

ABSTRACTS**Anti-mutagenics****THE DETOXIFICATION ENZYME SYSTEMS.**

The human body is exposed to a wide array of xenobiotics in one's lifetime, from food components to environmental toxins to pharmaceuticals, and has developed complex enzymatic mechanisms to detoxify these substances. These mechanisms exhibit significant individual variability, and are affected by environment, life-style, and genetic influences. The scientific literature suggests an association between impaired detoxification and certain diseases, including cancer, Parkinson's disease, fibromyalgia, and chronic fatigue/immune dysfunction syndrome. Data regarding these hepatic detoxification enzyme systems and the body's mechanisms of regulating them suggests the ability to efficiently detoxify and remove xenobiotics can affect these and other chronic disease processes. This article reviews the myriad detoxification enzyme systems, their regulatory mechanisms, and the dietary, lifestyle, and genetic factors influencing their activities, as well as laboratory tests available to assess their functioning.

Altern Med Rev. 1998 Jun;3(3):187-98

USE OF TRANSGENIC AND MUTANT ANIMAL MODELS IN THE STUDY OF HETEROCYCLIC AMINE-INDUCED MUTAGENESIS AND CARCINOGENESIS.

Heterocyclic amines (HCAs) are potent mutagens generated during the cooking of meat and fish, and several of these compounds produce tumors in conventional experimental animals. During the past 5 years or so, HCAs have been tested in a number of novel in vivo murine models, including the following: lacZ, lacI, cII, c-myc/lacZ, rpsL, and gptDelta. transgenics, XPA^{-/-}, XPC^{-/-}, Msh2^{+/-}, Msh2^{-/-} and p53^{+/-} knock-outs, Apc mutant mice (ApcDelta716, Apc1638N, Apcmin), and A33DeltaNbeta-cat knock-in mice. Several of these models have provided insights into the mutation spectra induced in vivo by HCAs in target and non-target organs for tumorigenesis, as well as demonstrating enhanced susceptibility to HCA-induced tumors and preneoplastic lesions. This review describes several of the more recent reports in which novel animal models were used to examine HCA-induced mutagenesis and carcinogenesis in vivo, including a number of studies which assessed the inhibitory activities of chemopreventive agents such as 1,2-dithiole-3-thione, conjugated linoleic acids, tea, curcumin, chlorophyllin-chitosan, and sulindac.

J Biochem Mol Biol. 2003 Jan 31;36(1):35-42

DIETARY SUPPLEMENTATION OF CURCUMIN ENHANCES ANTIOXIDANT AND PHASE II METABOLIZING ENZYMES IN DDY MALE MICE: POSSIBLE ROLE IN PROTECTION AGAINST CHEMICAL CARCINOGENESIS AND TOXICITY.

Dietary antioxidants protect laboratory animals against the induction of tumours by a variety of chemical carcinogens. Among possible mechanism of protection against chemical carcinogenesis could be mediated via-antioxidant-dependent induction of detoxifying enzymes. Curcumin, a yellow pigment from *Curcuma longa*, is a major component of turmeric and is commonly used as a spice and food colouring material and exhibits antiinflammatory antitumour, and antioxidant properties. In this study we therefore investigated the effect of dietary supplementation of curcumin on the activities of antioxidant and phase II-metabolizing enzymes involved in detoxification, and production of reactive oxygen species were quantified in ddY male mice. Dietary supplementation of curcumin (2%, w/v) to male ddY mice for 30 days significantly increased the activities of glutathione peroxidase, glutathione reductase, glucose-6-phosphate dehydrogenase and catalase to 189%, 179%, 189%, and 181% in liver and 143%, 134%, 167% and 115% in kidney respectively as compared with corresponding normal diet fed control ($P < 0.05-0.001$). Parallel to these changes, curcumin feeding to mice also resulted in a considerable enhancement in the activity of phase II-metabolizing enzymes viz. glutathione S-transferase and quinone reductase to 1.7 and 1.8 times in liver and 1.1 and 1.3 times in kidney respectively as compared with corresponding normal diet fed control ($P < 0.05-0.01$). In general, the increase in activities of antioxidant and phase II-metabolizing enzymes was more pronounced in liver as compared to kidney. The induction of such detoxifying enzymes by curcumin suggest the potential value of this compound as protective agent against chemical carcinogenesis and other forms of electrophilic toxicity. The significance of these results can be implicated in relation to cancer chemopreventive effects of curcumin against the induction of tumours in various target organs.

INHIBITION OF CARCINOGEN INDUCED C-HA-RAS AND C-FOS PROTO-ONCOGENES EXPRESSION BY DIETARY CURCUMIN.

BACKGROUND: We investigated the chemopreventive action of dietary curcumin on 7,12-dimethylbenz(a)anthracene (DMBA)-initiated and 12,0-tetradecanoylphorbol-13-acetate (TPA)-promoted skin tumor formation in Swiss albino mice. Curcumin, a yellow coloring matter isolated from roots of *Curcuma longa* Linn, is a phenolic compound possessing antioxidant, free radical scavenger, and antiinflammatory properties. It has been shown by previously reported work that TPA-induced skin tumors were inhibited by topical application of curcumin, and curcumin has been shown to inhibit a variety of biological activities of TPA. Topical application of curcumin was reported to inhibit TPA-induced c-fos, c-jun and c-myc gene expression in mouse skin. This paper reports the effects of orally administered curcumin, which was consumed as a dietary component at concentrations of 0.2 % or 1 %, in ad libitum feeding. **RESULTS:** Animals in which tumors had been initiated with DMBA and promoted with TPA experienced significantly fewer tumors and less tumor volume if they ingested either 0.2% or 1% curcumin diets. Also, the dietary consumption of curcumin resulted in a significantly decreased expression of ras and fos proto-oncogenes in the tumorous skin, as measured by enhanced chemiluminescence Western blotting detection system (Amersham). **CONCLUSIONS:** Whereas earlier work demonstrated that topical application of curcumin to mouse skin inhibited TPA-induced expression of c-fos, c-jun and c-myc oncogenes, our results are the first to show that orally consumed curcumin significantly inhibited DMBA- and TPA-induced ras and fos gene expression in mouse skin.

BMC Cancer. 2001;1(1):1. Epub 2001 Jan 17

ANTIPROLIFERATIVE EFFECT OF CURCUMIN (DIFERULOYLMETHANE) AGAINST HUMAN BREAST TUMOR CELL LINES.

Pharmacologically safe compounds that can inhibit the proliferation of tumor cells have potential as anticancer agents. Curcumin, a diferuloylmethane, is a major active component of the food flavor turmeric (*Curcuma longa*) that exhibits anticarcinogenic properties in vivo. In vitro, it suppressed c-jun/Ap-1 and NF-kappaB activation and type 1 human immunodeficiency virus long-terminal repeat-directed gene expression. We examined the antiproliferative effects of curcumin against several breast tumor cell lines, including hormone-dependent and -independent and multidrug-resistant (MDR) lines. Cell growth inhibition was monitored by [³H]thymidine incorporation, Trypan blue exclusion, crystal violet dye uptake and flow cytometry. All the cell lines tested, including the MDR-positive ones, were highly sensitive to curcumin. The growth inhibitory effect of curcumin was time- and dose-dependent, and correlated with its inhibition of ornithine decarboxylase activity. Curcumin preferentially arrested cells in the G2/S phase of the cell cycle. Curcumin-induced cell death was neither due to apoptosis nor to any significant change in the expression of apoptosis-related genes, including Bcl-2, p53, cyclin B and transglutaminase. Overall our results suggest that curcumin is a potent antiproliferative agent for breast tumor cells and may have potential as an anticancer agent.

Anticancer Drugs. 1997 Jun;8(5):470-81

POTENT INDUCTION OF PHASE 2 ENZYMES IN HUMAN PROSTATE CELLS BY SULFORAPHANE.

Two population-based, case-control studies have documented reduced risk of prostate cancer in men who consume cruciferous vegetables. Cruciferae contain high levels of the isothiocyanate sulforaphane. Sulforaphane is known to bolster the defenses of cells against carcinogens through up-regulation of enzymes of carcinogen defense (phase 2 enzymes). Prostate cancer is characterized by an early and near universal loss of expression of the phase 2 enzyme glutathione S-transferase (GST)-pi. We tested whether sulforaphane may act in prostatic cells by increasing phase 2 enzyme expression. The human prostate cancer cell lines LNCaP, MDA PCa 2a, MDA PCa 2b, PC-3, and TSU-Pr1 were treated with 0.1-15 microM sulforaphane in vitro. LNCaP was also treated with an aqueous extract of broccoli sprouts. Quinone reductase enzymatic activity, a surrogate of global phase 2 enzyme activity, was assayed by the menadione-coupled reduction of tetrazolium dye. Expression of NQO-1, GST-alpha, gamma-glutamylcysteine synthetase-heavy and -light chains, and microsomal GST was assessed by Northern blot analysis. Sulforaphane and broccoli sprout extract potently induce quinone reductase activity in cultured prostate cells, and this induction appears to be mediated by increased transcription of the NQO-1 gene. Sulforaphane also induces expression of gamma-glutamylcysteine synthetase light subunit but not the heavy subunit, and this induction is associated with moderate increases in intracellular glutathione levels. Microsomal and alpha-class glutathione transferases were also induced transcriptionally. Sulforaphane induces phase 2 enzyme expression and activity significantly in human prostatic cells. This induction is accompanied by, but not because of, increased intracellular glutathione synthesis. Our findings may help explain the observed inverse correlation between consumption of cruciferae and prostate cancer risk.

Cancer Epidemiol Biomarkers Prev. 2001 Sep;10(9):949-54

CHEMOPROTECTIVE GLUCOSINOLATES AND ISOTHIOCYANATES OF BROCCOLI SPROUTS: METABOLISM

AND EXCRETION IN HUMANS.

Broccoli sprouts are a rich source of glucosinolates and isothiocyanates that induce phase 2 detoxication enzymes, boost antioxidant status, and protect animals against chemically induced cancer. Glucosinolates are hydrolyzed by myrosinase (an enzyme found in plants and bowel microflora) to form isothiocyanates. In vivo, isothiocyanates are conjugated with glutathione and then sequentially metabolized to mercapturic acids. These metabolites are collectively designated dithiocarbamates. We studied the disposition of broccoli sprout glucosinolates and isothiocyanates in healthy volunteers. Broccoli sprouts were grown, processed, and analyzed for (a) inducer potency; (b) glucosinolate and isothiocyanate concentrations; (c) glucosinolate profiles; and (d) myrosinase activity. Dosing preparations included uncooked fresh sprouts (with active myrosinase) as well as homogenates of boiled sprouts that were devoid of myrosinase activity and contained either glucosinolates only or isothiocyanates only. In a crossover study, urinary dithiocarbamate excretion increased sharply after administration of broccoli sprout glucosinolates or isothiocyanates. Cumulative excretion of dithiocarbamates following 111-micromol doses of isothiocyanates was greater than that after glucosinolates (88.9 +/- 5.5 and 13.1 +/- 1.9 micromol, respectively; $P < 0.0003$). In subjects fed four repeated 50-micromol doses of isothiocyanates, the intra- and intersubject variation in dithiocarbamate excretion was very small (coefficient of variation, 9%), and after escalating doses, excretion was linear over a 25- to 200-micromol dose range. Dithiocarbamate excretion was higher when intact sprouts were chewed thoroughly rather than swallowed whole (42.4 +/- 7.5 and 28.8 +/- 2.6 micromol; $P = 0.049$). These studies indicate that isothiocyanates are about six times more bioavailable than glucosinolates, which must first be hydrolyzed. Thorough chewing of fresh sprouts exposes the glucosinolates to plant myrosinase and significantly increases dithiocarbamate excretion. These findings will assist in the design of dosing regimens for clinical studies of broccoli sprout efficacy.

Cancer Epidemiol Biomarkers Prev. 2001 May;10(5):501-8

SELECTIVE SENSITIVITY TO WASABI-DERIVED 6-(METHYLSULFINYL)HEXYL ISOTHIOCYANATE OF HUMAN BREAST CANCER AND MELANOMA CELL LINES STUDIED IN VITRO.

Recently, attention has focused on the anticancer properties of an aromatic component 6-(methylsulfinyl)hexyl isothiocyanate (6-MITC) in a typical Japanese spice, wasabi. In this paper, anticancer activity of 6-MITC in vitro was studied by using a human cancer cell (HCC) panel. 6-MITC directly affected the cells in the HCC panel and inhibited their growth in culture. The mean concentration required to inhibit 50% of control cell growth was 3.9 microM, which is a sufficiently low dosage for practical use. The suppression influenced not only the cell growth, but also the survival of these cells. The mean concentration to suppress cells to a 50% survival was 43.7 microM. The reduction activity of 6-MITC was differential, and it suppressed specific cells. These severely suppressed cell lines included breast cancer and melanoma cell lines. For example, one melanoma line was seriously damaged at a concentration of 0.3 microM of 6-MITC. Compared with other MITCs (2-MITC, 4-MITC and 8-MITC), 6-MITC showed the most effective suppression and with the most specific manner of the cells mentioned above. A "COMPARE" analysis using a computerized algorithm, which was based on the HCC database, suggested that the suppression mechanism of 6-MITC is unique and may be different from that of other known chemicals. The actual mechanism may not a simple one but may involve multiple pathways. On account of its sufficiently small size, 6-MITC is a new possible candidate for controlling cancer cells.

Cancer Detect Prev. 2005;29(2):155-60

ABSTRACTS

Zeaxanthin

MACULAR PIGMENT DENSITY IS REDUCED IN OBESE SUBJECTS.

PURPOSE: Because of the potential protective function of lutein (L) and zeaxanthin (Z) within the retina and lens, a better understanding of factors influencing tissue deposition is needed. The largest fractions of L and Z are stored in adipose tissue. Thus, higher body fat content and body mass index (BMI) may be expected to influence the quantities of L and Z in the retina (measured as macular pigment optical density, MPOD). **METHODS:** Six hundred eighty subjects were tested. Information on MPOD, body mass index (BMI), body fat percentage (n = 400, using bioelectric impedance), dietary intake (n = 280, using a food frequency questionnaire), and serum carotenoid content (n = 280, using reversed phase high-performance liquid chromatography) was obtained. **RESULTS:** There was an inverse relationship between MPOD and BMI (n = 680, r = -0.12, P < 0.0008) and between MPOD and body fat percentage (n = 400, r = -0.12, P < 0.01). These relationships were largely driven by data from the subjects with higher BMI (more than 29, 21% less MP) and higher body fat percentage (more than 27%, 16% less MP). Dietary carotenoid intake and serum carotenoid levels were also lower in subjects with higher BMI (n = 280). **CONCLUSIONS:** Obese subjects tend to have lower retinal L and Z. This reduction may be due to decreased dietary intake of L and Z and/or competition between retina and adipose tissue for uptake of L and Z.

Invest Ophthalmol Vis Sci. 2002 Jan;43(1):47-50

FRUITS AND VEGETABLES THAT ARE SOURCES FOR LUTEIN AND ZEAXANTHIN: THE MACULAR PIGMENT IN HUMAN EYES.

BACKGROUND: It has been suggested that eating green leafy vegetables, which are rich in lutein and zeaxanthin, may decrease the risk for age related macular degeneration. The goal of this study was to analyse various fruits and vegetables to establish which ones contain lutein and/or zeaxanthin and can serve as possible dietary supplements for these carotenoids. **METHODS:** Homogenates of 33 fruits and vegetables, two fruit juices, and egg yolk were used for extraction of the carotenoids with hexane. Measurement of the different carotenoids and their isomers was carried out by high performance liquid chromatography using a single column with an isocratic run, and a diode array detector. **RESULTS:** Egg yolk and maize (corn) contained the highest mole percentage (% of total) of lutein and zeaxanthin (more than 85% of the total carotenoids). Maize was the vegetable with the highest quantity of lutein (60% of total) and orange pepper was the vegetable with the highest amount of zeaxanthin (37% of total). Substantial amounts of lutein and zeaxanthin (30-50%) were also present in kiwi fruit, grapes, spinach, orange juice, zucchini (or vegetable marrow), and different kinds of squash. The results show that there are fruits and vegetables of various colours with a relatively high content of lutein and zeaxanthin. **CONCLUSIONS:** Most of the dark green leafy vegetables, previously recommended for a higher intake of lutein and zeaxanthin, have 15-47% of lutein, but a very low content (0-3%) of zeaxanthin. Our study shows that fruits and vegetables of various colours can be consumed to increase dietary intake of lutein and zeaxanthin.

Br J Ophthalmol. 1998 Aug;82(8):907-10

CAROTENOID ANALYSES OF SELECTED RAW AND COOKED FOODS ASSOCIATED WITH A LOWER RISK FOR CANCER.

We examined the carotenoid content of selected foods consistently found to be associated with a lower risk for various epithelial cancers in epidemiologic studies. Both raw and cooked samples of green, leafy vegetables and yellow or orange vegetables were quantitatively examined by high-performance liquid chromatography for individual carotenoid content. The results indicated that fresh, green, leafy vegetables were moderately high in beta carotene (0.5-14.6 mg/100 g) and very high in oxygenated carotenoids or xanthophylls, primarily lutein and its stereoisomers (2.3-63.0 mg/100g) [corrected]. The fresh, yellow or orange vegetables examined were very high in beta carotene (16.0-120.5 mg/100 g) [corrected] but had no detectable nonhydrocarbon carotenoids. Cooking differentially reduced the lutein content compared with the beta carotene content in green, leafy vegetables. These analyses suggest that consumption of carotenoids in addition to beta carotene may be associated with a lower risk for cancer.

J Natl Cancer Inst. 1990 Feb 21;82(4):282-5

KINETICS OF GASTRO-INTESTINAL TRANSIT AND CAROTENOID ABSORPTION AND DISPOSAL IN ILEOSTOMY VOLUNTEERS FED SPINACH MEALS.

BACKGROUND: Reports of low carotenoid absorption from food sources has undermined their postulated 'protective' role as one of the active agents in diets rich in vegetable matter. **AIM OF THE STUDY:** This study quantified beta-carotene and lutein absorption from a representative green vegetable with different degrees of processing, using both mass balance and metabolic modelling of triglyceride-rich lipoprotein plasma fraction (TRL) response. **METHODS:** Whole or chopped-leaf cooked spinach was fed to volunteers (n = 7, paired) with vegetable oil (40 g) in yoghurt. Blood and ileal effluent samples were collected for up to 24 h. Effluent and TRL samples were analysed for lutein and beta-carotene by HPLC. A digesta transit model was used to describe meal transit and a single compartment model used to predict percentage absorption from the plasma TRL response. **RESULTS:** Mass balance showed 25% of lutein and beta-carotene were absorbed from chopped spinach, compared with 25% beta-carotene and 40 % lutein from whole-leaf spinach. Increased lutein absorption correlated to slower gastrointestinal (GI) transit for the whole-leaf meal. An area under the curve (AUC) response for the TRL fraction, found in 50% of cases, was not confined to those with the greatest percentage absorption. Absorption by mass balance and TRL AUC indicate a half-life of newly absorbed carotenoid around 11 min **CONCLUSION:** GI residence time appears to have an effect on the absorption of lutein but not beta-carotene. Rapid clearance is probably the main reason for absence of measurable plasma concentration excursions. Lack of plasma response cannot be interpreted as lack of carotenoid absorption without knowledge of the absorption and disposal kinetics.

Eur J Nutr. 2004 Feb;43(1):15-22. Epub 2004 Jan 6

COMPARISON OF SERUM CAROTENOID RESPONSES BETWEEN WOMEN CONSUMING VEGETABLE JUICE AND WOMEN CONSUMING RAW OR COOKED VEGETABLES.

The objective of this study was to examine serum concentrations of alpha-carotene, beta-carotene, lutein, lycopene, and beta-cryptoxanthin due to consumption of vegetable juice versus raw or cooked vegetables. Subjects included female breast cancer patients who had undergone surgical resection and who were enrolled in a feasibility study for a trial examining the influence of diet on breast cancer recurrence. A high-vegetable, low-fat diet was the focus of the intervention, and some of the subjects were specifically encouraged to consume vegetable juice. At 12 months, blood samples were collected and analyzed for carotenoid concentrations via high-performance liquid chromatography methodology. Matched analysis and paired t test were conducted on two groups: those who consumed vegetable juice (the juice group) and those who consumed raw or cooked vegetables (no juice group). Serum concentrations of alpha-carotene and lutein were significantly higher in the vegetable juice group than in the raw or cooked vegetable group (P < 0.05 and P = 0.05, respectively). Paired t test analysis did not demonstrate a significant difference in serum values of beta-carotene, lycopene, and beta-cryptoxanthin between subjects consuming juice and those not consuming any juice. These results suggest that alpha-carotene and lutein appear to be more bioavailable in the juice form than in raw or cooked vegetables. Therefore, the food form consumed may contribute to the variability in serum carotenoid response to vegetable and fruit interventions in clinical studies.

Cancer Epidemiol Biomarkers Prev. 1999 Mar;8(3):227-31

STORAGE STABILITY OF LUTEIN DURING RIPENING OF CHEDDAR CHEESE.

Lutein (3,3'-dihydroxy-alpha-carotene) has been identified as a dietary factor that can delay the onset of age-related macular degeneration (AMD). However, available food sources of lutein contain only modest amounts of the carotenoid. Food fortification with lutein extract has been identified as a low-budget approach to prevent the onset or progression of AMD. The objectives of this study were to 1) incorporate various amounts of lutein into Cheddar cheese; 2) examine the color, pH, microbiological, and sensory characteristics of the Cheddar cheese during storage; and 3) analyze the stability of lutein during the cheese maturation process. Lutein extracted from corn was added to Cheddar cheese in quantities of 1, 3, and 6 mg per serving size. Measurements of the lutein stability were carried out by HPLC using a YMC C30 carotenoid column. Microbiological analyses of cheese samples included aerobic plate count, coliform, and yeast/mold counts. The color attributes a* and b* were significantly different between the treatment and control groups; however, no significant difference was observed in L* value and pH. Significant differences among 1, 3, and 6 mg lutein-enriched cheeses were observed in the aerobic plate count and yeast/mold compared with the control. Cheese samples contained no detectable levels of coliforms (< 10 cfu/g). The HPLC data showed quantitative recovery of lutein during the storage period, and no lutein degradation products were identified. These results indicate that lutein, a functional additive with purported ability to prevent or reduce the onset of AMD, can be incorporated into cheese adding value to this product.

J Dairy Sci. 2005 May; 88(5):1661-70

AMOUNT OF FAT IN THE DIET AFFECTS BIOAVAILABILITY OF LUTEIN ESTERS BUT NOT OF ALPHA-CAROTENE, BETA-CAROTENE, AND VITAMIN E IN HUMANS.

BACKGROUND: Fat-soluble vitamin E and carotenoids are regarded as being protective against chronic diseases. Little is known about the effect of dietary fat on the bioavailability of these compounds. **OBJECTIVE:** The objective of this study was to assess the effect of the amount of dietary fat on plasma concentrations of vitamin E and carotenoids after supplementation with these

compounds. DESIGN: During two 7-d periods, 4 groups of 14-15 volunteers received daily, with a low-fat hot meal, 1 of 4 different supplements: vitamin E (50 mg), alpha- plus beta-carotene (8 mg), lutein esters (8 mg lutein), or placebo. The supplements were provided in a low- or high-fat spread supplied in random sequence during either of the 2 experimental periods. RESULTS: As anticipated, plasma concentrations of vitamin E, alpha- and beta-carotene, and lutein were significantly higher in the supplemented groups than in the placebo group. The amount of dietary fat consumed with the hot meal (3 or 36 g) did not affect the increases in plasma concentrations of vitamin E (20% increase with the low-fat spread and 23% increase with the high-fat spread) or alpha- and beta-carotene (315% and 139% with the low-fat spread and 226% and 108% with the high-fat spread). The plasma lutein response was higher when lutein esters were consumed with the high-fat spread (207% increase) than with the low-fat spread (88% increase). CONCLUSION: Optimal uptake of vitamin E and alpha- and beta-carotene requires a limited amount of fat whereas the amount of fat required for optimal intestinal uptake of lutein esters is higher.

Am J Clin Nutr. 2000 May;71(5):1187-93

MODULATION OF MULTIDRUG RESISTANCE AND APOPTOSIS OF CANCER CELLS BY SELECTED CAROTENOIDS.

The multidrug resistance (MDR) proteins that belong to the ATP-binding cassette superfamily are present in a majority of human tumors and are an important final cause of therapeutic failure. Therefore, compounds which inhibit the function of the MDR-efflux proteins may improve the cytotoxic action of anticancer chemotherapy. The effects of carotenoids were studied on the activity of the MDR-1 gene-encoded efflux pump system. The carotenoids, isolated from paprika and other vegetables, were tested on the rhodamine 123 accumulation of human MDR-1 gene-transfected L1210 mouse lymphoma cells and human breast cancer cells MDA-MB-231 (HTB-26). Capsanthin and capsorubin enhanced the rhodamine 123 accumulation 30-fold relative to nontreated lymphoma cells. Lycopene, lutein, antheraxanthin and violaxanthin had moderate effects, while alfa- and beta-carotene had no effect on the reversal of MDR in the tumor cells. Apoptosis was induced in human MDR1 transfected mouse lymphoma cells and human breast cancer MDA-MB-231 (HTB-26) cell lines in the presence of lycopene, zeaxanthin and capsanthin. The data suggest the potential of carotenoids as possible resistance modifiers in cancer chemotherapy.

In Vivo. 2004 Mar-Apr;18(2):237-44

CORRELATES OF SERUM LUTEIN + ZEAXANTHIN: FINDINGS FROM THE THIRD NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY.

The determinants of blood levels of carotenoids were previously investigated in small or select samples. The relations of serum lutein + zeaxanthin to possible diet, lifestyle, and physiological determinants in 7059 participants of the Third National Health and Nutrition Examination Survey (1988-1994), > or = 40 y old, were examined. In a fully adjusted, multiple linear regression model, lower serum lutein + zeaxanthin was significantly associated with smoking, heavy drinking, being white, female, or not being physically active, having lower dietary lutein + zeaxanthin, higher fat-free mass, a higher percentage of fat mass, a higher waist-hip ratio, lower serum cholesterol, a higher white blood cell count, and high levels of C-reactive protein (P < 0.05). The model explained 24% of the variation present in serum lutein + zeaxanthin for the current sample. The correlation between dietary and serum lutein + zeaxanthin was 0.17 and increased to 0.18 after adjusting for the effects of given covariates. Each 10% increase in dietary lutein + zeaxanthin was associated with a 1% increase in serum conditional on other terms in the model. Many factors that influence the level of serum lutein + zeaxanthin remain unknown.

J Nutr. 2004 Sep;134(9):2387-94

ABSTRACTS

Flaxseed

HIGH ALPHA-LINOLENIC ACID FLAXSEED (LINUM USITATISSIMUM): SOME NUTRITIONAL PROPERTIES IN HUMANS.

Although high alpha-linolenic acid flaxseed (*Linum usitatissimum*) is one of the richest dietary sources of alpha-linolenic acid and is also a good source of soluble fibre mucilage, it is relatively unstudied in human nutrition. Healthy female volunteers consumed 50 g ground, raw flaxseed/d for 4 weeks which provided 12-13% of energy intake (24-25 g/100 g total fat). Flaxseed raised alpha-linolenic acid and long-chain n-3 fatty acids in both plasma and erythrocyte lipids, as well as raising urinary thiocyanate excretion 2.2-fold. Flaxseed also lowered serum total cholesterol by 9% and low-density-lipoprotein-cholesterol by 18%. Changes in plasma alpha-linolenic acid were equivalent when 12 g alpha-linolenic acid/d was provided as raw flaxseed flour (50 g/d) or flaxseed oil (20 g/d) suggesting high bioavailability of alpha-linolenic acid from ground flaxseed. Test meals containing 50 g carbohydrate from flaxseed or 25 g flaxseed mucilage each significantly decreased postprandial blood glucose responses by 27%. Malondialdehyde levels in muffins containing 15 g flaxseed oil or flour/kg were similar to those in wheat-flour muffins. Cyanogenic glycosides (linamarin, linustatin, neolinustatin) were highest in extracted flaxseed mucilage but were not detected in baked muffins containing 150 g flaxseed/kg. We conclude that up to 50 g high-alpha-linolenic acid flaxseed/d is palatable, safe and may be nutritionally beneficial in humans by raising n-3 fatty acids in plasma and erythrocytes and by decreasing postprandial glucose responses.

Br J Nutr. 1993 Mar;69(2):443-53

DIETARY FIBRE: MORE THAN A MATTER OF DIETETICS. II. PREVENTATIVE AND THERAPEUTIC USES.

A nutrition rich in fibre has a preventive effect against constipation, colon diverticulosis, carcinoma of the large bowel and stomach, type 2-diabetes, metabolic syndrome and cardiovascular disease. In case of constipation, diverticulosis and diabetes this effect solely depends on dietary fibre. Regarding carcinomas and cardiovascular diseases, so far unknown factors integrated in or associated with fibre-rich food may also contribute to the preventive effect. Therapy with dietary fibre is indicated for constipation, colon diverticulosis, diarrhea, diabetes, and hypercholesterinemia. The individual dietary fibres differ substance-specifically. Food-integrated dietary fibre such as whole-grain bread, vegetables and fruit have their place in prevention. Dietary fibre preparations such as wheat bran, flax seed or sugar-beet fibre are useful in the treatment of constipation, colon diverticulosis and adiposity. Oat bran is preferentially used in hypercholesterinemia. Purified dietary fibres such as cellulose, guar, psyllium, and beta-glucan have an anti-diabetic, all viscous fibres an anti-lipaemic effect. The therapeutic dosages of dietary fibre preparations are 20-40 g/day and of purified fibres substances 10-20 g/day respectively.

Wien Klin Wochenschr.2004 Aug 31;116(15-16):511-22

DIETARY LIGNAN INTAKES AND RISK OF PRE- AND POSTMENOPAUSAL BREAST CANCER.

Lignans are plant compounds metabolized in the mammalian gut to produce the phytoestrogens enterolactone and enterodiol. Because estrogens have been linked to breast cancer etiology, lignans could affect breast cancer risk through modulation of endogenous estrogen metabolism or competitive inhibition with estrogen receptors. We examined breast cancer risk and dietary lignan intake in a population-based case-control study of 1,122 women with primary, incident, histologically confirmed breast cancer and 2,036 controls frequency matched to cases on age and county of residence as part of the Western New York Exposures and Breast Cancer (WEB) Study. Diet was assessed with a self-administered 104-item food frequency questionnaire and other relevant data were collected by detailed in-person interviews. Lignans were expressed as the sum of the dietary precursors secoisolariciresinol and matairesinol. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated by unconditional logistic regression, adjusting for age, total energy and other breast cancer risk factors. Premenopausal women in the highest quartile of dietary lignan intake had reduced breast cancer risk (OR = 0.66; 95% CI = 0.44-0.98). No association was observed between lignan intakes and postmenopausal breast cancer. Our results suggest that dietary lignans may be important in the etiology of breast cancer, particularly among premenopausal women.

Int J Cancer. 2004 Sep 1;111(3):440-3

FLAXSEED INHIBITS METASTASIS AND DECREASES EXTRACELLULAR VASCULAR ENDOTHELIAL GROWTH FACTOR IN HUMAN BREAST CANCER XENOGRAPTS.

Angiogenesis is important in tumor growth, progression and metastatic dissemination. Vascular endothelial growth factor (VEGF) is one key factor in promotion of breast cancer angiogenesis. VEGFs are bioactive in the extracellular space where they become available to the endothelial cells. Phytoestrogens such as lignans have been shown to alter breast cancer incidence and be cancer-protective in rats. We show that supplementation of 10% flaxseed, the richest source of mammalian lignans, to nude mice with established human breast tumors reduced tumor growth and metastasis. Moreover, flaxseed decreased extracellular levels of VEGF, which may be one mechanistic explanation to the decreased tumor growth and metastasis.

Cancer Lett. 2002 Nov 8;185(1):31-7

ESSENTIAL FATTY ACIDS, DHA AND HUMAN BRAIN.

Essential fatty acids cannot be synthesized in the body but they are required for maintenance of optimal health. There are two classes of polyunsaturated fatty acids (PUFAs)—omega-6 and omega-3. The parent omega-6 fatty acid, linoleic acid (LA) is desaturated in the body to form arachidonic acid while parent omega-3 fatty acid alpha-linolenic acid (ALA) is desaturated by microsomal enzyme system through a series of metabolic steps to form eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). But there is a limited metabolic capability during early life to metabolize PUFAs to more active long-chain fatty acids. There is a critical role of EFAs and their metabolic products for maintenance of structural and functional integrity of central nervous system and retina. Most of the brain growth is completed by 5-6 years of age. At birth brain weight is 70% of an adult, 15% brain growth occurs during infancy and remaining brain growth is completed during preschool years. DHA is the predominant structural fatty acid in the central nervous system and retina and its availability is crucial for brain development. It is recommended that the pregnant and nursing woman should take at least 2.6 g of omega-3 fatty acids and 100-300 mg of DHA daily to look after the needs of her fetus and suckling infant. The follow-up studies have shown that infants of mothers supplemented with EFAs and DHA had higher mental processing scores, psychomotor development, eye-hand coordination and stereo acuity at 4 years of age. Intake of EFAs and DHA during preschool years may also have a beneficial role in the prevention of attention deficit hyperactivity disorder (ADHD) and enhancing learning capability and academic performance.

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THE EFFECT OF ESTROGENS AND PHYTOESTROGENIC LIGNANS ON MACROPHAGE UPTAKE OF ATHEROGENIC LIPOPROTEINS.

The present study examined the effect of estrogens and compounds with estrogenic activity on the uptake of atherogenic lipoproteins into macrophages, thought to be the initiating step in the development of atherosclerotic lesions. Isolated low density lipoprotein (LDL) and lipoprotein(a) (Lp(a)) were radiolabelled with (3)H-cholesterol linoleate, and incubated with J774 macrophages for 24 hours in the presence of pharmacological doses of estrogens and phytoestrogens. At a concentration of 0.1 microM, the estrogen 17beta-estradiol significantly reduced LDL uptake by macrophages by 14% ($p < 0.05$), but estrone did not have any effect. At 10 microM, both estrogens significantly reduced macrophage LDL uptake, but the phyto-estrogenic-lignans enterodiol and enterolactone had no effect on LDL uptake. Lp(a) uptake into cells was significantly reduced by both estrone and estradiol, and by enterolactone and enterodiol at concentrations of 10 microM ($p < 0.01$), with enterodiol being most effective. The results of this study suggest that the uptake of these structurally similar lipoproteins is regulated differently. Macrophage Lp(a) uptake appears more phytoestrogen sensitive than does LDL uptake.

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