Plasma pharmacokinetics of catechin metabolite 4'-O-Me-EGC in healthy humans.


Nestlé Research Center, Nestec Ltd., Vers-Chez-Les-Blanc, 1000, Lausanne 26, Switzerland, mathieu.renouf@rdls.nestle.com.

Abstract

BACKGROUND: Tea is an infusion of the leaves of the Camellia sinensis plant and is the most widely consumed beverage in the world after water. Green tea contains significant amounts of polyphenol catechins and represents a promising dietary component to maintain health and well-being. Epidemiological studies indicate that polyphenol intake may have potential health benefits, such as, reducing the incidence of coronary heart disease, diabetes and cancer. While bioavailability of green tea bioactives is fairly well understood, some gaps still remain to be filled, especially the identification and quantification of conjugated metabolites in plasma, such as, sulphated, glucuronidated or methylated compounds.

AIM OF THE STUDY: In the present study, we aimed to quantify the appearance of green tea catechins in plasma with particular emphasis on their methylated forms.

RESULTS: After feeding 400 mL of green tea, 1.25% infusion to 9 healthy subjects, we found significant amounts of EC, EGC and EGCg in plasma as expected. EGC was the most bioavailable catechin, and its methylated form (4'-O-Me-EGC) was also present in quantifiable amounts. Its kinetics followed that of its parent compound. However, the relative amount of the methylated form of EGC was lower than that of the parent compound, an important aspect which, in the literature, has been controversial so far. The quantitative results presented in our study were confirmed by co-chromatography and accurate mass analysis of the respective standards. We show that the relative abundance of 4'-O-Me-EGC is ~40% compared to the parent EGC.

CONCLUSION: 4'-O-Me-EGC is an important metabolite derived from catechin metabolism. Its presence in significant amounts should not be overlooked when assessing human bioavailability of green tea.

PMID: 21212969 [PubMed - as supplied by publisher]

Supplemental Content

Quantification of anthocyanins and flavonols in milk-based food products by ultra performance liquid chromatography-tandem mass spectrometry.

Nagy K, Redeuil K, Bertholet R, Steiling H, Kussmann M.

Functional Genomics Group, BioAnalytical Science Department, Nestlé Research Centre, Nestec Ltd., Lausanne, Switzerland. kornel.nagy@rdls.nestle.com

Abstract

The present article describes the development and validation of an ultra performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) method for the comprehensive quantification of anthocyanin and flavonol constituents of milk-based food products. Protein precipitation by acidified methanol and ultrafiltration was utilized as sample preparation to preserve overall polyphenol composition but to eliminate milk proteins in order to comply with UPLC. Reversed-phase chromatography was optimized to achieve separation of 27 analytes in 10 min in order to reduce suppression effects, achieve a wide dynamic range, and most importantly, to resolve isomeric compounds. Positive-ion electrospray mass spectrometric detection and fragmentation of analytes was optimized, final transitions were selected for maximized selectivity, reliable quantification, and reduction of false positives. The quantitative performance of the method was validated, the main features include (1) range of lower limits of detection 0.3-30 ng/mL for glycosylated analytes, 10-300 ng/mL for aglycones, (2) lower limits of quantification 1-100 ng/mL for glycosylated analytes, 30-1,000 ng/mL for aglycones, (3) averaged intraday precision 9%, (4) calibrated range 2-180,000 ng/mL for glycosylated analytes, 60-600,000 ng/mL for aglycones, and (5) averaged accuracy 101%. Applications for yogurt and ice cream products are given. The presented data suggest that this method will help to better characterize the polyphenol composition of milk-based food products for quality control, for assessment of dietary intake, and for polyphenol bioavailability/bioefficacy studies.

PMID: 20337399 [PubMed - indexed for MEDLINE]

Supplemental Content

Polyphenol-enriched apple extract attenuates food allergy in mice.

Zuercher AW, Holvoet S, Weiss M, Mercenier A.

Allergy Group, Department of Nutrition and Health, Nestle Research Center, Lausanne, Switzerland.

Abstract

BACKGROUND: The immune system may be modulated with nutrition to prevent the development or to treat the symptoms of allergy. Among other foods, consumption of apples has been linked to reduced incidence of atopic dermatitis and respiratory allergy.

OBJECTIVE: We evaluated the efficacy and mechanisms of a polyphenol-enriched apple extract in reducing symptoms of food allergy.

METHODS: In a model of food allergy to ovalbumin (OVA), BALB/c mice were fed with an apple extract either during sensitization or just before the challenge. After the challenge, allergic symptoms were scored, OVA-specific serum immunoglobulins were determined by ELISA, cytokine production by mesenteric lymph node (MLN) cells was measured by a multiplex assay and gene expression profiles in the intestine were addressed using quantitative real-time PCR.

RESULTS: Consumption of the apple extract reduced symptoms of food allergy upon challenge. This was paralleled by reduced levels of intestinal mast cell protease, diminished cytokine secretion by MLN cells and reduced local intestinal mRNA expression of various T-helper type-2 associated and pro-inflammatory genes. Mechanistic studies suggested decrease of mediator release by effector cells and reduction of allergenicity by protein-polyphenol interaction as potential mechanisms responsible for protection.

CONCLUSION: Polyphenol-enriched apple extract can attenuate food allergy symptoms in sensitized mice via two distinct possible mechanisms.

PMID: 20175787 [PubMed - indexed for MEDLINE]

Supplemental Content

Coffee and green tea as a large source of antioxidant polyphenols in the Japanese population.


Nestle Research Center, Vers-chez-les-Blanc, CH-1000 Lausanne 26, Switzerland. yoichi.fukushima@rdls.nestle.com

Abstract

Food and beverages rich in polyphenols with antioxidant activity are highlighted as a potential factor for risk reduction of lifestyle related diseases. This study was conducted to elucidate total polyphenol consumption from beverages in Japanese people. Total polyphenol (TP) contents in beverages were measured using a modified Folin-Ciocalteu method removing the interference of reduced sugars by using reverse-phase column chromatography. A beverage consumption survey was conducted in the Tokyo and Osaka areas in 2004. Randomly selected male and female subjects (10-59 years old, n = 8768) recorded the amounts and types of all nonalcoholic beverages consumed in a week. Concentration of TP in coffee, green tea, black tea, Oolong tea, barley tea, fruit juice, tomato/vegetable juice, and cocoa drinks were at 200, 115, 96, 39, 9, 34, 69, and 62 mg/100 mL, respectively. Total consumption of beverages in a Japanese population was 1.11 +/- 0.51 L/day, and TP contents from beverages was 853 +/- 512 mg/day. Coffee and green tea shared 50% and 34% of TP consumption in beverages, respectively, and contribution of each of the other beverages was less than 10%. TP contents in 20 major vegetables and 5 fruits were 0-49 mg and 2-55 mg/100 g, respectively. Antioxidant activities, Cu reducing power, and scavenging activities for DPPH and superoxide, of those samples correlated to the TP contents (p < 0.001). Beverages, especially coffee, contributed to a large share of the consumption of polyphenols, as antioxidants, in the Japanese diet.

PMID: 19187022 [PubMed - indexed for MEDLINE]

Supplemental Content


Interactions affecting the bioavailability of dietary polyphenols in vivo.

Scholz S, Williamson G.
Abstract

Polyphenols are widely abundant dietary constituents in plants that are associated with health-promoting effects. This review summarizes factors influencing the bioavailability of polyphenols, specifically flavanols, flavonols, flavanones, flavones, and hydroxycinnamic (phenolic) acids. Most factors tested so far indicate that bioaccessibility, defined as the amount of compound reaching the enterocyte in a form suitable for absorption, is the most important factor determining the absorption in the gut. Factors leading to an improved absorption of flavonols, notably quercetin and its metabolites, are primarily the nature of the attached sugar, and secondly, the solubility as modified by ethanol, fat, and emulsifiers. The absorption of flavanols, notably green tea catechins, is affected by epimerization reactions occurring during processing, the presence of lipid and carbohydrate, and is improved by the presence of piperine and tartaric acid. Flavanones, such as hesperidin, are strongly affected by the type of attached sugar. Phenolic acids are affected by the attached sugar, which can covalently link these compounds to the cereal bran matrix. In the few examples tested, absorption of polyphenols is dependent on release from the food matrix. There are only a few examples reported, but where information is available, the absorption increases with dose but is sometimes linear and sometimes saturated. The lack of systematic information on the effects of other components on the bioavailability of polyphenols needs to be addressed, and more human studies should be conducted in this field to establish general principles affecting absorption in vivo. Information derived from such experiments could be useful for the optimal design of future bioefficacy studies.


Predictive relationship between polyphenol and nonfat cocoa solids content of chocolate.

Cooper KA, Campos-Giménez E, Jiménez Alvarez D, Rytz A, Nagy K, Williamson G.

Nestlé Research Centre, Lausanne, Switzerland.

Abstract

Chocolate is often labeled with percent cocoa solids content. It is assumed that higher cocoa solids contents are indicative of higher polyphenol concentrations, which have potential health benefits. However, cocoa solids include polyphenol-free cocoa butter and polyphenol-rich nonfat cocoa solids (NFCS). In this study the strength of the relationship between NFCS content (estimated by theobromine as a proxy) and polyphenol content was tested in chocolate samples with labeled cocoa solids contents in the range of 20-100%, grouped as dark (n = 46), milk (n = 8), and those chocolates containing inclusions such as wafers or nuts (n = 15). The relationship was calculated with regard to both total polyphenol content and individual polyphenols. In dark chocolates, NFCS is linearly related to total polyphenols (r² = 0.73). Total polyphenol content appears to be systematically slightly higher for milk chocolates than estimated by the dark chocolate model, whereas for chocolates containing other ingredients,
the estimates fall close to or slightly below the model results. This shows that extra components such as milk, wafers, or nuts might influence the measurements of both theobromine and polyphenol contents. For each of the six main polyphenols (as well as their sum), the relationship with the estimated NFCS was much lower than for total polyphenols (r^2 < 0.40), but these relationships were independent of the nature of the chocolate type, indicating that they might still have some predictive capabilities.

PMID: 18052039 [PubMed - indexed for MEDLINE]

Supplemental Content

**Quantification of anthocyanins and flavonols in milk-based food products by ultra performance liquid chromatography-tandem mass spectrometry.**

Nagy K, Redeuil K, Bertholet R, Steiling H, Kussmann M.

Functional Genomics Group, BioAnalytical Science Department, Nestlé Research Centre, Nestec Ltd., Lausanne, Switzerland. kornel.nagy@rdls.nestle.com

Abstract

The present article describes the development and validation of an ultra performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) method for the comprehensive quantification of anthocyanin and flavonol constituents of milk-based food products. Protein precipitation by acidified methanol and ultrafiltration was utilized as sample preparation to preserve overall polyphenol composition but to eliminate milk proteins in order to comply with UPLC. Reversed-phase chromatography was optimized to achieve separation of 27 analytes in 10 min in order to reduce suppression effects, achieve a wide dynamic range, and most importantly, to resolve isomeric compounds. Positive-ion electrospray mass spectrometric detection and fragmentation of analytes was optimized, final transitions were selected for maximized selectivity, reliable quantification, and reduction of false positives. The quantitative performance of the method was validated, the main features include (1) range of lower limits of detection 0.3-30 ng/mL for glycosylated analytes, 10-300 ng/mL for aglycones, (2) lower limits of quantification 1-100 ng/mL for glycosylated analytes, 30-1,000 ng/mL for aglycones, (3) averaged intraday precision 9%, (4) calibrated range 2-180,000 ng/mL for glycosylated analytes, 60-600,000 ng/mL for aglycones, and (5) averaged accuracy 101%. Applications for yogurt and ice cream products are given. The presented data suggest
that this method will help to better characterize the polyphenol composition of milk-based food products for quality control, for assessment of dietary intake, and for polyphenol bioavailability/bioefficacy studies.

PMID: 20337399 [PubMed - indexed for MEDLINE]

**Supplemental Content**


**Intake of a milk-based wolfberry formulation enhances the immune response of young-adult and aged mice.**

Vidal K, Benvacoub J, Sanchez-Garcia J, Foata F, Segura-Roggero I, Serrant P, Moser M, Blum S.

Nutrition and Health Department, Nestlé Research Center, Lausanne, Switzerland. karine.vidal@rdls.nestle.com

**Abstract**

Aging is associated with alterations of immune responses. Wolfberry, a popular Chinese functional ingredient, is prized for its anti-aging properties; however, little is known about the immunological effect of wolfberry intake. The purpose of this study was to examine the effect of dietary intake of a milk-based formulation of wolfberry, named Lacto-Wolfberry, on in vivo and ex vivo parameters of adaptive immunity in young-adult and aged mice. Over 44 days, young-adult (2 months) and aged (21 months) C57BL/6J mice were fed ad libitum with a controlled diet and received drinking water supplemented or not with 0.5% (wt/vol) Lacto-Wolfberry. All mice were immunized on day 15 and challenged on day 22 with a T cell-dependent antigen, keyhole limpet hemocyanin (KLH). Lacto-Wolfberry supplementation significantly increased in vivo systemic immune markers that are known to decline with aging. Indeed, both antigen-(KLH) specific humoral response and cell-mediated immune responses in young-adult and aged mice were enhanced when compared to their respective controls. No significant effect of Lacto-Wolfberry supplementation was observed on ex vivo spleen cells proliferative response to mitogens and on splenocyte T cell subsets. In conclusion, dietary intake of Lacto-Wolfberry may favorably modulate the poor responsiveness to antigenic challenge observed with aging.

PMID: 20230278 [PubMed - indexed for MEDLINE]

**Supplemental Content**
Dietary supplementation with medium-chain TAG has long-lasting cognition-enhancing effects in aged dogs.


Nestlé Purina Research, St Louis, MO 63164, USA. yuanlong.pan@rdmo.nestle.com

Abstract

The present study focused on the hypothesis that dietary supplementation with medium-chain TAG (MCT) will improve cognitive function in aged dogs by providing the brain with energy in the form of ketones. Aged Beagle dogs were subjected to a baseline battery of cognitive tests, which were used to establish cognitively equivalent control or treatment groups. The dogs in the treatment group were maintained on a diet supplemented with 5.5 % MCT. After an initial wash-in period, all the dogs were tested with a battery of cognitive test protocols, which assessed sequentially landmark discrimination learning ability, egocentric visuospatial function and attention. The groups were maintained on the diets for 8 months. The MCT-supplemented group showed significantly better performance in most of the test protocols than the control group. The group differences also varied as a function of task difficulty, with the more difficult task showing greater supplementation effects than the easier tasks. The group given the MCT supplement showed significantly elevated levels of beta-hydroxybutyrate, a ketone body. These results indicate, first, that long-term supplementation with MCT can have cognition-improving effects, and second, that MCT supplementation increases circulating levels of ketones. The results support the hypothesis that brain function of aged dogs can be improved by MCT supplementation, which provides the brain with an alternative energy source.

PMID: 20141643 [PubMed - indexed for MEDLINE]
Rosemary (Rosmarinus officinalis L.) leaf extract limits weight gain and liver steatosis in mice fed a high-fat diet.

Harach T, Aprikian O, Monnard I, Moulin J, Membrez M, Béolor JC, Raab T, Macé K, Darimont C.

Nestlé Research Center, Lausanne, Switzerland.

Abstract

The objective of this study was to investigate the effects of rosemary (Rosmarinus officinalis L.) leaf extract (RE) on the prevention of weight gain and associated metabolic disorders in mice fed a high-fat diet. For this purpose, RE was administered for 50 days at 20 or 200 mg/kg body weight (BW) to mice fed a high-fat diet. Body weight was monitored during the study and body composition was measured before and at the end of the intervention. Glucose tolerance, assessed by an intraperitoneal glucose tolerance test (IPGTT), and hepatic and faecal lipid contents were determined at the end of the study. Treatment with 200 mg/kg BW of RE induced a significant reduction of weight and fat mass gain (-64% and -57%, respectively) associated with an increase of faecal lipid excretion. This effect appears to be related to the inhibition of pancreatic lipase activity induced by RE, as demonstrated IN VITRO. While glucose tolerance and fasting glycaemia were not affected by RE treatment, hepatic triglyceride levels were decreased by 39% in RE-treated mice. Administration of the lower dose of RE (20 mg/kg BW) was ineffective on all the parameters measured. In conclusion, our results demonstrate that consumption of 200 mg/kg BW of RE can limit weight gain induced by a high-fat diet and protect against obesity-related liver steatosis.


PMID: 19918713 [PubMed - indexed for MEDLINE]

Supplemental Content


Effects of tryptophan loading on human cognition, mood, and sleep.

Silber BY, Schmitt JA.

Cognitive Sciences Group, Nestlé Research Centre, P.O. Box 44, CH-1000 Lausanne, Switzerland. beata.silber@rdls.nestle.com
Abstract

Modulating central serotonergic function by acute tryptophan depletion (ATD) has provided the fundamental insights into which cognitive functions are influenced by serotonin. It may be expected that serotonergic stimulation by tryptophan (Trp) loading could evoke beneficial behavioural changes that mirror those of ATD. The current review examines the evidence for such effects, notably those on cognition, mood and sleep. Reports vary considerably across different cognitive domains, study designs, and populations. It is hypothesised that the effects of Trp loading on performance may be dependent on the initial state of the serotonergic system of the subject. Memory improvements following Trp loading have generally been shown in clinical and sub-clinical populations where initial serotonergic disturbances are known. Similarly, Trp loading appears to be most effective for improving mood in vulnerable subjects, and improves sleep in adults with some sleep disturbances. Research has consistently shown Trp loading impairs psychomotor and reaction time performance, however, this is likely to be attributed to its mild sedative effects.

(c) 2009 Elsevier Ltd. All rights reserved.

PMID: 19715722 [PubMed - indexed for MEDLINE]

Supplemental Content

Food ingredients and cognitive performance.

le Coutre J, Schmitt JA.

Perception Physiology Group, Nestlé Research Center, Lausanne, Switzerland.

Abstract

PURPOSE OF REVIEW: To integrate recent discoveries in the cognitive neuroscience field on overall brain development, performance and energy requirements, with insight obtained on the cellular and molecular mechanisms of stimulation with food at the periphery.

RECENT FINDINGS: A clear picture emerges of the brain energy demand, its changes through life and the nutritional requirements to provide an optimally functioning intellect at any time. Of particular importance is the dynamic range resulting from differences between 'poor diet' and 'optimal diet'. On the basis of a healthy brain, the question becomes: what drives transient cognitive performance, and to what extent does food-related input from the periphery modulate cognition in general? Over the last decade, vast achievements in the understanding of chemosensory signal transduction on the tongue have been made. Most molecular receptors for various taste modalities have been identified, and the logic of their
coding into the brain has been largely unravelled. Moreover, an intriguing discovery has been made that most of the known taste receptors are also expressed in the gastrointestinal tract.

SUMMARY: Brain energy supply and balanced diet are being unravelled on the molecular and cellular levels as prerequisites for proper cognitive development. With additional insight emerging into the fundamentals of sensory stimulation and perception, we are entering a scientific era that ultimately will link metabolic needs with food preferences, hedonics and healthy nutrition.

PMID: 18827573 [PubMed - indexed for MEDLINE]

**Supplemental Content**


**Antioxidant activity of oregano, parsley, and olive mill wastewaters in bulk oils and oil-in-water emulsions enriched in fish oil.**

Jimenez-Alvarez D, Giuffrida F, Golay PA, Cotting C, Lardeau A, Keely BJ.

Nestle Research Centre, Lausanne, Vers-Chez-les-Blanc, 1000 Lausanne, Switzerland.

**Abstract**

The antioxidant activity of oregano, parsley, olive mill wastewaters (OMWW), Trolox, and ethylenediaminetetraacetic acid (EDTA) was evaluated in bulk oils and oil-in-water (o/w) emulsions enriched with 5% tuna oil by monitoring the formation of hydroperoxides, hexanal, and t-t-2,4-heptadienal in samples stored at 37 degrees C for 14 days. In bulk oil, the order of antioxidant activity was, in decreasing order (p < 0.05), OMWW > oregano > parsley > EDTA > Trolox. The antioxidant activity in o/w emulsion followed the same order except that EDTA was as efficient an antioxidant as OMWW. In addition, the total phenolic content, the radical scavenging properties, the reducing capacity, and the iron chelating activity of OMWW, parsley, and oregano extracts were determined by the Folin-Ciocalteau, oxygen radical absorbance capacity, ferric reducing antioxidant power, and iron(II) chelating activity assays, respectively. The antioxidant activity of OMWW, parsley, and oregano in food systems was related to their total phenolic content and radical scavenging capacity but not to their ability to chelate iron in vitro. OMWW was identified as a promising source of antioxidants to retard lipid oxidation in fish oil-enriched food products.

PMID: 18636737 [PubMed - indexed for MEDLINE]
Flavonoids for controlling starch digestion: structural requirements for inhibiting human alpha-amylase.

Lo Piparo E, Scheib H, Frei N, Williamson G, Grigorov M, Chou CJ.

Nestlé Research Center, Vers-chez-les-Blanc, PO Box 44, CH-1000 Lausanne 26, Switzerland. elena.lopiparo@rdls.nestle.com

Abstract

In this study we investigated the structural requirements for inhibition of human salivary alpha-amylase by flavonoids. Four flavonols and three flavones, out of the 19 flavonoids tested, exhibited IC50 values less than 100 microM against human salivary alpha-amylase activity. Structure-activity relationships of these inhibitors by computational ligand docking showed that the inhibitory activity of flavonols and flavones depends on (i) hydrogen bonds between the hydroxyl groups of the polyphenol ligands and the catalytic residues of the binding site and (ii) formation of a conjugated pi-system that stabilizes the interaction with the active site. Our findings show that certain naturally occurring flavonoids act as inhibitors of human alpha-amylase, which makes them promising candidates for controlling the digestion of starch and postprandial glycemia.

PMID: 18507367 [PubMed - indexed for MEDLINE]
Abstract

The effect of any dietary compound is influenced by the active bioavailable dose rather than the dose ingested. Depending on the individual predisposition, including genetics and medication, a bioavailable dose may cause different magnitudes of effects in different people. Age might affect the predisposition and thus the requirements for nutrients including phytonutrients (e.g. phytochemicals such as flavonoids, phenolic acids and glucosinolates). These are not essential for growth and development but to maintain body functions and health throughout the adult and later phases of life; they are 'lifespan essentials'. Major mechanisms involved in chronic, age-related diseases include the oxidant/antioxidant balance, but the latest research indicates indirect effects of dietary bioactives in vivo and adaptive responses in addition to direct radical scavenging.

PMID: 18406129 [PubMed - indexed for MEDLINE]

Supplemental Content


Interactions affecting the bioavailability of dietary polyphenols in vivo.

Scholz S, Williamson G.

Nestlé Research Center, Vers chez les Blanc, 1000 Lausanne 26, Switzerland.

Abstract

Polyphenols are widely abundant dietary constituents in plants that are associated with health-promoting effects. This review summarizes factors influencing the bioavailability of polyphenols, specifically flavanols, flavonols, flavanones, flavones, and hydroxycinnamic (phenolic) acids. Most factors tested so far indicate that bioaccessibility, defined as the amount of compound reaching the enterocyte in a form suitable for absorption, is the most important factor determining the absorption in the gut. Factors leading to an improved absorption of flavonols, notably quercetin and its metabolites, are primarily the nature of the attached sugar, and secondly, the solubility as modified by ethanol, fat, and emulsifiers. The absorption of flavanols, notably green tea catechins, is affected by epimerization reactions occurring during processing, the presence of lipid and carbohydrate, and is improved by the presence of piperine and tartaric acid. Flavanones, such as hesperidin, are strongly affected by the type of attached sugar. Phenolic acids are affected by the attached sugar, which can covalently link these compounds to the cereal bran matrix. In the few examples tested, absorption of polyphenols is dependent on release from the food matrix. There are only a few
examples reported, but where information is available, the absorption increases with dose but
is sometimes linear and sometimes saturated. The lack of systematic information on the
effects of other components on the bioavailability of polyphenols needs to be addressed, and
more human studies should be conducted in this field to establish general principles affecting
absorption in vivo. Information derived from such experiments could be useful for the optimal
design of future bioefficacy studies.


Feeding a diet containing a
fructooligosaccharide mix can enhance
Salmonella vaccine efficacy in mice.

Benyacoub J, Rochat F, Saudan KY, Rochat I, Antille N, Cherbut C, von der Weid T,
Schiffrin EJ, Blum S.

Nestlé Research Center, CH-1000, Lausanne 26, Switzerland.
jalil.benyacoub@rdls.nestle.com

Abstract

Fructooligosaccharides (FOS) are considered prebiotics because of their ability to promote
growth of specific beneficial gut bacteria, such as bifidobacteria. Some studies reported
potential immune-modulating properties. The aim of this study was to investigate the effect of
FOS:inulin mix on murine response to Salmonella vaccine and evaluate the relevance toward
protection against Salmonella infection. Balb/c mice were fed a diet containing 5%
FOS:inulin mix or a control diet 1 wk before oral immunization with a suboptimal dose of
live attenuated Salmonella typhimurium vaccine. Four weeks after vaccination, mice were
infected with LD100 of virulent S. typhimurium. Specific blood Salmonella immunoglobulin
G and fecal immunoglobulin A significantly increased in mice fed the diet containing
prebiotics compared with control mice 4 wk postimmunization. Peritoneal macrophage
phagocytic activity also significantly increased in FOS:inulin-fed mice at 1 wk
postimmunization compared with control mice. No detectable effects were observed on the
percentage of lymphoid cell subsets in the spleen. However, production of cytokines,
interferon-gamma, interleukin-12, and tumor necrosis factor alpha, was numerically increased
in spleen cell cultures stimulated with mitogens from FOS:inulin-fed mice 1 and 4 wk
postimmunization. Salmonella translocation to lymphoid organs was not affected by feeding
FOS:inulin. However, the improved response to Salmonella vaccine was concomitant with an
increase in the survival rate of FOS:inulin-fed mice upon challenge with virulent Salmonella.
No detectable effects were observed on the composition or the metabolic activity of the
microbiota. Overall, the data suggest that a diet supplemented with FOS:inulin mix stimulates
mucosal immunity and seems to improve efficacy of an oral vaccine.


Supplemental Content
Review of the factors affecting bioavailability of soy isoflavones in humans.

Nielsen IL, Williamson G.

Nutrient Bioavailability Group, Nestle Research Center, Lausanne, Switzerland.

Abstract

Soy isoflavones have anticarcinogenic, antioxidant, and antiatherosclerotic activities. They also interact with the estrogen receptor, which makes them weak or moderate phytoestrogens. Because of their bioactivity, isoflavone bioavailability has been extensively studied in humans. This review summarizes data from intervention studies in humans, focusing on the factors that affect bioavailability. Summarizing data from 16 studies shows that the maximum concentration in plasma normalized to a constant dose of genistin is approximately 1.6 times that of genistein, and daidzin is approximately 1.8-fold higher than daidzein, whereas the half-life is not significantly different for aglycone and glucoside. There is a wide variation in the reported percentage urinary excretion that is not dependent on dose. Bioavailability is increased by a rapid gut transit time and by low fecal digestion rates and is decreased by a fiber-rich diet. There is no difference in bioavailability between pre- and postmenopausal women. The daily ingestion of soymilk for 1 wk does not affect bioavailability, but daily ingestion for a month increases excretion of equol in women. The factors or habitual diet characteristics that influence equol production are not clear, but equol production is limited with an immature flora. There is no consensus on which source of isoflavones results in the highest isoflavone bioavailability, and published studies present different results, although bioavailability is affected by whether the dose is given as food or drink. In conclusion, it is important to consider the factors affecting bioavailability of isoflavones when designing intervention studies.

Effect of 3-year folic acid supplementation on cognitive function in older adults in the FACIT trial: a randomised, double blind, controlled trial.

Durga J, van Boxtel MP, Schouten EG, Kok FJ, Jolles J, Katan MB, Verhoeef P.
Abstract

BACKGROUND: Low folate and raised homocysteine concentrations in blood are associated with poor cognitive performance in the general population. As part of the FACIT trial to assess the effect of folic acid on markers of atherosclerosis in men and women aged 50-70 years with raised plasma total homocysteine and normal serum vitamin B12 at screening, we report here the findings for the secondary endpoint: the effect of folic acid supplementation on cognitive performance.

METHODS: Our randomised, double blind, placebo controlled study took place between November, 1999, and December, 2004, in the Netherlands. We randomly assigned 818 participants 800 mug daily oral folic acid or placebo for 3 years. The effect on cognitive performance was measured as the difference between the two groups in the 3-year change in performance for memory, sensorimotor speed, complex speed, information processing speed, and word fluency. Analysis was by intention-to-treat. This trial is registered with clinicaltrials.gov with trial number NCT00110604.

FINDINGS: Serum folate concentrations increased by 576% (95% CI 539 to 614) and plasma total homocysteine concentrations decreased by 26% (24 to 28) in participants taking folic acid compared with those taking placebo. The 3-year change in memory (difference in Z scores 0.132, 95% CI 0.032 to 0.233), information processing speed (0.087, 0.016 to 0.158) and sensorimotor speed (0.064, -0.001 to 0.129) were significantly better in the folic acid group than in the placebo group.

INTERPRETATION: Folic acid supplementation for 3 years significantly improved domains of cognitive function that tend to decline with age.

PMID: 17240287 [PubMed - indexed for MEDLINE]

Supplemental Content

Effect of a fish oil and arginine-fortified diet in thermally injured patients.

Wibbenmeyer LA, Mitchell MA, Newel IM, Faucher LD, Amelon MJ, Ruffin TO, Lewis RD 2nd, Latenser BA, Kealey PG.

Department of Surgery, The University of Iowa Carver College of Medicine, Iowa City, Iowa 52246, USA.


Abstract

Burn injury induces a hypercatabolic inflammatory state, predisposing burn patients to malnutrition, poor wound healing, and infectious complications. We conducted this study to determine what effect a diet fortified with fish oil and arginine (FAD) would have on wound healing in a thermally injured population. Twenty-three thermally injured patients were enrolled in this randomized double blind enteral feeding study from July 2002 to August 2004. All study patients received isonitrogenous enteral intragastric feeding within 48 hours of admission. Patients were randomized to our standard diet (STD, ProBalance with Promix, Probalance from Nestlé, Glendale, CA; ProMix R.D., Navaco Laboratories, Phoenix, AZ) or a diet fortified with fish oil and arginine (FAD, Crucial, Nestlé Nutrition Glendale, CA) Diets were advanced as tolerated to meet 100% of estimated needs. The primary endpoint of the study was time to heal the first donor site. There were no statistical differences between the study groups with respect to baseline characteristics. Both diets were well tolerated, and there were no differences in the daily total kilocalories or protein intake per kilogram between the two diet groups throughout the study. Although nonsignificant, the patients in the FAD group showed a slightly faster healing time than those in the STD group (10.8 +/- 2.7 days vs 12.3 +/- 5.2 days, respectively). This trend was further accelerated when those with body surface area burns less than 30% were examined (patients with body surface area burns <30% in the FAD healed in 9.0 +/- 1.7 vs corresponding patients in the standard group who healed in 12.2 +/- 6.2, P = .63). Patients in the FAD group trended to more infections and more adverse complications. The adverse complications were predominantly associated with inhalation injuries. The role of fortified enteral diets in the outcomes of thermally injured patients deserves further study. Such a future study should be conducted in a multicenter trial and involve inhalation injury stratification systems to accurately score and randomize patients for inhalation injury. Finally, the frequency and pattern of infections in patients receiving fortified enteral diets deserves further evaluation.

PMID: 16998403 [PubMed - indexed for MEDLINE]

Supplemental Content
Osteoarthritis and nutrition. From nutraceuticals to functional foods: a systematic review of the scientific evidence.

Ameye LG, Chee WS.

Nutrition and Health Department, Nestlé Research Center, Vers-chez-les-Blanc, 1000 Lausanne 26, Switzerland. laurent.ameye@rdls.nestle.com

Abstract

The scientific and medical community remains skeptical regarding the efficacy of nutrition for osteoarthritis despite their broad acceptation by patients. In this context, this paper systematically reviews human clinical trials evaluating the effects of nutritional compounds on osteoarthritis. We searched the Medline, Embase, and Biosis databases from their inception to September 2005 using the terms random, double-blind method, trial, study, placebo, and osteoarthritis. We selected all peer-reviewed articles reporting the results of randomised human clinical trials (RCTs) in osteoarthritis that investigated the effects of oral interventions based on natural molecules. Studies on glucosamine and chondroitin sulfate were excluded. The quality of the RCTs was assessed with an osteoarthritic-specific standardised set of 12 criteria and a validated instrument. A best-evidence synthesis was used to categorise the scientific evidence behind each nutritional compound as good, moderate, or limited. A summary of the most relevant in vitro and animal studies is used to shed light on the potential mechanisms of action. Inclusion criteria were met by 53 RCTs out of the 2,026 identified studies. Good evidence was found for avocado soybean unsaponifiables. Moderate evidence was found for methylsulfonylmethane and SKI306X, a cocktail of plant extracts. Limited evidence was found for the Chinese plant extract duhuo jisheng Wan, cetyl myristoleate, lipids from green-lipped mussels, and plant extracts from Harpagophytum procumbens. Overall, scientific evidence exists for some specific nutritional interventions to provide symptom relief to osteoarthritic patients. It remains to be investigated whether nutritional compounds can have structure-modifying effects.

PMID: 16859534 [PubMed - indexed for MEDLINE]PMCID: PMC1779427Free PMC Article

Supplemental Content

Antioxidant status of pair-fed labrador retrievers is affected by diet restriction and aging.

Stowe HD, Lawler DF, Kealy RD.

Nestle Purina Petcare Company, St. Louis, MO 63164, USA. hdstowe@msu.edu

Abstract

Twenty-four sibling pairs of 8-wk-old Labrador Retrievers were assigned to an experiment to determine the effects of diet restriction (75% of control-fed pair mate) on the quality and span of canine life and to identify biological markers of aging in dogs. The antioxidant status of these dogs was monitored by annual assays for serum retinol (RT), retinyl palmitate (RP), total vitamin A (VA), vitamin E (VE), selenium (Se), copper (Cu), and ceruloplasmin (Cp), plasma ascorbic acid (AA), uric acid (UA), and total peroxyl-radical trapping activity (TRAP), and whole-blood glutathione peroxidase (Gpx). Data in this report are for the 6-y period of the experiment when the dogs were between 5 and 10 y of age. Diet restriction reduced RT, VE, Cu, and Cp. Aging was associated with decreased RP, VA, VE, Se, and Cu and with increased RT, Cp, and Gpx. Female dogs had lower RP, VA, Cu, and Cp than male dogs. Litter effects were observed for VE, Cu, UA, and Gpx. Treatment effects on serum RT and Cu suggest that these variables are not as regulated homeostatically by hepatic storage as in most other species. Although the antioxidant profiles did not elucidate how diet restriction contributes to longevity, they have the potential to enhance our understanding of canine clinical nutrition and to have practical applications in formulating canine diets.

PMID: 16772447 [PubMed - indexed for MEDLINE]

Bioavailability is improved by enzymatic modification of the citrus flavonoid hesperidin in humans: a randomized, double-blind, crossover trial.

Abstract

Hesperidin is the predominant polyphenol consumed from citrus fruits and juices. However, hesperidin is proposed to have limited bioavailability due to the rutinoside moiety attached to the flavonoid. The aim of this study was to demonstrate in human subjects that the removal of the rhamnose group to yield the corresponding flavonoid glucoside (i.e., hesperetin-7-glucoside) will improve the bioavailability of the aglycone hesperetin. Healthy volunteers (n=16) completed the double-blind, randomized, crossover study. Subjects randomly consumed hesperetin equivalents supplied as orange juice with natural hesperidin ("low dose"), orange juice treated with hesperidinase enzyme to yield hesperetin-7-glucoside, and orange juice fortified to obtain 3 times more hesperidin than naturally present ("high dose"). The area under the curve (AUC) for total plasma hesperetin of subjects consuming hesperetin-7-glucoside juice was 2-fold higher than that of subjects consuming the "low" dose hesperidin juice [3.45+/-1.27 vs. 1.16+/-0.52 mmol/(L.h), respectively, P>0.0001]. The AUC for hesperetin after consuming the hesperetin-7-glucoside juice was improved to the level of the "high" dose hesperidin juice [4.16+/-1.50 mmol/(L.h)]. The peak plasma concentrations (C(max)) of hesperetin were 4-fold higher (2.60+/-1.07 mmol/L, P<0.0001) after subjects consumed hesperetin-7-glucoside juice compared with those consuming "low" dose hesperidin juice (0.48 +/- 0.27 mmol/L), and 1.5-fold higher than those consuming "high" dose hesperidin juice (1.05+/-0.25 mmol/L). The corresponding T(max) was much faster (0.6+/-0.1 h, P<0.0001) after subjects consumed hesperetin-7-glucoside juice compared with "low" dose (7.0+/-3.0 h) and "high" dose (7.4+/-2.0 h) hesperidin juices. The results of this study demonstrated that the bioavailability of hesperidin was modulated by enzymatic conversion to hesperetin-7-glucoside, thus changing the absorption site from the colon to the small intestine. This may affect future interventions concerning the health benefits of citrus flavonoids.


Supplemental Content


Beneficial effect of amino acid supplementation, especially cysteine, on body nitrogen economy in septic rats.

Breuillé D, Béchereau F, Buffière C, Denis P, Pouyet C, Obled C.

Centre de Recherches Nestlé, Vers chez-les-blanc, P.O. Box 44 CH1000, Lausanne 26, Switzerland.
Abstract

BACKGROUND AND AIMS: Muscle wasting and increased synthesis of proteins and compounds involved in host defense characterize severe injury. The aims of the studies reported were to determine which amino acids exhibited an increased tissue content linked to anabolic processes in infected rats by comparison with healthy pair-fed controls, and to explore whether diets supplemented with these amino acids attenuate the catabolic response to infection.

METHODS: Total amino acid content of the liver and the rest of the body were measured in control well-fed rats, in infected rats and their pair-fed controls 2 days after infection. In the nutritional protocols, infected rats were fed with a diet supplemented with alanine (basal diet), or threonine, serine, aspartate, asparagine and arginine (AA) or AA+cysteine (complete diet).

RESULTS: Infection significantly increased liver total amino acid content by 38% for most amino acids. In contrast, the percentage increase was cysteine 79.3, threonine 45.3, aspartate-asparagine 46.3 and serine 46.5. Whole body without liver content of most amino acids decreased after infection due to the catabolic response, while the content of cysteine increased by 6% (P<0.05) and those of threonine and arginine did not decrease. After infection, animals fed the complete diet lost less weight than animals fed the basal diet (P<0.05). Furthermore, AA plus cysteine supplementation reduced significantly urinary nitrogen excretion and muscle wasting.

CONCLUSIONS: The results provide evidence that diet supplementation with cysteine, threonine, serine, aspartate-asparagine and arginine supports the synthesis of vital proteins to spare body protein catabolism during infection.

PMID: 16387396 [PubMed - indexed for MEDLINE]

Supplemental Content