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 useful as part of an antioxidant therapy to alleviate hypertension (Figure 1).

Figure 1. Mechanisms by which Astaxanthin reduces hypertension

- Maintains vessel integrity
- Anti-hypertension
- Restoration of Vessel Dilatation & Constriction
- Improved Blood Rheology

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 2006a) 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.

In a double blind controlled placebo study conducted in Japan, 20 healthy postmenopausal women, who ingested 12 mg everyday for 4 weeks, reduced their systolic and diastolic blood pressure by 7% and 4% (p<0.05) respectively (Iwabayashi et al., 2009). Another study conducted by Preuss et al., (2009), Zucker fatty rats fed with 25mg/kg of astaxanthin reduced their systolic blood pressure (SBP) by 9% in just 12 days and 13% (p<0.01) after 75 days (Preuss, et al., 2009). In the same study rats fed with 5 mg/kg of astaxanthin reduced their SBP by 7% (p<0.05) in 30 days compared to control group. 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).

The study 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 of astaxanthin post-treatment period. (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 neuronal protection of astaxanthin during ischemia was also confirmed in an earlier study by Kudo et al., (2001).

Figure 2. Astaxanthin (5mg/kg/day) treated SHR reduced mean blood pressure. Hussein et al., 2005b.

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).

In a human study conducted by Iwabayashi et al., (2009), 20 healthy women who ingested 6mg / day for 8 weeks increased ABI (ankle brachial pressure index) by 4% suggesting a reduction of lower limb vascular resistance. Another human study also prove that oral administration of 6 mg/day of astaxanthin for 10 days enhanced capillary blood flow by 10% (p<0.05) in 7 healthy individuals compared to control group (Miyawaki et al., 2008) (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 (Hussein et al., 2005b, 2006a, 2006b). The rennin angiotensin system regulates blood pressure and water (fluid) balance. Renin stimulates the production of which causes blood vessels to constrict, resulting in increased blood pressure. This is also a factor that leads to atherosclerosis – the restriction and hardening of the arteries. Rats administered with 50 mg/kg of astaxanthin show sharp improvements in all parameters measuring the rennin angiotensin system activity-losartan (36%; p<0.05), ACE activity (19%; p<0.05) and Angio II (14%; p<0.05). Decrease in angiotensin lead to direct and indirect decrease in free radicals, which in turns increase nitric oxide production in the vessels, inducing vasodilatation and therefore decreasing blood pressure.

Indeed, Hussein et al., (2006b) demonstrated that 5 mg/day of astaxanthin for 7 weeks decreased vascular wall thickness by 47% (p<0.05) improved vascular tone (elastin) by 36% in spontaneously hypertensive rats (Hussein et al., 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 the 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 3. Astaxanthin (5 mg/kg/day) treated SHR improved blood flow tested by MC-FAN. Hussein et al., 2005b.

Figure 4. Astaxanthin (6 mg/day) supplementation for 10 days improves blood flow in humans as tested by MC-FAN. 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., (2006a).

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