

## Effects of hydroalcoholic extract of *matricaria chamomilla* flower on testosterone and gonadotropins in adult male rats

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Received: 6/29/2014

Revised: 8/23/2014

Accepted: 8/29/2014

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Pars Journal of Medical Sciences, Vol. 12, No. 4, Winter 2015

Par J Med Sci 2015; 12(4):37-40

### Abstract

#### Introduction:

Chamomilla is a valuable plant that has been used in traditional medicine for thousands of years to treat different diseases. This study aimed to investigate the effects of chamomilla flower extract on pituitary-gonadal axis in adult male rats.

#### Materials and Methods:

In this experimental study, 45 adult male Wistar rats with a mean weight of 250-300 g were divided into five groups: control group, sham group and experimental groups 1, 2 and 3. The experimental groups, respectively received 10, 20 and 40 milligram per kilogram body weight of intraperitoneal injection of chamomile flower extract for 14 consecutive days. At the end of the treatment course, the rats were anesthetized with ether and their ventricular blood samples were collected for measuring serum concentration of gonadotropins and testosterone by radioimmunoassay. Data were analyzed using ANOVA.

#### Results :

The serum concentration of testosterone showed a significant decrease in experimental groups as compared with the sham group ( $p \leq 0.05$ ). Nonetheless, the serum concentration of gonadotropins no showed a significant difference in experimental groups as compared with that of the control group.

#### Conclusion:

Given the results of this study, intraperitoneal injection of chamomile flower extract reduces testosterone secretion in male rats.

**Keywords:** Chamomile, Testosterone, Gonadotropins, Rat

### Introduction

Increasing world population growth rate is a major concern, especially in developing countries. In the recent decade, mean annual growth rate in Iran is estimated at 1.2% (1). This overwhelming population growth is largely due to high fertility rates, and given adverse effects and side-effects

of chemical drugs, traditional medicine, especially herbal therapy may be able to offer a solution (2).

Chamomile is an annual herb from Asteraceae family that grows to 20 cm to 30 cm tall, and originated predominantly in Mediterranean region, but is now widely spread in Europe, temperate regions of

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Asia, and even America. Before Christ, shade-dried flowers and aerial parts of the plant, grown from May to October, were used as herbal medicine. In Iran and other countries, chamomile is traditionally used for its immune system boosting, hypnotic, sedative, analgesic, and nervous system strengthening properties (3). It has also been shown that this plant has an attenuating effect on the central nervous system (4-6). Chamomile contains flavonoids such as: apigenin and luteolin, volatile oils including chamazulene and bisabolol, sesquiterpene, lactones such as matricarine, mucilage including polysaccharides, capric and nonyl ethers, amphiphone, umbelliferone, furfural, amino acids, fatty acids, phenolic acids, and cholinocomarines (4,7). In traditional medicine, this plant is used as a sedative, appetizer, antispasmodic, menstruation regulator, and in treatment of oral, gum and skin infections. Studies have shown that this plant has the following properties: anxiolytic, analgesic, seizure control, immune system boosting, anti-allergic, anti-bacterial, reducing menopausal hot-flashes, protection against cardiovascular diseases, and osteoporosis. Strong antispasmodic effect of chamomile is attributed to spiroethers, its anti-allergic property to chamazulene, anti-inflammatory property to alpha-bisabolol, and anxiolytic, antioxidant and hormone-like properties with effects on central nervous system, to flavonoids. Currently, its extract is widely used in pharmaceuticals, cosmetics, health, and food products (8, 9).

Given that chamomile contains various compounds such as chamazulene, bisabolol and sesquiterpenes, it is likely that its use can be effective in production and secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from pituitary, and testosterone from testicles. Accordingly, the present study aimed to determine the effects of chamomile extract on testosterone and gonadotropins, for optimal use of this plant.

## Materials and Methods

This experimental study was conducted in autumn 2011 at Kazeroon Islamic Azad University on 45 adult male Wistar rats weighing between 250 grams and 300 grams. Room temperature was maintained constant at  $25\pm 2$  °C, and compressed food was made available to rats ad lib. Animals were housed according to the National Institute of Health guidelines. Rats were divided into 5 study groups. Control group received no particular treatment. Sham control group received a daily intraperitoneal dose of 0.2 ml of saline. Experimental groups 1, 2, and 3 received daily intraperitoneal doses of 10, 20, and 40 mg/kg of chamomile extract, respectively. After 14 days, ventricular blood samples were taken from all anesthetized rats. Blood serum was separated by centrifuging samples at 3000 rpm for 10 minutes. Hormone measurement was performed using radioimmunoassay (RIA) technique. To this end, unlabeled blood serum (unlabeled antigens) was poured into a container, and hormone labelled with <sup>125</sup>I (labeled antigens) was added. Both these antigens compete to bind with labeled and standard antibodies added to the solution.

To prepare chamomile extract, one kilogram of chamomile flower was milled into a powder, and dissolved in 4 liters of alcohol 96%, and then kept (at room temperature) for 4 days. Over this period, container was shaken frequently, to fully dissolve extract in alcohol. Solution was filtered, and then centrifuged at 4500 rpm for 8 minutes. The resulting liquid was poured into an open-top container to allow evaporation of alcohol. The resulting green thick syrup was dried at 80 °C. To prepare required concentrations, the resulting powder was dissolved in distilled water and alcohol.

Data were analyzed in SPSS software using variance analysis.  $P\leq 0.05$  was considered significant.

## Results

Normal distribution of data was investigated, and statistical results and comparison of mean testosterone and gonadotropin values among control, sham and experimental groups were in figures and tables.

Serum testosterone concentration showed a significant reduction in experimental

groups compared to control and sham groups due to the effect of different amounts of chamomile extract ( $P \leq 0.05$ ). Also, serum concentration of gonadotropin significantly changed in experimental groups compared to control and sham groups ( $P \leq 0.05$ ).

Hormone assay test results showed no significant difference in serum concentrations of FSH and LH compared to control and sham groups (table 1).

Table 1: Chamomile extract effect on FSH, LH, and testosterone

Group	LH	FSH	Testosterone
Control	0.30±0.02	0.24±0.02	7.66±2.51
Sham control	0.33±0.06	0.26±0.01	6.48±2.28
Experimental 1	0.31±0.01	0.21±0.01	2*±0.28
Experimental 2	0.31±0.03	0.23±0.02	2.23*±1.30
Experimental 3	0.28±0.02	0.26±0.02	3.83*±1.36

## Discussion

According to the present study results, administration of chamomile extract had no effect on FSH and LH. However, concentration of testosterone showed a significant reduction compared to control and sham groups ( $P \leq 0.05$ ). No significant difference was observed between control and sham groups in mean serum concentration of testosterone ( $P \geq 0.05$ ). The results showed a significant effect on serum concentration of testosterone due to administration of 10, 20, and 40mg/kg of chamomile extract over 14 days, and a significant reduction in serum concentration of this hormone in experimental groups compared to control ( $P \leq 0.05$ ). Chamomile extract contains phytoestrogen compounds, which stimulates prolactin secretion. Prolactin facilitates stimulation of LH in interstitial cells, and has a synergic effect on LH in stimulation of androgen production (10, 11). At physiological concentrations, prolactin maintains the number of LH receptors in leydig cells, and stimulates secretion of testosterone (12). Higher secretion of this hormone reduces sensitivity of these receptors to secretion of LH, thereby

producing a regulatory reduction in LH receptors (13). Spermatic macrophages and endothelial cells are in direct contact with leydig cells, and are considered a strong source of testicular nitric oxide secretion; and increased prolactin stimulates its production (14). Nitric oxide inhibits cleavage enzyme activity of cholesterol side-chain and cholesterol conversion into pregnenolone, and thus inhibits steroidogenesis (15). Accordingly, it is likely that chamomile extract reduces sensitivity of LH receptors in leydig cells through increased prolactin, reduces activity of enzymes involved in steroidogenesis process, and ultimately reduces production of testosterone, for which cholesterol is the precursor (16). Phytosterols reduce expression of steroidogenic acute regulatory (STAR) protein involved in cholesterol transfer to inner mitochondrial membrane and onset of steroidogenesis process (17). In addition, it has been found that phytosterols in chamomile extract reduce Side-chain Cleavage Cytochrome SCC-P450 of cholesterol desmolase, and thus reduce cholesterol conversion into mitochondrial pregnenolone, which

reduces steroid synthesis, including testosterone (18). Studies have shown that phytosterols have anti-androgenic properties and reduce activity of alpha-5 reductase. Inhibition of this enzyme leads to reduction in conversion of testosterone into dihydrotestosterone (active form of this hormone in tissues), and thus reduces sensitivity of tissues to androgens, and reduces their activity (19).

### Conclusion

According to the present study results, chamomile flower extract reduces testosterone, but has no effect on gonadotropins. Thus, use of this plant in

regulation of infertility in the male gender requires further studies.

### Acknowledgements

In This Way, The Authors From The University Of Medical Sciences And Jahrom Are Grateful For Health Services Research Funding.

### Conflict Of Interest

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this article.

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