

# New drug candidate reduces blood lipids

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People whose "bad" cholesterol and risk of future heart disease stay too high despite cholesterol-lowering statin therapy can safely lower it by adding a drug that mimics the action of thyroid hormone. In a report published in the Mar. 11, issue of the *New England Journal of Medicine*, Johns Hopkins and Swedish researchers say an experimental drug called eprotriome lowered cholesterol up to 32 percent in those already on statins, an effect equal to that expected from doubling the statin drug doses, without harmful side effects.

The researchers caution that the results don't suggest that eprotriome will or should replace statins, which are the current gold standard for treating high LDL cholesterol. However, the results of their small trial on 168 patients do suggest that eprotriome may eventually be a promising addition to statin therapy, a substitute for statins in people who can't tolerate their side effects, or a novel treatment for mixed dyslipidemia, a condition in which people have high levels of lipids other than cholesterol such as triglycerides or apolipoprotein B (apo B).

The researchers found that eprotriome lowered blood lipids that are little affected by statin therapy but known to increase the risk for cardiovascular disease, including triglycerides and lipoprotein A (Lp(a)).

"This drug represents a new class of medications that might offer hope to those at risk of future cardiovascular disease whose lipid profiles are not effectively altered with statin therapy, and perhaps for about a quarter of those who have tried statins but cannot tolerate their side effects," says study leader Paul W. Ladenson, M.D., professor of

endocrinology and metabolism at the Johns Hopkins University School of Medicine.

Ladenson is a consultant to Karo Bio, maker of eprotirome.

Researchers have long known that thyroid hormones, produced by the butterfly-shaped thyroid gland in the neck, act on numerous tissues in the body. One organ affected profoundly by thyroid hormones is the liver, which processes lipids, including cholesterol. Ladenson says previous research has shown that when people have abnormally high levels of thyroid hormones owing to a diseased thyroid gland, they tend to have low levels of bad, or LDL, cholesterol. However, high levels of a person's natural thyroid hormones also come with potentially dangerous side effects, including increased heart rate and irregular heart rhythms, loss of bone mass, and other troubling symptoms.

Seeking to seize upon thyroid hormones' benefits while avoiding these side effects, Ladenson and his colleagues tested eprotirome, a thyroid hormone mimetic developed by Swedish pharmaceutical company Karo Bio, on 168 patients at 15 sites in Sweden and Norway. All of the patients had been treated with statins for at least three months prior to the study start, but still had an LDL cholesterol higher than recommended, 116 mg/deciliter, with a mean level of 141 mg/deciliter (an optimal LDL measurement is considered less than 100 mg/deciliter).

These volunteers started the study with a four-week lead-in on a diet developed by the U.S. National Institutes of Health to reduce cholesterol. Continuing this diet, for the next 12 weeks, the patients took a placebo or 25, 50, or 100 mg of eprotirome in addition to whatever statin they had already been taking. The researchers then analyzed the patients' levels of LDL cholesterol, HDL (or "good") cholesterol, triglycerides, apo B, and Lp(a).

The researchers found that among the patients taking the 25, 50 or 100 mg doses of eprotirome reduced their LDL cholesterol levels by 22 percent, 28 percent, and 32 percent respectively, compared to only 6.5 percent in those taking placebo. Remarkably, they also found similar dose-related reductions in triglycerides, apo B, and Lp(a).

They also found modest reductions in HDL cholesterol of approximately 3 percent. Low HDL has been associated with increased cardiovascular disease risk, since HDL levels reflect how much artery-blocking cholesterol is being ferried away from blood vessels and back to the liver. However, Ladenson says he and his colleagues believe this small decrease could reflect the livers' increased processing of cholesterol in general, which could actually lower cardiovascular disease risk.

When the researchers evaluated study subjects for the harmful side effects that can accompany increased thyroid hormone, they found no indications of increased heartbeat abnormalities, increased bone turnover, or other symptoms of thyroid hormone excess.

Ladenson adds that though previous studies have shown that high levels of Lp(a) are associated with an increased risk of cardiovascular disease, no drug existed to lower this lipid.

"Although we've long known a high Lp(a) is strongly associated with increased risk of future cardiovascular disease, we've had no idea if lowering Lp(a) actually diminishes cardiovascular disease risk," he says. "We can finally address this question with this drug."

**More information:** 'Use of the Thyroid Hormone Analog Eprotirome in Statin-Treated Dyslipidemia', Paul W. Ladenson, Jens D. Kristensen, E. Chester Ridgway, Anders G. Olsson, Bo Carlsson, Irwin Klein, John D. Baxter and Bo Angelin, New England Journal of Medicine (NEJM), 10 March 2010. Read abstract:

[content.nejm.org/cgi/content/short/362/10/906](https://content.nejm.org/cgi/content/short/362/10/906)

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