

ABSTRACTS

Boron

Chemical composition and potential health effects of prunes: a functional food?

Prunes are dried plums, fruits of *Prunus domestica* L., cultivated and propagated since ancient times. Most dried prunes are produced from cultivar d'Agen, especially in California and France, where the cultivar originated. After harvest, prune-making plums are dehydrated in hot air at 85 to 90 degrees C for 18 h, then further processed into prune juice, puree, or other prune products. This extensive literature review summarizes the current knowledge of chemical composition of prunes and their biological effects on human health. Because of their sweet flavor and well-known mild laxative effect, prunes are considered to be an epitome of functional foods, but the understanding of their mode of action is still unclear. Dried prunes contain approximately 6.1 g of dietary fiber per 100 g, while prune juice is devoid of fiber due to filtration before bottling. The laxative action of both prune and prune juice could be explained by their high sorbitol content (14.7 and 6.1 g/100 g, respectively). Prunes are good source of energy in the form of simple sugars, but do not mediate a rapid rise in blood sugar concentration, possibly because of high fiber, fructose, and sorbitol content. Prunes contain large amounts of phenolic compounds (184 mg/100 g), mainly as neochlorogenic and chlorogenic acids, which may aid in the laxative action and delay glucose absorption. Phenolic compounds in prunes had been found to inhibit human LDL oxidation in vitro, and thus might serve as preventive agents against chronic diseases, such as heart disease and cancer. Additionally, high potassium content of prunes (745 mg/100 g) might be beneficial for cardiovascular health. Dried prunes are an important source of boron, which is postulated to play a role in prevention of osteoporosis. A serving of prunes (100 g) fulfills the daily requirement for boron (2 to 3 mg). More research is needed to assess the levels of carotenoids and other phytochemicals present in prunes to ensure correct labeling and accuracy of food composition tables in order to support dietary recommendations or health claims.

Crit Rev Food Sci Nutr. 2001 May;41(4):251-86

The biochemical effects of physiologic amounts of dietary boron in animal nutrition models.

This review summarizes evidence that supports working hypotheses for the roles of boron in animal model systems. It is well established that vascular plants, diatoms, and some species of marine algal flagellates have acquired an absolute requirement for boron, although the primary role of boron in plants remains unknown. Recent research findings suggest that physiologic amounts of supplemental dietary boron (PSB) affect a wide range of metabolic parameters in the chick and rat model systems. Much of the current interest in boron animal nutrition began with the initial finding that PSB stimulates growth in cholecalciferol (vitamin D3)-deficient chicks, but does not markedly affect growth in chicks receiving adequate vitamin D3 nutrition. The finding suggests that boron affects some aspect of vitamin D3 metabolism or is synergistic with vitamin D3 in influencing growth. Vitamin D3 regulates energy substrate utilization, and current research findings indicate that dietary boron modifies that regulatory function. The concentration of circulating glucose, the most thoroughly investigated metabolite to date, responds to PSB, especially during concomitant vitamin D3 deficiency. In chicks, PSB substantially alleviated or corrected vitamin D3 deficiency-induced elevations in plasma glucose concentrations. The influence of vitamin D3 on cartilage and bone mineralization is mediated in part through its role as a regulator of energy substrate utilization; calcification is an energy-intensive process. There is considerable evidence that dietary boron alleviates perturbations in mineral metabolism that are characteristic of vitamin D3 deficiency. In rachitic chicks, PSB alleviated distortion of the marrow sprouts of the proximal tibial epiphysial plate, a distortion characteristic of vitamin D3 deficiency.

Environ Health Perspect. 1994 Nov;102 Suppl 7:35-43

Studies on the relationship between boron and magnesium which possibly affects the formation and maintenance of bones.

Recent findings are reviewed indicating that changes in dietary boron and magnesium affect calcium, and thus bone, metabolism in animals and humans. In animals, the need for boron was found to be enhanced when they needed to respond to a nutritional stress which adversely affected calcium metabolism, including magnesium deficiency. A combined deficiency of boron and magnesium caused detrimental changes in the bones of animals. However, boron deprivation did not seem to enhance the requirement for magnesium. In two human studies, boron deprivation caused changes in variables associated with calcium metabolism in a manner that could be construed as being detrimental to bone formation and maintenance; these changes apparently were enhanced by low dietary magnesium. Changes caused by boron deprivation included depressed plasma ionized calcium and calcitonin as well as elevated plasma total calcium and urinary excretion of calcium. In one human study, magnesium deprivation depressed plasma ionized calcium and cholesterol. Because boron and/or magnesium deprivation causes changes similar to those seen in women with postmenopausal osteoporosis, these elements are apparently needed for

optimal calcium metabolism and are thus needed to prevent the excessive bone loss which often occurs in postmenopausal women and older men.

Magnes Trace Elem. 1990;9(2):61-9

Treatment of early recurrent prostate cancer with 1,25-dihydroxyvitamin D3 (calcitriol)

PURPOSE: Substantial experimental and epidemiological data indicate that 1,25-dihydroxyvitamin D3 (calcitriol) has potent antiproliferative effects on human prostate cancer cells. We performed an open label, nonrandomized pilot trial to determine whether calcitriol therapy is safe and efficacious for early recurrent prostate cancer. Our hypothesis was that calcitriol therapy slows the rate of rise of prostate specific antigen (PSA) compared with the pretreatment rate. **MATERIALS AND METHODS:** After primary treatment with radiation or surgery recurrence was indicated by rising serum PSA levels documented on at least 3 occasions. Seven subjects completed 6 to 15 months of calcitriol therapy, starting with 0.5 microg. calcitriol daily and slowly increasing to a maximum dose of 2.5 microg. daily depending on individual calciuric and calcemic responses. Each subject served as his own control, comparing the rate of PSA rise before and after calcitriol treatment. **RESULTS:** As determined by multiple regression analysis, the rate of PSA rise during versus before calcitriol therapy significantly decreased in 6 of 7 patients, while in the remaining man a deceleration in the rate of PSA rise did not reach statistical significance. Overall the decreased rate of PSA rise was statistically significant ($p = 0.02$ Wilcoxon signed rank test). Dose dependent hypercalciuria limited the maximal calcitriol therapy given (range 1.5 to 2.5 microg. daily). **CONCLUSIONS:** This pilot study provides preliminary evidence that calcitriol effectively slows the rate of PSA rise in select cases, although dose dependent calciuric side effects limit its clinical usefulness. The development of calcitriol analogues with decreased calcemic side effects is promising, since such analogues may be even more effective for treating prostate cancer.

J Urol. 1998 Jun;159(6):2035-9; discussion 2039-40

Boron neutron capture therapy for malignant gliomas.

Boron neutron capture therapy (BNCT) represents a promising modality for a relatively selective radiation dose delivery to the tumour tissue. Boron-10 nuclei capture slow 'thermal' neutrons preferentially and, upon capture, promptly undergo $^{10}\text{B}(n,\alpha)^7\text{Li}$ reaction. The ionization tracks of energetic and heavy lithium and helium ions resulting from this reaction are only about one cell diameter in length (approximately 14 microm). Because of their high linear energy transfer (LET) these ions have a high relative biological effectiveness (RBE) for controlling tumour growth. The key to effective BNCT of tumours, such as glioblastoma multiforme (GBM), is the preferential accumulation of boron-10 in the tumour, including the infiltrating GBM cells, as compared with that in the vital structures of the normal brain. Provided that a sufficiently high tumour boron-10 concentration (approximately 10^9 boron-10 atoms/cell) and an adequate thermal neutron fluence (approximately 10^{12} neutrons/cm²) are achieved, it is the ratio of the boron-10 concentration in tumour cells to that in the normal brain cells that will largely determine the therapeutic gain of BNCT.

Ann Med. 2000 Feb;32(1):81-5

Homocysteine

Prevalence and mechanisms of hyperhomocysteinemia in elderly hospitalized patients.

BACKGROUND: Plasma homocysteine concentrations increase with age and remain an independent risk factor for vascular disease in the elderly. There are negative correlations between plasma homocysteine and serum folate and vitamin B12 concentrations. Two mechanisms, poor nutritional status, and chronic atrophic gastritis, could explain hyperhomocysteinemia. **OBJECTIVE:** The purpose of the study was to determine prevalence and mechanisms of hyperhomocysteinemia in older hospitalized patients. **DESIGNS:** During a 12-month period, all the consecutive hospitalized patients who underwent gastric endoscopy were recruited in this observational prospective study. Clinical, histological, and biological data concerning nutritional status, gastric analysis, homocysteine, vitamin B12, and folate concentrations were collected during the study for each included patient. **RESULTS:** One hundred and ninety six patients (132 women and 64 men, mean age: 85.3 \pm 5.7 years) were included. Hyperhomocysteinemia (> 18 mmol/l) was diagnosed in 45.4 %, cobalamin deficiency in 13.3 %, and folate deficiency in 11.7 % patients. Hyperhomocysteinemia was significantly correlated to cobalamin deficiency ($r = -0.21$; $p = 0.005$). In a sub group of patients without hypothyroidism, or chronic renal impairment, univariate and multivariate analysis showed a significant association between hyper homocysteinemia and low MNA (OR: 0.92; 95% CI 0.85-0.99), and low albumin (OR: 0.92; 95% IC: 0.83-0.99; $p = 0.04$). No correlation was found between homocysteine concentrations and chronic atrophic gastritis or Helicobacter pylori infection. **CONCLUSION:** Hyperhomocysteinemia seems to be frequent in the elderly and is associated with poor nutritional status rather than chronic atrophic gastritis. *J Nutr Health Aging. 2003;7(2):111-6* Hyperhomocysteinemia and low pyridoxal phosphate. Common and independent reversible risk factors for coronary artery disease. **BACKGROUND:** High plasma homocysteine is associated with premature coronary artery disease in men, but the threshold concentration defining this risk and its importance in women and the elderly are unknown. Furthermore, although low B vitamin status increases homocysteine, the link between these vitamins and coronary disease is unclear. **METHODS AND RESULTS:** We compared 304 patients with coronary disease with 231 control subjects. Risk factors and concentrations of plasma homocysteine, folate, vitamin B12, and pyridoxal 5'-phosphate were documented. A homocysteine concentration of 14 $\mu\text{mol/L}$ conferred an odds ratio of coronary

disease of 4.8 ($P < .001$), and 5-mumol/L increments across the range of homocysteine conferred an odds ratio of 2.4 ($P < .001$). Odds ratios of 3.5 in women and of 2.9 in those 65 years or older were seen ($P < .05$). Homocysteine correlated negatively with all vitamins. Low pyridoxal 5'-phosphate (< 20 nmol/L) was seen in 10% of patients but in only 2% of control subjects ($P < .01$), yielding an odds ratio of coronary disease adjusted for all risk factors, including high homocysteine, of 4.3 ($P < .05$).

CONCLUSIONS: Within the range currently considered to be normal, the risk for coronary disease rises with increasing plasma homocysteine regardless of age and sex, with no threshold effect. In addition to a link with homocysteine, low pyridoxal-5'-phosphate confers an independent risk for coronary artery disease.

Circulation. 1995 Nov 15;92(10):2825-30

Hyperhomocysteinemia and related factors in 600 hospitalized elderly subjects.

Hyperhomocysteinemia (HHcy) is a metabolic disorder frequently occurring in the elderly population. Recently several reports have suggested abnormalities in homocysteine (tHcy) metabolism implicating HHcy as a metabolic link in the multifactorial processes characterizing many geriatric illnesses-with special emphasis on atherosclerotic vascular diseases and cognitive impairment. The present study was undertaken in a large sample of elderly hospitalized subjects to determine (1) the prevalence of HHcy, (2) the association of HHcy with vascular and cognitive disorders, and (3) the factors independently predicting HHcy. Six hundred elderly subjects (264 men and 336 women; mean age, 79 +/- 9 years) were randomly chosen from those admitted as inpatients over a period of 3 years. In all patients, body mass index (BMI), mid-upper arm muscle area (MUAMA), plasma cholesterol, triglycerides, total proteins, albumin, lymphocyte count, creatinine, homocysteine (fasting and 4 hours after methionine oral load), serum vitamin B(6), vitamin B(12), and folate concentrations were measured. The presence of disease or use of medications known to affect homocysteine plasma levels were also recorded. The mean fasting tHcy level was 16.8 +/- 12 micromol/L in the whole sample, 18.18 +/- 13.25 micromol/L in men, and 15.86 +/- 12.14 micromol/L in women ($P = .005$ men v women). The mean Hcy level 4 hours after methionine load was 37.95 +/- 20.9 in the whole sample. Prevalence of hyperhomocysteinemia (fasting Hcy ≥ 15 micromol/L or 4 hours after methionine load ≥ 35 micromol/L) was 61% (365/600) (67% in men and 56% in women, $P < .05$). HHcy was rarely (8%) an isolated disorder; in addition to diabetes (20%), renal failure (48.2%), and malnutrition (20.2%), it was often associated with heart failure (30%), malignancies (20.5%), and the use of diuretics (56%) and anticonvulsant drugs (13%). Plasma homocysteine progressively increases across subjects from those with no diabetes, malnutrition, renal failure, obesity, inflammatory bowel disease, heart failure to those with 1, 2, or more concurrent diseases. Multiple stepwise regression analysis showed that 72% of plasma total fasting tHcy variability was explained by age, serum folate, plasma albumin, use of diuretics, and renal function (measured as plasma creatinine clearance). In conclusion, the present study documents that hyperhomocysteinemia, in elderly hospitalized patients is (1) a common finding, (2) frequently associated with vascular and cognitive disorders, and (3) probably a secondary phenomenon in most cases. The major predictor of high plasma homocysteine levels were age, serum folate, plasma albumin, plasma creatinine clearance, and use of diuretic drugs. These variables explain a large proportion of plasma Hcy variability.

Metabolism. 2001 Dec;50(12):1466-71

Hyperhomocysteinemia in advanced age.

Nutritional deficiency does not fit the view of life in an affluent society and in fact typical diseases resulting from a deficiency of vitamins are actually a rarity. On the other hand, elderly people must be regarded as an essential risk group for vitamin deficiency because of various influence factors. The frequency of lowered vitamin concentrations in the blood increases with age. However, knowledge on the consequences for this population is insufficient, especially for hyperhomocysteinemia. Investigations have yielded the following results: 1. Hyperhomocysteinemia often occurs with advanced age; 2. Impairment of physical condition or social situation seems to increase the risk of hyperhomocysteinemia; 3. Administration of the vitamins B6, B12 and folate causes a significant decrease of elevated serum homocysteine concentrations in older persons. Homocysteine-lowering treatment should improve the prevention of chronic diseases. The question is which effects can be expected from such treatment in the elderly. Because of its great importance for both the persons concerned and society in general hyperhomocysteinemia in advanced age requires further systematic examination.

Clin Chem Lab Med. 2001 Aug;39(8):695-7

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