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Novel astaxanthin prodrug (CDX-085) attenuates thrombosis in a mouse model.

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Abstract

BACKGROUND: Cardiovascular disease remains the leading cause of morbidity and premature mortality in most industrialized countries as well as in developing nations. A pro-oxidative state appears to promote and/or exacerbate vascular disease complications. Furthermore, a state of low-grade chronic inflammation can promote increased oxidative stress and lead to endothelial cell and platelet dysfunction ultimately contributing to thrombogenesis.

OBJECTIVES: In this study, the effect of a proprietary astaxanthin prodrug (CDX-085) on thrombus formation was investigated using a mouse model of arterial thrombosis. The influence of free astaxanthin, the active drug of CDX-085, on human endothelial cells and rat platelets was evaluated to investigate potential mechanisms of action.

METHODS AND RESULTS: Oral administration of CDX-085 (0.4% in chow, approximately 500 mg/kg/day) to 6-8 week old C57BL/6 male mice for 14 days resulted in significant levels of free astaxanthin in the plasma, liver, heart and platelets. When compared to control mice, the CDX-085 fed group exhibited significant increases in basal arterial blood flow and significant delays in occlusive thrombus formation following the onset of vascular endothelial injury. Primary human umbilical vein endothelial cells (HUVECs) and platelets isolated from Wistar-Kyoto rats treated with free astaxanthin demonstrated significantly increased levels of released nitric oxide (NO) and significantly decreased peroxynitrite (ONOO-) levels.

CONCLUSION: Observations of increased NO and decreased ONOO- levels in endothelial cells and platelets support a potential mechanism of action for astaxanthin (CDX-085 active drug). These studies support the potential of CDX-085 and its metabolite astaxanthin in the treatment or prevention of thrombotic cardiovascular complications.

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