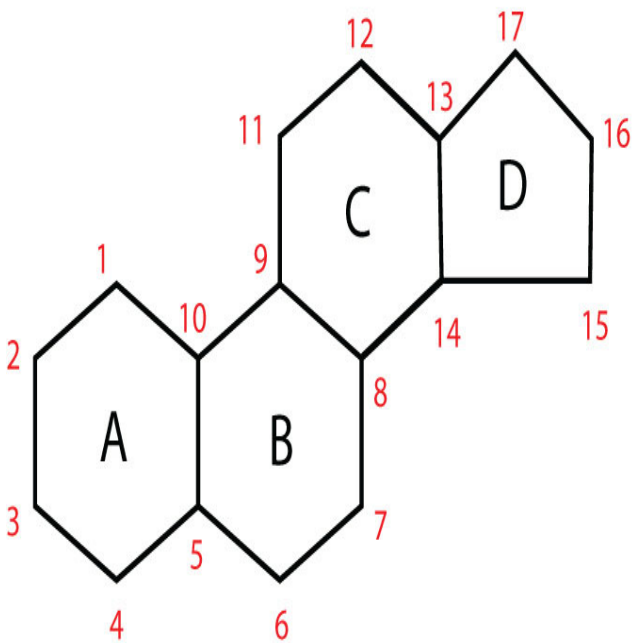
Cholesterol

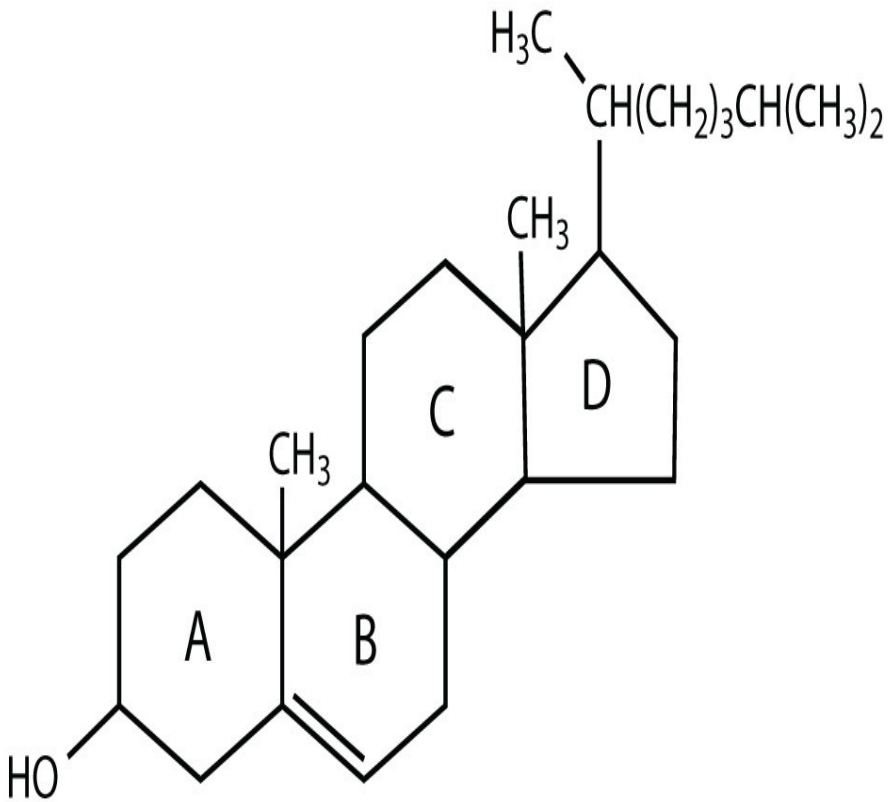
Functions

- Component of cell membrane
- Synthesis of biologically important compounds-
  - Bile acids,
  - Vitamin D &
  - steroid hormones – glucocorticoids, mineralocorticoids & sex hormones
- Membrane fluidity
- Electrical insulator

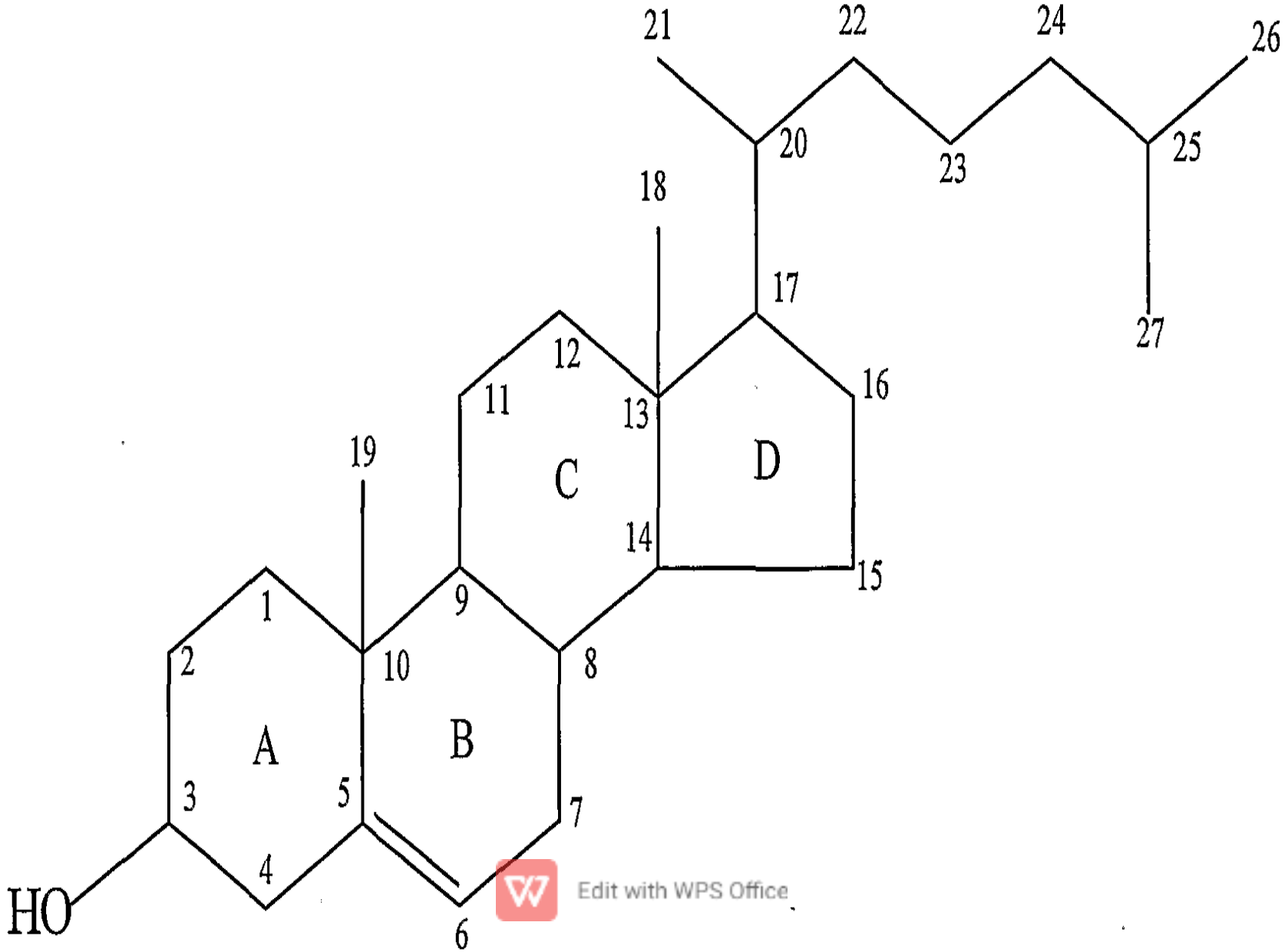
Structure



(a) Steroid skeleton



(b) Cholesterol



Synthesis

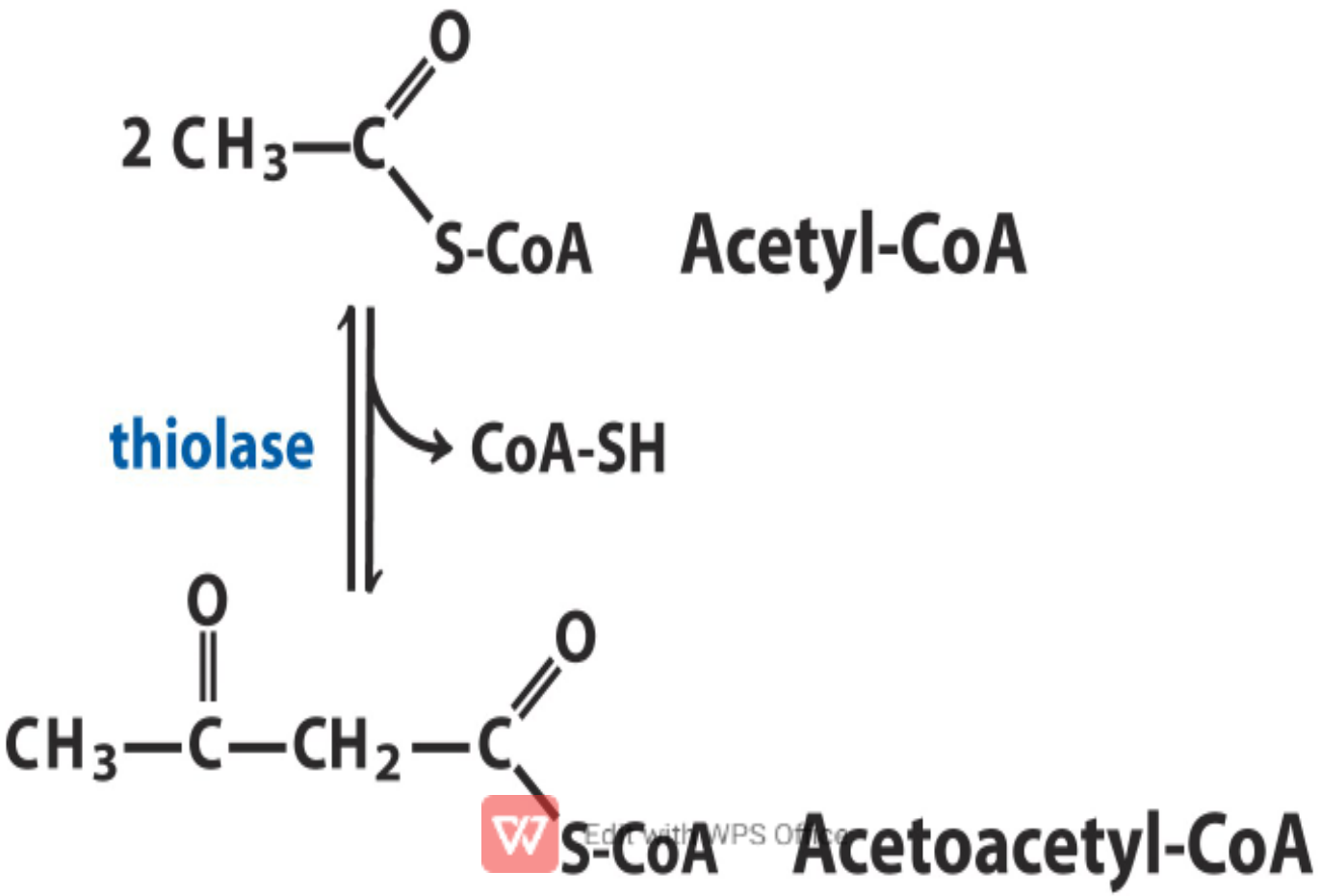
- **Site :**
- almost all tissues
- Mainly - liver, intestine, adrenal cortex & reproductive tissues
- cytosol & ER

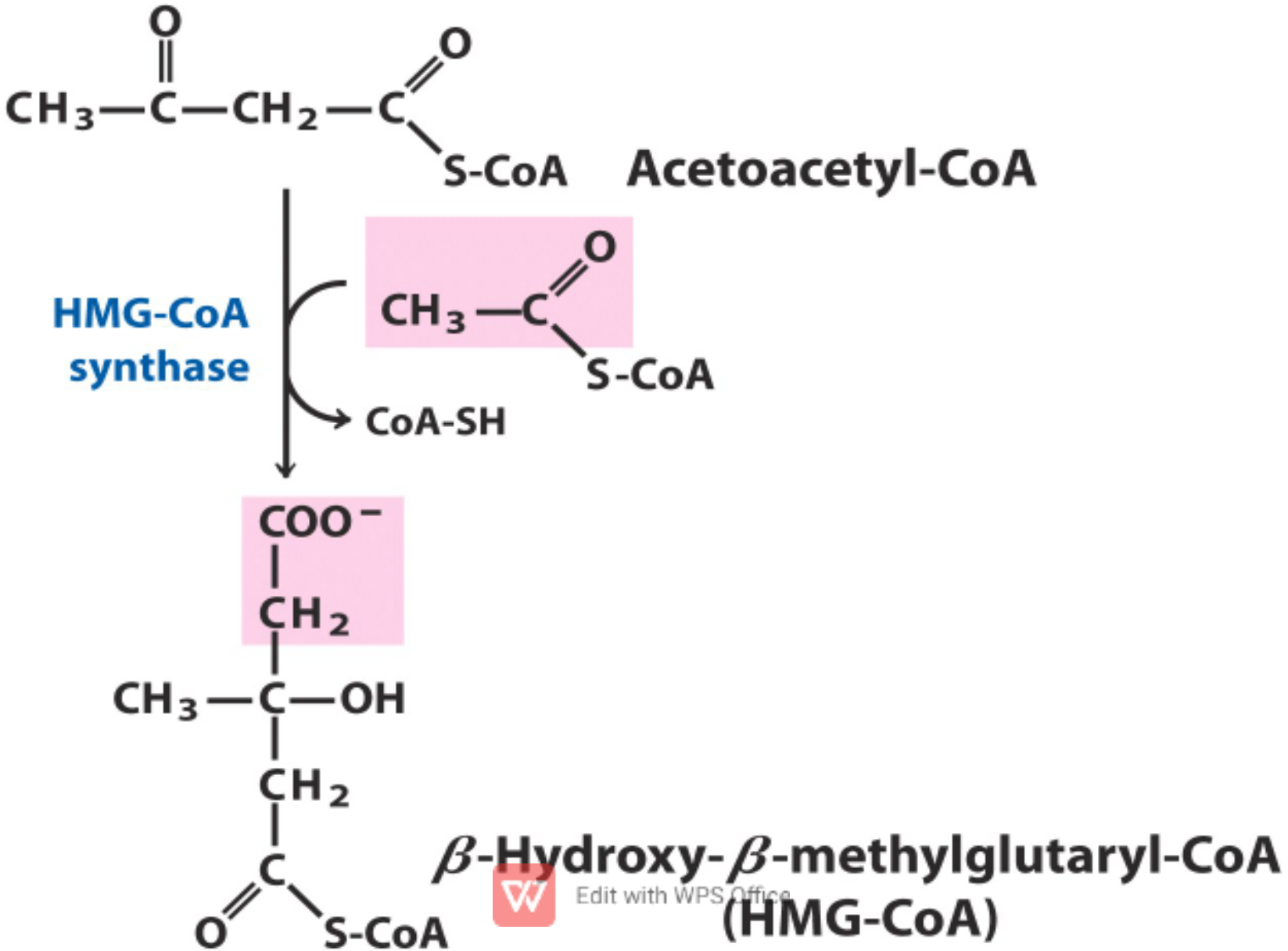
- **Requirements** :
- Acetyl CoA provides all C atoms
- NADPH + H^+
- ATP

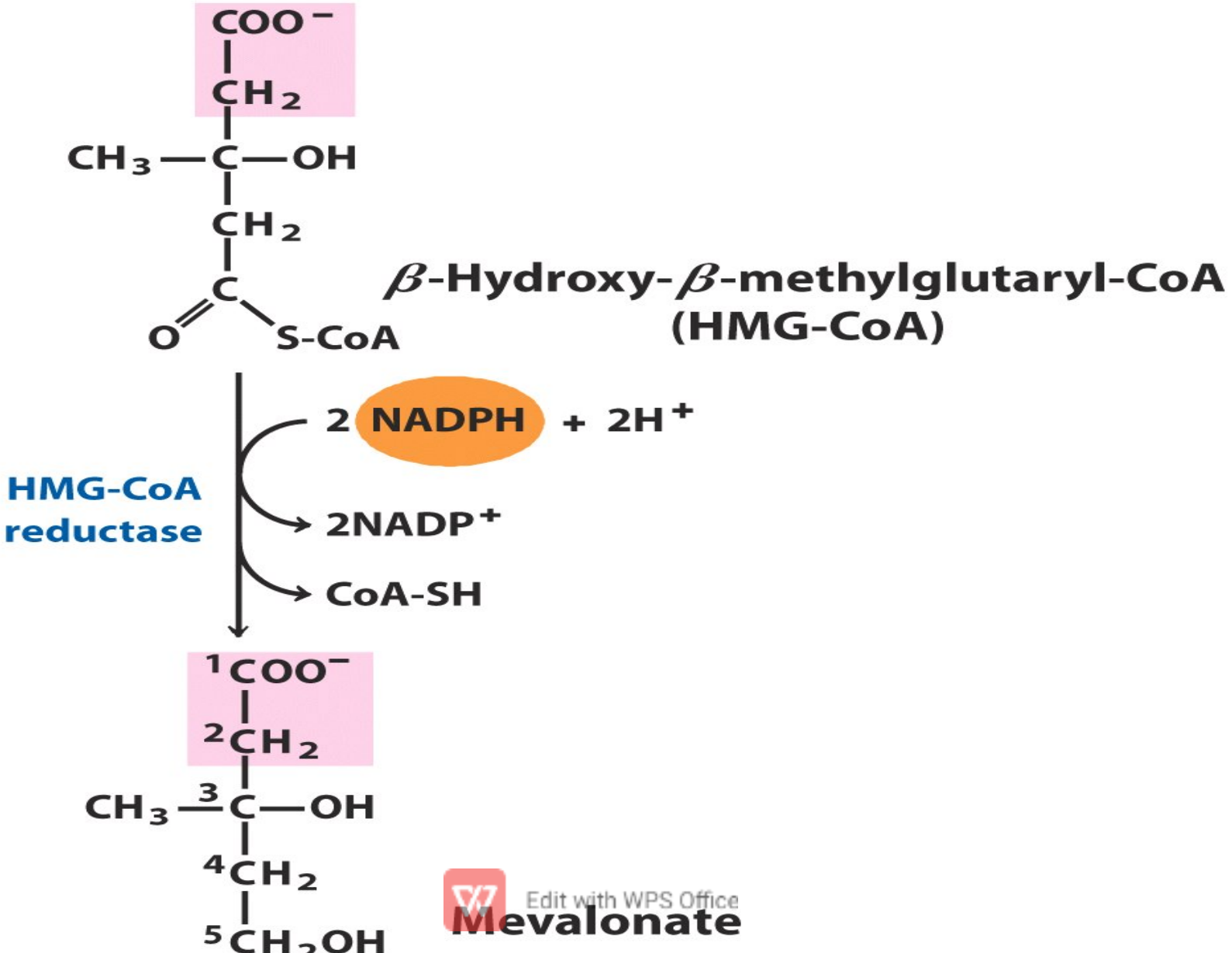
- Steps in biosynthesis :

1. Biosynthesis of Mevalonate
2. Formation of Isoprenoid units
3. Formation of Squalene
4. Formation of Lanosterol
5. Formation of Cholesterol

Cholesterol Synthesis: Stage 1







Important intermediates

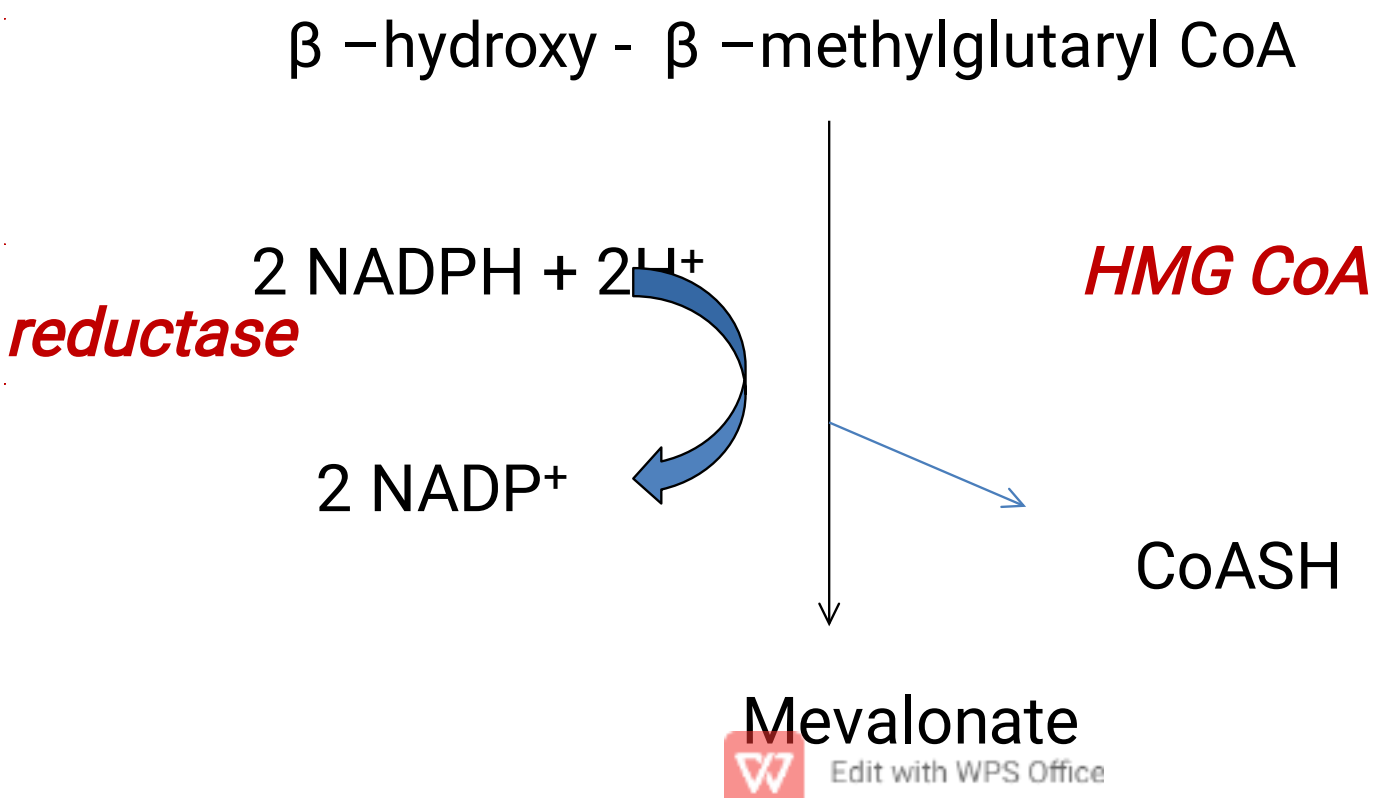
1. **Isoprenoid units** – used for biosynthesis of carotenoids (provitamin A)

2. **Farnesyl diphosphate** - synthesis of
   a. Ubiquinone
   b. Dolichols

3. **7-dehydrocholesterol** – synthesis of vitamin D

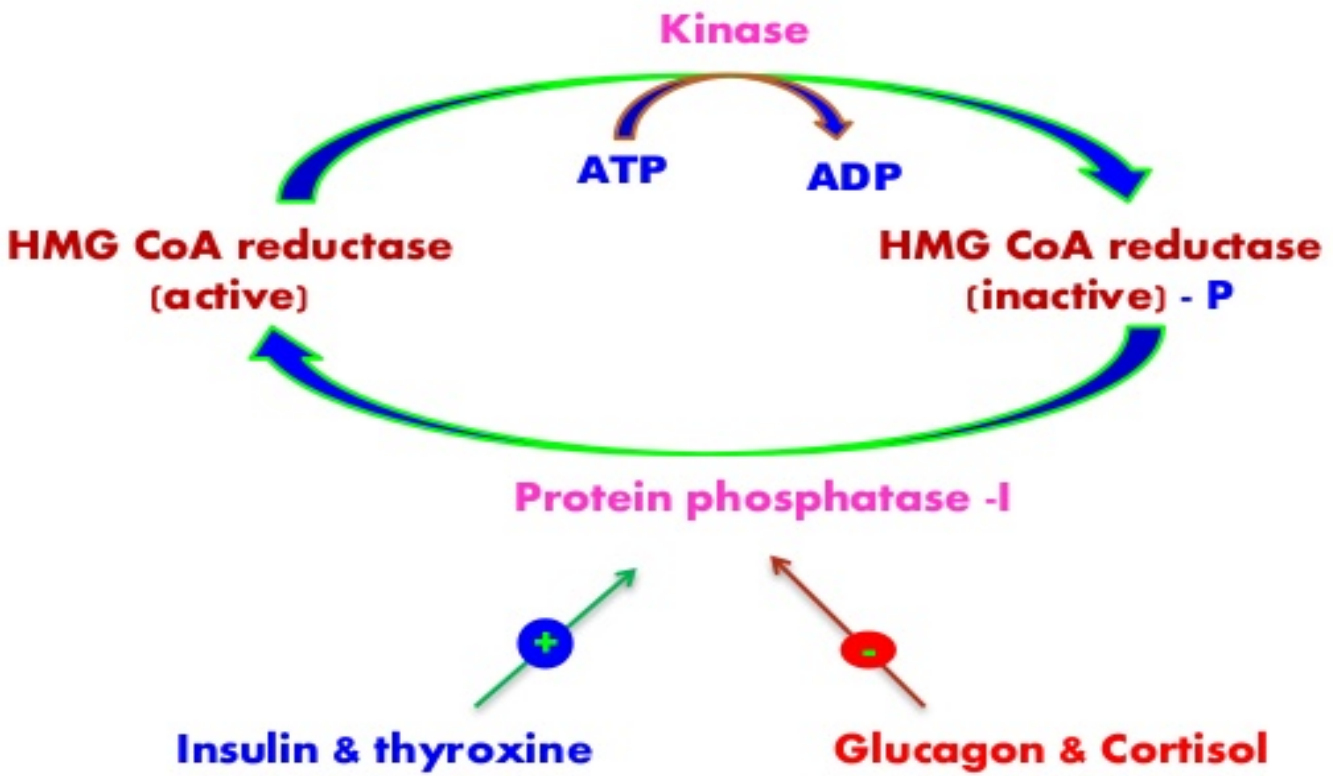
Regulation

Regulatory Enzyme – ***HMG CoA reductase***

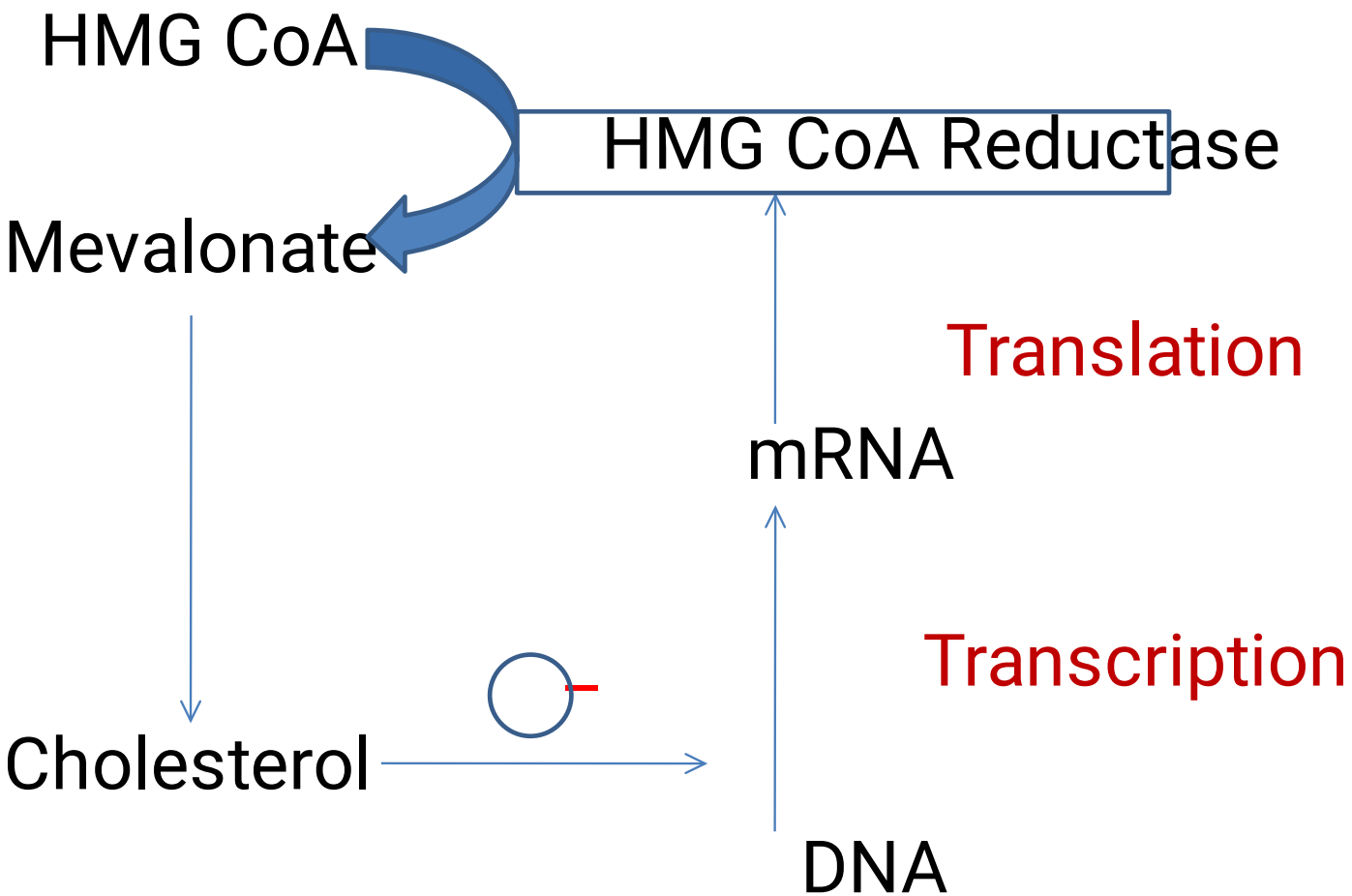


- Mechanisms –
- Covalent modification – Short term
- Repression - Long term
- Drug action

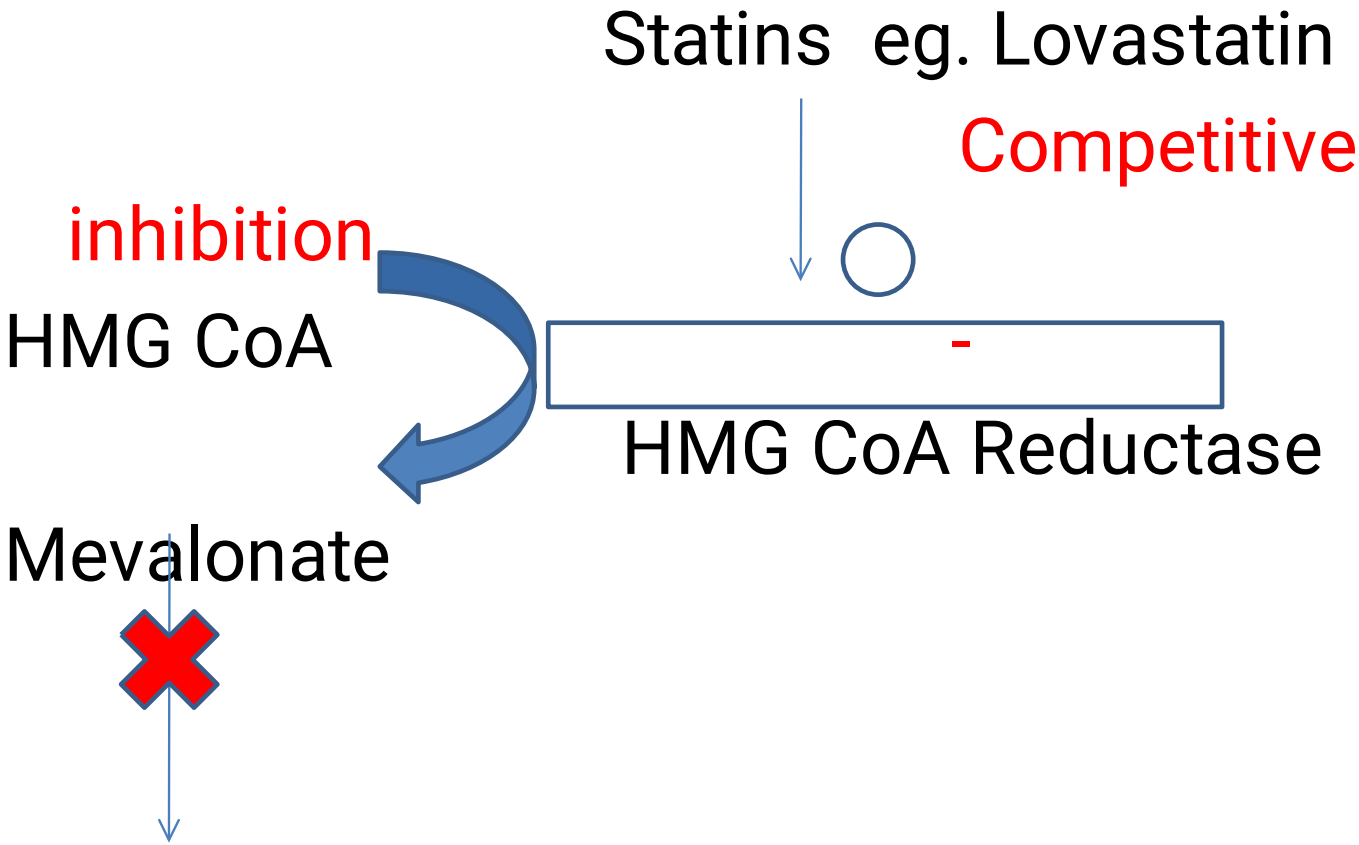
1. Covalent modification



2. Repression

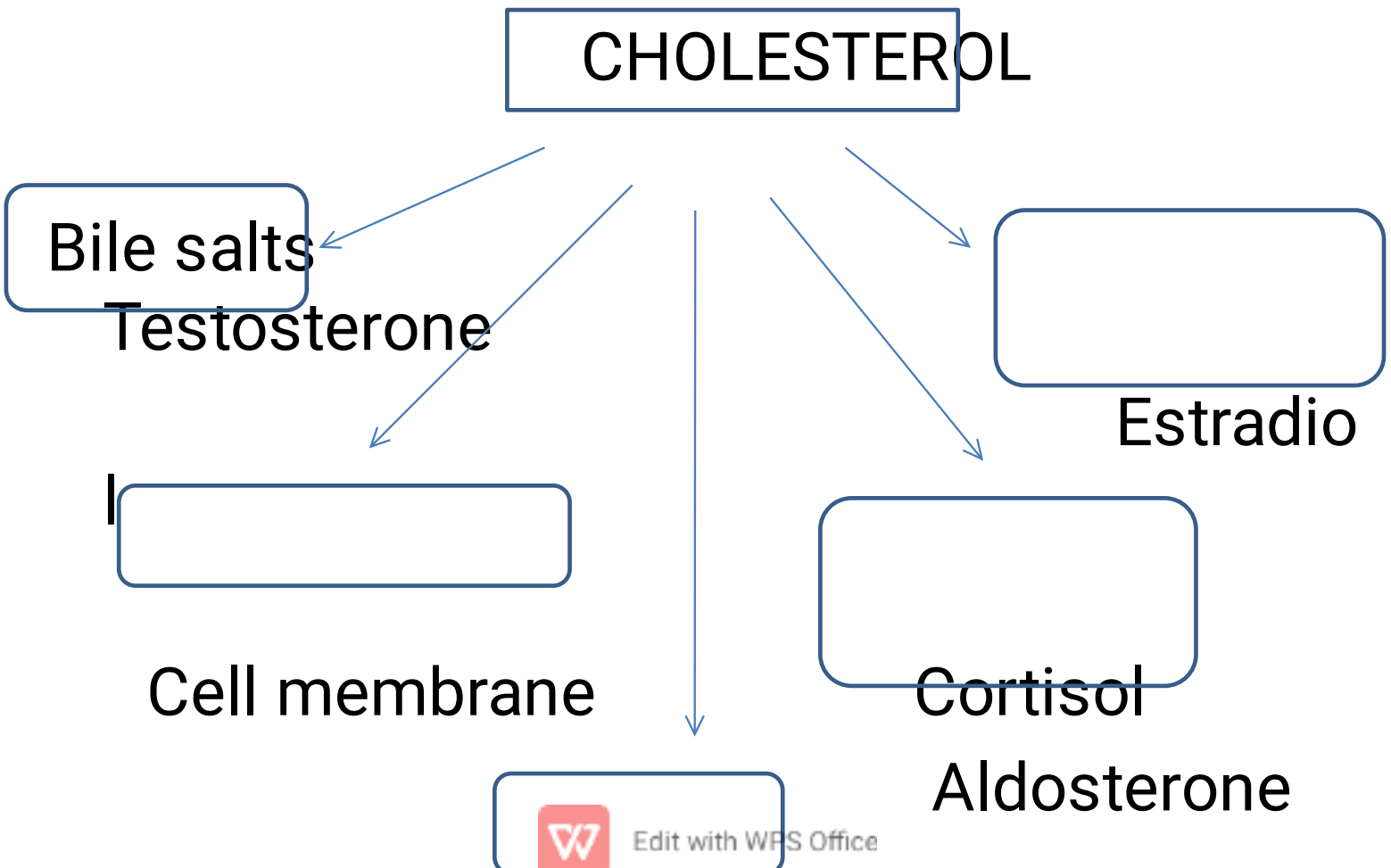


3. Drug action



Cholesterol (Clinically important to reduce cholesterol level in blood)

Fate of cholesterol



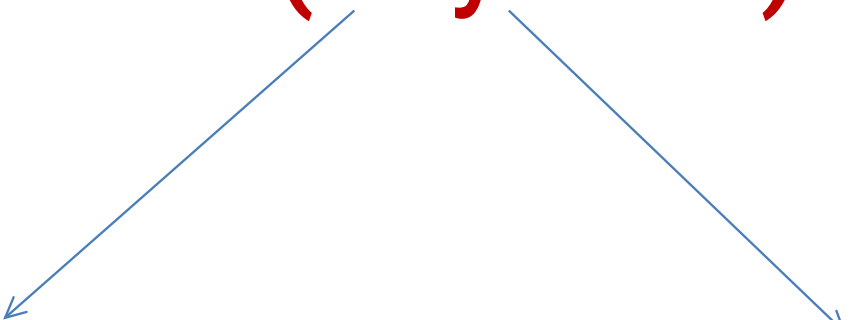
Transport of cholesterol

- By Lipoproteins
- Highest proportion of cholesterol found in lipoprotein - **LDL**

Cholesterol Excretion (≈ 1g/day)

Excreted in BILE

(only route)



Cholesterol salts)

(≈500mg/day)

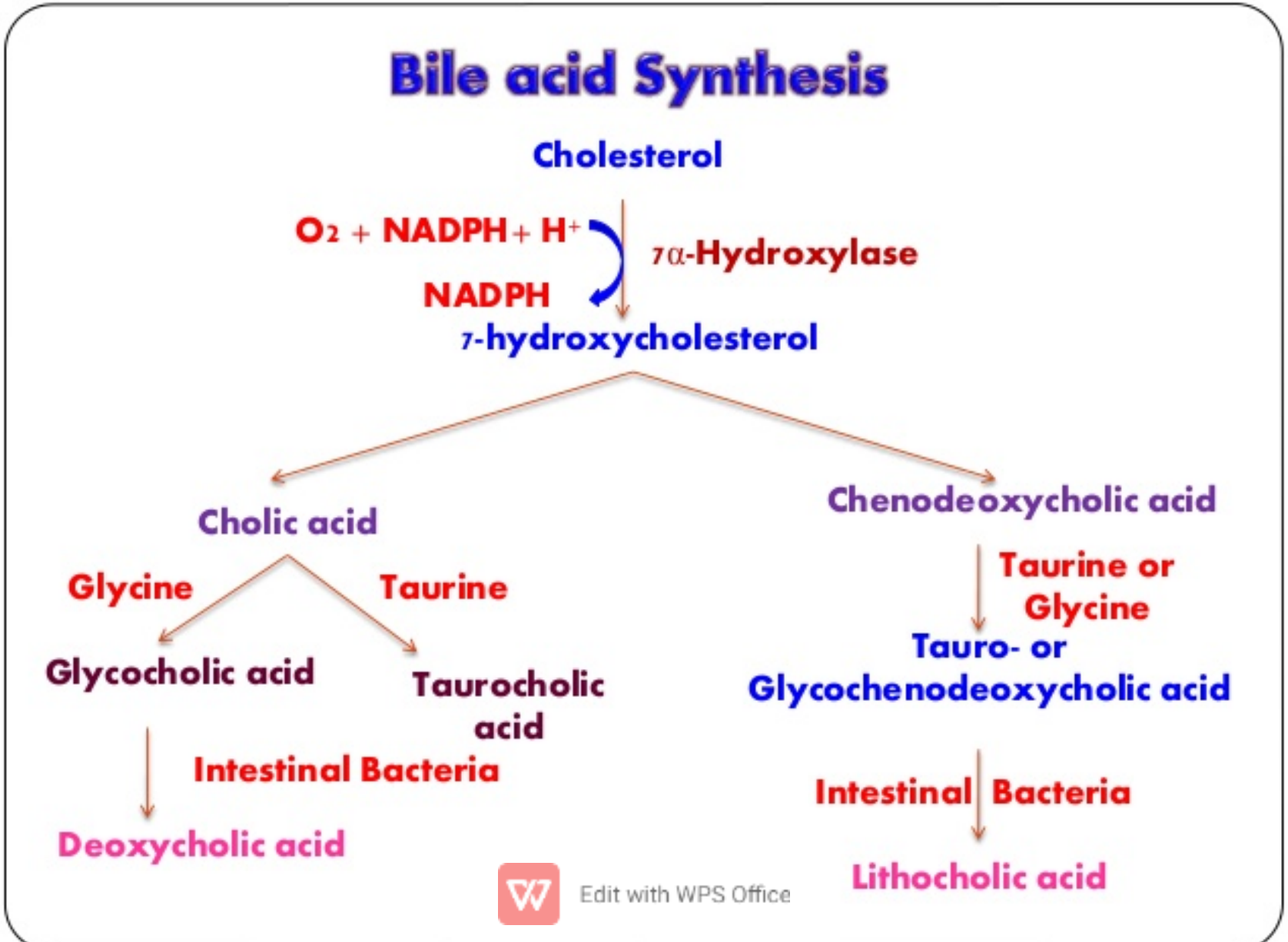
Bile acids (bile

(≈500mg/day)

Bile acids

- Synthesized in liver (peroxisomes) from cholesterol

Bile acid Synthesis



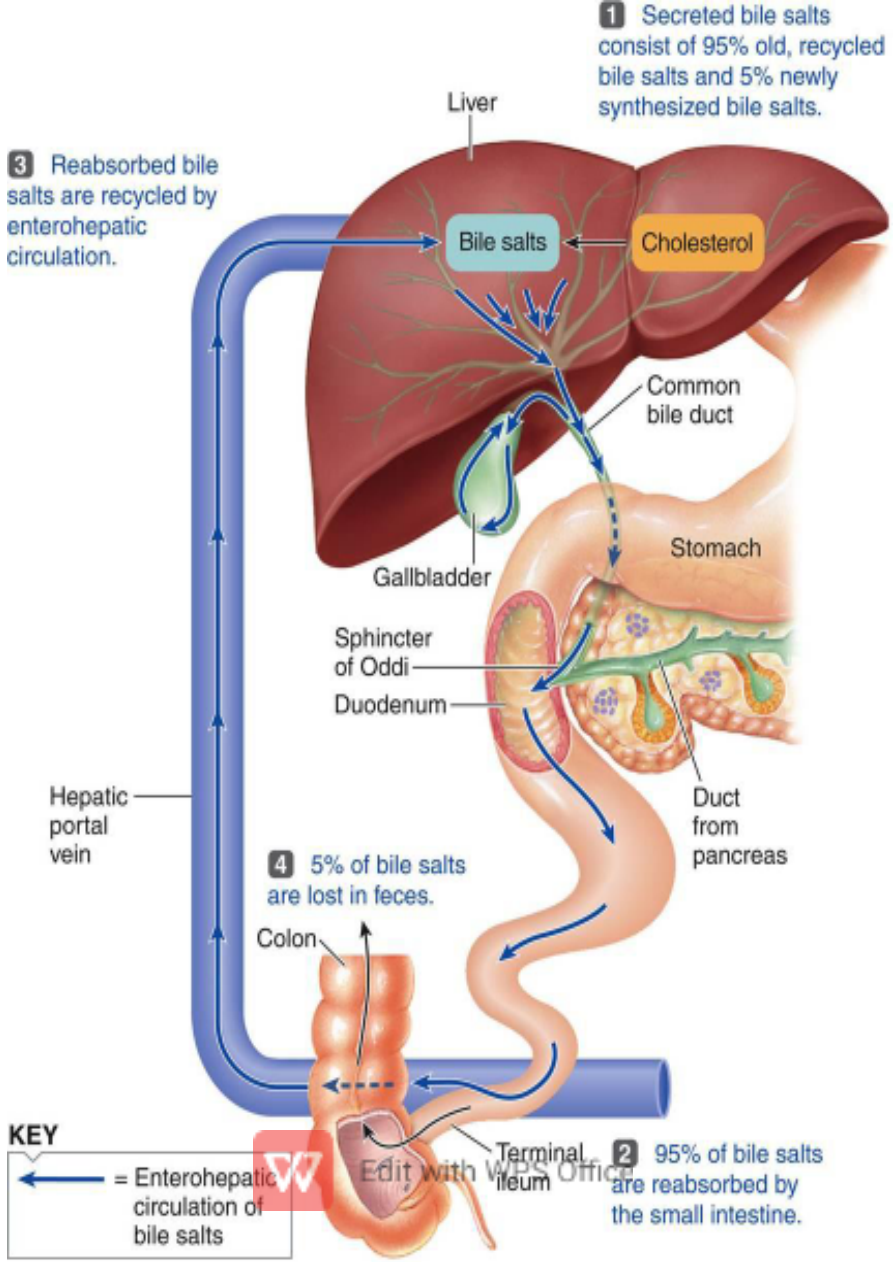
- Conj. Bile acids are excreted through BILE
- In bile they exist as BILE SALTS – Na & K salt of glyco & tauro cholic acid and chenodeoxycholic acid.

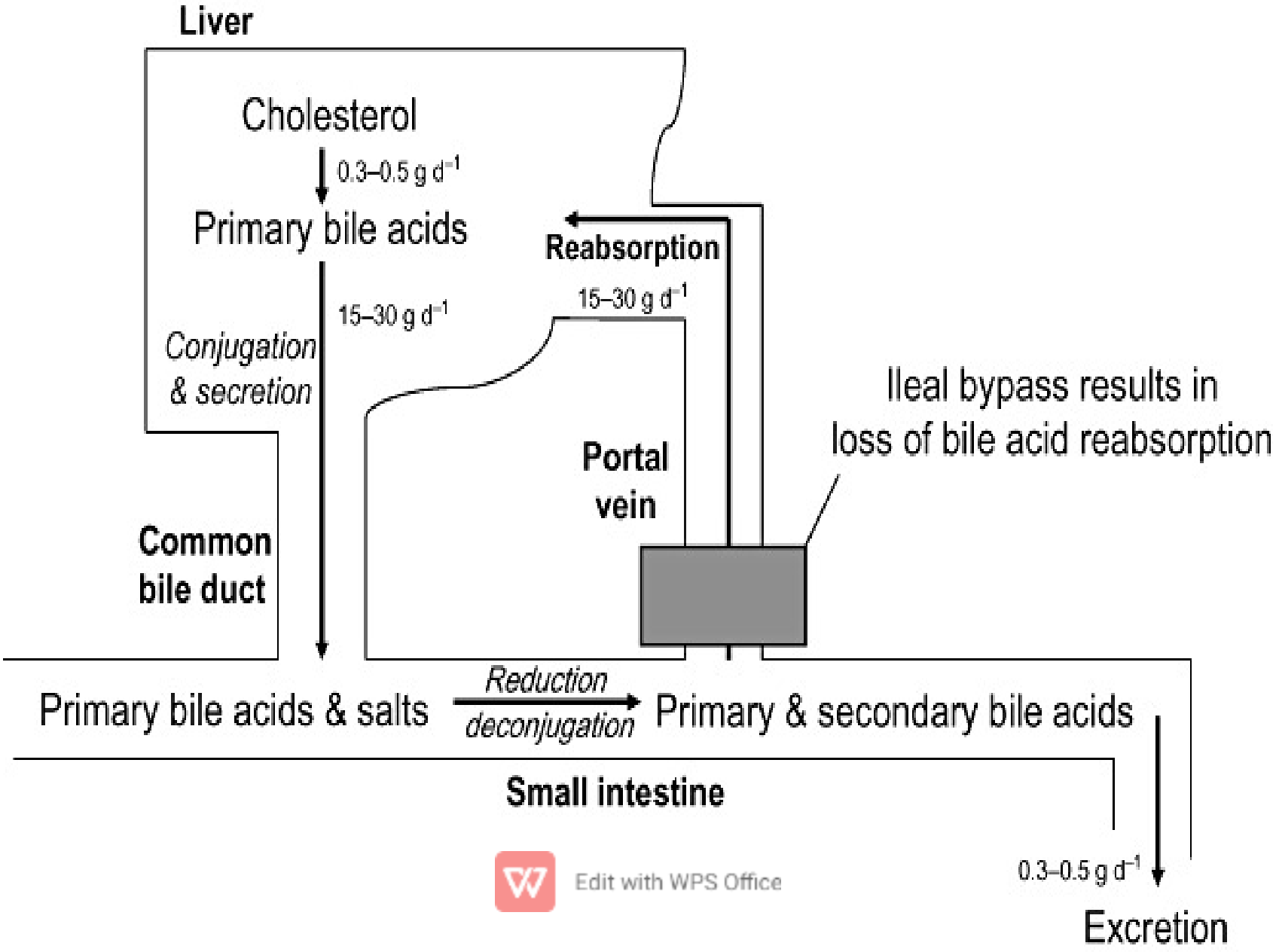
Functions

- Digestion & absorption of lipids by emulsification & micelle formation
- Absorption of fat soluble vitamins
- Bile salt has imp role in keeping cholesterol in solution

Enterohepatic circulation of bile salts

- Total bile salts reaching intestine – 15-30 g/day
- 98 – 99% of this is reabsorbed from ileum, reaches liver & re excreted through bile
- Very small fraction (300 -500 mg/day) is excreted in feces
- This is the major pathway for Cholesterol elimination


1 Secreted bile salts consist of 95% old, recycled bile salts and 5% newly synthesized bile salts.
Liver
3 Reabsorbed bile salts are recycled by enterohepatic circulation.
Bile salts
Cholesterol
Common bile duct
Gallbladder
Stomach
Sphincter of Oddi
Duodenum
Duct from pancreas
Hepatic portal vein
4 5% of bile salts are lost in feces.
Colon
Terminal ileum
2 95% of bile salts are reabsorbed by the small intestine.
KEY
= Enterohepatic circulation of bile salts
Edit with WPS Office



Clinical significance

1. Bile acid binding resin – **Cholestyramine** inhibits reabsorption of bile acids from ileum

- Return of bile acids to liver is ↓ – synthesis of bile acids by liver ↑ – cholesterol excretion ↑
- **used to ↓ plasma cholesterol**

2. **Bile salts are abnormal constituents of urine**

- **Seen in obstructive jaundice & hepatocellular jaundice**
- **Detected by Hay's test**