Astaxanthin ameliorates features of metabolic syndrome in SHR/NDmcr-cp.


International Research Center for Traditional Medicine, Toyama, Toyama Prefecture 939-8224, Japan. ghazihussein@hotmail.com

Glucose and lipid metabolic parameters play crucial roles in metabolic syndrome and its major feature of insulin resistance. This study was designed to investigate whether dietary astaxanthin oil (ASX-O) has potential effects on metabolic syndrome features in an SHR/NDmcr-cp (cp/cp) rat model. Oral administration of ASX (50 mg/kg/day) for 22 weeks induced a significant reduction in arterial blood pressure in SHRcp. It also significantly reduced the fasting blood glucose level, homeostasis index of insulin resistance (HOMA-IR), and improved insulin sensitivity. The results also showed an improved adiponectin level, a significant increase in high-density lipoprotein cholesterol, a significant decrease in plasma levels of triglycerides, and non-esterified fatty acids. Additionally, ASX showed significant effects on the white adipose tissue by decreasing the size of the fat cells. These results suggest that ASX ameliorates insulin resistance by mechanisms involving the increase of glucose uptake, and by modulating the level of circulating lipid metabolites and adiponectin.

Publication Types:

PMID: 17074368 [PubMed - indexed for MEDLINE]
Astaxanthin protects mesangial cells from hyperglycemia-induced oxidative signaling.


School of Nursing, Kyoto Prefectural University of Medicine, Kyoto 602-8566, Japan.

Astaxanthin (ASX) is a carotenoid that has potent protective effects on diabetic nephropathy in mice model of type 2 diabetes. In this study, we investigated the protective mechanism of ASX on the progression of diabetic nephropathy using an in vitro model of hyperglycemia, focusing on mesangial cells. Normal human mesangial cells (NHMCs) were cultured in the medium containing normal (5 mM) or high (25 mM) concentrations of D-glucose. Reactive oxygen species (ROS) production, the activation of nuclear transcription factors such as nuclear factor kappa B (NFκB) and activator protein-1 (AP-1), and the expression/production of transforming growth factor-beta 1 (TGFβ1) and monocyte chemoattractant protein-1 (MCP-1) were evaluated in the presence or absence of ASX. High glucose (HG) exposure induced significant ROS production in mitochondria of NHMCs, which resulted in the activation of transcription factors, and subsequent expression/production of cytokines that plays an important role in the mesangial expansion, an important event in the pathogenesis of diabetic nephropathy. ASX significantly suppressed HG-induced ROS production, the activation of transcription factors, and cytokine expression/production by NHMCs. In addition, ASX accumulated in the mitochondria of NHMCs and reduced the production of ROS-modified proteins in mitochondria. ASX may prevent the progression of diabetic nephropathy mainly through ROS scavenging effect in mitochondria of mesangial cells and thus is expected to be very useful for the prevention of diabetic nephropathy.

PMID: 17955498 [PubMed - indexed for MEDLINE]
Inhibitory effect of astraxanthin combined with Flavangenol on oxidative stress biomarkers in streptozotocin-induced diabetic rats.

Nakano M, Orimo N, Katagiri N, Tsubata M, Takahashi J, Van Chuyen N.

Department of Food and Nutrition, Japan Women's University, Tokyo, Japan. masako.nakano06@gr.jwu.ac.jp

In this study, the effect of dietary antioxidants, such as astaxanthin and Flavangenol, and a combination of both, in counteracting oxidative stress in streptozotocin-induced diabetes was investigated. Streptozotocin-induced diabetic rats were divided into four groups: control, astaxanthin, Flavangenol, and combined astaxanthin and Flavangenol (mix group). Each group other than the control group was fed with an astaxanthin diet (0.1 g/kg), Flavangenol diet (2.0 g/kg), or an astaxanthin (0.1 g/kg)-Flavangenol (2.0 g/kg) mixture diet, respectively. After 12 weeks of feeding, the results showed that the lipid peroxide levels of plasma and lens and the plasma triglyceride (TG) level in the mix group were significantly decreased by 44%, 20%, and 20%, respectively, compared with the control group. In the mix group, lipid peroxidation was also significantly reduced by 70% in the liver and 20% in the kidney compared with the control group. Furthermore, the level of urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) in the mix group was significantly lower, 36%, than the control group. The alpha-tocopherol concentrations in the plasma, liver, and kidney in the astaxanthin and mix groups were significantly higher, 3-9 times, than in the control group. The degree of cataract formation in the Flavangenol and mix groups tended to be lower than the control group. These results indicate that the combination of astaxanthin with Flavangenol has an improved protective effect on oxidative stress associated with streptozotocin-induced diabetes than either agent used alone. Thus, this combination may be beneficial in preventing the progression of diabetic complications.

PMID: 19326340 [PubMed - indexed for MEDLINE]
Effect of astaxanthin in combination with alpha-tocopherol or ascorbic acid against oxidative damage in diabetic ODS rats.

Nakano M, Onodera A, Saito E, Tanabe M, Yajima K, Takahashi J, Nguyen VC.

Department of Food and Nutrition, Japan Women's University Japan Women's University Tokyo 112-8681, Japan. masako.nakano06@gr.jwu.ac.jp

The present study was performed to investigate the effect of astaxanthin in combination with other antioxidants against oxidative damage in streptozotocin (STZ)-induced diabetic Osteogenic Disorder Shionogi (ODS) rats. Diabetic-ODS rats were divided into five groups: control, astaxanthin, ascorbic acid, alpha-tocopherol, and tocotrienol. Each of the four experimental groups was administered a diet containing astaxanthin (0.1 g/kg), in combination with ascorbic acid (3.0 g/kg), alpha-tocopherol (0.1 g/kg), or tocotrienol (0.1 g/kg) for 20 wk. The effects of astaxanthin with other antioxidants on lipid peroxidation, urinary 8-hydroxy-2-deoxyguanosine (8-OHdG) excretion, serum creatinine (Cr) level, creatinine clearance (Ccr), and urinary protein content were assessed. The serum lipid peroxide levels and chemiluminescent (CL) intensity in the liver of the alpha-tocopherol and tocotrienol groups were significantly reduced in comparison to that of the control group. In the alpha-tocopherol group, urinary 8-OHdG excretion, serum Cr level, Ccr, urinary albumin excretion, and urinary protein concentration were significantly decreased as compared with those in the control group. Additionally, the CL intensity in the kidney of the alpha-tocopherol group was significantly lower, but that of the ascorbic acid group was significantly higher than that in the control group. These results indicate that dietary astaxanthin in combination with alpha-tocopherol has an inhibitory effect on oxidative stress. On the other hand, our study suggests that excessive ascorbic acid intake increases lipid peroxidation in diabetic rats.

PMID: 18797156 [PubMed - indexed for MEDLINE]


Department of Medical Proteomics, Kyoto Prefectural University of Medicine, Kyoto 602-8566, Japan. ynaito@koto.kpu-m.ac.jp

We have demonstrated that astaxanthin reduces glomerular oxidative stress as well as inhibits the increase in urinary albumin in diabetic db/db mice. The aim of the present study was to determine the gene expression patterns in the glomerular cells of the diabetic mouse kidney, and to investigate the effects of astaxanthin on the expression of these genes using a high-density DNA microarray. The diet administered to the astaxanthin-supplementation group was prepared by mixing a control powder with astaxanthin at a concentration of 0.02%. Glomerular cells were obtained from the kidneys of mice by laser capture microdissection. Preparation of cRNA and target hybridization were performed according to the Affymetrix GeneChip eukaryotic small sample target labeling assay protocol. The gene expression profile was evaluated by the mouse expression set 430A GeneChip. Array data analysis was carried out using Affymetrix GeneChip operating and Ingenuity Pathway analysis software. Comparison between diabetic db/db and non-diabetic db/m mice revealed that 779 probes (3.1%) were significantly affected, i.e. 550 probes were up-regulated, and 229 probes were down-regulated, both at levels of \( \geq 1.5 \)-fold in the diabetic mice. Ingenuity signal analysis of 550 up-regulated probes revealed the mitochondrial oxidative phosphorylation pathway as the most significantly affected canonical pathway. The affected genes were associated with complexes I, III, and IV located on the mitochondrial inner membrane, and the expression levels of these genes were decreased in mice treated with astaxanthin as compared to the levels in the control mice. In addition, the expression of many genes associated with oxidative stress, collagen synthesis, and transforming growth factor-beta signaling was enhanced in the diabetic mice, and this enhancement was slightly inhibited in the astaxanthin-treated mice. In conclusion, this genome-wide nutrigenomics approach provided insight into genes and putative genetic pathways that are thought to be affected by stimulation by high-glucose concentrations. In addition, the present approach may help us gain a better understanding of the genes and pathways involved in the anti-diabetic mechanism of astaxanthin.

Publication Types:

PMID: 16964424 [PubMed - indexed for MEDLINE]
Prevention of diabetic nephropathy by treatment with astaxanthin in diabetic db/db mice.


Molecular Gastroenterology and Hepatology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kamigyo-ku, Kyoto 602-8566, Japan.

Oxidative stress is implicated as an important mechanism by which diabetes causes nephropathy. Astaxanthin, which is found as a common pigment in algae, fish, and birds, is a carotenoid with significant potential for antioxidative activity. In this study, we examined whether chronic administration of astaxanthin could prevent the progression of diabetic nephropathy induced by oxidative stress in mice. We used female db/db mice, a rodent model of type 2 diabetes, and their non-diabetic db/m littermates. The mice were divided into three groups as follows: non-diabetic db/m, diabetic db/db, and diabetic db/db treated with astaxanthin. Blood glucose level, body weight, urinary albumin, and urinary 8-hydroxydeoxyguanosine (8-OHdG) were measured during the experiments. Histological and 8-OHdG immunohistochemical studies were performed for 12 weeks from the beginning of treatment. After 12 weeks of treatment, the astaxanthin-treated group showed a lower level of blood glucose compared with the non-treated db/db group; however, both groups had a significantly high level compared with the db/m mice. The relative mesangial area calculated by the mesangial area/total glomerular area ratio was significantly ameliorated in the astaxanthin-treated group compared with the non-treated db/db group. The increases in urinary albumin and 8-OHdG at 12 weeks of treatment were significantly inhibited by chronic treatment with astaxanthin. The 8-OHdG immunoreactive cells in glomeruli of non-treated db/db mice were more numerous than in the astaxanthin-treated db/db mice. In this study, treatment with astaxanthin ameliorated the progression and acceleration of diabetic nephropathy in the rodent model of type 2 diabetes. The results suggested that the antioxidative activity of astaxanthin reduced the oxidative stress on the kidneys and prevented renal cell damage. In conclusion, administration of astaxanthin might be a novel approach for the prevention of diabetes nephropathy.

PMID: 15096660 [PubMed - indexed for MEDLINE]
Astaxanthin protects beta-cells against glucose toxicity in diabetic db/db mice.


First Department of Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan.

Oxidative stress induced by hyperglycemia possibly causes the dysfunction of pancreatic beta-cells and various forms of tissue damage in patients with diabetes mellitus. Astaxanthin, a carotenoid of marine microalgae, is reported as a strong anti-oxidant inhibiting lipid peroxidation and scavenging reactive oxygen species. The aim of the present study was to examine whether astaxanthin can elicit beneficial effects on the progressive destruction of pancreatic beta-cells in db/db mice--a well-known obese model of type 2 diabetes. We used diabetic C57BL/KsJ-db/db mice and db/m for the control. Astaxanthin treatment was started at 6 weeks of age and its effects were evaluated at 10, 14, and 18 weeks of age by non-fasting blood glucose levels, intraperitoneal glucose tolerance test including insulin secretion, and beta-cell histology. The non-fasting blood glucose level in db/db mice was significantly higher than that of db/m mice, and the higher level of blood glucose in db/db mice was significantly decreased after treatment with astaxanthin. The ability of islet cells to secrete insulin, as determined by the intraperitoneal glucose tolerance test, was preserved in the astaxanthin-treated group. Histology of the pancreas revealed no significant differences in the beta-cell mass between astaxanthin-treated and -untreated db/db mice. In conclusion, these results indicate that astaxanthin can exert beneficial effects in diabetes, with preservation of beta-cell function. This finding suggests that anti-oxidants may be potentially useful for reducing glucose toxicity.

PMID: 12688512 [PubMed - indexed for MEDLINE]
Astaxanthin protects β-cells against glucose toxicity in diabetic db/db mice

Kazuhiko Uchiyama1, Yuji Naito1, Goji Hasegawa1, Naoto Nakamura1, Jiro Takahashi2, Toshikazu Yoshikawa1

Oxidative stress induced by hyperglycemia possibly causes the dysfunction of pancreatic β-cells and various forms of tissue damage in patients with diabetes mellitus. Astaxanthin, a carotenoid of marine microalgae, is reported as a strong anti-oxidant inhibiting lipid peroxidation and scavenging reactive oxygen species. The aim of the present study was to examine whether astaxanthin can elicit beneficial effects on the progressive destruction of pancreatic β-cells in db/db mice – a well-known obese model of type 2 diabetes. We used diabetic C57BL/KsJ-db/db mice and db/m for the control. Astaxanthin treatment was started at 6 weeks of age and its effects were evaluated at 10, 14, and 18 weeks of age by non-fasting blood glucose levels, intraperitoneal glucose tolerance test including insulin secretion, and -cell histology. The non-fasting blood glucose level in db/db mice was significantly higher than that of db/m mice, and the higher level of blood glucose in db/db mice was significantly decreased after treatment with astaxanthin. The ability of islet cells to secrete insulin, as determined by the intraperitoneal glucose tolerance test, was preserved in the astaxanthin-treated group. Histology of the pancreas revealed no significant differences in the -cell mass between astaxanthin-treated and -untreated db/db mice. In conclusion, these results indicate that astaxanthin can exert beneficial effects in diabetes, with preservation of β-cell function. This finding suggests that anti-oxidants may be potentially useful for reducing glucose toxicity.
Acastaxanthin ameliorates the redox imbalance in lymphocytes of experimental diabetic rats.

Otton R, Marin DP, Bolin AP, Santos Rde C, Polotow TG, Sampaio SC, de Barros MP.

Postgraduate Program, Human Movement Sciences, Institute of Physical Activity and Sport Sciences, Universidade Cruzeiro do Sul, ZIP 01506000, Sao Paulo, SP, Brazil; Postgraduate Program, Health Sciences, CBS, Universidade Cruzeiro do Sul, ZIP 08060070, Sao Paulo, SP, Brazil.

Abstract

Diabetes mellitus is a syndrome of impaired insulin secretion/sensitivity and frequently diagnosed by hyperglycemia, lipid abnormalities, and vascular complications. The diabetic 'glucolipotoxicity' also induces immunodepression in patients by redox impairment of immune cells. Astaxanthin (ASTA) is a pinkish-orange carotenoid found in many marine foods (e.g. shrimp, crabs, salmon), which has powerful antioxidant, photoprotective, antitumor, and cardioprotective properties. Aiming for an antioxidant therapy against diabetic immunodepression, we here tested the ability of prophylactic ASTA supplementation (30 days, 20 mg ASTA/kg BW) to oppose the redox impairment observed in isolated lymphocytes from alloxan-induced diabetic Wistar rats. The redox status of lymphocytes were thoroughly screened by measuring: (i) production of superoxide (O(2)(-)), nitric oxide (NO), and hydrogen peroxide (H(2)O(2)); (ii) cytosolic Ca(2+); (iii) indexes of oxidative injury; and (iv) activities of major antioxidant enzymes. Hypolipidemic and antioxidant effects of ASTA in plasma of ASTA-fed/diabetic rats were apparently reflected in the circulating lymphocytes, since lower activities of catalase, restored ratio between glutathione peroxidase and glutathione reductase activities and lower scores of lipid oxidation were concomitantly measured in those immune cells. Noteworthy, lower production of NO and O(2)(-) (precursors of peroxynitrite), and lower cytosolic Ca(2+) indicate a hypothetical antiapoptotic effect of ASTA in diabetic lymphocytes. However, questions are still open regarding the proper ASTA supplementation dose needed to balance efficient antioxidant protection and essential NO/H(2)O(2)-mediated proliferative capacities of diabetic lymphocytes.

PMID: 20513374 [PubMed - indexed for MEDLINE]

Diabetes
In vivo astaxanthin treatment partially prevents antioxidant alterations in dental pulp from alloxan-induced diabetic rats.

Leite MF, de Lima A, Massuyama MM, Otton R.

Ciências Biológicas e da Saúde, Universidade Cruzeiro do Sul - São Paulo, Brazil.

Abstract

Leite MF, de Lima A, Massuyama MM, Otton R. In vivo astaxanthin treatment partially prevents antioxidant alterations in dental pulp from alloxan-induced diabetic rats. International Endodontic Journal. Abstract Aim To evaluate the effect of astaxanthin on antioxidant parameters of dental pulp from diabetic rats. The hypothesis tested was that supplementation of diabetic rats with astaxanthin might eliminate, or at least attenuate, the defect in their antioxidative status. Methodology Wistar rats (n = 32) were divided into four groups: untreated control, treated control, untreated diabetic and treated diabetic rats. A prophylactic dose of astaxanthin (20 mg kg(-1) body weight) was administered daily by gavage for 30 days. On day 23, diabetes was induced by injection of alloxan (60 mg kg(-1) body weight). After 7 days of diabetes induction, the rats were killed, and pulp tissue from incisor teeth removed. Superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx) and reductase activities were determined. Data were compared by anova and the Newman-Keuls test (P < 0.05). Results Diabetes caused a reduction in SOD, GPx and reductase activity in dental pulp tissue. Astaxanthin had no effect on SOD and catalase activities; however, it stimulated GPx in control and diabetic rats. Conclusions Diabetes altered the antioxidant system in dental pulp tissue; astaxanthin partially improved the diabetic complications.

PMID: 20546046 [PubMed - as supplied by publisher]
Astaxanthin restores the enzymatic antioxidant profile in salivary gland of alloxan-induced diabetic rats.

Leite MF, Lima AM, Massuyama MM, Otton R.

Universidade Cruzeiro do Sul, CEP, São Paulo, Brazil. mariana.leite@cruzeirodosul.edu.br
<mariana.leite@cruzeirodosul.edu.br>

Abstract

OBJECTIVE: To evaluate the effect of astaxanthin on antioxidant parameters of salivary gland from diabetic rats. The hypothesis of the study was whether the supplementation of diabetic rats with astaxanthin might antagonize, or at least prevent, the defect in their antioxidative status.

DESIGN: Wistar rats (n=32) were divided in 4 groups: untreated control, treated control, untreated diabetic and treated diabetic rats. Astaxanthin (20mg/kg body weight) was administered daily by gavage for 30 days. On day 23, diabetes was induced by injection of alloxan (60 mg/kg body weight). After 7 days of diabetes induction, the rats were killed and submandibular and parotid removed. Superoxide dismutase (SOD), catalase, glutathione peroxidase and reductase activities and the content of thiol groups were determined. Data were compared by ANOVA and the Tukey test (p<0.05).

RESULTS: Diabetes caused a reduction of SOD, and thiol content and increase of catalase and glutathione peroxidase activities of submandibular gland whilst in the parotid gland diabetes caused an increase of thiol content and no effect in the antioxidant system. The astaxanthin restores the enzymatic activities in the salivary gland, however does not prevent its oxidative damage.

CONCLUSION: The submandibular gland presented more susceptibility to oxidative alterations induced by diabetes. Astaxanthin presented a positive effect on the oxidative protection of the salivary gland from diabetic rats.

PMID: 20510163 [PubMed - in process]
Protection against oxidative stress, inflammation, and apoptosis of high-glucose-exposed proximal tubular epithelial cells by astaxanthin.

Kim YJ, Kim YA, Yokozawa T.

Department of Dental Hygiene, Busan Women's College, Busanjin-Gu, Busan, Korea.

Abstract

Astaxanthin is a carotenoid with powerful antioxidant properties that exists naturally in various plants, algae, and seafood. The purpose of the present study is to examine the protective action of astaxanthin against high-glucose-induced oxidative stress, inflammation, and apoptosis in proximal tubular epithelial cells (PTECs). To assess the efficacy of astaxanthin, several key markers and activities were measured, including lipid peroxidation, total reactive species (RS), superoxide (O2·−), nitric oxide (NO·), and peroxynitrite (ONOO−), as well as expressions of inflammatory proteins, inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), nuclear factor-kappa B (NF-kappaB) nuclear translocation, and levels of Bcl2/Bax protein. Results showed that astaxanthin effectively suppressed lipid peroxidation, total RS, O2·−, NO·, ONOO−, iNOS and COX-2 protein levels, NF-kappaB nuclear translocation, and pro-apoptotic Bax, whereas it increased anti-apoptotic Bcl2 protein levels. On the basis of these findings, it was concluded that in PTECs, astaxanthin has a protective efficacy against several deleterious effects caused by high glucose exposure and proposed that astaxanthin should be explored further as a potential antidiabetic remedy for the treatment of diabetic nephropathy.

PMID: 19731916 [PubMed - indexed for MEDLINE]