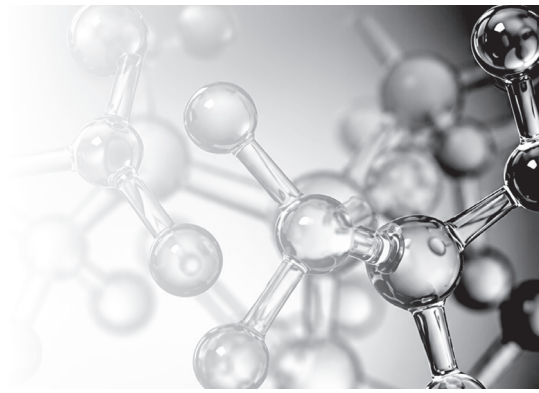
CHAPTER

3



Chemistry of lipids

CHAPTER OUTLINE

- Introduction to lipids
- Biological importance of lipids
- Classification of lipids
- Physical and chemical properties
- Cholesterol and lipoproteins

LEARNING OBJECTIVES

After studying this chapter, the student should be able to:

- Define lipids and describe their general characteristics.
- Explain the biological importance of lipids.
- Classify lipids with suitable examples.
- Describe the physical and chemical properties of lipids.
- Explain the structure, functions and clinical importance of cholesterol.
- Define lipoproteins and describe their structure and classification.
- Relate abnormalities of cholesterol and lipoproteins to cardiovascular disease.
- Understand the laboratory significance of lipid profile estimation.

LIPIDS

Lipids are a heterogeneous group of organic compounds that are insoluble in water but soluble in organic solvents like ether, chloroform, and benzene. They mainly contain carbon, hydrogen and oxygen. Some lipids also contain phosphorus, nitrogen, sulphur or carbohydrates.

BOLOGICAL IMPORTANCE OF LIPIDS

Lipids perform several essential functions in the human body.

1. **Energy storage**
   - Triacylglycerols are the major form of energy storage.
   - **1 gram of fat provides approximately 9 kcal of energy.**
   - Adipose tissue serves as the major storage site.
   - Lipids provide energy during fasting and prolonged exercise.

2. Structural components of cell membranes

Phospholipids, cholesterol and glycolipids are major components of biological membranes.

They contribute to:

- Membrane structure
- Membrane fluidity
- Selective permeability
- Cell recognition
- Cell signalling

The phospholipid bilayer provides the basic structural framework of the plasma membrane.

3. Thermal insulation & protection

Subcutaneous adipose tissue fat reduces heat loss from the body and helps maintain body temperature.

4. Mechanical protection

Deposits of adipose tissue around organs provide cushioning and protection.

For example, fat surrounding the kidneys and heart provides cushioning and protection against physical injury.

5. Absorption and transport of fat-soluble vitamins

Dietary lipids facilitate the intestinal absorption of vitamin A, Vitamin D, Vitamin E and Vitamin K

Defective fat digestion or absorption may therefore result in deficiency of these vitamins.

6. Source of essential fatty acids

Certain fatty acids cannot be synthesized adequately by the human body and must be supplied through the diet.

Examples include:

- Linoleic acid
- α-Linolenic acid

7. Precursors of biologically important compounds

Lipids serve as precursors for:

- Steroid hormones
- Bile acids
- Vitamin D
- Eicosanoids such as prostaglandins

CLASSIFICATION OF LIPIDS

Based on composition, lipids are classified into three classes, namely

1) SIMPLE LIPIDS

These are esters of fatty acids with alcohol.

- **Fats & Oils**

  They are esters of fatty acids with glycerol and are also called **triacylglycerols or triglycerides**.
- **Fats:** Usually solid at room temperature
- **Oils:** Usually liquid at room temperature
- **Waxes**

  These are esters of fatty acids with high molecular weight long chain alcohols.

  Examples:
  - Beeswax
  - Lanolin

2) COMPOUND (COMPLEX) LIPIDS

These contain fatty acids, alcohol and additional groups.

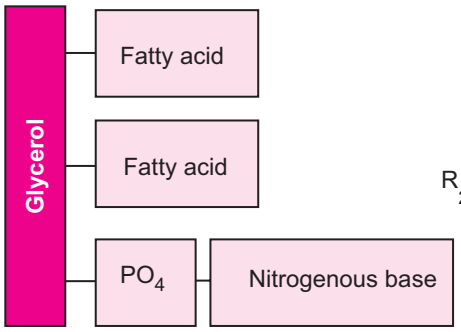
1. Phospholipids

Contain:

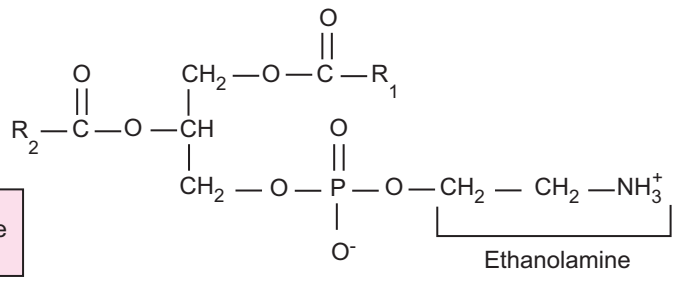
- Fatty acids
- Alcohol
- Phosphate group
- Nitrogenous base or other substituent

Examples:

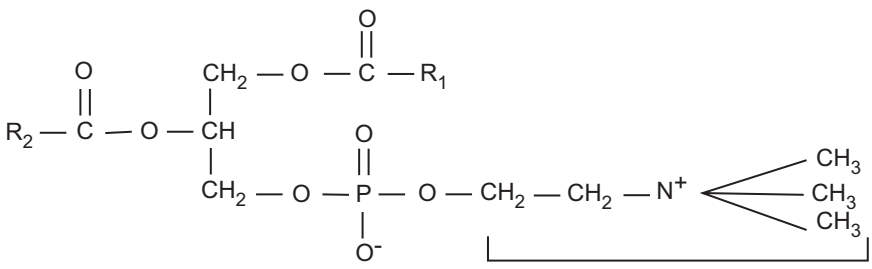
- Lecithin
- Cephalin
- Sphingomyelin



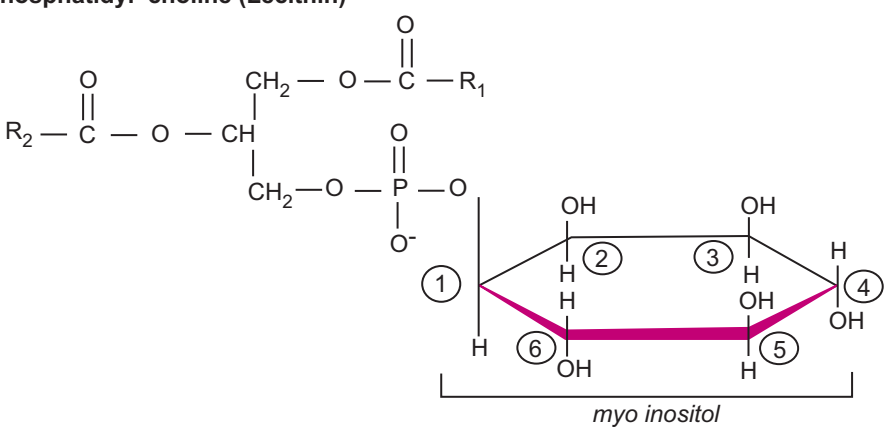
Glycerophospholipid



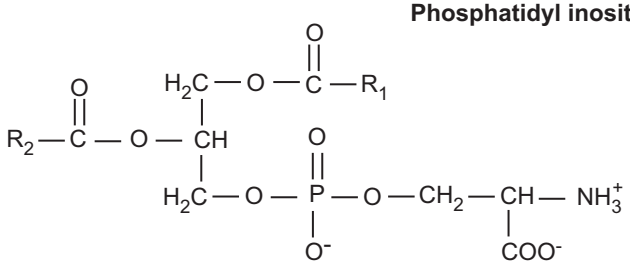
Phosphatidyl ethanaolamine (Cephalin)



Phosphatidyl choline (Lecithin)



Phosphatidyl inositol



Phosphatidyl serine

Fig. 3.1 : Structures of cephalin, lecithin, phosphatidylinositol and phosphatidyl serine

2. **Glycolipids**

   Contain carbohydrate in addition to lipid components.

   Examples:

   - Cerebrosides
   - Gangliosides

3. **Lipoproteins**

   Complexes of lipids and proteins involved in lipid transport in blood.

   Examples:

   - Chylomicrons
   - VLDL
   - LDL
   - HDL

3) DERIVED LIPIDS

These are substances derived from simple or complex lipids.

Examples:

- Fatty acids
- Glycerol
- Cholesterol
- Steroid hormones
- Ketone bodies
- Fat-soluble vitamins

PHYSICAL PROPERTIES OF LIPIDS

- **Insoluble** in water but soluble in organic solvents such as ether and chloroform.
- Most lipids have a **specific gravity less than water** and therefore tend to float on its surface.
- **Melting point**

  The melting point depends on:

  - Chain length of fatty acids
  - Degree of saturation

  Saturated fatty acids generally have higher melting points.

  Unsaturated fatty acids generally have lower melting points because double bonds introduce bends in the hydrocarbon chain and reduce close packing.

- **Emulsification**

  Large fat droplets can be broken into smaller droplets to form an **emulsion**.

  In the intestine, bile salts help emulsify dietary fats, increasing the surface area for digestion by lipases.

CHEMICAL PROPERTIES OF LIPIDS

1. **Hydrolysis**

   Triacylglycerols undergo hydrolysis to produce:

   Triacylglycerol + Water → Glycerol + Fatty acids

   This reaction occurs during digestion catalysed by **lipases**.

2. **Saponification**

   When fats are heated with strong alkali, they form:

   - Glycerol
   - Salts of fatty acids called **soap**

   Fat + Alkali → Glycerol + Soap

   This reaction is the basis of the **saponification number**.

3. **Hydrogenation**

   Unsaturated fatty acids contain double bonds. Hydrogen can be added across these double bonds to increase saturation.

   This process converts liquid oils into more solid fats.

   (Oils → Solid fats)

4. Rancidity

Unsaturated fatty acids are susceptible to oxidation.

Oxidation of lipids can produce **rancidity**, resulting in unpleasant taste and odour.

Antioxidants and appropriate storage conditions can reduce lipid oxidation in biological and food samples.

5. Iodine number

The iodine number indicates the degree of **unsaturation** of a lipid.

It is defined as the amount of iodine absorbed by **100 g of fat or oil**.

A higher iodine number generally indicates a greater degree of unsaturation.

FATTY ACIDS

- Fatty acids are carboxylic acids consist of non-polar hydrocarbon chain (tail), with methyl group at one end and a polar carboxyl group (head) at the other end. Thus, they are polar, with a hydrophilic(-COOH) and a hydrophobic ($-CH_3$) end.

  General formula is R - COOH
- Most fatty acids in humans contain an even number of carbon atoms (usually between 16 and 20).
- They are the simplest form of the lipids

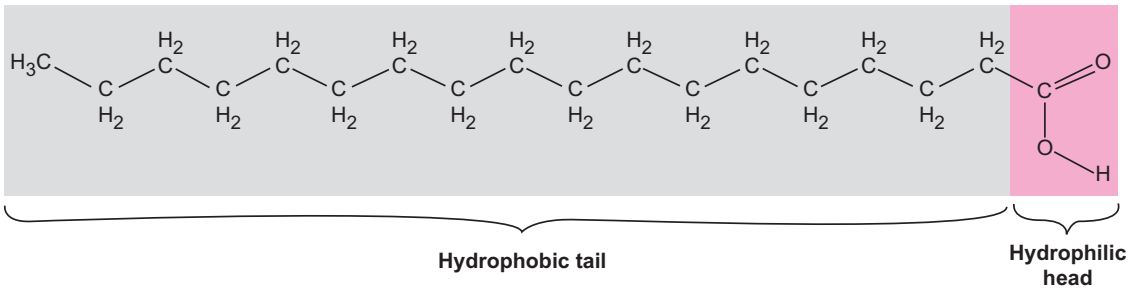


Fig. 3.2 : Structure of fatty acid

Occurrence of fatty acid

- They are not found free in nature but found as esterified forms as major constituents of various lipids
- Fatty acids of animal origin are much simpler in structure in contrast to those of plant origin.

Nomenclature of fatty acids

There are two systems of numbering the carbon atoms in a fatty acid

$$\overset{n}{CH_3} - (CH_2)_n - CH = CH - \overset{3}{CH_2} - \overset{2}{CH_2} - \overset{1}{CH_2} - COOH$$

$$\omega \qquad\qquad\qquad\qquad\qquad\qquad \beta \quad \alpha$$

1. Numbering starts from carboxyl carbon. The last carbon is the "n" carbon
2. The second carbon is the "α"and the third the "β" Carbon. The last carbon atom is omega.

ω terminus										Carboxy terminus
	CH_3-(CH_2)n		-CH_2	-CH_2	-CH_2-CH_2		-CH_2	-CH_2	-CH_2-COOH	
C numbering	n	9	8	7	6	5	4	3	2	1
n or ω numbering	1	2	3	4	5	6	7	8	9	10
Letter	ω1	ω2	ω3			δ	γ	β	α	
Designation	n1	n2	n3							

Eg:- CH_3–$(CH_2)_7$–CH_2–CH_2–$(CH_2)_7$–COOH stearic acid (saturated fatty acid)

Eg:- CH_3–$(CH_2)_7$–**CH=CH**–$(CH_2)_7$–COOH oleic acid (Unsaturated fatty acid)

Fatty acids can be represented as shown below where the delta indicates the position of the double bond and the next number shows the number of carbon atoms and the last number indicates the number of double bonds. In a different way the position of the double bond (s) can be indicated as shown in the second expression without the delta.

C18 : 1, Δ^9 or 18:1(9)

C18 indicates 18 carbons, 1 indicates the number of double bonds, delta 9(Δ^9) indicates the position of double bond between 9^{th} and 10^{th} carbon atoms.

Double bonds in naturally occurring fatty acids are in the cis- configuration and saturated fatty acids of C_{12} to C_{24} are solids at body temperature but the unsaturated once are liquids.

Common fatty acids

Table - 3.1 : Classification of fatty acids

Common name	Systematic name	Symbol
Palmitic acid	Hexadecanoic acid	16: 0
Stearic acid	Octadecanoic acid	18:0
Palmitoleic acid	9-hexadecaenoic acid or 9-hexadecenoic acid	16: 1;9
Oleic acid	9-octadecaenoic acid or 9-octadecenoic acid	18: 1;9
Linoleic acid	9,12-octadecadienoic acid	18: 2;9,12
Linolenic acid	9,12,15-octadecatrienoic acid	18: 3; 9,12,15
Arachidonic acid	5,8,11,14-eicosatetraenoic acid	20:4; 5,8,11,14

Table - 3.2 : Classification of fatty acids

Symbol	Common name	Systematic name
16: 1	Palmitoleic acid	9-hexadecaenoic acid
18: 1	Oleic acid	9-octadecaenoic acid
18: 2	Linoleic acid	9,12-octadecadienoic acid
18: 3	Linolenic acid	9,12,15-octadecatrienoic acid
20:4	Arachidonic acid	5,8,11,14-eicosatetraenoic acid

CH_3-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2 ——— CH_2-CH_2-COOH

Saturated fatty acid

Unsaturated fatty acids

Fatty acids which have one or more double bonds in the hydrocarbon chain are called unsaturated fatty acids.

- Contain one or more double C = C bonds
- A double bond makes the chain relatively rigid and causes a kink.
- Few interactions between chains
- Low melting points
- Liquids at room temperature
- Unsaturated fatty acids containing up to 30 carbons are identified
- They are subdivided into mono unsaturated fatty acids and polyunsaturated fatty acids (PUFA) based on number of double bonds.
- Monounsaturated fatty acids are palmitoleic acids and oleic acid. They contain one double bond.
- Poly unsaturated fatty acids are linoleic acid, linolenic acid and arachidonic acid.

CH_3-CH_2 -CH_2 -CH_2-CH_2=CH_2-CH_2-CH_2——— CH_2 -$(CH_2)_n$-COOH

Mono unsaturated fatty acid

CH_3-CH_2 -CH_2 =CH_2-CH_2=CH_2-CH_2=CH_2——— CH_2 -$(CH_2)_n$-COOH

Polyunsaturated fatty acid (PUFA)

Functions

- Fatty acids are source of energy for humans similar to glucose
- Fatty acids are components of nervous tissue, lipoproteins etc.,
- Polyunsaturated fatty acids (PUFAs) are essential fatty acids
- They are required for the synthesis of eicosanoids
- They are also the components of cell membrane.

Dietary intake

- Unsaturated fatty acids in diet are more beneficial than saturated fatty acids
- Monounsaturated and polyunsaturated fatty acids are beneficial
- ω3 fatty acids particularly are beneficial in reducing cardiovascular disease
- Consumption of trans fatty acids increase risk of atherosclerosis

Good sources of ω3 fatty acids

- Fish oils
- Flax seeds
- Walnuts
- Pecan nuts

Essential fatty acids

Fatty acids which cannot be synthesised in the body and they have to be taken through

diet only are called essential fatty acids. Polyunsaturated fatty acids such as **Linoleic acid** and **Linolenic acids** are essential for normal life functions. Therefore, they are called as essential fatty acids.

Arachidonic acid is considered as semi essential fatty acid since it can be synthesised from Linoleic acid.

- Essential polyunsaturated fatty acids can be classified as belonging to one of two "families", the omega-6 family or the omega-3 family.
- Fatty acids belonging to these two families differ not only in their chemistry, but also in their natural occurrence and biological functions.
  - Linoleic acid 18: 2; Δ 9, 12 (dienoic)
  - Linolenic acid 18: 3; Δ 9, 12, 15 (trienoic)
  - Arachidonic acid 20:4; Δ 5, 8, 11, 14 (tetraenoic)

Significance of essential fatty acids

- Components of cell membranes, structural elements of gonads and mitochondrial membrane
- Required for brain growth and development
- Precursors of Eicosanoids (Prostaglandins, Thromboxanes, Leukotrienes)
- Play an important role in vision
- They have a cardio protective role- Lowers serum cholesterol and increases HDL levels
- Prevent fatty liver formation
- Deficiencies of essential polyunsaturated fatty acids may cause a wide variety of symptoms, including retarded growth in children, reduced fertility and pathologic changes in the skin.

Sources of essential fatty acids

- Oils of plant origin (sunflower, corn, soya, flaxseeds)
- Nuts
- Fish
- Grains

Functions of lipids in the body:

- Source of energy
- Are structural components of cell membranes
- Contain fat soluble vitamins and essential fatty acids
- Provide **shape and contour** to the body
- Act as **metabolic regulators**
- Act as **thermal insulators** in the subcutaneous tissues and around certain organs
- Nonpolar lipids act as electrical insulators, **allowing** rapid propagation of depolarization waves along **myelinated nerves**
- Form protective padding around internal organs

CHOLESTEROL

Cholesterol is an important sterol found in animal tissues. It is an essential component of cell membranes and a precursor of several biologically important substances.

It is present in:

- Cell membranes
- Plasma lipoproteins
- Nervous tissue
- Adrenal glands
- Liver

Sources of cholesterol

Dietary source

Cholesterol is present mainly in foods of animal origin.

Endogenous synthesis

The body, particularly the **liver**, synthesizes cholesterol from acetyl-CoA.

STRUCTURE

Cholesterol is a 27-carbon sterol and an important component of animal cell membranes.

Cholesterol contains:

- A steroid nucleus (4 fused rings)
- A hydroxyl (-OH) group
- A hydrocarbon side chain
- Fused ring system contains four rings collectively known as **cyclopentanoper hydrophenanthrene ring**.

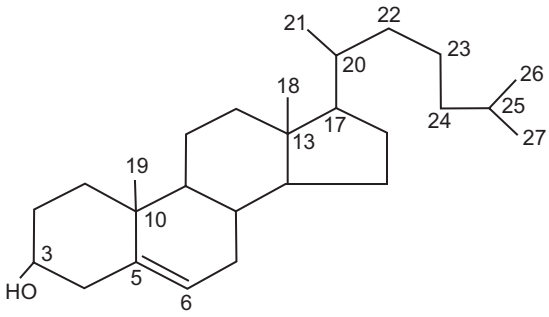


Fig. 3.3 : Structure of cholesterol (cyclopentano perhydro phenanthrene ring)

FUNCTIONS OF CHOLESTEROL

1. **Component of cell membranes**

   Cholesterol contributes to membrane structure and regulates membrane fluidity and integrity.

2. **Precursor of bile acids**

   Cholesterol is converted into **bile acids**, which are important for digestion and absorption of dietary lipids.

3. **Precursor of steroid hormones**

   Cholesterol is the precursor of:
   - Cortisol
   - Aldosterone
   - Progesterone
   - Oestrogens
   - Testosterone

4. **Precursor of vitamin D**

   A cholesterol derivative in the skin is converted to vitamin D following exposure to ultraviolet radiation.

Free cholesterol and cholesterol ester

Cholesterol occurs in two major forms:

- **Free cholesterol**

  Contains a free hydroxyl group and is present in cell membranes and the surface of lipoproteins.

- **Cholesteryl ester**

  The hydroxyl group of cholesterol is esterified with a fatty acid.

  Cholesterol + Fatty acid → Cholesteryl ester

  Cholesteryl esters are more hydrophobic and are stored within cells and transported in the core of lipoproteins.

Clinical significance of cholesterol
An increased concentration of circulating cholesterol, particularly cholesterol carried in certain LDL particles, is associated with atherosclerotic cardiovascular disease risk.Therefore, measurement of serum cholesterol forms an important part of the lipid profile.

Normal level of serum total cholesterol and variations

- Normal level of serum total cholesterol is **150-200 mg/dL** (Desirable <200 mg/dL)

Physiological variations

- Low at the time of birth, increases with advancing age.
- The level is increased during pregnancy.

Pathological Variations

a) Hypocholesterolaemia (Low serum cholesterol concentration) is observed in

- Hyperthyroidism
- Malnutrition
- Malabsorption syndrome
- Anaemia
- Haemolytic jaundice

b) Hypercholesterolemia (High serum cholesterol concentration)

is found in

- Diabetes Mellitus
- Nephrotic syndrome
- Obstructive Jaundice
- Myxoedema
- Biliary cirrhosis
- Hypopituitarism
- Familial Hypercholesterolemia
- Hypothyroidism

LIPOPROTEINS

Lipoproteins are spherical complexes of lipids and specific proteins called apolipoproteins that transport lipids through the aqueous blood plasma.

Because triglycerides and cholesteryl esters are poorly soluble in water, they require lipoproteins for transport in blood.

A lipoprotein consists of:

Core

The hydrophobic core contains:

- Triacylglycerols
- Cholesteryl esters

Surface

The surface contains:

- Phospholipids
- Free cholesterol
- Apolipoproteins

The hydrophilic components face the aqueous plasma, while the hydrophobic lipids are located in the core.

Basic structure

Lipoprotein = Lipid + Apolipoprotein

Apolipoproteins help in:

- Structural stability
- Enzyme activation
- Receptor recognition
- Regulation of lipoprotein metabolism **(Fig. 3.4)**

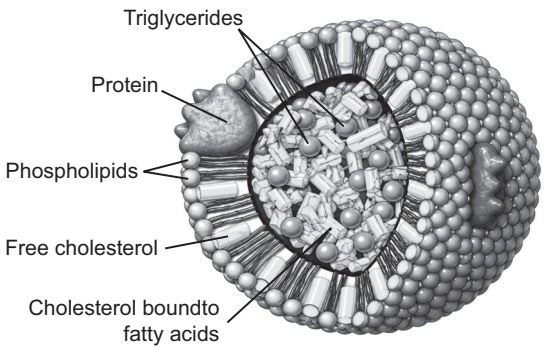


Fig. 3.4 : Lipoprotein

Classification of Lipoproteins

Lipoproteins are classified mainly according to their density. **(Table - 3.3)**

Clinical importance of lipoproteins

Abnormal concentrations of lipoproteins are associated with disorders of lipid metabolism and cardiovascular risk.

Hyperlipoproteinemia may result in:

- Increased triglycerides
- Increased cholesterol
- Atherosclerosis
- Coronary artery disease

Table - 3.3 : Common biologically important lipoproteins

Lipoprotein	Major lipid transported	Major function	Clinical importance
Chylomicrons	Dietary triglycerides	Transport dietary triglycerides	Post meal increase
VLDL	Endogenous triglycerides	Transport endogenous triglycerides from liver	↑ in hypertriglyceridemia
IDL	Remnant particles	Intermediate in VLDL metabolism	
LDL	Cholesterol	Delivers cholesterol to peripheral tissues	"bad cholesterol"
HDL	Cholesterol	Removes cholesterol from tissues. Participates in reverse cholesterol transport	'good cholesterol"

- Pancreatitis in severe hypertriglyceridemia

LDL vs HDL

- High LDL → Atherosclerosis risk
- High HDL → Protective effect
- Increased LDL → coronary artery disease (CAD)
- Decreased HDL → Risk factor

Lipid Profile

A routine lipid profile commonly includes:

- Total cholesterol
- Triglycerides
- HDL cholesterol
- LDL cholesterol
- VLDL cholesterol

Chylomicrons

Chylomicrons are the largest and least dense lipoproteins.

Major function

They transport dietary triglycerides from the intestine to peripheral tissues.

Very-low-density lipoprotein (VLDL)

VLDL is synthesized mainly in the liver.

Major function

It transports endogenous triglycerides from the liver to peripheral tissues.

VLDL is progressively metabolized to form:

VLDL → IDL → LDL

Intermediate-density lipoprotein (IDL)

IDL is formed during metabolism of VLDL.

It may be:

- Taken up by the liver, or
- Further metabolized to LDL

Low-density lipoprotein (LDL)

LDL is rich in cholesterol.

Major function

It transports cholesterol to peripheral tissues.