Antioxidant

Carotenoid Science, Vol.11, 2007, 16-20

Quenching Activities of Common Hydrophilic and Lipophilic Antioxidants against Singlet Oxygen Using Chemiluminescence Detection System

Yasuhiro Nishida*, Eiji Yamashita and Wataru Miki
Institute for Food Science Research, Japan

The singlet oxygen quenching activities among common hydrophilic and lipophilic antioxidants such as polyphenols, tocopherols, carotenoids, ascorbic acid, coenzyme Q10 and α-lipoic acid were recorded under the same test condition: the chemiluminescence detection system for direct 1O2 counting using the thermodissociable endoperoxides of 1,4-dimethylnaphthalene as 1O2 generator in DMF : CDCl3 (9 : 1). Carotenoids exhibited larger total quenching rate constants than other antioxidants, with astaxanthin showing the strongest activity. α-Tocopherol and α-lipoic acid showed considerable activities, whereas the activities of ascorbic acid, CoQ10 and polyphenols were only slight; these included capsaicin, probucol, edaravon, BHT and Trolox. This system has the potential of being a powerful tool to evaluate the quenching activity against singlet oxygen for various hydrophilic and lipophilic compounds.

Adapted from Nishida, Yamashita, Miki, Carotenoid Science, Vol. 11, 2007, 16-20 (in Japanese)

Astaxanthin has exceptional antioxidant activity to combat singlet oxygen when compared to other antioxidants. In particular, Astaxanthin can be used to defend against singlet oxygen damage for eye and skin health, which are especially susceptible to UV damage and aging effects.

Singlet oxygen is an active oxygen species generated in human skin by exposure to ultraviolet radiation (UV) that causes skin damage and eye damage. In this study, Astaxanthin extracted from *Haematococcus* microalgae powerfully quenched singlet oxygen. Results show that the quenching effect of Astaxanthin is 800 times greater than coenzyme Q10. Astaxanthin was also about 75 times greater than alpha lipoic acid, about 550 times greater than green tea catechins and about 6000 times greater than Vitamin C.

Antioxidant

Carotenoids as Singlet Oxygen Quenchers in Marine Organisms

Shimidzu, Gogo, Miki, 1995. Fisheries Science 62(1), 134-137

Results indicated that Astaxanthin was significantly stronger than all other antioxidants tested as singlet oxygen quenchers. Among the results Astaxanthin was shown to be 550X stronger than Vitamin E; 11X stronger than Beta-Carotene; 2.75X stronger than Lutein.

Antioxidant

OXYGEN FREE RADICAL SCAVENGING ABILITIES OF VITAMINS C, E, β-CAROTENE, PYCNOGENOL, GRAPE SEED PROANTHOCYANIDIN EXTRACT AND ASTAXANTHINS *IN VITRO*

Debasis Bagchi, Ph.D. Pharmacy Sciences, Creighton University School of Health Sciences, June 2001

Summary: Natural Astaxanthin (as BioAstin® from Cyanotech) showed significantly higher free radical scavenging activity than all other antioxidants tested. Results on a pure active basis were as follows:

Natural Astaxanthin	Alternate Antioxidant	Multiple of Greater Free Radical Scavenging Activity
BioAstin	Vitamin C	65X stronger
BioAstin	Vitamin E	14X stronger
BioAstin	Beta Carotene	54X stronger
BioAstin	Pycnogenol®	18X stronger
BioAstin	Synthetic Astaxanthin	21X stronger

Antioxidant

Comparison of Astaxanthin's Singlet Oxygen Quenching Activity with Common Fat and Water Soluble Antioxidants

United States Patent Application ***20060217445***
Kind Code **A1**
Chew; Boon P. ; et al. **September 28, 2006**

Natural astaxanthin extract reduces DNA oxidation

Abstract

Provided herein are methods for reducing oxidative DNA damage in a subject, by administering to the subject astaxanthin, for instance a natural, astaxanthin-enriched extract from Haematococcus pluvialis. It is shown that doses as low as 2 mg/day, given orally to a human subject for a period of four weeks, is sufficient to reduced measurable endogenous oxidative DNA damage by about 40%.

Antioxidant

Phytother Res. 2009 Jun 22. [Epub ahead of print]

Cytoprotective role of astaxanthin against glycated protein/iron chelate-induced toxicity in human umbilical vein endothelial cells.

Nishigaki I, **Rajendran P**, **Venugopal R**, **Ekambaram G**, **Sakthisekaran D**, **Nishigaki Y**.

NPO International Laboratory of Biochemistry, 1-166 Uchide, Nakagawa-ku Nagoya 454-0926, Japan.

Astaxanthin (ASX), a red carotenoid pigment with no pro-vitamin A activity, is a biological antioxidant that occurs naturally in a wide variety of plants, algae and seafoods. This study investigated whether ASX could inhibit glycated protein/iron chelate-induced toxicity in human umbilical-vein endothelial cells (HUVEC) by interfering with ROS generation in these cells. Glycated fetal bovine serum (GFBS) was prepared by incubating fetal bovine serum (FBS) with high-concentration glucose. Stimulation of cultured HUVECs with 50 mm 1 mL of GFBS significantly enhanced lipid peroxidation and decreased antioxidant enzyme activities and levels of phase II enzymes. However, preincubation of the cultures with ASX resulted in a marked decrease in the level of lipid peroxide (LPO) and an increase in the levels of antioxidant enzymes in an ASX concentration-dependent manner. These results demonstrate that ASX could inhibit LPO formation and enhance the antioxidant enzyme status in GFBS/iron chelate-exposed endothelial cells by suppressing ROS generation, thereby limiting the effects of the AGE-RAGE interaction. The results indicate that ASX could have a beneficial role against glycated protein/iron chelate-induced toxicity by preventing lipid and protein oxidation and increasing the activity of antioxidant enzymes.

PMID: 19548280 [PubMed - as supplied by publisher]

Antioxidant

Biochim Biophys Acta. 2001 Jun 6;1512(2):251-8.

Efficient radical trapping at the surface and inside the phospholipid membrane is responsible for highly potent antiperoxidative activity of the carotenoid astaxanthin.

Goto S, **Kogure K**, **Abe K**, **Kimata Y**, **Kitahama K**, **Yamashita E**, **Terada H**.

Faculty of Pharmaceutical Sciences, University of Tokushima, Japan.
Kogure@ph.tokushima-u.ac.jp

The effects of the carotenoids beta-carotene and astaxanthin on the peroxidation of liposomes induced by ADP and Fe(2+) were examined. Both compounds inhibited production of lipid peroxides, astaxanthin being about 2-fold more effective than beta-carotene. The difference in the modes of destruction of the conjugated polyene chain between beta-carotene and astaxanthin suggested that the conjugated polyene moiety and terminal ring moieties of the more potent astaxanthin trapped radicals in the membrane and both at the membrane surface and in the membrane, respectively, whereas only the conjugated polyene chain of beta-carotene was responsible for radical trapping near the membrane surface and in the interior of the membrane. The efficient antioxidant activity of astaxanthin is suggested to be due to the unique structure of the terminal ring moiety.

Publication Types:

PMID: 11406102 [PubMed - indexed for MEDLINE]

Antioxidant

Chem Biol Interact. 2009 Aug 14;180(3):398-406. Epub 2009 Apr 2.

Intervention of astaxanthin against cyclophosphamide-induced oxidative stress and DNA damage: a study in mice.

Tripathi DN, **Jena GB**.

Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research, Sector-67, S.A.S. Nagar, Punjab 160062, India.

Astaxanthin, a natural and nutritional red carotenoid pigment, is used as a dietary supplement. The intention of the present study was to investigate the beneficial effects of dietary pigment astaxanthin, against cyclophosphamide-induced oxidative stress and DNA damage. The end points of evaluation of the study included: (a) malondialdehyde, glutathione and superoxide dismutase concentration in liver to detect oxidative stress; (b) normal and modified alkaline comet assays (the latter includes lesion-specific enzymes formamidopyrimidine-DNA glycosylase and endonuclease-III) to detect normal and oxidative stress-induced DNA damage by cyclophosphamide in the mouse bone marrow and the peripheral blood lymphocytes. In addition, micronucleus assay and chromosomal aberration test capable of detecting the DNA damage were also carried out in peripheral blood and bone marrow of mice. Cyclophosphamide (100 mg/kg intra-peritoneal) treatment led to significant increase in liver malondialdehyde and decreased the antioxidant enzymes glutathione and superoxide dismutase. Further, cyclophosphamide also significantly increased the DNA damage as observed from normal and modified comet assays as well as micronucleus and chromosomal aberration assay. Pre-treatment with astaxanthin (12.5, 25 and 50 mg/kg/day for 5 days per oral) resulted in the restoration of oxidative stress markers such as malondialdehyde, glutathione and superoxide dismutase in liver. The amelioration of oxidative stress with astaxanthin pre-treatment correlated well with the decreased DNA damage as evident from normal and modified alkaline comet assays of bone marrow cells and peripheral blood lymphocytes. Further astaxanthin pre-treatment also reduced the frequency of chromosomal breakage and micronucleus formation in the mouse bone marrow cells and peripheral blood reticulocytes. It is thus concluded that pre-treatment with astaxanthin attenuates cyclophosphamide-induced oxidative stress and subsequent DNA damage in mice and it can be used as a chemoprotective agent against the toxicity of anticancer drug cyclophosphamide.

Research Support, Non-U.S. Gov't
PMID: 19539803 [PubMed - in process]

Antioxidant

J Agric Food Chem. 2000 Apr;48(4):1150-4.

Antioxidant activities of astaxanthin and related carotenoids.

Naguib YM.

Phytochem Technologies, Chelmsford, MA 01824, USA.

The antioxidant activities of astaxanthin and related carotenoids have been measured by employing a newly developed fluorometric assay. This assay is based on 4,4-difluoro-3,5-bis(4-phenyl-1, 3-butadienyl)-4-bora-3a,4a-diaza-s-indacene (BODIPY 665/676) as an indicator; 2,2'-azobis-2,4-dimethylvaleronitrile (AMVN) as a peroxyl radical generator; and 6-hydroxy-2,5,7, 8-tetramethylchroman-2-carboxylic acid (Trolox) as a calibrator in an organic and liposomal media. By employing this assay, three categories of carotenoids were examined: namely, the hydrocarbon carotenoids lycopene, alpha-carotene, and beta-carotene; the hydroxy carotenoid lutein; and the alpha-hydroxy-ketocarotenoid astaxanthin. The relative peroxyl radical scavenging activities of Trolox, astaxanthin, alpha-tocopherol, lycopene, beta-carotene, lutein, and alpha-carotene in octane/butyronitrile (9:1, v/v) were determined to be 1.0, 1.0, 1.3, 0.5, 0.4, 0.3, and 0.2, respectively. In dioleoylphosphatidyl choline (DOPC) liposomal suspension in Tri-HCl buffer (pH 7.4 at 40 degrees C), the relative reactivities of astaxanthin, beta-carotene, alpha-tocopherol, and lutein were found to be 1.00, 0.9, 0.6, and 0.6, respectively. When BODIPY 665/676 was replaced by 4,4-difluoro-5-(4-phenyl-1,3-butadienyl)-4-bora-3a, 4a-diaza-s-indacene-3-undecanoic acid (BODIPY 581/591 C(11)) as an indicator, astaxanthin showed the highest antioxidant activity toward peroxyl radicals. The relative reactivities of Trolox, astaxanthin, alpha-tocopherol, alpha-carotene, lutein, beta-carotene, and lycopene were determined to be 1.0, 1.3, 0.9, 0.5, 0.4, 0.2, and 0.4, respectively.

PMID: 10775364 [PubMed - indexed for MEDLINE]

J Nutr Biochem. 2009 May 6. [Epub ahead of print]

Astaxanthin protects mitochondrial redox state and functional integrity against oxidative stress.

Wolf AM, **Asoh S**, **Hiranuma H**, **Ohsawa I**, **Iio K**, **Satou A**, **Ishikura M**, **Ohta S**.

Department of Biochemistry and Cell Biology, Institute of Development and Aging Sciences, Nippon Medical School, Nakahara-ku, Kawasaki, Kanagawa 211-8533, Japan.

Mitochondria combine the production of energy with an efficient chain of reduction-oxidation (redox) reactions but also with the unavoidable production of reactive oxygen species. Oxidative stress leading to mitochondrial dysfunction is a critical factor in many diseases, such as cancer and neurodegenerative and lifestyle-related diseases. Effective antioxidants thus offer great therapeutic and preventive promise. Investigating the efficacy of antioxidants, we found that a carotenoid, astaxanthin (AX), decreased physiologically occurring oxidative stress and protected cultured cells against strong oxidative stress induced with a respiratory inhibitor. Moreover, AX improved maintenance of a high mitochondrial membrane potential and stimulated respiration. Investigating how AX stimulates and interacts with mitochondria, a redox-sensitive fluorescent protein (roGFP1) was stably expressed in the cytosol and mitochondrial matrix to measure the redox state in the respective compartments. AX at nanomolar concentrations was effective in maintaining mitochondria in a reduced state. Additionally, AX improved the ability of mitochondria to remain in a reduced state under oxidative challenge. Taken together, these results suggest that AX is effective in improving mitochondrial function through retaining mitochondria in the reduced state.

PMID: 19423317 [PubMed - as supplied by publisher]

Antioxidant

Zhongguo Gu Shang. 2008 Mar;21(3):187-9.

[Effects of Astaxanthin on the damage of osteoblast induced by H2O2]

[Article in Chinese]

Pei LP, **Dong FH**, **Hui BD**.

Institute of Orthopaedics and Traumatology, China Academy of Chinese Medical Science, Beijing 100700, China.

OBJECTIVE: To investigate the effect of Astaxanthin on enhancing the function of anti-oxidative damage in osteoblast. METHODS: MC3T3-E1 osteoblasts were randomly divided into five groups, including control group, model group, Astaxanthin group [low-dose (1 x 10(-7) mol/L), middle-dose (1 x 10(-6) mol/L), high-dose (1 x 10(-5) mol/L)], in which the activity of cells, activity of superoxide dismutase (SOD), the content of reactive oxygen species (ROS), lipid oxygen (LPO) and membrane fluidity were tested and compared. RESULTS: Compared with Astaxanthin groups, the activity of cells, SOD activity and membrane fluidity in the model group were significantly decreased ($P < 0.01$). However, the contents of ROS and LPO were significantly raised ($P < 0.01$). CONCLUSION: H2O2 can cause oxidative damage of MC3T3-E1 osteoblasts, but Astaxanthin can prevent or decrease its influence.

PMID: 19105434 [PubMed - indexed for MEDLINE]

Antioxidant

Phys Chem A. 2008 Sep 25;112(38):9037-42. Epub 2008 Aug 21.

Donator acceptor map for carotenoids, melatonin and vitamins.

Martínez A, **Rodríguez-Gironés MA**, **Barbosa A**, **Costas M**.

Instituto de Investigaciones en Materiales, Universidad Nacional Autonoma de Mexico, Circuito Interior, S N, Ciudad Universitaria, P. O. Box 70-360, Coyoacan, 04510, Mexico. martina@iim.unam.mx

Bright yellow and red colors in animals and plants are assumed to be caused by carotenoids (CAR). In animals, these pigments are deposited in scales, skin and feathers. Together with other naturally occurring and colorless substances such as melatonin and vitamins, they are considered antioxidants due to their free-radical-scavenging properties. However, it would be better to refer to them as "antiradicals", an action that can take place either donating or accepting electrons. In this work we present quantum chemical calculations for several CAR and some colorless antioxidants, such as melatonin and vitamins A, C and E. The antiradical capacity of these substances is determined using vertical ionization energy (I), electron affinity (A), the electrodonating power (omega(-)) and the electroaccepting power (omega(+)). Using fluor and sodium as references, electron acceptance (R(a)) and electron donation (R(d)) indexes are defined. A plot of R(d) vs R(a) provides a donator acceptor map (DAM) useful to classify any substance regarding its electron donating-accepting capability. Using this DAM, a qualitative comparison among all the studied compounds is presented. According to R(d) values, vitamin E is the most effective antiradical in terms of its electron donor capacity, while the most effective antiradical in terms of its electron acceptor capacity, R(a), is astaxanthin, the reddest CAR. These results may be helpful for understanding the role played by naturally occurring pigments, acting as radical scavengers either donating or accepting electrons.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 18714976 [PubMed - indexed for MEDLINE]

Antioxidant

Food Chem Toxicol. 2008 Jan;46(1):212-9. Epub 2007 Aug 14.

Effect of astaxanthin on kidney function impairment and oxidative stress induced by mercuric chloride in rats.

Augusti PR, **Conterato GM**, **Somacal S**, **Sobieski R**, **Spohr PR**, **Torres JV**, **Charão MF**, **Moro AM**, **Rocha MP**, **Garcia SC**, **Emanuelli T**.

Post-graduate Program on Toxicological Biochemistry, Center of Natural and Exact Sciences, Federal University of Santa Maria, 97105-900 Santa Maria, RS, Brazil.

Reactive oxygen species are implicated as mediators of tissue damage in the acute renal failure induced by inorganic mercury. Astaxanthin (ASX), a carotenoid with potent antioxidant properties, exists naturally in various plants, algae, and seafoods. This paper evaluated the ability of ASX to prevent HgCl(2) nephrotoxicity. Rats were injected with HgCl(2) (0 or 5 mg/kg b.w., sc) 6h after ASX had been administered (0, 10, 25, or 50mg/kg, by gavage) and were killed 12h after HgCl(2) exposure. Although ASX prevented the increase of lipid and protein oxidation and attenuated histopathological changes caused by HgCl(2) in kidney, it did not prevent creatinine increase in plasma and delta-aminolevulinic acid dehydratase inhibition induced by HgCl(2). Glutathione peroxidase and catalase activities were enhanced, while superoxide dismutase activity was depressed in HgCl(2)-treated rats when compared to control and these effects were prevented by ASX. Our results indicate that ASX could have a beneficial role against HgCl(2) toxicity by preventing lipid and protein oxidation, changes in the activity of antioxidant enzymes and histopathological changes.

Publication Types:

PMID: 17881112 [PubMed - indexed for MEDLINE]

Antioxidant

Biochem Biophys Res Commun. 2007 May 25;357(1):187-93. Epub 2007 Mar 28.

Cis astaxanthin and especially 9-cis astaxanthin exhibits a higher antioxidant activity in vitro compared to the all-trans isomer.

Liu X, **Osawa T**.

Laboratory of Food and Biodynamics, Graduate School of Bioagricultural Science, Nagoya University, Nagoya 464-8601, Japan.

In recent years, a number of studies have implicated the potent antioxidant property of astaxanthin in various experimental systems; however, these studies employed only the all-trans isomer. On the other hand, it has been reported that all-trans natural astaxanthin is readily isomerized to cis-trans, especially 9-cis and 13-cis isomers, under certain conditions by chemical analysis; however, the biological activities of the cis isomers of astaxanthin are little known. In the present study, we investigated the antioxidant activity of 9-cis and 13-cis astaxanthin compared to the all-trans isomer in vitro. In a stable radical DPPH scavenging activity test and in rat microsome and rabbit erythrocyte ghost membrane lipid peroxidation systems induced by AAPH and t-BuOOH, respectively, the results apparently showed that cis-astaxanthin, especially 9-cis astaxanthin, exhibited a higher antioxidant effect than the all-trans isomer. In addition, during polyunsaturated fatty acid (PUFA) oxidation, both DHA and linoleic acid hydroperoxides formation were markedly inhibited by astaxanthin isomers addition in the order 9-cis >13-cis >all-trans. Furthermore, 9-cis also exhibited the most effective inhibition of the generation of ROS induced by 6-hydroxydopamine (6-OHDA) in human neuroblastoma SH-SY5Y cells among the astaxanthin isomers, as well as on the degradation of collagen type II induced by DHA and linoleic acid hydroperoxides. The above-mentioned results suggest, for the first time, that cis isomer astaxanthin, especially 9-cis astaxanthin, has a much higher antioxidant potency than that of the all-trans isomer.

PMID: 17416351 [PubMed - indexed for MEDLINE]

Antioxidant

Biochim Biophys Acta. 2007 Jan;1768(1):167-74. Epub 2006 Sep 22.

Differential effects of carotenoids on lipid peroxidation due to membrane interactions: X-ray diffraction analysis.

McNulty HP, **Byun J**, **Lockwood SF**, **Jacob RF**, **Mason RP**.

Elucida Research, 100 Cummings Center, Suite 135L, P.O. Box 7100, Beverly, MA 01915-0091, USA. hmcnulty@elucidaresearch.com

The biological benefits of certain carotenoids may be due to their potent antioxidant properties attributed to specific physico-chemical interactions with membranes. To test this hypothesis, we measured the effects of various carotenoids on rates of lipid peroxidation and correlated these findings with their membrane interactions, as determined by small angle X-ray diffraction approaches. The effects of the homochiral carotenoids (astaxanthin, zeaxanthin, lutein, beta-carotene, lycopene) on lipid hydroperoxide (LOOH) generation were evaluated in membranes enriched with polyunsaturated fatty acids. Apolar carotenoids, such as lycopene and beta-carotene, disordered the membrane bilayer and showed a potent pro-oxidant effect (>85% increase in LOOH levels) while astaxanthin preserved membrane structure and exhibited significant antioxidant activity (40% decrease in LOOH levels). These findings indicate distinct effects of carotenoids on lipid peroxidation due to membrane structure changes. These contrasting effects of carotenoids on lipid peroxidation may explain differences in their biological activity.

PMID: 17070769 [PubMed - indexed for MEDLINE]

Antioxidant

Luminescence. 2005 Nov-Dec;20(6):419-27.

Comparative study of antioxidants as quenchers or scavengers of reactive oxygen species based on quenching of MCLA-dependent chemiluminescence.

Hosaka S, **Obuki M**, **Nakajima J**, **Suzuki M**.

Department of Applied Chemistry, Faculty of Engineering, Tokyo Polytechnic University, 1583 Atsugi, Kanagawa 243-0297, Japan. s-hosaka@parkcity.ne.jp

The quenching or scavenging effect of non-enzymatic antioxidants against reactive oxygen species (ROS) was studied by comparing the degree of suppression of chemiluminescence (CL) caused by the oxidation of MCLA (methoxylated Cypridina luciferin analogue) by ROS. MCLA-dependent CL caused by O2- was effectively quenched by ascorbic acid, beta-carotene, lycopene and astaxanthin, while it was enhanced by alpha-tocopherol. The CL by 1O2 was quenched effectively by beta-carotene, lycopene and astaxanthin, moderately by ascorbic acid, and slightly by alpha-tocopherol. beta-Carotene and alpha-tocopherol remarkably suppressed the CL when ROS was HO*. The present study revealed that MCLA-dependent CL assay provides a simple and rapid method for the evaluation of antioxidants as a quencher or scavenger against any kind of ROS. (c) 2005 John Wiley & Sons, Ltd.

Publication Types:

PMID: 15966055 [PubMed - indexed for MEDLINE]

Antioxidant

Bioorg Med Chem Lett. 2004 Aug 2;14(15):3985-91.

Synthesis, characterization, and direct aqueous superoxide anion scavenging of a highly water-dispersible astaxanthin-amino acid conjugate.

Jackson HL, **Cardounel AJ**, **Zweier JL**, **Lockwood SF**.

Hawaii Biotech, Inc., 99-193 Aiea Heights Drive, Suite 200, Aiea, HI 96701, USA.

The aqueous solubility and/or dispersibility of synthetic carotenoid analogs can be improved by varying the chemical structure(s) of the esterified moieties. In the current study, a highly water-dispersible astaxanthin (3,3'-dihydroxy-beta,beta-carotene-4,4'-dione) derivative was synthesized by esterification to the amino acid L-lysine, and subsequently converted to the tetrahydrochloride salt. Deep violet, evenly colored aqueous suspensions were obtained with addition of the novel derivative to USP purified water up to a maximum of 181.6 mg/mL. These aqueous suspensions were obtained without the addition of heat, detergents, co-solvents, or other additives. At higher concentrations (above 181.6 mg/mL), the dispersion became turbid and viscous. There was no saturation point up to 181.6 mg/mL. The direct superoxide scavenging ability of the tetrahydrochloride dilysine astaxanthin salt was also evaluated by electron paramagnetic resonance (EPR) spectroscopy in a well-characterized in vitro isolated human neutrophil assay. The novel derivative was an extremely potent (micromolar concentration) aqueous-phase scavenger, with near-complete suppression of the superoxide anion signal (as detected by spin-trap adducts of DEPMPO) achieved at 100 microM. To the authors' knowledge, this novel carotenoid derivative exhibits the greatest aqueous dispersibility yet described for a natural and/or synthetic C40 carotenoid, and as such, will find utility in those applications for which aqueous-phase singlet oxygen quenching and direct radical scavenging are required.

PMID: 15225712 [PubMed - indexed for MEDLINE]

Antioxidant

Chem Phys Lipids. 2001 Nov;113(1-2):11-22.

Molecular characteristics of astaxanthin and beta-carotene in the phospholipid monolayer and their distributions in the phospholipid bilayer.

Shibata A, **Kiba Y**, **Akati N**, **Fukuzawa K**, **Terada H**.

Faculty of Pharmaceutical Sciences, The University of Tokushima, Shomachi, Tokushima 770-8505, Japan. ashibata@ph.tokushima-u.ac.jp

The molecular characteristics of the monolayers of astaxanthin with polar group on the beta-ionone ring in the molecule and beta-carotene without polar group and their interactions in mixed carotenoid-phospholipid monolayers and the effects of carotenoids on the phase behavior of the phospholipid bilayers were examined by the monolayer technique and differential scanning calorimetry (DSC). We found from the monolayer study that beta-carotene had an amphiphilic nature. The molecular assembly of astaxanthin in the monolayer at the hydrophobic/hydrophilic interface was more stable than that of beta-carotene. Dimyristoylphosphatidylcholine (DMPC) in the monolayer was miscible with astaxanthin in the range of 0-0.4 mol fractions of astaxanthin, but not fully miscible with beta-carotene even at low concentrations below 0.1 mol fraction of beta-carotene. Surface potential and compression/expansion cycles of beta-carotene monolayer indicated the formation of molecular aggregates by itself. DSC study showed that when small amount of astaxanthin was added, the transition temperature of dipalmitoylphosphatidylcholine (DPPC) was markedly shifted to lower temperatures and that the transition peak was asymmetrically broadened, indicative of a significant depression in cooperativity of the gel to liquid-crystalline transition. The asymmetric DSC endothermic bands of DPPC incorporating small amounts of astaxanthin were well fit by deconvolution into two to three domains containing different concentrations of astaxanthin. On the contrary, the incorporation of beta-carotene resulted in a small depression of the main transition temperature with a slight broadening of the transition peak, suggesting a small miscibility of beta-carotene with the phospholipid bilayer or a formation of aggregates of beta-carotene in the membranes. These results suggest that there would be a high localized concentration in the phase separated membrane for astaxanthin or beta-carotene to function effectively as scavenger.

PMID: 11687223 [PubMed - indexed for MEDLINE]

Antioxidant

Biochem Biophys Res Commun. 2001 Oct 19;288(1):225-32.

Astaxanthin and peridinin inhibit oxidative damage in Fe(2+)-loaded liposomes: scavenging oxyradicals or changing membrane permeability?

Barros MP, **Pinto E**, **Colepicolo P**, **Pedersén M**.

Department of Botany, Stockholm University, SE-10691 Stockholm, Sweden. mpbarros@botan.su.se

Astaxanthin and peridinin, two typical carotenoids of marine microalgae, and lycopene were incorporated in phosphatidylcholine multilamellar liposomes and tested as inhibitors of lipid oxidation. Contrarily to peridinin results, astaxanthin strongly reduced lipid damage when the lipoperoxidation promoters-H(2)O(2), tert-butyl hydroperoxide (t-ButOOH) or ascorbate-and Fe(2+):EDTA were added simultaneously to the liposomes. In order to check if the antioxidant activity of carotenoids was also related to their effect on membrane permeability, the peroxidation processes were initiated by adding the promoters to Fe(2+)-loaded liposomes (encapsulated in the inner aqueous solution). Despite that the rigidifying effect of carotenoids in membranes was not directly measured here, peridinin probably has decreased membrane permeability to initiators (t-ButOOH > ascorbate > H(2)O(2)) since its incorporation limited oxidative damage on iron-liposomes. On the other hand, the antioxidant activity of astaxanthin in iron-containing vesicles might be derived from its known rigidifying effect and the inherent scavenging ability.

Publication Types:

PMID: 11594777 [PubMed - indexed for MEDLINE]

Antioxidant

Arch Biochem Biophys. 2001 Jan 1;385(1):13-9.

The interaction of dietary carotenoids with radical species.

Mortensen A, **Skibsted LH**, **Truscott TG**.

Department of Dairy and Food Science, Royal Veterinary and Agricultural University, Frederiksberg, Denmark.

Dietary carotenoids react with a wide range of radicals such as CCl3O2*, RSO2*, NO2*, and various arylperoxyl radicals via electron transfer producing the radical cation of the carotenoid. Less strongly oxidizing radicals, such as alkylperoxyl radicals, can lead to hydrogen atom transfer generating the neutral carotene radical. Other processes can also arise such as adduct formation with sulphur-centered radicals. The oxidation potentials have been established, showing that, in Triton X-100 micelles, lycopene is the easiest carotenoid to oxidize to its radical cation and astaxanthin is the most difficult. The interaction of carotenoids and carotenoid radicals with other antioxidants is of importance with respect to anti- and possibly pro-oxidative reactions of carotenoids. In polar environments the vitamin E (alpha-tocopherol) radical cation is deprotonated (TOH*+ --> TO* + H+) and TO* does not react with carotenoids, whereas in nonpolar environments such as hexane, TOH*+ is converted to TOH by hydrocarbon carotenoids. However, the nature of the reaction between the tocopherol and various carotenoids shows a marked variation depending on the specific tocopherol homologue. The radical cations of the carotenoids all react with vitamin C so as to "repair" the carotenoid.

Publication Types:

- Research Support, Non-U.S. Gov't
- Review

PMID: 11361009 [PubMed - indexed for MEDLINE]

Antioxidant

J Nutr. 2000 Jul;130(7):1800-8.

Depletion of alpha-tocopherol and astaxanthin in Atlantic salmon (Salmo salar) affects autoxidative defense and fatty acid metabolism.

Bell JG, **McEvoy J**, **Tocher DR**, **Sargent JR**.

Institute of Aquaculture, University of Stirling, Stirling FK9 4LA, Scotland, U.K.

Duplicate groups of Atlantic salmon post-smolts were fed four purified diets supplemented with both vitamin E and the carotenoid astaxanthin (Ax) (+E, +Ax), or supplemented with either vitamin E or Ax (-E, +Ax and +E, -Ax) or deficient in both vitamin E and Ax (-E, -Ax) for 22 wk. There were no effects of diet on growth rate, but an extensive lipoid liver degenerative lesion was observed in 15% of fish fed diets deficient in vitamin E. Tissue vitamin E concentrations varied in accordance with dietary vitamin E in liver, muscle, heart, plasma, brain and eye; levels were reduced to approximately 3% in liver but only to 40% in eye of fish fed diets deficient in vitamin E compared with those fed diets supplemented with vitamin E. An interactive sparing of Ax supplementation on tissue vitamin E concentration was observed, but only in brain. Dietary deficiency of both vitamin E and Ax significantly increased the recovery of desaturated and elongated products of both [1-(14)C] 18:3(n-3) and [1-(14)C] 20:5(n-3) in isolated hepatocytes, suggesting that conversion of fatty acids to their long-chain highly unsaturated products can be stimulated by a deficiency of lipid-soluble antioxidants. The antioxidant synergism of vitamin E and Ax was supported by their ability to reduce malondialdehyde formation in an in vitro stimulation of microsomal lipid peroxidation and to reduce plasma levels of 8-isoprostane. The results of this study suggest that both vitamin E and the carotenoid Ax have antioxidant functions in Atlantic salmon.

Publication Types:

PMID: 10867054 [PubMed - indexed for MEDLINE]

Antioxidant

Biochim Biophys Acta. 2000 Jan 15;1463(1):179-87.

Exogenously incorporated ketocarotenoids in large unilamellar vesicles. Protective activity against peroxidation.

Rengel D, **Díez-Navajas A**, **Serna-Rico A**, **Veiga P**, **Muga A**, **Milicua JC**.

Department of Biochemistry and Molecular Biology, University of the Basque Country, P.O. Box 644, 48080, Bilbao, Spain.

The ability of astaxanthin and canthaxanthin as chain-breaking antioxidants was studied in Cu(2+)-initiated peroxidation of phosphatidylcholine large unilamellar vesicles (LUVs). Both carotenoids increased the lag period that precedes the maximum rate of lipid peroxidation, though astaxanthin showed stronger activity. For these experiments, different amounts of xanthophylls were exogenously added to previously made LUVs, non-incorporated pigment being afterwards removed. Differential scanning calorimetry assays with L-beta,gamma-dimyristoyl-alpha-phosphatidylcholine LUVs demonstrated that xanthophylls incorporated as described interact with the lipid matrix becoming interspersed among the phospholipid molecules.

Publication Types:

PMID: 10631307 [PubMed - indexed for MEDLINE]

Antioxidant

FEBS Lett. 1997 Nov 24;418(1-2):91-7.

Comparative mechanisms and rates of free radical scavenging by carotenoid antioxidants.

Mortensen A, **Skibsted LH**, **Sampson J**, **Rice-Evans C**, **Everett SA**.

Department of Dairy and Food Science, Royal Veterinary and Agricultural University, Frederiksberg C, Denmark.

The comparative mechanisms and relative rates of nitrogen dioxide (NO2.), thiyl (RS.) and sulphonyl (RSO2.) radical scavenging by the carotenoid antioxidants lycopene, lutein, zeaxanthin, astaxanthin and canthaxanthin have been determined by pulse radiolysis. All the carotenoids under study react with the NO2. radical via electron transfer to generate the carotenoid radical cation (Car.+). In marked contrast the glutathione and 2-mercaptoethanol thiyl radicals react via a radical addition process to generate carotenoid-thiyl radical adducts [RS-Car].. The RSO2. radical undergoes both radical addition, [RSO2-Car]. and electron abstraction, Car.+. Both carotenoid adduct radicals and radical cations decay bimolecularly. Absolute rate constants for radical scavenging were in the order of approximately 10(7)-10(9) M(-1) s(-1) and follow the sequence HO(CH2)2S. > RSO2. > GS. > NO2.. Although there were some discernible trends in carotenoid reactivity for individual radicals, rate constants varied by no greater than a factor of 2.5. The mechanism and rate of scavenging is strongly dependent on the nature of the oxidising radical species but much less dependent on the carotenoid structure.

Publication Types:

PMID: 9414102 [PubMed - indexed for MEDLINE]

Antioxidant

J Nutr Sci Vitaminol (Tokyo). 1997 Jun;43(3):345-55.

Inhibition of beta-carotene and astaxanthin of NADPH-dependent microsomal phospholipid peroxidation.

Nakagawa K, **Kang SD**, **Park DK**, **Handelman GJ**, **Miyazawa T**.

Department of Applied Biological Chemistry, Tohoku University, Sendai, Japan.

To evaluate the antioxidant effects of beta-carotene and astaxanthin, rat liver microsomes were exposed to a mixture of chelated iron (Fe3+/ADP) and NADPH. The carotenoids (190 pmol/mg protein) were incorporated into some of these microsomal membranes, and phospholipid hydroperoxides (PLOOH), thiobarbituric acid reactive substances (TBARS) and endogenous alpha-tocopherol content were measured over time after the initiation of oxidant stress. In control microsomes, oxidant stress led to accumulation of 1,865 (+/- 371) pmol PLOOH/mg protein during the initial 10-min peroxidation reaction, followed by a more gradual decrease during the subsequent 20-min of reaction. PLOOH accumulation during the initial 10-min reaction period was reduced to 588 (+/- 169) pmol/mg protein with beta-carotene present and 800 (+/- 288) pmol/mg protein with astaxanthin present. During the following 20-min of incubation, PLOOH levels declined in the carotenoid-supplemented microsomes but continued to increase at a slower rate in control preparations. TBARS did not show such large accumulation as observed in PLOOH during the initial 10-min incubation in any microsomal sample. The presence of carotenoids in the microsomal membrane partially inhibited the loss of alpha-tocopherol, especially during the later phase of oxidant stress. When lipid peroxidation is generated by membrane-bound cyt-P450, the specific measurement of PLOOH clearly demonstrates that the presence of carotenoids provides antioxidant protection.

PMID: 9268922 [PubMed - indexed for MEDLINE]

Z Lebensm Unters Forsch. 1993 May;196(5):423-9.

Carotenoid scavenging of radicals. Effect of carotenoid structure and oxygen partial pressure on antioxidative activity.

Jørgensen K, **Skibsted LH**.

RVAU Centre for Food Research, Royal Veterinary and Agricultural University, Frederiksberg, Denmark.

Carotenoid scavenging of free radicals has been investigated in peroxidizing methyl esters of unsaturated fatty acids using (i) metmyoglobin as a water-based free-radical initiator in a heterogeneous lipid/water system, and (ii) azo-bis-isobutyronitrile as a free-radical initiator in a homogeneous chloroform solution. For the heterogeneous system, using a combination of electrochemical oxygen depletion measurements, spectrophotometric determination of lipid hydroperoxides and carotenoid degradation, it was demonstrated that each of the four carotenoids astaxanthin, beta-carotene, canthaxanthin, and zeaxanthin protects the methyl esters against oxidation. The antioxidative effect increases with increasing carotenoid concentration, increases with decreasing oxygen partial pressure ($0.010 < pO2 < 0.50$ atm), and shows little dependence on the structure of the carotenoid. For a homogeneous solution, the effect of the structure of the carotenoid was further investigated, and it was shown that the stability of the four carotenoids in the oxidizing system are different, with the order of decreasing stability being: astaxanthin > canthaxanthin > beta-carotene > zeaxanthin. Each of the four carotenoids can suppress lipid oxidation and the degree of suppression of peroxidation of methyl linoleate corresponds to the difference in stability.

PMID: 8511974 [PubMed - indexed for MEDLINE]

Arch Biochem Biophys. 1992 Sep;297(2):291-5.

Astaxanthin and canthaxanthin are potent antioxidants in a membrane model.

Palozza P, **Krinsky NI**.

Department of Biochemistry, Tufts University School of Medicine, Boston, Massachusetts 02111-1837.

When the conjugated keto-carotenoids, either astaxanthin or canthaxanthin, are added to rat liver microsomes undergoing radical-initiated lipid peroxidation under air, they are as effective as alpha-tocopherol in inhibiting this process. This contrasts with the effect of beta-carotene, which is a much less potent antioxidant when added in this system, without the addition of other antioxidants.

Publication Types:

PMID: 1497349 [PubMed - indexed for MEDLINE]

Antioxidant

Biochim Biophys Acta. 1992 Jun 22;1126(2):178-84.

Antioxidant activity of xanthophylls on peroxyl radical-mediated phospholipid peroxidation.

Lim BP, **Nagao A**, **Terao J**, **Tanaka K**, **Suzuki T**, **Takama K**.

National Food Research Institute, Ministry of Agriculture, Forestry and Fisheries, Ibaraki, Japan.

The ability of xanthophylls (canthaxanthin, zeaxanthin, and astaxanthin) as chain-breaking antioxidants was investigated in peroxyl radical-mediated peroxidation of phosphatidylcholine (PC) liposomes under atmospheric conditions using lipid-soluble and water-soluble radical generators. These xanthophylls retarded the chain propagation reaction of phosphatidylcholine hydroperoxides (PC-OOH) formation, although their activities to trap chain-carrying peroxyl radical were much less than that of alpha-tocopherol. In chick plasma studies, it was observed that endogenious xanthophylls participated in the antioxidant defenses against the attack of aqueous peroxyl radical. It was concluded that xanthophylls possess the ability to act as chain-breaking antioxidants in the peroxidation of membraneous phospholipids. Dietary xanthophylls may, therefore, be helpful in resisting membraneous phospholipids against oxidative damage in vivo.

PMID: 1627620 [PubMed - indexed for MEDLINE]

Physiol Chem Phys Med NMR. 1990;22(1):27-38.

Inhibition of oxidative injury of biological membranes by astaxanthin.

Kurashige M, **Okimasu E**, **Inoue M**, **Utsumi K**.

Department of Medical Biology, Kochi Medical School, Japan.

The value of astaxanthin, a carotenoid pigment, in the treatment of oxidative injury is assessed. Astaxanthin protects the mitochondria of vitamin E-deficient rats from damage by Fe2(+)-catalyzed lipid peroxidation both in vivo and in vitro. The inhibitory effect of astaxanthin on mitochondrial lipid peroxidation is stronger than that of alpha-tocopherol. Thin layer chromatographic analysis shows that the change in phospholipid components of erythrocytes from vitamin E-deficient rats induced by Fe2+ and Fe3(+)-xanthine/xanthine oxidase system was significantly suppressed by astaxanthin. Carrageenan-induced inflammation of the paw is also significantly inhibited by administration of astaxanthin. These data indicate that astaxanthin functions as a potent antioxidant both in vivo and in vitro.

PMID: 2084711 [PubMed - indexed for MEDLINE]

Antioxidant

Lipids. 1989 Jul;24(7):659-61.

Antioxidant activity of beta-carotene-related carotenoids in solution.

Terao J.

Research Institute for Food Science, Kyoto University, Uji, Kyoto 611, Japan.

The effect of the antioxidant activity of beta-carotene and related carotenoids on the free radical-oxidation of methyl linoleate in solution was examined by measuring the production of methyl linoleate hydroperoxides. Canthaxanthin and astaxanthin which possess oxo groups at the 4 and 4'-positions in the beta-ionone ring retarded the hydroperoxide formation more efficiently than beta-carotene and zeaxanthin which possess no oxo groups. The rates of autocatalytic oxidation of canthaxanthin and astaxanthin were also slower than those of beta-carotene and zeaxanthin. These results suggest that canthaxanthin and astaxanthin are more effective antioxidants than beta-carotene by stabilizing the trapped radicals.

Publication Types:

PMID: 2779372 [PubMed - indexed for MEDLINE]

Antioxidant

Critical Reviews in Food Science and Nutrition, 46:185–196 (2006)

Astaxanthin: A Review of its Chemistry and Applications

I. HIGUERA-CIAPARA, L. F ´ELIX-VALENZUELA, and F. M. GOYCOOLEA
Centro de Investigaci´on en Alimentaci´on y Desarrollo, A.C., P.O. Box 1735. Hermosillo, Sonora. M´exico. 83000

Astaxanthin is a carotenoid widely used in salmonid and crustacean aquaculture to provide the pink color characteristic of that species. This application has been well documented for over two decades and is currently the major market driver for the pigment. Additionally, astaxanthin also plays a key role as an intermediary in reproductive processes. Synthetic astaxanthin dominates the world market but recent interest in natural sources of the pigment has increased substantially. Common sources of natural astaxanthin are the green algae Haematococcus pluvialis, the red yeast, Phaffia rhodozyma, as well as crustacean byproducts. Astaxanthin possesses an unusual antioxidant activity which has caused a surge in the nutraceutical market for the encapsulated product. Also, health benefits such as cardiovascular disease prevention, immune system boosting, bioactivity against Helycobacter pylori, and cataract prevention, have been associated with astaxanthin consumption. Research on the health benefits of astaxanthin is very recent and has mostly been performed in vitro or at the pre-clinical level with humans. This paper reviews the current available evidence regarding astaxanthin chemistry and its potential beneficial effects in humans.

Antioxidant

Lebensm Unters Forsch (1993) 196: 423-429

Carotenoid Scavenging of Radicals
Effect of carotenoid structure and oxygen partial pressure on antioxidative activiy

Kevin Jorgensen and Leif H. Skibsted

Carotenoid scavenging of free radicals has been investigated in peroxidating methyl esters of unsaturated fatty acids using (i) metmyoglobin as a water-based free-radical initiator in a heterogeneous lipid/water system, and (ii) azo-*bis*-isobutyronitrile as a free-radical initiator homogeneous chloroform solution. For the heterogeneous system, using a combination of electrochemical oxygen depletion measurements, spectrophotometric determination of lipid hydroperoxides and carotenoid degradation, it was demonstrated that each of the four carotenoids astaxanthin, β-carotene, canthaxanthin, and zeaxanthin protects the methyl esters against oxidation. The antioxidant effect increases with increasing carotenoid concentration increases with decreasing oxygen partial pressure ($0.010 < 0.50$ atm), and shows little dependence on the structure of the carotenoid. For a homogeneous solution, the effect of the structure of the carotenoid was further investigated, and it was shown that the stability of the four carotenoids in the oxidizing system are different, with the order of decreasing stability being: astaxanthin > canthaxanthin > β-carotene > zeaxanthin. Each of the four carotenoids can suppress lipid oxidation and the degree of suppression of peroxidation of methyl linoleate corresponds to the difference in stability.

Antioxidant

Pure & Appl. Chem., Vol. 63, No. 1, pp. 141-146, 1991.
Printed in Great Britain.

Biological functions and activities of animal carotenoids

Wataru Miki

Astaxanthin, on of the dominant carotenoids in marine animals, showed both a strong quenching effect against singlet oxygen, and a strong scavenging effect against free radicals. These effects are considered to be defense mechanisms in the animals for attacking these active oxygen species. The activities of astaxanthin are approximately 10 times stronger than those of other carotenoids that were tested, namely zeaxanthin, lutein, tunaxanthin, canthaxanthin and β-carotene, and 100 times greater than those of a tocopherol. Astaxanthin also showed strong activity as an inhibitor of lipid peroxidation mediated by these active forms of oxygen. From these results, astaxanthin has a the properties of a "SUPER VITAMIN E".

Antioxidant

Am J Cardiol 2008;101[suppl]:20D–29D

Biologic Activity of Carotenoids Related to Distinct Membrane Physicochemical Interactions

Hyesun McNulty, PhD,[a] Robert F. Jacob, PhD,[a] and R. Preston Mason, PhD[a,b,]*

Carotenoids are naturally occurring organic pigments that are believed to have therapeutic benefit in treating cardiovascular disease (CVD) because of their antioxidant properties. However, prospective randomized trials have failed to demonstrate a consistent benefit for the carotenoid _-carotene in patients at risk for CVD. The basis for this apparent paradox is not well understood but may be attributed to the distinct antioxidant properties of various carotenoids resulting from their structure-dependent physicochemical interactions with biologic membranes. To test this hypothesis, we measured the effects of astaxanthin, zeaxanthin, lutein, _-carotene, and lycopene on lipid peroxidation using model membranes enriched with polyunsaturated fatty acids. The correlative effects of these compounds on membrane structure were determined using small-angle x-ray diffraction approaches. The nonpolar carotenoids, lycopene and _-carotene, disordered the membrane bilayer and stimulated membrane lipid peroxidation (>85% increase in lipid hydroperoxide levels), whereas astaxanthin (a polar carotenoid) preserved membrane structure and exhibited significant antioxidant activity (>40% decrease in lipid hydroperoxide levels). These results suggest that the antioxidant potential of carotenoids is dependent on their distinct membrane lipid interactions. This relation of structure and function may explain the differences in biologic activity reported for various carotenoids, with important therapeutic implications.

Antioxidant

Int. J. Vitam. Nutr. Res., 77(1), 2007, 3-11

Effects pf Astaxanthin Supplementation on Lipid Peroxidation

Jouni Karppi, Tiina H. Rissanen, kristiina Nyyssonen, Jari Kaikkonen, Anders G. Olsson, Sari Voutilainen and Jukka T. Salonen

Abstract: Astaxanthin, the main carotenoid pigment in aquatic animals, has greater antioxidant activity *in vitro* (protecting against lipid peroxidation) and aa more polar configuration then other carotenoids. We investigated the effect of three-month astaxanthin supplementation on lipid peroxidation in healthy non-smoking Finnish men, aged 19-33 years by using a randomized double-blind study design. Also absorption of astaxanthin from capsules into bloodstream and its safety were evaluate. The intervention group received two 4-mg astaxanthin (Astxan®) capsules daily, and the control group two identical-looking placebo capsules. Astaxanthin supplementation elevated plasma astaxanthin levels to 0.032 μmol/L ($p<0.001$ for the change compared with the placebo group). We observed that levels of plasma 12- and 15-hydroxy fatty acids were reduced statistically significantly in the astaxanthin group ($p=0.048$ and $p=0.047$ respectively) during supplementation, but not in the placebo group, as compared with the placebo group. The present study suggests that intestinal absorption of astaxanthin delivered as capsules is adequate, and well tolerated. Supplementation with astaxanthin may decrease *in vivo* oxidation of fatty acids in healthy men.

Antioxidant

J Agric Food Chem. 2006 Mar 22;54(6):2418-23.

Astaxanthin protects against oxidative stress and calcium-induced porcine lens protein degradation.

Wu TH, Liao JH, Hou WC, Huang FY, Maher TJ, Hu CC.

Department of Clinical Pharmacy, School of Pharmacy, Taipei Medical University, Taipei 110, Taiwan. thwu@tmu.edu.tw

Astaxanthin (ASTX), a carotenoid with potent antioxidant properties, exists naturally in various plants, algae, and seafoods. In this study, we investigated the in vitro ability of ASTX to protect porcine lens crystallins from oxidative damage by iron-mediated hydroxyl radicals or by calcium ion-activated protease (calpain), in addition to the possible underlying biochemical mechanisms. ASTX (1 mM) was capable of protecting lens crystallins from being oxidized, as measured by changes in tryptophan fluorescence, in the presence of a Fenton reaction solution containing 0.2 mM Fe2+ and 2 mM H2O2. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis analysis demonstrated that beta(high)-crystallin was the most vulnerable protein under these conditions of free radical exposure. The proteolysis of lens crystallins induced by calcium ion-activated calpain was also inhibited by ASTX (0.03-1 mM) as determined by daily measurement of the light-scattering intensity at 405 nm for five consecutive days. ASTX at 1 mM was as potent as a concentration of 0.1 mM calpain inhibitor E64 in protecting the oxidative damage/hydrolysis of porcine crystallins. At a concentration of 1 mM, ASTX provided better protection than the endogenous antioxidant glutathione in terms of suppressing calcium-induced turbidity of lens proteins. Thin-layer chromatography analysis indicated that ASTX interacted with calcium ions to form complexes, which we believe interfere with the hydrolysis of lens crystallins by calcium-activated calpain. This in vitro study shows that ASTX is capable of protecting porcine lens proteins from oxidative insults and degradation by calcium-induced calpain.

PMID: 16536628 [PubMed - indexed for MEDLIN

Antioxidant

Reprod Domest Anim. 2009 Nov 18. [Epub ahead of print]

Antioxidative Effects of Astaxanthin against Nitric Oxide-Induced Oxidative Stress on Cell Viability and Gene Expression in Bovine Oviduct Epithelial Cell and the Developmental Competence of Bovine IVM/IVF Embryos.

Jang HY, Ji SJ, Kim YH, Lee HY, Shin JS, Cheong HT, Kim JT, Park IC, Kong HS, Park CK, Yang BK.

College of Animal Life Science, Kangwon National University, Chuncheon, Korea.

Abstract

Contents The aim of the present study was to elucidate the fundamental mechanism of bovine oviduct epithelial cell (BOEC) co-culture on developmental capacity of bovine in vitro oocyte maturation/in vitro fertilization (IVM/IVF) embryos. We examined the effects of astaxanthin against nitric oxide-induced oxidative stress on cell viability by MTT assay, lipid peroxidation (LPO) by using thiobarbituric acid (TBA) reaction for malondialdehyde (MDA) and the expression of antioxidant genes (CuZnSOD, MnSOD and Catalase) or apoptosis genes (Bcl-2, Caspase-3 and Bax) by RT-PCR in BOEC. We also evaluated the developmental rates of bovine IVM/IVF embryos co-cultured with BOEC pre-treated with astaxanthin (500 mum) in the presence or absence of sodium nitroprusside (SNP, 1000 mum) for 24 h. Cell viability in BOEC treated with SNP (50-2000 mum) lowered, while astaxanthin addition (50-500 mum) increased it in a dose-dependent manner. Cell viability in astaxanthin plus SNP (1000 mum) gradually recovered according to the increase in astaxanthin additions (100-500 mm). The LPO in astaxanthin group (50-500 muM) gradually decreased in a dose dependent manner and among SNP or astaxanthin plus SNP group, SNP alone and astaxanthin (50 muM) plus SNP shown a significant increase than other groups ($p < 0.05$). Expression of apoptosis or antioxidant genes was detected by RT-PCR. Bcl-2 and antioxidant genes were detected in astaxanthin or astaxanthin plus SNP group, and Caspase-3 and Bax genes were only found in SNP group. When bovine IVM/IVF embryos were cultured for 6-7 days under co-culture system such as BOEC treated with astaxanthin in the presence or absence of SNP, the developmental ability to blastocysts in 500 mum astaxanthin group was the highest of all groups. These results suggest that astaxanthin has a antioxidative effect on cell viability and LPO of BOEC, and development of bovine IVM/IVF embryos due to the induction of antioxidant genes and suppression of apoptosis genes.

PMID: 19930137 [PubMed - as supplied by publisher]

Antioxidant

Cell Biol Toxicol. 2010 Oct;26(5):457-67. Epub 2010 Mar 14.

Astaxanthin prevents in vitro auto-oxidative injury in human lymphocytes.

Bolin AP, Macedo RC, Marin DP, Barros MP, Otton R.

Cellular Physiology Laboratory, Postgraduate Program-Health Science, CBS, Cruzeiro do Sul University, Tatuapé, São Paulo, Brazil.

Abstract

Upon mitogen sensitization, lymphocytes undergo proliferation by oxyradical-based mechanisms. Through continuous resting-restimulation cycles, lymphocytes accumulate auto-induced oxidative lesions which lead to cell dysfunction and limit their viability. Astaxanthin (ASTA) is a nutritional carotenoid that shows notable antioxidant properties. This study aims to evaluate whether the in vitro ASTA treatment can limit oxyradical production and auto-oxidative injury in human lymphocytes. Activated lymphocytes treated with 5 microM ASTA showed immediate lower rates of O(2)(*-) /H(2)O(2) production whilst NO* and intracellular Ca(2+) levels were concomitantly enhanced (<or=4 h). In long-term treatments (>24 h), the cytotoxicity test for ASTA showed a sigmoidal dose-response curve (LC50 = 11.67 +/- 0.42 microM), whereas higher activities of superoxide dismutase and catalase in 5 microM ASTA-treated lymphocytes were associated to significant lower indexes of oxidative injury. On the other hand, lower proliferative scores of ASTA lymphocytes might be a result of diminished intracellular levels of pivotal redox signaling molecules, such as H(2)O(2). Further studies are necessary to establish the ASTA-dose compensation point between minimizing oxidative damages and allowing efficient redox-mediated immune functions, such as proliferation, adhesion, and oxidative burst.

PMID: 20229275 [PubMed - in process]

Antioxidant

Eur J Nutr. 2010 Apr 2. [Epub ahead of print]

Astaxanthin addition improves human neutrophils function: in vitro study.

Macedo RC, Bolin AP, Marin DP, Otton R.

Postgraduate Program, Health Science, CBS, Cruzeiro do Sul University, Avenida Regente Feijó, 1295.

Tatuapé, São Paulo, SP, CEP 03342-000, Brazil.

Abstract

PURPOSE: The aim of the present study was to evaluate the in vitro effect of carotenoid astaxanthin (ASTA) on the phagocytic and microbicidal capacities, cytokine release, and reactive oxygen species production in human neutrophils.
METHODS: The following parameters were evaluated: cytotoxic effect of ASTA on human neutrophils viability, phagocytic and microbicidal capacities of neutrophils by using Candida albicans assay, intracellular calcium mobilization (Fura 2-AM fluorescent probe), superoxide anion (lucigenin and DHE probes), hydrogen peroxide (H(2)O(2), phenol red), and nitric oxide (NO.) (Griess reagent) production, activities of antioxidant enzymes (total/Mn-SOD, CAT, GPx, and GR), oxidative damages in biomolecules (TBARS assay and carbonyl groups), and cytokine (IL-6 and TNF-alpha) release.
RESULTS: Astaxanthin significantly improves neutrophil phagocytic and microbicidal capacity, and increases the intracellular calcium concentration and NO. production. Both functional parameters were accompanied by a decrease in superoxide anion and hydrogen peroxide and IL-6 and TNF-alpha production. Oxidative damages in lipids and proteins were significantly decreased after ASTA-treatment.
CONCLUSIONS: Taken together our results are supportive to a beneficial effect of astaxanthin-treatment on human neutrophils function as demonstrated by increased phagocytic and fungicide capacity as well as by the reduced superoxide anion and hydrogen peroxide production, however, without affecting neutrophils capacity to kill C. albicans. This process appears to be mediated by calcium released from intracellular storages as well as nitric oxide production.

PMID: 20361333 [PubMed - as supplied by publisher]

Antioxidant

Phytother Res. 2010 Jan;24(1):54-9.

Cytoprotective role of astaxanthin against glycated protein/iron chelate-induced toxicity in human umbilical vein endothelial cells.

Nishigaki I, Rajendran P, Venugopal R, Ekambaram G, Sakthisekaran D, Nishigaki Y.

NPO International Laboratory of Biochemistry, 1-166 Uchide, Nakagawa-ku Nagoya 454-0926, Japan.

nishigaki@se.starcat.ne.jp

Abstract

Astaxanthin (ASX), a red carotenoid pigment with no pro-vitamin A activity, is a biological antioxidant that occurs naturally in a wide variety of plants, algae and seafoods. This study investigated whether ASX could inhibit glycated protein/iron chelate-induced toxicity in human umbilical-vein endothelial cells (HUVEC) by interfering with ROS generation in these cells. Glycated fetal bovine serum (GFBS) was prepared by incubating fetal bovine serum (FBS) with high-concentration glucose. Stimulation of cultured HUVECs with 50 mm 1 mL of GFBS significantly enhanced lipid peroxidation and decreased antioxidant enzyme activities and levels of phase II enzymes. However, preincubation of the cultures with ASX resulted in a marked decrease in the level of lipid peroxide (LPO) and an increase in the levels of antioxidant enzymes in an ASX concentration-dependent manner. These results demonstrate that ASX could inhibit LPO formation and enhance the antioxidant enzyme status in GFBS/iron chelate-exposed endothelial cells by suppressing ROS generation, thereby limiting the effects of the AGE-RAGE interaction. The results indicate that ASX could have a beneficial role against glycated protein/iron chelate-induced toxicity by preventing lipid and protein oxidation and increasing the activity of antioxidant enzymes.

PMID: 19548280 [PubMed - indexed for MEDLINE]

Antioxidant