

The logo of Galgotias University is a stylized circular emblem composed of several overlapping, curved segments in shades of yellow, blue, and pink, creating a sense of motion or a spiral.

Anti-hyperlipidemic Drugs

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What is Hyperlipidemia?

- Hyperlipidemia a broad term, also called hyperlipoproteinemia, is a common disorder in developed countries and is the major cause of coronary heart disease.
- It results from abnormalities in lipid metabolism or plasma lipid transport or a disorder in the synthesis and degradation of plasma lipoproteins.
- Mostly hyperlipidemia is caused by lifestyle habits or treatable medical conditions.
- Obesity, not exercising, and smoking, diabetes, obstructive jaundice, and an under active thyroid gland inherit hyperlipidemia.

What are lipids?

- Lipids are the heterogenous mixtures of fatty acids and alcohol that are present in the body. The major lipids in the bloodstream are ***cholesterol and it's esters, triglycerides and phospholipids.***
- Cholesterol is C₂₇ steroid that serves as an important component of all cell membranes and important precursor molecule for the biosynthesis of bile acids, steroid hormones, and several fat-soluble vitamins.

Functions of cholesterol in the body?

- It is necessary for new cells to form and for older cells to repair themselves after injury.
- Cholesterol is also used by the adrenal glands to form hormones such as cortisol, by the testicles to form testosterone, and by the ovaries to form estrogen and progesterone.

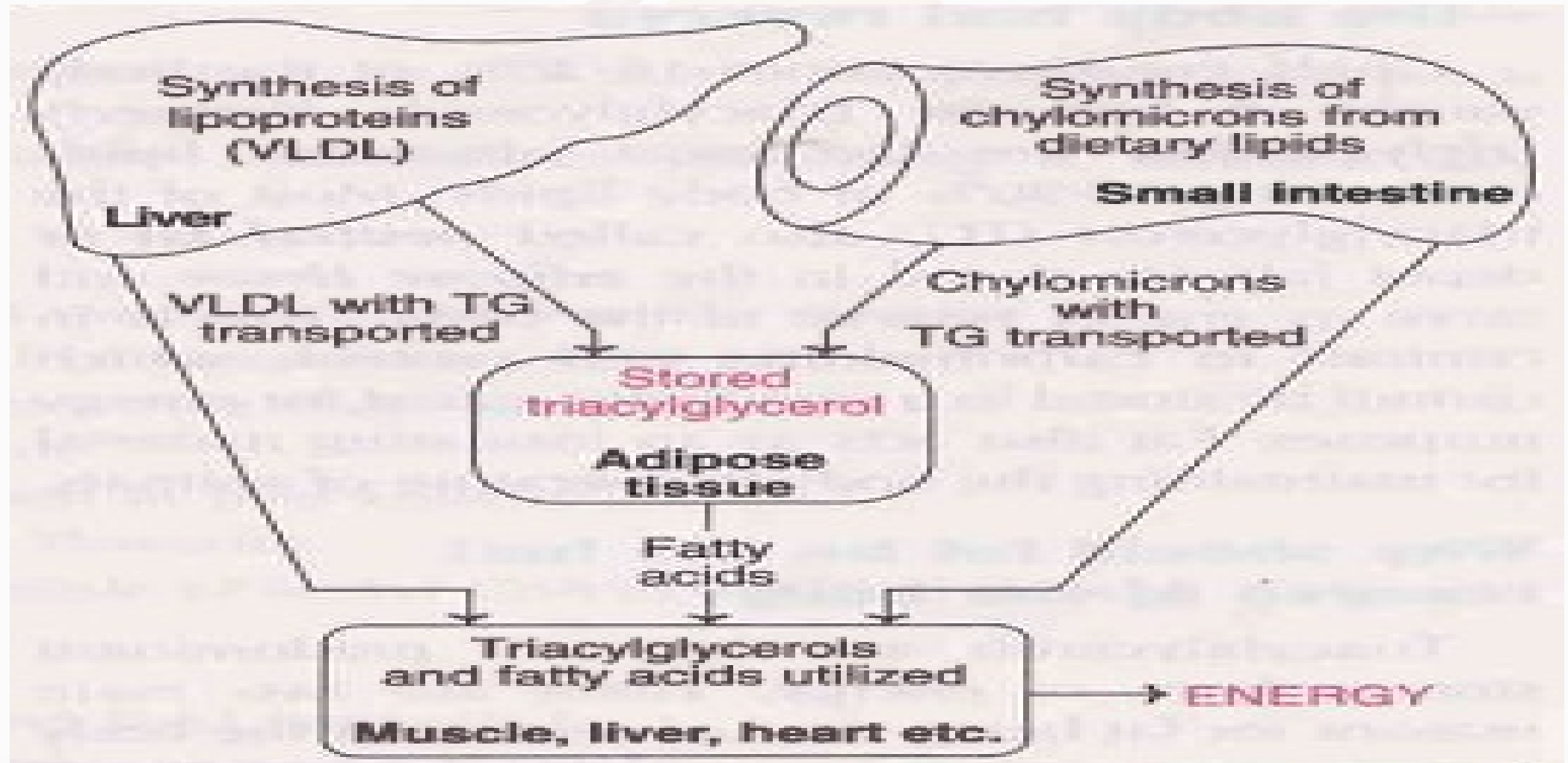
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- Triglycerides supply energy for the body. Triglycerides either meet immediate energy needs in muscles or stored as fat for future energy requirements.
- Phospholipids are compounds that are used to make cell membranes, generate second messengers, and store fatty acids for the use in generation of prostaglandins.

What are lipoproteins?

- Since blood and other body fluids are watery, so fats need a special transport system to travel around the body.
- They are carried from one place to another mixing with protein particles, called lipoproteins.
- There are four (or five) types of lipoproteins, each having very distinct job.
- A lipoprotein contains both proteins and lipids, bound to another proteins which is called apolipoproteins, which allow fats to move through the water inside and outside cells.

Overview of fat metabolism



CLASSIFICATION

1) HMG CoA Reductase inhibitors

Lovastatin, Simvastatin, Metastatin, Pravastatin, Fluvastatin, Atorvastatin, Pitavastatin, Rosuvastatin

2) Fibric acid derivatives Clofibrate, Fenofibrate, Gemfibrozil, Ciprofibrate, benzaffibrate, Fluvestatin.

3) Bile acid sequestrants Cholestyramine, Colestipol

4) LDL oxidation inhibitor

Probucol

5) Pyridine derivatives Nicotinic acid, Nicotinamide

6) Cholesterol absorption inhibitors

Ezetimibe

7) Miscellaneous agents

β -Sitosterol, Dextrothyroxine

- There are two classes of statins:
- Natural Statins: Lovastatin, Pravastatin, Simvastatin.
- Synthetic Statins: Atorvastatin, Fluvastatin.
- Statins are competitive inhibitors of HMG-CoA reductase.
- They are bulky and “stuck” in the active site.
- This prevents the enzyme from binding with its substrate, HMGCoA.

Fibrates

- Fibrates are antihyperlipidemic agents, widely used in the treatment of different forms of hyperlipidemia and hypercholesterolemia.
- Fibrates are 2-phenoxy-2-methyl propanoic acid derivatives. These drugs stimulate β -oxidation of fatty acids in mitochondria.
- This group of drugs is therefore known for decreasing plasma levels of fatty acid and triacylglycerol

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Bile acid sequestrants

- cholestyramine
- colestipol hydrochloride
- colesevelam

Also called bile acid-binding resins and ion-exchange resins

Cholestyramine

- is a non-absorbed bile acid sequestrant that is
- used as a therapy of hyperlipidemia and for the pruritis of chronic liver disease and biliary obstruction.
- is a large, highly positively charged anion exchange resin that binds to negatively charged anions such as bile acids.
- The binding of bile acids to cholestyramine creates an insoluble compound that cannot be reabsorbed and is thus excreted in the feces.

- Moderately effective with excellent safety record
- Large MW polymers containing Cl-
- Resin binds to bile acids and the acid-resin complex is excreted
 - prevents enterohepatic cycling of bile acids
 - obligates the liver to synthesize replacement bile acids from cholesterol.
- The levels of LDL-C in the serum are reduced as more cholesterol is delivered to the liver
- Little effect on levels of HDL-C and TG.
- Excellent choice for people that cannot tolerate other types of drugs

Colesevalam

- A third generation drug of this class resemble the previous ones but don't contain chloride ions.
- Strictly speaking, it is not an anion exchange resin.
- Selectivity for hydroxylated form of bile acids shows
- a reduced side effect (reduced constipation).

Adverse effects

- Constipation
- Heartburn, nausea, bloating
- These adverse effects tend to disappear over time.

Uses:

- Type IIa hyperlipoproteinemia.
- Relief of pruritus associated with partial biliary obstruction (cholestyramine).

Ezetimibe

- is a drug that lowers plasma cholesterol levels. It acts by decreasing cholesterol absorption in the intestine

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MOA of Cholesterol absorption inhibitors

- lowers plasma cholesterol levels by inhibiting the absorption from intestine
- This cause a decrease in the cholesterol delivery to the liver which in turn clears more cholesterol from the blood
- selective in its action ((not interfere with TGs, lipidsoluble vitamins absorption))
- The levels of LDL-C in the serum are reduced as in bile acid sequestrants.

Nicotinic acid (niacin)

- **Water soluble vitamin of the B family; Once converted to the amide, it is incorporated into NAD**
- **Vitamin B3**
- Lipid-lowering properties require much higher doses than when used as a vitamin
- Effective, inexpensive, often used in combination with other lipid-lowering drugs

Mechanism of action

- Increases activity of lipase, which breaks down lipids
- Reduces the metabolism of cholesterol and triglycerides

Indications

- Effective in lowering triglyceride, total serum cholesterol, and LDL levels
- Increases HDL levels
- Effective in the treatment of types IIa, IIb, III, IV, and V hyperlipidemias

Adverse effects

- Flushing (due to histamine release)
- Pruritus
- GI distress
- Liver dysfunction and jaundice. Serious liver damage is the most important risk.

LDL Oxidation inhibitor (Probucol)

- Molecule has two tertiary butylphenol groups linked by a dithiopropylidene bridge, giving it a high lipophilic character with strong antioxidant properties.

- In humans, it causes reduction of both liver and serum cholesterol levels, but it does not alter plasma triglycerides.
- It reduces LDL
- It reduces to a lesser extent HDL levels by a unique mechanism that is still not clearly delineated.
- The reduction of HDL may be caused by the ability of probucol to inhibit the synthesis of apoprotein A-1, a major protein component of HDL.
- It is effective at reducing levels of LDL and is used in hyperlipoproteinemias characterized by elevated LDL levels.

ADR: GI disorders and prolongation of GI intervals.

Use: It is used as antihyperlipoproteinemic agent.

Miscellaneous agent β -Sitosterol

- Sitosterol is a plant sterol, whose structure is identical with that of cholesterol, except for the substituted ethyl group on C-24 of its side chain.
- Although the mechanism of its hypolipidemic effect is not clearly understood, it is suspected that the drug inhibits the absorption of dietary cholesterol from the gastrointestinal tract.
- Sitosterols are absorbed poorly from the mucosal lining and appear to compete with cholesterol for absorption sites in the intestine.

ADR: Diarrhoea, constipation, GI disturbances

Use: Anti cholesteremic agent and treatment of prostatic oedema.

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