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Liver damage protection with epigallocatechin-3-gallate use (green tea) in wistar rats submitted to westernized diet: comparative study with sibutramine

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Abstract

Introduction: Obesity and its comorbidities are assuming alarming proportions in Brazil and worldwide. Hepatic steatosis, greatly present in many patients, could culminate in severe hepatic dysfunction. Objective: To evaluate the power of weight loss and protection against hepatic steatosis and steatohepatitis hepatitis Epigallocatechin-3-gallate (EGCG), the most important catechin of Camellia sinensis (green tea), in rats with obesity and compare it to Sibutramine. Methods: Experimental and comparative study, in which were used 57 pups from 13 Wistar female rats with different nutritional conditions. Male pups before 21 days were divided in control group (fed chow diet and standard offspring with 9 rats) or westernized group with reduced offspring of 3 rats (obese group. OG). After weaning, the male pups were fed either a standard laboratory chow or westernized diet ad libitum until the end of the fourth month. For the control group, a saline solution (NaCL 0.9%) was administered by gavage for 8 days and the group was called CSAL group. The WG received westernized diet for four months, starting on day 12 of lactation, and was divided into 3 subgroups, which received the following treatment: WSAL with saline (2 ml 0.9% NaCl); OSIB with sibutramine (7.5 mg / kg) and OEGCG with EGCG (50mg / kg / day) for the same period. Results: It was demonstrated that only the groups treated with EGCG and sibutramine showed significant reduction in food intake and body weight with percentage decline of 68% for the food intake and 16% for body weight (EGCG) and 62% for the food intake and 12% for body weight for OSIB. Histological evaluations showed no toxicity in the group with drugs. In animals that made use of EGCG, it has not been found nor pattern of hepatic steatosis nor inflammatory infiltrate, differing, thus, from other obese groups. Conclusion: The use of EGCG was effective in weight loss and promoted regression or fatty infiltration protection and liver inflammation.

Keywords: Camellia sinensis. Catechins. fat diet. Hepatic steatosis. Occidentalized diet.

Introduction

The prevalence of obesity has increased considerably, leading to serious challenges to public health (1). Studies point to frequent concomitant with hepatic steatosis and its consequences (2). Its pathophysiology is not well understood, but accumulation of triglycerides in hepatic cells, insulin resistance and mitochondrial oxidative stress (2) are described. Currently, there are few drugs to control obesity, given that drugs derived from amphetamine (Fenproporex, afepramona and Mazindol) had their trading suspended by the National Health Surveillance Agency (3). Camellia sinensis, with large amounts of polyphenols, especially epigallocatechin-3-gallate (EGCG), has potent antioxidant activity, with possible effects of weight loss and regression of their comorbidities (4). Our purpose was to evaluate the anti-obesity action and activity in hepatic steatosis vegetable from its main catechin, EGCG compared to sibutramine.

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Material and Methods

57 male Wistar pups were used, coming from the UFPE Nutrition Departement. Throughout the study, the rats were housed in a temperature-controlled (22 ± 1°C), with reversed light / dark cycle of 12-hour. After the third day of life, offspring composed of 9 and 3 rats constituted the following groups: control group (CG) and obese (GO), respectively. After the 21th day of life, the control group became part of the saline control group (CSAL), and received standard chow diet (Presence®) throughout the study, and 0.9% NaCl after the 4th month. The GO group was divided into three other subgroups: OSAL, OSIB and OEGCG, which received westernized diet based from Cavalcante, et al, modified, RIBEIRO, et al. (2016) (5-6) and treatment after the 4th month: OSAL, 2 ml 0.9% NaCl; OSIB, 7.5 mg / kg sibutramine (Aché Laboratório Farmacêuticos S. A.®) and OEGCG, 50mg / kg EGCG (Aktin Laboratory Chemicals, China®) by gavage once a day for 8 days. The animals were weighed weekly after the 21st day

and daily during the 8 days of treatment. Food consumption was measured daily after weaning and 8 days of drug use. The rats were anesthetized with xilazina® associated with Ketamina®, sacrificed and then were taken the organs for histopathology. A statistical analysis was performed according to ANOVA testing, Bonferroni test and "t" student and used Graphpad Prism 6.0 seconds. All results were considered significant at p <0.05.

Results

After weaning, significant weight gain were observed in the westernized diet group reduced offspring (OSAL, OSIB and OEGCG). The weight and daily food consumption during treatment showed significant reduction only in the treated groups and OSIB OEGCG, with a percentage decrease of 12% / 62% and 16% / 68%, respectively. Histopathology revealed severe hepatic steatosis, with strong presence of lymphocytic niches in OSAL and OSIB groups. However, OEGCG group showed resemblance to the slim control with insipient hepatic steatosis (figure 1).

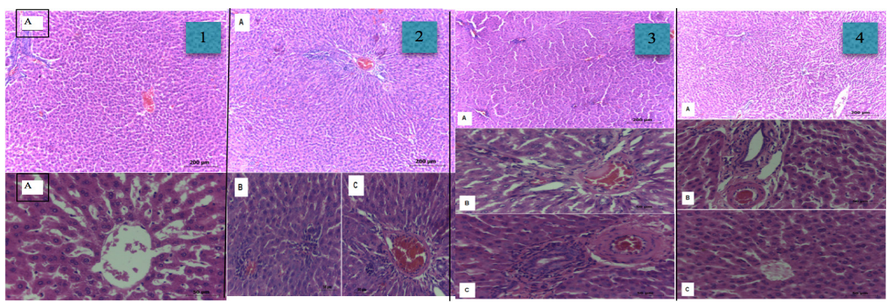

Figure 1 – Photomicrographs of liver portions of animals from CSAL group (photo 1), OSAL (photo 2), OSIB (photo 3) and OEGCG (photo 4), with preparations in hematoxylin-eosin. Observe in B and C (photo 2 and 3) evident hepatic steatosis in the OSAL and OSIB group, as well as increased amount of inflammatory infiltrate. Col HE Photo 4, watch absence of steatosis and inflammatory infiltrate.

Discussion and Conclusion

Both, sibutramine and EGCG were able to reduce body weight and food consumption. Our findings confirm previous study using EGCG at a dose of 15mg of 2 to 7 days by the intraperitoneal route in male rats, observing weight loss of 50% and consumption of 60%, with return to the previous condition of the suspension of the drug (7). The action of EGCG in obesity could be associated with reduced lipogenesis and possible mitotic modulation of MAP kinase protein, besides the reduction of preadipocyte proliferation (8-9). In addition, it may be involved in inhibiting COMIT complex, which promotes the stimulation of adrenaline in adipocytes with increased thermogenesis (10). EGCG can also promote various digestive enzymes lock (11) and central leptin receptors (12). As for histological studies, we observed clear pattern of steatosis in the EGCG group and absence of inflammation. The EGCG may have promoted reduction of liver damage caused by accumulation of fat, due to its antioxidant power, which corroborates the findings of Schmitz et al. (13). Those authors showed hepatoprotective activity of the alcoholic extract of Camellia sinensis in rat livers damaged by Diethylnitrosamine substance (DNT) and its important action mainly preventively in liver injury. We conclude that EGCG was able to decrease food intake and weight of obese rats with the same intensity as sibutramine. The use of the substance has led to the prevention or treatment of hepatic steatosis and steatohepatitis hepatitis produced by the occidentalized diet. Study suggests strong drug action in combating obesity and visceral fat.

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