



ENERGY+

SUGAR & CAFFEINE-FREE

All-Natural Mental Energy &
Motivation



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Technical Data Sheet



ENERGY+

SUGAR & CAFFEINE-FREE

A next-generation mental energy product that delivers rapid improvements in brain and physical performance, without the jitters or crash you might get from many high-stimulant or high-sugar energy drinks.*

KEY INGREDIENTS

Rooibos Powder — A south African red bush tea that has been used for centuries around the world. It is a caffeine-free alternative to black and green tea for energy and alertness, but also has antioxidant properties, inflammatory benefits, and blood sugar control properties. Laboratory studies have found that rooibos tea contains polyphenol antioxidants, including flavonoids and phenolic acids, that are potent free radical scavengers. The polyphenol antioxidants identified in rooibos tea include the monomeric flavonoids aspalathin, nothofagin, quercetin, rutin, isoquercitrin, orientin, isoorientin, luteolin, vitexin, isovitexin, and chrysoeriol. Currently, rooibos is the only known natural source of aspalathin.

Glycine — One of the amino acids that help produce proteins. It helps with the production of serotonin and overall transmission of chemical signals in the brain- which is why it helps with energy, brain fitness and strength. Glycine is also one of three amino acids needed to produce creatine, which in turn supplies energy to muscles and nerve cells. High concentrations of glycine are found in the muscles, the skin, and other connective tissues. Approximately 30 percent of collagen is composed of glycine.

Chicory Root Inulin — Medicinal use of chicory root dates back to ancient Egypt. Chicory contains exceptionally high levels of a fructan called inulin. One of the benefits of inulin is that it serves as a prebiotic fiber that helps beneficial probiotic bacteria flourish and can improve bowel movements and digestion. Some data also suggests that supplementing with inulin can also help improve blood sugar control.

Pomegranate Seed Extract — The pomegranate originates in the Middle East, with findings dating back to the early Bronze Age. Pomegranates are rich in antioxidants and flavonoids, both of which are known to prevent free radicals from damaging your cells. They also contain specialized polyphenols that help balance normal inflammatory pathways and open up blood vessels to stimulate blood circulation and boost vitality.

Asian Apple Polyphenols (Applephenon®) — Carefully extracted from specially selected wild green unripe apples sourced from Central Asia (where apples originated and were first cultivated thousands of years ago). Applephenon delivers powerful antioxidant properties from its optimized profile of proanthocyanidins, that deliver both “1st brain” and “2nd brain” effects to support mental and physical energy benefits.

New Zealand Pine Bark Polyphenols (Enzogenol™) — Produced from the ultra-clean New Zealand pine bark using proprietary pure water-only environmentally friendly extraction method. The finished extract is rich in OPCs (oligomeric proantho-cyanidins) that are known for their wide range of benefits in cellular protection, cardiovascular performance, alleviation of fatigue, memory enhancement, and enhanced mental acuity. *

French Grape Seed Polyphenols (Enovita®) — Contains polyphenol flavonoids with both antioxidant and antiinflammatory properties. In particular, specific research on grape seed extracts have shown biological properties, including cardioprotective, neuroprotective, and hepatoprotective activities, as well as specific “2nd brain” energy benefits via direct inflammatory-balancing effects within the GI tract. Enovita is a proprietary proanthocyanidin-rich extract made exclusively with grape seeds from white wine production and using only water as extraction solvent.

CLINICAL STUDIES

PLoS One. 2016 Oct 20;11(10):e0160305.

Pomegranate Supplementation Accelerates Recovery of Muscle Damage and Soreness and Inflammatory Markers after a Weightlifting Training Session. Ammar A, Turki M, Chtourou H, Hammouda O, Trabelsi K, Kallel C, Abdelkarim O, Hoekelmann A, Bouaziz M, Ayadi F, Driss T, Souissi N.

Abstract

PURPOSE: The aim of this study was to investigate the effect of natural Pomegranate juice supplementation on performance and acute and delayed responses of muscle soreness and biomarkers of muscle damage after a weightlifting training session. **METHODS:** Nine elite weightlifters (21 ± 0.5 years) performed two Olympic-Weightlifting-sessions after either placebo (PLA) or natural pomegranate juice (POMj) supplementations. Heart rate, blood pressure and blood samples (hematological parameters, muscle damage and C-reactive protein (CRP)) were collected at rest, 3min and 48h after each session. Weightlifting performance, RPE, and DOMS were also assessed after each training session.

RESULTS: T-test showed higher performance (+8.30%) and lower RPE values (-4.37%) using POMj supplementation ($p < 0.05$) in comparison with PLA. For the DOMS values, a significant improvement (13.4%) was shown only for the knee extensors ($p < 0.01$) using the POMj. Compared to PLA condition, POMj attenuated the acute (i.e., 3min) increase of systolic blood pressure (SBP), HR, CK and LDH ($p < 0.05$; -4.46%, -1.81%, -8.75%, -1.64%, respectively) and blunted the significant increase of ASAT, PAL and CRP ($p > 0.05$). Additionally, during the 48h following the training session, POMj improved the recovery kinetic of SBP ($p < 0.01$, 7.97%), CK ($p < 0.001$, 11.34%), LDH ($p < 0.05$, 7.30%) and ASAT ($p < 0.05$, 6.77%). Indeed, the present study showed that 48h of recovery associated to natural POMj supplementation was sufficient to reach the resting values of the selected muscle damage markers after intensive training session.

CONCLUSION: Natural POMj seems to ameliorate the capacity to adhere to an intensive training program. Therefore, elite weightlifters are advised to use natural POMj during intensive training program and competition to accelerate muscle recovery

Eur J Sport Sci. 2017 Apr;17(3):317-325.

Effects of pomegranate extract on blood flow and vessel diameter after high-intensity exercise in young, healthy adults.

Roelofs EJ, Smith-Ryan AE, Trexler ET, Hirsch KR1, Mock MG.

Abstract

The effects of pomegranate extract (PE) supplementation were evaluated on high-intensity exercise performance, blood flow, vessel diameter, oxygen saturation (SPO₂), heart rate (HR), and blood pressure (BP). In a randomized, crossover design, nineteen recreationally resistance-trained participants were randomly assigned to PE (1000 mg) or placebo (PL), which were consumed 30 min prior to a repeated sprint ability (RSA) test and repetitions to fatigue (RTF) on bench and leg press. The RSA consisted of ten six-second sprints on a friction-loaded cycle ergometer with 30 s recovery. Brachial artery blood flow and vessel diameter were assessed by ultrasound. Blood flow, vessel diameter, SPO₂, HR, and BP were assessed at baseline, 30 min post ingestion, immediately post exercise (IPost), and 30 min post exercise (30minPost). With PE, blood flow significantly increased IPost RSA (mean difference = 18.49 mL min⁻¹; $P < .05$), and IPost and 30minPost RTF ($P < .05$) according to confidence intervals (CI). Vessel diameter increased significantly 30minPost RSA according to CI and resulted in a significant interaction IPost and 30minPost RTF ($P < .05$). With PE, according to CI, average and peak power output increased significantly in sprint 5 of the RSA ($P < .05$). There was no significant difference between PE and PL for bench ($P = .25$) or leg press ($P = .15$) repetitions. Acute PE supplementation enhanced vessel diameter and blood flow, suggesting possible exercise performance enhancement from increased delivery of substrates and oxygen. The acute timing and capsule form of PE may be advantageous to athletic populations due to ergogenic effects, taste, and convenience.

Plant Foods Hum Nutr. 2012 Sep;67(3):309-14.

Effects of pomegranate juice supplementation on pulse wave velocity and blood pressure in healthy young and middle-aged men and women.

Lynn A, Hamadeh H, Leung WC, Russell JM, Barker ME.

Abstract

Pomegranate juice may improve cardiovascular risk because of its content of antioxidant polyphenols. We conducted a randomized placebo-controlled parallel study to examine the effect of pomegranate juice on pulse wave velocity (PWV), blood pressure (BP) and plasma antioxidant status (ferric reducing power; FRAP) in 51 healthy adults (30-50 years). Participants consumed 330 ml/day of pomegranate juice or control drink for four weeks. Measurements were made at baseline and at four weeks. There was no effect of the intervention on PWV ($P = 0.694$) and plasma FRAP ($P = 0.700$). However, there was a significant fall in systolic blood pressure (-3.14 mmHg, $P < 0.001$), diastolic blood pressure (-2.33 mmHg $P < 0.001$) and mean arterial pressure (-2.60 mmHg, $P < 0.001$). Change in weight was similar in the two groups over the intervention period ($P = 0.379$). The fall in BP was not paralleled by changes in concentration of serum angiotensin converting enzyme. We conclude that pomegranate juice supplementation has benefits for BP in the short term but has no effect on PWV. The mechanism for the effect is uncertain.

Complement Ther Clin Pract. 2011 May;17(2):113-5.

The effects of pomegranate juice consumption on blood pressure and cardiovascular health. Stowe CB.

Abstract

Hypertension (HTN) is the most common disease found in patients in primary care [JNC-7 Guidelines. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hyper* 2003; 42:1206.]. It eventually requires medication if lifestyle modifications are not initiated or do not control the blood pressure well enough. The majority of patients would prefer not to have to be medicated to manage their disease, and HTN can be found to be a comorbidity along with diabetes, CAD, and many other cardiovascular diseases. Adverse effects, forgetfulness and patient ignorance are multiple reasons for the hesitancy to begin drug management. Pomegranate juice is rich in tannins, possesses anti-atherosclerotic properties, has anti-aging effects, and potent anti-oxidative characteristics. As some antioxidants have been shown to reduce blood pressure, the purpose of this review was to discover the effect of pomegranate juice consumption on blood pressure and cardiovascular health. Pomegranate juice consumption may reduce systolic blood pressure, inhibits serum ACE activity, and is convincingly a heart-healthy fruit [Aviram M, Dornfeld L. Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure. *Athero* 2001;158:195-8.]. More clinical research is needed as a number of the studies discussed include small sample sizes and few studies seem to have been undertaken in the recent 5-10 years.

Am J Cardiol. 2009 Oct 1;104(7):936-42.

Effects of consumption of pomegranate juice on carotid intima-media thickness in men and women at moderate risk for coronary heart disease.

Davidson MH, Maki KC, Dicklin MR, Feinstein SB, Witchger M, Bell M, McGuire DK, Provost JC, Liker H, Aviram M.

Abstract

This randomized, double-blind, parallel trial assessed the influence of pomegranate juice consumption on anterior and posterior carotid intima-media thickness (CIMT) progression rates in subjects at moderate risk for coronary heart disease. Subjects were men (45 to 74 years old) and women (55 to 74 years old) with ≥ 1 major coronary heart disease risk factor and baseline posterior wall CIMT 0.7 to 2.0 mm, without significant stenosis. Participants consumed 240 ml/day of pomegranate juice (n = 146) or a control beverage (n = 143) for up to 18 months. No significant difference in overall CIMT progression rate was observed between pomegranate juice and control treatments. In exploratory analyses, in subjects in the most adverse tertiles for baseline serum lipid peroxides, triglycerides (TGs), high-density lipoprotein (HDL) cholesterol, TGs/HDL cholesterol, total cholesterol/HDL cholesterol, and apolipoprotein-B100, those in the pomegranate juice group had significantly less anterior wall and/or composite CIMT progression versus control subjects. In conclusion, these results suggest that in subjects at moderate coronary heart disease risk, pomegranate juice consumption had no significant effect on overall CIMT progression rate but may have slowed CIMT progression in subjects with increased oxidative stress and disturbances in the TG-rich lipoprotein/HDL axis.

Nutr Rev. 2009 Jan;67(1):49-56.

Pomegranate juice: a heart-healthy fruit juice.

Basu A, Penugonda K.

Abstract

Pomegranate juice is a polyphenol-rich fruit juice with high antioxidant capacity. In limited studies in human and murine models, pomegranate juice has been shown to exert significant antiatherogenic, antioxidant, antihypertensive, and anti-inflammatory effects. Pomegranate juice significantly reduced atherosclerotic lesion areas in immune-deficient mice and intima media thickness in cardiac patients on medications. It also decreased lipid peroxidation in patients with type 2 diabetes, and systolic blood pressure and serum angiotensin converting enzyme activity in hypertensive patients. Thus, the potential cardioprotective benefits of pomegranate juice deserves further clinical investigation, and evidence to date suggests it may be prudent to include this fruit juice in a heart-healthy diet.

Mol Nutr Food Res. 2009 Mar;53(3):322-31.

Vascular action of polyphenols.

Ghosh D, Scheepens A.

Abstract

Dietary patterns are widely recognized as contributors to cardiovascular and cerebrovascular disease. Endothelial function, the elastic properties of large arteries and the magnitude and timing of wave reflections are important determinants of cardiovascular performance. Several epidemiological studies suggest that the regular consumption of foods and beverages rich in flavonoids is associated with a reduction in the risk of several pathological conditions ranging from hypertension to coronary heart disease, stroke and dementia. The impairment of endothelial function is directly related to ageing and an association between decreased cerebral perfusion and dementia has been shown to exist. Cerebral blood flow (CBF) must be maintained to ensure a constant delivery of oxygen and glucose as well as the removal of waste products. Increasing blood flow is one potential way for improving brain function and the prospect for increasing CBF with dietary polyphenols is extremely promising. The major polyphenols shown to have some of these effects in humans are primarily from cocoa, wine, grape seed, berries, tea, tomatoes (polyphenolics and nonpolyphenolics), soy and pomegranate. There has been a significant paradigm shift in polyphenol research during the last decade. This review summarises our current knowledge in this area and points the way for the development of new types of functional foods targeted to brain health through improving vascular health.

Am J Cardiol. 2005 Sep 15;96(6):810-4.

Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease. Sumner MD, Elliott-Eller M, Weidner G, Daubenmier JJ, Chew MH, Marlin R, Raisin CJ, Ornish D.

Abstract

Pomegranate juice contains antioxidants such as soluble polyphenols, tannins, and anthocyanins and may have antiatherosclerotic properties. However, no study has investigated the effects of pomegranate juice on patients who have ischemic coronary heart disease (CHD). We investigated whether daily consumption of pomegranate juice for 3 months would affect myocardial perfusion in 45 patients who had CHD and myocardial ischemia in a randomized, placebo-controlled, double-blind study. Patients were randomly assigned into 1 of 2 groups: a pomegranate juice group (240 ml/day) or a placebo group that drank a beverage of similar caloric content, amount, flavor, and color. Participants underwent electrocardiographic-gated myocardial perfusion single-photon emission computed tomographic technetium-99m tetrofosmin scintigraphy at rest and during stress at baseline and 3 months. Visual scoring of images using standardized segmentation and nomenclature (17 segments, scale 0 to 4) was performed by a blinded independent nuclear cardiologist. To assess the amount of inducible ischemia, the summed difference score (SDS) was calculated by subtracting the summed score at rest from the summed stress score. The experimental and control groups showed similar levels of stress-induced ischemia (SDS) at baseline ($p > 0.05$). After 3 months, the extent of stress-induced ischemia decreased in the pomegranate group (SDS -0.8 ± 2.7) but increased in the control group (SDS 1.2 ± 3.1 , $p < 0.05$). This benefit was observed without changes in cardiac medications, blood sugar, hemoglobin A1c, weight, or blood pressure in either group. In conclusion, daily consumption of pomegranate juice may improve stress-induced myocardial ischemia in patients who have CHD.

J Nutr Health Aging. 2004;8(2):92-7.

Apple juice prevents oxidative stress and impaired cognitive performance caused by genetic and dietary deficiencies in mice.

Rogers EJ, Milhalik S, Orthiz D, Shea TB.

Abstract

Increased oxidative stress contributes to the decline in cognitive performance during normal aging and in neurodegenerative conditions such as Alzheimer's disease. Dietary supplementation with fruits and vegetables that are high in antioxidant potential have in some cases compensated for dietary and/or genetic deficiencies that promote increased oxidative stress. Herein, we demonstrate that apple juice concentrate, administered ad libitum in drinking water, can compensate for the increased reactive oxygen species and decline in cognitive performance in maze trials observed when normal and transgenic mice lacking apolipoprotein E are deprived of folate and vitamin E. In addition, we demonstrate that this protective effect is not derived from the sugar content of the concentrate.

J Agric Food Chem. 2008 Jul 9;56(13):4855-73.

Challenges for research on polyphenols from foods in Alzheimer's disease: bioavailability, metabolism, and cellular and molecular mechanisms.

Singh M, Arseneault M, Sanderson T, Murthy V, Ramassamy C.

Abstract

Polyphenols are the most abundant antioxidants in diet. Indeed, fruits, vegetables, beverages (tea, wine, juices), plants, and some herbs are loaded with powerful antioxidant polyphenols. Despite their wide distribution, research on human health benefits truly began in the mid-1990s (Scalbert, A.; Johnson, I. T.; Saltmarsh, M. *Am. J. Clin. Nutr.* 2005, 81, S15S-217S). Phenolic compounds have been receiving increasing interest from consumers and manufacturers because numerous epidemiological studies have suggested associations between consumption of polyphenol-rich foods or beverages and the prevention of certain chronic diseases such as cancers and cardiovascular diseases (Manach, C.; Mazur, A.; Scalbert, A. *Curr. Opin. Lipidol.* 2005, 16, 77-84; Duthie, S. J. *Mol. Nutr. Food Res.* 2007, 51, 665-674). Furthermore, in the past 10 years, research on the neuroprotective effects of dietary polyphenols has developed considerably. These compounds are able to protect neuronal cells in various *in vivo* and *in vitro* models through different intracellular targets (Ramassamy, C. *Eur. J. Pharmacol.* 2006, 545, 51-64). However, it is not at all clear whether these compounds reach the brain in sufficient concentrations and in a biologically active form to exert beneficial effects. On the other hand, it has become clear that the mechanisms of action of these polyphenols go beyond their antioxidant activity and the attenuation of oxidative stress. Therefore, there is a need for more research on their intracellular and molecular targets as special pathways underlying distinct polyphenol-induced neuroprotection. The focus of this review is aimed at presenting the role of some polyphenols from fruits, vegetables, and beverages in neuroprotection and particularly in Alzheimer's disease and the research challenges in this area.

J Alzheimers Dis. 2005 Dec;8(3):283-7.

Apple juice concentrate prevents oxidative damage and impaired maze performance in aged mice. Tchantchou F, Chan A, Kifle L, Ortiz D, Shea TB.

Abstract

Oxidative stress contributes to age-related cognitive decline. In some instances, consumption of fruits and vegetables rich in antioxidant can provide superior protection than supplementation with purified antioxidants. Our prior studies have shown that supplementation with apple juice concentrate (AJC) alleviates oxidative damage and cognitive decline in a transgenic murine model compromised in endogenous antioxidant potential when challenged with a vitamin-deficient, oxidative stress-promoting diet. Herein, we demonstrate that AJC, administered in drinking water, is neuroprotective in normal, aged mice. Normal mice aged either 9-10 months or 2-2.5 years were maintained for 1 month on a complete diet or a diet lacking folate and vitamin E and containing iron as a pro-oxidant, after which oxidative damage was assayed by thiobarbituric acid-reactive substances and cognitive decline as assayed by performance in a standard Y-maze. Mice 9-12 months of age were unaffected by the deficient diet, while older mice demonstrated statistically-increased oxidative damage and poorer performance in a Y maze test. Supplementation with AJC prevented these neurodegenerative effects. These data are consistent with normal aged individuals being susceptible to neurodegeneration following dietary compromise such as folate deficiency, and a hastened onset of neurodegeneration in those individuals harboring a genetic risk factor such as ApoE deficiency. These findings also support the efficacy of antioxidant supplementation, including consumption of antioxidant-rich foods such as apples, in preventing the decline in cognitive performance that accompanies normal aging.

Curr Med Chem. 2011;18(8):1195-212.

Neuroprotective actions of flavonoids. Gutierrez-Merino C1, Lopez-Sanchez C, Lagoa R, Samhan-Arias AK, Bueno C, Garcia-Martinez V.

Abstract

The experimental evidences accumulated during last years point out a relevant role of oxidative stress in neurodegeneration. As anti-cellular oxidative stress agents flavonoids can act either as direct chemical antioxidants, the classic view of flavonoids as antioxidants, or as modulators of enzymes and metabolic and signaling pathways leading to an overshoot of reactive oxygen species (ROS) formation, a more recently emerging concept. Flavonoids, a large family of natural antioxidants, undergo a significant hepatic metabolism leading to flavonoid-derived metabolites that are also bioactive as antioxidant agents. The development of more efficient flavonoid's based anti-oxidative stress therapies should also take into account their bioavailability in the brain using alternate administration protocols, and also that the major ROS triggering the cellular oxidative stress are not the same for all neurodegenerative insults and diseases. On these grounds, we have reviewed the reports on neuroprotection by different classes of flavonoids on cellular cultures and model animals. In addition, as they are now becoming valuable pharmacological drugs, due to their low toxicity, the reported adverse effects of flavonoids in model experimental animals and humans are briefly discussed.

Brain Res. 2014 Mar 25;1555:60-77. Neuroprotective effects of anthocyanin- and proanthocyanidin-rich extracts in cellular models of Parkinson's disease. Strathearn KE, Yousef GG, Grace MH, Roy SL, Tambe MA, Ferruzzi MG, Wu QL, Simon JE, Lila MA, Rochet JC.

Abstract

Neuropathological evidence indicates that dopaminergic cell death in Parkinson's disease (PD) involves impairment of mitochondrial complex I, oxidative stress, microglial activation, and the formation of Lewy bodies. Epidemiological findings suggest that the consumption of berries rich in anthocyanins and proanthocyanidins may reduce PD risk. In this study, we investigated whether extracts rich in anthocyanins, proanthocyanidins, or other polyphenols suppress the neurotoxic effects of rotenone in a primary cell culture model of PD. Dopaminergic cell death elicited by rotenone was suppressed by extracts prepared from blueberries, grape seed, hibiscus, blackcurrant, and Chinese mulberry. Extracts rich in anthocyanins and proanthocyanidins exhibited greater neuroprotective activity than extracts rich in other polyphenols, and a number of individual anthocyanins interfered with rotenone neurotoxicity. The blueberry and grape seed extracts rescued rotenone-induced defects in mitochondrial respiration in a dopaminergic cell line, and a purple basal extract attenuated nitrite release from microglial cells stimulated by lipopolysaccharide. These findings suggest that anthocyanin- and proanthocyanidin-rich botanical extracts may alleviate neurodegeneration in PD via enhancement of mitochondrial function.

Mol Nutr Food Res. 2013 Dec;57(12):2091-102. Role of standardized grape polyphenol preparation as a novel treatment to improve synaptic plasticity through attenuation of features of metabolic syndrome in a mouse model. Wang J, Tang C, Ferruzzi MG, Gong B, Song BJ, Janle EM, Chen TY, Cooper B, Varghese M, Cheng A, Freire D, Bilski A, Roman J, Nguyen T, Ho L, Talcott ST, Simon JE, Wu Q, Pasinetti GM.

Abstract

SCOPE: Metabolic syndrome has become an epidemic and poses tremendous burden on the health system. People with metabolic syndrome are more likely to experience cognitive decline. As obesity and sedentary lifestyles become more common, the development of early prevention strategies is critical. In this study, we explore the potential beneficial effects of a combinatory polyphenol preparation composed of grape seed extract, Concord purple grape juice extract, and resveratrol, referred to as standardized grape polyphenol preparation (SGP), on peripheral as well as brain dysfunction induced by metabolic syndrome.

METHODS AND RESULTS: We found dietary fat content had minimal effect on absorption of metabolites of major polyphenols derived from SGP. Using a diet-induced animal model of metabolic syndrome (DIM), we found that brain functional connectivity and synaptic plasticity are compromised in the DIM mice. Treatment with SGP not only prevented peripheral metabolic abnormality but also improved brain synaptic plasticity.

CONCLUSION: Our study demonstrated that SGP, comprised of multiple bioavailable and bioactive components targeting a wide range of metabolic syndrome related pathological features, provides greater global protection against peripheral and central nervous system dysfunctions and can be potentially developed as a novel prevention/treatment for improving brain connectivity and synaptic plasticity important for learning and memory.

Exp Gerontol. 2011 Nov;46(11):958-64. Grape seed proanthocyanidin lowers brain oxidative stress in adult and middle-aged rats. Asha Devi S, Sagar Chandrasekar BK, Manjula KR, Ishii N.

Abstract

There is growing concern over the increasing instances of decline in cognitive abilities with aging in humans. The present study evaluated the benefits of the natural antioxidant, grape seed proanthocyanidin extract (GSPE) in treating the effects of age-related oxidative stress (OS) and accumulation of lipofuscin (LF) on the cognitive ability in rats. Female Wistar rats of 3- and 12-months of age received a daily oral supplement of GSPE until they attained 6- and 15-months of age. During this period, rats were tested for their cognitive ability. At the end of this period, blood glucose and markers of OS were assessed in the hippocampus. GSPE lowered blood glucose, lipid peroxidation, hydrogen peroxide level, and increased protein sulphhydryl (P-SH) content in the hippocampus. In addition, GSPE significantly improved cognitive performance in the two age groups. These results demonstrate that the extent of OS-related LF accumulation is reducible by GSPE. They also suggest a critical role for GSPE as a neuroprotectant in the hippocampus and in preventing cognitive loss with aging.

Med Sci Monit. 2006 Apr;12(4):BR124-9. Epub 2006 Mar 28.

Grape seed proanthocyanidin extract (GSPE) and antioxidant defense in the brain of adult rats. Devi A, Jolitha AB, Ishii N.

Abstract

BACKGROUND: Proanthocyanidin (PA) is a naturally occurring antioxidant from grape seed extract. The present study aims at assessing the neuroprotective effects of grape seed proanthocyanidin (GSPE) on the cerebral cortex (CC), cerebellum (CB), and hippocampus (HC) in the adult rat brain.

MATERIAL/METHODS: GSPE was orally administered at 25, 50, and 75 mg per kg body weight daily and for a total period of 9 weeks. Antioxidant enzymes (AOEs), superoxide dismutase (SOD), and catalase (CAT) were analyzed along with malondialdehyde (MDA) and protein carbonyl content (PCC) as markers of lipid peroxidation (LPO) and protein oxidation (PO). The cholinergic system was studied by analyzing choline acetyl transferase (ChAT) and acetylcholine esterase (AChE) activities along with acetylcholine content (ACh).

RESULTS: The results obtained revealed an increased SOD activity in the 75-mg PA-supplemented animals, with a substantial decrease in MDA and PCC. The cholinergic neurotransmitter system analysis showed increased ChAT activity indicative of increased ACh content in the supplemented animals and the increase was more in the 75-mg PA group with a concomitant and moderate decrease in AChE activity. Regional changes were more with reference to HC.

CONCLUSIONS: Our study shows that PA intake in moderately low quantity is effective in up-regulating the antioxidant defense mechanism by attenuating LPO and PO. Changes in the cholinergic system, however, indicate an increase in the ACh concentration with a moderate reduction in AChE activity, suggesting further that PA may have a potent role in enhancing cognition in older rats.

Eur J Neurol. 2013 Aug;20(8):1135-44. Enzogenol for cognitive functioning in traumatic brain injury: a pilot placebo-controlled RCT. Theadom A, Mahon S, Barker-Collo S, McPherson K, Rush E, Vandal AC, Feigin VL.

Abstract

BACKGROUND AND PURPOSE: Enzogenol, a flavonoid-rich extract from *Pinus radiata* bark with antioxidant and anti-inflammatory properties has been shown to improve working memory in healthy adults. In traumatic brain injury (TBI), oxidation and inflammation have been linked to poorer cognitive outcomes. Hence, this phase II, randomized controlled trial investigated safety, compliance and efficacy of Enzogenol for improving cognitive functioning in people following mild TBI.

METHODS: Sixty adults, who sustained a mild TBI, 3-12 months prior to recruitment, and who were experiencing persistent cognitive difficulties [Cognitive Failures Questionnaire (CFQ) score > 38], were randomized to receive Enzogenol (1000 mg/day) or matching placebo for 6 weeks. Subsequently, all participants received Enzogenol for a further 6 weeks, followed by placebo for 4 weeks. Compliance, side-effects, cognitive failures, working and episodic memory, post-concussive symptoms and mood were assessed at baseline, 6, 12 and 16 weeks. Simultaneous estimation of treatment effect and breakpoint was effected, with confidence intervals (CIs) obtained through a treatment-placebo balance-preserving bootstrap procedure.

RESULTS: Enzogenol was found to be safe and well tolerated. Trend and breakpoint analyses showed a significant reduction in cognitive failures after 6 weeks [mean CFQ score, 95% CI, Enzogenol versus placebo -6.9 (-10.8 to -4.1)]. Improvements in the frequency of self-reported cognitive failures were estimated to continue until week 11 before stabilizing. Other outcome measures showed some positive trends but no significant treatment effects. **CONCLUSIONS:** Enzogenol supplementation is safe and well tolerated in people after mild TBI, and may improve cognitive functioning in this patient population. This study provides Class IIB evidence that Enzogenol is well tolerated and may reduce self-perceived cognitive failures in patients 3-12 months post-mild TBI.

Phytother Res. 2008 Sep;22(9):1168-74.

Improved cognitive performance after dietary supplementation with a *Pinus radiata* bark extract formulation.

Pipingas A, Silberstein RB, Vitetta L, Rooy CV, Harris EV, Young JM, Frampton CM, Sali A, Nastasi J.

Abstract

Dietary interventions may have the potential to counter age-related cognitive decline. Studies have demonstrated an improvement in age-related cognitive impairment in animals after supplementation with plant extracts containing flavonoids but there are few human studies. This double-blind, controlled study examined the effects on cognitive performance of a 5 week supplementation with Enzogenol *Pinus radiata* bark extract containing flavonoids, in 42 males aged 50-65 years, with a body mass index >25. Participants were supplemented for 5 weeks either with Enzogenol plus vitamin C, or with vitamin C only. A battery of computerized cognitive tests was administered, and cardiovascular and haematological parameters were assessed prior to and following supplementation. The speed of response for the spatial working memory and immediate recognition tasks improved after supplementation with Enzogenol plus vitamin C, whereas vitamin C alone showed no improvements. A trend in a reduction of systolic blood pressure was observed with Enzogenol plus vitamin C, but not with vitamin C alone. The blood safety parameters were unchanged. The findings suggest a beneficial effect of supplementation with Enzogenol on cognition in older individuals. Larger studies are needed to ascertain its potential as a preventive treatment for age-related cognitive decline.

The Effects of Glycine on Subjective Daytime Performance in Partially Sleep-Restricted Healthy Volunteers

By: Makoto Bannai,1,* Nobuhiro Kawai,1 Kaori Ono,1 Keiko Nakahara,2 and Noboru Murakami2

Abstract

Approximately 30% of the general population suffers from insomnia. Given that insomnia causes many problems, amelioration of the symptoms is crucial. Recently, we found that a non-essential amino acid, glycine subjectively and objectively improves sleep quality in humans who have difficulty sleeping. We evaluated the effects of glycine on daytime sleepiness, fatigue, and performances in sleep-restricted healthy subjects. Sleep was restricted to 25% less than the usual sleep time for three consecutive nights. Before bedtime, 3 g of glycine or placebo were ingested, sleepiness, and fatigue were evaluated using the visual analog scale (VAS) and a questionnaire, and performance were estimated by personal computer (PC) performance test program on the following day. In subjects given glycine, the VAS data showed a significant reduction in fatigue and a tendency toward reduced sleepiness. These observations were also found via the questionnaire, indicating that glycine improves daytime sleepiness and fatigue induced by acute sleep restriction. PC performance test revealed significant improvement in psychomotor vigilance test. We also measured plasma melatonin and the expression of circadian-modulated genes expression in the rat suprachiasmatic nucleus (SCN) to evaluate the effects of glycine on circadian rhythms. Glycine did not show significant effects on plasma melatonin concentrations during either the dark or light period. Moreover, the expression levels of clock genes such as *Bmal1* and *Per2* remained unchanged. However, we observed a glycine-induced increase in the neuropeptides arginine vasopressin and vasoactive intestinal polypeptide in the light period. Although no alterations in the circadian clock itself were observed, our results indicate that glycine modulated SCN function. Thus, glycine modulates certain neuropeptides in the SCN and this phenomenon may indirectly contribute to improving the occasional sleepiness and fatigue induced by sleep restriction.

Adjunctive high-dose glycine in the treatment of schizophrenia**D C Javitt 1, G Silipo, A Cienfuegos, A M Shelley, N Bark, M Park, J P Lindenmayer, R Suckow, S R Zukin****Affiliations expand PMID: 11806864 DOI: 10.1017/S1461145701002590****Abstract**

Glycine is an agonist at brain N-methyl-D-aspartate receptors and crosses the blood-brain barrier following high-dose oral administration. In a previous study, significant improvements in negative and cognitive symptoms were observed in a group of 21 schizophrenic patients receiving high-dose glycine in addition to antipsychotic treatment. This study evaluated the degree to which symptom improvements might be related to alterations in antipsychotic drug levels in an additional group of 12 subjects. Glycine treatment was associated with an 8-fold increase in serum glycine levels, similar to that observed previously. A significant 34% reduction in negative symptoms was observed during glycine treatment. Serum antipsychotic levels were not significantly altered. Significant clinical effects were observed despite the fact that the majority of subjects were receiving atypical antipsychotics (clozapine or olanzapine). As in earlier studies, improvement persisted following glycine discontinuation.

Oral glycine administration increases brain glycine/creatine ratios in men: a proton magnetic resonance spectroscopy study**Marc J. Kaufman,a,* Andrew P. Prescott,a Dost Ongur,a A. Eden Evins,b Tanya L. Barros,a Carissa L. Medeiros,a Julie Covell,a Liqun Wang,c Maurizio Fava,b and Perry F. Renshawa****Author information Copyright and License information Disclaimer****The publisher's final edited version of this article is available at Psychiatry Res****Abstract**

Oral high-dose glycine administration has been used as an adjuvant treatment for schizophrenia to enhance glutamate neurotransmission and mitigate glutamate system hypofunction thought to contribute to the disorder. Prior studies in schizophrenia subjects documented clinical improvements after 2 weeks of oral glycine administration, suggesting that brain glycine levels are sufficiently elevated to evoke a clinical response within that time frame. However, no human study has reported on brain glycine changes induced by its administration. We utilized a noninvasive proton magnetic resonance spectroscopy (1H-MRS) technique termed echo time-averaged (TEAV) 1H-MRS, which permits noninvasive quantification of brain glycine in vivo, to determine whether 2 weeks of oral glycine administration (peak dose of 0.8g/kg/day) increased brain glycine/creatine (Gly/Cr) ratios in 11 healthy adult men. In scans obtained 17 hours after the last glycine dose, brain (Gly/Cr) ratios were significantly increased. The data indicate that it is possible to measure brain glycine changes with proton spectroscopy. Developing a more comprehensive understanding of human brain glycine dynamics may lead to optimized use of glycine site agonists and glycine transporter inhibitors to treat schizophrenia, and possibly to treat other disorders associated with glutamate system dysfunction.

Health Effects and Sources of Prebiotic Dietary Fiber**Justin L Carlson,¹ Jennifer M Erickson,¹ Beate B Lloyd,² and Joanne L Slavin¹****Author information Article notes Copyright and License information Disclaimer****This article has been cited by other articles in PMC.****Abstract**

Prebiotic dietary fibers act as carbon sources for primary and secondary fermentation pathways in the colon, and support digestive health in many ways. Fructooligosaccharides, inulin, and galactooligosaccharides are universally agreed-upon prebiotics. The objective of this paper is to summarize the 8 most prominent health benefits of prebiotic dietary fibers that are due to their fermentability by colonic microbiota, as well as summarize the 8 categories of prebiotic dietary fibers that support these health benefits. Although not all categories exhibit similar effects in human studies, all of these categories promote digestive health due to their fermentability. Scientific and regulatory definitions of prebiotics differ greatly, although health benefits of these compounds are uniformly agreed upon to be due to their fermentability by gut microbiota. Scientific evidence suggests that 8 categories of compounds all exhibit health benefits related to their metabolism by colonic taxa.

Inulin: Properties, health benefits and food applications**Author links open overlay panel: Muhammad Shoaib, Aamir Shehzada, Mukama Omar, Allah Rakha Husnain Raza, Hafiz, Rizwan Sharif, Azam Shakeel, Anum Ansari, Sobia Niazi****Abstract**

Inulin is a water soluble storage polysaccharide and belongs to a group of non-digestible carbohydrates called fructans. Inulin has attained the GRAS status in USA and is extensively available in about 36,000 species of plants, amongst, chicory roots are considered as the richest source of inulin. Commonly, inulin is used as a prebiotic, fat replacer, sugar replacer, texture modifier and for the development of functional foods in order to improve health due to its beneficial role in gastric health. This review provides a deep insight about its production, physicochemical properties, role in combating various kinds of metabolic and diet related diseases and utilization as a functional ingredient in novel product development.

Effects of High Performance Inulin Supplementation on Glycemic Status and Lipid Profile in Women with Type 2 Diabetes: A Randomized, Placebo-Controlled Clinical Trial

Parvin Dehghan, 1 Bahram Pourghassem Gargari, 2 ,* and Mohammad Asgharijafarabadi 3

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Abstract

Background: Type 2 diabetes mellitus, as a noncommunicable disease, is the main public health challenge in the 21st century. The prevalence of diabetes mellitus adjusted for the world population in Iran was 8% until the year 2010. Lipid levels are considered as important parameters to be evaluated, as high serum lipid levels are often reported as a complication in patients with diabetes mellitus. It is claimed that functional foods may improve complications of diabetes mellitus, so this study was designed to evaluate the effects of high performance inulin on glycemic status and lipid profile of women with type 2 diabetes.

Methods: The study was a randomized controlled clinical trial. Forty-nine type 2 diabetic females (fiber intake <30g/d, 25<BMI<35 kg/m²) were divided into two groups. Patients in the intervention group (n=24) received 10g/d inulin and patients in the control group (n=25) received 10g/d maltodextrin for 8 weeks. Glycemic status and lipid profile indices were measured pre and post intervention. Data were analyzed using SPSS software (version 11.5). Paired, unpaired t-test and ANCOVA were used to compare quantitative variables.

Results: Supplementation with inulin caused a significant reduction in FBS (8.50%), HbA1c (10.40%), total cholesterol (12.90%), triglyceride (23.60 %), LDL-c (35.30 %), LDL-c/HDL-c ratio (16.25%) and TC/HDL-c ratio (25.20%) and increased HDL-c (19.90%). The changes for the control group parameters were not significant at the end of study.

Conclusion: Inulin may help to control diabetes and its complications via improving glycemic and lipid parameters.

Effects of Inulin-Type Fructans on Appetite, Energy Intake, and Body Weight in Children and Adults: Systematic Review of Randomized Controlled Trials

Liber A. · Szajewska H.

Ann Nutr Metab 2013;63:42-54

<https://doi.org/10.1159/000350312>

Abstract

Aim: To systematically evaluate the effects of inulin-type fructan (ITF) supplementation on appetite, energy intake, and body weight (BW) in children and adults.

Methods: The MEDLINE, EMBASE, and Cochrane Library databases were searched up to December 2012 for randomized controlled trials (RCTs) that compared the effects of supplementation with well-defined ITF with placebo or no intervention.

Results: For the pediatric population, 4 RCTs (n = 232) met the inclusion criteria. In infants, very limited evidence (1 RCT, n = 62) showed no effect of ITF supplementation on energy intake and BW. One RCT involving 97 nonobese adolescents aged 9 to 13 years found a reduced increase in BW in the oligofructose + inulin (8 g/day) group compared with the control group after 1 year. For the adult population, 15 RCTs (n = 545) met the inclusion criteria. Five RCTs found no effect of ITF supplementation on appetite sensations. Eleven RCTs found no effect of ITF supplementation on daily energy intake or energy intake during a meal tolerance test. Among 3 RCTs that assessed the effect of ITF supplementation on BW, 2 RCTs showed a (significant) reduction in BW. Of 3 RCTs that evaluated body mass index (BMI), 1 RCT showed a significant reduction in BMI in subjects supplemented with ITF.

Conclusion: Limited data suggest that long-term administration of ITF may contribute to weight reduction.

Prebiotic inulin-type fructans induce specific changes in the human gut microbiota**Doris Vandeputte,^{1,2,3} Gwen Falony,^{1,2} Sara Vieira-Silva,^{1,2} Jun Wang,^{1,2} Manuela Sailer,⁴ Stephan Theis,⁴ Kristin Verbeke,⁵ and Jeroen Raes^{1,2,3}**

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Contrary to the long-standing prerequisite of inducing selective (ie, bifidogenic) effects, recent findings suggest that prebiotic interventions lead to ecosystem-wide microbiota shifts. Yet, a comprehensive characterisation of this process is still lacking. Here, we apply 16S rDNA microbiota profiling and matching (gas chromatography mass spectrometry) metabolomics to assess the consequences of inulin fermentation both on the composition of the colon bacterial ecosystem and faecal metabolites profiles.

Design: Faecal samples collected during a double-blind, randomised, cross-over intervention study set up to assess the effect of inulin consumption on stool frequency in healthy adults with mild constipation were analysed. Faecal microbiota composition and metabolite profiles were linked to the study's clinical outcome as well as to quality-of-life measurements recorded.

Results: While faecal metabolite profiles were not significantly altered by inulin consumption, our analyses did detect a modest effect on global microbiota composition and specific inulin-induced changes in relative abundances of *Anaerostipes*, *Bilophila* and *Bifidobacterium* were identified. The observed decrease in *Bilophila* abundances following inulin consumption was associated with both softer stools and a favourable change in constipation-specific quality-of-life measures.

Conclusions: Ecosystem-wide analysis of the effect of a dietary intervention with prebiotic inulin-type fructans on the colon microbiota revealed that this effect is specifically associated with three genera, one of which (*Bilophila*) representing a promising novel target for mechanistic research.

Anti-Oxidative Effects of Rooibos Tea (*Aspalathus linearis*) on Immobilization-Induced Oxidative Stress in Rat Brain

In-Sun Hong,# 1 , 2 Hwa-Yong Lee,# 1 , 2 and Hyun-Pyo Kim 3 , *
Xianglin Shi, Editor

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Abstract:

Exposure to chronic psychological stress may be related to increased reactive oxygen species (ROS) or free radicals, and thus, long-term exposure to high levels of oxidative stress may cause the accumulation of oxidative damage and eventually lead to many neurodegenerative diseases. Compared with other organs, the brain appears especially susceptible to excessive oxidative stress due to its high demand for oxygen. In the case of excessive ROS production, endogenous defense mechanisms against ROS may not be sufficient to suppress ROS-associated oxidative damage. Dietary antioxidants have been shown to protect neurons against a variety of experimental neurodegenerative conditions. In particular, Rooibos tea might be a good source of antioxidants due to its larger proportion of polyphenolic compounds. An optimal animal model for stress should show the features of a stress response and should be able to mimic natural stress progression. However, most animal models of stress, such as cold-restraint, electric foot shock, and burn shock, usually involve physical abuse in addition to the psychological aspects of stress. Animals subjected to chronic restraint or immobilization are widely believed to be a convenient and reliable model to mimic psychological stress. Therefore, in the present study, we propose that immobilization-induced oxidative stress was significantly attenuated by treatment with Rooibos tea. This conclusion is demonstrated by Rooibos tea's ability to (i) reverse the increase in stress-related metabolites (5-HIAA and FFA), (ii) prevent lipid peroxidation (LPO), (iii) restore stress-induced protein degradation (PD), (iv) regulate glutathione metabolism (GSH and GSH/GSSG ratio), and (v) modulate changes in the activities of antioxidant enzymes (SOD and CAT).

Unfermented and fermented rooibos teas (*Aspalathus linearis*) increase plasma total antioxidant capacity in healthy humans

Author links open overlay panel: Débora Villaño, Monia Pecorari, Maria Francesca Testa, Anna Raguzzini, Angélique Stalmach, Alan Crozier, Claudio Tubili, Mauro Serafini.

<https://doi.org/10.1016/j.foodchem.2010.05.032>Get rights and content

Abstract:

The aim of the study was to assess the effect of drinking rooibos tea (*Aspalathus linearis*) on total antioxidant capacity (TAC), lipid triacylglycerols, cholesterol and glycaemia plasma levels in humans. In vitro, unfermented rooibos tea displayed a 28% higher value of TRAP than did the fermented beverage. An acute intervention study, cross-over design, was performed, with 15 healthy volunteers who consumed 500 ml of either water, unfermented or fermented rooibos teas. Plasma antioxidant capacity increased significantly with both teas, reaching a peak at 1 h post-consumption (+6.6%, $p < 0.05$ fermented tea; +2.9%, $p < 0.01$ unfermented tea). No changes in triacylglycerols, cholesterol or uric acid were observed with any of the treatments. A transitory increase in glycaemia at 30 min was linked to glucose upload. The data show that rooibos teas represent a source of dietary antioxidants in humans.

Bioavailability of C-linked dihydrochalcone and flavanone glucosides in humans following ingestion of unfermented and fermented rooibos teas

Angélique Stalmach 1, William Mullen, Monia Pecorari, Mauro Serafini, Alan Crozier

Affiliations expand

PMID: 19534535 DOI: 10.1021/jf9011642

Abstract:

High-performance liquid chromatography-mass spectrometry (HPLC-MS(n)) detected aspalathin and nothofagin, C-glycosides of apigenin and luteolin, and four eriodictyol-C-glycoside isomers in unfermented and fermented rooibos teas. The fermented drink contained 10-fold higher levels of aspalathin and nothofagin and a 4-fold lower eriodictyol-C-glycoside content than the fermented tea. The total flavonoid contents in 500 mL servings of the teas were 84 (fermented) and 159 μmol (unfermented). Following the ingestion of 500 mL of the teas by 10 volunteers, 0-24 h urine and plasma samples were collected for analysis. HPLC-MS(n) identified eight metabolites in urine. These were O-linked methyl, sulfate, and glucuronide metabolites of aspalathin and an eriodictyol-O-sulfate. The main compound excreted was an O-methyl-aspalathin-O-glucuronide (229 nmol) following ingestion of the unfermented drink and eriodictyol-O-sulfate (68 nmol) after ingestion of the fermented beverage. The overall metabolite levels excreted were 82 and 352 nmol, accounting for 0.09 and 0.22% of the flavonoids in the fermented and unfermented drinks, respectively. Most of the aspalathin metabolites were excreted within 5 h of tea consumption, suggesting absorption in the small intestine. Urinary excretion of the eriodictyol-O-sulfate occurred mainly during the 5-12 h collection period, indicative of absorption in the large intestine. Despite exhaustive searches, no flavonoid metabolites were detected in plasma.

Aspalathin from Rooibos (*Aspalathus linearis*): A Bioactive C-glucosyl Dihydrochalcone with Potential to Target the Metabolic Syndrome

Rabia Johnson 1 2, Dalene de Beer 3 4, Phiwayinkosi V Dlodla 1 2, Daneel Ferreira 5, Christo J F Muller 1 2 6, Elizabeth Joubert 3 4

Affiliations expand

PMID: 29388183 DOI: 10.1055/s-0044-100622

Abstract:

Aspalathin is a C-glucosyl dihydrochalcone that is abundantly present in *Aspalathus linearis*. This endemic South African plant, belonging to the Cape Floristic region, is normally used for production of rooibos, a herbal tea. Aspalathin was valued initially only as precursor in the formation of the characteristic red-brown colour of "fermented" rooibos, but the hype about the potential role of natural antioxidants to alleviate oxidative stress, shifted interest in aspalathin to its antioxidant properties and subsequently, its potential role to improve metabolic syndrome, a disease condition interrelated with oxidative stress. The potential use of aspalathin or aspalathin-rich rooibos extracts as a condition-specific nutraceutical is hampered by the limited supply of green rooibos (i.e., "unfermented" plant material) and low levels in "fermented" rooibos, providing incentive for its synthesis. In vitro and in vivo studies relating to the metabolic activity of aspalathin are discussed and cellular mechanisms by which aspalathin improves glucose and lipid metabolism are proposed. Other aspects covered in this review, which are relevant in view of the potential use of aspalathin as an adjunctive therapy, include its poor stability and bioavailability, as well as potential adverse herb-drug interactions, in particular interference with the metabolism of certain commonly prescribed chronic medications for hyperglycaemia and dyslipidaemia.

Hyperglycemia-induced oxidative stress and heart disease-cardioprotective effects of rooibos flavonoids and phenylpyruvic acid-2- O-β-D-glucoside

Phiwayinkosi V Dlodla 1 2, Elizabeth Joubert 3 4, Christo J F Muller 1 2 5, Johan Louw 1 5, Rabia Johnson 1 2

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PMID: 28702068 PMCID: PMC5504778 DOI: 10.1186/s12986-017-0200-8

Free PMC article

Abstract:

Diabetic patients are at an increased risk of developing heart failure when compared to their non-diabetic counterparts. Accumulative evidence suggests chronic hyperglycemia to be central in the development of myocardial infarction in these patients. At present, there are limited therapies aimed at specifically protecting the diabetic heart at risk from hyperglycemia-induced injury. Oxidative stress, through overproduction of free radical species, has been hypothesized to alter mitochondrial function and abnormally augment the activity of the NADPH oxidase enzyme system resulting in accelerated myocardial injury within a diabetic state. This has led to a dramatic increase in the exploration of plant-derived materials known to possess antioxidative properties. Several edible plants contain various natural constituents, including polyphenols that may counteract oxidative-induced tissue damage through their modulatory effects of intracellular signaling pathways. Rooibos, an indigenous South African plant, well-known for its use as herbal tea, is increasingly studied for its metabolic benefits. Prospective studies linking diet rich in polyphenols from rooibos to reduced diabetes associated cardiovascular complications have not been extensively assessed. Aspalathin, a flavonoid, and phenylpyruvic acid-2-O-β-D-glucoside, a phenolic precursor, are some of the major compounds found in rooibos that can ameliorate hyperglycemia-induced cardiomyocyte damage in vitro. While the latter has demonstrated potential to protect against cell apoptosis, the proposed mechanism of action of aspalathin is linked to its capacity to enhance the expression of nuclear factor (erythroid-derived 2)-like 2 (Nrf2) expression, an intracellular antioxidant response element. Thus, here we review literature on the potential cardioprotective properties of flavonoids and a phenylpropanoic acid found in rooibos against diabetes-induced oxidative injury.

Long-term administration of Aspalathus linearis infusion affects spatial memory of adult Sprague-Dawley male rats as well as increases their striatal dopamine content

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Authors:

Justyna Pyrzanowska, Izabela Fecka, Dagmara Mirowska-Guzel, Ilona Joniec

Abstract:

Ethnopharmacological relevance: Everyday use of the herbal tea rooibos, produced from *Aspalathus linearis* (Brum.f) Dahlg. (Fabaceae) is customary in South Africa, a continuation of its historical use by indigenous people. Although evidence of its traditional indications is anecdotal, rooibos tea is regarded as a general health tea. Aims of the study: Available contemporary research indicates to broad cell protective activity of rooibos focusing on its antioxidative, anti-inflammatory, anti-hyperglycaemic and antithrombotic features affecting metabolic syndrome, cardiovascular risk and neuroprotection. Nevertheless little is known about its impact on brain functions. The present experiment aimed to evaluate the possible behavioural and neurochemical effects of long-term oral administration of "fermented" rooibos herbal tea (FRHT) infusions to adult male Sprague-Dawley rats. Materials and methods: Infusions, prepared using 1, 2 and 4 g of "fermented" (oxidised) *A. linearis* leaves for 100 ml of hot water, were characterised in terms of flavonoid content by ultra-high and high performance liquid chromatography (UHPLC-qTOF-MS, HPLC-DAD) and administered to rats as sole drinking fluid for 12 weeks. Spatial memory behaviour was assessed in a modified version of the Morris water maze. Dopamine, noradrenaline, serotonin and their metabolite levels (DOPAC, 3-MT, HVA, MHPG, 5-HIAA) were quantified in prefrontal cortex, hippocampus and striatum by HPLC-ECD. Body weight and blood glucose level were additionally estimated. Results: All FRHT-treated rats showed improvement of long-term spatial memory defined as increased number of crossings over the previous platform position in SE quadrant of the water maze. It was not accompanied by excessive motor activity. Striatal dopamine and its metabolite 3-MT (3-methoxytyramine) levels were increased in treated rats. There were no differences in body weight gain between control and treated animals but blood glucose level was significantly lower in the latter ones. Conclusion: The improvement of long-term memory in FRHT-treated rats and stimulating impact of FRHT on their dopaminergic striatal transmission support the wellness enhancing effect of rooibos tea, contributing to a better understanding of the neurological background of traditional habitual consumption of this herbal tea.