

lipid (1)

lipid

- fats, oil, wax
- phospholipid, cholesterol
- bile salts, steroid hormone
- sphingolipids, eicosanoid.
- fat-soluble v. (A, P, E, K)

low solubility water
- High nonpolar solvent

like dissolve like

lipid → long hydrocarbon (nature)

yield large energy:-

- Represent highly reduced form of carbon.
- upon oxidation in (metabolism)

In Biological system

hydrocarbonic

- only non-polar
- ex: triacylglycerols.

amphipathic

- polar + non-polar
- Fatty acid.

Biological important

- energy (lipid > carbohydrate protein)

- nervous system → constituent.
- cell memb.

store energy
protect internal organs
subcutaneous thermal

- cholesterol: synthesis → steroid hormone
→ bile acid/salt

- supply body → essential fatty acid
fat soluble v. (A, P, E, K)

Fatty Acid

(composed)

- long, straight
- hydrophobic
- chain
- methyl group
- end
- w-carbon
- carboxyl group
- at other end
- pKa = 4, 8
- (COO⁻)

under physiological condition
It's amphipathic nature

- 2 = (α-carbon)
- 3 = (β-carbon)
- 4 = (γ-carbon)
- end = ω-carbon
- terminal methyl group

nature (FA): (14 - 24) C
- Human (16 - 20)

- certain marine orga. (odd) number
- (FA) ≥ 10 : insoluble in water (LCFA)

even x odd

C₂ building block
(even number)

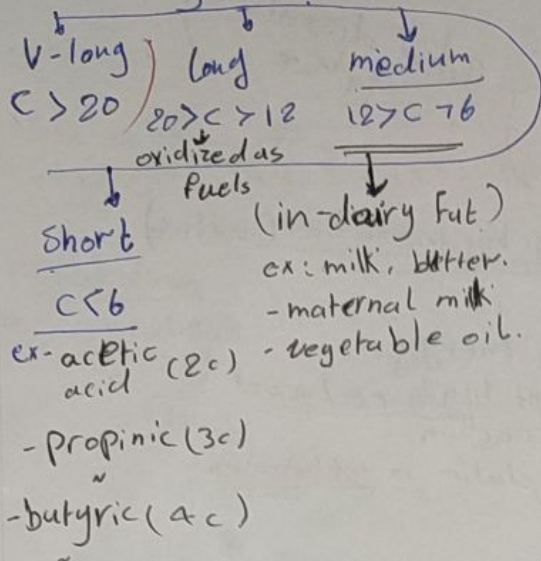
CH₂ ← acetyl group
(CH₃-CO)

Stearic acid
- Saturated
- 18:0

hydrophobic - CO-

long chain fatty acid

Classified



organic chain

animal
 - saturated
 monounsaturated
 (lo CFA)

plant (vegetable)
 - polyunsaturated
 (long chainy F.A)

chain

Saturated

- No double bond.
- packing tightly
- diet \rightarrow high satur. \rightarrow cause cholesterol in arteries.
- heart disease

mono unsat.

- single double bond
- olive oil
- more energy
- Rotation \rightarrow flexible molecule

unsaturated

poly unsat.

- double bonds \rightarrow one
- oil \rightarrow fish, sunflower, corn

each $C = 3$ space 3 carbon

(higher plant) \rightarrow oleic

- most common
- H cell \rightarrow palmitic acid (16)
- Stearic acid (18)
- No Rotation (restrict) Rigid.

(1-4) double bond less energy

- slightly more abundant
- most common \rightarrow oleic acid (18:1)

- 1- Cause (kink)
- 2- prevent packing tightly
- 3- keep liquid (Room T)

Cis (FA)

- H atoms same side of double bond

double bond

trans (FA)

- not nature.
- manufactured by hydrogenation
- It's raise (LDL) \rightarrow Bad cholesterol level
- \rightarrow heart disease.
- involved more linear way

It's favorable for food industry

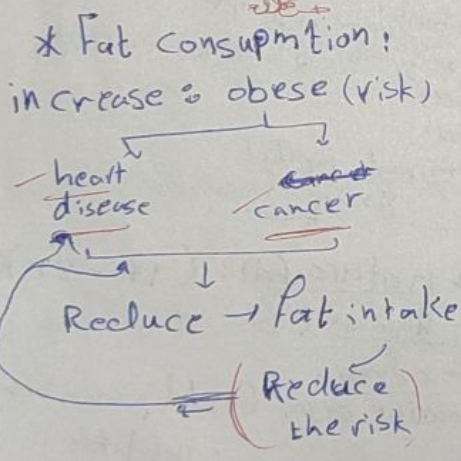
- used in - margarine
- baked goods.

change property

- (M.P)
- shelf life
- flavor
- stability.

- Natural trans: small amount in animal meat & dairy product.

H atoms: opposite side of a double bond

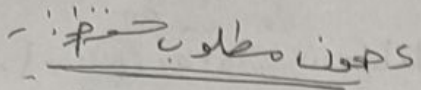


Numbering ~ carbon atom (low system)

Δ delta (w. 6)

numbering from (carboxyl-carbon) ^①

ex: arachidonic 20:4Δ^{5,8,11,14}
 # carbon # double bond # triple bond



(ω) omega

Numbering from methyl terminal end.

ex: Arachidonic ω6

the closest number double bond - (5,8,11,14)

- linolenic ~ ω3

contrast ↓

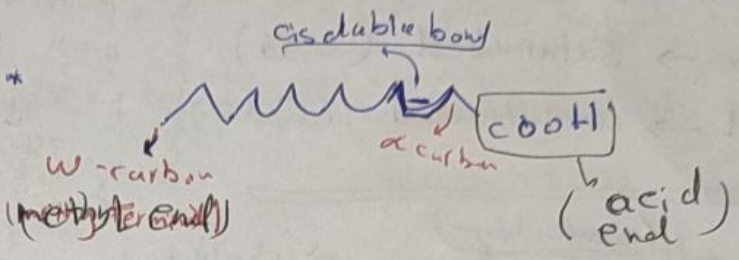
- linolenic ~ ω3 FA1

- Oleic acid (18:1Δ⁹) (ω9)

- α-linolenic ~ (18:3Δ^{4,12,15}) * (ω3)

eg. high in diet

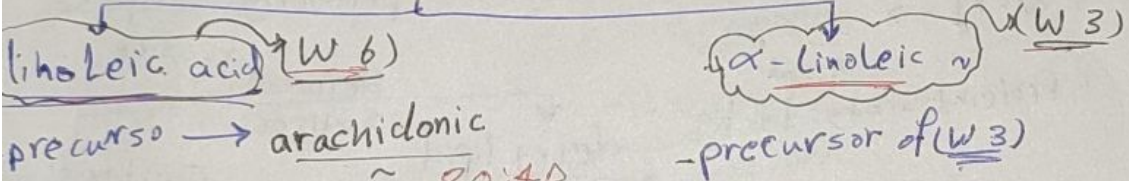
Arachidonic ~ 20:4^{5,8,11,14} (ω6)



Essential fatty acid

cant synthesize naturally
 get it from our diet.

In human include:



polyunsaturated present in phospholipid of cell/membrane
 substrate to synthesis: prostaglandin

growth development

important media in
 Pain inflammation responses

* deficiency of linolenic
 decrease vision
 altered learning behaviour

produce pain sleep
 blood coagulation
 reproduction

non-steroidal anti-inflammatory
 → aspirin
 → inhibiting prostaglandin synthesis

Saturated

- higher (m.p)
- linear → packed together
- close interacting between intermolecular.
- more solid at room temperature

unsaturated

- lower (m.p)
- double bond
- result: bend/kink
- intermolecular interaction weaker (low m.p)

* increase chain length increases T_m (M.D)

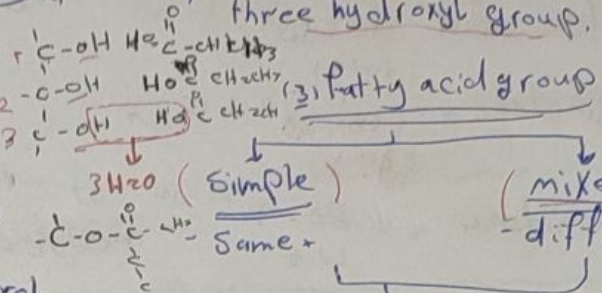
* oleate: - rigid, kink (cis double bond)

- oleate → ionized → oleic acid (unsaturated)
- palmitic → saturated (C16)
- oleic acid → unsaturated (C18)

Triglycerides

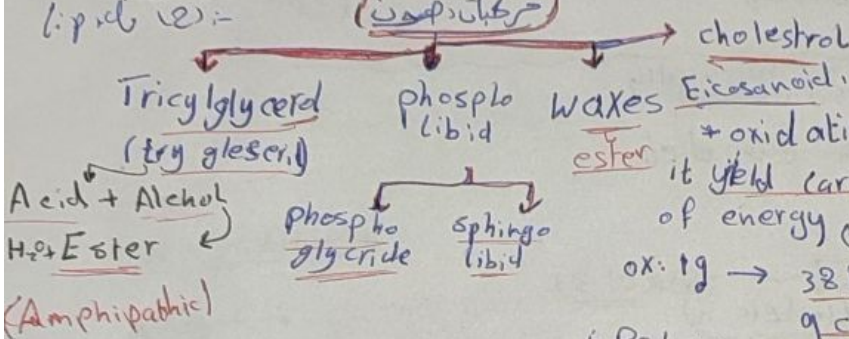
esterification

- consist → glycerol (C3H8O3) + three fatty acid
- TCG: - main component in animal fat @ vegetable oil
- most found: adipose tissue
- 90/95% → make the dietary fat
- Glycerine (glycerol) %
- colorless, viscous, sweet taste
- formula: $\text{CH}_2(\text{OH})\text{CH}_2(\text{OH})\text{CH}_2(\text{OH})$
- soluble in water (polar) with three hydroxyl group.



lipid (e):

(unsaturated)



natural fat → mixture of them

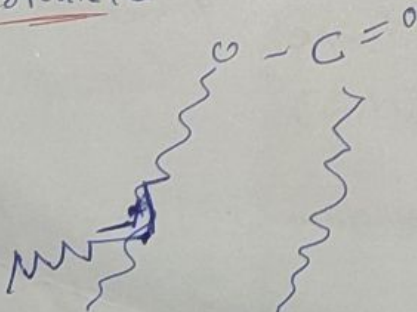
TCG animal → primarily: adipose tissue

(derived) (sources) synthesized in the liver (Kidney)

Phospholipid

- Amphipathic
- found mainly: cell membrane
- two classes.

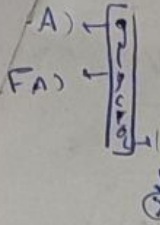
Both: play role: generation of lipid-sinalling molecule



Waxes

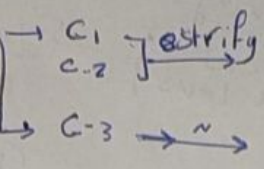
- Esters → fatty alcohol, fatty acid → long chain
- saturated → usually (solid)
- may → unsaturated
- include sterols: cholesterol
- water insoluble → weakly polar → ester group
- waxes → animal skin: water-repellant
- leave certain plant → bird feathers
- wax coating: cause: shiny surface of polished Apple.
- Ex: oleoyl alcohol esterify stearic acid

phosphoglyceride:

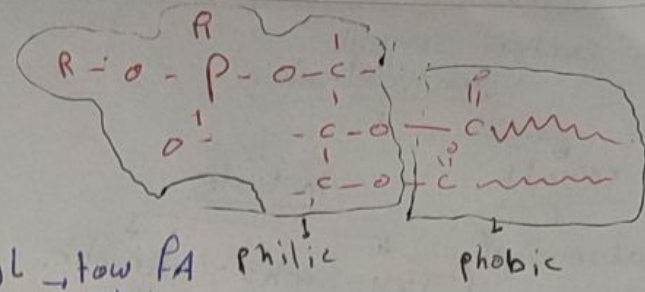


- glycerol → backbone.

- hydroxyl group

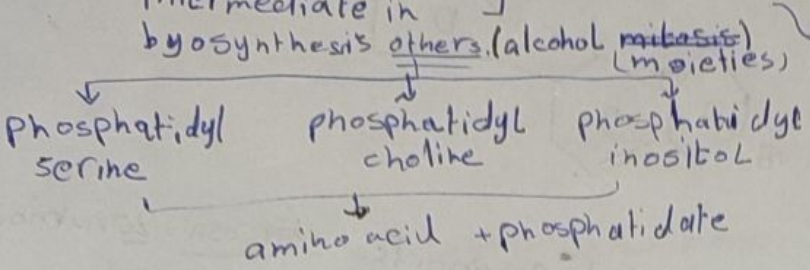


carboxyl group → low FA chain
phosphoric acid.



- the simplest one → intermediate in biosynthesis others (alcohol moieties)

Phosphatidate (Not addition)



phosphatidic acid (parent compound for phosphoglyceride)

3 types

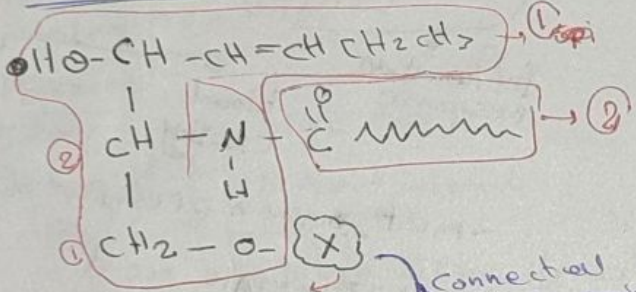
Sphingolipids

→ backbone: sphingosine.

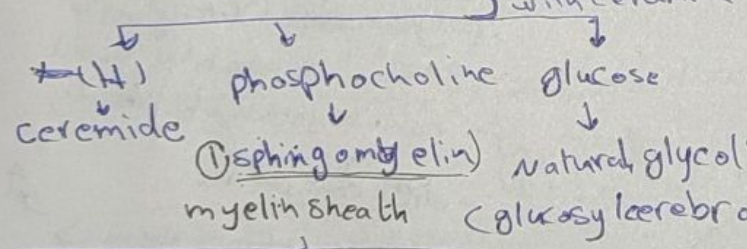
(2) major component

→ sphingosine: - 18 carbon
- amino alcohol
- unsaturated.
→ Fatty acid: amide linkage (between C and NH2)

General Structure

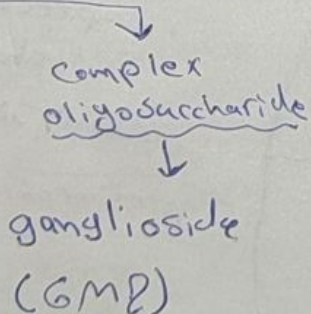
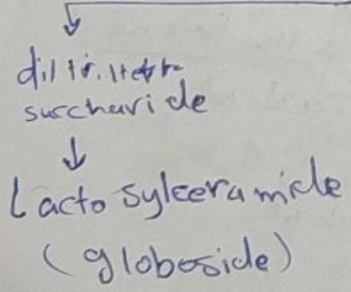
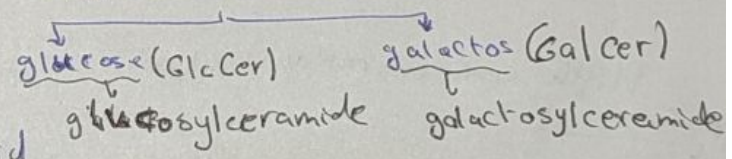


في الاربعة اماكن
توجد السفينوسين



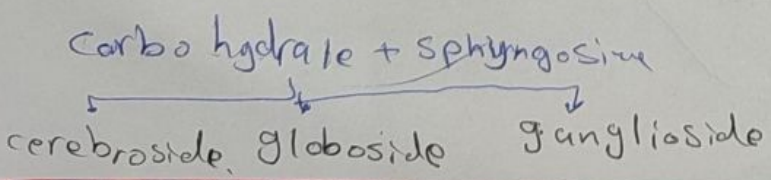
② cerebroside (neutral glycolipid)

- cell membrane
- monosaccharide



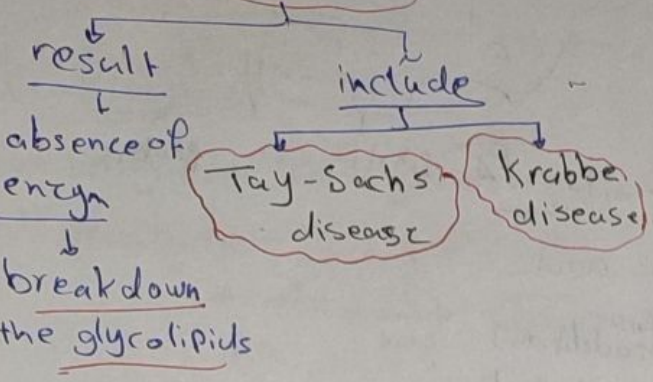
③ Ganglioside: complex glycosphingolipid

- oligo sacch → connecti ceramide
→ in head: Sialic acid - (presence)
(net negative charge) (at neutral)
→ outer layer: plasma membrane importance → antigens → receptor cell

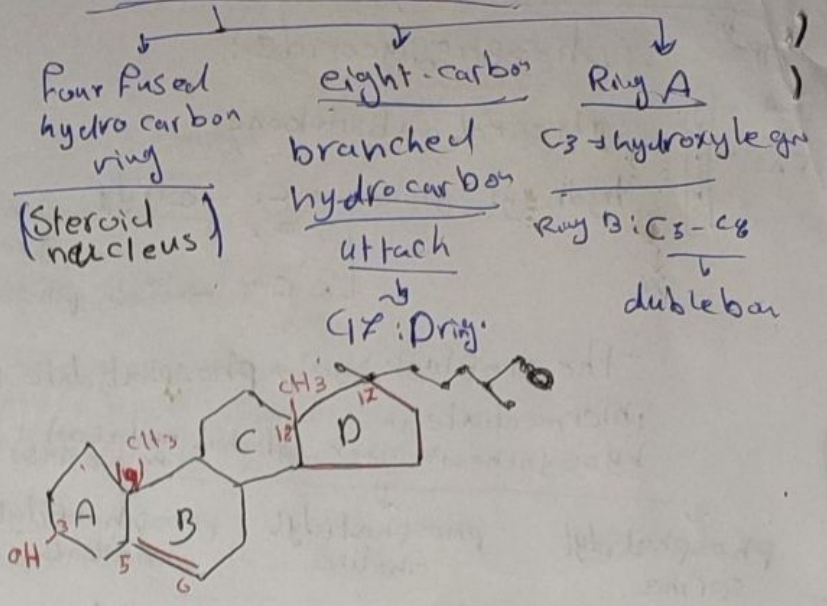


antigens: (sit → biological recognition) at cellular level

carbon several genetic disease



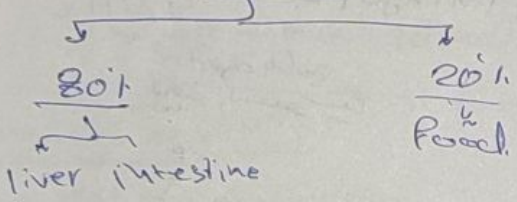
cholesterol structure



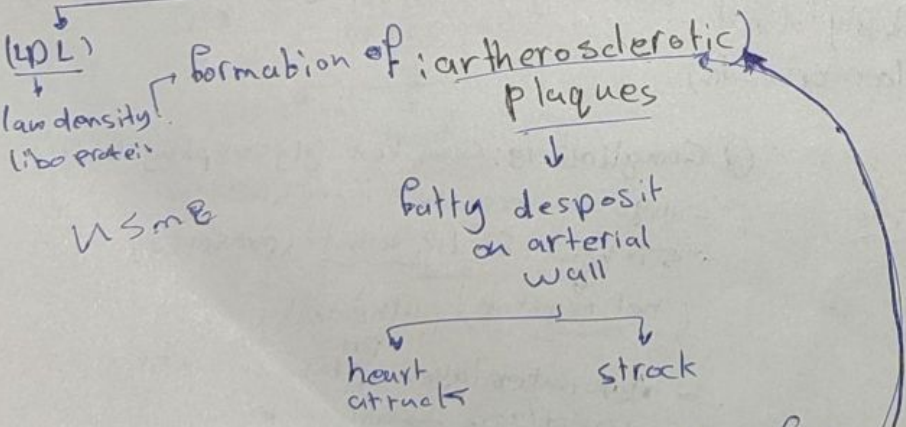
(cholesterol)

- waxy, whitish yellow fat
- other body make
 - cell membrane
 - steroid hormones
 - vit D
 - bile acids → digest absorb fat

Sources



- animal cell make, plant x
- can't oxidize the carbon in complex ring structure → No caloric value
- High concentration → blood



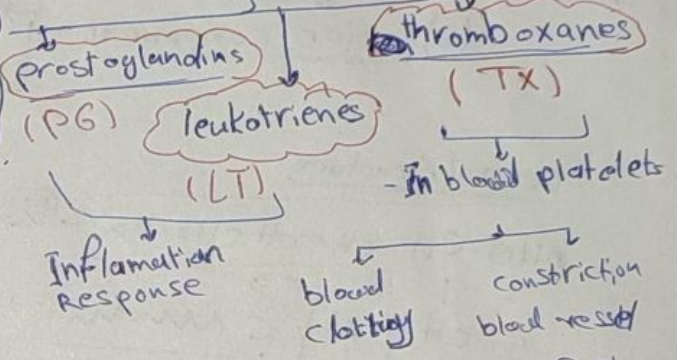
diets High concentration saturated fat → increase circulatory levels of LDL cholesterol

Eicosanoids

eicosan = 20 carbon

- From polyunsaturated fatty acid
- 20 carbon atoms

include



- most common precursor of Eicosan

Arachidonic acid

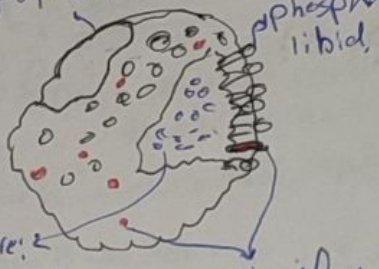
- polyunsaturated fatty acid
- 20C, 4 double bond
- can't synthesize by body
- diet contain it

precursor from them which is linoleic acid

precursor: linoleic acid

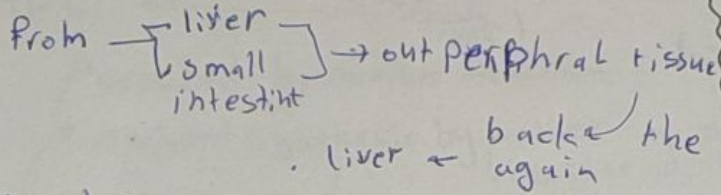
Lipoprotein

Apo protein

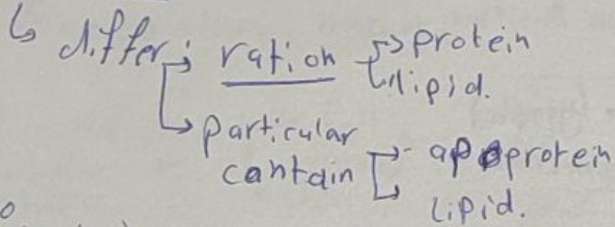


Plasma lipoprotein

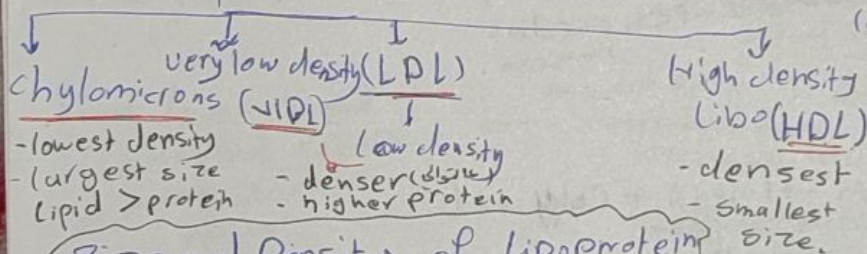
- Func: - transport lipid (tri, chole.)



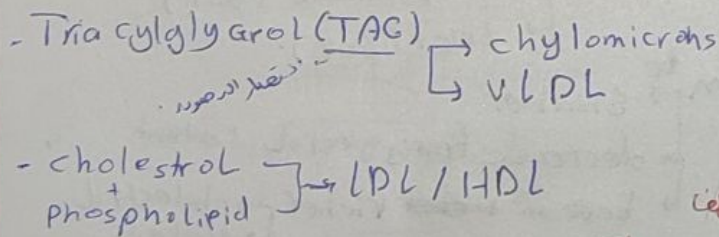
Lipo protein



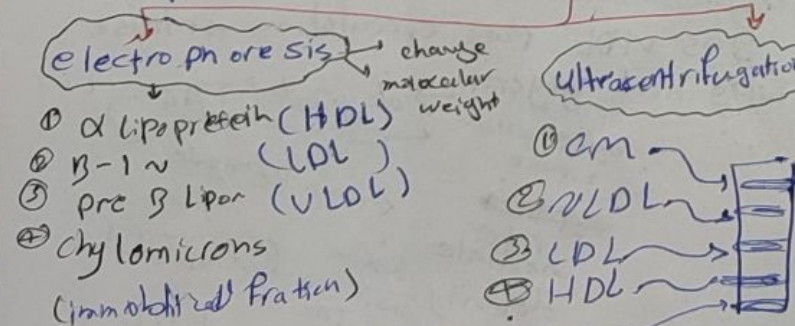
(Lipo particles):



Size and Density of lipoprotein



Separation (Plasma (Lipo protein))



(Revision)

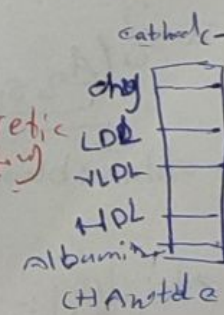
- (Am) ① fatty acid: long straight chain + met (in order) carboxyl + end
- (Hyl) ② Triglycerol: - glycerol (Gott) - fatty acid = est
- (Hyl) ③ waxes - fatty alcohol - fatty acid
- (Am) ④ phospho lipid. $\left\{ \begin{array}{l} \text{phosphoglyceride: } \left\{ \begin{array}{l} \text{phosphate} \\ \text{another amino acid} \end{array} \right. \left\{ \begin{array}{l} \text{FA} \\ \text{FA} \end{array} \right. \\ \text{Sphingolipid: } \left\{ \begin{array}{l} \text{sphingosine} \\ \text{fatty acid} \end{array} \right. \left\{ \begin{array}{l} \text{NH}_2 \\ \text{C} \\ \text{double bond} \end{array} \right. \end{array} \right.$
- (Am) ⑤ cholesterol: 4 cycles 8 carbon chain

Lipo structure

- ① enzyme
 - (outer) ② Apo protein - span the region - have part: exposed at surface. core outer envelop
 - ③ lipid \rightarrow ③ outer part: polar monophosphate - free cholesterol \rightarrow + charged point out \rightarrow water ③ core: - esterified cholesterol - Triacylglycerol
- Form the center of droplet (phobic)

صرفون، لا استروية بتال الكولسترول. صرفون، نصف الكثرية كور تيزول.

(* Albumin + FFA) \rightarrow free fatty acid - albumin complex (not true lipoprotein)



very large very negative

(Apoprotein) Function :-

- part of structure (lipoprotein) (apo B)
- enzymic cofactor (apo C-II)
- lipoprotein lipase
- inhibitors enzym. (Apo-A-II) } class
- lipoprotein lipase (Apo C-III) }
- Ligands (B-10) } interaction with lipoprotein receptor in tissue
- (apo E) }

chylomicrons

synthesized in intestinal mucosal cell.
 Function: Carry dietary lipids
 intestine → peripheral tissue

Fate: synthesize → M cell

- secreted by exocytosis (into lymph)
- pass blood → mature chylomicrons

Lipoprotein lipases

exist in:

- capillary wall (adipose tissue)
- muscle → esp. cardiac muscle.

extracellular Enzym

digest → triglycerol of CM → Fatty A. + Glycerol

deliver mainly →

- adipose tissue
- heart, muscle (80%)
- Liver (20%)

Result :- CM become

- smaller
- decrease triglycerol content
- become ~~richer~~ richer in cholest. protein

VLDL

Produce: liver
 Function: Carry lipid
 - liver → peripheral tissue.

FA synthesis liver

obtains blood synthesis from glucose.

healthy :- major source of fatty acid
 ↓
 VLDL → excess → dietary triglycerol glucose.

(Forming of LDL)

As VLDL pass circulation → release Fatty acid + glycerol → degraded TAG by lipoprotein lipase. → Remove
 ↓
 inter-mediate density lipoprote → Remove more TAG → form LDL

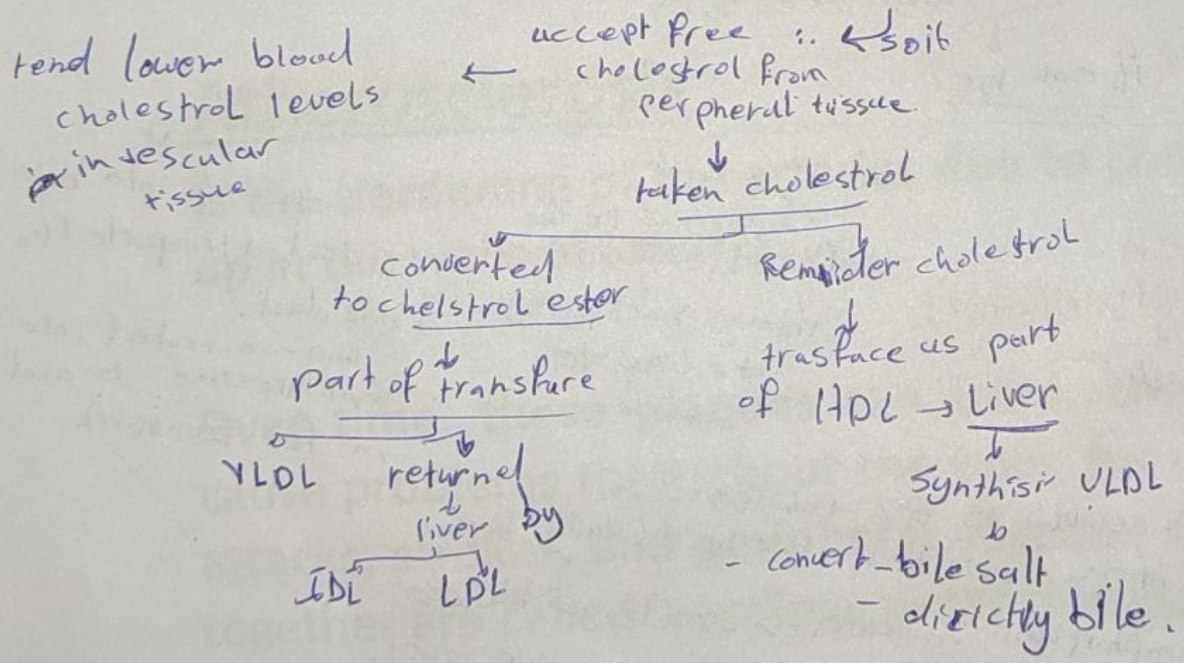
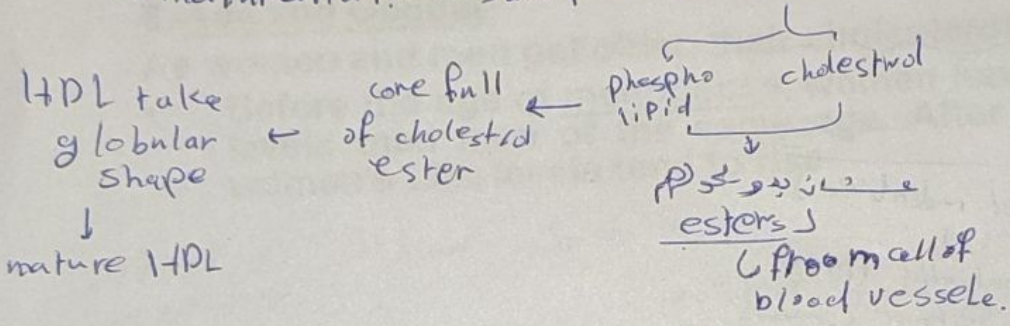
LDL (Bad FA)

* Nascent: immature

- func: - provide cholesterol to peripheral tissue.
- Rich → cholesterol and cholesterol ester.
- 60% back → liver.
- 40% extrahepatic → adrenocortical, gonad } cell synthesis steroid hormone.
- elevated level → atherosclerotic plaques

HDL (good cholesterol)

- Created by number mechanism:
- Nascent synthesis by liver & intestine } small molecule contain:
 - cholesterol
 - phospholipid.
 - apoprotein
- maturation: - nascent particles accumulate



Reverse cholesterol transport

(HDL) → remove cholesterol from loaded cell → liver
 esterification of cholesterol → prevent from leaving HDL
 → High level HDL → vasculo protective

Desired value

LDL cholesterol: less 100mg/dL (optimal - مثالي)

high (30-150)mg/dL (borderline high) - ارتفاع - خطير

HDL ~: greater 40-60 (desired) - المطلوب

Total cholesterol: less 200

Triglyceride: - Borderline high 200-239
 10-150 (normal) - طبيعي

VLDL: 2-38

hypercholesterolemia - زياده

cholesterol synthesized in liver

essentially three fates (ثلاثة)

it can be

esterified with fatty acid by enzyme (ACAT) & acyl-CoA to make cholesterol ester → stored in lipid droplet. (cholesterol acyl transferase)

- Exported to the peripheral tissue through packaging into lipoprotein particles

converted into bile acid → transported to bile duct and secreted into small intestine to aid in fat transport

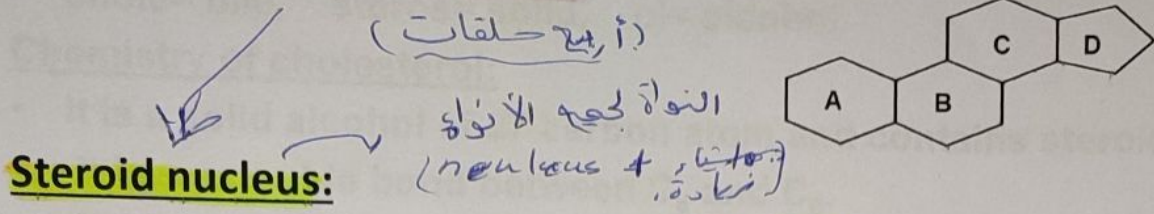
Bile Acids

as much as 50% → cholesterol in liver → converted → bile acid (daily basis).
 is amphipathic molecule → stored in gall bladder
 secreted into intestine through bile duct.
 Reabsorbed and returned to liver
 - greater 95% rest is excreted as waste.
 ~ 5% - قليل

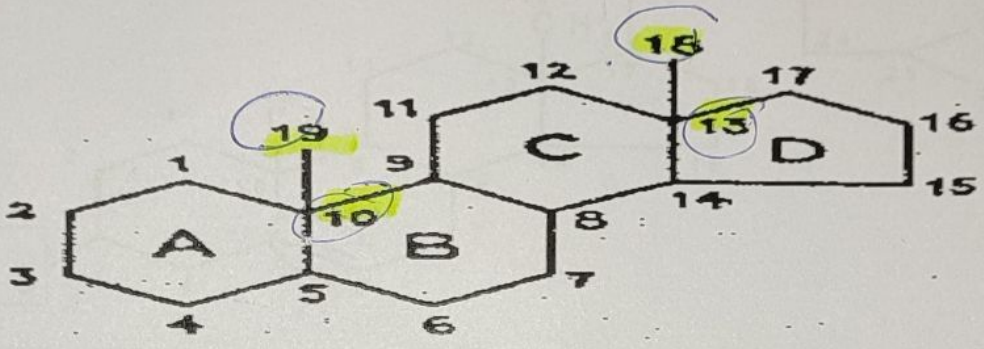
(hydrophobic) cholesterol → very large molecule → OH group

Steroids

- Steroids are group of plant and animal lipids that have a similar tetracyclic nucleus.



- So this tetracyclic nucleus is composed of **17** carbon atoms besides two methyl groups (C_{18} , C_{19}).
- There is a methyl group at C_{10} (it makes C 19).
- And there is another methyl group at C_{13} (it makes C18).



Steroids include:

1. **Sterols.**
2. **Bile acids and salts.**
3. **Steroid hormones.**
4. **Vitamin D.**

STEROLS: مجموعة الكوليسترول

- This group of steroids has a **hydroxyl group (OH)** at C_3 i.e. it is an alcohol, and an **aliphatic side chain** at C_{17} .

Types of sterols: ↳ side chain (only carbon, hydrogen atoms)

A. Animal sterols:

- **Cholesterol** and its derivative **7-dehydrocholesterol.**

B. Plant sterols:

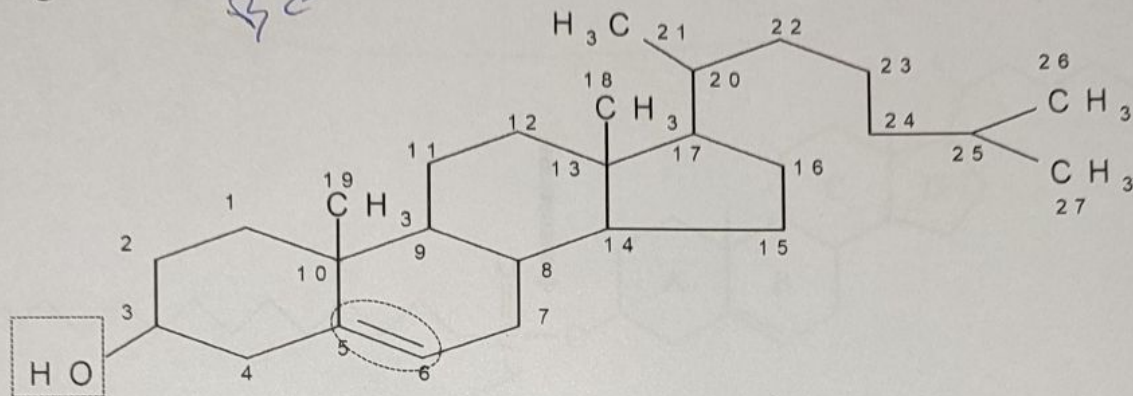
- **Ergosterol.**

Cholesterol

- **Naming:** The word cholesterol is derived from Greek words; chole= **bile**, steros= **solid**, ol= **alcohol**.

Chemistry of cholesterol:

- It is a solid alcohol of **27 carbon atom** and contains steroid ring.
- it has a **double bond** between **C₅** and **C₆**.
- One **hydroxyl group** at **C₃** which is characteristic to all sterols.
- The OH group is **beta oriented**, projecting above the plane of ring.



Properties of cholesterol:

- It has **amphipathic** properties which allow it to play structural role in **membrane** and in the outer layer of **lipoprotein**.

Cholesterol Sources

1. It is formed in the **body** from **acetyl CoA**. Most of the cholesterol is synthesized by the liver.
2. It is present in diet: **egg yolk**, **meat**, **liver** and **brain**. (It occurs in animal fats but not in plant fats).

Biomedical importance:

- 1- It is the **main sterol** in human body (**Nervous tissue**, **brain**, **suprarenal gland**, and in **bile**).
- 2- It is present in **blood** (normal level **150-200 mg / dl**). (Adrenal gland)
- 3- It is often found as **cholesterol ester** (in combination with **fatty acids**). The **fatty acid** is attached to the **hydroxyl group** e.g. **Cholesteryl oleate** or **linoleate**.

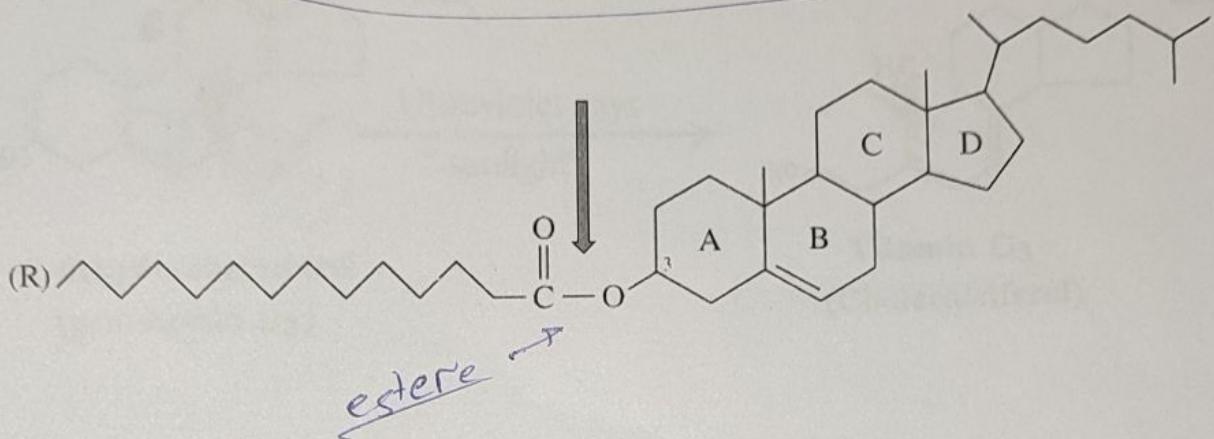
1. **cholesterol**

C₃

oleate

Cholesterol esters (CE)

- Cholesterol is converted to **cholesteryl esters** for cell storage or transport in blood
- Fatty acid is esterified to **C-3 OH** of cholesterol
- **Cholesterol esters** are very water insoluble (hydrophobic) and must be complexed with phospholipids or amphipathic proteins for transport



Biomedical importance:

4- It is a ^(main part) **major constituent** of the **plasma membrane**. The ^{rigid} fused **ring system** makes cholesterol **less flexible** than most other lipids.

5- It is the **precursor** of:

➤ Sex hormones

➤ Cortical hormones

➤ Vitamin D

➤ Bile acids.

secretion of Adrenal gland (Brain Suprarinal)

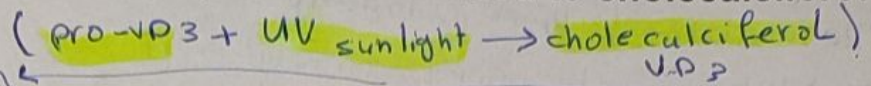
6- **High level of cholesterol in blood** will lead to its precipitation in the wall of blood vessels "**atherosclerosis**". Also high levels of blood cholesterol may lead to **stones** in **gall bladder** (**gall stone**).

high blood cholesterol → arteries → ^{Arteriosclerosis} ~~Arteriosclerosis~~

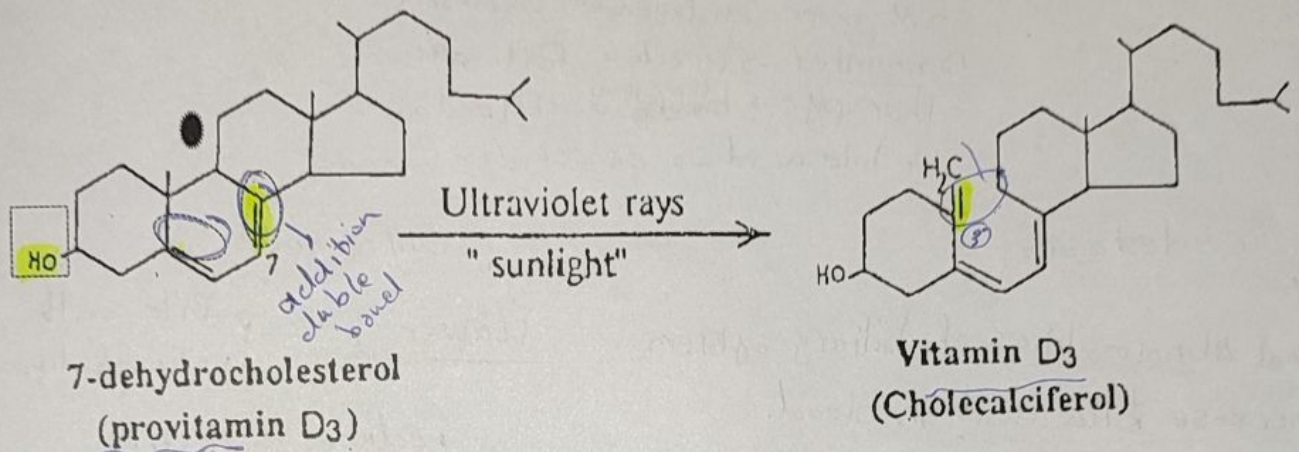
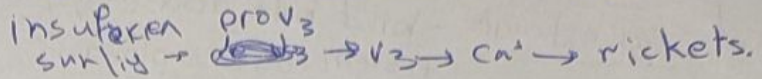
accumulation

7-dehydrocholesterol (pro-vitamin D3)

- 7-dehydrocholesterol is stored under the skin, and by the effect of ultraviolet rays (in sunlight) it is transformed to cholecalciferol (vit. D₃.)



Insufficient sunlight can lead to a deficiency of vitamin D₃, interfering with Ca²⁺ transport and bone development. Rickets can result.



Clinical correlation

- Low density lipoproteins (LDL) transports cholesterol from liver through blood to the tissues (Bad cholesterol)
 (liver → blood → tissue)
- High density lipoprotein (HDL) transports cholesterol from blood to the liver where it is metabolised (Good cholesterol)
 → blood → liver.

↑ LDL, ↑ Cholesterol High risk of heart attack

↑ HDL, ↓ Cholesterol Low risk of heart attack

lipid (4) → Bile acids
 → sex hormones

Bile Acid

hydroxylate steroid (OH be added)
 COOH ← acid negative

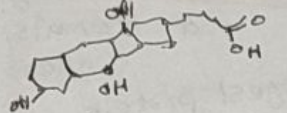
≈ 600 mg → bile salt
 synthesiz daily to replace
 losing in feces 5%.

amphipathic
 - stored in gall bladder

→ (liver)
 Peroxisomal enzym; assist hepatic biosynthesis → bile acid

- Found in the bile of → mammals & invertebrate
- conjugated → taurin, glycine } AA.
- residues give anion called bile salt (with cation)
- Liver → synthesize → via: cytochrome P450-mediate oxidation of cholesterol in multistep process.

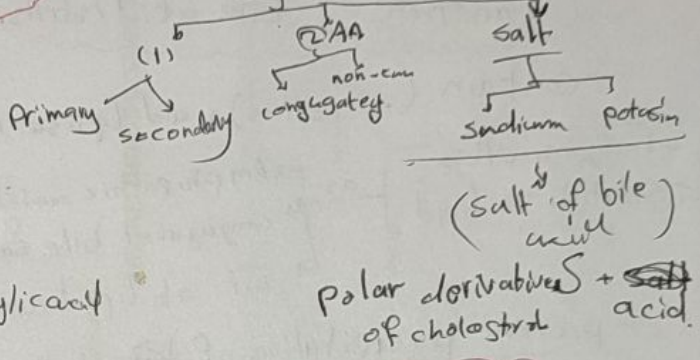
Primary bile salt (low only)
 cholic → chenodeoxycholic →



Structure

- large family of molecules
- steroid structure (nucleus ring)
- side chain terminate → COOH → carboxylic acid
- different number of hydroxyl group (double bond) is to *

(Classification)



conjugation

→ mainly four bile acid secreted from liver.
 - prior secretion → live conjugated them
 - glycine = NH₂CH₂COO⁻ with low A.A.
 - Taurine = NH₂CH₂CH₂SO₃⁻
 ↓ = 8 total possible conjugate bile acid.

From cholesterol → synthesis of bile acid

- 1) hydroxylation reaction
- 2) epimerization of 3rd hydroxyl group
- 3) saturation of double bond
- 4) side chain cleavage/oxidation

(Enterohepatic circulation)

In duodenum always in (deprotonate) form (A⁻).
 ↓
 match water soluble
 ↓
 able to emulsify Fats

- bile acid secreted into lumen of intestine
 - Bacterial partial dehydroxylation (secondary bile acid) Form
 - all these bile acids → taken back.
 Return liver → be secreted → blood stream → into

(enterohepatic circulation) process

5% excreted → faeces

Function of bile acid/salts

powerful detergent
or emulsifying agent

in intestine
↓
to aid digestion and absorption

- contain (micelles) → aid lipase to digest protein

- Form micelles
can solubilize lipid

as → Amphipathic molecule
conjugated bile salt.
sit at lipid/water interface.

< 2 > prevent precipitation of cholesterol in bile.

< 3 > Remove cholesterol from body → major pathway
5% lost → faeces.

⊕ Signaling molecule.

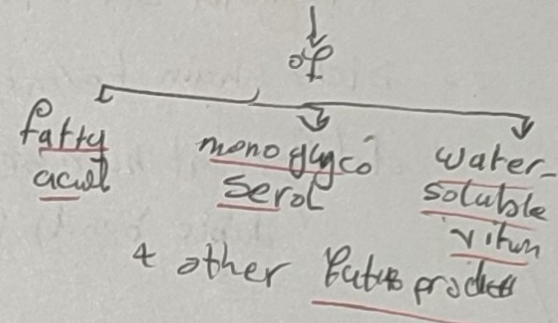
It has influence in metabolism → lipid.
→ glucose.

< 5 > inhibitory effect upon apoptosis (موت الخلية)

+ being study → Alzheimer's effect.

Beneficial.

بنيطاعون، فلبسا ← جراثيم، البصيرة العرجية
الأحراق من الزلال.



Slide 4

Clinical Significance of bile salt

(عنا صون عااله)
المراد

Hyperlipidemia

as → Bile acid made from endogenous cholesterol
↳ destruction of enterohepatic circulation of bile acid → lower cholesterol (المراد)

- Bile acid sequestrants - bind bile acid in gut
 - prevent reabsorption.
 - ↳ No more endogenous cholesterol is shunted → produce Bile salts
 - therapy → lowering cholest. level
 - ∴ bile acid → excreted in faeces.

Colon Cancer

- At high concentration bile salt is toxic.
- percentage relevant to colon cancer.

Cholestasis

- Functional abnormalities of biliary system results in increase bile acid in blood.

- Related to: the itching

Gallstones

[lower]

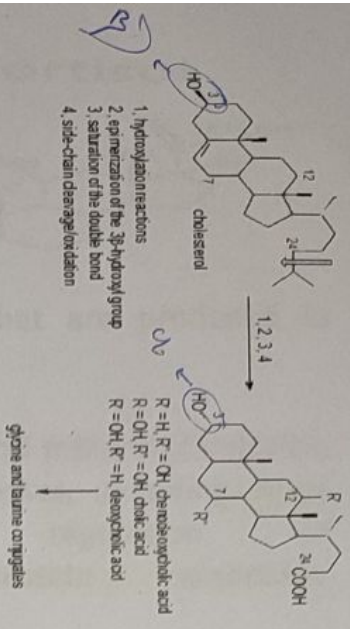
Bile salt
↳ phospholipid

- reduce cholesterol solubility
↓ level to
microcrystal formation

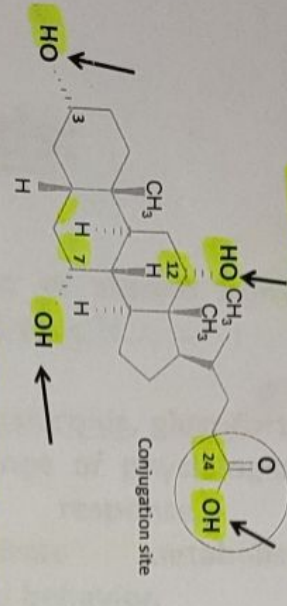
- oral therapy with chenodeoxycholic

dissolve cholesterol
gallstone ← use

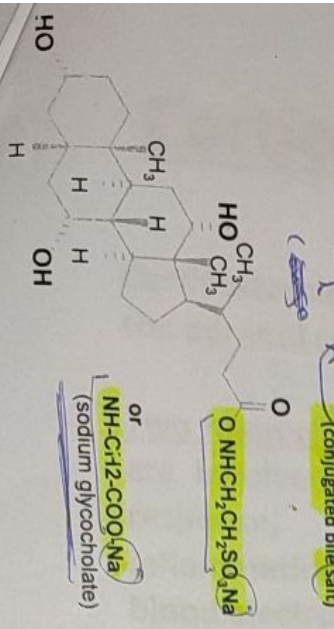
Biosynthesis of bile acids



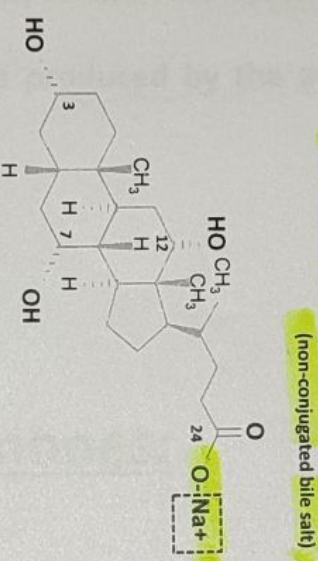
Bile acids: Cholic acid



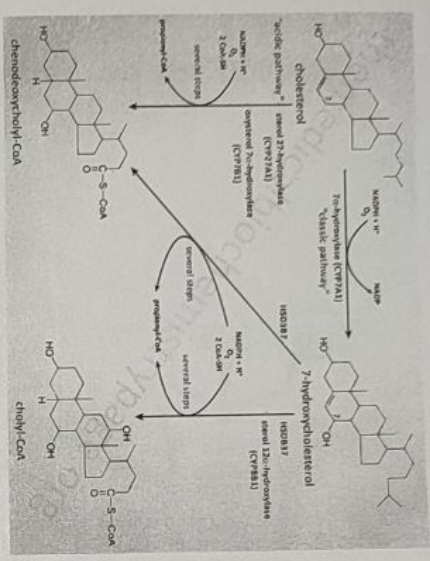
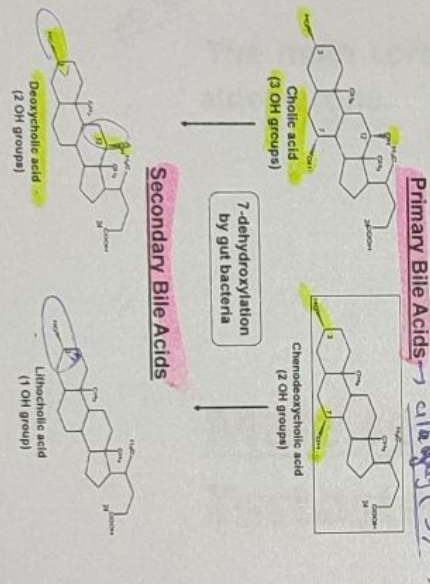
Bile salts: Sodium taurocholate



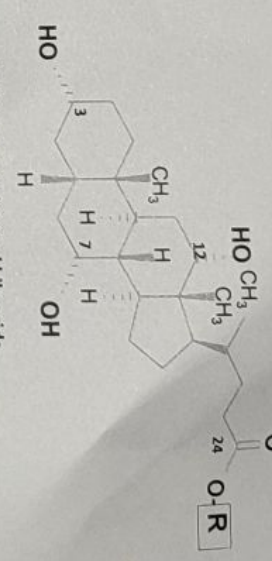
Bile salts: Sodium cholate



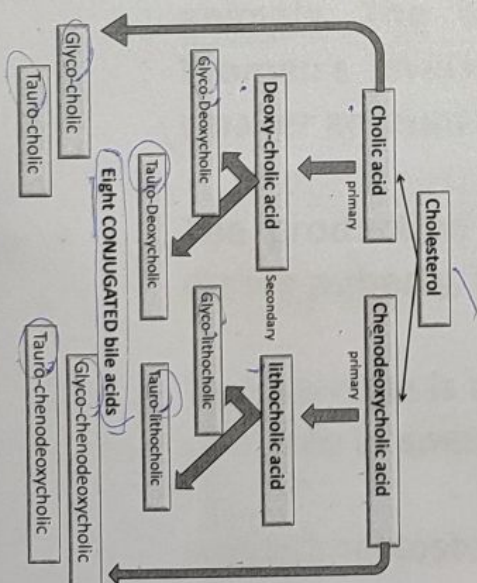
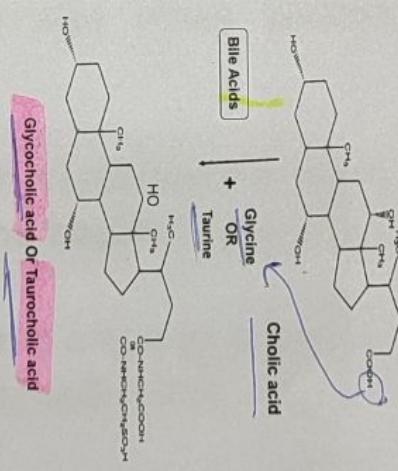
Primary and secondary bile acids



Bile acids/salts

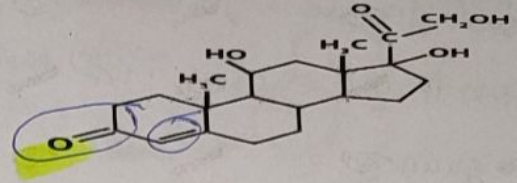


Bile Acid Conjugation



Corticosteroids:

Cortisol



Corticosteroids are a class of steroid hormones that are produced in the adrenal cortex of vertebrates. (الغدد الكظرية)

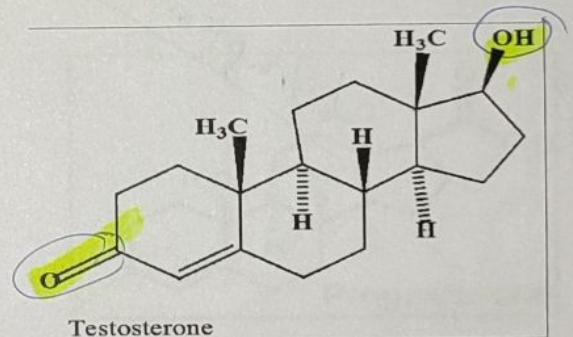
Two main classes of corticosteroids, glucocorticoids and mineralocorticoids, are involved in a wide range of physiological processes, including stress response, immune response, and regulation of inflammation, carbohydrate metabolism, protein catabolism, blood electrolyte levels, and behavior.

Some common naturally occurring steroid hormones are cortisol, corticosterone, cortisone and aldosterone.

The main corticosteroids produced by the adrenal cortex are cortisol and aldosterone.

Male sex hormones:

Testosterone



Testosterone is a hormone found in humans, as well as in animals. The testicles primarily make testosterone in men. Women's ovaries also make testosterone, though in much smaller amounts.

The production of testosterone starts to increase significantly during puberty, and begins to dip after age 30 or so.

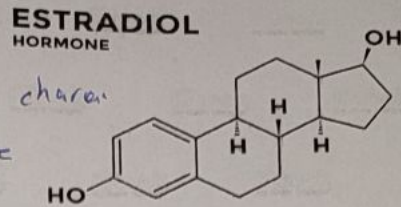
Testosterone is most often associated with sex drive, and plays a vital role in sperm production.

A man's testosterone levels can also affect his mood.

Female sex hormones:

Estradiol

26th secondary reproductive tissue



Estradiol, also spelled **oestradiol**, is an **estrogen** steroid hormone and the **major female sex hormone**.

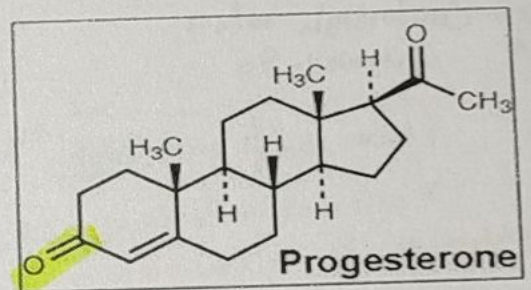
Estradiol is responsible for the **development** of **female secondary sexual characteristics** such as the **breasts**, **widening of the hips**, and a **female-associated pattern of fat distribution**.

It is important in the development and maintenance of female **reproductive tissues** such as the **mammary glands**, **uterus**, and **vagina** during **puberty**, **adulthood**, and **pregnancy**.

Female sex hormones:

Progesterone

ketone



Progesterone is an **endogenous steroid** and **progesterone** sex hormone involved in the **menstrual cycle**, **pregnancy**, and **embryogenesis** of humans and other species.

Progesterone has a variety of important functions in the body.

It is also a **crucial metabolic intermediate** in the production of other endogenous steroids, including the sex hormones and the corticosteroids, and plays an important role **in brain function** as a **neurosteroid**.