

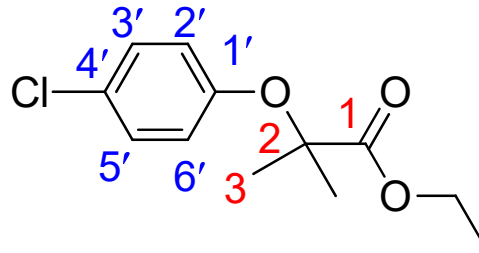
# Anti-hyperlipidemic agents

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## Clofibrate

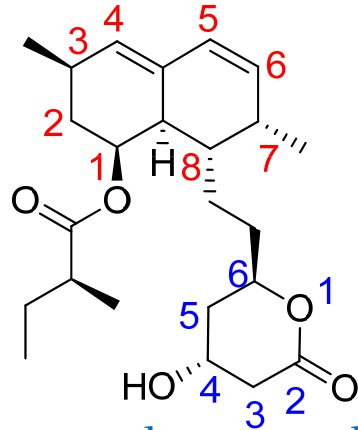


IUPAC: ethyl 2-(4-chlorophenoxy)-2-methylpropanoate

MOA: Clofibrate increases the activity of extrahepatic lipoprotein lipase (LL), thereby increasing lipoprotein triglyceride lipolysis. Chylomicrons are degraded, VLDLs are converted to LDLs, and LDLs are converted to HDL. This is accompanied by a slight increase in secretion of lipids into the bile and ultimately the intestine. Clofibrate also inhibits the synthesis and increases the clearance of apolipoprotein B, a carrier molecule for VLDL. Also, as a fibrate, Clofibrate is an agonist of the PPAR- $\alpha$  receptor in muscle, liver, and other tissues. This agonism ultimately leads to modification in gene expression resulting in increased beta-oxidation, decreased triglyceride secretion, increased HDL, increased lipoprotein lipase activity.

Uses: For Primary Dysbetalipoproteinemia (Type III hyperlipidemia) that does not respond adequately to diet. This helps control high cholesterol and high triglyceride levels.

## Lovastatin



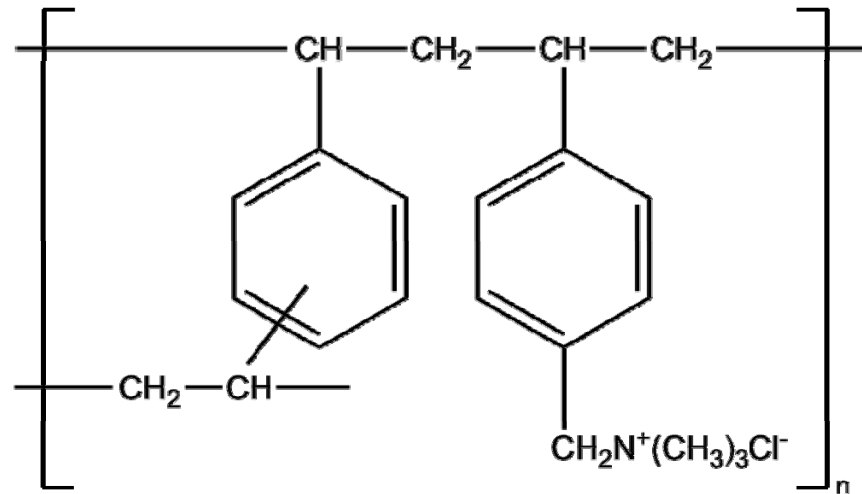
IUPAC: (1S,3R,7S,8S,8aR)-8- {2-[(2R,4R)-4-hydroxy-6-oxooxan-2-yl]ethyl} -3,7-dimethyl-1,2,3,7,8,8a-hexahydronaphthalen-1-yl (2S)-2-methylbutanoate

MOA: Lovastatin is a lactone which is readily hydrolyzed *in vivo* to the corresponding  $\beta$ -hydroxyacid and strong inhibitor of HMG-CoA reductase, a hepatic microsomal enzyme which catalyzes the conversion of HMG-CoA (3-hydroxy-3-methylglutaryl-coenzyme A ) to mevalonate, an early rate-limiting step in cholesterol biosynthesis. At therapeutic lovastatin doses, HMG-CoA reductase is not completely blocked, thereby allowing biologically necessary amounts of mevalonate to be available. Because the conversion of HMG-CoA to mevalonate is an early step in the biosynthetic pathway for cholesterol, therapy with lovastatin would not be expected to cause an accumulation of potentially toxic sterols.

Uses: Lovastatin is indicated to reduce the risk of myocardial infarction, unstable angina, and the need for coronary revascularization procedures in individuals without symptomatic cardiovascular disease.

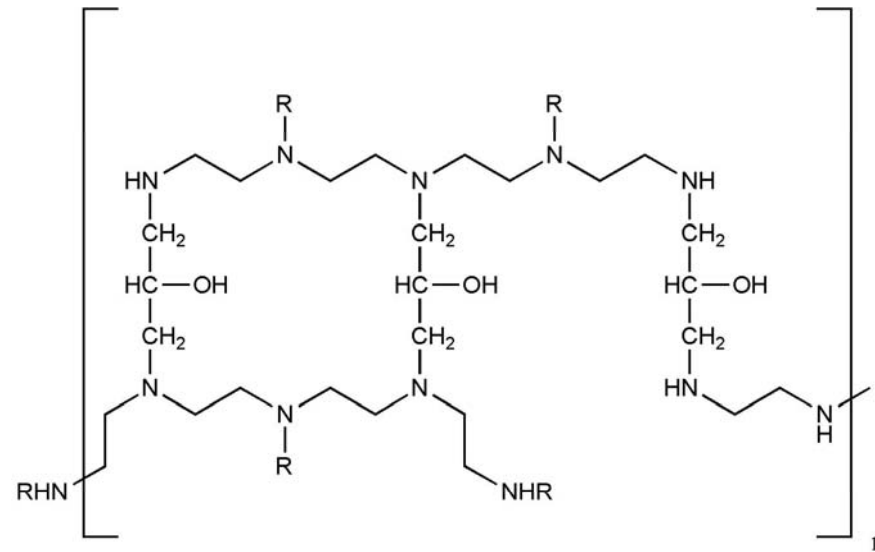
Lovastatin is also indicated to slow the progression of coronary atherosclerosis in patients with coronary heart disease.

## Cholesteramine



MOA: Cholestyramine forms a resin that acts as a bile acid sequestrant to limit the reabsorption of bile acids in the gastrointestinal tract. Cholestyramine resin is a strong anion exchange resin, allowing it to exchange its chloride anions with anionic bile acids present in the gastrointestinal tract and form a strong resin matrix. Cholestyramine consists of a functional group, which is a quaternary ammonium group attached to an inert styrene-divinylbenzene copolymer, in the anion exchange resin.

## Cholestipol



R = H or Cross Link

**MOA:** Colestipol is a lipid-lowering polymer that binds with bile acids in the intestine forming a complex that is excreted in the feces. This non-systemic action results in a continuous, partial removal of bile acids from the enterohepatic circulation preventing their reabsorption. This increased fecal loss of bile acids due to colestipol hydrochloride administration leads to increased oxidation of cholesterol to bile acids. This results in an increase in the number of hepatic low-density lipoprotein (LDL) receptors, and consequently an increased uptake of LDL and a decrease in serum/plasma beta lipoprotein or total and LDL cholesterol levels.

**Uses:** Colestipol is a bile acid sequestrant used to lower blood cholesterol, specifically low-density lipoprotein (LDL). It is also used to reduce stool volume and frequency, and in the treatment of chronic diarrhoea.