

Zeaxanthin as a Hepatoprotective

[Dig Dis Sci](#). 2009 May 8. [Epub ahead of print]

Protective Effects of the Carotenoid Zeaxanthin in Experimental Nonalcoholic Steatohepatitis.

[Chamberlain SM](#), [Hall JD](#), [Patel J](#), [Lee JR](#), [Marcus DM](#), [Sridhar S](#), [Romero MJ](#), [Labazi M](#), [Caldwell RW](#), [Bartoli M](#).

Section of Gastroenterology, Department of Medicine, Medical College of Georgia, BBR-2538, Augusta, GA, 30912, USA, schamberlain@mcg.edu.

Fat infiltration and inflammation cause liver injury and fibrosis and may progress to nonalcoholic steatohepatitis (NASH) and end-stage liver disease. Currently, there are no effective treatments for NASH. Zeaxanthin is a carotenoid which has been shown to be preferentially accumulated in the adipose tissue and liver. We hypothesized that treatment with zeaxanthin may decrease oxidative stress in the liver and, possibly, halt the inflammation and fibrosis associated with NASH. Here we tested zeaxanthin effects in preventing progression of liver injury in a model of NASH. Mongolian gerbils, fed a methionine-choline-deficient diet, were treated with different doses of zeaxanthin. We assessed histopathological changes by hematoxylin-eosin and Masson trichrome staining and determined oxidative stress by measuring lipid peroxidation. The obtained results show that zeaxanthin significantly prevented NASH progression by decreasing oxidative stress and liver fibrosis, thus suggesting a potential therapeutic application for this carotenoid in the management of NASH.

PMID: 19424798 [PubMed - as supplied by publisher]

Zeaxanthin dipalmitate from *Lycium chinense* has hepatoprotective activity.

[Kim HP](#), [Kim SY](#), [Lee EJ](#), [Kim YC](#), [Kim YC](#).

College of Pharmacy, Seoul National University, Korea.

We previously reported the isolation of zeaxanthin and zeaxanthin dipalmitate using bioactivity-guided fractionation to discover hepatoprotective components of *Lycium chinense* against carbon tetrachloride induced hepatotoxicity. The present study was designed to uncover the effects of zeaxanthin dipalmitate on hepatic parenchymal and nonparenchymal cells in vitro. Uptake of [3H]thymidine by cultured rat Ito cells in response to zeaxanthin dipalmitate was measured. Collagen synthesis was assessed by the collagenase digestion method. The effects of zeaxanthin dipalmitate on the formation of nitric oxide (NO) and the release of tumor necrosis factor-alpha (TNF-alpha) from Kupffer cells and peritoneal macrophages were also assayed. Zeaxanthin dipalmitate showed a significant hepatoprotective activity against carbon tetrachloride toxicity. Cellular malondialdehyde (MDA) levels declined significantly with the treatment of the compound in a concentration dependent manner. Zeaxanthin dipalmitate significantly inhibited the uptake of [3H]thymidine by Ito cells. Zeaxanthin dipalmitate also reduced collagen synthesis in Ito cells by 65.1% ($p < 0.05$) as compared to untreated controls. The formation of NO in either Kupffer cells or in peritoneal macrophages was significantly decreased by zeaxanthin dipalmitate in a concentration dependent manner. The release of TNF-alpha was somewhat less affected by the compound. From these results, we conclude that zeaxanthin dipalmitate exerts a potent hepatoprotective activity by inhibiting Ito cell proliferation, collagen synthesis and by inhibiting certain biochemical functions of Kupffer cells.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

PMID: 9387190 [PubMed - indexed for MEDLINE]

[Cancer Lett.](#) 2000 Apr 3;151(1):111-5.

Inhibitory effects of carotenoids on the invasion of rat ascites hepatoma cells in culture.

[Kozuki Y](#), [Miura Y](#), [Yagasaki K](#).

Department of Applied Biological Science, Tokyo Noko University, Fuchu, Japan.

The effects of carotenoids--alpha-carotene, beta-carotene, lycopene, beta-cryptoxanthin, zeaxanthin, lutein, canthaxanthin, astaxanthin--on the invasion of rat ascites hepatoma AH109A cells were investigated by co-culturing the hepatoma cells with rat mesentery-derived mesothelial cells (M-cells). All the carotenoids examined inhibited AH109A invasion in a dose-dependent manner up to 5 microM. Cancer cells previously cultured with hypoxanthine (HX) and xanthine oxidase (XO) showed a highly invasive activity. Carotenoids, 5 microM of beta-carotene and astaxanthin, suppressed this reactive oxygen species-potentiated invasive capacity by simultaneously treating AH109A cells with the carotenoids, HX and XO. These results suggest that the antioxidative property of these carotenoids may be involved in their anti-invasive action.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

PMID: 10766430 [PubMed - indexed for MEDLINE]

Plasma antioxidant levels in chronic cholestatic liver diseases.

[Floreani A](#), [Baragiotta A](#), [Martines D](#), [Naccarato R](#), [D'odorico A](#).

Department of Surgical and Gastroenterological Sciences, University of Padova, Italy.
aflor@ux1.unipd.it

BACKGROUND: [corrected] A predictable consequence of cholestasis is malabsorption of fat-soluble factors, (vitamins A, D, E, K) and other free radical scavengers, such as carotenoids. It has been suggested that oxygen-derived free radicals may be involved in the pathogenesis of chronic liver damage. **AIMS:** (i) To evaluate retinol, alpha-tocopherol and carotenoid plasma levels in two groups of patients with chronic cholestatic liver disease (primary biliary cirrhosis and primary sclerosing cholangitis); (ii) to compare the respective plasma levels with those of the general population; (iii) to correlate the plasma levels with disease severity. **METHODS:** A total of 105 patients with chronic cholestasis were included in the study: 86 with primary biliary cirrhosis (81 female, five male, mean age 55.5 +/- 11 years), 19 with primary sclerosing cholangitis (seven female, 12 male, mean age 35 +/- 11 years; six patients had associated inflammatory bowel disease); 105 sex- and age-matched subjects from the general population in the same geographical area (88 female, 17 male, mean age 51.3.5 +/- 10 years) served as controls. Carotenoids (lutein zeaxanthin, lycopene, beta-carotene, alpha-carotene, beta-cryptoxanthin), retinol and alpha-tocopherol were assayed by high-pressure liquid chromatography. A food frequency questionnaire was administered to each subject to evaluate the quality and the quantity of dietary compounds. Data were processed by analysis of variance and linear regression analysis, as appropriate. **RESULTS:** Both primary biliary cirrhosis and primary sclerosing cholangitis patients had significantly lower levels of retinol, alpha-tocopherol, total carotenoids, lutein, zeaxanthin, lycopene, alpha- and beta-carotene than controls ($P < 0.0001$). Among the cholestatic patients, no significant difference in the concentration of antioxidants was observed between primary biliary cirrhosis and primary sclerosing cholangitis subjects. Anti-oxidant plasma levels were not affected by the severity of the histological stage in primary biliary cirrhosis, but a negative correlation was found between total carotenoids and both alkaline phosphatase (ALP) and gamma-glutamyl transpeptidase (GGT) ($P < 0.013$ and $P < 0.018$, respectively). Within the primary sclerosing cholangitis group, no correlation was found between total carotenoids and cholestatic enzymes. Nutritional intake in cholestatic patients was comparable to controls, including fruit and vegetable intake. **CONCLUSIONS:** Although no clinical sign of deficiency is evident, plasma levels of antioxidants are low in cholestatic patients even in early stages of the disease. This is probably due to malabsorption of fat-soluble vitamins, as well as other mechanisms of hepatic release, suggesting the need for dietary supplementation.

Publication Types:

- [Clinical Trial](#)
- [Research Support, Non-U.S. Gov't](#)

PMID: 10735930 [PubMed - indexed for MEDLINE]

Zeaxanthin as a Hepatoprotective

Carotenoids and tocopherols in various hepatobiliary conditions.

[Leo MA](#), [Ahmed S](#), [Alevnik SI](#), [Siegel JH](#), [Kasmin F](#), [Lieber CS](#).

Section of Liver Disease and Nutrition, Alcohol Research Center, Bronx, NY 10468, USA.

BACKGROUND: Previous studies revealed hepatic interactions of beta-carotene with alcohol in non-human primates, but bile carotenoids and alpha-tocopherol have not previously been explored in man. **METHODS:** To compare the plasma and biliary concentrations of carotenoids, retinoids and tocopherols among controls and patients with biliary and pancreatic diseases, these compounds were measured by high performance liquid chromatography in bile collected during 41 endoscopic retrograde cholangiopancreatographies. **RESULTS:** In 14 subjects with normal endoscopic retrograde cholangiopancreatography (controls), bile contained beta-carotene, alpha-carotene, lycopene, cryptoxanthin, lutein+zeaxanthin (23.9 +/- 6.6, 3.9 +/- 1.1, 39.9 +/- 21.6, 22.5 +/- 4.6, 217.1 +/- 27.8 nmol/l, respectively) with corresponding plasma values of 399.7 +/- 72.6, 88.5 +/- 18.8, 588.2 +/- 75.0, 145.1 +/- 25.9, 319.3 +/- 33.7 nmol/l. In 13 patients in whom bile duct stones impaired biliary excretion (as reflected by raised serum bilirubin), beta-carotene was significantly decreased in both plasma (199.6 +/- 35.5 nmol/l) and bile (9.4 +/- 2.0 nmol/l), with a similar trend for other carotenoids. The beta-carotene plasma/bile ratio was maintained, as well as a correlation between the two ($r = 0.56$; $p = 0.048$). Furthermore, in three subjects with complete biliary obstruction, plasma beta-carotene (35.8 +/- 20.2 nmol/l) decreased even more, probably reflecting malabsorption. In 11 patients with pancreatic diseases, plasma and bile beta-carotene were 107.9 +/- 17.8 and 6.6 +/- 2.0 nmol/l respectively, while a correlation between the two ($r = 0.70$; $p = 0.018$) again persisted, confirming the role of plasma beta-carotene in determining bile concentrations. Indeed, for the entire group ($n = 41$), the correlation between plasma and bile or red blood cell beta-carotene was highly significant, whereas plasma/red blood cell ratios remained unchanged. Similar findings were observed for alpha-tocopherol, with 8.4 +/- 0.9 $\mu\text{mol/l}$ in control bile (vs. 23.2 +/- 1.7 $\mu\text{mol/l}$ in plasma), and no significant change in the various groups. **CONCLUSIONS:** 1) Carotenoids and tocopherols undergo biliary excretion in man. 2) Biliary concentrations reflect plasma levels in both normal and pathologic states. 3) Decreased biliary excretion of carotenoids does not increase plasma concentrations.

PMID: 8583143 [PubMed - indexed for MEDLINE]