Lipid Metabolism

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- Heterogenous group of biomolecules
- Water insoluble (hydrophobic)
- Soluble in organic and non-polar solvents
  acetone, ether, chloroform and benzene
Classes of lipids

Simple lipids
- e.g.
  - Triglycerides
  - Waxes

Conjugated (complex) lipids
- Phospholipids,
- Glycolipids
- Sphingo- phospholipids
- Lipoproteins.

Derived lipids
- Fatty acids
- Cholesterol
- Ketone bodies

Obtained on hydrolysis of simplex or complex lipids

Esters of FA with alcohols

Esters of FA with alcohols and additional group
Major **source of energy** for the body: Fat stored in the adipose tissue is a direct and potential source of energy.

- 1 gm lipids $\rightarrow$ 9.3 Kcal
- 1 gm CHO $\rightarrow$ 4.1 Kcal

**Functions**

- **Storage form of energy**: triglyceride
- Serves as **structural components** of cell membrane (Phospholipids, glycolipids)
- Some are **hormones** e.g. steroid hormone (cortisol, aldosterone, sex hormones)
- **Essential in the diet** to provide the body with some essential FA and of fat-soluble vitamins (A, D, E, K) which have regulatory or coenzyme function
In adult man ingests about **60-150 g of lipids/day** of which > 90% is normally TG, the remainder of dietary lipids is made of cholesterol, cholesteryl esters, PLs and FFAs.

In diabetes mellitus, The body 1st utilizes fats for energy production when glucose oxidation is impaired.

1- No digestion of Fat in the mouth.

2- Little fat digestion takes place in the stomach by Gastric Lipase that degrade TG with short chain FAs at optimum PH 5.

**Gastric Lipase** is valuable in infants due to high PH in their stomach and their milk diet with short chain FAs.

While it is insignificant in adults due to its inhibition by gastric acidity.
3- Digestion of dietary lipids start in the small intestine where they are first emulsified by the bile salts, mechanical mixing due to peristalsis, phospholipid and colipase.

- Emulsification increases the surface area of the lipid droplets, so that digestive enzymes can act effectively.
- After emulsification, lipids are hydrolysed by the **lipolytic enzymes** such as pancreatic lipase, phospholipase and cholesterol esterase, present in the pancreatic juice.
A-Pancreatic lipase:

- secreted into the intestine
- It is the major enzyme of TG hydrolysis, with optimum PH 7.
- This enzyme is specific for esters α-positions of TG (linkage in position 1,3)
- It catalyzes hydrolysis of triacylglycerols at positions 1 & 3, forming 1,2-diaclylglycerols, & then 2-monoacylglycerols.
- It prefers long chain FAs.
B- A protein colipase secreted by the pancreas, is required to stabilize the lipase to its TG substrate.

**Figure:** General structures of fatty acids and triacylglycerol Lipolysis of TG by pancreatic lipase produces fatty acids plus 2- Monoacylglycerol
**Figure 22.4. Action of Pancreatic Lipases.** Lipases secreted by the pancreas convert triacylglycerols into fatty acids and monoacylglycerol for absorption into the intestine.
C-cholesterol ester hydrolase (estrase)

Present in the pancreatic secretion.

None specific enzyme.

Hydrolyses cholesterol ester (CE) into cholesterol and FFA
Phospholipases

- Glycerol + two fatty acids + phosphorus + nitrogenous base.
- Phosphorus part makes it soluble in water.
- Fatty acids make it soluble in fat.
- Therefore can serve as an emulsifier.
- Key role is in cell membranes.
Phospholipase A₂

- Is secreted by the **pancreas** into the intestine where it is activated by **trypsin**
- It hydrolyzes the ester linkage between the fatty acid & the hydroxyl on C₂ of phospholipids
Lecithin (phosphatidyl choline) $\rightarrow$ Lysolecithin + FFA

Lysolecithin $\rightarrow$ Glycerolphosphorylbase + FFA

Glycerolphosphorylbase may be excreted in stool, or further degraded by phospholipase C to give phosphoryl base and glycerol, or degraded by phospholipase D to give glycerol phosphate and nitrogeous base.
The end products of dietary phospholipids digestion are lysophospholipids (mainly), free fatty acids, glycerol phosphate and the nitrogenous bases.
**Lipids:**
Triacylglycerol
Cholesterol esters
Phospholipids

**STEP 1**
Gastric Lipase
pH$_{opt} \sim 5$, Initiates hydrolysis and acts on TG with short chain FAs

**STEP 2**
Pancreas releases:
Lipase (+colipase)
cholesterol esterase
phospholipase A$_2$

**STEP 3**
Liver releases bile acids to solubilize lipid products in mixed micelles

**STEP 4**
Lipids absorbed from micelles into epithelial cells

**STEP 5**
Chylomicrons form and travel through lymphatics

**Figure:** Five steps of lipid digestion and absorption
At the intestinal lining, **shorter-chain fatty acids** and **glycerol** are absorbed and pass directly to liver by portal circulation.

The cells of the intestinal lining convert large lipid fragments back into **triglycerides** and combine them with protein forming **chylomicrons** that travel in the lymph.

* **lipoprotein** – how fat is transported in the body; a mixture of fat and protein

The end products of PL hydrolysis are absorbed along with the digestive products of the triglycerides.

Phospholipids are resynthesised in the intestinal mucosa and form part of the chylomicrons.
Cholesterol is absorbed in the free form
- The cholesterol esters are hydrolyzed by cholesterol esterase secreted in the pancreatic juice
- Cholesterol and free fatty acids are then absorbed from the intestine
- Cholesterol is re-esterified in the intestinal mucosa and passes along with triglycerides in the form of chylomicrons to the lymph vessel then systemic circulation. (milky appearance of serum after fatty meals which is cleared specific enzyme lipoprotein lipase on the surface of blood capillaries).
- After absorption, lipids are either oxidised mainly in the liver or are stored in the depot (adipose tissue)
Structure of a chylomicron

apolipoprotein

triacylglycerol

cholesteryl ester

phospholipid
Malabsorption of lipids (steatorrhea); causes loss of lipids include fat soluble vitamins and essential FAs in feces.