







# Biochemical aspects of bile acids and salts

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# Objectives

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



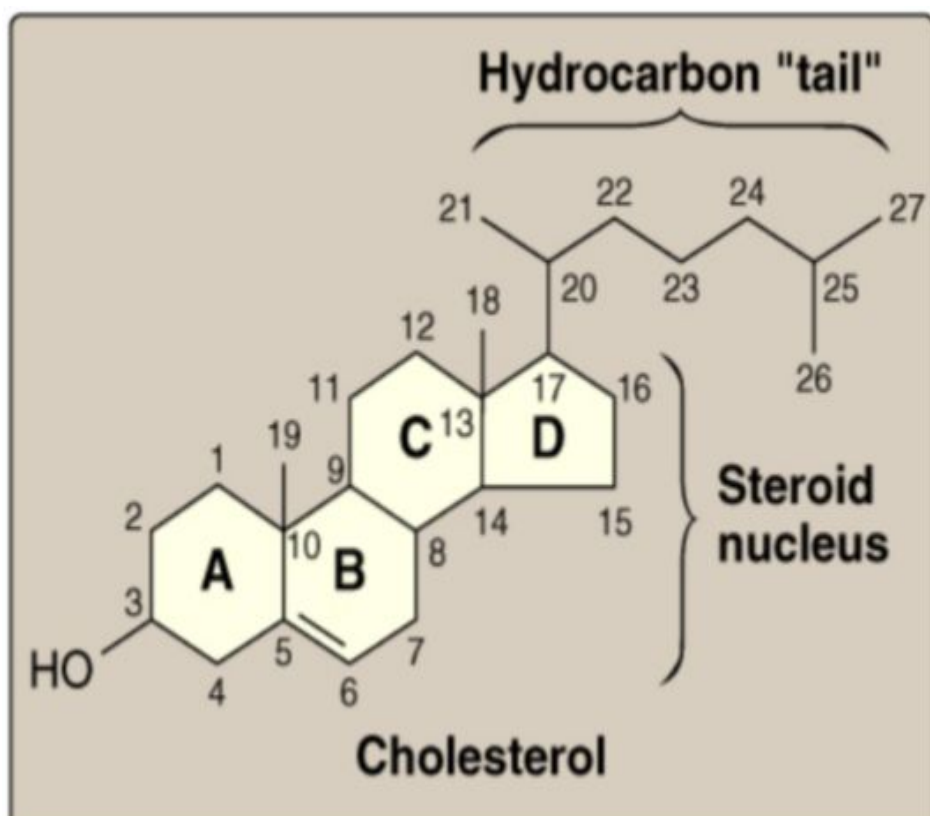
# Cholesterol and Primary Bile Acids

## Cholesterol

Cholesterol (27 C +double bond +Hydroxyl group) is the:

Parent steroid compound

Precursor of bile acids and salts



## Primary Bile Acids

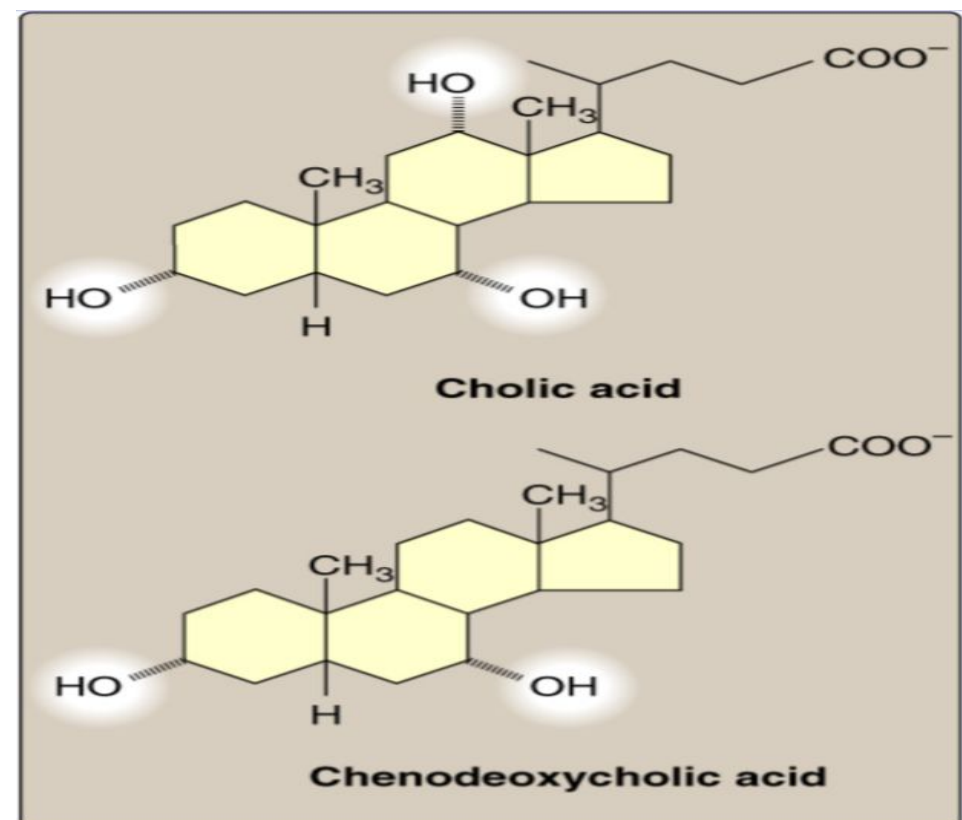
Primary bile acids (24 C):  
Amphipathic

-COOH at side chain

It's synthesized from Cholesterol by removing 3C, and adding Hydroxyl groups:

-Cholic acid: 3 OH (2 were added)

-Chenodeoxycholic: 2 OH (1 was added)



# Hepatic Synthesis of Bile Acids

The rate-limiting step is catalyzed by:

**Cholesterol 7- $\alpha$ -hydroxylase**

Function: adds OH on Carbon No.7

## Regulation:

### Down-regulated by

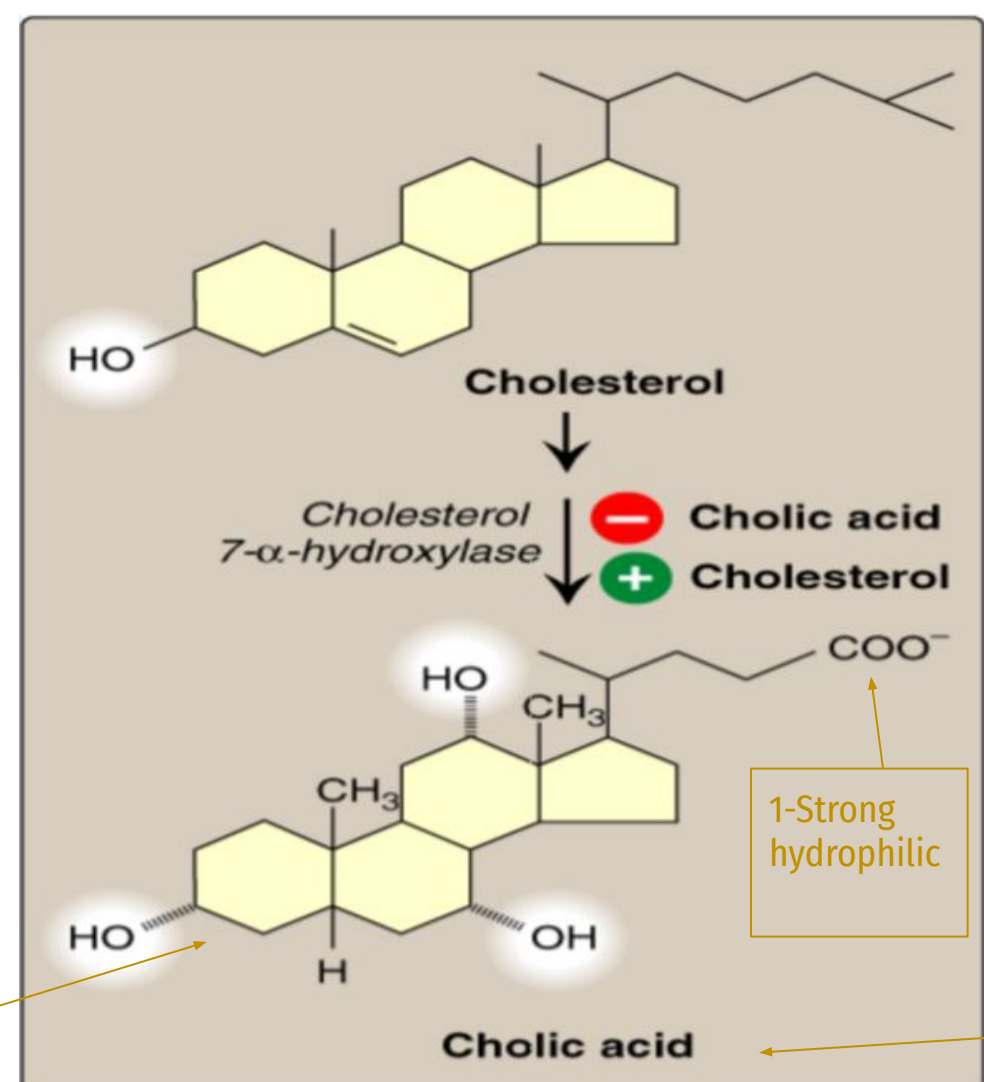
end products (bile acids)  
"Enzyme repression"

Explanation from 438 team: If we have too much of the product(bile acids) it will REPRESS the synthesis of the enzyme and inhibit the synthesis of bile acids

### Up-regulated by

cholesterol "Enzyme induction"

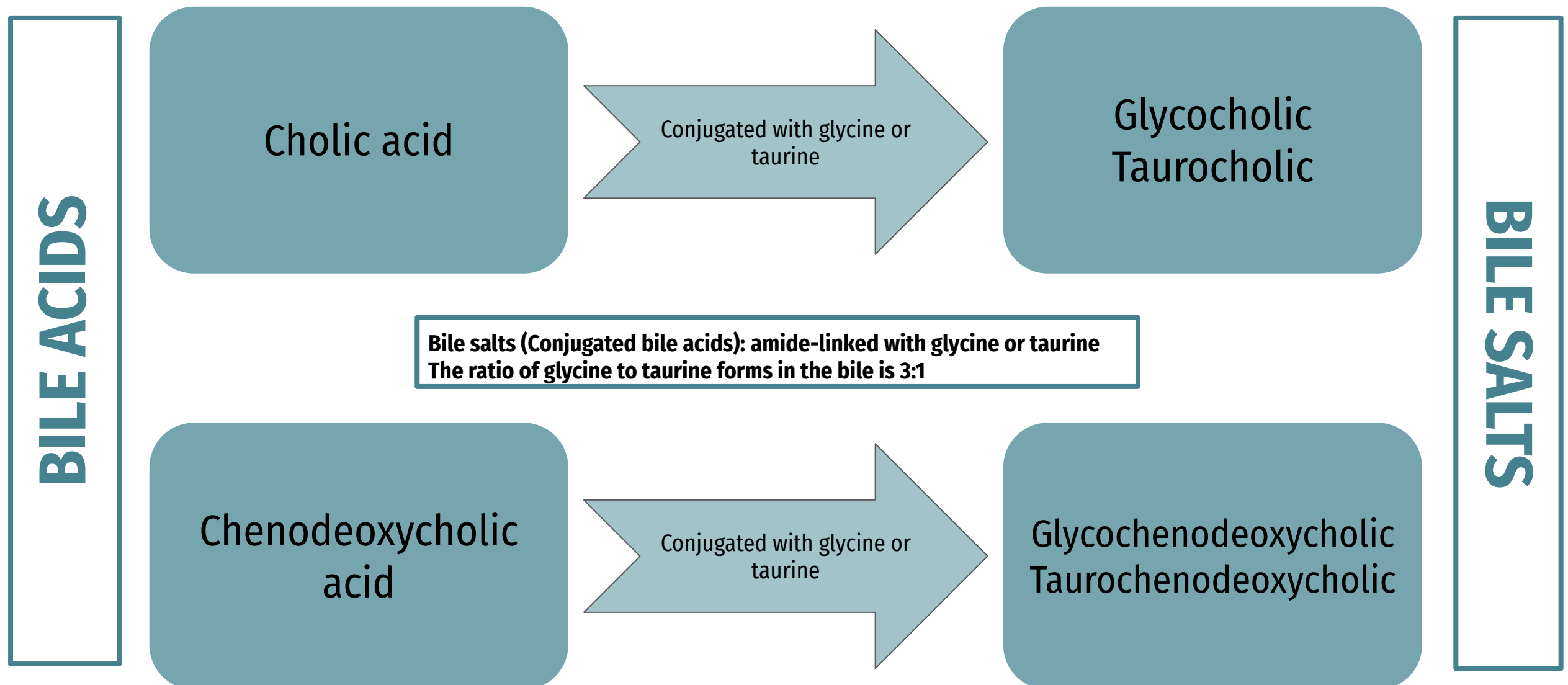
Explanation from 438 team: If we have too much of the precursor (Cholesterol) it will INDUCE the synthesis of the enzyme and increase bile acids



2-Hydrophobic

So, Cholic acid is Amphipathic

# Primary Bile Acids and Salts



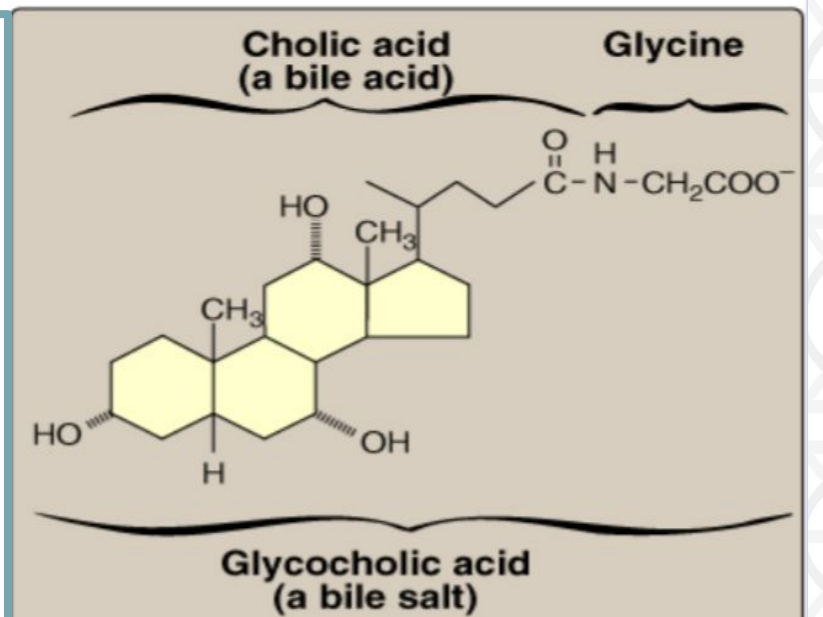
## Bile Salts

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

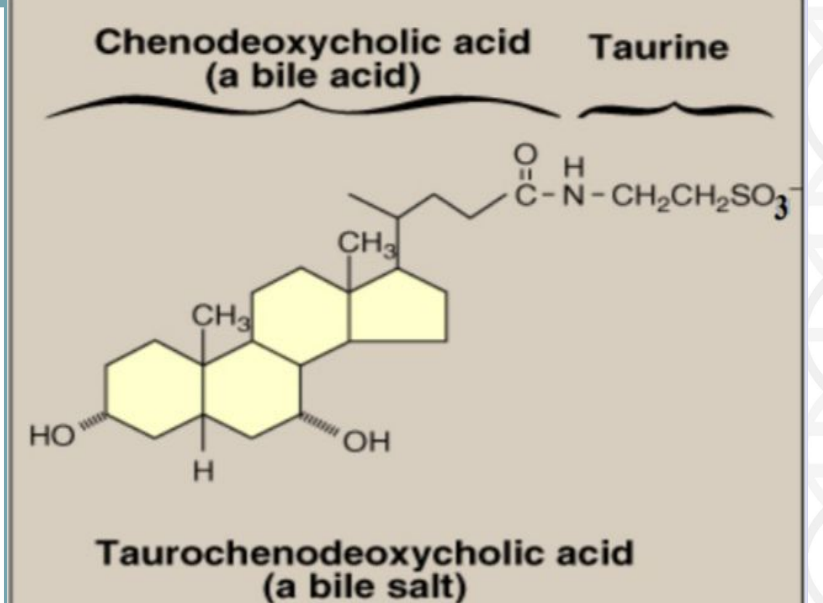
-COOH of glycine &  
-SO<sub>3</sub> of taurine  
(hence, its name as bile salts e.g.,  
Sodium or potassium glycocholate)

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

Na or K Glycocholate

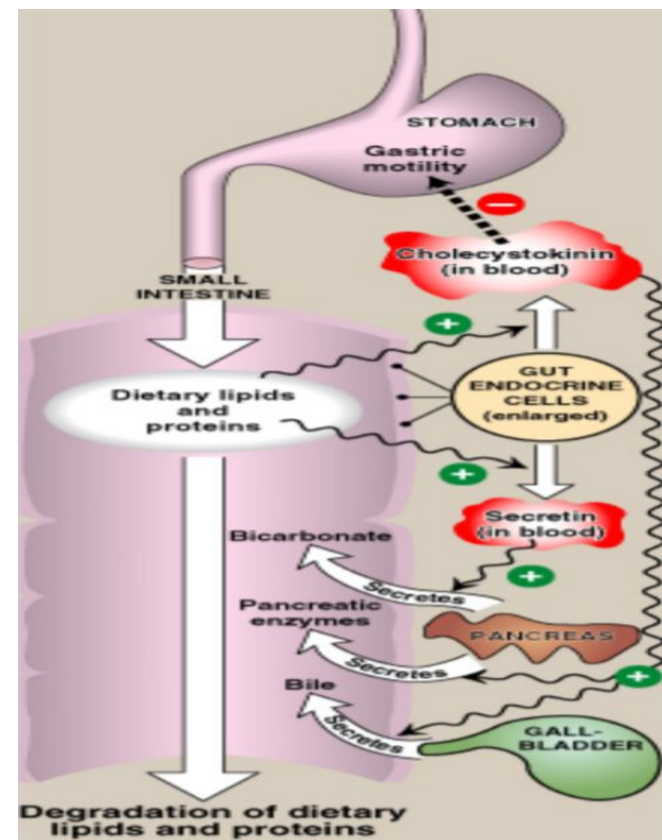


Na or K  
Taurochenodeoxycholate



# Hormonal Control of Bile Secretion

<b>Stimulus:</b>	Undigested lipids and partially digested proteins in duodenum
<b>Hormone from gut cells:</b>	Cholecystokinin (CCK)
<b>Responses</b>	<ol style="list-style-type: none"> <li>1. Secretion of pancreatic enzymes</li> <li>2. <b>Bile secretion</b></li> <li>3. Slow release of gastric contents</li> </ol>



Hormonal control of lipid digestion in the small intestine.

Explanation from 438 team: Cells in the mucosa of the lower duodenum and jejunum produce a small peptide hormone, cholecystokinin (CCK), in response to the presence of lipids and partially digested proteins entering these regions of the upper small intestine. CCK acts on the gallbladder (causing it to contract and release bile), and on the exocrine cells of the pancreas (causing them to release digestive enzymes). It also decreases gastric motility, resulting in a slower release of gastric contents into the small intestine. Other intestinal cells produce another small peptide hormone, secretin, in response to the low pH of the chyme entering the intestine. Secretin causes the pancreas and the liver to release a solution rich in bicarbonate that helps neutralize the pH of the intestinal contents, bringing them to the appropriate pH for digestive activity by pancreatic enzymes.

## Functions of Bile Salts

1

### Important for cholesterol excretion:

1. As metabolic products of cholesterol
2. Solubilizer of cholesterol in bile

3

### Cofactor for pancreatic lipase and PLA2

2

### Emulsifying factors for dietary lipids, a prerequisite step for efficient lipid digestion

4

### 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 (التحوصل).

# Functions of Bile Salts cont.

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

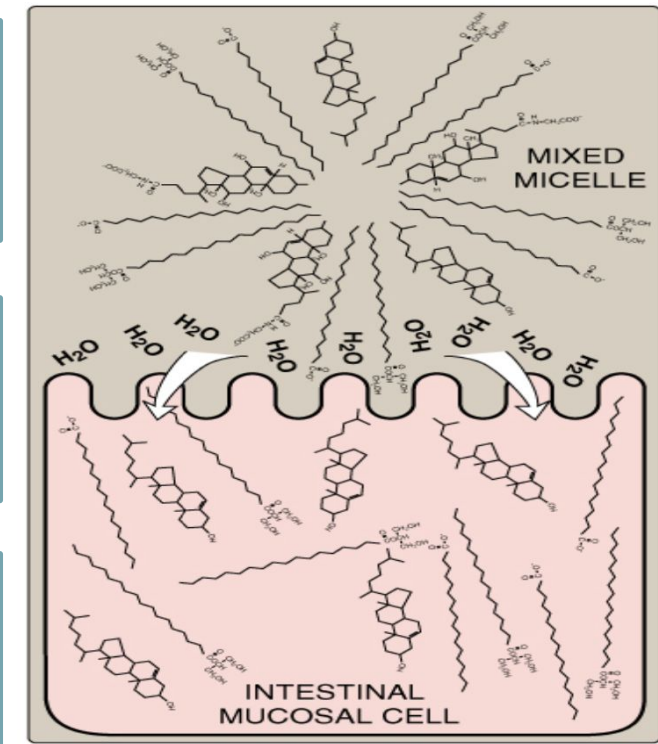
### Mixed micelles:

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

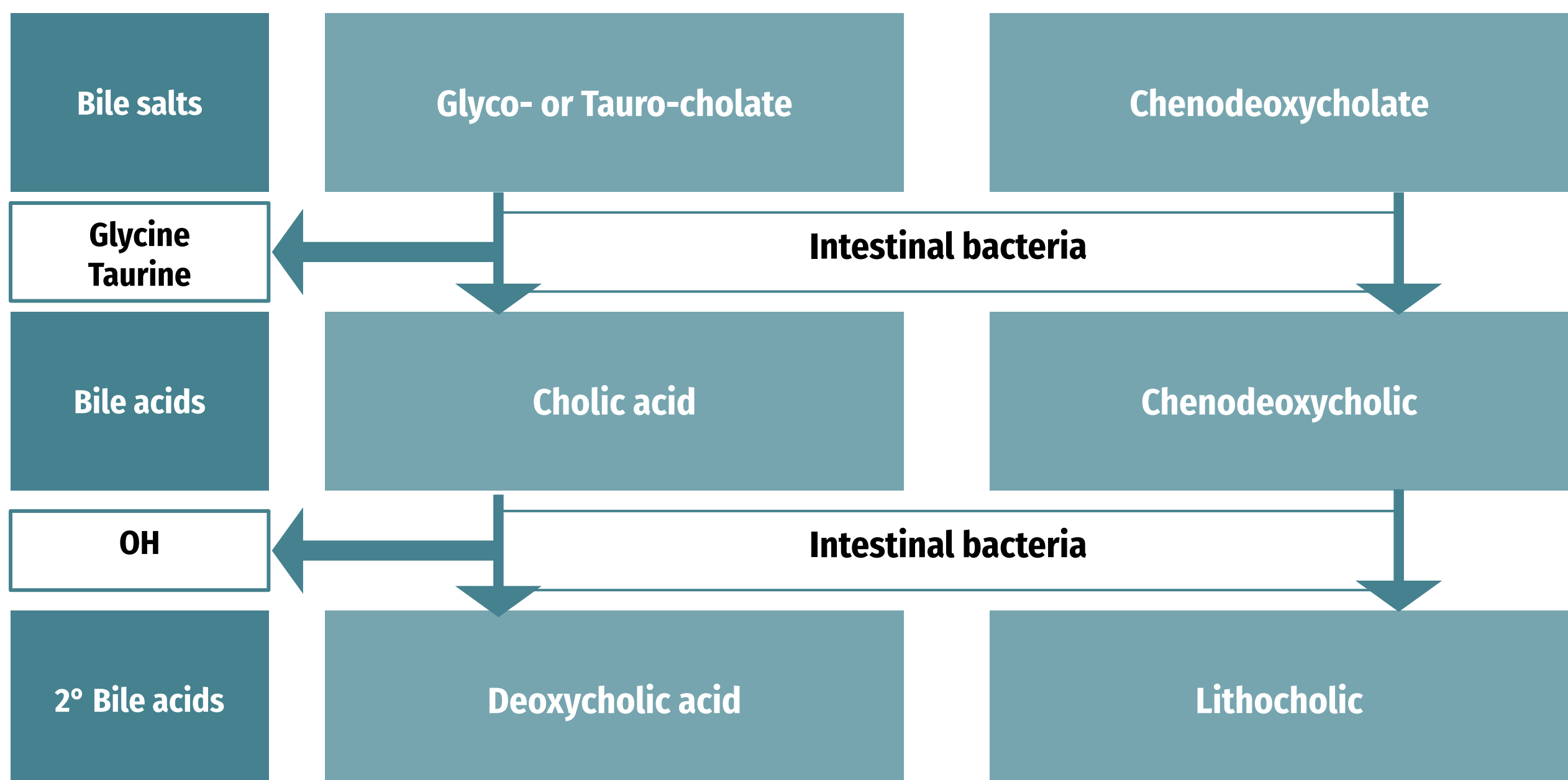
### Mixed Micelle Formation:

Bile salts, end products of lipid digestion, Fat-soluble vitamins



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

## Secondary Bile Acids



Note that Secondary Bile acid is synthesised outside the liver by Intestinal bacteria.

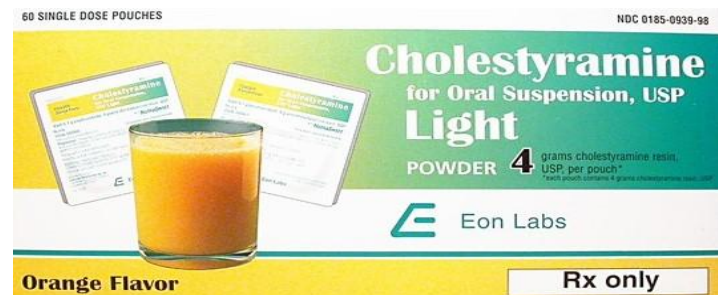
# Enterohepatic Circulation

## Cholestyramine:

Bile acid sequestrants

It binds to bile acids in the gut, preventing their reabsorption & Promoting their excretion.

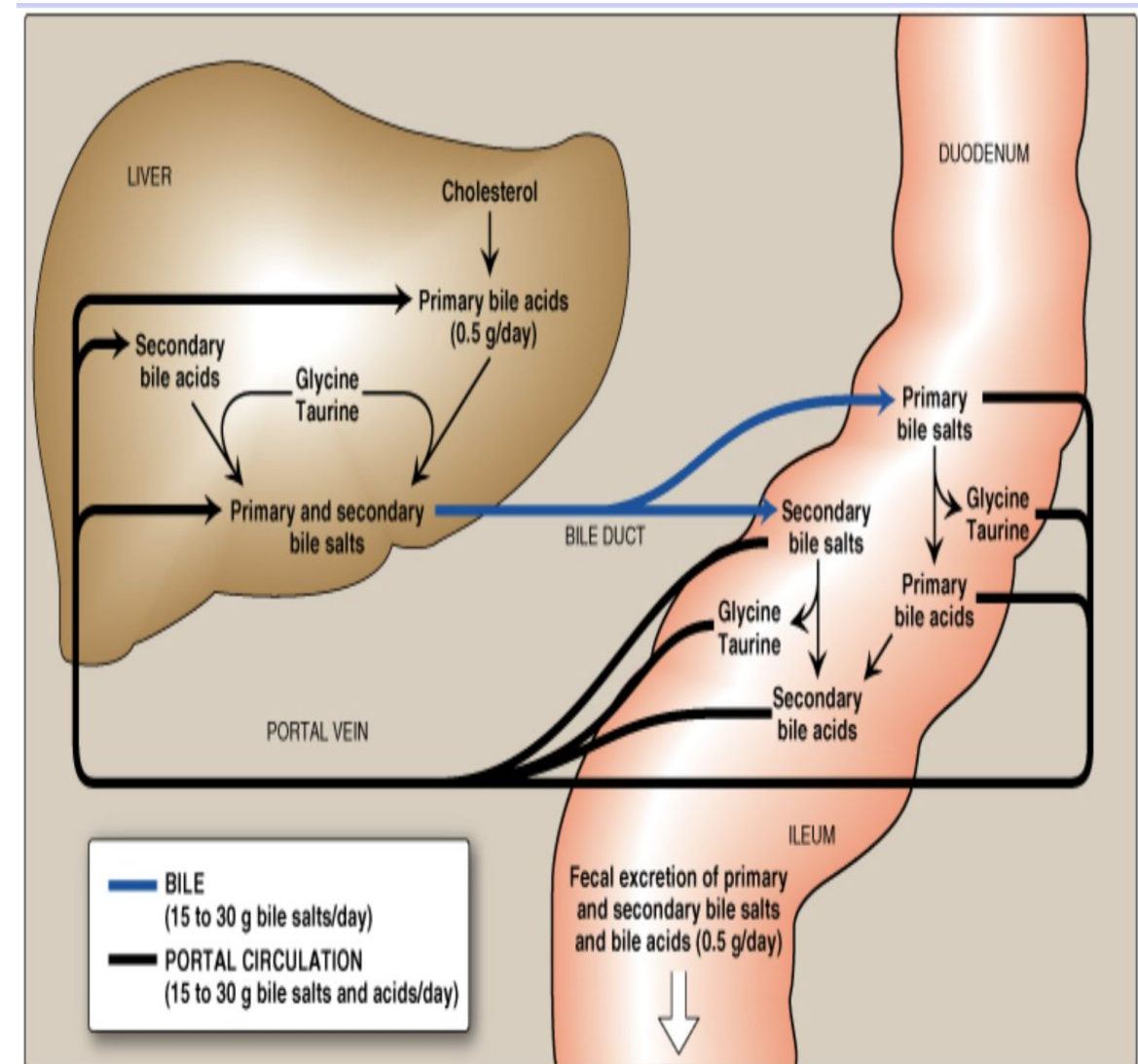
It is used for treatment of hypercholesterolemia.



## Dietary fiber:

It binds to bile acids, increasing their excretion.

Explanation from 438 team: Bile salts secreted into the intestine are efficiently reabsorbed 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<sup>+</sup>-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. 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



0.5 g/day of Bile lost in feces and 0.5 g/day of Bile synthesised in liver.

So, our body Regulate the excretion and synthesis of Bile.

## Maldigestion / Malabsorption of Lipids

Decreased bile secretion by:

Liver diseases:

e.g., Hepatitis or cirrhosis

Gall bladder diseases:

e.g., Gall stones

➔ Malabsorption of lipids

## Cholelithiasis: Cholesterol Gallstone Disease

Causes:

↓ Bile salts in bile:

Biliary tract obstruction

(interferes with enterohepatic circulation)

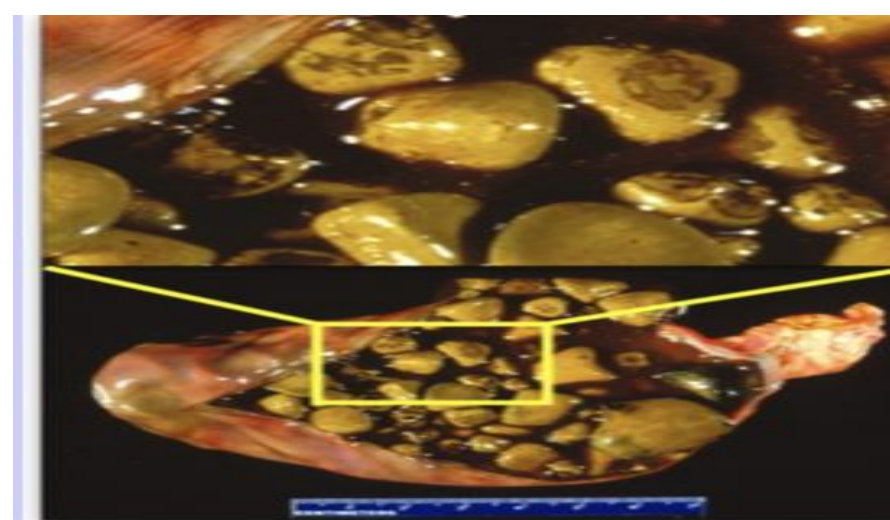
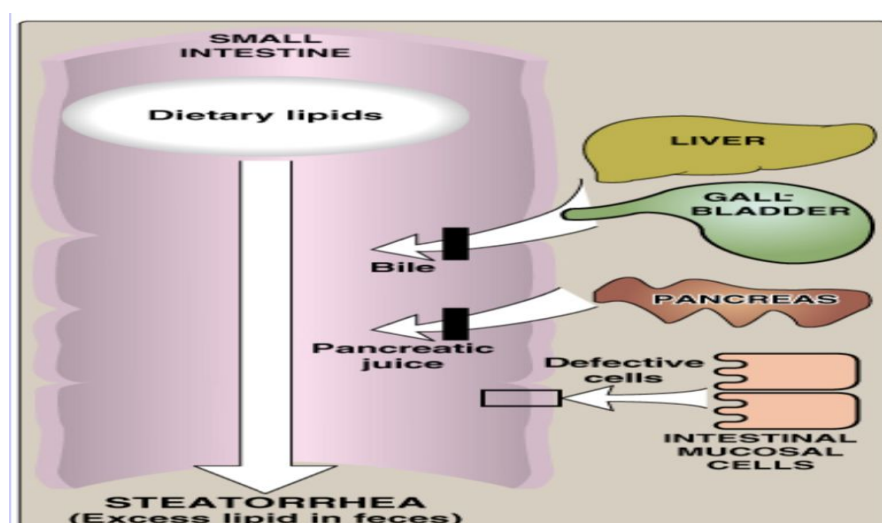
Hepatic dysfunction (↓ synthesis)

↑ Biliary cholesterol excretion

Treatment: 1- Bile acid replacement therapy

2-Surgical (majority) (Cholecystectomy)

Cholelithiasis are rigid and insoluble.



# Summary

<p><b>Structure of primary bile acids and salts</b></p>	<p>Cholesterol (27 C) (Precursor of bile acids and salts) removing 3C, and adding Hydroxyl group → Primary bile acids (24 C) The rate-limiting step is catalyzed by: Cholesterol 7-<math>\alpha</math>-hydroxylase (Down-regulated by bile acids)(Up-regulated by cholesterol)          Primary bile acids Conjugated with glycine or taurine → Primary Bile Salts          its named as bile salts because it have Sodium or potassium  <b>Only bile salts, but not acids, found in bile</b></p>
<p><b>Hormonal Control of Bile Secretion</b></p>	<p>Stimulus: Undigested lipids and partially digested proteins in duodenum</p> <p>Hormone from gut cells: Cholecystokinin (CCK)</p> <p>Responses: 1-Secretion of pancreatic enzymes 2-Bile secretion 3-Slow release of gastric contents</p>
<p><b>Structure of secondary bile acids and salts</b></p>	<p>Bile salts → Primary bile acid → Secondary bile acids</p> <p><b>Both Are Converted by intestinal bacteria.</b></p> <p>End products: Primary bile acids, By products: Glycine and taurine.          End products: Secondary bile acids, By products: OH.</p>
<p><b>Functions of bile salts</b></p>	<ol style="list-style-type: none"> <li>1. Important for cholesterol excretion.</li> <li>2. Emulsifying factors for dietary lipids, a prerequisite step for efficient lipid digestion.</li> <li>3. Cofactor for pancreatic lipase and PLA2.</li> <li>4. Facilitate intestinal lipid absorption by formation of mixed micelle.</li> </ol>
<p><b>Enterohepatic circulation</b></p>	<p>Cholestyramine:          Bile acid sequestrants, binds to bile acids in the gut, prevent their reabsorption, and so promote their excretion.          It is used in the treatment of hypercholesterolemia</p> <p>Dietary fibers:          It binds to bile acids, increasing their excretion.</p>
<p><b>Malabsorption syndrome</b></p>	<p>Decreased bile secretion by: Liver diseases: e.g., Hepatitis or cirrhosis</p> <p>Gall bladder diseases: e.g., Gall stones</p> <p>It Will Lead To Malabsorption of lipids</p>
<p><b>Cholelithiasis</b></p>	<p>Causes:          1-Decrease Bile salts in bile          2-Increase Biliary cholesterol excretion</p> <p>Treatment:          1- Bile acid replacement therapy          2-Surgical (majority) ( Cholecystectomy )</p>





# MCQs

**1- which of the following is not a property of primary bile acids ?**

A-Amphipathic	B-(-COOH) at both side chain	C-Cholic acid: 3 OH	D-Chenodeoxycholic: 2 OH
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**2- Bile salt linked with glycine or taurine by ?**

A-amide linkage	B-glycosidic linkage	C- ester linkage	D-peptide linkage
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**3-which hormone control bile secretion**

A-Cholecystokinin	B- Gastrin	C-secretin	D-Motilin
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**4-Which of the following not require mixed micelle for absorption?**

A-long chain fatty acid	B- short chain fatty acid	C-medium chain fatty acid	D-B&C
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**5- Which of the following cause of Cholelithiasis?**

A- Increased biliary cholesterol excretion	B- Decreased Bile salts in bile	C-Increased Bile salts in bile	D-A&B
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**6-Which of the following is bile salt?**

A-Cholic acid	B- Deoxycholic acid	C-Tauro-cholate	D-Lithotomic
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Answers key

1-B      2- A      3-A      4- D      5- D      6- C

## SAQs

### 1- What are the components of micelles?

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

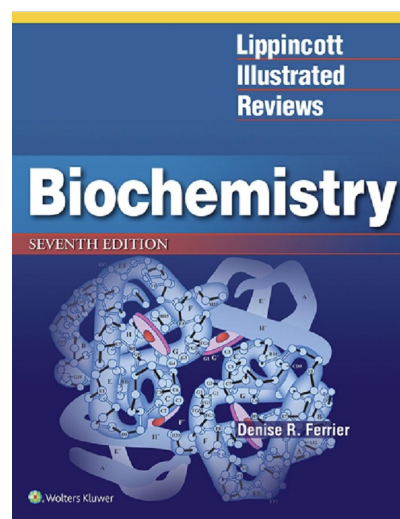
### 2- What is the mechanism of Cholestyramine?

It binds to bile acids in the gut, preventing their reabsorption & Promoting their excretion

### 3- list three functions of bile salts

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

## Resources Click on the book to download the resource





## Leaders



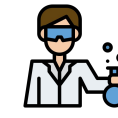
Albandari Alanazi



Sara Alharbi



Abdulaziz Alrabiah

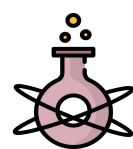


**Khalid Almutlaq**

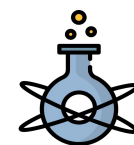
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Special thanks to Fahad AlAjmi for designing our team's logo.