Biochemistry of Lipids

- Fats and lipids are an essential component of the homeostatic function of the human body. Lipids contribute to some of the body's most vital processes.

- Lipids are fatty, waxy, or oily compounds that are soluble in organic solvents and insoluble in polar solvents such as water. Lipids include:

- Fats and oils (triglycerides) , Phospholipids, Waxes, Steroid

---

Plasma lipids and lipoprotein

The main four types of lipids present in plasma are:

1-Fatty acids are straight chain carbon compounds , saturated (no doble bonds) ,monounsaturated , or polyunsaturated. Esterified with glycerol to form triglycerides or non esterified (Free fatty acids) transported mainly bound to albumin .

2-Triglycerides are fatty acids esters of glycerol ,each containing 3 different fatty acids ,transported in plasma as lipoproteins or stored in Adipose tissue.

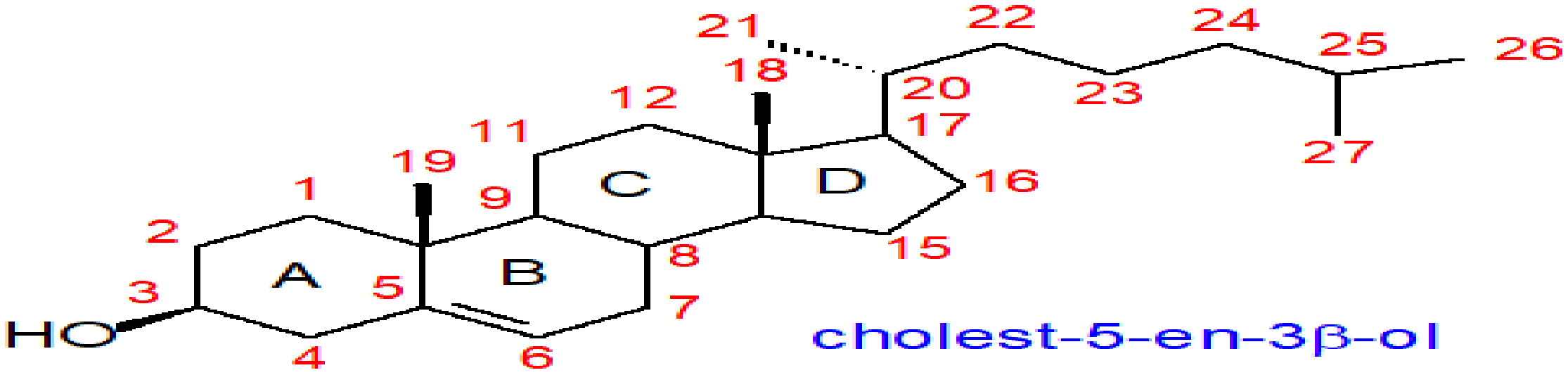
3- Cholesterol ,it is a precursor to many physiologically important steroids like bile acid and steroid hormones ,unlike that of triglycerides plasma cholesterol concentration does not rise after fatty meal

4-Phospholipids are complex lipids, like triglycerides but contain Nitrogen and Phosphate base instead of fatty acids, mainly in cell membranes .

Sterol is an organic compound with formula $C_{17}H_{28}O$, whose molecule is derived from that of gonane by replacement of a hydrogen atom in position 3 by a hydroxyl group. It is therefore an alcohol of gonane. More generally, any compounds that contain the gonane structure, additional functional groups, and/or modified ring systems derived from gonane are called steroids. Therefore, sterols are a subgroup of the steroids. They occur naturally in most eukaryotes, including plants, animals, and fungi, and can also be produced by some bacteria (however likely with different functions).

The most familiar type of animal sterol is cholesterol, which is vital to cell membrane structure, and functions as a precursor to fat-soluble vitamins and steroid hormones.

sterols are classified by biochemists as lipids (fats in the broader sense of the term)



Lipoproteins

Plasma lipids are either Exogenous (from the food) or Endogenous synthesized in the body .lipid are insoluble in water so they carried in plasma as soluble complexes with protein known as lipoproteins .The main five types of lipoproteins are :

- 1-Chylomicron ,which transport exogenous lipids from intestine to all cells.
- 2- VLDL (Very low density lipoproteins) .
- 3- IDL (intermediate density lipoproteins) it is normally transient and
- Undetectable .
- The upper 3 lipoproteins carry mainly triglycerides ,while the remaining 2 carry mainly cholesterol .
- 4- LDL (low density lipoproteins) .
- 5- HDL (high density lipoproteins).

Metabolism of lipoproteins

- Lipoproteins are synthesized in the intestine or liver ,its process of transport and metabolism is regulated by a protein component of lipoprotein particles called Apolipoprotein. They are different apolipoprotein :

- Apo A and apo B incorporated in the lipoprotein structure .
- Apo C and apo E interchange freely between lipoproteins .
- Apo A1 and apo C11 (ApoC2) activate enzymes of lipid metabolism.
- Apo B and apo E recognize receptors involved in cellular uptake of lipoprotein particles .

lipoproteins maintain solubility of lipids

. Exogenous pathways الطريق الخارجي

Fatty acid and cholesterol released from digestion of fat with cholesterol of bile absorbed and re-esterified to triglyceride and cholesterol esters .These with phospholipids ,apo A and apo B are secreted into lymphatic system as chylomicrons which inter systemic circulation by thoracic duct

Chylomicrons are metabolized in adipose tissue and muscles by the enzyme Lipoprotein lipase which is activated by apo C11 :

Its triglycerides→ fatty acid taken by adipose tissue or muscles, or bound to plasma albumin. and glycerol enter the hepatic glycolytic pathway .

The surface material of chylomicron (containing apo A , apo C and phospholipids)incorporated into HDL ,

and Chylomicron remnant (بقايا) (cholesterol ,apo B and apo E) bind to hepatic receptors, inter hepatic cells → protein catabolized and cholesterol released .

At the end of this pathway dietary triglyceride go to adipose tissue and muscles, and cholesterol go to the liver .

Endogenous pathwayالطريق الداخلي

The liver is the main source of endogenous lipids , triglycerides synthesized from glycerol and fatty acids which come from the fat stores or from glucose . Cholesterol synthesized locally or derived from chylomicron remnant . these lipids are transported from liver as VLDL .

VLDL metabolism

In peripheral tissues VLDL triglycerides are removed by lipoprotein lipase and the VLDL remnant (IDL) either taken by the liver or loses the remaining triglycerides and become LDL .

LDL metabolism

It is small cholesterol rich lipoprotein containing only apo B (about 70 percent of total cholesterol in plasma) .It is taken by specific receptors (LDL or apo B/E receptors)which more abundant in the liver . in the cells they are broken down by lysosomes ,the cholesterol released inter in membrane formation or in the adrenal cortex and gonads converted to steroid hormones .

Note : because of there small size LDL particles can infiltrate arterial walls and cause atherosclerosis

The liver has a central role in cholesterol metabolism because it :

* contain most of LDL receptors .
* synthesize most of endogenous cholesterol .
* receives cholesterol from diet and from lipoproteins .
* is the only organ that can secrete cholesterol from the body in bile .

Role of HDL

Cholesterol synthesized in cells would accumulate there if not removed , the only excretory rout is in the bile.

The transport of cholesterol from non hepatic cells to the liver involve HDL .

- HDL is synthesized in hepatic and intestinal cells and secreted as small particles containing phospholipids , free cholesterol and apo A and apo E (nascent HDL) .

- It may also be formed from the surface coat of VLDL or chylomicrons .

- esterification of cholesterol is catalyzed by LCAT enzyme which is part of HDL particle , this cholesterol is transferred to LDL, VLDL ,and chylomicron remnant. A small part stored in the core of spherical HDL .

- HDL synthesis is increased by estrogen so it is higher in menstruating women than menopause women and men .

Total cholesterol = LDL Ch. +HDL Ch. +VLDL Ch. .

VLDL Ch. =Triglycerides /5 , when triglycerides less than 5 mmol/L (425 mg/dl).

So LDL Ch. =Total cholesterol – (HDL Ch.+ triglyceride / 5) .