Lipid Digestion & Absorption

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Surat
**Digestion of lipids**

- The major dietary lipids
  - Triacylglycerol
  - Cholesterol
  - Phospholipids.
- Indian diet = 20-30 gm of lipids per day.
**Digestion in stomach**

- The *lingual lipase* from the mouth enters stomach along with the food.
- Optimum pH of 2.5 – 5.
- The enzyme therefore continues to be active in the stomach.
  - Acts on short chain triglycerides (SCT).
  - SCTs are present in milk, butter and ghee.
• **Gastric lipase** is acid stable
• with an optimum pH about 5.4.

• It is secreted by Chief cells, the secretion is stimulated by **Gastrin**.

• Up to 30% digestion of triglycerides occurs in stomach.
**Digestion in intestine**

- **Emulsification** is pre-requisite for digestion of lipids.
- smaller droplets
- surface tension is reduced
- surface area of droplets is increased.
- This process is favoured by:
  1. Bile salts (Detergent action)
  2. Peristalsis (mechanical mixing)
  3. Phospholipids
Bile salts are important for digestion of lipids

- sodium glycocholate
- sodium taurocholate
- lower surface tension
- Emulsify the fat droplets
- Increases the surface area of the particles for enhanced activity of enzymes
Action of Bile Salts

- The hydrophobic portions of bile salts intercalate into the large aggregated lipid, with the hydrophilic domains remaining at the surface.

- This leads to breakdown of large aggregates into smaller droplets.

- Thus the surface area for action of lipase is increased.
Lipolytic enzymes in intestine

1. Pancreatic lipase with co-lipase.
2. Cholesterol esterase.
4. The bile (pH 7.7)
   - Neutralise the acid of the stomach
   - Provides favourable pH.
   - Action of pancreatic enzymes occur.
Digestion of triglycerides

1. Pancreatic lipase
   1. Hydrolyses to 1\textsuperscript{st} and 3\textsuperscript{rd} carbon atoms of glycerol
   2. Form
      1. 2-monoacyl glycerol
      2. Two fatty acid.

2. Isomerase shifts FA position 2 to 1.

3. Than 1\textsuperscript{st} position is then hydrolysed by lipase to form free glycerol and fatty acid.
Triacylglycerol $\xrightarrow{\text{Lipase}}$ 2,3-diacylglycerol $\xrightarrow{\text{Lipase}}$ 2-monoacylglycerol

$+ \text{H}_2\text{O}$  $+ \text{H}_2\text{O}$  $+ \text{H}_2\text{O}$

+ fatty acid  + fatty acid  + fatty acid
3. Major end product
   • 2-MAG (78%)
   • 1-MAG (6%)
   • Glycerol and fatty acids (14%).
   • Thus digestion of TAG is partial (incomplete).

4. Cholesterol ester
   • free cholesterol and fatty acids.

5. Phospholipase A2
   • Lysophospholipid and fatty acid.
Co-lipase

- Bind to the triacylglycerol molecules at the oil-water interface is obligatory for the action of lipase.
- Secreted by the pancreas as zymogen.
- It is activated by trypsin.
Fat globule is broken up by lecithin and salts.
Absorption of lipids

1. Mixed micelle formation:
   • 2-monoglycerides, long chain fatty acids, cholesterol, phospholipids and lysophospholipids are incorporated into molecular aggregates to form mixed micelle.
   • The micelles are spherical particles with a hydrophilic exterior and hydrophobic interior core.
   • Due to their detergent action, the bile salts help to form micellar aggregates.
Bile salt

Pancreatic lipase

Fatty acid after lipase digestion

Triacyl glycerol
2. Micellar is essential for the absorption of fat soluble vitamins A, D and K.

3. The micelles are aligned at the microvillous surface of the jejunal mucosa.

4. Fatty acids, 2-MAG and other digested products passively diffuse into the mucosal cell.
2. Enterohepatic circulation of Bile Salts

- The bile salts are **reabsorbed** from the ileum and returned to the liver to be re-excreted.
- About 98% of dietary lipids are normally absorbed.
3. Re – esterification inside mucosal cell

1. Inside the intestinal mucosal cell
   – Long chain fatty acids are re-esterified to form triglyceride.

2. The fatty acids are first activated
   – to Fatty acyl CoA by the enzyme Acyl CoA synthetase or thiokinase.
   – This needs lysis of two high energy bonds.
3. Two such activated fatty acids react with mono acyl glycerol (MAG) to form the triglyceride.

4. Free glycerol absorbed from intestinal lumen directly.

So free glycerol is not available for re-esterification.

But the cells can convert glucose to glycerol phosphate, and synthesise TAG.
4. Chylomicrons

- Incorporated into Chylomicrons
  - Triacylglycerol
  - Cholesterol ester
  - Phospholipids
  - Apo protein B48 and apo-A

- The chyle (milky fluid) from the intestinal mucosal cells loaded with Chylomicrons are transported through the lacteals into the thoracic duct and then emptied into lymph circulation.
• Serum may appear milky after a high fat meal due to the presence of Chylomicrons in circulation.

• Normally the lipemia clears within a few hours by the uptake of Chylomicrons by tissues.
Chylomicron assembly and secretion from smooth ER of intestinal mucosal cells

2-Monoacylglycerol → Acyttransferase → CoA → Triacylglycerol

Phospholipids

R-group

Fatty acids

Fatty acyl-CoA synthetase → CoA, ATP → AMP+PPi

Chylomicron

apoB-48 (& other apolipoproteins)

To lymphatic system
5. Short chain fatty acid absorption is different

- SCF = Milk, Butter, Ghee
- MCF = Coconut oil and mother’s milk
- Do not need re-esterification.
- Directly enter into blood vessels, then to portal vein, finally to liver where they are immediately utilised for energy.
- Their absorption is rapid.
- They are better absorbed than long chain fatty acids.
Abnormalities in Absorption of lipids

1. Defective digestion:
   - **Steatorrhea** = daily excretion of fat in faeces is > 6 gm per day.
   - In pancreatic diseases = split steatorrhea.

2. Defective absorption:
   - if the absorption is also defective, most of the fat in stools may be split fat.
   - Gall bladder obstruction = Unsplit steatorrhea
Defective absorption may be due to diseases:

2. Surgical removal of intestine.
3. Obstruction of bile duct:
   1. Gallstones
   2. Tumours of head of pancreas
   3. Enlarged lymph glands

In such cases, triglycerides with short chain and medium chain fatty acids are digested and absorbed properly because they do not require micellerisation for absorption.

Since milk fat and coconut oil are made up of MCT, they are therapeutically useful in malabsorption syndromes.
Chyluria

• There is an abnormal connection between the urinary tract and lymphatic drainage system of the intestine. Urine appears milky due to lipid droplets.

Chylothorax

• can result from an abnormal connection between the pleural cavity and thoracic duct.
Fate of Chylomicrons

1. The absorbed (exogenous) triglycerides are transported in blood as Chylomicrons. They are taken up by adipose tissues and liver.

2. Liver synthesises endogenous triglycerides. These are transported as VLDL and are deposited in adipose tissue.

3. During starvation states, triglycerides in adipose tissue are hydrolysed to produce free fatty acids. In the blood, they are transported, complexed with albumin. These free fatty acids are taken up by the cells and are then oxidised to get energy.
Fats ingested in diet

① Bile salts emulsify dietary fats in the small intestine, forming mixed micelles.

② Intestinal lipases degrade triacylglycerols.

③ Fatty acids and other breakdown products are taken up by the intestinal mucosa and converted into triacylglycerols.

④ Triacylglycerols are incorporated, with cholesterol and apolipoproteins, into chylomicrons.

⑤ Chylomicrons move through the lymphatic system and bloodstream to tissues.

⑥ Lipoprotein lipase, activated by apoC-II in the capillary, converts triacylglycerols to fatty acids and glycerol.

⑦ Fatty acids enter cells.

⑧ Fatty acids are oxidized as fuel or reesterified for storage.
FIGURE 23-15 Metabolism of fatty acids in the liver.