



Apolipoprotein A-I mimetic improves HDL anti-inflammatory function

Administration of the apolipoprotein A-I (apoA-I) mimetic peptide D-4F improves anti-inflammatory activity of high-density lipoprotein (HDL) in patients at high risk of coronary heart disease. These data suggest that this agent may have therapeutic potential for attenuation of atherosclerosis.¹

ApoA-I is the main protein in HDL and is known to have anti-inflammatory and anti-oxidant activity, which protect against atherosclerosis. Administration of apoA-I mimetic peptides represents a promising strategy for improving HDL metabolism, raising HDL cholesterol levels and preventing atherosclerosis. However, as apoA-I and other apoA-I mimetics are rapidly degraded by the digestive system, oral administration is not feasible. D-4F is a synthetic apoA-I mimetic that is not degraded in the same way and can therefore be administered orally. Experimental studies have shown that oral administration of D-4F markedly reduces atherosclerosis in mice.

Researchers at the University of Pennsylvania, USA assessed the safety, tolerability, pharmacokinetics and pharmacodynamics of a single oral dose of D-4F or matching placebo in 50 patients with coronary heart disease or equivalent risk. Ten subjects per dose group were randomised to 30, 100, 300, or 500 mg D-4F or matching placebo (8 subjects received D-4F and 2 received placebo in each group) and fasted for 2 hours after study drug administration. A further 10 subjects received 500 mg or matching placebo with a standardised meal.

Administration of D-4F resulted in significant improvement in the HDL anti-inflammatory index at 2, 4, and 8 hours compared to baseline ($p < 0.01$ for all time points), whereas the placebo group had no significant change. The bioavailability of D-4F improved when food was delayed for 2 hours post-dose. Treatment was well tolerated.

The researchers concluded that D-4F was orally bioavailable and had measurable effects on HDL anti-inflammatory function in high-risk patients after a single dose.

Reference

1. Rader DJ. Oral administration of the apolipoprotein A-I mimetic peptide D-4F in humans with CHD improves HDL anti-inflammatory function after a single dose. Presented at the American Heart Association Scientific Sessions 2006, Abstract 1496.