Disodium Disuccinate Astaxanthin (Cardax™): Antioxidant and Antiinflammatory Cardioprotection

Samuel F. Lockwood¹ and Garrett J. Gross²

¹Hawaii Biotech, Inc., Aiea, Hawaii, USA
²Department of Pharmacology and Toxicology, Medical College of Wisconsin, Milwaukee, Wisconsin, USA

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ABSTRACT

Disodium disuccinate astaxanthin (Cardax™, DDA) has cardioprotective effects in the rat, rabbit, and canine models of experimental infarction. It is highly effective by parenteral administration in subchronic and acute dosing regimens. Unpublished data in rats suggest that oral cardioprotection is also readily achievable. DDA-induced myocardial salvage in the canine can reach 100% with a 4-day subchronic dosing regimen. At a single i.v. dose DDA is cardioprotective, when given 2 h before experimental coronary occlusion, but the protection is on the average two-thirds of that achieved with the subchronic regimen in dogs. In conscious animals DDA has no effects on hemodynamic parameters. The primary mechanism of cardioprotection appears to be antioxidant activity involving direct scavenging of superoxide anion, the lynchpin radical in ischemia-reperfusion injury. In addition, modulation of serum complement activity, as well as the reduction in the levels of C-reactive protein (CRP) and the membrane attack complex (MAC) in infarcted tissue suggest a significant antiinflammatory component in the mechanism of cardioprotective action of DDA. Stoichiometric binding of the meso-form of the compound to human serum albumin (HSA) has been demonstrated in vitro. This binding capacity overcomes the supramolecular assembly of the compound in aqueous solution, which by itself improves the stability and shelf life of aqueous formulations. Non-esterified astaxanthin readily enters cardiac tissue after either oral or parenteral administration, providing a reservoir of a cardioprotective agent with a significant half-life due to favorable ADME in mammals. Due to the well-documented safety profile of non-esterified astaxanthin in humans, disodium disuccinate astaxanthin may well find clinical utility in cardiovascular indications in humans following successful completion of preclinical and clinical pharmacology and toxicology studies.