

An anatomical illustration of a cross-section of an artery. The artery has a thick, reddish-brown outer wall. Inside, there is a yellow, irregularly shaped plaque (atherosclerosis) that has built up on the inner wall, narrowing the lumen. A thin white needle is shown entering the lumen from the right side. The background is dark, making the artery stand out.

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Hyperlipidemia

Presented by ;
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1. Definitions
2. Classification
3. Mechanism of actions

Hyperlipidemia :

Abnormally elevated level of lipid in blood, these lipids can adhere to the walls of the arteries and restrict blood flow which creates significant risk of heart attack and stroke

There are 3 major lipids in our blood

- ➔ Cholesterol
- ➔ Triglycerides
- ➔ Phospholipids

Cholestrol : which is necessary for the synthesis of bile acid.

Triglycerides : which provides energy to the cell.

Phospholipids : which is the major component of cell membrane .

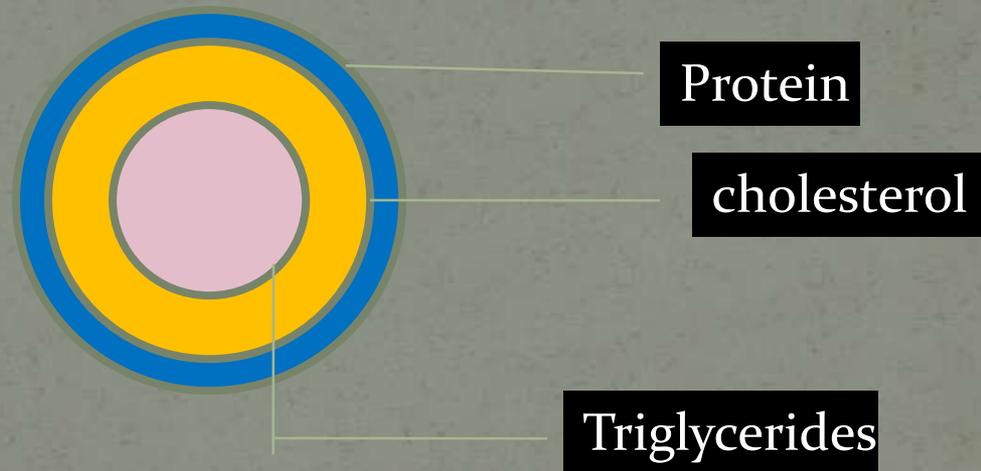
- ➔ Lipid produces in liver.
- ➔ From liver lipids not able to move to blood stream because they are insoluble in blood plasma .
- ➔ So, liver wraps protein around the lipid resulting in new molecule called lipoprotein
- ➔ Lipoprotein move to blood stream through out the body

Types of lipoprotein :

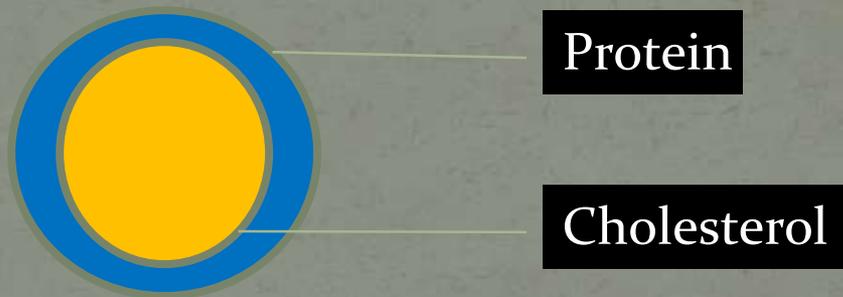
- ➔ Very low density lipoprotein
- ➔ Low density lipoprotein
- ➔ High density lipoprotein

➔ Very low density lipoprotein (VLDL)

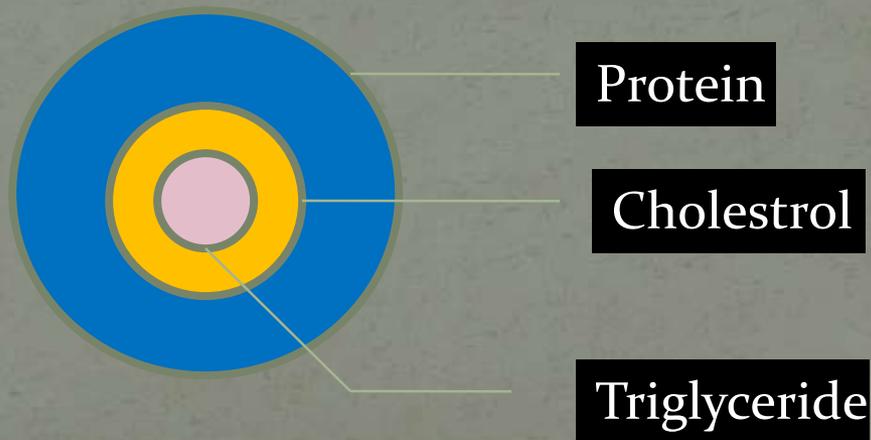
It composed of low level of protein , & high level of cholesterol & triglyceride



- ➔ Low density lipoprotein (LDL)
It composed of only protein and cholesterol.
It is also known as bad cholesterol.

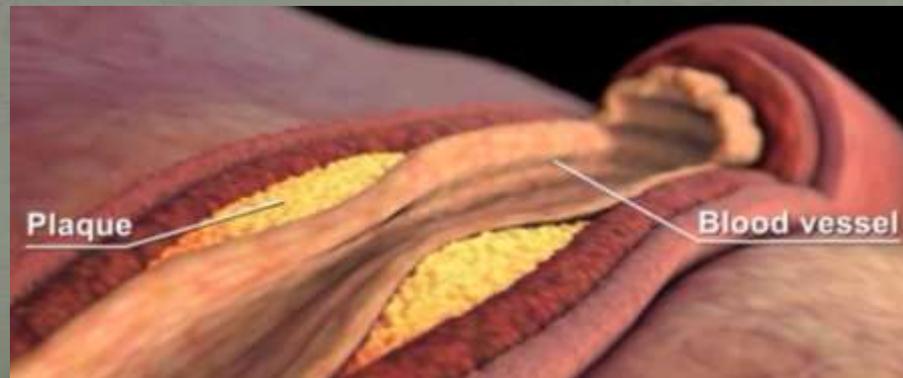


- ➔ High density lipoprotein (HDL) :
It composed of more amount of protein
and very less amount of cholestrol.
It is also known as good cholestrol

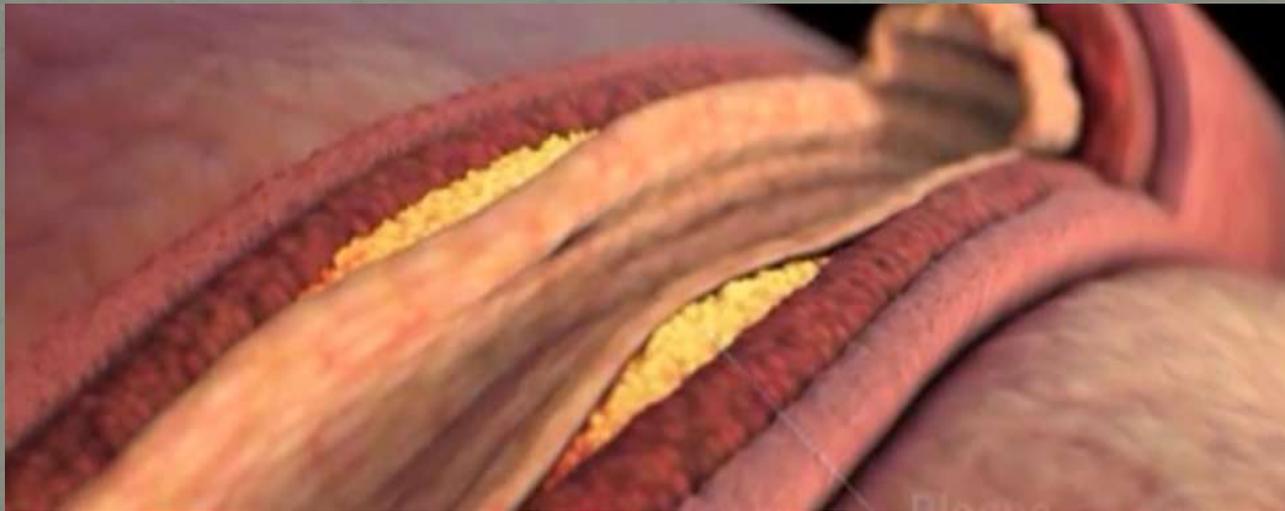


- ➔ Firstly liver releases VLDL in blood stream
- ➔ VLDL provides triglyceride to various cell for function .
- ➔ After utilizing triglyceride VLDL becomes LDL which contain only Protein and cholestrol.
- ➔ LDL provides cholestrol to various cell which required .

- ➔ If our body makes too much LDL, it will be deposited to the walls of artery causing a fat material called plaque.
- ➔ Due to which narrow blood vessel thereby reduce blood flow, that's why they are called bad cholesterol.



➔ Liver also makes HDL that removes excess of cholesterol from cells and plaque , and returns excess cholesterol to liver that's why they are called good cholesterol.



classification

Drug used to lower lipid levels :

- ➔ HMG-CoA reductases inhibitors
- ➔ Fabric acid derivatives
- ➔ Niacin (nicotinic acid)
- ➔ Bile acid sequestrates
- ➔ Cholesterol absorption inhibitors

HMG COA REDUCTASE INHIBITOR :

ATORVASTATIN,
FLUVASTATIN,
LOVASTATIN
PRAVATATIN,
ROSUVASTATIN,

FIBRATES :

FENOFIBRATES
GEMFIBROZIL,
CLOFIBRATE

BILE ACID SEQUESTRANTS INHIBITOR :

COLESEVELAM,
COLESTIPOL,
CHOLESTYRAMINE

NICOTINIC ACID :
NIACIN

CHOLESTROL ABSORPTION INHIBITOR :

EZETIMBE

Mechanism of action

HMG CoA REDUCTASE INHIBITOR :

In liver cell

HMG-CoA

HMG CoA REDUCTASE

Mevalonic acid

Cholesterol

HMG-CoA

HMG CoA REDUCTASE

Mevalonic acid

Cholesterol

Inhibit the enzyme HMG-CoA reductase , which
Is the rate limiting step in cholesterol synthesis.

➔ Decrease LDL, Increase HDL , Decrease triglyceride.

➔ The drugs which inhibit HMG CoA reductase enzyme includes :

Atorvastatin

Fluvastatin

Lovastatin

Pravastatin

Rosavastatin

➔ Side effects : liver toxicity , muscle toxicity.

Nicotinic acid

Triglycerides

Hormone sensitive lipase

Fatty acid

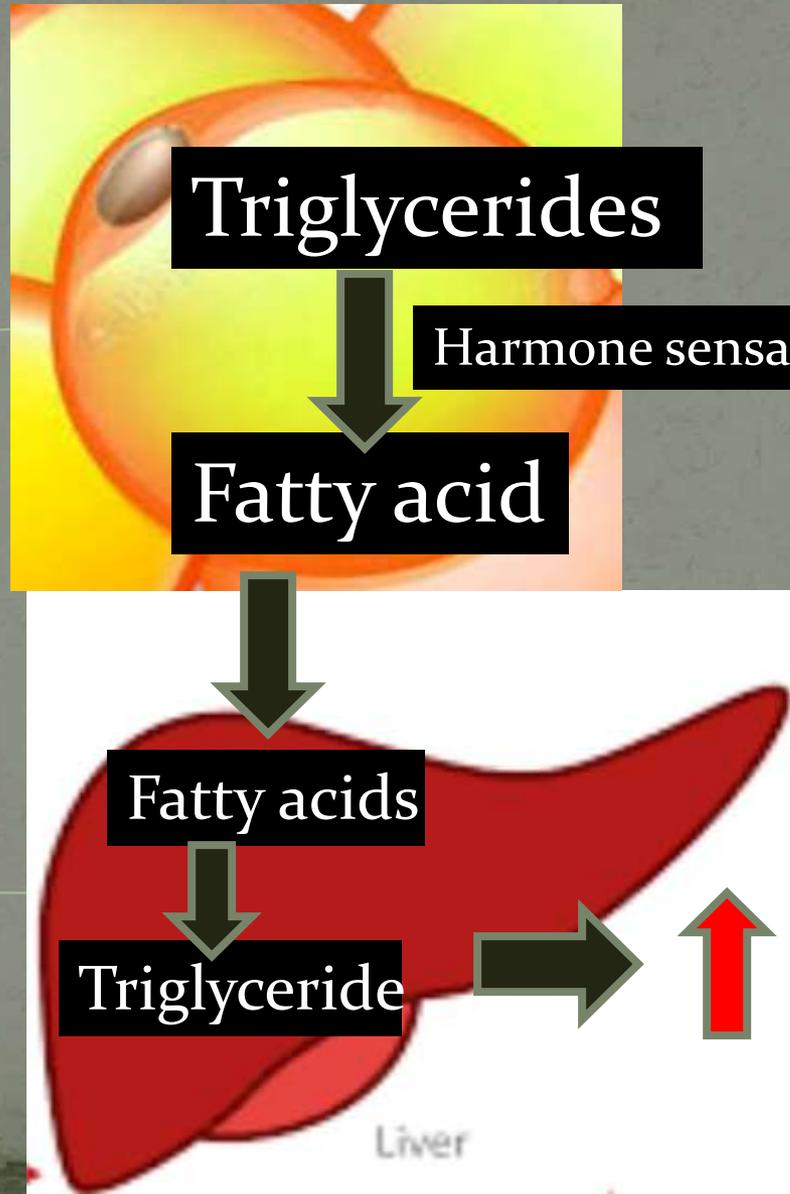
Fatty acids

Triglyceride

VLDL

ADIPOSE
TISSUE

LIVER



- ➔ Normally , Hormone sensitive lipase is responsible for break down of triglyceride to fatty acids in adipose tissue.
- ➔ These fatty acids is used by liver to makes its own triglyceride then become important component of VLDL

Nicotinic acid

Triglycerides

Hormone sensitive lipase

Fatty acid

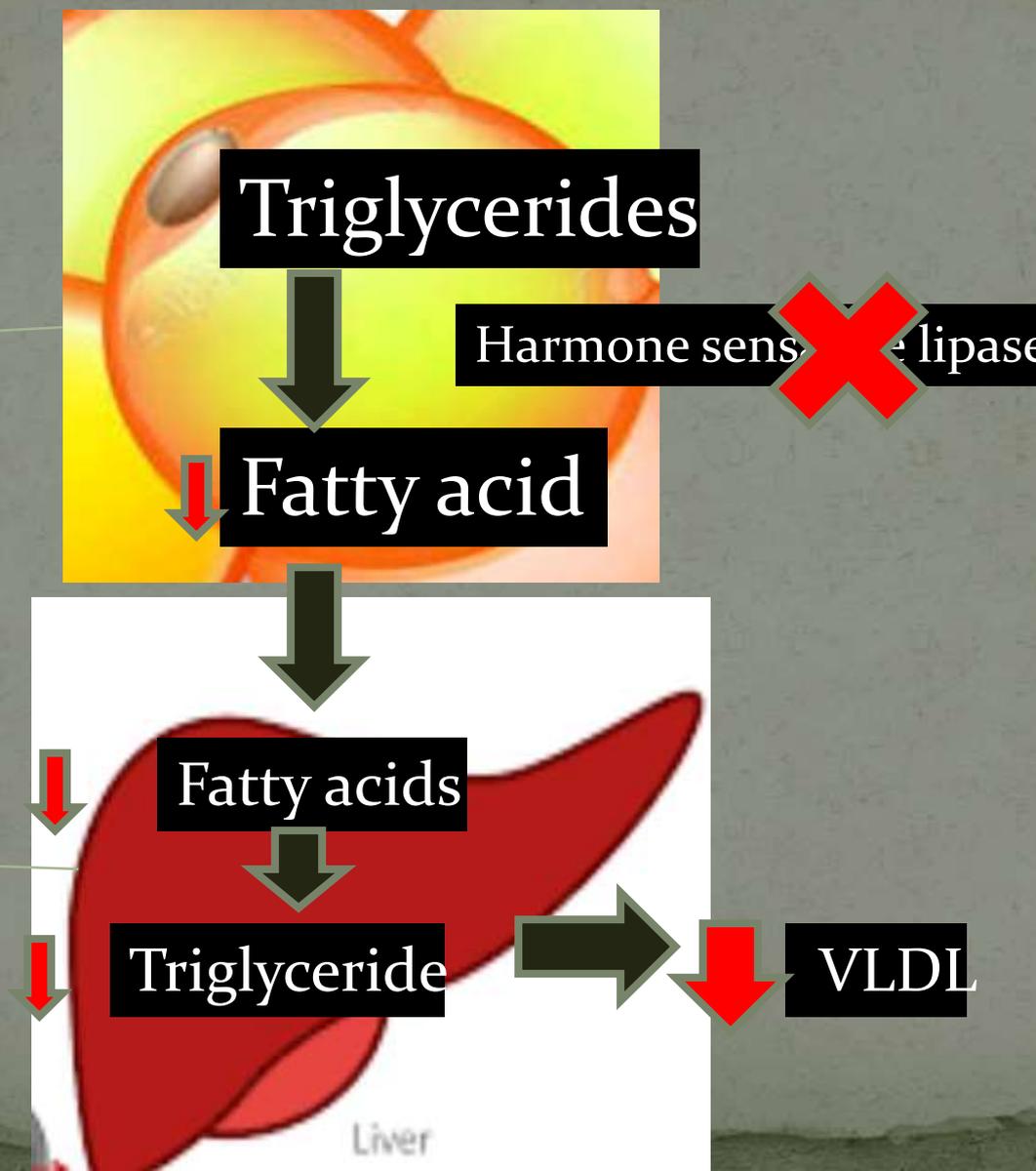
Fatty acids

Triglyceride

VLDL

ADIPOSE
TISSUE

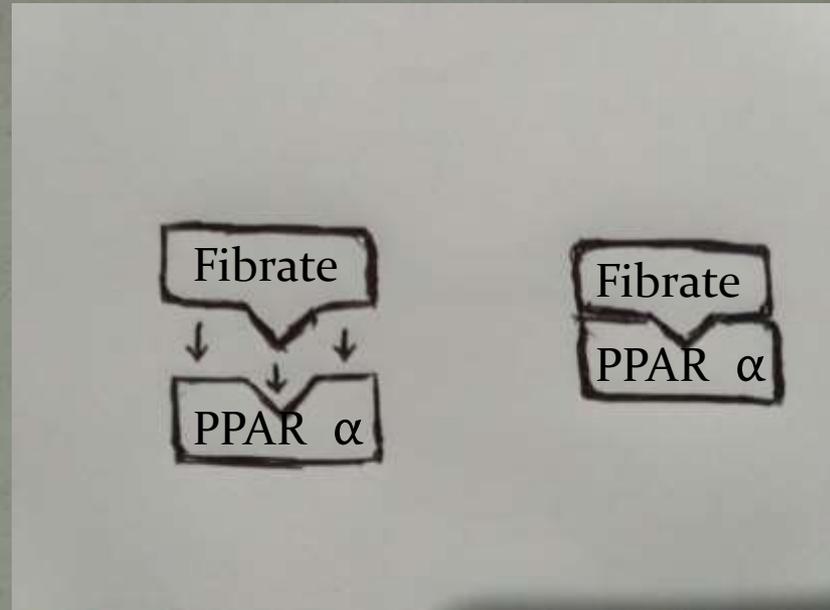
LIVER



- ➔ To decrease VLDL production NICOTINIC ACID
Inhibit hormone sensitive lipase .
- ➔ Increase HDL , decrease LDL , decrease triglycerides
- ➔ The drug which inhibit hormone sensitive lipase
is NIACIN .
- ➔ Side effects : Skin flushing , hyperglycemia,
And hepatotoxicity

FIBRATES

Fibrates work primarily by activating nuclear transcription receptor called PPAR α (Peroxisome proliferator activated receptor alpha).

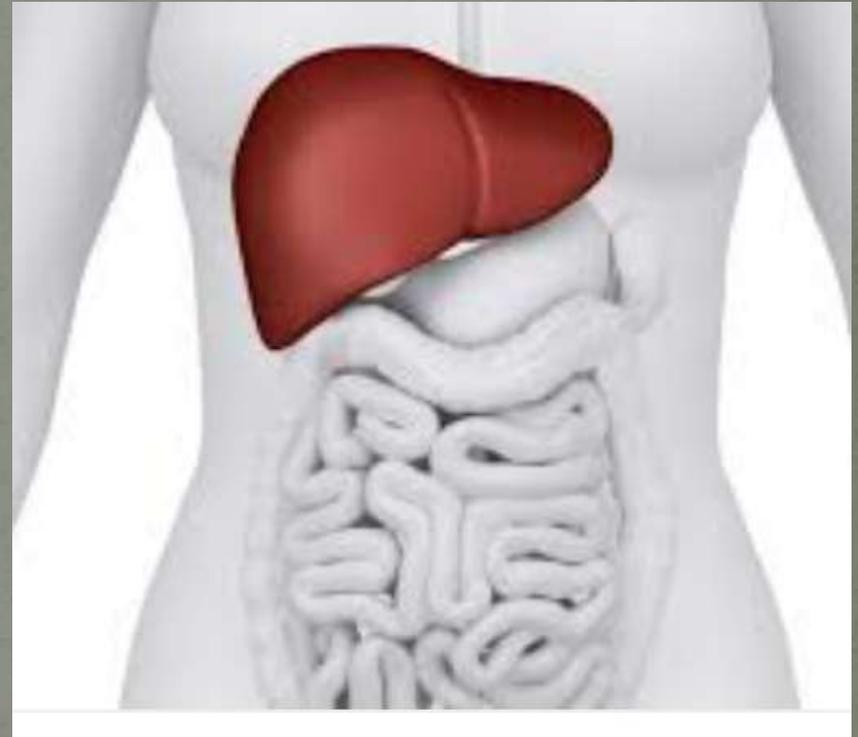


- ➔ PPAR α is found in metabolically active tissues such as liver and adipose tissue
- ➔ Binding of fibrates to PPAR α induces activation or inhibition of certain proteins involved in lipid metabolism. which ultimately decrease in the production of LDL and VLDL .
- ➔ The drugs belongs to this class include FINOFIBRATE GEMFIBRIZIL
- ➔ SIDE EFFECTS : GI distubance , rhabdomyolsis have been reported in patients with impared renal function

BILE ACID SEQUESTRANTS :

preventing the reabsorption of bile acid

- ➔ As we know bile acid are made from cholesterol .
Liver produce bile acid and stored in the gall bladder, and they excreted into the gut where they facilitate digestion & absorption of lipid



➔ Now bile acid sequestrants basically binds with bile acid and salt in the small intestine the formation of this insoluble complex prevents the reabsorption of bile acids and thus lead to their excretion

BILE ACID SEQUESTRANT + BILE ACID = FORMS A COMPLEX

➔ This increase in bile acid excretion in turn creates increase demand for their production

➔ Since bile acid are made from cholesterol liver cell increase their number of LDL receptors to bring in more LDL cholesterol in order to meet this new demand so the end result is decreased levels of circulating LDL

➔ The drugs belongs to this class include

CLESEVELAM,
COLESTIPOL ,
CHOLESTYRAMINE

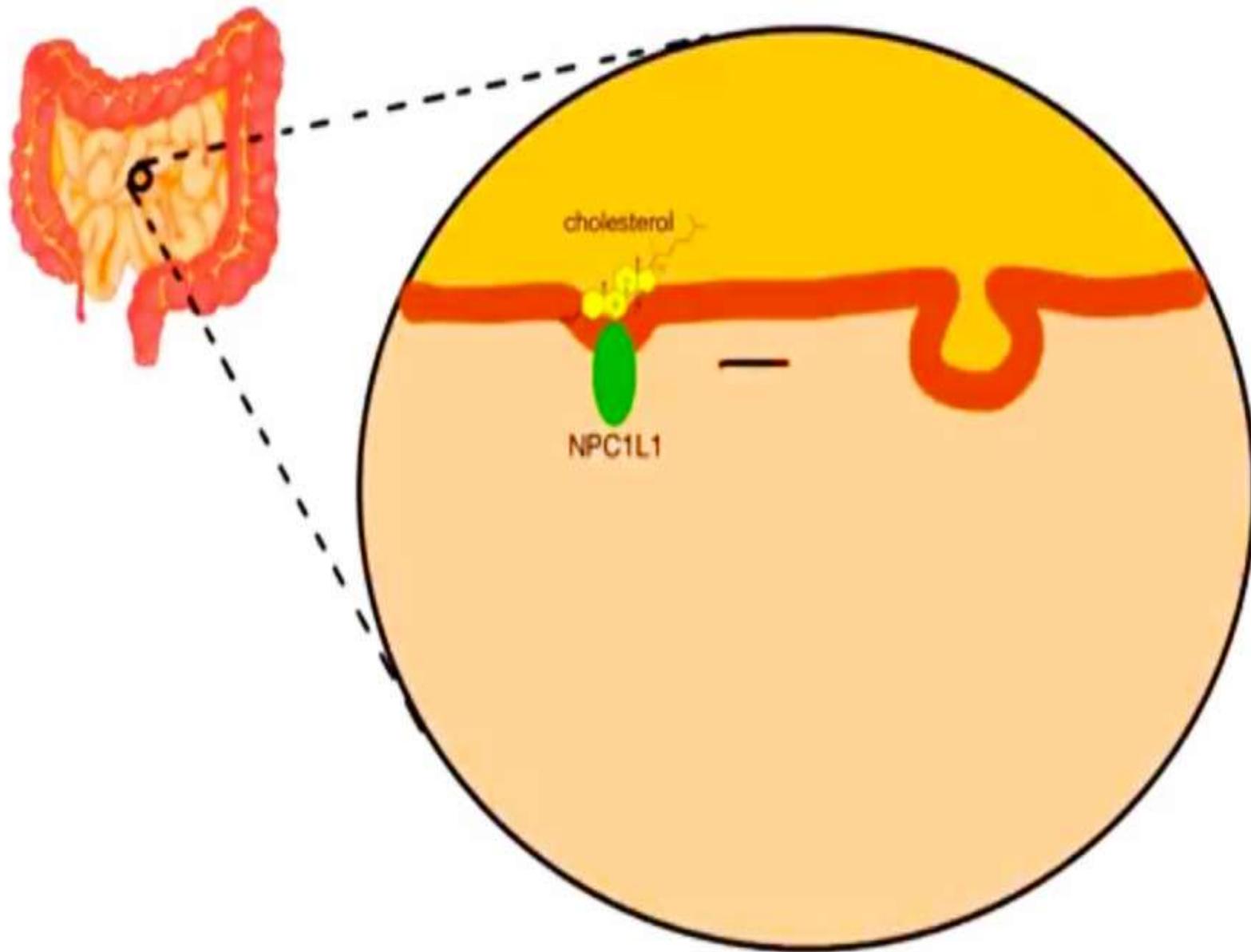
➔ SIDE EFFECTS : constipation
nausea are the common side
effects

CHOLESTEROL ABSORPTION INHIBITORS

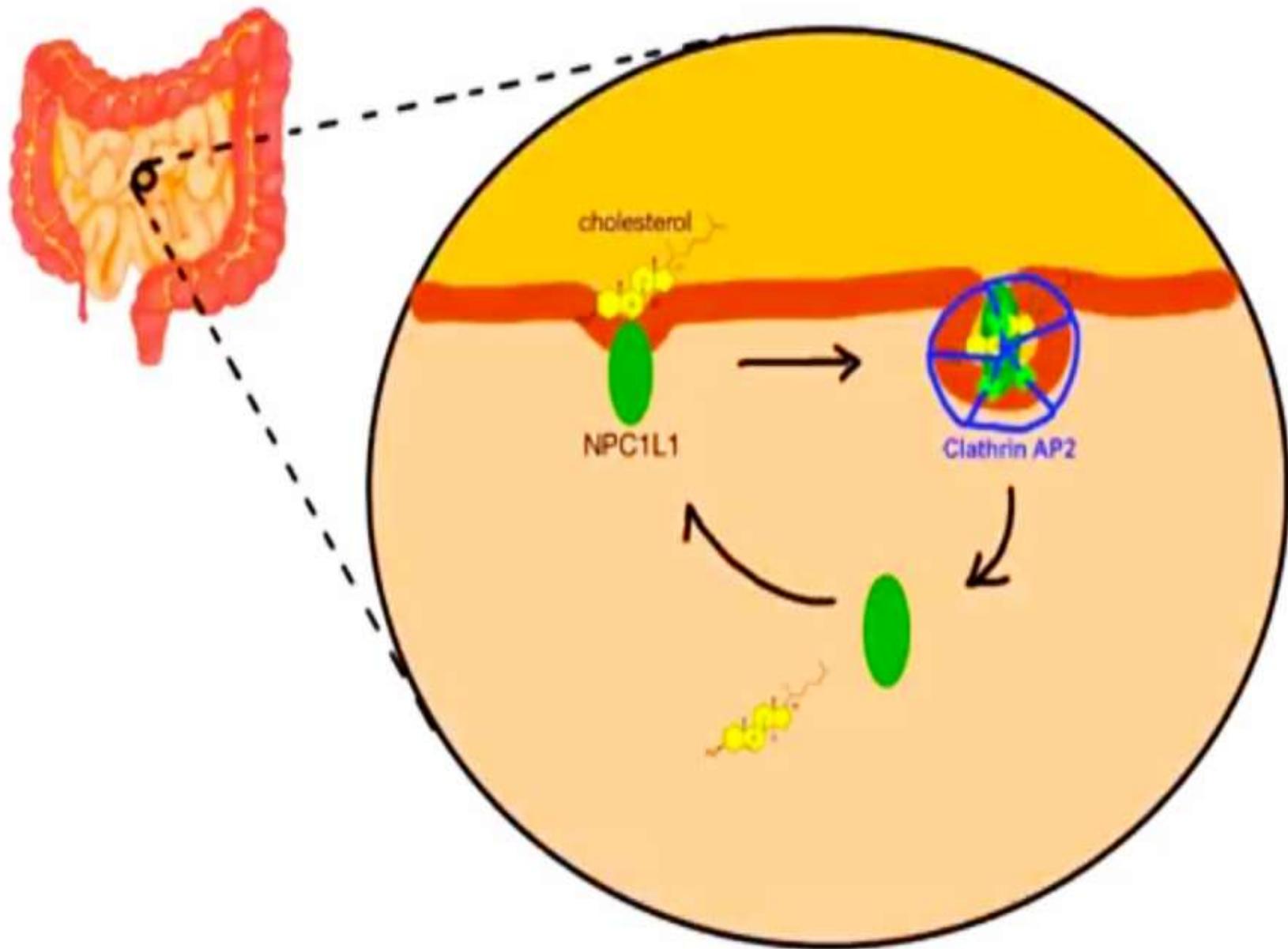
Under normal condition

Mechanism of cholesterol absorption in small intestine

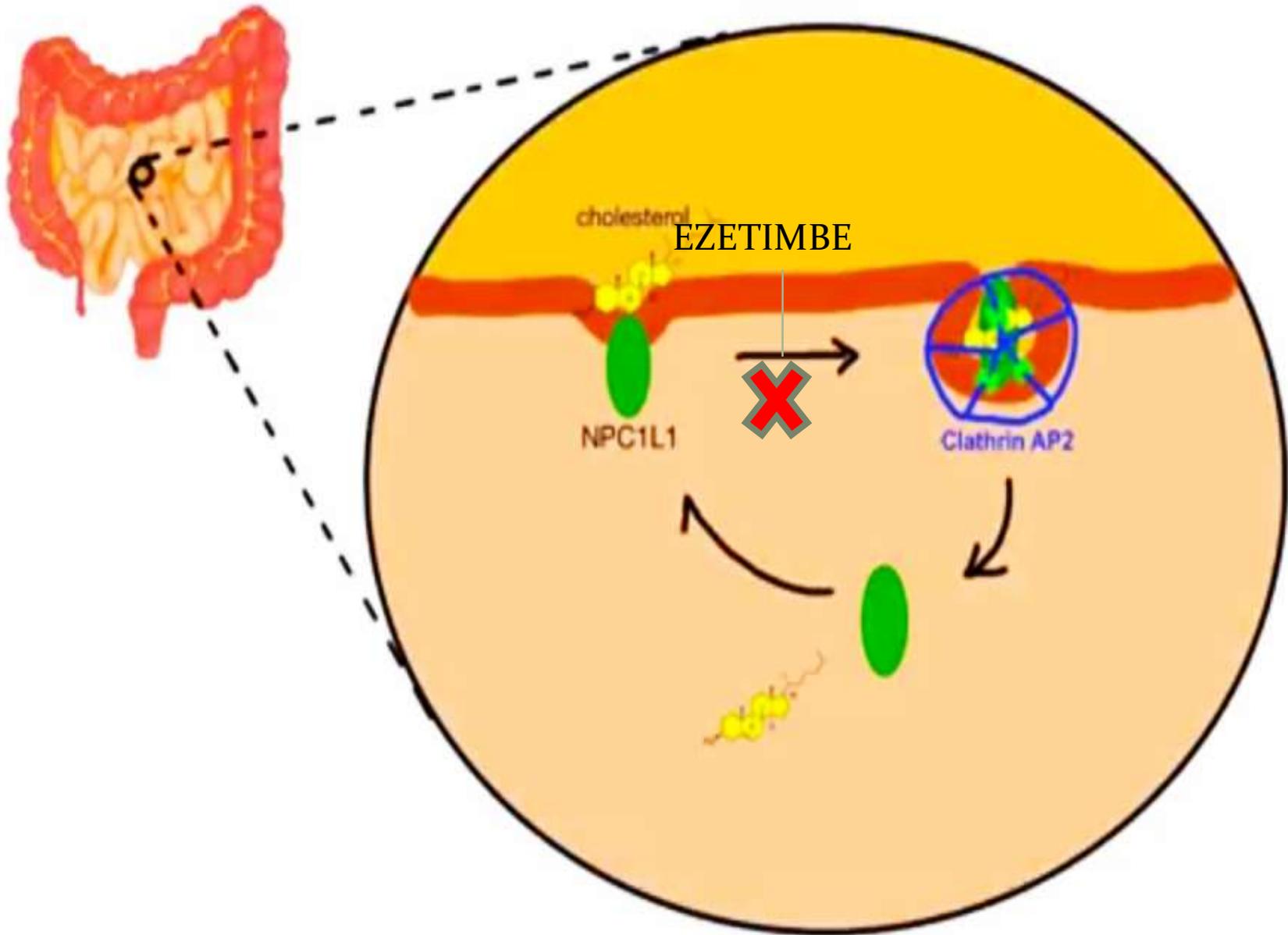
- ➔ Free cholesterol that comes either from bile or dietary sources first binds to protein abbreviated NPC1L1 which is located in the plasma membrane of the cells known as enterocytes that lines the intestinal walls .



- ➔ This Binding then triggers endocytosis which utilizes protein complex called clathrin AP₂ that works on the cell membrane to internalize the cholesterol cargo upon
- ➔ Upon endocytosis the cholesterol is released and the NPC1L1 return back to the plasma membrane



- ➔ Now the cholesterol absorption inhibitors simply binds to NPC1L1 and inhibits its ability to interact with clathrin AP2 complex that is necessary for endocytosis this lead to decreased delivery of intestinal cholesterol to the liver
- ➔ Which in turn causes decrease in hepatic cholesterol level & ultimately increased clearance of LDL cholesterol from the circulation



➔ Currently the only drug belongs to this class is EZETIMIBE

➔ The side effects of ezetimibe are mild and few which makes it a good choice for patients with intolerant or unresponsive to statins .

THANK YOU