

The Effect of Lycopene on Serum Ghrelin Levels and Body Weight in Adult Female Rats

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Abstract: Introduction: Lycopene is a red carotenoid that is effective in controlling body weight. Ghrelin is an appetite-stimulating peptide that plays a key role in the regulation of energy balance. The purpose of this study was to investigate the effects of lycopene on ghrelin serum level in adult female rats. Methods: In this experimental study, 32 adult female Wistar rats were divided into 4 groups of 8 rats including monitoring, control, experiments receiving lycopene (at concentrations of 5 and 10 mg/kg). The animals were fed by gavage of lycopene. Twenty-nine days after the start of the experiment and after weighing the animals, cardiac puncture was performed and serum ghrelin level was measured. The results were statistically analyzed by ANOVA and Duncan's test at $P \leq 0.05$. Results: The concentration of lycopene 10 mg/kg significantly decreased the ghrelin hormone as well as the average body weight more than the control group ($P \leq 0.05$). Conclusion: Lycopene reduces body weight by decreases serum ghrelin levels.

Keywords: *Lycopene, Ghrelin, Body Weight, Rat*

Introduction

Lycopene is a red carotenoid synthesized by some plants and microorganisms. This carotenoid is not a precursor of vitamin A, but it has a very powerful antioxidant activity due to the presence of 11 conjugated double bonds that eliminates free radicals [1]. Lycopene is the predominant carotenoid in human serum that prevents oxidation and radical degradation of important cellular biomolecules such as DNA, proteins and lipids with the protection of them and plays an important role in the prevention and treatment of prostate, cardiovascular, skeletal and digestive diseases [2, 3]. As lycopene is hydrophobic and there are high lipoprotein receptors in fat tissues for it, the storage site for lycopene and other carotenoids is adipose tissues [3].

The results indicated the effectiveness of lycopene in reducing inflammatory factors in obese and overweight people [4]. Luvizotto et al. in a study found that administered a dose of 10 mg/kg of lycopene for 6 weeks in obese rats in spite of the reduction in plasma levels as well as the decrease of adipokine gene expression of leptin, resistin and IL-6 in epididymal adipose tissue had no effect on body weight [4].

Markovits et al. and Gouranton et al. showed that lycopene inhibits inflammatory processes in obesity flow and helps weight loss through the decrease of expression of cytokines and chemokines in adipocytes (fat cells) [5, 6]. Guerendiain et al. on a study showed that there is a direct correlation

between increased carotenoids' plasma levels such as beta-carotene, retinol and lycopene with reduced adiposity and weight loss in adolescents with overweight or obese [7].

Therefore, according to the evidence of the effectiveness of lycopene in the regulation of body weight and some hormones affecting appetite, such as leptin and resistin, this study aimed to investigate the effects of lycopene on serum levels of orexigenic ghrelin hormone.

Materials and methods

In this study, 32 adult female Wistar rats were used with an average weight of 180-200 g. The rats were kept in animal breeding room of Jahrom University of Medical Sciences for a week to adapt to the environment. During the research, the animals were kept under 12 hours of light and 12 hours of darkness conditions and ambient temperature of 20-25 °C and freely had access to food and water.

According to the previous articles, prescribed concentrations of lycopene were determined in doses of 5 and 10 mg/kg of body weight [1] and rats were randomly divided into 4 groups of 8 animals as follows:

- **Monitoring Group:** This group did not receive any treatment during the experimental period (28 days).
- **Control Group:** This group received 1 ml of distilled water by gavage based on body weight during the experimental period (28 days).
- **Experimental Groups 1 and 2:** These groups received lycopene doses of 5 mg/kg and 10 mg/kg, respectively, by gavage based on body weight for 28 days.

Table 1: Comparison of changes in serum levels of ghrelin and body weight in experimental groups received different doses of lycopene with the control group

Group Variable	Monitoring	Control	Lycopene (5 mg/kg)	Lycopene (10 mg/kg)
Ghrelin (ng/ml)	1775.25 ± 46.26c	1837.62 ± 41.88c	1505.12 ± 78.20b	1248.87 ± 59.73a
Average of body weight changes	24.50 ± 1.00b	24.62 ± 0.822b	23.37 ± 0.885ab	1775.25 ± 46.26c

- According to Duncan test, the means in each row having at least one common letter, they are not significantly different at 5% level of Duncan test.
- The averages are presented as Mean ± SEM.

At the end of the study (on the 29th day) after weighing the animals, their blood were directly taken from the heart by 5 cc syringe (anesthetized by Diethyl ether); and their serum was collected by centrifugation (15 min, 3000 rpm); and they held in a freezer at -20 °C until examination time. Special ELISA kits for rats were used to measure the hormone ghrelin.

One-way analysis of variance (ANOVA) was used to analyze the data. Duncan test was used to find the differences between means in cases in which statistical difference was significant in different groups. Statistical analysis was performed using SPSS version 21 and significant levels were statistically considered with $P < 0.05$. The data were calculated and compared in the results' section as Mean ± SEM.

Results

According to the findings recorded in Table 1, doses of 5 and 10 mg/kg of lycopene resulted in a significant reduction in serum levels of hormone ghrelin compared with the monitoring group ($P < 0.05$). In the comparison of the groups received different doses of lycopene, it was also found that the concentration of 10 mg/kg had greater effect in reducing levels of the hormone ghrelin compared to the other concentrations (Table 1).

As well as the average of body weight changes showed that lycopene reduced at dose of 10 mg/kg resulted in a significant reduction in body weight compared with the control group ($P < 0.05$).

- $P < 0.05$ is statistically considered significant.

Discussion and Conclusion

The results of the present study showed that lycopene significantly reduced serum levels

of ghrelin and decreased body weight in female rats.

Ghrelin as an effective peptide in increasing appetite is mainly produced in the stomach and produced in lower levels in the brain, the hypothalamus, pituitary, adrenal cortex, pancreatic islet cells and other numerous tissues [8]. Ghrelin is a stimulant endogenous ligand for the growth hormone receptor which has different endocrine, paracrine and appetite-stimulating actions [9]. Ghrelin gene expression is increased in hunger states and is reduced in satiety states.

The injection of ghrelin in rats' cerebrospinal fluid (CSF) intensified their eating behaviors [10, 11]. On the other hand, temporary inhibition of ghrelin signaling by various methods reduces food consumption and body weight [12]. Ghrelin increases fat accumulation by increasing the expression of adipogenic genes such as acetyl CoA carboxylase [13]. The ghrelin injection independently affects adipose tissue metabolism by inhibition of lipolysis' enzymes and regulation of adipogenesis [14].

The results of our previous study showed

that lycopene increased serum levels of leptin and decreased serum levels of neuropeptide Y and decreased body weight in the female rats [15]. The interaction of hormone ghrelin with other hormones affecting appetite such as leptin and neuropeptide Y (NPY) is one of the main mechanisms of the hormone in regulation of appetite. Leptin and ghrelin are involved in parallel but opposite in body weight homeostasis.

Both the hormones apply their effect on the central nervous through receptors located in the center of appetite, Ventromedial and Arcuate Nuclei, in hypothalamus [16]. Ghrelin by stimulating [17, 18] and leptin by inhibiting of NPY-synthesizing neurons in the arcuate nucleus of the hypothalamus [19, 20] increased and decreased appetite, respectively. Therefore, reducing the hormone ghrelin serum levels in this study can be associated with increasing the levels of the hormone leptin and decreasing NPY by lycopene.

General Conclusion: Lycopene decreases body weight by reducing the serum levels of orexigenic ghrelin.

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