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Effects of guarana (*Paulinia cupana*) properties on antioxidant activity in the body

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Abstract

Guarana (Paulinia cupana) is composed of stimulants derived from methylxanthines (caffeine, theophylline and theobromine), condensed tannins (catechin and epicatechin), in addition to phosphorus, iron, magnesium, potassium, calcium, vitamin A and vitamin B1As. The components present in guarana have stimulating and antioxidant properties, which act to minimize the damage to the

body caused by oxidative stress, triggered by chronic diseases. In this sense, the purpose of this work is to present studies that have proven the effects of the properties of the use of guarana on the body's antioxidant activity. Studies have shown positive effects of guarana as a food source with anti-hyperglycemic potential, in the partial reduction of liver damage caused by hyperlipidemia and may have a potential use in the prevention of oral diseases.

Keywords: Stimulant, Xanthines, Tannins, Oxidative Stress, Food Source, Energetic.

1. INTRODUÇÃO

Guarana (*Paulinia cupana*) is a plant native to the Amazon and the largest regional production is in the municipality of Maués, State of Amazonas. Descendants of indigenous people from the Sateré-Mawé tribe traditionally use the fruit in a diet with healing and energetic properties. One of the first forms of commercialization of guaraná was through the use of smoked sticks, which are prepared by hand from dried seeds crushed in wooden pestle with the addition of small amounts of water (Rovellini & Fusari, 2015).

The socioeconomic relevance of guaraná planting is associated with the high caffeine content found in its seeds with levels ranging from 9.8 to 11.0%. Compared to other seeds, guarana extract has double or even triple levels of caffeine (Meurer-Grimes et al., 1998).

Scientific research since the 1960s has shown that guarana has a wide variety of biological properties, including antiproliferative (Fukumasu et al., 2008; Hertz et al., 2015), antimicrobial and antioxidant (Basile-doelsch et al., 2014; Yamaguti-Sasaki et al., 2007), cytoprotective (Schimpl et al., 2013), anxiolytic (Rangel et al., 2013), energetic and thermogenic (T. & J., 2001), in the prevention of oral diseases (Yamaguti-Sasaki et al., 2007), as well as in efforts to reduce oxidative effects and metabolic disorders (Portella et al., 2013).

According Yonekura et al. (2016), substances antioxidant bioactive of guarana, such as catechin and epicatechin, have the ability to reduce oxidative stress in healthy individuals and consequently

damage to the DNA molecule, while increasing the activities of catalases and glutathione, remaining the effect even after catechin be totally consumed.

Thus, the objective of this work is to present the characteristics and functional properties of guarana related to the antioxidant effect that its use is capable of causing in the body's metabolic syndrome.

2. ANTIOXIDANT ACTIVITY

Free radicals (FR) are defined as highly reactive chemical species, with one or more unpaired electrons in their orbitals, capable of existing independently and are naturally produced in organisms as a result of metabolism, with emphasis on Reactive Oxygen and Nitrogen Species - ERONs (Halliwell, 1991; Zhao et al., 2015).

The pathological activity of ERONs results from the peroxidation of lipid membranes, oxidative damage to nucleic acids and the oxidation of sulfhydryl functional groups of proteins (Dornas et al., 2007). In addition, harmful changes in cellular structures can enhance mitotic activity, increasing the likelihood of DNA damage and, consequently, harmful mutations to the functioning of the organism (Lu et al., 2014).

Among the ERONs, the greatest investigations are related to the superoxide anion (O2 • -), hydrogen peroxide (H2O2), hydroxyl radical (HO •) and nitric oxide (NO •) and proxinitrine (ONOO-) (de Souza et al., 2005; Valko et al., 2007).

The organism has a defense system against the FRs being formed by the antioxidant enzymes: superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione transferase (GSTP-1), glutathionearedutase and endothelial nitric oxide (eNOS); (Akimoto et al., 2010; Liu et al., 2015).

Physical exercise is one of the biggest sources of changes in the body, causing greater oxygenation and, consequently, potentiating the release of free radicals due to the oxidation-reduction reactions necessary to obtain energy that the muscle will use during contractions (Córdova et al., 2000). During electron transport chain (ETC) reactions in mitochondrial ridges, molecular oxygen (O2) is reduced by accepting 2 electrons (e-) and 2 protons (2H) forming, consequently, water (H2O),

but part of O2 (approximately 5%) receives only 1 electron, being converted to the superoxide anion (O2 • -) (Aguiar & Pinho, 2007).

During rest, the organism is able to synthesize the optimal amount of antioxidant enzymes that supply biological needs, and sometimes cell integrity (Prada et al., 2004). Some of the antioxidant enzymes that form a defense system against free radicals are: superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) (Akimoto et al., 2010; Y. Liu et al., 2015).

The imbalance between the production of ERONs and antioxidant agents can cause oxidative stress, which is able to increase the degradation of several biomolecules, such as: carbohydrates, lipids, proteins and nucleic acids (Fang et al., 2002; J. P. Soares et al., 2015) Another factor that also potentiates the establishment of oxidative stress is its high rate of body lipids. In subjects with dyslipidemia, as well as those with metabolic syndrome (MS), it was found that there is greater activity of ERONs compared to healthy people (Ohmori et al., 2005).

Another consequence of oxidative stress is the occurrence of chronic obstructive pulmonary disease (COPD), which results from damage to the respiratory tract (Cavalcante & Bruin, 2009). In diabetic rats, increases in superoxide levels were found in the prefrontal cortex, in the production of reactive species of thiobarbituric acid (TBARS), in the prefrontal cortex and in mitochondria of cells located in the amygdala (Ceretta et al., 2012).

2. PROPERTIES OF GUARANA (*Paulinia cupana*)

The chemical components found in the guarana fruit (Paulinia cupana) include stimulants derived from methylxanthines (caffeine, theophylline and theobromine), condensed tannins, which are composed of interconnected monomer units, the main ones being catechin and epicatechin (S A Sousa et al., 2010), in addition to phosphorus, iron, magnesium, potassium, calcium, vitamin A and vitamin B1. Caffeine, structurally identified as 1,3,7-trimethylxanthine, is the most consumed psychoactive chemical in the world, being then classified among the methylxanthine compounds (Tfouni et al., 2007). It is an alkaloid found in various plants, such as

coffee, tea, mate, cola nuts, cocoa and guarana (Adnadjevic et al., 2017), being a substance widely used in the pharmaceutical, food and cosmetic industries, acting as a stimulant for the heart, airways and central nervous system, being a vasodilator and a diuretic (Jun, 2009). One of the main uses worldwide is due to caffeine increasing the individual's alertness, thus improving cognitive capacity and resistance to physical tiredness (Kuskoski et al., 2005).

Guarana seed has a high percentage (2.5% to 6%) of caffeine (1,3,7-tri-methylxanthine) and has lower proportions of other purine alkaloids, such as theobromine (3, 7-dimethylxanthine) and theophylline (1,3-dimethylxanthine) (Heckman et al., 2010). They also contain a high concentration of polyphenols, particularly proanthocyanidins (Ruchel et al., 2016). There are other substances present in guarana that have therapeutic properties. The effects of antioxidant activity and anti-inflammatory activity are due to the high concentrations of phenolic compounds, such as tannins and the activity to the presence of saponins (KuskoskI et al., 2005). Among the therapeutic properties caused by the concentrations of phenolic compounds, the inhibition of platelet aggregation *in vitro* and *in vivo* stands out (Bydlowski et al., 1988).

Sousa et al., (2010b) found that the total tannin content found by the spectrophotometric method was 4.05% and by the chromatographic method, catechins and epicatechins were determined, totaling a percentage of 1.48%. The lower concentration of these compounds obtained by liquid chromatography (wavelength 280 nm) reinforces the importance of using specific methods in the analysis of herbal medicines. Guarana was considered a rich source of highly bioavailable catechins producing measurable effects on oxidative stress markers in humans by improving plasma ORAC (Oxygen Radical Absorbance Capacity), protecting erytrocytes DNA (against H2O2) and reducing the oxidation of low-fat lipoproteins density (LDL - Low Density Lipoproteins) (Yonekura et al., 2016).

For Moraes et al. (2004), the pharmacological activities of tannins are due to characteristics such as complexation with metal ions, the antioxidant and scavenger activity of free radicals and the ability to complex with other molecules, such as proteins and polysaccharides.

3. EFFECTS OF GUARANA ON METABOLIC SYNDROME

Yonekura et al. (2016) investigated the acute and cumulative effects of a 15-day intervention with daily doses of guarana powder, containing approximately 150 mg of catechins and 20 mg of proanthocyanidins. The daily intake of guarana had both acute and cumulative effects on glutathione peroxidase and catalase, which are phase II antioxidant enzymes that reduce oxides to water molecules The protective effect of guarana, on the anti-genotoxic / cytotoxic properties in hepatocytes of mice injected with N-nitrosodiethylamine (DEN), was evaluated both by the comet assay and by the DNA fragmentation technique in two-month-old female mice BALB. The treatment showed a 52.54% reduction in the length of the comet image when the animals were exposed to DEN ($p < 0.05$), showing that guarana has a protective effect against DNA damage induced by DEN in the liver of mice (Heidge Fukumasu et al., 2006). Studies carried out in rodents evaluated the toxicity of a semipurified extract (EPA fraction, containing caffeine and various flavonoids and proanthocyanidins) from guarana. Acute toxicity was tested in Swiss male mice, which received different doses orally (DR) and intraperitoneally (IP); control groups received water. Hematological and biochemical tests showed few changes, differing slightly between men and women; histopathological evaluation did not indicate significant changes. These results indicate that the guarana EPA fraction did not cause toxicity in rats at the lowest evaluated dose (30 mg / kg) (Antonelli-Ushirobira et al., 2010). Campos et al. (2003) sought to evaluate the effects of guarana extract in rats with acute gastric lesions induced by ethanol and indomethacin and compared to those produced by caffeine. Animals pretreated with guarana (50 and 100 mg / kg p.o.) showed a significant reduction in the severity of gastric lesions induced by absolute ethanol in a similar way to caffeine (20 and 30 mg / kg p.o.). Against gastric ulceration induced by indomethacin, guarana in higher doses offered significant protection.

Results found by Bonadiman et al. (2017) pointed out that the consumption of guarana can have beneficial effects on the vision of the elderly through preventive effects caused by oxidative stress. An *in vivo* analysis revealed that riverine elderly people with reports of good quality in vision were those with higher habitual consumption of

guarana than other elderly people. Portella et al. (2013) sought to investigate the potential association between the effect of guarana on LDL and serum oxidation also in the elderly. The results showed that guarana (GI) intake resulted in lower maximum production of conjugated diene. In addition, in vitro tests showed that guarana increased the lag phase in LDL and serum oxidation in vitro, as well as prevented the production of Thiobarbituric Acid (TBARS) and destruction of Tryptophan (Trp) in LDL oxidation.

Ruchel et al. (2016) determined the possible preventive effect of guarana powder on memory deficiency and acetylcholinesterase (AChE) activity in the brain structures of rats with Poloxamer-407-induced hyperlipidemia. The results revealed that the guarana powder was able to reduce the levels of CT and LDL-C in a similar way to simvastatin. Guarana powder also partially reduced liver damage caused by hyperlipidemia and was able to prevent changes in AChE activity and unforeseen impairment due to hyperlipidemia. In this case, guarana powder can be a source of promising phytochemicals used as adjunctive therapy in the management of hyperlipidemia and cognitive disorders, as the results showed that guarana powder was able to modulate enzymatic activity when associated with a hypercholesterolemic state. It was also observed that guarana decreased total cholesterol and LDL-C at baseline levels. In order to evaluate the potential inhibitory activity of guarana extracts after in vitro digestion in carbohydrate metabolism enzymes and to assess the bioaccessibility of guarana polyphenols. Silva et al. (2017) compare the guarana samples before and after enzymatic digestion in terms of total phenolic content and phenolic profile.

The result pointed to the use of guarana as a food source with anti-hyperglycemic potential. In order to investigate the polysaccharides present in guarana, Dalonso & Petkowicz (2012), isolated and characterized a pectic fraction and a xylan. The antioxidant activity tests were performed with methanolic extract and the pectic fraction in concentrations of 0.1 to 10 mg / ml. The methanolic extract exhibited a strong ability to eliminate DPPH radicals (90.9% at 10 mg / ml). At the same concentration, the polysaccharide showed a DPPH? Elimination activity of 68.4%. At a higher concentration, the methanolic extract and the polysaccharide exhibited similar effects of

eliminating hydroxyl radicals (-70%). The results suggest that the polysaccharides present in the extract may contribute to the possible biological effects of powdered guarana. Galduróz & Carlini (1996) sought to evaluate the effects of prolonged administration of guarana on the cognition of normal elderly volunteers. Forty-five volunteers were studied, with a random distribution in three experimental groups: placebo (n = 15), caffeine (n = 15) and guarana (n = 15), in a double-blind study. The results found point to flaws such as insufficient guarana treatment time, although studies with drugs to improve cognition state that a drug is not efficient when it does not show results after 5 to 6 months of administration.

Machado et al. (2015) exposed senescent adipocyte-mesenchymal cells (ASCs) obtained from human liposuction agents in contact with different concentrations of guarana hydroalcoholic extract for 72 h. Oxidative stress indicators and antioxidant enzymes (biochemical activity and gene expression by qRT-PCR analysis) were also evaluated in these senescent cells. In senescent cells exposed to guarana at a concentration of 5 mg / g, there was an increase in cell proliferation compared to untreated senescent cells (79.1 ± 15.7%).

Concomitantly, a decrease was observed in several oxidative stress indicators in senescent cells treated with guarana. A genomic effect of guarana exposure was observed when the modulation of antioxidant enzyme genes was analyzed. The results described in the study suggest that supplementation of dietary extract may reverse the initial senescence processes in ASCs. Matsuura et al. (2015) performed the in vitro evaluation of the effect of guarana on cell surface hydrophobicity (CSH), biofilm formation and the adhesion of C. albicans to polystyrene, composite resins and oral epithelial cells (BEC). The results showed that guarana did not show antifungal activity or reduced adherence of C. albicans to the surface of nanoparticle composites. However, it reduced the adhesion of C. albicans to BEC and polystyrene. These results indicate that guarana may have a potential use in the prevention of oral diseases. Oliveira et al. (2013) carried out the evaluation of the application of guaraná aiming to reduce the number and severity of hot flushes in women after breast cancer diagnosis. Women who survived breast cancer and who completed treatment at least 3 months before were evaluated, in

addition to having at least 14 episodes of hot flushes per week. The patients received 50 mg of the dried extract of Guarana orally 2 times a day for 6 weeks. The results showed that of the 15 patients who completed the study, 10 obtained a decrease of more than 50% in the severity rates of hot flushes. The use of guarana cupana was well tolerated, with no reports of toxicity as the cause of the study. Mara et al. (2007), evaluated in vitro the antibacterial potential of *Paulinia cupana* extracts against Streptococcus mutans in the prevention of dental plaque. The evaluation of the quality of *P. cupana* seeds established the minimum conditions for the drug, demonstrating the quality and equivalence in the content of characteristic chemical substances (methylxanthines and tannins). The total tannin content was 5.47% ± 0.19 (relative standard deviation - RSD% = 3.51) and methylxanthines 6.19% ± 0.08 (RSD% = 1.29). The results presented in the research showed that guarana extract can be used to prevent dental plaque.

L. Pomportes et al. (2015) compared the effects of a creatine-guaraná supplement (CRE + G) or placebo (Pl) on muscle power and cognitive performance in highly trained sportsmen. Seventeen high-level athletes in squash and fencing were analyzed and participated in two randomized experimental sessions, presented randomly one week apart, including the use of a nutritional supplement based on creatine (1000 mg) and guarana (1500 mg) (CRE + G) or placebo (Pl).

Muscle power was assessed during a 6-sprint test of 6 seconds, with 25 seconds of recovery performed on an ergocycle. Cognitive performance was measured before and after the speed test by simple reaction time, vigilance, ocular motility and decision-making tasks (Go / No-Go). Supplementation was presented to the athlete in two shots, spaced 30 minutes, 60 and 30 minutes before the beginning of the effort. The results indicate a positive effect of creatine + guarana supplement on muscle power (fatigue and peak power), as well as on cognitive performance measured after exercise for surveillance, Go / No-Go and eye motility tasks (Laura Pomportes et al., 2017).

Bittencourt et al. (2013) evaluated the antioxidant effects of hydroalcoholic extract of guarana (*Paulinia cupana* var. *Sorbilis Mart.)* on nitric oxide (NO) and other compounds generated by the degradation of sodium nitroprusside (SNP) in a culture of embryonic fibroblasts

(NIH-3T3 cells) . The bioactive compounds of guarana were: caffeine = 12,240 mg / g, theobromine = 6,733 mg / g and total catechins = 4,336 mg / g. The cells were exposed to 10 lM SNP over a 6 h period because the cells exhibited> 90% mortality in that concentration. These results demonstrate that guarana has an antioxidant effect on nitric oxide metabolism in situations with higher levels of cellular nitric oxide.

4. CONCLUSION

Considering the results presented, it is evident that the components present in guarana have stimulating and antioxidant properties that minimize damage to the body caused by oxidative stress in the body.

Studies have shown positive effects of guarana as a food source with anti-hyperglycemic potential, provided partial reduction of liver damage caused by hyperlipidemia, protection against gastric ulceration induced by indomethacin, beneficial results in the eyes of the elderly through preventive effects caused by stress oxidative, decreased cholesterol levels to baseline levels, as well as showing good results in preventing oral diseases and dental plaque.

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