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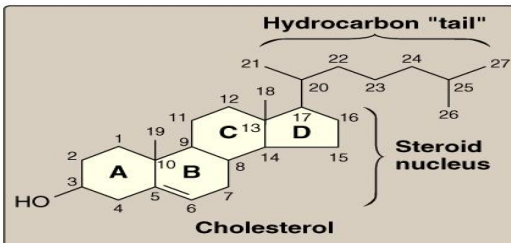
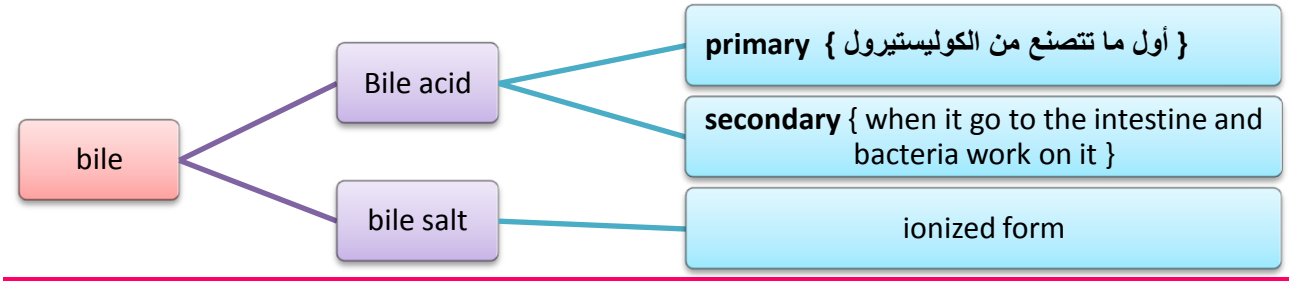
Biochemical Aspects of Bile Acids and Salts

Cholesterol

Cholesterol (27 C) is the:

- **Parent →steroid compound**
- **Precursor of → bile acids and salts**





Primary Bile Acids

Primary bile acids (24 C):

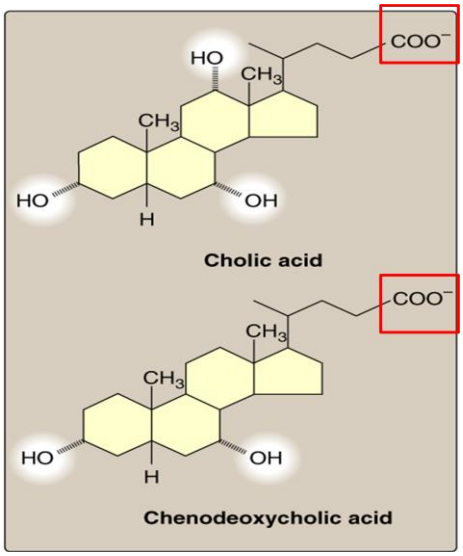
- **It is Amphipathic → has OH molecule**
- **-COOH at side chain**

1- Cholic acid:

- **3** OH
- - more efficient as a degernate
  - more soluble than Chenodeoxycholic

2- Chenodeoxycholic:

- **2** OH



Hepatic Synthesis of Bile Acids

cholesterol → cholic acid (by Cholesterol 7-α-hydroxylase)

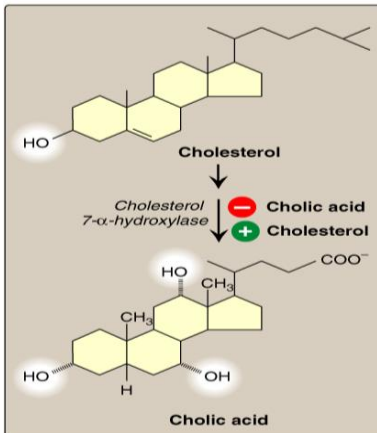
The rate-limiting step is catalyzed by: Cholesterol 7-α-hydroxylase

Location : liver

Regulation { at gene levels "not allosteric" } :

- **Down-regulated by end products (bile acids) "Enzyme repression"**
- **Up-regulated by cholesterol "Enzyme induction"**

❖ ↑ **cholesterol** → stimulate synthesis of bile acids
❖ ↑ **end product** → inhibit synthesis of bile acids



Bile Salts

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

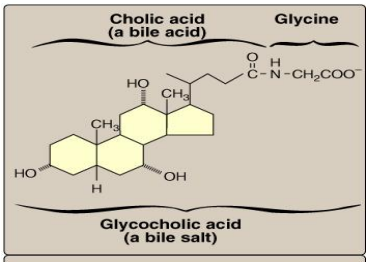
(-COOH) of glycine & (-SO_3) of taurine
(hence, its name as bile salts e.g., Sodium or potassium glycocholate)

➢ **More effective detergent than bile acids**

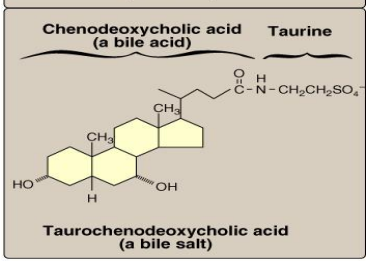
➢ **Only bile salts, but not acids, found in bile only .**

Conjucation of bile acids by glycine or taurine →convert it to bile salts→ ↑ **water solublity**

"bile salts is **more** soluble than bile acids"

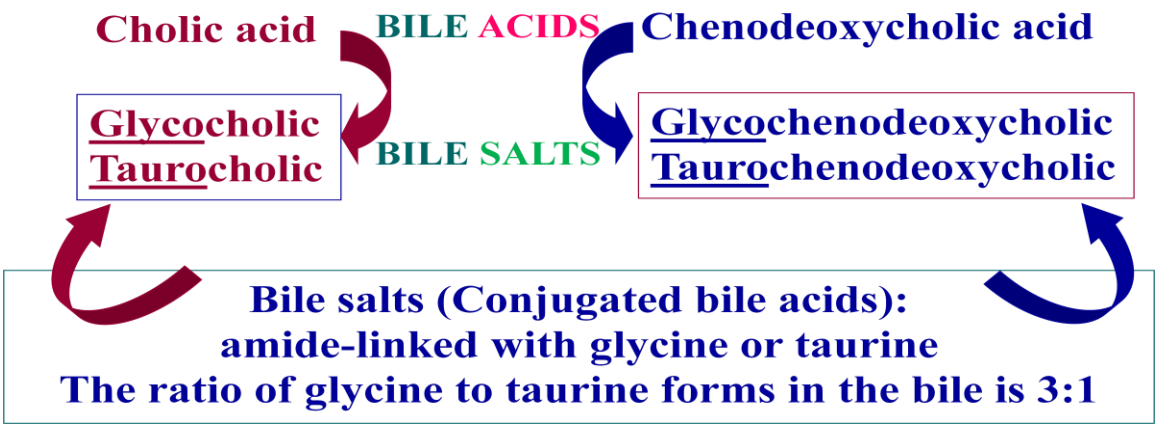


Na or K Glycocholate



Na or K Taurochenodeoxycholate

Primary Bile Acids and Salts

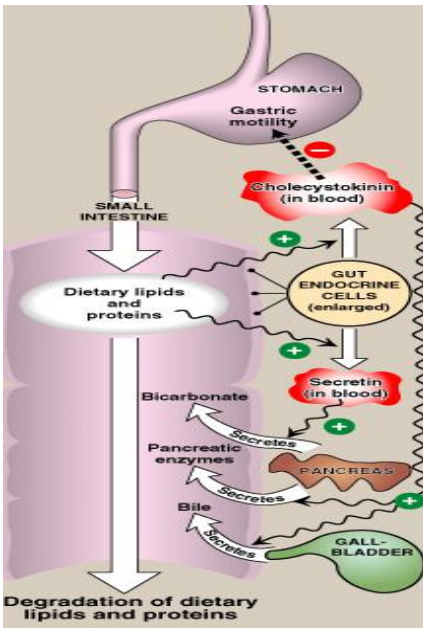


Hormonal Control of Bile Secretion:

- **Stimulus:** Undigested lipids and partially digested proteins in duodenum.
- **Hormone from gut cells:** Cholecystokinin (CCK)

Responses:

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



lipids and proteins in duodenum → secretion of CCK → secrete bile salts from gall bladder

Functions of Bile Salts:

Important for cholesterol excretion:

1. **As metabolic products of cholesterol:** As bile salt itself (because the origin of the bile salt Is cholesterol so if we lose them in stool we loss cholesterol)
2. **Solubilizer of cholesterol in bile**
    - Emulsifying factors for dietary lipids, a prerequisite step for efficient lipid digestion
    - Cofactor for pancreatic lipase and PLA2 (without bile salt the enzymes will not act)
    - formation of mixed micelle →Facilitate intestinal lipid absorption

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:

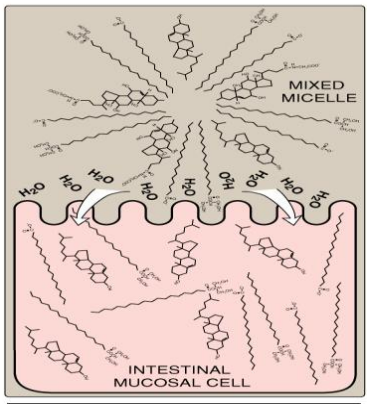
- Mixed micelles:
  Disc-shaped clusters of amphipathic lipids.
  Arranged with their hydrophobic groups on the inside and their hydrophilic groups on the outside.
- Micelle includes end products of lipid digestion, bile salts and fat-soluble vitamins

✓ 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:

1. **Bile salts**
2. **End products of lipid digestion**
3. **Fat-soluble vitamins**



Secondary Bile Acids

Bile salts Glyco- or Tauro-cholate -Chenodeoxycholate

Glycine / Taurine ← **Intestinal bacteria**

Bile acids Cholic acid Chenodeoxycholic

OH ← **Intestinal bacteria**

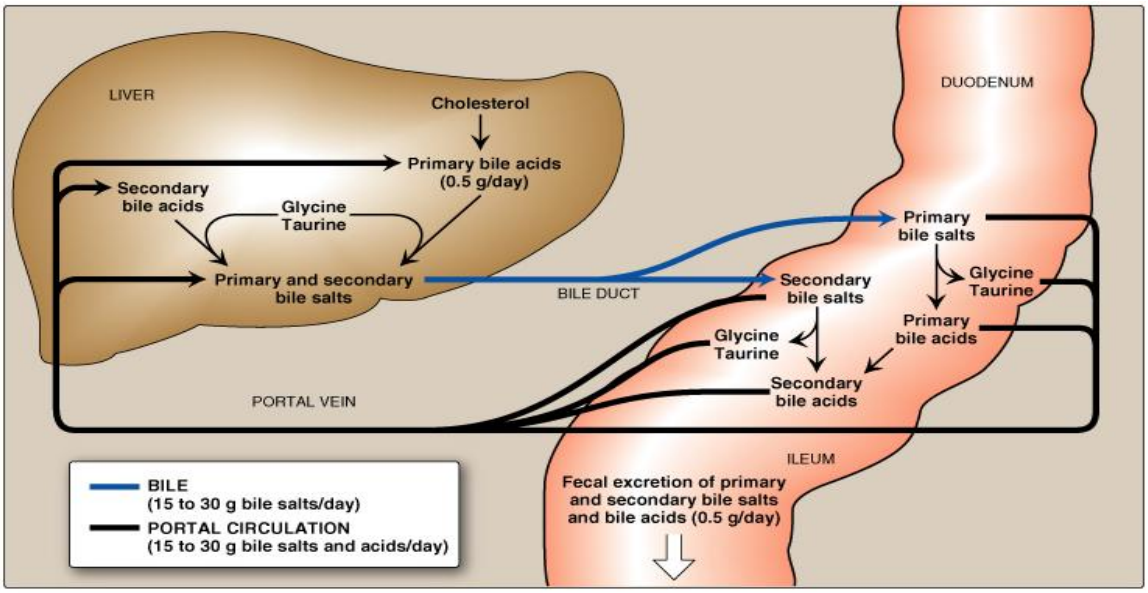
2° Bile acids Deoxycholic acid Lithocholic

- **Intestinal bacteria remove glycine & taurine → return bile salts again to primary acid**
- **Then the bacteria complete it's action and remove (OH) → result in secondary bile acids**

Can we find secondary BA in the liver?

secondary BA is not synthesis in the liver but we can see it there due to the enterohepatic circulatin ..

Enterohepatic Circulation



When we want to treat a case of hypercholesterolemia → intrubt enterohepatic circulation by:

1- Cholestyramine (drug): 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:

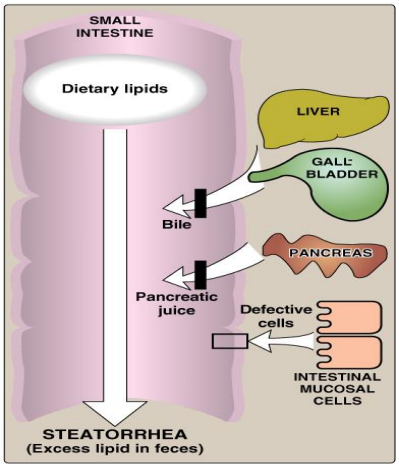
- It binds to bile acids, increasing their excretion

When we block the reabsorbion "by drugs"→ more cholesterol will be excreted in stools

Maldigestion/Malabsorption of Lipids:

Decreased bile secretion (→ Malabsorption of lipids) by:

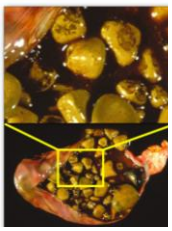
- **Liver diseases:** • e.g., Hepatitis or cirrhosis
- **Gall bladder diseases:** • e.g., Gall stones



Cholelithiasis " Cholesterol Gallstone Disease":

Causes:

- ↓ **Bile salts in bile:**
  - Biliary tract obstruction (intereferes with enterohepatic circulation)
  - Hepatic dysfunction (↓ synthesis)
- ↑ **Biliary cholesterol excretion**



Treatment:

- **Bile acid replacement therapy**
- **Surgical**