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Full Length Research Paper

Effects of *Psidium guajava* on the metabolic profile of Wister rats

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The consumption of a diet rich in fruits, vegetables, seeds and whole foods contributes to reduce the risk factors for chronic disorders such as insulin resistance, high blood pressure and dyslipidemia. The objective of this study was to evaluate the effect of the consumption of the pulp and seeds of guava (*Psidium guajava*) on the metabolic profile of Wistar rats. The animals were divided into a control group, G1, and two treatment groups: G2 – fed with guava pulp juice, and G3 – fed with rat food containing guava seeds. The duration of the treatment was 40 days. A significant reduction in glycemia and in the levels of triacylglycerides and total cholesterol, and augmented levels of High-density lipoprotein cholesterol (HDL-c) were observed in the animals fed with guava pulp juice and seeds. The levels of alanine aminotransferase (AST) and alanine aminotransferase (ALT) enzymes were also reduced. These findings indicate that the use of guava (*Psidium guajava*) pulp and seeds, the latter considered agroindustrial wastes, contribute significantly to the control of biochemical variables involved in the incidence of chronic degenerative disorders in the population.

Key words: *Psidium guajava*, glycemia, cholesterol, Wistar rats.

INTRODUCTION

One of the main risk factors for non-transmissible chronic diseases is a diet of inadequate composition, allied to the lack of physical activity and other lifestyle-related factors such as the use of tobacco and alcohol (Mccarthy et al., 2011). The incidence of chronic disorders such as obesity, diabetes, cardiovascular disease and metabolic syndrome has increased visibly, impairing the quality of life and increasing spending on hospitalizations, medications and other public health interventions (Remington and Brownson, 2011; Jeon et al., 2011).

Studies have demonstrated that the consumption of a diet rich in fruits, vegetables, seeds and whole foods contributes to diminish the risk factors associated with chronic disorders such as insulin resistance, high blood pressure and dyslipidemia (Devalaraja et al., 2011; Bamosa et al., 2010). Fruits and vegetables not only provide important components, such as ascorbic acid, β-carotene and folic acid, that play basic roles in the organism, but are also sources of bioactive compounds that are directly associated with the prevention of disorders such as diabetes and cardiovascular diseases (Faller and Fialho, 2009).

Psidium guajava L., known popularly as guava, belongs to the family Myrtaceae and has been used traditionally as a medicinal plant. Its leaves are used routinely in many countries to treat respiratory and gastrointestinal disorders, and as an antispasmodic and anti-inflammatory remedy (Kaneria and Shanda, 2011; Oh et al., 2005). Among Brazil's tropical fruits, the guava has placed Brazil among the world's top producers, with most of the country's production destined for the food industry, which produces candies, juices, jams and frozen guava

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pulp. The two most common varieties of guava are the red (*P. guajava* var. pomifera) and the white variety (*P. guajava* var. pyrifera). The main constituents of guava, in addition to vitamins, are tanins, phenolic compounds, flavonoids, essential oils, sesquiterpene alcohols and triterpenoid acids (Haida et al., 2011).

Guava fruit processing involves discarding the seeds, which make up the waste that is usually discarded in agro-industrial processes, together with part of the peel and pulp fraction not separated in the physical depulping process (Nascimento et al., 2010).

It is known that the seeds, peels and leaves of fruits contain considerable amounts of bioactive compounds with beneficial physiological and metabolic properties, such as antioxidant activity and control of biochemical variables (Felice et al., 2012; Bamosa et al., 2010; Guo et al., 2003). Numerous studies have demonstrated the antimicrobial, gastrointestinal and anticarcinogenic activity of guava seeds due to the presence of phenolic glycosides in the composition (Pelegrini et al., 2008; Salib and Michael, 2004; Lozoya et al., 2002; Hawrelak, 2003). However, the literature lacks data about their effects on the no lipid profile of animals. Therefore, the objective of this study was to evaluate the effect of the consumption of the pulp and seeds of guava (*P. guajava*) on the metabolic profile of Wistar rats.

MATERIALS AND METHODS

Groups of animals

This work was approved by the Animal Research Ethics Committee of the University of Marília (UNIMAR). The animals were treated according to the “Guide for the Care and Use of Experimental Animals” (that follows principles for the care of laboratory animals).

Thirty male Wistar rats were used, weighing approximately 250g, which were kept in the vivarium at UNIMAR (University of Marília) under a dark/light cycle of 12 h, room temperature of 22 ± 2℃, and relative air humidity of 60 ± 5%. After a period of seven days of acclimation to the laboratory, the animals were divided randomly into 3 groups (n = 10) treated for 40 days, as follows: G1 received water and rat food *ad libitum*; G2 received *Psidium guajava* pulp juice *ad libitum* and G3 received rat food supplemented with 30% of *Psidium* guava seeds (G3) also *ad libitum.*

Weight gain was monitored once a week on days 1, 8, 15, 23, 31 and 39 of the experiment. The animals were fed daily, and their consumption (of rat food and water) was recorded based on the leftovers found each day.

Preparation of *Psidium guajava* pulp juice and rat food supplemented

The *P. guajava* used in the experiment was obtained in the local market and was authenticated by experts from the Botanical Department of UNIMAR-Marília, SP, Brazil. The juice was prepared from *P. guajava* pulp by grinding them with water in a blender, in a proportion of 1:6 (pulp: water). The juice was filtered through gauze and stored in 500 ml plastic bottles at freezing temperature (-18℃).

The supplemented rat food was prepared from the seeds of guavas supplied by the company Predilecta for Matão, SP, Brazil. This is a large Brazilian company that produces a typical sweet guava paste called *goiabada*. The guava fruits this company uses come from large plantations that use Government-certified seeds.

The seeds were dehydrated in an air circulating oven (Marconi) at 100℃ for 11 h, knife mill mashed and mixed, and homogenized to rat food, previously crushed and milled at a ratio of 30: 70 (seeds: rat food). The mixture was modeled manually in the form of pellet similar to rat food, and the same was kiln dried by movement of forced air (Marconi) at a temperature of 65℃ for 5 h. The rat food supplemented was kept under refrigeration until their use.

Collection of blood samples and determination of the biochemical profile

After 40 days of treatment, the animals were anesthetized with Hypnol® (sodium pentobarbital) until complete sedation, after which blood samples were drawn to determine their biochemical profile: glycemia, total cholesterol, HDL-c, triacylglycerides, aspartate transaminase (AST) and alanine aminotransferase (ALT). The glucose and lipid levels were measured in mg/dl, and AST and ALT in U/L.

The exams were performed at the Clinical Analysis Lab of the University Hospital of UNIMAR (Laboratório São Francisco) and the results were interpreted according to the ADA (2010).

Statistical analysis

The variables are presented as means and standard deviations. The data were analyzed by Tukey-test with a 5% level of significance.

RESULTS

The results on the weight of the animals (Table 1) indicated that, at the end of the treatment, the weight of the group treated with guava pulp juice (G2) was significantly lower than that of the control group (G1). As for the group of animals treated with rat food containing guava seeds (G3), their weight did not vary significantly in relation to that of G1.

The results of the biochemical variables revealed that the treatments with guava pulp juice (G2) and with rat food supplemented with guava seeds (G3), significantly diminished the levels of glycemia, triacylglycerides and total cholesterol, and significantly augmented the levels of HDL-c when compared with the control group (G1) (Table 2).

Significant variations were also found in the levels of liver enzymes (AST and ALT) of the groups treated with pulp and with seed-supplemented rat food in relation to the control.

DISCUSSION

Overweight and obesity associated with elevated levels of low-density lipoprotein (LDL-c), hyperglycemia and high blood pressure increase the incidence of cardiovascular diseases and diabetes mellitus in the population. This finding has been confirmed in several clinical studies involving a large number of patients, as

Table 1. Comparison of the final weight of the animals of groups G1, G2 and G3 after 40 days of treatment.

	Group G1	Group G2	Group G3
Weight	312.91 ± 44.41	286.26 ± 41.42	308.09 ± 57.75
P-value		0.0052	0.1792

Table 2. Comparison of the biochemical profile of the animals of the control group (G1) and the treated groups (G2 and G3).

Variable	Groups			P-value
	G1	G2	G3	
Glycemia	163.20 ± 13.74^{B1}	136.80 ± 5.96^{A}	143.30 ± 9.80^{A}	0.0001
Triacylglycerides	104.90 ± 18.28^{C}	81.20 ± 9.37^{B}	38.00 ± 8.58^{A}	0.0000
Total cholesterol	80.00 ± 7.18^{B}	48.90 ± 3.48^{A}	51.50 ± 9.38^{A}	0.0000
HDL-c	17.10 ± 1.20^{B}	26.40 ± 2.01^{A}	26.10 ± 1.45^{A}	0.0000
AST	153.00 ± 15.19^{C}	132.70 ± 9.78^{B}	119.30 ± 9.75^{A}	0.0000
ALT	76.10 ± 16.57^{B}	78.80 ± 13.45^{B}	61.90 ± 7.98^{A}	0.0166

[1] Different letters in the vertical direction indicate a significant difference between the treatments at a level of 5%.

well as many other studies using animal models, which found augmented levels of total cholesterol, LDL-c and triglycerides, and reduced HDL-c levels. These lipids are risk factors for cardiovascular diseases. They are involved in the accumulation of lipids in the liver and are implicated in the development of type 2 diabetes and its correlated risks, such as metabolic syndrome and vascular diseases. The control of these risk factors through the consumption of healthy foods, especially those of vegetable origin, has been demonstrated in numerous studies (Dohadwala et al., 2011; Okarter and Liu , 2010; Hooper et al., 2008).

Huang et al. (2011) reported significant hypoglycemic effects of lyophilized pulp of *P. guajava* in diabetic rats, which they ascribed to the antioxidant activity of compounds present in the pulp of the fruit. Nascimento et al. (2010) observed the presence of total phenolic compounds in the agroindustrial wastes (seeds, skin and pulp) of guava (*P. guajava* L), confirming its antioxidant activity *in vitro*. Castro-Vargas et al. (2009) extracted and identified significant levels of β-carotene and total phenolic compounds from *P. guajava* L. seeds, and Ramírez and Delahaye (2011) found high concentrations of carotenoids, lycopene, vitamin C and polyphenols in guava pulp.

Other studies have reported the presence of higher amounts of phenolic compounds with antioxidant activity in the leaves of white (*P. guajava* var. pyrifera L.) and red guava (*P. guajava* var. pomifera L.) when compared with other vegetable species (Jiménez-Escrig et al., 2001; Wang et al., 2007; Haida et al., 2011). Moreover, tests on the leaves of the latter variety revealed the presence of gallic acid, catechins, epicatechins, rutin, naringenin and kaempferol (Melo et al., 2011; Chen et al., 2010). Bomtempo et al. (2012) reported that *P. guajava* pulp, peel and seeds extracts exert anti-cancer effects on both hematological and solid neoplasms, and suggested that these effects are due to the presence of antioxidant compounds.

Several studies have shown that phenolic compounds are beneficial in reducing glycemia and plasma lipids. For example, gallic acid, catechin and epicatechin inhibited pancreatic cholesterol esterase, which explains the decrease in cholesterol levels (Ngamukote et al., 2011). Park et al. (2009) have demonstrated that gallated catechins are important as a preventive treatment for type 2 diabetes and obesity. Akinmoladun et al. (2010) studied methanol extracts of some fruits, including *P. guajava*, and demonstrated that there is a good correlation between total phenolic contents and reductive potential and a fair correlation between total phenolic contents and lipid peroxidation inhibitory activity. They concluded that these plants possess significant antioxidant and radical scavenging activities.

Zhao et al. (2011) showed that rutin and kaempferol (also found in *P. guajava*) decreases HMG-CoA reductase activity in hepatic tissue and improves lipid profiles. *P. guajava* is also a source of ascorbic acid, carotenoids and flavonoids. Ascorbic acid is recognized for its important antioxidant effects (Thaipong et al., 2005; Monárrez-Espino et al., 2011; Thuaytong and Anprung, 2011). Among the carotenoids, lycopene has been correlated with the prevention of cardiovascular damage because of its positive effects on dyslipidemia (Lorenz et al., 2012; Sesso et al., 2012). Isoflavones also reportedly promote benefits in diabetes, dyslipidemia and heart disease. Curtis et al. (2012) studied the effect of dietary flavonoids on the risk of cardiovascular disease in postmenopausal women with type 2 diabetes and concluded that isoflavones improved biomarkers of cardiovascular risk. Singh and Marar (2011) studied the effects of *P. guajava* leaves on the inhibition of the activity intestinal glycosidases related with postprandial hyperglycemia, suggesting its use for the treatment of individuals with type 2 diabetes. Ojewole (2005) identified the presence of phenolic compounds in the leaves of the fruit, demonstrating their hypoglycemic and hypotensive effects on diabetic rats treated with aqueous leaf extract. Soman et al. (2011) reported a decline in the levels of glycated hemoglobin and fructosamines, as well as a significant reduction in the glycemic levels of diabetic rats treated for 30 days with guava leaf extract. Wu et al. (2009) also used guava leaves and found that the phenolic compounds, gallic acid, catechins and quercetins they contained significantly inhibited the glycation of proteins such albumin, suggesting their use for the prevention of diabetes complications.

Other studies have demonstrated that guava leaf and peel extracts also had hypoglycemic effects on experimental models drug-induced to severe conditions of diabetes (Rai et al., 2009; Shen et al., 2008; Oh et al., 2005). These data corroborate the findings of this study, since the groups treated with guava pulp juice and with rat food supplemented with seeds showed significantly lower levels of glycemia after the treatment.

Rai et al. (2010) reported hypolipidemic and hepato-protective effects in diabetic rats treated with aqueous extract of lyophilized guava peel (*P. guajava*). Deguchi and Miyazaki (2010) reported that guava leaves in the form of an infusion not only reduced postprandial glycemia and improved hyperinsulinemia in murine models but also contributed to reduce hypercholes-terolemia, hypertriglyceridemia and hypoadiponectinemia in the animals of their study. Several studies have shown that aqueous extract of *P. guajava* contains components with LDL-c antiglycation activity, suggesting its contri-bution to the prevention of neurodegenerative and cardiovascular diseases (Chen et al., 2010; Hsieh et al., 2005). Other studies have found cardioprotective effects of aqueous extract of *P. guajava* in myocardial ischemia-reperfusion injury in isolated rat hearts, primarily through their radical-scavenging actions (Yamashiro et al., 2003). Studies with humans have found that the consumption of guava for a period of 12 weeks reduced blood pressure by 8%, total cholesterol levels by 9%, triacylglycerides by almost 8%, and induced an 8% increase in the levels of HDL-c. The authors attributed these effects to the fruit's high potassium and soluble fibers contents (Singh et al., 1993; Singh et al., 1992). These results are consistent with those obtained in the present study, since both the guava pulp and the rat food containing guava seeds significantly reduced the triacylglycerides and total cholesterol levels, and increased the HDL-c values of treated Wistar rats when compared to the control.

Dutta and Das (2010) identified significant anti-inflammatory activity of the ethanol extract of guava leaves in experimental models, while Kawakami et al. (2009) observed the antiproliferative activity of the leaves through inhibition of the catalytic activity of prostaglandin endoperoxide H synthases (PGHS) involved in the inflammatory process.

Roy et al. (2006) reported that the use of *P. guajava* leaves lowered high serum AST and ALT levels in experimental models with induced liver injury. In the present study, the administration of guava pulp and rat food supplemented with guava seeds significantly diminished the AST levels, and the ALT levels of the animals of G3 were also lower than those of G1.

The results of this work indicate that the use of guava (*Psidium guajava*) pulp and seeds contributed signifi-cantly to control the biochemical variables of the experimental model under study. Moreover, since guava seeds are treated as wastes by the food processing industry and are therefore discarded, their use may not only minimize the disposal of pollutants but also promote important effects for the control and prevention of chronic degenerative diseases in the population.

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