



Biochemistry of the GIT

Biochemical Aspects of Bile Acids and Salts

Done By:

Hadeel Al-Madany

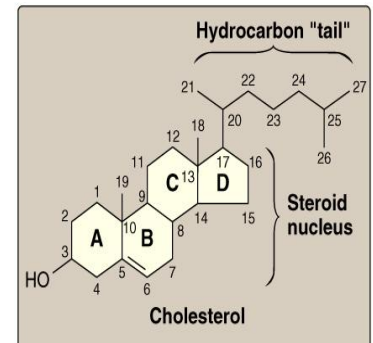
Mohanned AlEssa

Cholesterol

Cholesterol (27C) is the: **do not memorize the structure**

- ✓ Whenever you find a four-ringed-compound, you should know that its' parent compound is cholesterol
- ✓ **Parent** steroid compound
- ✓ **Precursor** of bile acids and salts

Bile acids are formed from cholesterol by transforming structure from 27 carbons to 24 carbons and adding hydroxyl groups.



Primary Bile Acids

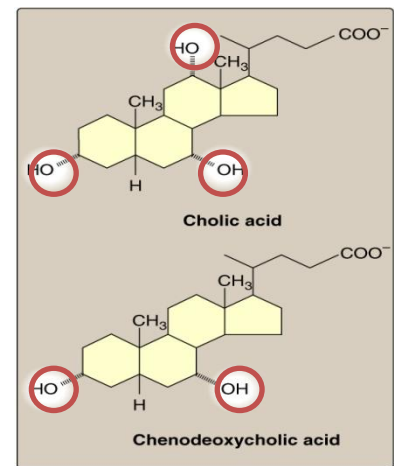
Primary bile acids (24 C):

Amphipathic (both hydrophilic and hydrophob

-COOH at side chain

(Structure)

- 2 Types:
 - Cholic acid: 3 OH
 - Chenodeoxycholic: 2 OH

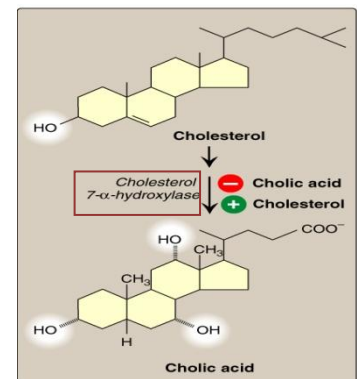


Hepatic Synthesis of Bile Acids

- ✓ The **rate-limiting step** is catalyzed by:
Cholesterol 7- α -hydroxylase (Regulating Hormone)
- ✓ Regulation:
 - Down-regulated by **end products** (increase bile acids) "**Enzyme repression**"
 - Up-regulated by **cholesterol** "increased cholesterol = increased substrate"

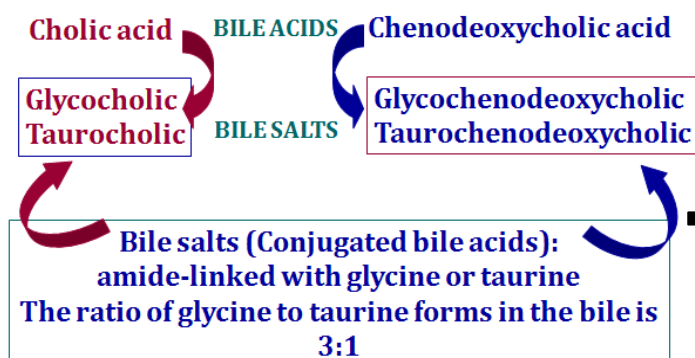
"Enzyme induction"

*Cholesterol had only 1 hydroxyl group which could be increased to 3 groups by Cholesterol 7- α -hydroxylase



Because the regulation is at the gene level, so the terms repression and induction are used instead of inhibition and stimulation. (Feedback +/-)

Primary Bile Acids and Salts



**Cholic acid is the most important Bile acid*
**the site of synthesis of bile acids is the liver*

Conjugation is the turning of substances into a hydrophilic state in the body. Here we mean the process by which the glycine (or taurine) binds to the bile acid to make bile salt through an amide linkage.

*Cholic acid + glycine = glycocholic (which is a bile salt)

*Cholic acid + taurine = Taurocholic (which is a bile salt)

*chenodeoxycholic acid + glycine = glycochenodeoxycholic

* chenodeoxycholic acid + taurine = Taurochenodeoxycholic

- Addition of glycine or taurine results in the presence of fully ionized groups at pH 7.0:

-COOH of glycine

-SO₃ of taurine

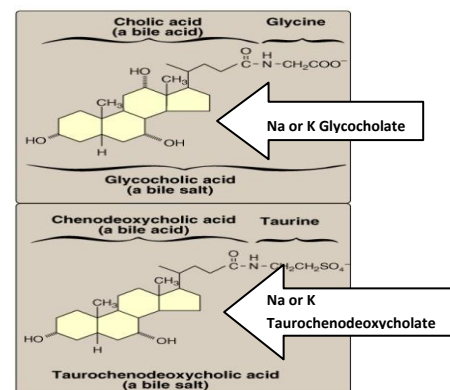
(hence, its name as bile salts e.g., Sodium or potassium glycocholate) because it has to bind with a positive atom for salt formation.

- More effective detergent than bile acids
- Only bile salts, but not acids, found in bile

Chose the correct answer:

Which one of the following is found in the bile:

- A. Bile acid
- B. Bile salts ✓



Hormonal Control of Bile Secretion

Stimulus:

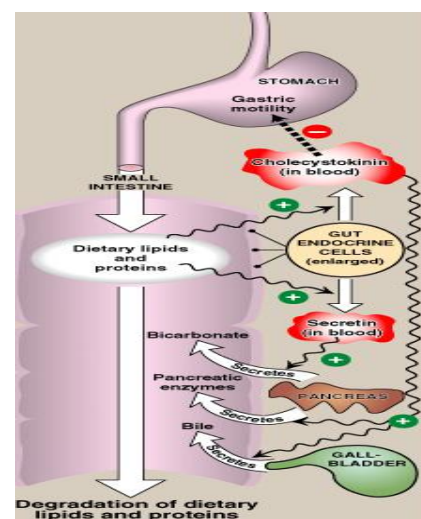
Undigested lipids and partially digested proteins in duodenum

Hormone from gut cells:

Cholecystokinin (CCK) → Contracts gall bladder for bile secretion.

Responses:

1. Secretion of pancreatic enzymes
2. **Bile secretion**
3. Slow release of gastric contents



Functions of Bile Salts

- Important for cholesterol excretion:
 1. As metabolic products of cholesterol
 2. Solubilizer of cholesterol in bile

- Cholesterol is excreted by bile salts as cholesterol (no change in form).
- Cholesterol is transformed into bile acids and excreted later on.

- Emulsifying factors for dietary lipids, a prerequisite step for efficient lipid digestion
- Cofactor for pancreatic lipase and PLA₂
- Facilitate intestinal lipid absorption by formation of mixed micelle

Emulsification of Dietary Lipids in Duodenum: Role of Bile Salts

- Emulsification increases the surface area of lipid droplets, therefore the digestive enzymes can effectively act.
- Mechanisms:
 1. Mechanical mixing by peristalsis
 2. Detergent effect of bile salts:
- Bile salts interact with lipid particles and aqueous duodenal contents, stabilizing the particles as they become smaller, and preventing them from coalescing.

Absorption of Lipids by Intestinal Mucosal Cells: Role of Bile salts

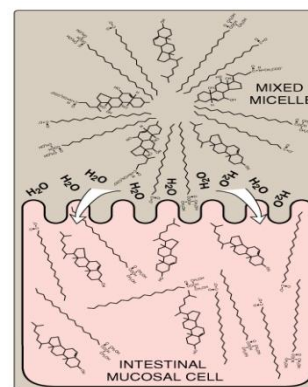
- Mixed micelles:
- Disc-shaped clusters of amphipathic lipids.
- Arranged with their hydrophobic groups on the inside and their hydrophilic groups on the outside.
- Micelle includes end products of lipid digestion, bile salts and fat-soluble vitamins

Note: Short- and medium-chain fatty acids do not require mixed micelle for absorption by intestinal cells

The Role of Bile Salts in Absorption of Lipids by Intestinal Cells

Mixed Micelle Formation:

- Bile salts
- End products of lipid digestion
- Fat-soluble vitamins



Secondary Bile Acids

Bile salts Glyco- or Tauro-cholate -Chenodeoxycholate



Bile acids Cholic acid Chenodeoxycholic



2° Bile acids Deoxycholic acid Lithocholic

This stage happens at the intestine by 2 steps:

- The intestinal bacteria acts on the bile salts to convert them back to bile acids by removing glycine or taurine
- Again, intestinal bacteria acts on bile salts to convert them into secondary bile acids by removing a hydroxyl group

Enterohepatic Circulation

Primary and secondary bile acids can be found in both intestine and liver

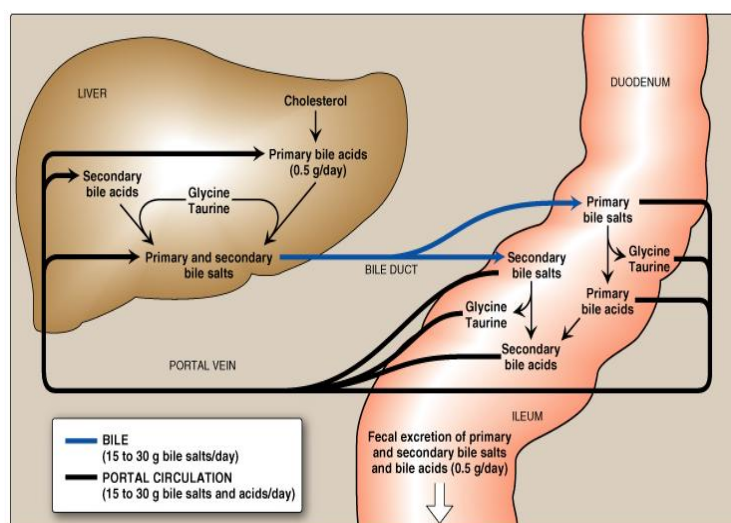
Bile duct contains only bile salts

Bile acids & salts are returned back to the liver by the Portal circulation.

Excretion of bile acids in enterohepatic circulation:

- 1- Cholestyramine: Bile acid sequestrants
 - It binds to bile acids in the gut,
 - preventing their reabsorption &
 - Promoting their excretion
 - It is used for treatment of hypercholesterolemia

- 2- Dietary fiber: (Less effective)
It binds to bile acids, increasing their excretion



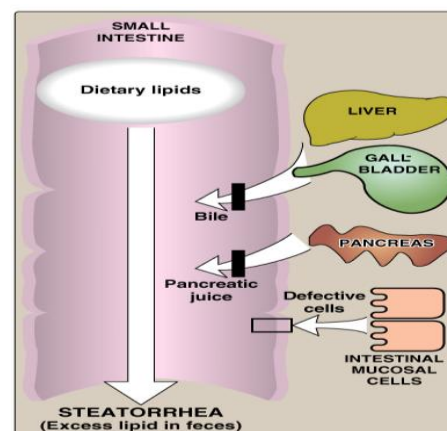
Used in treatment of Hypercholesteremia
because a large part of cholesterol will be transformed into bile acid. So it will decrease cholesterol.

Maldigestion/Malabsorption of Lipids

Decreased bile secretion by:

- Liver diseases:
e.g., Hepatitis or cirrhosis
- Gall bladder diseases:
e.g., Gall stones

Lead to → Malabsorption of lipids



Cholelithiasis [Cholelithiasis (calculi made out of cholesterol)]

Causes:

- ↓ Bile salts in bile:
 1. Biliary tract obstruction (interferes with enterohepatic circulation)
 2. Hepatic dysfunction (↓synthesis)
- ↑ Biliary cholesterol excretion (e.g. Hypercholesteremia)

Treatment:

- Bile acid replacement therapy
- Surgical (**Mostly used**)

Bile acid replacement therapy:

Introduction of bile acids → solubilizes cholesterol so it can be easily excreted.