

Effect of Ethanol Extract of Devil's Claw on Serum Levels of Cholecystokinin Hormone and Body Weight in Male Rats

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Abstract

Introduction: Cholecystokinin (CCK) is a 33 amino acid peptide that is produced by endocrine cells in the small intestine, a variety of neurons in the gastric intestinal region and the central nervous system. CCK hormone plays an effective role in lose weight. This study was conducted to evaluate the effect of devil's claw extract on serum levels of the hormone CCK and body weight in male rats. **Materials and Methods:** In this experimental study, 40 male Wistar rats weighing 180–200 g were divided randomly into 5 groups of 8 animals (control, experimental groups receiving devil's claw extract in concentrations of 150, 300, and 600 mg/kg of body weight). Devil's claw extract was administered orally to animals for 28 consecutive days. One day after the last injection, the mice were weighed, and after blood collection and serum separation, hormone CCK concentration was measured by special ELISA kits for male rats. Data analysis was performed with SPSS software (version 21) by one-way ANOVA and Duncan test. **Results:** Doses of 300 and 600 mg/kg devil's claw extract caused a significant increase in the hormone CCK as well as decreased body weight than the control group ($P < 0.05$). **Conclusion:** Devil's claw extracts reduce body weight by increasing the CCK hormone.

Key words: Body weight, cholecystokinin, devil's claw, rat

INTRODUCTION

By detecting peptides secreted from the digestive system affecting appetite, the role of this system in the balance of energy was determined, and like adipose tissue, muscle and liver, stomach is also known as an endocrine organ that affects energy balance. Cholecystokinin (CCK) hormone is among hormones secreted by the stomach that can play an important role in modulating appetite and weight loss.^[1] Devil's claw is a perennial plant with the scientific name *Harpagophytum procumbens* and belongs to the Pedaliaceae family that grows in South and East Africa. In traditional medicine, this herb has been used as an anti-inflammatory, antioxidant, anti-allergic, anti-diabetic, antirheumatic, anticancer, and appetite modulator.^[2-4] Scientific studies that have been conducted so far on devil's claw, also indicated its analgesic, anti-inflammatory effects and therapeutic value in the treatment of musculoskeletal diseases, rheumatoid arthritis,

and osteoarthritis.^[5,6] The main ingredient in the devil's claw is harpagoside, which belongs to the iridoid glycosides family and is the main composition of the plant.^[3] However, this plant also contains compounds such as flavonoids (such as campherol and apigenin), triterpenes, phytosterols, phenolic acids, and fibers.^[7] In a study conducted by Torres-Fuentes *et al.*, in 2014, devil's claw extract inhibitory effects on appetite have been reported.^[8] Based on the results of this research, the anti-anorexigenic effects of devil's claw are exerted through growth hormone secretagogue receptor (GHS-R1a).^[8] Ghrelin is the endogenous ligand for GHS-R1a.^[9] Therefore, by inhibiting the GHS-R1a, ghrelin hormone is not able to exert its anorexigenic effects

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(appetizer). In our previous studies, it was found that devil's claw extract reduced body weight in rats by increasing the secretion of obestatin,^[10] leptin and neuropeptide Y hormones.^[11] Given that previous studies have shown the efficacy of devil's claw on serum levels of ghrelin, obestatin, leptin, and neuropeptide Y hormones, this study was conducted to evaluate the effects of devil's claw extract on serum levels of other hormones affecting appetite, i.e., CCK in rats. The results of this study could help to identify more precisely the mechanisms that regulate appetite and body weight in plants.

MATERIALS AND METHODS

In this experimental study, 40 adult male Wistar rats with an average weight of 180–200 g were used. To adapt to the environment, animals were kept for a week in an animal room in Jahrom University of Medical Sciences. Throughout the study, animals were kept in conditions of 12 h of light and 12 h of darkness and ambient temperature 20–25°C and had free access to food and water. Humidity was about 50–55%. According to the earlier articles, prescribed devil's claw extract concentration was determined in the amount of 150, 300, and 600 mg/kg of body weight.^[5]

The rats were divided randomly into 5 groups of 8 animals as follows:

Control group

This group received no treatment during the experiment (28 days).

Experimental group

Duration of the experiment (28 days), the group received 1 ml of distilled water by gavage and in terms of body weight.

Experimental Groups 1, 2, and 3: Received doses of 150, 300, and 600 mg/kg of devil's claw extract by gavage for 28 days and in terms of body weight. At the end of the study (day 29), after weighing the animals, blood samples were directly taken from the heart by 5 cc syringe (under anesthesia by

diethyl ether), and their serum was collected by centrifuges (for 15 min and 3000 rpm) and was kept in freezer –20° until examination. To measure the CCK hormone, ELISA kits for rat were used. For data analysis, ANOVA was used. If different groups were statistically significant, Duncan test was used to understand the differences between means. Statistical analysis was performed using SPSS version 21, and statistically significant level ($P < 0.05$) was considered. The data were calculated and compared in the results in a mean \pm standard error of the mean.

FINDINGS

Based on the results listed in Table 1, the mean serum concentration in hormone CCK in rats receiving doses of 300 and 600 mg/kg of devil's claw extract showed a significant increase compared to the control group ($P \leq 0.05$). However, the mean serum concentration in hormone CCK in rats receiving doses of 150 mg kg of devil's claw extract did not show a significant increase compared to the control group ($P \leq 0.05$). The results of measuring the mean changes in body weight also showed that doses of 300 and 600 mg kg of devil's claw extract caused a significant decrease in body weight compared with the control group ($P \leq 0.05$) [Table 1].

DISCUSSION AND CONCLUSION

The results showed that oral administration of devil's claw extract by dose-dependent increases serum levels of the hormone CCK as well as reduces body weight in rats. CCK hormone plays a role in regulating energy balance and movements and digestive secretions. CCK slows down gastric emptying causing prolongation of abdominal distension and thus stimulates the stretch receptors in the stomach wall and could eventually create an indirect feeling of fullness and satiety. This hormone also acts as a neuropeptide.^[11] In humans and animals, CCK has various functions such as creating a feeling of satiety and reduced food intake, prevention of gastric emptying, prevention of gastric acid secretion, and stimulating intestinal peristalsis.^[12] Products of digestion in the intestinal lumen stimulate the release of CCK from the beginning of the small intestine.^[13] Research shows

Table 1: Comparison of changes in serum levels of the hormone cholecystokinin and body weight in the experimental groups receiving different doses of devil's claw extract with the control group

Variable	Group				
	Control	Sham	Devil's claw extract 150 (mg/kg)	Devil's claw extract 300 (mg/kg)	Devil's claw extract 600 (mg/kg)
Cholecystokinin	3066.20 \pm 49.28 ^a	3108.20 \pm 34.61 ^a	3163.80 \pm 58.75 ^a	3381.40 \pm 16.67 ^b	3385.40 \pm 28.38 ^b
Body weight change (r)	28.20 \pm 0.58 ^a	27.60 \pm 0.93 ^a	27.40 \pm 0.51 ^a	24.80 \pm 0.37 ^b	23.60 \pm 0.40 ^b

According to Duncan test, averages available in each row have at least a common letter; they have no significant difference in the level of 5% Duncan test. Averages were presented as mean \pm SEM. $P \leq 0.05$ was considered statistically significant. SEM: Standard error of the mean

that the effect of CCK on appetite control is exerted through the CCK-A and through the vagus nerve. Before the meal, antagonists of the receptor increase meal size in humans and other species.^[14] The results show that the CCK hormone exerts its effects on appetite by blocking the orexigenic neurons particularly Y neuropeptide neurons (NPY).^[15,16] Our previous study also showed that devil's claw extract reduces body weight by increasing the secretion of leptin hormone and reduced Y neuropeptide hormone.^[11] Furthermore, the ceased inhibitory effect of leptin hormone on food intake by CCK receptor antagonists has proved synergistic effects of these two hormones in the body weight and food intake.^[17] The presence of leptin hormone receptors in the arcuate nucleus (containing neurons secreting NPY) and the nucleus of the isolated stem (containing neurons stimulating CCK) is also another reason for the synergistic effects of the CCK and leptin hormone to inhibit the orexigenic effects of NPY.^[18] As a result, the weight loss observed by the devil's claw extract in this study can be linked to synergistic effects in leptin and CCK hormones in inhibiting related NPY orexigenic neurons.

CONCLUSION

Devil's claw extract reduces body weight by increasing the CCK hormone.

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