

Effects of Palmitoleic Acid on HDL levels and Cholesterol Deposition in Apo-E Mice

Research sponsored by Tersus Pharmaceuticals, LLC and performed at the Heart & Vascular Institute, Cleveland Clinic Foundation, Cleveland, Ohio, USA

Background & History of Development:

The beneficial effects of naturally-derived fatty acids in cardiovascular diseases have increasingly been recognized. Natural products are usually overlooked by traditional pharmaceutical companies for commercial development because they often lack patent appeal – not because they fail to possess a beneficial pharmacologic profile. It is unlikely that the Omega 3's are the only fatty acids with pharmacologic activity. To this end, Tersus Pharmaceuticals hypothesized that Omega 7 (palmitoleic acid; C16:1n7) may have activity against the development of atherosclerotic plaque and evaluated this compound in the Apo-E mouse model of atherosclerosis. Apo-E mice are genetically engineered to develop arterial plaque and cholesterol deposits.

Methods:

This randomized, blinded, controlled study was performed at the Cleveland Clinic by nationally-known and respected researchers. Two groups were studied – a control group that received no Palmitoleic acid and those who received Palmitoleic acid as part of their diet. HDL cholesterol levels were tracked during the study and the animals were sacrificed at 12 weeks. Their aortas and aortic roots were examined for the development of plaque and cholesterol deposition development. This method is essentially the same model utilized to qualify many cardiovascular disease drugs.

Results:

The treated animals showed dramatic reductions in aortic cholesterol deposition versus control. Aortic root cross-sections showed a virtual absence of atheroma formation after treatment with Palmitoleic acid. Additionally, treated animals showed an 85% increase in HDL levels. Equally impressive, a consistent antiatherogenic effect was seen in 100% of mice in the study as measured by the aortic root lesion area (mm²).

Conclusions & Implications:

Dramatic effects on HDL and plaque were seen within the group treated with Palmitoleic acid in this standard animal model. Palmitoleic acid should have a similar positive impact on humans with further research being warranted. The exact mechanism of action is not fully characterized and is undoubtedly multifactorial. As contributory factors in addition to effects on HDL, it has been documented in other international research studies that Palmitoleic acid also possesses strong anti-inflammatory activity causing a translationally-mediated decrease in TNF-alpha and an inhibition of MCP1 (monocyte chemoattractant protein), both of which are critical to the formation of atherosclerotic plaque.

Tersus Pharmaceutical believes it would be advantageous to all to have more attention given to natural substances and their potential efficacy against cardiovascular diseases as they characteristically carry a minimalistic side effect profile and are more cost-effective to our healthcare system, especially given the safety challenges seen with synthetic small molecules over the past several years.