

New Study Finds Astaxanthin Is Potent Inhibitor of Oxidation in C ell Membrane Model

Data supports platform for development of new class of cardiovascular drug

A study by Harvard researcher R. Preston Mason and colleagues at Elucida Research demonstrates that astaxanthin, a naturally occurring compound, shows promise as the scaffold for antioxidant/anti- inflammatory agents for the treatment of CV disease. Astaxanthin could be the basis for a first in class treatment for the inflammatory component of CV disease not fully addressed by current therapies.

Honolulu, HI, January 4, 2007: A just-published research study by Dr. R Preston Mason and colleagues at Elucida Research has determined that astaxanthin, a relatively unknown carotenoid found in nature, shows significant promise as a viable scaffold for a new therapy to treat cardiovascular disease based on its exceptional antioxidant properties in membrane models.

Combined with published proof-of-concept, pre-clinical and anecdotal human data, the results of the Mason study (*Differential effects of carotenoids on lipid peroxidation due to membrane interactions; xray diffraction analysis* by McNulty et al.) signify that astaxanthin exhibits potential utility for use as the scaffold for antioxidant/anti- inflammatory agents in the treatment of cardiovascular and other chronic inflammatory diseases. An astaxanthin derivative may improve, or augment, the restoration of the cellular oxidation balance (i.e. redox status) of mitochondria and cell signaling pathways upstream from the point that produces activation of bioactive inflammatory mediators.

"These data clearly demonstrate a differentiation within the carotenoid class of medically promising antioxidants and provided, in part, the impetus for Cardax Pharmaceuticals to advance an astaxanthin-based derivative into an IND development program," according to Fredric Pashkow, Executive Vice President and Chief Medical Officer of the Company and former head of U.S. Medical Affairs for cardiovascular drugs at Sanofi-Aventis.

Pashkow also said that the work from Mason's lab suggests astaxanthin could provide a platform for discovery of an entirely new class of safe, cardiovascular drugs. "These potent antioxidants may be the third big wave in the modern therapy for the secondary prevention of heart attack and stroke. In the heart, these agents probably will work by recalibrating the cellular oxidation balance in order to blunt the cell and tissue inflammatory response to injury and limit damage to the myocardium."

In addition, by limiting the amount of oxidative damage to LDL, the "bad cholesterol," an astaxanthin derivative could alter the progress of atherosclerosis, the underlying inflammatory process that clogs arteries and is responsible for most heart attacks and

strokes when an atherosclerotic plaque ruptures.

Pashkow maintains that statins represented the "first big wave" of cardiovascular preventive therapy. They proved to lower the risk of a second heart attack or cardiovascular death by 45% over 5 years, though more than half of the people treated did not realize their benefit. Increasing the dose of the statin improves the outcome and extends the benefits to people who have risk factors alone such as high cholesterol, but dose limiting side effects emerge especially when the drugs are taken for a long time.

Pashkow said that the recent problems encountered with Pfizer'storcetrapib highlight the impact of a late stage pipeline non-approval combined with the looming patent expiry of the current market leading therapy.

Antiplatelet therapies, particularly aspirin and aspirin in combination with other antiplatelet agents represent the "second big wave" of preventive therapies following a heart attack. In combination, they reduce the risk of future heart attacks and strokes by about 30% over a one-year period.

However, an appreciable segment of the population are 'resistant' to antiplatelet therapy and remain relatively unprotected. More potent antiplatelet therapies, or increased doses of aspirin increase the risk of bleeding. "This wave of treatments," said Pashkow "may be peaking as well."

Cardax Pharmaceuticals is exploring the use of astaxanthin and novel astaxanthin derivatives, as well as other carotenoids, for use as medical therapeutics (i.e. antioxidant/anti-inflammatory) in disease states characterized by abnormal cellular oxidation and chronic inflammation (e.g. cardiovascular, liver, ocular, prostatic and neurodegenerative diseases).

To read *Differential effects of carotenoids on lipid peroxidation due to membrane interactions; x-ray diffraction analysis* by Dr. McNulty et al. visit <u>http://dx.doi.org/10.1016/j.bbamem.2006.09.010</u>

To read more about Cardax go to <u>www.cardaxpharma.com</u>or contact Dr. Fredric J. Pashkow, MD at <u>fpashkow@cardaxpharma.com</u>.