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CAN *GARCINIA COCHINCHINENSIS* CHOISY AFFECT FOOD INTAKE AND BEHAVIOR IN EXPERIMENTAL MODELS?

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ABSTRACT

Studies have demonstrated an intrinsic relationship between obesity and anxiety, highlighting anxiety as both a frequent symptom among the obese and its strong relationship with an increase in food consumption. The objective of this study was to evaluate the effects of the consumption of the fruit and leaves from *Garcinia cochinchinensis Choisy*, the fruit known as yellow mangosteen, on the food intake and behavior of Wistar rats. 24 animals were used, divided into a control group (G1=8), which received water *ad libitum*, the G2 group (n=8) treated with juice from the pulp (40%), and the G3 group (n=8), treated with juice from the leaves (40%) of the fruit. After 40 days of experiment, behavioral analyses were carried out using the open field and elevated plus maze models, in addition to determining the weight of the animals' visceral fat. The data analysis was performed using analysis of variance (ANOVA) and Tukey's Test, using the SISVAR software and a significance level of 5% probability ($p < 0.05$). The results revealed a significant reduction in the visceral fat of the animals treated with the yellow mangosteen pulp and leaves compared to the control group.

The juices didn't have any effect on the behavior of the animals in the experimental models used. The results of this study can be used as reference for future works on this exotic fruit.

KEYWORDS: Yellow Mangosteen, Visceral Fat, Wistar Rats.

INTRODUCTION

In the last 25 years, obesity has emerged as an epidemic in both developed and developing countries. Population studies suggest that obesity is the cause of death of 2.8 million people per year, and currently around 12% of the world population is obese. It is also associated with numerous non-communicable diseases that contribute to increased morbidity and mortality due to various causes. Estimates indicate that in 2025, 50% of the world population will be obese if preventive measures are not taken.[1-4]

Various conditions are known to contribute to the etiology of obesity, including genetic, metabolic, endocrine, cultural, economic, emotional and behavioral factors that interact in different combinations in obese individuals. These multiple etiologies, behavioral correlates, psychosocial effects and medical consequences, therefore, make obesity an especially complex phenomenon.[5-7]

Studies have demonstrated an intrinsic relationship between obesity and anxiety, highlighting anxiety as both a frequent symptom among obese adults and its strong relationship with an increase in food consumption.[8] According to Segal, Cardinal and Cordás[11], mood changes and anxiety disorders have been described as enablers for weight gain and they could be classified as causes and/or complicating factors in obesity.

Anxiety is a generic term subjectively describing a wide variety of different mental states, which usually arise in response to some kind of external or internal stress.[12] According to Gross and Hen[13], the sensations related to anxiety are a normal part of human experience, but excessive or inappropriate anxiety can become a disease.

Several studies have therefore investigated the influence of psychological aspects on food intake, in addition to the effect of some food items on the feeding behavior in experimental models. The aim of this study was to evaluate the effects on the food intake and behavior of Wistar rats of the consumption of the fruit and leaves from *Garcinia cochinchinensis Choisy*, known as yellow mangosteen.

MATERIAL AND METHODS

Experimental models: This study was approved by the Animal Research Ethics Committee of the Faculty of Food Technology (Fatec), Marilia - SP, Brazil (protocol number 002/2016). Animals were fed *ad libitum* during the experimental period and were cared for according to the recommendations of the Canadian Council's "Guide to the care and use of experimental animals".

For the experiment, 24 Wistar rats (males) weighting 230 g - 250 g were housed in collective cages under a dark/light cycle of 12 hours, room temperature of 22 ± 2° C, and relative air humidity of 60 ± 5% at the Faculty of Food Technology (Fatec), Marilia - SP, Brazil.

Plant: The *Garcinia cochinchinensis* Choisy, known as yellow mangosteen, was obtained directly from the orchard in School of Food Technology (FATEC- Pompeia / São Paulo). The plant was identified and deposited in the Herbarium of the Department of Biology of FFCLRP-USP (Faculty of Philosophy, Sciences and Languages of Ribeirão Preto - USP), under nº SPFR 16037.

Preparation of the juices: After manually removing the seeds, the pulp of *G. cochinchinensis* Choisy was subjected to blast freezing (-80º C) for later use. The juices were prepared by grinding the pulp in a household blender with filtered water at a proportion of 40%. The juice was filtered in a fine sieve, poured in 500 mL bottles each day and administered through drinking fountains made of opaque PET (polyethylene terephthalate) bottles. The same procedure was used to prepare the juice of the leaves.

Groups of animals: After seven days of acclimation to laboratory conditions, the animals were divided randomly in G1 (n=8) that was fed water and rat food ad libitum, G2 (n=8) that was fed juice of the yellow mangosteen pulp, concentration of 40 % and rat food ad libitum, and G3 (n=8) that was fed juice from the leaves of the fruit (40%) and rat food ad libitum. The animals were fed daily, for a continuous period of 40 days, being the consumption (feed and water/juice) recorded from leftovers checked in each following day.

Behavioral analyses: After the period of 40 days of treatment, the animals were submitted to the Open field and Elevated Plus Maze models.

For the first test, a wooden box (1m x 1m x 20cm) with a white background, divided into quadrangles (10cm x 10cm) was used according to the methodology described by Barbosa[17]

e Vianna.[18] The exploratory behavior of each animal was observed individually for a period of 5 minutes, evaluating the time (in seconds) of locomotion (movement). The time of locomotion was considered from the time at which the animal moved its hind legs, and its vertical activity was also evaluated, i.e., the number of "rearings": the activity in which the animal seeks to stand on its hind legs.

The Elevated Plus Maze (EPM) is a validated method to explore the neurobiological bases of anxiety. The device consists of two open and two closed arms in the form of a Greek cross, which are connected by a central area. The device must be at a height of 45 cm from the ground. The test presents the animal with the conflict between its natural tendency to explore a new environment and its reluctance to expose itself in open territory, where the risks of falls and predators are higher. As a result, the less anxious animals tend to explore the open arms more.[19, 20]

The animals were placed in the central area facing one of the closed arms and the number of entries (frequency) and the dwell time (seconds) in each of the arms (open/closed) and in the central area were measured. Each animal was subjected to a single session of five minutes in the apparatus.

Visceral fat: In the 41º day of the experimental protocol, the rats were euthanized with a lethal intraperitoneal injection of thiopental (200 mg Kg^{-1}). After the euthanasia process, the visceral fat was removed from abdominal region it was weighed.

Statistical Analysis: The variables were presented as means and standard deviations. For the analysis of the elevated plus maze data, the experimental design was completely randomized in a 3 x 3 factorial scheme (treatment x location). The data was submitted to analysis of variance (ANOVA) and Tukey's Test, using the SISVAR software and a significance level of 5% ($p < 0.05$).[21]

RESULTS AND DISCUSSION

Feed and water/juice intake: The daily feed intake by the animals ranged between 11.37g and 12.48g and there was no statistically significant difference between the treated and control groups (Table 1). The mean volume of consumed water or juices from the pulp and leaves from *Garcinia cochinchinensis* Choisy also didn't differ among the experiment animals during the 40 days of treatment.

Table. 1: Mean daily feed and water/juice intake by the animals (mean ± standard deviation).

Consumption	Control (G1)	Pulp juice (G2)	Leaf juice (G3)
Water/juice mL day $^{-1}$	17.37 ± 6.75*	18.92 ± 7.04	20.63 ± 7.20
Feed mL day $^{-1}$	12.48 ± 3.44	11.37 ± 3.50	11.84 ± 3.51

*No significant difference was observed between the groups (ANOVA)

Similarly, no statistically significant difference was observed in a study by Sripradha et al.[22] regarding the consumption of feed between groups treated with an ethanolic extract of *Garcinia cambogia* and the control group during the treatment.

Visceral Fat: The weight of the visceral fat decreased significantly in animals treated with the juices from the pulp and leaves when compared to the control group (Figure 1).

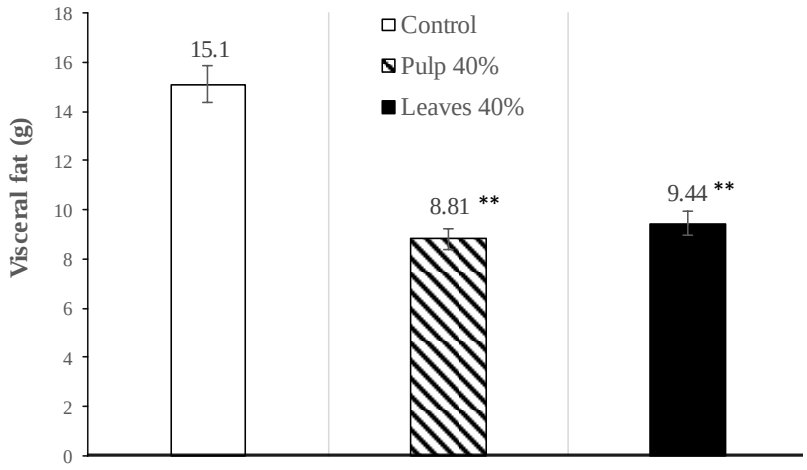

Figure. 1. Visceral fat weight (g) of the animals of the treated groups and control group.
(**) $p < 0.05$, compared to the control group (ANOVA)

Similarly, the consumption of *Garcinia cambogia* effectively reduced visceral fat in a study by Kim et al.[23] with animal models induced to obesity for a period of 12 weeks. The same fruit showed an effective reduction in total, subcutaneous and visceral fat in men and women between 20 and 65 years of age receiving its extract in a study by Hayamizu et al.[24]

The results of this study are relevant since visceral fat, also known as abdominal fat, is directly related to significant metabolic abnormalities in the body.

Visceral fat tissue can synthesize and secrete substances called adipokines, which have a pro-inflammatory nature, including interleukins (IL-1, IL-6, IL-8), tumor necrosis factor-alpha (TNF- α), leptin and resistin, involved in the physiopathogenesis of insulin resistance (IR) and atherogenesis.[25-27]

A reduction in visceral fat is therefore linked with positive health responses, since it contributes to a reduction in the inflammatory process related to obesity, and prevents chronic diseases as a result, such as cardiovascular disorders and mortality in obese subjects.[28-30]

Behavioral analyses: The administration of the juices from the yellow mangosteen pulp and leaves did not interfere significantly in the time spent by the animals in different locations of the elevated plus maze (EPM) ($p>0.05$). In general, however, the dwell time of the animals was significantly influenced by the location in the model ($p<0.01$) (Table 2), since the rats stayed for longer periods of time in the closed environment (165.1), differing statistically from the open (79.2) and central (58.8) environments, which didn't differ among themselves.

In EPM models, animals usually prefer to stay longer in the closed arms due to the aversion and fear of open spaces. According to Lister[31], a rat's order of preference is: closed > center > open arm. Drugs that induce animals to increase the exploitation of open environments are considered to be anti-anxiety agents. The pulp and leaf juices showed no anti-anxiety effect on the animals in the study's period of 40 days, therefore, making them not want to leave the protected environment.

Table. 2: Time and frequency means and standard deviations of the rats in the elevated plus maze model.

Attribute	Location	Treatment			Mean
		Control	Pulp juice	Leaf juice	
Time	Open	90.3 ± 47.2	76.3 ± 32.3	70.7 ± 28.9	79.2 b
	Center	59.6 ± 23.2	59.9 ± 23.4	56.8 ± 26.7	58.8 b
	Closed	150.1 ± 56.7	172.8 ± 55.5	172.5 ± 44.2	165.1 a
Frequency	Open	6.75 ± 3.6	5.87 ± 4.0	5.50 ± 1.9	6.04 b
	Center	12.75 ± 5.3	14.87 ± 5.7	12.50 ± 4.3	13.37 a
	Closed	9.37 ± 1.4	9.62 ± 3.7	7.25 ± 3.5	8.75 b

Means followed by the same capital letter in the row or small case letter in the column don't differ significantly among themselves at 5% of probability according to Tukey's test.

There was no statistically significant difference regarding the frequency of entry in the different areas of the model when the treatments were considered ($p>0.05$). However, it was observed that the frequency was also influenced significantly by the location ($p<0.01$). The frequency of rat visits was greater in the central area of the plus maze with a mean of 13.37 times, differing statistically from the frequency of the open (6.04) and closed (8.75) spaces, which did not differ among themselves.

According to Barbosa[17], the animals' frequency of entry in the central area of the device shows some measure of decision-making power and entries in the open and closed arm show an anti-anxiety effect and motor activity, respectively.

Despite the apparent simplicity of a test situation, many factors influence the aversion to open arms. Some are linked to the experimental procedure, such as a single or multiple exposures to the maze, time of day of the test, and the brightness of the experimental room.[32-35] The literature reports an increased avoidance of the open arms when the test room is very bright, and an increase in the percentage of entries and time spent in the open arms when animals are tested in the dark.[36-37] As such, the brightness on the test may have influenced the behavior of the animals in this study, since the EPM test was only performed in a bright environment.
Table 3 shows that there was no statistically significant difference regarding the roaming behavior of animals in the open field test, although the animals fed with the leaf juice from the yellow mangosteen moved 63.17% less than the control group. Some authors consider that an increased roaming of the animal indicates a reduction in stress factors.[38]

Table. 3: Movement and rearing rates of rats in the Open Field Model.

Treatments	Open field	
	Movement	Rearing
Control	140.4 ± 46.4 a*	21.4 ± 5.4 a
Mangosteen pulp juice	120.4 ± 39.9 a	14.6 ± 4.3 a
Mangosteen leaf juice	88.7 ± 39.8 a	13.9 ± 4.5 a

*Means followed by the same letter in the column do not differ among themselves according to Tukey's test at 5% level of significance.

Many plants have been studied for their potential behavioral and anti-anxiety effect in animal models. Mice treated orally with water-ethanol extracts of the burrito (*Aloysia polystachya* Griseb.) didn't alter their locomotor activity or motor coordination, but this plant did influence their behavior in the elevated plus maze, increasing the entry frequency and time spent in the open arms.[39] In a study by Rabbani et al.[40], the hydroalcoholic extract of *S. lavandulifolia* increased the number of entries and the time spent in the open arms and decreased the number of entries and time spent in the closed arms in animals subjected to EPM.

Some species of Garcinia have also been used in behavioral tests described in the literature. In a study conducted by George et al.[41], extracts from the bark and roots of *Garcina gummi*

gutta, administered in high doses (400 mg kg^{-1} weight), showed an anti-anxiety effect in animals, since it significantly increased the dwell time and the number of entries in the open arms of EPM models. The husks of *G. indica* had anti-anxiety and antidepressant effects in a study by Dhamija et al.[42], since the animals used in the experiment showed a higher frequency of entry and greater permanence in the open arms of the EPM model, but there was no significant difference in the locomotor activity of the animals in this experiment.

Garcinia cambogia has been used to influence the feeding behavior of experimental models, since its main chemical component, chromiumchelate acid, has an anorexigenic effect and increases the release of serotonin and its availability in the cerebral cortex.[43.44] The leaves of the bacupari, *G. brasiliensis*, were used in a study by Santa-Cecília et al.[45] and showed an antinociceptive effect in male Wistar rats and mice.

Other species of Garcinia has also been tested in behavioral studies, such as the effects of the *G. kola* seeds on cognitive development[46] and sexual behavior in experimental models[47, 48], the effects of *G. cambogia* on satiety in humans[49], the effects of *G. indica* on the locomotion and postural balance in animal models with Parkinson disease[50] and the protective effects of *G. kola* on the exploration activity in animals subjected to oxidative stress in the prefrontal cortex.[51]

CONCLUSION

The pulp and leaf juices of the yellow mangosteen did not interfere in the feed consumption of the animals, but significantly reduced the weight of the visceral fat after 40 days of treatment. In the dosages used, the juices didn't have an effect on the behavior of the animals in models in open field and elevated plus maze models, and the results can be used as reference for future works on this exotic fruit.

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