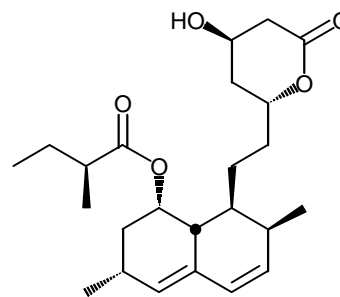


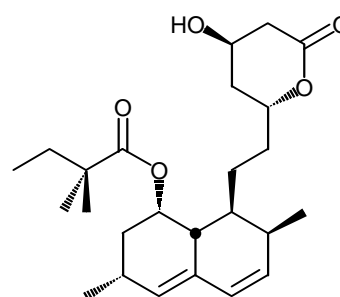
Statins and Cholesterol Reduction

Lovastatin is a polyketide derived natural product isolated from *Aspergillus terreus*. It is used as a cholesterol (lipid) reducing drug administered orally, and is marketed most prominently under the brand name Mevacor®. Lovastatin is an inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase, an enzyme which catalyzes the conversion of HMG-CoA to mevalonate. Mevalonate is a required building block for cholesterol biosynthesis, and lovastatin interferes with its production by acting as a competitive inhibitor for HMG-CoA, thus reducing the amount of HMG-CoA which binds to the HMG-CoA reductase. Lovastatin is inactive in its native form, the form in which it is administered. The lactone moiety is hydrolyzed to the β -hydroxy acid form in the body, and it is this form which is active. Presumably, the reductase is acting on the hydrolyzed lovastatin to reduce the carboxylic acid moiety.



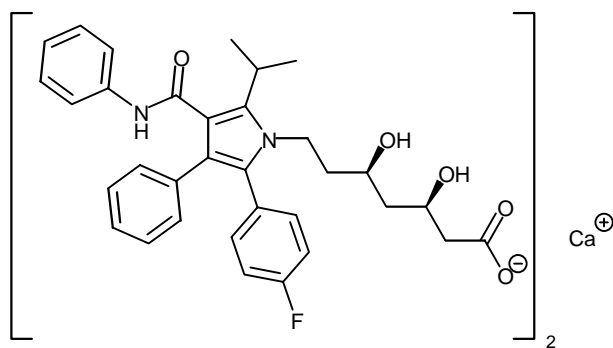
lovastatin

Several derivatives of lovastatin are now marketed as cholesterol reducing agents. Simvastatin (Zocor®) is another statin closely related to lovastatin, differing only by a methyl group in the butanoate moiety, which has many of the same properties. Both compounds are effective in lowering total cholesterol, LDL cholesterol (the bad cholesterol), and triglyceride levels. They increase the level of HDL (good cholesterol) at the same time.



simvastatin

Other statins have vastly different structures. Another popular cholesterol reducing drug is Lipitor® (atorvastatin). As you can see from the structure, this compound, administered as the calcium salt, is a pyrrole derivative. It is a synthetic compound, rather than a natural product, but also acts as a competitive inhibitor of HMG-CoA reductase.



atorvastatin calcium