



NEOLIFE

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Flavonoid Complex



This document contains studies conducted on Flavonoid Complex and peer reviewed studies that support ingredients found in Flavonoid Complex.

For more information on each study, please click on the link provided.

PEER REVIEWED STUDIES

Antiproliferative Effect of a Flavonoid Rich Fruit and Vegetable Blend on Human Breast Cancer Cells

ABSTRACT

Background:

The prevention of cancer by administration of food phytochemicals is currently regarded as a promising avenue for cancer control. Epidemiological studies have demonstrated the relationship between carcinogenesis and diet. Studies on animal models have also demonstrated that experimentally induced cancer is preventable with certain natural compounds in the diet. Many flavonoids have been shown to have potent anticarcinogenic and antitumor activity. For example, quercetin inhibits carcinogenesis in a number of models and is able to selectively inhibit a variety of tumor cell growth. Polymethoxylated citrus flavonoids have been shown to have anti-invasive and anti-metastatic activities.

Purpose:

To study the antiproliferative effect of a flavonoid rich fruit and vegetable blend (Flavonoid Complex Active Blend) on human mammary cancer cells (MCF7).

Method:

The polyphenol content of the blend contained quercetin, kaempferol, epicatechin, hesperidin, naringenin and myricetin. MCF7 (mammary adenocarcinoma cells) were harvested in RPMI 1640 media and seeded in 96 well plates. A polar and a non polar extract was prepared using 1:1 dichloromethane-methanol and 70% methanol respectively. The extracts were dissolved in DMSO, combined and serially diluted in the media. The cells were treated and incubated and for 3 days. Viable cells were quantified using the neutral Red Dye Uptake. Doxorubicin was used as the positive control.

Results:

There was a linear response on percent inhibition (Figure 1). The concentrations

used for regression were 150 to 200 ug/ml ($r^2 = 0.90$). Percent inhibition at these points were 41.5 and 82.1 respectively.

Conclusion:

This study demonstrates that a flavonoid rich blend of fruit and vegetable extracts strongly inhibits growth of human breast cancer cells.

Source

In Vitro Prescreening of Cruciferous and Flavonoid Blend Extracts using Chemoprevention Associated Biochemical Markers of the Carcinogenic Process Southern Research Institute (SRI) Birmingham, Alabama 35255-5305 Southern Research Institute (to Golden-Neolife, Inc) report #1, Sept 6, 1996

PEER REVIEWED STUDIES

Blood Sugar Balance

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

ABSTRACT

Objective:

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

Design

Systematic review and meta-analysis.

Data Sources:

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

Study Selection:

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

Results:

Six studies met the inclusion criteria; four of these studies also provided separate information on the consumption of green

leafy vegetables. Summary estimates showed that greater intake of green leafy vegetables was associated with a 14% (hazard ratio 0.86, 95% confidence interval 0.77 to 0.97) reduction in risk of type 2 diabetes ($P=0.01$). The summary estimates showed no significant benefits of increasing the consumption of vegetables, fruit, or fruit and vegetables combined.

Conclusion

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

Source

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

Habitual intake of flavonoid subclasses and incident hypertension in adults

ABSTRACT

Background:

Dietary flavonoids have beneficial effects on blood pressure in intervention settings, but there is limited information on habitual intake and risk of hypertension in population-based studies.

Objective:

We examined the association between habitual flavonoid intake and incident hypertension in a prospective study in men and women.

Design

A total of 87,242 women from the Nurses' Health Study (NHS) II, 46,672 women from the NHS I, and 23,043 men from the Health Professionals Follow-Up Study (HPFS) participated in the study. Total flavonoid and subclass intakes were calculated from semiquantitative food-frequency questionnaires collected every 4 y by using an updated and extended US Department of Agriculture database.

Results:

During 14 y of follow-up, 29,018 cases of hypertension in women and 5629 cases of

hypertension in men were reported. In pooled multivariate-adjusted analyses, participants in the highest quintile of anthocyanin intake (predominantly from blueberries and strawberries) had an 8% reduction in risk of hypertension [relative risk (RR): 0.92; 95% CI: 0.86, 0.98; $P < 0.03$] compared with that for participants in the lowest quintile of anthocyanin intake; the risk reduction was 12% (RR: 0.88; 95% CI: 0.84, 0.93; $P < 0.001$) in participants ≤ 60 y of age and 0.96 (0.91, 1.02) in participants >60 y of age (P for age interaction = 0.02). Although intakes of other subclasses were not associated with hypertension, pooled analyses for individual compounds suggested a 5% (95% CI: 0.91, 0.99; $P = 0.005$) reduction in risk for the highest compared with the lowest quintiles of intake of the flavone apigenin. In participants ≤ 60 y of age, a 6% (95% CI: 0.88, 0.97; $P = 0.002$) reduction in risk was observed for the flavan-3-ol catechin when the highest and the lowest quintiles were compared.

Conclusions:

Anthocyanins and some flavone and flavan-3-ol compounds may contribute to the prevention of hypertension. These vasodilatory properties may result from specific structural similarities (including the B-ring hydroxylation and methoxylation pattern).

Source

Cassidy A, et al. Habitual intake of flavonoid subclasses and incident hypertension in adults. *Am J Clin Nutr.* 2011 Feb; 93 (2): 338-347

Berries modify the postprandial plasma glucose response to sucrose in healthy subjects

ABSTRACT

Sucrose increases postprandial blood glucose concentrations, and diets with a high glycaemic response may be associated with increased risk of obesity, type 2 diabetes and CVD. Previous studies have suggested that polyphenols may influence carbohydrate digestion and absorption and thereby postprandial glycaemia. Berries are rich sources of various polyphenols and berry products are typically consumed with sucrose. We investigated the glycaemic

effect of a berry purée made of bilberries, blackcurrants, cranberries and strawberries, and sweetened with sucrose, in comparison to sucrose with adjustment of available carbohydrates. A total of twelve healthy subjects (eleven women and one man, aged 25-69 years) with normal fasting plasma glucose ingested 150 g of the berry purée with 35 g sucrose or a control sucrose load in a randomised, controlled cross-over design. After consumption of the berry meal, the plasma glucose concentrations were significantly lower at 15 and 30 min ($P < 0.05$, $P < 0.01$, respectively) and significantly higher at 150 min ($P < 0.05$) compared with the control meal. The peak glucose concentration was reached at 45 min after the berry meal and at 30 min after the control meal. The peak increase from the baseline was 1.0 mmol/l smaller ($P = 0.002$) after ingestion of the berry meal. There was no statistically significant difference in the 3 h area under the glucose response curve. These results show that berries rich in polyphenols decrease the postprandial glucose response of sucrose in healthy subjects. The delayed and attenuated glycaemic response indicates reduced digestion and/or absorption of sucrose from the berry meal.

Source

Törrönen R, et al. Berries modify the postprandial plasma glucose response to sucrose in healthy subjects. *Br J Nutr.* 2010 Apr;103(8):1094-7.

Cellular Health

Select dietary flavonoids are associated with markers of inflammation and endothelial dysfunction in US women

ABSTRACT

Flavonoids show antiinflammatory effects in vitro and human intervention studies have suggested beneficial effects of flavonoid-rich foods on biomarkers of inflammation and endothelial function. In the present study, we assessed the relationship between flavonoid intake and biomarkers of inflammation and endothelial dysfunction in a cross-sectional study of participants from

the Nurses' Health Study cohort. Intake of 6 flavonoid subclasses (flavonols, flavones, flavanones, flavan-3-ols, anthocyanidins, and polymeric flavonoids) was assessed using a FFQ administered in 1990. Also, the main food sources of these flavonoids were examined. Blood samples were collected in 1989-1990 and plasma C-reactive protein (CRP), IL-6, IL-18, soluble tumor necrosis factor receptor-2 (sTNF-R2), soluble intercellular adhesion molecule-1, soluble vascular adhesion molecule-1 (sVCAM-1), and E-selectin were measured in 1194-1598 women. The multivariate-adjusted geometric mean of plasma IL-8 were lower for women in the highest intake quintile of flavones, flavanones, and total flavonoids compared with those in the lowest quintiles by 9% (Q1: 264 ng/L, Q5: 241 ng/L; P -trend = 0.019), 11% (Q1: 273 ng/L, Q5: 244 ng/L; P -trend = 0.011), and 8% (Q1: 276 ng/L, Q5: 55 ng/L; P -trend = 0.034), respectively. The multivariate-adjusted geometric mean for women in the highest intake quintile of flavonol compared with those in the lowest quintile was 4% lower for sVCAM-1 (Q1: 578 μ g/L, Q5: 557 μ g/L; P -trend = 0.012). Among flavonoid-rich foods, higher intake of grapefruit was significantly associated with lower concentrations of CRP and sTNF-R2. In summary, higher intakes of selected flavonoid subclasses were associated with modestly lower concentrations of inflammatory biomarkers. In particular, flavonoids typically found in citrus fruits were modestly associated with lower plasma IL-18 concentrations.

Source

Landberg R, et al. Select dietary flavonoids are associated with markers of inflammation and endothelial dysfunction in US women. *Journal of nutrition.* April 2011, doi: 10.3945/jn.101.133843

Cognitive Health

Neural effects of green tea extract on dorsolateral prefrontal cortex

ABSTRACT

Background/Objectives:

Green tea is being recognized as a beverage with potential benefits for human health and cognitive functions. In vivo studies provide preliminary evidence that green tea intake may have a positive role in improving effects on cognitive functions. We aimed to examine the neural effects of green tea extract on brain activation in humans.

Subjects/Methods:

Functional magnetic resonance imaging was recorded while 12 healthy volunteers performed a working memory task following administration of 250 or 500 ml of a milk whey based green tea containing soft drink or milk whey based soft drink without green tea as control in a double-blind, controlled repeated measures within-subject design with counterbalanced order of substance administration. A whole-brain analysis with a cluster-level threshold of $P < 0.001$ (unadjusted) was followed by an a priori-defined region of interest (ROI) analysis of the dorsolateral prefrontal cortex (DLPFC) including a cluster-level threshold of $P < 0.05$ and family-wise error (FWE) adjustment for multiple comparisons.

Results:

Whole-brain analyses revealed no significant effects after correction for multiple comparisons (FWE $P < 0.05$). Using a ROI approach, green tea extract increased activation in the DLPFC relative to a control condition (FWE $P < 0.001$). This neural effect was related to green tea dosage. Green tea extract was not associated with any significant attenuation in regional activation relative to control condition.

Conclusions:

These data suggest that green tea extract may modulate brain activity in the DLPFC, a key area that mediates working memory processing in the human brain. Moreover, this is the first neuroimaging study implicating that functional neuroimaging methods provide a means of examining how green tea extract acts on the brain.

Source

Borgwardt S et. al. Neural effects of green tea extract on dorsolateral prefrontal cortex. *Eur J Clin Nutr.* 2012;66(11):1187-92.

Dietary intakes of berries and flavonoids in relation to cognitive decline

ABSTRACT

Objective:

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

Methods:

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

Results:

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

Interpretation:

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

Source

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

Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males

ABSTRACT

Rationale:

A significant proportion of the general population report supplementing their diet with one or more vitamins or minerals, with common reasons for doing so being to combat stress and fatigue and to improve mental functioning. Few studies have assessed the relationship between supplementation with vitamins/minerals and psychological functioning in healthy cohorts of non-elderly adults.

Objectives:

The present randomised, placebo-controlled, double-blind, parallel groups trial assessed the cognitive and mood effects of a high-dose B-complex vitamin and mineral supplement (Berocca®) in 215 males aged 30 to 55 years, who were in full-time employment.

Methods:

Participants attended the laboratory prior to and on the last day of a 33-day treatment period where they completed the Profile of Mood States (POMS), Perceived Stress Scale (PSS) and General Health Questionnaire (GHQ-12). Cognitive performance and task-related modulation of mood/fatigue were assessed with the 60 min cognitive demand battery. On the final day, participants also completed the Stroop task for 40 min whilst engaged in inclined treadmill walking and subsequent executive function was assessed.

Results:

Vitamin/mineral supplementation led to significant improvements in ratings on the PSS, GHQ-12 and the 'vigour' subscale of

the POMS. The vitamin/mineral group also performed better on the Serial 3s subtractions task and rated themselves as less 'mentally tired' both pre- and post-completion of the cognitive demand battery.

Conclusions:

Healthy members of the general population may benefit from augmented levels of vitamins/minerals via direct dietary supplementation. Specifically, supplementation led to improved ratings of stress, mental health and vigour and improved cognitive performance during intense mental processing.

Source

Kennedy DO et al. Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males. Psychopharmacol 211:55-68, 2010.

Berry fruit enhances beneficial signaling in the brain

ABSTRACT

Increased lifespans have led to population aging and brought attention to healthcare concerns associated with old age. A growing body of preclinical and clinical research has identified neurological benefits associated with the consumption of berry fruits. In addition to their now well-known antioxidant effects, dietary supplementation with berry fruits also has direct effects on the brain. Intake of these fruits may help to prevent age-related neurodegeneration and resulting changes in cognitive and motor function. In cell and animal models, berry fruits mediate signaling pathways involved in inflammation and cell survival in addition to enhancing neuroplasticity, neurotransmission, and calcium buffering, all of which lead to attenuation of age- and pathology-related deficits in behavior. Recent clinical trials have extended these antioxidant, anti-inflammatory, and cognition-sparing effects to humans. This paper reviews recent evidence for the beneficial signaling effects of berry fruits on the brain and behavior.

Source

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

A combination of green tea extract and L-theanine improve memory and attention in subjects with mild cognitive impairment: A double blind placebo controlled study

ABSTRACT

A combination of green tea extract and L-theanine (LGNC-07) has been reported to have beneficial effects on cognition in animal studies. In this randomized, double-blind, placebo-controlled study, the effect of LGNC-07 on memory and attention in subjects with mild cognitive impairment (MCI) was investigated. Ninety-one MCI subjects whose Mini Mental State Examination-K (MMSE-K) scores were between 21 and 26 and who were in either stage 2 or 3 on the Global Deterioration Scale were enrolled in this study. The treatment group (13 men, 32 women; 57.58±9.45 years) took 1,680mg of LGNC-07, and the placebo group (12 men, 34 women; 56.28±9.92 years) received an equivalent amount of maltodextrin and lactose for 16 weeks. Neuropsychological tests (Rey-Kim memory test and Stroop color-word test) and electroencephalography were conducted to evaluate the effect of LGNC-07 on memory and attention. Further analyses were stratified by baseline severity to evaluate treatment response on the degree of impairment (MMSE-K 21-23 and 24-26). LGNC-07 led to improvements in memory by marginally increasing delayed recognition in the Rey-Kim memory test (P=.0572). Stratified analyses showed that LGNC-07 improved memory and selective attention by significantly increasing the Rey-Kim memory quotient and word reading in the subjects with MMSE-K scores of 21-23 (LGNC-07, n=11; placebo, n=9). Electroencephalograms were recorded in 24 randomly selected subjects hourly for 3 hours in eye-open, eye-closed, and reading states after a single dose of LGNC-07 (LGNC-07, n=12; placebo, n=12). Brain

theta waves, an indicator of cognitive alertness, were increased significantly in the temporal, frontal, parietal, and occipital areas after 3 hours in the eye-open and reading states. Therefore, this study suggests that LGNC-07 has potential as an intervention for cognitive improvement.

Source

Park SK, et al. A combination of green tea extract and L-theanine improve memory and attention in subjects with mild cognitive impairment: A double blind placebo controlled study. Journal of Medicinal Foods, 2011; 14(4): 334-343

Total antioxidant capacity of diet and risk of stroke: a population-based prospective cohort of women

ABSTRACT

Background and Purpose:

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

Methods:

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

Results:

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

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

Conclusions:

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

Source

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

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

ABSTRACT

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

surface PrPC impaired its ability to inhibit the activity of the β -secretase BACE1, which cleaves the amyloid precursor protein to produce A β . The green tea polyphenol (-)-epigallocatechin gallate and the red wine extract resveratrol both remodeled the fibrillar conformation of A β oligomers. The resulting nonfibrillar oligomers displayed significantly reduced binding to PrPC-expressing cells and were no longer cytotoxic. These data indicate that soluble, fibrillar A β oligomers bind to PrPC in a conformation-dependent manner and require the integrity of lipid rafts and the transmembrane LRP1 for their cytotoxicity, thus revealing potential targets to alleviate the neurotoxic properties of A β oligomers in AD.

Source

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

Eye Health

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

ABSTRACT

Background:

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

Objective:

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

Design:

The Age-Related Eye Disease Study, an 11-center double-masked clinical trial, enrolled participants in an AMD trial if they had extensive small drusen, intermediate drusen, large drusen, noncentral geographic atrophy, or pigment abnormalities in 1 or

both eyes, or advanced AMD or vision loss due to AMD in 1 eye. At least 1 eye had best-corrected visual acuity of 20/32 or better. Participants were randomly assigned to receive daily oral tablets containing: (1) antioxidants (vitamin C, 500 mg; vitamin E, 400 IU; and beta carotene, 15 mg); (2) zinc, 80 mg, as zinc oxide and copper, 2 mg, as cupric oxide; (3) antioxidants plus zinc; or (4) placebo.

Main Outcome Measures:

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

Results:

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

Conclusions:

Persons older than 55 years should have dilated eye examinations to determine their risk of developing advanced AMD. Those with extensive intermediate size drusen, at least 1 large druse, noncentral geographic atrophy in 1 or both eyes, or advanced AMD or vision loss due to AMD in 1 eye, and without contraindications such as smoking, should consider taking a supplement of antioxidants plus zinc such as that used in this study.

Source

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

Heart Health

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

ABSTRACT

Background:

Dietary supplements are widely used in industrialized countries.

Objective:

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

Design:

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

Results:

During an average of 10.2 y of follow-up, 932 MI cases were identified in the CVD-

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

Conclusions:

The use of multivitamins was inversely associated with MI, especially long-term use among women with no CVD. Further prospective studies with detailed information on the content of preparations and the duration of use are needed to confirm or refute our findings.

Source

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

Total antioxidant capacity of diet and risk of stroke: a population-based prospective cohort of women

ABSTRACT

Background and Purpose:

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

Methods:

The study included women (31,035 CVD-free and 5680 with CVD history at baseline), aged 49 to 83 years, from the Swedish Mammography Cohort. Diet was assessed with a food frequency questionnaire. Dietary

TAC was calculated using oxygen radical absorbance capacity values. Stroke cases were ascertained by linkage with the Swedish Hospital Discharge Registry.

Results:

During follow-up (September 1997 to December 2009), we identified 1322 stroke cases (988 cerebral infarctions, 226 hemorrhagic strokes, and 108 unspecified strokes) among CVD-free women and 1007 stroke cases (796 cerebral infarctions, 100 hemorrhagic strokes, and 111 unspecified strokes) among women with a CVD history. The multivariable hazard ratio of total stroke comparing the highest with the lowest quintile of dietary TAC was 0.83 (95% CI, 0.70-0.99; P for trend=0.04) in CVD-free women. Among women with a CVD history, the hazard ratios for the highest versus lowest quartile of TAC were 0.90 (95% CI, 0.75-1.07; P for trend=0.30) for total stroke and 0.55 (95% CI, 0.32-0.95; P for trend=0.03) for hemorrhagic stroke.

Conclusions:

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

Source

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

Berries modify the postprandial plasma glucose response to sucrose in healthy subjects

ABSTRACT

Sucrose increases postprandial blood glucose concentrations, and diets with a high glycaemic response may be associated with increased risk of obesity, type 2 diabetes and CVD. Previous studies have suggested that polyphenols may influence carbohydrate digestion and absorption and thereby postprandial glycaemia. Berries are rich sources of various polyphenols and berry products are typically consumed with sucrose. We investigated the glycaemic effect of a berry purée made of bilberries, blackcurrants, cranberries and strawberries,

and sweetened with sucrose, in comparison to sucrose with adjustment of available carbohydrates. A total of twelve healthy subjects (eleven women and one man, aged 25-69 years) with normal fasting plasma glucose ingested 150 g of the berry purée with 35 g sucrose or a control sucrose load in a randomised, controlled cross-over design. After consumption of the berry meal, the plasma glucose concentrations were significantly lower at 15 and 30 min ($P < 0.05$, $P < 0.01$, respectively) and significantly higher at 150 min ($P < 0.05$) compared with the control meal. The peak glucose concentration was reached at 45 min after the berry meal and at 30 min after the control meal. The peak increase from the baseline was 1.0 mmol/l smaller ($P = 0.002$) after ingestion of the berry meal. There was no statistically significant difference in the 3 h area under the glucose response curve. These results show that berries rich in polyphenols decrease the postprandial glucose response of sucrose in healthy subjects. The delayed and attenuated glycaemic response indicates reduced digestion and/or absorption of sucrose from the berry meal.

Source

Törrönen R, et al. *Berries modify the postprandial plasma glucose response to sucrose in healthy subjects. Br J Nutr. 2010 Apr;103(8):1094-7.*

Immune Health

Physicians and nurses use and recommend dietary supplements: report of a survey

ABSTRACT

Background:

Numerous surveys show that dietary supplements are used by a large proportion of the general public, but there have been relatively few surveys on the prevalence of dietary supplement use among health professionals, including physicians and nurses. Even less information is available regarding the extent to which physicians and nurses recommend dietary supplements to their patients.

Methods:

An online survey was administered in October 2007 to 900 physicians and 277 nurses by Ipsos Public Affairs for the Council for Responsible Nutrition (CRN), a trade association representing the dietary supplement industry. The health professionals were asked whether they used dietary supplements and their reasons for doing so, and whether they recommend dietary supplements to their patients.

Results:

The "Life...supplemented" Healthcare Professionals Impact Study (HCP Impact Study) found that 72% of physicians and 89% of nurses in this sample used dietary supplements regularly, occasionally, or seasonally. Regular use of dietary supplements was reported by 51% of physicians and 59% of nurses. The most common reason given for using dietary supplements was for overall health and wellness (40% of physicians and 48% of nurses), but more than two-thirds cited more than one reason for using the products. When asked whether they "ever recommend dietary supplements" to their patients, 79% of physicians and 82% of nurses said they did.

Conclusions:

Physicians and nurses are as likely as members of the general public to use dietary supplements, as shown by comparing the results of this survey with data from national health and nutrition surveys. Also, most physicians and nurses recommend supplements to their patients, whether or not the clinicians use dietary supplements themselves.

Source

Dickinson A, et al. *Physicians and nurses use and recommend dietary supplements: report of a survey. Nutr J. 2009 Jul 1;8:29.*

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

ABSTRACT

The purpose of this manuscript is to review the impact of supplementation with vitamins E and C, carotenoids, and the B vitamins on parameters of innate and adaptive

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

Source

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

Skin Health

Polyphenols: Skin photoprotection and inhibition of photo-carcinogenesis

ABSTRACT

Polyphenols are a large family of naturally occurring plant products and are widely distributed in plant foods, such as, fruits, vegetables, nuts, flowers, bark and seeds, etc. These polyphenols contribute to the beneficial health effects of dietary products. Clinical and epidemiological studies suggest that exposure of the skin to environmental factors/pollutants, such as solar ultraviolet (UV) radiation induce harmful effects and leads to various skin diseases including the risk of melanoma and non-melanoma skin cancers. The incidence of non-melanoma skin cancer, comprising of squamous cell carcinoma and basal cell carcinoma, is a significant public health concern world-wide. Exposure of the skin to solar UV radiation results in inflammation, oxidative stress, DNA damage, dysregulation of cellular signaling pathways and immunosuppression thereby resulting in skin cancer. The regular intake of natural plant products, especially polyphenols, which are widely present in fruits, vegetables, dry legumes and beverages

have gained considerable attention as protective agents against the adverse effects of UV radiation. In this article, we first discussed the impact of polyphenols on human health based on their structure-activity relationship and bioavailability. We then discussed in detail the photoprotective effects of some selected polyphenols on UV-induced skin inflammation, proliferation, immunosuppression, DNA damage and dysregulation of important cellular signaling pathways and their implications in skin cancer management. The selected polyphenols include: green tea polyphenols, pomegranate fruit extract, grape seed proanthocyanidins, resveratrol, silymarin, genistein and delphinidin. The new information on the mechanisms of action of these polyphenols supports their potential use in skin photoprotection and prevention of photocarcinogenesis in humans.

Source

Afaq F et al. *Polyphenols: Skin photoprotection and inhibition of photocarcinogenesis. Mini Rev Med Chem* 11:1200-1215, 2011.

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

ABSTRACT

Ultraviolet radiation absorption is responsible for the production of free radicals in damaged cells. This side effect may be neutralized using antioxidant substances. It has been reported that ascorbic acid and d-alpha-tocopherol scavenge reactive oxygen species. In a single-blind controlled clinical trial we studied 45 healthy volunteers divided into three groups. Group 1 received d-alpha-tocopherol 1,200 I.U. daily; Group 2 ascorbic acid 2 g daily and Group 3 ascorbic acid 2 g plus d-alpha-tocopherol 1,200 I.U. daily. Treatment was sustained for one week. Before and after treatment, the minimal erythema dose was determined in all participants. The results show that the median minimal erythema dose increased from 60 to 65 mJ/cm² in Group 1 and from

50 to 70 mJ/cm² in Group 3. No modifications were observed in Group 2. We conclude that d-alpha-tocopherol prescribed in combination with ascorbic acid produces the best photoprotective effect.

Source

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

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

ABSTRACT

Background:

Dietary supplements are widely used in industrialized countries.

Objective:

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

Design:

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

Results:

During an average of 10.2 y of follow-up, 932 MI cases were identified in the CVD-free group and 269 cases in the CVD group. In the CVD-free group, use of multivitamins only, compared with no use of supplements, was associated with a multivariable-adjusted hazard ratio (HR) of 0.73 (95% CI: 0.57, 0.93). The HR for multivitamin use together with other supplements was 0.70 (95% CI: 0.57, 0.87). The HR for use of supplements other

than multivitamins was 0.93 (95% CI: 0.81, 1.08). The use of multivitamins for ≥5 y was associated with an HR of 0.59 (95% CI: 0.44, 0.80). In the CVD group, use of multivitamins alone or together with other supplements was not associated with MI.

Conclusions:

The use of multivitamins was inversely associated with MI, especially long-term use among women with no CVD. Further prospective studies with detailed information on the content of preparations and the duration of use are needed to confirm or refute our findings.

Source

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

Botanicals in Dermatology: An Evidence based Review

ABSTRACT

Botanical extracts and single compounds are increasingly used in cosmetics but also in over-the-counter drugs and food supplements. The focus of the present review is on controlled clinical trials with botanicals in the treatment of acne, inflammatory skin diseases, skin infections, UV-induced skin damage, skin cancer, alopecia, vitiligo, and wounds. Studies with botanical cosmetics and drugs are discussed, as well as studies with botanical food supplements. Experimental research on botanicals was considered to a limited extent when it seemed promising for clinical use in the near future. In acne therapy, Mahonia, tea tree oil, and *Saccharomyces* may have the potential to become standard treatments. Mahonia, *Hypericum*, *Glycyrrhiza* and some traditional Chinese medicines appear promising for atopic dermatitis. Some plant-derived substances like dithranol and methoxsalen (8-methoxypsoralen) [in combination with UVA] are already accepted as standard treatments in psoriasis; Mahonia and *Capsicum* (capsaicin) are the next

candidates suggested by present evidence. Oral administration and topical application of antioxidant plant extracts (green and black tea, carotenoids, coffee, and many flavonoids from fruits and vegetables) can protect skin from UV-induced erythema, early aging, and irradiation-induced cancer. Hair loss and vitiligo are also traditional fields of application for botanicals. According to the number and quality of clinical trials with botanicals, the best evidence exists for the treatment of inflammatory skin diseases, i.e. atopic dermatitis and psoriasis. However, many more controlled clinical studies are needed to determine the efficacy and risks of plant-derived products in dermatology. Safety aspects, especially related to sensitization and photodermatitis, have to be taken into account. Therefore, clinicians should not only be informed of the beneficial effects but also the specific adverse effects of botanicals used for dermatologic disorders and cosmetic purposes.

Source

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

Oral green tea catechin metabolites are incorporated into human skin and protect against UV radiation-induced cutaneous inflammation in association with reduced production of pro-inflammatory eicosanoid 12-hydroxyeicosatetraenoic acid

ABSTRACT

Green tea catechins (GTC) reduce UV radiation (UVR)-induced inflammation in experimental models, but human studies are scarce and their cutaneous bioavailability and mechanism of photoprotection are unknown. We aimed to examine oral GTC cutaneous uptake, ability to protect human skin against erythema induced by a UVR dose range and impact on potent cyclo-oxygenase- and lipoxygenase-produced mediators of UVR inflammation, PGE2 and 12-hydroxyeicosatetraenoic acid (12-HETE), respectively. In an open oral intervention study, sixteen healthy human subjects

(phototype I/II) were given low-dose GTC (540 mg) with vitamin C (50 mg) daily for 12 weeks. Pre- and post-supplementation, the buttock skin was exposed to UVR and the resultant erythema quantified. Skin blister fluid and biopsies were taken from the unexposed and the UVR-exposed skin 24 h after a pro-inflammatory UVR challenge (three minimal erythema doses). Urine, skin tissue and fluid were analysed for catechin content and skin fluid for PGE2 and 12-HETE by liquid chromatography coupled to tandem MS. A total of fourteen completing subjects were supplement compliant (twelve female, median 42.5 years, range 29-59 years). Benzoic acid levels were increased in skin fluid post-supplementation (P= 0.03), and methylated gallic acid and several intact catechins and hydroxyphenyl-valerolactones were detected in the skin tissue and fluid. AUC analysis for UVR erythema revealed reduced response post-GTC (P= 0.037). Pre-supplementation, PGE2 and 12-HETE were UVR induced (P= 0.003, 0.0001). After GTC, UVR-induced 12-HETE reduced from mean 64 (sd 42) to 41 (sd 32) pg/μl (P= 0.01), while PGE2 was unaltered. Thus, GTC intake results in the incorporation of catechin metabolites into human skin associated with abrogated UVR-induced 12-HETE; this may contribute to protection against sunburn inflammation and potentially longer-term UVR-mediated damage.

Source

Rhodes LE et al. Oral green tea catechin metabolites are incorporated into human skin and protect against UV radiation-induced cutaneous inflammation in association with reduced production of pro-inflammatory eicosanoid 12-hydroxyeicosatetraenoic acid. Br

Discovering the link between nutrition and skin aging

ABSTRACT

Skin has been reported to reflect the general inner-health status and aging. Nutrition and its reflection on skin has always been an interesting topic for scientists and physicians throughout the

centuries worldwide. Vitamins, carotenoids, tocopherols, flavonoids and a variety of plant extracts have been reported to possess potent anti-oxidant properties and have been widely used in the skin care industry either as topically applied agents or oral supplements in an attempt to prolong youthful skin appearance. This review will provide an overview of the current literature "linking" nutrition with skin aging.

Source

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

Sports Nutrition

Vitamin C status and perception of effort during exercise in obese adults adhering to a calorie-reduced diet

ABSTRACT

Objective:

Moderate energy restriction and exercise are recommended for effective weight loss. Obese individuals oxidize less fat and report a higher perceived exertion during exercise, characteristics that may negatively influence exercise behavior. Because vitamin C status has been linked to fatigability, we compared the effects of vitamin C supplementation on self-reported fatigue and on the respiratory exchange ratio and the Ratings of Perceived Exertion scale during moderate exercise in healthy obese adults adhering to a hypocaloric diet.

Methods:

Twenty adults (4 men and 16 women) were stratified and randomly assigned to receive 500 mg of vitamin C (VC) or placebo (CON) daily for 4 wk while adhering to a vitamin C-controlled, calorie-restricted diet. Feelings of general fatigue as assessed by the Profile of Mood States questionnaire were recorded on a separate day from the exercise session at weeks 0 and 4. Participants walked on a treadmill at an intensity of 50% predicted maximal oxygen consumption for 60 min at weeks 0 and

4, and heart rate, respiratory exchange ratio, and Ratings of Perceived Exertion were recorded.

Results:

After 4 wk, the two groups lost similar amounts of weight (≈ 4 kg), and the respiratory exchange ratio was not altered by group. Heart rate and the Ratings of Perceived Exertion during exercise were significantly decreased in the VC versus the CON group (-11 versus -3 beats/min, $P = 0.022$, and -1.3 versus +0.1 U, $P = 0.001$, respectively), and the general fatigue score was decreased 5.9 U for the VC group versus a 1.9 U increase for the CON group ($P = 0.001$).

Conclusion:

These data provide preliminary evidence that vitamin C status may influence fatigue, heart rate, and perceptions of exertion during moderate exercise in obese individuals.

Source

Huck CJ et al. *Vitamin C status and perception of effort during exercise in obese adults adhering to a calorie-reduced diet.* *Nutr* [Epub June 5, 2012].

established. Finally, there is emerging evidence that high doses of tea polyphenols may have adverse side effects. Given that the results of scientific studies on dietary components, including tea polyphenols, are often translated into dietary supplements, understanding the potential toxicities of the tea polyphenols is critical to understanding their potential usefulness in preventing obesity. In this review, we will critically evaluate the evidence for the prevention of obesity by tea, discuss the relevance of proposed mechanisms in light of tea polyphenol bioavailability, and review the reports concerning the toxic effects of high doses of tea polyphenols and the implication that this has for the potential use of tea for the prevention of obesity. We hope that this review will expose areas for further study and encourage research on this important public health issue.

Source

Grove KA and Lambert JD. *Critical Review. Laboratory, epidemiological, and human intervention studies show that tea (Camellia sinensis) may be useful in the prevention of obesity.* *J of Nutr* 140:446-53, 2010.

Weight Management

Laboratory, epidemiological, and human intervention studies show that tea (*Camellia sinensis*) may be useful in the prevention of obesity

ABSTRACT

Tea (*Camellia sinensis*, Theaceae) and tea polyphenols have been studied for the prevention of chronic diseases, including obesity. Obesity currently affects >20% of adults in the United States and is a risk factor for chronic diseases such as type II diabetes, cardiovascular disease, and cancer. Given this increasing public health concern, the use of dietary agents for the prevention of obesity would be of tremendous benefit. Whereas many laboratory studies have demonstrated the potential efficacy of green or black tea for the prevention of obesity, the underlying mechanisms remain unclear. The results of human intervention studies are mixed and the role of caffeine has not been clearly