Drugs Containing Carbohydrates and Derived Products

CHAPTER 14

14.1. INTRODUCTION

Carbohydrates, as the name suggest, were defined as a group of compounds composed of carbon, hydrogen and oxygen in which the latter two elements are in the same proportion as in water and were expressed by a formula $(CH_2O)_n$, that is, hydrates of carbon.

The term 'carbohydrates' arose from the mistaken belief that substances of this kind were hydrates of carbon, because the molecular formula of many substances could be expressed in the form $C_X(H_2O)_Y$, for example, glucose ($C_6H_{12}O_6$), sucrose ($C_{12}H_{22}O_{11}$), etc. In these examples, the hydrogen and oxygen are present in the same ratio as in water. But this definition has certain drawbacks as given below:

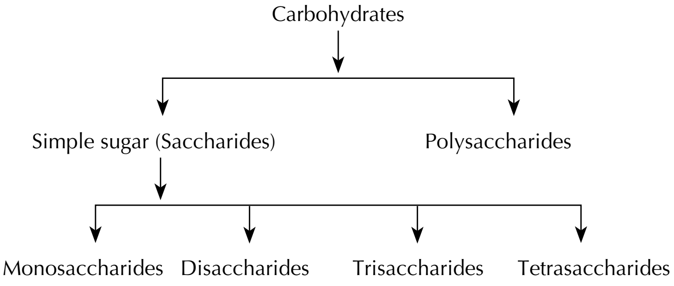
- It should be kept in mind that all organic compounds containing hydrogen and oxygen in the proportion found in water are not carbohydrates. For example, formaldehyde HCHO for the present purpose written as $C(H_2O)$; acetic acid CH_3COOH written as $C_3(H_2O)_2$; and lactic acid $CH_3CHOHCOOH$ written as $C_3(H_2O)_3$ are not carbohydrates.
- Also, a large number of carbohydrates such as rhamnose ($C_6H_{12}O_5$), cymarose ($C_7H_{14}O_4$), digitoxose ($C_6H_{12}O_4$), etc., are known which do not contain the usual proportions of hydrogen to oxygen.
- Finally, certain carbohydrates are also known which contain nitrogen or sulphur in addition to carbon, hydrogen and oxygen.

From the above discussion, it can be concluded that the definitions described above are not correct; however, carbohydrates are now defined chemically as polyhydroxy aldehyde or polyhydroxy ketones or compound that on hydrolyses produce either of the above.

Carbohydrates are among the first products to arise as a result of photosynthesis. They constitute a large proportion of the plant biomass and are responsible, as cellulose, for the rigid cellular framework and, as starch, for providing an important food reserve. Of special pharmacognostical importance is the fact that sugars unites with a wide variety of other compounds to form glycosides and secondary metabolites. Mucilage, as found in marshmallow root and psyllium seeds, act as water-retaining vehicles, where as gums and mucilage, which are similar in composition and properties, are formed in the plant by injury or stress and usually appear as solidified exudates; both are typically composed of uronic acid and sugar units. The cell walls of the brown seaweeds and the middle lamellae of higher plant tissues contain polysaccharides consisting almost entirely of uronic acid components.

Low molecular weight carbohydrates are crystalline, soluble in water and sweet in taste, for example, glucose, fructose, sucrose, etc. The high molecular weight carbohydrates (polymers) are amorphous, tasteless and relatively less soluble in water, for example, starch, cellulose, inulin, etc.

14.2. CLASSIFICATION



Monosaccharides

The term 'monosaccharides' is employed for such sugars that on hydrolysis yield no further, lower sugars. The general formula of monosaccharides is $C_n H_{2n} O_n$. The monosaccharides are subdivided as bioses, trioses, tetroses, pentoses, hexoses, heptoses, depending upon the number of carbon atoms they possess.

Bioses

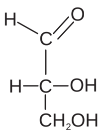
They contain two carbon atoms. They do not occur free in nature.

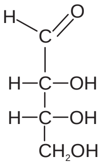
Trioses

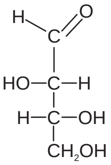
They contain three carbon atoms, but in the form of phosphoric esters, for example, glyceraldehydes.

Tetroses

They contain four carbon atoms, for example, erythrose, threose, etc.

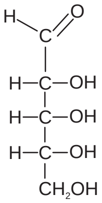

D -(+)-glyceraldehyde

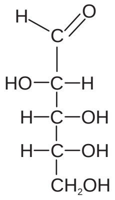

D -(-)-erythrose

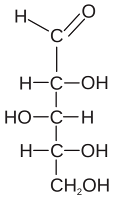

D -(-)-threose

Pentoses

They are very common in plants and are the products of hydrolysis of polysaccharides like hamicelluloses, mucilages and gums, for example, ribose, arabinose and xylose.


D -(-)-ribose

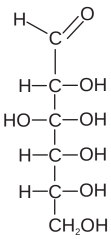

D -(-)-arabinose

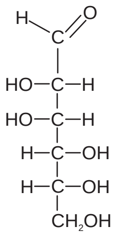

D -(+)-xylose

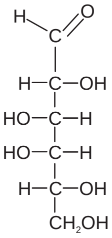
Hexoses

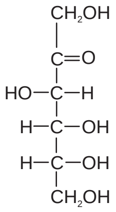
They are monosaccharides containing six carbon atoms and are abundantly available carbohydrates of plant kingdom. They are further divided into two types: aldoses and ketoses. They may be obtained by hydrolysis of polysaccharides like starch, insulin, etc.

Aldoses : Glucose, mannose, galactose
Ketoses : Fructose and sorbose


D -(+)-glucose


D -(+)-mannose


D -(+)-galactose


D -(-)-fructose

Heptoses

They contain seven carbon atoms, vitally important in the photosynthesis of plant and glucose metabolism of animals and are rarely found accumulated in plants, for example, glucoheptose and manoheptose.

Disaccharides

Carbohydrates, which upon hydrolysis yield two molecules of monosaccharides, are called as disaccharides.

Sucrose	$\xrightarrow{\text{Hydrolysis}}$	Glucose + fructose (sugarcane)
Maltose	$\xrightarrow{\text{Hydrolysis}}$	Glucose + Glucose (malt sugar)
Lactose	$\xrightarrow{\text{Hydrolysis}}$	Glucose + Galactose (cow's milk)

Trisaccharides

As the name indicates, these liberate three molecules of monosaccharides on hydrolysis.

Raffinose	$\xrightarrow{\text{Hydrolysis}}$	Glucose + fructose + galactose (in beet) (sugarcane)
Gentianose	$\xrightarrow{\text{Hydrolysis}}$	Glucose + Glucose + fructose (gentian roots)

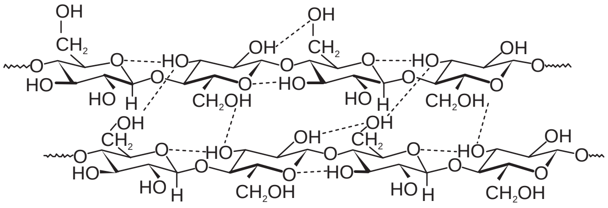
Tetrasaccharides

Stachyose, a tetrasaccharide, yields on hydrolysis, four molecules of monosaccharide, found in manna.

Polysaccharides

On hydrolysis they give an indefinite number of monosaccharides. By condensation, with the elimination of water, polysaccharides are produced from monosaccharides. Depending upon the type of product of hydrolysis these are further classified as Pentosans and Hexosans. Xylan is pentosan, whereas starch, insulin and cellulose are the examples of hexosans.

Cellulose is composed of glucose units joined by β-1, 4 linkages, whereas starch contains glucose units connected with α- 1, 4 and α- 1, 6 units. Polyuronides, gums and mucilages are the other pharmaceutically important polysaccharide derivatives.


Cellulose β-1, 4 linkages

14.3. TESTS FOR CARBOHYDRATES

The following are some of the more useful tests for sugars and other carbohydrates.

Reduction of Fehling's Solution

To the solution of carbohydrate, equal quantity of Fehling's solutions A and B is added. After heating, brick red precipitate is obtained.

Molisch Test

The test is positive with soluble as well as insoluble carbohydrates. It consists of treating the compounds with α-naphthol and concentrated sulphuric acid which gives purple colour. With a soluble carbohydrate this appears as a ring if the sulphuric acid is gently poured in to form a layer below the aqueous solution. With an insoluble, carbohydrate such as cotton wool (cellulose), the colour will not appear until the acid layer is shaken to bring it in contact with the material.

Osazone Formation

Osazones are sugar derivatives formed by heating a sugar solution with phenylhydrazine hydrochloride, sodium acetate and acetic acid. If the yellow crystals which form are examined under the microscope they are sufficiently characteristic for certain sugars to be identified. It should be noted that glucose and fructose form the same osazone (glucosazone, m.p. 205°C). Before melting points are taken, osazones should be purified by recrystalization from alcohol. Sucrose does not form an osazone, but under the conditions of the above test sufficient hydrolysis takes place for the production of glucosazone.

Resorcinol Test for Ketones (Selivanoff's Test)

A crystal of resorcinol is added to the solution and warmed on a water bath with an equal volume of concentrated hydrochloric acid. A rose colour is produced if a ketone is present (e.g. fructose, honey or hydrolysed inulin).

Test for Pentoses

Heat a solution of the substance in a test tube with an equal volume of hydrochloric acid containing a little phloroglucinol. Formation of a red colour indicates pentoses.

Keller-Kiliani Test for Deoxysugars

A Deoxysugar (found in cardiac glycosides) is dissolved in acetic acid containing a trace of ferric chloride and transferred to the surface of concentrated sulphuric acid. At the junction of the liquids a reddish-brown colour is produced which gradually becomes blue.

Furfural Test

A carbohydrate sample is heated in a test tube with a drop of syrupy phosphoric acid to convert it into furfural. A disk of filter paper moistened with a drop of 10% solution of aniline in 10% acetic acid is placed over the mouth of the test tube. The bottom of the test tube is heated for 30–60s. A pink or red stain appears on the reagent paper.

14.4. BIOSYNTHESIS OF CARBOHYDRATES

Production of Monosaccharides by Photosynthesis

Carbohydrates are products of photosynthesis, a biologic process that converts electromagnetic energy into chemical energy. In the green plant, photosynthesis consists of two classes of reactions. One class comprises the so-called light reactions that actually convert electromagnetic energy into chemical potential. The other class consists of the enzymatic reactions that utilize the energy from the light reactions to fix carbon dioxide into sugar. These are referred to as the dark reactions. The results of both of these types of reactions are most simply summarized in the following equation:

$$2H_2O + CO_2 + \text{light} \xrightarrow{\text{chlorophyll}} (CH_2O) + H_2O + O_2$$

Although this equation summarizes the overall relationships of the reactants and products, it gives no clue as to the nature of the chemical intermediates involved in the process. The elucidation of the reactions by which carbon dioxide is accepted into an organic compound and ultimately into sugars with regeneration of the carbon dioxide acceptor was a major achievement in biosynthetic research. The pathway of carbon in photosynthesis, as worked out primarily by Calvin and coworkers, is presented in Figure 14.1.

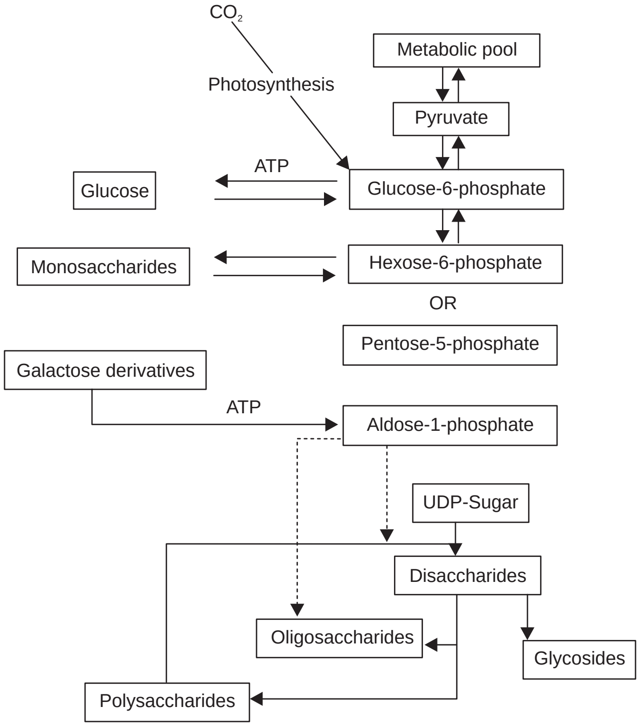


Fig. 14.1 Carbohydrate biosynthesis

CHAPTER 15

Drugs Containing Alkaloids

15.1. INTRODUCTION

One of the largest groups of chemicals produced by plants is the alkaloids. Many of these metabolic by-products are derived from amino acids and include an enormous number of bitter, nitrogenous compounds. More than 10,000 different alkaloids have been discovered in species from over 300 plant families. Alkaloids often contain one or more rings of carbon atoms, usually with a nitrogen atom in the ring. The position of the nitrogen atom in the carbon ring varies with different alkaloids and with different plant families. In some alkaloids, such as mescaline, the nitrogen atom is not within a carbon ring. In fact, it is the precise position of the nitrogen atom that affects the properties of these alkaloids. These compounds are renowned for their potent pharmacological activities. Whilst tiny amounts of some can immobilize an elephant or a rhinoceros, others have important clinical use, such as analgesics, antimalarial, antispasmodics, for pupil dilation, treatment of hypertension, mental disorders and tumours.

They are all nitrogen heterocycles which occur mainly in plants as their salts of common carboxylic acids, such as citric, lactic, oxalic, acetic, maleic and tartaric acids as well as fumaric, benzoic, aconitic and veratric acids. Their amine character produce an alkaline solution in water and hence the origin of their name—alkaloids.

Although they undoubtedly existed long before humans, some alkaloids have remarkable structural similarities with neurotransmitters in the central nervous system (CNS) of humans, including dopamine, serotonin and acetylcholine. The amazing effect of these alkaloids on humans has led to the development of powerful painkiller medications, spiritual drugs, and serious addictions by people who are ignorant of the properties of these powerful chemicals.

15.2. DEFINITION

An alkaloid is a nitrogenous organic molecule that has a pharmacological effect on humans and animals. They are a class of compounds which typically contain nitrogen and have complex ring structures. They occur naturally in seed bearing plants and are found in berries, bark, fruit, roots and leaves. Often, they are bases which have some physiological effect. The name derives from the word alkaline; originally, the term was used to describe any nitrogen-containing base (an amine in modern terms). Alkaloids are found as secondary metabolites in plants (e.g. in Vinca and Datura), animals (e.g. in shellfish) and fungi, and can be extracted from their sources by treatment with acids (usually hydrochloric acid or sulphuric acid, though organic acids, such as maleic acid and citric acid are sometimes used).

Usually alkaloids are derivatives from amino acids. Even though many alkaloids are poisonous (e.g. strychnine or coniine), some are used in medicine as analgesics (pain relievers) or anaesthetics, particularly morphine and codeine. Most alkaloids have a very bitter taste.

15.3. HISTORY

Evidence suggests that alkaloids have been used by humanity for thousands of years. The first civilizations to use them were probably the ancient Sumarians and Egyptians. However, it was not until the early nineteenth century that these compounds were reproducibly isolated and analysed. Advances in analytical separation techniques, such as chromatography and mass spectroscopy, led to the elucidation of the chemical structure of alkaloids. The term for these compounds is thought to have originated from the fact that the alkaloid, morphine, had similar properties to basic salts derived from the alkali ashes of plants thus, it was called a vegetable alkali or alkaloid. Since the first alkaloids were isolated, thousands more have .been identified and classified.

Prior to approximately 300 years ago, malaria was the scourge of Europe, likely having been introduced through the Middle East. Malaria is caused by protozoa of the genus

Plasmodium, contained as spores in the gut of the Anopheles mosquito, which then spreads the spores to humans when it bites. As the Spanish and Portuguese explorers began to colonize South America, they discovered a cure for malaria known to the native Indians. This was the bark of the Cinchona trees. The use of Cinchona bark to treat malaria was first reported in Europe in 1633, and the first bark reached Rome about 12 years later. Teas made from the bark cured people suffering from malaria, one of the major scourges in Europe at that time, and the bark was known as Jesuit's bark. Because of the philosophical differences between Protestants and Catholics, many Protestants refused to be treated with the bark. One of the most prominent Protestants of the time, Oliver Cromwell, reportedly died of malaria because of this stubbornness.

The French apothecary Derosne probably isolated the alkaloid afterwards known as narcotine in 1803 and the Hanoverian apothecary Serturner further investigated opium and isolated morphine (1806 and 1816). Morphine is the principal alkaloid and was first isolated between 1803 and 1806. It was widely used for pain relief beginning in the 1830s, but was also recognized as being addictive. Isolation of other alkaloids, particularly by Pelletier and Caventou, rapidly followed: strychnine (1817), emetine (1817), brucine (1819), piperine (1819), caffeine (1819), quinine (1820), colchicine (1820) and conine (1826). Coniine was the first alkaloid to have its structure established and to be synthesized, but for others, such as colchicine, it was well over a century before the structures were finally elucidated. In the second half of the twentieth century alkaloids featured strongly in the search for plant drugs with anticancer activity. A notable success was the introduction of catharanthus alkaloids and paclitaxel into medicine and there is much current interest in other alkaloids having anticancer properties as well as those exhibiting antiaging and antiviral possibilities.

15.4. CLASSIFICATION

Alkaloids are generally classified by their common molecular precursors, based on the biological pathway used to construct the molecule. From a structural point of view, alkaloids are divided according to their shapes and origins. There are three main types of alkaloids: (1) true alkaloids, (2) protoalkaloids, and (3) pseudoalkaloids. True alkaloids and protoalkaloids are derived from amino acids, whereas pseudoalkaloids are not derived from these compounds.

True Alkaloids

True alkaloids derive from amino acid and they share a heterocyclic ring with nitrogen. These alkaloids are highly reactive substances with biological activity even in low doses. All true alkaloids have a bitter taste and appear as a white solid, with the exception of nicotine which has a brown liquid. True alkaloids form water-soluble salts. Moreover, most of them are well-defined crystalline substances which unite with acids to form salts. True alkaloids may occur in plants (1) in the free state, (2) as salts and (3) as N-oxides. These alkaloids occur in a limited number of species and families, and are those compounds in which decarboxylated amino acids are condensed with a nonnitrogenous structural moiety. The primary precursors of true alkaloids are such amino acids as L-ornithine, L-lysine, L-phenylalanine/L-tyrosine, L-tryptophan and L-histidine. Examples of true alkaloids include such biologically active alkaloids as cocaine, quinine, dopamine and morphine.

Protoalkaloids

Protoalkaloids are compounds, in which the N atom derived from an amino acid is not a part of the heterocyclic. Such kinds of alkaloid include compounds derived from L-tyrosine and L-tryptophan. Protoalkaloids are those with a closed ring, being perfect but structurally simple alkaloids. They form a minority of all alkaloids. Hordenine, mescaline and yohimbine are good examples of these kinds of alkaloid. Chini et al. have found new alkaloids, stachydrine and 4-hydroxystachydrine, derived from *Boscia angustifolia*, a plant belonging to the Capparidacea family. These alkaloids have a pyrroline nucleus and are basic alkaloids in the genus *Boscia*. The species from this genus have been used in folk medicine in East and South Africa. *Boscia angustifolia* is used for the treatment of mental illness, and occasionally to combat pain and neuralgia.

Pseudoalkaloids

Pseudoalkaloids are compounds, the basic carbon skeletons of which are not derived from amino acids. In reality, pseudoalkaloids are connected with amino acid pathways. They are derived from the precursors or post-cursors (derivatives the indegradation process) of amino acids. They can also result from the amination and trans-amination reactions of the different pathways connected with precursors or post-cursors of amino acids.

These alkaloids can also be derived from nonaminoacid precursors. The N atom is inserted into the molecule at a relatively late stage, for example, in the case of steroidal or terpenoid skeletons. Certainly, the N atom can also be donated by an amino acid source across a trans-amination reaction, if there is a suitable aldehyde or ketone. Pseudoalkaloids can be acetate and phenylalanine derived or terpenoid, as well as steroidal alkaloids. Examples of pseudoalkaloids include such compounds as coniine, capsaicin, ephedrine, solanidine, caffeine and theobromine.

Alkaloids are mainly divided into two categories on the basis of their chemical structure, that is, heterocyclic rings (Table 15.1).

Atypical alkaloids

These are also known as nonheterocyclic alkaloids and contain nitrogen in aliphatic chain.

Typical alkaloids

These are also known as heterocyclic alkaloids and contain nitrogen in heterocyclic ring system.

Table 15.1 Classification of alkaloids

Groups	Example	Source	Uses
1. Nonheterocyclic Alkaloids			
Phenyl ethyl amine alkaloid	Ephedrine, Mescaline, Hordenine	Ephedra sp.	Asthma
Tropolone alkaloids	Colchicine	Colchicum sp.	Gout
Modified diterpene	Taxol	Taxus sp.	Anticancer
2. Heterocyclic Alkaloids			
a. Mono-nuclear Heterocyclic Alkaloids			
Pyridine	Lobeline	Lobelia sp.	Asthma
Piperidine	Piperine	Piper sp	Gonorrhoea, Antioxidant
Pyrrole	Hygrine	Coca sp.	CNS Stimulant
Pyrrolidine	Nicotine	Tobacco sp.	CNS Stimulant
Imidazole	Pilocarpine	Pilocarpus sp.	Contraction of pupil
b. Poly-nuclear Heterocyclic alkaloids			
Isoquinoline	Morphine, papaverine	Opium	Narcotic analgesic
Quinoline	Quinidine, quinidine	Cinchona	Antimalarial
Indole	Ergotamine, reserpine, vincristine, Strychnine	Ergot, Rauwolfia, Vinca, Nux vomica	Oxytocic, Anti-HT, Anticancer, CNS stimulant
Quinazoline	Vasicine	Vasaka	Antitussive
Tropane	Atropine, hyoscine	Datura, belladona	Parasympatholytic
Purine	Caffeine	Coffee, tea	CNS stimulant
Steroid	Solasodine	Solanum sp.	Steroidal precursor
Terpenoid	Aconitine	Aconite sp.	Neuralgia

The interrelationship between different ways of classifications can be summarized by the Table 15.2.

Table 15.2 Main types of alkaloids and their chemical groups

Alkaloid Type	Precursor Compound	Chemical Group of Alkaloids	Parent Compounds	Examples of Alkaloids
True alkaloids	l-ornithine	Pyrrolidine alkaloids	Pyrrolidine	Cuscohygrine Hygrine
		Tropane alkaloids	Tropane	Atropine Cocaine Hyoscyamine Scopolamine/ hyoscine
		Pyrrolizidine alkaloids	Pyrrolizidine	Ilamine Indicine-N-oxide Meteloidine Retronecine
	l-lysine	Piperidine alkaloids	Piperidine	Anaferine Lobelanine Lobeline Pelletierine Piperidine Piperine Pseudopelletierine Sedamine
		Quinolizidine alkaloids	Quinolizidine	Cytisine Lupanine Sparteine
		Indolizidine alkaloids	Indolizidine	Castanospermine Swansonine
	l-tyrosine	Phenylethylamino alkaloids	Phenylethyl amine	Adrenaline Anhalamine Dopamine Noradrenaline Tyramine
		Simple tetrahydroisoquinoline Alkaloids	Benzyltetrahydroisoquinoline	Codeine Morphine Norcoclaurine Papaverine Tetrandrine Thebaine Tubocurarine
	l-tyrosine or l-phenylanine	Phenethylisoquinoline alkaloids	Amaryllidaceae alkaloids	Autumnaline Crinine Floramultine Galanthamine Galanthine Haemanthamine Lycorine Lycorenine Maritidine Oxomaritidine Vittatine
	l-tryptophan	Indole alkaloids	Indole	
			Simple indole alkaloids	Arundacine Arundamine Psilocin Serotonin Tryptamine Zolmitriptan
			Simple β-carboline alkaloids	Elaeagnine Harmine

			Terpenoid indole alkaloids	Ajmalicine Catharanthine Secologanin Tabersonine
		Quinoline alkaloids	Quinoline	Chloroquinine Cinchonidine Quinine Quinidine
		Pyrroloindole alkaloids	Indole	Yohimbine Chimonantheine Chimonantheine Corynantheine Corynantheidine Corynanthine
		Ergot alkaloids		Ergotamine Ergocryptine
	l-histidine	Imidazole alkaloids	Imidazole	Histamine Pilocarpine Pilosine
		Manzamine alkaloids	Xestomanzamine	Xestomanzamine -A Xestomanzamine -B
	l-arginine	Marine alkaloids	β-carboline	Saxitoxin Tetrodotoxin
	Anthranilic acid	Quinazoline alkaloids	Quinazoline	Peganine
		Quinoline alkaloids	Quinoline	Acetylfolidine Acutine Bucharine Dictamnine Dubunidine Kokusaginine Maculosine Perfamine Perforine Polifidine Skimmianine
		Acridone alkaloids	Acridine	Acronycine Rutacridone
	Nicotinic acid	Pyridine alkaloids	Pyridine/ Pyrrolidine	Anabasine Cassinine Celapanin Evoline Evonoline Evorine Maymyrsine Nicotine Regelidine Wilforine
Proto alkaloids	l-tyrosine	Phenylethylamino alkaloids	Phenylethylamine	Hordenine Mescaline
	l-tryptophan	Terpenoid indole alkaloids	Indole	Yohimbine
	l-ornithine	Pyrrolizidine alkaloids	Pyrrolizidine	4-hydroxy stachydrine Stachydrine
Pseudo alkaloids	Acetate	Piperidine alkaloids	Piperidine	Coniine Coniceine Pinidine
		Sesquiterpene alkaloids	Sesquiterpene	Cassinine Celapanin Evonine Evonoline Evorine Maymyrsine Regelidine Wilforine
	Pyruvic acid	Ephedra alkaloids	Phenyl C	Cathine Cathinone Ephedrine Norephedrine
	Ferulic acid	Aromatic alkaloids	Phenyl	Capsaicin
	Geraniol	Terpenoid alkaloids	Terpenoid	Aconitine Actinidine Atisine Gentianine β-skytanthine
	Saponins	Steroid alkaloids		Cholestane Conessine Jervine Pregnenolone Protoveratrine A Protoveratrine B Solanidine Solasodine
	Adenine/ Guanine	Purine alkaloids	Purine	Caffeine Theobromine Theophylline

15.5. OCCURRENCE IN NATURE

Alkaloids are substances very well known for their biological activity at the beginning of world civilization. They were used in shamanism, in traditional herbal medicine for the cure of diseases and in weapons as toxins during tribal wars and during hunting. They also had, and still have, socio-cultural and personal significance in ethnobotany. Moreover, they have been and continue to be the object of human interest concerning new possibilities for their safe utilization and ensuing health benefits. Of all secondary compounds, historically and contemporaneously, only alkaloids are molecules of natural origin with highly important benefits and diagnostic uses. They can be characterized as the most useful and also the most dangerous products of nature.

Alkaloids are most abundant in higher plants. At least 25% of higher plants contain these molecules. In effect, this means that on average; at least one in fourth plants contains some alkaloids. In reality, it is not impossible that alkaloids occur more commonly. Using the latest equipment and technology, such slight traces of alkaloids may be detected (e.g. less than 10 gigagrams per kg of plant mass) that these have no real influence on biological receptors and activity. Generally these species are not considered as alkaloid species. Hegnauer has defined alkaloid plants as those species which contain more than 0.0l% of alkaloids. This is right from the point of view of the classification. From the genetic point of view, and the genetic mechanism of alkaloid synthesis, it is a real limitation. Paying attention to slight traces of alkaloids in plants, we see the members of the plant family which are relatives. They have a genetically determined alkaloid mechanism with a species expression. Moreover, this expression is also on the hybrid level.

The distribution of alkaloids in nature is restricted to some specific plants, animals or lower plants. The pattern of distribution of compound and its pharmacological activity have a great role in chemotaxonomical classification. Alkaloids are chiefly found to be distributed in angiosperms and to some extent in lower plants (mosses, liverworts) and animals. Nearly about 47–50% of various bacterial species also contain alkaloids, for example, pyocyanine from *Pseudomonas aeruginosa.* Alkaloids are commonly found in the families like, Chenopodiaceae, Lauraceae, Berberidaceae, Menispermaceae, Ranunculaceae, Papaveraceae, Fumariaceae, Leguminosae, Papilionaceae, Rutaceae, Apocynaceae, Loganiaceae, Rubiaceae, Boraginaceae, Convolvulaceae, Solanaceae, Campanulaceae, Compositae, etc. They may be present in any part of the plant like, roots (reserpine from Rauwolfia), aerial parts like (Ephedra), barks (quinine from cinchona), leaves (Cocaine from Coca), seeds (caffeine from Coca seeds) or even in entire plant (vinblastin from Vinca). 300 alkaloids belonging to more than 24 classes are reported to occur in the skins of amphibians.

15.6. PROPERTIES

Although numerous alkaloids exist, they have similar properties when separated. In general, they are colourless, crystalline solids which are basic, have a ring structure, and have definite melting points. They are also derived from plants and have a bitter taste. However, some exceptions are known. For instance, some alkaloids are not basic and others are brightly coloured (betanidine, beriberine, sanguinarine) or liquid (nicotine). Other alkaloids are produced synthetically. Most alkaloids are also chiral molecules which mean they have nonsuperimposable mirror images. This results in isomers that have different chemical properties. For example, one isomer may have a physiological function while the other does not.

Generally free bases of alkaloids are soluble in organic solvents and insoluble in water, where as alkaloidal salts are soluble in water and partially soluble in organic solvents. For example, strychnine hydrochloride is much more soluble in water than strychnine as a base.

15.7. EXTRACTION

The extraction of alkaloids is based on their basic character and solubility profiles. Generally alkaloids are extracted mainly using two methods.

Method A

The powdered material that contains alkaloidal salts is moistened with alkaline substances like sodium bicarbonate, ammonia, calcium hydroxide, etc., which combines with acids, tannins and other phenolic substances and sets free the alkaloids bases. Extraction is then carried out with organic solvents such as ether or petroleum spirit. The concentrated organic liquid is then shaken with aqueous acid and allowed to separate. Alkaloid salts will be present in aqueous liquid, while many impurities remain behind in the organic liquid.

Method B

The collected powdered material is extracted with water or aqueous alcohol containing dilute acid. Chloroform or other organic solvents are added and shaken to remove the pigments and other unwanted materials. The free alkaloids are then precipitated by the addition of excess alkalis like, sodium bicarbonate or ammonia and separated by filtration or by extraction with organic solvents.

Volatile liquid alkaloids (nicotine and coniine) are isolated by distillation. The powdered material that contains alkaloids is extracted with water and the aqueous extract is made alkaline with sodium carbonate or ammonia and the alkaloid is distilled off in steam. This could be collected and purified.

15.8. CHEMICAL TESTS

The chemical tests are performed from neutral or slightly acidic solution of drug.

Dragendorff's Test

Drug solution + Dragendroff's reagent (Potassium Bismuth Iodide), formation of Orangish red colour.

Mayer's Test

Drug solution + few drops of Mayer's reagent (potassium mercuric iodide), formation of creamy-white precipitant.

Hager's Test

Drug solution + few drops of Hagers reagent (Saturated aq. Solution of Picric acid), formation of crystalline yellow precipitate.

Wagner's Test

Drug solution + few drops of Wagner's reagent (dilute Iodine solution), formulation of reddish-brown precipitate.

Tannic Acid Test

Drug solution + few drops of tannic acid solution, formation of buff coloured precipitate.

CHAPTER 16

Drugs Containing Glycosides

16.1. INTRODUCTION

A glycoside is any molecule in which a sugar group is bonded through its anomeric carbon to another group via glycosidic bond. A glycosidic bond is a certain type of chemical bond that joins a sugar molecule to another molecule. Specifically, a glycosidic bond is formed between the hemiacetal group of a saccharide (or a molecule derived from a saccharide) and the hydroxyl group of an alcohol. A substance containing a glycosidic bond is a glycoside. The glycone and aglycone portions can be chemically separated by hydrolysis in the presence of acid. There are also numerous enzymes that can form and break glycosidic bonds.

The sugar group is known as the glycone and the nonsugar group as the aglycone or genin part of the glycoside. The glycone can consist of a single sugar group (monosaccharide) or several sugar groups (oligosaccharide). The sugars found in glycosides may be glucose and rhamnose (monosaccharides) or, more rarely, deoxysugars such as the cymarose found in cardiac glycosides.

In plants glycosides are both synthesized and hydrolysed under the influence of more or less specific enzymes. They are crystalline or amorphous substances that are soluble in water or alcohols and insoluble in organic solvents like benzene and ether. The aglycone part is soluble in organic solvents like benzene or ether. They are hydrolysed by water, enzymes and mineral acids. They are optically active. While glycosides do not themselves reduce Fehling's solution, the simple sugars which they produce on hydrolysis will do so with precipitation of red cuprous oxide. The sugars present in glycoside are of two isomeric forms, that is, α form and β form, but all the natural glycosides contain β-type of sugar.

The term 'glycoside' is a very general one which embraces all the many and varied combinations of sugars and aglycones.

16.2. CLASSIFICATION

The glycosides can be classified by the glycone, by the type of glycosidal linkage, and by the aglycone.

On the Basis of Glycone

If the glycone group of a glycoside is glucose, then the molecule is a glucoside; if it is fructose, then the molecule is a fructoside; if it is glucuronic acid, then the molecule is a glucuronide, etc.

On the Basis of Glycosidic Linkage

1. **O-glycosides:** Sugar molecule is combined with phenol or –OH group of aglycon, for example, Amygdaline, Indesine, Arbutin, Salicin, cardiac glycosides, anthraxquinone glycosides like sennosides etc.
2. **N-glycosides:** Sugar molecule is combined with N of the –NH (amino group) of aglycon, for example, nucleosides
3. **S-glycosides:** Sugar molecule is combined with the S or SH (thiol group) of aglycon, for example, Sinigrin.
4. **C-glycosides:** Sugar molecule is directly attached with C—atom of aglycon, for example, Anthraquinone glycosides like Aloin, Barbaloin, Cascaroside and Flavan glycosides, etc.

On the Basis of Aglycone

The various classes according to aglycone moiety are given below:

S. No.	Class	Examples
1.	Anthraquinone glycosides	Senna, Aloe, Rhubarb, etc.
2.	Sterol or Cardiac glycosides	Digitalis, Thevetia, Squill, etc.
3.	Saponin glycosides	Dioscorea, Liquorice, Ginseng, etc.
4.	Cyanogenetic and Cyanophoric glycosides	Bitter almond, Wild cherry bark, etc.
5.	Thiocynate and Isothiocynate glycosides	Black mustard
6.	Flavone glycosides	Ginkgo
7.	Aldehyde glycosides	Vanilla
8.	Phenol glycosides	Bearberry
9.	Steroidal glycosides	Solanum
10.	Bitter and Miscellaneous glycosides	Gentian, Picrrohiza, Chirata, etc.

16.3. DISTRIBUTION OF GLYCOSIDES

Glycosides are the class of compounds abundant in nature. Some plant families containing important glycosides are listed bellow:

1. Scrophulareaceae (*Digitalis purpurea* and *Digitalis lanata*, *Picrorhiza kurroa*).
2. Apocyanaceae (*Nerium oliander* and *Thevetia peruviana*).
3. Liliacea (*Urgenea indica* and *U. maritima*, *Aloe vera*)
4. Leguminocae (*Cassia acutefolia* and *C. angustefolia*, *Glycyrrhiza glabra, Psoralea corylifolia*)
5. Dioscoreaceae (*Dioscorea floribunda*)
6. Rosaceae (*Prunus amygdalus, Carategus oxycantha*)
7. Cruciferae (*Brassica* sp.)
8. Gentianaceae (Gentian and Chirata)
9. Acanthaceae (Kalmegh)
10. Simarubaceae (Quassia)
11. Umbelliferae (*Ammi majus, Ammi visnaga*)
12. Rutaceae: Citrus sp. (*Ruta graveolens*)
13. Polygonaceae (Fagopyrum sp.)
14. Myrtaceae (Eucalyptus sp.)

16.4. CHEMICAL TESTS OF GLYCOSIDES

Glycosides are the compounds with organic molecules having attached glucose or any mono-oligo sacchrid unit. Usually, these are crystalline or amorphous solids; optically active, soluble in water and alcohol but insoluble in organic solvents like ether, chloroform and benzene etc. Generally, aqueous or alcoholic extracts of crude drugs are tested with specific reagents for presence of various types of glycosides.

Chemical Tests for Anthraquinone Glycosides

Borntrager's test

To 1 gm of drug add 5–10 ml of dilute HCl boil on water bath for 10 min and filter. Filtrate was extracted with CCl_4/ benzene and add equal amount of ammonia solution to filtrate and shake. Formation of pink or red colour in ammonical layer due to presence of anthraquinone moiety.

Modified borntrager's test

To 1 gm of drug, add 5 ml dilute HCl followed by 5 ml ferric Chloride (5% w/v). Boil for 10 min on water bath, cool and filter, filtrate was extracted with carbon tetrachloride or benzene and add equal volume of ammonia solution, formation of pink to red colour due to presence of anthraquinone moiety. This is used C-type of anthraquinone glycosides.

Chemical Tests for Saponin Glycosides

Haemolysis test

A drop blood on slide was mixed with few drops of aq. Saponin solution, RBC's becomes ruptured in presence of saponins.

Foam test

To 1 gm of drug add 10–20 ml of water, shake for few minutes, formation frothing which persists for 60–120 s in presence of saponins.

Chemical Tests for Steroid and Triterpenoid Glycosides

Libermann burchard test

Alcoholic extract of drug was evaporated to dryness and extracted with $CHCl_3$, add few drops of acetic anhydride followed by conc. H_2SO_4 from side wall of test tube to the $CHCl_3$ extract. Formation of violet to blue coloured ring at the junction of two liquid, indicate the presence of steroid moiety.

Salkowaski test

Alcoholic extract of drug was evaporated to dryness and extracted with $CHCl_3$, add conc. H_2SO_4 from sidewall of test tube to the $CHCl_3$ extract. Formation of yellow coloured ring at the junction of two liquid, which turns red after 2 min, indicate the presence of steroid moiety.

Antimony trichloride test

Alcoholic extract of drug was evaporated to dryness and extracted with $CHCl_3$, add saturated solution of $SbCl_3$ in $CHCl_3$ containing 20% acetic anhydride. Formation of pink colour on heating indicates presence of steroids and triterpenoids.

Trichloro acetic acid test

Triterpenes on addition of saturated solution of trichloro acetic acid forms coloured precipitate.

Tetranitro methane test

It forms yellow colour with unsaturated steroids and triterpenes.

Zimmermann test

Meta dinitrobenzene solution was added to the alcoholic solution of drug containing alkali, on heating it forms violet colour in presence of keto steroid.

Chemical Tests for Cardiac Glycosides

Keller-kiliani test

To the alcoholic extract of drug equal volume of water and 0.5 ml of strong lead acetate solution was added, shaked and filtered. Filtrate was extracted with equal volume of chloroform. Chloroform extract was evaporated to dryness and residue was dissolved in 3 ml of glacial acetic acid followed by addition of few drops of $FeCl_3$ solution. The resultant solution was transferred to a test tube containing 2 ml of conc. H_2SO_4. Reddish brown layer is formed, which turns bluish green after standing due to presence of digitoxose.

Legal test

To the alcoholic extract of drug equal volume of water and 0.5 ml of strong lead acetate solution was added, shaked and filtered. Filtrate was extracted with equal volume of chloroform and the chloroform extract was evaporated to dryness. The residue was dissolved in 2 ml of pyridine and sodium nitropruside 2 ml was added followed by addition of NaOH solution to make alkaline. Formation of pink colour in presence of glycosides or aglycon moiety.

Baljet test

Thick section of leaf of digitalis or the part of drug containing cardiac glycoside, when dipped in sodium picrate solution, it forms yellow to orange colour in presence of aglycones or glycosides.

3,5-dinitro benzoic acid test

To the alcoholic solution of drug few drops of NaOH followed by 2% solution of 3,5-dinitro benzoic acid was added. Formation of pink colour indicates presence of cardiac glycosides.

Chemical Tests for Coumarin Glycosides

$FeCl_3$ test

To the concentrated alcoholic extract of drug few drops of alcoholic $FeCl_3$ solution was added. Formation of deep green colour, which turned yellow on addition of conc. HNO_3, indicates presence of coumarins.

Fluorescence test

The alcoholic extract of drug was mixed with 1N NaOH solution (one ml each). Development of blue-green fluorescence indicates presence of coumarins.

Chemical Tests for Cynophoric Glycoside

Sodium picrate test

Powdered drug was moistened with water in a conical flask and few drops of conc. Sulphuric acid was added. Filter paper impregnated with sodium picrate solution followed by sodium carbonate solution was trapped on the neck of flask using cork. Formation of brick red colour due to volatile HCN in presence of cynophoric glycosides takes place.

Chemical Tests for Flavonoid Glycosides

Ammonia test

Filter paper dipped in alcoholic solution of drug was exposed to ammonia vapor. Formation of yellow spot on filter paper.

Shinoda test

To the alcoholic extract of drug magnesium turning and dil. HCl was added, formation of red colour indicates the presence of flavonoids. To the alcoholic extract of drug zinc turning and dil. HCl was added, formation of deep red to magenta colour indicates the presence of dihydro flavonoids.

Vanillin HCl test

Vanillin HCl was added to the alcoholic solution of drug, formation of pink colour due to presence of flavonoids.

16.5. ISOLATION

Stas-Otto Method

The general method of extraction of glycosides is outlined here. The drug containing glycoside is finely powdered and the powder is extracted by continuous hot percolation using soxhlet apparatus with alcohol as solvent. During this process, various enzymes present in plant parts are also deactivated due to heating. The thermolabile glycosides, however, should be extracted at temperature preferably below 45°C. The extract is treated with lead acetate to precipitate tannins and thus eliminate nonglycosidal impurities. The excess of lead acetate is precipitated as lead sulphide by passing hydrogen sulphide gas through solution. The extract is filtered, concentrated to get crude glycosides. From the crude extract, the glycosides are obtained in pure form by making use of processes like fractional solubility, fractional crystallization and chromatographic techniques such as preparative thin layer and column chromatography.

The characterization of isolated purified compounds is done by IR, UV, visible, NMR and mass spectrometry and elemental analysis.

Drugs Containing Volatile Oils

CHAPTER

17

17.1. INTRODUCTION

Volatile oils are odorous volatile principles of plant and animal source, evaporate when exposed to air at ordinary temperature, and hence known as volatile or etheral oils. These represent essence of active constituents of the plant and hence also known as essential oils. In most instances the volatile oil preexists in the plant and is usually contained in some special secretory tissues, for example, the oil ducts of umbelliferous fruits, the oil cells, or oil glands occurring in the sub-epidermal tissue of the lemon and orange, mesophyll of eucalyptus leaves, trichomes of several plants, etc.

In few cases the volatile oil does not preexist, but is formed by the decomposition of a glycoside. For example, whole black mustard seeds are odourless, but upon crushing the seeds and adding water to it a strong odour is evolved. This is due to allyl isothiocyanate (the main constituent of essential oil of mustard) formed by decomposition of a glycoside, sinigrin, by an enzyme, myrosin. Glycoside and enzyme are contained in different cells of the seed tissue and are unable to react until the seeds are crushed with water present, so that the cell contents can intermingle.

Volatile oils are freely soluble in ether and in chloroform and fairly soluble in alcohol; they are insoluble in water. The volatile oils dissolve many of the proximate principles of plant and animal tissues, such as the fixed oils and fats, resins, camphor, and many of the alkaloids when in the free state.

These are chemically derived from terpenes (mainly mono and sesqui terpenes) and their oxygenated derivatives. These are soluble in alcohol and other organic solvents, practically insoluble in water, lighter than water (Clove oil heavier), possess characteristic odour, have high refraction index, and most of them are optically active. Volatile oils are colourless liquids, but when exposed to air and direct sunlight these become darker due to oxidation. Unlike fixed oils, volatile oils neither leave permanent grease spot on filter paper nor saponified with alkalis.

17.2. CLASSIFICATION OF VOLATILE OILS

Volatile oils are classified on the basis of functional groups present as given in Table 17.1.

Table 17.1 Classification of volatile oil

Groups	Drugs
Hydrocarbons	Turpentine oil
Alcohols	Peppermint oil, Pudina, Sandalwood oil, etc.
Aldehydes	Cymbopogon sp., Lemongrass oil, Cinnamon, Cassia, and Saffron
Ketones	Camphor, Caraway and Dill, Jatamansi, Fennel, etc.
Phenols	Clove, Ajowan, Tulsi, etc.
Phenolic ethers	Nutmeg, Calamus, etc.
Oxides	Eucalyptus, Cardamom, and Chenopodium oil
Esters	Valerian, Rosemary oil, Garlic, Gaultheria oil, etc.

17.3. EXTRACTION OF VOLATILE OILS

Volatile oils are prepared by means of several techniques and those techniques are discussed below:

Extraction by Distillation

The distillation is carried out either by water or steam. The volatile oils from fresh materials are separated by hydrodistillation, and volatile oils from air dried parts are separated by steam distillation. However it is better to use fresh materials in either case.

Extraction by Scarification

This method is used for the preparation of oil of lemon, oil of orange, and oil of bergamot. These oils are found in large oil glands just below the surface in the peel of the fruit. The two principal methods of scarification are the sponge and the ecuelle method.

(a) *Sponge Process:* In this process the contents of the fruit are removed after making longitudinal or transverse cut, and the peel is been immersed in water for a short period of time. Then it is ready for expression. The operator takes a sponge in one hand and with the other presses the softener peel against the sponge, so that the oil glands burst open and the sponge absorbs the exuded oil, which is transferred to a collecting vessel. The turbid liquid consisting of oil and water is allowed to stand for a short time, whereupon the oil separates from water and is collected. The whole of the above process is carried out in cool, darkened rooms to minimize the harmful effects of heat and light on the oil.

(b) *Ecuelle Process:* In this process, the rinds are ruptured mechanically using numerous pointed projections with a rotary movement and the oil is collected.

Extraction by Non-Volatile Solvent

A nonvolatile solvent, for example, a fine quality of either lard or olive oil, is used in this process. After saturation with the floral oil the lard or olive oil is sometimes used as a flavouring base for the preparation of pomades, brilliantine, etc., or converted to a triple extract. In the latter instance the lard or oil is agitated with two or three successive portions of alcohol, which dissolve the odorous substances. The mixed alcoholic solutions so obtained constitute the 'triple extract' of commerce.

There are three chief methods that come under this; they are enfleurage, maceration and a spraying process.

(a) *Enfleurage:* In this a fatty layer is prepared using lard and the flower petals are spreaded over it, after the imbibitions is over the fatty layer is replaced with fresh petals. After the saturation of fatty layer the odorous principles are removed by treating with alcohol and a triple extract then prepared. When oil is used as a solvent the flowers are placed on an oil-soaked cloth supported by a metal grid enclosed in a frame. Fresh flowers are added as required, and finally the oil is expressed from the cloths. It may then be used as perfumed oil, or extracted with alcohol to produce a triple extract.

(b) *Maceration:* This is also used to extract the volatile matters of flowers. The lard or oil is heated over a water bath, a charge of flowers added and the mixture stirred continuously for some time. The exhausted flowers are removed, pressed, the expressed fluid returned to the hot fat, fresh flowers, added and the process continued until defined weights of flowers and solvent have been used. Again, a triple extract is prepared by extracting the perfumed lard or oil with alcohol.

(c) *Spraying:* In this process a current of warm air is sprayed through a column of the flowers. Then oil or melted fat is sprayed over this oil-laden air which absorbs and dissolves most of the perfume, the collected oil or fat is then extracted with alcohol as described above.

Extraction by Volatile Solvent

In this the flowers are extracted by using the solvent light petroleum and the latter is distilled off at a low temperature, leaving behind the volatile oil.

17.4. TERPENOIDS

There are many different classes of naturally occurring compounds. Terpenoids also form a group of naturally occurring compounds majority of which occur in plants, a few of them have also been obtained from other sources. Terpenoids are volatile substances which give plants and flowers their fragrance. They occur widely in the leaves and fruits of higher plants, conifers, citrus and eucalyptus.

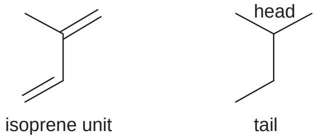
The term 'terpene' was given to the compounds isolated from terpentine, a volatile liquid isolated from pine trees. The simpler mono and sesquiterpenes is the chief constituent of the essential oils obtained from sap and tissues of certain plant and trees. The di- and triterpenoids are not steam volatile. They are obtained from plant and tree gums and resins. Tertraterpenoids form a separate group of compounds called 'Carotenoids'.

The term 'terpene' was originally employed to describe a mixture of isomeric hydrocarbons of the molecular formula $C_{10}H_{16}$ occurring in the essential oils obtained from sap and tissue of plants and trees. But there is a tendency to use more general term 'terpenoids', which includes hydrocarbons and their oxygenated derivatives. However, the term terpene is being used these days by some authors to represent terpenoids.

According to modern definition, 'Terpenoids are the hydrocarbons of plant origin of the general formula $(C_5H_8)_n$ as well as their oxygenated, hydrogenated, and dehydrogenated derivatives.'

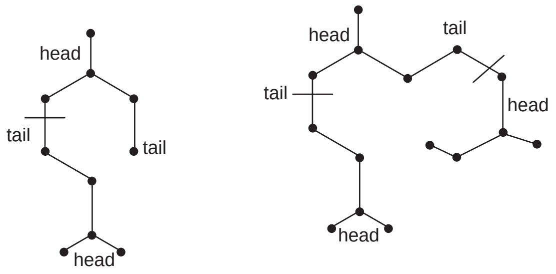
Isoprene Rule

Thermal decomposition of terpenoids gives isoprene as one of the product. Otto Wallach pointed out that terpenoids can be built up of isoprene unit. Isoprene rule states that the terpenoid molecules are constructed from two or more isoprene unit.

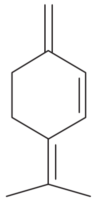


Special Isoprene Rule

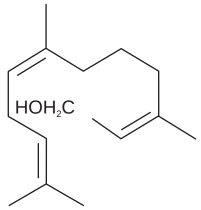
It states that the terpenoid molecules are constructed of two or more isoprene units joined in a 'head to tail' fashion.



Examples



Myrcene
(monoterpene)



Farnesol
(sesquiterpene)

But this rule can only be used as guiding principle and not as a fixed rule. For example carotenoids are joined tail to tail at their central, and there are also some terpenoids whose carbon content is not a multiple of five.

17.5. CLASSIFICATION OF TERPENOIDS

Most natural terpenoid hydrocarbons have the general formula $(C_5H_8)_n$. They can be classified on the basis of number of carbon atoms present in the structure.

Table 17.2 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	Triterpenoids ($C_{30}H_{48}$)
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.

1. Acyclic Terpenoids: They contain open structure.
2. Monocyclic Terpenoids: They contain one ring in the structure.
3. Bicyclic Terpenoids: They contain two rings in the structure.
4. Tricyclic Terpenoids: They contain three rings in the structure.
5. Tetracyclic Terpenoids: They contain four rings in the structure.

17.6. EVALUATION OF VOLATILE OILS

Product from different manufacturers varies considerably, since it is inherently difficult to control all the factors that affect a plants chemical composition. Environmental conditions such as sunlight and rainfall, as well as manufacturing process can create substantial variability in essential oil quality. Various procedures are given for the evaluation of essential oils. Preliminary examinations like odour, taste, and colour. Physical measurements, which includes optical rotation, relative density, and refractive index. Chromatographic techniques are used to determine the proportions of individual components of certain oils. The ketone and aldehyde content of oils are determined by reaction with hydroxylamine hydrochloride (oxime formation) and titration of the liberated acid. The oil, which passes the above examinations, would be having good quality and therapeutic value.

17.7. CHEMICAL TESTS

Natural drugs containing volatile oils can be tested by following chemical tests:

1. Thin section of drug on treatment with alcoholic solution of Sudan III develops red colour in the presence of volatile oils.
2. Thin section of drug is treated with tincture of alkana, which produces red colour that indicates the presence of volatile oils in natural drugs.

17.8. STORAGE OF VOLATILE OILS

Volatile oils are liable to oxidation on storage in presence of air, moisture, and light. The oxidation is followed by the change in colour, increase in viscosity, and change in odour. Hence, volatile oils must be stored in well-closed completely filled containers and away from light in cool places.

17.9. PHARMACEUTICAL APPLICATIONS

Volatile oils are used as flavouring agent, perfuming agent in pharmaceutical formulations, foods, beverages, and in cosmetic industries. These are also used as important medicinal agent for therapeutic purposes like:

1. Carminative (e.g. Umbilliferous fruits)
2. Anthelminitic (e.g. Chenopodium oil)
3. Diuretics (e.g. Juniper)
4. Antiseptic (e.g. Eucalyptus)
5. Counter irritant (e.g. Oil of winter green)
6. Local anesthetic (e.g. Clove)
7. Sedative (e.g. Jatamansi)
8. Local irritant (e.g. Turpentine)
9. Insect repellent (e.g. Citronella)
10. Source of vitamin A (e.g. Lemongrass)

Drugs Containing Resins

CHAPTER 18

18.1. DEFINITION

Resin can be defined as the complex amorphous product of more or less solid characteristics which on heating first sets softened and then melt. Resins are produced and stored in the schizogenous or schizolysigenous glands or cavities of the plants. Isolated resin products which come as an unorganized crude drug in the market are more or less solid, hard, transparent, or translucent materials. Resins are insoluble in most polar and nonpolar solvents like water and petroleum ether, respectively, but dissolve completely in alcohol, solvent ether, benzene, or chloroform.

18.2. CLASSIFICATION

Resins are classified mostly on the basis of two important features, that is, on the basis of their chemical nature and secondly as per their association with the other group of compounds like essential oils and gums.

Chemical classification of resins categorizes these products according to their active functional groups as given below:

Resin Acids

Resin acids are the carboxylic acid group containing resinous substances which may or may not have association with phenolic compounds. These compounds are found in free states or as the esters derivatives. Being acidic compounds they are soluble in aqueous solution of alkalies producing frothy solution. Resin acids can be derivatized to their metallic salts known as resinates, which finds their use in soap, paints and varnish industries. The abietic acid and commiphoric acid present in colophony and myrrh respectively are the examples of resin acids.

Resin Esters

Resin esters are the esters of the resin acids or the other aromatic acids like benzoic, cinnamic, salicylic acids, etc. They are sometimes converted to their free acids by the treatment with caustic alkali. Dragon's blood and benzoin are the common resin ester containing drugs.

Resin Alcohols

Resin alcohols or resinols are the complex alcoholic compounds of high molecular weight. Like resin acids they are found as free alcohols or as esters of benzoic, salicylic, and cinnamic acids. They are insoluble in aqueous alkali solution but are soluble in alcohol and ether. Resinols are present in benzoin as benzoresinol and in storax as storesinol.

Resin Phenols

Resin phenols or resinotannols are also high molecular weight compounds which occur in free states or as esters. Due to phenolic group they form phenoxoids and become soluble in aqueous alkali solution. However they are insoluble in water but dissolve in alcohol and ether. Resinotannols gives a positive reaction with ferric chloride. The resinotannol are found in balsam of Peru as peruresinotannol, in Tolu balsam as toluresinotannol and in benzoin as siaresinotannols.

Glucoresins

Resins sometimes get combined with sugars by glycosylation and produce glucoresins. Glycoresins can be hydrolysed by acidic hydrolysis to the glycone and aglycone.

Resenes

Chemically inert resin products are generally termed as resenes. They are generally found in free state and never form esters or other derivatives. Resenes are soluble in benzene, chloroform and to some extent in petroleum ether. Resenes are insoluble in water. Asafoetida is an example of resene-containing drug, which contains drug about 50% of asaresene B.

Accordingly, other simple classification based on the association of resin with gums and/or volatile oils is given below.

Oleoresins

Oleoresins are the homogenous mixture of resin with volatile oils. The oleoresins posses an essence due to volatile oils. A trace amount of gummy material may sometimes be found in oleoresins. Turpentine, ginger, copaiba, Canada resin are few important examples of oleoresins.

Gum Resins

Gum resins are the naturally occurring mixture of resins with gums. Due to solubility in water, gums can be easily separated out from resin by dissolving the gum in water. Ammoniacum is an example of natural gum resin.

Oleogum Resins

Oleogum resins are the naturally occurring mixtures of resin, volatile oil, and gum. The example includes gum myrrh, asafoetida, gamboage, etc. Oleogum resins oozes out from the incisions made in the bark and hardens.

Balsams

Balsams are the naturally occurring resinous mixtures which contain a high proportion of aromatic balsamic acids such as benzoic acid, cinnamic acid, and their esters. Balsams containing free acids are partially soluble in hot water. Some important balsams containing drugs are balsam of Peru, balsam of Tolu, benzoin, and storax. The oleogum resin containing drugs like copaiba and Canada are sometimes wrongly referred to as balsams.

18.3. CHEMICAL COMPOSITION

The chemical composition of the resin is generally quite complex and diverse in its nature. It can be a complex mixture of acids, alcohols, phenols, esters, glycosides, or hydrocarbons. When the resins are associated with volatile oils, contains the components like monoterpenoids, sesquiterpenonoids, and diterpenoids. The gums which are associated with resins are similar to acacia gum which sometimes possesses smaller quantities of oxidase enzymes. Resins can be of the physiological origin such as the secretions of the ducts. They can also be pathological products which are exuded through the incisions made on the plant.

18.4. ISOLATION

The process of the isolation of resin from crude drug can be a difficult task due to the presence of various combinations. However the most generalized technique can be the extraction of the drug with alcoholic solvents and then subsequent precipitation of resin by adding concentrated alcoholic extract to a large proportion of water. The method of distillation or hydrodistillation can be used for the separation of volatile oils from resin. This process is used largely for the separation of resin from turpentine.

ASAFOETIDA

Synonyms

Devil's dung; food of the gods; asafoda; asant; hing (Hindi).

Biological Source

Asafoetida is an oleo-gum resin obtained as an exudation by incision of the decapitated rhizome and roots of *Ferula asafoetida* L, *F. foetida,* Royel, *F. rubricaulis* Boiss, and some other species of Ferula, belonging to family Apiaceae.

Geographical Source

The plant grows in Iran, Turkestan and Afghanistan (Karam and Chagai districts).

Collection

The plant is a perennial branching, 3 m high herb possessing large schizogeneous ducts and lysigenous cavities containing milky liquid. Upon exudation and drying of the liquid, Asafoetida is obtained. For the collection of the drug the upper part of the root is laid bare and the stem cut off close to the crown in March–April. The exposed surface is covered by a dome-shaped structure made of twigs and earth. After separating each slice, exudation of oleo-gum-resin, present as whitish gummy resinous emulsion in the schizogenous ducts of the cortex of the stem, takes place. It hardens on the cut surface which is collected, packed in tin-line cases and exported. Removal of the exudation and exposure of fresh surface proceeds until the root is exhausted. The yield is usually soft enough to agglomerate into masses when packed.

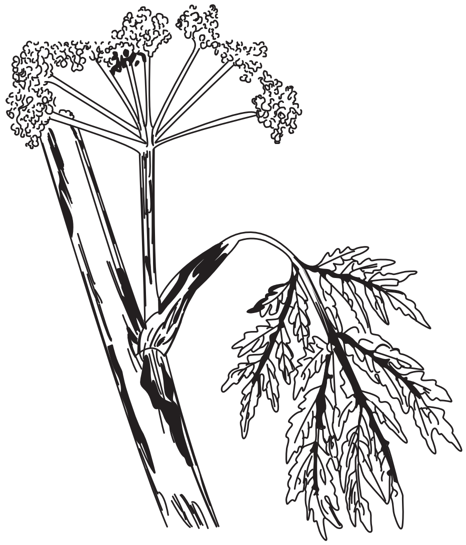


Fig. 18.1 *Ferula asafoetida*

Characteristics

Asafoetida occurs as a soft solid mass or irregular lumps or 'tears', sometimes almost semiliquid. Tears are rounded or flattened and about 5–30 mm in diameter, grayish-white or dull yellow or reddish brown in colour.

Asafoetida mass is mixed with fruits, fragments of root, sand and other impurities. Asafoetida has a strong garlic-like (alliaceous) odour and a bitter, acrid and alliaceous taste. When triturated with water, it makes a milky emulsion. It should not have more than 50% of matter insoluble in alcohol (90%) and not more than 15% of ash.

Chemical Constituents

Asafoetida contains volatile oil (4–20%), resin (40–65%), and gum (25%). The garlic-like odour of the oil is due to the presence of sulphur compounds. The main constituent of the oil is isobutyl propanyl disulphide ($C_6H_{16}S_2$). The three sulphur compounds, such as, 1-methylpropyl-1-propenyl disulphide, l-(methylthio)-propyl-1-pro-penyl disulphide, and l-methyl-propyl 3-(methylthio)-2-propenyl disulphide have also been isolated from the resin; the latter two have pesticidal properties. The flavour is largely due to R-2-butyl-l-propenyl disulphide and 2-butyl-3-methylthioallyl disulphide (both as mixtures of diastereoisomers).

The drug also contains a complex mixture of sesquiterpene umbelliferyl ethers mostly with a monocyclic or bicyclic terpenoid moiety. Resin consists of ester of asaresinotannol and ferulic acid, pinene, vanillin and free ferulic acid. On treatment of ferulic acid with hydrochloric acid, it is converted into umbelliferone (a coumarin) which gives blue fluorescence with ammonia.

Asafoetida also contains phellandrene, sec-butylpropenyl disulphide, geranyl acetate, bornyl acetate, α-terpineol, myristic acid, camphene, myrcene, limonene, fenchone, eugenol, linalool, geraniol, isoborneol, borneol, guaiacol, cadinol, farnesol, assafoetidin, foetidin, etc.

Chemical Tests

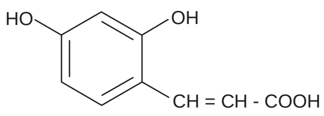
1. On trituration with water it produces a milky emulsion.
2. The drug (0.5 g) is boiled with hydrochloric acid (5 ml) for sometime. It is filtered and ammonia is added to the filtrate. A blue fluorescence is obtained.
3. To the fractured surface add 50% nitric acid. Green colour is produced.
4. To the fractured surface of the drug, add sulphuric acid (1 drop). A red colour is obtained which changes to violet on washing with water.

Uses

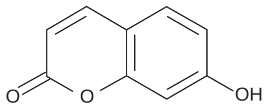
Asafoetida is used as carminative, expectorant, antispasmodic, and laxative as well as externally to prevent bandage chewing by dogs; for flavouring curries, sauces, and pickles; as an enema for intestinal flatulence, in hysterical and epileptic affections, in cholera, asthma, whooping cough, and chronic bronchitis.

Adulteration

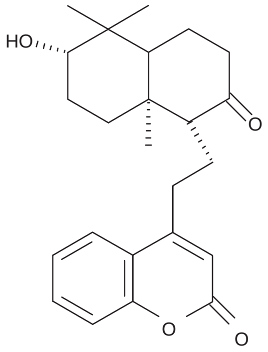
Asafoetida is adulterated with gum Arabic, other gum-resins, rosin, gypsum, red clay, chalk, barley or wheat flour, and slices of potatoes.



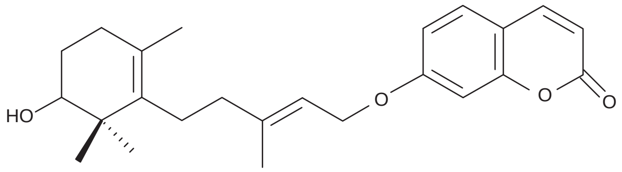
Umbellic acid



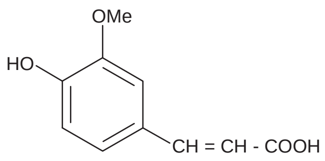
Umbelliferone



Foetidin



Assafoetidin



Ferulic acid

CHAPTER

19

Drugs Containing Lipids

19.1. INTRODUCTION

The lipids are a large and diverse group of naturally occurring organic compounds that are related by their solubility in nonpolar organic solvents (e.g. ether, chloroform, acetone, and benzene) and are generally insoluble in water. There is great structural variety among the lipids and comprise of fixed oils, fats, and waxes. The lipids of physiological importance for humans have the following major functions:

1. They serve as structural components of biological membranes.
2. They provide energy reserves, predominantly in the form of triacylglycerols.
3. Both lipids and lipid derivatives serve as vitamins and hormones.
4. Lipophilic bile acids aid in lipid solubilization.

19.2. FIXED OILS AND FATS

Fixed oils and fats are obtained from plants or animal. They are rich in calories and in plant source, they are present mostly in the seeds, as reserve substances and in animals they are present in subcutaneous and retroperitoneal tissues. They differ only according to their melting point and chemically they belong to the same group. If a substance is liquid at 15.5–16.5°C it is called fixed oil and solid or semisolid at the above temperature, it is called fat. They are made from two kinds of molecules: glycerol (a type of alcohol with a hydroxyl group on each of its three carbons) and three fatty acids joined by dehydration synthesis. Since there are three fatty acids attached, these are known as triglycerides. These fatty acids may be saturated, monounsaturated or polyunsaturated. The terms saturated, mono-unsaturated, and poly-unsaturated refer to the number of hydrogens attached to the hydrocarbon tails of the fatty acids as compared to the number of double bonds between carbon atoms in the tail. Fats, which are mostly from animal sources, have all single bonds between the carbons in their fatty acid tails, thus all the carbons are also bonded to the maximum number of hydrogens possible. Since the fatty acids in these triglycerides contain the maximum possible amount of hydrogens, these would be called saturated fats. The hydrocarbon chains in these fatty acids are, thus, fairly straight and can pack closely together, making these fats solid at room temperature. Oils, mostly from plant sources, have some double bonds between some of the carbons in the hydrocarbon tail, causing bends or ‘kinks’ in the shape of the molecules. Because some of the carbons share double bonds, they are not bonded to as many hydrogens as they could if they weren’t double bonded to each other. Therefore these oils are called unsaturated fats. Because of the kinks in the hydrocarbon tails, unsaturated fats can’t pack as closely together, making them liquid at room temperature.

Examples of saturated and unsaturated fatty acids are given in table 19.1.

Table 19.1 Examples of saturated and unsaturated fatty acids

Fatty acid	Source
Saturated fatty acids	
Butyric acid	Butter fat
Lauric acid	Coconut oil
Myristic acid	Palm oil
Palmitic acid	Arachis oil, sesame oil
Stearic acid	Arachis oil
Arachidic acid	Mustard oil
Unsaturated fatty acids	
Linolenic acid	Linseed oil
Linoleic acid	Sesame oil, sunflower oil
Arachidonic acid	Arachis oil
Oleic acid	Safflower oil, corn oil

Fixed oils and fats are insoluble in water and alcohol and are soluble in lipid solvents like light petroleum, ether, chloroform, and benzene. Only exception in this solubility is castor oil that is soluble in alcohol because of its hydroxy group of ricinoleic acid. They float in water since their specific gravity is less than one. They produce a permanent translucent stain on the paper and are called fixed oils. Fixed oils and fats cannot be distilled without their decomposition.

Analytical Parameters for Fats and Oils

Following are the parameters used to analyse the fats and oils.

1. **Iodine value:** The iodine value is the mass of iodine in grams that is consumed by 100 g of fats or oil. A iodine solution is violet in colour and any chemical group in the substance that reacts with iodine will make the colour disappear at a precise concentration. The amount of iodine solution thus required to keep the solution violet is a measure of the amount of iodine sensitive reactive groups. It is a measure of the extent of unsaturation and higher the iodine value, the more chance for rancidity.
2. **Saponification value:** The saponification value is the number of milligrams of potassium hydroxide required to saponify 1 g of fat under the conditions specified. It is a measure of the average molecular weight of all the fatty acids present.
3. **Hydroxyl value:** The hydroxyl value is the number of mg of potassium hydroxide (KOH) required to neutralize acetic acid combined to hydroxyl groups, when 1 g of a sample is acetylated.
4. Ester value: The ester value is the number of mg of potassium hydroxide (KOH) required to saponify the ester contained in 1 g of a sample.
5. **Unsaponifiable matter:** The principle is the saponification of the fat or oil by boiling under reflux with an ethanolic potassium hydroxide solution. Unsaponifiable matter is then extracted from the soap solution by diethyl ether. The solvent is evaporated and then the residue is dried and weighed.
6. **Acid value:** It is the amount of free acid present in fat as measured by the milligrams of potassium hydroxide needed to neutralize it. As the glycerides in fat slowly-decompose the acid value increases.
7. **Peroxide value:** One of the most widely used tests for oxidative rancidity; peroxide value is a measure of the concentration of peroxides and hydroperoxides formed in the initial stages of lipid oxidation. Milliequivalents of peroxide per kg of fat are measured by titration with iodide ion. Peroxide values are not static and care must be taken in handling and testing samples. It is difficult to provide a specific guideline relating peroxide value to rancidity. High peroxide values are a definite indication of a rancid fat, but moderate values may be the result of depletion of peroxides after reaching high concentrations.

19.3. WAXES

Waxes are esters of long-chain fatty acids and alcohols. The fatty acids are same in wax and fats, but the difference being saponification. Waxes are saponified only by alcoholic alkali but the fats may be saponified either by alcoholic alkali or by aqueous alkali. Along with fatty acids it also contains monohydroxy alcohols of high molecular weight especially cetyl alcohol, melissyl alcohol, and myricyl alcohol. Sometimes cholesterol or phytosterols are also present.

As such they are not suitable as food because hydrolysing enzymes of wax are not present in system. Waxes are widely distributed in nature. The leaves and fruits of many plants have waxy coatings, which may protect them from dehydration and small predators. The feathers of birds and the fur of some animals have similar coatings which serve as a water repellent.

Spermaceti, beeswax, carnuba wax, etc. are the examples of waxes.

ALMOND OIL

Biological Source

Almond oil is a fixed oil obtained by expression from the seeds of *Prunus amygdalus* (Rosaceae) var. dulcis (sweet almonds) or *P. amygdalus var. amara* (bitter almonds).

Geographical Source

The oil is mainly produced from almonds grown in the countries bordering the Mediterranean (Italy, France, Syria, Spain, and North Africa) and Iran.

Characteristics

Almond trees are about 5 m in height. The young fruits have a soft, felt-like pericarp, the inner part of which gradually becomes sclerenchymatous as the fruit ripens to form a pitted endocarp or shell. The shells, consisting mainly of sclerenchymatous cells, are sometimes ground and used to adulterate powdered drugs.

The sweet almond is 2–3 cm in length, rounded at one end, and pointed at the other. The bitter almond is 1.5–2 cm in length but of similar breadth to the sweet almond. Both varieties have a thin, cinnamon-brown testa which is easily removed after soaking in warm water. The oily kernel consists of two large, oily planoconvex cotyledons, and a small plumule and radicle, the latter lying at the pointed end of the seed. Some almonds have cotyledons of unequal sizes and are irregularly folded. Bitter almonds are found in samples of sweet almonds; their presence may be detected by the sodium picrate test for cyanogenetic glycosides.

Fig. 19.1 (a) Bitter almond and (b) Sweet almond

Chemical Constituents

Both varieties of almond contain 40–55% of fixed oil, about 20% of proteins, mucilage and emulsin. The bitter almonds contain in addition 2.5–4.0% of the colourless, crystalline, cyanogenelic glycoside amygdalin.

Almond oil is obtained by grinding the seeds and expressing, them in canvas bags between slightly heated iron plates. The oil is clarified by subsidence and filtration. It is a pale yellow liquid with a slight odour and bland nutty taste. It contains olein, with smaller quantities of the glycosides of linoleic and other acids. Bitter almonds, after maceration on hydrolysis of amygdalin yield a volatile oil that is used as a flavouring agent. Sweet almonds are extensively used as a food, but bitter almonds are not suitable for this purpose.

Essential or volatile oil of almonds is obtained from the cake left after expressing bitter almonds. This is macerated with water for some hours to allow hydrolysis of the amygdalin to take place. The benzaldehyde and hydrocyanic acid are then separated by stem distillation.

Almond oil consists of a mixture of glycerides of oleic (62–86%), linoleic (17%), palmitic (5%), myristic (1%), palmitoleic, margaric, stearic, linolenic, arachidic, gadoleic, behenic, and erucic acid. Bitter almond oil contains benzaldehyde and 2–4% of hydrocyanic acid. Purified volatile oil of bitter almonds has all its hydrocyanic acid removed and, therefore, consists mainly of benzaldehyde. The unsaponifiable matter contains β-sitosterol, Δ^5-avenasterol, cholesterol, brassicasterol and tocopherols.

Uses

Expressed almond oil is an emollient and an ingredient in cosmetics. Almond oil is used as a laxative, emollient, in the preparation of toilet articles and as a vehicle for oily injections. The volatile almond oils are used as flavouring agents.

Marketed Products

It is one of the ingredients of the preparations known as Baidyanath lal tail (Baidyanath Company), Himcolin gel, Mentat, Tentex Royal (Himalaya Drug Company), and Sage badam roghan (Sage Herbals).

ARACHIS OIL

Synonyms

Groundnut oil; monkeynut oil; peanut oil; katchung oil; earth-nut oil.

Biological Source

Arachis oil is obtained by expression of shelled and skinned seeds of *Arachia hypogaea* Linn., belonging to family Papilionaceae.

Geographical Source

South America (Brazil) is the original home of ground nut and now found in South and Central America, Peru, Argentina, Nigeria, Australia, India, Gambia, and other reasonably warm regions of all countries.

Characteristics

Groundnut plant is a small, prostrate, diffuse, erect, branched, annual herb, 30–60 cm in height, leaves alternate with adnate stipules and yellow papilionaceous flowers. After fertilization, the pedicel elongates rapidly and enters the ground, where the ovary begins to develop into a pod maturing in about two months. Pods or nuts are cylindrical, hard, reticulated, indehiscent, and inflated, 2.5–5.0 cm long, one to three seeded, with pericarp constricted between the seeds. The seeds are covered by a light or deep reddish brown seeds coat, and consisting of two white fleshy cotyledons rich in oil and proteins.

Fruits are dug out by raking the plants from the soil, seeds are separated by machine and expressed in a hydraulic press at ordinary temperature. The remaining oil of cakes is removed by solvent extraction. The two oil fractions are combined and purified.

Cultivation

Groundnut is predominantly a crop of the tropical and subtropical countries, up to an elevation of 1,160 m. It requires plenty of sunlight, timely and evenly distributed rainfall (50–125 cm) during its growth and a long season for its maturation and harvesting. It also requires a high

CHAPTER 20

Drugs Containing Tannins

20.1. INTRODUCTION

The name ‘tannin’ is derived from the French ‘tanin’ (tanning substance) and is used for a range of natural polyphenols. Tannins are complex organic, nonnitrogenous plant products, which generally have astringent properties. These compounds comprise a large group of compounds that are widely distributed in the plant kingdom. The term ‘tannin’ was first used by Seguin in 1796 to denote substances which have the ability to combine with animal hides to convert them into leather which is known as tanning of the hide. According to this, tannins are substances which are detected by a tanning test due to its absorption on standard hide powder. The test is known as Goldbeater’s skin test.

20.2. CLASSIFICATION

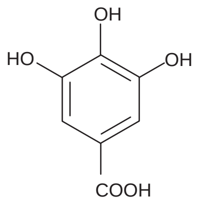
The tannin compounds can be divided into two major groups on the basis of Goldbeater’s skin test. A group of tannins showing the positive tanning test may be regarded as true tannins, whereas those, which are partly retained by the hide powder and fail to give the test, are called as pseudotannins.

Most of the true tannins are high molecular weight compounds. These compounds are complex polyphenolics, which are produced by polymerization of simple polyphenols. They may form complex glycosides or remains as such which may be observed by their typical hydrolytic reaction with the mineral acids and enzymes. Two major chemical classes of tannins are usually recognized based on this hydrolytic reaction and nature of phenolic nuclei involved in the tannins structure. The first class is referred to as hydrolysable tannins, whereas the other class is termed as condensed tannins.

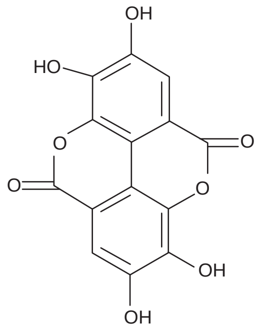
Hydrolysable Tannins

As the name implies, these tannins are hydrolysable by mineral acids or enzymes such as tannase. Their structures involve several molecules of polyphenolic acids such as gallic, hexahydrodiphenic, or ellagic acids, bounded through ester linkages to a central glucose molecule. On the basis of the phenolic acids produced after the hydrolysis, they are further categorized under gallotannins composed of gallic acid or ellagitannins which contains hexahydrodiphenic acid which after intraesterification produces ellagic acid.

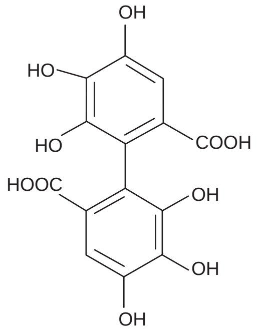
Hydrolysable tannins are sometimes referred to as pyrogallol tannins as the components of phenolic acids on dry distillation are converted to pyrogallol derivatives. The hydrolysable tannins are soluble in water, and their solution produces blue colour with ferric chloride.



Gallic acid



Ellagic acid

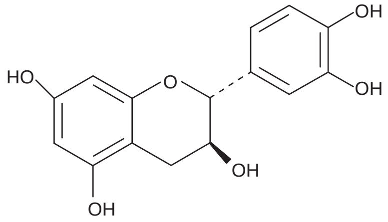


Hexahydroxydiphenic acid

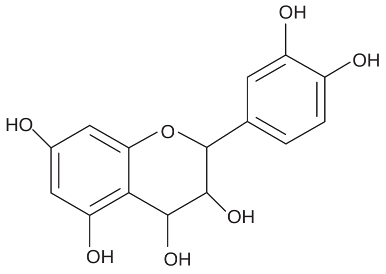
Nonhydrolysable or Condensed Tannins

Condensed tannins, unlike the previously explained group are not readily hydrolysable to simpler molecules with mineral acids and enzymes, thus they are also referred to as nonhydrolysable tannins. The term proanthocyanidins is sometimes alternatively used for these tannins. The compounds containing condensed tannins contain only phenolic nuclei which are biosynthetically related to flavonoids. Catechin which is found in tannins is flavan-3-o1, whereas leucoanthocyanidins are flavan-3,4-diol structures. These phenolics are frequently linked to carbohydrates or protein molecules to produce more complex tannin compounds. When treated with acids or enzymes, they tend to polymerize yielding insoluble red coloured products known as phlobaphens. The phlobaphens give characteristic red colour to many drugs such as cinchona and wild cherry bark. On dry distillation, they yield catechol derivatives. Condensed tannins are also soluble in water and produces green colour with ferric chloride.

The families of the plants rich in both of the above groups of tannins include Rosaceae, Geraniaceae, Leguminosae, Combretaceae, Rubiaceae, Polygonaceae, Theaceae, etc. The members of families Cruciferae and Papaveraceae on the other hand are totally devoid of tannins. In the plants in which tannins are present, they exert an inhibitory effect on many enzymes due to their nature of protein precipitation and therefore contribute a protective function in barks and heartwood.



Catechin



Leucoanthocyanidin

Pseudotannins

Pseudotannins are simple phenolic compounds of lower molecular weight. They do not respond to the tanning reaction of Goldbeater's skin test. Gallic acid, Chlorogenic acid, or the simple phenolics such as catechin are pseudotannins which are abundantly found in plants, especially in dead tissues and dying cells.

20.3. CHARACTERISTICS OF TANNINS

1. Tannins are colloidal solutions with water.
2. Non crystalline substance.
3. Soluble in water (exception of some high molecular weight structures), alcohol, dilute alkali, and glycerin.
4. Sparingly soluble in ethyl acetate.
5. Insoluble in organic solvents, except acetone.
6. Molecular weight ranging from 500 to >20,000.
7. Oligomeric compounds with multiple structure units with free phenolic groups.
8. Can bind with proteins and form insoluble or soluble tannin—protein complexes.

20.4. BIOSYNTHESIS OF TANNINS

Tannins belong to the phenolics class of secondary metabolites. All phenolic compounds; either primary or secondary are in one way or another formed through shikirnic acid pathway (phenylpropanoid pathway). Other phenolics such as isoflavones, coumarins, lignins, and aromatic amino acids (tryptophan, phenylalanine, and tyrosine) are also formed by the same pathway. Hydrolysable tannins (Hts) and condensed tannins (proanthocyanidins) are the two main categories of tannins that impact animal nutrition.

Common tannins are formed as follows:

- Gallic acid is derived from quinic acid.
- Ellagotannins are formed from hexahydroxydiphenic acid esters by the oxidative coupling of neighbouring gallic acid units attached to a D-glucose core.
- Further oxidative coupling forms the hydrolysable tannin polymers.
- Proanthocyanidin (PA) biosynthetic precursors are the leucocyanidins (flavan-3,4-diol and flavan-4-ol) which on autoxidation, in the absence of heat, form anthocyanidin and 3-deoxyanthocianidin, which, in turn, polymerize to form PAs.

20.5. CHEMICAL TESTS

1. *Goldbeater's skin test*: Goldbeater's skin is a membrane produced from the intestine of Ox. It behaves just like untanned animal hide. A piece of goldbeaters skin previously soaked in 2% hydrochloric acid and washed with distilled water is placed in a solution of tannin for 5 minutes. It is then washed with distilled water and transferred to 1% ferrous sulphate solution. A change of the colour of the goldbeater's skin to brown or black indicates the presence of tannin.

Hydrolysable and condensed tannins both give the positive goldbeater's test, whereas pseudotannins show very little colour or negative test.

2. *Phenazone Test:* To 5 ml of aqueous solution of tannin containing drug, add 0.5 g of sodium acid phosphate. Warm the solution, cool, and filter. Add 2% phenazone solution to the filtrate. All tannins are precipitated as bulky, coloured precipitate.
3. *Gelatin Test:* To a 1% gelatine solution, add little 10% sodium chloride. If a 1% solution of tannin is added to the gelatine solution, tannins cause precipitation of gelatine from solution.
4. *Test for Catechin* (*Matchstick Test*): Catechin test is the modification of the well-known phloroglucinol test for lignin. Matchstick contains lignin. Dip a matchstick in the dilute extract of the drug, dry, moisten it with concentrated hydrochloric acid, and warm it near a flame. Catechin in the presence of acid produces phloroglucinol which stains the lignified wood pink or red.
5. *Test for chlorogenic acid*: A dilute solution of chlorogenic acid containing extract, if treated with aqueous ammonia and exposed to air, slowly turns green indicating the presence of chlorogenic acid.
6. *Vanillin-hydrochloric acid test:* Drug shows pink or red colour with a mixture of vanillin: alcohol : dilute HCl in the ratio 1:10:10. The reaction produces phloroglucinol which along with vanillin gives pink or red colour.

20.6. ISOLATION

Both hydrolysable and condensed tannins are highly soluble in water and alcohol but insoluble in organic solvents such as solvent ether, chloroform, and benzene. Tannin compounds can be easily extracted by water or alcohol. The general method for the extraction of tannic acid from various galls is either with water-saturated ether, or with mixture of water, alcohol, and ether. In such cases, free acids such as Gallic and ellagic acid go along with ether, whereas true tannin gets extracted in water. If the drug consists of chlorophyll or pigment, it may be removed by ether. After extraction, the aqueous and ethereal layers are separately concentrated, dried, and subjected to further isolation and purification using various separation techniques of chromatography.

20.7. MEDICINAL PROPERTIES AND USES

Tannins occur in crude drugs either as major active constituent as in oak bark, hammamelis leaves, and bearberry leaves, etc. or as a subsidiary component as in clove, cinnamon, peppermint, or garden sage. In many cases, they synergistically increase the effectiveness of active principles. Tannins are medicinally significant due to their astringent properties. They promote rapid healing and the formation of new tissues on wounds and inflamed mucosa. Tannins are used in the treatment of varicose ulcers, haemorrhoids, minor burns, frostbite, as well as inflammation of gums. Internally tannins are administered in cases of diarrhoea, intestinal catarrh, and in cases of heavy metal poisoning as an antidote. In recent years, these compounds have demonstrated their antiviral activities for treatment of viral diseases including AIDS. Tannins are used as mordant in dyeing, manufacture of ink, sizing paper and silk, and for printing fabrics. It is used along with gelatine and albumin for manufacture of imitation horn and tortoise shell. They are widely used in the leather industry for conversion of hide into leather, the process being known as tanning. Tannins are also used for clarifying beer or wine, in photography or as a coagulant in rubber manufacture. Tannins are used for the manufacture of gallic acid and pyrogallol, and sometimes as a reagent in analytical chemistry.

20.8. HYDROLYSABLE TANNINS

MYROBALAN

Synonyms

Chebulic myrobalan, harde, haritaki.

Biological Sources

Myrobalan is the mature dried fruits of *Terminalia chebula,* belonging to family Combretaceae.

Geographical Source

Myrobalan trees are found at an elevation of 300 to 900 m in North India, Satpura ranges of Madhya Pradesh, Maharashtra, and Panchamahal district in Gujarat. It is also found in Myanmar and Sri Lanka.

Collection and Preparation

T. chebula is a moderate-sized or large deciduous tree attaining a height of 25–30 m. The plant lacks natural regeneration. The plant requires direct overhead light and cannot tolerate shady situations. It is a frost and draught resistant tree. The fruits ripen from November to March depending upon the locality, and fall soon after ripening. The mature fruits are collected from January to April by shaking the trees, and then drying by spreading in thin layers preferably in shades. The dried myrobalan fruits are graded under different trade names. Gradation is done on the basis of fruits colour, solidness, and freedom from insect attack.

Characteristics

Papain occurs as white or greyish-white, slightly hygroscopic powder. It is incompletely soluble in water and glycerol. It may digest about 35 times its weight of lean meat. Best grades render digestion of 200–300 times their weight of coagulated egg albumin in alkaline media. A temperature range of 60–90°C is favourable for the digestive process with 65° the optimum point. Best pH is 5.0, but it functions also in neutral or alkaline media. It is activated by reduction (HCN and H_2S) and inactivated by oxidation (H_2O_2, iodoacetate).

Fig. 21.2 Plant of *Carica papaya*

Chemical Constituents

Papain contains several enzymes such as proteolytic enzymes peptidase I capable of converting proteins into dipeptides and polypeptides, rennin-like enzyme, clotting enzyme similar to pectase and an enzyme having a feeble activity on fats.

The enzymes, papain, papayaproteinase, and chymopapain, have been isolated in crystalline form from the latex. Papain is atypical protein digesting enzyme with isoelectric point. It contains 15.5% nitrogen and 1.2% sulphur. Crystalline papain is most stable in the pH range 5–7 and is rapidly destroyed at 30°C below pH 2.5 and above pH 12. Papain is a protein of 212 amino acids and having a molecular weight of about 23,000 daltons. It is resistant to heat, inactivated by metal ions, oxidants and reagents which react with thiols, and is an endopeptidase activated by thiols and reducing moieties, for example, cysteine, thiosulphate, and glutathione.

The leaves possess dehydrocarpaines I and II, fatty acids, carpaine, pseudocarpaine, and carotenoids.

The fruits yield lauric, myristoleic, palmitoleic and arachidic acids, malonated benzyl-p-o-glucosides, 2-phenyl ethyl glucoside, and 4-hydroxy-phenyl-2-ethyl glucoside.

Uses

Papain is used to prevent adhesions; in infected wounds; internally as protein digestant, as anathematic (nematode), to relieve the symptoms of episiotomy (incision of vulva), in meat industry for tenderizing beef, for treatment of dyspepsia, intestinal and gastric disorders, and diphtheria, for dissolving diphtheria membrane; in surgery to reduce incidence of blood clots where thromboplasma is undesirable and for local treatment of buccal, pharyngeal, and laryngeal disorders.

It is used in digestive mixtures, liver tonics, for reducing enlarged tonsils, in prevention of postoperative adhesions, curbuncles, and eschar burns. It is an allergic agent causing severe paroxysmal cough, vasomotor rhinitis and dyspnea. It is a powerful poison when injected intravenously. In industry it is used in the manufacture of proteolytic preparations of meat, lever, and casein, with dilute alcohol and lactic acid as meat tenderizer, as a substitute for rennet in cheese manufacture, in brewing industry for making chill-proof bear, for degumming natural milk, in preparation of tooth pastes and cosmetics, in tanning industry for bathing skin and hides, and as an ingredient in cleansing solutions for soft contact lenses.

Test

1. Papain is reacted with a gelatin solution at 80°C in the presence of an activating cysteine chloral hydrate solution for an hour. The solution is cooled to 4°C for long time. The treated solution must not regel in comparison to a blank solution under identical conditions.

Adulteration

Commercial papain is often adulterated with arrowroot starch, dried milk of cactus, gutta percha, rice flour, and pepsin.

21.2. PROTEINS

A protein is a complex, high molecular weight organic compound that consists of amino acids joined by peptide bonds. The word protein is derived from greek '*protos*' meaning '*of primary importance*'. Proteins are essential to the structure and function of all living cells. Many proteins are enzymes or subunits of enzymes. Other proteins play structural or mechanical roles, such as those that form the struts and joints of the cytoskeleton, serving as biological scaffolds for the mechanical integrity and tissue signalling functions.

They are obtained from both plant and animal sources. In plants they are stored in the form of aleurone grains.

In animals they are present in structural material in the form of collagen (connective tissue), keratin (hair, wool, hairs, feathers, and horns), elastin (epithelial connective tissue), casein (milk), and plasma proteins. Casein, gelatin, heparin, and hemoglobin are pharmaceutically important proteins of animal origin.

Proteins are generally large molecules, having molecular masses of up to 3,000,000 (the muscle protein titin has a single amino-acid chain 27,000 subunits long). However, protein masses are generally measured in kiloDaltons (kDa). Such long chains of amino acids are almost universally referred to as proteins, but shorter strings of amino acids are referred to as 'polypeptides', 'peptides', or rarely, 'oligopeptides'. The dividing line is undefined, though 'polypeptide' usually refers to an amino-acid chain lacking tertiary structure which may be more likely to act as a hormone (like insulin), rather than as an enzyme (which depends on its defined tertiary structure for functionality).

There are about 20 different amino acids, eight of which must be present in the diet. The eight essential amino acids required by humans are: leucine, isoleucine, valine, threonine, methionine, phenylalanine, tryptophan, and lysine. For children, histidine is also considered to be an essential amino acid. Unlike animal proteins, plant proteins may not contain all the essential amino acids in the necessary proportions, and so the proteins derived from plants are grouped as incomplete and from animals are grouped as complete. However, a varied vegetarian diet means a mixture of proteins are consumed, the amino acids in one protein compensating for the deficiencies of another.

The structure of protein could be differentiated into four types:

1. Primary structure: the amino-acid sequence
2. Secondary structure: highly patterned substructures–alpha helix and beta sheet–or segments of chain that assume no stable shape. Secondary structures are locally defined, meaning that there can be many different secondary motifs present in one single protein molecule.
3. Tertiary structure: the overall shape of a single protein molecule; the spatial relationship of the secondary structural motifs to one another
4. Quaternary structure: the shape or structure that results from the union of more than one protein molecule, usually called protein subunits in this context, which function as part of the larger assembly or protein complex.

Proteins are sensitive to their environment. They may only be active in their native state, over a small pH range, and under solution conditions with a minimum quantity of electrolytes. A protein in its native state is described as folded and that is not in its native state is said to be denatured. Denatured proteins generally have no well-defined secondary structure. Many proteins denature and will not remain in solution in distilled water also they are denatured due to heat, changes in pH, treatment of organic solvents or by ultra violet radiation.

Proteins are essential for growth and repair. They play a crucial role in virtually all biological processes in the body. All enzymes are proteins and are vital for the body's metabolism. Muscle contraction, immune protection and the transmission of nerve impulses are all dependent on proteins. Proteins in skin and bone provide structural support. Many hormones are proteins. Protein can also provide a source of energy. Generally the body uses carbohydrate and fat for energy but when there is excess dietary protein or inadequate dietary fat and carbohydrate, protein is used. Excess protein may also be converted to fat and stored.

The important proteins are given hereunder.

MALT EXTRACT

Synonym

Diastase, malt extract.

Biological Source

Malt extract is the extract obtained from the dried barley grains of one or more varieties of *Hordeum vulgare* Linne, family Poaceae.

Geographical Source

Barley is widely cultivated throughout the world. The major producers are United States, Russia, Canada, India, and Turkey. It is also cultivated in highlands of China and Tibet.

Cultivation, Collection, and Preparation

Barley is one of the oldest cultivated cereals. It is an annual erect stout herb resembling wheat. The crop becomes ready for harvest in about four months after sowing. The grains are threshed out by beating with sticks or trampling by oxen. Dried barley grains are artificially germinated by keeping their heaps wet with water in a warm room. When the caulicle of the grains starts protruding out, the germinated grams are dried. Dry germinated barley or dry malt is subjected to extraction. The malt is infused with water at 60°C. An infusion is concentrated below 60°C under reduced pressure and then dried. Less purified malt extract contains sugars, and amylolytic enzymes. Its further purification affords diastase.

Characteristics

Malt extract contains enzymes, which are most active in neutral solution. The acidic conditions destroy the activity. It converts starch into disaccharide maltose. The enzyme is destroyed by heat. Many heat sterilized malt extracts do not contain diastase. It is completely soluble in cold water, more readily in warm water. The aqueous solution shows flocculant precipitate on standing. Limit for arsenic should not exceed one part per million.

Chemical Constituents

Malt extract contains dextrin, maltose, traces of glucose and about 8% of amylolytic enzyme diastase.

Uses

Malt extract and purified diastase, both are used as amylolytic enzymes and as an aid in digesting starch. They are used as bulk producing laxatives.

GELATIN

Synonyms

Gelfoam; puragel; gelatinum.

Biological Source

Gelatin is a protein derivative obtained by evaporating an aqueous extract made from bones, skins, and tendons of various domestic animals. Some important sources are: Ox, *Bos taurus*, and Sheep, *Ovis aries* belonging to family Bovidae

Preparation

The process of manufacture of gelatin vary from factory to factory. However, the general outline of the process is given below.

Raw material

Bones, skins, and tendons of Bovideans is collected and subjected to liming operation.

Liming Process

The raw material is first subjected to the treatment known as 'liming'. In this process, the skins and tendons are steeped for fifteen to twenty and sometimes for 40 days in a dilute milk of lime. During this, fleshy matter gets dissolved, chondroproteins of connective tissues gets removed and fatty matter is saponified. The animal skin is further thoroughly washed in running water.

Defattying

In case of bones, the material is properly ground and defatted in close iron cylinders by treatment with organic solvents such as benzene. The mineral and inorganic part of the bone is removed by treatment with hydrochloric acid.

Extraction

The treated material from bones, skins and tendons is boiled with water in open pans with perforated false bottom. This process can also be carried out under reduced pressure. The clear liquid runs of again and again and is evaporated until it reaches to above 45 per cent gelatin content.

Setting

The concentrated gelatin extract is transferred to shallow metal trays or trays with glass bottom. It is allowed to set as a semisolid jelly.

Drying

The jelly is transferred to trays with a perforated wire netting bottom and passed through series of drying compartments of 30–60°C increasing each time with 10°C. About a month is taken for complete drying.

Bleaching

In case of darker colour, finished product is subjected to bleaching by sulphur dioxide. Bleaching affords a light coloured gelatin.

Characteristics

Gelatin occurs as a colourless or slightly yellow, transparent, brittle, practically odourless, tasteless sheet, flakes or course granular powder. In water it swells and absorbs 5–10 times its weight of water to form a gel in solutions below 35–40°C. It is insoluble in cold water and organic solvents, soluble in hot water, glycerol, acetic acid; and is amphoteric. In dry condition it is stable in air, but when moist or in solution, it is attacked by bacteria. The gelatinizing property of Gelatin is reduced by boiling for long time. The quality of gelatin is determined on the basis of its jelly strength (Bloom strength) with the help of a Bloom gelometer. Jelly strength is used in the preparation of suppositories and pessaries.

Commercially two types of gelatin, A and B, are available. Type A has an isoelectric point between pH 7 and 9. It is incompatible with anionic compounds such as Acacia, Agar and Tragacanth. Type B has an isoelectric point between 4.7 and 5, and it is used with anionic mixtures. Gelatin is coloured with a certified colour for manufacturing capsules or for coating of tablets. It may contain various additives.

Chemical Constituents

Gelatin consists of the protein glutin which on hydrolysis gives a mixture of amino acids. The approximate amino-acid contents are: glycine (25.5%), alanine (8.7%), valine (2.5%), leucine (3.2%), isoleucine (1.4%), cystine and cysteine (0.1%), methionine (1.0%), tyrosine (0.5%), aspartic acid (6.6%), glutamic acid (11.4%), arginine (8.1%), lysine (4.1%), and histidine (0.8%). Nutritionally, gelatin is an incomplete protein lacking tryptophan. The gelatinizing compound is known as chondrin and the adhesive nature of gelatin is due to the presence of glutin.

Chemical Tests

1. *Biuret reaction:* To alkaline solution of a protein (2 ml), a dilute solution of copper sulphate is added. A red or violet colour is formed with peptides containing at least two peptide linkages. A dipeptide does not give this test.
2. *Xanthoproteic reaction:* Proteins usually form a yellow colour when warmed with concentrated nitric acid. This colour becomes orange when the solution is made alkaline.
3. *Millon's reaction:* Millon's reagent (mercuric nitrate in nitric acid containing a trace of nitrous acid) usually yields a white precipitate on addition to a protein solution which turns red on heating.
4. *Ninhydrin test:* To an aqueous solution of a protein an alcoholic solution of ninhydrin is added and then heated. Red to violet colour is formed.
5. On heating gelatin (1 g) with soda lime, smell of ammonia is produced.
6. A solution of gelatin (0.5 g) in water (10 ml) is precipitated to white buff coloured precipitate on addition of few drops of tannic acid (10%).
7. With picric acid gelatin forms yellow precipitate.

Uses

Gelatin is used to prepare pastilles, pastes, suppositories, capsules, pill-coatings, gelatin sponge; as suspending agent, tablet binder, coating agent, as stabilizer, thickener and texturizer in food; for manufacturing rubber substitutes, adhesives, cements, lithographic and printing inks, plastic compounds, artificial silk, photographic plates and films, light filters for mercury lamps, clarifying agent, in hectographic matters, sizing paper and textiles, for inhibiting crystallization in bacteriology, for preparing cultures and as a nutrient.

It forms glycerinated gelatin with glycerin which is used as vehicle and for manufacture of suppositories. Combined with zinc, it forms zinc gelatin which is employed as a topical protectant. As a nutrient, Gelatin is used as commercial food products and bacteriologic culture media.

CASEIN

Biological Source

Casein is a proteolytic enzyme obtained from the stomachs of calves. It is extracted from the proteins of the milk; in the milk, casein is structured in voluminous globules. These globules are mainly responsible for the white colour of the milk. According to various species, the casein amount within the total proteins of the milk varies.

The casein content of milk represents about 80% of milk proteins. The principal casein fractions are alpha (s1) and alpha (s2)-caseins, β-casein and κ-casein. The distinguishing property of all casein is their low solubility at pH 4.6. The common compositional factor is that caseins are conjugated proteins, most with phosphate group(s) esterified to serine residues. These phosphate groups are important to the structure of the casein micelle. Calcium binding by the individual caseins is proportional to the phosphate content.

Within the group of caseins, there are several distinguishing features based on their charge distribution and sensitivity to calcium precipitation:

Alpha (s1)-casein: (molecular weight 23,000; 199 residues, 17 proline residues).

Two hydrophobia regions, containing all the proline residues, separated by a polar region, which contains all but one of eight phosphate groups. It can be precipitated at very low levels of calcium.

Alpha (s2)-casein: (molecular weight 25,000; 207 residues, 10 prolines).

Concentrated negative charges near N-terminus and positive charges near C-terminus. It can also be precipitated at very low levels of calcium.

β-*casein:* (molecular weight 24,000; 209 residues, 35 prolines).

Highly charged N-terminal region and a hydrophobia C-terminal region. Very amphiphilic protein acts like a detergent molecule. Self association is temperature-dependent; will form a large polymer at 20°C but not at 4°C. Less sensitive to calcium precipitation.

κ-*casein:* (molecular weight 19,000; 169 residues, 20 prolines).

Very resistant to calcium precipitation, stabilizing other caseins. Rennet cleavage at the Phe l05 – Met l06 bond eliminates the stabilizing ability, leaving a hydrophobia portion, para- κ-casein and a hydrophilic portion called κ-casein glycomacropeptide (GMP), or more accurately, caseinomacropeptide (CMP).

Characteristics

The isoelectric point of casein is 4.6. The purified protein is water insoluble. While it is also insoluble in neutral salt solutions, it is readily dispersible in dilute alkalis and in salt solutions such as sodium oxalate and sodium acetate. Casein does not coagulate on heating. It is precipitated by acids and by a proteolytic enzyme (rennet).

Chemical Constituents

Milk consists of 80% of milk proteins (casein). The major constituents of casein are alpha (s1) and alpha (s2)-caseins, β-casein and kappa-casein. These caseins are conjugated proteins with phosphate group(s) which are esterified into serine residues they have a low solubility at pH 4.6.

Uses

It is used in the manufacture of binders, adhesives, protective coatings, plastics (such as for knife handles and knitting needles), fabrics, food additives, and many other products. It is commonly used by bodybuilders as a slow-digesting source of amino acids. There is growing evidence that casein may be addictive for some individuals, particularly those on the autism spectrum or having schizophrenia.

COLLAGEN

Synonym

Ossein.

Biological Source

It is the protein which consists of major portion of white fibres in connective tissues of the animal body specifically, from the tendons, skin, bones, and teeth.

Characteristics

The molecule of collagen is similar to three strand rope, each strand consisting of polypeptide chain with molecular weight of 10,000. These three strands are left-handed helices and are wrapped together in a right-handed superhelix. The strands are held together by hydrogen bonds, which give the molecule its strength.

Collagen fibres range from 10 to 100 μm in diameter and visible by microscope as banded structure in the extra cellular matrix of connective tissues.

Chemical Constituents

Glycine and proline are the important amino acids in the central core of the triple helical molecule of collagen. It can be differentiated from other accompanying fibrous proteins like elastin and reticulin. Elastin is highly crossed linked hydrophobic protein. Collagen is characterized by the presence of glycine, proline, hydroxyproline, and hydroxylysine and low tyrosine and sulphur contents, whereas elastin contains nonpolar amino acids like valine, isoleucine, and leucine. Various types of collagen exist depending upon the amino-acid sequence. Collagen is converted to gelatin by boiling with water.

Uses

It is used in the preparation of sutures, as a gel in food casings and in photographic emulsions.

FICIN

Biological Source

Ficin is found in the latex of the plants of the Genus Ficus. Commercial ficin is purified from the latex of the fig tree, *Ficus glabatra* or *Ficus carica.*

Refined ficin microgranulate is a protease, which can be used when a degradation of proteolytical stuff is required.

Characteristics

The optimum pH of ficin depends on the substrate and its concentration. Generally the optimum pH is between 5 and 8, although ficin keeps its activity over the range of pH 4–9 at 60°C. Though the optimum temperature of ficin is 45–55°C, it is effective in temperatures between 15 and 60°C. It is obtained as a white to yellow microgranular powder. The moisture content should not exceed 6%.

Uses

It is generally used in alcohol and beer industries, hydrolization of proteins, meat processing, baking industry, pet food, health food, contact lens cleaning. Cancer treatment, antiarthritis, digestive aid, etc.

CHAPTER

29

Nutraceuticals and Cosmeceuticals

29.1. NUTRACEUTICALS

Food and drugs from nature plays quite a significant role in public healthcare system throughout the world. Human inquisitiveness and search for specific constituents of plant, animals, minerals and microbial origin which are beneficial to our overall health have caused coining of terminologies such as functional foods or nutraceuticals. The idea of nutraceuticals has evolved from the recognition of the link between diet and health. Nutraceuticals have caused heated debate because they blurred the traditional dividing lines between food and medicine. Dr Stephen L. Defelice defines nutraceuticals as any substance that may be considered as food or part of food which in addition to its normal nutritive value provides health benefits including prevention of disease. The American Association of Nutritional Chemists mentions nutraceuticals as the products that has been isolated or purified from food and generally sold in medicinal forms not usually associated with food. When nutraceuticals are referred to as functional foods, most of the researchers of concerned field agree that they are foods marketed as having specific health effects. Functional foods are ordinary foods that have components or ingredients incorporated in them to give them a specific medical or physiological benefit other than a purely nutritional effect.

All foods are functional in the sense that we eat it, and it provides the energy and nutrients we needed to live. As we approach towards the 21st century, nutritional science has come into its own with manufacturers and consumers, placing for more emphasis on the benefits to be derived from food. Nutraceuticals or functional foods have been found to be associated with the prevention and/or treatment of many chronic diseases and ailments, such as cancer, diabetes, heart diseases, hypertension, arthritis, osteoporosis, etc. Statistical data indicates that 35% of all cancers are related to the food that we eat and certain dietary habits have long been associated with cancer risk. It certainly makes the old saying 'you are what you eat', more relevant in the context of the health benefits of the food. As the importance of dietary changes to optimize health is gaining recognition and acceptance, the food industry is responding to consumer demand for more healthful, nutrients-rich food products. The figure of 1997 statistical data shows that the European market for functional foods was estimated at £830 million.

29.1.2. CLASSIFICATION

Nutraceuticals or functional foods can be classified on the basis of their natural sources, pharmacological conditions or as per chemical constitution of the products. On the basis of natural source, these are the products obtained from plants, animals, minerals or microbial sources.

The classification of nutraceuticals based upon its therapeutical implications for the treatment or prevention of specific condition may produce a big list. Some of the important conditions in which the nutraceuticals are specially directed for its treatment, prevention or support are given in Table 29.1.

Table 29.1 Nutraceuticals used in various disease conditions

Conditions	Nutraceuticals
Allergy relief	*Ginkgo biloba*
Arthritis support	Glucosamine
Cancer prevention	Flax seeds, Green tea
Cardiac diseases	Garlic
Cholesterol lowering	Garlic
Digestive support	Digestive enzymes
Diabetic support	Garlic, Momordica
Female hormone support	Black Cohosh, False Unicorn
Immunomodulators	Ginseng
Prostate support	Tomato lycopenes

A systematic classification on the basis of therapeutically important compounds of the nutraceuticals products responsible for the specific health benefit can be done as given in Table 29.2.

Table 29.2 Classification of nutraceuticals as per chemical groupings

Sr. No.	Class	Examples
1.	Inorganic mineral supplements	Minerals
2.	Vitamin supplements	Vitamins
3.	Digestive enzymes	Enzymes
4.	Probiotics	Helpful bacteria
5.	Prebiotics	Digestive enzymes
6.	Dietary fibres	Fibres
7.	Cereals and grains	—
8.	Health drinks	—
9.	Antioxidants	Natural antioxidants
10.	Phytochemicals	
	Polysaccharides	Arabinogalactans
	Isoprenoids	Carotenoids
	Flavanoids	Bioflavanoids
	Phenolics	Tea polyphenols
	Fatty acids	Omega-3-fatty acids
	Lipids	Spingolipids
	Proteins	Soya proteins
11.	Herbs as a functional foods	—

However, in many cases the health benefit is not mainly due to a single group of compounds but the overall effect of variety of proteins, lipids, carbohydrates, vitamins and mineral constitution of the product.

Inorganic Mineral Supplements

Large number of elements control variety of physiological and biochemical functions of human body. Most of these minerals are provided through the diet but their deficiently in diet may develop variety of health-related problems and diseases.

Calcium: Calcium is an important element in the treatment of bone loss and prevention. Calcium deficiency is found in 25% of women, even though much higher percentage has osteopenia or osteoporosis. Prepuberty is the best time to begin supplementing the diet with calcium-rich minerals along with exercise regimen. Sufficient intake of calcium and vitamin D postmenopausally can significantly reduce the risk for fracture.

Magnesium: Magnesium is an essential element involved in well over 300 enzymatic processes and critical in the proper use and maintenance of calcium. Many individuals with calcium deficiency are actually magnesium deficient which prevent proper use of calcium.

Manganese: Manganese is required in several enzymatic reactions and necessary for proper bone and cartilage formation.

Boron: Boron is reported to be helpful in supporting the calcium and estrogen levels in postmenopausal women.

Copper: Copper is an essential element needed by all tissues in the body; copper and zinc must be in proper proportion. Copper is best absorbed when bound to an amino acid.

Zinc: Zinc is one of the most important trace mineral. Zinc supports the body's overall antioxidant system by scavenging free radicals. It also performs many other vital functions.

Phosphorous: Phosphorous is important in maintaining bone structure and modulating plasma and bone formation.

Silicon: Silicon is concentrated in the active growth areas of the bone. It influences bone formation and calcification.

Vitamin Supplement

Vitamins are the complex substances of organic origin which in small quantities are necessary for the maintenance of human and animal life. Some of the important water-soluble and water-insoluble vitamins are discussed below.

Vitamins B complex: Specific B vitamins are recommended as the daily requirement to combat high levels of homocysteine, a known risk factor for heart diseases. Homocysteine accumulates in the blood secondary to protein intake, especially from meat. Vitamins B extra is generally recommended to those who use caffeine, alcohol, excessive sugar or oral birth pills in their diet, since B vitamins are water soluble and easily excreted. Vitamins B_1 or thiamine deficiency is mostly observed in white rice eaters. Ribofalvin-5-phosphate is a cofactor for vitamin B_2 which is beneficial in people who lack the enzyme to convert vitamin B_2 because of nutritional factors or disease condition. Niacinamide deficiency may cause neurological and skin problems. The body can also synthesize niacin from tryptophan. Pantothenic acid-A deficiency affect adrenal gland, immune and cardiovascular system. Vitamin B_6 is crucial for glucose production, hormone modulation and neurotransmitter synthesis. Pyridoxal 5-phosphate is considered as an active form of vitamin B_6. Vitamin B_{12} deficiency may be observed in vegetarian people as plants have no appreciable vitamins B_{12}. Folic acid is a B complex vitamin which contributes to healthy bone formation.

Among the other vitamins, vitamin C is the body's main water-soluble antioxidant. It is necessary for proper maintenance of bones. Inositol helps move fatty material from the liver into intestine. Biotin produced by several species of intestinal flora prevents yeast from converting to a more pathogenic fungal form. Choline bitartrate is helpful in moving fat out of liver into the bile.

Digestive Enzymes

Much of the reflux is not caused by too much acid in the stomach but from poor digestion because of too little acid. As we ages, stomach cells responsible for acid production slow down, this in turn slows the transit time of food in the stomach causing reflux of food from the oesophagus. Taking antacids often worsen the problem. Variety of digestive enzymes can be used as digestive aid to help absorb and digest the food material. Pepsin, principal digestive enzymes in gastric juices is a digestive aid for proteins. Pancreatin, an enzyme from pancreas is often found in enzymatic formulation.

Pancrilipase helps the body to break down fat in small intestine while amylase helps in improve digestion of carbohydrates and sugars. Betaine HCl is used as a phase I digestive aid for proper digestion. The plant proteolytic enzyme, papain obtained from *Carica papaya* fruits and bromelain derived from stem and fruit of pineapple are used as an aid in digestion and are commonly found in digestive products.

Probiotics

Probiotics (for life) can be described as a live microorganism which when ingested with or without food improves the intestinal microbial balance and consequently the health and functioning of large intestine. Probiotics or friendly bacteria present in the dairy food are another area of functional foods. Approximately 95% of all bacteria found in human body are located in colon; some of which are desirable and helpful while others harmful. The natural balance between these two groups of microbes plays an important role in the health and functioning of the large intestine. Probiotics bacteria promote gut health. Bioyoghurts containing *Lactobacillus acidophillus* and *Bifidobacteria* lead the probiotics. *Lactobacillus acidophillus* can reduce the incidence of vaginal infections including thrush and bacterial vaginosis. Specially fermented products such as yakult containing *L. Casei, L johnsonii* and *Lactobacillus* GG are also used as probiotics to restore the imbalance; *Biofidobacteria* may help fight wide range of harmful food poisoning bacteria including potentially harmful *E.coli-0157*. *Bifidobacteria* and *Streptococcus thermophilus* both found in yoghurt can prevent young children suffering from diarrhoea. *Lactohacillus* GG may also be helpful in treating antibiotics associated diarrhoea. It has also been reported to be effective at treating causes of travellers' diarrhoea and rotavirus infection—the most common cause of diarrhoea in children throughout the world. Probiotics may also help reduce certain food allergies. Probiotics only have a transient effect and regular daily intake is needed to bring about health benefits.

Prebiotics

Prebiotics are the food components that escape digestion by normal human digestive enzymes and safely in intact form reach the colon after passage through the stomach and small intestine, where they selectively promote the growth of probiotics. Probiotics alone can hardly survive the rigours of digestive enzymes and acids in the upper gut before reaching the colon. Such difficulties have emphasized the alternative ways of boosting the levels of probiotics in the large intestine by supply of probiotics. Insulin as fructosan obtained commercially from Jerusalem artichoke tubers, *Helianthus tuberosus,* family Compositae or raw chicory is the best known prebiotics. Fructo-oligosaccharides (FOS) are increasingly used in food supplements and can have more long-lasting effect as they encourage the growth of *Bifidobacteria* already present in the gut. At least, 10 g FOS is needed daily.

Unlike probiotics, prebiotics are easier to formulate into regular foods and therefore offer a better chance of success in restoring natural balance of the colonic micro-flora and enriching the health of the large intestine.

Dietary Fibres

Dietary fibres play critical role in keeping good health in human individuals and animals. Fibres are those parts of the plant, leaves, stem, fruits and seeds which cannot be digested or absorbed in the body. These fibres are necessary for our body to function properly. Dietary fibres can be divided into two broad categories such as water-insoluble and water-soluble fibres. Water-insoluble fibres absorb water to a certain extent and mainly contribute to bulking of stool, and allow quick passage of wastes through the elementary canal. Soluble fibres get dissolved in water and form a gel that binds the stool. It slows down the absorption of glucose and reduces blood cholesterol levels.

It has been recommended that about 30–40 g of dietary fibre should be consumed daily in order to obtain significant health benefits. The major sources of water insoluble fibres include whole grain cereals, whole wheat products, brown rice, fruits and vegetables with the peels. The sources of water soluble fibres are oats, dried beans, legumes, lentils, fruits and vegetables. Processed food can also be formulated to contain significant properties of both soluble and insoluble dietary fibres. The examples of such marketed processed products include breads, breakfast cereals and high-fibre beverages.

Cereals and Grain

Cereals and grain are largely used throughout the world as the major food material in the form of entire cereals and grains, sprouted cereals and grains and their milled flours. These products of cereals and grains are rich with normal food nutrients, vitamins, minerals and specific phytochemicals. Breads of soya flour and linseed provide phyto-oestrogenic natural substances that mimic the structure of the hormone oestrogen. Phytoestrogens have been documented to enhance oestrogen levels when hormonal levels are low to weaken the effects of oestrogen when levels are high. This action may protect against both hot flushes and breast cancer. Cereals and grains helps in calcium fortification, maintaining healthy heart and a healthy immune system.

Health Drinks

Drinks are the fast-developing area of functional foods. Some of these health drinks are fortified with the antioxidants, vitamins A, C, E and others with herbal extracts. The fruits and vegetable juices have also been shown to produce the health benefits. A new range of herb and vitamin-enhanced drinks claims to help overcome problems ranging from PMS to lack of energy. A Tropicana fruit juice fortified with calcium provides about 365 mg calcium per 250 ml glass. Drinks containing caffeine can also be described as functional foods as it vitalizes body and mind, increases physical endurance, improves and increases concentration and reaction speed.

Antioxidants

Antioxidants are the nutraceuticals whose deficiency states are associated with variety of dreaded disease conditions, viz. cardiovascular diseases, diabetes, cataracts, rheumatoid arthritis, Alzheimer disease and many others.

Phytochemicals might exert antioxidant action *in vivo* or in food by inhibiting generation of reactive oxygen species (ROS) or by directly scavenging free radicals. Certain compound may act *in vivo* as antioxidants by raising the levels of endogenous antioxidants defenses by up-regulating expression of the genes encoding superoxide dismutase (SOD), catalase or glutathione peroxidase.

Antioxidants can be broadly divided into three categories: (a) True antioxidants, (b) Reducing agents and (c) Antioxidant synergists. True antioxidants react with the free radicals and block the chain reaction of free radical. Reducing agents have a lower redox potential and readily get oxidized and are found effective against oxidizing agents while antioxidant synergists are the substance which on their own have little antioxidant effect but may enhance the effect of true antioxidants by reacting with heavy metals ions which catalyse autooxidation.

Natural antioxidant compounds can be classified as vitamins. carotenoids, hydroxycinnamates and flavonoids. Among the all above, flavonoid is a largest group of antioxidant which are almost ubiquitous in nature in most of the fruits, vegetables and plants. The various types of natural antioxidants and their dietary sources are given in Table 29.3.

Vitamins C or ascorbic acid is often claimed to be an important antioxidant *in vivo.* Its antioxidant property is regarded to be due to free radical scavenging by ascorbate and dehydro-ascorbate radical. Vitamin E or α-tocopherol delays lipid peroxidation by reacting with chain-propagating peroxy radicals faster than these radical can react with proteins or fatty acid side chains; β-carotene has remarkable antioxidant properties by interacting with a free radical to form β-carotone-derived radical which in the presence of oxygen forms a peroxyl radical. Antioxidants act at different levels in the oxidative sequence involving lipids and the extent to which oxidation of fatty acids and their esters occurs depends on the chemical nature of the fatty acid.

Table 29.3 Naturally occurring antioxidants

Antioxidants	Sources
Vitamins	
Vitamin C	Citrus fruits, vegetables
Vitamin E	Grains, nuts, oils
Carotenoids	
Carotenes	
Lycopene	Tomatoes
β-carotene	Carrots, sweet potato, green vegetables
Xanthophylls	
β-Cryptoxanthin	Mango, papaya, oranges
Lutein	Banana, egg yolk, green vegetables
Zeaxanthin	Paprika
Hydroxycinnamates	
Ferulic acid	Cabbage, spinach, grains
Caffeic acid	White grapes, olive, spinach
Flavonoids	
Flavone	
Rutin	Buckwheat, tobacco, *Eucalyptus* Spp.
Luteolin	Lemon, red pepper, olive
Flavonols	
Quercetin	Onion, apple skin, black grapes
Kaempferol	Grape fruit, tea
Flavanone	
Naringin	Citrus peel
Taxifolin	Citrus fruits
Chalcones	
Liquiritin	Liquorice
Anthocyanidins	
Cyanidin	Grapes, strawberry
Deiphinidin	Aubergin skin
Catechins	
Epicatechin gallate	Green tea polyphenols
Epigailocatechin gallate	Green tea polyphenols

Polyunsaturated Fatty Acids

Human body is capable of synthesizing most of the fatty acids it needs except the two major polyunsaturated fatty acids (PUFA), i.e. omega-3-fatty acid and omega-6-fatty acids. These fatty acids are required to be supplemented from the diet. The PUFA are the known precursors for arachidonic acid (AA), eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA). These fatty acids have been found to regulate blood pressure, heart rate, blood clotting and immune response. Omega-3-fatty acids have been reported to be important fatty acids in the prevention of heart diseases and also in the treatment of arthritis. Omega-3 fatty acids are mostly found in cold water fishes, such as tuna, salmon and macaerel. It is also present in dark green leafy vegetables, flaxseed oil and in certain vegetable oils. The fatty acids such as AA and DMA are essential for the development of the foetus and also during the first six months after birth. The deficiency of these fatty acids may result in poor development of foetus and may also cause a variety of problems such as premature birth to underweight babies. Breast milk is a very rich source of DHA. Most of the infant formulas which are used as a substitute of breast milk should be supplemented with DHA, as per the recommendation by WHO.

Herbs as Functional Foods

A great attention has nowadays been given to discover the link between dietary nutrients and disease prevention. Large numbers of herbs which had been in use since unknown time have been shown to play a crucial role in the prevention of disease. In addition to the macro- and micro-nutrients such as proteins, fats, carbohydrates, vitamins or minerals necessary for normal metabolism—a plant based diet contains numerous nonnutritive phyto-constituents which may also play an important role in health enhancement. A brief overview of the role of various herbs in disease prevention, with a focus on bioactive components from flaxseeds, spirulina, ginseng, garlic, green tea, citrus fruits, soyabean, tomato, *Ginkgo biloba,* turmeric, black cohosh and fenugreek has been given in this part of the nutraceuticals.

Flaxseeds

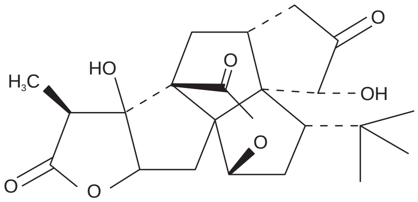
Flaxseeds are the dried ripe seeds of *Linum usitatissimum,* family Linaceae. Canada is the largest producer and exporter of flaxseeds which is about 40% of the world supply. It is also cultivated in the Mediterranean countries, the Middle East, United States, Russia and India. Generally flaxseed is cultivated for the oil but many medicinal properties are found to be associated with flaxseeds and its constituents. It is an abundant source of gamma-linolenic acid (GLA), viscous fibre components and phytochemicals such as lignans and proteins. The components are of great interest as functional food. Flaxseed incorporations into the diet are particularly attractive from the perspective of specific health benefit. Flaxseed has been recorded as one of the six plant materials as cancer-preventive foods. Alpha-linolenic acid (ALA) has a broad spectrum of health advantages. It inhibits the production of ecosanoids, alters the production of several prostanoids, reduces blood pressure in hypertensive patients and lowers triglycerides and cholesterol. Dietary ALA may retard tumour growth and plays an important role in metastatis. It has been suggested that ALA is dietary essential for optimal neurological development of humans especially during fetal and early postnatal life. GLA and its metabolites are effective in suppression of inflammation, in the treatment of diabetic neuropathy, atopic eczema, and certain cancers like malignant human brain glioma.

Dietary fibres of flaxseeds contain about 6% mucilage which has nutritional value. It appears to play a role in reducing diabetes and coronary heart disease risk, preventing colon and rectal cancer and reduces the incidence of obesity. Flaxseed mucilage has hypolipidaemic, cholesterolaemic and atherogenic effects in animals and humans.

The lignan compounds of flaxseeds such as secoisolariciresinol diglycoside (SDG) have been reported to be the precursors for enterodiol and enterolactone. It has also been reported to be a protective agent against mammary and colon cancer. Flaxseed extract and purified lignans exhibit antioxidant effect and inhibits the activation of promutagens and procarcinogens.

Ginkgo biloba

Ginkgo biloba, family Ginkgoaceae, known as fossil tree is an important drug used in traditional Chinese medicine since more than 2,800 years. Mainly leaves and edible seeds are used as drugs. The leaves contain dimeric flavones such as bilobelin, ginkgetin, isoginkgetin and flavonols along with their glycosides. The diterpenoids Ginkgolides A, B, C and bilobalide are also the therapeutically active constituents. Leaf contains 6-hydroxykynurenic acid, a metabolite of tryptophan.



Ginkgolide

The leaves are recommended as being beneficial to the heart and lungs. Ginkgolides present in the leaves are able to alleviate the adverse effects of platelet-activating factor in a number of tissues and organs both in animals and in humans. It is also effective in the treatment of arterial insufficiency in the limbs and in the brain. Inhalation of the decoction of leaves is used for the treatment of asthma. Ginkgo preparations are beneficial in the treatment of geriatric illness, including impairment of memory. Standardized concentrated extracts of *G. biloba* leaves are marketed throughout the world.

Spirulina

Spirulina is a blue green algae obtained from *Spindina platensis* or *S. maxima,* family Oscillatoriaceae. It is a simplest photosynthetic algae which grows in fresh water in planktonic form. The major producers of the algae are United States, China, Thailand, Mexico and India.

Spirulina is a potential source of food containing nutraceuticals. It contains about 50–70% of proteins and 5–6%

of lipids. Lipids mostly contain essential fatty acids, such as γ-linoleic, linoleic and oleic acid. It also contains glycolipids and sulpholipids. Spirulina is rich in vitamins B contents and also possesses β-carotenes. Its mineral content, which is about 3–6%, contains the appreciable proportion of iron which is shown to be better absorbed as compared to other natural irons.

Spirulina has been reported to have immunostimulant activities and shows promises for the treatment and management of HIV and other viral infection, such as Herpes, Cytomegalovirus, Influenza, Mumps and Measles virus. The glycolipid part of the spirulina is reported to be responsible for its antiHIV potential. It stimulates the activity of spleen, thymus and bone marrow stem cells. Spirulina also acts as an antioxidant due to the presence of enzyme superoxide dismulase and thereby found helpful in the treatment of atherosclerosis, arthritis, cataract, diabetes and aging process.

Ginseng

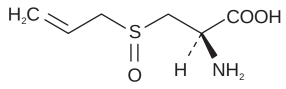
Ginseng roots obtained from *Panax ginseng* or from various other *Panax* Spp., family Araliaceae have been extensively studied for its wide range of pharmacological activities. White ginseng represents the peeled and sun-dried roots whilst red ginseng is unpeeled steamed and dried. Ginseng contains variety of tetracyclic dammarane-type sapogenins such as protopanaxadiol and their glycosides. It also contains other constituents which include traces of volatile oil, polyacetylenes, sterols, polysaccharides, starch, β-amylase, free sugars, choline, fats and minerals along with vitamins $B_{1,}$ B_2, B_{12}, pantothenic acid and biotin.

Ginseng is widely renowned for its adoptogenic properties as it is used to help the body cope with stress and fatigue and to promote recovery from diseases like hypertension or hypoglycaemia. In many countries it is self administered and taken in the form of tablets or capsules containing dried extracts of the roots. Ginseng preparations with multivitamins and trace elements have been shown to modify metabolic and liver function in elderly patients. It has been shown to reduce blood sugar concentrations in diabetics and nondiabetics and has been reported to successfully treat cases of diabetics polyneuropathy, reactive depression, psychogenic impotence and various child psychiatric disorders. When used appropriately, ginseng appears to be relatively nontoxic. Ginseng products are available in most of the developed countries as food supplements in combination with vitamins and minerals.

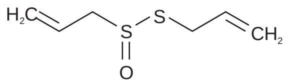
Garlic organosulphur compounds

Garlic consists of the fresh or dried bulbs of *Allium sativum,* family Liliaceae. It is a perennial, erect bulbous herb indigenous to Asia but commercially cultivated in most countries. The bulb shows a number of concentric bulblets which has a characteristics strong alliaceous odour and very persistently pungent and acid taste.

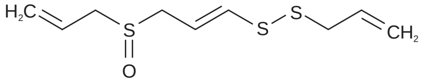
Garlic is used as an adjunct to dietic management in the treatment of hyperlipidaemia and in the prevention of athrosclerotic (age-dependent) vascular changes. Fresh garlic juice, aged garlic extract or the volatile oil, all lowers cholesterol and plasma lipids, lipid metabolism, and atherogenesis both *in vitro* and *in vivo.* The mechanism of garlic's antihypercholesterolaemic and antihyperlipidaemic activity appears to involve the inhibition of hepatic HMG-CoA reductase and remodelling of the plasma lipoprotein and cell membrane. The overall activity of garlic is mainly due to the presence of sulphur compound, such as allin, allicin, ajoene and others.



Allin



Allicin

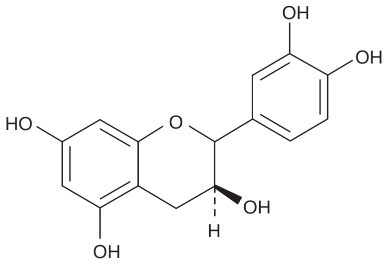


Ajoene

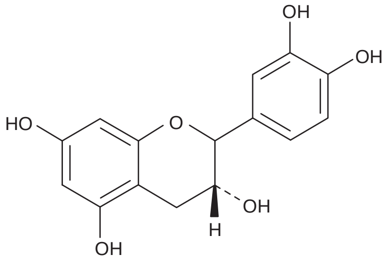
Cancers-preventive effect of garlic has been observed in a number of epidemiologic studies with stomach cancers appearing to be the type of neoplasia whose risk is clearly reduced by garlic consumption. Garlic has been reported to reduce the risk of colon cancer and lung carcinoma. Consumption of one or more servings of fresh or powdered garlic per week resulted in a 50% lower risk of cancer of the distal colon and a 35% lower risk of cancers anywhere in the colon. Garlic also shows antihypertensive, hypoglycaemic and antispasmodic activities.

Tea catechins

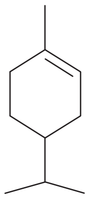
Tea is second only to water as the most widely consumed beverage in the world. About two to five million ton of dried tea is annually manufactured out of which about 78% is black tea, the reminder 20% is green tea while a smaller 2% is of oolong tea. Approximately 30% of the total dry weight of fresh is due to the presence of polyphenols, referred to as catechins. The four major green tea catechins are (-) epicatechin (EC), (-) epicatechin-3-gallate (ECG), (-) epigallocatechin (EGC) and (-) epigallocatechin-3-gallate (EGCG). Green tea polyphenols have been shown to afford protection against cancers of skin, lung, forestomach, oesophagus, duodenum, pancreas, liver breast and colon. Tea consumption is likely to have preventive effect in reducing cancer risk.



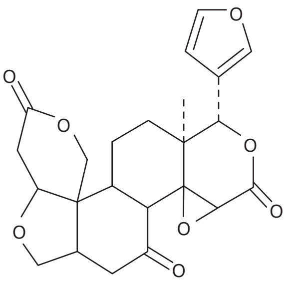
Catechin



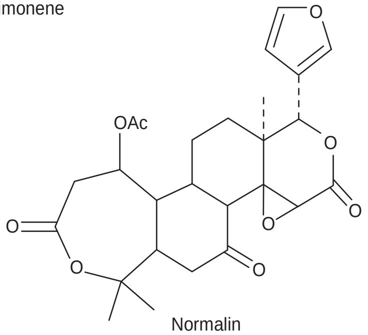
Epicatechin



Limonene



Limonin



Normalin

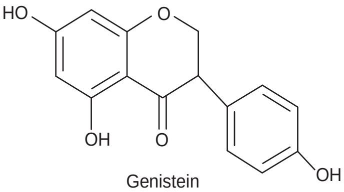
Citrus limonoids

Citrus fruit consumption has been shown to protect against a variety of human cancers. The citrus fruits such as oranges, lemons, limes and grapefruits are the principal source of important nutrients like vitamins C, folate, fibres and vitamins E, but the other monoterpene compounds known as limonoids are reported to be responsible for the anticancer activity, d-limonene— a predominant monocyclic monoterpene found in essential oil of citrus fruits has been reported to be a cancer-chemopreventive agent. This compound has been shown to be effective against both spontaneous and chemically induced rodent mammary tumours. Two most abundant limonoids of citrus, limonin and normalin have been found to inhibit or prevent chemically induced carcinogenesis. The mechanism of antitumour activity of limonoids includes the induction of hepatic detoxification enzymes, glutathione S-transferase and uridine diphosphoglucoronosyl transferase. Limonene has little or no toxicity in humans and has been suggested as a good candidate for human clinical chemoprevention.

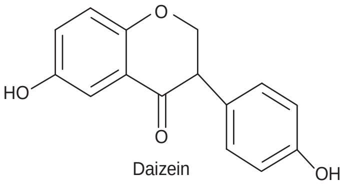
Soya products

Soyabean, *Glycin max,* family Leguminoseae has clearly been a plant food in the spotlight in the 1990s. It has been recognized as an excellent source of protein, equivalent to quality to animal protein. Soya has been extensively investigated for its ability to treat and prevent a variety of chronic diseases including cancer. Soyabean meals, concentrates and isolates are used as meat substitute and have many healthful benefits. Soyabean is also a major source of lecithins which yields liposomes used to formulate stable emulsions and finds major use in food technology.

The primary isoflavones in soya, genistein and daidzein are structurally similar to the estrogenic steroids and have been reported to have estrogenic and antiestrogenic activities. Due to their weaker activity, Isoflavones may act as antiestrogens by competing with the more potent, naturally occurring estrogens for binding to the estrogen receptor. Due to this, soya consumption may reduce the risk for estrogen-dependent cancers. South East Asian populations who consume 20–80 mg of genistein per day are found to have significantly lower incidence of breast and prostate cancer. Genistein has been reported to be a potent and specific inhibitor of protein tyrosine kinase. Genistein also inhibits DNA topoisomerase II activity, alters cell cycle specific events, induce apoptosis and inhibits angiogenetic process which is essential for tumour growth.



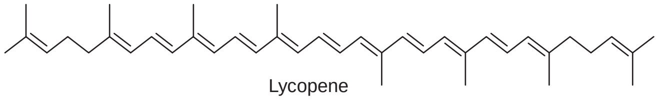
Genistein



Daizein

Tomato lycopenes

Lycopene is a carotenoid principle present in lycopersicon family Solanaceae known throughout the world as tomato. Clinical studies have indicated that lycopene significantly lowered the risk of prostate cancer. The candidates that consumed processed tomato products about 10 times per week had less than one-half the risk of developing prostate cancer. Lycopene activity is likely to be related to its antioxidant function because lycopene has been reported to be the most efficient quencher of singlet oxygen in biological system. Lycopene has also been shown to reduce risk of other types of cancers of digestive tract, pancreas, cervix, bladder and skin. Recently, it has been proved that low-plasma lycopene levels may be an independent risk factor for lung cancers especially in smokers.



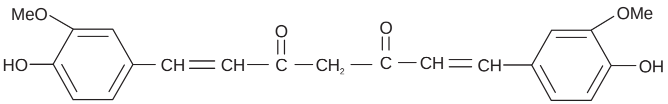
Lycopene

Momordica charantia

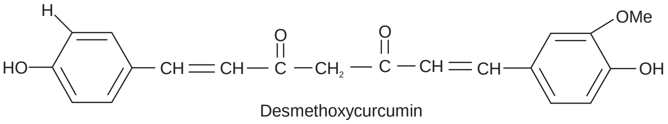
Momordica charantia, family Cucurbitaceae, known in India as karela is used in the form of extracts and health drinks as an antidiabetic agent. The alcoholic extract of karela pulp demonstrates a significant hypoglycemic activity in various experimental models of diabetes. The extract also increases the rate of glycogen synthesis from 14c-glucose by four- to five-fold in liver of experimental animals. Momordica antidiabetics activity could be partly attributed to increased glucose utilization in the liver rather than an insulin secretion effect.

Turmeric curcuminoids

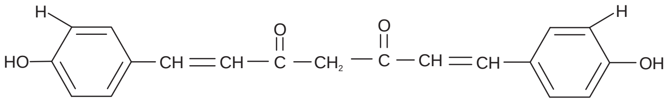
The tuber of *Curcuma longa*, family Zmgiberaceae known as turmeric is used as a spice in the culinary all over the world. It contains diaryl heptanoid compounds consisting mainly curcumin, desmethoxycurcumin and bisdesmethoxycurcumin. Curcumin has been shown to protect the experimental animals against decrease in heartbeat rate, blood pressure and biochemical changes It also demonstrates significant hepato-protective activity. It is used as condiment, colouring agent, and as a drug in various condition in various traditional systems of medicine. Recent findings indicate the potential of turmeric as an inhibitors of integrase enzyme of HIV virus.



Curcumin



Desmethoxycurcumin



Bisdesmethoxycurcumin

Black cohosh

Black cohosh consists of roots and rhizomes of *Cimicifuge racemosa,* family Rananculaceae is also known as Black snakeroot and is listed by the Food and Drug Administration (FDA) as a herb of unlimited safety. Black cohosh roots and rhizomes contain quinolizidine alkaloid N-methylcytisine, terpenoids like actein, 12-acetylactein and cimigoside, tannins and 15–20% of cimicifugin.

Black cohosh is stated to possess antirheumatic, antitussive, sedative and emmenagogue properties. It has been used for intercostal myalgia, sciatica, whooping cough, dysmenorrhoea and specially for rheumatism and rheumatoid arthritis. It has shown promises in reducing leutinizing hormone levels which are thought to be responsible for postmenopausal symptoms.

Fenugreek

Fenugreek seeds obtained from *Trigonella foenum-graecum,* family Leguminosae is an important food material as well as drug. Fenugreek is listed by the Council of Europe as a natural source of food flavouring. In United States, fenugreek extracts are permitted in food. Fenugreek seeds contain variety of constituents, such as alkaloids, flavonoids, coumarins, proteins and amino acids, steroidal saponins, vitamins and lipids.

Gentianine and trigonelline are the major alkaloids. Steroidal sapogenins, such as diosgenin and yamogenin are the major saponins. Fenugreek is stated to possess mucilaginous demulcent, laxative, nutritive, expectorant and orexigenic properties. Traditionally, it has been used in the treatment of anorexia, dyspepsia, gastritis and convalescence. Fenugreek has found to be a potential hypoglycaemic agent. Fenugreek seeds contain a high proportion of mucilaginous fibre which works as the dietary fibres. In addition, hypocholesterolaemic action has been documented for fenugreek.

29.1.3. MARKET SCENARIO OF NUTRACEUTICALS

In a wider context, there is a growing demand for plant-based medicines, health products, pharmaceuticals, food supplements, cosmetics, etc., in the national and international markets. Global demand for nutraceuticals ingredients will grow 5.8% annually through 2010. Best prospects include probiotics, soy additives, lycopene, lutein, sterol-based additives, green tea, glucosamine, chondroitin and coenzyme Q10. China and India will be the fastest growing markets, while the US will remain the largest. This study analyses the 11.7 billion dollars world nutraceutical industry. Nutraceuticals is one huge business opportunity awaiting the Indian pharmaceutical industry in the coming years. At least a dozen large companies currently produce and market nutraceuticals today. Many of these are just food supplements with no specific curative values. South based Parry Nutraceuticals, a leading player, has a well-known product, Spirulina. Some of the other major players are