College of pharmacy

Biochemistry I third stage

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Lecture 1

Lipids

Lipids

The lipids are a heterogeneous group of compounds, including fats, oils, steroids, waxes, and related compounds. They have the common property of being relatively insoluble in water and soluble in nonpolar solvents such as ether and chloroform. Lipids are a major source of energy for the body, and they also provide additional functions in the body, for example, some fat soluble vitamins have regulatory or coenzyme functions, and the prostaglandins and steroid hormones play major roles in the control of the body's homeostasis. Fat is stored in adipose tissue, where it also serves as a thermal insulator in the subcutaneous tissues.

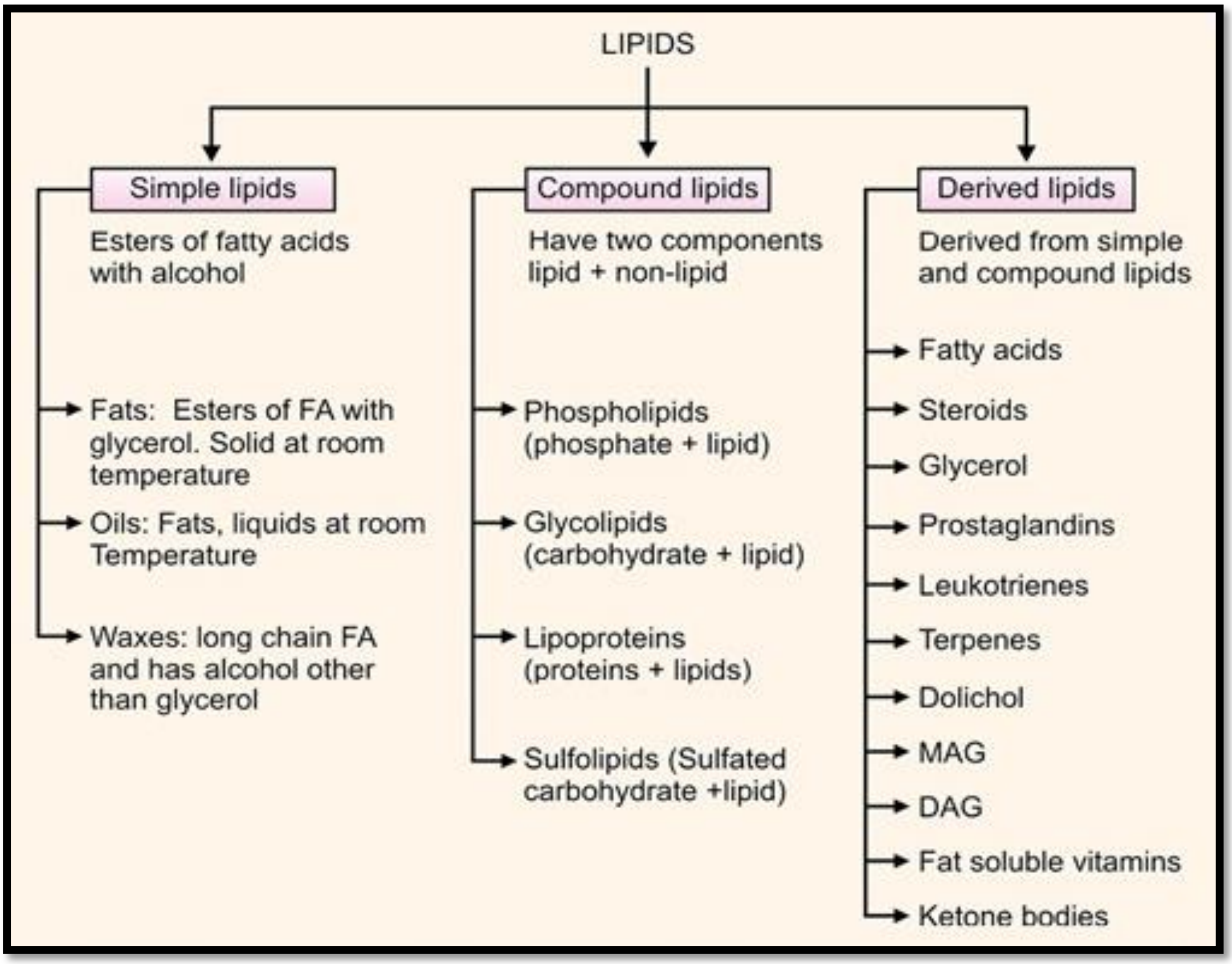
Classification of lipids

1- Simple lipids: Esters of fatty acids with various alcohols.

2- Complex lipids: Esters of fatty acids containing groups in addition to an alcohol and a fatty acid.

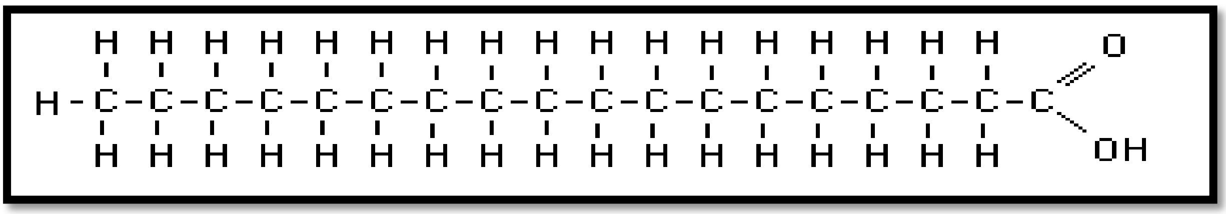
3- Precursor and derived lipids: These include fatty acids, glycerol, steroids, other alcohols, fatty aldehydes, and ketone bodies, hydrocarbons, lipid-soluble vitamins, and hormones.

Because they are uncharged, acylglycerols (glycerides), cholesterol, and cholesteryl esters are termed **neutral lipids.**



Fatty Acid

A fatty acid is a molecule characterized by the presence of a carboxyl group attached to a long hydrocarbon chain. Therefore these are molecules with a formula R–COOH where R is a hydrocarbon chain.



Classification of fatty acids: Fatty acids can be classified according to:

1. Chain length ™

A. Short chain fatty acids: 2-4 carbon atoms ™

B. Medium chain fatty acids: 6 –10 carbon atoms ™

C. Long chain fatty acids: 12 – 26 carbon atoms

2. Saturated and unsaturated fatty acids

A. Saturated fatty acids do not have any double bonds. A fatty acid is saturated when every carbon atom in the hydrocarbon chain is saturated with hydrogen. Saturated fatty acids are solids at room temperature. Animal fats are a source of saturated fatty acids.

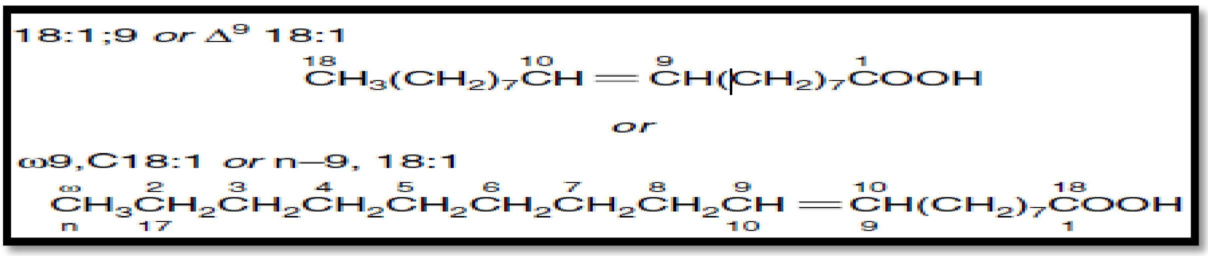
Saturated fatty acid chain $–CH_2 – CH_2 – CH_2 –$

B. Unsaturated fatty acids can have one or more double bonds along its hydrocarbon chain. A fatty acid with one double bond is called monounsaturated. If it contains two or more double bonds, we say that the fatty acid is polyunsaturated. The **melting point** of a fatty acid is influenced by the **number** of double bonds that the molecule contains and by the **length** of the hydrocarbon tail. The more double bonds it contains, the lower the melting point. As the length of the tail increases, the melting point increases. Plants are the source of unsaturated fatty acids.

Unsaturated fatty acid chain $–CH = CH – CH = CH –$

Nomenclature of Fatty Acids

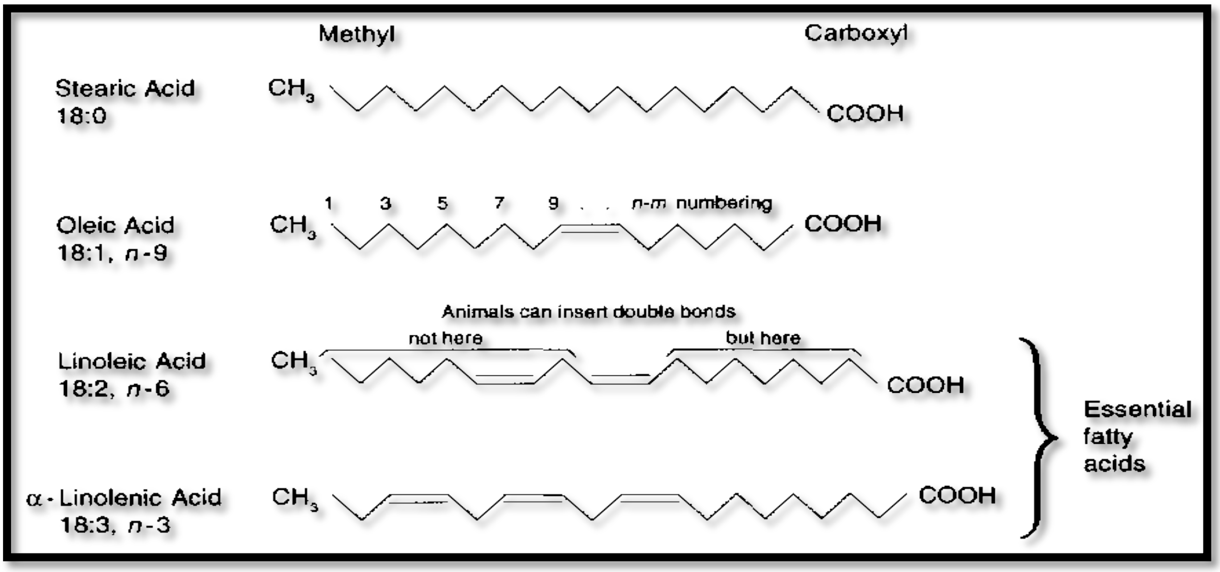
Carbon atoms are numbered from the carboxyl carbon (carbon No. 1). The carbon atoms adjacent to the carboxyl carbon (Nos. 2, 3, and 4) are also known as the α, β, and γ carbons, respectively, and the terminal methyl carbon is known as the ω or n-carbon. The Δ indicating the number and position of the double bonds; eg, Δ9 indicates a double bond between carbons 9 and 10 of the fatty acid; ω9 indicates a double bond on the ninth carbon counting from the ω- carbon.

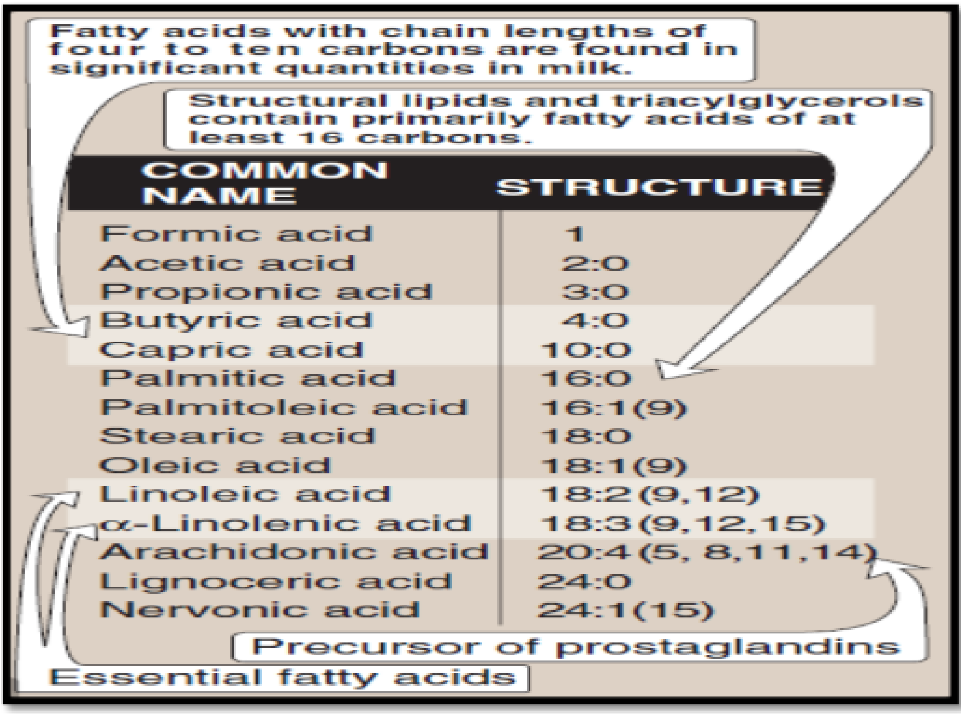


Oleic acid

3. Essential and non-essential fatty acids

If a fatty acid can only be obtained from the diet (for humans) then the fatty acid is an essential fatty acid. Two fatty acids cannot be synthesized in the human body and are therefore essential. These are linoleic and linolenic fatty acids, which are both unsaturated. Non-essential fatty acids can be made by the human body and so do not need to be obtained from diet alone. These are made from carbohydrates and proteins or from other fatty acids.



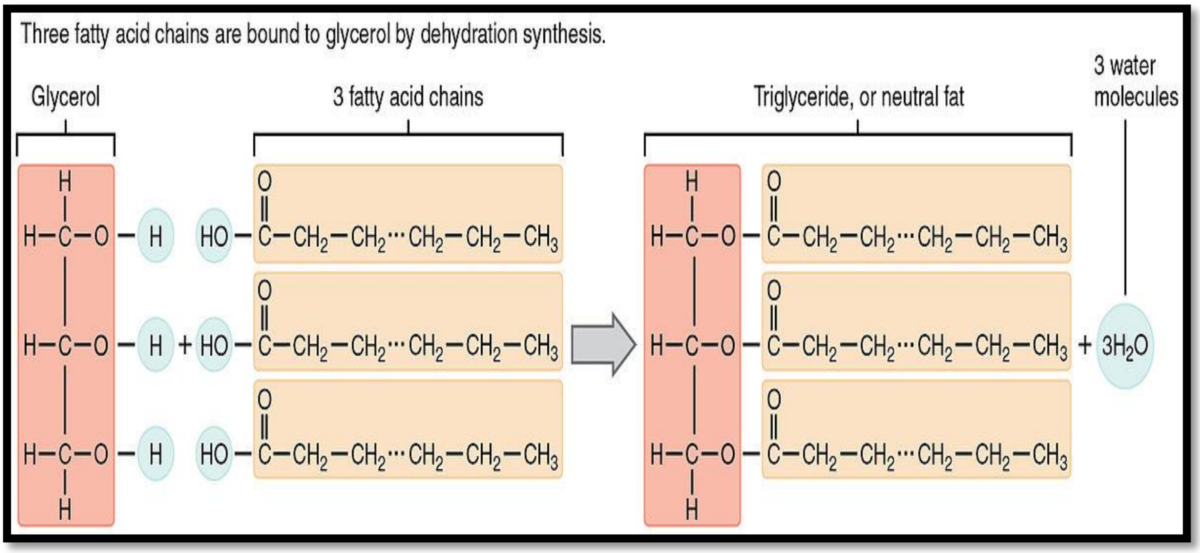


COMMON NAME	STRUCTURE
Formic acid	1
Acetic acid	2:0
Propionic acid	3:0
Butyric acid	4:0
Capric acid	10:0
Palmitic acid	16:0
Palmitoleic acid	16:1(9)
Stearic acid	18:0
Oleic acid	18:1(9)
Linoleic acid	18:2(9,12)
α-Linolenic acid	18:3(9,12,15)
Arachidonic acid	20:4(5, 8,11,14)
Lignoceric acid	24:0
Nervonic acid	24:1(15)

Some fatty acids of physiologic importance

Triacylglycerols

Triacylglycerols, also called triglycerides (TG), are the simplest of lipids composed of three fatty acids each in ester linkage with a single glycerol molecule. Those containing the same kind of fatty acid in all three positions are called simple triacylglycerols. For example, tripalmitin, tristearin and triolein that contain three palmitic, stearic and oleic acids respectively. However, majority of the naturally occurring triacylglycerides contain more than one type of fatty acids and are hence called mixed triacylglycerides. For example, a triacylglycerides with palmitic acid at position 1, oleic acid at position 2 and stearic acid at position 3 referred to as 1-palmitoyl 2-oleoyl 3-stearoylglcerol.



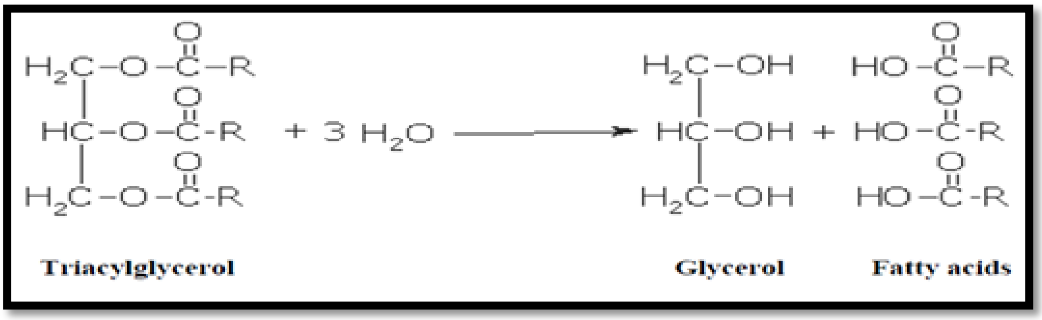
Physical properties

Triacylglycerols are non-polar, hydrophobic and essentially insoluble in water since the polar hydroxyls of glycerol and the polar carboxylates of fatty acids are bound in ester linkage.

Chemical properties

1. Hydrolysis

Triglycerides are very slowly hydrolyzed to glycerol and fatty acids when boiled at atmospheric pressure. They may also be hydrolyzed by the action of the enzymes known as lipases that are widespread in human.

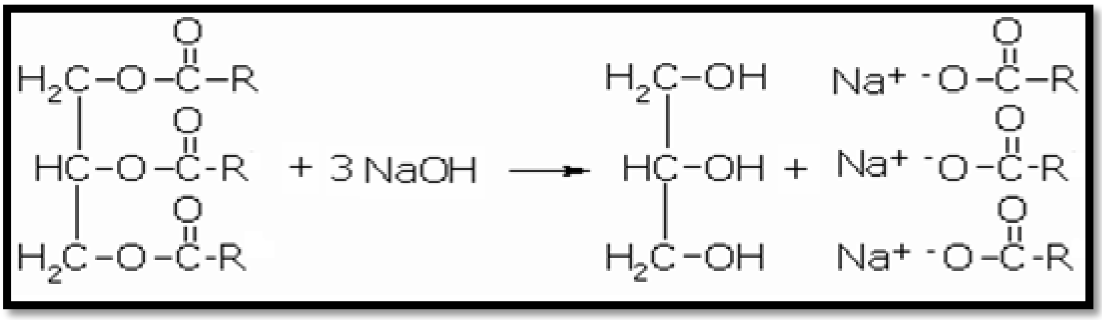


Iodine number

The relative unsaturation of fat is determined by measuring the quantity of halogen absorbed by the glycerides. The **iodine number** of a given fat is defined as the percent of iodine absorbed by the fat, or the grams of iodine absorbed by 100 grams of fat.

2. Saponification

The triglycerides may be readily decomposed into glycerol and salts of constituent fatty acids (soaps) by boiling with strong bases such as NaOH or KOH. This process is called saponification.



Triacylglycerol **Glycerol** **Soap**

Saponification number

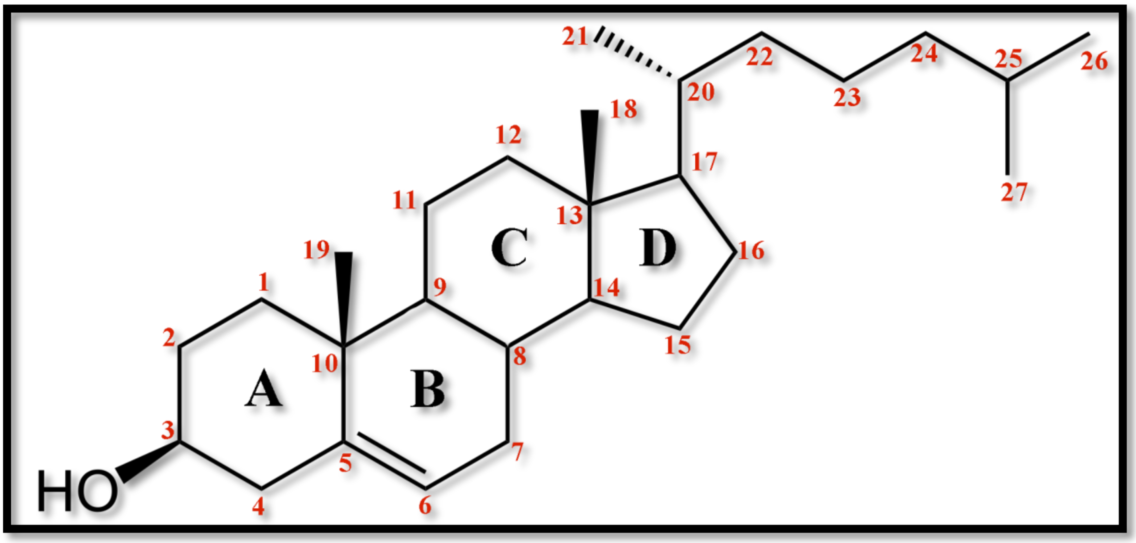
The number of milligrams of potassium hydroxide required to completely saponify one gram of oil or fat is called saponification number.

Cholesterol

Cholesterol, the characteristic steroid alcohol of animal tissues, performs a number of essential functions in the body. For example, cholesterol is a **structural** component of all cell membranes, cholesterol is a precursor of **bile acids**, **steroid hormones**, and **vitamin D**. High levels of blood cholesterol are associated with plaque formation, causing the narrowing of blood vessels (**atherosclerosis**) and increased risk of cardio-, cerebro- and peripheral vascular disease.

Structure of cholesterol

Cholesterol is a very hydrophobic compound, composed from 27 carbon atom. It consists of four fused hydrocarbon rings (A-D) called the “steroid nucleus”(three cyclohexane A, B, C, and one cyclopentane D), and it has an eight-carbon, branched hydrocarbon chain attached to carbon 17 of the D ring. Ring A has a hydroxyl group at carbon 3, and ring B has a double bond between carbon 5 and 6.



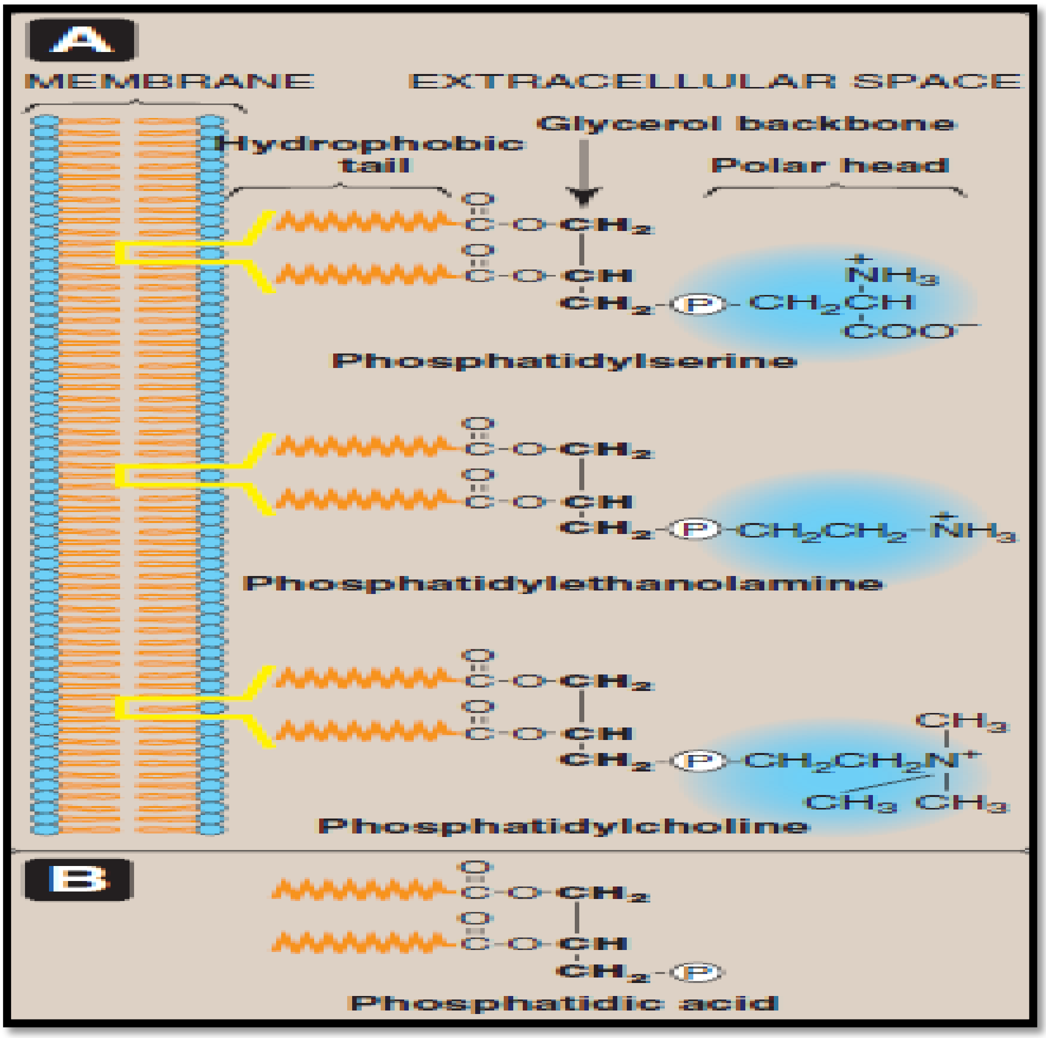
Structure of cholesterol

Most plasma cholesterol is in an esterified form with a fatty acid attached at carbon 3, which makes the structure even more hydrophobic than free (unesterified) cholesterol. Because of their hydrophobicity, cholesterol and its esters must be **transported** in association with protein as a component of a **lipoprotein** particle.

Phospholipids

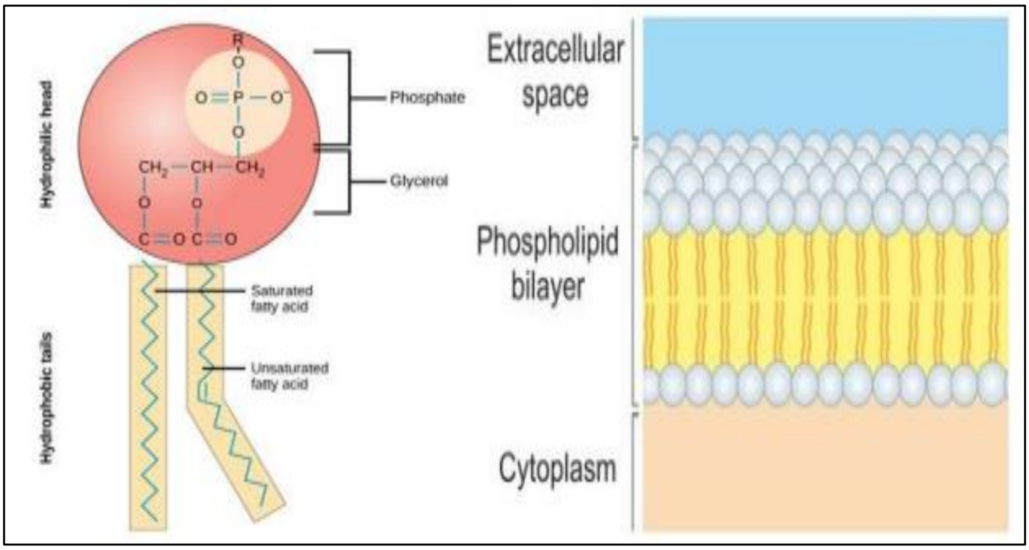
Phospholipids are polar, ionic compounds composed of an alcohol that is attached by a **phosphodiester bridge** to either diacylglycerol or sphingosine. Like fatty acids, phospholipids are **amphipathic** in nature, that is, each has a **hydrophilic head** (the phosphate group plus whatever alcohol is attached to it, for example, serine, ethanolamine, and choline) and a long, **hydrophobic tail** (containing fatty acids).

Phospholipids are the predominant lipids of cell membranes. In membranes, the hydrophobic portion of a phospholipid molecule is associated with the nonpolar portions of other membrane constituents, such as glycolipids, and cholesterol. The hydrophilic (polar) head of the phospholipid extends outward, interacting with the intracellular or extracellular aqueous environment.



Phosphatidic acid (PA) + Ethanolamine → phosphatidylethanolamine (cephalin)

Phosphatidic acid (PA) + Choline → phosphatidylcholine (lecithin)



Digestion of dietary lipid

About **90%** of **dietary** lipids is **triacylglycerol**. The remainder of the dietary lipids consists primarily of cholesterol, cholesteryl esters, phospholipids, and unesterified (free) fatty acids.

1. Digestion by mouth

A few things happen in the mouth that start the process of lipid digestion. Chewing mechanically breaks food into smaller particles and mixes them with saliva. An enzyme called lingual lipase is produced by cells on the tongue and begins some enzymatic digestion of triglycerides, cleaving individual fatty acids from the glycerol backbone.

2. Digestion by stomach

Cells in the stomach produce another lipase, called gastric lipase that also contributes to enzymatic digestion of triglycerides. Lingual lipase swallowed with food and saliva also remains active in the stomach. Triglycerides molecules, particularly those containing fatty acids of **short or medium chain length** (fewer than 12 carbons, such as are found in milk fat), are the **primary target** of this enzyme.

3. Emulsification of dietary lipid in the small intestine

The emulsification of dietary lipids occurs in the duodenum. Emulsification increases the surface area of the hydrophobic lipid droplets so that the digestive enzymes, which work at the interface of the droplet and the surrounding aqueous solution, can act effectively. Emulsification is accomplished by two complementary mechanisms, namely, use of the detergent properties of the bile salts, and mechanical mixing due to peristalsis. Bile salts, made in the liver and stored in the gallbladder, are derivatives of cholesterol.

4. Degradation of dietary lipids by pancreatic enzymes

The dietary TAG, cholesteryl esters, and phospholipids are enzymically degraded by pancreatic enzymes, whose secretion is hormonally controlled.

A. Triglycerides degradation:

Pancreatic lipase, which preferentially removes the fatty acids at carbons 1 and 3. The primary products of hydrolysis are thus a mixture of 2-monoacylglycerol (2-MAG) and free fatty acids (FFA).

B. Cholesteryl ester degradation:

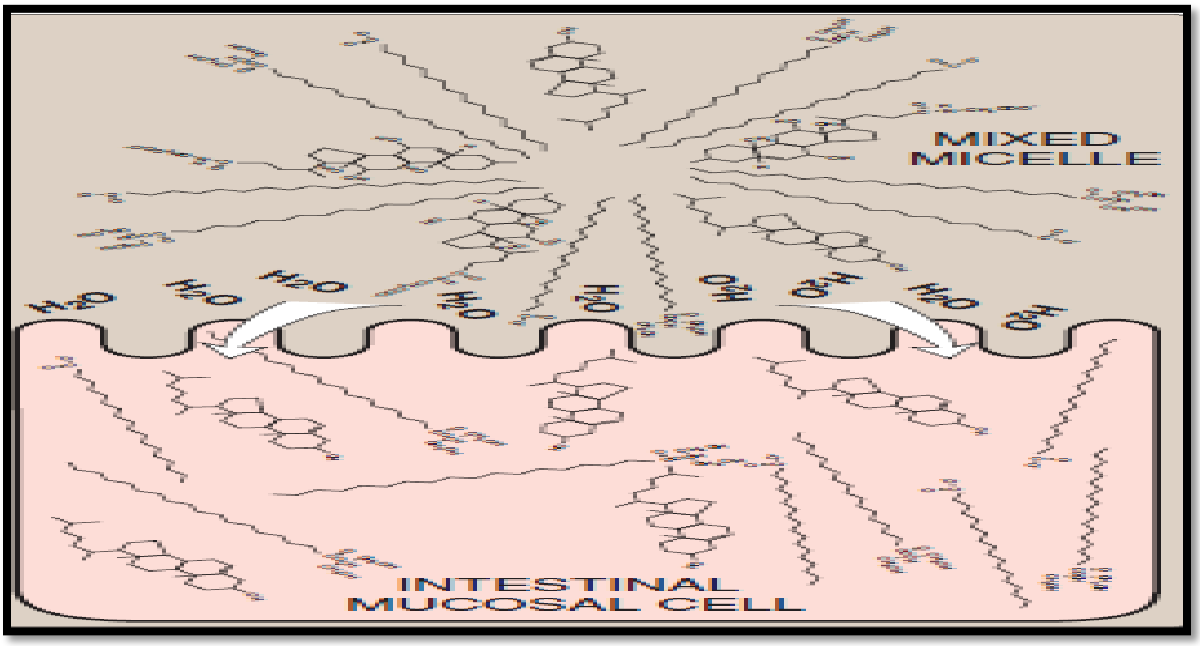
Most dietary cholesterol is present in the free (nonesterified) form, with 10–15% present in the esterified form. Cholesteryl esters are hydrolyzed by pancreatic cholesterol esterase, which produces cholesterol plus free fatty acids.

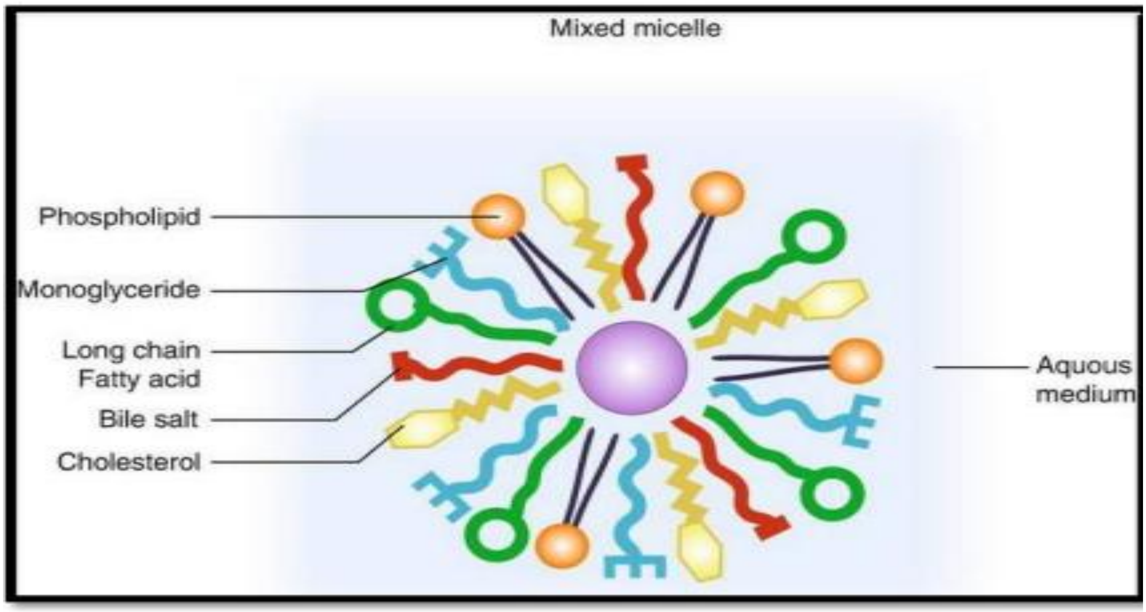
C. Phospholipid degradation:

Phospholipase A_2 removes one fatty acid from carbon 2 of a phospholipid, leaving a lysophospholipid. For example, phosphatidylcholine becomes lysophosphatidylcholine. The remaining fatty acid at carbon 1 can be removed by lysophospholipase, leaving a glycerylphosphoryl base.

Absorption of lipids

Free fatty acids, free cholesterol, and 2-monoacylglycerol are the primary products of lipid digestion in the jejunum. These, plus bile salts and fat soluble vitamins (A, D, E, and K), form mixed micelles disk shaped clusters of amphipathic lipids that combine with their hydrophobic groups on the inside and their hydrophilic groups on the outside. Mixed micelles are, therefore, soluble in the aqueous environment of the intestinal lumen. The hydrophilic surface of the micelles facilitates the transport of the hydrophobic lipids through the unstirred water layer to the brush border membrane where they are absorbed. Short and medium chain length fatty acids do not require the assistance of mixed micelles for absorption by the intestinal mucosa.





Absorption of lipids contained in a mixed micelle