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Journal ABSTRACTS

Weight Loss

EMOTIONAL INFLUENCES ON FOOD CHOICE: SENSORY, PHYSIOLOGICAL AND PSYCHOLOGICAL PATHWAYS.

Sensory, physiological and psychological mechanisms are reviewed that underlie emotional influences on food choice. Both moods and emotions are considered. Eating a meal will reliably alter mood and emotional predisposition, typically reducing arousal and irritability, and increasing calmness and positive affect. However, this depends on the meal size and composition being close to the eater's habit, expectations and needs. Unusual meals—e.g. too small, unhealthy—may negatively affect mood. Sweetness, and sensory cues to high energy density, such as fatty texture, can improve mood and mitigate effects of stress via brain opioidergic and dopaminergic neurotransmission. However, adaptation in these pathways, perhaps enhanced by inherited sensitivity, with chronic exposure to such sensory qualities, could lead to overeating of energy-dense foods and consequent obesity. Sweet, fatty foods low in protein may also provide alleviation from stress in vulnerable people via enhanced function of the serotonergic system. Moreover, in rats, such foods seem to act as part of a feedback loop, via release of glucocorticoid hormones and insulin, to restrain activity of the hypothalamic pituitary adrenal axis during stress. However, this effect is also associated with abdominal obesity. In humans, a number of psychological characteristics predict the tendency to choose such foods when stressed, such as restrained or emotional eating, neuroticism, depression and premenstrual dysphoria, all of which could indicate neurophysiological sensitivity to reinforcing effects of such foods. Greater understanding of such predictive traits and the underlying mechanisms could lead to tailoring of diet to meet personal emotional needs.

Physiol Behav. 2006 Aug 30;89(1):53-61

KEYNOTE REVIEW: PHOSPHODIESTERASE-4 AS A THERAPEUTIC TARGET.

Cyclic AMP (cAMP) is a key second messenger in all cells. It is compartmentalized within cells and its levels are controlled, as a result of spatially discrete signaling cassettes controlling its generation, detection and degradation. Underpinning compartmentalized cAMP signaling are approximately 20 members of the phosphodiesterase-4 (PDE4) family. The selective inhibition of this family generates profound, functional effects and PDE4 inhibitors are currently under development to provide potential, novel therapeutics for the treatment of inflammatory diseases, such as asthma, chronic obstructive pulmonary disease and psoriasis, as well as treating depression and serving as cognitive enhancers. Here, we delineate the range of PDE4 isoforms, their role in signaling, their structural biology and related preclinical and clinical pharmacology.

Drug Discov Today. 2005 Nov 15;10(22):1503-19

EVALUATION OF INTERACTIONS BETWEEN CCK AND GLP-1 IN THEIR EFFECTS ON APPETITE, ENERGY INTAKE, AND ANTRYPYLORODUODENAL MOTILITY IN HEALTHY MEN.

There is evidence that CCK and glucagon-like peptide-1 (GLP-1) mediate the effects of nutrients on appetite and gastrointestinal function and that their interaction may be synergistic. We hypothesized that intravenous CCK-8 and GLP-1 would have synergistic effects on appetite, energy intake, and antropyloroduodenal (APD) motility. Nine healthy males (age 22 +/- 1 yr) were studied on four separate days in a double-blind, randomized fashion. Appetite and APD pressures were measured during 150-min intravenous infusions of 1) isotonic saline (control), 2) CCK-8 (1.8 pmol.kg(-1).min(-1)), 3) GLP-1 (0.9 pmol.kg(-1).min(-1)), or 4) both CCK-8 (1.8 pmol.kg(-1).min(-1)) and GLP-1 (0.9 pmol.kg(-1).min(-1)). At 120 min, energy intake at a buffet meal was quantified. CCK-8, but not GLP-1, increased fullness, decreased desire to eat and subsequent energy intake, and increased the number and amplitude of isolated pyloric pressure waves and basal pyloric pressure ($P < 0.05$). Both CCK-8 and GLP-1 decreased the number of antral and duodenal pressure waves (PWs) ($P < 0.05$), and CCK-8+GLP-1 decreased the number of duodenal PWs more than either CCK-8 or GLP-1 alone ($P < 0.02$). This was not the case for appetite or isolated pyloric PWs. In conclusion, at the doses evaluated, exogenously administered CCK-8 and GLP-1 had discrepant effects on appetite, energy intake, and APD pressures, and the effects of CCK-8+GLP-1, in combination, did not exceed the sum of the effects of CCK-8 and GLP-1, providing no evidence of synergism.

Am J Physiol Regul Integr Comp Physiol. 2005 Jun;288(6):R1477-85

INTERACTION BETWEEN GLP-1 AND CCK-33 IN INHIBITING FOOD INTAKE AND APPETITE IN MEN.

Glucagon-like peptide-1 (GLP-1) and CCK-33 were intravenously infused alone or in combination into normal weight men for 60 min before they were served a lunch of ham sandwiches, chocolate mousse, and orange juice. Infusion of GLP-1 (dose: $0.9 \text{ pmol} \times \text{kg}(-1) \times \text{min}(-1)$) or CCK-33 (dose: $0.2 \text{ pmol} \times \text{kg}(-1) \times \text{min}(-1)$) each reduced calorie intake of the test meal. However, simultaneous infusion of these peptide doses reduced calorie intake less than the sum of the peptides' individual effects. Infusions of the same doses of GLP-1 plus CCK-33 had neither individual nor interactive effects on meal size or calorie consumption. The combination of GLP-1 plus CCK-33 induced, however, a significant reduction in hunger feelings in the premeal period ($P = 0.036$ vs. all other treatments). In summary, intravenous infusion of near physiological doses of CCK-33 and GLP-1 produced specific inhibitions of hunger feeling in men; the simultaneous infusion resulted in an infra-additive reduction in calorie consumption, rejecting thereby the hypothesis that the two peptides exert a positive synergistic effect on food intake compared with the effects observed with infusion of individual peptides. In conclusion, CCK and GLP-1 are meal-related satiety signals that are released from the gastrointestinal tract during food intake.

Am J Physiol Regul Integr Comp Physiol. 2004 Sep;287(3):R562-7

GLUCAGON-LIKE PEPTIDE-1 IN THE PATHOGENESIS OF OBESITY.

The recently discovered gut peptide glucagon-like peptide-1 (GLP-1) is one of many peptides implicated in the short-term regulation of appetite. GLP-1 is a 30-amino-acid peptide that is produced in and secreted from the L cells of the intestinal mucosa after intake of a mixed meal. The amino acid sequence of GLP-1 is highly conserved and all mammals studied to date have identical GLP-1 sequences. GLP-1 receptors have been found in the lung and stomach, and binding of GLP-1 to skeletal muscle and fat cells has been demonstrated. At physiological plasma levels GLP-1 inhibits meal- and pentagastrin-induced gastric acid secretion. In addition, gastric emptying is delayed. Plasma GLP-1 is acutely elevated in normal-weight subjects after a meal, but obese subjects seem to have an attenuated GLP-1 release in response to meals. Consequently, GLP-1 may be a candidate for meal termination and intermeal satiety by either peripheral or central pathways. In terms of the importance of GLP-1 in the pathogenesis of obesity, research points in the direction of a vicious circle where overfeeding results in a down-regulation of postprandial GLP-1 release, which may result in the consumption of a larger amount of calories to elicit a "normal" GLP-1 satiety signal, thus perpetuating the obese state.

Drug News Perspect. 1998 Mar;11(2):92-7

ICE-CREAM CONSUMPTION, TENDENCY TOWARD OVEREATING, AND PERSONALITY.

OBJECTIVE: The exploration of the mechanisms underlying the tendency toward overeating by investigating the Dutch Eating Behavior Questionnaire (DEBQ)/Revised Eating Disorders Inventory (EDI-R) disinhibition, in sequence to the milkshake-ice cream study (van Strien, Cleven, and Schippers, in press). **METHOD:** In hierarchical multiple regression analyses, the relative predictive power for ice-cream consumption was assessed, that is, emotional versus external versus bulimic eating using scales of the DEBQ and the EDI-R. In nonplanned stepwise multiple regression analyses, the association was assessed between these three types of eating behaviors and non-eating-related EDI-R scales. **RESULTS:** Emotional eating was the most important variable for ice-cream consumption. External eating was borderline significant and bulimic eating nonsignificant when emotional and external eating had been partialled out. Emotional eating was best predicted by the EDI-R scales Asceticism, Interoceptive Awareness, and Social Insecurity. **DISCUSSION:** Results are consistent with psychosomatic theory, which focuses on emotional eating as the result of confusion and apprehension in recognizing and accurately responding to emotional and visceral states related to hunger and satiety.

Int J Eat Disord. 2000 Dec;28(4):460-4

THE ROLE OF CONJUGATED LINOLEIC ACID IN REDUCING BODY FAT AND PREVENTING HOLIDAY WEIGHT GAIN.

Objective: The incidence of obesity and overweight in the US has increased considerably during the past two decades and currently affects 65% of the adult population. Research has indicated that small, yet irreversible, gains during the holiday season contribute to increases in weight during adulthood. Conjugated linoleic acid (CLA), a naturally occurring dietary fatty acid, has been found to reduce weight gain and dramatically decrease fat mass in animals. Although research in humans has shown inconsistent results, most studies have been of insufficient duration or have utilized body composition methods that are less accurate than the currently accepted criterion. **Design:** Randomized, double-blind, placebo-controlled study of 3.2 g/day CLA for 6 months. **Subjects:** Forty healthy, overweight subjects (age: 18-44 years; body mass index: 25-30 kg/m²). **Measurements:** Body composition by the four-compartment model, resting metabolic rate (RMR) by indirect calorimetry, self-reported physical activity and dietary intake, and blood chemistries were determined at baseline and after 6 months. Body weight was measured monthly during the pre-holiday season (August-October), holiday season (November-December) and post-holiday season (January-

March). Adverse events were assessed monthly. Results: Compared to CLA, the placebo group showed a greater rate of weight gain during the holiday season ($P=0.01$). Within the placebo group, holiday weight change was significantly greater compared to the pre-holiday period (August-October) ($P=0.03$). Six-month change in body composition was improved with CLA compared to placebo ($P=0.02$), and body fat was significantly reduced within the CLA group (-1.0 ± 2.2 kg, $P=0.05$). CLA had no effect on RMR, physical activity or dietary intake. The rate of reported negative emotions decreased significantly with CLA, although there was no difference in any other category of adverse event. In comparison to the placebo, CLA did not affect insulin resistance, blood lipids and markers of liver function or markers of inflammation, with the exception of a significant decrease in a biomarker of endothelial dysfunction. Conclusion: CLA supplementation among overweight adults significantly reduced body fat over 6 months and prevented weight gain during the holiday season. Although no adverse effects were seen, additional studies should evaluate the effect of prolonged use of CLA.

Int J Obes (Lond). 2006 Aug 22

THE TRANS-10,CIS-12 ISOMER OF CONJUGATED LINOLEIC ACID DOWNREGULATES STEAROYL-COA DESATURASE 1 GENE EXPRESSION IN 3T3-L1 ADIPOCYTES.

Conjugated linoleic acids (CLA) are a group of positional and geometric conjugated dienoic isomers of linoleic acid. The objective of this study was to determine the effects of the cis-9,trans-11 and trans-10,cis-12 isomers of conjugated linoleic acid on lipid composition and gene expression during the differentiation of mouse 3T3-L1 preadipocytes. Treatment of differentiating 3T3-L1 preadipocytes with trans-10,cis-12 conjugated linoleic acid (CLA) resulted in a dose-dependent decrease in the expression of the stearoyl-CoA desaturase 1 gene (SCD1). The expression of other adipocyte genes such as adipose P2 (aP2), fatty acid synthase (FAS), SCD2 and the key adipogenic transcription factors, peroxisome proliferator-activated receptor gamma2 (PPARgamma2) and CCAAT enhancer binding protein alpha (C/EBPalpha), remained elevated. Cells treated with trans-10,cis-12 CLA exhibited smaller lipid droplets, with reduced levels of the major monounsaturated fatty acids, palmitoleate and oleate. By contrast, the cis-9,trans-11 isomer did not alter adipocyte gene expression. Repression of the stearoyl-CoA desaturase gene expression in adipocytes by the trans-10,cis-12 isomer may contribute to the mechanisms by which CLA reduces body fat in mice.

J Nutr. 2000 Aug;130(8):1920-4

EFFECT OF CONJUGATED LINOLEIC ACID SUPPLEMENTATION AFTER WEIGHT LOSS ON APPETITE AND FOOD INTAKE IN OVERWEIGHT SUBJECTS.

OBJECTIVE: To study the effects of 13 weeks conjugated linoleic acid (CLA) supplementation in overweight subjects on body-weight maintenance, parameters of appetite and energy intake (EI) at breakfast after weight loss. **DESIGN:** This study had a double-blind, placebo-controlled randomized design. **SUBJECTS:** A total of 26 men and 28 women (age 37.8 ± 7.7 y; body mass index 27.8 ± 1.5 kg/m²). **INTERVENTIONS:** Subjects were first submitted to a very-low-calorie diet (VLCD; 2.1 MJ/day) for 3 weeks after which they started with the 13-week intervention period. They either received 1.8 g CLA or placebo per day or 3.6 g CLA or placebo per day. Additionally, subjects of the high dosage intervention replaced their habitual lunch by one meal of a protein-rich, low-energy supplement. EI was measured at breakfast and appetite profile after an overnight fast. **RESULTS:** The mean body weight loss was $6.9\pm 1.7\%$ of their original body weight. Multiple regression analysis showed that at the end of the 13-week intervention, CLA did not have an effect on body weight regain. Feelings of fullness and satiety were increased and feelings of hunger were decreased after 13 weeks intervention by CLA compared to placebo, independent of %body weight regain. However, EI measured at breakfast was not affected by CLA. **CONCLUSION:** Appetite (hunger, satiety and fullness) was favorably, dose-independently affected by a 13-week consumption of 1.8 or 3.6 g CLA/day. This did not result in a lower EI at breakfast or an improved body-weight maintenance after weight loss.

Eur J Clin Nutr. 2003 Oct;57(10):1268-74

GREEN TEA AND THERMOGENESIS: INTERACTIONS BETWEEN CATECHIN-POLYPHENOLS, CAFFEINE AND SYMPATHETIC ACTIVITY.

The thermogenic effect of tea is generally attributed to its caffeine content. We report here that a green tea extract stimulates brown adipose tissue thermogenesis to an extent which is much greater than can be attributed to its caffeine content per se, and that its thermogenic properties could reside primarily in an interaction between its high content in catechin-polyphenols and caffeine with sympathetically released noradrenaline (NA). Since catechin-polyphenols are known to be capable of inhibiting catechol-O-methyl-transferase (the enzyme that degrades NA), and caffeine to inhibit transcellular phosphodiesterases (enzymes that break down NA-induced cAMP), it is proposed that the green tea extract, via its catechin-polyphenols and caffeine, is effective in stimulating thermogenesis by relieving inhibition at different control points along the NA-cAMP axis. Such a synergistic interaction between catechin-polyphenols and caffeine to augment and prolong sympathetic stimulation of thermogenesis could be of value in assisting the management of obesity.

Int J Obes Relat Metab Disord. 2000 Feb;24(2):252-8

GREEN TEA EXTRACT THERMOGENESIS-INDUCED WEIGHT LOSS BY EPIGALLOCATECHIN GALLATE INHIBITION OF CATECHOL-O-METHYLTRANSFERASE.

Epidemiological studies have shown that intake of tea catechins is associated with a lower risk of cardiovascular disease. The antioxidative activity of tea-derived catechins has been extensively studied. Reports have shown that green tea extract intake is associated with increased weight loss due to diet-induced thermogenesis, which is generally attributed to the catechin epigallocatechin gallate. That catechin-polyphenols are known to be capable of inhibiting catechol-O-methyltransferase (the enzyme that degrades norepinephrine) is a possible explanation for why the green tea extract is effective in stimulating thermogenesis by epigallocatechin gallate to augment and prolong sympathetic stimulation of thermogenesis. Knowledge about thermogenesis-induced weight loss produced by green tea's epigallocatechin gallate and its ability to inhibit catechol-O-methyltransferase is important for health benefits and for prolonging the action of norepinephrine in the synaptic cleft.

J Med Food. 2006 Winter;9(4):451-8

EFFECTS ON BLOOD PRESSURE OF DRINKING GREEN AND BLACK TEA.

BACKGROUND: The flavonoid components of tea have been associated in epidemiological studies with a decreased risk of cardiovascular disease. Flavonoids have been shown to have antioxidant and vasodilator effects in vitro; we therefore postulated that drinking green or black tea attenuates the well-characterized acute pressor response to caffeine and lowers blood pressure during regular consumption. **OBJECTIVE:** To determine whether green and black tea can attenuate the transient pressor effect of caffeine, or lower blood pressure during regular consumption. **METHODS:** In the first study, the acute effects of four hot drinks - green tea and black tea (at a dose equivalent to four standard cups), water matched to the teas for caffeine content ('caffeine') and water - were assessed in 20 normotensive men using a Latin-Square designed study. Clinic blood pressure was measured before and 30 and 60 min after each drink had been ingested. In the second study, the effects on blood pressure of regular green and black tea ingestion were examined in 13 subjects with high-normal systolic blood pressure and mild systolic hypertension (systolic blood pressure in the range 130-150 mmHg) using a three-period crossover study. Five cups per day of green tea, black tea and caffeine (in hot water and matched to the teas) were consumed for 7 days each, in random order. Twenty-four hour ambulatory blood pressure was measured at the end of each seven-day intervention. Results are presented as means and 95% confidence intervals (CI). **RESULTS:** An acute pressor response to caffeine was observed. Relative to caffeine, there were further acute increases in systolic and diastolic blood pressure at 30 min among those drinking green tea [5.5 mmHg (95%CI -1.4 to 12.4) and 3.1 mmHg (95%CI -0.1 to 6.3), respectively] and black tea [10.7 mmHg (95%CI 4.0 to 17.4) and 5.1 mmHg (95%CI 1.8 to 8.4), respectively]. The changes in blood pressure at 60 min were not significant. The effect on 24-h ambulatory systolic and diastolic blood pressure of regular drinking of green tea [increases of 1.7 mmHg (95%CI -1.6 to 5.0) and 0.9 mmHg (95%CI -1.3 to 3.1), respectively] or black tea [increase of 0.7 mmHg (95%CI -2.6 to 4.0) and decrease of 0.7 mmHg (95%CI -2.9 to 1.5), respectively] was not significant relative to caffeine. **CONCLUSIONS:** Contrary to our initial hypothesis, tea ingestion caused larger acute increases in blood pressure than caffeine alone. However, any acute effects of tea on blood pressure did not translate into significant alterations in ambulatory blood pressure during regular tea consumption.

GREEN TEA EXTRACT IMPROVES RUNNING ENDURANCE IN MICE BY STIMULATING LIPID UTILIZATION DURING EXERCISE.

A series of polyphenols known as catechins are abundant in green tea, which is consumed mainly in Asian countries. The effects of catechin-rich green tea extract (GTE) on running endurance and energy metabolism during exercise in BALB/c mice were investigated. Mice were divided into four groups: nonexercise control, exercise control (Ex-cont), exercise+0.2% GTE, and exercise+0.5% GTE groups. Treadmill running time to exhaustion, plasma biochemical parameters, skeletal muscle glycogen content, beta-oxidation activity, and malonyl-CoA content immediately after exercise were measured at 8-10 wk after the initiation of the experiment. Oxygen consumption and respiratory exchange ratio were measured using indirect calorimetry. Running times to exhaustion in mice fed 0.5% GTE were 30% higher than in Ex-cont mice and were accompanied by a lower respiratory exchange ratio, higher muscle beta-oxidation activity, and lower malonyl-CoA content. In addition, muscle glycogen content was high in the GTE group compared with the Ex-cont group. Plasma lactate concentrations in mice fed GTE were significantly lower after exercise, concomitant with an increase in free fatty acid concentrations. Catechins, which are the main constituents of GTE, did not show significant effects on peroxisome proliferator-activated receptor-alpha or delta-dependent luciferase activities. These results suggest that the endurance-improving effects of GTE were mediated, at least partly, by increased metabolic capacity and utilization of fatty acid as a source of energy in skeletal muscle during exercise.

Am J Physiol Regul Integr Comp Physiol. 2006 Jun;290(6):R1550-6

STRUCTURE-ACTIVITY RELATIONSHIPS OF TEA COMPOUNDS AGAINST HUMAN CANCER CELLS.

The content of the biologically active amino acid theanine in 15 commercial black, green, specialty, and herbal tea leaves was determined as the 2,4-dinitrophenyltheanine derivative (DNP-theanine) by a validated HPLC method. To define relative anticarcinogenic potencies of tea compounds and teas, nine green tea catechins, three black tea theaflavins, and theanine as well as aqueous and 80% ethanol/water extracts of the same tea leaves were evaluated for their ability to induce cell death in human cancer and normal cells using a tetrazolium microculture (MTT) assay. Compared to untreated controls, most catechins, theaflavins, theanine, and all tea extracts reduced the numbers of the following human cancer cell lines: breast (MCF-7), colon (HT-29), hepatoma (liver) (HepG2), and prostate (PC-3) as well as normal human liver cells (Chang). The growth of normal human lung (HEL299) cells was not inhibited. The destruction of cancer cells was also observed visually by reverse phase microscopy. Statistical analysis of the data showed that (a) the anticarcinogenic effects of tea compounds and of tea leaf extracts varied widely and were concentration dependent over the ranges from 50 to 400 mug/mL of tea compound and from 50 to 400 mug/g of tea solids; (b) the different cancer cells varied in their susceptibilities to destruction; (c) 80% ethanol/water extracts with higher levels of flavonoids determined by HPLC were in most cases more active than the corresponding water extracts; and (d) flavonoid levels of the teas did not directly correlate with anticarcinogenic activities. The findings extend related observations on the anticarcinogenic potential of tea ingredients and suggest that consumers may benefit more by drinking both green and black teas. Keywords: HPLC; theanine; catechins; theaflavins; teas; cancer cells; growth inhibition; structure-activity relationships; dietary significance.

J Agric Food Chem. 2007 Jan 24;55(2):243-253

INTRACELLULAR SIGNALING NETWORK AS A PRIME CHEMOPREVENTIVE TARGET OF (-)-EPIGALLOCATECHIN GALLATE.

Chemoprevention is an attempt to use either naturally occurring or synthetic substances or their mixtures to intervene in the progress of carcinogenesis. Recently, it has been shown that some edible phytochemicals alter gene expression, directly or indirectly, thereby regulating the carcinogenic processes. (-)-Epigallocatechin gallate (EGCG), a principal antioxidant derived from green tea, is one of the most extensively investigated chemopreventive phytochemicals. EGCG has been known to block each stage of carcinogenesis by modulating signal transduction pathways involved in cell proliferation, transformation, inflammation, apoptosis, metastasis and invasion. This review addresses the molecular target-based chemoprevention with EGCG by focusing on the common events mediated by transcription factors, such as NF-kappa B, activator protein-1 and nuclear factor erythroid 2 p45-related factor, and upstream kinases involved in the cellular signaling network.

Mol Nutr Food Res. 2006 Feb;50(2):152-9

GREEN TEA POLYPHENOLS IN THE PREVENTION OF COLON CANCER.

Several plant-based nutrients and non-nutrients that can inhibit mutagenesis and proliferation have been identified. Some of the most promising nutrients identified as chemopreventive agents in colon cancer prevention include isoflavones, curcumin, calcium, vitamin D and more recently Green tea polyphenols (GTP). In addition to inhibiting mutagenesis and proliferation, these compounds are relatively non-toxic, are of low cost and can be taken orally or as a part of the daily diet. Epidemiological and

laboratory studies have identified epigallocatechin gallate (EGCG) in green tea polyphenols (GTP), as the most potent chemopreventive agent that can induce apoptosis, suppress the formation and growth of human cancers including colorectal cancers (CRC). It is only logical then, that future clinical studies should focus on examining the efficacy of phytochemicals such as EGCG in cancer chemoprevention as an alternative to pharmacological agents, especially in populations where administration of COX-2 inhibitors, Aspirin and NSAIDs is contraindicated. The goal of this review is to provide the rationale, and discuss the use of EGCG in GTP as a chemopreventive agent for prevention of colon carcinogenesis and present evidence for the efficacy and safety of these agents based on epidemiological, animal, in vitro studies and Phase I clinical trials.

Front Biosci. 2007 Jan 1;12:2309-15

MECHANISMS OF HYPOLIPIDEMIC AND ANTI-OBESITY EFFECTS OF TEA AND TEA POLYPHENOLS.

Among the health-promoting effects of tea and tea polyphenols, the cancer-chemopreventive effects in various animal model systems have been intensively investigated; meanwhile, the hypolipidemic and antiobesity effects in animals and humans have also become a hot issue for molecular nutrition and food research. It has been demonstrated that the body weights of rats and their plasma triglyceride, cholesterol, and LDL-cholesterol have been significantly reduced by feedings of oolong, black, pu-erh, and green tea leaves to the animals. It has been suggested that the inhibition of growth and suppression of lipogenesis in MCF-7 breast cancer cells may be through down-regulation of fatty acid synthase gene expression in the nucleus and stimulation of cell energy expenditure in the mitochondria. The experimental data indicated that the molecular mechanisms of fatty acid synthase gene suppression by tea polyphenols (EGCG, theaflavins) may invite down-regulation of EGFR/PI3K/Akt/Sp-1 signal transduction pathways.

Mol Nutr Food Res. 2006 Feb;50(2):211-7

GREEN TEA, BLACK TEA AND BREAST CANCER RISK: A META-ANALYSIS OF EPIDEMIOLOGICAL STUDIES.

Experimental studies have shown that tea and tea polyphenols have anti-carcinogenic properties against breast cancer. A number of epidemiologic studies, both case-control and cohort in design, have examined the possible association between tea intake and breast cancer development in humans. This meta-analysis included 13 papers which examined populations in eight countries and provided data on consumption of either green tea or black tea, or both in relation to breast cancer risk. Summary odds ratios (ORs) for highest versus non/lowest tea consumption level were calculated based on fixed and random effects models. Heterogeneity between studies was examined via the Q statistics. For green tea, the combined results from the four studies indicated a reduced risk of breast cancer for highest versus non/lowest intake (OR = 0.78, 95% CI = 0.61-0.98). For black tea, conflicting results were observed in case-control versus cohort studies. The combined results from the eight case-control studies showed a minor inverse association between black tea consumption and risk of breast cancer (OR = 0.91, 95% CI = 0.84-0.98). This inverse association was stronger in hospital-based (OR = 0.77, 95% CI = 0.50-1.19) than population-based case-control studies (OR = 0.94, 95% CI = 0.81-1.09). Five cohort studies demonstrated a modest increase in risk associated with black tea intake (OR = 1.15, 95% CI = 1.02-1.31). The results of this meta-analysis indicate a lower risk for breast cancer with green tea consumption. Available data suggest a possible late-stage, promotional effect of black tea on breast carcinogenesis.

Carcinogenesis. 2006 Jul;27(7):1310-5

THE EFFECTS OF GREEN TEA CONSUMPTION ON INCIDENCE OF BREAST CANCER AND RECURRENCE OF BREAST CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS.

BACKGROUND: Green tea is widely used by women for the prevention and treatment of breast cancer. The authors aimed to determine the efficacy of green tea ingestion on the risk of breast cancer development and the risk of breast cancer recurrence. **METHODS:** The authors conducted a systematic review and meta-analyses of observational studies from systematic searches of 8 electronic data sources and contact with authors. They included studies assessing breast cancer incidence and recurrence. **RESULTS:** Results: The pooled relative risk (RR) of developing breast cancer for the highest levels of green tea consumption in cohort studies was 0.89 (95% confidence interval [CI], 0.71-1.1; P= .28; I(2)= 0%), and in case control studies, the odds ratio was 0.44 (95% CI, 0.14-1.31; P= .14; I(2)= 47%). The pooled RR of cohort studies for breast cancer recurrence in all stages was 0.75 (95% CI, 0.47-1.19; P= .22; I(2)= 37%). A subgroup analysis of recurrence in stage I and II disease showed a pooled RR in cohort studies of 0.56 (95% CI, 0.38-0.83; P= .004; I2= 0%). Dose-response relationships were evident in only 3 of the 7 studies. **CONCLUSION:** To date, the epidemiological data indicates that consumption of 5 or more cups of green tea a day shows a non-statistically significant trend towards the prevention of breast cancer development. Evidence indicates that green tea consumption may possibly help prevent breast cancer recurrence in early stage (I and II) cancers. However, conclusions as to the potential therapeutic application of green tea are currently impossible to make due to the small number of studies conducted, the lack of any clinical trial evidence, the lack of a consistent dose-response relationship, and the potential for interaction with standard care.

BLACK AND GREEN TEAS EQUALLY INHIBIT DIABETIC CATARACTS IN A STREPTOZOTOCIN-INDUCED RAT MODEL OF DIABETES.

Green and black teas were given at 1.25% in the drinking water to streptozotocin-induced diabetic rats for 3 months. Normal and diabetic control groups were also studied. As expected, diabetic animals had significantly increased glucose in lens and plasma. Lens and red blood cell sorbitol were significantly increased as a result of the aldose reductase pathway activation. Plasma and lens lipid thiobarbituric acid-reactive substances and protein glycation were also significantly elevated. Both teas significantly inhibited diabetic cataracts and caused significant reductions in the biochemical pathway implicated in the development of the pathology. After corrections for glucose, it was found that the teas retard the development of diabetic cataracts by a hypoglycemic effect that in turn inhibits the biochemical indicators of pathology. There were significant correlations between glucose, cataract score, and these indicators. Green tea but not black tea caused a significant decline in triglycerides in the diabetic animals. Tea may be a simple, inexpensive means of preventing or retarding human diabetes and the ensuing complications. Tea also should be investigated as an adjunct therapy for diabetes treatment.

J Agric Food Chem. 2005 May 4;53(9):3710-3

A NEW APPROACH TO MANAGING ORAL MANIFESTATIONS OF SJOGREN'S SYNDROME AND SKIN MANIFESTATIONS OF LUPUS.

Sjogren's syndrome (SS) is an autoimmune disorder that affects the salivary glands, leading to xerostomia, and the lacrimal glands, resulting in xerophthalmia. Secondary SS is associated with other autoimmune disorders such as systemic rheumatic diseases and systemic lupus erythematosus (SLE), which can affect multiple organs, including the epidermis. Recent studies have demonstrated that green tea polyphenols (GTPs) possess both anti-inflammatory and anti-apoptotic properties in normal human cells. Epidemiological evidence has indicated that, in comparison to the United States, the incidence of SS, clinical xerostomia and lupus is considerably lower in China and Japan, the two leading green tea-consuming countries. Thus, GTPs might be responsible, in part, for geographical differences in the incidence of xerostomia by reducing the initiation or severity of SS and lupus. Consistent with this, molecular, cellular and animal studies indicate that GTPs could provide protective effects against autoimmune reactions in salivary glands and skin. Therefore, salivary tissues and epidermal keratinocytes could be primary targets for novel therapies using GTPs. This review article evaluates the currently available research data on GTPs, focusing on their potential application in the treatment of the oral manifestations of SS and skin manifestations of SLE.

J Biochem Mol Biol. 2006 May 31;39(3):229-39

PHASE II STUDY OF POMEGRANATE JUICE FOR MEN WITH RISING PROSTATE-SPECIFIC ANTIGEN FOLLOWING SURGERY OR RADIATION FOR PROSTATE CANCER.

PURPOSE: Phytochemicals in plants may have cancer preventive benefits through antioxidation and via gene-nutrient interactions. We sought to determine the effects of pomegranate juice (a major source of antioxidants) consumption on prostate-specific antigen (PSA) progression in men with a rising PSA following primary therapy. **EXPERIMENTAL DESIGN:** A phase II, Simon two-stage clinical trial for men with rising PSA after surgery or radiotherapy was conducted. Eligible patients had a detectable PSA > 0.2 and < 5 ng/mL and Gleason score < or = 7. Patients were treated with 8 ounces of pomegranate juice daily (Wonderful variety, 570 mg total polyphenol gallic acid equivalents) until disease progression. Clinical end points included safety and effect on serum PSA, serum-induced proliferation and apoptosis of LNCaP cells, serum lipid peroxidation, and serum nitric oxide levels. **RESULTS:** The study was fully accrued after efficacy criteria were met. There were no serious adverse events reported and the treatment was well tolerated. Mean PSA doubling time significantly increased with treatment from a mean of 15 months at baseline to 54 months posttreatment ($P < 0.001$). In vitro assays comparing pretreatment and posttreatment patient serum on the growth of LNCaP showed a 12% decrease in cell proliferation and a 17% increase in apoptosis ($P = 0.0048$ and 0.0004 , respectively), a 23% increase in serum nitric oxide ($P = 0.0085$), and significant ($P < 0.02$) reductions in oxidative state and sensitivity to oxidation of serum lipids after versus before pomegranate juice consumption. **CONCLUSIONS:** We report the first clinical trial of pomegranate juice in patients with prostate cancer. The statistically significant prolongation of PSA doubling time, coupled with corresponding laboratory effects on prostate cancer in vitro cell proliferation and apoptosis as well as oxidative stress, warrant further testing in a placebo-controlled study.

Clin Cancer Res. 2006 Jul 1;12(13):4018-26

IN VITRO ANTIPROLIFERATIVE, APOPTOTIC AND ANTIOXIDANT ACTIVITIES OF PUNICALAGIN, ELLAGIC ACID AND A TOTAL POMEGRANATE TANNIN EXTRACT ARE ENHANCED IN COMBINATION WITH OTHER POLYPHENOLS AS FOUND IN POMEGRANATE JUICE.

Pomegranate (*Punica granatum* L.) fruits are widely consumed as juice (PJ). The potent antioxidant and anti-atherosclerotic activities of PJ are attributed to its polyphenols including punicalagin, the major fruit ellagitannin, and ellagic acid (EA). Punicalagin is the major antioxidant polyphenol ingredient in PJ. Punicalagin, EA, a standardized total pomegranate tannin (TPT) extract and PJ were evaluated for in vitro antiproliferative, apoptotic and antioxidant activities. Punicalagin, EA and TPT were evaluated for antiproliferative activity at 12.5-100 microg/ml on human oral (KB, CAL27), colon (HT-29, HCT116, SW480, SW620) and prostate (RWPE-1, 22Rv1) tumor cells. Punicalagin, EA and TPT were evaluated at 100 microg/ml concentrations for apoptotic effects and at 10 microg/ml concentrations for antioxidant properties. However, to evaluate the synergistic and/or additive contributions from other PJ phytochemicals, PJ was tested at concentrations normalized to deliver equivalent amounts of punicalagin (w/w). Apoptotic effects were evaluated against the HT-29 and HCT116 colon cancer cell lines. Antioxidant effects were evaluated using inhibition of lipid peroxidation and Trolox equivalent antioxidant capacity (TEAC) assays. Pomegranate juice showed greatest antiproliferative activity against all cell lines by inhibiting proliferation from 30% to 100%. At 100 microg/ml, PJ, EA, punicalagin and TPT induced apoptosis in HT-29 colon cells. However, in the HCT116 colon cells, EA, punicalagin and TPT but not PJ induced apoptosis. The trend in antioxidant activity was $PJ > TPT > punicalagin > EA$. The superior bioactivity of PJ compared to its purified polyphenols illustrated the multifactorial effects and chemical synergy of the action of multiple compounds compared to single purified active ingredients.

J Nutr Biochem. 2005 Jun;16(6):360-7.

BIOACTIVE COMPOUNDS FROM THE SEEDS OF PUNICA GRANATUM (POMEGRANATE).

Two new compounds, coniferyl 9-O-[beta-D-apiofuranosyl(1-->6)]-O-beta-D-glucopyranoside (1) and sinapyl 9-O-[beta-d-apiofuranosyl(1-->6)]-O-beta-D-glucopyranoside (2), were isolated from the seeds of *Punica granatum* (pomegranate), together with five known compounds, 3,3'-di-O-methylellagic acid (3), 3,3',4'-tri-O-methylellagic acid (4), phenethyl rutinoside, icariside D1, and daucosterol. The structures of 1 and 2 were elucidated by spectroscopic data analysis. Compounds 1-4 exhibited antioxidant activity, which was evaluated by measurement of low-density lipoprotein (LDL) susceptibility to oxidation and by determination in vitro of malondialdehyde (MDA) levels in the rat brain.

PRENEOPLASTIC PROSTATE LESIONS: AN OPPORTUNITY FOR PROSTATE CANCER PREVENTION.

Environmental factors, especially the diet, play a prominent role in the epidemic of prostate cancer (PCA), in the United States. Many candidate dietary components have been proposed to influence human prostatic carcinogenesis, including fat, calories, fruits and vegetables, anti-oxidants, and various micronutrients, but the specific roles dietary agents play in promoting or preventing PCA remain controversial. We have collected evidence to suggest that GSTP1, the gene encoding the pi-class glutathione S-transferase (GST), may serve a "caretaker" function for prostatic cells. Although GSTP1 can be detected in normal prostatic epithelium, in almost all PCA cases, PCA cells fail to express GSTP1 polypeptides, and lack of GSTP1 expression most often appears to be the result of somatic "CpG island" DNA methylation changes. Loss of GSTP1 function also appears to be characteristic of prostatic epithelial neoplasia (PIN) lesions, thought to represent PCA precursors. We have recently learned that a new candidate early PCA precursor lesion, proliferative inflammatory atrophy (PIA), characterized by proliferating prostatic cells juxtaposed to inflammatory cells, contains epithelial cells that express high levels of GSTP1. These findings have formed the basis for a new model of prostatic carcinogenesis, in which prostatic cells in PIA lesions, subjected to a barrage of inflammatory oxidants, induce GSTP1 expression as a defense against oxidative genome damage. When cells with defective GSTP1 genes appear amongst the PIA cells, such cells become vulnerable to oxidants and electrophiles that inflict genome damage that tends to promote neoplastic transformation to PIN and PCA cells. Subsequently, PIN and PCA cells with defective GSTP1 genes remain vulnerable to similar stresses tending to promote malignant progression. This new model for prostatic carcinogenesis has implications for the design of new prostate cancer prevention strategies. Rational prevention approaches might include: (i) restoration of GSTP1 expression via treatment with inhibitors of CpG methylation, (ii) compensation for inadequate GSTP1 activity via treatment with inducers of general GST activity, and (iii) abrogation of genome-damaging stresses via avoidance of exogenous carcinogens and/or reduction of endogenous carcinogenic (particularly oxidant) stresses.

Ann N Y Acad Sci. 2001 Dec;952:135-44

THE ROLE OF INFLAMMATION IN THE PATHOGENESIS OF PROSTATE CANCER.

PURPOSE: A new hypothesis for the etiology of prostate cancer is that chronic or recurrent prostate inflammation may initiate and promote prostate cancer development. **MATERIALS AND METHODS:** We reviewed the current direct and indirect evidence from epidemiology, genetics, molecular biology and histopathology implicating inflammation in the pathogenesis of prostate cancer. **RESULTS:** The case for prostate inflammation as a cause of prostate cancer is compelling. Epidemiology data have correlated prostatitis and sexually transmitted infections with increased prostate cancer risk and intake of anti-inflammatory drugs and antioxidants with decreased prostate cancer risk. Genetic studies have identified RNASEL, encoding an interferon inducible ribonuclease, and MSR1, encoding subunits of the macrophage scavenger receptor, as candidate inherited susceptibility genes for familial prostate cancer. Somatic silencing of GSTP1, encoding a glutathione S-transferase capable of defending against oxidant cell and genome damage, has been found in almost all prostate cancer cases. Proliferative inflammatory atrophy lesions containing activated inflammatory cells and proliferating epithelial cells appear likely to be precursors to prostatic intraepithelial neoplasia lesions and prostatic carcinomas. **CONCLUSIONS:** Emerging hints that prostate inflammation may contribute to prostatic carcinogenesis will provide opportunities for the discovery and development of new drugs and strategies for prostate cancer prevention.

J Urol. 2004 Nov;172(5 Pt 2):S6-11

RANDOMIZED, CONTROLLED CHEMOPREVENTION TRIALS IN POPULATIONS AT VERY HIGH RISK FOR PROSTATE CANCER: ELEVATED PROSTATE-SPECIFIC ANTIGEN AND HIGH-GRADE PROSTATIC INTRAEPITHELIAL NEOPLASIA.

This is a report of research efforts underway at the Arizona Cancer Center. These efforts build upon Larry Clark's unanticipated clinical prevention trial results: those results indicated that 200 microg/day of selenium in selenized yeast decreased prostate cancer risk by almost 60%. The trials underway address various phases of the possible preventive activity of selenium. The first of these, for men who are suspected to have prostate cancer but who have had a biopsy revealing no evidence of cancer, will test the ability of selenium to prevent the development of clinical prostate cancer. The second is for men with high-grade prostatic intraepithelial neoplasia; the trial will test whether selenium will prevent the development of prostatic cancer in this high-risk group. The third trial is for men who have been diagnosed with prostate cancer and are scheduled for prostatectomy: the trial is designed to test whether evidence of selenium-linked changes can be identified in the tissue removed at prostatectomy. The fourth trial is for men who have been diagnosed with prostate cancer but who have chosen neither surgery nor irradiation; this trial will evaluate whether treatment with selenium will inhibit the progress of prostate cancer. Together, these trials will provide important information as to the prostate cancer chemopreventive potential of selenium.

Urology. 2001 Apr;57(4 Suppl 1):185-7

DESIGNING THE SELENIUM AND VITAMIN E CANCER PREVENTION TRIAL (SELECT).

Prostate cancer continues to be a major health threat, especially among African American men. The Selenium and Vitamin E Cancer Prevention Trial (SELECT), which opened on July 25, 2001, was planned to study possible agents for the prevention of prostate cancer in a population of 32,400 men in the United States, including Puerto Rico, and Canada. SELECT is a phase III randomized, placebo-controlled trial of selenium (200 microg/day from L-selenomethionine) and/or vitamin E (400 IU/day of all rac alpha-tocopheryl acetate) supplementation for a minimum of 7 years (maximum of 12 years) in non-African American men at least 55 years of age and African American men at least 50 years of age. SELECT is a large, simple trial that conforms as closely as possible with community standards of care. This commentary discusses the design problems the SELECT investigators had to resolve in developing the trial, including the role of prostate cancer screening, the best forms and doses of the study agents, and estimation of the event (prostate cancer) rate of men on the placebo arm.

J Natl Cancer Inst. 2005 Jan 19;97(2):94-102

CONSUMPTION OF ONE EGG PER DAY INCREASES SERUM LUTEIN AND ZEAXANTHIN CONCENTRATIONS IN OLDER ADULTS WITHOUT ALTERING SERUM LIPID AND LIPOPROTEIN CHOLESTEROL CONCENTRATIONS.

Lutein and zeaxanthin accumulate in the macular pigment of the retina, and are reported to be associated with a reduced incidence of age-related macular degeneration. A rich source of lutein and zeaxanthin in the American diet is the yolk of chicken eggs. Thus, the objective of the study was to investigate the effect of consuming 1 egg/d for 5 wk on the serum concentrations of lutein, zeaxanthin, lipids, and lipoprotein cholesterol in individuals >60 y of age. In a randomized cross-over design, 33 men and women participated in the 18-wk study, which included one run-in and one washout period of no eggs prior to and between two 5-wk interventions of either consuming 1 egg or egg substitute/d. Serum lutein 26% ($P < 0.001$) and zeaxanthin 38% ($P < 0.001$) concentrations increased after 5-wk of 1 egg/d compared with the phase prior to consuming eggs. Serum concentrations of total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides were not affected. These findings indicate that in older adults, 5 wk of consuming 1 egg/d significantly increases serum lutein and zeaxanthin concentrations without elevating serum lipids and lipoprotein cholesterol concentrations.

J Nutr. 2006 Oct;136(10):2519-24

ASSOCIATIONS BETWEEN INTERMEDIATE AGE-RELATED MACULAR DEGENERATION AND LUTEIN AND ZEAXANTHIN IN THE CAROTENOIDS IN AGE-RELATED EYE DISEASE STUDY (CAREDS): ANCILLARY STUDY OF THE WOMEN'S HEALTH INITIATIVE.

OBJECTIVE: To evaluate the relationship between dietary lutein plus zeaxanthin and intermediate age-related macular degeneration (AMD). **DESIGN:** Women aged 50 to 79 years in Iowa, Wisconsin, and Oregon with intake of lutein plus zeaxanthin above the 78th (high) and below the 28th (low) percentiles at baseline in the Women's Health Initiative Observational Study were recruited 4 to 7 years later into the Carotenoids in Age-Related Eye Disease Study (CAREDS), when the presence of AMD was determined by fundus photographs. Logistic regression analyses examined the prevalence of AMD in 1787 CAREDS participants, after accounting for potential covariates. **RESULTS:** The prevalence of intermediate AMD was not statistically different between the high and low lutein plus zeaxanthin intake recruitment groups after adjusting for age (odds ratio, 0.96; 95% confidence interval, 0.75-1.23). Limiting analyses to women younger than 75 years with stable intake of lutein plus zeaxanthin, without a history of chronic diseases that are often associated with diet changes, substantially lowered odds ratios (0.57; 95% confidence interval, 0.34-0.95). Exploratory analyses of advanced AMD in 34 participants resulted in protective, but statistically nonsignificant, associations in the overall sample and in women younger than 75 years. **CONCLUSION:** Diets rich in lutein plus zeaxanthin may protect against intermediate AMD in healthy women younger than 75 years.

Arch Ophthalmol. 2006 Aug;124(8):1151-62

LUTEIN, BUT NOT ALPHA-TOCOPHEROL, SUPPLEMENTATION IMPROVES VISUAL FUNCTION IN PATIENTS WITH AGE-RELATED CATARACTS: A 2-Y DOUBLE-BLIND, PLACEBO-CONTROLLED PILOT STUDY.

OBJECTIVE: We investigated the effect of long-term antioxidant supplementation (lutein and alpha-tocopherol) on serum levels and visual performance in patients with cataracts. **METHODS:** Seventeen patients clinically diagnosed with age-related cataracts were randomized in a double-blind study involving dietary supplementation with lutein (15 mg; $n = 5$), alpha-tocopherol (100 mg; $n = 6$), or placebo ($n = 6$), three times a week for up to 2 y. Serum carotenoid and tocopherol concentrations were determined with quality-controlled high-performance liquid chromatography, and visual performance (visual acuity and glare sensitivity) and biochemical and hematologic indexes were monitored every 3 mo throughout the study. Changes in these parameters were assessed by General Linear Model (GLM) repeated measures analysis. **RESULTS:** Serum concentrations of lutein and alpha-tocopherol increased with supplementation, although statistical significance was reached only in the lutein group. Visual performance (visual acuity and glare sensitivity) improved in the lutein group, whereas there was a trend toward the maintenance of and decrease in visual acuity with alpha-tocopherol and placebo supplementation, respectively. No significant side effects or changes in biochemical or hematologic profiles were observed in any of the subjects during the study. **CONCLUSIONS:** Visual function in patients with age-related cataracts who received the lutein supplements improved, suggesting that a higher intake of lutein, through lutein-rich fruit and vegetables or supplements, may have beneficial effects on the visual performance of people with age-related cataracts.

ARE LUTEIN AND ZEAXANTHIN CONDITIONALLY ESSENTIAL NUTRIENTS FOR EYE HEALTH?

The carotenoids lutein and zeaxanthin are found in the macula in high concentrations and may play a role in the pathogenesis of age-related macular degeneration (ARMD). Lutein and zeaxanthin may protect the macula and photoreceptor outer segments throughout the retina from oxidative stress and play a role in an antioxidant cascade that safely disarms the energy of reactive oxygen species. Although lutein and zeaxanthin are not essential nutrients, studies are beginning to suggest that they fit the criteria for conditionally essential nutrients. Low plasma lutein and zeaxanthin concentrations or dietary intake are associated with low macular pigment density and increased risk of ARMD. Dietary deprivation of lutein and zeaxanthin in primates causes pathological changes in the macula. Should controlled clinical trials show lutein and/or zeaxanthin supplementation protects against the development or progression of ARMD and other eye diseases, then lutein and zeaxanthin could be considered as conditionally essential nutrients for humans.

Med Hypotheses. 2003 Oct;61(4):465-72

DOUBLE-MASKED, PLACEBO-CONTROLLED, RANDOMIZED TRIAL OF LUTEIN AND ANTIOXIDANT SUPPLEMENTATION IN THE INTERVENTION OF ATROPHIC AGE-RELATED MACULAR DEGENERATION: THE VETERANS LAST STUDY (LUTEIN ANTIOXIDANT SUPPLEMENTATION TRIAL).

BACKGROUND: Age-related macular degeneration (ARMD) is the leading cause of vision loss in aging Western societies. The objective of the lutein antioxidant supplementation trial (LAST) is to determine whether nutritional supplementation with lutein or lutein together with antioxidants, vitamins, and minerals, improves visual function and symptoms in atrophic ARMD. **METHODS:** The study was a prospective, 12-month, randomized, double-masked, placebo-controlled trial conducted at an urban midwestern Veterans Administration Hospital from August 1999 to May 2001. Ninety patients with atrophic ARMD were referred by ophthalmologists at two Chicago-area veterans medical facilities. Patients in Group 1 received lutein 10 mg (L); in Group 2, a lutein 10 mg/antioxidants/vitamins and minerals broad spectrum supplementation formula (L/A); and in Group 3, a maltodextrin placebo (P) over 12 months. **RESULTS:** In Groups 1 L and 2 L/A, mean eye macular pigment optical density increased approximately 0.09 log units from baseline, Snellen equivalent visual acuity improved 5.4 letters for Group 1 L and 3.5 letters for Group 2 L/A, and contrast sensitivity improved. There was a net subjective improvement in Amsler grid in Group 1 L. VFO-14 questionnaires concerning subjective glare recovery were nearly significant at 4 months for Group 2 L/A. Patients who received the placebo (Group 3) had no significant changes in any of the measured findings. **CONCLUSION:** In this study, visual function is improved with lutein alone or lutein together with other nutrients. Further studies are needed with more patients, of both genders, and for longer periods of time to assess long-term effects of lutein or lutein together with a broad spectrum of antioxidants, vitamins, and minerals in the treatment of atrophic age-related macular degeneration.

Optometry. 2004 Apr;75(4):216-30

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 analyze 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. **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

A PROSPECTIVE STUDY OF CAROTENOID AND VITAMIN A INTAKES AND RISK OF CATARACT EXTRACTION IN US WOMEN.

BACKGROUND: Oxidation of lens proteins plays a central role in the formation of age-related cataracts, suggesting that dietary antioxidants may play a role in prevention. However, the relation between specific antioxidants and risk of cataract remains uncertain. **OBJECTIVE:** Our objective was to examine prospectively the association between carotenoid and vitamin A intakes

and cataract extraction in women. METHODS: A prospective cohort of registered female nurses aged 45-71 y and free of diagnosed cancer was followed; in 1980, 50461 were included and others were added as they became 45 y of age for a total of 77,466. Information on nutrient intake was assessed by repeated administration of a food-frequency questionnaire during 12 y of follow-up. RESULTS: During 761,762 person-years of follow-up, 1,471 cataracts were extracted. After age, smoking, and other potential cataract risk factors were controlled for, those with the highest intake of lutein and zeaxanthin had a 22% decreased risk of cataract extraction compared with those in the lowest quintile (relative risk: 0.78; 95% CI: 0.63, 0.95; P for trend = 0.04). Other carotenoids (alpha-carotene, beta-carotene, lycopene, and beta-cryptoxanthin), vitamin A, and retinol were not associated with cataract in multivariate analysis. Increasing frequency of intakes of spinach and kale, foods rich in lutein, was associated with a moderate decrease in risk of cataract. CONCLUSIONS: Lutein and zeaxanthin and foods rich in these carotenoids may decrease the risk of cataracts severe enough to require extraction.

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