

The Effect of *Apium Graveolens* Extract on Pituitary-Testis Axis in Mice

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Abstract: Celery (*Apium graveolens*) has many therapeutic effects. This plant has many phytoestrogens that can affect on the reproductive endocrine system and can reduce fertility. In this study, hydro alcoholic extracts of celery leaves on the reproductive parameters in young male mice of Balb/C was investigated. The samples were randomly divided into 5 groups (3 treatment groups, placebo and control). Celery leaves hydro-alcoholic extract in different doses (50, 100, 150 mg/kg/2 day) was injected (IP) for 20 days. The placebo group was used for injection of normal saline. The samples were randomly divided into 5 groups (3 treatment groups, placebo and control). After 10 injections, samples bloods were analyzed for FSH, LH and testosterone using RIA method. Results showed that concentrations of FSH in 100 and 150 mg kg⁻¹ decreased significantly while LH and testosterone concentrations in all experimental groups decreased ($p < 0.05$). This study showed dose dependent negative effect of celery extracts in male reproductive potential.

Key words: Celery extract, reproductive hormones, mice, FSH, LH

INTRODUCTION

Medicinal plants, dating back several 1,000 years in the treatment of diseases and their therapeutic effects has been proved (Modaresi, 2012) and expensive chemical drugs cause side effects and herbal medicine is people's attitudes. But along with increased consumption, due to false beliefs and attitudes that herbal medicines are completely safe, adverse side effects, especially in cases of uncontrolled consumption to come from consumers (Elisabetsky and Castilhos, 1990). Celery contains vitamin C and other materials that are health enhancing substances, such as phalides which lowers cholesterol and coumarrins that helps prevent cancer. Celery seeds of anti-rheumatism, sedative, antiseptic urinary tract, increased excretion of uric acid, blood pressure lowering, to some extent against fungal diseases, diuretic, analgesic, anti-inflammatory, detoxification, anti-spasmodic, anti-bacteria, binding rules, anti-contractions, seizures, stomach tonic and is carminative (Blumenthal *et al.*, 2000).

In recent years, numerous studies have shown that the percentage prevalence of infertility and reproductive system abnormalities in all the world is increasing. Infertility can be one of the natural plant compounds (phytoestrogens) that are widely used in life which can affect the reproductive endocrine system and can reduce fertility. According to available reports contain phytoestrogens might celery plants and in this respect can be effective in reproductive physiology (Modaresi, 2012).

The high rate of consumption of herbal medicines and are available in the market. The important point in relation to the dose of herbal medicines. The aim of this research, was determine the effect of three doses of herbal extracts in the celery on the pituitary-gonad and reproductive potential in Balb/C mice.

MATERIALS AND METHODS

The study was conducted in Khorasgan Branch of Islamic Azad University. Total 50 male mice from Balb/C race and in weight range of 30±5 g were prepared and kept for 2 weeks in similar condition with free access to food, water, normal light and appropriate temperature and moisture. These favorite conditions were continued for whole period of study. Experimental groups were selected as follows:

- Control group: In order to basal hormones LH, FSH and testosterone in the group treated groups in the same conditions but without injecting the test period was recorded
- Placebo group: To ensure the injection of the test result and its comparison with the control group, this group daily rate 0.5 mL normal saline was injected
- Treatment group 1 consisted of 10 mice that daily received 50 mg/kg/2 day celery hydro alcoholic extract
- Treatment group 2 consisted of 10 mice that daily received 100 mg/kg/2 day celery hydro alcoholic extract
- Treatment group 1 consisted of 10 mice that daily received 150 mg/kg/2 day celery hydro alcoholic extract

Injections were done for 20 days every other day and 1 day after last injection, blood samples were prepared using guillotine method. Eliza method and gamma counter machine were used to measure FSH, LH and testosterone hormones. The study was done in completely randomized design and obtained data were analyzed using SPSS program and Duncan's multiple ranges test ($p \leq 0.05$) was used to compare means.

RESULTS AND DISCUSSION

Evaluation of FSH: The mean level of FSH in the blood serum of experimental groups and control in comparison level ($p < 0.05$) was determined using Duncan test between 2 experimental groups 2 (100 mg kg^{-1}) and 3 (150 mg kg^{-1}) decreased significantly (Fig. 1).

Evaluation of LH: The mean level of LH in the blood serum of experimental groups and control in comparison level ($p < 0.05$) was determined using Duncan test between 3 experimental groups 1 (50 mg kg^{-1}), 2 (100 mg kg^{-1}) and 3 (150 mg kg^{-1}) decreased significantly. Figure 2 shows this difference.

Evaluation of testosterone: The mean level of testosterone in the blood serum of experimental groups and control in comparison level ($p < 0.05$) was determined using Duncan test between 3 experimental groups 1 (50 mg kg^{-1}), 2 (100 mg kg^{-1}) and 3 (150 mg kg^{-1}) decreased significantly. Figure 3 shows this difference.

In this research, extract celery on the pituitary-gonad in male mice was investigated. Concentration of LH, FSH and testosterone hormone were examined and compared with a control group.

Changes in the levels of FSH and LH: The results showed in this study, celery extracts, caused significant reduction in mean of LH, FSH which seems to inducted an inhibitory effect on the pituitary-gonadal in mice.

The main pathway of sexual control is the Hypothalamic-Pituitary-Gonadal (HPG). The center, under the direct influence of feedback control, the regulation of sexual activity in humans and other mammals are. The axis of the male hormone testosterone and spermatogenesis for very precise control of such acts:

- Hypothalamic releasing hormones, stimulating the secretion of pituitary and gonadal hormone (LH, FSH) from which these cells
- The hormone LH, go with the Leydig cells of the testes to secrete androgens (testosterone) increase. FSH is the hormone that stimulates spermatogenesis

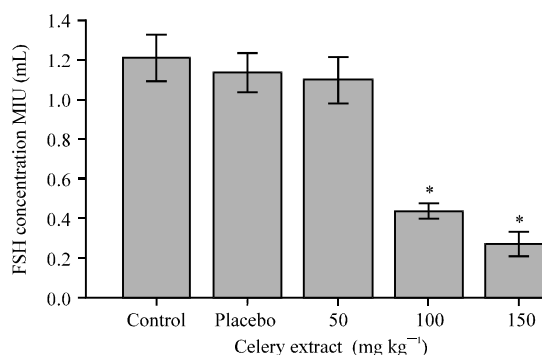


Fig. 1: The concentration of FSH in various groups

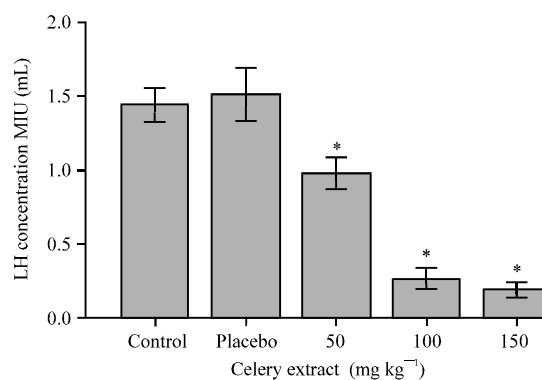


Fig. 2: The concentration of LH in various groups

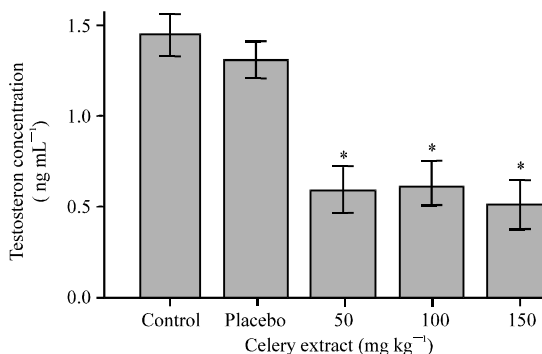


Fig. 3: The concentration of testosterone in various groups

With the rising levels of androgen hormones to regulate and control the axis hormone secretion through its negative effect. Increase in LH and testosterone effects on the hypothalamus and inhibits FSH partly through self-regulation mechanism is negative. Low testosterone also removed the inhibitory effect of testosterone on the hypothalamus.

Inhibin is an endocrine hormone that is secreted by sertoli cells in testis. This hormone is secreted in

response to FSH levels and a negative feedback effect on its secretion and inhibit pituitary FSH and spermatogenesis is regulated. Thus, the axis as the main pathway in the regulation of sexual acts. Axis hypothalamus-pituitary-gonadal can be influenced by various factors and regulate and balance is impaired. One of these factors are phytoestrogens. Studies have shown that phytoestrogens and structurally similar compounds can act through an anti-estrogen, male reproductive health and the damage to endangered. Some studies have suggested that central nervous system-gonadal and sexual behavior in rats during development is sensitive to phytoestrogens (Santti *et al.*, 1998; Ogawa *et al.*, 2002). Celery has plenty of vitamin C and has oestrogenic effects (Zamansoltani *et al.*, 2009). Some research suggests that anti-androgenic properties of celery extracts. Decrease in FSH and LH levels can be raised following possibilities:

- Estrogen-like compounds such as flavonoids in this plant can be increased estrogen levels (Armanini and Bonanni, 1999) However, excessive secretion of pituitary FSH producing estrogen reduces
- Celery compounds can cause toxic effects can create barriers in FSH and LH synthesis and thus reduce its rates

CONCLUSION

Assessment of changes in testosterone levels, the results showed in this study, Celery extracts, caused significant reduction in mean serum levels of testosterone have been shown in Fig. 3. Decrease in testosterone levels compared to control group raised the following reasons:

- Due to decreased synthesis of LH hormone testosterone decreases
- Due to reduced number of Leydig cells, also decreases the amount of testosterone synthesis
- It can be reduced due to the influence testosterone synthesis directly on the celery extracts or its metabolism is increased

The 3 enzyme, 17-hydroxy steroid dehydrogenase, 3 hydroxy steroid dehydrogenase and 17-20 lyase, making testosterone and aromatase is involved in its metabolism. Aromatase that converts testosterone to estradiol and thus, may reduce testosterone levels (Aramaini, 2003).

According to the results, it seems that the endocrine function of the celery on pituitary-testis can cause negative effects on male reproductive potential.

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