

Biomedical
Science

Molecular
Genetics



BMS 44110B | Fall 2026-2027

Metabolic Disease 2

Digestion & Absorption



Free Session

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Functions of Digestion & Absorption

The main function of digestion is to **hydrolyze large dietary components** such as:

Starch

poly saccharides, oligo saccharides

Starch →

mono saccharides

Proteins

large dietary protein components

Proteins →

amino acid

Fats

large dietary fat components

Fats →

fatty acids



Release of Bound Vitamins

In addition, digestion serves to release some vitamins from their **protein-bound forms.**

Biotin

released from its protein-bound form

Vitamin B12

released from its protein-bound form



Organs of the Gastrointestinal System

The well-coordinated functioning of organs of gastrointestinal system is required for **efficient digestion and absorption** of the essential nutrients in foods. The organs include:

Stomach

Produces **hydrochloric acid** which **denatures proteins**, making it susceptible to proteolysis both by **pepsin**, produced by the stomach, and by pancreas-derived proteases.

Pancreas

Secretes numerous digestive enzymes such as **proteases** that act in the small intestine and large amounts of **sodium bicarbonate**, which neutralize stomach acid, thus providing the nearly neutral pH required for the activity of pancreatic enzymes in the lumen of the small intestine.

Liver

Secretes **bile salts** required for the digestion and **absorption of fats**.

Gall bladder

Stores and concentrates the **bile salt** secreted by liver.

Small intestine

Is the **body's largest endocrine organ**, as it produces a variety of hormones that regulate digestion and energy balance.

- Enterocytes that line the lumen of the small intestine provide the surface to which disaccharidases and peptidases are attached and also provide surface for absorption of nutrients.



Ileum & Colon

Ileum

Integral element of the **enterohepatic circulation** that accounts for the **recycling of bile salts** and the absorption of essential nutrients such as **vitamin B12**.

Colon

Colon is a major site of **absorption of water and sodium and chloride** ions.

ALSO THE SITE OF ABSORPTION OF

Some of the metabolic by-products of **colonic bacteria**, particularly **lactate**, **short-chain fatty acids** such as **propionate and butyrate**, and **ammonia**, which is generated by hydrolysis of urea by bacterial urease.

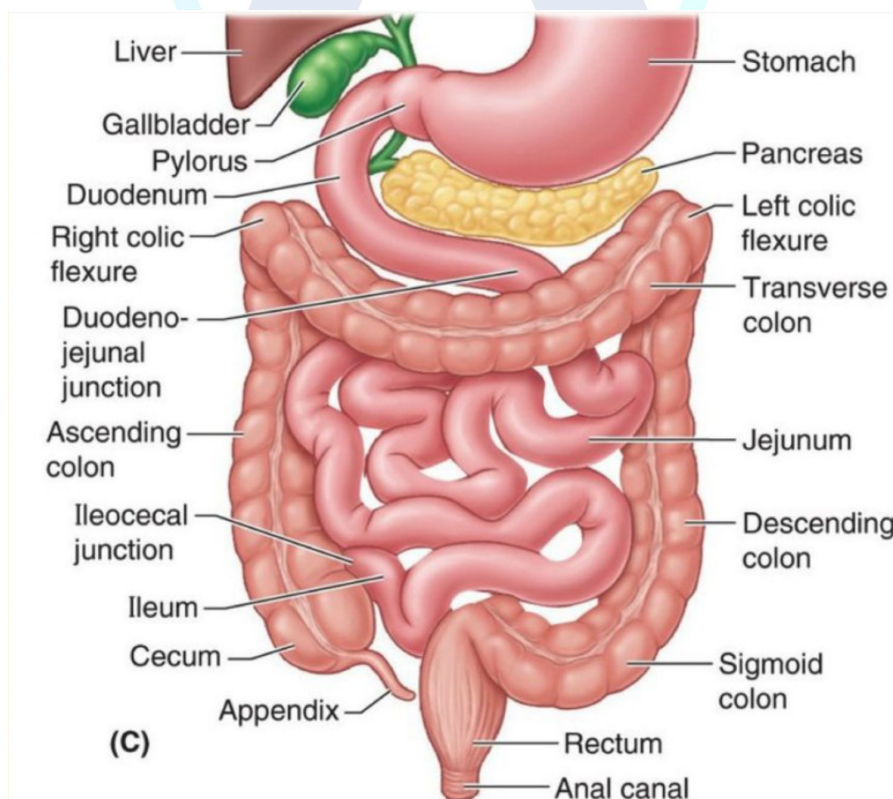


Figure adopted from Walter Kluwer Health | Lippincot Wilkins and Wilkins 2014



The Digestive Enzymes

DIGESTIVE GLANDS	ENZYMES	SUBSTRATE (NUTRIENT)	PRODUCT OF DIGESTION
Salivary glands	Ptyalin (Salivary amylase)	Starch	Maltose
Gastric glands	Pepsin	Proteins	Peptones
	Rennin (in infants)	Milk protein or caseinogen	Curdles milk to produce casein protein
Pancreas	Pancreatic amylase	Starch	Maltose
	Trypsin	Proteins and peptones	Peptides and amino acids
	Chymotrypsin	Protein	Proteoses, Peptones, Polypeptide, tri and dipeptides
	Pancreatic lipase	Emulsified fats	Fatty acids and Glycerol
Intestinal glands	Maltase	Maltose	Glucose and Glucose
	Lactase	Lactose	Glucose and Galactose
	Sucrase	Sucrose	Glucose and Fructose
	Lipase	Fats	Fatty acids and Glycerol

Table 8.3: Chart showing the Digestive Enzymes



Dietary Carbohydrates

THE MAJOR DIETARY CARBOHYDRATES ARE

Starch

Sucrose

Lactose

Cellulose

Starch

Polymeric, **storage form of carbohydrate in plants.**

Amylose is a straight-chain polymer
→ glucose joined by **alpha-1,4 glycosidic** links

Amylopectin is a branched structure
→ glucose joined by **alpha-1,4 glycosidic** links and **alpha 1, 6 glycosidic links** at branch points

Sucrose

Non reducing disaccharide present in most fruits.

$\text{Glc}(1 \rightarrow 2)\beta\text{-Fru}$

Lactose

Reducing disaccharide present in milk.

$\beta\text{-Gal}(1 \rightarrow 4)$

Cellulose

Polymeric, not digested in humans, forms the source of fiber in food
→ glucose are linked by **beta-1,4 glycosidic bonds.**

Most common monosaccharides and disaccharides are **reducing sugars** since they have a free aldehyde or ketone group.

In an alkaline solution, a reducing sugar will reduce **cupric ion (Cu^{2+})** to **cuprous ion (Cu^{+})**. By contrast, **sucrose is not a reducing sugar.**



Digestion of Starch

1

Salivary amylase (ptyalin)

initiates hydrolysis of the glucose polymers

2

Up to 40% of dietary starch

hydrolyzed before the enzyme is inactivated

3

Low pH in the stomach

inactivates salivary amylase

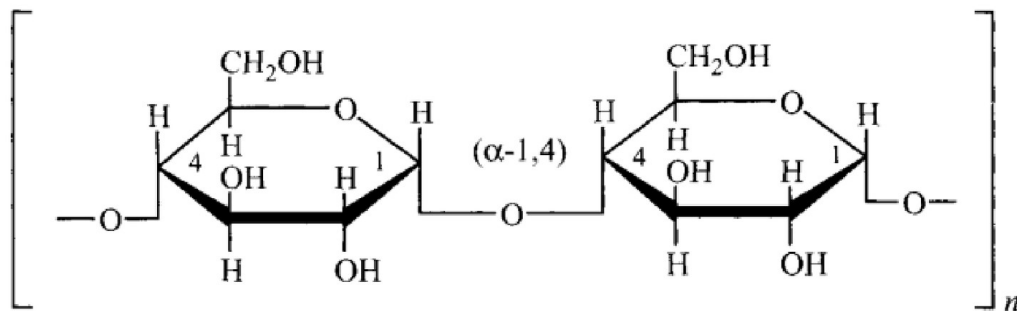
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Pancreatic α -amylase

continues starch digestion in the small intestine

Salivary and pancreatic amylases are both **endoglycosidases** that randomly hydrolyze internal **alpha-1,4 glycosidic bonds** of amylose and amylopectin to form smaller polysaccharides called **dextrins**.

A



B

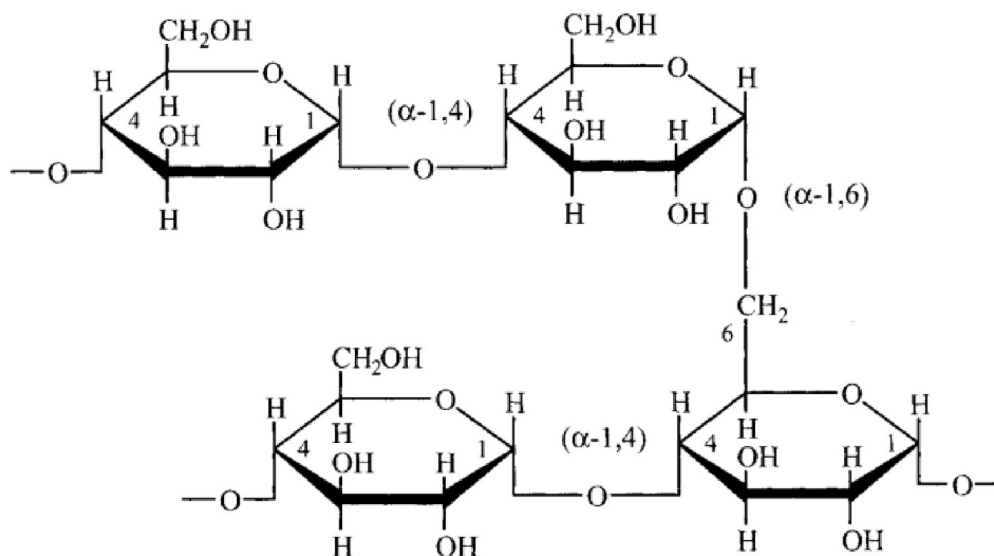


FIGURE 3-1 Structure of dietary starch: (A) the straight-chain structure of amylose (n indicates the number of repeating units, which may be in the thousands); (B) an α -1,6 glycosidic branch point in amylopectin.



Enzymes of Carbohydrate Digestion

ENZYME	SPECIFICITY	NATURAL SUBSTRATE	PRODUCT
Amylase	α -(1→ 4) Glucose	Amylose	Glucose
Isomaltase	α -(1→ 6) Glucose	Isomaltose, α -dextrin	Glucose
Maltase	α -(1→ 4) Glucose	Maltose, maltriose	Glucose
Sucrase	α -(1→ 2) Glucose	Sucrose	Glucose, Fructose
Lactase	β -(1→ 4) Galactose	Lactose	Glucose, Galactose



Digestion of Oligosaccharides

Starch are hydrolyzed by enzymes that are localized on the surface of the **brush border of the intestinal mucosa** to yield disaccharides and oligosaccharides digestion of dietary

sucrose

Maltose

Isomaltose

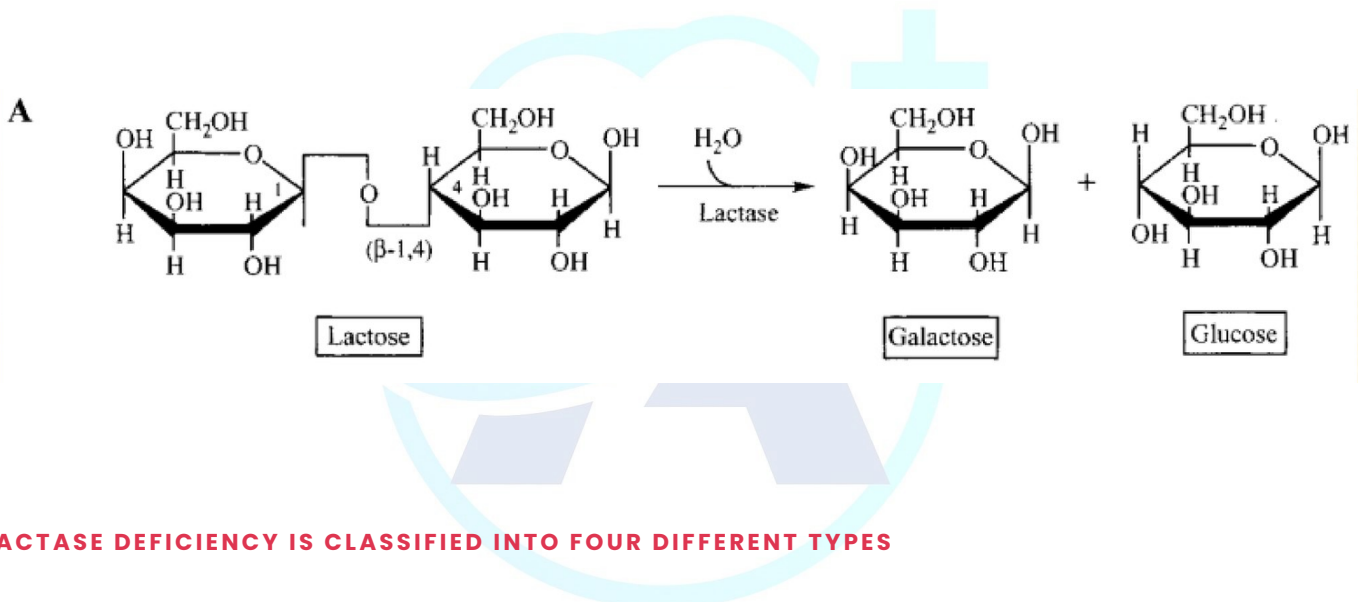
Lactose

derived from milk



Lactase

Lactase is a **β -galactosidase** that hydrolyzes **lactose to glucose and galactose**.



Primary

Secondary

Developmental

Congenital

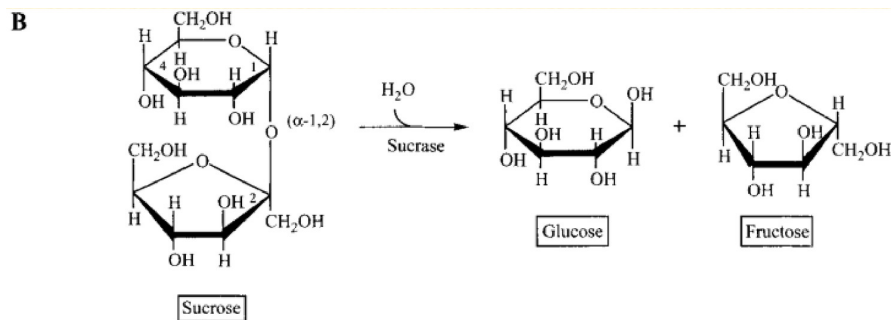
PRIMARY LACTASE DEFICIENCY

The **most common cause of lactose intolerance worldwide**. This type of lactase deficiency is caused by an inherited genetic fault that runs in families. Primary lactase deficiency develops when your lactase production decreases as your diet becomes less reliant on milk and dairy products.



Sucrase

Sucrase is a **disaccharidase** that hydrolyzes sucrose.

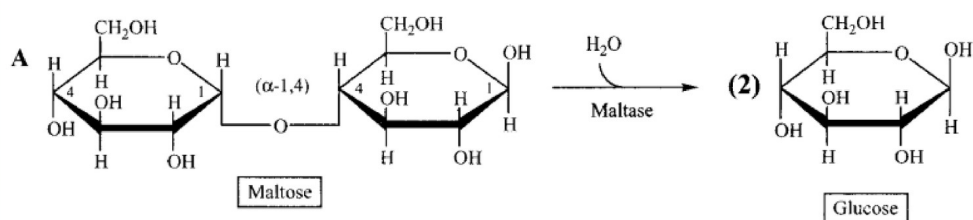


Congenital sucrase-isomaltase deficiency is a disorder that affects a person's ability to **digest certain sugars**. People with this condition cannot break down the disaccharides **sucrose and maltose**.



Maltase

Maltase is an **alpha-glucosidase** that hydrolyzes both maltose and maltotriose.



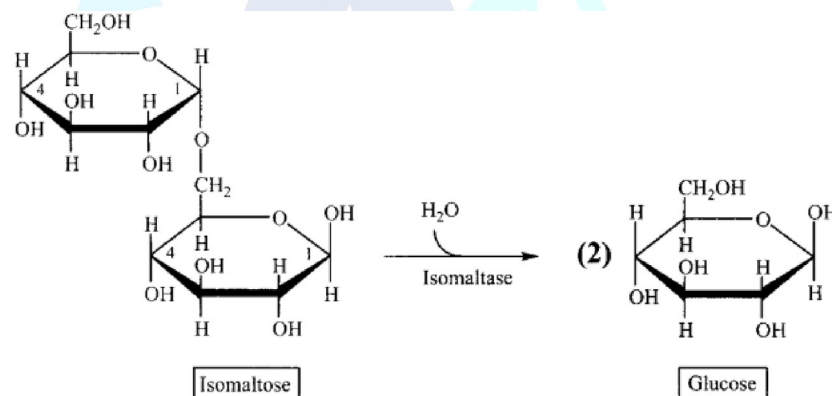


Isomaltase

Iso-maltase is an **alpha glycosidase** that hydrolyzes the **α -1,6 glycosidic bond** of isomaltose and limit dextrans.

Congenital sucrase-isomaltase deficiency is a disorder that affects a person's ability to digest certain sugars. People with this condition cannot break down the sugar **sucrose and maltose**.

B



α -Dextrinase

This **exoglycosidase** hydrolyzes glucose α -1,4-glucose linkages starting at the **nonreducing end** of the oligosaccharide chain.

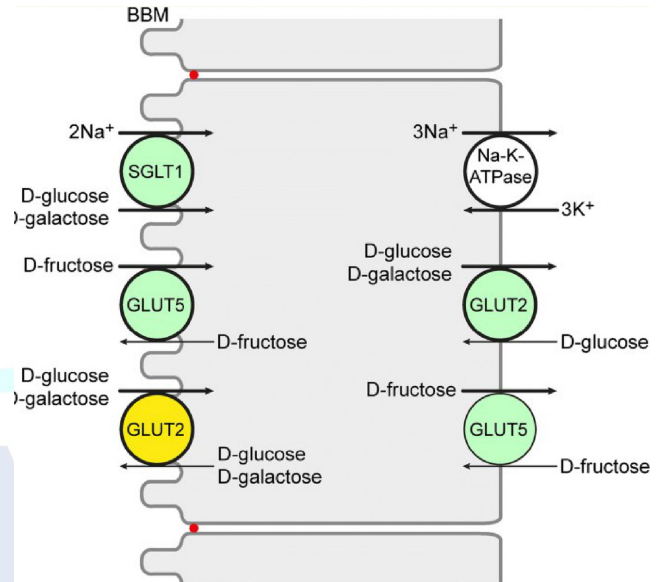
Although α -dextrinase has greater activity for oligosaccharides with relatively longer chains, it also hydrolyzes **maltose and maltotriose**.



Absorption of Sugars

GLUCOSE AND GALACTOSE

- Glucose is absorbed into the cells of the intestinal mucosa in cotransport with Na^+ by **SGLT1**, the sodium glucose-dependent symporter.
- This process is driven by the **active transport of Na^+** out of the cell through the basolateral membrane, which also serves to maintain a low concentration of intracellular Na^+ .
- Galactose is also transported by the **same symporter**.



SGLT1 deficiency causes intestinal glucose-galactose malabsorption, a condition that presents with **severe osmotic diarrhea and dehydration** soon after birth.



Fructose

- Fructose is specifically and passively transported by the facilitative **glucose transporter 5 (GLUT5, Slc2a5)** across the intestinal apical membrane and then is transported from the cytosol to the blood by **GLUT2 (Slc2a2)**.
- Fructose malabsorption** or Dietary Fructose Intolerance is a dietary disability of the small intestine, where the amount of fructose carrier in enterocytes is deficient.
- In humans the GLUT5 protein is **encoded by the SLC2A5** gene.



Digestion & Absorption of Dietary Lipids

The major dietary lipids are **triacylglycerols** containing three long-chain fatty acids (usually C16-C20) esterified to glycerol.

OTHER DIETARY LIPIDS INCLUDE

Free cholesterol and
cholesteryl esters
(animal source)

Phospholipids

Vitamins A, D, E, and K

The carotenoids

Lipids are **hydrophobic** form aggregate of **large lipid droplets**.

EFFICIENT DIGESTION OF THESE DROPLETS REQUIRES EMULSIFICATION

- 1 The physical effects of **peristaltic churning**.
- 2 Chemical dispersion of the droplets by the **detergent action of bile salts**.
- 3 Providing **greater surface area** for access by hydrolytic enzymes to their substrates.



Hydrolysis of Triacyl Glycerol (TAG)

1-Palmitoyl-2-linoleoyl-3-stearoylglycerol

→

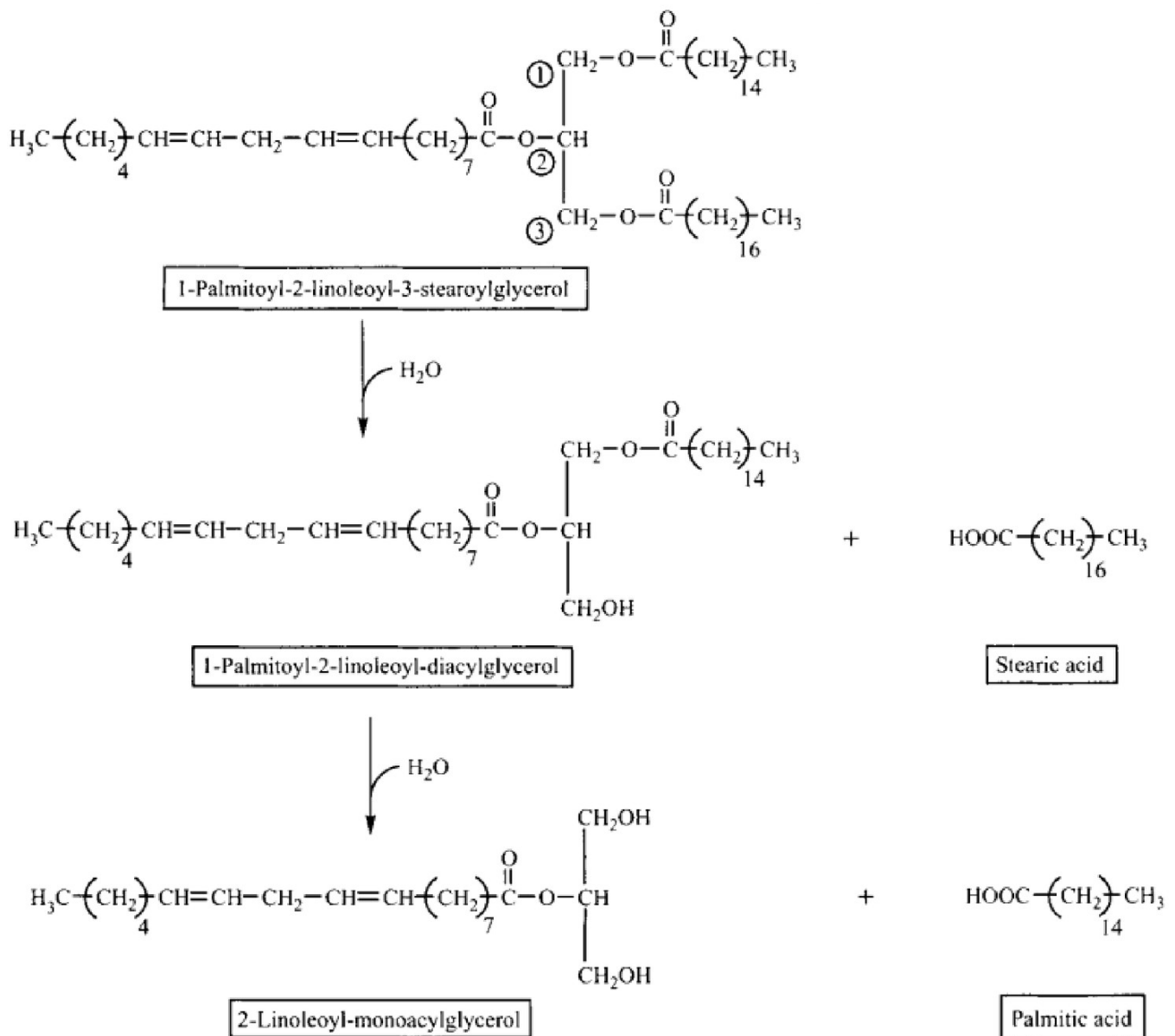
1-Palmitoyl-2-linoleoyl-diacylglycerol

+ Stearic acid

→

2-Linoleoyl-monoacylglycerol

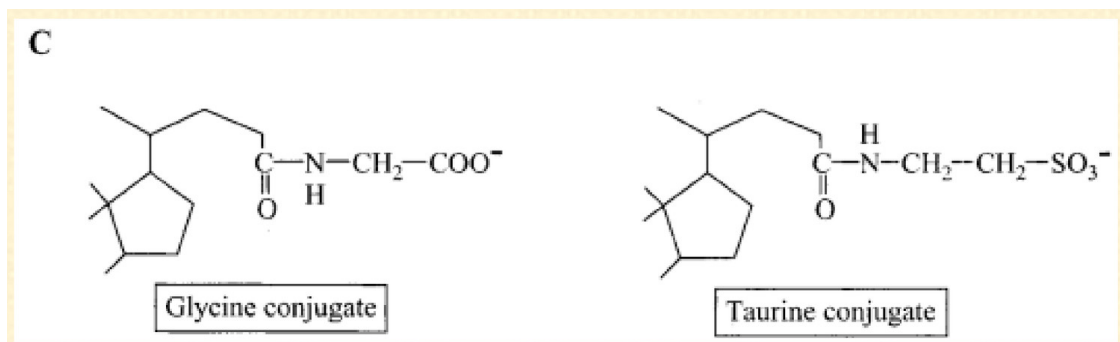
+ Palmitic acid





Bile Acid and Bile Salts

Bile acids are **cholesterol derivatives** with several hydroxyl groups and a hydrocarbon tail ending in a carboxyl group to which **glycine or taurine** linked via an amide bond forming bile salts (conjugated bile acids) (Fig. 3-5). (Fig. 3-5C).



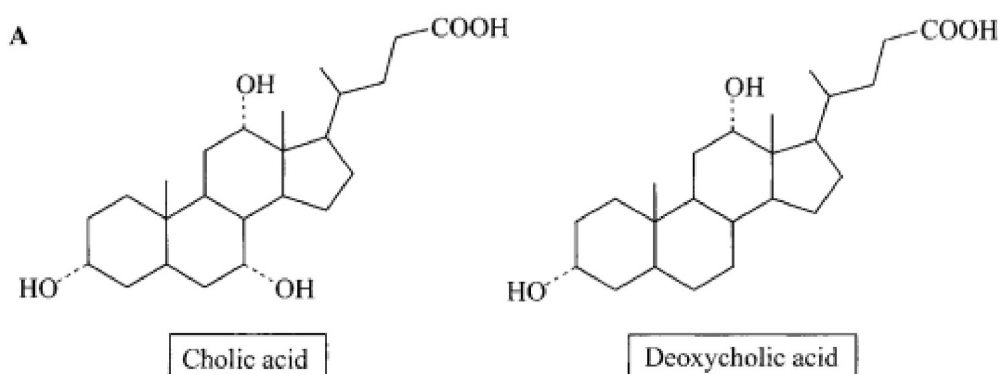
Weak acids

Bile acids are weak acids (**pK = 6**).

Conjugation lowers the pK

Conjugation decreases the pK, of the bile salts; glycocholic acid has a pK, of about **4**, whereas the pK, of taurocholic acid is about **2**.

Bile salts containing **three hydroxyl groups** (e.g., cholic acid) **are better emulsifiers** than those that have only two hydroxyl groups (e.g., deoxycholic acid).





Mixed Micelles

- 1 A second role that **bile salts** play in the process of forming small aggregates called **mixed micelles** that solubilizes the relatively hydrophobic products of lipid hydrolysis.
- 2 Mixed micelles have structures similar to **small disks cut out of a membrane bilayer**, with the bile salts stabilizing the cut edges.
- 3 Stabilization of mixed micelles by bile salts is required for the products of lipid hydrolysis to diffuse through the water layer near the surface of the intestine to the plasma membrane of the enterocyte brush border where they are absorbed.



B

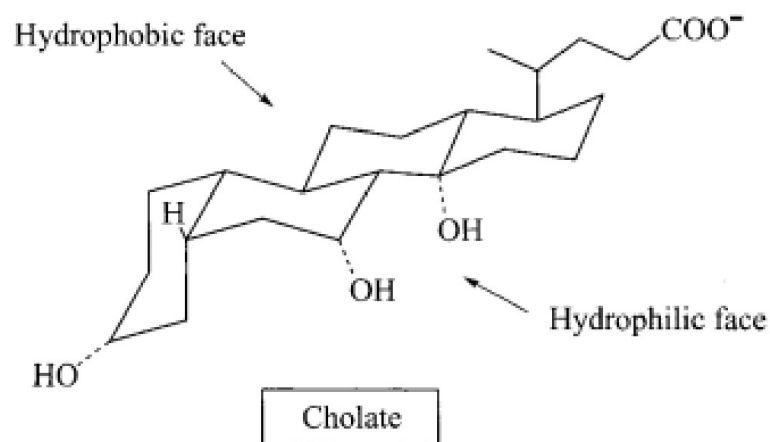


Figure 3-5 Structures of bile acids and bile salts: (A) the primary bile acids, cholic acid and deoxycholic acid; (B) the hydroxyl groups of bile salts such as taurocholic acid generate a polar face on an otherwise nonpolar steroid ring; (C) bile salts are formed by conjugation of bile acids with glycine or taurine.

⇒ Hydrolysis of Dietary Lipids

The digestive **lipases** catalyse the partial hydrolysis of dietary fats.

LIPIDS ARE ABSORBED AS A MIXTURE OF

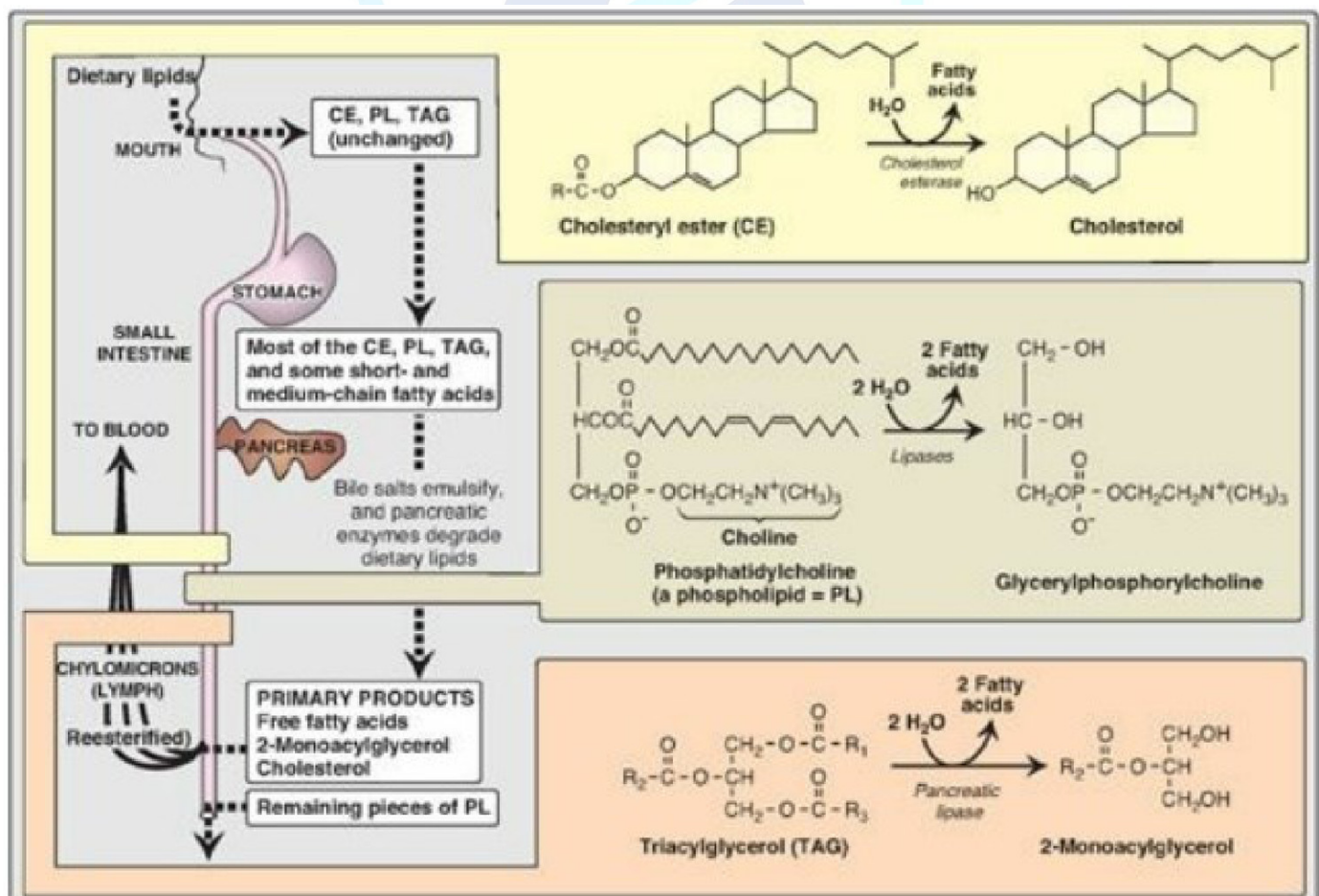
Monoacylglycerols

Diacylglycerols

Lysophospholipids

Free fatty acids

These products are then **reassembled within the enterocytes** for transport within the body.





Hydrolysis TAG

Triacylglycerols. The enzymes that hydrolyze triacylglycerols (triglycerides) are called **lipases:**

PANCREATIC LIPASE

Most important lipase — requires a **colipase** (non protein) that reduces the surface tension at the lipid-aqueous interface, facilitating the interaction between the lipase and the lipid droplet. Involved in the digestion of **long chain (C16-C20) fatty acids.**

LINGUAL LIPASE

Contribution is very little but is **not inactivated by the acid pH** of the stomach. In the absence of pancreatic secretion of bicarbonate, remains active in the small intestine as well. Thus, particularly in the absence of pancreatic lipase activity, lingual lipase can contribute significantly to the digestion of dietary triacylglycerols.

GASTRIC LIPASES

Active against **short-chain (C4-C6)** and **medium chain (C8-C12)** fatty acids, particularly important in the infant.

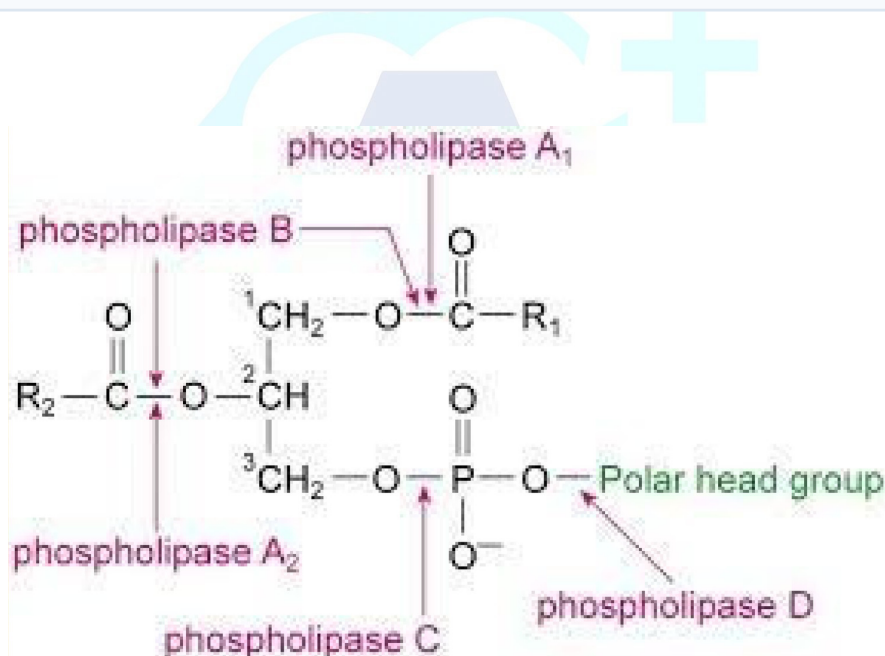
BILE SALT-STIMULATED LIPASE

A neutral pH optimum lipase, present in **human milk but not in cow's milk,** contributes substantially to triacylglycerol hydrolysis in the intestine of breast-fed infants.



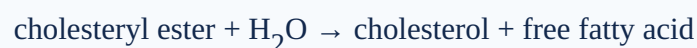
Hydrolysis of Phospholipids

- Pancreatic **phospholipase A2** is secreted as a **zymogen** activated by trypsin-catalyzed hydrolysis.
- Phospholipase A2 is specific for fatty acids in the **2-position of phospholipids**.
- Phospholipase A2 catalyzes the partial hydrolysis of dietary phospholipids, and of phosphatidylcholine secreted by the liver and contained in the bile.



Hydrolysis of Cholesteryl Esters

Dietary cholesterol is a mixture of **free cholesterol** and cholesterol esterified with **long-chain fatty acids**. Pancreatic juice also contains a **cholesterol esterase** or cholesteryl ester hydrolase which catalyzes the following reaction:





Absorption of Lipids & Chylomicrons

All the products of lipid digestion are solubilized by bile salts to form small **mixed micelles** that diffuse from the lumen of the intestine toward the **apical surface of the epithelium** of the duodenum and jejunum.

Instead, the absorbed fatty acids are **reesterified** into less polar products for transport in the form of large lipoprotein aggregates called **chylomicrons** (Fig. 3-7).

Hydrophobic core

Consists primarily of **triacylglycerol** molecules. It also contains cholesteryl esters and other absorbed lipophilic molecules, such as **fat-soluble vitamins**.

Surface layer

Phospholipids, free cholesterol, and proteins, primarily **apoprotein B48 (apo B48)** and **apoA1**.

After assembly, the chylomicrons are secreted from the enterocytes into the **lymphatic circulation**, from whence they eventually enter the blood via the **thoracic duct**.

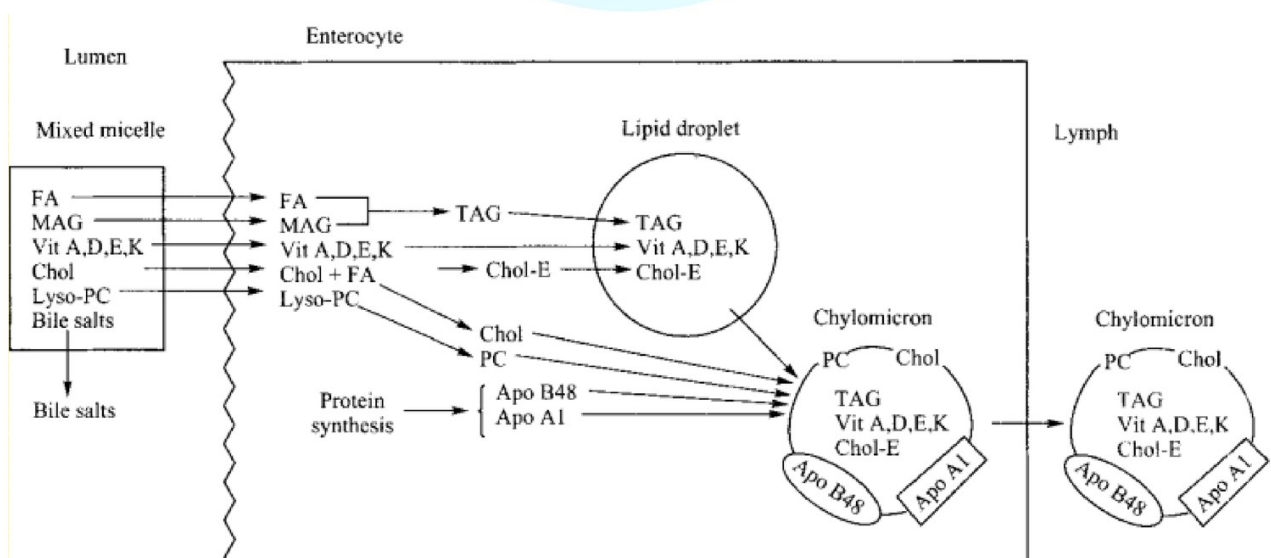


FIGURE 3-7 Absorption of dietary lipids into the enterocyte leads to chylomicron formation. apo A1, apoprotein A1; apo B48, apoprotein B48; Chol, cholesterol; Chol-E, cholesteryl ester; FA, free fatty acid; lyso-PC, 2-lysophosphatidylcholine; MAG, 2-monoacylglycerol; PC, phosphatidylcholine; TAG, triacylglycerol.



Resynthesis of Triacylglycerol

In enterocytes, synthesis of triacylglycerol occurs through the sequential action of **monoacylglycerol acyltransferase** and **diacylglycerol acyltransferase**, for a net reaction:



The conversion of free fatty acids to fatty acyl-CoA in enterocytes utilizes the ubiquitous **fatty acyl-CoA synthetase** reaction:



Reesterification of Absorbed Lipids

- Secretion of cholesterol and phosphatidylcholine in bile and reabsorption of cholesterol and lysophosphatidyl-choline in the small intestine provides enterocytes with a supply of the components involved in **chylomicron assembly**.
- **Lysophosphatidyl-choline acyltransferase** catalyzes the reassembly of the phospholipid:



Any free (nonesterified) cholesterol in excess of that which can be accommodated on the surface of the chylomicron particle is esterified by **acyl-CoA: cholesterol acyltransferase (ACAT)** and transported in the core of the chylomicron.



Absorption of Bile Acids

- Bile salts remain in the intestinal lumen until they reach the **distal ileum**, where most are absorbed by an active transport mechanism that utilizes a **Na⁺-bile salt cotransport system**.
- The bile salts are transported through the **portal vein** to the liver, where they are extracted from the circulation by hepatocytes and then secreted back into bile.
- Specific transporters on both ileal and hepatic cells are required for this process. This **enterohepatic circulation** results in the secretion and reabsorption of the same pool of bile salts some **4 to 10 times a day**, thus enabling the bile salts to be efficient promoters of fat digestion and absorption.

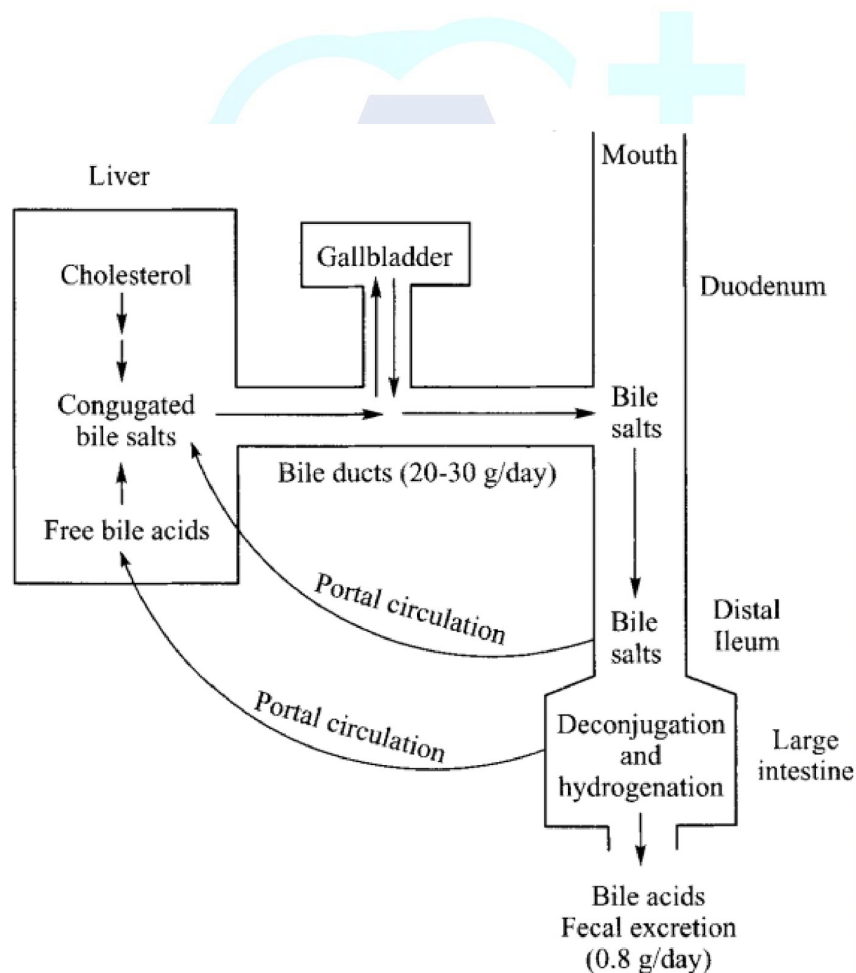


FIGURE 3-8 Enterohepatic circulation of bile salts.

Approximately **0.8 g/day** is excreted in the feces.



Medium-Chain Fatty Acids

The digestion and absorption of TAG containing **short- and medium-chain** fatty acids **differs in several ways** from TAG that containing long-chain fatty acids.

- 1 Additional lipases are available for shorter-chain fatty acids hydrolysis.
- 2 **Gastric lipase** preferentially hydrolyzes TAG in breast milk containing medium-chain fatty acids.
- 3 TAG containing medium-chain **(C6-C12)** fatty acids can also be absorbed by intestinal mucosa, where they are hydrolyzed by a mucosal lipase.
- 4 Medium-chain triacylglycerols, such as those in **coconut oil and human milk**, can also be digested and absorbed in the **absence of bile salts**, although the presence of bile salts does enhance their absorption.
- 5 Short- and medium-chain fatty acids are more soluble than C16 and C18 fatty acids, they can be transported as free fatty acids in the **portal blood** and are not reesterified and incorporated into chylomicrons.

CLINICAL USE

People with a reduced capacity for hydrolyzing triacylglycerols in circulating chylomicrons or persons who produce insufficient amounts of pancreatic lipase (e.g., patients with **cystic fibrosis**) are sometimes prescribed diets in which triacylglycerols that contain **medium-chain fatty acids** are used in place of common dietary fats.



To Summarise...

ORGANS

7

Gastrointestinal system

- Stomach: HCl denatures proteins for pepsin
- Pancreas: proteases + sodium bicarbonate
- Ileum recycles bile salts; colon absorbs water

STARCH

40%

Salivary amylase (ptyalin)

- Hydrolyzes as much as 40% of dietary starch
- Inactivated by the low pH in the stomach
- Pancreatic α -amylase continues the process

ENZYMES

5

Carbohydrate digestion

- Amylase, isomaltase, maltase, sucrase, lactase
- Localized on the intestinal brush border
- Yield glucose, fructose and galactose

UPTAKE

SGLT1

Absorption of sugars

- Glucose + galactose cotransported with Na^+
- Fructose crosses apically by GLUT5 (Slc2a5)
- GLUT2 moves sugars from cytosol to blood

BILE

4–10×

Enterohepatic circulation

- Same bile salt pool recycled 4 to 10 times a day
- Absorbed in the distal ileum by Na^+ cotransport
- Approximately 0.8 g/day excreted in the feces

LIPIDS

C16–C20

Chylomicron formation

- TAG core plus cholesteryl esters and vitamins
- Surface of phospholipids, apo B48 and apoA1
- Secreted to lymph, reach blood via thoracic duct

DEFICIENCIES COVERED IN THIS LECTURE

Primary lactase deficiency

Congenital sucrase-isomaltase deficiency

SGLT1 deficiency — glucose-galactose malabsorption

Fructose malabsorption

Cystic fibrosis — insufficient pancreatic lipase