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ORIGINAL PAPER

Guaraná, a supplement rich in caffeine and catechin, modulates cytokines: evidence from human in vitro and in vivo protocols

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Abstract Guaraná powder is an antiobesogenic supplement; however, its effect on inflammatory biomarkers has not yet been determined. Therefore, this study analysed whether guaraná supplementation can differentially modulate the levels of proinflammatory cytokines [interleukin 6 (IL-6), tumour necrosis factor-alpha, interleukin 1 beta (IL-1β), interferon-gamma (Ig-γ)] and anti-inflammatory interleukin 10 (IL-10) from in vitro and in vivo protocols. In the pilot in vitro protocol, human peripheral blood mononuclear cells were exposed to guaraná, as well as to resveratrol, quercetin and ascorbic acid as positive controls. The effect of guaraná on cytokine levels was also evaluated in culture medium supplemented with glucose and insulin. A randomised, placebo-controlled in vivo assay was also performed to evaluate the potential influence of guaraná on the blood cytokine levels of 14 healthy volunteers supplemented for 14 days. The effect of guaraná was similar to that of resveratrol, a known anti-inflammatory molecule, decreasing IL-1β, IL-10 and Ig-γ levels and increasing IL-10 levels compared to those of the control group. The in vitro insulin supplementation potentiated the effect of guaraná on some cytokines. A decreasing effect on the blood inflammatory cytokine levels, along with an increase in IL-10 levels, was also observed in volunteers supplemented with guaraná. In conclusion, guaraná positively modulates cytokines associated with inflammatory metabolism.

Keywords *Paullinia cupana* · Guaraná · Cytokines · Inflammation · Metabolic disorders

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Introduction

Guaraná (*Paullinia cupana*, Mart. var. sorbilis) is an Amazonian fruit that contains bioactive compounds such as methylxanthines (caffeine) and catechins [1, 2]. Guaraná extracted from seeds is listed in the official Brazilian Pharmacopoeia and is also approved in the United States as a food additive and is considered a dietary supplement. Therefore, guaraná is present in a variety of drinks, foods, dietary/herbal supplements and pharmaceuticals, and due its widespread use and potential abuse, the Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency has recently encouraged the submission of scientific data on guaraná in order to prepare a corresponding herbal monograph [3].

Unfortunately, the pharmacokinetic studies involving guaraná are limited to that performed by Bempong and Houghton [4] in rat intestines, which showed that the release and uptake of caffeine from guaraná was the same as for preparations containing free caffeine. An additional study performed by Haller et al. [5] assessed the human pharmacokinetics and pharmacodynamics of a dietary supplement containing ephedra from Ma Huang, a Chinese herb, and caffeine from guaraná and demonstrated that the plasma clearance and elimination half-lives for ephedrine and caffeine were comparable to published values reported for drug formulations. The authors concluded that botanical stimulants using guaraná as a caffeine source presented characteristics similar to those of their pharmaceutical counterparts. These results support the several biological actions of guaraná that are described in the literature, including positive effects on metabolic variables associated with cardiovascular diseases risks factors, such as obesity [6–8], and decreases in the lipid parameters [9]. An additional investigation using in vitro and in vivo assays showed that guaraná decreases the oxidation of LDL cholesterol [10].

From these results, an epidemiological study performed by Costa Krewer et al. [11] in an elderly population of the Amazon Riverine region (Maués, Brazil) analysed the association between habitual guaraná ingestion and cardiometabolic risk factors. The authors found a lower prevalence of hypertension, obesity and metabolic syndrome in the elderly that reported habitual guaraná powder ingestion compared to other individuals that never ingest this food. Complementary investigations demonstrated that guaraná modulates the oxidative stress caused by high nitric oxide levels [12] and decreases the oxidised LDL levels [13].

As metabolic disorders, including obesity, are associated with low-grade inflammation and other immune dysfunctions [14, 15], the potential effect of guaraná on blood inflammation biomarkers is unknown. Therefore, the present study analysed if guaraná supplementation could differentially modulate the levels of proinflammatory cytokines [interleukin 6 (IL-6), tumour necrosis factor-alpha (TNF-α), interleukin 1 beta (IL-1β), and interferon-gamma (IFN-γ)] and anti-inflammatory interleukin 10 (IL-10) from in vitro and in vivo protocols. In the in vitro protocol, human peripheral blood mononuclear cells (PBMCs) were exposed to guaraná extract, whereas the in vivo protocol was performed with 14 healthy adults who were given daily supplements of guaraná or placebo capsules.

Materials and methods

Drugs and reagents

The drugs and reagents used in the experiments, including insulin, Dulbecco Modified Eagle Medium (DMEM, 1640), phytohaemagglutinin (PHA), HEPES, resveratrol, quercetin, ascorbic acid and other chemical reagents, were purchased from Sigma-Aldrich (San Louis, MO, USA). Foetal bovine serum, heat-inactivated horse serum, penicillin and streptomycin were purchased from Gibco (Grand Island, NY, USA). Vacutainer® by BD Diagnostics (Plymouth, UK) cytokines kits for ELISA immunoassays were purchased from Biomyx Technology (San Diego, CA, USA).

Guaraná origin

Guaraná powder was supplied by EMBRAPA, Amazônia Ocidental (Agropecuary Research Brazilian Enterprise), a non-profit Brazilian governmental sector that offers technical support for guaraná production in Amazonas State. The bioactive compounds present in guaraná powder were previously determined by Bittencourt et al. [8], and the bromatological characteristics were determined by EMBRAPA.

General experiment design

This study was approved by the Universidade Federal de Santa Maria Ethical Board under number 0146.0.243.000-07. All of the participants gave consent. Two in vitro and in vivo protocols were used. The in vitro assay was performed using a hydro-alcoholic guaraná extract described in detail in Bittencourt et al. [8]. In the in vivo protocol, the volunteers were supplemented with capsules containing a minimal dose of guaraná powder (90 mg per day) estimated to contain caffeine (12.24 %), theobromine (6.7 %) and catechin (4.3 %).

The in vitro protocols

The in vitro protocols were performed in PBMCs obtained from peripheral blood samples of three healthy human volunteers. The blood samples were collected after 12 h of overnight fasting and were routinely centrifuged within 1 h of collection for 15 min at 2,500×*g*; the leucocyte samples were used to obtain PBMCs through gradient centrifugation using Ficoll–Hypaque. The PBMCs were immediately transferred to culture media containing 5 ml RPMI 1,640 with 10 % foetal calf serum (FCS), and 1 % penicillin/streptomycin and PHA [16]. Initially, the cells were expanded in suspension culture at 37 °C in a humidified 5 % CO_2 atmosphere for 72 h. Furthermore, the cells were centrifuged for 10 min (3 rpm) and washed twice with HBSS buffer (118 mM NaCl, 4.6 mM KCl, 10 mM D-glucose, 20 mM HEPES and 0.4 mM CaCl2, pH 7.4). After washing, the cells were transferred to the same buffer with and without the supplementation with guaraná and other chemicals.

These cells were used to perform two in vitro protocols. The first protocol evaluated the effect of 5 mg/ml guaraná supplementation on cytokine levels. The guaraná concentration was based on the study of Bittencourt et al. [8]. Resveratrol, quercetin and ascorbic acid, which are bioactive molecules with anti-inflammatory properties that were previously described in the literature [17, 18], were used as positive controls at 0.20 μM. Functional foods are generally represented by a nutritional matrix with several bioactive molecules. Guaraná, similar to coffee and tea, is richest in caffeine and catechins. However, the isolation of these molecules does not guarantee that the potential decreasing effect of guaraná on proinflammatory cytokine levels is specifically due to these molecules or their mixture. Some chemical molecules, such as resveratrol, quercetin and ascorbic acid, have been recognised for their effective anti-inflammatory effects on cytokines. Therefore, we evaluated whether guaraná presented properties similar to those of these compounds, although these molecules are not present in guaraná.

Because guaraná is an antiobesogenic and thermogenic food [4, 5], a second in vitro experiment was performed to evaluate the potential effect of supplementation with glucose and insulin on the cytokine levels of PBMCs. In this protocol, the following treatments were performed: control (C), guaraná (GUA), D-glucose at 15 nM (G) and insulin at 10 nM (I) [19].

In both of the in vitro protocols, the PBMCs were exposed to each treatment for six hours, and the cells were stored at −20 °C until cytokine analysis. The concentration of PBMCs in each treatment was 5×10^7 cells/ml. All of the treatments were performed in triplicate.

The in vivo protocol

A pilot in vivo protocol was performed using a randomised, placebo-controlled design to evaluate the potential influence of guaraná on the blood cytokine levels of 14 volunteers (six male and eight female). The volunteers were non-smokers and recreationally active, with body mass indices (BMI) >23 and <30 kg/m and without chronic morbidities. The body weight, height, body mass index (BMI, kg/m^2), waist circumference (WC) and systemic blood pressure were measured as previously described by Krewer et al. [7]. In addition, the fasting glucose level was evaluated using the standard enzymatic method using Ortho-Clinical Diagnostics® reagents on a fully automated analyser (Vitros 950® dry chemistry system; Johnson & Johnson, Rochester, NY, USA). Seven volunteers were supplemented with guaraná capsules and the others with placebo capsules.

The protocol began with an initial washout period (3 days), during which the participants were advised to not ingest foods rich in caffeine, such as coffee, tea, chimarrao (a traditional yerba mate beverage) and other nutritional supplements, that could have an influence on the analysed biochemical variables. The National Brazilian Ethics Committee (CONEP) does not permit payment to volunteers for clinical research. Therefore, long-term intervention studies were very difficult due the discontinuity of potential volunteers. Therefore, the present study was performed over a short period (14 days). The cytokine levels were determined in fasting blood samples collected at baseline and on the 7th and 14th days of treatment.

Cytokines analysis

The levels of the cytokines IL-β, IL-6, TNF-α, IFN-γ and IL-10 were measured in cell-free supernatants using ELISA immunoassay kits according to the manufacturer's instructions [20]. The results were calculated as pg cytokine/ml culture medium. The results obtained from the in vitro protocols were expressed as per cent control. The in vivo results were expressed as cytokine unit measure (pg/ml).

Statistical analysis

The results are presented as the mean ± standard deviation (SD). The comparison of the cytokine levels of PBMCs exposed to guaraná and positive controls was performed via a one-way analysis of variance followed by Dunnett's post hoc test. The comparison of the cytokines levels of PBMCs supplemented with guaraná with and without glucose and insulin was performed via a two-way analysis of variance followed by Bonferroni's post hoc test. The statistical analysis of the in vivo protocol was performed using a repeated measures analysis of variance followed by Bonferroni's post hoc test for each treatment group (placebo and guaraná). The influence of metabolic parameters such as glucose, BMI, WC and blood pressure on the cytokine levels was evaluated by Pearson's correlation. The potential influence of sex, age and BMI on the placebo and glucose response was estimated using a multivariate analysis (logistic regression, *Backward Wald* method). The p values were two-tailed, and the differences were considered statistically significant at $p \leq 0.05$.

Results

The cytokine levels observed in the C-PBMC group were IL-1β = 57.5 ± 13.1, IL-6 = 94.2 ± 9.9; TNF-α = 110.6 ± 12.4; IFN-γ = 150.5 ± 23.5 and IL-10 = 45.3 ± 3.5 pg/ml. The level of IL-1β, IL-10 and IL-1β decreased when the PBMCs were exposed to guaraná and resveratrol. The ascorbic acid did not change the IL-1β level, and quercetin did not change the IL-6 level

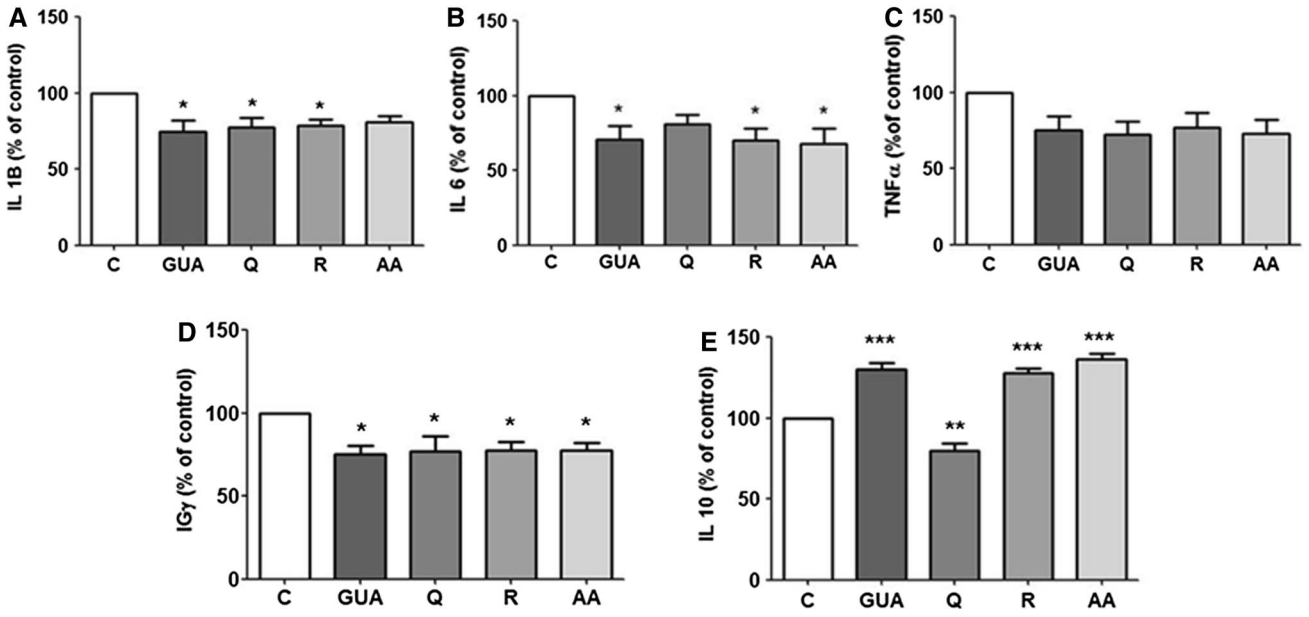

Fig. 1 The cytokine levels of PBMCs not treated (Control, *C*) or treated with guaraná (*G*), quercetin (*Q*), resveratrol (*R*) and ascorbic acid (*AA*). IL-1B. The statistical comparison was performed using a one-way analysis of variance followed by Dunnett's post hoc test that compared the treatment group with the control group. $*p < 0.05$; $**p < 0.01$; $***p < 0.001$

compared to that of the PBMC-C group. However, each treatment altered the levels of TNF-α. Similar to resveratrol and ascorbic acid, guaraná extract significantly increased the IL-10 levels. However, quercetin decreased the IL-10 cytokine level compared to that of the C-PBMC group (Fig. 1).

The second protocol analysed the potential effect of glucose and insulin on the cytokine levels of PBMCs with and without guaraná supplementation, and the results are presented in Fig. 2. After 6 h of guaraná treatment, the addition of glucose and insulin in the culture medium did not change the cytokine levels compared to those of the PBMC control group. However, guaraná with glucose or insulin significantly decreased the IL-β levels compared to those of the PBMCs treated only with guaraná. The levels of IL-6 as well as TNF-α also significantly decreased when treated with guaraná and insulin. The levels of IFN-γ remained unchanged in cells treated only with guaraná and with glucose and insulin. The level of IL-10 also significantly increased in the PBMCs treated with guaraná and insulin compared to those of cells treated only with guaraná.

As illustrated in Table 1, the general characteristic baselines of volunteers that participated in the in vivo protocol were similar. The results of the treatments with placebo and guaraná are presented in Table 2. The guaraná supplementation significantly decreased the levels of all of the inflammatory cytokines beginning on the 7th day of supplementation. The decreasing effect of guaraná on the blood inflammatory cytokine levels was maintained after 14 days of supplementation. In addition, the IL-10 levels of the volunteers that ingested the guaraná capsule also increased.

The correlation between metabolic parameters such as glucose, BMI, WC and blood pressure with the cytokine levels of subjects were supplemented with placebo or guaraná was analysed. The results showed a positive correlation between the levels of glucose and IL-6 cytokine ($r = 0.566$, $p = 0.035$) in the subjects supplemented with placebo. However, this correlation was not observed in the subjects supplemented with guaraná.

A multivariate analysis was also performed to evaluate whether sex, age or BMI could influence the effect of guaraná on cytokine levels. The analysis showed that results were independent of these variables.

Discussion

To the best of our knowledge, this is the first study that described the effect of guaraná on the levels of human cytokines and demonstrated an immunomodulatory effect independent of body weight loss. It is important to contextualise the results described here from an epidemiological perspective.

Several foods and their bioactive molecules have being associated with decreases in chronic disease and decreases especially in the levels of metabolic morbidities that increase the risk of cardiovascular disease. However, many of these studies investigated specific populations, including

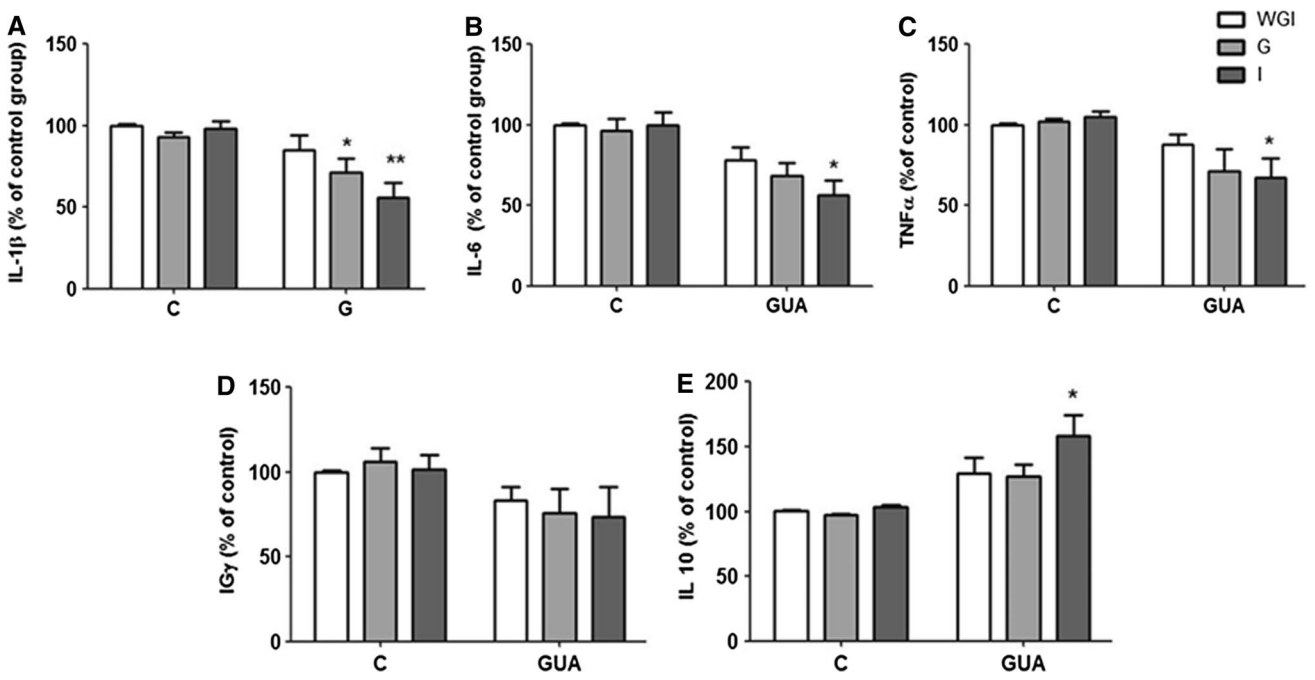

Fig. 2 The cytokine levels of PBMCs not treated (Control, *C*) or treated with guaraná (*G*) plus glucose (*G*) and insulin (*I*) or without concomitant glucose and insulin (*WGI*). The statistical comparison was performed using a one-way analysis of variance followed by Dunnett's post hoc test that compared the treatment group with each untreated group (control or guaraná). $*p < 0.05$; $**p < 0.01$; $***p < 0.001$

Table 1 Characteristics baseline

Variables	Supplementation	
	Placebo	Guaraná
	Mean ± SD	Mean ± SD
Age (years)	37.1 ± 8.7	36.8 ± 8.6
SBP (mmHg)	120.6 ± 12.0	116.7 ± 12.1
DBP (mmHg)	75.0 ± 5.3	70.0 ± 8.9
Waist circumference (cm)	90.4 ± 8.8	93.2 ± 14.2
BMI (kg/m^2)	27.3 ± 3.6	27.1 ± 3.8
Glucose (mg/dl)	95.7 ± 12.3	94.6 ± 17.3

SD standard deviation, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

the Mediterranean diet and some foods such as green tea and soybean that are present in the Asian diet [21, 22]. Due to the lack of epidemiological evidence, foods originating from other world regions, such as foods consumed during pre-Columbian periods, are less studied.

A previous study performed by our team evaluated the habitual ingestion of guaraná an Amazonian fruit that today is used to produce energy drinks [11]. The results demonstrated a lower prevalence of hypertension, obesity and metabolic syndrome in the elderly that habitually ingest guaraná than in others. Additionally, a significant association was found between lower levels of advanced oxidative protein products and habitual guaraná consumption, suggesting that guaraná could protect against metabolic disorders.

Table 2 Cytokine levels in volunteers supplemented with guaraná or placebo capsules

Cytokines	Supplementation groups					
	Placebo			Guaraná		
	Periods (days)			Periods (days)		
	1st	7th	14th	1st	7th	14th
IL-1β	104.7 ± 11.8	109.4 ± 0.6	105.0 ± 8.1	117.3 ± 14.3	91.6 ± 11.7*	78.6 ± 10.1**
IL-6	133.3 ± 3.5	128.7 ± 5.2	126.8 ± 6.2	132.8 ± 5.8	118.7 ± 3.8**	93.1 ± 9.6***
TNF-α	151.9 ± 7.9	147.6 ± 5.5	143.0 ± 6.2	160.7 ± 3.9	92.1 ± 8.6**	95.3 ± 11.9**
Igγ	219.3 ± 15.6	212.8 ± 8.5	212.1 ± 9.3	223.1 ± 21.7	129.4 ± 4.7**	148.7 ± 9.3*
IL-10	59.3 ± 3.6	60.6 ± 4.9	56.3 ± 4.8	55.6 ± 8.4	82.1 ± 4.8**	118.5 ± 9.9

Cytokines unit = pg/ml; data presented as mean ± standard deviation; * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$ significant difference among cytokines levels after 7 and 14 days of placebo or guaraná supplementation compared with baseline (1st) day

As metabolic disorders, including obesity, are associated with low-grade inflammation and other immune dysfunctions [23, 24], the potential effect of guaraná on blood inflammation biomarkers was tested here. However, it is difficult to isolate the potential immunomodulatory, antiobesogenic effect of guaraná that has been suggested by previous studies [6–9, 25]. Because the inflammatory response is generally acute and does not require a large intervention time for evaluation, the present investigation analysed the effect of guaraná on the levels of blood cytokines independent of body weight loss.

Cytokines are immunomodulating factors that include interleukins and interferons that are stimulated in response to inflammation, infection and trauma [26]. In addition, evidence has also demonstrated that in metabolic diseases such as obesity and diabetes type 2, there is an enhanced secretion of some interleukins and inflammatory cytokines [27, 28]. The inflammatory response of these diseases promotes the activation of transcriptional factors and pro-inflammatory cytokines, which can lead to an unresolved inflammatory response associated with a high risk for cardiovascular morbidities [29]. Epidemiological and intervention studies have suggested the influence of dietary patterns, foods and bioactive compounds with protective anti-inflammatory effects [29]. Therefore, the results described here from in vitro and in vivo protocols demonstrating the effect of guaraná on cytokine levels are in accordance with previous data from other foods and related molecules.

The results described here were obtained from in vitro and in vivo protocols. The in vitro protocol constituted two assays using PBMCs as the experimental model. These cells are considered a promising target tissue in the field of nutrigenomics because they seem to reflect the effects of dietary modifications at the level of gene expression [30]. Initially, the effect of guaraná on the level of cytokines in the PBMCs was evaluated using a negative control group and resveratrol, ascorbic acid and quercetin molecules as positive immunomodulatory control groups.

Generally, in studies of functional foods, the isolated effect of the main bioactive molecules is concomitantly evaluated to determine the contribution of these molecules to the results obtained. However, there are a few studies involving the effect of caffeine and catechin on the level of proinflammatory cytokines in human PBMCs. Moreover, a previous study by Nevestani et al. [31] that investigated the effect of black tea extract (BTE) and some of its pure phenolics on human PBMCs showed that BTE but not the pure molecules suppressed pro-inflammatory cytokines.

In addition, some bioactive molecules present in the human diet decrease the level of proinflammatory cytokines human PBMCs. This is the case of resveratrol [32, 33], ascorbic acid [34, 35] and quercetin [36]. Therefore, we believe that a comparison of effect of guaraná on cytokines and these molecules can help determine whether guaraná presents a similar immunomodulatory action. Because this experimental design is not traditional, the results are informative and relevant.

The effect of guaraná on the PBMCs was similar to those of the bioactive molecules tested here, such as resveratrol. Resveratrol is a polyphenolic phytoalexin that is found in several plant, such as grapes, berries and peanuts, and has some well-studied anti-inflammatory, antagonising and catabolic effects on TNF-α and (IL)-1β via the inhibition of nuclear factor (NF)-κB [37–39]. NF-κB is a transcription factor that plays an important role in inflammation, the autoimmune response, cell proliferation and apoptosis as is regulates several genes related to these processes. This molecule can be stimulated by several cellular stress variables, such as reactive oxygen species, and induces the transcription of pro-inflammatory cytokines, NO and other molecules [28]. Guaraná is an antioxidant food that regulates cell oxidative stress caused by high concentrations of NO [12]. Therefore, we can speculate that guaraná decreases the level of proinflammatory cytokines from NF-κB by downregulation. However, additional studies are required to determine if guaraná differentially modulates genes related to the cell inflammatory response.

The effect of food and bioactive compounds on interferon cytokines has been less studied than that on interleukin molecules. INF-γ, also called type II interferon, plays a key role in the innate and adaptive immunity against viral, intracellular bacterial infections and tumour cells. This molecule is an important activator of macrophages. In the body, INF-γ is secreted by lymphocytes such as T helper, cytotoxic T and NK cells, as well as by myeloid cells, dendritic cells and macrophages. INF-γ is highly expressed in atherosclerotic lesions and has emerged as a significant factor in atherogenesis [26]. It is possible that the decreasing effect of guaraná on INF-γ levels could be associated with the positive effect of guaraná on metabolic variables, such as the lipid profile, blood pressure and body weight, which are associated with low-grade and chronic inflammation.

To confirm these results, an additional in vitro protocol was performed that evaluated the effect of guaraná on the levels of cytokines in the PBMCs in the presence of high insulin and glucose levels that mimic ‘metabolic disorder conditions’. The results also suggested a potential interaction between guaraná and insulin on the cytokine levels in the PBMCs. Some molecules, including proinflammatory cytokines such as TNF-α, IL-6 and IL-1β that are produced by adipocytes and macrophages, are important modulators of chronic inflammation contributing to the development of obesity and atherosclerosis.

This effect is probably related to the caffeine content of guaraná. Many studies have indicated that caffeine has immunomodulatory effects similar to those of other

members of the methylxanthine family [40]. A study of Horrigan et al. using diluted human whole blood that was pre-incubated with caffeine demonstrated the suppression of TNF-α by caffeine. Unfortunately, the in vivo mechanisms of T cell interaction with insulin have not been fully elucidated. However, there is evidence that T cells from diabetic patients and from healthy subjects that were exposed to different glucose concentrations present different responses [41]. While in the PBMCs from diabetic patients the exogenous glucose did not affect cell stimulation or respiratory burst, the PBMCs from healthy patients displayed a dose-dependent decrease in the responsiveness to mitogens. From these results, the authors concluded that hyperglycaemic states cause changes in the immune system cells due to the repeated 'continuous' exposure to excess sugar.

The in vivo results described in this study also demonstrate a decreasing effect of guaraná on the levels of inflammatory cytokines. These results are in agreement with data obtained from the in vitro assays. In addition, the decrease in the cytokine levels in healthy adult volunteers after guaraná supplementation is in accordance with the results of previous epidemiological studies that suggested an effect of caffeine on inflammation biomarkers. Chavez Valdez et al. [42] performed a cross-sectional study that measured changes in the peripheral blood cytokine levels associated with caffeine treatment in a cohort of preterm infants and determined that 1 week of caffeine treatment (<20 μg/ml) decreased the peripheral blood concentrations of IL-1β, IL-6 and TNF-α.

Finally, it is important to comment on the potential methodological limitations of this study design: in the in vitro assay, the effect of guaraná on cytokine levels was measured at only one guaraná concentration (5 mg/ml) and only once after the supplementation (6 h). Another question that must be considered is related to the effect of insulin on the PBMCs. Insulin itself has been reported to have an anti-inflammatory effect at low concentrations. However, in this study, the experimental conditions that used PBMCs exposed to insulin did not demonstrate significant cytokine modulation. In fact, the biological effects of some chemicals are influenced by the molecule and cell concentrations, the time of exposure and the time of analysis relative to the treatment. Because there are no standardised protocols in the literature to define anti-inflammatory analyses, we believe that the lack of significant results regarding the effect of insulin on PBMCs in our experiments compared to other studies that used insulin as treatment may be due to these variables.

Another important methodological concern related to studies performed here is the low number of subjects that were supplemented with guaraná ($n = 14$). Due to this low number, this study was considered a pilot investigation that requires confirmation by other experiments involving more individuals. Despite the low sample number, the results are relevant because the subjects that participated in this investigation were carefully selected to avoid environmental and biological interferences in the results obtained. Therefore, the results presented are realistic and are in accordance with the results of the controlled in vitro protocols. Despite this limitation, guaraná significantly decreased the most inflammatory cytokine analysed here.

In conclusion, guaraná positively affects the levels of cytokines associated with inflammatory metabolism. This effect may be associated with the previously reported antiobesogenic effect of guaraná due the bioactive molecules present in its nutritional matrix (caffeine and catechin). Because this study included healthy adults, complementary studies evaluating the potential anti-inflammatory effect of guaraná supplementation on patients suffering from obesity or metabolic syndrome are needed.

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Conflict of interest None.

Compliance with Ethics Requirements The present study was by Ethical Board of Federal University of Santa Maria and all volunteers signed consent term (process number: 23081.015838/2011-10). The authors also declare have Brazilian governmental authorization to perform studies using guaraná fruit (number: 010547/2014-4).

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