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PHYSIOLOGY HONOURS (CBCS) SEMESTER-I (MODULE-CC-2)



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LIPID CHEMISTRY

Introduction:

Lipids are non-polar bio-molecules, mostly insoluble in water but soluble in non-polar organic solvent. They are mostly fatty acid ester of different alcohols. Lipids are molecules with C, H and O but may also carry N, P, S in their structure.

Classification:

1. Simple lipids: These are fatty acid esters of alcohols.

They are of two types: Glycerides and Waxes.

Glycerides are ester of fatty acid with glycerol. They are classified into **monacylglycerol, diacylglycerol and triacylglycerol** depending upon number of fatty acids esterified with glycerol. Triacylglycerol are known as **'fats'**. Fats can be simple triglyceride or mixed glycerides as one or more than one type of fatty acids are incorporated. **Oils** are fats which remain liquid at room temperature.

Waxes are esters of long chain fatty acids with long chain monohydric alcohols. Eg, myricyl palmitate of beeswax.

2. Compound Lipids: They are ester of fatty acids which carry in addition other substance such as nitrogenous base, phosphate, carbohydrates and proteins etc. Eg., Phospholipid, glycolipid, lipoproteins etc

3. Derived lipid: They are derived from simple or compound lipid by hydrolysis.

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Mono, Di, Tri Glycerides formed by esterification of one, two, three fatty acids

Triacylglycerols

are esters of glycerol and fatty acids.

Natural fats and oils (butterfat, lard, olive oil, etc.) consists not of a single triacylglycerol, but of a complex mixture of triacylglycerols. A small portion of diacyl- and monoacylglycerols may be included.





Classification of fatty acids: Fatty acids are long chain mono-carboxylic organic acid.

1. Straight chain fatty acid: Carbons are arranged linearly. It can be saturated or unsaturated.

Saturated fatty acids:

Even chain: Butyric(C4), caproic (C6),capric (C10), myristic (C14), palimitic (C16), Staeric (C18), arachidic (C20) and lignoceric acid (C24) etc. **Odd chain :** Valeric (C5)



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2. Unsaturated Fatty acids: They contain double bonds between some carbons. They are further classified into

- a) Monoenoic acid: single double bond Eg. Oleic acid (C18)
- b) Dienoic acid: two double bonds. Eg., Linoleic acid (C18)
- c) Trienoic acid: three double bonds. –Eg., Linolenic acid (C18)
- d) Tetraenoic acid: four double bonds . Eg., Arachidonoc acid (C20).



*Omega (ω) series fatty acids: Unsaturated fatty acids may belong to omega (ω) series according to the position of double bond closest to ω -methyl carbon. Thus both lenoleic and arachidonic acids are ω -6 fatty acids. On the contrary linolenic acid belong to ω -3 fatty acids.

2. Branched chain fatty acids:

These fatty acids have branch in their linear hydrocarbon chain. Eg., Isovaleric acid, isobutyric acid.



3. Substituted fatty acids:

They have one or more hydrogen atoms of hydrocarbon chain of fatty acids to be replaced by other groups such as –OH, -CH3 and other halide groups. Eg., **Cerebronic acid (2-hydroxylignoceric acid), hydroxy-nervonic acid,** leukotrienes (polyunsaturated C20 fatty acids) etc.

CH₃—(CH₂)₇—
$$\overset{16}{CH} = \overset{15}{CH}$$
—(CH₂)₁₂—CH—COOH
hydroxynervonic acid (24:1 (n-9) OH)
CH₃—(CH₂)₂₁—CH—COCH
I
OH
CH³ (CH₂)₂₁—CH—COCH

4. Cyclic fatty acids:

These are fatty acids with a cyclic ring in their carbon chain. Eg., Prostaglandins and thromboxanes synthesized in animal tissues.

Prostaglandins are unsaturated, -hydroxy and- keto substituted C20 fatty acids with a saturated C5 ring (cyclopentane ring) at the middle of the linear carbon chain. They are classifieds into PG1, PG2 and PG3 series according to the presence of 1,2 and 3 double bonds. Each series have different molecules like PGD₂, PGE₂, PGF₂ etc depending on substitutions.



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The common naturally occurring fatty acids

Number of carbons and double bonds		Common name	Systematic name	
Saturated fatty acids				
4:0		Butyric	butanoic	
6:0		Caproic	hexanoic	
8:0		Caprylic	octanoic	
10:0		Capric	decanoic	
12:0		Lauric	dodecanoic	
14:0		Myristic	tetradecanoic	
16:0		Palmitic	hexadecanoic	
18:0		Stearic	octadecanoic	
20:0		Arachidic	eicosanoic	
22:0		Behenic	docosanoic	
24:0		Lignoceric	tetracosanoic	
Unsaturated fatty ac	ids			
16:1 (9)	(n-7)	Palmitoleic	cis -hexadec-9-enoic	
18:1 (9)	(<i>n</i> –9)	Oleic	cis-octadec-9-enoic	
18:2 (9,12)	(<i>n</i> -6)	Linoleic	cis, cis -octadeca-9,12-dienoic	
18:3 (6,9,12)	(<i>n</i> –6)	α-Linolenic	cis, cis -octadeca-6,9,12-trienoic	
18:3 (9,12,15)	(<i>n</i> -3)	γ-Linolenic	all - cis - octadeca-9,12,15-trienoic	
20:4 (5,8,11,14)	(<i>n</i> -6)	Arachidonic	all - cis -eicosa-5,8,11,14-tetraenoic	
20:4 (5,8,11,14,17)	(<i>n</i> -3)	(Timnodonic) EPA	all - cis - e icosa-5,8,11,14,17-pentaenoic	

PG	Receptor	Functions	
PGD ₂ ,	DP	X P. aggregation, Vasodilatation, Relaxation of GIT & uterus, regulates Sleep-wake cycle.	
PGF ₂	FP	Contractions Uterus & Bronchi.	
PGI ₂	IP	X platelet aggregation, Vasodilatation, Renin release & Natriuresis	
TXA ₂	TP	P. aggregation, Vasoconstriction, Bronchoconstriction.	
PGE ₂	EP ₁ PEF ₂	Bronchonstrction, GIT motility, increases colon cancer.	
	EP ₂	Br.dilation, Vasodilatation, GIT relaxation, Intestinal fluid secretion, Ovulation & Fertilization	
	EP ₃ EP ₄	X gastric acid secretion, Cytoprotective action, contraction of pregnant uterus & GIT muscle, X lipolysis & ANS neurotransmitter release. -Maintains patency of ductus arteriosus.	

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PROPERTIES OF FAT AND FATTY ACIDS

1. CIS-TRANS ISOMERISM:

Configuration and position of double bonds in unsaturated fatty acids give rise to this type of isomerism. If the double bond is 'cis' in nature (i.e., groups held by the carbons at the two ends of double bonds are situated on the same side of the axis) it produces a **bending of the carbon chain by about 30^o at the cis-double bond.** The chain will have as many bendings as the number of cis-double bonds. In contrast, if the double bond is 'trans' in nature (i.e., groups held by the carbons at the two ends of a double bond are oriented on opposite sides of the axis), then the carbon chain shows little or no bending at the double bond. Therefore, an unsaturated fatty acid with a double bond may exist in two isomeric forms- a **cis-isomer** and a **trans-isomer**. This is known as cis-trans isomerism.

For example, **Oleic acid and Elaidic acid are both C18 acids with a single double bond**. They are cis-trans isomer to each other. In animal tissues and foods, cis-isomers of unsaturated fatty acids are far more common

than trans-isomers. Intake of trans-fat is extremely unhealthy.

Learning Resources cis-trans isomer of fatty acids



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2. MELTING POINT:

Melting points of cis-unsaturated fatty acids are low. Because of their bendings at double bonds, they are less closely packed and have lower hydrophobic interactions. Such molecules need much less heat to break up. For eg., unsaturated oleic acid has a melting point of only 16^o C. So, they are usually liquid at room temperature. Fats rich in such unsaturated glycerides are called oils. Eg., sunflower oil, saffola oil, mustard oil etc.
 Melting points of trans-unsaturated fatty acids are higher than cis-fatty acids. This is because the approximate of trans-optimized provides are called on the second point.

carbon chains of trans-fatty acids are more closely packed and strongly held together by hydrophobic interactions.

☐ Higher saturated fatty acids also have higher melting points just like trans-fats. The melting points rise with chain length. For example, saturated stearic acid is solid at room temperature and has a melting point of 72° C. Fats rich in such saturated fatty acids are solid at room temperature. Butter, margarine, vanaspati etc.





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Trans-fatty acids are present in certain foods.

The shape of trans-unsaturated acids resembles that of saturated fatty acids:



The presence of *trans*-fatty acids in human nutrition seems to be harmful (e.g., an unfavourable effect on cholesterol metabolism).

Most arise as a <u>by-product during the "hardening" of vegetable oils into margarines</u> by means of metal-catalyzed hydrogenation.

An additional contribution comes from the ingestion of ruminant fat that contains *trans*-fatty acids (beef tallow 3-7 %, butter 3 %) arising from the action of microorganisms in the rumen.

Trans-fatty acids



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Fatty acid composition of some fats and oils



Trans Fat Content per Serving			
Food Item	TRAFA (g)		
Fast food chicken pot pie	14		
Fast foods- harsh brown/ French fries (large order)	6-13		
KFC chicken and biscuits	9		
Onion rings	4-10		
Fish and chips	10-12		
Chicken strips 5 pieces	5		
Donuts per piece	4		
Biscuit	5-6		
Apple pie / pound cakes per slice	5		
Berger	4-5		
Cheese sticks/cheese fries French toast sticks	4-5		
Vegetable shortening/tbsp	4.2		
Margarine, especially stick margarine per table spoon	2.8		



WHAT ARE TRANS FATS & HOW THEY HIDE IN POPULAR FOODS

The WHO ceiling for trans fats is 5 gm a day. Are you within limits? Check out how your choicest snacks and savouries stack up

Trans fats are man-made and lurk unlabelled in a range of foods. These form when hydrogen atoms are added to vegetable oils at high temperature.

The food and beverage industry's best-loved fat, it's less likely to spoil, can be repeatedly recycled, has a less greasy feel and is fabulously cheap.

Trans fats clog linings of blood vessels and surfaces in the brain. They are linked to obesity, coronary and cholesterol problems, diabetes and other lifestyle diseases.

Vanaspati is the biggest source of trans fat in India. Commercial and street food producers invariably use vanaspati.

The daily dose

The average trans fat content per serving





5 REASONS WHY YOU SHOULD AVOID TRANS FATS





FATS

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INTAKE

PUFA

Polyunsaturated fatty acids (omega-3 and omega-6) are the good fats.

Found in

Omega-3: fatty fish, canola oil, walnuts, flaxseeds and chia seeds.

Omega-6: Vegetable oils such as olive oil, safflower oil, sunflower oil, almonds and pumpkin seeds.

Recommendation

5-10% (incl. at least 1% of omega-3)

Fats to Include	Fats to Limit
Polyunsaturated, Monounsaturated &	Saturated & Trans-fats
Omega-3	 whole milk dairy products
 non-fried fish (salmon, flounder, 	 high fat animal meat (marbled
herring, sardines)	beef, bacon, sausage)
 olive oil, flax oil, 	 butter & margarine
- nuts/nut butters	 French fries & other deep-fried
 flax seed (in moderation) 	foods
- wheat germ	 partially hydrogenated oils in
- avocado	pastries, crackers, processed foods
	(Check the ingredients!)
Plant based and medium chain	
triglyceride rich	
 coconut oil, coconut milk 	

3. SOLUBILITY:

All fats are soluble in non-polar organic solvents such as benzene, chloroform etc. It is due to the presence of their non-polar hydrocarbon fatty acid tails. They are insoluble in water.

4. HYDROLYSIS:

Triglycerides are hydrolyzed into glycerol and fatty acids in presence of lipase or when boiled in presence of acids.

5. SAPONIFICATION NUMBER:

When triglycerides are boiled with alcoholic solution of strong metallic alkali (NaOH or KOH), fatty acids are released; which then react with alkali to form metallic salts called soaps. This alkaline hydrolysis of fat resulting in soap formation is called saponification. For eg., sodium stearate, potassium palmitate etc.

Saponification number is defined as the **number of mg of KOH required to saponify 1 gm of fat**. Each fatty acid in a fat uses 1KOH molecule for being saponified. Therefore saponification number of fat is inversely proportional to the average chain-length (or MW) of the fatty acids in its triglycerides molecules. So higher is the saponification number in a fat, lower is the average chain length of fatty acids in it. For eg., saponification number of butter is 210-230 castor oil is 175-180 etc.

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It is defined as **number of gm of iodine absorbed by 100 gm of a fat**. Iodine is absorbed only at double bonds of unsaturated fatty acids in a fat. Therefore higher iodine number indicates greater proportion of unsaturated fatty acids in a fat or greater number of double bonds in the fatty acids compared to saturated fat.

Eg., lodine number of butter is 25-28 and safflower oil is 141-155. A fat with only saturated fatty acid will have a iodine number of zero.



Type of oil	Double bond % ^a	Iodine value
Canola	~114	110-120
Coconut	~12	6-11
Corn	~142	102-130
Olive	~83	79-88
Peanut	~105	84-100
Sunflower	~153	110-143
Sesame	~132	103-116
Soy bean	~97	120-143

^aAssuming that maximum percentage of double bonds (300 %) is given by an oil containing triglycerides with 100 % of linolenic acid.

Learning Resources 7. ACETYL NUMBER:

It is defined as the **number of mg of KOH required to neutralize the acetic acid released by the saponification of 1 gm of acetylated fat**. The acetyl group is only accepted by –OH groups of hydroxyl fatty acids in a fat. This is a measure of amount of hydroxy-fatty acids in a fat.

For Eg., acetyl number of castor oil is 146-150 and olive oil is 10-12 etc.

Acetyl number

some fatty acids have hydroxyl groups



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8. ACID NUMBER:

It is defined as the **number of mg of KOH required to neutralize free fatty acids in 1 gm fat or oil**. Free fatty acids are released due to hydrolysis of fat. Higher acid number also indicates higher tendency of rancidity. Lower is the value purer is the fat.

9. REICHERT-MEISSL NUMBER:

It is a measure of relative amount of steam-volatile lower fatty acids in a fat. A fat is first saponified and then treated with a mineral acid to liberate free fatty acids from soaps. Steam is then allowed to pass through the mixture. Lower fatty acids (up to capric acid C_{10}) are volatilized and carried away with steam to condense in a receptacle. R-M number is defined as the **amount of N/10 KOH (in ml) required to neutralize volatile fatty acids in the distillate from 5 gm of fat.**

Eg., R-M number of butter is 20-33, olive oil is 0.5-1.5 etc.

Importance:

1. It is confined to butter and coconut oil.

2. Reichert-Meisel value is reduced when animal fat is used as adulterant in butter or ghee.

3. The determination of Reichert-Meisel number is important to the food chemist because it helps to detect the adulteration in butter and ghee. .

10. RANCIDITY:

Rancidity is the generation of **offensive odour and taste of oils and fats** when they are exposed to air, moisture and warmth for a long time. This may happen due to two reasons.

Atmospheric O2 and O3 can oxidize double bonds of unsaturated fatty acids in a fat to produce obnoxious aldehydes (oxidative rancidification).

□Enzymes of contaminating microbes can cause hydrolysis of ester bonds in fat molecules to release free fatty acids (hydrolytic rancidification).



Fig 5.14: Types of rancidity

Rancidity

Hydrolytic Rancidity

- caused by a breakdown of the fat into glycerol and fatty acid. (in general known as lipolysis and also lipolytic rancidity)
- Important in milk and milk product undesirable flavour mainly due to low fatty acids
- In most of the product other type of rancidity is observed.

Oxidative Rancidity

- results from oxidation of unsaturated and polyunsaturated fatty acids producing undesirable flavors and odors.
- by reacting with oxygen in the air.
- Air, Heat/Sun Exposure, moisture further supports OR Unsaturated fats are more susceptible to oxidative rancidity than saturated fatty acids.
- The reaction occur due to free radical formation at the site of double bonds
- Antioxidants added to foods prevent rancidity/autooxidation
- As antioxidants have lower energy for making free radicals so enter in to reaction preventing attack on unsaturated fat



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Lipid Chemistry-1







The principal class of storage and membrane lipids



From Lehninger Principles of Biochemistry

PHOSPHOLIPIDS

Phospholipids are class of **compound lipids** which are fatty acid esters carrying in addition a **phosphate group** and **nitrogenous/non-nitrogenous substance**.

CLASSIFICATION:

Phospholipids are of two types: **Glycerophospholipids and sphingolipids.** In glycerophospholipids, the alcohol is glycerol. In sphingolipids the alcohol is sphingosine. Glycerophospholipids are further sub-divided into **lecithins, cephalins, lipoaminoacids, plasmalogens and nitrogen-free phospholipids**.



Glycerophospholipids

Glycerophospholipids (or phosphoglycerides) are fatty acid esters of glycerol carrying an additional phosphate group and nitrogenous or non-nitrogenous substance.

Phosphoglycerides are derivatives of phosphatidic acid. In most of them, one of the primary alcohol groups of glycerol is esterified with a **saturated fatty acid**, the secondary alcohol group is esterified with an **unsaturated fatty acid** and the other primary alcohol group is esterified with a **phosphate** which in turn remain bound to a either a **nitrogenous substance** (choline, ethanol mine etc) or a **non-nitrogenous substance** (Inositol, another glycerol or another phosphatidic acid etc.)



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Phosphatidic acid

1,2-diacyl-sn-glycerol 3-phosphate



Phosphatidyl is the name of a remainder obtained by taking off –OH group.


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Phospholipids are 'Amphipathic' molecule.

Because they have **polar head groups** (phosphate group and the nitrogenous/nonnitrogenous substance) and **non-polar tails** (hydrocarbon chains of two fatty acids).



****Amphipathic molecules** are chemical compounds that have both polar and nonpolar regions, giving them both hydrophilic (water-loving) and lipophilic (fat-loving) properties. The word *amphiphile* comes from the Greek words *amphis*, which means "both," and *philia*, which means "love." **1. Lecithins:** It has nitrogenous base choline attached to the phosphate group. Also known as phosphatidyl choline.

2. Cephalins: It has nitrogenous base ethanolamine attached to the phosphate group. Also known as phosphatidylethanolamine.



3. Lipoaminoacids: It has a hydroxy amino acid (serine, threonine etc.) attached to the phosphate group. Eg., Phosphatidyl serine.

4. Plasmalogens: they are also known as ether phospholipids. Instead of being linked to a fatty acid by an ester bond, the a'-carbon of glycerol is linked to an alkene radical by an ether linkage.



5. Nitrogrn-free phosphoglycerides: They contain non-nitrogenous substance instead of a nitrogenous group. Example, lipositol (or phospatidyl Inositol) which contains Inositol connected to the phosphate group.



Phosphatidyl inositol



Phospholipids (and glycolipids) are the main lipid constituents of membranes:

Membrane proteins are inserted in lipid bilayer or bound to either surface.



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Sphingolipids:

Sphingolipids (or sphingomyelin) are phospholipids that carry **sphingosine** (a c18, nitrogenous, dihydroxy alcohol) instead of glycerol.

In each molecule of sphingomyelin, a fatty acid remains bound to $-NH_2$ group of sphingosine. The CH2OH group of shingosine in turn remains esterified to a phosphocholine.



Sphingosine	ÓН
	CH₂O-R NH
Fatty acid (N-acyl chain)	\sim
Substituent (R)	Sphingolipid
Substituent (R) H	Sphingolipid Ceramides
Substituent (R) H Phosphocholine	Sphingolipid Ceramides Sphingomyelins
Substituent (R) H Phosphocholine Sugar (s)	Sphingolipid Ceramides Sphingomyelins Glycosphingolipids
Substituent (R) H Phosphocholine Sugar (s) - Single sugar (glucose or galactose)	Sphingolipid Ceramides Sphingomyelins Glycosphingolipids - Cerebrosides
Substituent (R) H Phosphocholine Sugar (s) - Single sugar (glucose or galactose) - Lactose (disaccharide)	Sphingolipid Ceramides Sphingomyelins Glycosphingolipids - Cerebrosides - Lactosylceramides
Substituent (R) H Phosphocholine Sugar (s) - Single sugar (glucose or galactose) - Lactose (disaccharide) - Oligosaccharide	Sphingolipid Ceramides Sphingomyelins Glycosphingolipids - Cerebrosides - Lactosylceramides - Gangliosides

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Sphingolipids – schematic structure





A sphingophospholipid









Importance/Significance of Phospholipids:

1. Phospholipids provide **basic structure to a cell's membrane, and aids in the membrane's flexibility and fluidity.**

2. Phospholipids make membranes highly dynamic. They control curvature and charge.

3. They are also essential to regulate **exocytosis**, **chemotaxis**, **cytokinesis**, **phagocytosis**, and **endocytosis**.

4. Helps in assembling circulating lipoproteins.

- 5. Works as **emulsifiers** in the body to make micelles for fatty-substance absorption.
- 6. Lecithin or PC serves as a component substrate for generation of acetylcholine.
- 7. **Phosphatidyl Inositol (PI)** works as a precursor that aids in message transmission in the nervous system.
- 8. **Phosphatidyl serine (PS)** helps nerve cells to function and regulates nerve impulse conduction.

9. **Sphingomyelin** is found in the membranous **myelin sheath** that surrounds many nerve cell axons and electrically insulates it. So it acts as an insulator of nerve fibre. They play a significant role in **cell signaling pathways**.

10. **Cardiolipin (CL**), a signature phosopholipid in mitochondrial membrane. It makes up a significant amount of cardiac tissues and is found in cells and tissues that require high energy.

Glycerophospholipids

are

- essential structural components of all biological membranes,
- essential components of all types of lipoproteins in extracellular fluids,
- supply polyunsaturated fatty acids for the synthesis of eicosanoids,
- act in anchoring of some proteins to membranes,
- serve as a component of lung surfactant
- phosphatidyl inositols are precursors of second messengers (PIP₂, DG), etc.

Functions of phospholipids

- In association with proteins phospholipids form the structural components of membranes and regulate membrane permeability
- Phospholipids in the mitochondria maintain the conformation of electron transport chain components and thus cellular respiration
- They participate in the absorption of fats from the intestine
- They are essential for the synthesis of different lipoproteins and thus participate in transport of lipids
- The prevent accumulation of fats in liver (lipotropic factors)

FUNCTIONS OF PHOSPHOLIPIDS

1. Along with structural component of membrane regulate membrane permeability

2. (lecithin /cephalin /cardiolipin)—present in electron transport chain –assist in cell respiration

- 3. Amphipathic nature combine with polar & nonpolar compounds
- 4 .absorption of fat from intestine
- 5.lipoprotein synthesis---lipid transport (LDL/VLDL/HDL)
- 6.PREVENT FATTY LIVER-REGARDED AS LIPOTROPIC FACTORS

7.SYNTHESIS OF PROSTAGLANDINS / PROSTCYCLINS / THROMBOXANES

PHOSPHOLIPIDS→ARACHIDONIC ACIDS-→EICOSANOIDS



Lung surfactant

The major component of lung surfactant is dipalmitoylphosphatidylcholine.

It contributes to a reduction in the surface tension within the alveoli (air spaces) of the lung, preventing their collapse in expiration. Less pressure is needed to reinflate lung alveoli when surfactant is present.



The respiratory distress syndrome (RDS) of premature infants is caused, at least in part, by a deficiency in the synthesis of lung surfactant.

CARDIOLIPIN



Cardiolipin (CL) is a phospholipid, which is exclusively located in inner mitochondrial membrane, where it constitutes about 20% of the total lipid composition.

Cardiolipin plays an important role in regulating various kinds of mitochondrial proteins such as electron transport complexes, carrier proteins etc.

It is essential for the organization of particular mitochondrial structures such as cristae and contact sites.

Highly sensitive to oxidative damage.

GLYCOLIPIDS

They are compound lipids. Each molecule is made up of a **sphingosine (a nitrogenous alcohol)**, a fatty acid and a carbohydrate molecule. The combination of sphingosine and a fatty acid is called a 'ceramide'.

□All glycolipids are amphipathic. They have polar heads and non-polar tails. According to the carbohydrate molecule, glycolipids are classified into following:

Cerebrosides: The ceramide is connected to either a single galactose or glucose to produce a galacto-cerebroside or a gluco-cerebroside. The anomeric carbon (C1) of the monosaccharide remains connected to the CH₂OH of sphingosine by a glycosidic bond.
 Sulfatides: They are very similar to galacto-cerebrosides in which one or more OH groups of galactose remain sulfated. As a result, polar head group becomes anionic and acidic.

3. Gangliosides: The ceramide is connected to an **oligosaccharide chain which bears one or more sialic acid (NANA) residues.** Sialic acids make these molecules anionic and acidic.

4. Globosides: The ceramide is connected to **an oligosaccharide chain but it does not contain any sialic acid residue**. The polar head group therefore remains uncharged.

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Sphingosine	OH
Fatty acid (N-acyl chain)	
Substituent (R)	Sphingolipid
н	Ceramides
Phosphocholine	Sphingomyelins
Sugar (s)	Glycosphingolipids
- Single sugar (glucose or galactose)	- Cerebrosides
 Lactose (disaccharide) 	- Lactosylceramides
 Oligosaccharide 	- Gangliosides
 Sugar + sulfate 	- Sulfatides

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Significance of Glycolipids

- Cell-membrane interaction: Glycolipid is commonly found in all membranes. 2/3rd of all glycolipids are distributed in intracellular membranes such as golgi apparatus, nuclear membrane, endosome, lysosome and mitochondria. They not only play a structural role in membrane stability but also facilitate cell-cell communication by acting as receptors, anchors proteins and regulates signal transduction.
- 2. Part of nervous system: Galactocerebrosides (like kerasins, cerebrons, nervons and oxxynervons) occur in myelin sheath and white matter of CNS. Sulfatides also occur in white matter of brain. Gangliosides are found in grey matter of brain, membranes of neurons, ganglion cells, splenic cells and RBCs.
- **3. Immune response**: Glycolipid are crucial for immune responses.
- 4. Blood groups: Blood group antigens (ABO) on RBCs are glycolipids.

Functions of Glycolipid

- The glycolipids are an essential part of cell membranes.
- Glycolipids also help determine the blood group of an individual.
- Glycolipids act as receptors at the surface of the red blood cell.

 some viruses, bacteria (eg., cholera) use glycolipids on their cell surface as well. This helps the immune system destroy and clear the pathogen from the body.



Importance of Glycolipids

Essential components of all membranes of the body

but are found in greatest amounts in <u>nerve tissue</u> They are located <u>on the outer leaflet of plasma membrane</u> where they interact with the extracellular environment

Glycolipids are antigenic:

e.g identified as source of <u>blood group antigens</u> Carbohydrate portion is the antigenic determinant

Glycolipids are cell surface receptors

e.g. for: cholera, tetanus toxins certain bacteria & viruses

S.No	Cerebrosides	Gangliosides
1	Structurally Simple Ceramide linked with Glucose or Galactose.	Structurally complex Ceramide linked to Glucose, Galactose , NAGalactosamine ,and NANA
2	Occur in White matter of brain and Myelin Sheaths.	Occur in Grey matter of brain and Ganglions .
3	Types : Glucocerebrosides Galactocerebrosides	Types : GM1,GM2, GM3,GM4
4	Function : Conducts nerve impulse	Transfer Biogenic Amines
5	Related Disorder: Gauchers Disease	Related Disorder: Tay Sachs Disease

CHOLESTEROL

1. Cholesterol is a steroid compound with an alcoholic –OH group in its structure. Each **steroid** compound consist of a 'steroid nucleus' which is a fused, reduced tetracyclic ring system known as **'cyclopentanoperhydrophenanthrene'**. The first three rings (A, B and C) are cyclohexanes and the fourth ring (D) is a cyclopentane.

2. **Sterols** are steroid-alcohols in which there is an –OH group at C3 and a C_8 - C_{10} side chain attached to C17.

3. Cholesterol is **3** β -**OH**- Δ^5 -**cholestene**. It means it carries a –OH group on C3, methyl substitutions on C10 and C13, a C₈ hydrocarbon chain substitution on C17 and a double bond between C5 and C6.

4. Cholesterol is an animal sterol. It is a white, crystalline solid, insoluble in water but soluble in ether, chloroform, benzene, acetone etc. it is levorotatory in nature.

5. Cholesterol can form **'cholesterol-ester'** with fatty acids like oleic acid and linoleic acid at C3.

6. Cholesterol itself is **amphipathic**. Because its C3-OH group is polar and hydrocarbon ring system and the side chain is non-polar. But the cholesterol-ester are totally non-polar molecules as C3-OH group is not free.



Cyclopentano-perhydrophenanthrene (steroid) nucleus



Sterol structure







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Cholesterol ester



Foods High in Cholesterol





Significance of Cholesterol:

- 1. It is an animal sterol found in liver, adrenal gland, blood, nerve tissue, egg yolk, fishliver oil, bile, milk, butter etc.
- Normal adults typically synthesize about 1 g (1,000 mg) cholesterol per day and the total body content is about 35g. Typically about 50% of the excreted cholesterol is reabsorbed by the small intestines back into the bloodstream for reuse.
- 3. Its main function is to maintain the integrity and fluidity of cell membranes.
- 4. Cholesterol also helps in **nerve conduction**. The myelin sheath is rich in cholesterol.
- 5. It serves as a **precursor for the synthesis of steroid hormones.**
- 6. Cholesterol must also be present for the skin to manufacture vitamin D.
- 7. Cholesterol also enables the body to **form bile acids**, which are needed to help breakdown fats in the digestive tract so that they can be absorbed into the body.
- 8. High level cholesterol in blood increase the risk of atherosclerosis.
- 9. High levels of cholesterol can also result in the formation of gall stones.

5

FUNCTIONS OF CHOLESTEROL

Cholesterol is the most abundant sterol in humans and performs a number of essential functions. For example-

- It is a major constituent of the plasma membrane and of plasma lipoproteins.
- It is a precursor of bile salts,
- It is a precursor of steroid hormones that include adrenocortical hormones, sex hormones, placental hormones etc
- Also a precursor of vitamin D, cardiac glycosides, Sitosterol of the plant kingdom, and some alkaloids.
- It is required for the nerve transmission. Cholesterol is widely distributed in all cells of the body but particularly abundant in nervous tissue.



YOUR BRAIN NEEDS CHOLESTEROL

Cholesterol Levels in Tissues

Mouse Brain having cholesterol ~15mg/g tissue

Adrenal gland ~19mg/g

Lung ~6mg/g

- Cholesterol in the Brain exists in two pools
 - One pool is largely containing ~70% (white matter), conc. ~40 mg/g tissue
 - Second pool is small having ~30% (gray matter),
 - conc. ~8mg/g tissue





TOTAL CHOLESTEROL

Total Cholesterol Level in mg/dl*	Category
Less than 200	Desirable
200 to 239	Borderline high
240 and above	High

* Cholesterol levels are measured in milligrams (mg) of cholesterol per deciliter (dL) of blood.
| Test | Desirable | Borderline | Undesirable |
|----------------------|-----------|------------|-------------|
| Total cholesterol | <200 | 200-240 | >240 |
| HDL cholesterol | >45 | 35-45 | <35 |
| Triglycerides | <200 | 200-400 | >400 |
| LDL cholesterol | <130 | 130-160 | >160 |
| Cholesterol/HDL | <4.5 | 4.5-7.5 | >5.5 |
| LDL/HDL | <3.0 | 3.5 | >5.0 |
| Source: Medical Essa | y (1993) | | |

Table I Lipid levels (mg/DL) in human beings with known heart disease

LIPOPROTEINS

- 1. Lipoproteins are **compound lipids** which are made up of lipid molecules (triglycerides, cholesterol, fatty acids etc) and proteins. Water insoluble lipids are transported in plasma as lipoproteins.
- 2. Each lipoprotein particle of plasma has a **2 nm thick surface monolayer of amphipathic lipids** (such as phopsholipids, glycolipids, free cholesterol etc). The **polar heads** of these lipids oriented on the outer surface of the particle towards the aqueous medium and **nonpolar tails** or hydrocarbon rings are buried deep inside the non-aqueous central core. Thus a lipoprotein can be easily transported in aqueous body fluids.
- 3. Each lipoprotein contains some proteins (apolipoproteins). Some of them are integral proteins embedded in the lipid monolayer such as apo-B-100. Some are peripheral proteins present on the outer surface of the particles. Eg., apo-A, apo-C, apo-D and apo-E.
- 4. The higher is the lipid content of a lipoprotein, the larger will be its diameter, lower will be its density and higher will be its floatation rate (in Svedberg units).
- 5. Depending on their densities and floatation rate, lipoproteins are classified into VLDL, LDL, IDL, HDL and chylomicrons.

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The higher is the lipid content of a lipoprotein, the larger will be its diameter, lower will be its density and higher will be its floatation rate (in Svedberg units).

Class Origin		Major function	Diameter (nm)	Density (g/ml)	Major protein	Concentration in interstitial fluid	Average composition by weight (%)				
					170		TG	CE	PL	Chol	Protein
Chylomicrons	lleum	Transport ingested fat and fat-soluble vitamins	200–1,000	<0.95	apoB48	Absent	85	3	8	2	1
VLDL	Liver	Transport synthesized glyceride	30-90	0.95-1.006	apoB100	Absent	55	18	20	5	9
LDL	Lipolysis of VLDL	Deliver cholesterol to cells	22-28	1.006-1.063	apoB100	~9% that in plasma	10	50	29	11	20
HDL	Liver and ileum	Reverse cholesterol transport	7–11	1.063–1.21	apoA1	~20% that in plasma	6	40	46	7	50

TG, triglyceride; PL, phospholipid; Chol, cholesterol.

				Composition			
Lipoprotein	Source	Diameter (nm)	Density (g/mL)	Protein (%)	Lipid (%)	Main Lipid Components	Apolipoproteins
Chylomicrons	Intestine	90–1000	< 0.95	1–2	98–99	Triacylglycerol	A-I, A-II, A-IV,¹ B-48, C-I, C-II, C-III, E
Chylomicron remnants	Chylomicrons	45–150	< 1.006	6–8	92–94	Triacylglycerol, phospholipids, cholesterol	B-48, E
VLDL	Liver (intestine)	30-90	0.95–1.006	7–10	90-93	Triacylglycerol	B-100, C-I, C-II, C-III
IDL	VLDL	25–35	1.006–1.019	11	89	Triacylglycerol, cholesterol	B-100, E
LDL	VLDL	20–25	1.019–1.063	21	79	Cholesterol	B-100
HDL	Liver, intestine, VLDL, chylomicrons					Phospholipids, cholesterol	A-I, A-II, A-IV, C-I, C-II, C-III, D, ² E
HDL,		20–25	1.019-1.063	32	68		
HDL ₂		10–20	1.063-1.125	33	67		
HDL ₃		5–10	1.125-1.210	57	43		
Preβ-HDL ³		< 5	> 1.210				A-I
Albumin/free fatty acids	Adipose tissue		> 1.281	99	1	Free fatty acids	

¹Secreted with chylomicrons but transfers to HDL. ²Associated with HDL₂ and HDL₃ subfractions. ³Part of a minor fraction known as very high density lipoproteins (VHDL). **Abbreviations:** HDL, high-density lipoproteins; IDL, intermediate-density lipoproteins; LDL, low-density lipoproteins; VLDL, very low density lipoproteins.

Learning Resources Major functions of lipoproteins:

- 1. VLDL: They transport endogenous triglyceride, synthesized in liver cells, from liver to extra-hepatic tissues, particularly to adipose tissue for storage. The removal of triglycerides from VLDL by muscle and adipose tissue results in the formation of IDL particles which are enriched in cholesterol.
- 2. LDL: They are rich in cholesterol and cholesterol-esters and transport them from liver to extra-hepatic tissues. Intake of high-fat diet is often associated with elevated plasma LDL level and indicates deposition of cholesterol in wall of arteries.
- 3. HDL: They transport cholesterol and its esters from extra-hepatic tissues to the liver. They help in scavenging of cholesterol from extra-hepatic tissues including plasma and its delivery to the liver for catabolism. High plasma HDL indicates a greater capacity for this reverse cholesterol transport.
- 4. Chylomicrons: They transport triglyceride (endogenous and dietary), cholesterol esters, fat soluble vitamins etc. from the intestine to liver, adipose tissue and muscles. Cholesterol esters are mainly taken up by liver where as triglycerides are delivered to adipose tissues and muscles. Chylomicrons pass to blood plasma via lymph.



Learning Resources HDL (Good cholesterol) vs. LDL (Bad-cholesterol):

- As a general rule, HDL is considered "good" cholesterol, while LDL is considered "bad." This is because HDL carries cholesterol to liver, where it can be removed from the bloodstream before it builds up in the arteries. LDL, on the other hand, takes cholesterol directly to the arteries. This can result in atherosclerosis, a plaque buildup that can even cause heart attack and stroke.
- 2. High LDL/HDL ratio in plasma leads to deposition of cholesterol-rich lipids in vascular wall resulting in formation of fibrous, calcified plaques on the walls and subsequent thickening, hardening of arterial walls, a condition called **atherosclerosis.** High LDL/HDL ratio is therefore an indicator of increased risk of cardiovascular disorders including myocardial infarctions and coronary occlusions.



	LDL	HDL
Fuli Name	Low Density Lipoproteins	High Density Lipoproteins
Size	Larger (carry more cholesterol)	Smaller (carry more proteins)
Myth	Bad Cholesterol	Good Cholesterol
Reality	Transports cholesterol to the cells as necessary to function	Removes excess cholesterol from the blood stream to the liver- converted to bile acids
Risk	High LDL	Low HDL
Optimal	<100	>60



Your Cholesterol Reading

Cholesterol	Ideal	Borderline	High	
Type	Range	High		
Total	less	200-239	240 and	
cholesterol	than 200		higher	
LDL cholesterol	less	130-159	160 and	
(bad cholesterol)	than 130		higher	
HDL cholesterol	50 and	40-49	less	
(good cholesterol)	higher		than 40	
Triglycerides	less than 200	200-399	400 and higher	

Cholesterol Ratio

A ratio tells us how much of one thing we have compared to another. This ratio compares Total Cholesterol to HDL. To calculate the Cholesterol Ratio you divide your TOTAL Cholesterol by HDL Cholesterol.

5:1	Say your Total Cholesterol is 220 (which is borderline) and your HDL is 44, your ratio would be 5:1. This is not a healthy ratio. To improve it you need to focus on increasing your HDL.
4:1	If your Total is 200 and your HDL is 50 your ratio is 4:1 This is an acceptable ratio.
3:1	If your Total is 180 and your HDL is 60, your ratio is 3:1 This is a good ratio.



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8 Good Cholesterol Foods Should be in Your Diet

Fruits, and vegetables Nuts Seeds Extra-virgin Olive oil Fatty fish Whole grains Beans Soy

FOODS TO AVOID if you've HIGH CHOLESTEROL

/thefitnesscafe1

www.fitnesscafe.co



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Eicosanoids:

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1. Eicosanoids are unsaturated and **substituted C20 fatty acids**.

2. They belong to three main classes: **Cyclic Prostanoids** (Prostaglendins and thrmoboxanes), **Leukotrienes and Lipoxins.** Compound of each class belong to different series according to the number and positions of double bonds and substituent groups.

3. They are mostly synthesiszed from arachidonic acid (20:4) and timnodonic acid (20:5).



(Prostaglandins) Cyclic unsaturated fatty acid



(Leukotrienes) Hydroxy (2) tetra-unsaturated fatty acids



(Lipoxins) Hydroxy (3) tetra-unsaturated fatty acids **Functions of eicosanoids:** They have diverse biological roles as **paracrine hormones** and influence the cells in the immediate neighbourhood.

- Prostaglandin E (PGE) decreases adipose tissue lipolysis and lowers plasma FFA level. It also enhances Ca+2 mobilizations from bones. PGE stimulates pancreatic and intestinal secrestions. It also lowers arterial BP by producing general vasodilatation. PGE increases glomerular filtration in kidney by producing renal vasodilation and enhancing renal blood flow. It also increases the release of other hormone such as GH, LH, TSH, ACTH, glucagon, corticosteroids etc. it produces inflammation at the site of trauma or injury.
- 2. PGF stimulates contractions of smooth muscles of uterus, GI tract, arterioles, bronchi etc.
- **3.** Thromboxanes particularly TXA2 are found in platelets. It promotes platelet aggregation and thrombus formation. PGI, PGE and PGD inhibits aggregation.
- 4. Leukotrienes (LTC4, LTD4, LTE4) are released from mast cells during anaphylactic reactions (immediate hypersensitivity or allergy). They cause sustained contractions of smooth muscles in bronchi. They also cause vasodilatation and increased capillary permeability. LTB4 stimulates chemotaxis and chemokinesis of neutrophils and eosinophils during anaphylaxis.

Amphipathic molecules (phospholipids, soaps, bile salts etc.) sometimes aggregate into **small, stable droplets of 4-10 nm** when they are present in excess of a specific concentration (called CMC or critical micelle concentration) in aqueous medium. These are called micelles. They **have polar head groups** on the outer surface and nonpolar tails in central core. The polar heads remain bound to neighboring water molecules by hydrogen bonds. **Non-polar tails** are closely held together by van der Waals forces and hydrophobic forces.

Micelles formed in the intestinal lumen help in intestinal absorption of fat. Micelle formed in gallbladder bile helps biliary excretion of cholesterol.



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Liposomes are **stable**, **large vesicles of colloidal dimension** (10-5 to 10-7 cm) enclosing hollow, water-filled central cores. They are formed from the Sonification or Ultrasonification of aqueous suspension of amphipathic molecules.

They are covered by either a **single closed bilayer of amphipathic molecules (unilamellar liposome)** or they may contain many concentric bilayers **(multilamellar liposomes)**.

The lipid bilayer in a liposome is impermeable to polar materials and thus successfully maintains the composition of enclosed aqueous fluid. They are used to **deliver drugs** to specific cells.

