



Biochemical Aspects of Bile Acids and Salts

OBJECTIVES

- Structure of primary bile acids and salts
- Structure of secondary bile acids and salts
- Functions of bile salts
- Enterohepatic circulation
- Malabsorption syndrome
- Cholelithiasis

Cholesterol: contain 27C¹ and serve as :

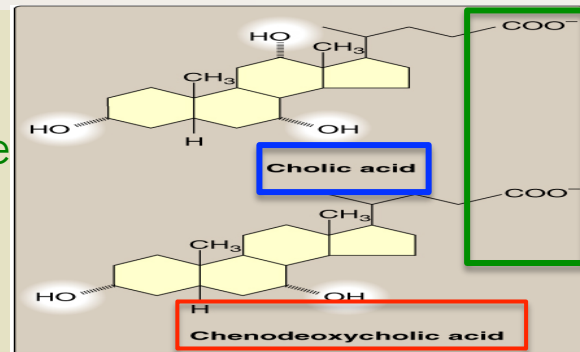
- ❑ steroid Parent compound
- ❑ Precursor of bile acids and salts

Primary bile acids

They are amphipathic structures with a side chain that terminate in a carboxyl (COOH) group.

They have either: 3 (OH) groups => **CHOLIC ACID**

OR 2 (OH) groups => **CHENOXYCHOLIC ACID**



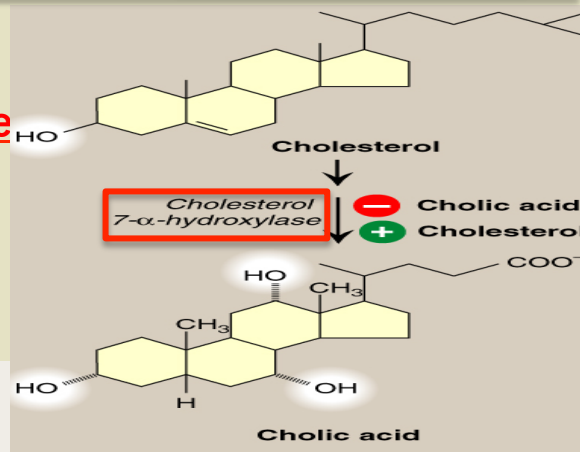
Hepatic Synthesis of Bile Acids

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

◆ Regulation of “Cholesterol 7- α -hydroxylase”

⇒ Down-regulation (**Enzyme repression**) by end products (**Bile acids**)

⇒ Up-regulated (**Enzyme induction**) by **Cholesterol**.



1:Cholesterol is very hydrophobic, has one (OH) group attached to c3 which is the ONLY hydrophilic part. (the more OH in a molecule, the more hydrophilic it becomes)

PRIMARY BILE ACIDS AND SALTS

Cholic acid

Chenodeoxycholic acid

+ Glycine*
Taurine

=>

Glycochenodeoxycholic acid

Taurochenodeoxycholic acid

Glycocholic acid

Taurocholic acid

Primary Bile acids

Bile salts

Bile salts: (Conjugated bile acids)¹

- Before bile acids leave the liver, they are conjugated to either **(Glycine or Taurine)** by an **amide bond**. The ratio of glycine to taurine forms in the bile is **3:1**
- Addition of glycine or taurine results in the presence COOH group (from GLYCINE) Or a sulfonate (SO₃ group (from TAURINE)), both are fully ionized² at physiologic PH.
- More effective detergent than bile acids
- **ONLY Conjugated forms (bile salts) are found in the bile .**

1. More hydrophilic (negatively charged) and more ionized

2. That's why they are usually exist as salts of various cations (e.g., Na or K glycocholate OR Na or K Taurochenodeoxycholate

Hormonal Control of Bile Secretion

Stimulus	Hormone from gut cells	Response
Undigested lipids and partially digested proteins in duodenum	Cholecystokinin (CCK)	<ol style="list-style-type: none">1. Secretion of pancreatic enzymes2. Bile secretion3. 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

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

Role of bile salts in:

1. Emulsification of dietary Lipids in Duodenum

- ❑ Emulsification increases the surface area of lipid droplets, therefore the digestive enzymes can effectively act.
- ❑ Mechanism of Emulsification:
 - 1) Mechanical mixing: By peristalsis
 - 2) Detergent effect of bile salt.

2. Absorption of Lipids by Intestinal Mucosal Cells.

❑ Mixed micelles:

Disc-shaped clusters of amphipathic lipids arranged with their hydrophobic groups on the inside and their hydrophilic groups on the outside.

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

❑ They include:

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

Secondary bile acids

Bile salts

Glycochenodeoxycholic acid
Taurochenodeoxycholic acid
Glycocholic acid
Taurocholic acid

Taurine

By Intestinal
bacteria

Glycine

Primary Bile acids

Cholic acid
Chenodeoxycholic acid

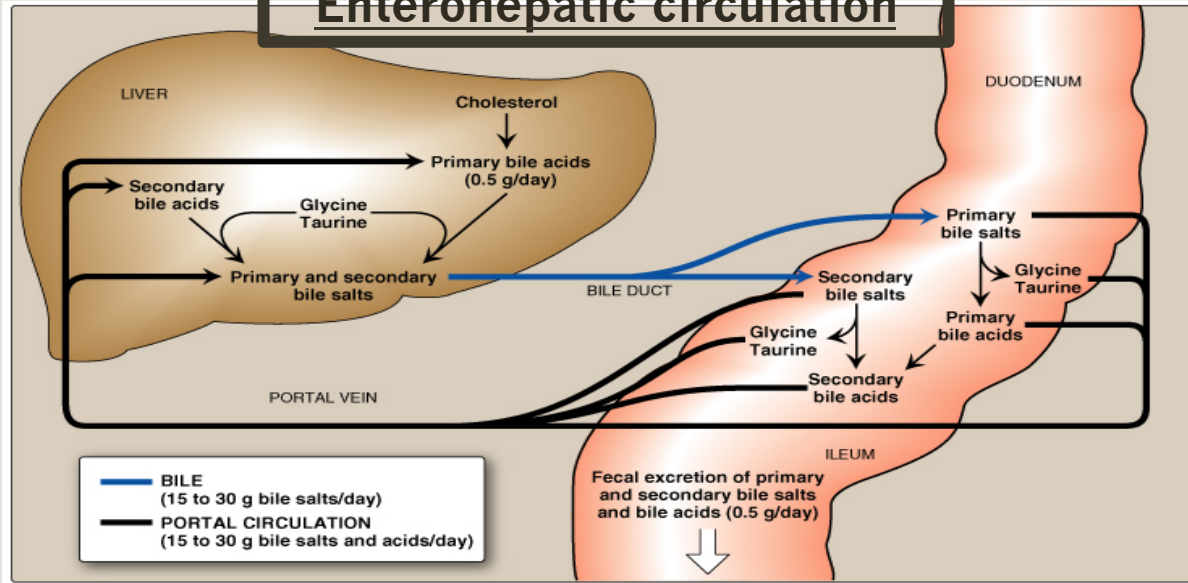
OH

By Intestinal
bacteria

Secondary Bile acids

Deoxycholic acid
(from cholic acid)
Lithocholic
(from chenodeoxycholic acid)

Enterohepatic circulation



Bile salts secreted into the intestine are efficiently reabsorbed (greater than 95%) and reused. The liver converts both primary and secondary bile acids into bile salts by conjugation with glycine or taurine, and secretes them into the bile. The mixture of bile acids and bile salts is absorbed primarily in the ileum via a Na^+ -bile salt cotransporter. They are actively transported out of the ileal mucosal cells into the portal blood, and are efficiently taken up by the hepatocytes via an isoform of the cotransporter. [Note: Bile acids are hydrophobic and require a carrier in the portal blood. Albumin carries them in a noncovalent complex, just as it transports fatty acids in blood (see p. 181).] The continuous process of secretion of bile salts into the bile, their passage through the duodenum where some are converted to bile acids, their uptake in the ileum, and subsequent return to the liver as a mixture of bile acids and salts is termed the enterohepatic circulation (see Figure 18.11). Between 15

Clinical applications:

Cholestyramine:

Bile acid sequestrant

Binds to bile acids in the gut => preventing their reabsorption & Promoting their excretion

It is used for **treatment of hypercholesterolemia**

How do they work ?

Dietary fibers

It binds to bile acids, increasing their excretion

Cholelithiasis (Cholesterol Gallstone Disease)

Causes:

1. ↓ Bile salts in bile:

- ✓ Biliary tract obstruction (Disrupt enterohepatic circulation)
- ✓ Hepatic dysfunction (↓ synthesis)

2. ↑ Biliary cholesterol excretion

Treatment

- Bile acid replacement therapy
- Surgical removal (Cholecystectomy)

Maldigestion/Malabsorption of Lipids

↓ Bile secretion due to :

1. Liver diseases:

e.g., Hepatitis or cirrhosis

2. Gall bladder diseases:

e.g., Gall stones

=> Malabsorption of lipids

COMPARISON BETWEEN BILE ACIDS & BILE SALTS

Bile acids	Bile salts
Unconjugated	Conjugated
Amphipathic	Enhanced amphipathic function
Formed from cholesterol (by Cholesterol 7-α-hydroxylase)	Formed from Bile acid + glycine or Taurine
Partially ionized	Fully ionized
Less polar	More polar
Less detergent effect	More detergent effect
NOT found in bile	Found in bile

1) Which ONE of the following molecules is more hydrophobic:

- A. Cholic acid
- B. Chenodeoxycholic acid
- C. Cholesterol
- D. Bile salts

2) Primary Bile Acids are:

- A. Amphipathic
- B. Hydrophobic
- C. Hydrophilic
- D. None of the Above

3) The synthesis of Bile Acids is up-regulated by:

- A. Cholesterol
- B. Cholic acid
- C. Beta-Hydroxylase
- D. None of the Above

4) What is the ratio of Glycine to Taurine from inside the Bile?

- A. 1:3
- B. 2:1
- C. 3:1
- D. 4:1

5) Bile secretion is stimulated by:

- A. Undigested Protein & partially digested Lipids in Duodenum
- B. Undigested Lipids & partially digested Protein in Duodenum
- C. Undigested Carbohydrates
- D. Partially digested Carbohydrates

6) Mixed Micelles contain all the following EXCEPT:

- A. Short & Medium Chain Fatty Acids
- B. Lipids
- C. Fat-soluble Vitamins
- D. None of the Above

7) Bile secretion is decreased by:

- A. Gall Stones
- B. Hepatitis
- C. Adenocarcinoma
- D. Both a & b

8) Cholelithiasis is treated with:

- A. Bile Acid replacement therapy
- B. Surgery
- C. Drugs
- D. Both a & b

9) Which ONE of the following is the secondary bile acid derived from chenodeoxycholate:

- A. Lithocholic acid
- B. Deoxycholate
- C. Taurocholate
- D. Deoxycholic acid

10) An 56-year obese woman presented to her general physician with right upper quadrant colicky pain. Her symptoms are aggravated after ingestion of fatty food, she was diagnosed with gallstones.

The most-likely underlying cause of her condition is:

- A. Decreased levels of cholesterol
- B. Decreased bile salts in bile
- C. Insufficient dietary fat intake.
- D. Increased bile acid synthesis

Answers: 1) C 2)A 3)A 4)C 5)B 6)A 7)D 8)D 9)A 10) B



Thank You!

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