

Effects of slim-quick and FAT STOP on Leptin and Cholecystokinin in Rats

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ABSTRACT

Introduction: Orlistat or FAT STOP is one of the pharmaceutical drugs and Slim-Quick is one of the most common herbal medicines that are used to treat obesity and overweight. The aim of this study was to evaluate the effects of Slim-Quick and Fat-Stop and compare these two drugs in serum concentrations of leptin hormones, cholecystokinin, and body weight changes in adult female rats. **Method:** In this experimental study, 32 adult female Wistar rats were divided into 4 groups that each of them consisted of 8 rats, and these groups were: control, 200 mg/kg Slim-Quick, 200 mg/kg FAT STOP, and Slim-quick and FAT STOP (each of them with a dosage of 200 mg/kg). Slim-Quick and Fat-Stop were fed to animals by means of gavage. On the 29th day after the start of the experiment and after weighing the animals, blood samples were taken from the heart and serum concentrations of cholecystokinin and leptin hormones were measured. The results were analyzed by ANOVA and Duncan's test at a significant level of $p \leq 0.05$. **Findings:** By comparing the group receiving fat-stop with the slim-quick recipient group, it was found that slim-quick increases serum levels of both leptin and cholecystokinin hormones. While fat stop only affects the serum concentration of cholecystokinin hormone. **Conclusion:** Simultaneous application of Slim-Quick and Fat Stop reduces body weight by increasing serum levels of appetite lowering hormones (leptin and cholecystokinin).

Keywords: Slim-quick, fat stop, Leptin, Cholecystokinin, body weight, rat.

Introduction

Today, national and global health organizations are increasingly focusing on obesity and its prevalence as one of the major global problems. Even some experts go further and believe that the increase in body mass (overweight) has stopped the process of hope for humanity and may even have reversed it. In response to these concerns, health organizations all over the world are seeking ways or incentives to reduce the incidence of disease [1]. Orlistat or Fat-stop (trade name Xenical), is one of the synthetic drugs and Slim-Quick, as one of the herbal drugs are considered as common drugs for obesity and overweight treatment. Fat-stop is one of the Lipase enzyme inhibitors that inhibit the absorption of one-third of the fat in the food by

inhibiting the enzyme. By doing this, the fat entry to the body will be gradually decreased, and the body uses its reserves and the weight loss phenomenon will occur [2, 3].

Slim-Quick tablets have celery, dill and green tea extracts [4]. Clinical studies have shown that essential oils of celery and dill have a positive effect on the center of appetite in the brain and cause an interruption in the transmission of the sense of hunger. In addition, flavonoids in the product have an inhibitory effect on the lipogenesis enzyme. The active ingredients in this product increase fat metabolism and reduce blood lipids and, in addition, prevent lipid absorption in the intestine. Catechin and caffeine in green tea inhibit phosphodiesterase enzyme and strengthen the effect of body norepinephrine [5, 6]. Green tea boosts insulin's effect in the body. Green tea reduces fat in all parts of the body by increasing the oxidation of fat in the liver [7]. Thus, taking this pill reduces the risk of developing type 2 diabetes.

The storage and use of adipose tissue are controlled through a complex network of neural signals that activates the absorption and use of energy from the food. Many hormones are the basis of this physiological system for regulating homeostasis of body weight. Leptin is mainly secreted from the white adipose tissue and to a lesser extent from the gastric and peritoneal epithelial

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cells. Leptin reduces the intake of food, increases energy consumption, and thus inhibits appetite [8]. In rodents, leptin is necessary for the feedback loop in the hypothalamus centers [9]. Leptin is capable of directly inhibit the expression of the neuropeptide Y (NPY), which increases the intake of food and reduces the energy use [10].

Cholecystokinin hormone (CCK) is a polypeptide hormone secreted from the stomach into the upper intestine from the cells in the duodenum mucosa and upper jejunum [11]. Studies have shown that CCK injections in laboratory animals and humans prior to eating can reduce the amount of food eaten during a meal, and the higher the injection rate of CCK led to the greater the amount of consumed food [12]. Anti-orexigenic effects of cholecystokinin are induced by CCK-A receptors, these receptors are located in both the central nervous system and the peripheral nervous system [12].

Considering the efficacy of a Slim-quick as a herbal medicine and a Fat-stop as a pharmaceutical drug in line with weight loss, the present study aimed to compare the effects of these two drugs on two hormones affecting appetite (leptin and cholecystokinin) and body weight changes.

Method

In this experimental study, 32 adult female Wistar rats weighing 200-180 g were used. Rats were kept in Jahrom University of Medical Sciences for one week in order to adapt to the environment. Throughout the study, the animals were kept in 12 hours of daylight and 12 hours of darkness, and at an ambient temperature of 25 to 20 degrees Celsius, and were free to have access to water and food.

Rats have randomly divided into 4 groups that each one consisted of 8 rats and these groups can be introduced as follows:

Control group: This group did not receive any treatment during the experiment (28 days).

Experimental group 1 (Slim-quick): Based on the body weight this group received a 200 mg/kg dosage of slim-quick dissolved in 1 ml of distilled water in the course of the experiment (28 days) in the form of gavage.

Experimental group 2 (Fat stop): Based on the body weight this group received a 200 mg/kg dosage of Fat Stop dissolved in 1 ml of distilled water in the course of the experiment (28 days) in the form of gavage.

Experimental group 3 (Slim-quick and Fat stop): Based on the body weight this group received a 200mg/kg dosage of fat stop and a 200 mg/kg dosage of slim-quick dissolved in 1 ml of distilled water in the course of the experiment (28 days) in the form of gavage.

At the end of the study (day 29), after weighing the animals, blood samples were taken directly from the heart of the animals by using a 5cc syringe (anesthetized by diethyl ether) and their serum was collected by centrifuge (for 15 minutes and 3000 RPM) and stored at -20 °C until the test is completed. For the measurement of leptin and cholecystokinin hormones, Elisa kits for rat are used.

One-way ANOVA test was used to analyze the data. In cases where the difference between the groups was significant, Duncan's test was used to find out the difference between the means. Statistical analysis was performed by SPSS software version 21 and significant level ($P < 0.05$) was considered. Data were computed and compared in the results section as Mean \pm SEM.

Findings

Based on the findings listed in Table 1, 200 mg/kg dosage of Slim-quick increased the serum level of leptin and cholecystokinin hormones compared to the control group ($P < 0.05$). Mean changes in body weight also showed that all three experimental groups significantly decreased body weight compared to control group ($P < 0.05$).

In the group receiving Fat Stop, there was also an increase in serum level of cholecystokinin hormones and body weight loss. However, the serum level of leptin hormone did not change significantly in this group compared with the control group ($P < 0.05$).

By means of comparing the fat Stop receptor group with the Slim-quick receptor group, we found that slim-quick increases the serum levels of both leptin and cholecystokinin hormones. While Fat Stop only affects the serum level of cholecystokinin hormone.

In the group that received both Fat Stop and Slim-quick drugs simultaneously, an increase in serum levels of leptin and cholecystokinin hormones and body weight loss was observed compared to the control group ($P < 0.05$).

Table 1: Comparison of serum level of leptin and cholecystokinin hormones and body weight changes in experimental groups receiving different doses of lycopene with the control group

Group / Variable	Control	Slim-quick 200 mg/kg	Fat stop 200 mg/kg	Slim-quick 200 mg/kg and Fat stop 200 mg/kg
ng/ml (Leptin)	0.675 \pm 0.047 a	1.7 \pm 0.025 b	0.77 \pm 0.151 a	2.075 \pm 0.278 b
Cholecystokinin (ng/L)	172 \pm 12.12 a	375.72 \pm 29.46 b	492.45 \pm 21.12 c	433.35 \pm 4.60 bc
Average body weight changes	31.25 \pm 1.65 d	9.75 \pm 1.37 b	17.5 \pm 2.88 c	-4.25 \pm 1.36 a

- Based on Duncan's test, the averages in each row, which have at least one common letter, do not differ significantly in Duncan's test at the 5% level.

-Means are given as Mean \pm SEM.

Discussion and Conclusion

Based on the results of this study, in the group receiving Fat stop, increased serum level of cholecystokinin hormone and body weight loss in normal diets were observed. However, the serum level of leptin hormone in this group did not change significantly compared to the control group. Derosa et al., (2016), in a systematic study reviewed studies performed between 2004 and 2010 on Orlistat. Their results showed that in all of these studies, Orlistat increased plasma concentrations of Adiponectin and reduced leptin and C-reactive protein (CRP) levels in obese or overweight individuals [13]. The difference between the results of the present study and previous studies, i.e., the lack of changes in serum levels of leptin hormone in the Fat stop group, may be due to differences in the conditions of this study with previous studies. Previous studies have been conducted on overweight or obese rats, while the current study was conducted on rats receiving a normal diet.

The present study also showed that Slim-quick increases serum levels of leptin and cholecystokinin hormones and decreases body weight in rats with normal diets. Increasing the secretion of leptin in the recipient of Slim-quick is probably linked with the enhancement of the effect of norepinephrine and insulin by the compounds present in this drug, especially green tea. Caffeine in green tea inhibits phosphodiesterase enzyme and strengthens the body norepinephrine effect. The green tea catechin with caffeine inhibits the Catechol-o-methyl-transferase (COMT) enzyme, thereby raises the level of catecholamines, and increases metabolism [5, 6]. Studies have shown that epinephrine injection can increase the plasma insulin concentration in humans [14]. Insulin is one of the main factors regulating the level of secretion of the leptin hormone. Studies on mice show that insulin increases the *ob* gene and increases plasma leptin levels in healthy and diabetic rats [15]. The possible mechanism for expressing how to stimulate leptin secretion by insulin can be expressed in this way that Insulin transmits glucose into fat cells via GLUT4 (glucose transporter protein). Glucose then acts as an intracellular signal and stimulates the secretion of leptin from fat cells [16].

In the third experimental group (which received both Fat stop and Slim-quick drugs) an increase was also observed in serum levels of leptin and cholecystokinin hormones and weight loss in comparison with the control group. Comparing the group with the received Fat stop with Slim-quick group made it clear that the effect of the Slim-quick drug on both leptin and cholecystokinin hormone levels is the same. While the Fat stop drug has a greater effect on the cholecystokinin hormone and has had no effect on the leptin hormone.

It has been shown that the synergistic effects of cholecystokinin and leptin hormones play an important role in weight loss [17].

Research results indicate that the inhibitory effects of leptin hormone on food intake are stopped by CCK-A receptor antagonists [18]. Synergistic effects of leptin and cholecystokinin are applied on body weight loss through the central nervous system. Parabrachial nucleus (BPN) on the brain bridge is one of the places where the synergistic effects of these two hormones are applied [19]. This nucleus receives inputs from arcuate nucleus of the hypothalamus, as well as the solitary nucleus (NTS). The arcuate nucleus contains neuropeptide Y secretion neurons and solitary nucleus contain the vagus nerves (a stimulant of cholecystokinin secretion) [20]. On the other hand, the presence of leptin hormone receptors in the arcuate nucleus and solitary nucleus has been proven [21].

Conclusion

Simultaneous use of Slim-quick and Fat Stop reduces body weight by increasing serum levels of appetite lowering hormones (leptin and cholecystokinin). Considering the greater popularity of using herbal medicines, the simultaneous use of an herbal drug with a chemical product may, in part, reduce the side effects of synthetic drugs and increase the effectiveness of herbal drugs in reducing body weight.

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