# GBX PEP

Good-For-Your-Gut Energy Drink

amare®

TECHNICAL DATA SHEET

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.


# GBX PEP

Good-For-Your-Gut Energy Drink

Cutting edge gut-brain axis science packed into a refreshing strawberry cream beverage that puts other energy drinks to shame. Put a "pep" in your step with prebiotics and probiotics that help support cognitive function, improved concentration, healthy digestion, and happy taste buds…anytime, anywhere.* #GBXPepSquad

## Why You'll Love It

- Supports mental alertness and improved concentration.*
- Clean energy from organic natural caffeine.*
- Supports a healthy gut microbiome.*
- Helps aid in healthy digestion.*
- Zero Sugar. No gluten, dairy, or soy.*
- All pep!

## What It Is

- A delicious infusion of probiotics, prebiotics, and organic caffeine.*
- Probiotics: DE111® Bacillus subtilis, Organic Live Kombucha
- Prebiotics: PFBc (Palm Fruit Bioactives), Sunfiber®
- Clean energy: Organic Green Coffee Bean (contains caffeine), Suntheanine®

## How It Works

- The crisp taste puts a smile on your face :)
- Specific probiotics to help aid in healthy digestion.*
- Specific prebiotics to support cognitive function and microbiome diversity.*
- Organic caffeine for improved mental alertness.*
- Suntheanine for improved concentration.*

## CLINICAL STUDIES

### Tolerance and Effect of a Probiotic Supplement Delivered in Capsule FormGina Labellarte, Margaret Maher

Biology Department, University of Wisconsin, La Crosse, USA.

DOI: 10.4236/fns.2019.106046 PDF HTML XML 1,006 Downloads 3,716 Views Citations

**Abstract**
Probiotic supplements have shown benefits in increasing frequency and efficiency of bowel movements and some strains have shown to reduce serum glucose levels. Bacillus subtilis is used in the fermentation of some foods for probiotic effects and may be useful in concentrated supplement form. The first objective of this clinical study was to determine if daily consumption of Bacillus subtilis strain DE111 at a dose of 5 × 109 CFU is safe for human consumption. The second objective was to determine the effectiveness at increasing frequency of normal bowel movements and improving consistency of bowel type, by increasing beneficial gut microbes and reducing pathogenic ones. The tolerance and efficacy of encapsulated Bacillus subtilis DE111 was assessed in an average 20-day double-blind, randomized, and placebo-controlled human study. Most blood parameters remained within normal ranges throughout; however, fasted serum glucose levels in the probiotic group (91.0 ± 1.0 to 85.9 ± 1.4 mg/dl, $\alpha \leq 0.05$; $P = 0.012$) were significantly reduced. Although there was a significant increase in the average number of bowel movements per day within the placebo group ($\alpha \leq 0.05$; $P = 0.015$), there was no significant change in the type. Triglyceride levels were maintained within the probiotic group, while the control group displayed a significant increase from pre to post by paired T-test ($\alpha \leq 0.05$; $P \leq 0.042$) (Figure 2). Additionally, significant differences in microbe colonization were present for Bacillus subtilis and Bifidobacterium in the fecal colony counts. Daily consumption of Bacillus subtilis can be recognized as safe, and has potential to be effective as a supplement to improve glucose tolerance.

## Examining the Gastrointestinal and Immunomodulatory Effects of the Novel Probiotic Bacillus subtilis DE111

Kimberley E Freedman 1, Jessica L Hill 2, Yuren Wei 1, Allegra R Vazquez 1 3, Diana S Grubb 1, Roxanne E Trotter 1, Scott D Wrigley 1, Sarah A Johnson 3, Michelle T Foster 2, Tiffany L Weir 1

### Abstract

Probiotics make up a large and growing segment of the commercial market of dietary supplements and are touted as offering a variety of human health benefits. Some of the purported positive impacts of probiotics include, but are not limited to, stabilization of the gut microbiota, prevention of gastrointestinal disorders and modulation of the host immune system. Current research suggests that the immunomodulatory effects of probiotics are strain-specific and vary in mode of action. Here, we examined the immunomodulatory properties of Bacillus subtilis strain DE111 in a healthy human population. In a pilot randomized, double blind, placebo-controlled four-week intervention, we examined peripheral blood mononuclear cells (PBMCs) at basal levels pre- and post-intervention, as well as in response to stimulation with bacterial lipopolysaccharide (LPS). We observed an increase in anti-inflammatory immune cell populations in response to ex vivo LPS stimulation of PBMCs in the DE111 intervention group. Overall perceived gastrointestinal health, microbiota, and circulating and fecal markers of inflammation (Il-6, sIgA) and gut barrier function (plasma zonulin) were largely unaffected by DE111 intervention, although the study may have been underpowered to detect these differences. These pilot data provide information and justification to conduct an appropriately powered clinical study to further examine the immunomodulatory potential of B. subtilis DE111 in human populations.

**Examining the Gastrointestinal and Immunomodulatory Effects of the Novel Probiotic Bacillus subtilis DE111**

Joan Colom, [1] , † Daniela Freitas, [2], † Annie Simon, [1] Andre Brodkorb, [2] Martin Buckley, [3] John Deaton, [4] , * and Alison M. Winger [1]

**Abstract**
Spore-based probiotics offer important advantages over other probiotics as they can survive the harsh gastric conditions of the stomach and bile salts in the small intestine, ultimately germinating in the digestive tract. A novel clinical trial in 11 ileostomy participants was conducted to directly investigate the presence and germination of the probiotic strain Bacillus subtilis DE111® in the small intestine. Three hours following ingestion of DE111®, B. subtilis spores (6.4 × 104 ± 1.3 × 105 CFU/g effluent dry weight) and vegetative cells (4.7 × 104 ± 1.1 × 105 CFU/g effluent dry weight) began to appear in the ileum effluent. Six hours after ingestion, spore concentration increased to 9.7 × 107 ± 8.1 × 107 CFU/g and remained constant to the final time point of 8 h. Vegetative cells reached a concentration of 7.3 × 107 ± 1.4 × 108 CFU/g at 7 h following ingestion. These results reveal orally ingested B. subtilis DE111® spores are able to remain viable during transit through the stomach and germinate in the small intestine of humans within 3 h of ingestion.

**Daily intake of probiotic strain Bacillus subtilis DE111 supports a healthy microbiome in children attending day-care**

November 2020Beneficial Microbes 11(7):611-620

Authors:

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**Abstract and Figures**

There is ample evidence suggesting that modulations in gut microbiota play an important role in inflammation and immunity. In particular, the microbiota of children is highly susceptible to environment influences, such as infections. Consequently, probiotics and their ability to promote and support a healthy microbiome have been increasingly studied. This study aimed at investigating the effects of a probiotic supplement (Bacillus subtilis DE111) on the microbiome composition of preschool aged children attending day care. Healthy children aged 2-6 years old were randomised to receive either probiotic or placebo once a day for 8 weeks. No significant changes of the overall microbiome equilibrium were seen in between the two groups or from baseline to week 8. However, alpha diversity was increased in the probiotic group from baseline to week 8 ($P<0.05$), with no change in the placebo group. A decrease in the Firmicutes/Bacteroidetes ratio following probiotic supplementation ($P<0.05$) was also observed. Differential abundance analysis revealed an increase in Alistepes ($P<0.01$), Bacteroides ($P<0.05$), Parabacteroides ($P<0.01$), Odoribacter ($P<0.001$) and Rikenellaceae ($P<0.001$) in the probiotic group, most of which are involved in inflammation reduction. In addition, a decrease in Eisenbergiella ($P<0.001$), Lactobacillales ($P<0.01$) and Streptococcaceae ($P<0.01$), which is considered pro-inflammatory, were also observed in the probiotic group. Together with a reduction of the F/B ratio observed in the probiotic group, these results suggest probiotic supplementation with Bacillus subtilis DE111 introduce subtle but positive changes in the microbiome of children aged 2-6 years old

## Effects of Probiotic (Bacillus subtilis) Supplementation During Offseason Resistance Training in Female Division I Athletes

Jeremy C Toohey 1, Jeremy R Townsend 1, Sean B Johnson 1, Ann M Toy 1, William C Vantrease 1, David Bender 1, Chelsea C Crimi 1, Kathryn L Stowers 1, Matthew D Ruiz 1, Trisha A VanDusseldorp 2, Yuri Feito 2, Gerald T Mangine 2

### Abstract

Toohey, JC, Townsend, JR, Johnson, SB, Toy, AM, Vantrease, WC, Bender, D, Crimi, CC, Stowers, KL, Ruiz, MD, VanDusseldorp, TA, Feito, Y, and Mangine, GT. Effects of probiotic (Bacillus subtilis) supplementation during offseason resistance training in female Division I athletes. J Strength Cond Res 34(11): 3173-3181, 2020-We examined the effects of probiotic (Bacillus subtilis) supplementation during offseason training in collegiate athletes. Twenty-three Division I female athletes (19.6 ± 1.0 years, 67.5 ± 7.4 kg, and 170.6 ± 6.8 cm) participated in this study and were randomized into either a probiotic (n = 11; DE111) or placebo (n = 12; PL) group while counterbalancing groups for sport. Athletes completed a 10-week resistance training program during the offseason, which consisted of 3-4 workouts per week of upper- and lower-body exercises and sport-specific training. Athletes consumed DE111 (DE111; 5 billion CFU/day) or PL supplement daily for the entire 10-week program. Before and after training, all athletes underwent 1 repetition maximum (1RM) strength testing (squat, deadlift, and bench press), performance testing (vertical jump and pro-agility), and isometric midthigh pull testing. Body composition (body fat [BF]%) was completed using BODPOD and bioelectrical impedance analysis, as well as muscle thickness (MT) measurement of the rectus femoris (RF) and vastus lateralis using ultrasonography. Separate repeated-measures analyses of variance were used to analyze all data. Significant ($p \leq 0.05$) main effects for time were observed for improved squat 1RM, deadlift 1RM, bench press 1RM, vertical jump, RF MT, and BF%. Of these, a significant group × time interaction was noted for BF% ($p = 0.015$), where greater reductions were observed in DE111 (-2.05 ± 1.38%) compared with PL (-0.2 ± 1.6%). No other group differences were observed. These data suggest that probiotic consumption in conjunction with post-workout nutrition had no effect on physical performance but may improve body composition in female Division I soccer and volleyball players after offseason training.

**Effects of Probiotic ( Bacillus subtilis DE111) Supplementation on Immune Function, Hormonal Status, and Physical Performance in Division I Baseball Players**

Jeremy R Townsend [1], David Bender [2], William C Vantrease [3], Philip A Sapp [4], Ann M Toy [5], Clint A Woods [6], Kent D Johnson [7]

**Abstract**

We sought to determine the effects of probiotic supplementation (Bacillus subtilis DE111; 1 billion CFU·d-1) on markers of immune and hormonal status in collegiate male athletes following 12 weeks of offseason training. Twenty-five Division I male baseball athletes (20.1 ± 1.5 years, 85.5 ± 10.5 kg, 184.7 ± 6.3 cm) participated in this double blind, placebo-controlled, randomized study. Participants were randomly assigned to a probiotic (PRO; n = 13) or placebo (PL; n = 12) group. Pre- and post-training, all athletes provided resting blood and saliva samples. Circulating concentrations of testosterone, cortisol, TNF-α, IL-10, and zonulin were examined in the blood, while salivary immunoglobulin A (SIgA) and SIgM were assayed as indicators of mucosal immunity. Separate analyses of covariance (ANCOVA) were performed on all measures collected post intervention. No differences in measures of body composition or physical performance were seen between groups. TNF-α concentrations were significantly ($p = 0.024$) lower in PRO compared to PL, while there were no significant group differences in any other biochemical markers examined. A main effect for time was observed ($p < 0.05$) for increased testosterone ($p = 0.045$), IL-10 ($p = 0.048$), SIgA rate ($p = 0.031$), and SIgM rate ($p = 0.002$) following offseason training. These data indicate that probiotic supplementation had no effect on body composition, performance, hormonal status, or gut permeability, while it may attenuate circulating TNF-α in athletes.

**Bacillus subtilis DE111 intake may improve blood lipids and endothelial function in healthy adults**

R E Trotter 1, A R Vazquez 1, D S Grubb 1, K E Freedman 1, L E Grabos 1, S Jones 1, C L Gentile 1, C L Melby 1, S A Johnson 1, T L Weir 1

**Abstract**
Cardiovascular disease (CVD) is the leading cause of death in the US and worldwide. By 2030 it is anticipated that CVD will claim the lives of more than 24 million people. Throughout the last decade, researchers have investigated the role of the gut microbiota in the development of CVD. Evidence exists for a positive correlation between Bifidobacterium and vascular function, glucose tolerance, and reduced systemic inflammation. Another probiotic species, Bacillus subtilis, has also been found to reduce cholesterol levels in human and animal models. In light of these data, we examined various measures of cardiovascular health after consumption of Bifidobacterium animalis subsp. lactis strain BL04, with and without a cocktail of Escherichia coli-targeting bacteriophages (marketed as PreforPro), Bacillus subtilis strain DE111 or a maltodextrin-based placebo in a healthy human population. In a randomised, double-blind, placebo-controlled 4-week intervention conducted in individuals 18 to 65 years of age with a body mass index of 20 to 34.9, we saw no significant changes in measured CVD parameters among individuals consuming B. lactis with or without bacteriophages. However, B. subtilis supplementation resulted in a significant reduction in total cholesterol relative to baseline measures (-8 mg/dl; P=0.04, confidence interval (CI): -13.40, -0.19), as well as non-high-density lipoprotein-cholesterol (-11 mg/dl; P=0.01, CI: -12.43, -2.07). In addition we observed trending improvements in endothelial function (P=0.05, CI: -0.003, 0.370) and in low-density lipoprotein-cholesterol (P=0.06, CI:-12.29, 0.2864). Strikingly, these effects were seen in a largely healthy population. These data suggest that B. subtilis supplementation may be beneficial for improving risk factors associated with CVD. Further studies in populations of older adults or those with dyslipidaemia and endothelial dysfunction is warranted.

Keywords: Bacillus subtilis; Bifidobacterium lactis; bacteriophage; cardiovascular disease; probiotic; vascular function.

**Palm Fruit Bioactives modulate human astrocyte activity in vitro altering the cytokine secretome reducing levels of TNFα, RANTES and IP-10**

Robert P Weinberg [1,2], Vera V Koledova [3,4], Kirsten Schneider [3,4], T G Sambandan [3,4], Adlai Grayson [3,4], Gal Zeidman [3,4], Anastasia Artamonova [3,4], Ravigadevi Sambanthamurthi [5], Syed Fairus [5], Anthony J Sinskey [3,4], ChoKyun Rha [6]

**Abstract**

Neurodegenerative diseases, including Alzheimer's disease and Parkinson's disease, are becoming more prevalent and an increasing burden on society. Neurodegenerative diseases often arise in the milieu of neuro-inflammation of the brain. Reactive astrocytes are key regulators in the development of neuro-inflammation. This study describes the effects of Palm Fruit Bioactives (PFB) on the behavior of human astrocytes which have been activated by IL-1β. When activated, the astrocytes proliferate, release numerous cytokines/chemokines including TNFα, RANTES (CCL5), IP-10 (CXCL10), generate reactive oxygen species (ROS), and express specific cell surface biomarkers such as the Intercellular Adhesion Molecule (ICAM), Vascular Cellular Adhesion Molecule (VCAM) and the Neuronal Cellular Adhesion Molecule (NCAM). Interleukin 1-beta (IL-1β) causes activation of human astrocytes with marked upregulation of pro-inflammatory genes. We show significant inhibition of these pro-inflammatory processes when IL-1β-activated astrocytes are exposed to PFB. PFB causes a dose-dependent and time-dependent reduction in specific cytokines: TNFα, RANTES, and IP-10. We also show that PFB significantly reduces ROS production by IL-1β-activated astrocytes. Furthermore, PFB also reduces the expression of ICAM and VCAM, both in activated and naïve human astrocytes in vitro. Since reactive astrocytes play an essential role in the neuroinflammatory state preceding neurodegenerative diseases, this study suggests that PFB may have a potential role in their prevention and/or treatment.

## The Pharmacological Potential of Oil Palm Phenolics (OPP) Individual Components

Syed-Badrul Syarifah-Noratiqah,[1] Mohamed S Zulfarina,[1] Shihab Uddin Ahmad,[1] Syed Fairus,[2] and Isa Naina-Mohamed[1]

**Abstract**

The oil palm tree (Elaeis guineensis) from the family Arecaceae is a high oil-producing agricultural crop. A significant amount of vegetation liquor is discarded during the palm oil milling process amounting to 90 million tons per year around the world. This water-soluble extract is rich in phenolic compounds known as Oil Palm Phenolics (OPP). Several phenolic acids including the three isomers of caffeoylshikimic acid (CFA), p-hydroxybenzoic acid (PHBA), protocatechuic acid (PCA) and hydroxytyrosol are among the primary active ingredients in the OPP. Previous investigations have reported several positive pharmacological potentials by OPP such as neuroprotective and atheroprotective effects, anti-tumor and reduction in Aβ deposition in Alzheimer's disease model. In the current review, the pharmacological potential for CFA, PHBA, PCA and hydroxytyrosol is carefully reviewed and evaluated.

## Oil Palm Phenolics Inhibit the In Vitro Aggregation of β-Amyloid Peptide into Oligomeric Complexes

Robert P. Weinberg, [1] Vera V. Koledova, [1] Hyeari Shin, [1] Jennifer H. Park, [1] Yew Ai Tan, [2] Anthony J. Sinskey, [3] Ravigadevi Sambanthamurthi, [2] and ChoKyun Rha[1]

### Abstract

Alzheimer's disease is a severe neurodegenerative disease characterized by the aggregation of amyloid-β peptide (Aβ) into toxic oligomers which activate microglia and astrocytes causing acute neuroinflammation. Multiple studies show that the soluble oligomers of Aβ42 are neurotoxic and proinflammatory, whereas the monomers and insoluble fibrils are relatively nontoxic. We show that Aβ42 aggregation is inhibited in vitro by oil palm phenolics (OPP), an aqueous extract from the oil palm tree (Elaeis guineensis). The data shows that OPP inhibits stacking of β-pleated sheets, which is essential for oligomerization. We demonstrate the inhibition of Aβ42 aggregation by (1) mass spectrometry; (2) Congo Red dye binding; (3) 2D-IR spectroscopy; (4) dynamic light scattering; (5) transmission electron microscopy; and (6) transgenic yeast rescue assay. In the yeast rescue assay, OPP significantly reduces the cytotoxicity of aggregating neuropeptides in yeast genetically engineered to overexpress these peptides. The data shows that OPP inhibits (1) the aggregation of Aβ into oligomers; (2) stacking of β-pleated sheets; and (3) fibrillar growth and coalescence. These inhibitory effects prevent the formation of neurotoxic oligomers and hold potential as a means to reduce neuroinflammation and neuronal death and thereby may play some role in the prevention or treatment of Alzheimer's disease.

**Palm Fruit Bioactive Complex (PFBc), a Source of Polyphenols, Demonstrates Potential Benefits for Inflammaging and Related Cognitive Function**

Susan J Hewlings [1,2], Kristin Draayer [3], Douglas S Kalman [2,4]

**Abstract**
Cognitive function is a key aspect of healthy aging. Inflammation associated with normal aging, also called inflammaging is a primary risk factor for cognitive decline. A diet high in fruits and vegetable and lower in calories, particularly a Mediterranean Diet, may lower the risk of age-related cognitive decline due in part to the associated high intake of antioxidants and polyphenols. A phenolic, Palm Fruit Bioactive complex (PFBc) derived from the extraction process of palm oil from oil palm fruit (Elaeis guineensis), is reported to offset inflammation due to its high antioxidant, especially vitamin E, and polyphenol content. The benefit is thought to be achieved via the influence of antioxidants on gene expression. It is the purpose of this comprehensive review to discuss the etiology, including gene expression, of mild cognitive impairment (MCI) specific to dietary intake of antioxidants and polyphenols and to focus on the potential impact of nutritional interventions specifically PFBc has on MCI. Several in vitro, in vivo and animal studies support multiple benefits of PFBc especially for improving cognitive function via anti-inflammatory and antioxidant mechanisms. While more human studies are needed, those completed thus far support the benefit of consuming PFBc to enhance cognitive function via its anti-inflammatory antioxidant functions.

Keywords: PFBc; Palm Fruit Bioactive complex; anti-inflammatory; antioxidant; cognitive function; inflammaging; mild cognitive impairment; polyphenols.

**The Use of Green Coffee Extract as a Weight Loss Supplement: A Systematic Review and Meta-Analysis of Randomised Clinical Trials**

Igho Onakpoya, * Rohini Terry, and Edzard Ernst

**Abstract**
The purpose of this paper is to assess the efficacy of green coffee extract (GCE) as a weight loss supplement, using data from human clinical trials. Electronic and nonelectronic searches were conducted to identify relevant articles, with no restrictions in time or language. Two independent reviewers extracted the data and assessed the methodological quality of included studies. Five eligible trials were identified, and three of these were included. All studies were associated with a high risk of bias. The meta-analytic result reveals a significant difference in body weight in GCE compared with placebo (mean difference: −2.47 kg; 95%CI: −4.23, −0.72). The magnitude of the effect is moderate, and there is significant heterogeneity amongst the studies. It is concluded that the results from these trials are promising, but the studies are all of poor methodological quality. More rigorous trials are needed to assess the usefulness of GCE as a weight loss tool.

**The effects of green coffee extract supplementation on glycemic indices and lipid profile in adults: a systematic review and dose-response meta-analysis of clinical trials**

Omid Asbaghi, Mehdi Sadeghian, Morteza Nasiri, Mahmoud Khodadost, Azad Shokri, Bahman Panahande, Aliyar Pirouzi & Omid Sadeghi

Nutrition Journal volume 19, Article number: 71 (2020) Cite this article

**Abstract**

Background

The role of coffee consumption in the risk of cardiovascular diseases has been debated for many years. The current study aimed to summarize earlier evidence on the effects of green coffee extract (GCE) supplementation on glycemic indices and lipid profile.

Methods

We searched available online databases for relevant clinical trials published up to October 2019. All clinical trials investigating the effect of GCE supplementation, compared with a control group, on fasting blood glucose (FBG), serum insulin, total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were included. Overall, 14 clinical trials with a total sample size of 766 participants were included in the current meta-analysis.

Results

We found a significant reducing effect of GCE supplementation on FBG (weighted mean difference (WMD): -2.35, 95% CI: −3.78, −0.92 mg/dL, P = 0.001) and serum insulin (WMD: -0.63, 95% CI: −1.11, −0.15 μU/L, P = 0.01). With regard to lipid profile, we observed a significant reduction only in serum levels of TC following GCE supplementation in the overall meta-analysis (WMD: -4.51, 95% CI: −8.39, −0.64, P = 0.02). However, subgroup analysis showed a significant reduction in serum TG in studies enrolled both genders. Also, such a significant reduction was seen in serum levels of LDL and HDL when the analyses confined to studies with intervention duration of ≥8 weeks and those included female subjects. In the non-linear dose-response analyses, we found that the effects of chlorogenic acid (CGA) dosage, the main polyphenol in GCE, on FBG, TG and HDL were in the non-linear fashions.

**Dietary supplementation with decaffeinated green coffee improves diet-induced insulin resistance and brain energy metabolism in mice**

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Affiliations expand

PMID: 22305652 DOI: 10.1179/1476830511Y.0000000027

**Abstract**

Objectives

There is accumulating evidence that coffee consumption may reduce risk for type 2 diabetes, a known risk factor for Alzheimer's and other neurological diseases. Coffee consumption is also associated with reduced risk for Alzheimer's disease and non-Alzheimer's dementias. However, preventive and therapeutic development of coffee is complicated by the cardiovascular side effects of caffeine intake. As coffee is also a rich source of chlorogenic acids and many bioactive compounds other than caffeine, we hypothesized that decaffeinated coffee drinks may exert beneficial effects on the brain.

Methods

We have investigated whether dietary supplementation with a standardized decaffeinated green coffee preparation, Svetol®, might modulate diet-induced insulin resistance and brain energy metabolism dysfunction in a high-fat diet mouse model.

Results

As expected, dietary supplementation with Svetol® significantly attenuated the development of high-fat diet-induced deficits in glucose-tolerance response. We have also found that Svetol®) treatment improved brain mitochondrial energy metabolism as determined by oxygen consumption rate. Consistent with this evidence, follow-up gene expression profiling with Agilent whole-genome microarray revealed that the decaffeinated coffee treatment modulated a number of genes in the brain that are implicated in cellular energy metabolism.

Discussion

Our evidence is the first demonstration that dietary supplementation with a decaffeinated green coffee preparation may beneficially influence the brain, in particular promoting brain energy metabolic processes.

# The Effect of Green Coffee Bean Extract on Cardiovascular Risk Factors: A Systematic Review and Meta-analysis

Makan Pourmasoumi [1], Amir Hadi [2], Wolfgang Marx [3], Ameneh Najafgholizadeh [4], Sukhdeep Kaur [5], Amirhossein Sahebkar [6 7 8]

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PMID: 34981487

DOI: 10.1007/978-3-030-73234-9_21

**Abstract**

Background and aim: Cardiovascular disease remains the primary cause of noncommunicable disease- related death. The present systematic review and meta-analysis was performed to assess the possible benefit of the green coffee bean extract on cardio-metabolic markers.

Methods: PubMed, Scopus, Web of Science, and Cochrane Library were systematically searched to identify clinical trials that examined the effect of green coffee bean extract on cardio-metabolic risk factors including serum lipid profiles, glycemic status-related markers, blood pressure, and anthropometric indices. Since the included RCTs were carried out in different settings, random effect models were used to conduct all meta-analyses.

Results: Fifteen studies (19 arms) consisting of 637 participants were included. The results indicated that green coffee bean extract significantly reduced levels of total cholesterol (-5.93 mg/dl; 95% CI: -9.21, -2.65; I2: 0%), fasting plasma glucose (-2.21 mg/dl; 95% CI: -3.94, -0.48; I2: 32%), systolic blood pressure (-3.08 mmHg; 95% CI: -4.41, -1.75; I2: 26%), diastolic blood pressure (-2.27 mmHg; 95% CI: -3.82, -0.72; I2: 61%), body weight (-1.24 kg; 95% CI: -1.82, -0.66; I2: 15%), and BMI (-0.55 kg/m2; 95% CI: -0.88, -0.22; I2: 73%). Although the pooled effect size of LDL-C, fasting insulin, and waist circumstance were significant, the results were significantly influenced by individual studies. No significant effect was detected for triglycerides, HDL-C, HbA1C, and HOMA-IR. However, the nonsignificant pooled effect size for triglyceride levels was influenced by one individual study.

Conclusion: The present study suggests that green coffee been extract consumption can improve total cholesterol, triglycerides, body weight, blood pressure, and fasting plasma glucose.

Keywords: CVD; Cardiovascular disease; Chlorogenic acid; Green coffee.

**Modulation of brain insulin signaling in Alzheimer's disease: New insight on the protective role of green coffee bean extract**

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PMID: 29712510

DOI: 10.1080/1028415X.2018.1468535

**Abstract**

Objective: Alzheimer's disease (AD), a neurodegenerative disorder, involves brain insulin signaling cascades and insulin resistance (IR). Because of limited treatment options, new treatment strategies are mandatory. Green coffee bean extract (GCBE) was reported to attenuate IR and improve brain energy metabolism. We aimed to investigate the possible use of GCBE as a prophylactic strategy to delay the onset of AD or combined with pioglitazone (PIO) as a strategy to retard the progression of AD. Methods: Rats received 10% fructose in drinking water for 18 weeks to induce AD. GCBE-prophylactic group received GCBE for 22 weeks started 4 weeks prior to fructose administration. The PIO group treated with PIO for 6 weeks started on week 12 of fructose administration. The GCBE+PIO group received GCBE for 22 weeks started 4 weeks prior to fructose administration and treated with PIO for the last 6 weeks of fructose administration. Results: Pretreatment with GCBE, either alone or combined with PIO, alleviated IR-induced AD changes. GCBE improved cognition, decreased serine phosphorylation of insulin receptor substrate, increased phosphoinositol-3 kinase (PI3K) activity and protein kinase B (Akt) gene expression, decreased glycogen synthase kinase-3β (GS3Kβ) gene expression and Tau hyperphosphorylation. Discussion: GCBE exerted neuroprotective effects against IR-induced AD mediated by alleviating IR and modulating brain insulin signaling cascade.

**Effect of Repeated Consumption of Partially Hydrolyzed Guar Gum on Fecal Characteristics and Gut Microbiota: A Randomized, Double-Blind, Placebo-Controlled, and Parallel-Group Clinical Trial**

Zenta Yasukawa [1 2], Ryo Inoue [3], Makoto Ozeki [4 5], Tsutomu Okubo [6 7], Tomohisa Takagi [8], Akira Honda [9], Yuji Naito [10]

**Abstract**

Partially hydrolyzed guar gum (PHGG) is a water-soluble dietary fiber and is used in solid and liquid food to regulate gut function. The aim of this study was to investigate effects of PHGG on bowel movements (stool form and frequency), plasma bile acids, quality of life, and gut microbiota of healthy volunteers with a tendency toward diarrhea, i.e., irritable bowel syndrome diarrhea (IBS-D)-like symptoms. A randomized, double-blind, placebo-controlled, and parallel trial was performed on 44 healthy volunteers (22 males, 22 females, 41.9 ± 6.3 years old (average ± SD)) with minimum 7 bowel movements every week, wherein above 50% of their stool was between the Bristol stool scale (BSS) value of 5 and 6. Intake of the PHGG for 3 months significantly improved stool form, evaluated using BSS, and had no effects on stool frequency. BSS was significantly normalized in the group consuming the PHGG compared with the placebo. Comprehensive fecal microbiome analysis by the 16S rRNA-sequence method detected significant changes in the ratio of some bacteria, such as an increase of Bifidobacterium ($p < 0.05$) in the PHGG group. Our results suggest that intake of PHGG improves human stool form via regulating intestinal microbiota.

**Role of guar fiber in improving digestive health and function**

Author links open overlay panelTheertham PradyumnaRaoaGiuseppinaQuartaroneb

https://doi.org/10.1016/j.nut.2018.07.109Get rights and content

Highlights

Digestive health is important for daily quality of life.

Guar fiber has dual action to reduce both constipation and diarrhea.

Guar fiber alleviated the conditions and symptoms associated with irritable bowel syndrome.

All the digestive health effects were observed with intake of about 5 to 6 g of guar fiber.

Guar fiber provided a natural remedy for maintaining proper digestive health.

Guar fiber offered potential prebiotic effects for protection of digestive health.

**Abstract**
Digestive health plays key role in our active daily life; but maintaining proper bowel movements, i.e., being free from constipation, diarrhea, irritable bowel syndrome, inflammatory bowel disease, flatulence, bloating, and abdominal pain, is complex. Dietary fibers often are recommended to maintain proper digestive health, but none seems to provide a single comprehensive solution for overall maintanance of proper digestive health. Guar fiber, however, has emerged as a credible candidate for just such a solution. This review focused on summarizing the clinically observed effects of guar fiber on digestive health. Several clinical studies suggest the guar fiber normalizes both constipation and diarrheal conditions. Also, it was effective in alleviating the symptoms associated with irritable bowel syndrome. The studies suggest that a regular intake of 5 to 10 g/d guar fiber is effective to treat most of the morbidities associated with digestive health. Guar fiber is all natural. It may offer potential protection and promotion of digestive health both alone and when combined with probiotics as a synbiotic formula.

**Dietary supplementation with partially hydrolyzed guar gum helps improve constipation and gut dysbiosis symptoms and behavioral irritability in children with autism spectrum disorder**

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Supplementary Materials

**Abstract**
Prebiotic dietary water-soluble fiber obtained from partially hydrolyzed guar gum was added to diets of children with autism spectrum disorders who presented constipation symptoms. Supplementation with partially hydrolyzed guar gum altered gut microbiota and significantly increased the frequency of defecation per week and altered the gut microbiota. In addition, supplementation with partially hydrolyzed guar gum significantly ($p<0.05$) decreased and tended to decrease ($p = 0.07$) the concentrations of serum interleukin-1β and tumor necrosis factor-α, respectively. More importantly, supplementation with partially hydrolyzed guar gum significantly ameliorated behavioral irritability as per the Aberrant Behavior Checklist, Japanese Version. The present study demonstrated that supplementation with partially hydrolyzed guar gum to diets of constipated autism spectrum disorders children helped improve constipation and gut dysbiosis symptoms, which in turn helped attenuate the level of serum inflammation cytokines and behavioral irritability.

**Partially hydrolyzed guar gum in the treatment of irritable bowel syndrome with constipation: effects of gender, age, and body mass index**

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PMID: 25843197

PMCID: PMC4392570

DOI: 10.4103/1319-3767.153835

**Abstract**

Background/aims:
Partially hydrolyzed guar gum (PHGG) relieves symptoms in constipation-predominant irritable bowel syndrome (IBS) and may have prebiotic properties. However, the correlation between the effectiveness of PHGG and patient characteristics has not been examined. We aimed to investigate the effect of PHGG in symptom relief on constipation-predominant IBS according to gender, age, and body mass index (BMI).

Patients and methods:
Sixty-eight patients with IBS entered a 2-week run-in period, followed by a 4-week study period with PHGG. Patients completed a daily questionnaire to assess the presence of abdominal pain/discomfort, swelling, and the sensation of incomplete evacuation. The number of evacuations/day, the daily need for laxatives/enemas and stool consistency-form were also evaluated. All patients also underwent a colonic transit time (CTT) evaluation.

Results:
PHGG administration was associated with a significant improvement in symptom scores, use of laxatives/enemas, stool form/consistency and CTT. At the end of the study period and compared with baseline, the number of evacuations improved in women, patients aged ≥ 45 years and those with BMI ≥ 25 ($P < 0.05$ for all comparisons); abdominal bloating improved in males ($P < 0.05$), patients < 45 years ($P < 0.01$) and those with BMI < 25 ($P < 0.05$). A decrease in the number of perceived incomplete evacuations/day was reported in patients with a BMI ≥ 25 ($P < 0.05$). Reductions in laxative/enema use were recorded in females ($P < 0.05$), patients < 45 years ($P < 0.01$), and patients with BMI < 25 ($P < 0.05$).

Conclusions:
Gender, age, and BMI seem to influence the effect of PHGG supplementation in constipated IBS patients. Further studies are needed to clarify the interaction of such parameters with a fiber-enriched diet.

**Randomized clinical study: Partially hydrolyzed guar gum (PHGG) versus placebo in the treatment of patients with irritable bowel syndrome**

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**Abstract**

Background

The treatment of Irritable bowel syndrome (IBS) is still challenging. Partially hydrolyzed guar gum (PHGG) is a known prebiotic fiber. To assess the effects of PHGG on clinical symptoms of IBS patients in a prospective randomized double blind placebo-controlled study.

Methods

Suitable IBS patients were recruited into an 18-week-long study (2 weeks of run-in, 12 weeks of treatment and 4 weeks of follow-up). They were blindly randomized to receive 6 gr of PHGG or placebo. Treatment efficacy was evaluated by the Francis Severity IBS score, the IBS quality-of-life scores and scored parameters of weekly journal of symptoms. Deltas of changes between the final and baseline scores were compared between two groups.

Results

Of 121 patients who underwent randomization, 108 patients (49 in the PHGG group and 59 in the placebo group) had all the data needed for intention-to-treat analysis. A 12-week administration of PHGG led to a significant improvement of journal bloating score in the PHGG group versus placebo (-4.1±13.4 versus -1.2±11.9, P=0.03), as well as in bloating+gasses score (-4.3±10.4 versus -1.12±10.5, P = 0.035). The effect lasted for at least 4 weeks after the last PHGG administration. PHGG had no effect on other journal reported IBS symptoms or on Severity and Quality of life scores. There were no significant side effects associated with PHGG ingestion. The rate of dropouts was significantly higher among patients in the placebo group compared with the PHGG group (49.15% versus 22.45%, respectively, P = 0.01).

## The Effect of L-Theanine Incorporated in a Functional Food Product (Mango Sorbet) on Physiological Responses in Healthy Males: A Pilot Randomised Controlled Trial

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**Abstract**

Consumption of L-Theanine (L-THE) has been associated with a sensation of relaxation, as well as a reduction of stress. However, these physiological responses have yet to be elucidated in humans where L-THE is compared alongside food or as a functional ingredient within the food matrix. The aim of this study was to determine the physiological responses of a single intake of a potential functional food product (mango sorbet) containing L-THE (ms-L-THE; 200 mgw/w) in comparison to a flavour and colour-matched placebo (ms). Eighteen healthy male participants were recruited in this randomised, double-blind, placebo-controlled trial. The participants were required to consume ms-L-THE or placebo and their blood pressure (BP) (systolic and diastolic), heart rate (HR), and heart rate variability (HRV) were monitored continuously over 90 minutes. Eleven males (age 27.7 ± 10.8 years) completed the study. Changes in area under the curve for systolic and diastolic blood pressure and HRV over the 90 minute observation period indicated no differences between the three conditions (all $p > 0.05$) or within individual groups (all $p > 0.05$). The values for heart rate were also not different in the placebo group ($p = 0.996$) and treatment group ($p = 0.066$), while there was a difference seen at the baseline ($p = 0.003$). Based on the findings of this study, L-THE incorporated in a food matrix (mango sorbet) demonstrated no reduction in BP or HR and showed no significant parasympathetic interaction as determined by HRV high-frequency band and low-frequency/high-frequency ratio. Further studies should be focussed towards the comparison of pure L-THE and incorporation within the food matrix to warrant recommendations of L-THE alongside food consumption.

**Effects of L-theanine-caffeine combination on sustained attention and inhibitory control among children with ADHD: a proof-of-concept neuroimaging RCT**

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PMID: 32753637

PMCID: PMC7403383

DOI: 10.1038/s41598-020-70037-7

**Abstract**

We examined the acute effects of L-theanine, caffeine and their combination on sustained attention, inhibitory control and overall cognition in boys with attention deficit hyperactivity disorder (ADHD). L-Theanine (2.5 mg/kg), caffeine (2.0 mg/kg), their combination and a placebo were administered in a randomized four-way repeated-measures crossover with washout, to five boys (8-15 years) with ADHD. Functional magnetic resonance imaging (fMRI) was performed during a Go/NoGo task and a Stop-signal task ~ 1 h post-dose. NIH Cognition Toolbox was administered ~ 2 h post-dose. Treatment vs. placebo effects were examined in multi-level mixed-effects models. L-Theanine improved total cognition composite in NIH Cognition Toolbox ($p = 0.040$) vs. placebo. Caffeine worsened and L-theanine had a trend of worsening inhibitory control (i.e. increased Stop-signal reaction time; $p = 0.031$ and $p = 0.053$ respectively). L-Theanine-caffeine combination improved total cognition composite ($p = 0.041$), d-prime in the Go/NoGo task ($p = 0.033$) and showed a trend of improvement of inhibitory control ($p = 0.080$). L-Theanine-caffeine combination was associated with decreased task-related reactivity of a brain network associated with mind wandering (i.e. default mode network). L-Theanine-caffeine combination may be a potential therapeutic option for ADHD-associated impairments in sustained attention, inhibitory control and overall cognitive performance.

**Effects of L-Theanine Administration on Stress-Related Symptoms and Cognitive Functions in Healthy Adults: A Randomized Controlled Trial**

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**Abstract**
This randomized, placebo-controlled, crossover, and double-blind trial aimed to examine the possible effects of four weeks L-theanine administration on stress-related symptoms and cognitive functions in healthy adults. Participants were 30 individuals (nine men and 21 women; age: 48.3 ± 11.9 years) who had no major psychiatric illness. L-theanine (200 mg/day) or placebo tablets were randomly and blindly assigned for four-week administration. For stress-related symptoms, Self-rating Depression Scale, State-Trait Anxiety Inventory-trait, and Pittsburgh Sleep Quality Index (PSQI) scores decreased after L-theanine administration ($p = 0.019$, 0.006, and 0.013, respectively). The PSQI subscale scores for sleep latency, sleep disturbance, and use of sleep medication reduced after L-theanine administration, compared to the placebo administration (all $p < 0.05$). For cognitive functions, verbal fluency and executive function scores improved after L-theanine administration ($p = 0.001$ and 0.031, respectively). Stratified analyses revealed that scores for verbal fluency ($p = 0.002$), especially letter fluency ($p = 0.002$), increased after L-theanine administration, compared to the placebo administration, in individuals who were sub-grouped into the lower half by the median split based on the mean pretreatment scores. Our findings suggest that L-theanine has the potential to promote mental health in the general population with stress-related ailments and cognitive impairments.

Keywords: L-theanine; cognition; emotion; sleep; stress.

Conflict of interest statement

Yasukawa Z. and Ozeki M. are employees of Taiyo Kagaku Co., Ltd. which supplied the L-theanine and placebo tablets used in this trial.

**The effect of L-theanine supplementation on the immune system of athletes exposed to strenuous physical exercise**

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**Abstract**

Background

The aim of this study was to analyze the response of selected components of the immune system in rowers to maximal physical exercise, and to verify if this response could be modulated by supplementation with L-theanine.

Method

The double-blind study included 20 members of the Polish Rowing Team. The subjects were randomly assigned to the supplemented group (n = 10), receiving 150 mg of L-theanine extract for 6 weeks, or to the placebo group (n = 10). The participants performed a 2000-m test on a rowing ergometer at the beginning (1st examination) and at the end of the supplementation period (2nd examination). Blood samples were obtained from the antecubital vein before each exercise test, 1 min after completing the test, and after a 24-h recovery. Subpopulations of T regulatory lymphocytes (Tregs) (CD4+/CD25+/CD127-), cytotoxic lymphocytes (CTLs) (CD8+/TCRαβ+), natural killer (NK) cells (CD3-/CD16+/CD56+) and TCRδγ-positive (Tδγ) cells were determined by means of flow cytometry. The levels of interleukin 2 (IL-2), interleukin 4 (IL-4), interleukin 10 (IL-10), interferon gamma (INF-ɤ) and total antioxidant capacity (TAC) were determined with commercially available diagnostic kits.

Results

Supplementation with L-theanine contributed to a significant post-exercise decrease in IL-10 concentration, which was reflected by higher values of IL-2 to IL-10 and IFN-γ to IL-10 ratios. Moreover, a significant post-recovery decrease in CTL count, Treg to NK and Treg to CTL ratios was observed in the supplemented group.

Conclusion

Despite the decrease in the number of some cytotoxic cells (CTLs) and an increase in the proportion of Tregs to CTLs, supplementation with LTE seems to exert a beneficial effect on a disrupted Th1/Th2 balance in elite athletes, as shown by the decrease in IL-10 concentration.

**Anti-stress effect of theanine on students during pharmacy practice: positive correlation among salivary α-amylase activity, trait anxiety and subjective stress**

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PMID: 24051231

DOI: 10.1016/j.pbb.2013.09.004

**Abstract**

Purpose

Theanine, an amino acid in tea, has significant anti-stress effect on experimental animals under psychosocial stress. Anti-stress effect of theanine on humans was evaluated in 5th-year university students during pharmacy practice.

Method

The study design was a single-blind group comparison and participants (n=20) were randomly assigned to theanine or placebo groups. Theanine or placebo (lactose) tablets (200 mg, twice a day, after breakfast and lunch) were taken from 1 week prior to the pharmacy practice and continued for 10 days in the practice period. To assess the anxiety of the participants, the state-trait anxiety inventory test was carried out before the pharmacy practice. Salivary α-amylase activity (sAA) was measured as a marker of sympathetic nervous system activity.

Results

n the placebo-group, sAA in the morning (pre-practice sAA) was higher than in theanine-group during the pharmacy practice (p=0.032). Subjective stress was significantly lower in the theanine-group than in the placebo-group (p=0.020). These results suggest that theanine intake had anti-stress effect on students. Furthermore, students with higher pre-practice sAA showed significantly higher trait anxiety in both groups (p=0.015). Similarly, higher pre-practice sAA was correlated to shorter sleeping time in both groups (p=0.41×10(-3)).

Conclusion

Stressful condition increased the level of sAA that was essentially affected by individual trait anxiety. The low levels of pre-practice sAA and subjective stress in the theanine-group suggest that theanine intake suppressed initial stress response of students assigned for a long-term commitment of pharmacy practice.