



NEOLIFE

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Carotenoid Complex



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NEOLIFE STUDIES

Modulated mitogenic proliferative responsiveness of lymphocytes in whole-blood cultures after a low-carotene diet and mixed-carotenoid supplementation in women

ABSTRACT

To determine the effects of dietary carotenes on the mitogenic proliferative responsiveness of blood lymphocytes in vitro, nine premenopausal women were fed a low-carotene diet for 120 d. Low-dose beta-carotene (0.5 mg/d) was given to five subjects on days 1-60, while four received a placebo. All subjects received a low-dose beta-carotene (0.5 mg/d) supplement on days 61-120, plus a carotenoid complex on days 101-120. The mean (+/-SEM) serum beta-carotene concentration for the combined beta-carotene supplemented and placebo subjects (n = 9) was not significantly reduced from that on day 1 (1.27 +/- 0.24 mumol/L) on days 60 (0.66 +/- 0.14 mumol/L) and 100 (0.91 +/- 0.38 mumol/L), but on day 120 (3.39 +/- 0.44 mumol/L) it was increased above that on days 1, 60, and 100. Maximum mitogenic proliferative responsiveness of blood lymphocytes in vitro to optimal dose phytohemagglutinin (PHA) was reduced on days 60 (P = 0.025) and 100 (P < 0.0001), but corrected itself on day 120 to a value above those on day 1 (P = 0.04), day 60 (P = 0.0001), and day 100 (P < 0.0001). Present findings show that a diet low in carotene had a suppressive effect on the maximum mitogenic proliferative responsiveness of blood lymphocytes in vitro, which was not corrected with low-dose beta-carotene supplementation but was with a carotenoid complex from vegetables rich in carotenoids.

Source

<http://carotenoidcomplex.com/pdfs/Modulated.pdf>

Plasma carotenoid concentrations before and after supplementation with a carotenoid mixture

ABSTRACT

Plasma carotenoid concentrations were determined by HPLC in 11 individuals consuming low-carotenoid diets and after taking a carotenoid supplement. Subjects first consumed low-carotenoid diets for 2 wk, then supplemented these diets daily with 8.5 mg beta-carotene, 3.5 mg alpha-carotene, and 0.5 mg lycopene, from natural sources for 4 wk. Serum cholesterol, triglycerides, and lipoproteins were determined before and after supplementation. After 2 wk on the low-carotenoid diet, plasma concentrations of the three carotenoids fell to approximately 60% of baseline values. One week after supplementation, alpha- and beta-carotene concentrations returned to baseline and by the end of the supplementation period they were significantly higher than baseline values (P < 0.05). Lycopene concentrations increased only slightly. Serum lipids did not change significantly. Overall, plasma concentrations of these carotenoids reflect the amount provided by the supplement. This is the first study reporting increments of serum carotenoids, other than beta-carotene, after supplementation.

Source

<http://carotenoidcomplex.com/pdfs/Plasma.pdf>

PEER REVIEWED STUDIES

Absorption of Carotenoids

Influence of olive oil on carotenoids bioavailability—A review

ABSTRACT

Bioavailability is defined as “the fraction of an ingested nutrient that is available for utilization in normal physiological functions or for storage”. Available studies on carotenoids bioavailability are based on the measurement of their levels in serum or plasma. Dietary components were reported to affect the rate of carotenoids absorption.

On digestion, carotenoids are incorporated into the lipid phase and then are emulsified into small lipid droplets. The nature and amount of lipids in the diet greatly affect the emulsification, secretion of bile salts, and formation of mixed micelles all of which are currently important subjects to understand the carotenoids bioavailability. Specific lipids, vegetable oils and their fatty acid moiety have been shown to affect the mixed micelles formation that positively influences the absorption of carotenoids. Gavage and dietary studies revealed that oleic acid micelles and olive oil (oleic acid, C18:1) enhance the intestinal accessibility of carotenoids more than linoleic acid micelles or vegetable oils rich in polyunsaturated fatty acids (PUFA). The chemistry of fats or oils which may act differently at various stages of absorption and metabolism of carotenoids is discussed. This review shows that dietary unsaturated fat appears to be a suitable carrier for carotenoids when oxidative stress is a critical issue in nutrition-related degenerative disorders.

Source

Lakshminarayana R et al. Influence of olive oil on carotenoids bioavailability—A review. *Eur J Lipid Sci Tech* DOI: 10.1002/ejlt.201200254, Epub ahead of print, 2012.

Blood Sugar Balance

Fruit and vegetable intake and incidence of type 2 diabetes mellitus: systematic review and meta-analysis

ABSTRACT

Objective:

To investigate the independent effects of intake of fruit and vegetables on incidence of type 2 diabetes.

Design:

Systematic review and meta-analysis.

Data Sources:

Medline, Embase, CINAHL, British Nursing Index (BNI), and the Cochrane library were searched for medical subject headings and keywords on diabetes, prediabetes, fruit, and vegetables. Expert opinions were sought and reference lists of relevant

articles checked.

Study Selection:

Prospective cohort studies with an independent measure of intake of fruit, vegetables, or fruit and vegetables and data on incidence of type 2 diabetes.

Results:

Six studies met the inclusion criteria; four of these studies also provided separate information on the consumption of green leafy vegetables. Summary estimates showed that greater intake of green leafy vegetables was associated with a 14% (hazard ratio 0.86, 95% confidence interval 0.77 to 0.97) reduction in risk of type 2 diabetes ($P=0.01$). The summary estimates showed no significant benefits of increasing the consumption of vegetables, fruit, or fruit and vegetables combined.

Conclusion:

Increasing daily intake of green leafy vegetables could significantly reduce the risk of type 2 diabetes and should be investigated further.

Source

Carter P, et al. Fruit and vegetable intake and incidence of type 2 diabetes mellitus: systematic review and meta-analysis. *BMJ*. 2010 Aug 18;341:c4229. doi: 10.1136/bmj.c4229.

Breast Health

Circulating Carotenoids and Risk of Breast Cancer: Pooled Analysis of Eight Prospective Studies

ABSTRACT

Background:

Carotenoids, micronutrients in fruits and vegetables, may reduce breast cancer risk. Most, but not all, past studies of circulating carotenoids and breast cancer have found an inverse association with at least one carotenoid, although the specific carotenoid has varied across studies.

Methods:

We conducted a pooled analysis of eight cohort studies comprising more than 80% of the world's published prospective data

on plasma or serum carotenoids and breast cancer, including 3055 case subjects and 3956 matched control subjects. To account for laboratory differences and examine population differences across studies, we recalibrated participant carotenoid levels to a common standard by reassaying 20 plasma or serum samples from each cohort together at the same laboratory. Using conditional logistic regression, adjusting for several breast cancer risk factors, we calculated relative risks (RRs) and 95% confidence intervals (CIs) using quintiles defined among the control subjects from all studies. All P values are two-sided.

Results:

Statistically significant inverse associations with breast cancer were observed for α -carotene (top vs bottom quintile RR = 0.87, 95% CI = 0.71 to 1.05, $P(\text{trend}) = .04$), β -carotene (RR = 0.83, 95% CI = 0.70 to 0.98, $P(\text{trend}) = .02$), lutein+zeaxanthin (RR = 0.84, 95% CI = 0.70 to 1.01, $P(\text{trend}) = .05$), lycopene (RR = 0.78, 95% CI = 0.62 to 0.99, $P(\text{trend}) = .02$), and total carotenoids (RR = 0.81, 95% CI = 0.68 to 0.96, $P(\text{trend}) = .01$). β -Cryptoxanthin was not statistically significantly associated with risk. Tests for heterogeneity across studies were not statistically significant. For several carotenoids, associations appeared stronger for estrogen receptor negative (ER(-)) than for ER(+) tumors (eg, β -carotene: ER(-): top vs bottom quintile RR = 0.52, 95% CI = 0.36 to 0.77, $P(\text{trend}) = .001$; ER(+): RR = 0.83, 95% CI = 0.66 to 1.04, $P(\text{trend}) = .06$; $P(\text{heterogeneity}) = .01$).

Conclusions:

This comprehensive prospective analysis suggests women with higher circulating levels of α -carotene, β -carotene, lutein+zeaxanthin, lycopene, and total carotenoids may be at reduced risk of breast cancer.

Source

Eliassen AH, et al. Circulating Carotenoids and Risk of Breast Cancer: Pooled Analysis of Eight Prospective Studies. *J Natl Cancer Inst*. 2012 Dec 19;104(24):1905-16

Dietary carotenoids and risk of breast cancer in Chinese women

ABSTRACT

There has been considerable interest in the role of carotenoids in the chemoprevention of cancer. However, the protective effect of carotenoids on breast cancer has been inconclusive. To investigate whether intake of lycopene, alpha-carotene, beta-carotene, beta-cryptoxanthin, and lutein/zeaxanthin is inversely associated with breast cancer risk, a case-control study was conducted in China during 2004-2005. The cases were 122 female patients aged 24-87 years with histopathologically confirmed breast cancer. 632 healthy women age-matched were randomly recruited from outpatient clinics. Habitual dietary intake and lifestyle were collected by face-to-face interview using a validated and reliable food frequency questionnaire. The USDA nutrient composition database was used to calculate intake of the specific carotenoids. Unconditional logistic regression analyses were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs), accounting for age, locality, education, body mass index, smoking, passive smoking, physical activity, number of children breastfed, menopausal status, oral contraceptive use, biopsy-confirmed benign breast diseases, family history of breast cancer, and total energy intake. Compared with the highest versus lowest quartile of intake, the adjusted ORs were 0.26 (95% CI 0.14-0.46) for lycopene, 0.38 (95% CI 0.21-0.71) for beta-carotene, 0.43 (95% CI 0.23-0.82) for beta-cryptoxanthin, and 0.37 (95% CI 0.20-0.68) for total carotenoids, with statistically significant tests for trend. There was no association with breast cancer for alpha-carotene and lutein/zeaxanthin. It is concluded that higher intake of lycopene, beta-carotene and beta-cryptoxanthin is associated to a lower risk of breast cancer among Chinese women. More research to examine the relationship between carotenoids and breast cancer risk is warranted.

Source

Huang JP, et al. *Dietary carotenoids and risk of breast cancer in Chinese women. Asia Pac J Clin Nutr. 2007;16 Suppl 1:437-42.*

Intake of specific carotenoids and the risk of epithelial ovarian cancer**ABSTRACT**

There has been considerable interest in the role of carotenoids in the chemoprevention of cancer. However, few studies have examined the association between intake of specific carotenoids and the risk of epithelial ovarian cancer and the results for carotenoids have been inconclusive. To investigate whether the intake of alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein and zeaxanthin, and lycopene is inversely associated with ovarian cancer risk, a case-control study was conducted in China during 1999-2000. The cases were 254 patients with histologically confirmed epithelial ovarian cancer and 652 age-matched controls were randomly recruited during the same period. Habitual dietary intake and lifestyle were collected by face-to-face interview using a validated and reliable FFQ. The US Department of Agriculture nutrient composition database was used to calculate the intake of specific carotenoids. Unconditional logistic regression analyses were used to estimate OR and 95 % CI, accounting for age, locality, education, BMI, smoking, tea drinking, parity, oral contraceptive use, hormone replacement therapy, menopausal status, family history of ovarian cancer, physical activity and energy intake. Compared with the highest v. the lowest quartile of intake, the adjusted OR were 0.39 (95 % CI 0.23, 0.66) for alpha-carotene, 0.51 (95 % CI 0.31, 0.84) for beta-carotene, 0.51 (95 % CI 0.31, 0.83) for beta-cryptoxanthin, 0.45 (0.27, 0.76) for lutein and zeaxanthin, and 0.33 (95 % CI 0.20, 0.56) for total carotenoids, with statistically significant tests for trend. It is concluded that a higher intake of carotenoids can reduce the risk of epithelial ovarian cancer.

Source

Zhang M, et al. *Intake of specific carotenoids and the risk of epithelial ovarian cancer. Br J Nutr. 2007 Jul;98(1):187-93. Epub 2007 Mar 19.*

Cellular Health**Recent advances in clinical research involving carotenoids****ABSTRACT**

Epidemiological studies show consistent decreased risk of lung cancer and certain other cancers, cataracts, age-related macular degeneration, and coronary heart disease in populations with the highest intakes of carotenoid-rich diets. Intervention studies show reductions in precancerous oral lesions, enhancement in immune parameters, and reduced incidence of cardiovascular events in individuals supplemented with β -carotene.

Source

Bendich A, et al. *Recent advances in clinical research involving carotenoids. Pure & Appl Chem. 1994;66(5): 1017-1024.*

Effect of low carotene diet on malondialdehyde (MDA) concentration**ABSTRACT****Objective:**

The purpose of the study was to evaluate the effect of a low carotenoid diet (83 micrograms Beta-carotene) on malondialdehyde-thiobarbituric acid (MDA-TBA) concentrations of nine pre-menopausal women.

Methods:

Subjects lived on the metabolic research unit of the Western Human Nutrition Research Center (WHNRC), where diet, exercise and other activities were controlled. Five subjects (Group C, control group) consumed a low carotenoid diet and received an additional 0.5 mg/day of Beta-carotene while four subjects (Group P, placebo group) received only the low carotenoid diet during days 1 to 60 (period 1). All subjects received 0.5 mg/day of Beta-carotene during days 60 to 100 (period 2), plus three capsules/day mixed carotenoid supplement (Neo-Life Company) during study days 100 to 120. Changes in MDA-TBA concentrations were analyzed during the study periods and between the groups.

Results:

At the start of the study (day 1), no significant difference in the MDA-TBA concentration was observed between the control (Group C) and the placebo (Group P) subjects. During period 1 (days 2 to 60), when Group P subjects consumed the low carotenoid diet without supplementation, the MDA-TBA values for Group P rose markedly and were significantly ($p < 0.05$) higher than the MDA-TBA values for Group C subjects who were receiving carotenoid supplementation. During period 2 (days 60 to 100) when both groups received carotenoid supplementation, the MDA-TBA values of Group P subjects were significantly ($p < 0.05$) reduced to the point where they were similar to the MDA-TBA values for Group C subjects.

Conclusions:

These findings provide evidence to support the beneficial effects of carotenoids in preventing lipid peroxidation in the cells. Further studies are needed to identify the exact mechanism by which carotenoids prevent lipid peroxidation and the amount needed for normal activity.

Source

Dixon ZR, et al. *Effect of low carotene diet on malondialdehyde (MDA) concentration; Free Radic Biol Med. 1996.*

Effects of a carotene-deficient diet on measures of oxidative susceptibility and superoxide dismutase activity in adult women**ABSTRACT**

The effect of consuming a low carotene diet (approximately 60 micrograms carotene/day) on oxidative susceptibility and superoxide dismutase (SOD) activity in women living in a metabolic research unit was evaluated. The diet had sufficient vitamins A, E, and C. The women ate the diet supplemented with 1500 micrograms/day beta-carotene for 4 days (baseline), then the unsupplemented diet for 68 days (depletion), followed by the diet supplemented with > 15,000 micrograms/day carotene for 28 days (repletion). Production of hexanal, pentanal, and pentane by copper-oxidized plasma low

density lipoproteins from carotene-depleted women was greater than their production of these compounds when repleted with carotene. Erythrocyte SOD activity was depressed in carotene-depleted women; it recovered with repletion. Thiobarbituric acid reactive substances in plasma of carotene-depleted women were elevated and diminished with repletion. Dietary carotene seems to be needed, not only as a precursor of vitamin A, but also to inhibit oxidative damage and decrease oxidation susceptibility.

Source

Dixon ZR, et al. Effects of a carotene-deficient diet on measures of oxidative susceptibility and superoxide dismutase activity in adult women. *Free Radic Biol Med.* 1994 Dec;17(6):537-44.

Bioavailability, and Potential Healthy Effects of Capsanthin, Natural Red Pigment from Capsicum

ABSTRACT

Capsanthin, uniquely found in capsicum spp., is a fat soluble red pigment. Capsanthin is synthesized during carotenogenesis and enhances liposolubility by esterifying with short-chain saturated fatty acids. Capsanthin and derivatives have been analyzed and identified by diverse techniques as spectrophotometry, TLC, HPLC, LC/MS, NMR, and FABMS/MS, etc. The absorptive pathways of carotenoids are similar to those of other dietary lipids. Capsanthin is found abundantly distributed at the polar surfaces of lipoproteins, and the clearance of capsanthin is much faster than those of lycopene in the human body. Capsanthin is regarded as a functional material by antioxidative activity and anti-tumor-promotion activity, even though it exhibits no provitamin A activity. In epidemiological studies, capsanthin appears to possibly exert a potent inhibitory effect on colon carcinogenesis. Therefore, increased intake of capsanthin rich foods may be helpful for the improvement of health.

Source

Kim S, et al. Analysis, Bioavailability, and Potential Healthy Effects of Capsanthin,

Natural Red Pigment from Capsicum. *Food Reviews International*, March 2009; 25 (3)

Serum α -carotene concentrations and risk of death among US Adults: the Third National Health and Nutrition Examination Survey Follow-up Study

ABSTRACT

Background:

Much research has been conducted relating total carotenoids--and β -carotene in particular--to risk of cancer and cardiovascular disease (CVD). Limited data are emerging to implicate the important role of α -carotene in the development of CVD or cancer.

Methods:

We assessed the direct relationship between α -carotene concentrations and risk of death among 15,318 US adults 20 years and older who participated in the Third National Health and Nutrition Examination Survey Follow-up Study. We used Cox proportional hazard regression analyses to estimate the relative risk for death from all causes and selected causes associated with serum α -carotene concentrations.

Results:

Compared with participants with serum α -carotene concentrations of 0 to 1 $\mu\text{g}/\text{dL}$ (to convert to micromoles per liter, multiply by 0.01863), those with higher serum levels had a lower risk of death from all causes ($P < .001$ for linear trend): the relative risk for death was 0.77 (95% confidence interval, 0.68-0.87) among those with α -carotene concentrations of 2 to 3 $\mu\text{g}/\text{dL}$, 0.73 (0.65-0.83) among those with concentrations of 4 to 5 $\mu\text{g}/\text{dL}$, 0.66 (0.55-0.79) among those with concentrations of 6 to 8 $\mu\text{g}/\text{dL}$, and 0.61 (0.51-0.73) among those with concentrations of 9 $\mu\text{g}/\text{dL}$ or higher after adjustment for potential confounding variables. We also found significant associations between serum α -carotene concentrations and risk of death from CVD ($P = .007$), cancer ($P = .02$), and all other causes ($P < .001$). The association between serum α -carotene concentrations and risk of death from all causes was significant in most subgroups stratified by demographic characteristics, lifestyle habits, and health risk factors.

Conclusions:

Serum α -carotene concentrations were inversely associated with risk of death from all causes, CVD, cancer, and all other causes. These findings support increasing fruit and vegetable consumption as a means of preventing premature death.

Source

Li C, et al. Serum α -carotene concentrations and risk of death among US Adults: the Third National Health and Nutrition Examination Survey Follow-up Study. *Arch Intern Med.* 2011 Mar 28;171(6):507-15.

The carotenoid beta-cryptoxanthin stimulates the repair of DNA oxidation damage in addition to acting as an antioxidant in human cells

ABSTRACT

The role of dietary antioxidants in human health remains controversial. Fruits and vegetables in the diet are associated with lower rates of chronic disease, and this is often attributed to their content of antioxidants, and a resulting protection against oxidative stress. However, large-scale human trials with antioxidant supplements have shown, if anything, an increase in mortality. We have investigated the biological properties of beta-cryptoxanthin, a common carotenoid, in cell culture model systems, using the comet assay to measure DNA damage. At low concentrations, close to those found in plasma, beta-cryptoxanthin does not itself cause damage, but protects transformed human cells (HeLa and Caco-2) from damage induced by H₂O₂ or by visible light in the presence of a photosensitizer. In addition, it has a striking effect on DNA repair, measured in different ways. Incubation of H₂O₂-treated cells with beta-cryptoxanthin led to a doubling of the rate of rejoining of strand breaks and had a similar effect on the rate of removal of oxidized purines by base excision repair. The latter effect was confirmed with an in vitro assay: cells were incubated with or without beta-cryptoxanthin before preparing an extract, which was then incubated with substrate DNA containing 8-oxo-7,8-dihydroguanine; incision was more rapid with the extract

prepared from carotenoid-preincubated cells. No significant increases were seen in protein content of human 8-oxoguanine DNA glycosylase 1 or apurinic endonuclease 1. The apparent cancer-preventive effects of dietary carotenoids may depend on the enhancement of DNA repair as well as antioxidant protection against damage.

Source

Lorenzo Y, et al. *The carotenoid beta-cryptoxanthin stimulates the repair of DNA oxidation damage in addition to acting as an antioxidant in human cells. Carcinogenesis. 2009 Feb;30(2):308-14.*

In vitro protective effects of colon-available extract of *Camellia sinensis* (tea) against hydrogen peroxide and beta-amyloid (A β ((1-42))) induced cytotoxicity in differentiated PC12 cells

ABSTRACT

There is mounting evidence that the deposition and aggregation of β -amyloid peptides (A β) in the brain play a significant role in the development and pathogenesis of Alzheimer's disease. There is further evidence that free radical species such as hydrogen peroxide (H₂O₂) mediate A β induced toxicity. Previous studies have demonstrated that green tea polyphenols possess neuroprotective properties through their ability to ameliorate oxidative stress induced by free radical species. Green tea polyphenols have also been shown to enhance cognition in various animal models of induced cognitive impairment. Upon ingestion, green tea polyphenols are metabolised and undergo bio-transformation which affects their bioavailability and therefore efficacy. These results demonstrate that potentially bioavailable green tea metabolites are able to ameliorate both H₂O₂ and A β ((1-42)) induced cytotoxicity.

Source

Okello EJ, et al. *In vitro protective effects of colon-available extract of *Camellia sinensis* (tea) against hydrogen peroxide and beta-amyloid (A β ((1-42))) induced cytotoxicity in differentiated PC12 cells. Phytomedicine. 2010 Dec 21. [Epub ahead of print*

Children's Health

Associations of maternal serum concentrations of antioxidants with Asthma in children; Proceedings of the Midwest Nursing Research Society

ABSTRACT

Introduction:

Studies linking maternal serum concentrations of carotenoids with asthma in children are lacking. The objective of this study was to examine the relationships of life-time doctor-diagnosed asthma in children with maternal serum levels of beta-carotene, alpha-carotene, and beta-cryptoxanthin in a population-based and representative sample of the United States' children.

Methods:

This cross-sectional study analyzed data on 2290 pairs of mothers and their children aged 2 months-6 years who were examined in the third National Health and Nutrition Examination Survey (NHANES III). Bivariate and multiple logistic regression analyses were conducted treating serum concentrations of the antioxidants as categorical variables (quintiles). IRB approval was deemed unnecessary because the study was based on publicly available data.

Results:

Mothers of children with asthma had significantly lower serum concentrations of alpha-carotene, beta-carotene, and beta-cryptoxanthin than mothers of children without asthma with significant dose-dependent inverse associations between serum levels of these nutrients and the odds of asthma. The odds ratios (ORs) comparing children of mothers whose serum concentrations were in the 5th quintile with children whose mothers' serum concentrations were in the 1st quintile were 2.53 (95% CI: 1.06-6.03), 3.48 (95% CI: 1.32-9.17), and 2.60 (95% CI: 1.24-5.47), for alpha-carotene, beta-carotene, and beta-cryptoxanthin, respectively, with significant tests for trends obtained for the three nutrient markers. These associations persisted after adjusting for age, sex,

ethnicity, maternal smoking during pregnancy, and educational level of the family reference person.

Conclusion:

Our study demonstrated inverse associations of maternal serum levels of alpha-carotene, beta-carotene, and beta-cryptoxanthin with the odds of asthma in children. These findings add to the growing body of literature linking asthma in children with maternal dietary factors and highlight the need for longitudinal studies to further examine the relationships of maternal diet during pregnancy or early in the child's life with the risk of asthma in children.

Source

Eldeirawi, K. *Associations of maternal serum concentrations of antioxidants with Asthma in children; Proceedings of the Midwest Nursing Research Society. University of Illinois at Chicago: College of Nursing-Health Systems Science; 15 April 2010.*

Cognitive Health

Antioxidative and anti-inflammatory neuroprotective effects of astaxanthin and canthaxanthin in nerve growth factor differentiated PC12 cells

ABSTRACT

Nerve growth factor differentiated PC12 cells were used to examine the antioxidative and anti-inflammatory effects of astaxanthin (AX) and canthaxanthin (CX). PC12 cells were pretreated with AX or CX at 10 or 20 μ M, and followed by exposure of hydrogen peroxide (H₂O₂) or 1-methyl-4-phenylpyridinium ion (MPP(+)) to induce cell injury. H₂O₂ or MPP(+) treatment significantly decreased cell viability, increased lactate dehydrogenase (LDH) release, enhanced DNA fragmentation, and lowered mitochondrial membrane potential (MMP) (P < 0.05). The pretreatments from AX or CX concentration-dependently alleviated H₂O₂ or MPP(+)-induced cell death, LDH release, DNA fragmentation, and MMP reduction (P < 0.05). Either H₂O₂ or MPP(+) treatment significantly increased malonyldialdehyde (MDA) and reactive oxygen species (ROS) formations, decreased glutathione content, and lowered glutathione peroxidase (GPX) and

catalase activities ($P < 0.05$). The pretreatments from AX or CX significantly retained GPX and catalase activities, and decreased MDA and ROS formations ($P < 0.05$). H₂O₂ or MPP(+) treatment significantly decreased Na(+)-K(+)-ATPase activity, elevated caspase-3 activity and levels of interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-alpha ($P < 0.05$); and the pretreatments from these agents significantly restored Na(+)-K(+)-ATPase activity, suppressed caspase-3 activity and release of IL-1, IL-6, and TNF-alpha ($P < 0.05$). Based on the observed antioxidative and anti-inflammatory protection from AX and CX, these 2 compounds were potent agents against neurodegenerative disorder.

Source

Chan KC, et al. Antioxidative and anti-inflammatory neuroprotective effects of astaxanthin and canthaxanthin in nerve growth factor differentiated PC12 cells. *J Food Sci.* 2009 Sep;74(7):H225-31.

Dietary intakes of berries and flavonoids in relation to cognitive decline

ABSTRACT

Objective:

Berries are high in flavonoids, especially anthocyanidins, and improve cognition in experimental studies. We prospectively evaluated whether greater long-term intakes of berries and flavonoids are associated with slower rates of cognitive decline in older women.

Methods:

Beginning in 1980, a semiquantitative food frequency questionnaire was administered every 4 years to Nurses' Health Study participants. In 1995-2001, we began measuring cognitive function in 16,010 participants, aged ≥ 70 years; follow-up assessments were conducted twice, at 2-year intervals. To ascertain long-term diet, we averaged dietary variables from 1980 through the initial cognitive interview. Using multivariate-adjusted, mixed linear regression, we estimated mean differences in slopes of cognitive decline by long-term berry and flavonoid intakes.

Results:

Greater intakes of blueberries and strawberries were associated with slower rates of cognitive decline (eg, for a global score averaging all 6 cognitive tests, for blueberries: p-trend = 0.014 and mean difference = 0.04, 95% confidence interval [CI] = 0.01-0.07, comparing extreme categories of intake; for strawberries: p-trend = 0.022 and mean difference = 0.03, 95% CI = 0.00-0.06, comparing extreme categories of intake), after adjusting for multiple potential confounders. These effect estimates were equivalent to those we found for approximately 1.5 to 2.5 years of age in our cohort, indicating that berry intake appears to delay cognitive aging by up to 2.5 years. Additionally, in further supporting evidence, greater intakes of anthocyanidins and total flavonoids were associated with slower rates of cognitive decline (p-trends = 0.015 and 0.053, respectively, for the global score).

Interpretation:

Higher intake of flavonoids, particularly from berries, appears to reduce rates of cognitive decline in older adults.

Source

Devore EE, Kang JH, Breteler MM, Grodstein F. Dietary intakes of berries and flavonoids in relation to cognitive decline. *Ann Neurol.* 2012;72(1):135-43.

Berry fruit enhances beneficial signaling in the brain

ABSTRACT

Increased lifespans have led to population aging and brought attention to healthcare concerns associated with old age. A growing body of preclinical and clinical research has identified neurological benefits associated with the consumption of berry fruits. In addition to their now well-known antioxidant effects, dietary supplementation with berry fruits also has direct effects on the brain. Intake of these fruits may help to prevent age-related neurodegeneration and resulting changes in cognitive and motor function. In cell and animal models, berry fruits mediate signaling pathways involved in inflammation and cell survival in addition to enhancing neuroplasticity, neurotransmission, and

calcium buffering, all of which lead to attenuation of age- and pathology-related deficits in behavior. Recent clinical trials have extended these antioxidant, anti-inflammatory, and cognition-sparing effects to humans. This paper reviews recent evidence for the beneficial signaling effects of berry fruits on the brain and behavior.

Source

Miller MG, Shukitt-Hale B. Berry fruit enhances beneficial signaling in the brain. *J. Agric. Food Chem.*, 2012, 60 (23): 5709–5715.

Rautiainen S, Larsson S, Virtamo J, Wolk A. Total antioxidant capacity of diet and risk of stroke: a population-based prospective cohort of women. *Stroke* 2012;43(2):335-40.

ABSTRACT

Background and Purpose:

Consumption of antioxidant-rich foods may reduce the risk of stroke by inhibition of oxidative stress and inflammation. Total antioxidant capacity (TAC) takes into account all antioxidants and the synergistic effects between them. We examined the association between dietary TAC and stroke incidence in cardiovascular disease (CVD)-free women and in women with CVD history at baseline.

Methods:

The study included women (31,035 CVD-free and 5680 with CVD history at baseline), aged 49 to 83 years, from the Swedish Mammography Cohort. Diet was assessed with a food frequency questionnaire. Dietary TAC was calculated using oxygen radical absorbance capacity values. Stroke cases were ascertained by linkage with the Swedish Hospital Discharge Registry.

Results:

During follow-up (September 1997 to December 2009), we identified 1322 stroke cases (988 cerebral infarctions, 226 hemorrhagic strokes, and 108 unspecified strokes) among CVD-free women and 1007 stroke cases (796 cerebral infarctions, 100 hemorrhagic strokes, and 111 unspecified strokes) among women with a CVD history. The multivariable hazard ratio of total stroke

comparing the highest with the lowest quintile of dietary TAC was 0.83 (95% CI, 0.70-0.99; P for trend=0.04) in CVD-free women. Among women with a CVD history, the hazard ratios for the highest versus lowest quartile of TAC were 0.90 (95% CI, 0.75-1.07; P for trend=0.30) for total stroke and 0.55 (95% CI, 0.32-0.95; P for trend=0.03) for hemorrhagic stroke.

Conclusions:

These findings suggest that dietary TAC is inversely associated with total stroke among CVD-free women and hemorrhagic stroke among women with CVD history.

Source

Rautiainen S, Larsson S, Virtamo J, Wolk A. Total antioxidant capacity of diet and risk of stroke: a population-based prospective cohort of women. *Stroke* 2012;43(2):335-40.

Prion protein-mediated neurotoxicity of amyloid- β oligomers requires lipid rafts and the transmembrane LRP1

ABSTRACT

Soluble oligomers of the amyloid- β ($A\beta$) peptide cause neurotoxicity, synaptic dysfunction, and memory impairments that underlie Alzheimer disease (AD). The cellular prion protein (PrPC) was recently identified as a high affinity neuronal receptor for $A\beta$ oligomers. We report that fibrillar $A\beta$ oligomers recognized by the OC antibody, which have been shown to correlate with the onset and severity of AD, bind preferentially to cells and neurons expressing PrPC. The binding of $A\beta$ oligomers to cell surface PrPC, as well as their downstream activation of Fyn kinase, was dependent on the integrity of cholesterol-rich lipid rafts. In SH-SY5Y cells, fluorescence microscopy and co-localization with subcellular markers revealed that the $A\beta$ oligomers co-internalized with PrPC, accumulated in endosomes, and subsequently trafficked to lysosomes. The cell surface binding, internalization, and downstream toxicity of $A\beta$ oligomers was dependent on the transmembrane low density lipoprotein receptor-related protein-1 (LRP1). The binding of $A\beta$ oligomers to cell surface PrPC impaired its ability to inhibit the activity of the β -secretase BACE1, which cleaves the

amyloid precursor protein to produce $A\beta$. The green tea polyphenol (-)-epigallocatechin gallate and the red wine extract resveratrol both remodeled the fibrillar conformation of $A\beta$ oligomers. The resulting nonfibrillar oligomers displayed significantly reduced binding to PrPC-expressing cells and were no longer cytotoxic. These data indicate that soluble, fibrillar $A\beta$ oligomers bind to PrPC in a conformation-dependent manner and require the integrity of lipid rafts and the transmembrane LRP1 for their cytotoxicity, thus revealing potential targets to alleviate the neurotoxic properties of $A\beta$ oligomers in AD.

Source

Rushworth JV et. al. Prion protein-mediated neurotoxicity of amyloid- β oligomers requires lipid rafts and the transmembrane LRP1. *Journal of Biological Chemistry* 2013;288: 8935-8951.

Eye Health

Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8.

ABSTRACT

Background:

Observational and experimental data suggest that antioxidant and/or zinc supplements may delay progression of age-related macular degeneration (AMD) and vision loss.

Objective:

To evaluate the effect of high-dose vitamins C and E, beta carotene, and zinc supplements on AMD progression and visual acuity.

Design:

The Age-Related Eye Disease Study, an 11-center double-masked clinical trial, enrolled participants in an AMD trial if they had extensive small drusen, intermediate drusen, large drusen, noncentral geographic atrophy, or pigment abnormalities in 1 or both eyes, or advanced AMD or vision loss due to AMD in 1 eye. At least 1 eye had best-corrected visual acuity of 20/32 or better. Participants were randomly assigned to receive daily oral tablets containing: (1)

antioxidants (vitamin C, 500 mg; vitamin E, 400 IU; and beta carotene, 15 mg); (2) zinc, 80 mg, as zinc oxide and copper, 2 mg, as cupric oxide; (3) antioxidants plus zinc; or (4) placebo.

Main Outcome Measures:

(1) Photographic assessment of progression to or treatment for advanced AMD and (2) at least moderate visual acuity loss from baseline (> or =15 letters). Primary analyses used repeated-measures logistic regression with a significance level of .01, unadjusted for covariates. Serum level measurements, medical histories, and mortality rates were used for safety monitoring.

Results:

Average follow-up of the 3640 enrolled study participants, aged 55-80 years, was 6.3 years, with 2.4% lost to follow-up. Comparison with placebo demonstrated a statistically significant odds reduction for the development of advanced AMD with antioxidants plus zinc (odds ratio [OR], 0.72; 99% confidence interval [CI], 0.52-0.98). The ORs for zinc alone and antioxidants alone are 0.75 (99% CI, 0.55-1.03) and 0.80 (99% CI, 0.59-1.09), respectively. Participants with extensive small drusen, nonextensive intermediate size drusen, or pigment abnormalities had only a 1.3% 5-year probability of progression to advanced AMD. Odds reduction estimates increased when these 1063 participants were excluded (antioxidants plus zinc: OR, 0.66; 99% CI, 0.47-0.91; zinc: OR, 0.71; 99% CI, 0.52-0.99; antioxidants: OR, 0.76; 99% CI, 0.55-1.05). Both zinc and antioxidants plus zinc significantly reduced the odds of developing advanced AMD in this higher-risk group. The only statistically significant reduction in rates of at least moderate visual acuity loss occurred in persons assigned to receive antioxidants plus zinc (OR, 0.73; 99% CI, 0.54-0.99). No statistically significant serious adverse effect was associated with any of the formulations.

Conclusions:

Persons older than 55 years should have dilated eye examinations to determine their risk of developing advanced AMD. Those with extensive intermediate size drusen, at least 1 large druse, noncentral geographic atrophy in

1 or both eyes, or advanced AMD or vision loss due to AMD in 1 eye, and without contraindications such as smoking, should consider taking a supplement of antioxidants plus zinc such as that used in this study.

Source

Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. Arch Ophthalmol

Clinical trial of lutein in patients with retinitis pigmentosa receiving vitamin A

ABSTRACT

Objective:

To determine whether lutein supplementation will slow visual function decline in patients with retinitis pigmentosa receiving vitamin A.

Design:

Randomized, controlled, double-masked trial of 225 nonsmoking patients, aged 18 to 60 years, evaluated over a 4-year interval. Patients received 12 mg of lutein or a control tablet daily. All were given 15,000 IU/d of vitamin A palmitate. Randomization took into account genetic type and baseline serum lutein level.

Main Outcome Measures:

The primary outcome was the total point score for the Humphrey Field Analyzer (HFA) 30-2 program; prespecified secondary outcomes were the total point scores for the 60-4 program and for the 30-2 and 60-4 programs combined, 30-Hz electroretinogram amplitude, and Early Treatment Diabetic Retinopathy Study acuity.

Results:

No significant difference in rate of decline was found between the lutein plus vitamin A and control plus vitamin A groups over a 4-year interval for the HFA 30-2 program. For the HFA 60-4 program, a decrease in mean rate of sensitivity loss was observed in the lutein plus vitamin A group ($P = .05$). Mean decline with the 60-4 program was slower among those with the highest serum lutein level or with the highest increase in macular pigment optical density at follow-up ($P = .01$ and $P =$

$.006$, respectively). Those with the highest increase in macular pigment optical density also had the slowest decline in HFA 30-2 and 60-4 combined field sensitivity ($P = .005$). No significant toxic effects of lutein supplementation were observed.

Conclusion:

Lutein supplementation of 12 mg/d slowed loss of midperipheral visual field on average among nonsmoking adults with retinitis pigmentosa taking vitamin A. Application to Clinical Practice Data are presented that support use of 12 mg/d of lutein to slow visual field loss among nonsmoking adults with retinitis pigmentosa taking vitamin A.

Source

Berson EL, et al. Clinical trial of lutein in patients with retinitis pigmentosa receiving vitamin A. *Arch Ophthalmol*. 2010 Apr;128(4):403-11.

UVB photoprotection with antioxidants: effects of oral therapy with d-alpha-tocopherol and ascorbic acid on the minimal erythema dose

ABSTRACT

Ultraviolet radiation absorption is responsible for the production of free radicals in damaged cells. This side effect may be neutralized using antioxidant substances. It has been reported that ascorbic acid and d-alpha-tocopherol scavenge reactive oxygen species. In a single-blind controlled clinical trial we studied 45 healthy volunteers divided into three groups. Group 1 received d-alpha-tocopherol 1,200 I.U. daily; Group 2 ascorbic acid 2 g daily and Group 3 ascorbic acid 2 g plus d-alpha-tocopherol 1,200 I.U. daily. Treatment was sustained for one week. Before and after treatment, the minimal erythema dose was determined in all participants. The results show that the median minimal erythema dose increased from 60 to 65 mJ/cm² in Group 1 and from 50 to 70 mJ/cm² in Group 3. No modifications were observed in Group 2. We conclude that d-alpha-tocopherol prescribed in combination with ascorbic acid produces the best photoprotective effect.

Source

Mireles-Rocha H, et al. UVB photoprotection with antioxidants: effects of oral therapy with d-alpha-tocopherol and ascorbic acid on the minimal erythema dose. Acta Derm Venereol 82:21-4, 2002.

Biological role of lutein in the light induced retinal degeneration

ABSTRACT

Lutein, a xanthophyll of a carotenoid, is anticipated as a therapeutic product to prevent human eye diseases. However, its biological mechanism is still unclear. Here, we show the molecular mechanism of lutein's effect to reduce photodamage of the retina. We analyzed the light-exposed retinas of Balb/c mice given lutein-supplemented or normal diet. Visual function was measured by electroretinogram, and histological changes were observed. Immunohistochemical and immunoblot analyses were performed to analyze molecular mechanism. The reactive oxygen species induced in the retina was evaluated by fluorescent probes. In the mice after light exposure, reduction of a-wave and b-wave amplitudes in electroretinogram, indicating visual impairment, and thinning of the photoreceptor cell layer owing to apoptosis were both attenuated by lutein diet. Interestingly, γ -H2AX, a marker for double-strand breaks (DSBs) in DNA, was up-regulated in the photoreceptor cells after light exposure, but this increase was attenuated by lutein diet, suggesting that DSBs caused by photodamage contributed to the photoreceptor cell death and that this change was suppressed by lutein. Moreover, the expression of eyes absent (EYA), which promotes DNA repair and cell survival, was significantly up-regulated with lutein diet in the light-exposed retina. Therefore, lutein induced EYA for DNA repair, which could suppress DNA damage and photoreceptor cell apoptosis. Lutein reduced light-induced oxidative stress in the retina, which might contribute to promote DNA repair. The lutein-supplemented diet attenuated light-induced visual impairment by protecting the photoreceptor cells' DNA.

Source

Sasaki M., *Biological role of lutein in the light induced retinal degeneration. Journal of nutritional Biochemistry. 2011; doi:10.1016/j.jnutbio.2011.01.006*

Photoprotection by dietary carotenoids: concept, mechanisms, evidence and future development
ABSTRACT

Carotenoids are micronutrients present mainly in fruits and vegetables, and they are ingested from these sources with the diet. They exhibit specific antioxidant activity but also influence signaling and gene expression at the cellular level. β -Carotene and lycopene, the colorants of carrots and tomatoes, respectively, are among the most prominent members of this group of lipids, and they are usually the dominating carotenoids in human blood and tissues. Both compounds modulate skin properties when ingested as supplements or as dietary products. There is evidence that they protect the skin against sunburn (solar erythema) by increasing the basal defense against UV light-mediated damage. Their photoprotective efficacy, however, is not comparable to the use of a sunscreen. In vitro data show that also other carotenoids are efficient photoprotectors. Among them are lutein and structurally unusual phenolic polyenes like 3,3'-dihydroxyisorenieratene.

Source

Stahl W and Sies H. *Photoprotection by dietary carotenoids: concept, mechanisms, evidence and future development. Mol Nutr Food Res 56:287-95, 2012.*

Carotenoids and carotenoids plus vitamin E protect against ultraviolet light-induced erythema in humans
ABSTRACT**Background:**

Carotenoids and tocopherols, known to be efficient antioxidants and capable of scavenging reactive oxygen species generated during photooxidative stress, may protect the skin from ultraviolet light-induced erythema. β -Carotene is widely used as an oral sun protectant but studies

on its protective effects are scarce.

Objective:

The objective of this study was to investigate the protective effects of oral supplementation with carotenoids and a combination of carotenoids and vitamin E against the development of erythema in humans.

Design:

A carotenoid supplement (25 mg total carotenoids/d) and a combination of the carotenoid supplement and vitamin E [335 mg (500 IU) RRR- α -tocopherol/d] were given for 12 wk to healthy volunteers. Erythema was induced by illumination with a blue-light solar simulator. Serum β -carotene and α -tocopherol concentrations and skin carotenoid levels were assessed by HPLC and reflection photometry.

Results:

Serum β -carotene and α -tocopherol concentrations increased with supplementation. Erythema on dorsal skin (back) was significantly diminished ($P < 0.01$) after week 8, and erythema suppression was greater with the combination of carotenoids and vitamin E than with carotenoids alone.

Conclusion:

The antioxidants used in this study provided protection against erythema in humans and may be useful for diminishing sensitivity to ultraviolet light.

Source

Stahl, W et al. *Carotenoids and carotenoids plus vitamin E protect against ultraviolet light-induced erythema in humans. Am J Clin Nutr 71:795-8, 2000.*

Heart Health
Effects of lycopene supplementation on oxidative stress and markers of endothelial function in healthy men
ABSTRACT**Objective:**

The objective was to determine the effects of lycopene supplementation on endothelial function assessed by reactive hyperemia

peripheral arterial tonometry (RH-PAT) and oxidative stress.

Methods:

Healthy men ($n = 126$) were randomized to receive placebo ($n = 38$), 6 mg ($n = 41$), or 15 mg ($n = 37$) lycopene daily for 8-week.

Results:

Serum lycopene increased in a dose-dependent manner after 8-week supplementation ($P < 0.001$). The 15 mg/day group had greater increase in plasma SOD activity ($P = 0.014$) and reduction in lymphocyte DNA comet tail length ($P = 0.042$) than the placebo group. Intragroup comparison revealed a 23% increase in RH-PAT index from baseline (1.45 ± 0.09 vs. 1.79 ± 0.12 ; $P = 0.032$) in the 15 mg/day group after 8-week. hs-CRP, systolic blood pressure, sICAM-1 and sVCAM-1 significantly decreased, and β -carotene and LDL-particle size significantly increased only in the 15 mg/day group. Interestingly, the beneficial effect of lycopene supplementation on endothelial function (i.e., RH-PAT and sVCAM-1) were remarkable in subjects with relatively impaired endothelial cell function at initial level. Changes in RH-PAT index correlated with SOD activity ($r = 0.234$, $P = 0.017$) especially in the 15 mg lycopene/day group ($r = 0.485$, $P = 0.003$), lymphocyte DNA comet tail moment ($r = -0.318$, $P = 0.001$), and hs-CRP ($r = -0.238$, $P = 0.011$). In addition, changes in lycopene correlated with hs-CRP ($r = -0.230$, $P = 0.016$) and SOD activity ($r = 0.205$, $P = 0.037$).

Conclusion:

An increase in serum lycopene after supplementation can reduce oxidative stress which may play a role in endothelial function.

Source

Kim JY, et al. *Effects of lycopene supplementation on oxidative stress and markers of endothelial function in healthy men. Atherosclerosis. 2011 Mar;215(1):189-95.*

Multivitamin use and the risk of myocardial infarction: a population-based cohort of Swedish women

ABSTRACT

Background:

Dietary supplements are widely used in industrialized countries.

Objective:

The objective was to examine the association between multivitamin use and myocardial infarction (MI) in a prospective, population-based cohort of women.

Design:

The study included 31,671 women with no history of cardiovascular disease (CVD) and 2262 women with a history of CVD aged 49-83 y from Sweden. Women completed a self-administered questionnaire in 1997 regarding dietary supplement use, diet, and lifestyle factors. Multivitamins were estimated to contain nutrients close to recommended daily allowances: vitamin A (0.9 mg), vitamin C (60 mg), vitamin D (5 µg), vitamin E (9 mg), thiamine (1.2 mg), riboflavin (1.4 mg), vitamin B-6 (1.8 mg), vitamin B-12 (3 µg), and folic acid (400 µg).

Results:

During an average of 10.2 y of follow-up, 932 MI cases were identified in the CVD-free group and 269 cases in the CVD group. In the CVD-free group, use of multivitamins only, compared with no use of supplements, was associated with a multivariable-adjusted hazard ratio (HR) of 0.73 (95% CI: 0.57, 0.93). The HR for multivitamin use together with other supplements was 0.70 (95% CI: 0.57, 0.87). The HR for use of supplements other than multivitamins was 0.93 (95% CI: 0.81, 1.08). The use of multivitamins for ≥5 y was associated with an HR of 0.59 (95% CI: 0.44, 0.80). In the CVD group, use of multivitamins alone or together with other supplements was not associated with MI.

Conclusions:

The use of multivitamins was inversely associated with MI, especially long-term use among women with no CVD. Further prospective studies with detailed information on the content of preparations and the

duration of use are needed to confirm or refute our findings.

Source

Rautiainen S et al. Multivitamin use and the risk of myocardial infarction: a population-based cohort of Swedish women. Am J Clin Nutr. 95:1251-6, 2010.

Immune Health

Recent advances in clinical research involving carotenoids.

ABSTRACT

Epidemiological studies show consistent decreased risk of lung cancer and certain other cancers, cataracts, age-related macular degeneration, and coronary heart disease in populations with the highest intakes of carotenoid-rich diets. Intervention studies show reductions in precancerous oral lesions, enhancement in immune parameters, and reduced incidence of cardiovascular events in individuals supplemented with β-carotene.

Source

Bendich A, et al. Recent advances in clinical research involving carotenoids. Pure & Appl Chem. 1994;66(5): 1017-1024.

Vitamin D controls T cell antigen receptor signaling and activation of human T cells

ABSTRACT

Phospholipase C (PLC) isozymes are key signaling proteins downstream of many extracellular stimuli. Here we show that naive human T cells had very low expression of PLC-gamma1 and that this correlated with low T cell antigen receptor (TCR) responsiveness in naive T cells. However, TCR triggering led to an upregulation of approximately 75-fold in PLC-gamma1 expression, which correlated with greater TCR responsiveness. Induction of PLC-gamma1 was dependent on vitamin D and expression of the vitamin D receptor (VDR). Naive T cells did not express VDR, but VDR expression was induced by TCR signaling via the alternative mitogen-activated protein kinase p38 pathway. Thus,

initial TCR signaling via p38 leads to successive induction of VDR and PLC-gamma1, which are required for subsequent classical TCR signaling and T cell activation.

Source

von Essen MR, et al. Vitamin D controls T cell antigen receptor signaling and activation of human T cells. Nat Immunol. 2010 Apr;11(4):344-9.

Update:

effects of antioxidant and non-antioxidant vitamin supplementation on immune function

ABSTRACT

The purpose of this manuscript is to review the impact of supplementation with vitamins E and C, carotenoids, and the B vitamins on parameters of innate and adaptive immune function as reported from clinical trials in humans. There is evidence to support causal effects of supplementation with vitamins E and C and the carotenoids singly and in combination on selected aspects of immunity, including the functional capacity of innate immune cells, lymphocyte proliferation, and the delayed-type hypersensitivity (DTH) response. Controlled intervention trials of B vitamin-containing multivitamin supplements suggest beneficial effects on immune parameters and clinical outcomes in HIV-positive individuals.

Source

Webb AL, et al. Update: effects of antioxidant and non-antioxidant vitamin supplementation on immune function. Nutr Rev. 2007 May;65(5):181-217.

Lung Health

Intake of specific carotenoids and risk of lung cancer in 2 prospective US cohorts

ABSTRACT

Background:

Carotenoids may reduce lung carcinogenesis because of their antioxidant properties; however, few studies have

examined the relation between intakes of individual carotenoids and lung cancer risk.

Objective:

The aim of this study was to examine the relation between lung cancer risk and intakes of alpha-carotene, beta-carotene, lutein, lycopene, and beta-cryptoxanthin in 2 large cohorts.

Design:

During a 10-y follow-up period, 275 new cases of lung cancer were diagnosed in 46924 men; during a 12-y follow-up period, 519 new cases were diagnosed in 77283 women. Carotenoid intakes were derived from the reported consumption of fruit and vegetables on food-frequency questionnaires administered at baseline and during follow-up. The data were analyzed separately for each cohort and the results were pooled to compute overall relative risks (RRs).

Results:

In the pooled analyses, alpha-carotene and lycopene intakes were significantly associated with a lower risk of lung cancer; the association with beta-carotene, lutein, and beta-cryptoxanthin intakes were inverse but not significant. Lung cancer risk was significantly lower in subjects who consumed a diet high in a variety of carotenoids (RR: 0.68; 95% CI: 0.49, 0.94 for highest compared with lowest total carotenoid score category). Inverse associations were strongest after a 4-8-y lag between dietary assessment and date of diagnosis. In subjects who never smoked, a 63% lower incidence of lung cancer was observed for the top compared with the bottom quintile of alpha-carotene intake (RR: 0.37; 95% CI: 0.18, 0.77).

Conclusion:

Data from 2 cohort studies suggest that several carotenoids may reduce the risk of lung cancer.

Source

Michaud DS, et al. Intake of specific carotenoids and risk of lung cancer in 2 prospective US cohorts. *Am J Clin Nutr.* 2000 Oct;72(4):990-7.

Men's Health

The association of folate, zinc and antioxidant intake with sperm aneuploidy in healthy non-smoking men

ABSTRACT

Background:

Little is known about the effect of paternal nutrition on aneuploidy in sperm. We investigated the association of normal dietary and supplement intake of folate, zinc and antioxidants (vitamin C, vitamin E and beta-carotene) with the frequency of aneuploidy in human sperm.

Methods:

Sperm samples from 89 healthy, non-smoking men from a non-clinical setting were analysed for aneuploidy using fluorescent in situ hybridization with probes for chromosomes X, Y and 21. Daily total intake (diet and supplements) for zinc, folate, vitamin C, vitamin E and beta-carotene was derived from a food frequency questionnaire. Potential confounders were obtained from a self-administered questionnaire.

Results:

After adjusting for covariates, men with high folate intake (>75th percentile) had lower frequencies of sperm with disomies X, 21, sex nullisomy, and a lower aggregate measure of sperm aneuploidy ($P \leq 0.04$) compared with men with lower intake. In adjusted continuous analyses, total folate intake was inversely associated with aggregate sperm aneuploidy (-3.6% change/100 microg folate; 95% CI: -6.3, -0.8) and results were similar for disomies X, 21 and sex nullisomy. No consistent associations were found between antioxidant or zinc intakes and sperm aneuploidy.

Conclusions:

Men with high folate intake had lower overall frequencies of several types of aneuploid sperm.

Source

Young SS, et al. The association of folate, zinc and antioxidant intake with sperm aneuploidy in healthy non-smoking men. *Human Reprod*

Epub Mar 19, 2008.

Ovarian Health

Dietary carotenoids and risk of breast cancer in Chinese women

ABSTRACT

There has been considerable interest in the role of carotenoids in the chemoprevention of cancer. However, the protective effect of carotenoids on breast cancer has been inconclusive. To investigate whether intake of lycopene, alpha-carotene, beta-carotene, beta-cryptoxanthin, and lutein/zeaxanthin is inversely associated with breast cancer risk, a case-control study was conducted in China during 2004-2005. The cases were 122 female patients aged 24-87 years with histopathologically confirmed breast cancer. 632 healthy women age-matched were randomly recruited from outpatient clinics. Habitual dietary intake and lifestyle were collected by face-to-face interview using a validated and reliable food frequency questionnaire. The USDA nutrient composition database was used to calculate intake of the specific carotenoids. Unconditional logistic regression analyses were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs), accounting for age, locality, education, body mass index, smoking, passive smoking, physical activity, number of children breastfed, menopausal status, oral contraceptive use, biopsy-confirmed benign breast diseases, family history of breast cancer, and total energy intake. Compared with the highest versus lowest quartile of intake, the adjusted ORs were 0.26 (95% CI 0.14-0.46) for lycopene, 0.38 (95% CI 0.21-0.71) for beta-carotene, 0.43 (95% CI 0.23-0.82) for beta-cryptoxanthin, and 0.37 (95% CI 0.20-0.68) for total carotenoids, with statistically significant tests for trend. There was no association with breast cancer for alpha-carotene and lutein/zeaxanthin. It is concluded that higher intake of lycopene, beta-carotene and beta-cryptoxanthin is associated to a lower risk of breast cancer among Chinese women. More research to examine the relationship between carotenoids and breast cancer risk is warranted.

Source

Huang JP, et al. *Dietary carotenoids and risk of breast cancer in Chinese women. Asia Pac J Clin Nutr. 2007;16 Suppl 1:437-42.*

Prostate Health

Carotenoids and prostate cancer risk

ABSTRACT

Chemoprevention is presumably one of most effective means to combat prostate cancer (PCa). Patients usually require more than a decade to develop a clinically significant Pca, therefore, an ideal target for chemoprevention. This review will focus on recent findings of a group of naturally occurring chemicals, carotenoids, for potential use in reducing PCa risk.

Source

Young CY, et al. *Carotenoids and prostate cancer risk. Mini Rev Med Chem. 2008 May;8(5):529-37.*

Skin Health

Dietary carotenoids contribute to normal human skin color and UV photosensitivity.

ABSTRACT

The aim of the current study was to determine whether dietary carotenoids influence skin pigmentation and UV photosensitivity in a healthy unsupplemented panel (n = 22) of Caucasian (skin Type II) subjects. Skin spectrophotometric and tristimulus (L*a*b*) CR200 chromameter readings were made at various body sites to objectively measure skin carotenoid levels and skin color, respectively. The minimal erythemal dose (MED) was also measured to determine the intrinsic UV photosensitivity of the skin. We found that tristimulus b* values (but not L* and a* values) were consistently and closely correlated with skin carotenoid levels at a number of body sites including the back (r = 0.85, P < 0.00001), forehead (r = 0.85, P < 0.00001), inner forearm (r = 0.75, P < 0.0001) and palm of the hand (r = 0.78, P < 0.0001). Skin carotenoid levels and MED were also correlated in these subjects (r =

0.66, P < 0.001), as were tristimulus b* values and MED (r = 0.71, P < 0.0002). From these observations, we conclude that carotenoids from a normal, unsupplemented diet accumulate in the skin and confer a measurable photoprotective benefit (at least in lightly pigmented Caucasian skin), that is directly linked to their concentration in the tissue. Carotenoids also appear to contribute measurably and significantly to normal human skin color, in particular the appearance of "yellowness" as defined objectively by CR200 tristimulus b* values. On the basis of these findings we believe that objective measurements of skin color, in particular tristimulus b* values, may be a potentially useful means of monitoring dietary carotenoid status and assessing UV photosensitivity in Caucasian populations.

Source

Alaluf S, et al. *Dietary carotenoids contribute to normal human skin color and UV photosensitivity. J Nutr 132: 399-403, 2002.*

UVB photoprotection with antioxidants: effects of oral therapy with d-alpha-tocopherol and ascorbic acid on the minimal erythema dose

ABSTRACT

Ultraviolet radiation absorption is responsible for the production of free radicals in damaged cells. This side effect may be neutralized using antioxidant substances. It has been reported that ascorbic acid and d-alpha-tocopherol scavenge reactive oxygen species. In a single-blind controlled clinical trial we studied 45 healthy volunteers divided into three groups. Group 1 received d-alpha-tocopherol 1,200 I.U. daily; Group 2 ascorbic acid 2 g daily and Group 3 ascorbic acid 2 g plus d-alpha-tocopherol 1,200 I.U. daily. Treatment was sustained for one week. Before and after treatment, the minimal erythema dose was determined in all participants. The results show that the median minimal erythema dose increased from 60 to 65 mJ/cm² in Group 1 and from 50 to 70 mJ/cm² in Group 3. No modifications were observed in Group 2. We conclude that d-alpha-tocopherol prescribed in combination with ascorbic acid produces the best photoprotective effect.

Source

Mireles-Rocha H, et al. *UVB photoprotection with antioxidants: effects of oral therapy with d-alpha-tocopherol and ascorbic acid on the minimal erythema dose. Acta Derm Venereol 82:21-4, 2002.*

Botanicals in Dermatology: An Evidence based Review

ABSTRACT

Botanical extracts and single compounds are increasingly used in cosmetics but also in over-the-counter drugs and food supplements. The focus of the present review is on controlled clinical trials with botanicals in the treatment of acne, inflammatory skin diseases, skin infections, UV-induced skin damage, skin cancer, alopecia, vitiligo, and wounds. Studies with botanical cosmetics and drugs are discussed, as well as studies with botanical food supplements. Experimental research on botanicals was considered to a limited extent when it seemed promising for clinical use in the near future. In acne therapy, Mahonia, tea tree oil, and Saccharomyces may have the potential to become standard treatments. Mahonia, Hypericum, Glycyrrhiza and some traditional Chinese medicines appear promising for atopic dermatitis. Some plant-derived substances like dithranol and methoxsalen (8-methoxypsoralen) [in combination with UVA] are already accepted as standard treatments in psoriasis; Mahonia and Capsicum (capsaicin) are the next candidates suggested by present evidence. Oral administration and topical application of antioxidant plant extracts (green and black tea, carotenoids, coffee, and many flavonoids from fruits and vegetables) can protect skin from UV-induced erythema, early aging, and irradiation-induced cancer. Hair loss and vitiligo are also traditional fields of application for botanicals. According to the number and quality of clinical trials with botanicals, the best evidence exists for the treatment of inflammatory skin diseases, i.e. atopic dermatitis and psoriasis. However, many more controlled clinical studies are needed to determine the efficacy and risks of plant-derived products in dermatology. Safety aspects, especially related to

sensitization and photodermatitis, have to be taken into account. Therefore, clinicians should not only be informed of the beneficial effects but also the specific adverse effects of botanicals used for dermatologic disorders and cosmetic purposes.

Source

Reuter J et al. *Botanicals in Dermatology: An Evidence based Review. Am J Clin Dermatol* 11:247-67, 2010.

Significant correlations of dermal total carotenoids and dermal lycopene with their respective plasma levels in healthy adults

ABSTRACT

Carotenoids in skin have been known to play a role in photoprotection against UV radiation. We performed dermal biopsies of healthy humans (N=27) and collected blood samples for pair-wise correlation analyses of total and individual carotenoid content by high performance liquid chromatography (HPLC). The hydrocarbon carotenoids (lycopene and beta-carotene) made up the majority of carotenoids in both skin and plasma, and skin was somewhat enriched in these carotenoids relative to plasma. Beta-cryptoxanthin, a monohydroxycarotenoid, was found in similar proportions in skin as in plasma. In contrast, the dihydroxycarotenoids, lutein and zeaxanthin, were relatively lacking in human skin in absolute and relative levels as compared to plasma. Total carotenoids were significantly correlated in skin and plasma ($r = 0.53, p < 0.01$). Our findings suggest that human skin is relatively enriched in lycopene and beta-carotene, compared to lutein and zeaxanthin, possibly reflecting a specific function of hydrocarbon carotenoids in human skin photoprotection.

Source

Scarmo S et al. *Significant correlations of dermal total carotenoids and dermal lycopene with their respective plasma levels in healthy adults. Arch Biochem Biophys* 504:34-39, 2010.

Discovering the link between nutrition and skin aging

ABSTRACT

Skin has been reported to reflect the general inner-health status and aging. Nutrition and its reflection on skin has always been an interesting topic for scientists and physicians throughout the centuries worldwide. Vitamins, carotenoids, tocopherols, flavonoids and a variety of plant extracts have been reported to possess potent anti-oxidant properties and have been widely used in the skin care industry either as topically applied agents or oral supplements in an attempt to prolong youthful skin appearance. This review will provide an overview of the current literature "linking" nutrition with skin aging.

Source

Schagen S et al. *Discovering the link between nutrition and skin aging. Review. Dermato-Endocrinol* 4:298-307, 2012.

Photoprotection by dietary carotenoids: concept, mechanisms, evidence and future development

ABSTRACT

Carotenoids are micronutrients present mainly in fruits and vegetables, and they are ingested from these sources with the diet. They exhibit specific antioxidant activity but also influence signaling and gene expression at the cellular level. β -Carotene and lycopene, the colorants of carrots and tomatoes, respectively, are among the most prominent members of this group of lipids, and they are usually the dominating carotenoids in human blood and tissues. Both compounds modulate skin properties when ingested as supplements or as dietary products. There is evidence that they protect the skin against sunburn (solar erythema) by increasing the basal defense against UV light-mediated damage. Their photoprotective efficacy, however, is not comparable to the use of a sunscreen. In vitro data show that also other carotenoids are efficient photoprotectors. Among them are lutein and structurally unusual phenolic polyenes like 3,3'-dihydroxyisorenieratene.

Source

Stahl W and Sies H. Photoprotection by dietary carotenoids: concept, mechanisms, evidence and future development. *Mol Nutr Food Res* 56:287-95, 2012.

Carotenoids and carotenoids plus vitamin E protect against ultraviolet light-induced erythema in humans

ABSTRACT

Background: Carotenoids and tocopherols, known to be efficient antioxidants and capable of scavenging reactive oxygen species generated during photooxidative stress, may protect the skin from ultraviolet light-induced erythema. β -Carotene is widely used as an oral sun protectant but studies on its protective effects are scarce.

Objective:

The objective of this study was to investigate the protective effects of oral supplementation with carotenoids and a combination of carotenoids and vitamin E against the development of erythema in humans.

Design:

A carotenoid supplement (25 mg total carotenoids/d) and a combination of the carotenoid supplement and vitamin E [335 mg (500 IU) RRR- α -tocopherol/d] were given for 12 wk to healthy volunteers. Erythema was induced by illumination with a blue-light solar simulator. Serum β -carotene and α -tocopherol concentrations and skin carotenoid levels were assessed by HPLC and reflection photometry.

Results:

Serum β -carotene and α -tocopherol concentrations increased with supplementation. Erythema on dorsal skin (back) was significantly diminished ($P < 0.01$) after week 8, and erythema suppression was greater with the combination of carotenoids and vitamin E than with carotenoids alone.

Conclusion:

The antioxidants used in this study provided protection against erythema in humans and may be useful for diminishing sensitivity to ultraviolet light.

Source

Stahl, W et al. Carotenoids and carotenoids plus vitamin E protect against ultraviolet light-induced erythema in humans. *Am J Clin Nutr* 71:795-8, 2000.

A randomized controlled trial of an appearance-based dietary intervention

ABSTRACT**Objective:**

Inadequate fruit and vegetable consumption precipitates preventable morbidity and mortality. The efficacy of an appearance-based dietary intervention was investigated, which illustrates the beneficial effect that fruit and vegetable consumption has on skin appearance.

Methods:

Participants were randomly allocated to three groups receiving information-only or a generic or own-face appearance-based intervention. Diet was recorded at baseline and 10 weekly follow-ups. Participants in the generic and own-face intervention groups witnessed on-screen stimuli and received printed photographic materials to illustrate the beneficial effect of fruit and vegetable consumption on skin color.

Results:

Controlling for baseline diet, a significant effect of intervention group was found on self-reported fruit and vegetable intake among 46 completers who were free of medical and personal reasons preventing diet change. The own-face appearance-based intervention group reported a significant, sustained improvement in fruit and vegetable consumption whereas the information-only and generic appearance-based intervention groups reported no significant dietary changes.

Conclusions:

Seeing the potential benefits of fruit and vegetable consumption on own skin color may motivate dietary improvement.

Source

Whitehead RD et al. A randomized controlled trial of an appearance-based dietary intervention. *Health Psychol*, Epub ahead of print, 2013.

You are what you eat: Within-subject increases in fruit and vegetable consumption confer beneficial skin-color changes

ABSTRACT**Background:**

Fruit and vegetable consumption and ingestion of carotenoids have been found to be associated with human skin-color (yellowness) in a recent cross-sectional study. This carotenoid-based coloration contributes beneficially to the appearance of health in humans and is held to be a sexually selected cue of condition in other species.

Methodology and Principal Findings:

Here we investigate the effects of fruit and vegetable consumption on skin-color longitudinally to determine the magnitude and duration of diet change required to change skin-color perceptibly. Diet and skin-color were recorded at baseline and after three and six weeks, in a group of 35 individuals who were without makeup, self-tanning agents and/or recent intensive UV exposure. Six-week changes in fruit and vegetable consumption were significantly correlated with changes in skin redness and yellowness over this period, and diet-linked skin reflectance changes were significantly associated with the spectral absorption of carotenoids and not melanin. We also used psychophysical methods to investigate the minimum color change required to confer perceptibly healthier and more attractive skin-coloration. Modest dietary changes are required to enhance apparent health (2.91 portions per day) and attractiveness (3.30 portions).

Conclusions:

Increased fruit and vegetable consumption confers measurable and perceptibly beneficial effects on Caucasian skin appearance within six weeks. This effect could potentially be used as a motivational tool in dietary intervention.

Source

Whitehead RD et al. *You are what you eat: Within-subject increases in fruit and vegetable consumption confer beneficial skin-color changes. PLoS ONE* 7:e32988, 2012.

Sports Nutrition

The Role of Nutritional Supplements in the Prevention and Treatment of Resistance-Induced Skeletal Muscle Injury

ABSTRACT

The topic of exercise-induced skeletal muscle injury has received considerable attention in recent years. Likewise, strategies to minimise the injury resulting from heavy resistance exercise have been studied.

Over the past 15 years, several investigations have been performed focused on the role of nutritional supplements to attenuate signs and symptoms of muscle injury. Of these, some have reported favourable results, while many others have reported no benefit of the selected nutrient. Despite these mixed findings, recommendations for the use of nutritional supplements for the purposes of attenuating muscle injury are rampant within the popular fitness media and athletic world, largely without scientific support. Those nutrients include the antioxidant vitamin C (ascorbic acid) and vitamin E (tocopherol), N-acetyl-cysteine, flavonoids, L-carnitine, astaxanthin, beta-hydroxy-beta-methylbutyrate, creatine monohydrate, essential fatty acids, branched-chain amino acids, bromelain, proteins and carbohydrates. A discussion of all published peer-reviewed articles in reference to these nutrients and their impact on resistance exercise-induced skeletal muscle injury is presented, in addition to a brief view into the potential mechanism of action for each nutrient. Based on the current state of knowledge, the following conclusions can be made with regard to nutritional supplements and their role in attenuating signs and symptoms of skeletal muscle injury occurring as a consequence of heavy resistance exercise: (i) there appears to be a potential role for certain supplements (vitamin C, vitamin E, flavonoids, and L-carnitine); (ii) these supplements cannot effectively eliminate muscle injury, only attenuate certain signs and symptoms; (iii) it is presently unclear what the optimal

dosage of these nutrients is (whether used alone or in combination); (iv) it is unclear what the optimal pretreatment period is; and (v) the effectiveness is largely specific to non-resistance trained individuals.

Ultimately, because so few studies have been conducted in this area, it is difficult to recommend with confidence the use of selected nutrients for the sole purpose of minimising signs and symptoms of resistance exercise-induced muscle injury, in particular with regard to resistance-trained individuals.

Source

Bloomer R, et al; The Role of Nutritional Supplements in the Prevention and Treatment of Resistance-Induced Skeletal Muscle Injury. Sports Medicine, 2007.