Astaxanthin-Rich Extract from the Green Alga \textit{Haematococcus pluvialis} Lowers Plasma Lipid Concentrations and Enhances Antioxidant Defense in Apolipoprotein E Knockout Mice$^{1-3}$

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Abstract

Dyslipidemia and oxidative stress contribute to atherogenesis. Astaxanthin (ASTX) is a red-colored carotenoid well known for its high antioxidant capacity. However, its effects on lipid metabolism and antioxidant defense mechanisms have received only limited investigation. We fed male apoE knockout (apoE$^{-/-}$) mice, a mouse model for atherosclerosis, a high-fat (15%)/high-cholesterol (0.2%) diet alone (control) or supplemented with ASTX-rich \textit{Haematococcus pluvialis} extract (0.03% ASTX by weight) for 4 wk. ASTX-fed apoE$^{-/-}$ mice had significantly lower plasma total cholesterol and TG concentrations than controls, but body weight and plasma alanine aminotransferase and aspartate aminotransferase did not differ between the groups. qRT-PCR analysis demonstrated significantly greater mRNA levels of LDL receptor (LDLR), 3-hydroxy-3-methylglutaryl CoA reductase, and sterol regulatory element binding protein 2 (SREBP-2) and greater mature SREBP-2 protein in the livers of ASTX-fed mice, indicating that increased LDLR expression may be responsible for the hypocholesterolemic effect of ASTX. Hepatic lipogenic gene expression was not altered, but carnitine palmitoyl transferase 1, acetyl-CoA carboxylase \( \beta \), and acyl-CoA oxidase mRNA abundance were significantly increased by ASTX supplementation, suggesting the TG-lowering effect of ASTX may be due to increased fatty acid \( \beta \)-oxidation in the liver. Expression of the nuclear factor E2 related factor 2-responsive endogenous antioxidant gene also was induced with concomitantly lower glutathione disulfide levels in the livers of ASTX-fed apoE$^{-/-}$ mice compared to controls. In conclusion, these results suggest that supplementation of ASTX-rich \textit{H. pluvialis} extract improves cholesterol and lipid metabolism as well as antioxidant defense mechanisms, all of which could help mitigate the progression of atherosclerosis. J. Nutr. 141: 1611–1617, 2011.

Introduction

CHD$^6$ is the leading cause of death in the United States and other industrialized countries (1). Major CHD risk factors include hypertension, hyperglycemia, hypercholesterolemia (2), increased oxidative stress and inflammation also contribute to the CHD risk (3,4). Various foods have been shown to lower plasma cholesterol levels, including garlic (5), soy protein (6), artichoke (7), and soluble fibers (8). In addition, nuts and berries also lower plasma cholesterol levels as well as protect against oxidative stress (9).

ASTX is a xanthophyll carotenoid abundant in marine animals such as salmon, crustaceans, and trout that live on ASTX-containing planktons and microalgae (10,11). \textit{Haematococcus pluvialis}, a green alga, is thought to have the greatest capacity to accumulate ASTX in nature (12) and is a primary source of ASTX used in the food industry and aquaculture. The FDA awarded “generally recognized as safe” status to ASTX extracted from \textit{H. pluvialis} in 2010. Accordingly, ASTX consumption is expected to increase, because it can be readily incorporated into various food products. However, its physiological functions are not well understood.

ASTX is readily esterified and extracted from \textit{H. pluvialis} primarily in a monoester form (12). With the presence of a keto and a hydroxyl moiety on each of its 2 ionone rings, ASTX is more polar than other carotenoids, thereby allowing its transmembrane positioning in the phospholipid bilayer of cell membranes (11,13,14). ASTX cannot be converted to vitamin A but...
is a potent biological antioxidant. Due to its distinct molecular structure, ASTX functions as a ROS quencher as well as a powerful free radical scavenger. ASTX also effectively scavenges peroxyl radicals and destroy peroxides, thereby protecting fatty acids and biological membranes from lipid peroxidation (15,16). The antioxidant capacity of ASTX has been shown in vitro to be superior to that of other antioxidants at ~100-500 times higher than α-tocopherol (17,18) and 5-15 times better than other carotenoids such as β-carotene, lutein, and lycopene (17). The strong antioxidant property of ASTX is possibly due to its transmembrane alignment in the lipid bilayer of the cellular membrane. In the cell membrane, the hydrophobic ends of ASTX are exposed to an aqueous environment, potentially facilitating the removal of ROS via the conjugated double bond system of its hydrocarbon backbone (11). Moreover, its polar ends may provide proximity to cofactors such as vitamin C that can serve as a free radical scavenger to potentiate the antioxidant activity of ASTX (19).

Studies have shown that ASTX prevents UV light-mediated DNA damage (19), enhances immune response (20), and exerts antitumor activity (21). It may also protect against atherosclerosis through its antioxidant and antiinflammatory properties. Indeed, ASTX inhibits the oxidation of LDL in vitro and in vivo (22,23) and represses macrophage activation and proinflammatory cytokine production (24). In RAW 264.7 macrophages, expression of proinflammatory mediators, such as prostaglandin E2, TNFα, and IL-1β, was reduced by ASTX through the inhibition of NF-κB, a key transcription factor for inflammatory gene expression (25). Furthermore, ASTX prevented the development of hepatic steatosis and lowered plasma concentrations of TC and TG in obese mice fed a high-fat diet (26). In human clinical trials, ASTX supplementation exerted hypolipidemic and antioxidant effects (13,23,27). Little is known, however, about the mechanisms by which ASTX exerts these biological functions. The objective of this study was to better define the mechanism by which ASTX regulates hepatic lipid metabolism and antioxidant defense in vivo using apoE−/− mice, the most commonly used mouse model of atherosclerosis.

**Materials and Methods**

**Mouse feeding and care.** Sixteen male apoE−/− mice at 8 wk old were purchased from Jackson Laboratory and randomly assigned to a control or ASTX group. They were housed in a polycarbonate cage under a 12-h-light/-dark cycle and were fed a high-fat (15%), high-cholesterol (0.2%) diet alone (control) or supplemented with 0.5% *H. pluvialis* supercritical CO2 extract [6.1% ASTX (wt/wt) in the extract; 0.03% ASTX (wt/wt) in diet] for 4 wk. Mice had free access to food and water. The *H. pluvialis* extract contains 99.9% fat that mostly consists of acylglycerols and carotenoids. The carotenoids in the extract include ASTX, β-carotene, and canthaxanthin. However, ~98.5% of the carotenoids is ASTX and each of the other carotenoids is present at ~0.5%. The extract also contains a small quantity of tocopherols, free fatty acids, free sterols, and phospholipids. As fatty acid composition of the extract is similar to that of soybean oil, the extract was added to the experimental diet at the expense of soybean oil. Based on different energy needs estimated for humans and mice, the ASTX supplementation level of 0.03% used in our study would be equivalent to ~200 mg/kg in humans. The composition of the experimental diets is shown in Table 1. The supercritical CO2 extract from *H. pluvialis* was generously provided by Algena. Body weight and food consumption were recorded weekly. At the end of the 4-wk experimental period, mice were feed deprived for 4 h, anesthetized with ketamine HCl (50 mg/kg)/xylazine (10 mg/kg), and subsequently killed by cardiac puncture and cervical dislocation. Blood was collected into tubes containing EDTA (BD Vacutainer) and centrifuged for 20 min at 5000 × g at 4°C and then plasma was collected and stored at −80°C. Liver samples were excised, immediately frozen in liquid nitrogen, and stored at −80°C until use. All procedures were approved by the Institutional Animal Care and Use Committee of the University of Nebraska-Lincoln.

**Plasma chemistry.** Plasma TC, TG, and glucose concentrations were measured using Cholestech LDX Lipid Profile/Glucose cassettes by the Cholestech LDX System (Cholestech). Plasma levels of ALT (28) and AST were also analyzed using Cholestech LDX ALT/AST test cassettes.

**Liver lipids.** Lipid from liver samples was extracted using the method of Folch et al. (29) as described (30). Liver lipids were determined using reagents for TC. (Roche Diagnostics), TG (Roche Diagnostics), and free cholesterol (Free Cholesterol E, Wako Chemicals) by enzymatic analysis. Esterified cholesterol was calculated as the difference between TC and free cholesterol.

**Gene expression analysis by qRT-PCR.** qRT-PCR analysis for hepatic gene expression was conducted as previously described using the SYBR Green procedure and CFX96 real-time PCR detection system (Bio-Rad) (31,32). Primer sequences were designed according to the GenBank database using the Beacon Designer software (Premier Biosoft) and lists of primer sequences are shown in [Supplemental Table 1](#).

**Western-blot analysis.** Liver samples (~0.5 g) were homogenized in 1 mL of RIPA buffer (150 mmol/L NaCl, 1.0% Igepal CA-630, 0.5% sodium deoxycholate, 0.1% SDS, and 50 mmol/L Tris, pH 8.0) containing Protease Inhibitor Cocktail set III (Calbiochem). Tissue lysates were incubated on ice for 30 min, after which they were centrifuged at 12 000 × g for 5 min at 4°C. The supernatant was collected and protein concentrations were measured by bichinonic acid assay (Pierce) using BSA as a standard. Western-blot analysis was performed as previously described (32) using antibodies against sterol regulatory element-binding protein-2 (SREBP-2; Santa Cruz Biotechnology) and β-actin (Sigma). The blots were developed using a HRP system (Pierce) and densitometry analysis was performed using a Chemidoc XR+ (Bio-Rad) and Image Lab software (Bio-Rad). β-Actin was used as a loading control.

**Glutathione redox status in the liver.** Hepatic GSH and GSSG levels were measured using HPLC-Boron Doped Diamond detection (ESA Biosciences), as previously described (33). In brief, livers were homogenized in PBS containing 1 mmol/L diethylenetriaminepentaacetic acid,
thoroughly mixed with 10% PCA containing 1 mmol/L diethylenetriaminepentaacetic acid, and centrifuged at 15,000 \times g for 5 min at 4°C. The acidified supernatant was collected, transferred to a light-shielded vial, and injected on the HPLC system equipped with a conditioning cell set to +500 mV and a HPLC-Boron Doped Diamond cell set to +1475 mV. GSH and GSSG were quantified at +1475 mV relative to external standards prepared in 5% PCA.

**Statistical analysis.** A Student’s paired t-test was performed using GraphPad Prism 5 (GraphPad Software) to compare group means. Differences were considered significant at P < 0.05. Data are expressed as means ± SEM.

**Results**

**Plasma and liver lipids.** Male apoE \(^{-/-}\) mice were fed a high-fat, high-cholesterol control diet or the same diet containing ASTX (0.03% ASTX by weight) for 4 wk. Food intake (data not shown) and body mass did not differ between the male apoE \(^{-/-}\) mice fed control and ASTX-supplemented diets for 4 wk (Table 2). Plasma concentrations of aspartate aminotransferase, ALT, and glucose did not differ between control and ASTX-fed mice. However, ASTX supplementation significantly decreased the plasma concentrations of TC and TG compared with controls (Table 2). Hepatic TG, free cholesterol, and esterified cholesterol concentrations did not differ between the groups (data not shown).

**Expression of hepatic genes involved in lipid metabolism.** To evaluate the underlying mechanism for the hypocholesterolemic effect of ASTX in apoE \(^{-/-}\) mice, qRT-PCR analysis was performed to measure the expression of the genes involved in the hepatic cholesterol metabolism. In mice fed the ASTX-supplemented diet, mRNA levels of LDLR (Fig. 1A) and 3-hydroxy-3-methylglutaryl CoA reductase (HMGR) (Fig. 1B), the rate-limiting enzyme for cholesterol biosynthesis, were significantly greater than those of control mice. The 2 genes are transcriptionally regulated by SREBP-2 in response to cellular cholesterol levels (34). SREBP-2 mRNA (Fig. 1C) and its active mature form (Fig. 1D) of protein were significantly increased by ASTX feeding.

Because ASTX lowered the plasma TG concentration in apoE \(^{-/-}\) mice, we evaluated the expression of genes involved in lipogenesis and fatty acid \(\beta\)-oxidation. Lipogenic genes, including SREBP-1c, acetyl-CoA carboxylase (ACC)-\(\alpha\), fatty acid synthase, and stearoyl CoA desaturase 1 (SCD-1) expression, were not differentially induced in mice fed the ASTX-rich diet compared with the control diet (Fig. 2A–C).

**Endogenous antioxidant genes and GSH redox status.** Nuclear factor E2 related factor 2 (Nrf2) regulates the expression of a variety of genes for antioxidant defense and xenobiotic metabolism (35). We examined whether ASTX supplementation alters the expression of Nrf2-responsive genes by qRT-PCR. ASTX significantly increased hepatic mRNA expression levels of Nrf2 as well as its target genes, such as glutamate-cysteine ligase modifier subunit (GCLm), superoxide dismutase 1 (SOD-1), SOD-2, and GSH peroxidase 1 (GPX-1). In contrast, the expression of GCL catalytic subunit (GCLc), catalase (CAT), and GPX-4 mRNA abundance were unaffected by ASTX (Table 3). Expression of uncoupling protein 2 (UCP-2), which inhibits ROS production (36–38), was also greater in ASTX-fed mice than in controls. Although hepatic levels of GSH, an endogenous antioxidant, were not significantly different between the control and ASTX-fed groups, ASTX supplementation significantly lowered GSSG levels in the liver (data not shown), suggesting a protective effect against oxidative stress.

**Discussion**

ASTX is best known for its antioxidant properties. However, its role in the regulation of lipid metabolism and endogenous antioxidant defense mechanisms has yet to be determined. In this study, we investigated the modulation of plasma lipid levels and the expression of genes involved in lipid metabolism and antioxidant defense by ASTX in a well-established mouse model of atherosclerosis. Our results demonstrated that ASTX has hypocholesterolemic and hypotriglyceremic effects that are potentially mediated by increasing LDL uptake and fatty acid \(\beta\)-oxidation, respectively, in the liver. ASTX also enhanced the expression of Nrf2-responsive endogenous antioxidant genes in the livers of apoE \(^{-/-}\) mice. This study therefore provides the first evidence, to our knowledge, that ASTX exerts its effects on lipid metabolism and antioxidant defense mechanism via the modulation of gene expression in vivo.

Plasma TC and TG concentrations were lower in the ASTX-fed mice than in controls in this study. Consistent with our findings, the lipid-lowering activities of ASTX have been reported in humans and animals. In humans, ASTX administration at 12 and 18 mg/d for 12 wk significantly reduced plasma TG levels compared with placebo control (27). ASTX also lowered plasma TC and TG levels in obese mice fed a high-fat diet with daily i.p. administration of ASTX at 6 and 30 mg/kg body weight for 60 d (26). However, the mechanisms by which ASTX exerts its lipid-lowering effect have not been well defined. In the livers of ASTX-fed mice, we observed that mRNA abundance of LDLR and HMGR was greater than those of controls. The expression of LDLR and HMGR are known to be induced in response to low cellular cholesterol via SREBP-2, a key transcription factor that regulates the expression of genes important for cholest-

### TABLE 2

<table>
<thead>
<tr>
<th>Initial body weight</th>
<th>Final body weight</th>
<th>Alanine aminotransferase</th>
<th>Aspartate aminotransferase</th>
<th>Glucose</th>
<th>TC</th>
<th>TG</th>
</tr>
</thead>
<tbody>
<tr>
<td>g</td>
<td>g</td>
<td>U/L</td>
<td>U/L</td>
<td>mmol/L</td>
<td>mmol/L</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Control</td>
<td>22.3 ± 2.0</td>
<td>28.2 ± 2.1</td>
<td>30.6 ± 7.1</td>
<td>80.3 ± 22</td>
<td>15.9 ± 0.6</td>
<td>22.2 ± 0.7</td>
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<tr>
<td>ASTX</td>
<td>21.6 ± 1.4</td>
<td>28.0 ± 1.8</td>
<td>27.9 ± 2.6</td>
<td>76.0 ± 22</td>
<td>15.1 ± 0.7</td>
<td>19.4 ± 1.1*</td>
</tr>
</tbody>
</table>

* Values are means ± SEM, n = 8. *Different from control, P < 0.06.

Lipid-lowering and antioxidant properties of astaxanthin 1613
terol metabolism (39–43). Transcriptional activity of SREBP-2 is primarily regulated at the posttranscriptional level involving INSIG and SREBP cleavage-activating protein (SCAP). SCAP/SREBP-2 precursor complex retains in the endoplasmic reticulum via sterol-induced interaction of SCAP with INSIG (44,45). When cellular cholesterol is low, dissociation of SCAP from INSIG frees SCAP/SREBP-2 to the Golgi, where mature SREBP-2 is released by 2-step proteolytic cleavages (46,47). The mature SREBP-2 then enters the nucleus to induce transcription of its target genes such as HMGR and LDLR. We observed increased SREBP-2 mRNA and its mature protein levels in the livers of mice fed a ASTX-supplemented diet. Although the hepatic free cholesterol and esterified cholesterol levels did not differ between the 2 groups, esterified cholesterol tended to be lower in the livers of ASTX-fed mice than in controls (P = 0.09). We speculate that ASTX supplementation may decrease the regulatory cholesterol pool, activating the SREBP-2 pathway to increase LDLR expression, which in turn increases the uptake of LDL from the circulation. ASTX did not alter the expression of cholesterol and bile acid transporters in the liver and small intestine or hepatic cholesterol 7α-hydroxylase, a rate-limiting enzyme in bile acid synthesis (data not shown). Interestingly, intestinal scavenger receptor class B, type I (SR-BI) mRNA was significantly higher in ASTX-fed mice than in controls (data not shown). Despite continued controversy, SR-BI has been suggested to play a role in intestinal cholesterol absorption (48,49). Further study is necessary to evaluate the possibility that the hypocholesterolemic effect of ASTX may be due to reduced lipogenesis, because the expression of lipogenic genes such as SREBP-1c, ACCα, fatty acid synthase, and stearoyl CoA desaturase-1 was not significantly different between control and ASTX-fed mice. Instead, we speculate that increased β-oxidation of fatty acids is likely responsible for the TG-lowering effect of ASTX based on significantly higher mRNA levels of marker genes for mitochondrial and peroxisomal fatty acid β-oxidation, i.e. CPT-1 and ACOX, respectively (53), as well as ACCβ in the livers of ASTX-fed mice. Interestingly, CPT-1 and ACOX are under transcriptional regulation by PPARα (54,55). UCP-2, another PPARα target gene (56), was also induced in the liver by ASTX supplementation. It is therefore possible that ASTX may exert its hypotriglyceridemic effect by reducing VLDL TG secretion consequent to enhanced fatty acid β-oxidation in the liver. This is consistent with previous studies demonstrating that ASTX increases fat utilization in muscle by activating CPT-1, thereby reducing adiposity in mice (57).

ASTX has stronger antioxidant potency than other carotenoids (17) and vitamin E (18) in vitro. It increased GSH levels and SOD activities in rat liver (58) and also lowered plasma levels of 12- and 15-hydroxy fatty acids, indicating a decrease in the lipid peroxidation in humans (59). The studies strongly support an antioxidant function of ASTX. Gaps in our knowledge exist, however, as to the mechanisms for the antioxidant effect of ASTX. Nrf2 plays a critical role in cellular defense against oxidative stress by inducing the transcription of antioxidant genes (60). Under basal conditions, Nrf2 is sequestered in the cytoplasm by Keap1, a negative regulator of Nrf2. When cells are under oxidative stress, oxidative modifications or phosphorylation in Keap1 release Nrf2 that subsequently enters the nucleus, activating the transcription of genes containing an antioxidant response element in their promoters (61). Nrf2-

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**FIGURE 1** Expression of genes involved in cholesterol metabolism in the livers of male apoE knockout (apoE−/−) mice fed a high-fat, high-cholesterol diet alone (control) or supplemented with astaxanthin (ASTX) for 4 wk. qRT-PCR was used to measure LDLR (A), HMGR (B), and SREBP-2 (C) mRNA levels. (D) Western-blot analysis for mature SREBP-2 protein levels in the liver. Densitometry analysis was performed using β-actin as a loading control. Values are means ± SEM, n = 8. *Different from control, P < 0.05.

**FIGURE 2** Expression of genes involved in fatty acid β-oxidation in the livers of male apoE knockout (apoE−/−) mice fed a high-fat, high-cholesterol diet alone (control) or supplemented with astaxanthin (ASTX) for 4 wk. qRT-PCR was used to measure CPT-1 (A), ACCα (B), and ACOX (C). Data are expressed as relative expression to control. Values are means ± SEM, n = 8. *Different from control, P < 0.05.
responsive genes include GCLc, GCLm, glutathione synthetase (GS), glutathione-S-transferase (GST), GPx, heme oxygenase 1, and SOD (62,63). In the present study, we observed that ASTX supplementation significantly increased the expression of Nrf2 and most of its target genes in the livers of apoE−/− mice. The increased expression of its downstream targets may provide a stronger endogenous defensive system against oxidative stress in the body. Consistent with this notion, levels of GSSG, an oxidized form of GSH, were lower in the livers of ASTX-fed mice compared to controls. The question to be answered is how ASTX induces the Nrf2 pathway. On the basis of induced PPARα target genes, e.g. CPT-1, ACOX, and UCP-2, in the livers of ASTX-fed mice, we speculate that ASTX may activate PPARα. PPARα has been implicated in the prevention of cellular oxidative damage that may occur during normal cellular metabolism or under oxidative stress (64,65). Ppara−/− mice had perturbations in the redox system with diminished SOD-2 expression in the heart (66). Fibrates increased SOD expression in the liver (67) and brain (68) of mice. Because a primary role of PPARα in the liver is to increase FA β-oxidation, its activation could burden mitochondrial machinery of oxidative phosphorylation due to elevated FA β-oxidation, resulting in ROS production. In this case, Nrf2-dependent antioxidant mechanisms would need to be turned on to offset the production of ROS for the protection against oxidative damage. The interplay between Nrf2 and PPARα has been suggested by demonstrating the presence of ARE in the promoter of Ppary in mice and, surprisingly, Pparγ has been shown to act on upstream signaling pathway for the activation of Nrf2 (69). Whether such a mutual regulation also exists between Nrf2 and PPARα needs further investigation.

In conclusion, supplementation of ASTX extracted from H. pluvialis decreased plasma TC and TG concentrations as well as increased endogenous antioxidant mechanism in apoE−/− mice. Our results suggest that ASTX achieves the effects at least in part by modulating the expression of genes involved in cholesterol and lipid metabolism as well as antioxidant mechanism. To our knowledge, this is the first study to demonstrate that ASTX plays a role as a regulator of the expression of genes involved in lipid metabolism and antioxidant mechanism. Given that progression of atherosclerosis is accelerated by dyslipidemia and chronic inflammation, and oxidative stress due to excessive presence of ROS is a major contributor to cardiovascular inflammation, ASTX has great potential for human consumption as a food ingredient to lower the risk of CHD.

Acknowledgments
Y.Y., J.M.S., A.N., T.X.P., Y.P., H.J.P., and R.S.B. conducted experiments; Y.Y. contributed to writing the manuscript; and J.L. designed the experiments and wrote the manuscript. All authors read and approved the final manuscript.

Literature Cited

Literature Cited

### TABLE 3

Antioxidant gene expression in the livers of male apoE knockout (apoE−/−) mice fed a high-fat, high-cholesterol diet alone (control) or supplemented with Astaxanthin (ASTX) for 4 wk

<table>
<thead>
<tr>
<th>Gene</th>
<th>Control</th>
<th>ASTX</th>
<th>fold of control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nrf2</td>
<td>0.85 ± 0.08</td>
<td>1.43 ± 0.08*</td>
<td></td>
</tr>
<tr>
<td>GCLc</td>
<td>0.83 ± 0.08</td>
<td>0.80 ± 0.09</td>
<td></td>
</tr>
<tr>
<td>GCLm</td>
<td>0.95 ± 0.08</td>
<td>1.35 ± 0.08*</td>
<td></td>
</tr>
<tr>
<td>SOD-1</td>
<td>1.03 ± 0.11</td>
<td>1.36 ± 0.11*</td>
<td></td>
</tr>
<tr>
<td>SOD-2</td>
<td>0.97 ± 0.05</td>
<td>1.33 ± 0.08*</td>
<td></td>
</tr>
<tr>
<td>CAT</td>
<td>0.98 ± 0.08</td>
<td>1.14 ± 0.10</td>
<td></td>
</tr>
<tr>
<td>GPx-1</td>
<td>0.81 ± 0.04</td>
<td>1.24 ± 0.09*</td>
<td></td>
</tr>
<tr>
<td>GPx-4</td>
<td>0.86 ± 0.08</td>
<td>1.04 ± 0.13</td>
<td></td>
</tr>
<tr>
<td>UCP-2</td>
<td>0.76 ± 0.06</td>
<td>1.14 ± 0.07*</td>
<td></td>
</tr>
</tbody>
</table>

*Values are means ± SEM, n = 8. *Different from control, P < 0.05.

2 ASTX, astaxanthin.


