Astaxanthin Reduces Hypertension

Epidemiological and clinical data suggest that dietary carotenoids such as astaxanthin may protect against cardiovascular disease (CVD) which includes hypertension. This condition is associated with blood vessel dysfunction, altered contractility and tone; mediated by relaxant (nitric oxide NO; prostacyclin) and constrictor factors (thromboxane; endothelin) in the blood. Furthermore, blood flow properties serve an important role in the pathological complications seen in atherosclerosis and coronary heart disease. Research presented here suggests that astaxanthin may be a useful as part of an antioxidant therapy to alleviate hypertension (Figure 1).

Reduction of Arterial Blood Pressure

An early study involving a composition of carotenoids have been used against hypertension or high blood pressure (BP), but Hussein et al., (2005a) published the first study involving astaxanthin with spontaneously hypertensive rats (SHR) and stroke prone (SHR-SP). This study investigated the effects of astaxanthin on the aortic vessel blood pressure (BP) in relation to endothelium and nitric oxide (NO) to elucidate mechanism and response. The arterial BP in hypertensive rats (N=5-6, p<0.05) fell by almost 10% when they were treated with 50 mg astaxanthin/kg/day for two weeks. Long term supplementation in SHR-SP rats revealed that 5 mg/kg/day also had the same effect as 50 mg/kg/day (8-9% BP reduction, N=5, p<0.001). At the same time, the control group BP increased by 8% at week 5. Two further studies (N=5-8) by Hussein et al., (2005b and 2006) confirmed this observation by reducing BP almost 16% (p<0.001) at 7 weeks in SHR (Figure 2). Furthermore, astaxanthin had no effect on the normal blood pressure in healthy rats.

Interestingly, the authors reported a 50% reduction of incidence of stroke in the treated (50 mg/kg/day) SHR-SP group compared to the control group after 14 days. (Hussein et al., 2005a).

In addition, astaxanthin treated mice also showed significant neuroprotective effects at relatively high doses by preventing the ischemia-induced impairment of spatial memory in mice negotiating a water maze (Hussein et al., 2005a). This effect is suggested to be due to the significant antioxidant property of astaxanthin on ischemia-induced free radicals and their consequent pathological cerebral and neural effects. The neurological protection of astaxanthin during ischemia was also confirmed in an earlier study by Kudo et al., 2001.

Mechanism of Anti-hypertension

The antihypertensive mechanism may be in part explained by the changes of vascular reactivity and hemorheology.

Microchannel Array Flow Analysis (MC-FAN) measured a significant increase of blood flow of 11% (Figure 3) in the astaxanthin treated group (N=6-7, p<0.05). Although plasma fluidity is largely influenced by fibrinogen, in this study, the fibrinogen levels did not change and therefore, the improved deformation and reduced blood aggregation are the likely mechanisms (Hussein et al., 2005b). This is supported by Miyawaki et al., (2005) who also used the MC-FAN to demonstrate...
the significant improvement of blood flow (N=10, p<0.05) in humans treated with 6 mg astaxanthin for 10 days (Figure 4).

A systematic investigation in both relaxant and constrictor responses revealed that astaxanthin can restore the NO dependent relaxation and sensitivity to constriction mechanisms (Figure 5). Astaxanthin reduced sensitivity to angiotensin II (AngII) which is involved in vessel contraction, and scavenged ROS which would normally hinder nitric oxide (NO) dependent dilation (Hussein et al., 2005b, 2006a, 2006b).

Astaxanthin treatment also maintained the structural composition of the vessel wall structure. Hypertension normally produces thick walled vessels which alter stiffness and internal volume; thereby reducing volume of blood flow and increasing pressure. Astaxanthin treated rats were protected from such structural changes (Figure 6) as seen in the reduction of number of branched elastin bands (p<0.001) and improved vessel wall to lumen thickness ratio (p<0.01). Li et al., (2004) substantiated the same structural preservation effect after treating hyperlipidemic rabbits (WHHL) with astaxanthin. The intactness of the internal elastic membranes of aortic segments was an important gauge of atheroma.

Figure 4. Astaxanthin (6 mg/day) supplementation for 10 days improves blood flow in humans as tested by MC-FAN. *p<0.01 vs. start; #p<0.05 vs control. Miyawaki et al., 2005,

Figure 5. Astaxanthin increases relaxant and reduces constrictor mechanisms to help reduce blood pressure in SHR.

Figure 6. A) Coronary artery wall is thinner and lumen is wider in astaxanthin treated rats. B) Elastin bands are also fewer in number and smoother compared to the control groups. Hussein et al., 2006.

A. Arterial wall of control and astaxanthin groups. Staining: hematoxylin-eosin. Magnification: 20x

B. Sections of the aorta of control and astaxanthin groups showing elastin bands. Staining: Verhoff’s. Magnification: 40x.

Outlook

The oxidative status and physiological condition during hypertension are successfully mediated by astaxanthin. The mechanisms of action include improved blood rheology, modulation of constrictor and dilator factors and blood vessel remodelling. Although, these findings are based on spontaneous hypertensive rat models, these serve as a solid basis for extending the hypothesis to human clinical trials.

References