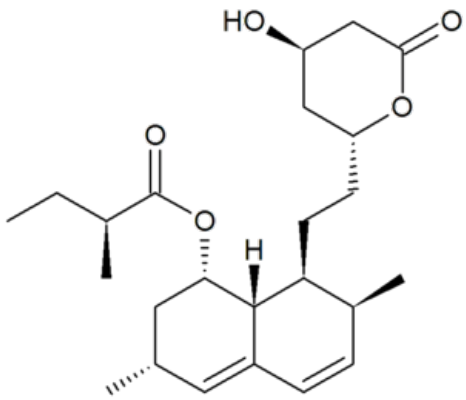
# Statins

Statins are **competitive inhibitors of HMG-CoA reductase**. HMG-CoA (3-hydroxy-3-methylglutaryl-coenzyme A) reductase is an enzyme that catalyzes the major step in cholesterol synthesis, the conversion of HMG-CoA to mevalonic acid. HMG-CoA is subsequently converted to coenzyme A during this blockade.

Its inhibition reduces intrahepatic cholesterol synthesis, which leads to an increase in the number of LDL-receptors on hepatocytes, increased uptake of LDL by the liver, and thus a decrease in circulating blood cholesterol. LDL cholesterol levels are thus reduced by 20 to 50%, and HDL levels may increase slightly.

Another effect of statins is inhibition of smooth muscle cell proliferation in the vessel wall, improvement of endothelial cell function, stabilization of the atherosclerotic plaque, it also has antiplatelet and anti-inflammatory effects.



Chemical formula of lovastatin

## Pharmacokinetics

About 30 % of the administered dose is absorbed from the intestine, statins are taken up by the liver, where they are metabolized and then excreted by the bile.

Statins have both lipophilic (simvastatin, atorvastatin) and hydrophilic representatives (rosuvastatin). In addition, some are substrates of P-glycoprotein and CYP3A4, which carries the risk of drug interactions. This is especially true for lipophilic agents, which must be converted to hydrophilic compounds during elimination.

The effect of statins is determined by the concentration at the site of action (hepatocytes). Their transfer to hepatocytes is facilitated by the OATP1B1 pump (organic anion transporting polypeptide), which is polymorphic (dysfunctional in up to 15% of the population), which poses a higher risk of side effects and a lower therapeutic effect for patients.

Simvastatin, for example, has more side effects and, in addition, less therapeutic effect due to low bioavailability and short half-life. Rosuvastatin, on the other hand, is one of the most effective statins (hydrophilic, more available, less side effects, 90% bound to plasma proteins).

## Indications

The main indication for statin therapy is the treatment of hypercholesterolemia, as well as the achievement of target LDL cholesterol levels in high-risk patients with normal cholesterolemia. They are used in the treatment of familial hypercholesterolemia type IIa. With statin therapy, up to a 40 % reduction in LDL-cholesterol levels can be achieved (in combination with ion exchangers up to 60 %). According to current recommendations, patients with acute coronary syndrome seek to reduce LDL levels by at least 50% of baseline values. In high-risk patients even below 1.4 mmol / l.

## Contraindications

Pregnancy, lactation, childhood, myopathy, allergies.

## Side effects

Side effects occur in up to 3% of patients with statin therapy. Some of them can be solved by simply reducing the dose or changing the prescribed product. However, it is necessary to properly educate patients and think about rare, but potentially very serious complications in the form of rhabdomyolysis and subsequent renal failure. Patients with significant drug interactions are at risk, which at the level of CYP enzymes (verapamil, citrus juices, some ATBs, antifungals), glycoprotein P or OATP1B1 increase the exposure of mainly lipophilic statins.

According to some studies, statin treatment significantly reduces coenzyme Q10 (cholesterol is a precursor of CoQ10), which may be a factor in some of the side effects listed below (myopathy, rhabdomyolysis, neuropathy) – probably due to damage to membrane structure.

- Increased activity of aminotransferases (regular checks) and creatine kinase;
- myalgia (usually not a reason to discontinue therapy, dose reduction or statin change is sufficient);
- severe skeletal muscle myopathy with pain, high creatine kinase activity and hyperkalemia; necessary interruption of therapy, otherwise the possibility of transition to rhabdomyolysis with myoglobinuria and renal failure - these conditions may rarely occur in monotherapy, the much higher incidence is reported in combination with CYP3A4 inhibitors (erythromycin, SSRI, azole antifungals, fibrates, cyclosporine);
- polyneuropathy - predilection for HD (up to 10% of patients?);
- tendinitis, tendon ruptures (t. Achillei, m. quadriceps, m. biceps femoris);
- sleep disorders (up to 10 %?);

- cataracts;
- CNS bleeding;
- increased risk of DM.

**Due to the above findings, some professional societies recommend substituting coenzyme Q10 in statin therapy.** Especially with long-term therapy, in the event of an emergency or with an increased risk of cellular damage.

### Representatives (by increasing lipid-lowering efficacy)

- **pravastatin** tbl.10 a 20 mg,
- **lovastatin**,
- **fluvastatin** (ve formě s prodlouženým účinkem),
- **simvastatin** tbl. 10–40 mg,
- **atorvastatin** tbl. 10, 20 a 40 mg,
- **rosuvastatin** tbl. 10, 20 a 40 mg.

## References

### Related articles

- Statin myopathy
- Hypolipidemics
- Lipoproteins

### References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### External links

- Statiny (Czech wikipedia)
- Statin (English wikipedia)

### Source


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