

Digestion and absorption of lipids (Cc4, unit 2)

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Definition



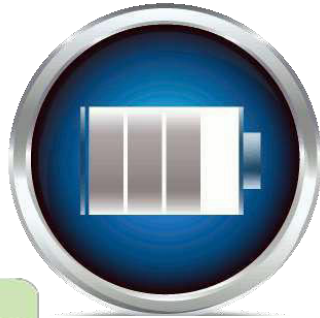
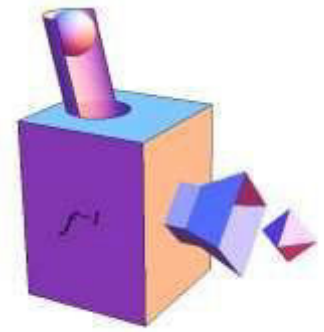
They have the common property of being

(1) relatively **insoluble in water**

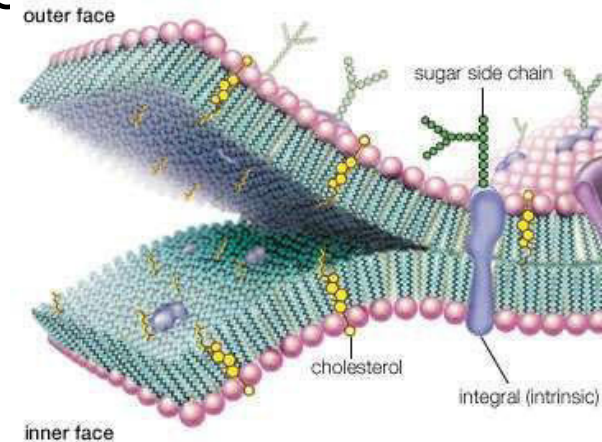
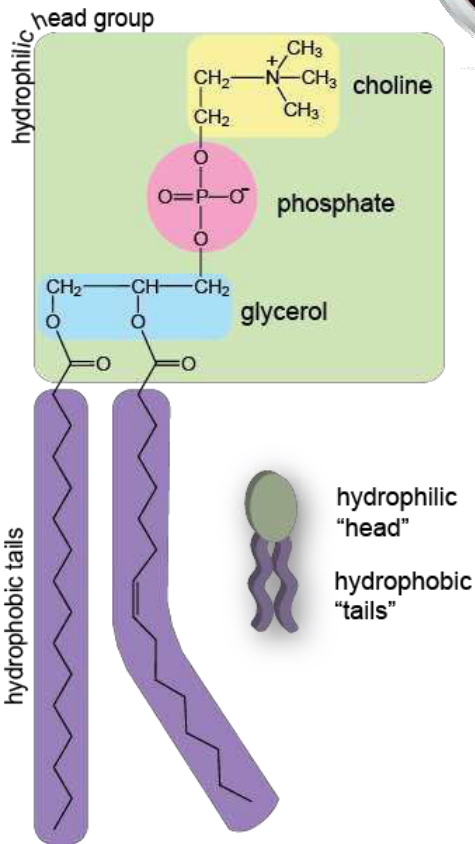
(2) **soluble in nonpolar solvents** such as alcohol, ether and chloroform.

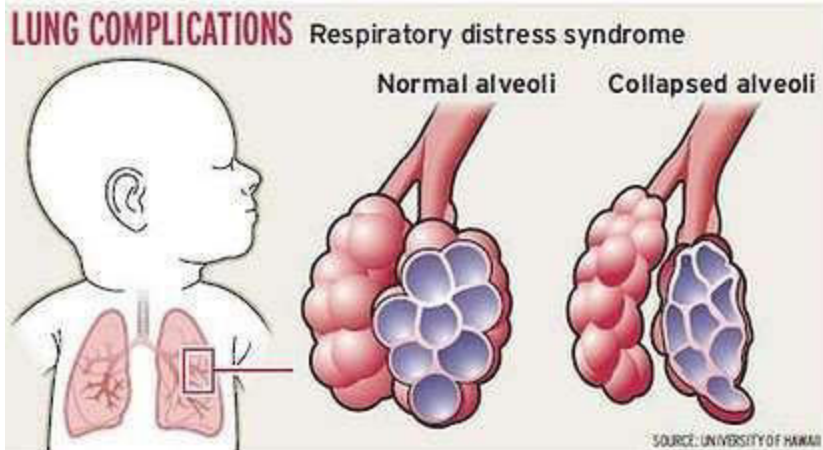


Functions

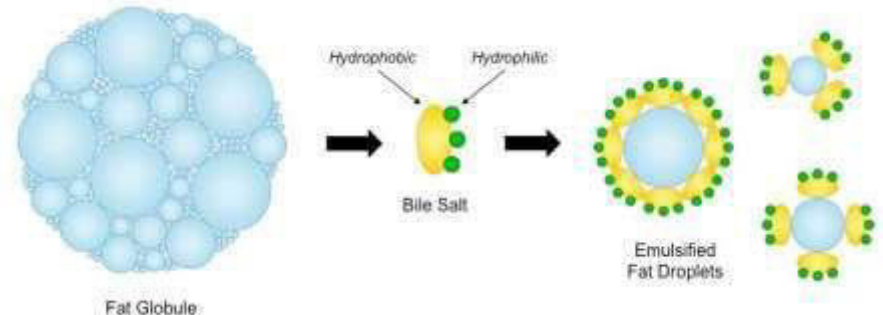


- Storage form of energy
 - Concentrated storage
 - 9.24kcal/g
- Bio membrane
 - Structural components
 - Phospholipids
 - Glycolipids





- Metabolic regulator
 - Steroid hormones
 - Prostaglandins
- Surfactant
 - Diphosphatidylcholine (Lecithine)
- Detergent emulsifier



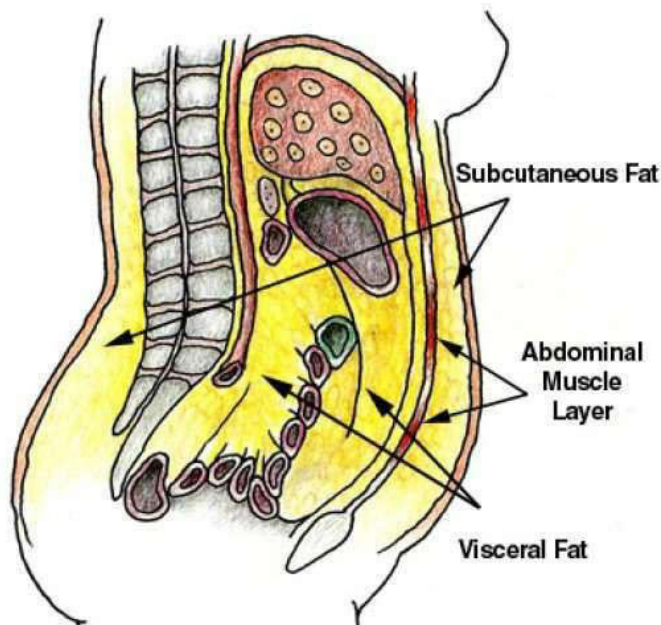


- Electric insulator of neuron
- Insulator from external temperature
- Shape and contour to the body





- Cushioning to internal organs
- Fat soluble vitamins
- Taste and palatability



Vs



To Eat or Not to Eat

Dietary fat Composition

- ❑ >More than 95% : TG
- ❑ Cholesterol,
- ❑ Cholesteryl esters,
- ❑ Phospholipids, and
- ❑ Unesterified fatty acids.



Dietary sources of Lipids



Fatty meats
and fish



Cheese



Butter



Avocado

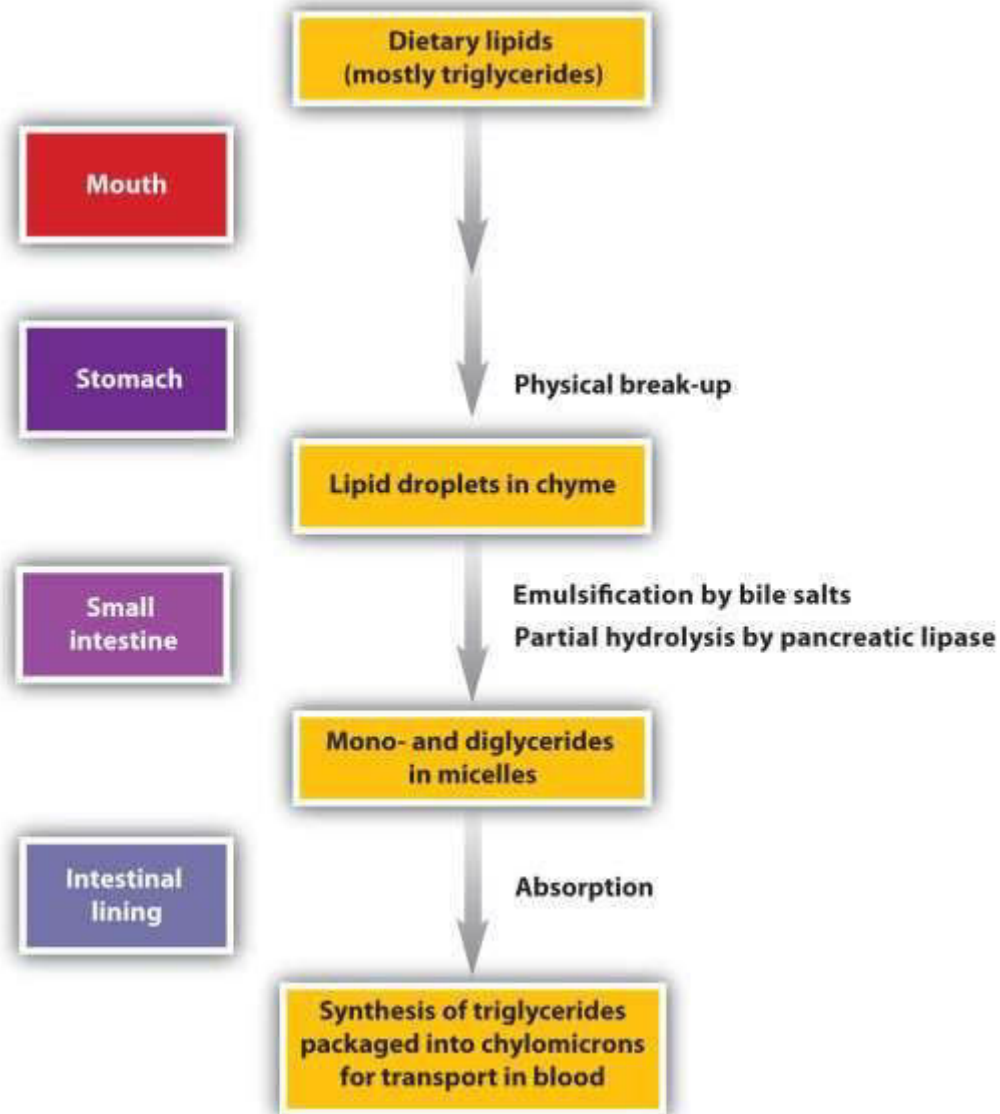


Nuts and seeds



Chocolate

Overview



Digestion in Mouth

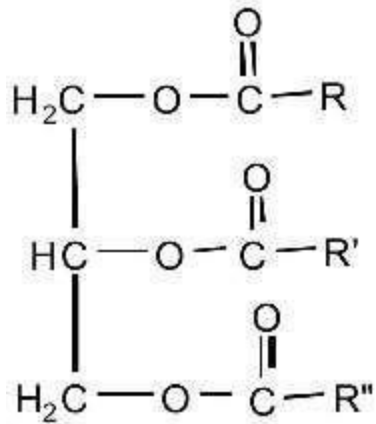


Lingual lipase:

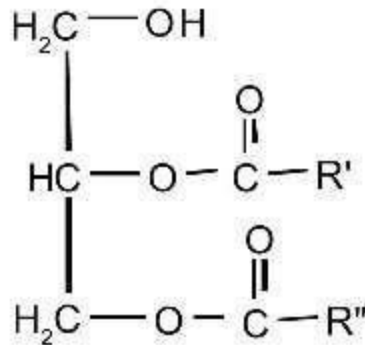
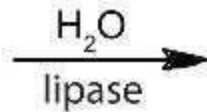
- ❑ Secreted by dorsal surface of tongue
- ❑ Active at low pH (pH 2.0 – 7-5)
- ❑ optimum pH 4.0-4.5
- ❑ Ideal substrate-Short chain TGS
- ❑ Enzymatic action continues in stomach
- ❑ Short chain fatty acids: absorbed directly from the stomach wall
- ❑ Enter the portal vein.



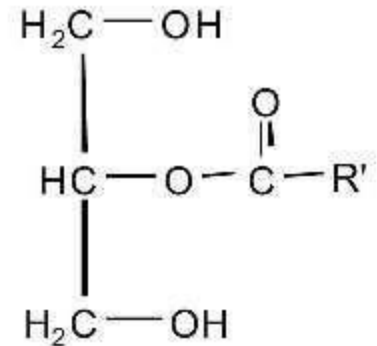
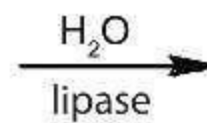
Triglyceride degradation



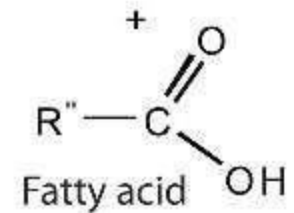
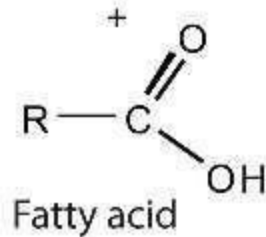
Triglyceride



Diglyceride



Monoglyceride

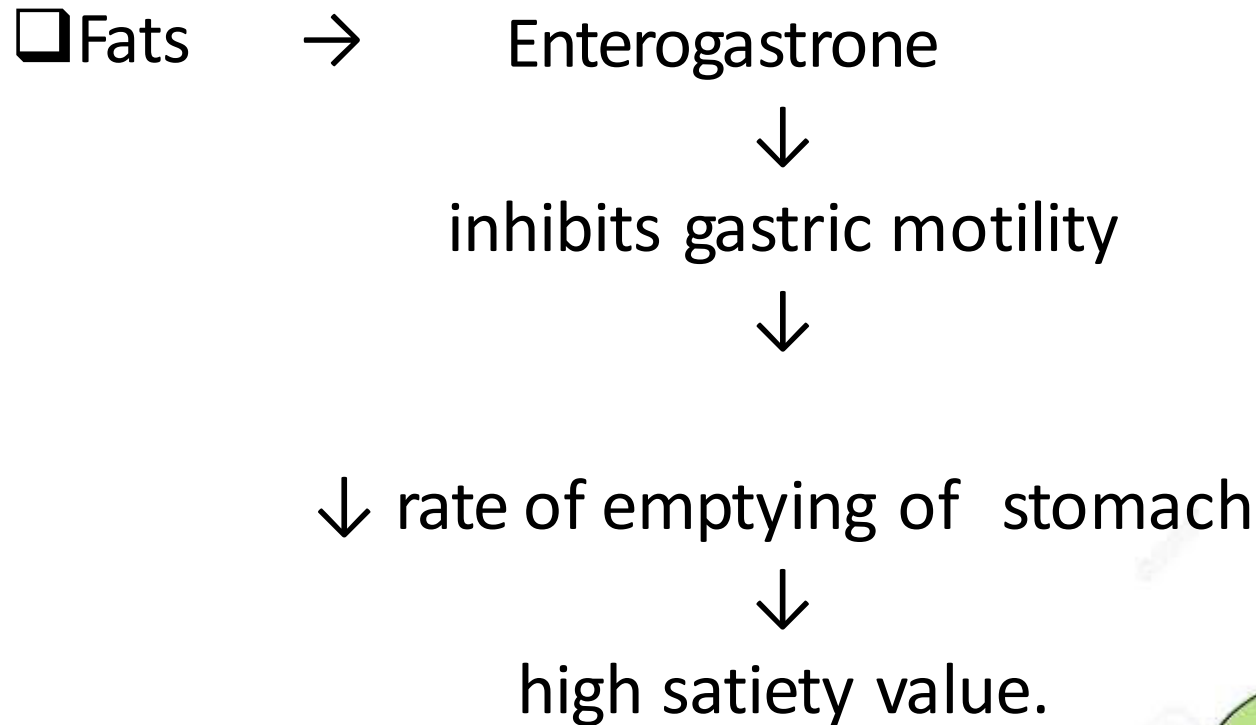


Digestion in Stomach

Gastric Lipase

- Optimum p H 5.4 (4-7)
- Acid stable
- Gastrin → Chief cells
- Requires the presence of Ca^{++}
- Short and medium chain fatty acid (30%)

Fats in gastric emptying : Satiety



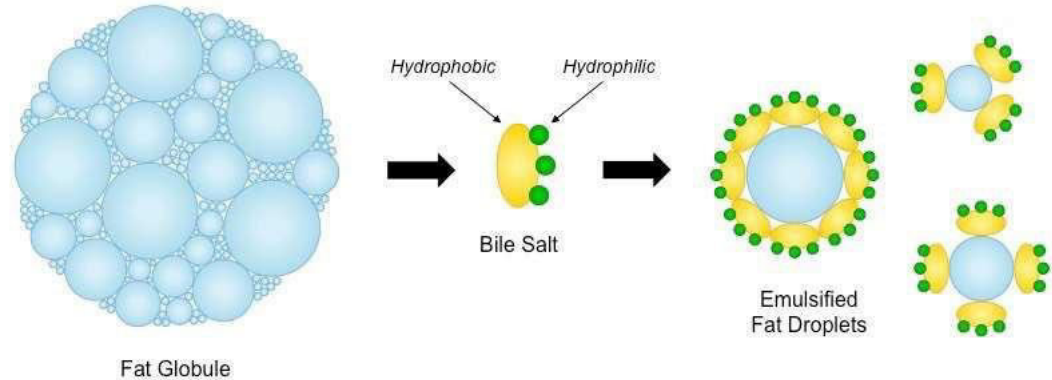
Significance of Lingual & Gastric Lipases

- **Neonates**
- Pancreatic insufficiency
 - **Cystic fibrosis**
 - **other pancreatic disorders**
- short and medium chain fatty

Emulsification and digestion

□ Lipids

- hydrophobic
- poorly soluble in the aqueous environment



- **Lipase**, : water soluble
- can only work at the surface of fat globules.

□ Digestion is greatly aided by

Emulsification : breaking up of fat globules into much smaller **emulsion droplets**.

Emulsification and digestion

TG digestion :

- occurs at lipid-water interfaces

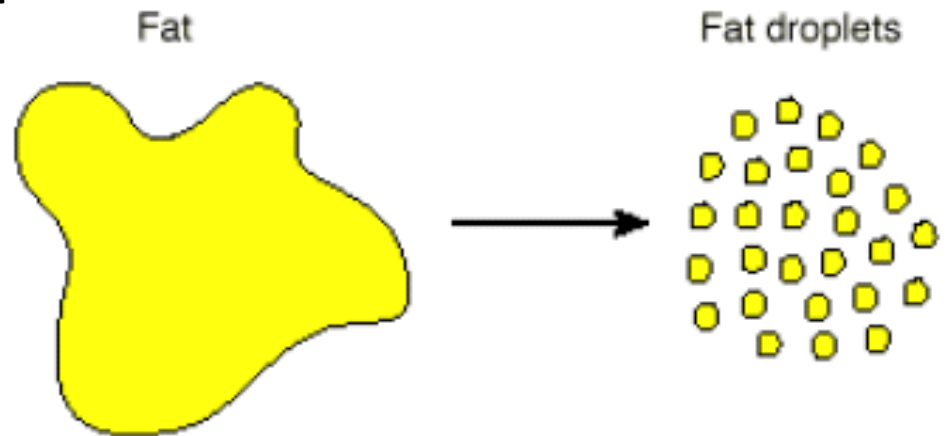
- Rate \propto surface area

- increased by

- churning peristaltic movements of the intestine

- emulsifying action of bile salts

- Emulsification takes place in the duodenum.



Digestion in small intestine

- Major site of fat digestion
- Effective → Pancreatic lipase and bile salts.
- Bile salts → effective emulsifying agents
- Secretion of pancreatic juice is stimulated by?
- acid gastric /Protein rich content in duodenum
- Secretin/ Cholecystokinin Pancreozymin

GI hormones

Secretin- ↑ secretion of electrolytes and HCO_3^- -rich fluid components of pancreatic juice

Pancreozymin of CCK –

stimulates the secretion of the pancreatic enzymes

Cholecystokin of CCK-PZ-

Contraction of the gall bladder

Dilatation of sphincter of Oddi

Hepatocrinin-

Released by intestinal mucosa

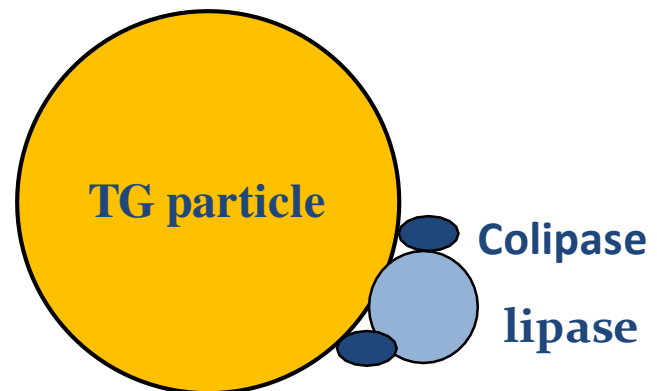
stimulates more bile formation (poor in bile acid)

Contents of Pancreatic Juice

- ❑ Pancreatic Lipase- triglycerides
- ❑ Phospholipase A2- Phospholipids
- ❑ Cholesterol esterase- Cholesteryl esters

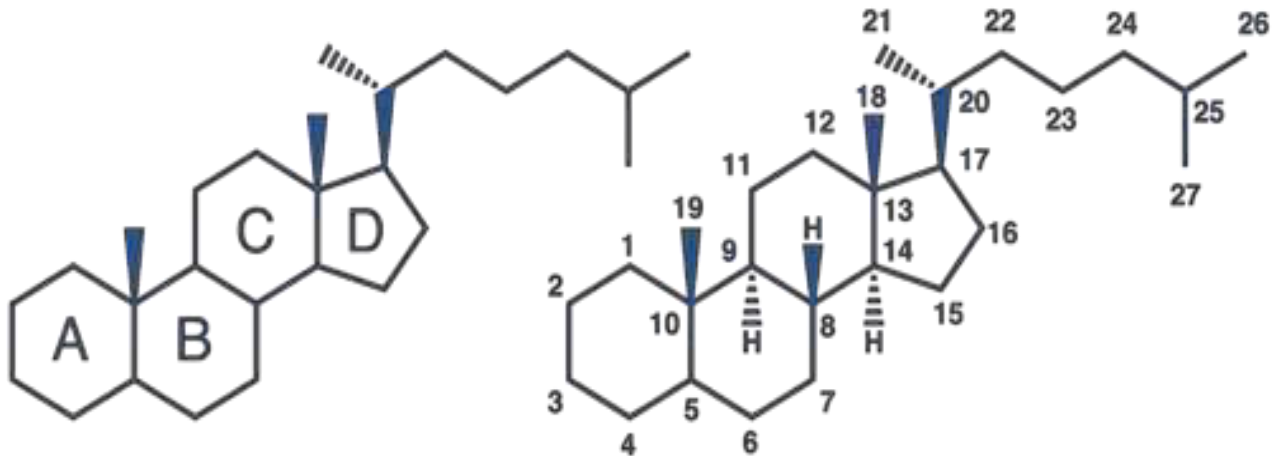
Bile Salts

- Required for the proper functioning of the pancreatic lipase enzyme
- Combines **lipase** + 2 X **Colipase**.
- Enhances the lipase activity
- Emulsification of fats

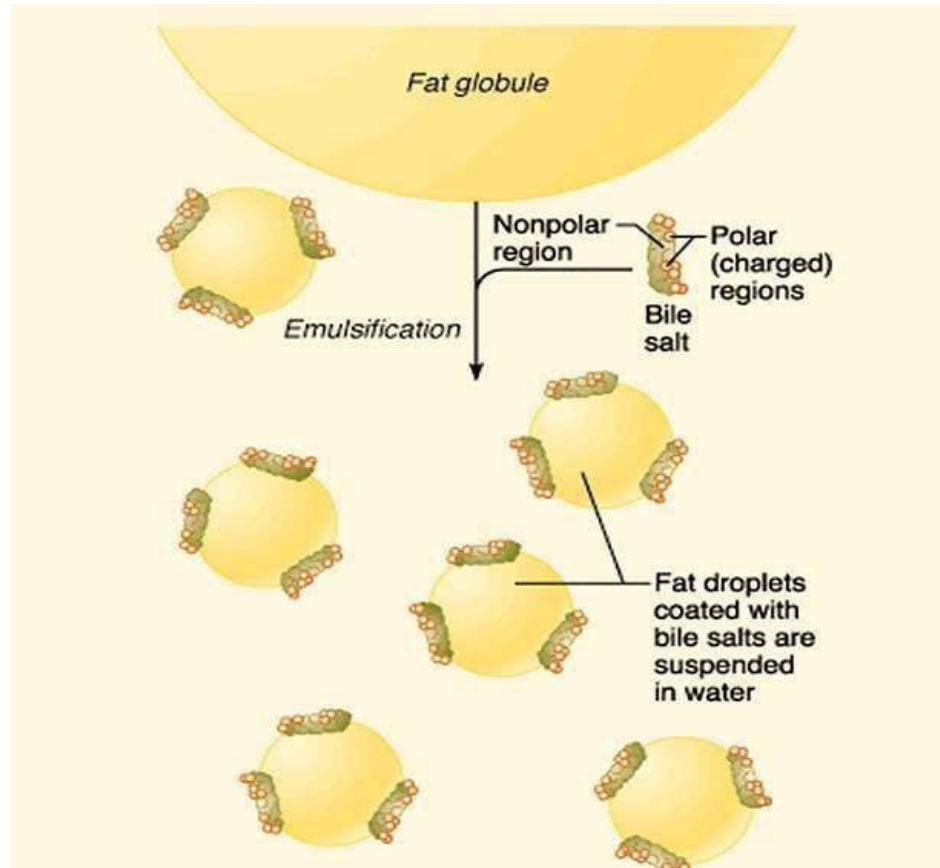


Bile Salts

- Synthesized in the liver
- Stored in the gall bladder
- Derivatives of cholesterol
- sterol ring + side chain + glycine / Taurine
- Na & K salts of Glycocholic & Taurocholic acid
- Entero-hepatic circulation



Emulsification by bile salts

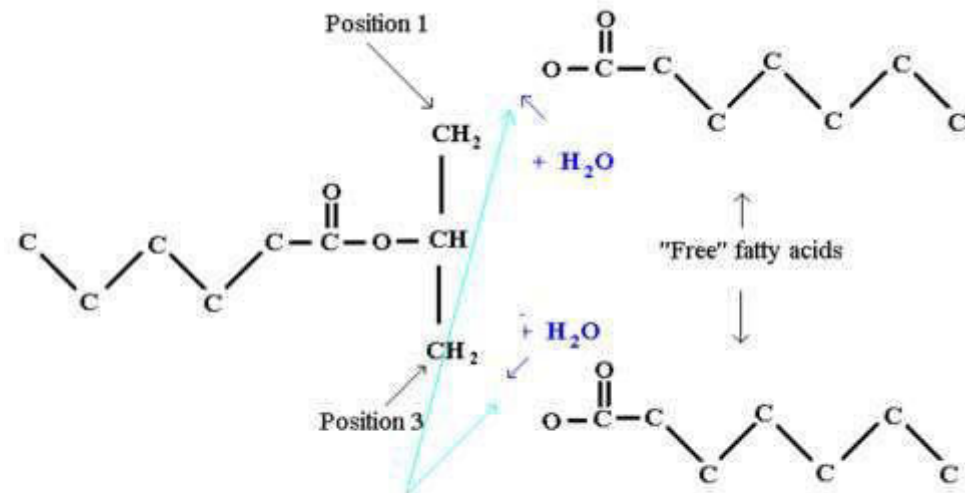


interact with the dietary lipid particles and the aqueous duodenal contents stabilizing the lipid particles as smaller preventing them from coalescing

TG degradation by pancreatic lipase

- specific for 1^o ester linkages
- Cant act on '2
- Acts on FA present at position 1 and 3

↓
α,β diglyceride
↓
β mono glyceride

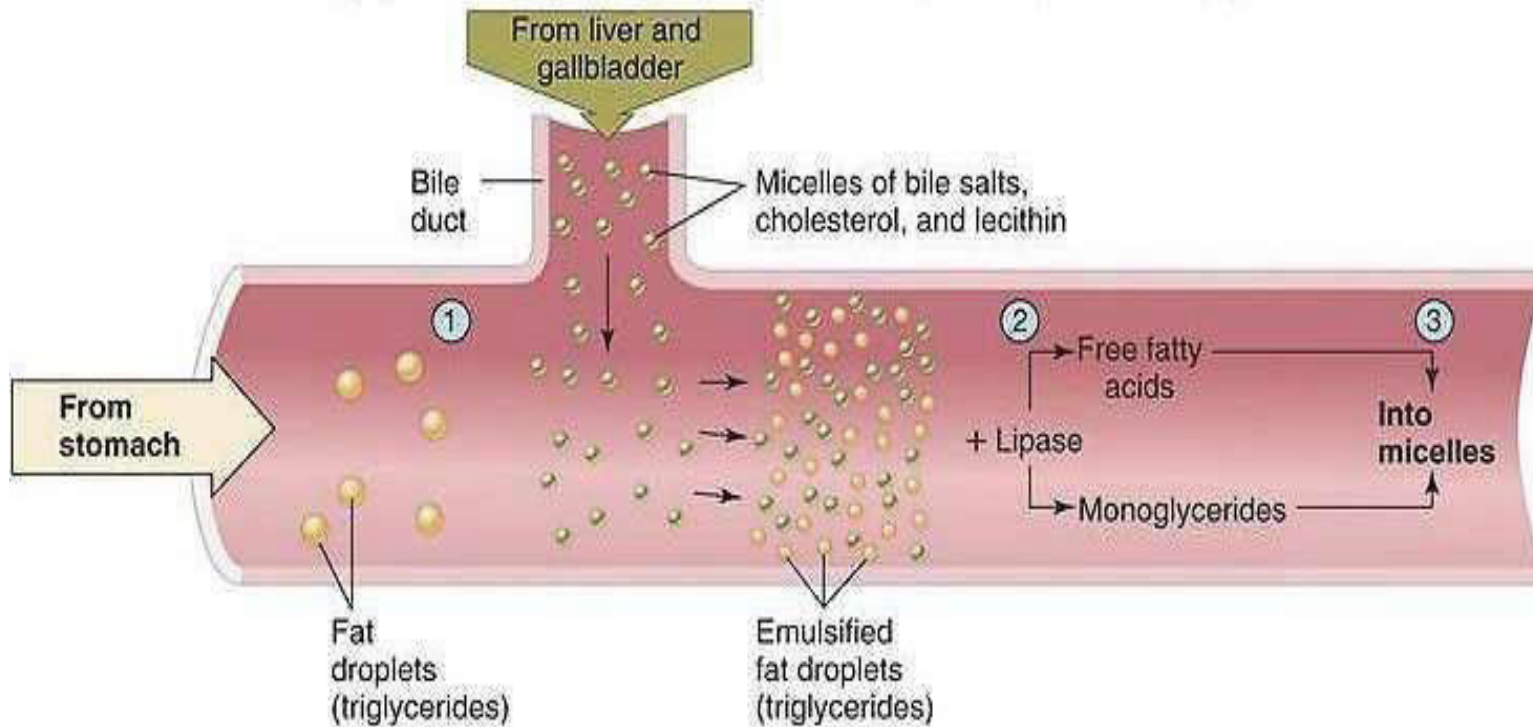


Pancreatic lipase is an enzyme that breaks the bonds between glycerol and the fatty acids at positions 1 and 3, liberating the 2 fatty acids.

TG degradation by pancreatic lipase

- β - Mono acyl glycerol $\xrightarrow[\text{Pancreatic lipase}]{\text{Isomerase}}$ α - Mono acyl glycerol
- α - Mono acyl glycerol $\xrightarrow{\text{Pancreatic lipase}}$ Glycerol + FA
- Primary product
 - β - Mono acyl glycerol (78%)
 - α - Mono acyl glycerol (6%)
 - free fatty acids
 - glycerol (14%)

Emulsification and Digestion of TG



Step 1: Emulsification of fat droplets by bile salts

Step 2: Hydrolysis of triglycerides in emulsified fat droplets into fatty acid and monoglycerides

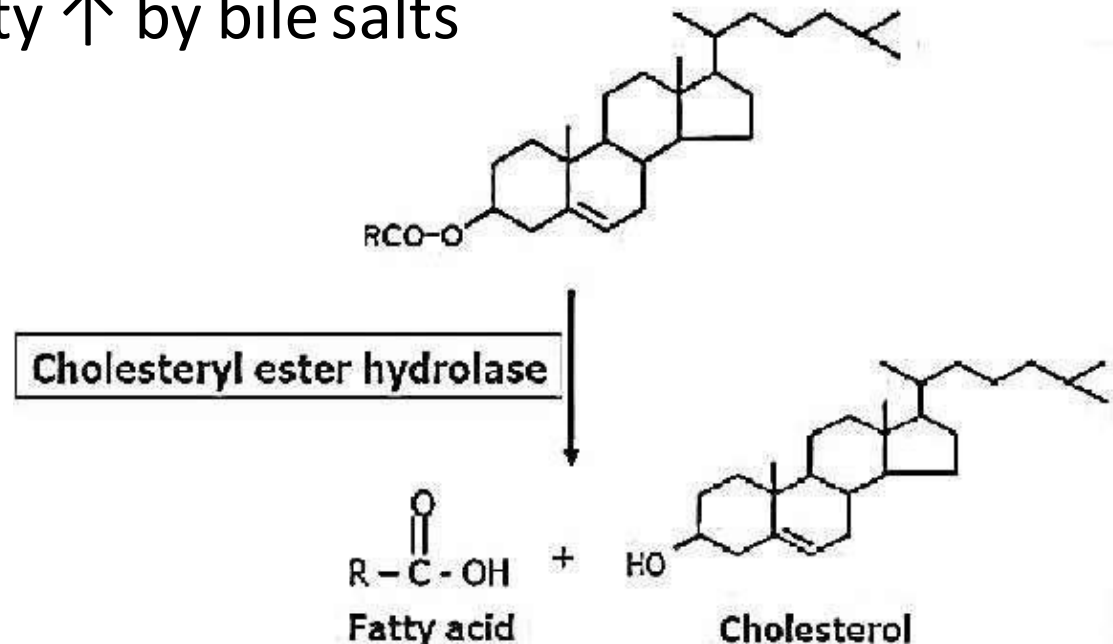
Step 3: Dissolving of fatty acids and monoglycerides into micelles to produce "mixed micelles"

Significance of Pancreatic lipase

- High concentration in pancreas.
- severe **pancreatic deficiency** such
 - **cystic fibrosis**
 - malabsorption of fats
- **Orlistat**
 - antiobesity drug
 - inhibits gastric and pancreatic lipases
 - decreasing fat digestion and absorption
 - weight loss.

Cholesteryl ester degradation

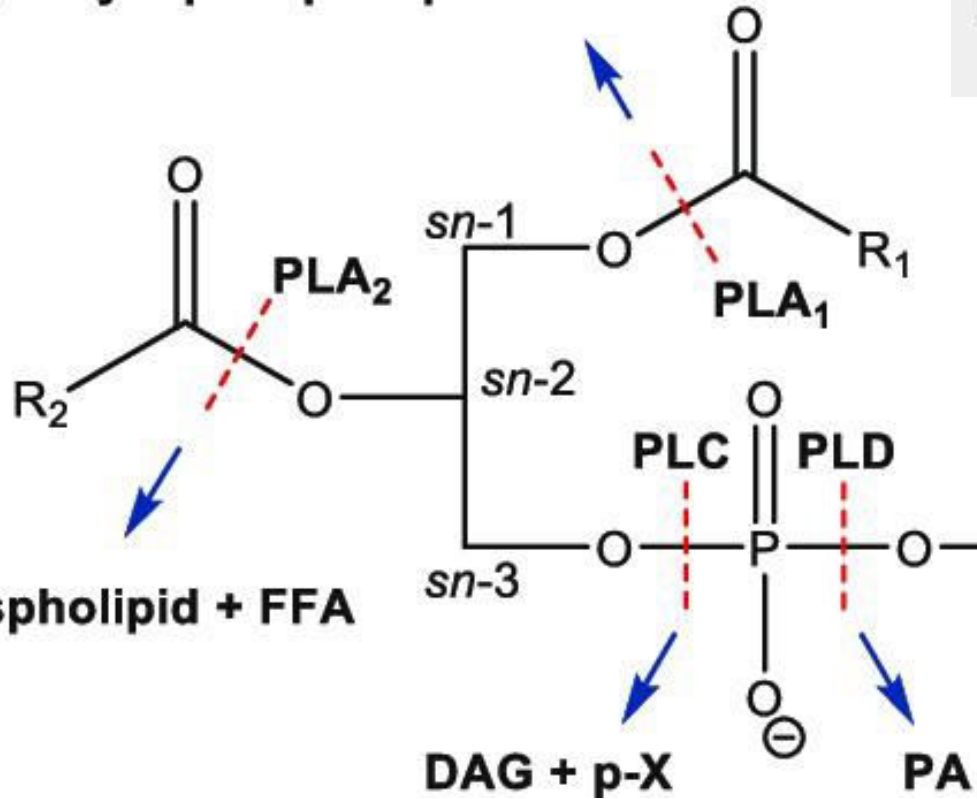
- Dietary cholesterol
 - mainly free (Non esterified) form
 - 10-15% is in esterified form *cholesteryl esters*
- Hydrolase : activity \uparrow by bile salts



Phospholipid degradation

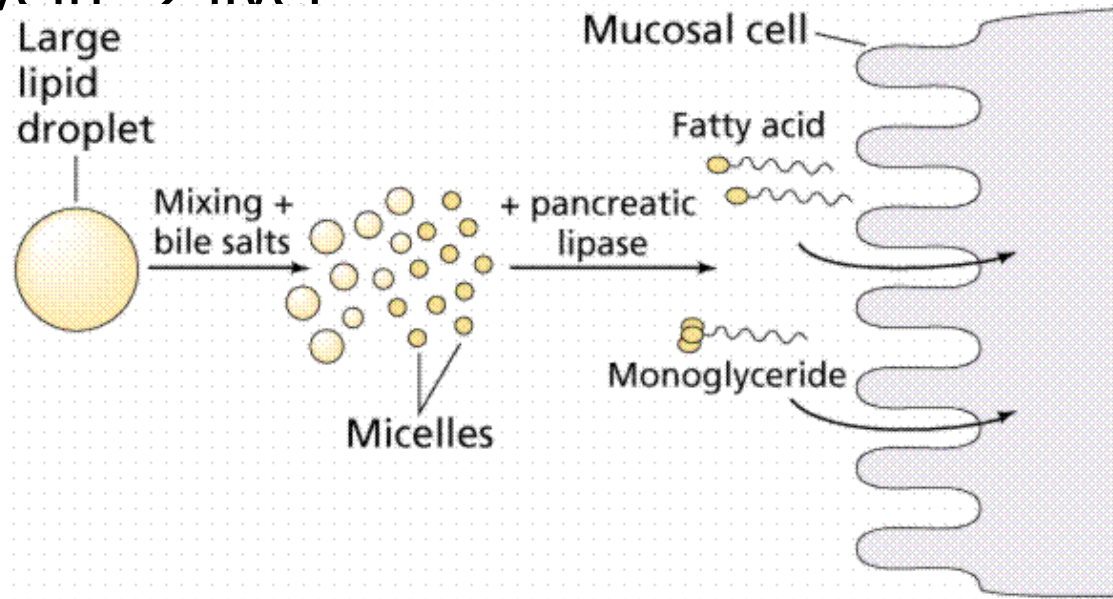


2-acyl-1-lysophospholipid + FFA



Absorption of Lipids

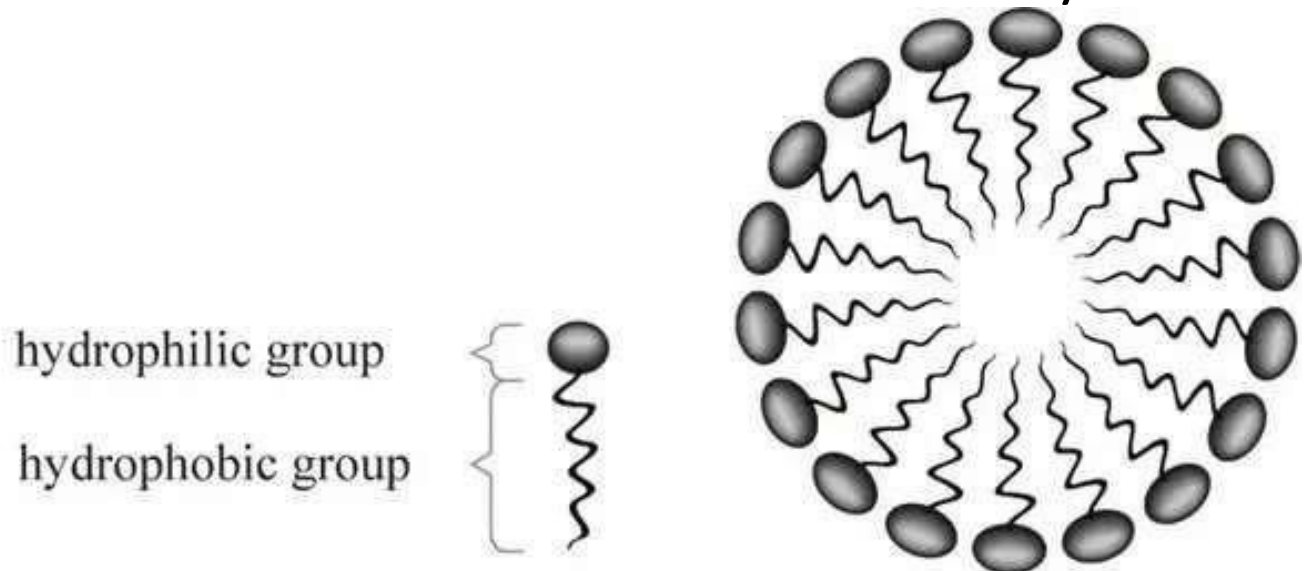
Glycerol, short chain FA & medium chain FA
directly absorbed from the intestinal lumen →
portal vein → liver



Long chain fatty acids, free cholesterol and β -acyl glycerol
With bile salts form mixed micelles

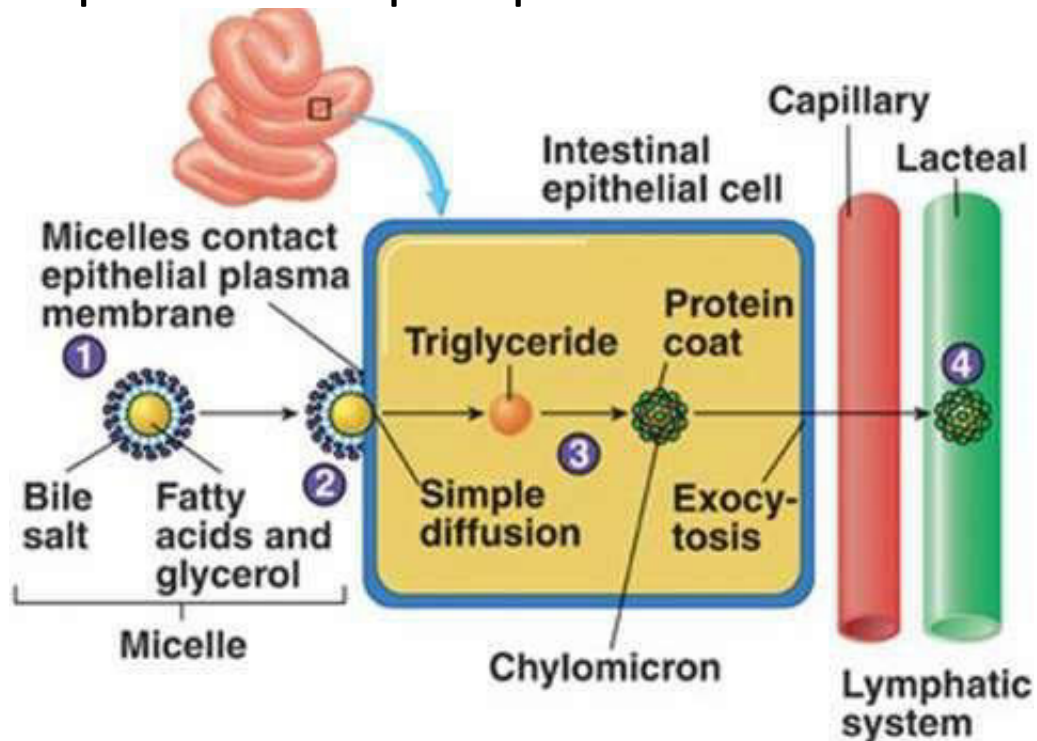
Micelles

- Spherical
- Clusters of amphipathic lipids
 - hydrophobic groups on the inside
 - hydrophilic groups on the outside of clusters
- Mixed micelles : soluble in the aqueous environment of the intestinal lumen
- Approach the brush border membrane of the enterocytes



Micelles

- Micelles constantly break down and re-form,
- MAG & FA :
 - nonpolar
 - diffuse across the plasma membrane of the enterocyte.
 - Some : specific transport proteins



Clinical Significance of Cholesterol Absorption

Ezetimibe

- Blocks a protein mediating cholesterol transport across enterocytes
- Effective at reducing levels of LDL cholesterol
- Clinical trials are in progress

Resynthesis of TAG and CHE

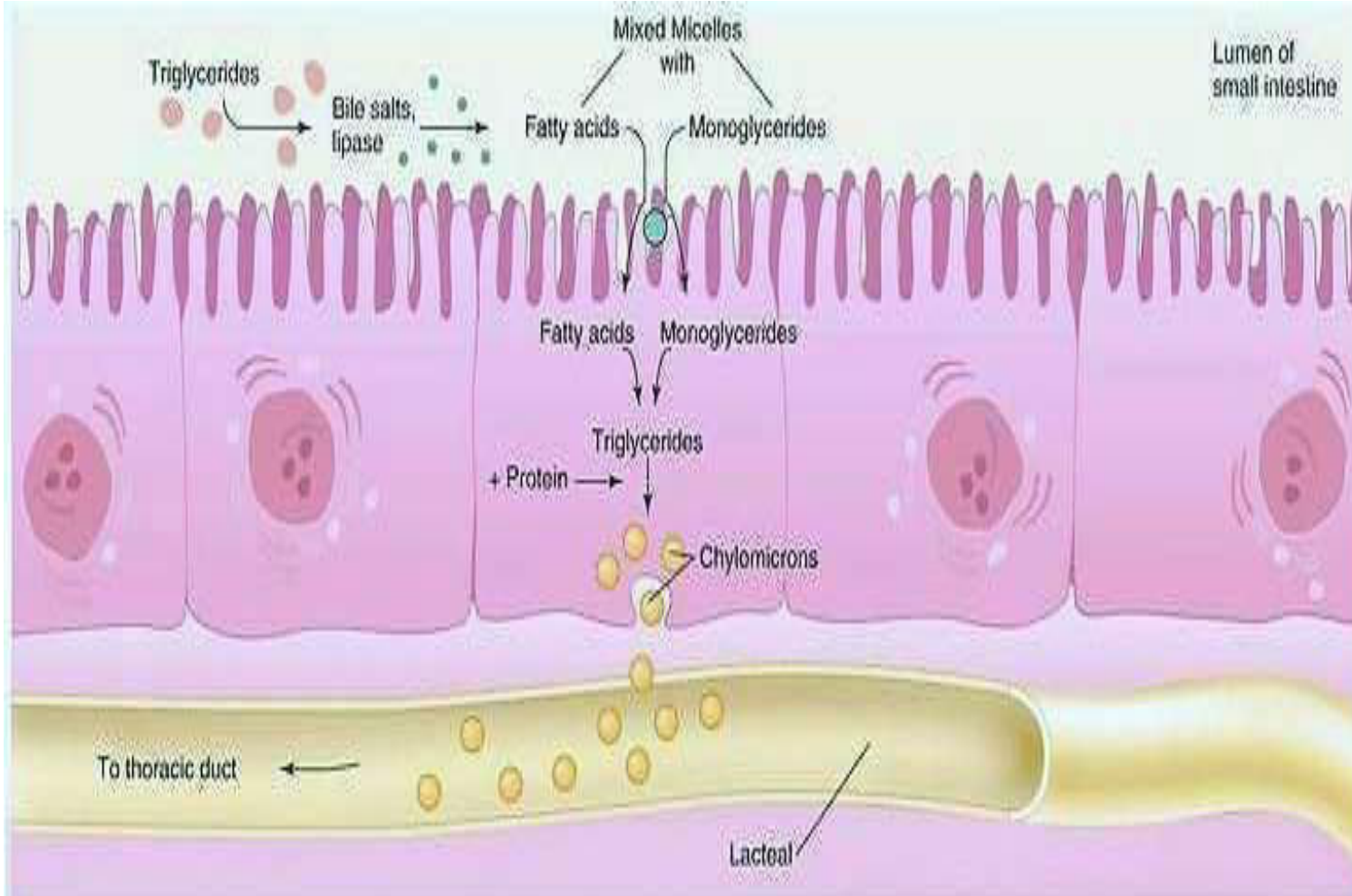
Within the intestinal epithelium

- 1- monoacylglycerols → FA + glycerol
- 2-monoacylglycerols → TAG

(monoacylglycerol pathway)

- Lysophospholipids → phospholipids.
- Cholesterol → Cholesteryl esters
- LCFA → TGs, PL, CHE.
- SCFA & MCFA → portal circulation
- carried by serum albumin to liver.

Formation and Transportation of Chylomicrons



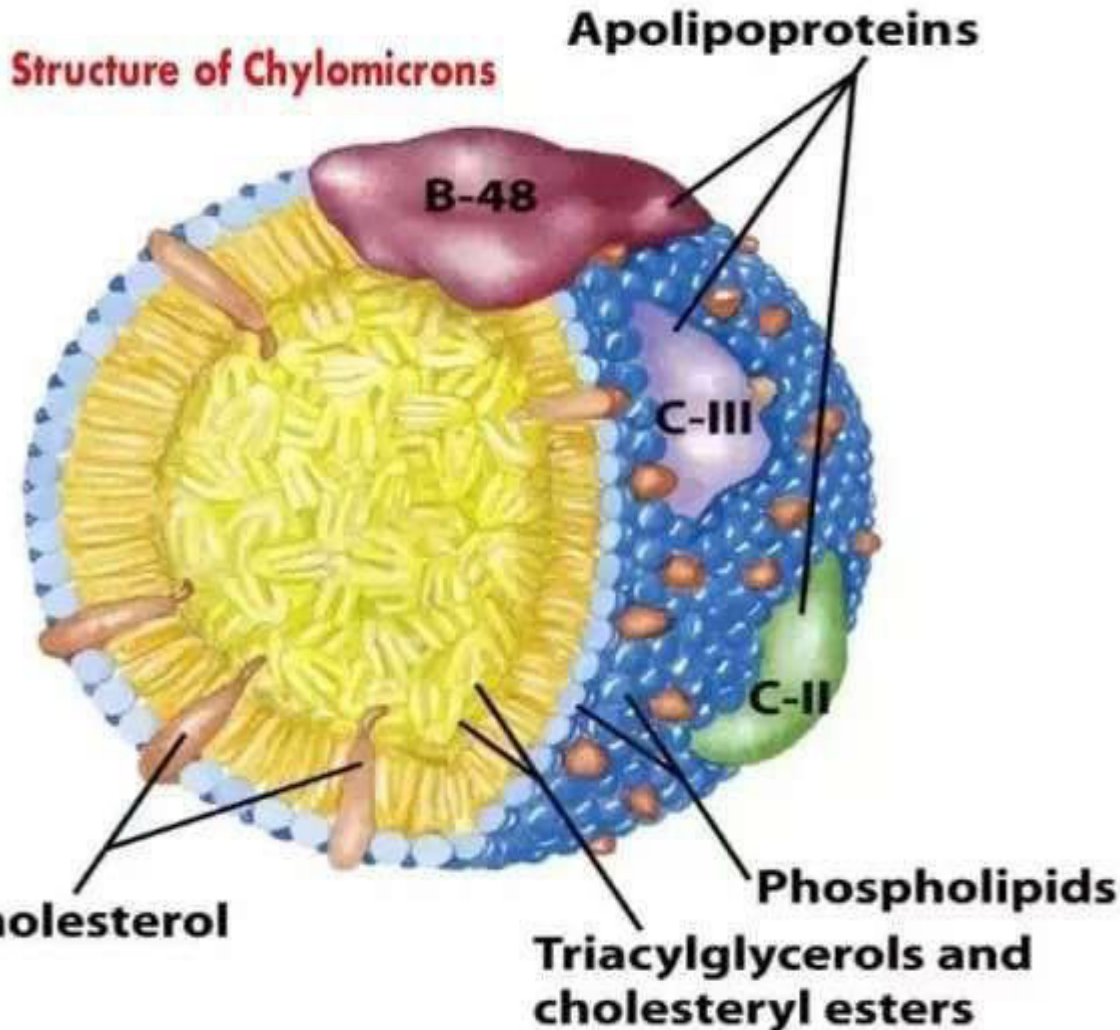
Lipid Malabsorption (Steatorrhea)

- **lipids loss** (including fat soluble vitamins A,D E and K) in the feces.
- **Cause**
 - pancreatic insufficiency
 - cystic fibrosis
 - chronic diseases of pancreas
 - surgical removal of pancreas
 - Shortened bowel, Celiac diseases, sprue or crohn's disease
 - Bile duct obstruction
- Milk and coconut oil are used therapeutically since they contain medium chain fatty acids.

Secretion of lipids from enterocytes

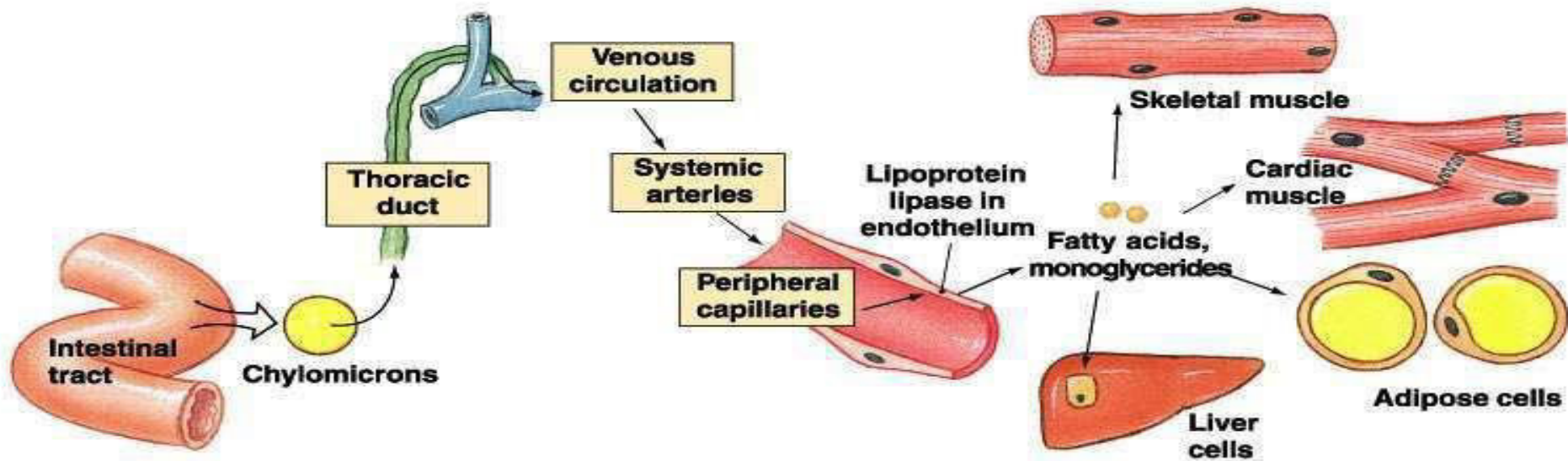
- Once inside the enterocyte
- monoglycerides and fatty acids → TAG.
- TAG + CH & Fat soluble vitamins → **chylomicrons**.
- Chylomicrons are **lipoproteins**, special particles that are designed for the transport of lipids in the circulation.
- Chylomicrons are released by exocytosis at the basolateral surface of the enterocytes.
- too large to enter typical capillaries.
- enter **lacteals**
- Chylomicrons then flow into the circulation via lymphatic vessels.

Structure of Chylomicron



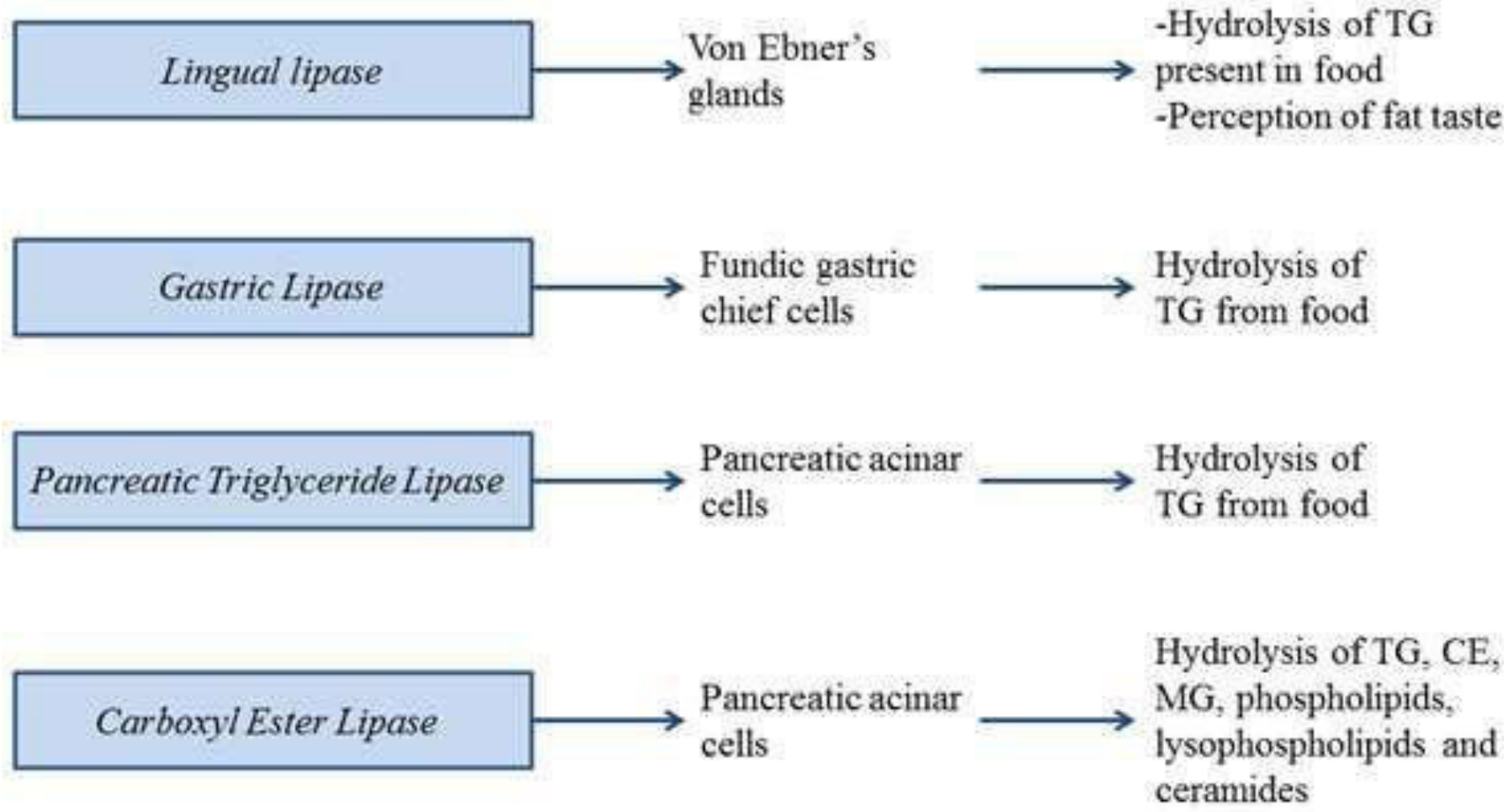
- ❑ *Size: 0.1–1 μm*
- ❑ *Average composition*
 - TG (84%)
 - Cholesterol(2%)
 - Ester Cholesterol (4%)
 - Phospholipid (8%)
 - Apo lipoproteins (2%)

Transport and Utilization of chylomicrons



Clinical significance of Chylomicron synthesis and utilization

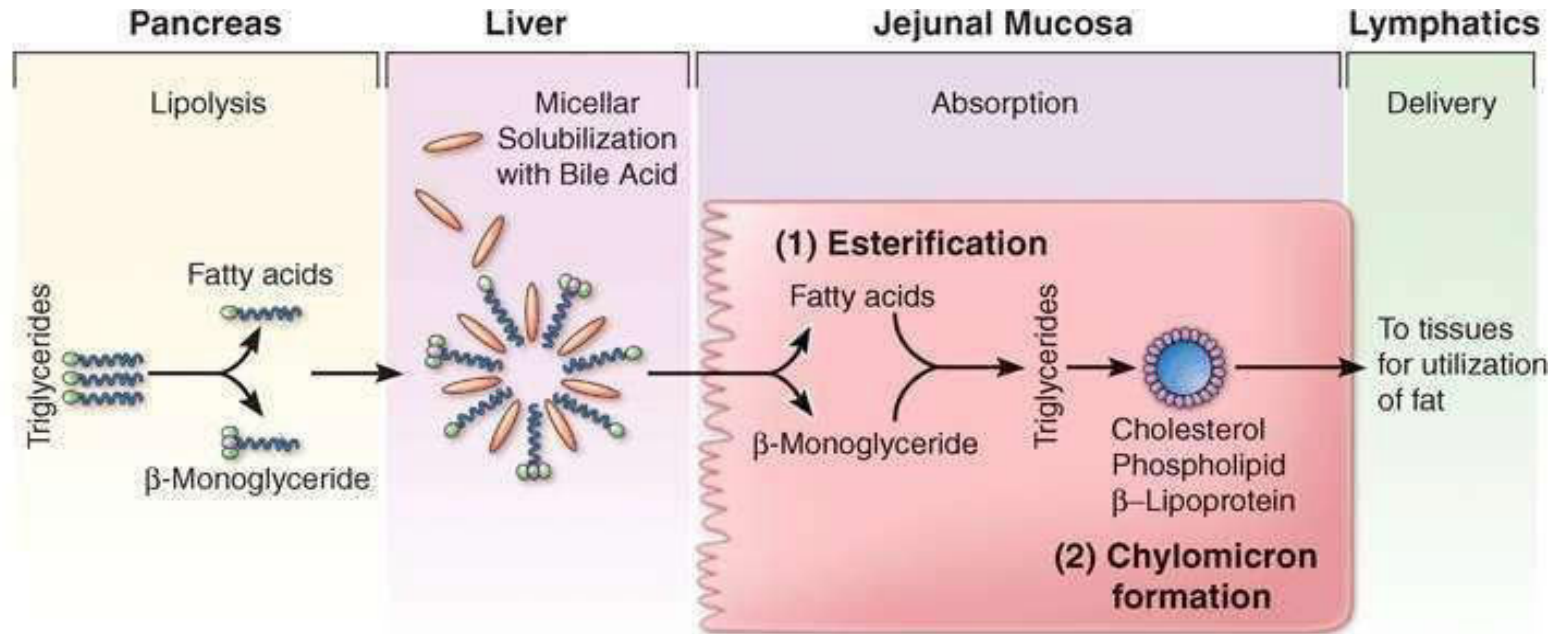
- **Defective synthesis-** Deficiency of apo-B 48 protein.
- The triglyceride may accumulate in intestinal cells.
- **Chyluria-** abnormal connection between urinary tract and lymphatic drainage system of the intestines
 - forming Chylous fistula
 - passage of Milky urine.
- **Chylothorax-** Small intestine resulting in accumulation of lymph in pleural cavity giving Milky pleural effusion



Physiologically important lipases

Lingual / acid stable lipase	Mouth , stomach	TAGs with medium chain FAs	FFA+DAG
Pancreatic lipase + co-lipase	Small intestine	TAGs with long chain FAs	FFA+2MAG
Intestinal lipase with bile acids	Small intestine	TAGs with medium chain FAs	2FFA+glycerol
Phospholipase A ₂ + bile acids	Small intestine	PLs with unsat. FA at position 2	Unsat FFA lysolecithin
Lipoprotein lipase insulin (+)	Capillary walls	TAGs in chylomicron or VLDL	FFA+ glycerol
Hormone sensitive lipase	Adipose cell	TAG stored in adipose cells	FFA+ glycerol

Summary of lipid digestion and Absorption



Chylomicrons deliver absorbed TAG to the body's cells. TAG in chylomicrons and other lipoproteins are hydrolyzed by **lipoprotein lipase**, an enzyme that is found in capillary endothelial cells. Monoglycerides and fatty acids released from digestion of TAG then diffuse into cells.