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Guarana and Its Possible Effects on Health

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Abstract

Botanically known as *Paullinia cupana* (Sapindaceae), guarana is widely grown in Amazon region and naturally in Brazil, Ecuador, Venezuela, Colombia, Peru and the Cooperative Republic of Guyana. It is used in sugar and/or carbonated soft drinks, herbal teas and energy drinks in the form of guarana extract. Guarana has antioxidant, antibacterial, antifungal, antidepressant effects; improves cognitive performance; triggers weight loss and reduces lipid peroxidation. It has important effects on various methods and treatments from cardiovascular to neurological diseases, from memory and liveliness to cancer. It is also known that guarana enhances biological activities and psychological effects on the body. This compilation has been conducted to evaluate the chemical and physical properties of guarana, its metabolites, the mechanism of its effect on psychological activities and health.

1. Introduction

Guarana is a herbal substance extracted from Paullinia cupana Kunth (Sapindaceae) which is from maple family in South America and a rain forest ivy rooted from Amazon for the products rich in caffeine (Pennay, Lubman, & Miller, 2011; de Lima Portella et al., 2013). The main components of guarana seeds were shown in Table 1 (Hamerski, Somner, & Tamaio, 2013).

The proportion of caffeine in dry weight of guarana plant seeds is 2-6%, which corresponds to 2 fold of the caffeine present in the coffee beans (de Oliveira Campos et al., 2011; Lima et al., 2005; Haskell, Kennedy, Wesnes, Milne, & Scholey, 2007; EFSA, 2008; Pennay et al., 2011). Caffeine contents of leaves, seeds and crusts of the dry weight of guarana are different. According to a study by Baumann et al. (1995) examining guarana's purine alkaloid contents, the caffeine content of guarana was found to be 0.02% in the fruit husk (pericarp) and 1.6% in the seed husk (testa). The caffeine content of the guarana tinctures is 9.82-11.02%, which is about 2-3 times higher than the caffeine in seed (Meurer-Grimes, Berkov, & Beck, 1998). The caffeine content of guarana is around 1-2%, while this percentage may rise up to 3% in coffee beans in some cases; its percentage in yoco husk is around 3%, in tea leaves between 2-4% while it may rise to very high levels in some cases, in cola nuts between 1-3% and yerba mate leaves around 0.4-2% (EFSA, 2008). In other words, guarana has 30 times more caffeine than cacao and 10 times more than yerba tea (Edwards et al., 2005). With this feature, guarana contains the highest dose of natural caffeine in the world (Hamerski et al., 2013). As its absorption in the gastrointestinal system is slower, it can be considered that guarana has a longer effect than the caffeine in coffee beans (Pennay et al., 2011).

The popularity of energy drinks has increased in adolescents and young adults (de Lima Portella et al., 2013). Such beverages are used to enhance physical performance and mental alertness with the addition of herbal supplements and caffeine, such as guarana, yerba mate and coke nuts (U.S. Food and Drug Administration, 2012). It is necessary to consider the combinations of substances as the ingredients of energy drinks may give a different reaction in the same formulation. It is also necessary to understand how these ingredients effect physiology (Moustakas et al., 2015). Guarana is sold as a stimulant of energy drinks and also often as capsules combined with ginseng (Woods, 2012). The different components found in energy drinks were presented in Table 2 (Zeidán-Chuliá et al., 2013). In energy drinks, it is anticipated that low doses of guarana seeds have short term stimulating effect when combined with caffeine and glucose but high doses do not have a long term effect (Moustakas et al., 2015).

2. Biological Activities, Molecular Activities, Molecular Purposes of Guarana and Relevant Diseases

It is claimed that guarana reduces the effects of aging, relieves fatigue, improves vitality, endurance, strength, concentration and performance in athletes, reduces rheumatic diseases, tension, migraine, constipation and diarrhea, facilitates weight loss and suppresses appetite (Woods, 2012). Guarana is rich in caffeine and catechins like green tea, and its

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Table 1. Basic composition of renewable guarana beans (Hamerski et al., 2013)

Determination	Content medium (%)
Starch	30
Protein	15
Tannins	12
Catechutannic acid	5
Caffeine	4
Catechic acid	0.6
Kalium	0.27
Oil	0.16
Calcium	0.08
Magnesium	0.05
Phosphorus	0.01

functional properties related to metabolic disorders are very similar to green tea (de Lima Portella et al., 2013; da Costa Krewer et al., 2011). Guarana has antioxidant, antitumoral, anticarcinogenic, antimicrobial and antidepressive effects. It is also suggested that guarana has important biological effects such as improving cognitive performance and antidepressive effect (da Costa Krewer et al., 2011). Guarana is also used as a diuretic and as a pain reliever for migraine treatment (Hamerski et al., 2013). Guarana was alos reported to have hepatoprotective activity and preventive effect on DNA strand breakage in liver damage caused by carbon tetrachloride (CCl_4) in rats (Kober et al., 2016). It is also considered that the high concentration of caffeine available in guarana powder contributes to the mating success of lab-reared male flies (de Aquino, Souza, de Jesus Santos, & Joachim-Bravo, 2016).

2.1. Effects on Cancer

Guarana extracts have an antioxidant effect on NO (Hamerski et al., 2013). It is known that it has an antioxidant effect even at low concentrations (1.2 µg / mL). It is stated that it is a natural and powerful antioxidant beneficial to human health and also protects the organism from oxidative damage (EFSA, 2010).

The antioxidant properties of the guarana extract are thought to be caused from the tannins, catechins, epicatechins, saponins, proanthocyanidols as well as methylxanthines such as theophylline, theobromine and caffeine (de Lima Portella et al., 2013; Hamerski et al., 2013). Guarana also protects the body from damage stimulated by cadmium (Hamerski et al., 2013). It was reported that guarana supplementation reduces oxidative stress at maximum 5 mg/mL (Bittencourt et al., 2013). There is also a significant

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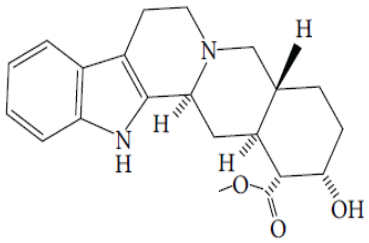
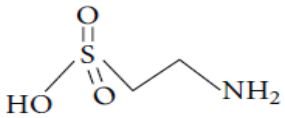
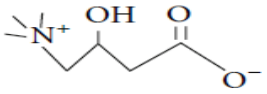
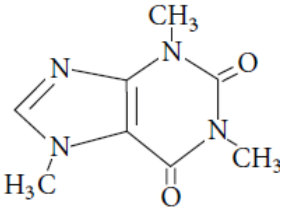
Table 2. Different components found in energy drinks (Zeidán-Chuliá et al., 2013)

Plant extract	Guarana *Paullinia cupana*	*Methylxanthines *Epicatechins Caffeine *Tannins Theobromine *Saponins Theophylline *Catechins *Proanthocyanidins *Other compounds
	Ginseng *Panax ginseng*	*Saponins * Other compounds Ginsenosides
Yohimbine	Yohimbine *Pausinystalia yohimbe*	
	Snakeroot or sarpagantha *Rauwolfia serpentina*	
Ginkgo *Ginkgo biloba*		*Flavonoids *Terpenes Quercetin Ginkgolide A Kaempferol Ginkgolide B Biflavone Ginkgolide C Ginkgetin Bilobalide Bilobetin Sciadopitysin
Amino acids	Taurine	
	L-carnitine	
B vitamins		
Caffeine		

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decrease in oxidative stress types such as protein carbonylation level, intracellular reactive oxygen species (ROS) and lipoperoxidation in aging adipose-derived stem cells (ASCs) of the 5 mg / mL supplemented plant extract (Machado et al., 2015). Guarana has been reported to significantly reduce fatigue after chemotherapy in cancer patients (dos Santos Martins, Ferreira, & del Giglio, 2017). In a study conducted on cancer patients with anorectic - cachectic syndrome causing body weight loss and appetite reduction of more than 5% of normal weight, all participants were given guarana extract twice a day for 4 weeks and the body weight of the patients remained the same and their appetite increased (Palma et al., 2016). In another study, it was found out that *Paullinia cupana* (PC-18) can be effective for the treatment of fatigue associated with chemotherapy in 40 patients who had various solid tumors and was given 37,5 mg PC-18 twice a day orally for 3 weeks one week after chemotherapy in induction phase and either the same dose of PC-18 or placebo randomly for following three weeks (damping phase) (del Giglio et al., 2013). Besides the studies revealing the positive effects of guarana, in another study, the patient group who were treated with 50 mg guarana twice a day and received chemoradiotherapy as they have head and neck cancer suffered from more intense body weight loss and used more nasogastric tube (dos Santos Martins et al., 2017). However, further studies are required to examine its positive effects.

2.2. Antibacterial and Antifungal Effects

Guarana is a bioactive substance which shows significant antibacterial effect against gram-positive and gram-negative bacteria (Basile et al., 2013). It was found out that alcoholic guarana seed extracts showed strong antimicrobial activity against the bacteria such as *Pseudomonas fluorescens, P. aeruginosa, Proteus vulgaris, Escherichia coli, Bacillus cereus, Proteus mirabilis* and *Streptococus mutans* and the harmful fungi such as *Trichoderma viride, Aspergillus niger* and *Penicillium cyclopium* (Hamerski et al., 2013). It is also claimed that sodium benzoate, flavonoids, vitamins, carbon monoxide and tannins contained in the guarana have a protective effect on teeth erosion (Barac et al., 2015). It is used in tooth paste due to its antimicrobial effects (de Camargo Smolarek et al., 2015).

This plant has also a strong effect against some pathogens in the digestive tract. Besides in another study, it was found out that guarana can ethnopharmacologically be used against dysentery and diarrhea (Basile et al., 2005). Owing to its strong antimicrobial and antioxidant properties, it is suggested that guarana can be used as a natural additive in food, cosmetic and pharmaceutical industries. As a result of another study, it was found out that guarana seed extract has a significant activity against growth of th bacteria such as *E. coli, B. cereus and P. fluorescens* and fungi such as *A. niger, T. viride* and *P. cyclopium* which are responsible for the food poisoning (Majhenič, Škerget, & Knez, 2007).

2.3. Effects on Nervous System and Memory

Guarana extracts have antidepressive, anxiolytic and anti-amnestic effects so it is claimed that guarana reduces the symptoms of depression, when consumed moderately (Silvestrini, Marino, & Cosentino, 2013). It was found out that multivitamin-mineral supplementation prepared with guarana supplement

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improves decision making performance and ensures a stable autonomous nervous system regulation in the first hour (Pomportes, Davranche, Brisswalter, Hays, & Brisswalter, 2014). In a randomized, prospective and placebo-controlled study also conducted on 27 healthy individuals (9 of them were given guarana extract and 15 of them placebo), it was suggested that guarana extract in recommended quantities (350 mg x 3/day) has no effect on anxiety, state of mind and psychological wellness (Silvestrini et al., 2013).

Guarana is considered to promote cognitive performance, memory and reduces mental fatigue in healthy young adults (Haskell et al., 2007; Kennedy et al., 2008). Although guarana is reported to protect nerves and promote cognitive ability, its possible mechanism is not fully understood (Ruchel et al., 2017). In a randomized and controlled study, subjects were given guarana in 4 different doses and it was found out that 75 mg of guarana had positive effects on memory and cognitive functions (Haskell et al., 2007). As a result of a study in which guarana was used as a multivitamin, it was observed that there is an acute beneficial effect on mood and cognitive performance (Scholey et al., 2013). Moreover, in a study it was reported that acrolein has a role in Alzheimer's disease and acrolein-induced toxicity on neuronal-like cells (SH-SY5Y) was stated to be inhibited by guarana; therefore, it can be used as a therapeutic agent for neurodegenerative diseases (Bittencourt et al., 2014).

According to EFSA, in order to observe guarana's effect on vitality and fatigue, it is recommended to consume guarana; as fruit-seed-root equivalent to minimum 8 mg caffeine or equivalent to 75 mg extract (11-13% caffeine), 1-6 g/day pulverized seeds, as 3% fruit extract equivalent to 1-3 g/day caffeine or only minimum 50 mg of guarana (EFSA, 2011).

2.4. Relation with Obesity

Guarana seed is increasingly used as a weight loss product in tablets in powdered and compressed form (Hamerski et al., 2013). It is considered that guarana reduces appetite and energy intake and promotes state of mind (Alkhatib, Seijo, Larumbe, & Naclerio, 2015). Using guarana in natural caffeine sources has increased significantly in recent years in order to improve athletic performance and reduce body weight (Pendleton, Brown, Thomas, & Odle, 2012). It is extensively consumed by athletes, as it is believed to be ergogenic and "fat burning" (Hamerski et al., 2013). Guarana is used in fruit juice drinks, candy (such as chocolate products), energy drinks, as well as dietary and herbal supplements and in highly controversial herbal body weight loss products (Kennedy, Haskell, Wesnes, & Scholey, 2004).

The metabolic pathways associated with body weight are related with the role of bioactive components (de Lima Portella et al., 2013). In a study conducted on six hundred and thirty-seven elderly individuals (≥60 years), the prevalence of obesity and metabolic syndrome was found to be lower in guarana-consuming group than in the group not consuming guarana. It was found out that the waist circumference of the male group consuming guarana was lower than that of the non-consuming group (da Costa Krewer et al., 2011). In addition, there was no evidence that weight loss increases when guarana is consumed alone (Hamerski et al., 2013).

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2.5. Effects on Cardiovascular Diseases and Hypertension

Lipid peroxidation induced by independent radicals is involved in the pathogenesis of various diseases. Using a 2 µg/mL concentration of guarana extract reduces 62.5% of lipid peroxidation depending on the dose (Basile et al., 2005). The effect of guarana on serum oxidation and LDL is probably associated with some bioactive components (xanthine and catechin) (de Lima Portella et al., 2013; da Costa Krewer, 2011). However, there is not a certain information on whether guarana consumption increases low density lipoprotein (LDL) oxidation resistance (de Lima Portella et al., 2013).

In the study conducted by da Costa Krewer et al. (2011), the prevalence of hypertension in individuals who consumed guarana was lower than those who did not consume, and cholesterol levels of the female group consuming guarana were lower than that of the control group. In another study conducted on 42 healthy adults, it was emphasized that guarana has a positive effect on LDL oxidation and may have protective effects, in part, on cardio-metabolic diseases (de Lima Portella et al., 2013). As a result of another study, it was found out that the cells with higher cellular nitric oxide levels exposed to different concentrations of guarana reduced the level of lipid peroxidation (Bittencourt et al., 2013).

3. Safe Dose and Toxicology

The results of several studies on long-term intake of guarana are contradictory (Silvestrini et al., 2013). The consumption of excessive amounts of energy drinks and more than 200 mg caffeine per day may cause health problems (Pennay et al., 2011). The consumption of caffeine more than 20 mg/kg is considered as potential toxic amount. Moreover, its consumption more than 150 mg/kg is regarded as lethal dose (Pendleton et al., 2012).

Generally, the daily dosage of 20 to 30 mg of caffeine is recommended (Silvestrini et al., 2013). The caffeine content of a plant depends on several conditions such as climate, hydration state and harvest time (de Carvalho Ferrari, 2011). For this reason, it is not recommended to consume more than 2 energy drinks per day whether it is alcoholic or not (Pennay et al., 2011). In the light of this information, as a result of the calculations made by considering human dose recommendations and body weight, it is recommended to consume 150-250 mg extracts of guarana seeds containing 9-11% of caffeine per day (Dimpfel, 2013).

Guarana was described as safe by the US Food and Drug Administration (FDA), although it has side effects when taken in various quantities (de Lima Portella et al., 2013). EFSA recommends the use of 125 mg of guarana dry powder extract per day (EFSA, 2012). However, it is suggested in some sources that elderly people, which are considered to be sensitive, should be kept under constant supervision (Lüde et al., 2016).

4. Conclusion

Guarana is a herb which has been used as a medical plant for many years. *In vivo, in vitro* and human experimens have shown that it can be effective in the treatment and prevention of many diseases. Although the positive effects of guarana on health are stated, safe dosing and interactions of its active ingredient, caffeine, should be taken into consideration in the

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treatment of diseases. However, studies show conflicting results about the safe dose.

Due to the increasing consumption of guarana which has antioxidant features, it can be used for body weight loss and it is known to reduce cardiovascular disease prevalence but there is a need for further human and animal studies on its functional properties.

Conflict of interest

The authors declare they have no conflict of interest. The authors alone are responsible for the content and writing of this article.

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