



Get the Science Vitamin C: All-C & Super-C

Get the science behind All-C and Super-C with Peer Reviewed Studies that support ingredients found in these amazing products.



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Peer Reviewed Studies

Antioxidant Support

Vitamin C supplementation lowers urinary levels of 4-hydroperoxy-2-nonenal metabolites in humans

ABSTRACT

The lack of suitable biomarkers of oxidative stress is a common problem for antioxidant intervention studies in humans. We evaluated the efficacy of vitamin C supplementation in decreasing biomarkers of lipid peroxidation in nonsmokers and in cigarette smokers, a commonly studied, free-living human model of chronic oxidative stress. Participants received ascorbic acid (500mg twice per day) or placebo for 17 days in a double-blind, placebo-controlled, randomized crossover design study. The urinary biomarkers assessed and reported herein are derived from 4-hydroperoxy-2-nonenal (HPNE) and include the mercapturic acid (MA) conjugates of 4-hydroxy-2(E)-nonenal (HNE), 1,4-dihydroxy-2(E)-nonene (DHN), and 4-oxo-2(E)-nonenol(ONO). Vitamin C supplementation decreased the urinary concentrations of both ONO-MA ($p=0.0013$) and HNE-MA ($p=0.0213$) by ~30%; however, neither cigarette smoking nor sex affected these biomarkers. In contrast, vitamin C supplementation decreased urinary concentrations of DHN-MA (three-way interaction $p=0.0304$) in nonsmoking men compared with nonsmoking women ($p<0.05$), as well as in nonsmoking men compared with smoking men ($p<0.05$). Vitamin C supplementation also decreased ($p=0.0092$) urinary total of metabolites by ~20%. Thus, HPNE metabolites can be reduced favorably in response to improved plasma ascorbic acid concentrations, an effect due to ascorbic acid antioxidant function.

Source: Kuiper HC, Bruno RS, Traber MG, Stevens JF. Vitamin C supplementation lowers urinary levels of 4-hydroperoxy-2-nonenal metabolites in humans. Free Radic Biol Med. 2011;50(7):848-853. doi:10.1016/j.freeradbiomed.2011.01.004

Effects of vitamin C on oxidative stress, inflammation, muscle soreness, and strength following acute exercise: meta-analyses of randomized clinical trials

ABSTRACT

Background: The combined supplementation of vitamins C and E potentially can mitigate oxidative stress (OS) and accelerate recovery following exercise. However, there is little evidence and a lack of consensus on the effects of these vitamins for this purpose. The objective of this systematic review was to summarize the evidence on the effects of the combined supplementation of vitamins C and E in OS, inflammatory markers, muscle damage, muscle soreness, and musculoskeletal functionality following acute exercise.

Methods: The search was carried out from inception until March 2021, on MEDLINE, EMBASE, Cochrane CENTRAL, Web of Science, and SPORT Discus. We included placebo-controlled randomized clinical trials (RCTs) that evaluated the effects of combined supplementation of vitamins C and E in OS, inflammatory markers, muscle damage, muscle soreness, and muscle strength following a single bout of exercise. Random-effect meta-analyses were used to compare pre- to post-exercise mean changes in subjects who received supplementation with vitamins C and E or placebo versus controls. Data are presented as standard mean difference (SMD) and 95% confidence interval (95% CI).

Results: Eighteen RCTs, accounting for data from 322 individuals, were included. The use of vitamins attenuated lipid peroxidation (SMD= -0.703; 95% CI= -1.035 to -0.372; $p < 0.001$), IL-6 (SMD= -0.576; 95%CI= -1.036 to -0.117; $p = 0.014$), and cortisol levels (SMD= -0.918; 95%CI= -1.475 to -0.361; $p = 0.001$) immediately, and creatine kinase levels 48 h following exercise (SMD= -0.991; 95%CI= -1.611 to -0.372; $p = 0.002$). Supplementing the combination of vitamins had no effects on protein carbonyls, reduced/oxidized glutathione ratio, catalase, interleukin-1Ra, C-reactive protein, lactate dehydrogenase, muscle soreness, and muscle strength.

Conclusion: Prior supplementation of the combination of vitamins C and E attenuates OS (lipid peroxidation), the inflammatory response (interleukin-6), cortisol levels, and muscle damage (creatinase) following a session of exercise.

Source: Santos de Lima K, Schuch FB, Camponogara Righi N, et al. Effects of the combination of vitamins C and E supplementation on oxidative stress, inflammation, muscle soreness, and muscle strength following acute physical exercise: meta-analyses of randomized controlled trials. Crit Rev Food Sci Nutr. 2023;63(25):7584-7597. doi:10.1080/10408398.2022.2048290

Faster plasma vitamin E disappearance in smokers is normalized by vitamin C supplementation

ABSTRACT

Vitamin E disappearance is accelerated in cigarette smokers due to their increased oxidative stress and is inversely correlated with plasma vitamin C concentrations. Therefore, we hypothesized that ascorbic acid supplementation (500 mg, twice daily; 2 weeks) would normalize smokers' plasma alpha- and gamma-tocopherol disappearance rates and conducted a double-blind, placebo-controlled, randomized crossover investigation in smokers (n=11) and nonsmokers (n=13) given a single dose of deuterium-labeled alpha- and gamma-tocopherols (50 mg each d6-RRR-alpha and d2-RRR-gamma-tocopheryl acetate). During the placebo trial, smokers, compared with nonsmokers, had significantly (P<0.05) greater alpha- and gamma-tocopherol fractional disappearance rates and shorter half-lives. Ascorbic acid supplementation doubled (P<0.0001) plasma ascorbic acid concentrations in both groups and attenuated smokers', but not nonsmokers', plasma alpha- and gamma-tocopherol (P<0.05) fractional disappearance rates by 25% and 45%, respectively. Likewise, smokers' plasma deuterium-labeled alpha- and gamma-tocopherol concentrations were significantly higher (P<0.05) at 72 h during ascorbic acid supplementation compared with placebo. Ascorbic acid supplementation did not significantly change (P>0.05) time of maximal or maximal-labeled alpha- and gamma-tocopherol concentrations. Smokers' plasma F2alpha-isoprostanes were approximately 26% higher than nonsmokers (P>0.05) and were not affected by ascorbic acid supplementation in either group (P>0.05). In summary, cigarette smoking increased plasma alpha- and gamma-tocopherol fractional disappearance rates, suggesting that the oxidative stress from smoking oxidizes tocopherols and that plasma ascorbic acid reduces alpha- and gamma-tocopheroxyl radicals to nonoxidized forms, thereby decreasing vitamin E disappearance in humans.

Source: Bruno RS, Leonard SW, Atkinson J, et al. Faster plasma vitamin E disappearance in smokers is normalized by vitamin C supplementation. Free Radic Biol Med. 2006;40(4):689-697. doi:10.1016/j.freeradbiomed.2005.10.051

Novel repair action of vitamin C upon in vivo oxidative DNA damage

ABSTRACT

There appears to be a paucity of data examining the effect of dietary antioxidants on levels of oxidative DNA damage in vivo, limiting evidence-based assessment of antioxidant efficacy, mechanisms and recommendation for optimal intake. We have examined levels of 8-oxo-2'-deoxyguanosine (8-oxodG) in mononuclear cell DNA, serum and urine from subjects undergoing supplementation with 500 mg/day vitamin C. Significant decreases in DNA levels of 8-oxodG were seen, correlating strongly with increases in plasma vitamin C concentration. Furthermore we established a timecourse for sequential, significant increases in serum and urinary 8-oxodG levels. These results illustrate, for the first time in humans, the kinetics of 8-oxodG removal and processing in vivo, suggesting a role for vitamin C in the regulation of DNA repair enzymes and thereby demonstrating a non-scavenging antioxidant effect.

Source: Cooke MS, Evans MD, Podmore ID, et al. Novel repair action of vitamin C upon in vivo oxidative DNA damage. *FEBS Lett.* 1998;439(3):363-367. doi:10.1016/s0014-5793(98)01403-3

Collagen Production for Connective Tissue Health

Dietary nutrient intakes and skin-aging appearance among middle-aged American women

ABSTRACT

Background: Nutritional factors play a key role in normal dermatologic functioning. However, little is known about the effects of diet on skin-aging appearance.

Objective: We evaluated the associations between nutrient intakes and skin-aging appearance.

Design: Using data from the first National Health and Nutrition Examination Survey, we examined associations between nutrient intakes and skin aging in 4,025 women (40-74 y). Nutrients were estimated from a 24-h recall. Clinical examinations of the skin were conducted by dermatologists. Skin-aging appearance was defined as having a wrinkled appearance, senile dryness, and skin atrophy.

Results: Higher vitamin C intakes were associated with a lower likelihood of a wrinkled appearance [odds ratio (OR) 0.89; 95% CI: 0.82, 0.96] and senile dryness (OR: 0.93; 95% CI: 0.87, 0.99). Higher linoleic acid intakes were associated with a lower likelihood of senile dryness (OR: 0.75; 95% CI: 0.64, 0.88) and skin atrophy (OR: 0.78; 95% CI 0.65, 0.95). A 17-g increase in fat and a 50-g increase in carbohydrate intakes increased the likelihood of a wrinkled appearance (OR: 1.28 and 1.36, respectively) and skin atrophy (OR: 1.37 and 1.33, respectively). These associations were independent of age, race, education, sunlight exposure, income, menopausal status, body mass index, supplement use, physical activity, and energy intake.

Conclusions: Higher intakes of vitamin C and linoleic acid and lower intakes of fats and carbohydrates are associated with better skin-aging appearance. Promoting healthy dietary behaviors may have additional benefit for skin appearance in addition to other health outcomes in the population.

Source: Cosgrove MC, Franco OH, Granger SP, Murray PG, Mayes AE. Dietary nutrient intakes and skin-aging appearance among middle-aged American women. *Am J Clin Nutr.* 2007;86(4):1225-1231. doi:10.1093/ajcn/86.4.1225

Do antioxidant micronutrients protect against the development and progression of knee osteoarthritis?

ABSTRACT

Objective: Cumulative damage to tissues, mediated by reactive oxygen species, has been implicated as a pathway that leads to many of the degenerative changes associated with aging. We hypothesized that increased intake of antioxidant micronutrients might be associated with decreased rates of osteoarthritis (OA) in the knees, a common age-related disorder.

Methods: Participants in the Framingham Osteoarthritis Cohort Study underwent knee evaluations by radiography at examinations 18 (1983-1985) and 22 (1992-1993). Usual dietary intake was assessed using the Food Frequency Questionnaire, administered at examination 20 (1988-1989). Knees without OA at baseline (Kellgren and Lawrence [K&L] grade < or = 1) were classified as having incident OA if they had a K&L grade > or = 2 at followup. Knees with OA at baseline were classified as having progressive OA if their score increased by > or = 1 at followup. Knees were also classified as having cartilage loss or osteophyte growth if their maximal joint space narrowing or osteophyte growth score increased by > or = 1 (range 0-3). The association of vitamin C, beta carotene, and vitamin E intake, ranked in

sex-specific tertiles, with incidence and progression of OA was compared with that of a panel of nonantioxidant vitamins, B1, B6, niacin, and folate, using logistic regression and generalized estimation equations to adjust for correlation between fellow knees. The lowest tertile for each dietary exposure was used as the referent category. Odds ratios (OR) were adjusted for age, sex, body mass index, weight change, knee injury, physical activity, energy intake, and health status.

Results: Six hundred forty participants received complete assessments. Incident and progressive OA occurred in 81 and 68 knees, respectively. We found no significant association of incident OA with any nutrient. A 3-fold reduction in risk of OA progression was found for both the middle tertile (adjusted OR = 0.3, 95% confidence interval [95% CI] 0.1-0.8) and highest tertile (adjusted OR = 0.3, 95% CI 0.1-0.6) of vitamin C intake. This related predominantly to a reduced risk of cartilage loss (adjusted OR = 0.3, 95% CI 0.1-0.8). Those with high vitamin C intake also had a reduced risk of developing knee pain (adjusted OR = 0.3, 95% CI 0.1-0.8). A reduction in risk of OA progression was seen for beta carotene (adjusted OR = 0.4, 95% CI 0.2-0.9) and vitamin E intake (adjusted OR = 0.7, 95% CI 0.3-1.6), but was less consistent. No significant associations were observed for the nonantioxidant nutrients.

Conclusion: High intake of antioxidant micronutrients, especially vitamin C, may reduce the risk of cartilage loss and disease progression in people with OA. We found no effect of antioxidant nutrients on incident OA. These preliminary findings warrant confirmation.

Source: McAlindon TE, Jacques P, Zhang Y, et al. Do antioxidant micronutrients protect against the development and progression of knee osteoarthritis?. Arthritis Rheum. 1996;39(4):648-656. doi:10.1002/art.1780390417

Immune Health

Vitamin C reduces the severity of common colds: a meta-analysis

ABSTRACT

Background: Randomized trials have shown that vitamin C shortens the duration of common colds. Some trials reported greater effects on severe cold symptoms compared with mild symptoms. This review systematically compares the effects of vitamin C on severe and mild common cold symptoms.

Methods: We included all placebo-controlled trials of orally administered vitamin C in doses of at least 1 g/day for the common cold for people in good health at baseline. The analysis was restricted to trials which reported both the total duration of the common cold, and the severity of the common cold measured using severity scales, the duration of more severe stages of the cold, or proxies for severe colds such as days indoors. Findings were pooled using the inverse variance, fixed effect options of the metacont function of the R package meta to calculate the ratio of means estimate.

Results: Fifteen comparisons from 10 trials which reported both mild and severe symptoms were identified. All trials were randomized and double-blind. Compared to placebo, vitamin C significantly decreased the severity of the common cold by 15% (95% CI 9-21%). The direct comparison of the effect of vitamin C on mild and severe symptoms was limited to five comparisons which found that vitamin C had a significant benefit on the duration of severe symptoms. In this subset, there was a significant difference in the size of the effect of vitamin C on the overall duration of colds versus the duration of severe colds ($P = 0.002$), and vitamin C had no significant effect on the duration of mild symptoms.

Conclusions: The common cold is the leading cause of acute morbidity and a major cause of absenteeism from work and school. However, absenteeism is dependent on the severity of symptoms. The finding that vitamin C may have a greater effect on more severe measures of the common cold is therefore important. Further research on the therapeutic effects of vitamin C on the common cold should measure outcomes of differing levels of severity.

Source: Hemilä H, Chalker E. Vitamin C reduces the severity of common colds: a meta-analysis. BMC Public Health. 2023;23(1):2468. Published 2023 Dec 11. doi:10.1186/s12889-023-17229-8

Nutritional modulation of exercise-induced immunodepression in athletes: a systematic review and meta-analysis

ABSTRACT

Background: Heavy exercise induces marked immunodepression that is multifactorial in origin. Nutrition can modulate normal immune function.

Objective: To assess the efficacy of nutritional supplements in exercise-induced immunodepression in athletes.

Design: Systematic review.

Review methods: Randomised and/or controlled trials of athletes undertaking nutritional supplements to minimise the immunodepression after exercise were retrieved. The primary outcome measure was incidence of upper respiratory tract (URT) illness symptoms after exercise, and secondary outcomes included cortisol, cell counts, plasma cytokine concentration, cell proliferative response, oxidative burst, natural killer cell activity and immunoglobulins. When data were available for a pooled estimate of the effect of intervention, meta-analyses were conducted for direct comparisons.

Results: Forty-five studies were included (1603 subjects). The studies were heterogeneous in terms of exercise interventions, selection of athletes, settings and outcomes. The overall methodological quality of most of the trials was poor. Twenty studies addressed carbohydrate supplementation, eight glutamine, 13 vitamin C and four others interventions. Three trials assessed the effect of intervention on prevention of URT infections. The pooled rate ratio for URT infections after vitamin C supplementation against placebo was 0.49 (0.34-0.71). Carbohydrate supplementation attenuated the increase in cortisol and neutrophils after exercise; vitamin C attenuated the decrease in lymphocytes after exercise. No other interventions had significant or consistent effect on any of the studied outcomes.

Conclusions: Although the prevention of URT infections by vitamin C was supported by two trials, further studies are needed. The available evidence failed to support a role for other nutritional supplements in preventing exercise-induced immune suppression. Larger trials with clinically relevant and uniform end points are necessary to clarify the role of these nutritional interventions.

Source: Moreira A, Kekkonen RA, Delgado L, Fonseca J, Korpela R, Hahtela T. Nutritional modulation of exercise-induced immunodepression in athletes: a systematic review and meta-analysis. Eur J Clin Nutr. 2007;61(4):443-460. doi:10.1038/sj.ejcn.1602549

Energy Metabolism

Vitamins and minerals for energy, fatigue and cognition: A narrative review of the biochemical and clinical evidence

ABSTRACT

Vitamins and minerals are essential to humans as they play essential roles in a variety of basic metabolic pathways that support fundamental cellular functions. In particular, their involvement in energy-yielding metabolism, DNA synthesis, oxygen transport, and neuronal functions makes them critical for brain and muscular function. These, in turn, translate into effects on cognitive and psychological processes, including mental and physical fatigue. This review is focused on B vitamins (B1, B2, B3, B5, B6, B8, B9 and B12), vitamin C, iron, magnesium and zinc, which have recognized roles in these outcomes. It summarizes the biochemical bases and actions of these micronutrients at both the molecular and cellular levels and connects them with cognitive and psychological symptoms, as well as manifestations of fatigue that may occur when status or supplies of these micronutrients are not adequate.

Source: Tardy AL, Pouteau E, Marquez D, Yilmaz C, Scholey A. Vitamins and Minerals for Energy, Fatigue and Cognition: A Narrative Review of the Biochemical and Clinical Evidence. Nutrients. 2020;12(1):228. Published 2020 Jan 16. doi:10.3390/nu12010228

Iron Absorption

Enhancers of iron absorption: ascorbic acid and other organic acids

ABSTRACT

Ascorbic acid (AA), with its reducing and chelating properties, is the most efficient enhancer of non-heme iron absorption when its stability in the food vehicle is ensured. The number of studies investigating the effect of AA on ferrous sulfate absorption far outweighs that of other iron fortificants. The promotion of iron absorption in the presence of AA is more pronounced in meals containing inhibitors of iron absorption. Meals containing low to medium levels of inhibitors require the addition of AA at a molar ratio of 2:1 (e.g., 20 mg AA: 3 mg iron). To promote absorption in the presence of high levels of inhibitors, AA needs to be added at a molar ratio in excess of 4:1, which may be impractical. The effectiveness of AA in promoting absorption from less soluble compounds, such as ferrous fumarate and elemental iron, requires further investigation. The instability of AA during food processing, storage, and cooking, and the possibility of unwanted sensory changes limits the number of suitable food vehicles for AA, whether used as vitamin fortificant or as an iron enhancer. Suitable vehicles include dry-blended foods, such as complementary, precooked cereal-based infant foods, powdered milk, and other dry beverage products made for reconstitution that are packaged, stored, and prepared in a way that maximizes retention of this vitamin. The consumption of natural sources of Vitamin C (fruits and vegetables) with iron-fortified dry blended foods is also recommended. Encapsulation can mitigate some of the AA losses during processing and storage, but these interventions will also add cost. In addition, the bioavailability of encapsulated iron in the presence/absence of AA will need careful assessment in human clinical trials.

Source: Teucher B, Olivares M, Cori H. Enhancers of iron absorption: ascorbic acid and other organic acids. *Int J Vitam Nutr Res.* 2004;74(6):403-419. doi:10.1024/0300-9831.74.6.403

Ascorbic acid can reverse the inhibition of phytic acid, sodium oxalate and sodium silicate on iron absorption in caco-2 cells.

ABSTRACT

The objective of the present study is to determine the effect of phytic acid (PA), sodium oxalate (SO) and sodium silicate (SS) on non-heme iron bioavailability in both the presence and absence of ascorbic acid (AA) using an in vitro digestion/Caco-2 cell model, and the levels of AA needed to promote Fe absorption from Fe complexed with PA, SO or SS were also determined. The results indicated that adding PA at 1:1, 3:1, 5:1 and 10:1 molar as compared to Fe decreased ferrous iron uptake by 55.80 % (P < 0.05), 72.33 % (P < 0.05), 73.32 % (P < 0.05), and 73.26 % (P < 0.05), respectively. Adding SS at 1:1, 3:1, 5:1 and 10:1 molar as compared to Fe also decreased ferrous iron uptake by 51.40 % (P < 0.05), 66.12 % (P < 0.05), 60.19 % (P < 0.05) and 45.11 % (P < 0.05), respectively. Adding SO at 5:1 and 10:1 molar as compared to Fe decreased ferrous iron uptake by 40.81 % (P < 0.05) and 33.14 % (P < 0.05), respectively. When adding AA to iron plus organic acid medias reached molar ratios of 5:5:1 AA:PA:Fe, 3:5:1 AA:SO:Fe and 5:5:1 AA:SS:Fe, iron absorption from FeSO₄ were significantly increased (P < 0.05). However, no significant effect was observed in iron absorption from FeCl₃ when adding AA to the media. The results showed that PA, SS or SO decreases iron uptake from ferrous Fe, and AA can counteract their inhibiting effect on ferrous iron absorption and thus increase ferrous iron uptake. The results may be important for elucidating factors affecting iron bioavailability in the small intestine and for the development of foods with improved iron bioavailability.

Source: He W, Li X, Ding K, Li Y, Li W. Ascorbic Acid can Reverse the Inhibition of Phytic Acid, Sodium Oxalate and Sodium Silicate on Iron Absorption in Caco-2 cells. *Int J Vitam Nutr Res.* 2018;88(1-2):65-72. doi:10.1024/0300-9831/a000503