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Research Article

Effect of Astaxanthin Supplementation on Cardiorespiratory Function in Runners

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Abstract

Purpose: Marine microalgae is the predominant source of natural astaxanthin (NAX), a red-orange carotenoid with powerful antioxidant and anti-inflammatory properties. Studies in both rodents and humans suggest that NAX supplementation improves antioxidant capacity and reduces oxidative stress, while also improving fat utilization and exercise endurance. The purpose of this study was to assess the effects of a moderate dose of NAX supplementation (12mg/day for 8 weeks) on cardiorespiratory function during both higher and lower intensity exercise in recreational runners.

Patients and Methods: Using a double-blind parallel design, 28 recreational runners (male = 14, female = 14, age = 42) were supplemented with NAX (*Haematococcus pluvialis algal extract*) or a placebo. Before and after the supplementation period, subjects performed a maximal running test (VO2max on treadmill) and a maximal cycling test (watts on cycle ergometer).

Results: There was no improvement in maximal oxygen uptake (running VO_2 max) or maximal power output (cycling watts) with NAX supplementation. However, subjects in the NAX group showed a significant ~10% lower average heart rate at submaximal running intensities compared to placebo (aerobic threshold, AeT; NAX 130+17 v. PL 145+14; and anaerobic threshold, AT; NAX 139+20 v. PL 154+11, $p < 0.05$).

Conclusion: Supplementation with 12 mg/day of NAX for 8 weeks reduced average heart rate at submaximal endurance intensities (AeT and AT), but not at higher "peak" intensities. These results suggest that NAX may be a beneficial ergogenic aid for long/ultra-distance endurance athletes, but not necessarily for athletes competing in shorter higher intensity efforts. In addition, these data are also suggestive of a general "cardiotonic" effect of NAX, that should be investigated in non-athletic populations including elderly subjects and those with cardiac complications including post-myocardial infarction, heart failure, statin usage, mitochondrial dysfunction, chronic fatigue, and related conditions.

Keywords: *Antioxidant; Cardiovascular; Carotenoid; Athlete; Endurance*

Introduction

Natural astaxanthin (NAX) is a red-orange carotenoid that provides pink flamingo feathers, pink shrimp shells, and red salmon flesh their characteristic colors. The high level of NAX in these tissues is reflective of the animal's dietary intake of NAX from microalgae,

copepods, krill, and other lower food chain organisms [1,2]. The primary dietary source of astaxanthin for humans is from seafood such as salmon, shrimp, crabs, lobster [3-5]. NAX can exist in 3 sterioisomeric forms (ambati), two chiral (3S/3'S and 3R/3'R), and one meso (3R/3'S) that exist in nature in variable ratios depending on the diet of the animal (e.g. wild salmon consuming natural algae versus farmed salmon consuming synthetic AX). Synthetic astaxanthin (SAX), derived from petrochemicals and approved as a food coloring for fish aquaculture, is equimolar in (3R/3'S), resulting in farmed salmon having high levels of synthetic 3R/3'S, while wild salmon have predominantly 3S/3'S [6].

NAX can be produced commercially from the microalgae *Haematococcus pluvialis* (*H. pluvialis*) and is the only source currently approved for human consumption [6] by both the FDA and EFSA (both in dried form or extracted with ethanol or supercritical CO_2). *H. pluvialis* as a source of NAX provides the benefits of esterified 3S/3'S astaxanthin stereoisomers (96% of carotenoids) plus other naturally-occurring carotenoids (beta-carotene, lutein, zeaxanthin), which may provide synergistic benefits and improved absorption compared to SAX [7,8].

NAX has been studied for its antioxidant, anti-inflammatory, and cardioprotective activities in humans [9-13]. Rodent studies have further shown NAX to reduce blood pressure and improve blood flow [14,15], possibly via modulation of cellular stress pathways, including nuclear factor kB (NFkB), nuclear factor E2 related factor 2 (Nrf2), and nitric oxide [16].

With respect to exercise effects, astaxanthin has shown positive results for reducing lactic acid accumulation, increasing fat oxidation, and improving endurance performance with most studies demonstrating benefits [17-24].

Material and Methods

Participants

We recruited 30 recreational runners, evenly split between males and females. Two subjects, one from each group, withdrew from the study due to inability to complete the training regimen, resulting in 28 subjects completed the 8-week supplementation period (age 42 ± 8, range 26 - 63 years; height 169¬+10 cm; BW 69¬+¬6 kg). Runners were recruited based on their desire to train for and compete in a mountainous half-marathon trail race (Snowbird Ski Resort, Utah, USA) and to consume a commercially-available dietary supplement containing 12 mg/day of natural astaxanthin (or placebo). All participants completed informed consent documents approved by an external ethics review board.

Dietary Supplement

Participants were randomly divided in double-blind fashion into two groups to receive the natural astaxanthin (NAX) supplement (AstaZine® Natural Astaxanthin, BGG/AlgaeHealth Sciences) or matching placebo (PL). The NAX supplement provided 12 mg/day of natural astaxanthin extracted with ethanol from *Haematococcus pluvialis* suspended in edible MCT oil (medium chain triglyceride) with d-alpha tocopherol as an antioxidant. Subjects consumed NAX or PL daily for 8 weeks. No adverse events related to the dietary supplement were reported.

Training Program

During the 8-week supplementation period, subjects participated in a gradually-progressive trail running training program designed to ensure success in completing the half-marathon target event. Weekly mileage and specific workouts were recommended for each of the 8 weeks (e.g. hills, intervals, long runs). To enhance compliance with the supplementation regimen, participants also attended weekly educational seminars covering topics related to training, diet, and recovery.

Performance Assessment

Before and after the supplementation period, subjects performed a maximal running test (VO_2max on a treadmill, CardioCoach, Korr Medical Technologies) and a maximal cycling test (watts on a cycle ergometer, Spinner Blade Ion). We also measured body composition by bioelectrical impedance analysis, including body weight, body fat percentage, and basal metabolic rate (Tanita TBF-350).

Participants performed all three assessments (running VO_2max, body composition, and cycling watts) in a single visit at baseline and week 8. Pre-assessment diets were not controlled, but subjects were instructed to eat as they would prior to a race, and maintain diet consistency the day before and day of each assessment. The VO_2max test was performed first, followed by body composition and survey completion, followed by cycling watts test. This format was selected to maximize time efficiency and minimize laboratory visits for subjects. Each visit lasted approximately 60 minutes and allowed a rest period between running/cycling efforts of approximately 20 minutes, which our participants felt was adequate to allow them to perform optimally on each physical test.

The running VO_2max assessment was designed for participants to reach maximal oxygen consumption and voluntary fatigue within 15 minutes. The protocol consisted of a gradual warmup of self-selected easy jogging, followed by progressive increases in speed and incline each minute until exhaustion. Heart rate (beats per minute, bpm) and oxygen consumption (ml/kg/min) were recorded at maximum and at two submaximal levels (aerobic threshold, AeT and anaerobic threshold, AT). The cycling watts assessment was performed as a 20-minute time trial with participants instructed to generate their highest average watts with self-selected workload and target pedal cadence of 90 rpm (range between 80 - 100 rpm).

Data Management and Analysis

All participant data was maintained in a central location and transcribed to a central database. Data were identified by subject number and examined for accuracy and completeness. Tabulated data were analyzed with JMP 8.0 (SAS Institute, Cary, NC) using standard parametric paired t tests, and significance was assessed with a 2-tailed alpha level set at 0.05.

Results

Subject baseline characteristics are presented in table 1. There was no improvement in maximal oxygen uptake (VO_2max while running) or maximal power output (watts while cycling) with NAX supplementation (Figure 1). However, subjects in the NAX group showed a significant ~10% lower average heart rate at submaximal running intensities (aerobic threshold and anaerobic threshold) compared to both pre-supplementation values and compared to placebo (Figure 2), suggesting a profound "cardiotonic" effect of AX supplementation with superior metabolic efficiency at submaximal aerobic endurance intensities, but not at maximal efforts. At submaximal running intensities, aerobic threshold (AeT) and anaerobic threshold (AT) heart rates were significantly lower post-supplementation in NAX versus PL (AeT; NAX 130 ± 17 v. PL 145 ± 14; and AT; NAX 139 ± 20 v. PL 154 ± 11, $p < 0.05$). There were no significant changes in body composition in either group (Table 1).

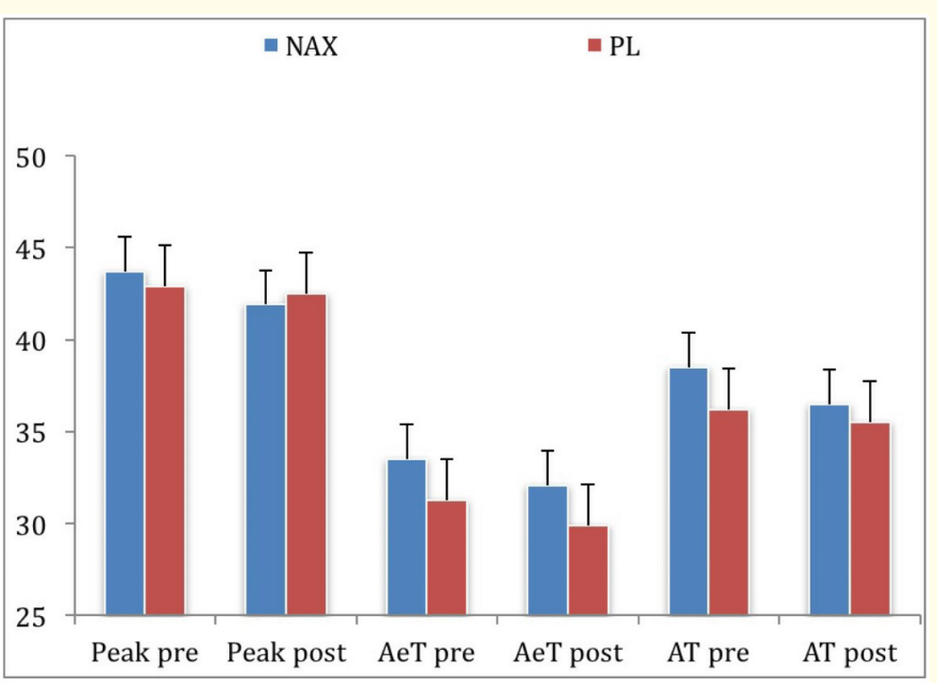

Figure 1: *Oxygen consumption at baseline (pre-supplementation) and week 8 (post-supplementation). There were no significant differences in absolute oxygen consumption at any time point. Abbreviations: NAX: Natural Astaxanthin Group; PL: Placebo Group; pre: Baseline; post: Week 8; Peak: Maximal Oxygen Consumption; AeT: Aerobic Threshold; AT: Anaerobic Threshold*

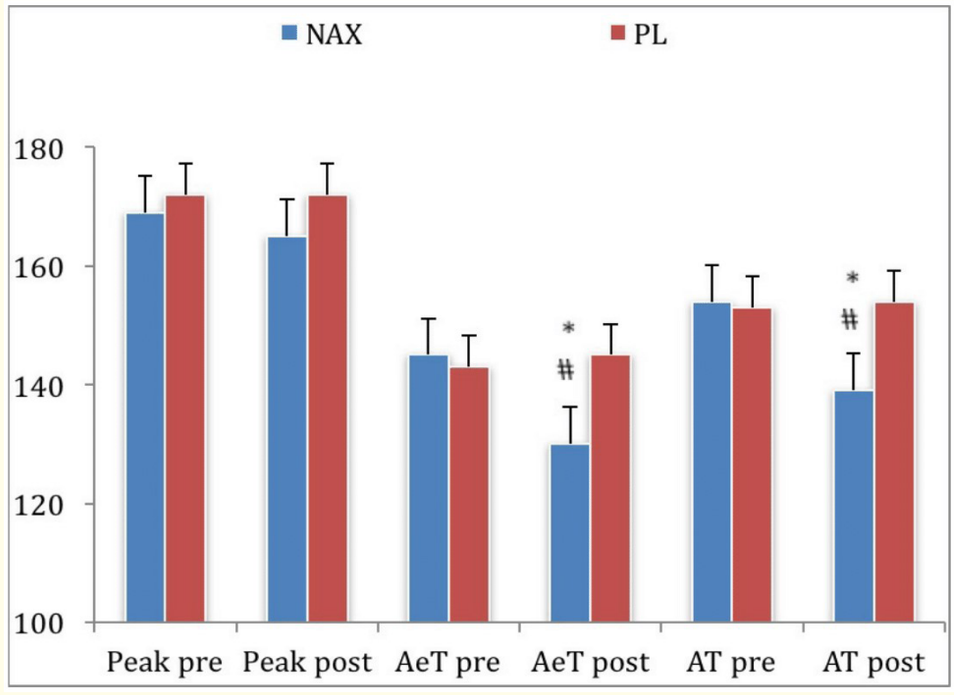

Figure 2: *Heart Rate at baseline (pre-supplementation) and week 8 (post-supplementation). At submaximal running intensity (AeT, aerobic threshold and AT, anaerobic threshold), the NAX group had significantly lower heart rate (HR) compared to pre-supplementation values (*) and compared to placebo (PL) values (#, both p<0.05) after 8 weeks (post) of supplementation with 12mg/day of natural astaxanthin.*

Abbreviations: NAX: Natural Astaxanthin Group; PL: Placebo Group; HR: Heart Rate; pre: Baseline; post: Week 8; Peak: Maximal HR at VO2max; AeT: Aerobic Threshold; AT: Anaerobic Threshold

	NAX	PL
Height (cm)	169 (11)	168 (9)
Weight (kg)	70.0 (7.1)	69.3 (7.0)
Body Fat (%)	20.3 (6.3)	24.9 (8.4)
VO_2max (ml/kg/min)	43.7 (9.1)	42.9 (7.2)
Peak HR (bpm)	169 (9)	172 (9)
AeT VO_2 (ml/kg/min)	33.5 (7.5)	31.3 (3.8)
AeT HR (bpm)	145 (13)	143 (11)
AT VO_2 (ml/kg/min)	38.5 (8.3)	36.2 (4.7)
AT HR (bpm)	154 (15)	153 (11)
Watts (cycling)	140 (50)	119 (37)
Watts HR (bpm)	154 (14)	158 (12)

Table 1: *Baseline subject characteristics Data represent average (Mean) values (±SD).*

Abbreviations: *NAX: Natural Astaxanthin Group; PL: Placebo Group; VO_2max: Maximal Oxygen Consumption; Peak HR: Heart Rate at VO_2max; AeT: Aerobic Threshold; AT; Anaerobic Threshold*

Discussion

Astaxanthin (AX) is a naturally occurring carotenoid, synthesized primarily by marine microalgae, with powerful antioxidant and anti-inflammatory properties. In mammals, dietary AX accumulates in muscle, where it attenuates muscle damage and inhibits peroxidation of DNA and lipids due to prolonged exercise [17]. In addition, AX has been identified as a nutrient that may strongly stimulate fat oxidation during exercise. AX supplementation of mice (4 - 5 weeks with 6 - 30 mg/kg BW) improves fat utilization and increases swimming and treadmill running time to exhaustion [19,20]. These effects were theorized to be attributable to an improved mitochondrial capacity for fatty acyl-CoA uptake via an improvement in carnitine palmitoyltransferase 1 (CPT1) function, subsequent to inhibition of oxidative damage to the mitochondrial membrane. Such pre-clinical results provide suggestive evidence that AX may have potential ergogenic effects for endurance athletes.

Previous studies of NAX administration in animal models has shown a decrease in exercise-induced damage to skeletal and cardiac muscle, as well as an increase in redox balance, fat oxidation and time to exhaustion during exercise [17-20,22]. Some positive rodent studies have administered NAX at fairly high dosages of 6 - 30 mg/kg [18-21], while others have used lower amounts (1 mg/kg) to delay physical exhaustion and improve redox balance [22] relatively higher than the amounts of NAX supplemented in human trials (2 - 20 mg/day).

Humans studies of NAX supplementation have noted improved antioxidant status as well as reduced oxidative damage in sedentary obese subjects [25,26] and untrained men [27]. In athletes, NAX supplementation for 4 weeks reduced lactic acid accumulation following 1200m of running [21]. Earnest., *et al*. [23] found significant improvements in power output (+15% = 20W mean power increase) and faster completion of a 20 km cycling time trial (5% = 2 min mean change) following NAX supplementation (4 mg/day for 4 weeks).

The current study, while failing to show benefits of NAX supplementation on maximal-effort exercise (watts during cycling time trial and maximal oxygen consumption during running) found intriguing "submaximal" endurance and possible cardiotonic benefits of NAX supplementation. At submaximal exercise intensities, supplementation with 12 mg/day of NAX for 8 weeks significantly reduced heart rate at the same relative workload at aerobic threshold (AeT) and anaerobic threshold (AT). Submaximal running heart rates were ~10% lower following NAX supplementation, where average heart rates were ~130 - 145 bpm (aerobic threshold) to ~139 - 154 bpm (anaerobic threshold), but not at higher "peak" intensities (e.g. ~154 - 158 bpm during cycling time trial or ~165 - 172 bpm at peak running VO_2max).

Conclusion

These results suggest that NAX supplementation may be a beneficial ergogenic aid for long-distance and ultra-distance endurance athletes (e.g. marathon runners, Ironman triathletes, and ultra-runners/cyclists), but not necessarily for athletes competing in shorter distance higher intensity efforts. In addition, these data are also suggestive of a general "cardiotonic" effect of NAX supplementation, that should be investigated in non-athletic populations including elderly subjects and those with cardiac complications including post-myocardial infarction, heart failure, statin usage, mitochondrial dysfunction, chronic fatigue, and related conditions.

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Disclosure

This work was funded by Algae Health Sciences, a division of BGG. Talbott was principal investigator and reports no conflicts of interest in this work. Hantla reports no conflict of interest. Capelli and Ding are employees of Algae Health Sciences, and Li and Artaria are employees of BGG and BGG Europe respectively.

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