Lipids—II
Classification

Bloor (1943) has proposed the following classification of lipids based on their chemical composition.

A. Simple lipids or Homolipids. These are esters of fatty acid with various alcohols.
   1. Fats and oils (triglycerides, triacylglycerols). These are esters of fatty acids with a trihydroxy alcohol, glycerol. A fat is solid at ordinary room temperature whereas an oil is liquid.
   2. Waxes. These are esters of fatty acids with high molecular weight monohydroxy alcohols.

B. Compound lipids or Heterolipids. These are esters of fatty acids with alcohol and possess additional group(s) also.
   1. Phospholipids (phosphatids). These are compounds containing, in addition to fatty acids and glycerol, a phosphoric acid, nitrogen bases and other substituents.
   2. Glycolipids (cerebrosides). These are the compounds of fatty acids with carbohydrates and contain nitrogen but no phosphoric acid. The glycolipids also include certain structurally-related compounds comprising the groups, gangliosides, sulfolipids and sulfatids.

C. Derived lipids. These are the substances derived from simple and compound lipids by hydrolysis. These include fatty acids, alcohols, mono- and diglycerides, steroids, terpenes and carotenoids.
Glycerides and cholesterol esters, because of their uncharged nature, are also called neutral lipids. However, Conn and Stumpf (1976) have traditionally classified lipids into following 6 classes:

1. Acyl glycerols
2. Waxes
3. Phospholipids
4. Sphingolipids
5. Glycolipids
6. Terpenoid lipids including carotenoids and steroids

**SIMPLE LIPIDS**

**FATS AND OILS**

(= Triglycerides or Triacylglycerols)

The triglycerides are the most abundant of all lipids. They constitute about 98% of total dietary lipids; the remaining 2% consists of phospholipids and cholesterol and its esters. They are the major components of storage or depot fats in plant and animal cells but are not normally found in membranes. They are nonpolar, hydrophobic molecules since they contain no electrically charged or highly polar functional groups. In animals, the fat cells or adipocytes contain very large quantities of triglycerides in the form of fat droplets, which fill almost the entire cell volume (Fig. 13-1). Adipocytes are abundantly found under the skin, in the abdominal cavity and in the mammary glands. Triglycerides can be stored in quantities, sufficient to supply the energy needs of the body for many months, as in the case of obese persons. On the contrary, the body can store the carbohydrate glycogen in meagre amounts, sufficient to supply energy need of a day only. Triglycerides are much better adapted than glycogen to serve as storage form of energy. They are not only stored in large amounts but also yield over twice as much energy as carbohydrates. Since fats tend to remain in the stomach longer than carbohydrates and are digested more slowly, they also have greater satiety value than carbohydrates. The arctic and antarctic animals (Fig. 13-2) such as whales, seals, walruses and penguins are amply padded with triglycerides to serve both as energy storage depots and as an insulation against very low temperatures. Most fats and oils, upon hydrolysis, yield several fatty acids as well as glycerol. However, the milk of spiny anteater is an exception in that it comprises almost pure triolein. Human body contains enough fat to make 7 bars of soap!

In a normal man, weighing 70 kg, at least 10-20% of the body weight is lipid, the bulk of which is triacylglycerol (TAG). TAG is found in all organs of the human body, particularly in adipose
tissue, in which droplets of triacylglycerols may represent more than 90% of the cytoplasm of the cells. Body lipid is a reservoir of potential chemical energy. About 100 times more energy is stored as mobilizable lipid than as mobilizable carbohydrate in the normal human being. TAG is stored in a relatively water-free state in the tissue, in comparison to carbohydrate, which is heavily hydrated.

Chemically, triglycerides are esters of glycerol with 3 fatty acid molecules. Their generic formula is shown in Fig. 13–3.

\[
\begin{align*}
\text{CH}_2 & \text{OOOCR}_1 \\
\text{CH} & \text{OOOCR}_2 \\
\text{CH}_2 & \text{OOOCR}_3
\end{align*}
\]

Fig. 13–3. Generic formula of triglycerides

Obviously, when the groups attached to carbon 1 and 3 differ, a centre of asymmetry is created at C 2. The 2 optical isomers may, thus, be represented as shown in Fig. 13–4. The naturally-occurring fats are of L-type.

\[
\begin{align*}
\text{CH}_2 & \text{OOOCR}_1 & \text{CH}_2 & \text{OOOCR}_1 \\
\text{H} & \text{C} & \text{OOOCR}_2 & \text{R}_2\text{COO} & \text{C} & \text{H} \\
\text{CH}_2 & \text{OOOCR}_3 & \text{CH}_2 & \text{OOOCR}_3
\end{align*}
\]

D-isomer

L-isomer

Fig. 13–4. Two optical isomers of triglycerides

A fat molecule contains 3 moles of fatty acids which may be similar or dissimilar. Those containing a single kind of fatty acid in all 3 positions (α, β, α′) are called simple (or symmetrical) triglycerides; they are named after the fatty acids they contain (Fig. 13–5). Examples are tripalmitin, tristearin and triolein. They occur very infrequently in natural fats. Such simple triglycerides have, however, been synthesized in the laboratory e.g., tristearin and triolein.

Most of the triglycerides of nature are mixed (or asymmetrical) triglycerides, i.e., they contain 2 or 3 different fatty acid units in the molecule. Representatives of such mixed triglycerides are oleodipalmitin and oleopalmistearin (Fig. 13–6).

\[
\begin{align*}
\text{CH}_2 & \text{OOC.C}_{17}\text{H}_{33} & \text{CH}_2 & \text{OOC.C}_{17}\text{H}_{33} \\
\text{CH} & \text{OOC.C}_{17}\text{H}_{33} & \text{CH} & \text{OOC.C}_{17}\text{H}_{33} \\
\text{CH}_2 & \text{OOC.C}_{17}\text{H}_{33} & \text{CH}_2 & \text{OOC.C}_{17}\text{H}_{33}
\end{align*}
\]

Tristearin
(tristearoylglycerol)

Tristearin
(tristearoylglycerol)

Fig. 13–5. Two simple triglycerides

Most animal fats such as those from meat, milk and eggs are relatively rich in saturated fatty acids but contain a rather low content of polyunsaturated fatty acids (Table 13–1); two exceptions
are chicken fat and fish fat. The large proportion of saturated fatty acids (esp., palmitic and stearic) with high melting point confers solid state to the animal fats. The plant fats, on the other hand, contain a large proportion of unsaturated fatty acids (esp., polyunsaturated). The unsaturated fatty acids have low melting point and confer liquid state to the plant fats.

### Table 13–1. Fatty acid composition of important animal and plant fats

<table>
<thead>
<tr>
<th>Fat/Oil</th>
<th>Percentage of total fatty acids</th>
<th>Saturated</th>
<th>Monounsaturated</th>
<th>Polyunsaturated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal fats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Butter fat</td>
<td></td>
<td>60</td>
<td>36</td>
<td>4</td>
</tr>
<tr>
<td>Pork fat</td>
<td></td>
<td>59</td>
<td>39</td>
<td>2</td>
</tr>
<tr>
<td>Beef fat</td>
<td></td>
<td>53</td>
<td>44</td>
<td>2</td>
</tr>
<tr>
<td>Chicken fat</td>
<td></td>
<td>39</td>
<td>44</td>
<td>21</td>
</tr>
<tr>
<td>Plant fats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olive oil*</td>
<td></td>
<td>20</td>
<td>26</td>
<td>54</td>
</tr>
<tr>
<td>Corn oil</td>
<td></td>
<td>15</td>
<td>31</td>
<td>53</td>
</tr>
<tr>
<td>Soybean oil</td>
<td></td>
<td>14</td>
<td>24</td>
<td>53</td>
</tr>
<tr>
<td>Soft margarine</td>
<td></td>
<td>23</td>
<td>22</td>
<td>52</td>
</tr>
</tbody>
</table>

* data not confirmed.

The differences between the animal and plant fats are presented in Table 13–2.

### Waxes

Far less spread but equally important are the waxes. The term `wax' originates in the Old English word weax, meaning “the material of the honeycomb”, reminding of beeswax, the honeycomb is made of. These are esters of long-chain saturated and unsaturated fatty acids with long-chain monohydroxy alcohols. The fatty acids range in between C\textsubscript{14} and C\textsubscript{36} and the alcohols range from C\textsubscript{16} to C\textsubscript{36}. In vertebrates, waxes are secreted by cutaneous glands as a protective coating to keep the skin pliable, lubricated and water-proof. Hair, wool and fur are also coated with wax. Birds, particularly waterfowl, secrete waxes in their preen glands to make their feathers water-repellent. The leaves of many plants such as Rhododendron, Calotropis etc., are shiny because of the deposition of protective waxy coating. Waxes also serve as the chief storage form of fuel in planktons. Since marine organisms (whale, herring, salmon) consume planktons in large quantities, waxes act as major food and storage lipids in them.

### Table 13–2. Differences between animal and plant fats

<table>
<thead>
<tr>
<th>Animal fat</th>
<th>Plant fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Relatively rich in saturated fatty acids, esp., C\textsubscript{16} and C\textsubscript{18} acids.</td>
<td>1. Relatively rich in unsaturated fatty acids, esp., polyunsaturated acids.</td>
</tr>
<tr>
<td>2. Solid at ordinary room temperature.</td>
<td>2. Liquid at ordinary room temperature.</td>
</tr>
<tr>
<td>3. These have usually low iodine number.</td>
<td>3. These have usually high iodine number.</td>
</tr>
<tr>
<td>4. These have usually high Reichert-Meissl number.</td>
<td>4. These have usually low Reichert-Meissl number.</td>
</tr>
<tr>
<td>5. These are stored mainly in liver and bone marrow</td>
<td>5. These are stored mainly in seeds and fruits.</td>
</tr>
<tr>
<td>6. Oxidative rancidity is observed more frequently.</td>
<td>6. Oxidative rancidity is observed less frequently.</td>
</tr>
<tr>
<td><strong>Examples</strong>– Butterfat, Beef fat, Tallow</td>
<td><strong>Examples</strong>– Olive oil, Castor oil, Soybean oil, Corn oil</td>
</tr>
</tbody>
</table>
Most of the waxes are mixtures of esters. Thus, sperm whale wax (spermaceti) and beeswax are composed mainly of palmitic acid esterified with either hexacosanol, \( \text{CH}_3(\text{CH}_2)_{24}\text{CH}_2\text{OH} \) or triacontanol, \( \text{CH}_3(\text{CH}_2)_{30}\text{CH}_2\text{OH} \).

\[
\text{CH}_3(\text{CH}_2)_{14}\text{COOH} + \text{H}_2\text{O} \rightarrow \text{CH}_3(\text{CH}_2)_{14}\text{COO}\text{CH}_3
\]

Palmitic acid Hexacosanol Hexacosanyl palmitate

Moreover, sperm whale wax is also rich in cetyl palmitate and the beeswax in myricyl palmitate.

\[
\text{CH}_3(\text{CH}_2)_{14}\text{COOH} \bigg\longrightarrow \bigg\rightarrow \text{CH}_3(\text{CH}_2)_{28}\text{CH}_3
\]

Cetyl palmitate Myricyl palmitate

Carnauba wax, the hardest known wax, consists mainly of fatty acids esterified with tetracosanol, \( \text{CH}_3(\text{CH}_2)_{22}\text{CH}_2\text{OH} \) and tetraatriacontanol, \( \text{CH}_3(\text{CH}_2)_{32}\text{CH}_2\text{OH} \).

The waxes from the conifers contain polymers formed by the ester-linking of many \( \omega \)-hydroxy acids, such as juniperic acid, with each other.

\[
\text{HOOC.(CH}_2)_{14}\text{CH}_2\text{OH} \bigg\longrightarrow \bigg\rightarrow \text{HOOC.(CH}_2)_{14}\text{CH}_2\text{OH}
\]

\( \text{Juniperic acid} \)

There are certain waxes which have a characteristic odour. This is due to the presence of hydroxy acids in the form of lactones in them. For example, a wax named ambretolide, which is extracted from the seeds of lady’s finger, \( \text{Abelmoschus esculentus} \), has a characteristic musky smell.

Lipids of marine organisms such as starfish, squid and shark contain fatty alcohols that are long-chain alkyl ethers of glycerol. Three such glyceryl ethers (Fig. 13–7), as they are called have been isolated from shark oil.

Waxes are unusually inert due to their saturated nature of the hydrocarbon chain. However, they can be split slowly with hot alcoholic KOH. They are insoluble in water and highly resistant to atmospheric oxidation. Hence, these are used in polishing furnitures and automobiles and also in wax-coated paper used to wrap perishable food products such as biscuits, cakes, etc. Lanolin (from lamb’s wool), beeswax (from honeycomb), carnauba wax (from a Brazilian palm tree) and spermaceti oil (from sperm whales) are widely used in the manufacture of lotions, ointments and polishes.

**COMPOUND LIPIDS**

**PHOSPHOLIPIDS**

(= Phosphatids)

Phospholipids are the most abundant membrane lipids. They serve primarily as structural components of membranes and are never stored in large quantities. As their name implies, phospholipids contain phosphorus in the form of phosphoric acid groups. They differ from triglycerides in possessing usually one hydrophilic polar “head” group and usually two hydrophobic nonpolar “tails”. For this reason, they are often called polar lipids. Thus, phospholipids are amphipathic, whereas the storage...
lipids (triglycerides and waxes) are not. In phospholipids, two of the OH groups in glycerol are linked to fatty acids while the third OH group is linked to phosphoric acid. The phosphate is further linked to one of a variety of small polar head groups (alcohols). Folch and Sperry (1955) have classified phospholipids into phosphoglycerides, phosphoinositides and phosphosphingosides.

A. Phosphoglycerides

These are the major phospholipids found in membranes and contain two fatty acid molecules or “tails” esterified to the first and second hydroxyl groups of glycerol. The third hydroxyl group of glycerol forms an ester linkage with phosphoric acid. In addition, phosphoglycerides contain a second alcohol, which is also esterified to the phosphoric acid. This is referred to as ‘head alcohol group’ as it is present at one end (‘head’) of the long phosphoglyceride molecule.

The various phosphoglycerides differ in their head alcohol groups. However, all of them contain two nonpolar tails, each consisting of a long chain (usually C₁₆ or C₁₈) fatty acid. Usually one of the fatty acids is saturated and the other unsaturated; the latter is always esterified to the middle or β-hydroxy group of glycerol. A noteworthy feature of the phosphoglycerides is that they contain an asymmetric carbon atom at position 2 in the glycerol part of their molecule. It has the L-configuration since it is related to L-glyceraldehyde. All phosphoglycerides have a negative charge on phosphoric group at pH 7. In addition, the head alcohol group may also have one or more electric charges at pH 7.

1. Lecithins (= phosphatidyl cholines) – Lecithins (likithos = yolk) are widely distributed in nature. Various oil seeds like soybean and the yeasts are important sources from plant world. In animals, the glandular and nervous tissues are rich in these lipids. The lecithins are required for the normal transport and utilization of as other lipids esp. in the liver of animals. In their absence, accumulation of lipids occurs in the liver to as much as 30% against a normal value of 3-4%, giving rise to a condition called “fatty liver”. This fatty infiltration may lead to fibrotic changes, characteristic of the liver disease cirrhosis.

In addition to glycerol and 2 moles of fatty acids, the lecithins (Fig. 13–8) also contain phosphoric acid and a nitrogen base choline at either the end or middle carbon atom of glycerol unit. Accordingly, two forms of lecithins, α and β are recognized.

![Fig. 13–8. Structure of α-lecithin](image)

On complete hydrolysis, lecithin yields choline, phosphoric acid, glycerol and 2 moles of fatty acids. But partial hydrolysis of lecithins by lecithinases (active principles found in snake venoms) causes removal of only one fatty acid to yield substances called lysolecithins (Fig. 13–9). These, therefore, contain only one acyl radical. When subjected into the blood stream by sting as a result of snake bite or by needle, the lysolecithins cause rapid rupture (hemolysis) of the red blood corpuscles.

![Fig. 13–9. Structure of α-lysolecithin](image)
2. Cephalins – The cephalins (kephalus = head) are closely associated with lecithins in animal tissues. These have also been identified from soybean oil. These are similar in structure to the lecithins except that the choline is replaced by either ethanolamine or serine. Serine is the biochemical precursor of ethanolamine.

Accordingly, two types of cephalins are recognized, phosphatidyl ethanolamine and phosphatidyl serine. Like lecithins, the cephalins (Fig. 13–10) also exist in 2 forms, \( \alpha \) and \( \beta \), depending upon the relative positions of the two substituent fatty acids.

Since the primary amino group of ethanolamine is a weaker base than the quaternary ammonium group of choline, the cephalins are more acidic than lecithins. Moreover, the cephalins are comparatively less soluble in alcohol than lecithins.

Venoms containing lecithinases also split off fatty acids from cephalins, leaving hemolytic lysocephalins.

3. Plasmalogens (=Phosphoglyceracetals) – Plasmalogens constitute about 10% of the phospholipids of the brain and muscle. These are apparently not found in significant quantities in plant tissues. Structurally, these resemble lecithins and cephalins but have one of the fatty acids replaced by an unsaturated ether. Since the nitrogen base can be choline, ethanolamine or serine, three types of plasmalogens (Fig. 13–11) are accordingly distinguished: phosphatidal choline, phosphatidal ethanolamine and phosphatidal serine.

---

**Fig. 13–10. The two cephalins**

Since the primary amino group of ethanolamine is a weaker base than the quaternary ammonium group of choline, the cephalins are more acidic than lecithins. Moreover, the cephalins are comparatively less soluble in alcohol than lecithins.

Venoms containing lecithinases also split off fatty acids from cephalins, leaving hemolytic lysocephalins.

**Fig. 13–11. The three plasmalogens**
B. Phosphoinositides (=Phosphatidyl inositols)

Phosphoinositides (Fig. 13−12) have been found to occur in phospholipids of brain tissue and of soybeans and are of considerable importance because of their role in transport processes in cells. These are phospholipids where a cyclic hexahydroxy alcohol called inositol replaces base. The inositol is present as the stereoisomer, myo-inositol. On hydrolysis, the phosphoinositides yield 1 mole of glycerol, two moles of fatty acid, 1 mole of inositol and 1, 2, or 3 moles of phosphoric acid. Accordingly, mono-, di- or triphosphoinositides are found.

![Fig. 13–12. The two phosphoinositides](image)

Phosphoinositides are also classified as glycolipids, in as much as they contain carbohydrate residue.

C. Phosphosphingosides (=Sphingomyelins)

These compounds are commonly found in nerve tissue esp., in the myelin sheath of the nerve (hence their name, sphingomyelins) and apparently lack in plants and the microorganisms. In a syndrome called Niemann−Pick disease, the sphingomyelins are stored in the brain in large quantities. These differ from other phospholipids in their lack of glycerol and the presence of another nitrogenous base sphingosine or a closely related dihydrosphingosine, besides choline, in place of glycerol. Sphingomyelins are electrically charged molecules and contain phosphocholine as their polar head groups.

**CLINICAL IMPLICATIONS**

Niemann−Pick disease (= sphingomyelin lipidosis) is a rare genetic disorder, inherited as an autosomal recessive condition. The disease is caused by a deficiency of the enzyme sphingomyelinase, which cleaves ceramide-phosphocholine bond of sphingomyelin. As a result, sphingomyelin accumulates in large amounts in the reticuloendothelial system since their synthesis is normal in rate but their degradation is interrupted. Niemann−Pick cells (prototype of ‘foam cells’) are found in the bone marrow, spleen, lymphoid tissues, liver, lung and tissues, of virtually any organ. Clinically, the disease manifests itself in two forms:

(a) *Early or infantile form*. This is characterized by hepatosplenomegaly, macular degeneration, cherry-red retinal spot (= macula) in nearly half of the cases, mental retardation and blindness. Death ensues by two years of age.

(b) *Late or adult form*. This perhaps is the most common of the two forms and reveals intellectual impairment during late infancy, slow evolution of the disease, no changes in the ocular fundi and survival beyond the age of five. However, death of the patient occurs by the second decade.
On hydrolysis, the phosphosphingosides yield equimolar amounts of fatty acid, phosphoric acid, choline and sphingosine or dihydrosphingosine but no glycerol. Thus, in these compounds the atomic ratio N/P is 2, in contrast to phosphoglycerides where this ratio equals unity. Phosphoinositides, however, do not contain a nitrogen base.

![Fig. 13–13. Structure of sphingomyelin](image)

It may be observed from the formula of sphingomyelin (Fig. 13–13) that sphingosine carries the phosphoric acid on its primary alcohol group and the fatty acid by amide linkage on its primary amino group.

**GLYCOLIPIDS (= Cerebrosides or Glycosphingosides)**

The cerebrosides, as the name suggests, are important constituent of brain where they amount to about 8% of the solid matter. These may also occur in tissues other than brain. Since the head group characteristically consists of one or more sugar units, cerebrosides are often called glycosphingosides. Like phospholipids, glycolipids are composed of a hydrophobic region, containing 2 long hydrocarbon tails, and a polar region, which now contains one or more sugar residues and no phosphate. Both phospholipids and glycolipids form self-sealing lipid bilayers that are the basis for all cellular membranes. In Gaucher disease, the cerebrosides appear in relatively large amount in the liver and the spleen. They are also present in large amount in the brain in Niemann–Pick disease. These are present in much higher concentration in medullated than in nonmedullated nerve fibres. There is evidence that they also occur in some plant organs.

The structure of cerebrosides (Fig. 13–14) is somewhat similar to that of phosphosphingosides. They contain a high molecular weight fatty acid, sphingosine and either galactose or glucose instead of choline but no phosphoric acid. They have no electric charge since their polar head groups are neutral. In general properties, they resemble sphingomyelins.

**CLINICAL IMPLICATIONS**

**Gaucher disease** (= glucocerebrosidosis) is a not-so-rare, autosomal recessive, hereditary syndrome, often familial and of Jewish origin. It is 30 times more prevalent among the Ashkenazic Jews, with 1 case in 2,500 births. The disease is due to a deficiency of the enzyme glucosyl ceramide hydrolase (= glucocerebrosidase), which cleaves ceramide from ceramide trihexoside, causing deposition of the later. Gaucher's cells (pale lipid-containing cells) are found in abundance in all the organs specifically in the lungs and bone marrow, resulting in marked hepatosplenomegaly. Thus, the disease affects the lungs and causes destruction of bones. Clinically, two patterns of the disease have been reported:

(a) **Infantile or acute form.** In this, the symptoms appear early with hepatosplenomegaly, mental retardation, hypertonicity and signs of respiratory involvement. Most patients die during infancy.

(b) **Adult or chronic form.** This is more common a form of this disease. There is slow evolution of the disease with hepatosplenomegaly, hypersplenism, pathological fractures and often no neurological deficit.
Fig. 13–14. Structure of a cerebroside

The name ceramide is commonly used to designate the sphingosine–fatty acid (or N-acylsphingosine) portion of the cerebrosides. Here again the sphingosine carries the galactose by glycosidic linkage on its primary alcohol group and the fatty acid by an amide linkage on its primary amino group.

Individual cerebrosides are differentiated on the basis of their fatty acid component (Fig. 13–15). The various classes, so differentiated, are as follows:

(a) Kerasin—contains saturated C 24 lignoceric acid.
(b) Phrenosin (cerebron)—contains a 2-hydroxy derivative of lignoceric acid called cerebronic acid.

Fig. 13–14. Structure of a cerebroside

![Structure of a cerebroside](image)

**Fig. 13–14. Structure of a cerebroside**

![Structure of a cerebroside](image)

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Individual cerebrosides are differentiated on the basis of their fatty acid component (Fig. 13–15). The various classes, so differentiated, are as follows:

(a) Kerasin—contains saturated C 24 lignoceric acid.
(b) Phrenosin (cerebron)—contains a 2-hydroxy derivative of lignoceric acid called cerebronic acid.

![Characteristic fatty acids of cerebrosides](image)

**Fig. 13–15. Characteristic fatty acids of cerebrosides**

(c) Nervon—contains an unsaturated homologue of lignoceric acid called nervonic acid,
(d) Oxynervon—contains a 2-hydroxy derivative of nervonic acid called oxynervonic acid.

Gangliosides

In 1955, Klenk isolated a new type of glycolipid from brain tissue and named it as ganglioside. These are found in significant concentrations in ganglion cells of nervous tissue (hence so named) and also in most parenchymatous tissues like spleen and erythrocytes. They make up about 6% of the membrane lipids in the gray matter of the brain. They are also found in lesser amounts in the membranes of most nonneural tissues. Gangliosides are thought to act as receptors for toxic agents like the pathogens, *Vibrio cholerae* influenza virus and tetanus toxin. They are also implicated to play a role in cell-cell interaction.

The structure of gangliosides (Fig. 13–16) is complex and related to that of cerebrosides in that they contain a ceramide (N-acylsphingosine) linked to a carbohydrate (galactose or glucose).

![The three gangliosides](image)

**Fig. 13–16. The three gangliosides**
In addition to these, the gangliosides also generally contain 2 additional moles of carbohydrates, 1 mole of N-acetylgalactosamine and from 1 to 5 moles of N-acetylneuraminic acid (NANA). In Tay–Sachs disease, the gangliosides are stored in relatively large amounts in the brain and spleen.

**CLINICAL IMPLICATIONS**

Tay-Sachs disease (named after an English physician Warren Tay who first described the disease and an American neurologist Bernard Sachs who worked out its details), also called $G_{M2}$ gangliosidosis, was first described in 1881. This is the oldest medically described lipid storage disease or lipidosis. It is a common hereditary disorder. Although the disease is rare in the population at large (1 in 3,00,000 births), it has a very high incidence (1 in 3,600 births) in Ashkenazi Jews, who make up about 90% of the Jewish population in America. One in 30 Ashkenazi Jews carries the defective gene in recessive form (i.e., the carrier rate is 1/30), whereas the carrier rate is 1/300 in non-Jewish Americans. Consequently, the incidence of the disease is about 100 times higher in Jewish Americans. When both parents are carrier, their children are likely to develop Tay-Sachs disease even though the parents show no symptoms of the disease. Because the disease is irreversible and needs intensive care, genetic counseling of parents has become important in averting its consequences. The disease is caused due to a deficiency of the enzyme N-acetylgalactosaminidase ($=\text{hexosaminidase A}$), which cleaves a specific bond ($\beta-8\rightarrow4$) between an N-acetyl-D-galactosamine and a D-galactose residue in the polar head of the ganglioside, $G_{M2}$. In effect, $G_{M2}$ is not degraded to $G_{M1}$. With the result, $G_{M2}$, which is also called Tay–Sachs ganglioside, is accumulated in large amounts in the lysosomes, particularly in the brain cells to the tune of 100-300 times the normal $G_{M2}$ content, causing degeneration of the nervous system. In Tay–Sachs disease, the symptoms are evident before an affected infant is a year old. Weakness, retardation in development and difficulty in eating are typical early symptoms. Mental retardation and blindness usually follow a few months later; death, between two and five years, is inevitable. Over 90% of the patients have a characteristic cherry-red spot in the retina. Tay–Sachs disease can be diagnosed during fetal development. Amniotic fluid is obtained by amniocentesis and assayed for $b$-N-acetylgalactosaminidase activity. As mentioned, Tay–sachs disease shares the tragic element of Niemann–Pick and Gaucher diseases in that the affected child seldom lives beyond age three.

More than 15 different gangliosides have been characterized and their structures determined. These are commonly abbreviated by the letter G, with a subscript $M$, $D$, or $T$ to designate that they contain one, two or three sialic acid and (N-acetylneuramine or N-glycocolyl neuraminate) residues respectively, and a number or letter to distinguish different members of a group from one another. In essence, they consist of an oligosaccharide chain attached to ceramide (N-acylsphingosine) by a sugar residue which is usually glucose. They lack phosphoric acid.

**Sulfolipids.**

A glycolipid that contains sulfur is widely distributed in plants. It is localized in the chloroplasts but is also found in the chromatophores of photosynthetic bacteria. As the sulfur in this compound is present as a sulfonic group in a hexose, this may be included under a class of compounds called sulfolipids. Its structure is given in Fig. 13–17.

**Sulfatides.**

A sulfate ester analogue of phrenosin, abundant in white matter of brain, is another sulfur-containing glycolipid. In it, the sulfate is present in ester linkage at C 3 of the galactose portion of the molecule. Members of this group of cerebrosides sulfuric esters have been designated as sulfatides.

The classification of compound lipids as presented here is now becoming obsolete. It is, however, more logical to classify them according to the main alcohol component (refer Table 13–3). According to this system, the compound lipids fall under 2 categories : one in which the main alcohol component is glycerol (glycerophosphatides) and the other in which sphingosine is the main alcohol component (sphingolipids). The further classification of these two categories depends on the nature of the other alcohol components.
### Table 13–3. Classification of compound lipids

<table>
<thead>
<tr>
<th>Name</th>
<th>Main alcohol component(s)</th>
<th>Other alcohol component(s)*</th>
<th>N:P ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glycerophosphatides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phosphatidic acids</td>
<td>Diglyceride (= glycerol diester)</td>
<td>Choline</td>
<td>0 : 1</td>
</tr>
<tr>
<td>Lecithins</td>
<td>Diglyceride (= glycerol diester)</td>
<td>Ethanolamine, serine</td>
<td>1 : 1</td>
</tr>
<tr>
<td>Cephalins</td>
<td>Diglyceride (= glycerol diester)</td>
<td>Inositol</td>
<td>0 : 1</td>
</tr>
<tr>
<td>Inositides</td>
<td>Diglyceride (= glycerol diester)</td>
<td>Choline, ethanolamine, serine</td>
<td>1 : 1</td>
</tr>
<tr>
<td>Plasmalogens</td>
<td>Monoglyceride (= glycerol ester) + Enol ether</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sphingolipids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sphingomyelins</td>
<td>N-acylsphingosine</td>
<td>Choline</td>
<td>2 : 1</td>
</tr>
<tr>
<td>Cerebrosides</td>
<td>N-acylsphingosine</td>
<td>Galactose, glucose</td>
<td>1 : 0</td>
</tr>
<tr>
<td>Sulfatides</td>
<td>N-acylsphingosine</td>
<td>Galactose</td>
<td>(1H₂SO₄)</td>
</tr>
<tr>
<td>Gangliosides</td>
<td>N-acylsphingosine</td>
<td>N-acetylgalactosamine + N-acetylneuraminic acid</td>
<td>No P</td>
</tr>
</tbody>
</table>

* The other alcohol components in all the sphingolipids except sphingomyelins are not present as phosphoric esters, but rather in glycosidic linkages. For this reason, these sphingolipids are grouped under glycolipids.

### DERIVED LIPIDS

The group derived lipids is a “catch all” group in Bloor’s classification. It includes the hydrolysis products of simple and compound lipids and also various other compounds such as steroids, terpenes, fatty acids, alcohols, fatty aldehydes, ketones etc.

**STEROIDS**

The steroids (stereos = solid) are one of the most studied classes of biological compounds and are often found in association with fat. Since they contain no fatty acids, they are nonsaponifiable, i.e., cannot be hydrolyzed by heating with alkali to yield soaps of their fatty acid components. Fats, on the other hand, are saponifiable and form soaps when hydrolyzed with alkali. The steroids may be separated from the fat after the latter is saponified since they occur in ‘nonsaponifiable residue’. All steroids may be considered as derivatives of a fused and fully saturated ring system called **cyclopentanoperhydrophenanthrene** or **sterane**. This system consists of 3 cyclohexane rings (A, B and C) fused in nonlinear or phenanthrene manner and a terminal cyclopentane ring (D). The sterane nucleus along with the conventional numbering of the carbon atoms is shown in Fig. 13–18.

![Phenanthrene and sterane nucleus](image)

Fig. 13–18. Phenanthrene and sterane nucleus
It may, however, be emphasized that in steroids the hexagonal rings are not the benzene rings as in them the valences of C atoms are fully satisfied by hydrogen bonds, unless shown otherwise. The double bonds, if present, are shown as such. The ‘angular’ methyl groups occur typically at positions 10 and 13 and constitute carbon atoms 19 and 18 respectively. The steroids may have one or more hydroxyl groups, one OH group being present usually on C 3. A side chain at C 17 is usual. This side chain serves as a convenient basis for classification of steroids. For example, the side chain contains 8, 9 or 10 C atoms in sterols, 5 C atoms in bile acids, 2 C atoms in adrenal cortical steroids and in progesterone and none in naturally occurring estrogens and androgens.

Stereochemical considerations of steroids. Without even considering the substituent groups, there are 6 possible asymmetric centres present in the steroid nucleus (Fig. 13–19). Consequently, the steroids have many potential stereoisomers. Each of 3 cyclohexane rings, on the basis of the tetrahedral theory, is capable of existing in 3-dimensional conformation either of a ‘chair’ or of a ‘boat’ (Fig. 13–20).

These 2 forms are aplanar and strainless and were first proposed by Sachse in 1890. The ‘chair’ form is rigid (in the sense that it resists distortion) and when it is changed to the ‘boat’ form, some angular deformity invariably takes place. The ‘chair’ conformation of cyclohexane itself is more stable than the ‘boat’ conformation. The ‘chair’ and ‘boat’ forms are both free from angle strain but because of differences in steric strain and bond opposition strain, the two forms differ in energy content (Finar, 1975).

In naturally occurring steroids, all the rings are in ‘chair’ form. With respect to each other, the rings can be either -cis or -trans (Fig. 13–21). The junction between the rings A and B (A/B junction) in naturally-occurring steroids may be either -cis or -trans. But the B/C and C/D junctions are, with certain exceptions, always in -trans form. The idea of -cis and -trans forms with respect to A/B junction may be explained as below. The hydrogen atom on C 5 may be either on the same side of the plane of molecule as the methyl group on C 10 or on the opposite side. In the former case, rings A and B will be -cis to each other and the molecule is said to belong to normal configuration. If the hydrogen atom and the methyl group are on the opposite sides, the rings A and B are -trans to each other and the molecule is of allo configuration.

Steroids containing hydroxyl groups (hydroxy steroids) are often referred to as sterols. Broadly speaking, the various steroids fall under 2 groups based on their source: the animal sterols or zoosterols (cholesterol, cholestanol, coprostanol) and the plant sterols or phytosterols (ergosterol, stigmasterol, spinasterol). A third group of sterols, which are obtained from fungi including yeasts, is sometimes separately referred to as mycosterols. This classification, however, is not rigid as some sterols are obtained from more than one of these sources.
In the structural representation of the steroids, substituents that are above the plane of the ring (or $\beta$-oriented) are shown with solid lines, while those which are below the plane of the ring (or $\alpha$-oriented) are represented with broken lines. The methyl groups at C 10 and C 13, the hydroxyl group on C 3 and the side chain at C 17 are all $\beta$-oriented.

Certain common steroids are described below.

**C 29, C 28 and C 27 Steroids**

1. **Cholesterol** (chole$^G$ = bile). Cholesterol is undoubtedly the most publicized lipid in nature, because of the strong correlation between high levels of cholesterol in the blood and the incidence of diseases of the cardiovascular system in humans. It is not only an important component of some cell membranes and of plasma lipoproteins but also the precursor of many other biologically important steroids, such as bile acids and various steroid hormones. It is the principal sterol of higher animals and is especially abundant in nerve tissues and in gallstones. It occurs either free or as fatty esters in all animal cells. It was first isolated in 1784, from human gallstones which consist almost entirely of cholesterol and hence so named (cholesterol literally means ‘solid alcohol from bile’). Its main sources are fish liver oils and the brain and spinal cord of cattle. White matter contains as much as 14%, gray matter 5%, spinal cord 7%, and gallstones 99%.

**Cholesterol** is generally believed to be notorious as a major cause of heart disease. There are 2 types of cholesterol, the low-density lipoprotein cholesterol (LDL-C) and the high-density lipoprotein cholesterol (HDL-C). The LDL-C grows with intake of eggs and dairy products and triggers heart trouble. However, in a study conducted by Dr. Ian Craig of the Goteborg University, Sweden in the early 70s showed that patients with heart trouble such as myocardial infarction had low levels of HDL-C, as compared to other people. He pointed out that most of the preventive heart attack studies have so far been aimed at lowering the LDL-C levels through drugs and diet, but it seemed that normal variations in diet made little difference in HDL-C levels. Also, HDL-C levels were generally found higher in women than men. Perhaps this is the reason why fewer women than men have heart attacks. There are, thus, hopeful signs that incidence of heart disease may be lowered by increasing the HDL-C level in heart patients.
cord 12% and liver about 1% cholesterol. Cholesterol is, however, not found in plant fats. Its parent hydrocarbon is cholestane, \( \text{C}_{27}\text{H}_{45} \). The structure of cholesterol was determined by the German chemist, Adolph Windaus (LT, 1879 – 1959), who received 1928 Nobel Prize in Chemistry. Cholesterol (Fig. 13–22) has a molecular formula, \( \text{C}_{27}\text{H}_{45}\text{OH} \). In addition to an OH group at C3, there is a double bond at C5. The hydroxyl group constitutes its polar head, the rest of the molecule is hydrophobic. It is a white crystalline solid and is optically active, \([\alpha]_D \, 39^\circ\). The crystals are rhombic plates with one of the angles broken. It has a melting point of 149°C. Konrad S. Bloch, a Germany-born American biochemist, elucidated the biosynthetic pathway of cholesterol synthesis, one of the most complex known, for which he received the coveted Nobel Prize in Chemistry along with Feodor Lynen, a German and John Cornforth, a Briton, in 1964. Bloch combined work and pleasure by traveling to Bimini for collection of shark livers.

On receiving the Nobel Prize in 1985 for their work on cholesterol, Michael Brown and Joseph Goldstein recounted in their lecture the extraordinary history of cholesterol:

“Cholesterol is the most highly decorated small molecule in biology. Thirteen Nobel Prizes have been awarded to scientists who devoted major parts of their careers to cholesterol. Ever since it was isolated from gallstones in 1784, cholesterol has exerted an almost hypnotic fascination for scientists from the most diverse areas of science and medicine... Cholesterol is a Janus-faced molecule. The very property that makes it useful in cell membranes, namely its absolute insolubility in water, also makes it lethal.”

(Courtesy: The Nobel Foundation, 1985)

Table 13-4 provides data on fat and cholesterol contents of some notable animal foods.
<table>
<thead>
<tr>
<th>Food Item</th>
<th>Fat  g/100 g</th>
<th>Saturated fatty acids  g/100 g</th>
<th>Cholesterol  mg/100 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butter</td>
<td>80</td>
<td>50</td>
<td>250</td>
</tr>
<tr>
<td>Ghee</td>
<td>100</td>
<td>65</td>
<td>300</td>
</tr>
<tr>
<td>Milk (cow)</td>
<td>4</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>Milk (buffalo)</td>
<td>8</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Milk (skimmed)</td>
<td>0.1</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>Milk (condensed)</td>
<td>10</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>Cream</td>
<td>13</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td>Cheese</td>
<td>25</td>
<td>15</td>
<td>100</td>
</tr>
<tr>
<td>Egg (whole)</td>
<td>11</td>
<td>4</td>
<td>400</td>
</tr>
<tr>
<td>Egg (yolk)</td>
<td>30</td>
<td>9</td>
<td>1120</td>
</tr>
<tr>
<td>Chicken (with skin)</td>
<td>18</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>Chicken (without skin)</td>
<td>4</td>
<td>1</td>
<td>60</td>
</tr>
<tr>
<td>Beef</td>
<td>16</td>
<td>8</td>
<td>70</td>
</tr>
<tr>
<td>Mutton</td>
<td>13</td>
<td>7</td>
<td>65</td>
</tr>
<tr>
<td>Pork</td>
<td>35</td>
<td>13</td>
<td>90</td>
</tr>
<tr>
<td><strong>Organ meats</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>6</td>
<td>2</td>
<td>2000</td>
</tr>
<tr>
<td>Heart</td>
<td>5</td>
<td>2</td>
<td>150</td>
</tr>
<tr>
<td>Kidney</td>
<td>2</td>
<td>1</td>
<td>370</td>
</tr>
<tr>
<td>Liver</td>
<td>9</td>
<td>3</td>
<td>300</td>
</tr>
</tbody>
</table>

* The data are based on per 100 g edible portion of the food item.

No vegetable oil contains any cholesterol; hence, it is misleading for oil manufacturers to advertise any oil as ‘low cholesterol’ oil. Saturated fats of animals origin (such as butter, ghee and lard) do contain cholesterol but vanaspati, which is derived from vegetable oils, does not contain cholesterol. Only a little portion of the body cholesterol is derived from diet. The bulk of it is synthesized in the body. Unsaturated fatty acids lower blood cholesterol levels by controlling cholesterol’s synthesis as well as its elimination from the body. Thus, vegetable oils when consumed within the recommended amounts help to maintain proper levels of lipids in the blood than do the saturated fats like butter, ghee, lard and vanaspati. These saturated fats elevate blood lipids (cholesterol and triglycerides) and reduce the ratio of good to bad cholesterol even when consumed within the recommended limits. High intake of dietary cholesterol can probably raise blood cholesterol levels and hence should be avoided, esp., by the elderly people and those having high blood cholesterol.

The level of cholesterol in the blood is measured in milligrams per decilitre (mg/dl, which is equivalent to parts per 1,00,000). The levels range from less than 50 in infants to an average of 215 in adults to 1,200 or more in individuals suffering from a rare inherited disease called familial cholesterolemia. For those persons in the normal range, about two-thirds of their cholesterol is transported as LDLs. Most of the rest is carried by HDLs.

An often-posed question relates to the consumption of eggs and meat, and sometimes even milk, because of the relatively high content of cholesterol in these foods. Milk is no doubt a very good and safe food. Persons aspiring to control their cholesterol intake (and calories) must use defatted or skimmed milk. Egg and meat proteins are of high grade and desirable especially for the growing children. Those desirous of reducing their cholesterol intake should eat only the white of egg and lean on white meat like chicken and fish. Nutritionally, fish is a very good food since it has high-quality...
protein (fish fat is rich in $n$-3 PUFA) and its flesh has very little cholesterol. Organ meats like brain and liver are rich in cholesterol and should hence be avoided by those wanting to restrict cholesterol.

The notion that cholesterol is a poisonous substance in the body is misleading. It is the parent hydrocarbon from which many important hormones (corticosteroids and sex steroids, for example) are synthesized. The problem creates when blood cholesterol level rise and the level of LDL-cholesterol, which carries cholesterol to the tissues, goes below the desired level. HDL-cholesterol or good cholesterol removes cholesterol from the tissues and helps eliminating it from the body. High blood cholesterol results in the deposition of cholesterol in the arteries and narrows the passage, a condition called atherosclerosis. Also, the arterial surface roughens due to cholesterol deposition, which leads to frequent blood clotting or thrombosis. Both are major health hazards. Studies, however, point out that even very low levels of blood cholesterol are too not desirable. The thumb rule, therefore, is moderation. Both too much and too little of fat may be harmful.

In blood about two-thirds of the cholesterol is esterified mainly to unsaturated fatty acids, the remaining portion occurring as the free alcohol. Reduction of the double bond gives rise to 2 products, coprostanol and cholestanol.

2. **Coprostanol (≡ coprosterol).** It occurs in feces and is produced in the intestine as a result of bacterial action on the double bond of cholesterol. The A/B junction is -cis in coprostanol in contrast to -trans in cholesterol.

3. **Cholestanol.** It occurs as a minor constituent of the sterols of blood and other tissues. Here the A/B junction is in -trans form.

4. **Ergosterol.** It is present in ergot (hence its nomenclature), yeast and the mould *Neurospora*. Its parent hydrocarbon is ergostane, $C_{28}H_{49}$. Ergosterol (Fig. 13–23) has a molecular formula, $C_{28}H_{48}OH$ with one OH group at C$_3$ and 3 double bonds at C$_5$, C$_7$ and C$_{22}$. It is also optically active, $[\alpha]_D$ -135°.

Rupture of the ring B by UV radiation produces vitamin D$_2$ which is chemically known as ergocalciferol. A similar compound cholecalciferol (or vitamin D$_3$) is, however, obtained from 7-dehydrocholesterol on irradiation with UV light (refer Chapter 32).

![Structure of ergosterol](image1)

![Structure of lanosterol](image2)

5. **Lanosterol (= cryptosterol).** It is a major constituent of wool fat and is also present in minor quantities in liver and yeast. Lanosterol (Fig. 13–24) is a C$_{30}$ compound with twin methyl groups at C$_4$ and a third angular methyl group on C$_{14}$. There are 2 double bonds at C$_8$ and C$_{24}$. It is an intermediate in the biosynthesis of cholesterol.

A number of sterols have also been obtained from various plant and animal sources, for example *stigmasterol* (from soybean and wheat germ oils), *spinasterol* (spinach and cabbage), *sitosterol* (many higher plants), *ostreasterol* (oysters) and *chondrillasterol* (marine sponges).
C 24 Steroids or Bile Acids

The bile acids are the important end products of cholesterol metabolism in higher plants. About 20 natural bile acids have been characterized (Table 13−4). All these are derived from a C 24 parent steroid, cholanic acid and resemble coprostanol in having rings A and B in cis form. The most abundant bile acids in human bile are cholic acid (25-60% of the total bile acids), chenodeoxycholic acid (30-50%) and deoxycholic acid (5-25%). Various bile acids differ from each other in the number and position of OH groups which are all in a configuration. In the bile acids, the number of OH group(s) may be 1, 2, or 3 and the position of OH group(s) may be any of the following : 3, 6, 7, 11, 12 and 23. The side chain is usually made up of 5 carbon atoms and bears the carboxyl group.

Table 13-5. Some important natural bile acids

<table>
<thead>
<tr>
<th>Name</th>
<th>Formula</th>
<th>Melting point, °C</th>
<th>Position of OH group(s)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monohydroxycholanic acid</td>
<td>C_{23}H_{36}(OH).COOH</td>
<td>186</td>
<td>3</td>
<td>Man, Ox</td>
</tr>
<tr>
<td>Lithocholic acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dihydroxycholanic acids</td>
<td>C_{23}H_{37}(OH)_{2}.COOH</td>
<td>172</td>
<td>3, 12</td>
<td>Man, Ox</td>
</tr>
<tr>
<td>Deoxycholic acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chenodeoxycholic acid</td>
<td></td>
<td></td>
<td>3, 7</td>
<td>Man, Ox, Hen</td>
</tr>
<tr>
<td>α-hydroxydeoxycholic acid</td>
<td></td>
<td></td>
<td>3, 6</td>
<td>Pig</td>
</tr>
<tr>
<td>Trihydroxycholanic acid</td>
<td>C_{23}H_{36}(OH)_{3}.COOH</td>
<td>195</td>
<td>3, 7, 12</td>
<td>Man, Ox</td>
</tr>
<tr>
<td>Cholanic acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The structure of two principal bile acids is given in Fig. 13–25.

These acids are coupled in amide linkage to the amino acids glycine (NH\textsubscript{2}−CH\textsubscript{2}−COOH) and taurine (NH\textsubscript{2}−CH\textsubscript{2}−CH\textsubscript{2}−SO\textsubscript{3}H) to form glycocholic and taurocholic acids respectively (Fig. 13–26). The reaction is characteristic of COOH group and involves the side chain only. The salts of these conjugated acids have high surface activity and hence promote the intestinal absorption of lipids like cholesterol. They are water-soluble and are powerful detergents.
C 21, C 19 and C 18 Steroids

On account of their hormonal role, these have been described in Chapter 30.

Several important poisons are based on the steroid structure. Digitoxior digitalin (Fig. 13-27 a, b) is present in the foxglove plant (Digitalis purpurea) and has a powerful heart stimulating action. Another cardiac glycoside, Quabain, (Fig. 13-27 c) is isolated from the East African Ouabio tree and has the sugar, rhamnose, attached to a modified sterol nucleus. It is of interest to note that it is a powerful inhibitor of the ‘sodium pump’, a device which normally ensures that the cell content of potassium is higher and that of sodium is lower than in the circumambient fluid.

Fig. 13.27. The foxglove plant and two most-commonly prescribed cardiac drugs

(a) The foxglove plant, Digitalis purpurea. The leaves of purple foxglove plant are the source of the popular heart muscle stimulant, digitalis.

(b) Digitoxin. It is extracted from the dried leaves of foxglove plant and is the major component of digitalis, one of the most-widely used cardiac muscle stimulant.

(c) Quabain. It is a cardiac glycoside, isolated from the East African Quabio tree. (Courtesy: (a) Derek Fell)

Table 13–6 lists the occurrence and biological role of some important steroids.

<table>
<thead>
<tr>
<th>Group</th>
<th>Representative</th>
<th>Formula</th>
<th>Occurrence</th>
<th>Biological role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterols</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C 30</td>
<td>Lanosterol</td>
<td>C 30H 51O</td>
<td>Wool fat</td>
<td>Biosynthesis of cholesterol</td>
</tr>
<tr>
<td>C 28</td>
<td>Ergosterol</td>
<td>C 28H 44O</td>
<td>Yeast</td>
<td>Provitamin D</td>
</tr>
<tr>
<td>C 27</td>
<td>Cholesterol</td>
<td>C 27H 46O</td>
<td>Animal fats</td>
<td>Structural component and precursor</td>
</tr>
</tbody>
</table>
**TERPENES**

Among the nonsaponifiable lipids found in plants are many hydrocarbons known as terpenes (from *turpentine*). In general, these hydrocarbons and their oxygenated derivatives have lesser than 40 carbon atoms. The simplest terpenes are called *monoterpens* and conform to the formula \( C_{10}H_{16} \) (equivalent to 2 isoprene units, Fig. 13–28), those with the formula \( C_{15}H_{24} \) are called as *sesquiterpens*, with \( C_{20}H_{32} \) as *diterpens* and with \( C_{30}H_{48} \) as *triterpens*. Terpenes with 40 carbon atoms (or *tetraterpens*) include compounds called carotenoids (refer Chapter 32).

![Fig. 13–28. Structure of isoprene](2-methyl-1, 3-butadiene)

In fact, O. Wallach (1910 Nobel Laureate in Chemistry) was the first to point out, in 1887, that nearly all the terpenoids are made of varying number of repetitive units (\( C_5H_8 \)), called isoprene units. His finding later came to be known as the *isoprene rule*. Structurally, isoprene is a 5-carbon diene. The carbon skeletons of open-chain monoterpens and sesquiterpens are:

![Monoterpoid and Sesquiterpenoid](head-to-tail linkages or 1,4 linkages)

Even not only the presence of isoprene units but their special type of arrangement is found to be present in nearly all the terpenoids. Ingold, in 1925, formulated this observation under another rule, the *special isoprene rule*, according to which the isoprene units in terpenoids are usually joined in *head-to-tail linkages* or 1,4 linkages (the branched end of the isoprene unit was considered as the head).
Exceptions, however, do occur for these two isoprene rules. For example, cryptone, a natural terpenoid, contains only 9 carbon atoms instead of 10. Also, in lavandulol, the 2 isoprene units are not joined in head-to-tail manner, and in carotenoids, the two halves (each with 4 isoprene units) are linked with each other by tail-to-tail at the centre.

**Monoterpenes and Sesquiterpenes**

The fragrances of many plants arise from volatile C\(_{10}\) and C\(_{15}\) terpenes. These and their oxygenated derivatives occur as components of the essential oils, some of which are used as perfumes. Important monoterpenes (Fig. 13–29) are myrcene (from oil of bay), geraniol (from rose oil), limonene (from lemon oil) and menthol (from peppermint oil).

Among the sesquiterpenes, farnesol (Fig. 13–30) is widely distributed but is present in essential oils in small amounts.

**Diterpenes**

These are usually found as substituents of the resins and balsams. The two resin acids, abietic and sapietic (Fig. 13–31) are the best known tricyclic diterpenes.
Vitamins A₁ and A₂ and their aldehydes called retinenes are important monocyclic derivatives of diterpenes.

**Phytol.**

\((C_{20}H_{40}O; \text{b.p. } 145°C)\) is an acyclic diterpene and is obtained from the hydrolysis of chlorophyll. It was isolated from nettles by Paul Karrer et al. in 1943. The phytol molecule (Fig. 13–32) has 2 chiral (= asymmetric) centres, 7 and 11. Natural phytol is very weakly dextrorotatory.

**Triterpenes**

These are not widespread in nature but are significant in that some of them are intermediates in the biosynthesis of cholesterol. Two such compounds are: a tetracyclic alcohol, **lanosterol** (see page 260) and an acyclic hydrocarbon, **squalene**. Squalene \((C_{30}H_{50}; \text{b.p. } 240–242°C)\) was first isolated from the liver of sharks (genus *Squalus*), hence so named. The olive oil and several other vegetable oils are other sources. It has also been detected in the leaves. Each squalene molecule (Fig. 13–33) has 6 double bonds. The double-bond system present is of nonconjugated type. The conjugated double bonds are, however, absent from the molecule.

**Polyterpene**

Mention, however, should also be made of **rubber** \((\text{MW } = \text{ca } 3,00,000)\), a polyterpene present in the latex of many tropical plants. A molecule of rubber (Fig. 13–34) is composed of about 500 to 5,000 isoprene units joined in a long straight chain. When the bark of the rubber tree is cut, latex slowly exudes from the cut. Addition of acetic acid coagulates the rubber, which is then separated from the liquor and either processed into blocks or rolled into sheets, and finally dried in a current of warm air, or smoked.

**Carotenoids**

The carotenoids are tetraterpenes. These are widely distributed in both the plant and animal kingdoms but are exclusively of plant origin. These occur in unsaponifiable residue of plant and animal lipids. They are isoprene derivatives with a high degree of unsaturation. Because of the presence of many conjugated double bonds, they are coloured red or yellow. As an example, the pigment of...
tomato (lycopene) and that of carrot (α- and β-carotene) are red while many oxygen-containing carotenoids are yellow (xanthophylls). Since the olefinic (= double) bonds permit cis-trans isomerism, numerous forms are possible. Most carotenoids, however, exist in all-trans form. The presence of long hydrocarbon chain in carotenoids makes them lipid-soluble; they are hence also called lipochromes or chromolipids.

**Lycopene**

Lycopene ($C_{40}H_{56}$) is the main pigment of tomato, paprika and many other fruits. It is a highly unsaturated, unbranched, long chain hydrocarbon (a polyene) and is composed of two identical units ($C_{20}H_{28}$), joined by a double bond between $C_{15}$ and $C_{15}'$. Each of these units may, in turn, be considered to have been derived from 4 isoprene units ($C_5H_8$). A molecule of lycopene (Fig. 13–35) in all contains as many as 13 double bonds, of which 11 are conjugated.

![Fig. 13–35. Structure of lycopene](image)

(Dotted lines mark the positions where various isoprene-like sements are joined with each other.)

**Carotene**

Another group of naturally occurring carotenoids, with the same molecular formula as that of lycopene, is carotene. Carotene was first isolated by Wackenroder (1831) from carrots (this was the origin of the name carotin, which was later on modified to carotene). The 3 types of carotenoids are:

1. α-carotene—violet crystals; m.p. 187°C; optically active (dextrorotatory).
2. β-carotene—red crystals; m.p. 183°C; optically inactive.
3. γ-carotene—dark red crystals; m.p. 152–154°C; optically inactive.

(The prefixes α, β and γ in the carotenones were assigned not on the basis of structural properties but rather as a result of observations of their elution patterns on a CaCO$_3$ chromatographic column, eluted with petroleum ether).

The carotenones are obtained commercially by chromatography. The two best sources are carrots and alfalfa. Their relative proportion, however, varies with the source; for example carrots contain 15% α-, 85% β- and 0.1% γ-form. These are unstable to air, heat, acids and alkalies.

It is to be noted that the ends of the lycopene chain can easily close up to form rings, with the disappearance of the double bonds. Ring closure on only one end results in the production of γ-carotene while closure of the ring at both ends produces β- and α-carotenes which differ from each other in the position of the double bonds in the rings. The ring is structurally related to the ionones. (Fig. 13–36). In β-carotene, both annular double bonds are in conjugation with the system of double bonds of the long chain (β-ionone structure). In α-carotene, one of the annular double bonds is removed from the system of conjugation by one position (α-ionone structure). Of particular interest is β-carotene (Fig. 13–37), which is precursor of vitamin A.

![Fig. 13–36. Structure of β-ionone](image)
CLASSIFICATION OF LIPIDS

Contents

LIPIDS

SIMPLE LIPIDS or HOMOLIPIDS
- Fats and oils (Triglycerides)
  - Simple triglycerides
  - Mixed triglycerides
- Waxes
  - Sperm whale wax
  - Beeswax
  - Carnauba wax

COMPOUND LIPIDS or HETEROLIPIDS
- Phospholipids (Phosphatids)
  - Phosphoglycerides
  - Lecithins
  - Cephalins
  - Plasmalogens
- Phosphoinositides (Phosphatidylinositol)
- Phosphosphingosides (Sphingomyelins)
- Glycolipids (Cerebrosides)
  - Kerasin
  - Phrenosin
  - Nervon
  - Oxynervon

DERIVED LIPIDS
- Steroids
  - C 29, C 28, C 27 steroids
  - C 24 steroids
  - C 21, C 19, C 18 steroids
- Terpenes
  - Monoterpenes
  - Sesquiterpenes
  - Diterpenes
  - Triterpenes
  - Tetraterpenes
  - Polyterpenes
- Carotenoids
  - Lycopene
  - Carotenes
  - Xanthophylls
**Xanthophylls**

Xanthophylls are characterized by the presence of hydroxyl groups in the ionone rings of carotenes, in the para position to the long chain. The xanthophyll of the leaf (lutein, C₄₀H₅₆O₂, Fig. 13–38) is derived from α-carotene while that of corn (zeaxanthine) from β-carotene. The xanthophyll of crustaceans (astaxanthine) is, however, more rich in oxygen. Astaxanthine is responsible for the appetizing redness of boiled lobsters.

![Fig. 13–38. Structure of lutein](3, 3'-dihydroxy-α-carotene)

The classification of lipids described above may be summarized as depicted on page 252.

### REFERENCES

See list following Chapter 14.

### PROBLEMS

1. A common structural feature of membrane lipid molecules is their amphipathic nature. For example, in phosphatidylcholine, the two fatty acid chains are hydrophobic and the phosphocholine head group is hydrophilic. For each of the following membrane lipids, name the components that serve as the hydrophobic and hydrophilic units:
   - (a) phosphatidylethanolamine
   - (b) sphingomyelin
   - (c) galactosylcerebroside
   - (d) cholesterol

2. Which of the following could not be classified as a lipid?
   - (a) steroids
   - (b) fats and oils
   - (c) waxes
   - (d) photosynthetic pigments
   - (e) anthocyanin pigments