlorophyll and proteins.
- Lecithin is a fat that is essential in the cells of the body. It can be found in many foods, including Soybeans and Egg Yolks. Lecithin is taken as a medicine and is also used in the manufacturing of medicines. Lecithin is used for treating memory disorders, such as Dementia and Alzheimer's disease.
- Chlorophyll is a green pigment found in plants. People use chlorophyll as medicine. Common sources of chlorophyll used for medicine include Alfalfa (*Medicago sativa*) and Silkworm Droppings.
- Garcinia Cambogia contains an ingredient called HydroxyCitric Acid (HCA), which has been used to aid weight loss.
- Blue Tea or Butterfly Pea Flower Tea, is a caffeine-free herbal concoction, made by seeping dried or fresh leaves of the *Clitoria ternatea* plant.
- Aloe Vera is a gelatinous substance that is obtained from the thick leaves of the cactus-like Aloe Vera plant. The most popular and most familiar use of this extract is for topical use in cosmetic preparations and after-sun lotions.
- Aloe Vera is also used as an ingredient of ointments to treat skin conditions because it is claimed to have anti-inflammatory, itch relieving, painkilling and healing properties.

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- Oat products are a dietary source of the cholesterol-lowering soluble fibre beta-glucan. There is now significant scientific agreement that consumption of this particular plant food can reduce total and Low Density Lipoprotein (LDL) cholesterol, thereby reducing the risk of Coronary Heart Disease (CHD).
- The health benefits of flaxseeds are mainly attributed to the omega-3 fatty acids, lignans and fiber that they contain.
- Bees and their pollination facilities contribute to maintain the biological balance in nature and enable various animals and plant species, including humans, to thrive.
- The bees provide the bee products that are an entirely natural food source.
- Together with honey, which is definitely the most widespread bee product, bees also provide us with Pollen, Propolis, Royal Jelly and Wax.
- Bee venom is another product from which people can be benefitted.
- Honey is the most used of the products derived from beekeeping and is the naturally obtained food.
- Three by-products of beekeeping include Royal Jelly, Bee Pollen and Bee Propolis – are used as dietary supplements.
- Functional foods fall into two broad categories - plant origin and animal origin. The plant based foods have some components that act against lethal diseases, such as cancer.
- A vast number of components, such as fish oil and dairy products naturally present in animal sources are potentially beneficial to health. Nutraceuticals deliver a concentrated form of a biologically active component from a food to enhance health.
- The use of probiotics in combination with prebiotic has been very effective against several chronic diseases.
- Probiotics and prebiotics provide an alternate source for the management of different intestinal disorders. The major contributions associated with the work of probiotics on human health are proper colonic function and increased metabolism.
- Fish contains high levels of nutrients and protein, particularly oily fish, such as salmon and tuna. Fish often has less cholesterol and saturated fat than meat, and it is a staple of the healthful Mediterranean diet. Fish also provides Vitamins and Minerals, including B Vitamins, Zinc, and Iron.
- Oily fish contains omega-3 fatty acids, which are beneficial fats that humans must obtain from their diet. Omega-3 fatty acids have potential health benefits, such as helping prevent cardiovascular disease. As fish is a low-fat protein source, incorporating it into the diet can also potentially lead to weight loss.

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- Fish oil is one of the most commonly consumed dietary supplements. It is rich in Omega-3 fatty acids, which are vital and essential for the health.
- Fish oil is the fat or oil that is extracted from fish tissues. It usually comes from oily fish, such as herring, tuna, anchovies, and mackerel. Yet it is sometimes produced from the livers of other fish, as is the case with Cod Liver Oil.
- The World Health Organization (WHO) recommends eating 1–2 portions of fish per week. This is because the omega-3 fatty acids in fish provides many health benefits, including protection against a number of diseases.
- The dairy products are functional foods. They are one of the best sources of Calcium, an essential nutrient which can prevent Osteoporosis and possibly Colon Cancer.
- In addition to Calcium, recent research has focused specifically on other components in dairy products, particularly fermented dairy products known as 'Probiotics'.
- Probiotics are defined as, 'live microbial feed supplements which beneficially affect the host animal by improving its intestinal microbial balance'.
- Marine ecosystems have a high diversity of living organisms compared to terrestrial ecosystems providing numerous resources for human nutrition and health.

11.5 KEY WORDS

- **Nutraceutical:** A nutraceutical or bioceutical is a pharmaceutical alternative which provides physiological benefits.
- **Spirulina:** It is a small, single-celled microorganism which is rich in chlorophyll, a plant pigment that provides their dark Blue-Green colour to so many lakes and ponds.
- **Kelp:** It is a Brown Algae that grows only in the sea. The name refers to any of the numerous long-stemmed seaweeds that belong to the order Laminariales or Fucales.
- **Wheatgrass:** It is the freshly sprouted first leaves of the common wheat plant, used as a food, drink, or dietary supplement.
- **Aloe Vera:** It is a gelatinous substance that is obtained from the thick leaves of the cactus-like Aloe Vera plant and this extract is used for topical use in cosmetic preparations and after-sun lotions.
- **Probiotics:** These are defined as live microbial feed supplements which beneficially affect the host animal by improving its intestinal microbial balance.

11.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

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Short Answer Questions

1. Explain the terms nutraceutical or bioceutical.
2. What is the advantage of Spirulina and Kelp?
3. Explain the features of green tea and grape tea.
4. What is Wheatgrass?
5. Explain the nutritional significance of Aloe Vera and Blue Tea.
6. What are functional foods?

Long Answer Questions

1. Explain nutraceutical rich supplements with examples.
2. Briefly discuss the significance of nutraceutical or bioceutical with the help of appropriate examples.
3. Explain the nutritional and health benefits of Spirulina and Kelp.
4. Discuss the significance of Wheatgrass as food component?
5. Briefly explain the nutritional components and benefits of caffeine, green tea, grape tea, wheat grass, lecithin, mushroom extract and chlorophyll.
6. Explain the nutritional components and health benefits of Garcinia Cambogia, Aloe Vera and Blue Tea.
7. Discuss the nutraceutical components that are obtained from the animal sources with the help of examples.

11.7 FURTHER READINGS

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UNIT 12 FOOD AS REMEDIES: NUTRACEUTICALS IN TREATMENT FOR COGNITIVE DISORDERS

Structure

12.0 INTRODUCTION

Over the past few years, various types of dietary supplements are available in supermarkets, health food shops and also in chemist shops or pharmacies.

The term 'nutraceutical' is used to describe these medicinally or nutritionally functional foods. Nutraceuticals, are also termed as medical foods, exclusive health foods, phytochemicals, functional foods and nutritional supplements, include the everyday products, such as 'bio' yoghurts and fortified breakfast cereals, as well as vitamins, herbal remedies and even genetically modified foods and supplements. Many different terms and definitions are used in different countries to describe nutraceuticals. Stephen De Felice, founder and chairman of the Foundation for Innovation in Medicine (an American organization) defines a nutraceutical as, 'a food or parts of a food, that provide medical or health benefits, including the prevention and treatment of disease'. Different scientists have given different definitions for functional foods and nutraceuticals, such as, 'a functional food is similar in appearance to conventional foods … consumed as part of a usual diet' whereas, 'a nutraceutical is a product produced from foods but sold in the form of pills, powders, medicines and other medicinal forms not generally associated with food'.

Hence, a functional food is essentially a food, but a nutraceutical is an isolated or concentrated form termed as 'medical foods' and 'dietary supplements'. Many of these health food products are available in the market to treat various disease states. These nutraceutical foods have their origins from the plant and animal kingdoms. The plants produce secondary compounds, such as alkaloids to protect themselves from infection and these constituents are also significant in the treatment of human infection.

In this unit, you will study about the food as remedies, nutraceuticals bridging the gap between the food and drug, nutraceuticals in treatment for cognitive disorders, medicinal plant derived nutraceuticals, anti-aging and anti-inflammatory compounds.

12.1 OBJECTIVES

After going through this unit, you will be able to:

- Discuss the food as remedies
- Understand how nutraceuticals bridge the gap between the food and drug
- Explain how nutraceuticals are used in treatment of cognitive disorders
- Analyse the medicinal plant derived nutraceuticals for anti-aging and anti-inflammatory compounds

12.2 NUTRACEUTICALS FOODS AS REMEDY MEDICINES

Over the past few years, various types of dietary supplements are available in supermarkets, health food shops and also in chemist shops or pharmacies.

The term 'nutraceutical' is used to describe these medicinally or nutritionally functional foods. Nutraceuticals, are also termed as medical foods, exclusive health foods, phytochemicals, functional foods and nutritional supplements, include the everyday products, such as 'bio' yoghurts and fortified breakfast cereals, as well as vitamins, herbal remedies and even genetically modified foods and supplements. Many different terms and definitions are used in different countries to describe nutraceuticals. Stephen De Felice, founder and chairman of the Foundation for Innovation in Medicine (an American organization) defines a nutraceutical as, 'a food or parts of a food, that provide medical or health benefits, including the prevention and treatment of disease'. Different scientists have given different definitions for functional foods and nutraceuticals, such as, 'a functional food is similar in appearance to conventional foods … consumed as part of a usual diet' whereas, 'a nutraceutical is a product produced from foods but sold in the form of pills, powders, medicines and other medicinal forms not generally associated with food'.

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Hence, a functional food is essentially a food, but a nutraceutical is an isolated or concentrated form termed as 'medical foods' and 'dietary supplements'. Many of these health food products are available in the market to treat various disease states. These nutraceutical foods have their origins from the plant and animal kingdoms. The plants produce secondary compounds, such as alkaloids to protect themselves from infection and these constituents are also significant in the treatment of human infection.

Nutraceuticals as Remedy/Therapy

Nutraceuticals are non-specific biological therapies used to promote wellness, prevent malignant processes and control symptoms. These can be grouped into the following three broad categories:

- **Nutrients:** The nutrients are the substances with established nutritional functions, such as Vitamins, Mineral, Amino Acids and Fatty Acids.
- **Herbals:** The herbs or botanical products, such as concentrates and extracts.
- **Dietary Supplement:** Reagents derived from other sources (Pyruvate, Chondroitin Sulphate, Steroid Hormone Precursor) serving specific functions, such as sports, nutrients, weight loss supplements and meal replacement.

The Relationship between Nutraceuticals, Foods and Medicines

The major nutraceuticals have a number of origins, being either endogenous human metabolites, dietary constituents, animal or plant constituents normally not present in the diet in therapeutic levels, or synthetic compounds particularly MSM.

For both patients and pharmacists, the choice of nutraceutical is based upon the disease state, and the efficacy and safety data. The information in this unit is set out according to disease states, which is a logical arrangement for patients and pharmacists wishing to identify a suitable product for treating a particular ailment. The nutraceuticals discussed will be those popularly available, whether or not there is a large body of clinical or scientific evidence to substantiate their use.

Overall, lifestyle and dietary choices are probably the main determinants of health/bad health, and therefore the main question today is:

Can nutraceuticals help in the prevention of diseases and in their treatment?

'Nutraceutical' is the term used to describe a medicinal or nutritional component that includes a food, plant or naturally occurring material, which may have been purified or concentrated, and that is used for the improvement of health, by preventing or treating a disease. It is often thought that nutraceuticals have to occupy a narrow strip of legislative ground between pharmaceuticals and food, but in reality their position is much more complex. Figure 12.1 shows the inter-relationship between nutraceuticals and other health products. This relationship is confused due to the overlap between the various entities, in terms of legal status, origins, marketing and public perception. Pharmaceuticals are usually classed as

medicines by law, but some are freely available without legal constraints and some are legally classed as medicines. For example, in certain countries melatonin is classed as a medicine and is not freely available. Most nutraceuticals, however, are openly on sale and available via the Internet. Herbal remedies may be categorised as medicines because of their perceived risks with self-medication. For example, plants containing potent pharmacological entities, such as digitalis are categorised as medicines. Functional foods are closely related to nutraceuticals as they often contain nutraceuticals in a food-based formulation, such as carotenoids, but others are novel biotechnological entities derived from foods, for instance, prebiotic and probiotics. A new term for these has recently been coined – 'Phoods' – which presumably aims to blur the distinction between pharmaceuticals and foods in the minds of consumers. Further new terms to attract consumers include cosmeceuticals and aquaceuticals, which aim to convey pharmaceutical activity and quality in the areas of cosmetics and soft drinks, respectively.

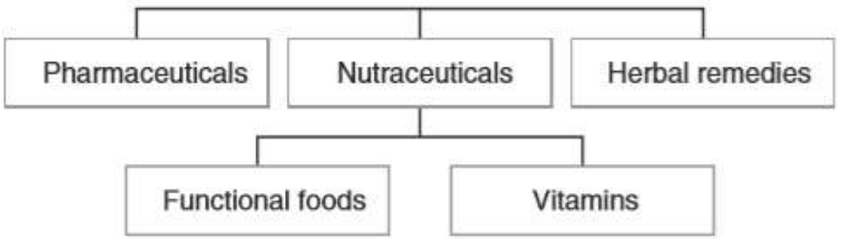

Fig. 12.1 *Relationship between Nutraceuticals and Other Health Foods*

Vitamins can also be categorised as medicines, but may be freely available. The distinction between certain vitamins and nutraceuticals is not distinct, for example Carotene, which is a Vitamin A precursor. Many nutraceuticals are derived from plants or foods and marketing usually follows legal status, medicines and non-medicines being clearly separate. Public perception may involve little distinction between any of these entities, except when legal status affects availability. Most people are guided by the marketing. The nutraceuticals usually appear to be packaged and labelled as if they were medicines. Many terms and definitions are used in different countries and this is quite confusing.

12.3 NUTRACEUTICALS FOR MENTAL HEALTH

Two of the most important mental ailments are **Cognitive Decline** and **Depression**. The most commonly available nutraceuticals claimed to be effective in age-related cognitive decline include Acetyl-L-Carnitine, Phosphatidylserine, n-3 Fatty Acids, particularly DocosaHexaenoic Acid (DHA), Soy Isoflavones, Citicoline (Cytidine Diphosphate Choline), reduced form of Nicotinamide Adenine Dinucleotide (NADH), Green Tea and Carnosine. Depression has been treated with n-3 fatty acids and S-Adenosyl Methionine (SAMe).

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Many people believe that their memory declines with age. Many changes do occur in the ageing brain, including loss of myelin, accumulation of lipofuscin and a reduction in the branching of dendrites, consequently the brain makes fewer new connections. Other changes that may occur during ageing are reduced availability of acetylcholine and reduced cerebral blood flow. The Central Nervous System (CNS) does not generally divide or regenerate cells; it relies on a regular supply of glucose to continuously repair the neurons. Memory loss is probably related to the death of neurons. Increased glutamate and intracellular Calcium levels will lead to necrosis, which can cause inflammation of the brain. Hydroxyl radicals and Hydrogen Peroxide can be produced as by-products of respiration under given conditions, and these are extremely reactive species and will attack DNA, Enzymes and Lipid Membranes. The body's natural defences against these radicals are Antioxidants, such as Superoxide Dismutase, Vitamin C and Alpha-Tocopherol (Vitamin E). Normal memory loss is believed to be caused by a combination of these factors taking place over many years in the brain.

Alzheimer's disease is a form of Dementia that has no specific precipitating factors. It is diagnosed by patients scoring 27 or less on the Mini-Mental State Examination (MMSE). The brain tissue shrinks and there is a loss of neurons, particularly in the hippocampus. Other specific aspects of the disease are the formation of Amyloid Plaques and Neurofibrillary Tangles. These cause damage and are thought to subject the brain to more oxidative stress and ischaemia. Another major feature of Alzheimer's disease is the loss of cholinergic neurons; all the drugs used in the UK to treat mild to moderate Alzheimer's are Acetylcholinesterase Inhibitors. Donepezil, Rivastigmine and Galantamine have a success rate of up to 50% in slowing the disease process. These products are not without side effects and there is great interest in developing dietary and supplementary regimens to help the memory.

Another form of memory loss is that associated with cardiovascular disease. Arteriosclerosis in the cerebral arteries can lead to transient ischaemic attacks, in which not enough blood reaches one part of the brain for a short period of time, or in the worst case scenario, stroke occurs. Small memory lapses may be early symptoms of ischaemia, and the degree of ischaemia and subsequent loss of respiration in the brain have been linked to the severity of certain Dementias. The current pharmacological treatments for Dementia are only partially effective. There is a great deal of interest in whether diet and/or supplementation could slow down or reverse the ageing process in the brain. The following nutraceuticals are marketed as enhancing 'Brain Power Nutraceuticals'.

12.3.1 Acetyl-L-Carnitine

Acetyl-L-Carnitine is a common nutraceutical sold to combat cognitive decline or to enhance memory. The Acetyl form of Carnitine can easily cross the blood–brain barrier and it appears to be well tolerated and safe in humans. Acetyl-L-Carnitine is a very promising agent for the treatment of patients with mild Alzheimer's

disease. It is thought to have many actions on brain cells and to increase the availability of acetylcholine to neurons, possibly by providing acetyl groups to conjugate with choline. It is also believed to be a partial cholinergic agonist, working in a similar way to the current pharmacological treatments for Alzheimer's disease. In addition, Acetyl-L-Carnitine assists the movement of fatty acids from the cytoplasm into mitochondria, where they are converted to ATP, and helps with the removal of toxic long-chain fatty acids. This could lead to a synergism with long-chain fatty acids such as the n-3 group; Acetyl-L-Carnitine is sometimes combined with a linolenic acid in supplements.

Acetyl-L-Carnitine has also been shown to increase the levels of Nerve Growth Factor (NGF), one of a group of substances known as neurotrophins. NGF is involved in the formation of neurons in the developing brain, and has been recently discovered to be implicated in the repair and maintenance of neurons and the formation of new connections between them. The branching of dendrites and formation of new connections is critical in the memory storage process. Acetyl-L-Carnitine may also boost the levels of phosphomonoesters, which are phospholipid components that are reduced in Alzheimer's disease patients. This means that Acetyl-L-Carnitine might synergise with another nutraceutical called phosphatidylserine, which has beneficial effects on the neuron membrane. Other reports state that it could increase Protein Kinase C (PKC) activity and reverse an age-related decline in glutamate N-Methyl D-Aspartate receptors, possibly reducing the risk of excitotoxicity (the death of neurons stimulated by glutamate).

12.3.2 Phosphatidylserine

Phosphatidylserine is a membrane phospholipid found in every cell in the body and is part of a normal diet. It is particularly concentrated in the central nervous system, and is usually found on the inside of the neuron plasma membrane. It was originally derived from bovine brain but with fears about Creutzfeldt–Jakob disease in recent years the production source has been switched to soy. Like other nutraceuticals, phosphatidylserine has many proposed mechanisms of action. Levels are thought to decline with age, which has consequences for the communication and transmission between neurons. Phosphatidylserine supplementation is thought to maintain the ability of the neurons to transmit electrical potentials, which aids the communication between neurons necessary for the formation of memory. It also activates PKC, a substance that helps the release of neurotransmitters such as dopamine, serotonin and acetylcholine, from synaptic vesicles. PKC also upregulates genes that are believed to produce the long-term changes needed to form memory. In addition to this it has been postulated that it could reduce the age-related loss in the number of dendritic spines formed by neurons.

Clinical trials have shown that phosphatidylserine produces minimally significant benefits in a number of clinical and psychometric tests. However the trial with the best results for phosphatidylserine appears to have used subjects who were significantly less mentally impaired than in the rest of the clinical studies.

Phosphatidylserine has generally been tested in patients with mild to moderate dementia, or those with mild cognitive impairment. A double-blind crossover study later reported that the CGI of patients treated with phosphatidylserine was significantly increased compared with the placebo group, and these effects continued for weeks after phosphatidylserine had stopped being administered. However, amongst a battery of psychometric tests administered to the subjects, only reaction times were significantly reduced (no improvements were measured in tests such as logical memory and mental arithmetic). CGI is the most sensitive of tests and only a modest improvement was observed in this work. Use of phosphatidylserine has been shown to result in a consistent improvement in verbal memory tests (e.g., immediate word-list recall) and was found to be better than placebo for face recognition in a trial conducted on normally ageing adults.

12.3.3 DocosaHexaenoic Acid (DHA)

DocosaHexaenoic Acid (DHA) is widely available from fish oils, and the prevalence of Alzheimer's disease correlates negatively with fish consumption. There are high levels of DHA in the brain, and DHA deficiency has been reported to cause a reduction in learning ability in rats. A diet containing a high ratio of n-6 to n-3 fatty acids was shown to have a negative effect on the maintenance of the cognitive functions of the brain, whereas a low ratio was beneficial, using the MMSE evaluation in men aged 69–89 years. A 4:1 ratio of n-6 to n-3 fatty acids was shown to give the best results in learning tasks in rats, and was later tested in 100 patients with Alzheimer's disease. Overall improvement was reported in 49 out of the 60 patients receiving the preparation of fatty acids.

A further study produced similar results, in which participants who consumed fish once weekly or more had a 60% lower risk of Alzheimer's disease compared with those who rarely or never ate fish. Total n-3 PolyUnsaturated Fatty Acids (PUFAs) and DHA were associated with reduced risk, but EicosaPentaenoic Acid (EPA) had no association with Alzheimer's disease.

12.3.4 Soy Isoflavones

Research into feeding a high Soy Isoflavone diet (0.6 mg/g isoflavones) to rats investigated the neuro-behavioural effects. It was found that soy consumption resulted in very high plasma isoflavone levels, which significantly altered dimorphic brain regions, anxiety, learning and memory. Few trials have been carried out in humans, and most of these concentrated on the effects in menopausal women. Evidence that postmenopausal women suffer cognitive decline is possibly due to decreased oestrogen levels, and soy has been considered to be an alternative to Hormone Replacement Therapy (HRT), after controversy over evidence suggesting this leads to increase risk in breast cancer, and additionally that the cognitive benefits of HRT may actually be reversed over long term usage. There is limited evidence to substantiate the benefits of soy isoflavones, one trial on 53 postmenopausal women over six months showed a significant improvement in one of five cognitive

tests, insignificant improvement in two tests and no improvement in the rest. Other work using low levels of isoflavone (60 mg) over short time periods (12 weeks) has been reported to increase memory, pattern recognition and mental flexibility. Another trial carried out with young subjects over a ten-week period found that a dose of 100 mg per day of total isoflavones caused significant cognitive improvements in both young males and females, in both short- and long-term memory, but also in mental flexibility. Soy phytoestrogens have been subjected to a number of investigations in the area of cognitive function in both menopausal and postmenopausal women.

12.3.5 Other Nutraceuticals

Choline compounds, such as phosphatidylcholine, found in lecithin, have been postulated as having beneficial effects on Dementia by increasing the brain levels of acetylcholine. They work in a similar way to the current pharmaceutical treatments, cholinesterase inhibitors, and it is thought that increased acetylcholine levels help any remaining neurons in a diseased brain to work more efficiently. Other forms of choline include citicoline and choline alphoscerate. Citicoline is a combination of choline and cytidine, which may work synergistically to promote dopamine levels, as well as acetylcholine levels.

12.3.6 Treatments for Depression

Mental depression is thought to affect 8–10% of people in Europe, associated with psychological, environmental and hereditary factors. Epidemiological research has shown that populations with low intakes of seafood have a higher prevalence of severe depression. As with risk factors associated with cognitive impairment, red blood cell DHA and EPA levels are significantly lower in people with depression. Two studies investigating the effect of supplementation with n-3 fatty acids have shown significant improvements in depressive symptoms in patients. Supplementation with 6.2 g EPA and 3.4 g DHA daily for four months, 4.2 and 2 g EPA for four weeks showed positive results, but supplementation with 2 g DHA daily for six weeks was found to produce no significant effect. S-Adenosyl Methionine (SAMe) is the most widely investigated nutraceutical for treatment of depression, and has been the subject of clinical trials since 1973. SAMe is a methyl donor and is involved in the synthesis of neurotransmitters in the brain. It is believed that it is as effective as tricyclic antidepressants in alleviating depression, and may even potentiate their activity. Most investigations involved either parenteral dosing at 45–400 mg per day or 200–1600 mg orally daily, and meta-analyses appear to confirm the efficacy of SAMe. Two analyses report significant improvement when compared with placebo, and a third agrees a definite role for its use.

Acetyl-L-Carnitine and Citicoline may be useful supplements for age related decline of varying causes. Further research, specifically largescale, placebo controlled, double-blind trials should be carried out into their use before their

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efficacy is firmly established. Phosphatidylserine appears to have a minimal effect, but it may be beneficial when used in combination with other products. The mechanisms that cause Dementia and Mild Cognitive Impairment are not clearly understood. Loss of memory could be caused by a number of factors including ischaemia, amyloid plaques, a decrease in cholinergic neurons, loss of phospholipid components and oxidative stress. It is likely that combinations of these pathologies are present in any patient with memory loss. Diagnostic tests should improve in the future and scans may be able to show what is really happening in the brain to cause memory loss. Physicians may then be able to prescribe a specific treatment(s) for a specific patient.

12.4 SYNERGISM, BENEFICIAL INTERACTIONS AND COMBINATION PRODUCTS

As more and more combination products becoming available, some involving more than one nutraceutical, some including other entities with claimed biological activity, the identification and study of synergistic and additive effects becomes more important. Synergy is the interaction between two or more constituents, resulting in potentiation of the therapeutic effects and a quantitative increase in the particular effect, above and beyond that expected simply by adding the effects seen by the individual constituents. Synergistic interactions may result from events taking place at many possible loci - absorption, distribution, metabolism, site of action or excretion. Any or all of these can vary with route of administration, age, gender, health, nutritional status, etc. Additive effects, on the other hand, require independent mechanisms and that any rate-limiting or effect-limiting steps in the process are not saturated by any of the individual components acting alone.

Synergism has been reported to occur between conventional medicines, herbal medicines and biologically active food constituents. The major benefits of synergistic reactions between two or more active constituents include reduced dosing levels required to obtain the same response, concomitant reduction of adverse effects, and avoidance of use of potentially toxic medicines. Consumption of plant foods, such as fruit and vegetables, as well as grains, has been strongly associated with reduced risk of many disease states, including cardiovascular disease, cancer, diabetes, Alzheimer's disease and age-related disorders. Plant foods contain a wide range of pharmacologically and physiologically active constituents, including antioxidants. It is now thought that a number of these constituents may act synergistically, and increasingly those examples are being used as nutraceutical supplementation to our diets.

Data are emerging concerning a number of both additive and synergistic interactions between nutraceuticals and other biologically active constituents. A number of patents have been filed concerning these synergistic interactions with nutraceuticals. Some examples are listed in Table 12.1.

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Table 12.1 *Examples of Claimed Synergistic Effects between Nutraceuticals and Medicines, Other Nutraceuticals and Biologically Active Natural Products in Filed Patents*

Medical application	*Nutraceutical*	*Nutraceutical/medicine*
Analgesic[2]	Glucosamine	NSAID/opioid
Articular cartilage repair[3]	Chondroitin/MSM	Four glucosamine derivatives
Anti-inflammatory[4]	Glucosamine	Green-lipped mussel extract
Growth hormone release[5]	Acetyl-L-carnitine	L-Ornithine
Antioxidant effect[6]	Astaxanthin	Mixed tocotrienols
	Carotenoid	Tocotrienol
	Melatonin	Astaxanthin
Treatment of vascular disease[7]	Propionyl carnitine	Chitosan plus derivatives

NSAID, non-steroidal anti-inflammatory drug.

The synergistic effects claimed in patents are usually not corroborated by parallel publications in the medical/scientific literature concerning their in vitro activity, whole animal in vivo results, or randomised clinical trials in either patients or human volunteers. An increasing number of research papers are now being published in the area of synergistic and beneficial interactions of the nutraceuticals.

Check Your Progress

1. Why is the term nutraceutical used?
2. Define nutraceuticals as non-specific biological therapies. What are the three categories of the nutraceuticals?
3. What are the most commonly available nutraceuticals that are effective in age-related cognitive decline?
4. Explain the changes that occur in the ageing brain.
5. What is Acetyl-L-Carnitine?
6. Explain the terms synergy and synergistic interactions.

12.5 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. The term 'nutraceutical' is used to describe the medicinal or nutritional functional foods. Nutraceuticals, are also termed as medical foods, exclusive health foods, phytochemicals, functional foods and nutritional supplements, include the everyday products, such as 'bio' yoghurts and fortified breakfast cereals, as well as vitamins, herbal remedies and even genetically modified foods and supplements. Many different terms and definitions are used in different countries to describe nutraceuticals. Stephen De Felice, founder

and chairman of the Foundation for Innovation in Medicine (an American organization) defines a nutraceutical as, 'a food or parts of a food, that provide medical or health benefits, including the prevention and treatment of disease'. Hence, a nutraceutical is an isolated or concentrated form termed as 'medical foods' and 'dietary supplements'.

2. Nutraceuticals are non-specific biological therapies used to promote wellness, prevent malignant processes and control symptoms. These can be grouped into the following three broad categories:
   - **Nutrients:** The nutrients are the substances with established nutritional functions, such as Vitamins, Mineral, Amino Acids and Fatty Acids.
   - **Herbals:** The herbs or botanical products, such as concentrates and extracts.
   - **Dietary Supplement:** Reagents derived from other sources (Pyruvate, Chondroitin Sulphate, Steroid Hormone Precursor) serving specific functions, such as sports, nutrients, weight loss supplements and meal replacement.
3. The most commonly available nutraceuticals claimed to be effective in age-related cognitive decline include Acetyl-L-Carnitine, Phosphatidylserine, n-3 Fatty Acids, particularly DocosaHexaenoic Acid (DHA), Soy Isoflavones, Citicoline (Cytidine Diphosphate Choline), reduced form of Nicotinamide Adenine Dinucleotide (NADH), Green Tea and Carnosine. Depression has been treated with n-3 fatty acids and S-Adenosyl Methionine (SAMe).
4. Many changes occur in the ageing brain, including loss of myelin, accumulation of lipofuscin and a reduction in the branching of dendrites, consequently the brain makes fewer new connections. Other changes that may occur during ageing are reduced availability of acetylcholine and reduced cerebral blood flow. The Central Nervous System (CNS) does not generally divide or regenerate cells; it relies on a regular supply of glucose to continuously repair the neurons. Memory loss is probably related to the death of neurons. Increased glutamate and intracellular Calcium levels will lead to necrosis, which can cause inflammation of the brain.
5. Acetyl-L-Carnitine is a common nutraceutical sold to combat cognitive decline or to enhance memory. The Acetyl form of Carnitine can easily cross the blood–brain barrier and it appears to be well tolerated and safe in humans. Acetyl-L-Carnitine is a very promising agent for the treatment of patients with mild Alzheimer's disease.
6. Synergy is the interaction between two or more constituents, resulting in potentiation of the therapeutic effects and a quantitative increase in the particular effect, above and beyond that expected simply by adding the effects seen by the individual constituents. Synergistic interactions may result from events taking place at many possible loci - absorption, distribution, metabolism, site of action or excretion. Any or all of these can vary with

route of administration, age, gender, health, nutritional status, etc. Synergism has been reported to occur between conventional medicines, herbal medicines and biologically active food constituents.

12.6 SUMMARY

- Over the past few years, various types of dietary supplements are available in supermarkets, health food shops and also in chemist shops or pharmacies. The term 'nutraceutical' is used to describe these medicinally or nutritionally functional foods.
- Nutraceuticals, are also termed as medical foods, exclusive health foods, phytochemicals, functional foods and nutritional supplements, include the everyday products, such as 'bio' yoghurts and fortified breakfast cereals, as well as vitamins, herbal remedies and even genetically modified foods and supplements.
- Many different terms and definitions are used in different countries to describe nutraceuticals. Stephen De Felice, founder and chairman of the Foundation for Innovation in Medicine (an American organization) defines a nutraceutical as, 'a food or parts of a food, that provide medical or health benefits, including the prevention and treatment of disease'.
- Different scientists have given different definitions for functional foods and nutraceuticals, such as, 'a functional food is similar in appearance to conventional foods … consumed as part of a usual diet' whereas, 'a nutraceutical is a product produced from foods but sold in the form of pills, powders, medicines and other medicinal forms not generally associated with food'.
- Nutraceuticals are non-specific biological therapies used to promote wellness, prevent malignant processes and control symptoms.
- The nutrients are the substances with established nutritional functions, such as Vitamins, Mineral, Amino Acids and Fatty Acids.
- The herbs or botanical products, such as concentrates and extracts.
- Dietary supplement are the reagents derived from other sources (Pyruvate, Chondroitin Sulphate, Steroid Hormone Precursor) serving specific functions, such as sports, nutrients, weight loss supplements and meal replacement.
- Functional foods are closely related to nutraceuticals as they often contain nutraceuticals in a food-based formulation, such as carotenoids, but others are novel biotechnological entities derived from foods, for instance, prebiotic and probiotics.
- Two of the most important mental ailments are Cognitive Decline and Depression. The most commonly available nutraceuticals claimed to be effective in age-related cognitive decline include Acetyl-L-Carnitine,

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Phosphatidylserine, n-3 Fatty Acids, particularly DocosaHexaenoic Acid (DHA), Soy Isoflavones, Citicoline (Cytidine Diphosphate Choline), reduced form of Nicotinamide Adenine Dinucleotide (NADH), Green Tea and Carnosine. Depression has been treated with n-3 fatty acids and S-Adenosyl Methionine (SAMe).

- Many changes occur in the ageing brain, including loss of myelin, accumulation of lipofuscin and a reduction in the branching of dendrites, consequently the brain makes fewer new connections. Other changes that may occur during ageing are reduced availability of acetylcholine and reduced cerebral blood flow.
- The Central Nervous System (CNS) does not generally divide or regenerate cells; it relies on a regular supply of glucose to continuously repair the neurons.
- Memory loss is probably related to the death of neurons. Increased glutamate and intracellular Calcium levels will lead to necrosis, which can cause inflammation of the brain.
- Alzheimer's disease is a form of Dementia that has no specific precipitating factors. It is diagnosed by patients scoring 27 or less on the Mini-Mental State Examination (MMSE). The brain tissue shrinks and there is a loss of neurons, particularly in the hippocampus.
- Small memory lapses may be early symptoms of ischaemia, and the degree of ischaemia and subsequent loss of respiration in the brain have been linked to the severity of certain Dementias.
- Acetyl-L-Carnitine is a common nutraceutical sold to combat cognitive decline or to enhance memory. The Acetyl form of Carnitine can easily cross the blood–brain barrier and it appears to be well tolerated and safe in humans. Acetyl-L-Carnitine is a very promising agent for the treatment of patients with mild Alzheimer's disease.
- Phosphatidylserine is a membrane phospholipid found in every cell in the body and is part of a normal diet. It is particularly concentrated in the central nervous system, and is usually found on the inside of the neuron plasma membrane.
- DocosaHexaenoic Acid (DHA) is widely available from fish oils, and the prevalence of Alzheimer's disease correlates negatively with fish consumption. There are high levels of DHA in the brain, and DHA deficiency has been reported to cause a reduction in learning ability in rats.
- Feeding a high Soy Isoflavone diet (0.6 mg/g isoflavones) to rats investigated the neuro-behavioural effects. It was found that soy consumption resulted in very high plasma isoflavone levels, which significantly altered dimorphic brain regions, anxiety, learning and memory.
- Choline compounds, such as phosphatidylcholine, found in lecithin, have been postulated as having beneficial effects on Dementia by increasing the brain levels of acetylcholine.

- Citicoline is a combination of choline and cytidine, which may work synergistically to promote dopamine levels, as well as acetylcholine levels.
- Epidemiological research has shown that populations with low intakes of seafood have a higher prevalence of severe depression. As with risk factors associated with cognitive impairment, red blood cell DHA and EPA levels are significantly lower in people with depression.
- Acetyl-L-Carnitine and Citicoline may be useful supplements for age related decline of varying causes.
- Synergy is the interaction between two or more constituents, resulting in potentiation of the therapeutic effects and a quantitative increase in the particular effect, above and beyond that expected simply by adding the effects seen by the individual constituents.
- Synergistic interactions may result from events taking place at many possible loci - absorption, distribution, metabolism, site of action or excretion. Any or all of these can vary with route of administration, age, gender, health, nutritional status, etc.
- Synergism has been reported to occur between conventional medicines, herbal medicines and biologically active food constituents.
- The major benefits of synergistic reactions between two or more active constituents include reduced dosing levels required to obtain the same response, concomitant reduction of adverse effects, and avoidance of use of potentially toxic medicines.

12.7 KEY WORDS

- **Nutrients:** The nutrients are the substances with established nutritional functions, such as Vitamins, Mineral, Amino Acids and Fatty Acids.
- **Herbals:** The herbs or botanical products, such as concentrates and extracts.
- **Dietary supplement:** Reagents derived from other sources (Pyruvate, Chondroitin Sulphate, Steroid Hormone Precursor) serving specific functions, such as sports, nutrients, weight loss supplements and meal replacement.
- **Acetyl-L-Carnitine:** It is a common nutraceutical sold to combat cognitive decline or to enhance memory as the Acetyl form of Carnitine can easily cross the blood–brain barrier and is a very promising agent for the treatment of patients with mild Alzheimer's disease.
- **Synergy:** It is the interaction between two or more constituents, resulting in potentiation of the therapeutic effects and a quantitative increase in the particular effect, above and beyond that expected simply by adding the effects seen by the individual constituents.

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- **Synergistic interactions:** These may result from events taking place at many possible loci - absorption, distribution, metabolism, site of action or excretion. Any or all of these can vary with route of administration, age, gender, health, nutritional status, etc.

12.8 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. Explain the term food as remedies.
2. How nutraceuticals food helps in treatment of Alzheimer's disease.
3. What are cognitive disorders?
4. Explain anti-aging and anti-inflammatory compounds.
5. What is synergy?

Long Answer Questions

1. Briefly discuss the concept nutraceuticals food as remedies for many diseases giving appropriate examples.
2. The nutraceuticals bridge the gap between food and drugs. Justify the statement giving relevant examples.
3. Discuss how nutraceuticals help in the treatment of cognitive disorders. Give any one example as case study.
4. Explain how the nutraceuticals derived from medicinal plant help in anti-aging and anti-inflammatory effects.

12.9 FURTHER READINGS

Vattem, Dhiraj A. and Vatsala Maitin. 2016. *Functional Foods, Nutraceuticals and Natural Products, Concepts and Applications*. USA: DEStech Publications, Inc.

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UNIT 13 NUTRACEUTICAL REMEDIES FOR ARTHRITIS, BRONCHITIS, CIRCULATORY PROBLEMS AND HYPOGLYCEMIA

Structure

13.0 INTRODUCTION

Nutraceuticals are food or part of food that plays a significant role in modifying and maintaining normal physiological functions that maintains the health of human beings. The nutraceutical market is gaining popularity worldwide as the population is more conscious about the health trends. The food products used as nutraceuticals can be categorized as dietary fibre, prebiotics, probiotics, polyunsaturated fatty acids, antioxidants and other different types of herbal/ natural foods. These nutraceuticals help in combating some of the major health problems of the century, such as obesity, cardiovascular diseases, cancer, osteoporosis, arthritis, diabetes, cholesterol, etc. In whole, 'nutraceutical' has led to the new era of medicine and health, in which the food industry has become a research oriented sector.

In this unit, you will study about nutraceutical remedies for arthritis, bronchitis, circulatory problems and hypoglycemia in detail.

13.1 OBJECTIVES

After going through this unit, you will be able to;

- Understand how nutraceutical remedies are helpful in arthritis, bronchitis, circulatory problems and hypoglycemia
- Discuss about various ways to cure different diseases

13.2 NUTRACEUTICAL REMEDIES FOR ARTHRITIS

Arthritis is a progressive degenerating joint disease that has a major impact or joint-function and quality of life. Nutraceutical are dietary compounds which have a role in the balance of anabolic and catabolic signals in joints. It is a degenerative disease characterized by cartilage and synovium inflammation that can cause joint stiffness, swelling, pain and loss of mobility. Current literature existing nutraceutical compounds that could be used as integrators in a daily diet, such as in olive oil, fish oil and botanical extracts used as non-pharmacological treatment.

Nutraceuticals

- **Fish Oil:** Omega-3 blocks inflammatory cytokines and prostaglandin and are converted by the body into powerful anti-inflammatory chemicals called resolving, the competition for receptors of n-3 products with proinflammatory molecules; the reduction in gene expression of cytokines, cyclo-oxygenase 2, with degrading proteinases; the interference in the signaling pathway of inflammation and the reduction in lymphocytes proliferation.
- **Olive Oil:** Olive oil is the principal fat and one of the Mediterranean diet. The anti-inflammatory properties of Olive oil are attributed to its phytochemicals, such as the Phenolic Compounds and Mono-Unsaturated Fatty Acids, PCMUFAs. In Olive oil improved pain and physical functions in patients affected by knee osteoarthritis.
- **Methionine:** It is an essential amino acid for humans, since the human organism is not able to synthesize it and it is therefore taken with diet. The active form of methionine is S-Adenosyl Methionine (SAMe) is a precursor of glutathione. SAMe has antioxidant properties and, in the joints, provides levels of glutathione peroxidase, an antioxidant enzyme. In patients with is arthritis, treatment with SAMe has a more beneficial effect in long term compared to treatment with Compounds of Non-Steroidal Anti-Inflammation Drugs, CNSAIDs.
- **Gamma Linolenic Acid (GLA):** It is an Omega-6-fatty acid that the body converts into anti-inflammatory chemicals. In one trial, 56 patients with active RA showed significant improvement in joint pain.

- **Botanical Extracts:** Botanical extracts are a large variety of substances obtained from plants and used as additives in diet.
- **Avocado/Soy Unsaponifiable (ASU)**: Avocado/Soy Unsaponifiable or ASU components are a sterol rich hydrolysed lipid fraction extract from avocado and Soyabean. ASU has anabolic and anti-inflammatory properties on chondrocytes. ASU blocks pro-inflammatory chemicals, prevents deterioration of synovial cells which line joints, and may help regenerate normal connective tissue.
- **Capsaicin (*Capsicum frutescens*):** Capsicum temporarily reduces substance P, a pain transmitter. Its pain relieving properties have been shown in many studies which revealed a 50 per cent reduction in joint pain after three weeks of use.
- **Turmeric/Curcumin:** Curcumin is extracted from the Indian spice Turmeric, it is an aromatic molecule with an anti-inflammatory effect that in vitro showed to inhibit the activity of COX-2 and 5-LOX enzyme. It can reduce joint pain and smelling by blocking inflammatory cytokines and enzymes. Turmeric supplement showed long term improvement in pain and function in patients with knee OA.
- **Bromelain:** Bromelain is extracted from stems and immature fruits of pineapple and it contains proteolytic enzymes that may have anti-inflammatory, analgesic and anti-fibrinolytic properties.
- **Boswellia Serrate:** The active components have anti-inflammatory and pain relieving properties. It may also help prevent cartilage loss and inhibit the autoimmune process. In a study, the extract also known as Loxin 5, significantly improved OA pain and function within seven days. An Indian study revealed that it showed cartilage damage after three months of use.

13.3 NUTRACEUTICAL REMEDIES IN BRONCHITIS

Respiratory disorders are among the leading causes of morbidity and mortality, affect people of all ages and are a major global health problem. They involve the air passages, such as nasal passages, large and small airways and the lungs. Bronchial Asthma, Chronic Obstructive Pulmonary Disease (COPD), Pulmonary Tuberculosis, Pneumonia, Fibrosis, Lung Cancer and Pneumoconiosis are commonly seen respiratory conditions. The COPD is caused by inhalation of toxins and irritants for longer durations, resulting in chronic inflammation of airways and damage of alveolar structure of the lungs. This finally results in condition like Chronic Bronchitis, Chronic Bronchiolitis and Emphysema.

Nutraceutical is a combination of two words, nutrient and pharmaceutical. Nutraceuticals are products that are used for the maintenance of health and prevention and treatment of disease. They also have basic nutritions value.

Alternatively, a nutraceutical may simply be considered as any substances that has physiological benefit or provides protection against chronic disease.

Prebiotics and Probiotics

Probiotics are living microbial food supplements that when administered in adequate amounts, benefit the host organism by improving its intestinal microbial balance. Lactobacilli, Gram Positive Cocci and Bifidobacteria are mostly found in the gut. There is evidence that administration of probiotics decreases the risk of systemic conditions, such as dietary ingredients that act by selectively altering the composition or metabolism of the gut microbiota. These are short chain Polysaccharides (Fructose-Based Oligosaccharides). The prebiotics consumption generally promotes the lactobacillus and bifidobacterial growth in the gut, thus, helping metabolism. Because of the immuno-modulating properties of Probiotics, Prebiotics and Synbiotics may be valuable tool to treat and prevent immune disorders, such as Allergies.

- ***Adhatoda vasica:*** It is a shrub used by Asian and European medical practitioners. The leaves, roots, flowers and bark of this plant have been used in cough, colds, asthma, liquefy sputum, bronchodilator, bronchitis and tuberculosis. An essential oil from the leaves showed an airways smooth muscle relaxant property in the isolated Guinea Pigs. Vasicine, an alkaloid is one of the major components of the plant and is responsive for most of its antioxidant, anti-inflammatory and bronchodilatory activities.
- ***Bryophyllum pinnatum* or *Kalanchoe integra:*** It has shown various activities, such as immune suppressive, wound healing, hepatoprotective, anti-inflammatory, antidiabetic, antioxidant, antimicrobial, analgesic, anti-convulsant. In respiratory disorders, boiled leaf extracts are useful in the management of acute and chronic bronchitis, pneumonia, bronchial asthma and palpitation.
- ***Zingiber officinale:*** It is a dietary component that is commonly known as ginger. This is the rhizome of the plant which has been used in the treatment of cold, asthma and bronchitis. The ethanolic extracts of ginger rhizome exhibited antibacterial activity against respiratory tract pathogens. Fresh ginger has antiviral activity against human respiratory syncytial virus-induced plaque formation on airway epithelium.

13.4 NUTRACEUTICAL REMEDIES FOR CIRCULATORY SYSTEM

The three major factors that cause circulation problems including Heart Diseases are smoking, high blood pressure levels, etc. The Cardio Vascular Diseases (CVD) ranks amongst the most common health issues worldwide.

Many studies have now linked excessive consumption of fats to subsequent heart disease and other circulatory problem. There are following two types of fat:

- Unsaturated Fat found in Seed Oils and Fish Oils.
- Saturated Fats are obtained mostly from Animal Sources. Pecent guidelines suggested that saturated fats should be limited to 10% of yours total calorie intake.

The circulation system carries blood to and from all parts of the body through arteries, veins and tiny blood vessels that would stretch for about 160000 km (100000 miles) if they were laid out end to end. The heart is four chambered pump that powers the entire system. The body's extremities, which are farthest from it, are particularly prone the circulatory problems.

The most common and serious disorders associated with poor circulation is ATHRESCLEROSIS, in which the walls of the arteries develop fatty deposits, thicken, become less supple and so impede the blood flow. This increases the risk of heart attacks, strokes and a variety other disorders depending on which arteries affected.

Various CVD's

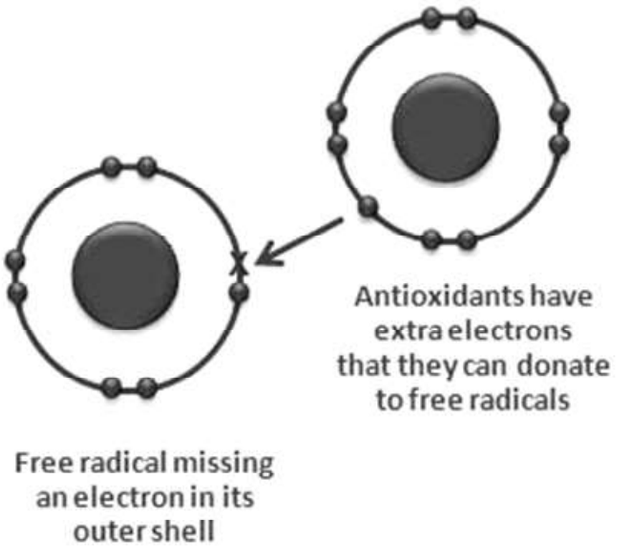
- Arrhythmia (Irregular Heartbeat)
- Angina (Chest Pain)
- Coronary Artery Diseases (Narrowing of the Blood Vessels)
- Arteries that Supply Oxygen and Blood to the Heart
- Heart Attack
- Heart Failure
- Stroke
- Blood Clotting Disorders
- Atherosclerosis

Role of Nutraceutical in CVD

Averting vascular disease is now a central calling for the nutraceutical industry. This is because the mechanisms of vascular damage have increasingly indicated a major culprit; a lack of nutrition hygiene.

There are following three strategies the nutraceutical can offer to prevent and reverse vascular diseases.

- The first is to reduce circulating levels of LDL-cholesterol by forming micelle with bile salts as it contains cholesterol.
- The second strategy is to reduce the possibility of oxidation by neutralizing radicals with antioxidants.
- The third is to reduce artery plaque through fibrinolytic activity. A fibrin clot is broken down a product of coagulation. Enzyme plasmin, cuts the fibrin mesh at various places leading to production of fragments that are cleared by kidney and liver.



Role of Nutraceuticals in Vascular Diseases and CVD

Sterols and Stanols

- Plant derived sterols and stanols compete with cholesterol to form micelles with bile salts. This reduces cholesterolis absorption into the blood stream.
- All plants contain sterol, such as stigmasterol, beta-sitosterol and campesterol. Significant amounts appear in vegetables, nuts and seeds.
- Significant stanol content is found in avocados, pumpkin seeds, cashmes, rice bran and others. Plants favored for sterol and stanol extraction include cord, soya beans and wheat.

Phenols

Phenols have been shown to reduce cholesterol levels and LDC oxidation. Polyphenolic cathechin which is present in Green Tea reduces the CVD by enhancing antioxidant activity by improving endothelial dysfunction preventing cardiac hypertrophy and mitochondria.

Super Fibers

- Dietary fibres found in plant foods, fruits, vegetables and whole grains are essential to maintain healthy digestive system.
- Two types of fiber is soluble fiber, such as gums and pectins which can dissolve in water which helps to lower blood fat and maintain blood sugar.
- Insoluble fibers cannot dissolve in water, so directly passes through the digestive tract and helps to trap cholesterol, toxins, etc., that are then expelled through faeces.

Tocotrienols

Tocotrienol are members of a subgroup of the Vitamin E family, which includes tocopherols. Both tocotrienols and tocopherols are antioxidants but only tocotrienols have been shown to reduce cholesterol, inhibit certain cancers and manage diabetes.

Vitamin D (Calciferol)

- Vitamin D acts as a hormone which regulates more than 200 genes throughout the body. It does an impressive amount of work.
- Helps regulate blood pressure in the Kidney.
- Helps regulate blood sugar levels in the Pancreas.
- It directly effects the arterial wall and may protect them against Atherosclerosis. Through the inhibition of macrophage, cholesterol is responsible for cell formation, reduced vascular smooth cell proliferation and reduced expression of adhesion molecules in endothelial cells.

Pantethine

- It is a dimer form of Pantothenic Acid (Vitamin B5).
- It reduces cardio vascular risk by inhibiting platelet dumping and the production of the inflammation in producing chemical, Thromboxane A2 (CVR).
- Pantethine (300 mg 3 times daily) reduced serum triglycerides 32%, total cholesterol 19%, and LDC cholesterol 21% HDL cholesterol levels increased 23%.

Sources: Milk, Egg, Peas, Cereals

Fish

People with high intake of dietary fish and fish oil supplements have a low rate of CVD. Both EicosaPentaenoic Acid (EPA) and DocosaHexaenoic Acid (DHA) are only found in fish, such as Salmon, Tuna, Lake Trout and Herrings. Fish oil supplements have favourable effects on lipid profile and blood pressure. Fish ingestion has been related to a reduced risk for mycocardial imfarction which may relate to beneficial effects of EPA and DHA on plaque stability.

Fruits and Vegetables

There are various literature that has ben reported the beneficial effects of diets rich in vegetables and fruits on CVD risks. Inadequate consumption of fruits and vegetables may cause higher incidences of CVD as compared to increased frequency of fruits and vegetable intake.

Fruits and vegetables have been found to decrease susceptibility of particles to oxidation due to their antioxidant and anti-inflammatory effects. Several bioactive

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components in fruits and vegetables, such as Carotenoids Vitamin C, Fiber, Magnesium and Potassium act synergistically to promote a holistic beneficial effect.

Nuts and Legumes

Nuts are complex foods containing cholesterol lowering mono and polyunsaturated fatty acids, arginine, soluble fiber, and several antioxidant polyphenols. Cardioprotective effects of diets high in nuts is robust as multiple mechanisms work together to reduce risk.

Legumes are also complex foods rich in soluble fibers and polyphenols, as well as folic acid. Cholesterol lowing effect of legumes are probably due to the combined effects of several bioactive components, such as protein, soluble and in soluble fibres and phytosterols.

Whole Grains

Whole grain products contain intact grain kernels rich in fiber and trace elements. They are nutritionally more important because they contain cytoprotective substances that might work synergistically to reduce cardio vascular risk.

The mechanisms underlying the protective effects of whole grains on CVD risk include its effect on insulin sensitivity, blood pressure, lipids and inflammation. Antiinflammatory mechanism may be related to higher intake of antioxidant nutrients present in the germ of whole grains.

Soy Proteins

Soy is the main source of protein. Soy products are rich in polyunsaturated fatty acids, fiber and vitamin and minerals and low saturated fat content. In some studies there is remarkable decrease in reduction of total cholesterol and LDL as well as of chromic and cerebrovascular events with a daily intake of Soya Protein.

Soy products contain many isoflavonoids, such as Genistin, Daidzin and Glycitin that are natural phytoestrogens able to inhibit LDL. Oxidation thus decreasing the risk of Atherosclerosis.

Dark Chocolates

Cocoa is a flavonoids-rich food that has been recently investigated for its possible role in prevention of CVD (Refer Table 13.1). In healthy adults, drinking flavonoid-rich cocoa may improve no-dependent vasorelaxation and flow-mediated dialation in the brachial arteries. Administration of dark chocolates in essential hypertensives reduced ambulatory blood pressure and serum LDL.

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Table 13.1 *Potential Cardio Vascular Protective Effects of Function*

Functional foods	Bioactive compounds	Potential mechanism
- Nuts	- Tocopherols, omega-3 fatty acids	Lowering blood cholesterol
- Legumes	- Fiber and polyphenols	
- Fruits and vegetables	- Fiber (pectin)	
- Margarine	- Phytosterols	
- Fish oil	- Omega-3 fatty acids	
- Whole grains	- Fiber and phytochemicals	
- Soy proteins	- Genistein and daidzein	
- Dark chocolate	- Flavonoid	
- Fish	- Omega-3 fatty acids	Inhibition of LDL-C oxidation
- Green leafy vegetables, fruits	- Carotenoids	
- Citrus fruits and vegetables	- Vitamin C	
- Tomato	- Lycopene	
- Extravirgin olive oil	- Polyphenolics and oleic acid	
- Green tea	- Tea polyphenolics	
- Soy proteins	- Genistein, daidzein, and glycitein	
- Dark chocolate	- Flavonoid	
- Pomegranate	- Polyphenols	
- Fish	- Omega-3 fatty acids	Lowering blood triglycerides
- Fish	- Omega-3 fatty acids	Decreasing blood pressure
- Legumes	- Fiber	
- Whole grains	- Fiber and phytochemicals	
- Citrus fruits	- Ascorbic acid	
- Ginseng	- Ginsenosides	
- Onion and garlic	- Quercetin	
- Green and black teas	- Tea polyphenols	
- Grapes and red wines	- Grape polyphenols	
- Dark chocolate	- Flavonoid	
- Fruits and vegetables	- Folate - Phytochemicals	Lowering blood homocysteine
- Whole grains	- Fiber and phytochemicals	
- Citrus fruits and vegetables	- Vitamin C	
- Nuts, seeds, and oils	- Vitamin E	
- Tomatoes	- Lycopene	Antioxidant action
- Green leafy vegetables, fruits	- Carotenoids	
- Vegetable oils	- Tocopherol, tocotrienols	
- Citrus fruits and vegetables	- Vitamin C	
- Soy proteins	- Genistein and daidzein	
- Green and black teas	- Tea polyphenols	
- Grapes and red wines	- Anthocyanins, catechins, cyanidins, and flavonols, myricetin and quercetin	

Table 13.2 *Classification of Nutraceuticals*

Chemical Constituent	Source	Potential Benefit
1. Carotenoids (Isoprenoids)		
Lycopene	Tomatoes, Grapefruit, Guava, Papaya, Watermelon	Antioxidant activity, protects against formation of Cancer mainly Prostate, Bladder, Cervical, Leukemia.
Lutin	Corn, Avocado, Egg York, Spinach	Anticancer activity (colon) cataracts, protects the eyes against development of age related muscular degeneration.
β-Carotene	Carrots, various Fruits and Vegetables, Carrots	Antioxidant activity which neutralizes free radicals, protect cornea against UV Light, Antioxidants.
α-Carotene	Orange and	Anticarcinogenic
α-Cryptoxanthin	Tangerines	Antioxidants, Anticancer
Zeaxanthin	Corn, Avocado	Protects Eye from Macular Degeneration and Cataracts
2. Dietary Fibres		
Solube Fibre	Legumes, oats, barely, some fruits	Anticancer, helpful in maintaining the digestive tract
Insoluble Fibre	Whole grain foods Wheat and corn bran, nuts	Anticancer (colon), helpful in maintaining the digestive tract
3. Polyphenolic Compounds		
Flavonones	Citrus fruits	Antioxidants, Anti-cancer
Flavones	Fruits, Vegetables, Soyabean	Antioxidants, Anti-cancer
Flavonols	Onions, apples, tea, broccoli	Antioxidants
Anthocyanins	Blueberries, blackberries, black raspberries	Anti-oxidants, counteracts inflammation in the body, Lower blood sugar levels in people with diabetes
Phenolic Acids	Berries, legumes	Phenolic acids reduce oxidation of LDL cholesterol. Reduce formation of cancer
Resveratrol	Dark grapes, Raisins, berries, peanuts	Lowers total serum cholesterol increasing HDL
Curcumin	Turmeric root	Strongly anti- inflammatory and strongly anti-oxidant, effective anti-clotting agent

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4. Fatty Acids		
Omega 3 Fatty Acids (Poly Unsaturated Fatty Acids)	Salmon, Flax seed	Potent controllers of the inflammatory processes, Maintenance of brain function, Reduce cholesterol disposition
Monosaturated Fatty Acids	Tree nuts	Reduce risk of coronary heart disease
5. Isothiocyanates **6. Sulporaphane**	Cauliflower, broccoli, cabbage, kale, Horseradish	May enhance detoxification of undersirable compounds and bolster cellular antioxidant defences
7. Phenols Caffeic Acid Ferulic Acid	Apples, pears, citrus fruits, some vegetables	May bolster cellular antioxidant defences: May contribute to maintenance of vision and heart health
8. Plant Stanols/Sterols	Fortified table	May reduce risk of
Stanol/Sterol Esters	spreads, stanol ester dietary supplements	coronary heart disease
Tocotrienol (Isoprenoids)	Grains, Palm Oil	Anticancer (breast cancer), Promotes cardiovascular health
9. Saponins	Chickpeas and soybeans	Lowers cholesterol level, Anticancer activity (colon)
10. Probiotics/Prebiotics Lactobacilli, bifidobacteria	Yogurt, other dairy and non dairy Applications	May improve gastrointestinal health and systematic Immunity
11. Minerals Calcium, selenium, potassium, zinc, copper	Food	Important constituent of balanced diets
12. Polyols Sugar Alcohols (xylitol, sorbital)	Fruits	Reduces risk of dental caries
13. Sulphides/Thiol s Dithiothiones	Cruciferous vegetables	May contribute to maintenance of healthy immune function
14. Gulcosinolates	Cruciferous vegetables, Cauliflower	Anticancer (bladder cancer)
15. Phytoestrogens		
Isoflavanes (genistein, daidzein)	Soybeans, legumes	Lowers LDL cholesterol antioxidant, anticancer (prostate, breast, bowel)
Liganans	Flaxseed, rye, vegetables	Inhibit the development of breast cancer and colon cancer

16. Alkaloids		
Quinine	Cinchona	Anti-malarial
Tropane Alkaloids	Solanaceous members: Deadly night shade, Datura	In treatment of heart ailments
Morphine	Opium poppy	Antidepressant, pain killer
Ergot Alkaloids	Fungus: (Claviceps purpurea)	Abortifiacients
Vincristine	Periwinkle	Antineoplastic
Vinblastine	Periwinkle	Antineoplastic
Coumarin	Fenugreek	Hypoglycaemic
Scopoletin	Fenugreek	Hypoglycaemic
Fenugreekine	Fenugreek	Hypoglycaemic
Trigonelliine	Fenugreek	Hypoglycaemic
17. Non-Carotenoid terpenoids		
Perillyl Alcohol	Cherries and mints	Anticancer
Saponins	Legumes (Chicks, peas, fenugreek, all	Reduces cholesterol levels in blood
	pulse crops)	
Terpenol	Carrots	Anticancer
Terpene Limonoids	Peels and membranes of citrus fruits	Anticarcinogenic
18. Anthraquinones		
Senna	Legumes and pulses	Purgative
Barbaloin	Aloe	Laxative, anti-helminthic
Hypericn	St. John's Wort	Analgesic
Capsaicin	Capsicum (hot peppers)	Anticancer, anti-inflammatory, anti- apoptotic
Piperine	Black peppers, jalapeno peppers	Helps in digestion

13.5 NUTRACEUTICAL REMEDIES IN TREATMENT OF HYPOGLYCAEMIA

Diabetes mellitus as a metabolic disorder characterised by hyperglycaemia or high blood sugar. The characteristic symptoms of diabetes are polyuria (excessive urine, polydipsia thirst and increased fluid intake) and blurred vision. The World Health Organizations (WHO) recognizes three main forms of Diabetes Mellitus - Type 1, Type 2, Gestational Diabetes (occurring during pregnancy). All forms are

due to the beta cells of the pancreas being unable to produce sufficient insulin to prevent hyperglycaemia Type 1 is usually due to the autoimmune destruction of the pancreatic beta cells, which produce insulin. Type 2 is characterised by tissue wide insulin resistance, but impairment of beta cell function is necessary for its development.

Diabetes can cause many complications. Acute complications include hypoglycaemia, ketoacidosis or non-ketonic hyperosmolar coma, if the disease is not adequately controlled.

Uncontrolled glucose levels are one of the most common health problems in the world. Hypoglycaemia symptoms frequently affect people with prediabetes or diabetes. Anyone who consumes a poor diet and has trouble with normal glucose metabolism can develop symptom of hypoglycaemia.

Hypoglycaemia is a condition caused by a low blood sugar levels, also sometimes referred to as low glucose.

Symptoms

- Hunger
- Symptoms of Anxiety
- Sweating
- Feeling Dizzy or Light Headed
- Becoming Fatigued and Tired
- Trouble Sleeping
- Feeling Irritable
- Paleness in the Face
- Headaches
- Muscle Weakness

Nutraceutical: New Weapon for Holistic Treatment

Food and drugs from nature are playing a quite significant role in healthcare system. Human inquisitiveness and search for specific constituents of plants, animals, minerals and microbial origins which are beneficial to our overall health has coined termed like functional food or nutraceuticals. The term nutraceuticals came from a combination of nutrition and pharmaceuticals and can be defined as a food or part of a food that provides medical or health benefit including the prevention and treatment of a disease.

- **Aloe Vera:** Aloe Vera extract is useful for skin infections, wound and burn healing due to the presence of compounds as Polysaccharides, *Anthraquinone* and Lectins, which have also been reported for anti-diabetic activity. In a study, diabetes receiving 15 ml of Aloe Gel trice a day for 42 days experienced 44% reductions in Blood Sugar.

- ***Acacia arabica* or Babul:** It is generally known as Babul or Prickly Acacia. It has been used to treat high cholesterol, diabetes stomatitis, gingivitis and pharyngitis.
- ***Allium cepa* or Onion:** Onions have been known the have several putative health benefits since ancient times. They are rich in flavonoids, such as quercetin as well as sulphur compounds. In a study of 100 g of onion resulted in 89 mg/dl reduction in fasting blood glucose level (4 hours later) fasting blood glucose was lowered by 145 mg/dl in response to administration of insulin.
- ***Cucurbita maxima* or Pumpkin:** In a recent report, the low molecular weight fraction in pumpkin juice at the dose of 300 mg/kg produced significant reductions in plasma glucose at the end of the treatment. The pumpkin extract also reduces or eliminates the need for insulin injections in Type 1 Diabetics by increasing insulin production, a regenerate damaged pancreatic cells.
- **Jamun:** Jamun is a boon for diabetics as it has a low glycaemic index and keeps blood sugar levels under check. It also contains Oleanolic acid which as antidiabetic properties. The seeds have Jamboline, which prevents the starch from turning into sugar, thus monitoring the blood sugar levels in the body.
- **Ginseng:** Both Panax Ginseng and American Ginseng have been used to manage diabetes. Panax Ginseng has been found to remarkably reduce the blood sugar levels.

Check Your Progress

1. What is fish oil?
2. How is olive oil a principal fat and one of the Mediterranean diet?
3. How is Curcumin extracted?
4. What are probiotics?
5. What is *Adhatoda vasica*?
6. How many types of fats are there?
7. List the strategies nutraceutical can offer to prevent and reverse vascular diseases.
8. What are tocotrienols?
9. Write in short about pantethine. Give its source.

13.6 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Omega-3 blocks inflammatory cytokines and prostaglandin and are converted by the body into powerful anti-inflammatory chemicals called

resolving, the competition for receptors of n-3 products with proinflammatory molecules; the reduction in gene expression of cytokines, cyclo-oxygenase 2, with degrading proteinases; the interference in the signaling pathway of inflammation and the reduction in lymphocytes proliferation.

2. Olive oil is the principal fat and one of the Mediterranean diet. The anti-inflammatory properties of Olive oil are attributed to its phytochemicals, such as the Phenolic Compounds and Mono-Unsaturated Fatty Acids, PCMUFAs. In Olive oil improved pain and physical functions in patients affected by knee osteoarthritis.
3. Curcumin is extracted from the Indian spice Turmeric, it is an aromatic molecule with an anti-inflammatory effect that in vitro showed to inhibit the activity of COX-2 and 5-LOX enzyme. It can reduce joint pain and smelling by blocking inflammatory cytokines and enzymes. Turmeric supplement showed long term improvement in pain and function in patients with knee OA.
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6. There are following two types of fat:
   - Unsaturated Fat found in Seed Oils and Fish Oils.
   - Saturated Fats are obtained mostly from Animal Sources. Pecent guidelines suggested that saturated fats should be limited to 10% of yours total calorie intake.
7. There are following three strategies nutraceutical can offer to prevent and reverse vascular diseases.
   - The first is to reduce circulating levels of LDL-cholesterol by forming micelle with bile salts as it contains cholesterol.
   - The second strategy is to reduce the possibility of oxidation by neutralizing radicals with antioxidants.
   - The third is to reduce artery plaque through fibrinolytic activity. A fibrin clot is broken down a product of coagulation. Enzyme plasmin, cuts the fibrin mesh at various places leading to production of fragments that are cleared by kidney and liver.

8. Tocotrienol are members of a subgroup of the Vitamin E family, which includes tocopherols. Both tocotrienols and tocopherols are antioxidants but only tocotrienols have been shown to reduce cholesterol, inhibit certain cancers and manage diabetes.
9. Pantethine is a dimer form of Pantothenic Acid (Vitamin B5). It reduces cardio vascular risk by inhibiting platelet dumping and the production of the inflammation in producing chemical, Thromboxane A2 (CVR). Pantethine (300 mg 3 times daily) reduced serum triglycerides 32%, total cholesterol 19%, and LDC cholesterol 21% HDL cholesterol levels increased 23%. Sources: Milk, Egg, Peas, Cereals

13.7 SUMMARY

- Arthritis is a progressive degenerating joint disease that has a major impact or joint-function and quality of life.
- Nutraceutical are dietary compounds which have a role in the balance of anabolic and catabolic signals in joints. It is a degenerative disease characterized by cartilage and synovium inflammation that can cause joint stiffness, swelling, pain and loss of mobility.
- Current literature existing nutraceutical compounds that could be used as integrators in a daily diet, such as in olive oil, fish oil and botanical extracts used as non-pharmacological treatment.
- Omega-3 blocks inflammatory cytokines and prostaglandin and are converted by the body into powerful anti-inflammatory chemicals called resolving, the competition for receptors of n-3 products with proinflammatory molecules; the reduction in gene expression of cytokines, cyclo-oxygenase 2, with degrading proteinases; the interference in the signaling pathway of inflammation and the reduction in lymphocytes proliferation.
- Olive oil is the principal fat and one of the Mediterranean diet. The anti-inflammatory properties of Olive oil are attributed to its phytochemicals, such as the Phenolic Compounds and Mono-Unsaturated Fatty Acids, PCMUFAs.
- In Olive oil improved pain and physical functions in patients affected by knee osteoarthritis.
- Methionine is an essential amino acid for humans, since the human organism is not able to synthesize it and it is therefore taken with diet.
- The active form of methionine is S-Adenosyl Methionine (SAMe) is a precursor of glutathione.
- SAMe has antioxidant properties and, in the joints, provides levels of glutathione peroxidase, an antioxidant enzyme.

- In patients with is arthritis, treatment with SAMe has a more beneficial effect in long term compared to treatment with Compounds of Non-Steroidal Anti-Inflammation Drugs, CNSAIDs.
- Respiratory disorders are among the leading causes of morbidity and mortality, affect people of all ages and are a major global health problem. They involve the air passages, such as nasal passages, large and small airways and the lungs.
- Bronchial Asthma, Chronic Obstructive Pulmonary Disease (COPD), Pulmonary Tuberculosis, Pneumonia, Fibrosis, Lung Cancer and Pneumoconiosis are commonly seen respiratory conditions.
- The COPD is caused by inhalation of toxins and irritants for longer durations, resulting in chronic inflammation of airways and damage of alveolar structure of the lungs.
- Nutraceutical is a combination of two words, nutrient and pharmaceutical. Nutraceuticals are products that are used for the maintenance of health and prevention and treatment of disease. They also have basic nutritions value.
- Alternatively, a nutraceutical may simply be considered as any substances that has physiological benefit or provides protection against chronic disease.
- Probiotics are living microbial food supplements that when administered in adequate amounts, benefit the host organism by improving its intestinal microbial balance.
- Lactobacilli, Gram Positive Cocci and Bifidobacteria are mostly found in the gut. There is evidence that administration of probiotics decreases the risk of systemic conditions, such as dietary ingredients that act by selectively altering the composition or metabolism of the gut microbiota. These are short chain Polysaccharides (Fructose-Based Oligosaccharides).
- The prebiotics consumption generally promotes the lactobacillus and Bifidobacteria growth in the gut, thus, helping metabolism.
- The immuno-modulating properties of Probiotics, Prebiotics and Synbiotics may be valuable tool to treat and prevent immune disorders, such as Allergies.
- The three major factors that cause circulation problems including Heart Diseases are smoking, high blood pressure levels, etc.
- The Cardio Vascular Diseases (CVD) ranks amongst the most common health issues worldwide.
- Averting vascular disease is now a central calling for the nutraceutical industry. This is because the mechanisms of vascular damage have increasingly indicated a major culprit; a lack of nutrition hygiene.
- Phenols have been shown to reduce cholesterol levels and LDC oxidation. Polyphenolic Cathechin which is present in Green Tea reduces the CVD by

enhancing antioxidant activity by improving endothelial dysfunction preventing cardiac hypertrophy and mitochondria.

- Tocotrienol are members of a subgroup of the Vitamin E family, which includes tocopherols.
- Both tocotrienols and tocopherols are antioxidants but only tocotrienols have been shown to reduce cholesterol, inhibit certain cancers and manage diabetes.
- People with high intake of dietary fish and fish oil supplements have a low rate of CVD.
- Both EicosaPentaenoic Acid (EPA) and DocosaHexaenoic Acid (DHA) are only found in fish, such as Salmon, Tuna, Lake Trout and Herrings.
- Fish oil supplements have favourable effects on lipid profile and blood pressure.
- Fish ingestion has been related to a reduced risk for mycocardial imfarction which may relate to beneficial effects of EPA and DHA on plaque stability.
- Nuts are complex foods containing cholesterol lowering mono and polyunsaturated fatty acids, arginine, soluble fiber, and several antioxidant polyphenols.
- Cardio protective effects of diets high in nuts is robust as multiple mechanisms work together to reduce risk.
- Legumes are also complex foods rich in soluble fibers and polyphenols, as well as folic acid.
- Cholesterol lowing effect of legumes are probably due to the combined effects of several bioactive components, such as protein, soluble and in soluble fibres and phytosterols.
- Whole grain products contain intact grain kernels rich in fiber and trace elements. They are nutritionally more important because they contain cytoprotective substances that might work synergistically to reduce cardio vascular risk.
- The mechanisms underlying the protective effects of whole grains on CVD risk include its effect on insulin sensitivity, blood pressure, lipids and inflammation.
- Anti-inflammatory mechanism may be related to higher intake of antioxidant nutrients present in the germ of whole grains.
- Diabetes mellitus as a metabolic disorder characterised by hyperglycaemia or high blood sugar.
- The characteristic symptoms of diabetes are polyuria (excessive urine, polydipsia thirst and increased fluid intake) and blurred vision.

- The World Health Organizations (WHO) recognizes three main forms of Diabetes Mellitus - Type 1, Type 2, Gestational Diabetes (occurring during pregnancy).
- All forms are due to the beta cells of the pancreas being unable to produce sufficient insulin to prevent hyperglycaemia Type 1 is usually due to the autoimmune destruction of the pancreatic beta cells, which produce insulin.
- Type 2 is characterised by tissue wide insulin resistance, but impairment of beta cell function is necessary for its development.
- Food and drugs from nature are playing a quite significant role in healthcare system.
- Human inquisitiveness and search for specific constituents of plants, animals, minerals and microbial origins which are beneficial to our overall health has coined termed like functional food or nutraceuticals.
- The term nutraceuticals came from a combination of nutrition and pharmaceuticals and can be defined as a food or part of a food that provides medical or health benefit including the prevention and treatment of a disease.

13.8 KEY WORDS

- **Arthritis:** Arthritis is a progressive degenerating joint disease that has a major impact or joint-function and quality of life.
- **Nutraceutical**: Nutraceutical are dietary compounds which have a role in the balance of anabolic and catabolic signals in joints.
- **Hypoglycaemia**: Hypoglycaemia is a condition caused by a low blood sugar levels, also sometimes referred to as low glucose.

13.9 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. What are nutraceuticals?
2. Distinguish between prebiotics and probiotics.
3. Write a short note on *Bryophyllum pinnatum* or *Kalanchoe integra.*
4. Expand the term CVD. What are the various CVD's?
5. Explain the role of nutraceutical in CVD.
6. Discuss briefly the role of nutraceuticals in vascular diseases and CVD.
7. Write a note on 'Nutraceutical: New Weapon for Holistic Treatment'.

Long Answer Questions

1. Discuss about nutraceutical remedies for arthritis.
2. How are nutraceutical remedies helpful in bronchitis?
3. 'Nutraceutical remedies for circulatory problems'. Explain.
4. How hypoglycemia is cured using nutraceutical remedies?
5. Discuss with the help of table potential cardiovascular protective effects of function.
6. List the symptoms of hypoglycaemia.

13.10 FURTHER READINGS

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UNIT 14 NUTRACEUTICAL REMEDIES FOR NEPHROLOGICAL DISORDERS

Structure

14.0 INTRODUCTION

Nutraceuticals are defined as substances that have physiological benefits or proved protection against diseases like renal diseases, nephrological disorders, liver disorders, osteoporosis, psoriasis and ulcers. The nutraceuticals substances can be used to improve health, increase life expectancy and functions of human body. It comprises of food supplements, such as prebiotics and probiotics dietary supplements, herbal products and medical foods meant for the prevention and treatment of disease. Since these nutraceuticals possess multiple therapeutic effects without undesirable effects, hence it is popular to the consumers. The nutraceuticals products are available in the form of capsule, tablet and are also available as form of food or included in foods or as complete food itself. Researches are still going on regarding nutraceutical agents that may help in prevention or delay in the onset of chronic renal diseases.

Chronic Kidney Disease (CKD) is a common condition where in dialysis and renal transplantation places an enormous pressure on the healthcare system. Kidney failure patients are susceptible to malnutrition, protein energy wasting and gastrointestinal symptoms. The mechanism by which these nutraceuticals may benefit patients with kidney disease include reduction of inflammation, modulation of oxidative stress and inhibition of interstitial fibrosis, promotion of renal blood flow, Glomerular Filtration Rate (GFR) and stimulation of tubular regeneration.

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The liver is the biggest organ that sits just under the rib cage on the right side of the abdomen and is essential for digesting food and for the removal of toxic substances from the body. Osteoporosis is a disease in which bone weakening increases the risk of a broken bone. Bones that commonly break include the vertebrae in the spine, the bones of the forearm, and the hip. Psoriasis is a long-lasting autoimmune disease characterized by patches of abnormal skin. These skin patches are typically red, dry, itchy, and scaly. Psoriasis varies in severity from small, localized patches to complete body coverage. An ulcer is a discontinuity or break in a bodily membrane that impedes the organ of which that membrane is a part from continuing its normal functions. The nutraceutical foods help to cure the nephrological disorders, liver disorders, osteoporosis, psoriasis and ulcers by adding appropriate food supplements in the diet.

In this unit, you will study about the nutraceutical remedies for the nephrological disorders, liver disorders, osteoporosis, psoriasis and ulcers.

14.1 OBJECTIVES

After going through this unit, you will be able to:

- Understand the significance of nutraceutical foods as remedies for various chronic diseases and disorders
- Discuss the nutraceutical foods as remedies for nephrological disorders
- Explain the role of nutraceutical foods as remedies for liver disorders
- Analyse nutraceutical foods as remedies for osteoporosis, psoriasis and ulcers

14.2 NUTRACEUTICAL REMEDIES FOR NEPHROLOGICAL DISORDERS

Chronic Kidney Disease (CKD) is a common condition where in dialysis and renal transplantation places an enormous pressure on the health of the patient. Kidney failure patients are susceptible to malnutrition, protein energy wasting and gastrointestinal symptoms.

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Nutraceuticals and Chronic Kidney Diseases (CKD)

Chronic Kidney Disease (CKD) is one of the most common chronic diseases worldwide. According to the Kidney Disease - Improving Global Outcomes (KDIGO) Guideline 2012, CKD is defined as abnormalities of kidney structure or function, present for more than 3 months, with implications for health and is categorised into five stages according to severity using estimated Glomerular Filtration Rate (GFR) or into three stages based on Albuminuria.

The incidence of CKD is subject to variation worldwide. The global prevalence of CKD is estimated to vary between 8% and 16%. Diabetes and Hypertension are the main risk factors for CKD. The global prevalence of CKD is likely to increase in view of the growing number of patients with diabetes and/or hypertension.

Under normal conditions, Homeostasis is maintained owing to interactions between the host and intestinal microflora. However, quantitative and qualitative alterations in the intestinal microflora are present in patients with CKD. This dysbiotic intestinal microflora is characterised by an increase in the pathogenic flora relative to the symbiotic flora. The pathogenic gut microbiota produce Uraemic Toxins, in particular Indoxyl Sulfate (IS) and P-Cresyl Sulfate (PCS) among others, which have been associated with increased inflammation, greater oxidative stress and higher risk for Cardio Vascular Disease (CVD), progression of CKD and death due to CKD.

Probiotics refer to the living microorganisms which colonise or implant in the host's Gastro-Intestinal (GI) environment and exert beneficial health effects. Prebiotics are defined as non-digestible food ingredients that induce the growth and/or activity of beneficial microorganisms in the host. Synbiotics are a mixture of probiotics and prebiotics.

Recently, probiotics, prebiotics or synbiotics have been reported to reduce inflammation, improve kidney function and retard progression of CKD by restoring the symbiosis of gut microflora in patients with CKD. A randomised trial found synbiotics decreased serum PCS without reducing serum IS in non-dialysis CKD. A pilot study suggested probiotic dietary supplements are more effective than placebo in reducing Blood Urea Nitrogen (BUN) and improving the quality of life of patients with Stage 3 or 4 CKD. Another study found that synbiotics delayed CKD progression.

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Probiotics and Chronic Kidney Diseases (CKD)

The use of probiotics with chronic kidney disease is gaining momentum because altered gut micro flora affects the patient in a myriad of ways. Probiotics are bacteria containing foods, such as Refit, that may alter the floral composition of the gut through completion of one type of culture with another.

Following are the benefits of probiotics:

- Suppression of growth or epithelial binding/invasion by pathogenic bacteria.
- Improvement of intestinal barrier function.
- Modulation the immune system.

Increased used of medication that are prescribed at any given point of time to a patient with CKD or patient on dialysis causes disorder on his gastrointestinal systems. Phosphorus binders may result in constipation while other medications may cause diarrhoea, heartburn, stomachache, vomiting and kill the good bacteria in the gut. Thus, probiotics may seem promising in restoring the good bacteria in the gut and hence improving immune function and providing anti-inflammatory effects.

14.3 NUTRACEUTICAL REMEDIES FOR LIVER DISORDERS

Liver is protected by ribs. The liver is located in the upper right part of the abdomen. It is the largest organ in the body and performs more than 500 jobs including at least 22 vital functions. It is the main detoxifier of the body as it removes and neutralises poisons, drugs, nicotine and alcohol in the blood stream.

Other functions include strong glucose in the form of glycogen and maintaining blood sugar levels, manufacturing important proteins and breaking down excess amino acid, the by-products of Protein digestion into Urea which is eliminated by the kidneys. It also manufactures bile which is stored in the gall bladder and passes into the duodenum where it breaks down Fat into thing Globules to make them more digestible. All of these functions are impaired by severe liver disease, most commonly caused by infections, such as Viral Hepatitis or by drugs, such as Alcohol. Chronic inflammation of the liver leads to scar tissues being formed due to the condition known as Cirrhosis. Another common liver problem is the failure of the liver to secrete bile because of stones forming in the gall bladder.

Although the liver has a remarkable ability to regenerate itself, but due to the health effects or continued and long term alcohol abuse may cause Liver Failure. Signs of chronic liver disease can include Jaundice, Fever, loss of Body Hair, distension in the Abdomen and Yellow Fatty deposits in the Upper Eyelids.

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Liver Health Supplements

Following are the liver health supplements.

1. N-Acetyl Cysteine (NAC)

N-Acetyl Cysteine (NAC) is a supplement form of cysteine. Cysteine is a semi-essential amino acid because the human body can produce it from other Amino Acids, namely Methionine and Serine. It becomes essential only when the dietary intake of Methionine and Serine is low.

Cysteine is found in most high-protein foods, such as Chicken, Turkey, Yogurt, Cheese, Eggs, Sunflower Seeds and Legumes. Consuming adequate cysteine and NAC is important for various health reasons including replenishing the Glutathione, most powerful antioxidant of the human body. These amino acids also help with chronic respiratory conditions, fertility and brain health.

2. Glutathione

The Glutathione (GSH) is the most abundant and important antioxidant formed in our body and in the cells of any living thing on the planet. Fundamentally, the Glutathione (GSH) is an antioxidant found in plants, animals, fungi, and some Bacteria and Archaea. Glutathione (GSH) is essential in order to maintain immune function and combat oxidative stress levels. Because Glutathione is the master detoxifier to the human body, hence majority of it is found in our liver. Glutathione is capable of preventing damage to important cellular components caused by reactive oxygen species, such as Free Radicals, Peroxides, Lipid Peroxides, and heavy metals. It is a Tripeptide with a Gamma Peptide Linkage between the Carboxyl group of the Glutamate side chain and the Amine group of Cysteine, and the Carboxyl group of Cysteine is attached by normal Peptide linkage to a Glycine.

While most antioxidants are found in the foods that we eat, Glutathione is produced by our body. It is primarily made up of three Amino Acids, namely the Glutamine, Glycine and Cysteine. There are a number of reasons why the Glutathione level in the body is depleted or decreased including poor diet, chronic disease, infection and constant stress. Glutathione can also decrease with age.

3. Milk Thistle Extract

Milk Thistle is used as a natural remedy to treat a range of health conditions. The active ingredient in milk thistle is called 'Silymarin'. Milk thistle is also known as Mary Thistle or Holy Thistle. It is mainly used to treat Liver problems, but it is also used to lower Cholesterol level and to manage Type 2 Diabetes.

Milk Thistle is a flowering plant and belongs to the same family of plants as the Daisy. It grows in Mediterranean countries and is typically used to make natural remedies. Different parts of the Milk Thistle plant may be used to treat various health conditions. The Milk Thistle not only used for liver problems but it also help in the treatment of Cirrhosis, Jaundice, Hepatitis and Gallbladder Disorders.

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4. Licorice Root Extract

A Licorice root extract called Glycyrrhizin has also shown remedy for Chronic Hepatitis C and Liver Cancer. The supplements are available as teas, capsules, tablets and liquid extracts that contain Glycyrrhizin, the biologically active component of Licorice.

5. Burdock Root

Burdock root is one of the best blood purifier for detoxifying the liver.

6. Selenium

The mineral Selenium also plays a role in maintaining the body's Glutathione levels as it is directly involved in the Methylation Cycle. Selenium is important for our liver health, partially due to its ability to enhance Glutathione levels.

Studies and researches reveal that taking a Selenium supplement regularly can help in reducing the risk of developing Liver Cancer. It provides protection against Liver damage.

7. L-Carnitine

L-Carnitine plays a critical role in the intracellular and metabolic functions, such as Fatty Acid Transport into the Mitochondria, stabilization of cell membranes and reduction of Serum Lipid Levels. Moreover, it is also important in the regulation of energy balance in tissues that derive much of their energy from Fatty Acid Oxidation, and is able to modulate the inflammatory response. L-Carnitine supplement is beneficial in several chronic health conditions, such as Obesity, Type 2 Diabetes and Liver Cirrhosis.

8. Polyphenols

Polyphenols are members of a large family of plant derived compounds classified as Flavonoids and Non-Flavonoids. Non-Flavonoids include Stilbenes and Phenolic Acids. Polyphenols act as antioxidants, reducing liver fat accumulation, mainly by inhibiting Lipogenesis.

Probiotic Treatment

In cirrhotic patients there was imbalance in bacterial gut flora which contributes significantly to ammonia production resulting in varying degrees of encephalopathy. So these patients should intake supplements with combinations of probiotic which reduces the Blood Ammonia Concentrations. Those patients which are treated with a combination of probiotics and fiber had a lower rate of getting bacterial infections than those treated with selective intestinal decontamination indicatives, a beneficial effect on the prevention of bacterial translocation.

Following Table 14.1 illustrates the major nutraceuticals essential for the treatment of non-alcoholic fatty liver and the mechanism of action.

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Table 14.1 *Major Essential Nutraceuticals and the Mechanism of Action*

Nutraceuticals	Target/Mechanism of Action
Vitamin D	• Chronic Inflammation • Vitamin D Deficiency • Insulin Resistance
Vitamin E	• Oxidative Stress • Hepatocellular Protection
Carnitine	• Insulin Resistance • Chronic Inflammation • Hepatocellular Protection • Atherogenic Dyslipidemia (AD)
Vitamin C	• Oxidative stress • Hepatocellular protection
Omega-3 Fatty Acids	• Atherogenic Dyslipidemia • Cardiovascular Risk • Oxidative Stress • Hepatocellular Protection
Silymarin	• Oxidative Stress • Chronic Inflammation • Insulin Resistance • Hepatocellular Protection
Resveratrol	• Oxidative Stress • Insulin Resistance • Cardiovascular Risk • Hepatocellular Protection

14.4 NUTRACEUTICAL REMEDIES FOR OSTEOPOROSIS

Our skeletons provide us with a strong yet light protective framework due to a unique structure comparable to reinforced concrete. Bone is a highly dynamics metabolic reservoir of calcium ions. The skeleton stores 99% of all Calcium ions contained in the body. There are two main types of bones in the skeleton. These are differentiated by their microscopic architecture.

Cortical bone is hard and dense, and comprises the shafts of the long bones which bear most of the body weight.

Can Cellar bones are found in the end of long bones, vertebrae and pelvis. The structure has honey comb like appearance with plates known as Trabeculae which are arranged in such a way that it provide resistance to forces.

Bone consist of an organic phase (matrix) and an inorganic mineral phase, together with a highly varied population of cells responsible for its development and maintenance. The matrix composed of structural proteins, collagen and mucopolysaccharides which provide resistance and flexibility. The main mineral

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present is Hydroxyapatite (Crystalline Calcium Phosphate) which is responsible for the rigidity and compressibility of bone.

Growth of bones begins in fatal development and continues to between 25-40 years of age when peak bone mass is said to be attained. During puberty there is an accelerated period of growth where most of this mass is laid down. The timing and nature of this process initially dictated by genetic factors, followed by environmental factors in adulthood. After modelling there follows a process of consolidation, known as remodelling which is necessary to allow the skeleton to respond to external forces and maintain body minerals up to 10 per cent of existing bone per year is restructured at sites known as bone multicellular units.

Bone multicellular units consist of Osteoblasts and Osteoclasts acting in a coordinated fashion under the influence of numerous cellular factors.

- Osteoblasts initiate remodelling through specific activation of their membrane receptors. They attach to internal bone surfaces and secrete protons and enzymes which degrade and release minerals from the tissue.
- Osteoblasts the replace the resorbed material with immature matrix Protein (Osteoid), which later becomes mineralised.

Factors necessary for coordinating Osteoblasts and Osteoclasts includes,

- Calcium Availability
- Mechanical Forces Experienced by the Skeleton
- Endocrine, Autocrine and Paracrine Factors

Endocrine Factors

Endocrine factors are released into the systemic circulation and have a generalised effect in the skeleton.

Parathyroid hormone is a peptide hormone secreted in response to low concentrations of Serum Calcium and directly enhances Osteoclasts activation via interaction with a membrane receptor. This stimulates resorption and release of free Calcium irons to restore the imbalance.

Vitamin D is obtained from the diet or synthesised in the skin by Ultra Violet (UV) light. It acts by increasing intestinal Calcium absorption and promoting Osteoclast resorption.

Calcitonin is a Peptide Hormone that inhibits the action of Osteoclasts in response to elevated Serum Calcium levels.

Growth hormone promotes the synthesis of collagen and other bone proteins by Osteoblasts.

Estrogens, such as Estradiol are thought to be important in maintaining bone mass in women and are thought to act by inhibiting paracrine factors that promote

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bone resorption. Androgens, such as Testosterone have a similar role to Estrogens in men and also contribute to the sudden growth spurt at puberty.

Autocrine and Paracrine factors are secreted by cells within bone tissue and have more localised targets of action.

Prostaglandins are derived from membrane Lipid precursors and are thought to be the main local mediators of bone metabolism prostaglandins E_1 and E_2 (PGE_1 and PGE_2), both act via binding to various membrane receptors, and their effects are also mediated through cytokines known as Insulin like Growth Factors (IGF). PGE_1 is made through the action of the enzyme Cyclooxygenase 1 (COX-1) in many tissues and is thought to increase bone formation inhibit osteoclasts and promote Calcium uptake.

PGE_2 is synthesised by the COX-2 isoenzyme in response to factors released during inflammation and can inhibit bone formation and promote Osteoclast activity. This may be through promoting expression of IGF.

Cytokines and growth factors are peptides seceded by osteoblasts and other cells and have both inhibitory and stimulatory effects on bone remodelling. Examples of Cytokines include InterLeukin-1 (IL-1) and Tumours Necrosis Factor-α (alpha) or TNF-α.

Bone multicellular units are thus tightly regulated to present overall changes in bone mass, but this can be lost with the ageing or disease. Until peak mass formation, 100 percent of the bone multicellular units are active. Following this is a gradual decline in bone strength and increasing porosity due to reduced activity at each bone multicellular unit – a reduction with age, by 30 percent in men and 50 percent in women. This can lead to the most prevalent disease of bone known as osteoporosis.

Osteoporosis means 'Porous Bones' and is defined as a progressive, systemic skeletal disease that leads to loss of bone and its microscopic structure. The consequences of this are reduce strength and an increased risk of low impact fracture. This can lead to associated complications of mortality, mobility and reduced quality of life. The three most important and common sites of fractures are due to their having the greatest proportion of cancellous bone namely the hip (femoral neck), lumbar vertebrae and the forearms or wrist. Prevalence of osteoporosis with age (seen in up to 70 percent of people over 80 years of age) and it is often not diagnosed until a fracture occurs. The World Health Organisation (WHO) has estimated that over 75 million Osteoporotic Fractures will occur each year by 2025.

There is mounting evidence to suggest that eating more calcium rich foods, during childhood and adolescence is the most effective way of preventing or at least minimizing the extent of osteoporosis. In this condition which most commonly affects are middle aged and elderly women, the bones become weak and brittle, other symptoms may include pain in the hips and back, loss of height and sometimes stooped posture as the bones of the spinal column become weak and compressed.

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Who is at Risk?

Throughout life, our bones are continuously being replaced. Cells called Osteoclasts eat away at the existing bone, thereby releasing Calcium into blood stream. At the same time cells called Osteoblasts form the new bone and deposit Calcium into it. In young and healthy people there is equal activity between the two types of cell, with the result that bone mass and structure are maintained.

Women have a far greater risk than men of developing Osteoporosis. They have less bone mass to begin with and with the menopause lose the hormone Estrogen, within strong bone loss. While postmenopausal women are more at risk, some younger women – marathon runners, gymnasts, dancers and anorexics can also suffer from Osteoporosis. A low body weight increases the risk of Osteoporosis because it puts less stress on bones. Body fat also promotes Estrogen production.

Diet low in Calcium, Vitamin D or high in Animal Protein can increase risk of Osteoporosis. Although Protein is necessary in the diet, a large intake of animal protein containing larger quantities of acidic or sulphurous amino acids interferes with Renal Calcium Reabsorption.

Smoking is a significant risk factor as large numbers of children and teenagers continue to smoke. Toxic free radicals in cigarette smoke interfere with blood supply to bone and directly damage Osteoblast. In women, smoking can reduce active Estrogen levels and promote an earlier onset of menopause.

Alcohol has both direct and indirect toxic effects on bone formation, such as directly inhibiting Osteoblast activity and interfering with the balance of Cytokine activity. Caffeine consumption should not exceed 3-4 cups of coffee a day, as Caffeine removes Calcium from the blood stream.

Corticosteroids are strongly associated with Osteoporosis and increased fracture risk, particularly at vertebral column. They mediate their effects via Osteoblast activity and bone mineral content within month of their initiation. They can also cause adrenal suppression which reduces Estrogen and Androgen Synthesis.

Nutraceuticals for Bone – Melatonin

Melatonin is an endogenous hormone secreted by the pineal gland of the brain. It occurs naturally in various fruits and vegetables, particularly in Tomatoes, Cucumbers, Bananas although only in small quantities compared with those in the body (5-25 mg secreted daily). In order to obtain significant physiological concentration large quantities of Melatonin rich foods would have to be eaten.

There is also variation in the total amounts of Melatonin found in the body once the lifespan the greatest quantities being found around 1-3 years of age

followed by a rapid decline by old age. It is for this reason that Melatonin has been implicated as a protective nutraceutical against degenerative conditions associated with old age, including Osteoporosis.

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Polyunsaturated Fatty Acids

Fatty acids are derived from triglycerides in the dies, and many can also be synthesised. There is however a group which can only be obtained from the diet because body lacks the ability to synthesise them, and hence these are known as essential fatty acids.

Many of those derive from Fish and Plant Oils include,

Linoleic Acid: Mainly found in Evening Primrose, Corn and Sunflower Oils.

EicosaPentaenoic Acid (EPA): Mainly found in Oily Fish.

DocosaHexaenoic Acid (DHA): Mainly found in certain algae, a rich source of Omega-3s.

Alpha Lindemic Acid (ALA): Mainly found in Soy and Flaxseed.

All these fatty acids possess multiple unsaturated double bounds and hence are termed as PolyUnsaturated Fatty Acids (PUFAs).

Metabolic pathways have been identified which outline how the n-3 and n-6 PUFAs act as precursors for the formation of Prostaglandins. These prostaglandins are released into the immediate bone tissue environment and have conflicting actions.

Dietary fat intake, predominantly of saturated acids is thought to be detrimental to bone mineral density, leading to a greater risk of fracture.

There are two potential mechanisms by which PUFA's may promote bone health:

- Directly through influencing the metabolism of professional precursors involved in Bone Homeostatic.
- Indirectly via Growth Hormone Action.

Phytoestrogens

The use of phytoestrogens to treating menopausal symptoms, including Osteoporosis has been recently reviewed. The major examples of phytoestrogens are derived from a large number of plant sources. These include,

- Isoflavones found in chickpeas, red clonee and soya bean. Soy is the richest source. The main isoflovones that have been extracted and purified, are genistein (60 per cent of the isoflovones content in Soy) daidzein (25% of the isoflavones content in Soy are found in their glycosylated (glycone) form with in plant tissues.
- Lignans found in various legumes, grains and flaxseeds.

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Studies have shown strong evidence that Soy isoflavones have a positive effect on bone mineral density.

Take plenty of,

- Foods rich in Calcium, such as Milk and Dairy Products.
- Food sources of Vitamin D, such as Oily Fish and Eggs.
- Sensible exposure of skin to sunlight.

Cut down on,

- Food rich in Phytic Acid, such as Wheat Bran, Brown Rice and Nuts.
- Alcohol
- Smoking
- Salt
- Caffeine

14.5 NUTRACEUTICAL REMEDIES IN PSORIASIS

Psoriasis is a skin disorder that causes skin cells to multiply up to 10 times faster than normal. This makes the skin build up into bumpy red patches covered with white scales. It is considered as an autoimmune disease. The patches can come and go over the course of a few days to over a month. They can grow anywhere, but most appear on the scalp, elbows, knees, and lower back. Psoriasis cannot be passed from person to person.

Psoriasis usually appears in early adulthood. For some people, it effects some areas of skin. In severe cases, Psoriasis can cover large parts of the body. The patches can heal and then come back throughout a person's life.

Symptoms

The most common symptoms of Psoriasis include,

- Red Patches on Skin.
- Scaly, sometimes Silvery Skin Patches.
- Itchy Skin.
- Joint Swelling, Stiffness.
- Disorders of the Fingernails and Toenails, including Discoloration and Pitting of the Nails.

The symptoms of Psoriasis also vary based on the type. There are five official types of Psoriasis:

- Plaque Psoriasis
- Pustular Psoriasis

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- Guttate Psoriasis
- Erythrodermic Psoriasis
- Scalp Psoriasis
- Nail Psoriasis
- Crythrodermic Psoriasis
- Psoriatic Arthritis

1. Plaque Psoriasis or **Psoriasis Vulgaris** is the most common form of Psoriasis. 80% of people have lose Plaque Psoriasis, which is characterized by thick red patches of skin, often with a sliver or white scaly layer. Patches are usually 1 to 10 cm wide, but can also be larger and cover more of the body. If you scratch them more it will get worse. These patches often appear on,

- Elbows
- Knees
- Lower Back
- Scalp

People with Psoriasis can also get a type of Arthritis called Psoriatic Arthritis. It causes pain and swelling in the joints.

2. **Pustular Psoriasis** is a severe form of Psoriasis. It develops fast in the form of many white pustules surrounded by red skin. It causes red and scaly skin with tiny pustules on the palms of the hands and soles of the feet.

Some people experience cyclic periods of pustules and remission, while the pus is non-infectious. This condition can cause flu like symptoms, such as:

- Fever
- Chills
- Rapid Pulse
- Muscle Weakness
- Loss of Appetite

There are two kinds of pustular Psoriasis:

- Von Zumbusch
- PalmoPlantar Pustulosis (PPP)

3. **Guttate Psoriasis**

It appears as small red spots on the skin. It is the second most common type, which starts in adulthood or childhood and causes small, red spots, mainly on the torso and limbs, but can also appears on the face and scalp. Spots are usually not as thick as Plaque Psoriasis, but they can develop into Plaque Psoriasis over time.

NOTES

The following can happen after certain triggers:

- Strep Throat
- Stress
- Skin Injury
- Infection
- Medication

4. **Erythrodermic Psoriasis**

It is a rare kind of Psoriasis, look like severe burns. It is a serious condition and can be a medical emergency. This form of Psoriasis is widespread, red and scaly. It may cover large positions of the body. Exfoliation often occurs in larger pieces than the small scales typical to most Psoriasis.

Erythrodermic Psoriasis can develop from,

- Pustular Psoriasis.
- Widespread, Poorly Controlled Plaque Psoriasis.
- A Bad Sunburn.
- Alcoholism.
- Significant Stress.
- Abrupt Discontinuation of a Systemic Psoriasis Medicines.

5. **Scalp Psoriasis** is common in people with Plaque Psoriasis. For some people, it may cause severe dandruff, for some it can be painful, itchy at the hairline. It can be extended to neck, face and ears in one large patch or many smaller patches.

Excessive scratching can cause hair loss and scalp infections. The condition may also cause feeling of social stress.

6. **Nail Psoriasis**

Nail Psoriasis is also a type of Psoriasis. It can often be confused with fungal infections and other infections of the nail.

It can cause,

- Nail Pitting
- Grooves
- Discoloration
- Loosening or Crumbling of the Nail
- Thickened Skin under the Nail
- Colored Patches or Spots under the Nail

NOTES

Aloe Vera for Psoriasis

It is a succulent plant that thrives in tropical areas of the world and has been used for millennia for its soothing qualities, especially for skin conditions, such as burns, rashes, cuts and scrapes. Aloe plants are made up a four layers:

- Rind, the tough, protective layer.
- Sap, a layer of bitter find which helps protect the plant from animals.
- Mucilage (Gee) in the inner part of the leaf.
- Inner Gel.

It is the gel that contains most of the healing compounds, including essential amino acids. Your body needs but cannot manufacture, Antioxidants, Fatty Acids, Vitamins, Minerals and many lesser known but vital compounds. Aloe is antimicrobial, antiviral, anti-fungal, antibiotic and antibacterial, etc.

Part of the discomfort from Psoriasis is that skin can crack, which could be described as rivaling a dozen paper cuts all in one place.

- **Wound Healing:** Properties related to a compound called Glucomannan help accelerate wound healing and skin cell growth.
- **Skin Hydration:** Keeping skin irritation moist and hydrate always feels better and Aloe Vera gel does that.
- **Inflammation Reduction:** The study showed the gel to be more effective than a placebo in treating skin conditions, including UV-induced erythema or skin reddening due to the dilation of blood vessels.
- **Collagen Production:** Aloe Vera helps the skin stay elastic by making more collagen.

14.6 NUTRACEUTICAL REMEDIES IN ULCERS

Herbs, vegetables and fruits are being considered to be the potential source for treating and controlling various ailments.

Ulcer is an open sore on an external or internal surface of the body, caused by a break in the skin or mucous membrane which fails to heal. Ulcers range from small, painful sores in the mouth to bedsores and serious lesions of the stomach or intestine.

An ulcer is a painful sore that is slow to heal and sometimes recurs. Ulcers are not uncommon. How they appear and corresponding symptoms depend on what caused them and where they occur on your body.

Ulcers can appear anywhere in or on the body, from the lining in the stomach to the outer layer of the skin. Some cases of ulcers disappear on their own, but others require medical treatment to prevent serious complications.

NOTES

Different Types of Ulcers

The most common types of ulcers are peptic ulcers, but there are many types, including:

- Arterial Ulcers
- Venous Ulcers
- Mouth Ulcers
- Genital Ulcers

Peptic Ulcers

Peptic ulcers are sores or wounds that develop on the inside lining of the stomach, the upper portion of the small intestine, or the esophagus. They form when digestive juices damage the walls of the stomach or intestine.

Peptic ulcers are most often caused from inflammation after being infected with *Helicobacter pylori* (*H. pylori*) bacteria and long-term use of painkillers.

Following are the three types of peptic ulcers:

- Gastric Ulcers are ulcers that develop in the Stomach Lining.
- Esophageal Ulcers are ulcers that develop in the Esophagus.
- Duodenal Ulcers are ulcers that develop in the Duodenum (Small Intestine).

The most common symptom of this condition is a burning pain. Other symptoms may include,

- Bloating or the feeling of Being Full
- Belching
- Heartburn
- Nausea
- Vomiting
- Unexplained Weight Loss
- Chest Pain

Treatment depends on the underlying cause of the ulcer, for example if the infection is due to an *Helicobacter pylori* infection, then the doctor may prescribe antibiotics to kill the harmful bacteria.

If the ulcers formed as a result of prolonged use of painkillers or medication, then the doctor may prescribe medication that reduces the stomach acid or protectively coats the stomach to prevent acid damage.

Arterial Ulcers

Arterial (Ischemic) Ulcers are open sores that primarily develop on the outer side of the ankle, feet, toes, and heels. Arterial ulcers develop from damage to the

arteries due to lack of blood flow to tissue. These forms of ulcers can take months to heal and require proper treatment to prevent infection and further complications.

Venous Ulcers

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Venous ulcers are the most common type of leg ulcers. These are open wounds often forming on the leg, below the knee and on the inner area of the ankle. They typically develop from damage to the veins caused by insufficient blood flow back to the heart. In some cases, venous ulcers cause little to no pain unless they are infected. Other cases of this condition can be very painful.

Mouth Ulcers

Mouth ulcers are small sores or lesions that develop in the mouth or the base of the gums, commonly known as Canker Sores. These ulcers are triggered by a number of causes, such as food allergies, hard teeth brushing, hormonal changes, vitamin deficiencies, bacterial infection, etc.

Genital Ulcers

Genital ulcers are sores that develop on genital areas, including the penis, vagina, anus or surrounding areas. They are usually caused by Sexually Transmitted Infections (STIs), but genital ulcers can also be triggered by trauma, inflammatory diseases, or allergic reactions to skin care products.

Treatment and Remedy

The conventional treatment for ulcers is to take Antacids, Antibiotics, Ranitidine or Cimetidine. These medications treat the symptoms of ulcers however and not the cause. They also do not repair the damaged tissue. In addition, they have various side effects, among them they can cause a rebound in acid production. Some natural interventions, such as a meal and drink of natural juice, like carrot and cabbage juice, to heal the mucosal lining.

Fruits and vegetables, such as spinach, cucumber, avocado, cabbage, potato, banana, apple, melon and cantaloupe. Eat soothing foods that produce a protective coating over the digestive tract, for example, ground flax seed, yogurt, porridge and congee. Consume fermented products like yogurt, kefir, quark, buttermilk and natural cheeses to replenish the friendly bacteria that assist with nutrient digestion.

Dietary change is often the only way to completely resolve an ulcer. Eliminate all processed and refined foods from the diet. Also avoid fatty, rich foods, vinegar, citrus fruits, plums, coffee and black tea.

NOTES

Check Your Progress

1. What is Chronic Kidney Disease (CKD)?
2. By which mechanism the nutraceuticals benefit patients with kidney disease?
3. Where is liver located? What is its key function?
4. What are the common liver problems?
5. What is Milk Thistle? Why is it used?
6. Explain the constituents of bone.
7. Define osteoporosis.
8. What is psoriasis?
9. Explain about ulcers.

14.7 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Chronic Kidney Disease (CKD) is a common condition where in dialysis and renal transplantation places an enormous pressure on the health of the patient. Kidney failure patients are susceptible to malnutrition, protein energy wasting and gastrointestinal symptoms.
2. The mechanism by which the nutraceuticals may benefit patients with kidney disease include reduction of inflammation, modulation of oxidative stress and inhibition of interstitial fibrosis, promotion of renal blood flow, Glomerular Filtration Rate (GFR) and stimulation of tubular regeneration.

   The probiotics, prebiotics or synbiotics have been reported to reduce inflammation, improve kidney function and retard progression of CKD by restoring the symbiosis of gut microflora in patients with CKD.
3. Liver is protected by ribs. The liver is located in the upper right part of the abdomen. It is the largest organ in the body and performs more than 500 jobs including at least 22 vital functions. It is the main detoxifier of the body as it removes and neutralises poisons, drugs, nicotine and alcohol in the blood stream.
4. Chronic inflammation of the liver leads to scar tissues being formed due to the condition known as Cirrhosis. Another common liver problem is the failure of the liver to secrete bile because of stones forming in the gall bladder.

   Although the liver has a remarkable ability to regenerate itself, but due to the health effects or continued and long term alcohol abuse may cause Liver

Failure. Signs of chronic liver disease can include Jaundice, Fever, loss of Body Hair, distension in the Abdomen and Yellow Fatty deposits in the Upper Eyelids.

5. Milk Thistle is used as a natural remedy to treat a range of health conditions. The active ingredient in milk thistle is called 'Silymarin'. Milk thistle is also known as Mary Thistle or Holy Thistle. It is mainly used to treat Liver problems, but it is also used to lower Cholesterol level and to manage Type 2 Diabetes.

   Milk Thistle is a flowering plant and belongs to the same family of plants as the Daisy. It grows in Mediterranean countries and is typically used to make natural remedies. Different parts of the Milk Thistle plant may be used to treat various health conditions. The Milk Thistle not only used for liver problems but it also help in the treatment of Cirrhosis, Jaundice, Hepatitis and Gallbladder Disorders.

6. Bone consist of an organic phase (matrix) and an inorganic mineral phase, together with a highly varied population of cells responsible for its development and maintenance. The matrix composed of structural proteins, collagen and mucopolysaccharides which provide resistance and flexibility. The main mineral present is Hydroxyapatite (Crystalline Calcium Phosphate) which is responsible for the rigidity and compressibility of bone.

   Bone multicellular units consist of Osteoblasts and Osteoclasts acting in a coordinated fashion under the influence of numerous cellular factors.

   - Osteoblasts initiate remodelling through specific activation of their membrane receptors. They attach to internal bone surfaces and secrete protons and enzymes which degrade and release minerals from the tissue.
   - Osteoblasts the replace the resorbed material with immature matrix Protein (Osteoid), which later becomes mineralised.

7. Osteoporosis means 'Porous Bones' and is defined as a progressive, systemic skeletal disease that leads to loss of bone and its microscopic structure. The consequences of this are reduce strength and an increased risk of low impact fracture. Diet low in Calcium, Vitamin D or high in Animal Protein can increase risk of Osteoporosis.

8. Psoriasis is a skin disorder that causes skin cells to multiply up to 10 times faster than normal. This makes the skin build up into bumpy red patches covered with white scales. It is considered as an autoimmune disease. The patches can come and go over the course of a few days to over a month. They can grow anywhere, but most appear on the scalp, elbows, knees, and lower back. Psoriasis cannot be passed from person to person.

NOTES

9. Ulcer is an open sore on an external or internal surface of the body, caused by a break in the skin or mucous membrane which fails to heal. Ulcers range from small, painful sores in the mouth to bedsores and serious lesions of the stomach or intestine.

   An ulcer is a painful sore that is slow to heal and sometimes recurs. Ulcers are not uncommon. How they appear and corresponding symptoms depend on what caused them and where they occur on your body.

14.8 SUMMARY

- Chronic Kidney Disease (CKD) is a common condition where in dialysis and renal transplantation places an enormous pressure on the health of the patient. Kidney failure patients are susceptible to malnutrition, protein energy wasting and gastrointestinal symptoms.
- The mechanism by which the nutraceuticals may benefit patients with kidney disease include reduction of inflammation, modulation of oxidative stress and inhibition of interstitial fibrosis, promotion of renal blood flow, Glomerular Filtration Rate (GFR) and stimulation of tubular regeneration.
- Under normal conditions, Homeostasis is maintained owing to interactions between the host and intestinal microflora. However, quantitative and qualitative alterations in the intestinal microflora are present in patients with CKD. This dysbiotic intestinal microflora is characterised by an increase in the pathogenic flora relative to the symbiotic flora.
- The pathogenic gut microbiota produce Uraemic Toxins, in particular Indoxyl Sulfate (IS) and P-Cresyl Sulfate (PCS) among others, which have been associated with increased inflammation, greater oxidative stress and higher risk for Cardio Vascular Disease (CVD), progression of CKD and death due to CKD.
- Probiotics, prebiotics or synbiotics have been reported to reduce inflammation, improve kidney function and retard progression of CKD by restoring the symbiosis of gut microflora in patients with CKD.
- Liver is protected by ribs. The liver is located in the upper right part of the abdomen. It is the largest organ in the body and performs more than 500 jobs including at least 22 vital functions. It is the main detoxifier of the body as it removes and neutralises poisons, drugs, nicotine and alcohol in the blood stream.
- Chronic inflammation of the liver leads to scar tissues being formed due to the condition known as Cirrhosis. Another common liver problem is the failure of the liver to secrete bile because of stones forming in the gall bladder.

NOTES

- Although the liver has a remarkable ability to regenerate itself, but due to the health effects or continued and long term alcohol abuse may cause Liver Failure. Signs of chronic liver disease can include Jaundice, Fever, loss of Body Hair, distension in the Abdomen and Yellow Fatty deposits in the Upper Eyelids.
- Milk Thistle is used as a natural remedy to treat a range of health conditions. The active ingredient in milk thistle is called 'Silymarin'. Milk thistle is also known as Mary Thistle or Holy Thistle. It is mainly used to treat Liver problems, but it is also used to lower Cholesterol level and to manage Type 2 Diabetes.
- Bone consist of an organic phase (matrix) and an inorganic mineral phase, together with a highly varied population of cells responsible for its development and maintenance. The matrix composed of structural proteins, collagen and mucopolysaccharides which provide resistance and flexibility. The main mineral present is Hydroxyapatite (Crystalline Calcium Phosphate) which is responsible for the rigidity and compressibility of bone.
- Bone multicellular units consist of Osteoblasts and Osteoclasts acting in a coordinated fashion under the influence of numerous cellular factors.
- Osteoblasts initiate remodelling through specific activation of their membrane receptors. They attach to internal bone surfaces and secrete protons and enzymes which degrade and release minerals from the tissue.
- Osteoblasts the replace the resorbed material with immature matrix Protein (Osteoid), which later becomes mineralised.
- Parathyroid hormone is a peptide hormone secreted in response to low concentrations of Serum Calcium and directly enhances Osteoclasts activation via interaction with a membrane receptor. This stimulates resorption and release of free Calcium irons to restore the imbalance.
- Vitamin D is obtained from the diet or synthesised in the skin by ultraviolet (UV) light. It acts by increasing intestinal Calcium absorption and promoting Osteoclast resorption.
- Calcitonin is a Peptide Hormone that inhibits the action of Osteoclasts in response to elevated Serum Calcium levels.
- Growth hormone promotes the synthesis of collagen and other bone proteins by Osteoblasts.
- Osteoporosis means 'Porous Bones' and is defined as a progressive, systemic skeletal disease that leads to loss of bone and its microscopic structure. The consequences of this are reduce strength and an increased risk of low impact fracture.
- Diet low in Calcium, Vitamin D or high in Animal Protein can increase risk of Osteoporosis.

NOTES

- Melatonin is an endogenous hormone secreted by the pineal gland of the brain. It occurs naturally in various fruits and vegetables, particularly in Tomatoes, Cucumbers, Bananas although only in small quantities compared with those in the body (5-25 mg secreted daily). In order to obtain significant physiological concentration large quantities of Melatonin rich foods would have to be eaten.
- Psoriasis is a skin disorder that causes skin cells to multiply up to 10 times faster than normal. This makes the skin build up into bumpy red patches covered with white scales. It is considered as an autoimmune disease. The patches can come and go over the course of a few days to over a month. They can grow anywhere, but most appear on the scalp, elbows, knees, and lower back. Psoriasis cannot be passed from person to person.
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- An ulcer is a painful sore that is slow to heal and sometimes recurs. Ulcers are not uncommon. How they appear and corresponding symptoms depend on what caused them and where they occur on your body.
- Peptic ulcers are sores or wounds that develop on the inside lining of the stomach, the upper portion of the small intestine, or the esophagus. They form when digestive juices damage the walls of the stomach or intestine.
- Peptic ulcers are most often caused from inflammation after being infected with *Helicobacter pylori* (*H. pylori*) bacteria and long-term use of painkillers.

14.9 KEY WORDS

- **Chronic Kidney Disease (CKD):** It is a common condition where in dialysis and renal transplantation places an enormous pressure on the health of the patient.
- **Parathyroid hormone:** It is a peptide hormone secreted in response to low concentrations of Serum Calcium and directly enhances Osteoclasts activation via interaction with a membrane receptor.

NOTES

- **Calcitonin:** It is a Peptide Hormone that inhibits the action of Osteoclasts in response to elevated Serum Calcium levels.
- **Growth hormone:** It promotes the synthesis of collagen and other bone proteins by Osteoblasts.
- **Osteoporosis:** It means 'Porous Bones' and is defined as a progressive, systemic skeletal disease that leads to loss of bone and its microscopic structure. The consequences of this are reduce strength and an increased risk of low impact fracture.

14.10 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. What is CKD?
2. Give some benefits of probiotics.
3. What is Licorice root?
4. How methionine and serine are useful?
5. List the factors necessary for coordinating osteoblasts and osteoclasts.
6. Write a short note on nutraceuticals for bone melatonin.
7. Explain about phytoestrogens in short.
8. What are the most common symptoms of psoriasis?
9. What are ulcers?

Long Answer Questions

1. Discuss about nutraceutical remedies for nephrological disorders.
2. How the probiotics are helpful in chronic kidney disease? Explain with examples.
3. List some of the nutraceutical remedies for liver disorders.
4. Elaborate a note on liver health supplements,
5. Explain with the help of table the nutraceutical principal for the treatment of non-alcoholic fatty liver and possible targets.
6. Discuss about nutraceutical remedies for osteoporosis.
7. What are endocrine factors? What are its preventions and treatment?
8. Explain the symptoms and types of psoriasis and the remedy for its cure.

14.11 FURTHER READINGS

NOTES

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