Guarana as a source of bioactive compounds

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Abstract

A high daily intake of fruits and vegetables is an important strategy to promote health. The mechanism explaining the health benefits of plant food materials is attributed, at least in part, to their high content of bioactive phenolics. Guarana (Paullinia cupana) is a typical product from Amazon biota and, mainly as a source of caffeine; its seeds are commonly used as stimulants. However, guarana seeds are also rich in catechin, epicatechin, procyanidin B1, and procyanidin B2. Guarana exhibits potential health benefits in cognitive function and prevention of cardiovascular disease. Furthermore, it is a promising source of antihyperglycemic and antibacterial compounds for prevention and/or management of type 2 diabetes and oral diseases. However, to confirm these benefits in humans, clinical trials are needed to provide evidence for these anecdotal observations.

Keywords: Caffeine; Phenolic compounds; Antioxidant properties; Anti-Inflammatory potential; Antimicrobial activity.

Non-communicable diseases (NCDs) are the major health challenges of the 21st century. In 2016, they were responsible for 71% (41 million) death around the globe. NCDs include cardiovascular diseases (17.9 million death), cancers (9 million death), chronic respiratory diseases (3.8 million death), and diabetes (1.6 million death) (WHO, 2018).

Unhealthy diet is a behavioral risk factor linked to the main NCDs. However, several studies have shown that a high daily intake of vegetables and fruits may be helpful in health promotion. The mechanisms explaining these health benefits are related to the action of bioactive molecules such as phenolic compounds (Boeing et al., 2012; Abbas et al., 2017; Karasawa and Mohan, 2018), mainly due to their antioxidant potential.

Guarana (Paullinia cupana) is a typical product from Amazon biota. As a source of caffeine, its seeds are commonly used as a stimulant. In food processing, guarana seed extract is the base flavor used in the manufacture of one of the most popular Brazilian carbonated drinks. Furthermore, it is also used in the energy drink industry. Besides that, guarana has been listed in the Brazilian Pharmacopoeia (Agência Nacional de Vigilância Sanitária, 2017) and is also introduced in the U.S. Pharmacopeia, under monographs for guarana seed, its powder and dry extract. The Brazilian Food Supplement Law recently recognized that guarana presents bioactive substances, hence supporting its role as a functional food ingredient (Agência Nacional de Vigilância Sanitária, 2018).

Literature data show that guarana seeds are good sources of catechin, epicatechin, procyanidin B1, and procyanidin B2 (Schimpl et al., 2013; Yonekura et al., 2016). Due to its bioactive compounds, guarana has attracted considerable interest as an ingredient for the development of functional foods and food supplements. However, the health benefits of bioactive compounds depend not only on the intake levels but also on their bioavailability (BAv). The bioavailability is involved with digestion, absorption, metabolism, distribution, transporting, excretion, and colonic fermentation. Therefore, these parameters have to be considered (de Camargo et al., 2018; Shahidi and Peng, 2018; Shahidi et al., 2019).

In vitro methods to simulate gastrointestinal digestion allow determination of the bioaccessibility (BAcs) of bioactive compounds...
and evaluate the effect of food processing and to anticipate their action under systemic conditions. In line with this, recent studies have suggested the use of gastrointestinal digestion in functional food design (Cilia et al., 2018; Santana and Macedo, 2018).

Yonekura et al. (2016) have shown BACs and BAV of phenolic compounds of guarana seed in their in vivo study. Mendes et al. (2019) evaluated the effect of macronutrients (milk casein, potato starch and vegetable oil) on BACs of guarana catechins in Caco-2 cells. The results demonstrated that the interaction with other food macronutrients did not affect the permeability values of all tested compounds.

Guarana consumption may induce changes in lipid metabolism. Krewer et al. (2011) evaluated the associations of metabolic disorders and anthropometric and biochemical biomarkers of lipid, glucose and oxidative metabolism and the habitual ingestion of guarana by an elderly population. The reduction of prevalence of various metabolic disorders (hypertension, obesity and metabolic syndrome) was associated with guarana ingestion, thus suggesting a potential protective effect of regular consumption of guarana ingestion against metabolic disorders.

Oxidation of low-density lipoprotein-cholesterol (LDL-c) is known as a biomarker related to the development of coronary heart disease (Amarowicz, 2016). To investigate how guarana consumption protects against metabolic disorders, Portella et al. (2013) carried out an in vivo study to better understand the potential effects of guarana on LDL-c oxidation. Healthy elderly subjects who habitually ingested guarana demonstrated lower LDL-c oxidation than that of the control group (reduction of 27%, p < 0.0014). Furthermore, guarana exhibited a high antioxidant activity in vitro, mainly at concentrations of 1 and 5 μg/mL, as demonstrated by decreased values of conjugated dienes (CDs) and thiobarbituric acid reactive substances (TBARS), tryptophan destruction and high total peroxyl radical-trapping potential (TRAP) activity.

Many studies suggest the link between the intake of dietary antioxidants and the reduction/prevention of cardiovascular diseases (CVD) (Chiu et al., 2018). The impact of these antioxidants stems from their protection towards LDL-c oxidation, which is recognized by its role in the early atherogenic process (Vauzour et al., 2010; Billingsley and Carbone, 2018).

Yonekura et al. (2016) assessed the effects of guarana consumption on plasma catechins, erythrocyte antioxidant enzyme activity (superoxide dismutase, catalase, and glutathione peroxidase) and biomarkers of oxidative stress (ex vivo LDL-c oxidation, plasma total antioxidant status and oxygen radical absorbance capacity (ORAC) values, and lymphocyte single cell gel electrophoresis) in healthy overweight subjects. These authors showed that daily intake of guarana had both acute and cumulative effects on GPx (glutathione peroxidase) and catalase, which are phase II antioxidant enzymes that reduce peroxides to water molecules. However, the antioxidant status markers such as reducing ex vivo LDL-c oxidation and hydrogen peroxide-induced DNA damage in lymphocytes improved only transiently. The authors believe that the daily dose of guarana was probably not enough to keep the fasting plasma catechin concentration above a threshold level required to exert direct antioxidant effects.

The anti-hyperglycemic potential of guarana seed consumption has been pointed as another important health benefit. The aqueous extract of guarana seeds was able to inhibit α-glucosidase (Cires et al., 2017; Hanhimeva et al., 2010; Kim et al., 2016). Therefore, to confirm this hypothesis, further studies with guarana are warranted.

Gut microbiome is involved in the etiology of obesity and obesity-related complications such as non-alcoholic fatty liver disease (NAFLD), insulin resistance and type 2 diabetes mellitus (T2DM). The main species of the colonic microbiota are the genera Bacteroides, Bifidobacterium, Ruminococcus, Escherichia and Lactobacillus (Canfora et al., 2019). Silveira et al. (2018) evaluated the effects of guarana seed powder (GSP) on gut microbial composition in Wistar rats after 21 days of treatment. GSP altered gut microbiota in a negative way, loss in diversity, decreased Bacteroidetes and increased Cyanobacteria abundance, probably due to other metabolites than caffeine. The modulation of gut microbiota by polyphenols is not fully understood. Human intervention studies provide the best models for studying the effect of phenolic compounds on modulation of gut microbiota. However, human intervention studies hold inevitable practical and ethical limitations (Ozdal et al., 2016).

Several phenolic compounds (e.g. catechins and proanthocyanidins) have been recognized as potential antimicrobial agents with bacteriostatic or bactericidal actions (de Camargo et al., 2017; Ozdal et al., 2016). Majhenic et al. (2007) tested guarana seed extracts against three food-borne fungi: Aspergillus niger, Trichoderma viride and Penicillium cyclopium, and three pathogenic bacteria: Escherichia coli, Pseudomonas fluorescens and Bacillus cereus. The results suggested that seed extracts of guarana possess strong antimicrobial action. Besides that, in vitro assessment of the antibacterial potential of the guarana extracts against Streptococcus mutans showed that these could be used in the prevention of bacterial dental plaque (Yamaguti-Sasaki et al., 2007).

Numerous plant extracts such as guarana have shown the ability to prevent carcinogenesis by reducing tumor size or relieve cancer-related symptoms. Fukumasu et al. (2008) evaluated the effects of guarana extracts against three food-borne fungi: Aspergillus niger, Trichoderma viride and Penicillium cyclopium, and three pathogenic bacteria: Escherichia coli, Pseudomonas fluorescens and Bacillus cereus. The results suggested that seed extracts of guarana possess strong antimicrobial action. Besides that, in vitro assessment of the antibacterial potential of the guarana extracts against Streptococcus mutans showed that these could be used in the prevention of bacterial dental plaque (Yamaguti-Sasaki et al., 2007).

Hertz et al. (2015) evaluated the effects of guarana on breast cancer cell response to 7 chemotherapeutic agents currently used in the treatment of breast cancer. MCF-7 breast cancer cells were cultured under controlled conditions and exposed to 1, 5 and 10 μg.mL⁻¹ guarana concentrations, with and without chemotherapeutics (gemcitabine, vinorelbine, methotrexate, 5-fluorouracil, paclitaxel, doxorubicin and cyclophosphamide). The main results demonstrated the antiproliferative effect of guarana at concentrations of 5 and 10 μg.mL⁻¹ and a significant effect on chemotherapeutic drug action.

Cadonà et al. (2017) investigated the in vitro antitumor effect of guarana by inhibiting the AKT/mTOR/S6K and MAPKs pathways. Colorectal and breast cancer cell lineages, HT-29 and MCF-7 cells, respectively, were exposed to different guarana concentrations (0.1, 1, 10, and 100 μg.mL⁻¹) as well as its main bioactive molecule, caffeine, at proportional concentrations to those found in the extract. The results showed that guarana could serve as an important agent in antitumor pharmacologic therapies by inhibiting mTOR and MAPKs pathways. However, the most published studies are in vitro so it is necessary to explore novel ways to extrapolate the overwhelming beneficial evidence seen in pre-clinical studies to humans Table 1.

Increasing evidence suggests that ingested food polyphenols can have beneficial effects in neuronal protection by acting against oxidative stress and inflammatory injury (Ashfaq et al., 2012; de Camargo et al., 2019; John and Shahidi, 2019; Wang et al., 2018; Zhang and Tsao, 2016; Zhang et al., 2018). Moreover, polyphenols...
have been reported to promote cognitive functions (Filosa et al., 2018). A double-blind, randomised, placebo-controlled, parallel groups study assessed the acute effects of either a vitamin/mineral/guarana supplement or placebo drink in 129 healthy young adults (18–24 years). Participants completed a 10 min version of the Cognitive Demand Battery. Thirty minutes following their drink participants made six consecutive completions of the battery (i.e. 60 min). The vitamin/mineral/guarana combination resulted in improved task performance, in comparison to placebo and the increase in mental fatigue associated with extended task performance was also attenuated by the supplement (Kennedy et al., 2008; Scholey et al. (2013) also confirmed the acute benefits of multivitamins with guarana on mood and cognitive performance.

It is, however, not fully understood which bioactive compound of guarana improves the mental health. Probably the effect of guarana is due to its caffeine content (Scholey et al., 2013). Adenosine seems to inhibit the release of many neurotransmitters in the central nervous system such as serotonin, noradrenaline and dopamine. Therefore, adenosine receptor antagonists, such as caffeine, promote the release of these various neurotransmitters (McLellan et al., 2016; Kolahdouzan and Hamadeh, 2017). However, animal studies suggest that the powerful neuroprotective effects are due phenolic compounds content (chlorogenic acid, epigallocatechin gallate, curcumin, tannins). Their mode of action range from pro-oxidative stress to interaction with signaling pathways involved in maintaining energy homeostasis (Kennedy et al., 2008; Gomez-Pinilla and Nguyen, 2012). Therefore, further studies with guarana should investigate its role in modulation of BDNF.

In summary, this contribution shows that the potential health benefits of guarana go beyond the action of caffeine. Prevention of metabolic comorbidities (obesity, hypertension, type 2 diabetes, and metabolic syndrome) can be improved by moderate intake of guarana. In addition, guarana helps to extend mental fatigue associated with extended task performance, in comparison to placebo and the increase in mental fatigue associated with extended task performance was also attenuated by the supplement (Kennedy et al., 2008; Scholey et al. (2013) also confirmed the acute benefits of multivitamins with guarana on mood and cognitive performance.

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Globally, depression is rising in an alarming manner, in almost every community of the world. The pathophysiology of depression is very complex, but the literature has shown the involvement of brain-derived neurotrophic factor (BDNF) as a crucial biomarker of this neural disorder. Some studies with phenolic compounds from blueberry and grape have shown that phenolic compounds are able to modulate important marker in brain tissue and could be an important factor to prevent brain diseases (Williams et al; 2008; Gomez-Pinilla and Nguyen, 2012; Dani et al., 2017). Therefore, further studies with guarana should investigate its role in modulation of BDNF.

In summary, this contribution shows that the potential health benefits of guarana go beyond the action of caffeine. Prevention of
cardiovascular diseases and benefits on cognitive performance related to phenolics from guarana have been reported. Besides that, due to their inhibitory effect towards α-glucosidase and α-amylase, its promising action as a new antihyperglycemic agent for prevention and/or management of type 2 diabetes has been highlighted. Finally, as antibacterial ingredient, phenolic bioactives from guarana may counteract oral diseases (plaque and periodontal diseases). However, to confirm the benefits of guarana in humans, these evidences must be further addressed in clinical trials.

References


