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A hormonal study of the effect of sesame oil in female albino rats whose ovaries had been removed

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Abstract---This study was conducted to investigate the physiological effect of sesame seed oil (*Sesamum indicum*) in the case of oral treatment on post-menopause and the occurrence of surgical menopause as a result of the removal of the ovaries, by studying the changes in some hormones in the blood serum of adult female albino rats (Albino Rats), as 15 adult rats about three months old, with weights ranging from 160-180 g, were used. The animals were randomly divided into three groups with five animals for each group. The first group represented the negative control, which was normal without removal of the ovaries, and the second represented the positive control that was removed. The ovaries were completely removed, and the third group completely removed the ovaries and treated them orally with sesame oil at a concentration of 4 ml / kg of body weight per day for 30 days. The results of laboratory tests for serum samples of the completely removed ovaries group compared to the negative control group showed a significant decrease ($P < 0.05$) in the levels of estrogen and progesterone, while an insignificant increase ($P > 0.05$) in prolactin levels was observed, and significant ($P < 0.05$) for follicle-stimulating hormone (FSH) and luteal stimulating hormone (LH). When the treatment with sesame oil, the tests showed a non-significant increase ($P > 0.05$) in the serum levels of all studied hormones, namely estrogen, progesterone, prolactin, follicle-stimulating hormone and luteinizing hormone. We conclude from this, that sesame oil has positive effects in the body by stimulating

an increase in the production and effectiveness of ovarian hormones and hormones of the anterior lobe of the pituitary gland.

Keywords---ovariectomy, sesame oil, hormones, rats.

Introduction

The demand for the use of drugs has increased strongly among different peoples as a result of the huge increase in the world's population and their frequent exposure to diseases, so synthetic chemical drugs were used instead of natural ones, and due to the emergence of harmful side effects from the use of manufactured drugs came the call for the need to return to medicinal plants and natural medicinal raw materials. Thus, medicinal plants have become a source of drugs and active substances that are included in the preparation of the drug in the form of an extract, active substances or raw materials for use in the treatment of many disease conditions such as cortisone, sex hormones, plasma substitute, and others. Among the blessings of God (Almighty and Glory be to Him) over His creation is the presence of medicinal plants that are a food and medicinal source for various diseases because the herbs or their plant parts contain chemicals of great benefit and importance due to their physiological and physiological effects and their therapeutic activity for humans and animals, and phytochemicals are micronutrients and biologically compatible elements. And it has extraordinary efficacy in treating multiple diseases with minimal or no harmful effect (1) (2). Some scientific research has directed the study of medicinal plants in order to investigate the role of antioxidants in these plants in order to prevent oxidative damage resulting from the reactions of radicals. Free in a number of pathological conditions, thus protecting the vital function of the cell (3).

The sesame plant (*Sesamum indicum*) stands out among those important medicinal plants that have several benefits, as sesame belongs to the Pedaliaceae family, and its cultivation is often spread in the tropical and subtropical regions of Asia, Africa and South America, and the word "Sesame" is derived from the word The Arabic "Simsim" (4), and it is also called in the Arab countries by this name "Simsim" (5), and it is also known by other names such as Al-Shamsham, Sheraj or Al-Serj, Jaljalan and Al-Saleet (6). Globally, it is also known as "Sesame" or "Simsim" in Asia and Africa (7). According to prehistoric studies, the cultivation of sesame was discovered in wild groups in southern Asia, and cultivation originated there around 2000 BC, specifically from the time of the Harappan civilization (8).

Sesame seeds and the oil extracted from them also have a potential power of great importance in treating female and male sexual problems and increasing the fertility of both sexes. The oil of this plant increases sexual orientation, stimulates the formation of sperms, increases their number and stimulates their movement, in addition to increasing the production of testosterone (9) (10) (11) (12). Other studies have confirmed this great role of sesame from a medical point of view in treating many Diseases and health conditions, including those related to dysmenorrhea, as well as disorders associated with menopause in females (13) (14) (15).

Materials and Methods

Various devices, tools and chemicals were used in this study, in addition to the ready-made kits obtained in the form of standard kits for the purpose of conducting the required laboratory tests. Experimental animals, represented by female Albino Rats, were three months-old adult virgins. Approximately, and with weights ranging between 160-180 g, they were obtained from the animal house of the Faculty of Pharmacy at Karbala University. The animals were housed in a miniature animal house that was prepared in the researcher's house, and the place was with specifications and laboratory conditions suitable for conducting the experiment, including ventilation, lighting, heating and cooling ..etc., the animals were placed in special cages for raising rats made of plastic and equipped with a clamped iron cover and equipped with special water drinking bottles with a nipple at the end. The floor of the cages was spread with a quantity of sawdust, which is replaced from time to time to maintain the cleanliness of the place and the animals. The pelt and the necessary drinking water were also given freely. The animals were left for two weeks to ensure that they are free of various diseases and to adapt to the conditions of the experiment before being subjected to the study, which is the removal of the ovaries and the treatment with sesame seed oil and the physiological tests that accompanied this study.

Sesame seeds were also used in this study, which are available in the local markets of Karbala governorate. Sesame seed oil was used in the experiment of the current study, and this oil was previously extracted according to the standard AOAC method (16), as the method of preparing seeds for the purpose of extraction included several different and sequential steps to extract the oil, this method was summarized by bringing a quantity of dry sesame seeds (seeds weighing 20 g and sizes ranged between 1-2 mm) and exposing them to direct sunlight in order to reduce the moisture content of the seeds and then grinding them well using an electric grinder, and the ground product is placed through a funnel Covered with a cotton tampon and inserted into the Soxhlet extractor, then 250 ml of hexane was poured into the round bottom beaker and connected to the extractor, The condenser was also connected to the extractor, and the rubber hose connected to the inlet of the condenser was connected to a water tap allowing water to flow in and out of the outlet hole, and a heater device was set at 70°C to provide heat to the bottom of the flask placed on the heating plate, with heating continuing for some time, it was observed The presence of a colored solution (sesame oil extract) in the bottle, then filter the resulting oil containing some sesame seed crumbs using a fine sieve, then this pure, pure oil was placed in a clean glass bottle, and this process was repeated several times for the purpose of obtaining the required amount of oil from For later use in dosing experimental animals.

The oil dose given to the experimental animals was 4 ml/kg body weight of the animal, which is the appropriate dose that could have the effective effectiveness to perform the purpose for which the oil of this plant was used (17). The treated groups of experimental animals (white rats) were dosed with sesame oil orally and on a daily basis for one month only (while ensuring that the oil reaches the stomach directly) after calculating the exact dose of oil in relation to the animal's body weight. The 15 experimental animals (female white rats) were randomly divided into

three groups with five replicates for each group, according to the following description (Fig. 1):

- The first group: is the negative control group called Sham, during which an operation was performed on the animal's abdomen (opening the skin and abdominal muscles only) without excision of the ovaries and closing the skin in the same way as for the removal of the ovaries, then giving a break for two weeks after the operation and then conducting tests after one month.
- The second group: The positive control group, in which a complete ovarian excision was performed, then a break was given for two weeks after the operation, then tests were performed after one month.
- The third group: The group treated with sesame oil by direct gastric dosing method after a complete removal of the ovaries, as the rats were dosed with sesame oil for one month after completely removing the ovaries and giving a break for two weeks after the operation.

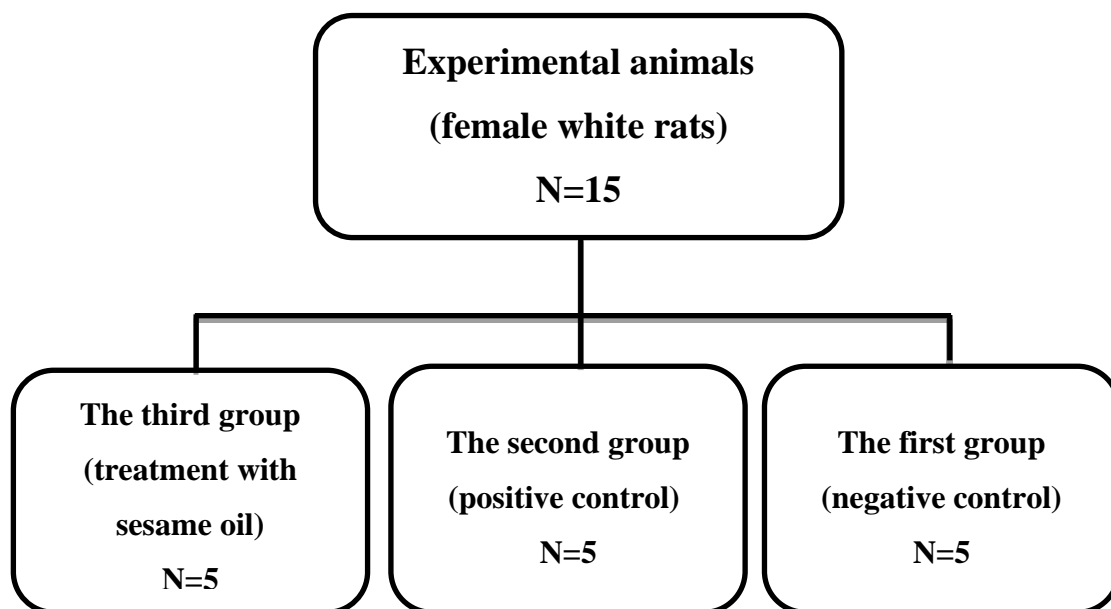


Figure 1. Experimental design

Ovaries were removed from female albino rats under sterile surgical conditions. The animals were anesthetized by general anesthesia by intramuscular injection. The rat was injected with Xylazine at a dose of 10 mg/kg body weight of the animal and ketamine at a dose of 50 mg. kg of body weight of the animal (18). 3-5 minutes after injecting the rat with the anesthetic, the rat was placed in a lying position on the back, then body hair was removed from the abdominal area, the area was cleaned and the area was sterilized with 70% ethyl alcohol. The middle abdomen is below the navel, as the skin, the abdominal muscles and the peritoneum were opened, and the intestines were pushed aside so that the uterus appeared clear. After following the uterus upwards from the right and left sides, the right and left ovaries were easily reached, after which the ovaries were removed using electric cautery, after connecting the uterine tube near the ovary twice with absorbable surgical thread. The abdomen (peritoneum and muscles) was made with absorbable surgical

sutures, type Cat Gut 0/3, by continuous suture method. The skin was also sutured with non-absorbable surgical wires type 3/0 and by intermittent sutures method (19), and finally the external wound was sterilized with iodine solution to prevent any infection. Ovaries were removed from all experimental groups except for the negative control group (Sham), where only the skin and abdominal muscles were opened (without removing the ovaries), and the area was closed in the same way as before.

After the procedure of removing the ovaries and dosing with sesame oil on the experimental animals, blood was drawn from the heart of the animal directly (after starving it overnight) while it was lying on its back using clean, sterile 5 ml medical syringes. 3 ml of the drawn blood was placed in marked plastic test tubes. Free of anticoagulant and containing gel tubes for the purpose of obtaining a sufficient and pure amount of serum in order to reach the best results, as the serum was separated from the blood mediated by a centrifuge at 3000 rpm for 15 minutes. With the use of ordinary plastic tubes (Plain Tubes), in which a certain amount of water is placed for the purpose of calibrating the centrifuge. The clear and free serum from the rest of the blood components was withdrawn by means of a micropipette, then the separated serum was placed in small, dry, marked Eppendorf Tubes. Conducting tests for measuring serum levels of the hormones estrogen, progesterone, prolactin, follicle-stimulating hormone and luteinizing hormone. The levels of these hormones were measured using the Enzyme Linked Fluorescent Assay Technique and using the (Mini VIDAS) device with the use of the numbers required for examination, and the principle of measurement was based on the method Enzyme immunoassay sandwich method with a final Fluorescent detection. The results of the current study experiment were analyzed according to the factorial experiment model and in a completely randomized design (Factorial Experiments with Completely Randomized Design), as the Least Significant Difference (L.S.D.) test was used under the probability level of 0.05, to show the significance of the differences between the different treatments (20).

Results and Discussion

- Estrogen level measurement:
The results showed a significant decrease ($P < 0.05$) in the estrogen level in the positive control case (represented by complete removal of ovaries) compared to the negative control group (Sham). While the results also showed an insignificant increase ($P > 0.05$) in the level of estrogen in the case of treatment with sesame oil for the group of complete removal of ovaries compared to the positive control group (represented by complete removal of ovaries).
- Progesterone level measurement:
The results showed a significant decrease ($P < 0.05$) in the level of progesterone hormone in the case of complete removal of the ovaries compared to the negative control group (Sham). While the results also showed a non-significant increase ($P > 0.05$) in the level of progesterone hormone in the case of group treated with sesame oil compared to the positive control group (represented by the complete removal of the ovaries).
- Measurement of the level of the hormone prolactin:
The results showed that there was a non-significant increase ($P > 0.05$) in the level of prolactin hormone in the positive control case (represented by

complete removal of the ovaries) compared to the negative control group (Sham). The results also showed a non-significant increase ($P>0.05$) in the level of the hormone prolactin in the case of group treated with sesame oil compared to the group of the positive control.

- Follicle-stimulating hormone (FSH) level measurement:
The results showed a significant increase ($P<0.05$) in the level of follicle-stimulating hormone in the case of complete removal of the ovaries compared to the negative control group (Sham). The results also showed a non-significant increase ($P>0.05$) in the level of follicle-stimulating hormone in the group treated with sesame oil compared to the positive control group (represented by complete removal of ovaries).
- Measuring the level of Luteinizing Hormone (LH):
The results showed a significant increase ($P<0.05$) in the level of luteinizing hormone in the case of complete removal of the ovaries compared to the negative control group (Sham). The results also showed a non-significant increase ($P>0.05$) in the level of luteinizing hormone in the case of group treated with sesame oil compared to the positive control group (represented by complete removal of ovaries).

Table 1
Effect of ovariectomy and treatment with sesame oil on some hormones
in female white rats

Parameter / (Unit)	Sham	Ovariectomized females	Ovariectomized females treated with sesame oil
Estrogen / (pg/mL)	1.62 A ± 32.30	1.21 B ± 11.09	0.97 B ± 13.51
Progesterone / (ng/mL)	0.53 A ± 5.95	0.31 B ± 3.88	0.24 B ± 4.04
Prolactin / (ng/mL)	0.25 A ± 3.70	0.30 A ± 4.09	0.29 A ± 4.19
FSH / (pg/mL)	0.01 A ± 0.177	0.02 B ± 0.205	0.01 B ± 0.219
LH / (pg/mL)	0.02 A ± 0.135	0.01 B ± 0.175	0.01 B ± 0.186

- The values represent the mean of five animals ± Standard Error.
- Different capital letters in the horizontal direction represent the presence of significant differences at the level of probability ($P<0.05$).

The ovary (one of the components of the female reproductive system) secretes steroid hormones, estrogen and progesterone, as well as sexual cells. These hormones are responsible for the growth of female reproductive organs, the emergence of secondary sexual characteristics, and the growth of mammary glands. The lining of the uterus thickens and fatty tissue increases (21). The significant decrease in the level of estrogen and progesterone hormones in the blood serum of female rats as a result of removing the ovaries from them, could be due to a loss in the manufacture and production of these two hormones as a result of the loss of the ovaries, which are the main center for the production of estrogen and progesterone, and consequently a decrease in their concentration (22) (23) (24) (25).

The results of the current study agreed with the study conducted by Hadi (26) on rabbits, which indicated a decrease in the level of estrogen hormone in the blood serum of rabbits with bilateral ovaries. Steroid production is significantly reduced in postmenopausal women as well as in women subjected to surgical removal of their ovaries, resulting in an increase in the levels of luteinizing hormone (LH) and follicle stimulating hormone (FSH), by means of a negative feedback mechanism. Between the pituitary and ovarian hormones to produce steroid hormones, FSH also rises due to the sharp drop in Inhibin (27) (23). The results also agreed with the studies of Kharode *et al.* (28) and Al-Saadi (29) regarding the increase in the level of FSH and LH hormones in the serum, which may be the reason for attacking the free radicals of the ovarian tissues and destroying the ovarian follicles in the ovary, and in the case of surgical removal of the ovaries in women, which is the main source of the hormone Estrogen, the level of this hormone decreases, thus showing the symptoms of menopause.

It is worth noting here, that the level of estrogen in the serum of rats reached low levels and did not completely disappear from the blood serum, due to the presence of other sources that manufacture it, but in a limited way, such as the adrenal cortex, while the other main sites for estrogen production are: tissues fatty (adipose tissue), skin (muscles) and others (30) (31) (23). The physiological imbalance of the ovaries in women with polycystic ovaries or other diseases leads to a decrease in the level of the hormones estrogen and progesterone, as a result of the imbalance in the gonadotropic hormones (32) (33) (34), and in addition, the levels of ovarian hormones in the blood serum decrease And significantly in the case of eradication of one or both ovaries. The significant decrease in the concentration of the hormone progesterone agreed with the results of the study of researchers Johnson *et al.* (35) and Yart *et al.* (25), which showed that the process of removing the ovaries led to a suppression in the periodic secretion of estrogen and progesterone, and this is definitely a result of the decrease in hormones due to the removal process because the ovaries It is the main source of secretion of these hormones. Also, the high level of LH hormone in the patients' blood serum was due to the decrease in estrogen and progesterone levels through the negative feedback mechanism (36).

The results of the current study are consistent with research and studies that indicate a coincidence between a decrease in the level of progesterone and an increase in the level of LH and FSH hormones, as a result of an imbalance in the function of the pituitary gland, which causes early ovarian impotence (37). The results show an increase in the level of female hormones, which include: estrogen, progesterone and prolactin in the blood serum of female rats dosed with sesame oil. Types of flavonoids in addition to being a type of plant estrogen (38), as quercetin stimulates the receptors of the prolactin hormone and releases it from the pituitary gland, thus increasing the secretion of this hormone (39). Amino acids play a major role in influencing the endocrine glands system, as Agiang *et al.* (40) indicated that sesamin, the main component in sesame oil, contains a plant estrogen that binds to estrogen receptors and increases the level of the hormone in the blood in addition to its role in an increase in the hormone prolactin.

On the other hand, it is not hidden, the indirect role of the amino acid tryptophan, which acts as a stimulator of serotonin, which in turn through its pathways

stimulates the hormone prolactin (41). The natural phytochemical compounds called sesamin on the one hand and Quercetin on the other hand have been compared with the commercial product Dimensional used to increase milk secretion. Thus, milk production increases (42). The results of the current study agreed with the study of Martin *et al.* (43) to know the effect of sesame seeds and oil on beta-estrogen receptors in the uterus, which are also present in the mammary glands, as it was noted that an increase in the number of cells expressing these receptors, which in turn affects the increase in the effect of estrogen (44). Another study demonstrated the effectiveness of sesame as an alternative hormonal treatment without side risks, as 60 g of sesame seeds were used to treat menstrual dysfunction (Oligomenorrhea) compared with the medroxy progesterone product, as it was noted that there was an increase in the rate of menstruation and an increase in estrogen receptors in the uterus (9).

On the other hand, the study of Mahabadi *et al.* (11) indicated an increase in the luteinizing hormone (LH) when using sesame, as this hormone in turn stimulates the secretion of progesterone (45), and as a result of the effectiveness of sesame in stimulating pancreatic cells, it increases The hormone insulin, which activates the hypothalamus pituitary gonads to stimulate the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), as these hormones affect the level of estrogen and progesterone in the serum (46).

Conclusion

The results of our study experiment indicate that sesame oil has positive effects in the body through stimulating the increase in the production and effectiveness of ovarian hormones and hormones of the anterior lobe of the pituitary gland.

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