Curcuma longa on the Metabolic Profile and Atherogenic Index of Rats Fed with a Hyper Caloric Diet

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Abstract: The chronic diseases such as diabetes mellitus, metabolic syndrome and cardiovascular diseases have reached epidemic proportions in developed and developing countries. The high costs of the allopathic medicines represent a growing demand for non-allopathic alternatives. *Curcuma longa* is usually used as a spice in curries and as a dietary pigment and is considered a medicinal plant due important properties, with anti-inflammatory, anti-oxidant, anti-bacterial and anti-tumor action. The aim of this work was to evaluate the effects of *Curcuma longa* on the metabolic profile of Wistar rats treated with hyper caloric diet. Forty eight male rats were divided randomly into 4 groups (n=12) and treated for 40 days: G1 that received water (Control Group); G2 that received condensed milk solution *ad libitum*; G3 that received *C. longa* by gavage route and G4 that received condensed milk solution *ad libitum* and *C. longa* by gavage route. No significant differences for body weight and cholesterol were observed among the groups. Visceral fat, triglycerides and glycaemia were higher in the groups treated with condensed milk but did not differ when comparing G1 with G3 and G2 with G4. Analyzing our results it is possible to say that *C. longa* may not be efficient to promote benefits in lipid and glycemic profile as well as in the body weight and visceral fat of animals treated with hyper caloric diet.

Keywords: *Curcuma longa*, glycaemia, cholesterol, triglycerides, HDL-c.

INTRODUCTION

In recent years the chronic diseases have reached epidemic proportions in developed and developing countries. High blood pressure, insulin resistance, dyslipidemia and weight gain are the main risk factors for developing chronic diseases such as diabetes mellitus, metabolic syndrome and cardiovascular diseases. These diseases have serious repercussions because they can interfere in the ability to work and may be related to high morbidity and mortality. The combination of these factors and the high costs of the allopathic drugs represent a growing demand for non-allopathic alternatives [1-4].

There is a long historical use of spices for medicinal purposes, and several authors are showing their potential in health. The benefits are related to a possible role in prevention or as adjuvant in the treatment of chronic diseases [5,6].

Curcuma longa is usually used as spice in curries, food additive and as a dietary pigment. It is a rhizomatous perennial herbaceous plant belonging to Zingiberaceae family, native to tropical South Asia, where it was harvested for over 5,000 years. It bears many rhizomes on its root system which are the source of its culinary spice known as turmeric and its medicinal extract called curcumin. It is considered a medicinal plant due to important properties, with anti-inflammatory, anti-oxidant, anti-bacterial and anti-tumor action. In Indian and Chinese traditional medicine it is used for prevention and treatment of eye infections, burns and bruises, respiratory discomfort, digestive disorders and cancer [7-12].

Turmeric possesses three major curcuminoids coumponds called curcumin, demethoxycurcumin, and bisdemethoxycurcumin. The first one is the most abundant of the three and it is known chemically as diferuloylmethane or 1,7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-dione. Curcumin is obtained by solvent extraction of turmeric that is, the ground rhizomes of *C. longa* [13, 14].

OBJECTIVE

The aim of this work was to evaluate the effects of *Curcuma longa* on the metabolic profile of Wistar rats treated with hyper caloric diet.

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MATERIALS AND METHODS

Ethical Principles

This work was approved by the Animal Research Ethics Committee of the University of Marilia (UNIMAR) with registration number 48. 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).

Preparation of Aqueous Extracts of *C. longa*

The extracts of *C. longa* were prepared at a concentration of 200mg/mL (powder/water). The extract was prepared immediately before its use. The powder of the plant was obtained in local markets at Marilia city.

Preparation of the Solution of Condensed Milk

Condensed milk is a very popular product used in Brazil to the preparation of candies and cakes. Its formulation includes high percentage of sugar and fats (in 20 g it contains: 12 g of carbohydrates, 1,7g of fat and 1,4 g of protein; 69 Kilo calories or 290 KJ). The solution was used to the animals of G2 and G4 groups and was prepared in a 1:1 proportion (condensed milk/water) every day immediately before its offer to the animals. Animals that received this solution instead of water were considered receiving a hyper caloric diet because the amount of carbohydrates is higher than the group that received only water and rat food.

Experimental Model

Forty eight male Wistar rats weighing approximately 250g were used in our study. They were kept in the vivarium at UNIMAR (University of Marília) under a dark/light cycle of 12 hours, room temperature of 22 ± 2°C, and relative air humidity of 60 ± 5%. After a period of seven days of acclimation to the laboratory, the animals were divided randomly into 4 groups (n=12) treated for 40 days, as follows (animals of all groups received food *ad libitum* during the treatment period):

G1 received water and food *ad libitum* (Control Group);

G2 received condensed milk solution and food, both *ad libitum*;

G3 received *C. longa* by gavage route and water and food *ad libitum*;

G4 received condensed milk solution and food, both *ad libitum,* and *C. longa* by gavage route.

Administration of *C. longa*

The administration of the plant extracts was done twice a day (intragastric route): in the early morning and late afternoon and the treatment lasted for 40 days. The administered doses were 200mg/mL of aqueous extract of the plant for G3 and G4 and saline solution for G1 and G2. Animals received 1 mL of the plant extract.

Collection of Blood Samples and Determination of the Biochemical Profile, Atherogenic Index (AI) and Protection Index (PI)

After treating animals for 40 days, they were anesthetized with Thiopental (sodium pentobarbital) until complete sedation, after which blood samples were drawn to determine their biochemical profile: total cholesterol, LDL-c, HDL-c, triglycerides, glycaemia and hepatic transaminases (ALT: aspartate transaminase and AST: alanine aminotransferase). The glucose and lipid levels were measured in mg/dL and the enzymes in U/L and the results were interpreted according to the ADA [15].

Atherogenic Index (AI) and Protection Index (PI) were calculated after Schulpis, Karikas [16] and also used by Munshi, Joshi, Rane [17]: AI = (Total cholesterol – HDL-c)/HDL-c.

Statistical Analysis

The results were expressed as mean ± S.E.M. and evaluated by analysis of variance (ANOVA) complemented with Tukey test. The level of significance was set at $p < 0.05$.

RESULTS

Figure **1** shows that there are no significant differences for body weight in the different groups.

Significant differences were observed between G1 and G2, G1 and G3, G2 and G3 and G3 and G4 when comparing visceral fat. These results show that this type of diet increases visceral fat in the groups treated with condensed milk (Figure **2**).

Glycaemia showed significant differences between G1 and G2 and between G2 and G3, showing that the hyper caloric diet increases plasmatic glucose levels and the treatment with the plant (G4) was not enough to prevent hyperglycemia (Figure **3**). However, lower values of glucose in the blood were observed in the group that received hyper caloric diet and treatment with *C. longa.*

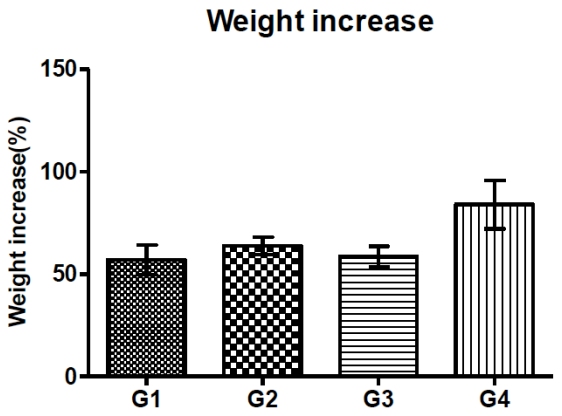

Figure 1: Values of weight (mean ± S.E.M.) in G1 (control group), G2 (condensed milk), G3 (*C. longa*) and G4 (condensed milk and *C. longa*). No significant differences were found between the groups.

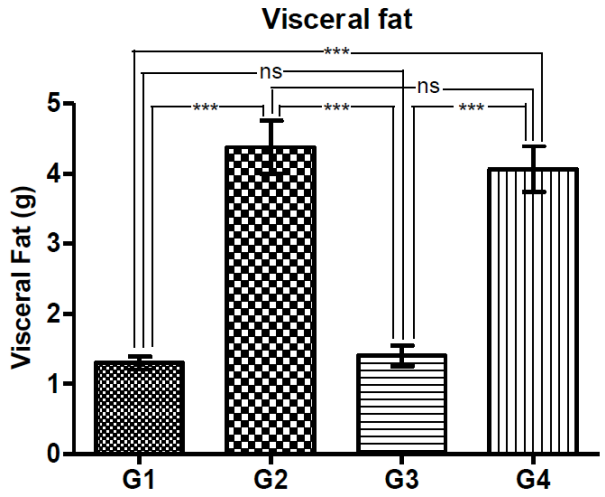

Figure 2: Values of visceral fat weight (mean ± S.E.M.) in G1 (control group), G2 (condensed milk), G3 (*C. longa*) and G4 (condensed milk and *C. longa*). ns – not significant; ***p<0.0001.

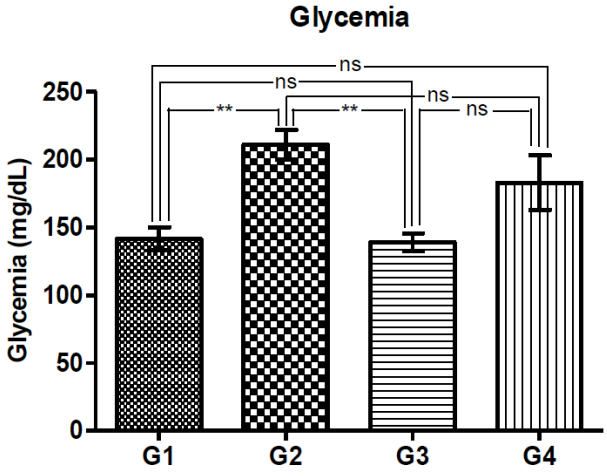

Figure 3: Values of glycaemia (mean ± S.E.M.) in G1 (control group), G2 (condensed milk), G3 (*C. longa*) and G4 (condensed milk and C. longa). ns – not significant; **p<0.001.

Figure **4** shows that there are no significant differences in cholesterol levels in the different groups, even in those treated with hyper caloric diet.

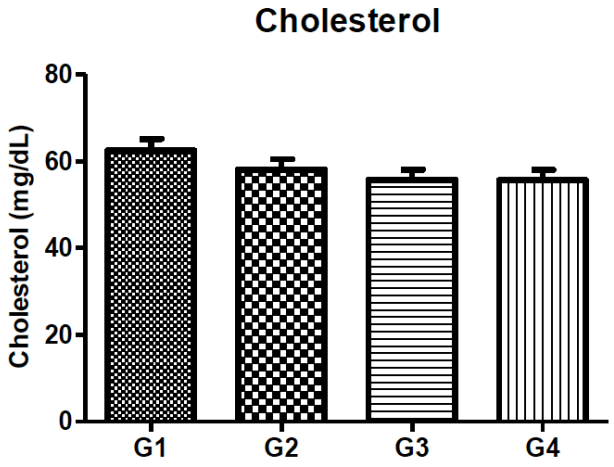

Figure 4: Values of cholesterol total (mean±S.E.M.) in G1 (control group), G2 (condensed milk), G3 (*C. longa*) and G4 (condensed milk and *C. longa*). No significant differences were found between the groups.

The levels of HDL-c were significantly different when comparing groups G2 and G3 showing that *C. longa* where not efficient to increase this lipoprotein (Figure **5**).

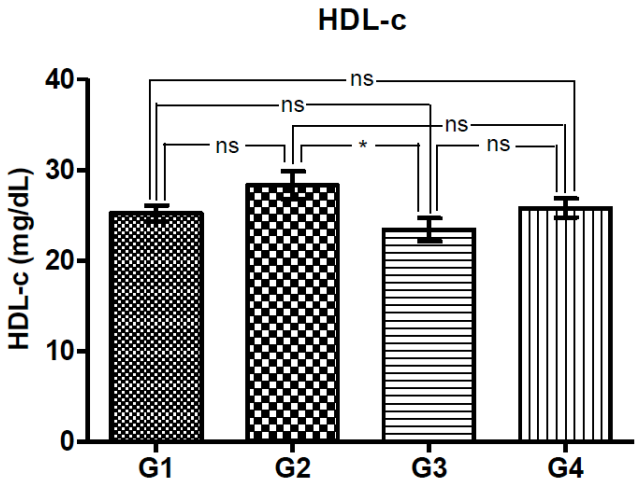

Figure 5: Values of HDL-c (mean ± S.E.M.) in G1 (control group), G2 (condensed milk), G3 (*C. longa*) and G4 (condensed milk and *C. longa*). ns – not significant; *p<0.05.

Triglycerides showed significant differences between: G1 and G2; G1 and G4; G2 and G3; G3 and G4. The hyper caloric diet increases the levels of this lipid and the treatment with the plant is not enough to prevent alterations in animals fed with a hyper caloric diet (Figure **6**) 4 when comparing to G3.

The hepatic enzymes AST were significantly different between G1 and G2; G1 and G3, G1 and G4,

G2 and G4 and between G3 and G4 (Figure **7**). Higher levels were observed in the control group.

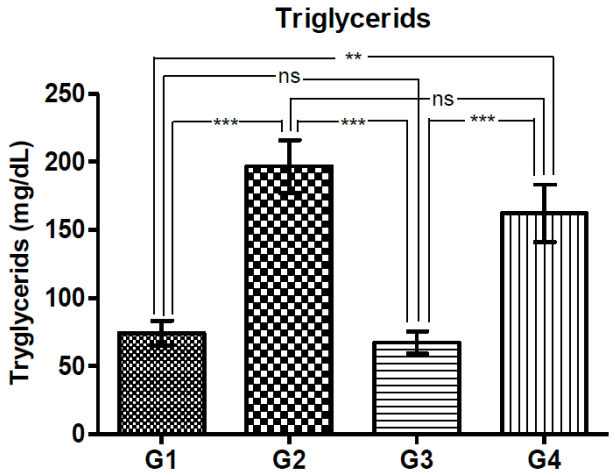

Figure 6: Values of triglycerides (mean ± S.E.M.) in G1 (control group), G2 (condensed milk), G3 (*C. longa*) and G4 (condensed milk and *C. longa*). ns – not significant; **p<0.001; ***p<0.0001.

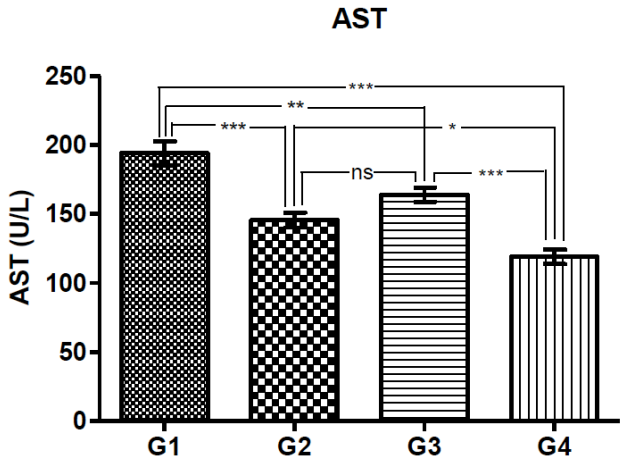

Figure 7: Values of AST (mean ± S.E.M.) in G1 (control group), G2 (condensed milk), G3 (*C. longa*) and G4 (condensed milk and *C. longa*). ns – not significant; *p<0.05; **p<0.001; ***p<0.0001.

AST were significantly different between G1 and G2; G1 and G3; G1 and G4; G2 and G3; G3 and G4 (Figure **8**). As in ALT levels, the higher values were found in the control group.

The AI were calculated among the groups and we observed that *C. longa* reduces the value in animals that received the hyper caloric diet and were treated with with the plant (Table **1**).

When calculating the percentage of cardiovascular protection (PI), we found that C. longa reduces the risk of cardiovascular disease by 13% when the animals consume the hyper caloric diet.

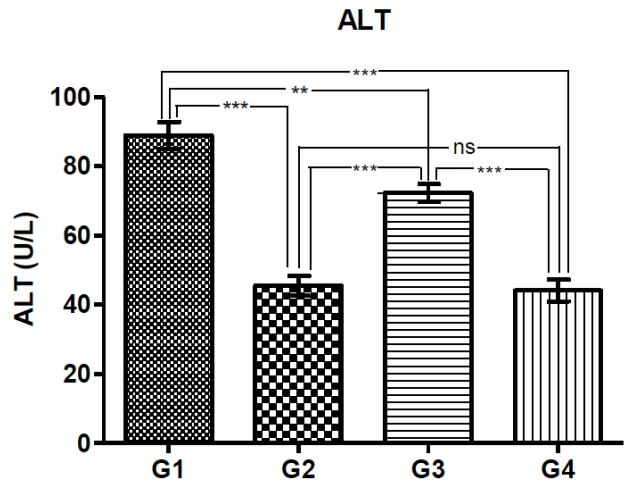

Figure 8: Values of ALT (mean ± S.E.M.) in G1 (control group), G2 (condensed milk), G3 (*C. longa*) and G4 (condensed milk and *C. longa*). ns – not significant; **p<0.001; ***p<0.0001.

Table 1: Atherogenic Index (AI) in Groups G1 (Control Group), G2 (Condensed Milk), G3 (*C. longa*) and G4 (Condensed Milk and *C. longa*).

	G1	G2	G3	G4
AI	1,47	1,87	1,43	1,55

DISCUSSION

C. longa is widely used in traditional medicine and several authors have shown importance in the treatment and prevention of many diseases as anti-oxidant, anti-inflammatory, anti-carcinogenic, anti-thrombotic, and cardiovascular protective effects. It possesses curcumin (diferuloylmethane) which is a yellow-colored bioactive constituent (polyphenol) responsible for the yellow color of the curry spice turmeric [18-20].

Our results show that visceral fat is increased in both groups of animals treated with hyper caloric diet and the use of *C. longa* improves this parameter but not significantly. The accumulation of lipids in adipocyte leads to obesity that is directly related to the metabolic syndrome, diabetes and cardiovascular diseases. Um *et al.* [21] showed that curcumim reduces the body-weight and adipose tissue weight of mice treated with a high fed diet as well reduces the levels of total cholesterol, fasting glucose and insulin. It also has the ability to activate AMP-activated protein kinase (AMPK) and increase the gene expression of PPARα (peroxisome proliferator-activated receptor α) and decreased the activity of Acetyl-CoA carboxylase 1 and fatty acid synthase. They also found that it protects

against the development of hepatic steatosis by reducing hepatic fat accumulation. Other study show that gambigyeongsinhwan, a curcuminoid compound, inhibits lipid accumulation and mRNA levels of adipocyte-specific genes as peroxisome proliferator-activated receptor γ (PPAR γ) and activating adipose PPARα. These conditions lead to the decrease of body weight gain, adipose tissue mass, and visceral adipocyte size in rats [22].

Our results do not exhibit positive effects of the plant in the levels of total cholesterol and in the glycaemia, however decreased levels of glucose are found in the group treated with hyper caloric diet and *C. longa.* Similar results are found to the triglycerides levels. Tranchida *et al.* [23] also studied the use of this plant in rats fed with a high level of fructose and saturated fatty acid diet and found that *C. longa* did not prevent the observed increase in glycaemia, triglycerides, cholesterol and insulin levels. Lee *et al.* [23] did not found differences in glycaemia between users of turmeric. Contradicting these results, authors have shown that the anti-oxidant properties of curcumin may attenuate cardiotoxicity and may show protection against diabetic cardiovascular complications. Moreover, anti-diabetic effects of this component may occur due to its ability to reduce oxidative stress and inflammation. Associated to that, it may reduce blood glucose, and the levels of glycosylated hemoglobin in diabetic rats as well as advanced glycation, which takes to the reducing of production of advanced glycation end products that are related to the complications of diabetes. It also initiates a down-regulation of nuclear factor-kappa B and show benefits on the diabetes-induced endothelial dysfunction [18, 25-27]. There are evidences that curcumim may be related to the reduction of cholesterol levels protecting from the pathological changes observed in the atherosclerosis. Li *et al.* [26] evaluated the effects of curcumim in animals treated with high-fat diet and obtained significant reduction in cholesterol, LDL-c, triglycerides and increase in HDL-c levels [19, 27]. Lin *et al.* [20] showed a possible mechanism for understanding the anti-atherogenic effects of curcumin on attenuating the progression of atherosclerosis. They found that curcumin increases the expression of ATP-binding cassette transporter 1, promoting cholesterol efflux from macrophage-derived foam cells, reducing cellular cholesterol levels and attenuating the progression of atherosclerosis [20, 28]

Curcuminoids also were found to improve lipid profile in patients with metabolic syndrome after eight weeks of treatment [29]. Shin *et al.* [30] found that *C. longa* improves lipid profile, Atherogenic Index, reactive oxygen species and inflammatory cytokines (tumor necrosis factor-α, and interlukin-6) in mice. Despite our results did not show improvement in the lipid profile, there was a reduction of AI in the animals treated with *C. longa.* Besides we also observed a PI of 13%.

Our results show that the lowest values of the hepatic enzymes (AST and ALT) are in G4 and any other group showed values higher than control group. This leads to suppose that *C. longa* does not cause damages to the liver in the amount used in this experimental model. Nevertheless, Al-Rubaei, Mohammad, Ali [31] found significant increase in levels of ALT and AST in animals treated with curcumim. Kim *et al.* [32] studied the effects of fermented *C. longa* in rats under induced oxidative stress and verified it may protect liver against increase of AST and ALT under this condition.

Analyzing our results we may conclude that *C. longa* obtained from local markets may not be efficient to promote the benefits that several authors have shown in lipid and glycemic profile as well as in the body weight. One possibility to explain these data is that dietary curcumin is only poorly absorbed by the digestive tract what leads to its excretion [33]. This could confound the reasons of how dietary curcumin shows benefits in glycaemia, dyslipidemia and other diseases in some studies and no effects in others.

AUTHORS' CONTRIBUTIONS

ELG, ACA and SMB carried out the conception and design of the study, treated the animals and drafted the manuscript.

PCSB and DPC performed the statistical analysis.

MSSS prepared the extracts of the plants and treated the animals.

CGM, SSB and EPS performed the laboratorial analysis.

All authors read and approved the final manuscript.

CONFLICT OF INTERESTS

Authors declare no conflict of interests.

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