**Journal of Diseases and Medicinal Plants**
2022; 8(2): 24-27
http://www.sciencepublishinggroup.com/j/jdmp
doi: 10.11648/j.jdmp.20220802.11
ISSN: 2469-8202 (Print); ISSN: 2469-8210 (Online)

# The Effect of Saffron (*Crocus sativus L. Iridaceae*) Orally Administration on Blood Level of Sex Hormones in Rats

**Babaev Khanaga Fizuli[1], Shukurova Parvana Agababa[1], Ibragimov Anar Shamistan[2, *], Abbasov Ragif Yusub[1], Ibragimova Jale Muchtar[1], Alieva Ravana Iqbal[1], Gasimova Gulnara Zair[1]**

[1]Institute of Physiology Named After A. I. Karaev, Azerbaijan National Academy of Sciences, Baku, Republic of Azerbaijan

[2]Department of Biology, Khazar University, Baku, Republic of Azerbaijan

## Email address:

medkrim@list.ru (I. A. Shamistan), jaluzi2009@gmail.com (I. J. Muchtar)

[*]Corresponding author

## To cite this article:

Babaev Khanaga Fizuli, Shukurova Parvana Agababa, Ibragimov Anar Shamistan, Abbasov Ragif Yusub, Ibragimova Jale Muchtar, Alieva Ravana Iqbal, Gasimova Gulnara Zair. The Effect of Saffron (*Crocus sativus L. Iridaceae*) Orally Administration on Blood Level of Sex Hormones in Rats. *Journal of Diseases and Medicinal Plants*. Vol. 8, No. 2, 2022, pp. 24-27. doi: 10.11648/j.jdmp.20220802.11

**Received**: February 20, 2022; **Accepted**: March 15, 2022; **Published**: April 14, 2022

**Abstract:** Modern medicine is currently marked by an increased interest in herbal pharmaceutical drugs traditionally applied in folk medicine in a significant number of diseases. In this regard, saffron (*Crocus sativus L. Iridaceae*) is of particular importance. This paper presents the results of study of the effects of Azerbaijan-grown saffron on blood level of follicle-stimulating hormone (FSH) in female rats, as well as on blood level of testosterone in male rats. In the blood serums of animals, using hormonal test systems for enzyme immunoassay, FSH and testosterone levels were determined. The findings revealed a decrease in blood levels of FSH in 12-month-old female rats as compared to the control group (comprising animals of the same age which did not receive the saffron extract), as they approximated the registered levels of 6-month-old female rats. Saffron increased the blood level of testosterone as compared to untreated controls, which did not receive saffron. Saffron's unique medicinal properties largely owe to the diversity of biologically active substances it contains The effects of saffron treatment observed in the course of this study could be explained by the direct impact of saffron and its components on the sex glands and the central nervous system. Findings of diverse pharmacological effects of the saffron extract open new horizons for the development of scientifically corroborated recommendations for application in practical medicine.

**Keywords:** Saffron Extract, Female Rats, Follicle-Stimulating Hormone, Male Rats, Testosterone, Phytoprotector

## 1. Introduction

Population ageing is a matter of concern in most of the developed countries, and a number of developing ones [1, 2]. To this point, the objective of modern physiology, gerontology and medicine is to extend the active period of life and maintain reproductive health. Reproductive system is one of the most important systems of entire body, and age-related decline in reproductive functions is one of the manifestations of biological ageing in humans and animals [3-5]. The activity of the reproductive system is directly related to age, and the level of sex hormones reflects and determines the biological age of a person. As the body ages, the function of the sex glands gradually decreases until it fades completely. This is particularly manifestant in women in the form of a complex multifaceted symptoms (syndrome) called menopause. It is noteworthy that in the last 150 years women's life expectancy following the onset of menopause has significantly increased; currently women spend approximately one third of their lives in the estrogen-deficient state, that makes the medical and social status of middle- and senior-aged women a matter of acute concern. [6].

Prevention and correction of premature aging are the key issues facing anti-ageing medicine and preventive geriatrics. They make the studies of properties of plant-derived medicines extremely relevant; according to World Health Organization (WHO) the global market for these substrates is steadily growing, in Europe and Central Asia, in particular [7].

Saffron is one of the most valuable ingredients of folk medicine, the curable characteristics of which are known from the famous book "Canon" by doctor, scientist-encyclopedist Ibn-Sina. The best is considered to be Khorasan saffron, which is cultivated widely in Azerbaijan.

To date, there are enough experimental data indicating the stimulating effect of saffron and its components on the sexual behavior of animals. [8-10]. The effect of an aqueous extract of saffron and its main components, safranal and crocin, on the sexual behavior of male rats was studied in their studies by Hosseinzade H. et al.. In this study, it was shown that safranal did not affect the sexual behavior of male rats, while an aqueous extract of saffron and its other component, crocin, increased the sexual activity of males [11]. The positive effect of saffron extract at a dose of 100 mg/kg on the pituitary-testis axis in mice was established by Modaresi M. et al. [12]. When studying the effect of an aqueous extract from saffron stigmas on the serum levels of follicle-stimulating hormone, luteinizing hormone, progesterone and estrogen, as well as on folliculogenesis in 45 adult rats, it was found that an extract from saffron stigmas at a dose of 80 mg/kg significantly increased the serum levels of all studied hormones, as well as the number of primary, secondary and tertiary follicles in treated rats [13]. Some clinical studies have also found the effectiveness of saffron in the treatment of premenstrual syndrome (PMS) [14]. For example, in a double-blind and placebo-controlled study, it was found that oral administration of saffron capsules at a dose of 30 mg / day (15 mg 2 times a day, day, morning and evening) in women aged 20-45 years with a regular menstrual cycle and symptoms of PMS for two menstrual cycles, reduced the severity of PMS symptoms [14].

The above-mentioned discoveries speak in favour of investigating the effects of saffron on the functioning of reproductive systems in both sexes, in experimental model, so as to understand the mechanisms that underlie pharmacological effects of saffron, and develop scientifically based recommendations for its application in medicine.

## 2. Objective

The objective of the research was to study the effects of the *Crocus sativus L. Iridaceae* stigma extract on blood level of follicle-stimulating hormone in female rats, and blood level of testosterone in male rats.

## 3. Material and Methods

In the present study the saffron grown in the Bilgah village of the Absheron peninsula was used. The saffron stigma extract was obtained by a percolation method. The ethanol extract was filtered, the residue was washed with 75% alcohol and filtered again, then distilled off alcohol. The obtained liquid extract was further vacuum dryed to concentrate to a dry residue. The yield of the active extract as viscous gumlike substance constituted 56% of total mass of row material.

The tests was conducted on 45 Wistar rats, kept in standard cages (10 animals per cage) at a room temperature of 22 ± 2°C. All animals were fed ad libitum with standard laboratory chow, and had an access to tap water.

The work was carried out in accordance with the international principles of the Helsinki Declaration on Humane Treatment of Animals, the Principles of Humanity set out in the European Community Directive (86/609/U), Directive 2010/63/EU of the Europen Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes.

Before the tests on female rats began, the animals were kept separately during 21 days to avoid accidental pregnancy. Female rats suitable for experiments were selected in the following manner: for the duration of two weeks, vaginal smear samples were taken from animals on a daily basis, for cytological evaluation of the estrous cycle. Females with a regular estrous cycle (4-5 days) were selected. Animals with an impaired estrous cycle were excluded from the study. All animals were at diestrus phase at the start of the experiment.

The female rats were divided into four groups as follows: two control and two experimental groups, 10 females in each subgroup. The experimental groups consisted of 12-month old animals, which were subjected to daily morning saffron extract administration at the dose of 120 mg/kg for a course of 14 days (the 1st experimental group) and 21 days (the 2nd experimental group). Control groups included 6-month-old (the 1st controls) and 12-month old (the 2nd controls); animals were treated with physiological saline in the same manner.

Male rats were divided into 3 groups: the 1st group included intact animals, the 2nd group (control) included animals that received physiological saline, the 3rd group (experimental) included animals that received the saffron extract at the dose of 120 mg/kg for 21 days. The saffron extract and the physiological saline were administered to animals *per os* using a thin metal probe.

The follicle-stimulating hormone (FSH) blood test was performed after finishing treatment course. Upon completion of the experiments with saffron extract administration, the blood samples were collected from animals of the control and experimental groups. The blood testosterone level was studied on the 7th, 14th and 21st days of administration of the saffron extract. For the indicated time intervals, the blood sampling was carried out in the male rats of the control and experimental groups. Procedure was conducted in the morning (9-10 a.m.), blood was obtained from the tail vein under light (1 min) diethyl ether anesthesia. The level of FSH and testosterone was determined in the blood serum using hormonal test kits for enzyme immunoassay *in vitro* for mammals ("Pishtaz", Iran).

Data analysis was performed using Microsoft Excel statistical package. Statistical significance of differences was proven by Student's t-test.

## 4. Results and Their Discussion

The results of the experiments revealed significant differences in the blood level of FSH between the control groups, reflecting age-related variation in hormonal production. In this case, the level of FSH was 0.7 ± 0.04 IUL/L

in the 1st controls vs 1.13 ± 0.05 IUL/L in the 2nd controls. Referring to previously published data, a decline in sex-motivated behavior in Wistar rats is observed at the age of 18 months [4]. Observed natural signs signalling the ageing of reproductive systems in 15- to 18-month old female rats are the following: short estrous cycles disappear, long ovulatory cycles prevail (more than 7 days), regular cycles gradually transit to irregular cycles and the syndrome of constant estrus develops, that ultimately turns into anestrus. Premenopause and menopause are characterized by a significant and stable increase of FSH in the blood level. An increase of FSH level in the rats of the 2nd control group may be due to the appearance of the first signs of the reproductive system ageing.

An analysis of data obtained in the course of the experiments with female rats showed (Figure 1) that 21-day treatment with saffron extract led to almost 33% decrease in FSH level in the animals from the 2nd experimental groups as compared to the same age rats of the 2nd control group ($p < 0.01$), and brought it closer to the level that was noted in the 1st control group, that included 6-month old animals.

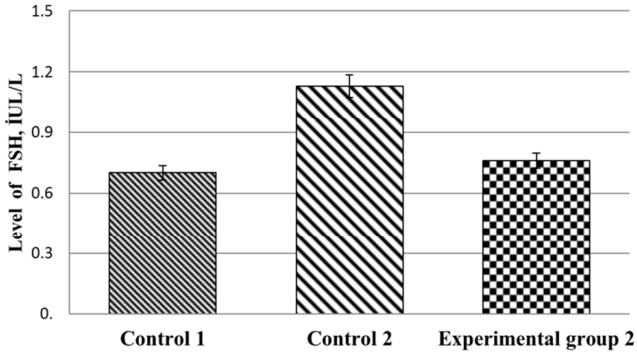


***Figure 1.*** *The level of follicle-stimulating hormone (FSH) in the serum in the female rats of both control groups and the 2nd experimental group.*

* $p < 0.01$ - differences in the group with the index in the rats of the 2nd control group

The results of this study clearly exhibited, that the saffron extract in a 21-day treatment regimen brought the FSH blood level of 12-month old female rats to the reference values of younger age. Given that FSH regulates the development, growth, pubertal maturation and reproductive processes of the body, the obtained data allow to surmise that the administration of saffron can help to slow down the age-related changes in the female reproductive system.

***Table 1.*** *The serum testosterone level in male rats under saffron extract.*

| Groups | Testosterone, IU/L | | |
|---|---|---|---|
| Intact | 1.35 ± 0.44 | | |
| | 7th day | 14th day | 21st day |
| Control group (saline) | 1.35 ± 0.44 | 1.38 ± 0.22 | 1.4 ± 0.24 |
| Experimental group (the saffron extract) | 1.38 ± 0.22 p<0,05 | 1.42 ± 0.14 p<0,05 | 2.27 ± 0.28 p<0,001 |

Analysis of the obtained results showed that the use of saffron extract for 21 days led to a statistically significant increase in the level of total testosterone in experimental animals. The initial testosterone content in control animals was 1.35 ± 0.44 IU/L. After 7 days of taking saffron extract, it reached 1.38 ± 0.22 IU/l. ($p<0.05$) (see Table 1). Consecutive changes in the total testosterone content occurred as follows: on day 14 of saffron extract treatment, the testosterone concentration was 1.42±0.14 IU/L ($p<0.05$); on day 21 of saffron extract administration it reached the point of 2.87±0.28 IU/L ($p<0.01$). It is noteworthy that the difference in testosterone levels on day 7 and day 21 of the treatment are statistically significant ($p<0.001$) (see Table 1).

Having evaluated the results, we conclude that the administration of saffron had an effect both on the level of FSH in treated female rats. In this case, saffron treatment significantly lowered the blood level of FSH in 12-month old female rats. Administration of the extract to male rats raised their sexual motivation and had positive influence on the serum testosterone level.

Therefore, saffron extract application adds to maintaining of the reproductive functions of the body, which is biologically significant.

# 5. Conclusion

The unique chemical composition of saffron is rich with carotinoids, flavonoids, many vitamins, quite a number of amino acids (including the essential ones), microelements and others provides a wide spectrum of its biological effect, including antioxidizing, directed to different structural, metabolic and regulatory systems of organism [15]. The positive effects of saffron revealed in the course of this study can be explained by the direct effect of saffron and its components on the sex glands and the central nervous system.

Some literature evidence indicate that saffron extract is used for the treatment of moderate depression [16]. Similar to the action of antidepressants, safranal, one of the main elements of saffron, inhibits the reuptake of serotonin and acts as a mild psychoactive agent [17], contributing to the normalization of the functions of the hypothalamic-pituitary-ovarian system.

Our study showed that oral administration of the saffron extract at a dose of 50 mg /kg stabilized certain parameters of lipid metabolism, specifically, total lipids (TL), triglycerides (TG) and total cholesterol (TC). Henceforth, the administration of the saffron extract to animals receiving high-calorie diet promoted their weight loss, and reduced their blood levels of TL, TG and TC, compared to similar indicators in untreated animals [18], ultimately leading to lipid metabolism normalization.

Also, Verma SK, Bordia A. in their study noted that a dose of 50 mg of saffron stigmas dissolved in milk, administered twice a day, reduced the susceptibility of lipoproteins to oxidation both in healthy controls and in patients with coronary heart disease [19]. It is widely recognized, that lipoproteins are the transport forms of cholesterol. As cholesterol participates in the synthesis of vital hormones and all steroids, including testosterone and estradiol, as well as in the formation of cell membranes structure, its delivery to the body's peripheral tissues plays a key role. Saffron's ability to

regulate lipid metabolism and reduce lipoproteins oxidizability may be one of the mechanisms behind the biological effects of saffron.

Taking into consideration that the imbalance of the neuroimmunoendocrine system lies at the base of premature aging, the effects of saffron on neuroendocrine relationships are of principal importance for the theory as much as the practice of the anti-aging medicine. Overall, the new findings of diverse pharmacological effects of the saffron extract open new horizons for the development of scientifically corroborated recommendations for application in practical medicine as a potential phyto-geroprotector.

# References

[1] Safarova G. L. (2009) DEMOGRAPHY OF AGING: CURRENT STATE AND PRIORITY-DRIVEN RESEARCH DIRECTIONS. Advances in gerontology. 22 (1): 49-59.

[2] World Population Prospects: The 2008 Revision Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat. June 2009.

[3] Mustafina O. E., Somova R. Sh. (2015) SOME RESULTS OF MOLECULAR GENETIC RESEARCHES OF AGING AND LONGEVITY. Advances in gerontology. 28 (1): 11–26.

[4] ANDREEVA E. N., SHEREMETYEVA E. V., GRIGORYAN O. R. (2020) Environmental factors and menopause. Russian Journal of Human Reproduction 26 (4): 14-21.

[5] Wu D., Gore A. C. (2010) Changes in androgen receptor, estrogen receptor alpha, and sexual behavior with aging and testosterone in male rats. Norm. Behav. 58 (2): 306-316.

[6] Minici F., Tiberi F., Tropea A. et al. (2007) Paracrine regulation of endometriotic tissue. Gynecol. Endocr. 23. (10): 574–580.

[7] WHO monographs on medicinal plants, Widely used in the Newly Independent States (2010) World Health Organization: 464.

[8] Salahshoor M. R., Khazaei M., Jalili C., Keivan M. Crocin Improves Damage Induced by Nicotine on A Number of Reproductive Parameters in Male Mice (2016) International Journal of Fertility and Sterility 10 (1): 71-78.

[9] Khayatnouri M., Safavi S. E., Safarmashaei S., Babazadeh D., Mikailpourardabili B. (2011) The effect of Saffron Orally Administration on Spermatogenesis Index in Rat. Advances in Environmental Biology, 5 (7): 1514-1521.

[10] Shamsa A., Hosseinzadeh H., Molaei M. et al. 2009 Evaluation of *Crocus sativus L. (saffron)* on male erectile dysfunction: a pilot study. Phytomedicine 8 (16): 690-693.

[11] Hosseinzadeh H., Zeall T., Sadeghi A. (2008) The effect of saffron, *Crocus sativus stigma*, extract and its constituents safranal and crocin on sexual behaviors in normal male rats. Phytomedicine 15 (6-7): 491-495.

[12] Modaresi M. Messripour M., AsadiMarghmaleki M. et al. (2008) Effect of saffron (Crocus sativus) extract on level of FSH, LH and testosterone in mice. ZUMS Journal 16 (63): 11-18.

[13] Ai J., Nekooeian A. A., Takhshid M. A., Mostafizi N. et al. (2009) Effect of Aqueous Extract of *Crocus sativus L. (Saffron)* Stigma on Serum Levels of Gonadotropins and Folliculogenesis in Adult Rats. Journal of Applied Animal Research 35: 49-52.

[14] Agha-Hosseini M., Kashani L., Aleyaseen A. et al. (2008) *Crocus sativus L. (saffron)* in the treatment of premenstrual syndrome: a double-blind, randomized and placebo-controlled trial. BJOG 115 (4): 515-519.

[15] Abdullayev F. I. (1993) Biological effects of saffron. J. BioFactors 4: 83-86.

[16] Akhondzadeh S., Fallah-Pour H., Afkham K. et al. (2004) Comparison of *Crocus sativus L.* and imipramine in the treatment on mild of moderate depression: a pilot double-blind randomized trial [ISRCT N 45683816] // BMC Complement Altern. Med. 2: 6771.

[17] Georgiadou G, Tarantilis PA, Pitsikas N. (2012) Effects of the active constituents of *Crocus Sativus L.*, crocins, in an animal model of obsessive-compulsive disorder. NeurosciLett. 528 (1): 27-30.

[18] Hashimova U. F., Babaev Kh. F., Sadykh-zade R. A., Shukurova P. A. (2016) Potential anti-aging properties of saffron (*Crocus sativus, L.*) Vrach 6: 35-38.

[19] Verma SK, Bordia A. (1998) Antioxidant property of Saffron in man Indian J. Med. Sci. 52. (5): 205-207.