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## THE POTENTIAL ROLE OF *HYPOTHALAMUS* (HOMEOPATHY) IN THE TREATMENT OF OBESITY

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### ABSTRACT

Obesity has reached alarming proportions around the world, and it is responsible for an important burden for the health systems and increase of deaths both in developed and developing countries. Homeopathy has been used to treat several diseases, and this study aimed to evaluate the effect of *Hypothalamus* on the metabolic parameters of animals fed a hypercaloric diet. Thirty animals were treated with a hypercaloric diet and water *ad libitum* for 50 days and then, were divided into three groups (n=10); G1: treated with hypercaloric diet and water mixed with *Hypothalamus* 30CH *ad libitum*; G2: treated with hypercaloric diet and water mixed with *Hypothalamus* 15CH *ad libitum*; G3: Control group that received hypercaloric diet and water *ad libitum*. Our results show that there was no interference of *Hypothalamus* in the initial and final weight, in the percentage of weight gain, Lee's index, glycemia, and total cholesterol, but there was a reduction in the thoracic and abdominal circumference as well as in the abdominal fat in the treated groups. Increase in the levels of triglycerides was also observed. We may conclude that *Hypothalamus* may interfere in some metabolic parameters but other studies should be performed with the aim of establishing the doses and period of administration.

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### INTRODUCTION

Obesity has reached alarming proportions in many parts of the world, and it is responsible for an important burden for the health systems both in developed and developing countries. The modifications in the lifestyle include reduction in physical activity and changes in diet that may lead to overweight and obesity that affect nearly 50% of the adult population and nearly 30% of the child population. For these reasons, it is considered by the World Health Organization as a global epidemic. In Brazil, approximately 17.1% of the population may be classified as obese (Krishna *et al.*, 2017; Brasil, 2014; Ruiz *et al.*, 2015; WHO, 2017). Increased Body Mass Index (BMI) is a risk factor for insulin resistance, diabetes, hypertension, hypercholesterolemia, metabolic syndrome, cardiovascular diseases, and cancer that may be consequences

of obesity and can contribute to the increase in the morbidity and mortality of the population. Many authors have shown that there are gene and environment interactions associated with this pathology besides the impact of food intake, metabolism, fat mass accumulation and body composition (McCuen-Wurst *et al.*, 2017; Wahab *et al.*, 2017). The nutritional intervention, that is a major challenge in obesity studies, addresses modifications in the feeding behavior and metabolic and anthropometric outcomes such as body mass composition, insulin resistance and biomarkers of inflammation resulting from fat mass accumulation (Toro-Martin *et al.*, 2017; Agrawal, Kern, Nikolajczyk, 2017). The modifications in the nutritional habits to treat overweight and obesity are not always efficient and several studies have shown the role of different drugs that may help in the approach of this pathology. On the other hand, the available drugs are costs and related to

several side-effects that reduce the efficiency of the therapeutic conduct. For these reasons, many alternatives have been studied to help in the weight loss as shown with the use of medicinal plants and bioactive compounds (Kandouliet *al.*, 2017; Freitas Junior, de Almeida, 2017; Mopuri, Islam, 2017; Choi *et al.*, 2017). Another alternative approach that has been used since ancient times for treating many health conditions is the Homeopathy. This kind of therapy is based on the *Principle of Similars* that claims that a substance related to the cause of symptoms of illness may be used to treat similar symptoms in an ill individual (Vilhena, Castilho, 2016). As the incidence of obesity and related pathologies is increasing in the world population and the existing treatments are often high cost and not effective, the objective of this study was to evaluate the effect of and Homeopathic formulation on the metabolic parameters of animals fed a hypercaloric diet.

## MATERIALS AND METHODS

### Ethical principles

Our research was approved by the Animal Research Ethics Committee of the Medical School of Marilia (UNIMAR), Marilia – São Paulo, Brazil, and the animals were cared for in accordance with the recommendations of the Canadian Council's "Guide for the care and use of experimental animals".

### Group of Animals

Thirty female Wistar rats, weighing 83 to 100g, were obtained from the Animal Experimentation Center (CEMA) / University of Marilia (UNIMAR), Marilia – São Paulo, Brazil. Seven days before initializing the experimental protocol, all the females were acclimated to the laboratory conditions and were housed in plastic boxes (40x30x17cm) at controlled room temperature (20°C to 25°C) and light/dark cycle of 12 hours (five animals per box).

The animals of the three groups were treated with a hypercaloric diet and water *ad libitum* for 50 days and then, were divided into three groups (n=10) G1, G2 and G3 according to the following:

- G1:** Group treated with hypercaloric diet and water mixed with *Hypothalamus* 30 CH *ad libitum* for 30 days;
- G2:** Group treated with hypercaloric diet and water mixed with *Hypothalamus* 15 CH *ad libitum* for 30 days;
- G3:** Control group that received hypercaloric diet and water *ad libitum*;

*Hypothalamus* is a Homeopathic product that was obtained from local Pharmacy in the city of Marilia – São Paulo – Brazil. The administration was performed *ad libitum* for 30 days. For the preparation of this solution, we mixed 15 drops of *Hypothalamus* in 500mL of water. The weight of each animal and the consumption (average per box) of water and feed were evaluated three times per week. The percentage and specific rate of weight gain and Lee index were calculated. The thorax and abdominal circumferences were also performed at the end of the experimental protocol.

### Preparation of the hypercaloric diet

The hypercaloric diet was prepared with commercial rat feed and added with condensed milk (395g of condensed milk/500g

of commercial rat feed). The mixture was modeled, pelletized and dried in an air circulating oven at a temperature of 65 °C for 6 hours for drying. The feed was kept under refrigeration (5°C) until use.

### Blood and visceral fat collection

At the end of the experiment, the animals were anesthetized with thiopental (200mg/kg) and immediately after death, blood samples were collected to delineate the biochemical profile: glycemia, total cholesterol (TC), and triglycerides (TG). The glucose and lipid levels were measured in mg/dL. Abdominal adipose tissue was also removed for weight assessment.

### Statistical analysis

For the Statistical analysis, ANOVA and Tukey test were performed. Variables were presented as a mean and standard deviation, adopting a 5% level of significance.

## RESULTS

Table 1 and 2 show the results for the anthropometric and biochemical parameters of the animals after the treatment with *Hypothalamus*. Significant modifications were seen only for Thoracic and abdominal circumference and abdominal fat, although no modifications were observed in the body weight. Levels of triglycerides increased in a significant manner in the treated groups

**Table 1. Body weight at the beginning, at the end, and percentage of the experimental protocol in G1 (treated with *Hypothalamus* 30 CH), G2 (treated with treated with *Hypothalamus* 15 CH), and G3 (control group)**

Parameters	G1 (30CH)	G2 (15CH)	G3 (Control)	p-value
Weight1	99.8 ± 25.4	83.5 ± 19.3	83.1 ± 26.8	0.2262
Weight2	242.25 ± 21.9	258.7 ± 24.2	256.22 ± 15.8	0.1923
%WG	164.66 ± 101.7	226.6 ± 85.7	246.7 ± 116.6	0.1977

Weight 1: Weight at the beginning of the experimental protocol; Weight 2: Weight at the end of the experimental protocol; %WG: Percentage of weight gain

**Table 2. Anthropometric and biochemical parameters of the animals at the end of the experimental protocol in the G1 (treated with *Hypothalamus* 30 CH), G2 (treated with treated with *Hypothalamus* 15 CH), and G3 (control group)**

Parameters	G1 (30CH)	G2 (15CH)	G3 (Control)	p-value
BMI	0.58 ± 0.057	0.60 ± 0.058	0.52 ± 0.04	0.0096
Lee Index	80.75 ± 7.3	86.23 ± 8.05	85.4 ± 5.27	0.1923
Thorax circ.	10 ± 0	11.35 ± 1.49	14.22 ± 1.12	<0.0001
Abd. Circ.	12.5 ± 0.85	13.55 ± 0.92	16.11 ± 0.99	<0.0001
Abd. Fat	1.54 ± 0.33	2.21 ± 0.73	1.96 ± 0.42	0.0253
Glycaemia	144.4 ± 35.57	156.3 ± 40.1	161.4 ± 29.48	0.5701
Cholesterol	169.8 ± 4.1	163.9 ± 9.65	166.66 ± 7	0.2124
Triglycerides	142 ± 30.82	113.5 ± 31.49	101.77 ± 22.05	0.0142

BMI: Body Mass Index; Thorax circ.: Circumference; Abd. Circ. Abdominal Circumference; Abd. Fat: Abdominal Fat

## DISCUSSION

Our results show that there was no interference of *Hypothalamus* in the initial, and final weight, in the percentage of weight gain, Lee's index, glycemia, and total cholesterol, but there was a reduction in the thoracic and abdominal

circumference as well as in the abdominal fat in the treated groups. Obesity has no longer considered only as an aesthetic problem, but rather a disease requiring treatment. Weight loss can improve comorbidities, avoid a plethora of illness conditions, and improve the quality and life expectancy of the patient. The use of hypercaloric diets has been widely used as a model for inducing obesity in laboratory animals and further comparisons with humans. Rat models are useful in the research with obesity because they share similarity to initiation and to the metabolic responses that lead to obesity in humans. In many cases, obesity may be only the consequence of a positive energy balance resulted from excessive consumption of high-calorie foods and sedentary lifestyle. The standardization of an animal model for the induction of obesity and its complications allows evaluating the efficacy of new drugs and natural compounds in the treatment of this pathology (Choi *et al.*, 2017; Mopuri *et al.*, 2017).

One possibility of treatment is the homeopathy that is based on the belief that there is stimulation of a self-regulatory healing process in the patient (Vilhena, Castilho, 2016; Mathie *et al.*, 2017). *Hypothalamus* is a formulation commonly used in the Homeopathic Medicine to reduce appetite. However, no modifications were observed in the body weight and Lee Index of the animals treated with this Homeopathic formulation. On the other hand, there was a reduction in the measures of thoracic and abdominal circumference and the weight of the abdominal fat, and increase in the triglycerides. Authors have shown that the visceral fat is not a mere storage site for triglycerides, but, in fact it may be considered as an endocrine organ capable of producing a plethora of pro-inflammatory cytokines, such as Tumor Necrosis Factor- $\alpha$  (TNF- $\alpha$ ), Interleukin-2 (IL-2), IL-1 $\beta$ , IL-6, IL-18, resistin, lipocalin-2, adiponectin, leptin, Plasminogen-1 (PAI-1), and other biomarkers of inflammation. The unbalance in the expression of these inflammatory markers modifies many factors linked to the cardiovascular diseases. These factors may include energy imbalance, insulin resistance, and elevation of blood pressure, increase in the blood lipids, interference in the metabolism of lipoproteins, imbalance in the immune response and loss of homeostasis. These conditions favor the development of a low-intensity inflammatory scenario that leads to a local immune response, increasing the release of adipokines and resulting in the oxidative species. A vicious cycle is established and the increase of inflammation and oxidative stress is observed (Visser *et al.*, 2017; Guzik *et al.*, 2017; Yao *et al.*, 2017; Muredda *et al.*, 2017; Stolarczyk, 2017; Wang *et al.*, 2017; Krishna *et al.*, 2017). We did not find in the literature studies involving animal models or humans that have evaluated the use of *Hypothalamus* in the treatment of obesity. Nevertheless, we may say that homeopathic formulations are easily accessible, not expensive and rarely are associated with side effects. The formulation used in our work may provide benefit effects once it could help in the reduction of visceral fat and in consequence, could reduce the release of inflammatory cytokines that are related to oxidative stress and cardiovascular complications.

## Conclusions

Our results show that the use of *Hypothalamus* improved thoracic and abdominal circumference, and abdominal fat, suggesting that it may have potential to be used as an adjuvant in the treatment of obesity. However, there was a significant augment in the levels of triglycerides, indicating that further

studies are necessary with humans to establish the effective therapeutic approach.

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