CHY2026: General Biochemistry

Unit 3: Lipid Chemistry

Lipids

- The are heterogeneous and are related to fatty acids
- They include fats, oils and waxes
- Fatty acids have the general formula R-COOH

  where R = H, hydrocarbon chain

- At pH 7 all free fatty acids have an ionized carboxylate
- The long R group makes the molecule non polar and is hydrophobic

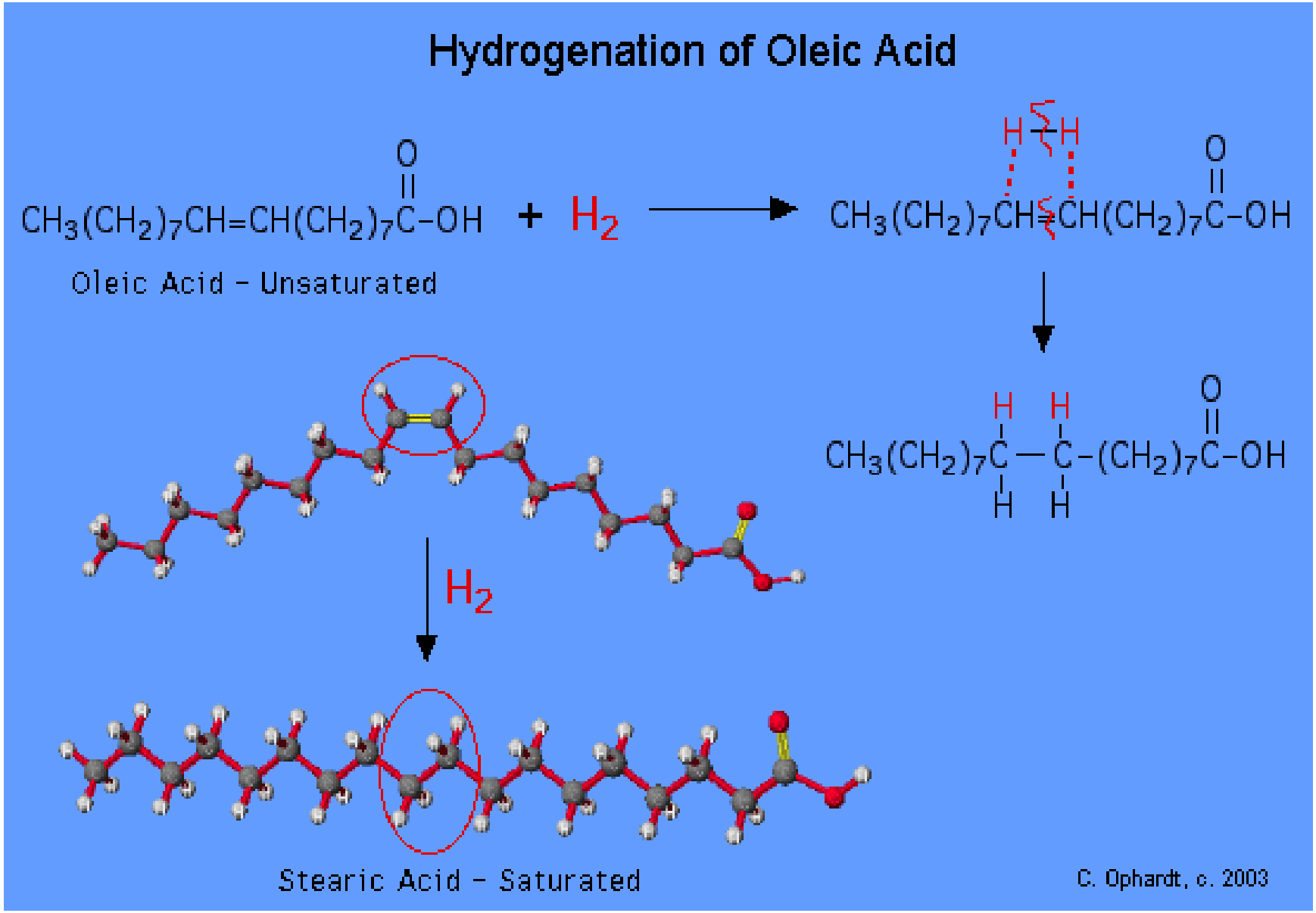
Physical Properties of Fats and Oils

- Colourless, odourless
- Absorb a variety of odours
- Insoluble in water abut soluble in organic solvents such as choloform, ether, acetone and benzene
- They have relatively high melting and boiling point (increases with an increase in chain length)

Chemical Properties

Hydrogenation

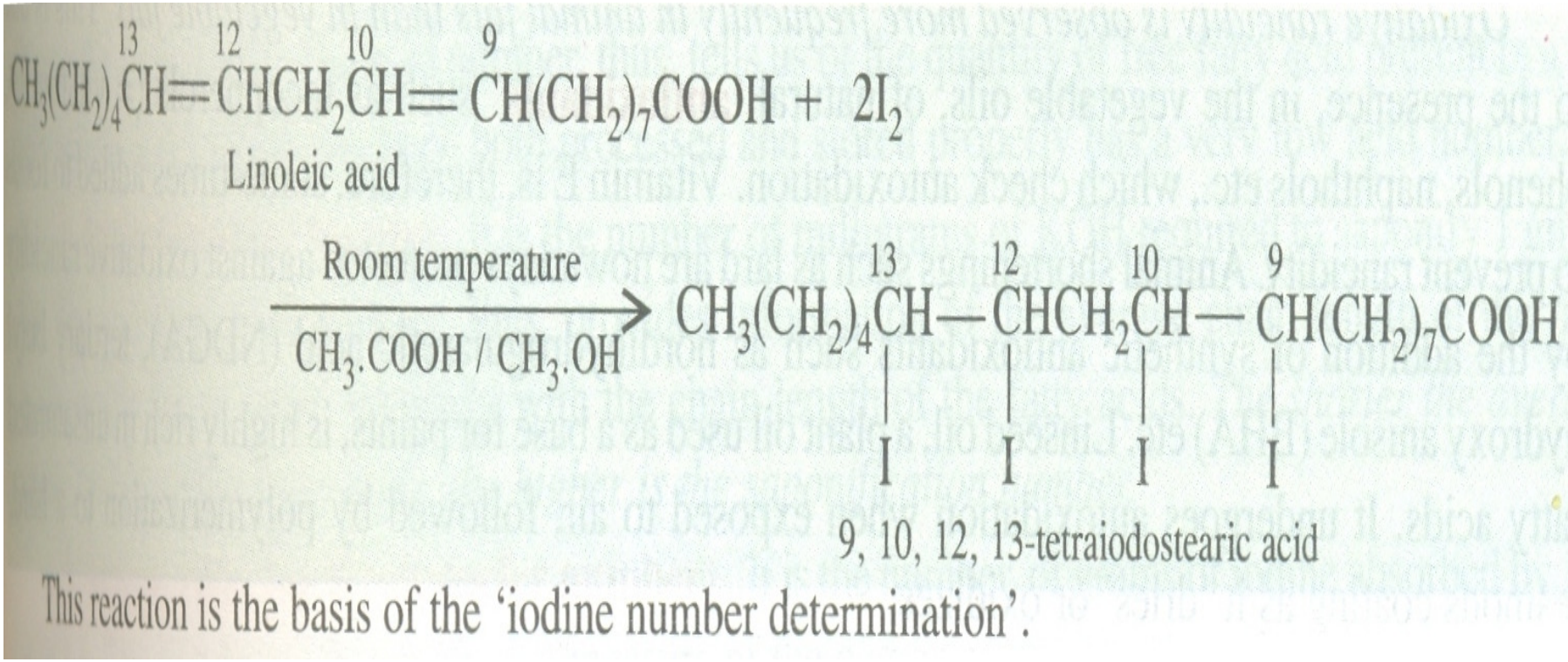
- Unsaturated fatty acids react with gaseous hydrogen to yield saturated fatty acids
- Catalyst:Pt or Ni
- This reaction is used in the manufacture of candles, vegetable shortening and margarines
- During partial hydrogenation, some of the unsaturated fatty acids, which are normally found as the cis isomer about the double bonds, are changed to a **trans** double bond and remain **unsaturated**
- **Trans fat** have a more linear shape than **cis fat**
- **Trans fat** give products a longer shelf life but raises bad cholesterol (LDL)
- Complete hydrogenation is avoided because a completely saturated fatty acid is hard and brittle



http://chemwiki.ucdavis.edu/Biological_Chemistry/Lipids/Hydrogenation_of_Unsaturated_Fats_or_Trans_Fat

Halogenation

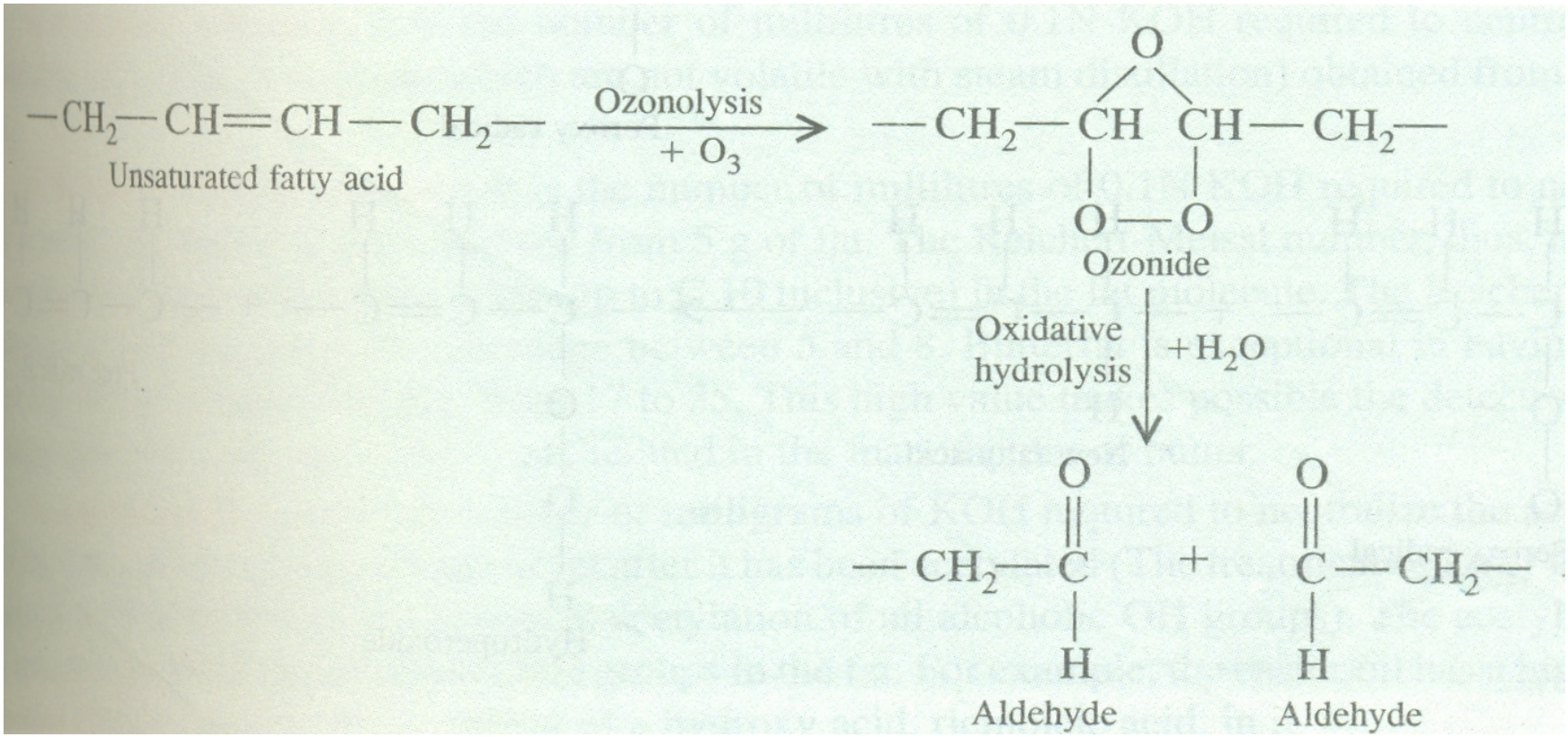
- Halogens (Br_2 and I_2) can be added to unsaturated fatty acids at room temperature in acetic acid



Oxidation

(a) Ozone

The reaction with ozone yields two aldehyde groups



(b) With $KMnO_4$

(*b*) With $KMnO_4$ – Under mild conditions, the *glycols* are formed at the sites of double bon

$$CH_3(CH_2)_7\overset{10}{C}H{=}\overset{9}{C}H(CH_2)_7COOH \xrightarrow{KMnO_4} CH_3(CH_2)_7\overset{10}{C}H(OH){-}\overset{9}{C}H(OH)(CH_2)_7COOH$$

Oleic acid

9, 10-dihydroxystearic acid

Under vigorous conditions, the same reagent cleaves the molecule at the double bond oxidizes the terminal portions to the *carboxyl group*.

$$CH_3(CH_2)_7\overset{10}{C}H{=}\overset{9}{C}H(CH_2)_7COOH \xrightarrow{KMnO_4} CH_3(CH_2)_7COOH + HOOC(CH_2)_7CO$$

Oleic acid — Pelargonic acid — Azelaic acid

The oxidation reactions have been extensively used in establishing the position of double bon in the fatty acid chain. This gives important clues regarding lipid structure.

Oxidative Rancidity

- Highly unsaturated oils are spontaneously oxidized by atmospheric oxygen and ordinary temperatures
- This is a slow reaction → short chain fatty acids and aldehydes resulting in a rancid odour or taste to the fats

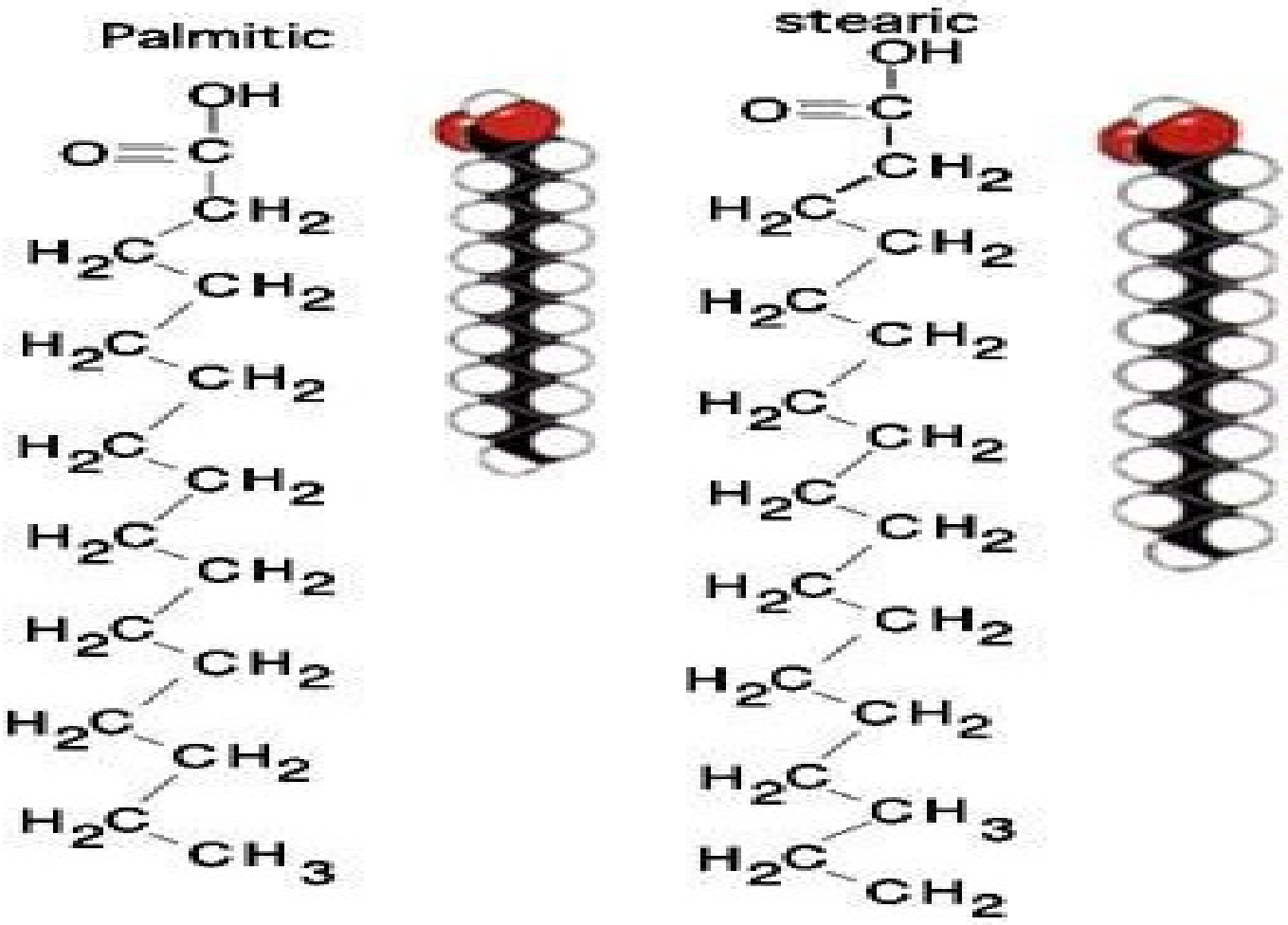
Fatty Acids

- General formula $C_nH_{2n+1}COOH$
- When the fatty acids are not attached to other molecules: "free" fatty acids
- Fatty acids are amphipathic compounds: hydrophilic carboxylic group and hydrophobic aliphatic tail
- If the hydrocarbon chain contains no double bonds then the fatty acid is **saturated**
- Even number straight chain fatty acids are found abundantly in plants and animals (C16 – palmitic acid; C18 stearic acid ……C10)… reflecting the pathway for their biosynthesis from the two-carbon building-block acetyl CoA
- Less than 1% of the total fatty acids are odd number fatty acids
- Bacteria, however, possess the ability to synthesize odd- and branched-chain fatty acids. As a result, ruminant animal fat contains odd-numbered fatty acids (15), due to the action of bacteria in the rumen

Table 12–2. Straight chain saturated fatty acids, commonly found in natural fats

Trivial name	*Systematic name**	*Carbon skeleton*	*Structure†*	*Common sourc*
Butyric	*n*-Butanoic	4 : 0	$CH_3(CH_2)_2COOH$	Butter
Caproic	*n*-Hexanoic	6 : 0	$CH_3(CH_2)_4COOH$	Coconut and palm oils
Caprylic	*n*-Octanoic	8 : 0	$CH_3(CH_2)_6COOH$	Coconut and palm oils
Capric	*n*-Decanoic	10 : 0	$CH_3(CH_2)_8COOH$	Coconut and palm oils
Lauric (*laurus*^{L} = laurel plant)	n-Dodecanoic	12 : 0	$CH_3(CH_2)_{10}COOH$	Laurel oil, Spermaceti
Myristic (*Myristica*^{L} = nutmeg genus)	*n*-Tetradecanoic	14 : 0	$CH_3(CH_2)_{12}COOH$	Butter and wo fats
Palmitic (*palma*^{G} = palm tree)	*n*-Hexadecanoic	16 : 0	$CH_3(CH_2)_{14}COOH$	Animal and plant fats
Stearic (stear = hard fat)	*n*-Octadecanoic	18 : 0	$CH_3(CH_2)_{16}COOH$	Animal and plant fats
Arachidic (*Arachis*^{L} = legume genus)	*n*-Eicosanoic	20 : 0	$CH_3(CH_2)_{18}COOH$	Groundnut oil
Behenic	*n*-Docosanoic	22 : 0	$CH_3(CH_2)_{20}COOH$	Groundnut oil
Lignoceric (*lignum*^{L} = wood; *cera*^{L} = wax)	*n*-Tetracosanoic	24 : 0	$CH_3(CH_2)_{22}COOH$	Groundnut and Rapeseed oils
Cerotic	*n*-Hexacosanoic	26 : 0	$CH_3(CH_2)_{24}COOH$	Wool fat
Montanic	*n*-Octacosanoic	28 : 0	$CH_3(CH_2)_{26}COOH$	—

Saturated Fatty Acids



Fatty acids

- The hydrocarbon chain of fatty acids sometimes contain double bond(s) and are called **unsaturated fatty acids**
- Unsaturated fatty acids may be classified based on the degree of unsaturation

monoethanoid acids: oleic acid

Diethanoid acids: linoleic acid

linolenic acid

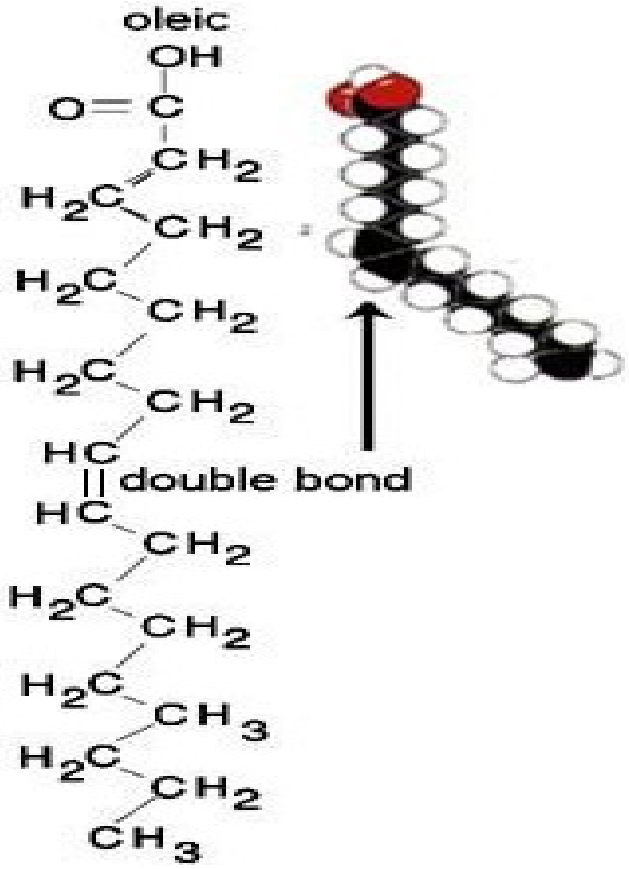
} EFA (must be obtained from Triethanoid acid: diet)

N.B all foods contain small quantities of bound fats or invisible fats (takes care of half to the daily fat requirements

- Many fatty acids are unsaturated, some are polyunsaturated, e.g., those derived from linoleic acid

Trivial name	*Systematic name*	*Carbon skeleton*	*Structure*	*Common source*
Crotonic	2-butenoic	4 : 1 ; 2	$CH_3CH=CHCOOH$	Croton oil
Myristoleic	9-tetradecenoic	14 : 1 ; 9	$CH_3(CH_2)_3CH=CH(CH_2)_7COOH$	*Pycnanthyus*
Palmitoleic	9-hexadecenoic	16 : 1 ; 9	$CH_3(CH_2)_5CH=CH(CH_2)_7COOH$	Animal and plant fats
Oleic (*oleum*^{G} = oil)	9-octadecenoic	18 : 1 ; 9	$CH_3(CH_2)_7CH=CH(CH_2)_7COOH$	Animal and plant fats
Vaccenic	11-octadecenoic	18 : 1 : 11	$CH_3(CH_2)_5CH=CH(CH_2)_9COOH$	Bacterial fat
Linoleic (*linon*^{G} = flax)	9, 12-octadecadienoic	18 : 2 ; 9, 12	$CH_3(CH_2)_4CH=CHCH_2CH=CH(CH_2)_7COOH$	Linseed and cottonseed oils
Eleostearic	9, 11, 13-octadecatrienoic	18 : 3 ; 9, 11, 13	$CH_3(CH_2)_3CH=CH—CH=CH—CH=CH(CH_2)_7COOH$	Tung oil
Linolenic	9, 12, 15-octadecatrienoic	18 : 3 ; 9, 12, 15	$CH_3CH_2CH=CHCH_2CH=CHCH_2CH=CH(CH_2)_7COOH$	Linseed oil
Arachidonic	5, 8, 11, 14-eicosatetraenoic	20 : 4 ; 5, 8, 11, 14	$CH_3(CH_2)_4CH=CHCH_2CH=CHCH_2CH=CHCH_2CH=CH(CH_2)_3COOH$	Animal fat
Nervonic	15-tetracosenoic	24 : 1 ; 15	$CH_3(CH_2)_7CH=CH(CH_2)_{13}COOH$	–

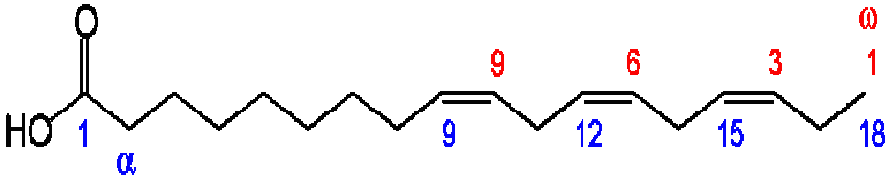
Unsaturated Fatty Acids

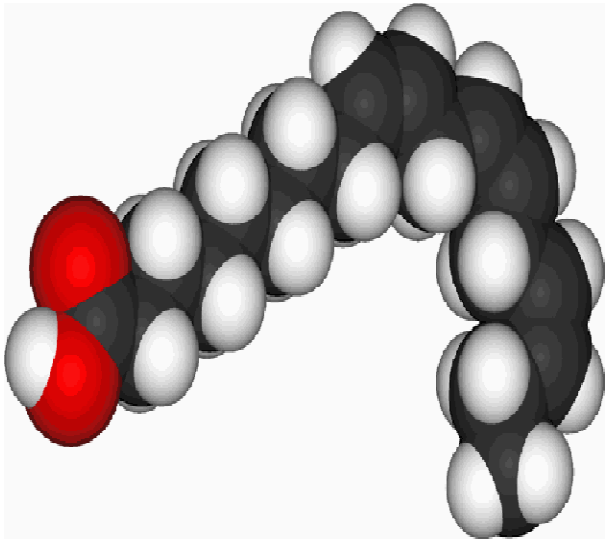


Linoleic Acid

(once called vitamin F)

Linolenic Acid





Saturated fatty acids	Unsaturated fatty acids
Solids at room temperature	Liquid at room temperature
They are found in animals	They are found in plants
Stored mainly in liver and bone	Stored in seeds and fruits
Oxidative rancidity is observed less frequently	Oxidative rancidity observed more frequently

Fatty acids

- The body is able to convert stearic acid to oleic acid by inserting a double bond but incapable of inserting further double bonds
- Unsaturated fatty acids from vegetable oil can have their double bonds removed by adding hydrogen (Hydrogenation): hydrogenated fat (saturated fat even though derived from vegetable oil)

Chemical Properties of Fatty Acids

- Fatty acids are important sources of fuel …when metabolized they yield large quantities of ATP
- Many cell types can use either glucose or fatty acids for fuel. In particular the heart and skeletal muscle prefer fatty acids
- Many naturally occurring fatty acids contain 2-3 double bonds in the cis position
- The carbon chains of saturated fatty acid tend to be fully extended because this minimizes repulsion between neighboring methylene groups
- The cis conformation of the double bond of an unsaturated fatty acid puts a rigid bend in the carbon chain that interferes with packing causing reduced van der Waals attractions between molecules
- Therefore unsaturated fatty acids have lower melting points

Functions of Lipids

- Storage form of energy
- They are insoluble and can act as food storage
- Membrane structure involvement
- They have high insulating capacity
- Absorption and transport of fatty acids (phospholipids)
- They play a role in hormone synthesis (cholesterol)
- They are carriers of fat soluble vitamins (Vit. A, D, E, K)
- Antibiotic agent (squalamine – steroid found in sharks)

Classification of Lipids

- Lipids can be classified as –

  (a) **Simple lipids/homolipids** – e.g. triglycerides (triacylglycerol), oils and waxes

  (b) **Compound lipids/ heterolipids** – e.g. phospholipids and glycolipids,

  (c) **Derived Lipids** - they are derived from simple and compound lipids e.g. steroids

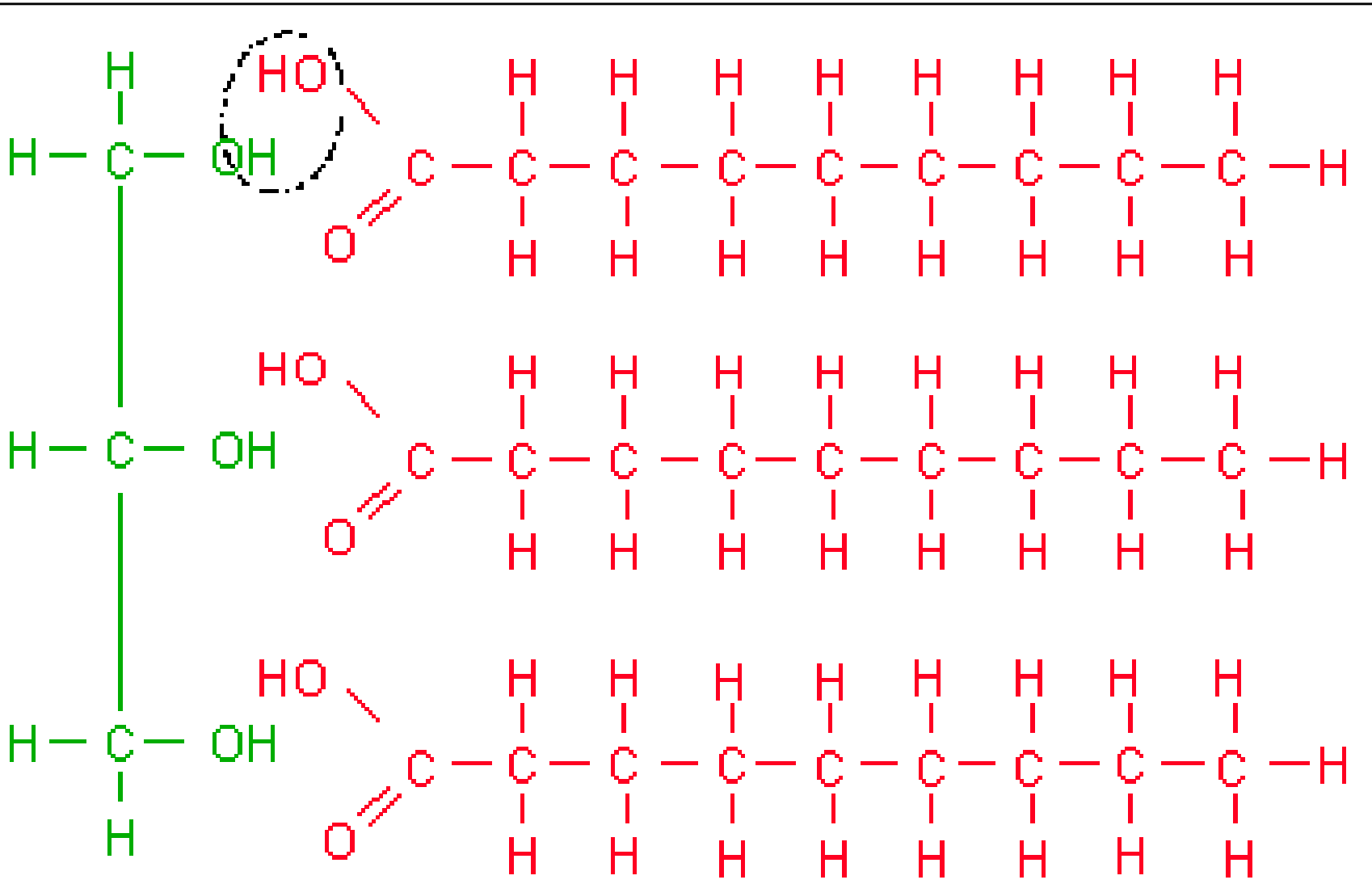
Simple Lipids: Triglycerides/triacylglycerols

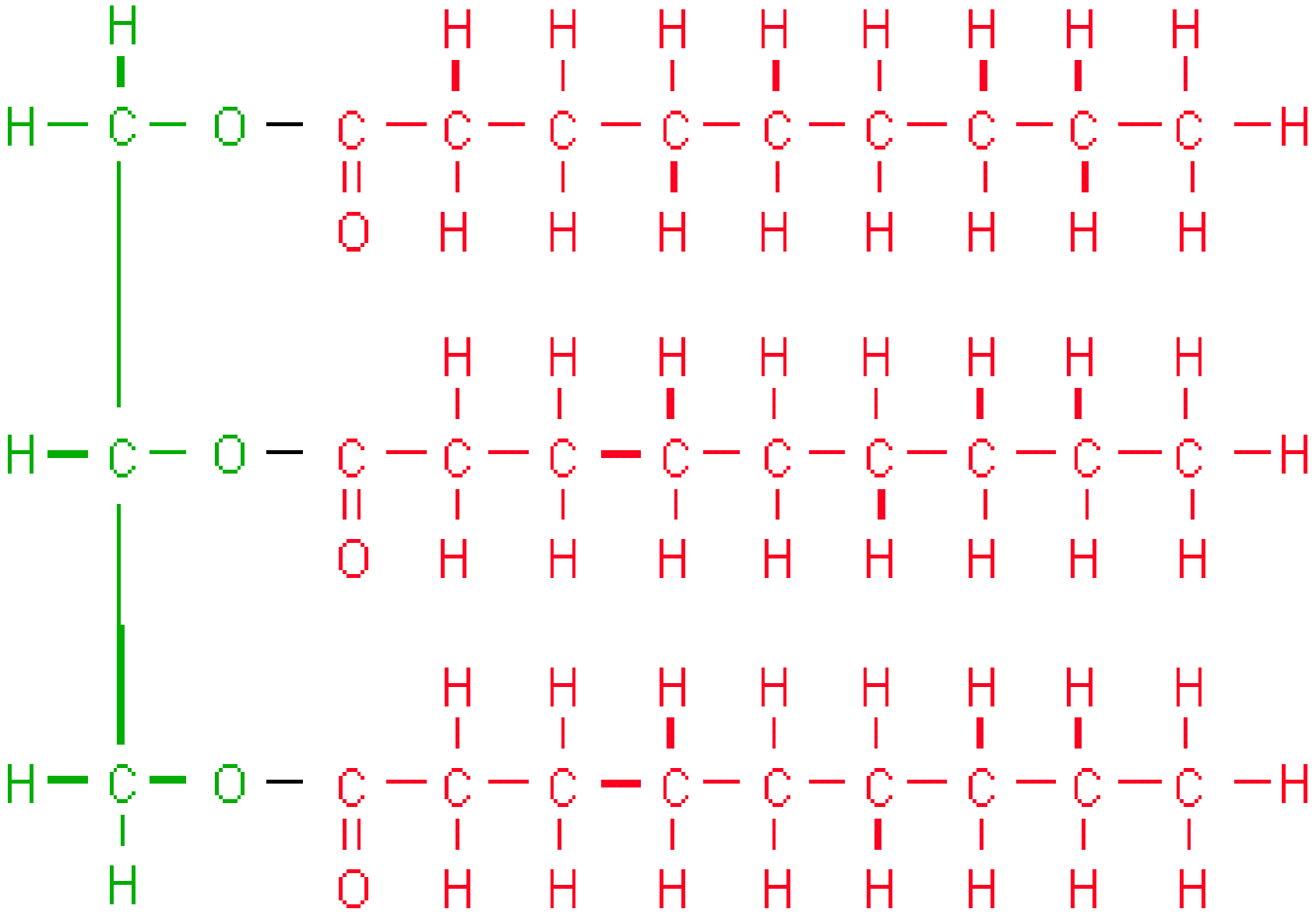
- They are the most abundant of all lipids
- Make up 98% of total dietary lipids (remaining 2 %: phospholipids and cholesterol)
- Major component of fat storage in plant and animal cells (adipocytes)

  (triglycerides are much better adapted than glycogen to serve as a storage form of energy…longer to digest…greater satiety value)
- They are non polar and are therefore insoluble in water
- They are less dense than water → floats
- It is formed via **esterification** - reaction between an alcohol **(glycerol)** and a tricarboxylic acid
- Triglycerides can undergo hydrolysis to form free glycerol and fatty acids

Chemical Nature of Triglycerides

- The chain lengths of the fatty acids in naturally occurring triglycerides vary, but most contain 16, 18, or 20 carbon atoms


Glycerol
Fatty Acids



Functions of Triglycerides/Fats

- They store long term energy

  The provide more energy per gram (9 kcal/gram) than proteins or carbohydrates (~4.0 kcal/gram)

- They have greater satiety value than carbohydrates
- They act as insulators for the body (FACT! The human body has enough fat to make 7 bars of soap)
- They act as shock absorbers for organs
- May make up more than 90% of the cytoplasm
- % fat women 25 – 31 % and males 18 – 24 %
- The % fat stored is sufficient to allow us to survive 2 -3 months. Glycogen only provides 1 day of energy

Functions of Triglycerides/Fats

- When the body has used up the calories from carbohydrates, which occurs after the first 20 minutes of exercise, it begins to depend on the calories from fat.
- Healthy skin and hair are maintained by fat. Fat helps the body absorb and move the vitamins A, D, E, and K through the bloodstream
- About 98% of the lipids in our diet are triglycerides, the remaining 2% consists of complex lipids and cholesterol
- Triglycerides cannot pass through cell membranes freely. Enzymes called lipoprotein lipases must break down triglycerides into free fatty acids and glycerol. The hormone glucagon stimulates the process
- The lipid is first emulsified by bile salts produced in the liver
- The glycerol component of triglycerides can be converted into glucose for brain fuel

Functions of Triglycerides

- The amount of fat in the diet, especially saturated fat is a health concern for a number of years…High levels of triglycerides in the bloodstream may result in atherosclerosis (hardening of the arteries) resulting in the risk of heart disease and stroke

Waxes

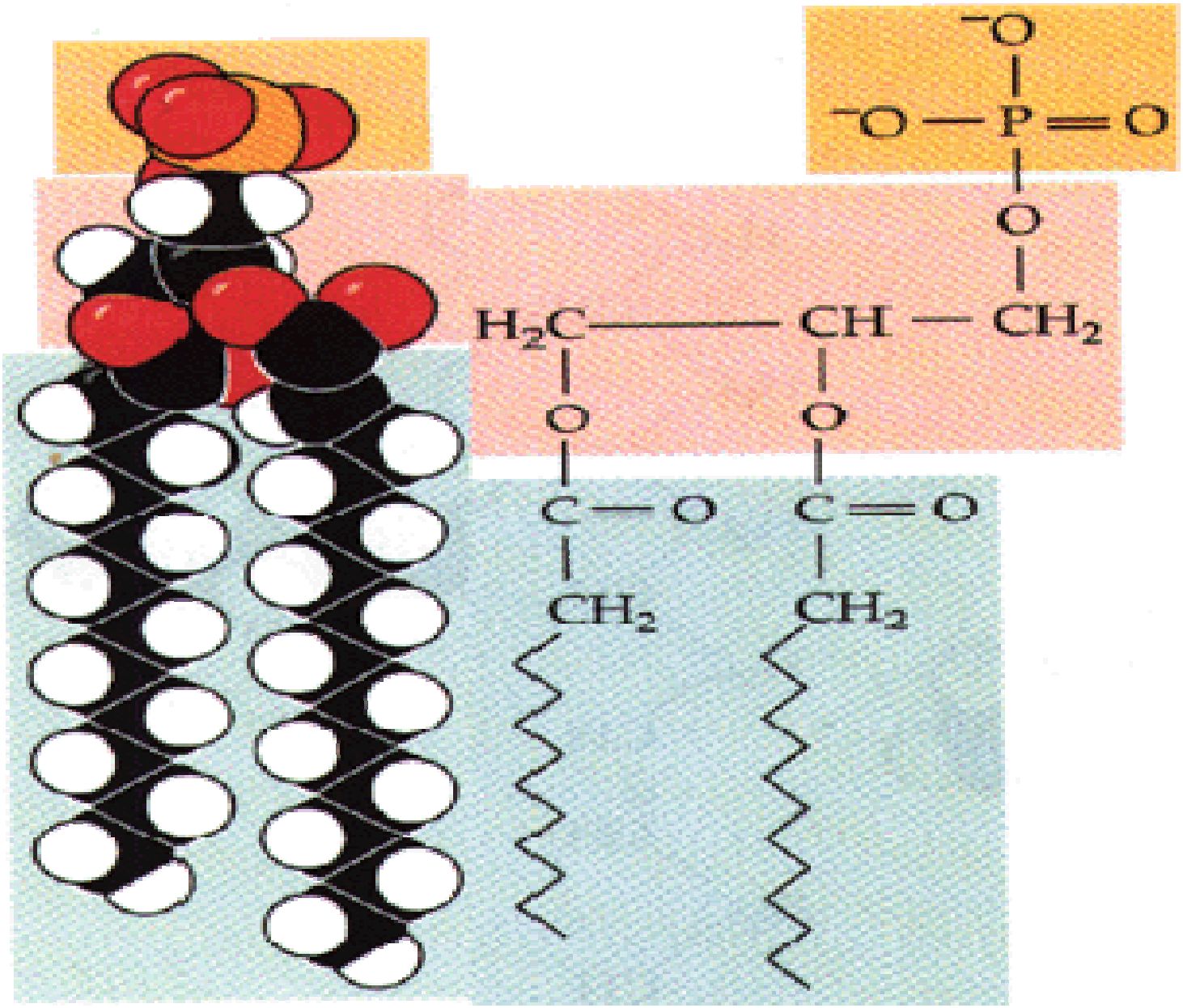
- They are esters of long chain saturated and unsaturated fatty acids
- Vertebrates: They are secreted by cutaneous glands as a protective clothing to keep skin pliable, lubricated and waterproof
- Waxes are used in cosmetics, polishes and ointments

Compound Lipids: Phospholipids

- They are the most abundant membrane lipids
- They differ from triglycerides having one polar head and two hydrophobic tails
- They are the structural components of the membrane (never stored in large amounts)
- Cell membranes separate the cell from the external environment and provide selective transport for nutrients and waste in and out of the cell
- Most lipids in the bilayer contains at least one unsaturated fatty acid
- This prevents the tight packing of the hydrophobic chain in the lipid bilayer giving fluid-like character to the membranes
- This property allows metabolic by-products to cross the cell membrane

Industrial Importance of Phospholipids

- Phospholipids have been commercially available as dietary supplements clinically proven safe and beneficial for the brain, liver, circulation, and intestinal tract
- Phospholipids are used for processing food and other products as it aids in the mixing of vegetable oils, butters, and other fatty ingredients so that they are uniformly distributed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$^{-}O-P=O$
O
H_2C CH CH_2
O O
C O C O
CH_2 CH_2

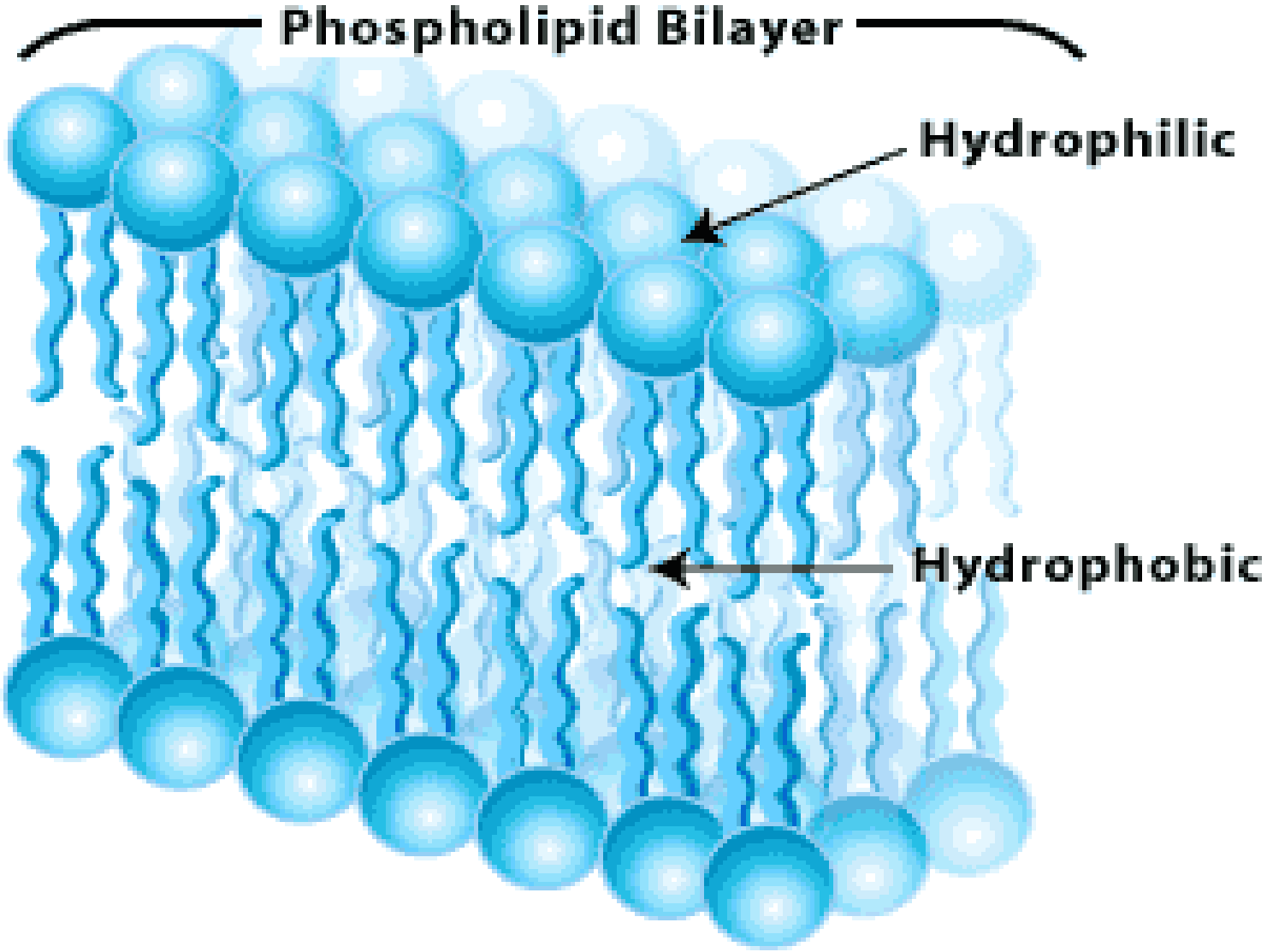
Compound Lipids: Phospholipids

- There are two types of phospholipids

  (a) phosphoglycerides – most common

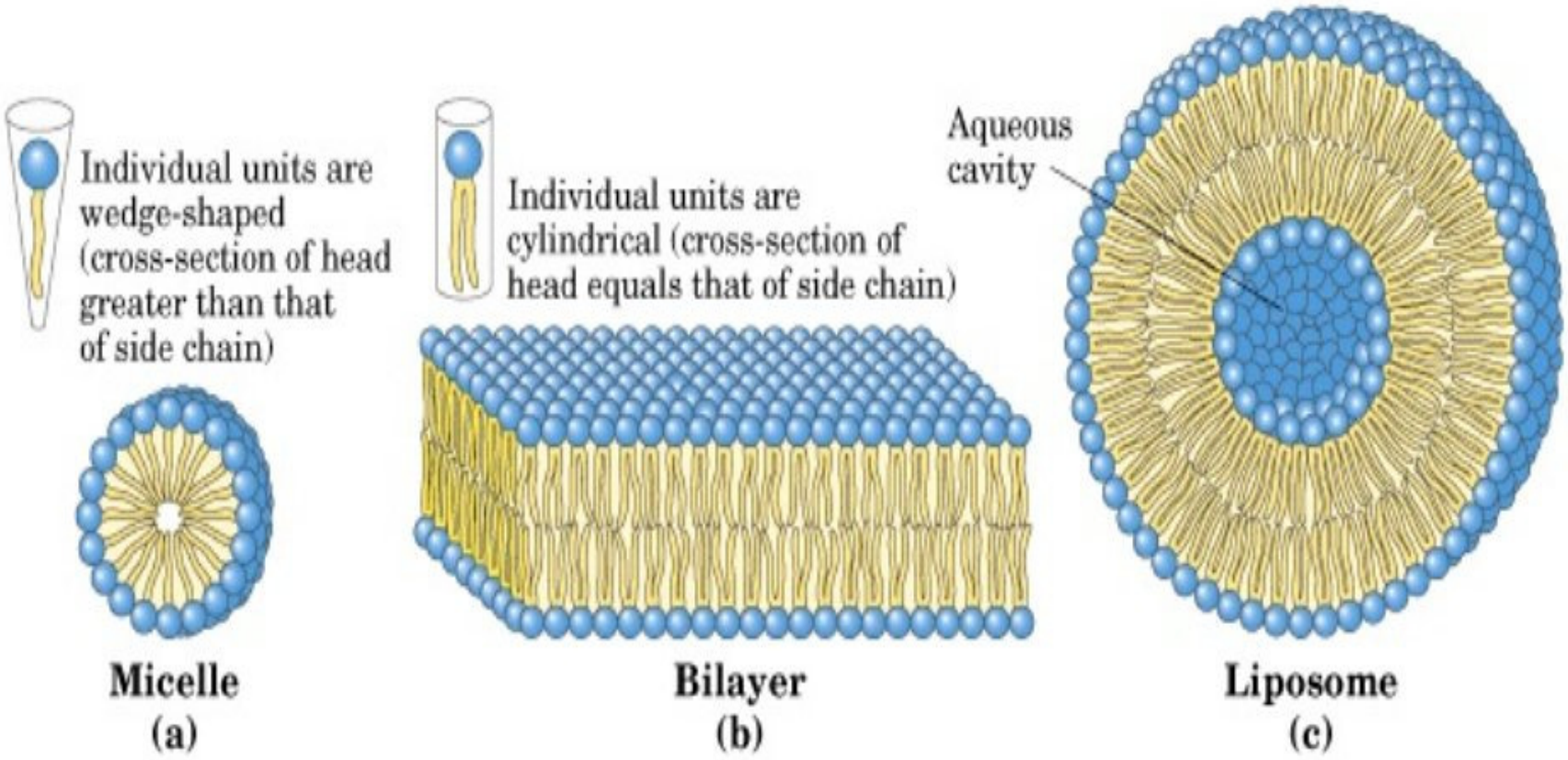
  (b) sphingomyelin

- The bipolar nature of phospholipids allows for the formation of bimolecular sheets **(bilayers)**



http://www.bioteach.ubc.ca/Bio-industry/Inex/graphics/lipidbilayer.gif

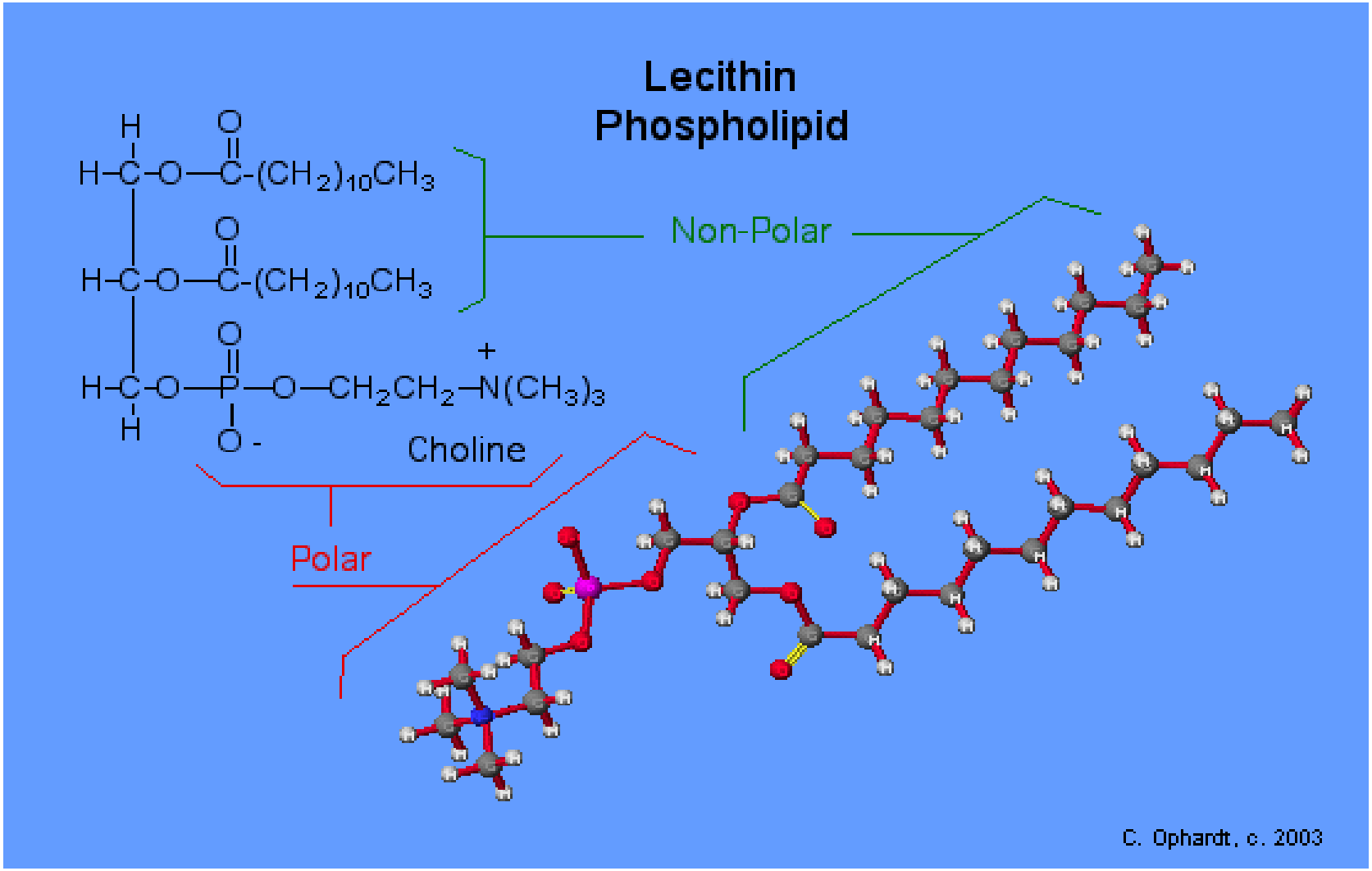
Lipid Bilayers



http://courses.cm.utexas.edu/jrobertus/ch339k/overheads-2/ch12_lipid-bilayer.jpg

Phosphoglyceride: Lecithin

- Found in oil seeds (soybean)
- Grandular and nervous tissues rich in these lipids
- They are required for the transport and utilization of other lipids…In its absence accumulation of lipids occur in the liver which can lead to cirrhosis
- It is able to emulsify (break up) fats in the bloodstream, enabling them to pass through the cell walls to be utilized for energy
- By emulsifying fats and helping in absorption for use by the body, lecithin will **reduce the cholesterol level in the blood**



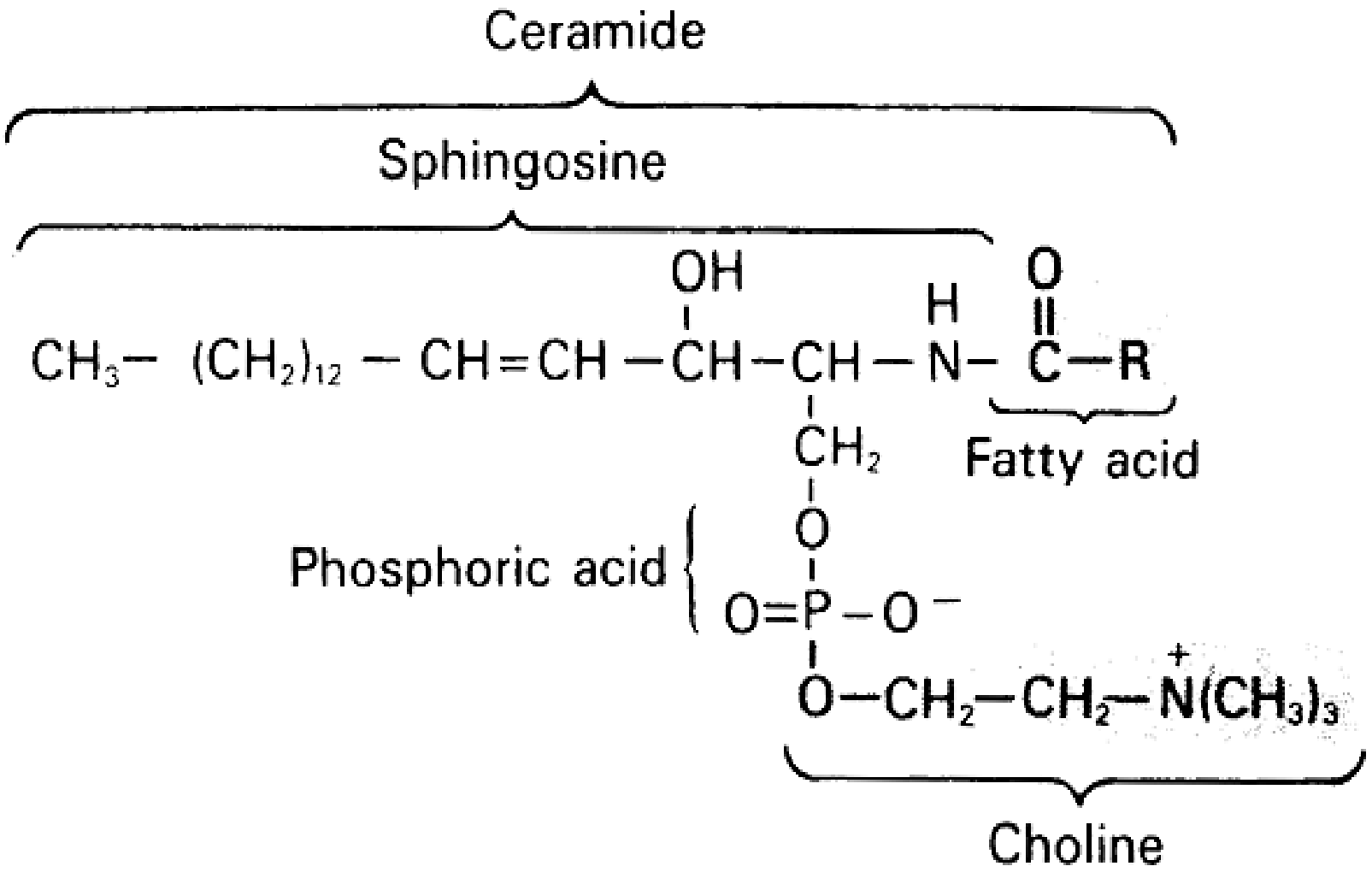
http://www.elmhurst.edu/~chm/vchembook/images/553lecithin.gif

Sphingolipids

- Sphingolipids are a class of lipids containing a backbone of sphingoid bases, where the alcohol portion is sphingosine
- A long chain fatty acid is connected to the amino group by an amide bond and the –OH group at the end of the chain is esterified by phosphorylcholine
- The combination of fatty acid and sphingosine is called the **ceramide** portion of the molecule because many of they are found in cerebrosides

Sphingomyelins

- Found in nerve tissues (myelin sheath)
- The myelin sheath consists of about 70% lipid and 30% protein in the lipid bilayer
- They differ from other lipids in that they lack glycerol in the structure
- Neimann-Pick Disease- is caused by a deficiency of an enzyme that breaks down excessive sphingomyelin which are therefore stored in the brain, spleen, marrow in large quantities causing mental retardation and blindness
- The myelin sheath allows for insulation and rapid conduction of electrical signals
- In multiple sclerosis, the myelin sheath gradually deteriorates resulting in muscle weariness, lack of coordination and lack of vision as demyelinated axons cannot conduct electricity



http://chemistry.gravitywaves.com/CHE450/Images14-20/Sphingomyelin.gif

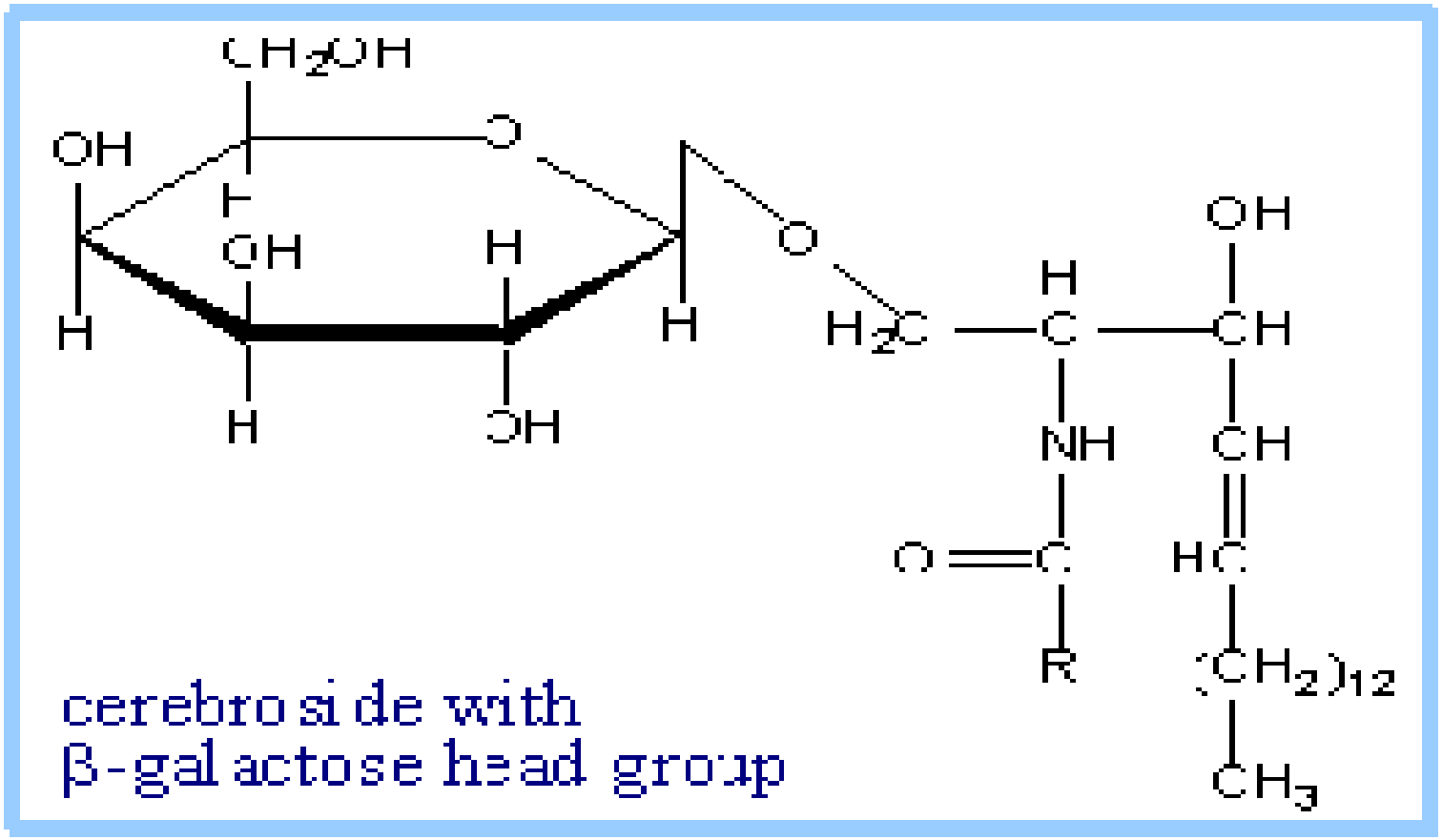
Industrial Importance of Sphingolipids

- Mammalian sphingolipid metabolites, such as ceramide and sphingosine-1-phospate, are important mediators in the signaling cascades involved in apoptosis, proliferation, and stress responses
- Sphingolipids are used in the preparation of a cosmetic or dermopharmaceutical composition protecting the skin and hair
- Dietary sphingolipids are used to lower plasma cholesterol and triacylglycerol and prevent liver steatosis (fatty liver- large droplets of fat, containing mostly triglycerides, collect within cells of the liver)

Compound Lipids: Glycolipids

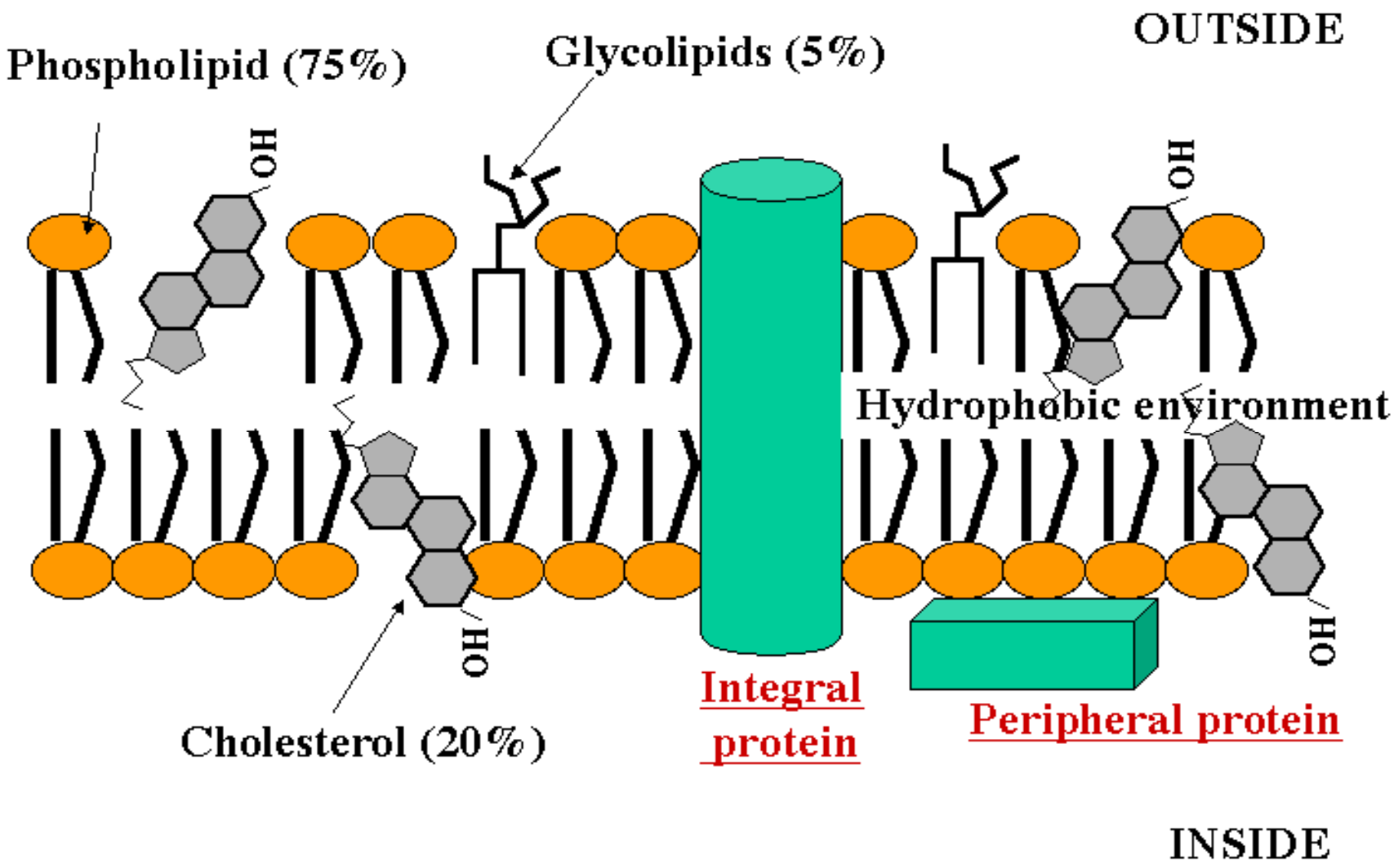
- These comprise of lipids linked to carbohydrates
- The carbohydrate portion forms a polar head
- They are an important constituent of cell membranes, particularly in the myelin sheath and outer surface of the nerve cells and the chloroplast membrane
- Both phospholipids and glycolipids form self-sealing lipid bilayers that are the basis of all cellular membranes

Compound Lipids: Glycolipids



http://www.rpi.edu/dept/bcbp/molbiochem/MBWeb/mb1/part2/images/cerebro.gif

Plasma membrane



Derived Lipids: Steroids (cholesterol)

- It is the most abundant steroid
- It is absent from plant cells, which is why vegetable oil is considered as cholesterol free…Found in the blood of all animals…Blood plasma levels range from 15 – 250 mg/100mls
- It is an important component of cell membrane
- Important precursor of many biological compounds e.g. bile acids and steroid hormones
- The end products of cholesterol metabolism ⟶ steroids (bile salts)
- These salts are formed in the liver and secreted into the small intestines to absorb lipids
- When the bile salts are attached to the lipid the complex is called a **chylomicron**
- Bile salts are largely reabsorbed during lipid absorption

Derived Lipids: Steroids (cholesterol)

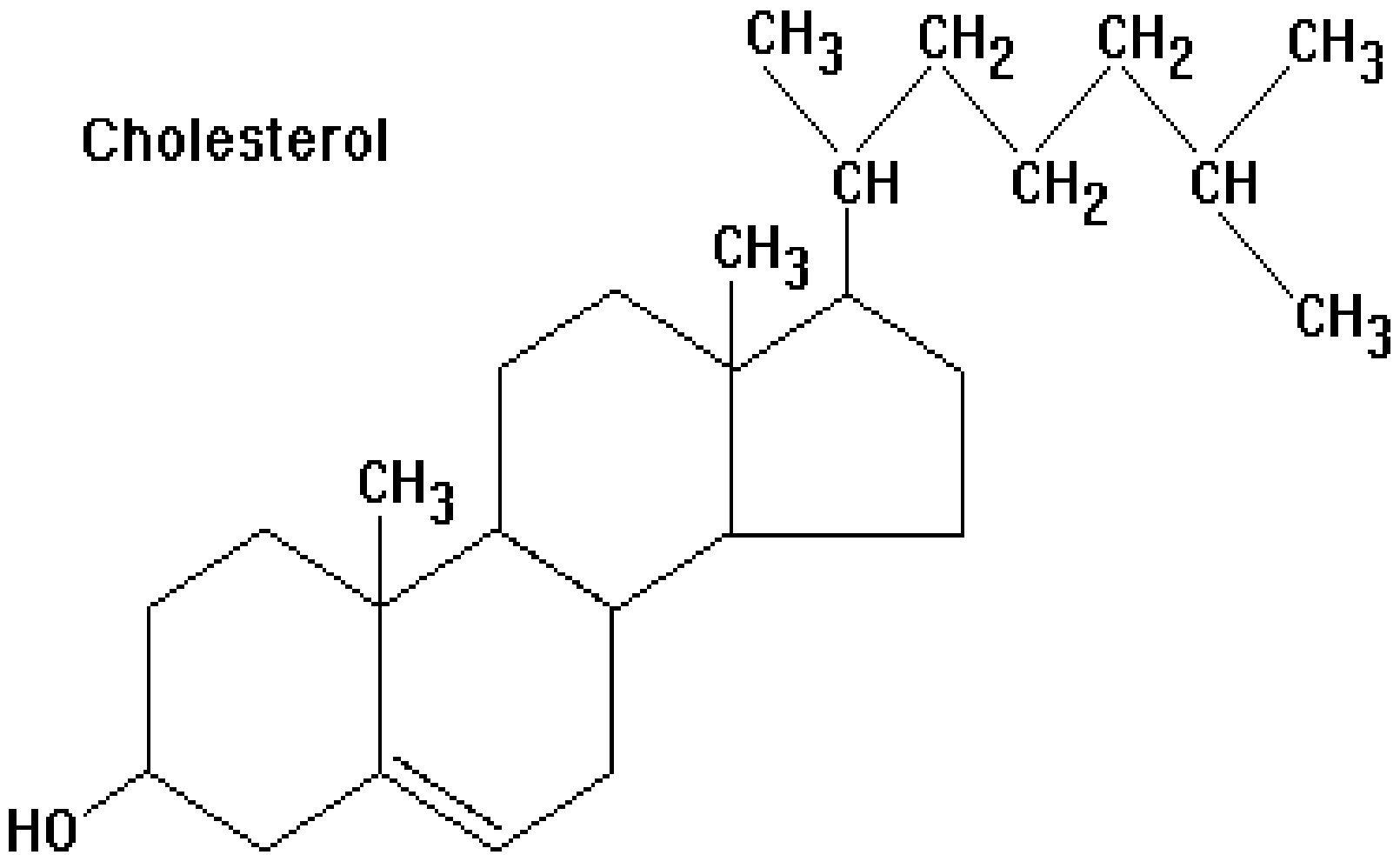
- Cholesterol is acquired by the body in **two ways** -

  (a) Production in the cells of the body

  (b) Dietary sources e.g. meat and dairy products

- Sites of production includes – liver, gonads, adrenal glands, nervous tissues and intestines
- Cholesterol exist in the free and esterified form

Cholesterol



Derived Lipids: Cholesterol

- Many steroid hormones are formed from cholesterol:
  - Aldosterone
  - Progesterone
  - Cortisol
  - Testosterone
  - Estradiol

- For transport in an aqueous medium, sterols and other lipids are bound to specific proteins, forming lipoprotein particles.
- These particles are classified based on their composition and density

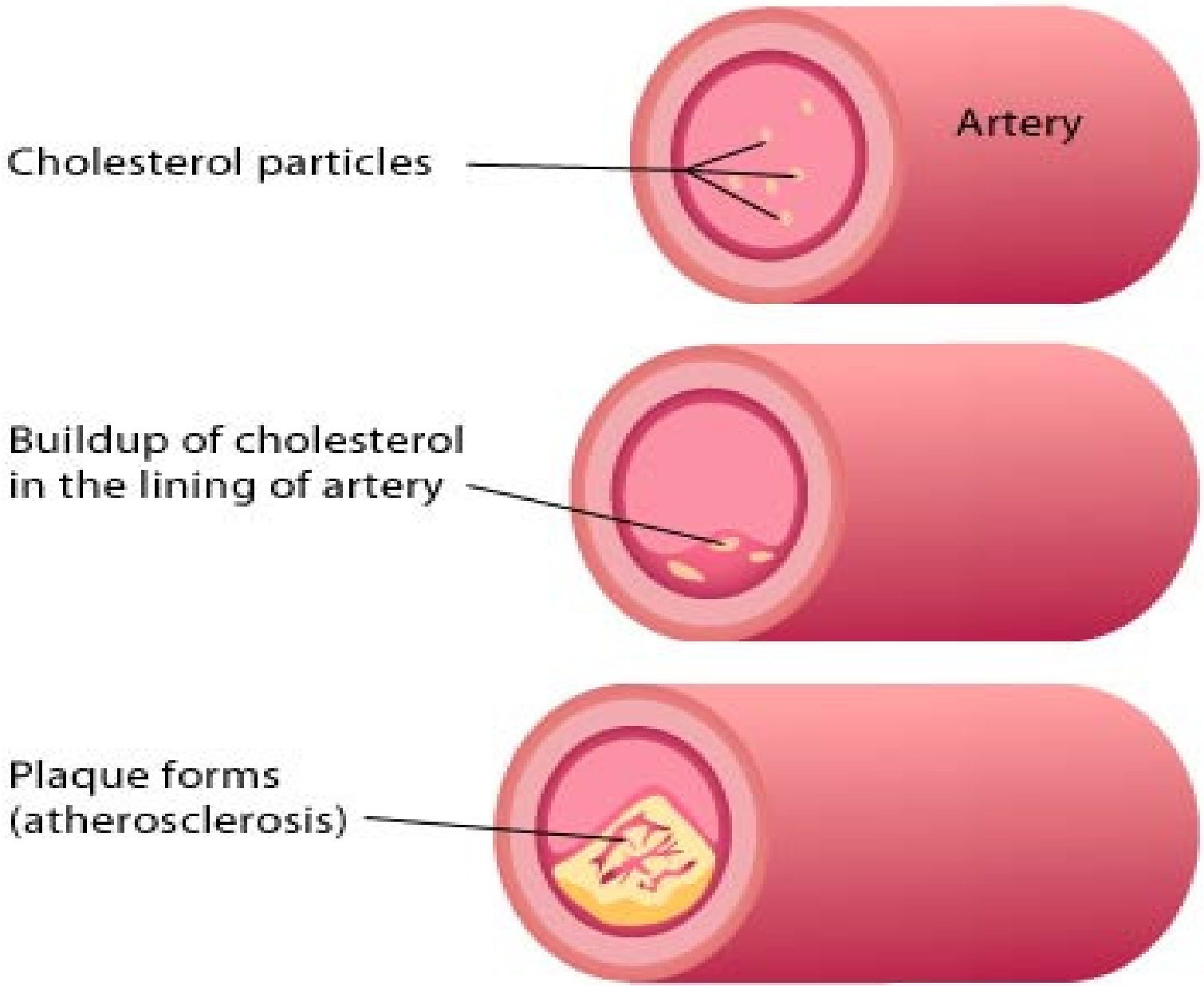
  Lipoproteins – contains lipid surrounded by hydrophilic molecules such as proteins and phospholipids

Four kinds of lipoproteins:

- HDL- 33% protein, 30% cholesterol. Delivers cholesteryl esters mainly to the liver to be used in the synthesis of bile acids and steroid hormones
- LDL- 25% protein, 50% cholesterol. Delivers cholesterol to the cell to be used mostly as a membrane component
- VLDL – mostly carries triglycerides synthesized by the liver
- Chylomicrons – carry dietary lipids synthesized in the intestine

Derived Lipids: Cholesterol

- HDLs carry LDLs away from artery walls
- LDL sticks to the artery walls and can lead to plaque build up (atherosclerosis)
- Higher proportion of LDL compared to HDL → associated with cardiovascular diseases such as heart attack and stroke


Artery
Cholesterol particles
Buildup of cholesterol
in the lining of artery
Plaque forms
(atherosclerosis)

Derived Lipids: Cholesterol

- Diet and exercise help to maintain balance in the LDL and HDL
- Two important cholesterol diseases

  (a) Familial hypercholesterolemia : Over production of cholesterol

  (b) Zanthomatosis: Build up of cholesterol in the skin

Terpenoids

- Terpenoids are a large and diverse class of naturally occurring organic chemicals
- Most terpenoids are multicyclic structures that differ from one another not only in functional groups but also in their basic carbon skeletons
- Essential oils can be obtained from plants by heating or applying steam distillation to certain plant material. These can be used in medicine or in the perfume industry
- Hydrocarbons known as terpenes and oxygen containing compounds known as terpenoids are the most important constituent of these oils

# OF CARBON ATOMS	CLASS
10	Monoterpenes
15	Sesquiterpenes
20	Diterpenes
30	Triterpenes

Biological Importance of Terpenoids

- The steriods and sterols in animals are biologically produced from terpenoid precursors
- Sometimes terpenoids are added to proteins, e.g., to enhance their attachment to the cell membrane; this is known as isoprenylation

Industrial Importance of Terpenoids

- Plant terpenoids are used extensively for their aromatic qualities
- Terpenoids play a role in traditional herbal remedies and are under investigation for antibacterial, antineoplastic, and other pharmaceutical functions
- Terpenoids contribute to the scent of eucalyptus, the flavors of cinnamon, cloves, and ginger, and the color of yellow flowers
- Well-known terpenoids include citral, menthol, camphor and the cannabinoids found in Cannabis