Protective effect of some herbs extracts upon the gonad of born rats treated with anti depression fluoxetine

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ABSTRACT
Fluoxetine is an antidepressant widely used to alleviate mood disorders and anxiety disorders. Many studies suggest how antidepressants to treat depression in women with PCOS, in addition to its negative impact on the testis and testicular sperm in men. So, the objective of this study was to demonstrate the effectiveness of herbal extracts in the treatment of gonad treated with fluoxetine drug. In order to achieve that, white baby rats were divided with the age one month into two groups “The first treated with fluoxetine daily for one month with an oral dose (5 mg/kg) while, the second group was treated with a similar dose mixed with an aqueous extract of mixed set of herbs (ring, linen, Nigella, Neu, almond, anise and cinnamon). The results indicated the occurrence of polycystic ovarian syndrome in rats treated with the drug as most property damage to sperm cells leading to inhibition of sperm formation process. While, the herbal treatment with the drug to return to the natural composition gonads asymptotic for the control group also vanished from ovarian cysts liposome confirming the effectiveness of herbal extracts used in fertility treatment and raise.

KEYWORDS: Testicle, Spermatheca, Tail of epididymis, Spermatheca, Nigella satia, Oviduct, Uterus

INTRODUCTION
Antidepressants are medicines that address aspects of depression, evolved first in 1950 and used regularly since then. Today there are about 30 species of antidepressants used to alleviate mood disorders and anxiety disorders such as social phobia disorder and works by increasing the activity of certain chemicals within the brain of these substances called neurotransmitters. That send signals from one brain cell to other cells. These chemicals that play a role in depression called serotonin and noradrenaline some who take antidepressants have problems in the stomach and intestines. This has also caused [7] drugs, sexual problems may reduce sexual desire.

Fluoxetine is an antidepressant widely used, when used on two freshwater prosobranch molluscs: (Valvata piscinalis and Potamopyrgus antipodarum) the fertility is not affected [8], also confirms [9] that using the drug has led to improved social concerns, sexual concerns, fears, and the desire to have children, and a need for more parenting. Shahine and Lathi [10] disagree with those opinion, he stating that many women of childbearing age to take the property, despite the negative impact on the function of gonad.

While, Cochrane breen how antidepressants able to treat depression in women with Polycystic Ovary Syndrome (PCOS). when a disruption or malfunction of the hormones the ovary it is possible for a member of the disease PCOS. This imbalance is called Stein-Leventhal syndrome, which he described as a common hormonal disorder in women (about 6-10% of reproductive age) [23]. Aquat Toxicol (2009) examined the effect of Fluoxetine on reproduction and the results indicated that the disruption of reproduction of the low
levels of the hormone estrogen decreasing birth rate and significantly decreased levels of estradiol 17beta (E) ovarian hormones, hormone stimulus for the formation of vesicles (FSHR), hormone receptor (LHR) indicating that this was due to the negative effect of inflammation on the ovary which affected standards develop eggs. Possible mechanisms involved in the effect of this drug on reproduction is still unknown.

Results showed by Pawlowski et al., that, alflokstin dose of 5 mg/kg/day resulted in the proliferation of cells in a layer of granular cells in the ovary of female adult rat. Flokstin is an antidepressant prescribed widely and works physiologically as selective serotonin reuptake inhibitors (SSRI) and to determine their ability to disrupt reproductive function use fluoxetine at concentrations of 0, 0.1, 0.5, 1 and 5 µg/l for 4 weeks. Noted a significant changes were observed in egg production, fertility and ovulation rate, and hatching, however a birth defects have been observed at all concentrations of the drug. Also, reproductive glands in adult liver, increased plasma levels of estradiol in females significantly by 0.1 and 0.5. Olcese (1985), found when giving injections daily of fluoxetine (5 mg/kg) a decrease in testicular weight. Moreover, the animals showed signs of regression in the gonads. De Oliveira [15] stated that floxtin exposure has led to reduced body weights of testis in births. As wellas, the pipe tubes size of sperm and epithelial lining epithelium, cells decomposition were observed s

The results by showed a decrease in the weight of the seminal vesicle in sperm count. Moreover, reducing the number and tubes radius when babies affected by the fluoxetine drug. Gouvêa [16] study the effects of exposure assessment FLX on sexual behavior and testis in male rats, that treated every day, through the feeding tube, with 7.5 mg/kg FLX during pregnancy and lactation. There was no moral change in outcome measurement distance anogenital and testosterone concentration, testis weight, epididymis, seminal vesicle and the pituitary gland. While, the sexual behavior was not affected when treated with FLX. However, this exposure indicates low sex drive and is a classic side effects in people who eat these antidepressant drugs. Studying the impact of long-term ingestion alflokstin on fertility in male mice(adult male mice exposed to fluoxetine when concentration of 200 mg/kg for 60 days). This Caused a significant decrease in sperm in vitro sperm from the testes and sperm density and decreased genital weights (testes, epididymis, seminal vesicle). Hormonal examination also showed a significant reduction in levels of testosterone and FSH levels. Testicular also showed a decline in the number of sperm in primary and secondary system. The number of female rats that got pregnant by male rats long-term treatment with the flokstin, as the number of live fetuses and uterine implantation rate, as well as, a slight decrease in body weight. These results confirm that taking fluoxetine has a negative effect on fertility and reproductive system in male rats. Therefore, we must further study to investigate the effect of treatment with the drug long term fertility.

Recent studies have shown adverse effects on male reproductive system after treatment with flokstin. Rats were treated orally with fluoxetine (5, 10, and 20 mg/kg) for 13 days from pregnancy to breastfeeding 21 days. The results showed in births at age 90 on a decrease in the weight of the testes (16%), Epididymis (28%), spermatheca (18%) in animals exposed to flokstin 20 mg/kg compared to control. The seminal epithelium decreased 17% total cells edge 30% reduction in the risk group with flokstin at 20 mg/kg. Furthermore, reduced Leydig-cell 29% at 5 mg/kg group. Sperm pipe length reduction of 17% and decreased sperm production in the risk group with flokstin at 20 mg/kg. Because of the side effects caused by the use of medications used herbs and plants as alternative treatment and security of traditional medicine for the treatment of various diseases, including infertility and impotence [31]. Cinnamon belong to the family Lauraceae, cinnamon bark is used widely in spice because of its fragrance and was used to treat impotence and frigidity [24]. Bolin (2010) illustrated that the improvement of patients with ovarian syndrome of multiple pouches when you use cinnamon and sweet almond is considered safe when taken by mouth. Sweet almond may lower blood sugar levels. So that has estrogen-like activity. Apricot rich diet may have a preventive role on histopathological changes caused by alcohol in rat testes [6].

Flax Seed belongs to flax family Linaceae and helps to reduce the growth of breast cancer cells. The study by DILSHAD, [22] showed that the use of flax seed delayed puberty in cows and Buffalo. Ali, illustrated that Palm pollen (Phoenix dactylifera) belong to the family Arecaceae, Palm is called the tree of life by the Arabs, it is a good source of protein, amino acids, vitamins, and dietary fiber, fatty acids, enzymes, hormones, minerals and used to enhance the reproductive function and fertility in male laboratory animals [26] and used by ancient Egyptians to stimulate and increase the fertility of females. Rasha et al. [30] showed results of the fenugreek seeds led to an increase in the rate and primary and secondary follicles diameter and yellow objects has led to improved fertility in female mice in aggregates treated with the extract of fenugreek compared with control group. The results of Mabrouk [1] to the extract of Nigella sativa reverse biochemical changes caused by totally lead to control values, is very effective in preventing bullets that cause oxidative stress in testicular.

[2] indicates that black seed can modify the properties of the sperm where its antioxidant activity in rats. Therefore the aim of this study was to demonstrate the effectiveness of herbal extracts in the treatment of gonad treatment drug fluoxetine.
MATERIALS AND METHODS

The rat was divided into two groups at the age of one month "the first group was treated by an oral dose (5 mg/kg) of fluoxetine for one month, while the second group was treated with a similar dose of previous group mixed with a similar dose of an aqueous extract of mixed set of herbs (ring, linen, black seed, date, cinnamon, almonds and anise)."

RESULTS AND DISCUSSION

Testicle:
Deformation of tubes and lack of sperm were observed, as well as epithelial cell disorder in neutered rats treated compared to control one. Where, vanguard sperm separated from sperm cells in some tubes and sperm cells clash, differentiated vanguard, empty cavities of sperm as noted gap decomposition and sertoli cells disintegrate were observed. Cold plasma and cells interface fabric ledge and filled in the gaps as the tubes lost their spherical or oval as a result of contraction, increased thickness of the basal membrane and its susceptibility to pigmentation and vacuum interface with loss of germ cells by eosinophilia shows some sperm cells where heightened pigmentation cytoplasm by eosin.

Tail of epididymis:
Tail of epididymis explains the small size bore channel epididymis and low sperm count compared to control subjects and enclosed epithelial in some warped in the other. Where, an event epithelial dissolution and increased thickness as well as, not to distinguish cell boundaries and crash edge.

Spermatheca:
Spermatheca found at histological examination fuse sperm of male rat of group treatment mucous layer creases Palace overlooking the cavity and the small size of the cells of the mucous layer and size of nuclei was nominated few lymphocytes epithelial mucosa and lack of secretory material limited by sperm sacs cavity. Also, abnormal cell proliferation in the basal portion epithelial muscle layer surrounding hyperplasia and follicular banoeh cells appear large and analyzes the air clear cytoplasm in some areas.

These results support the hypothesis that, serotonergic function change caused by inhibition of the gonads effect property on gonads, testes in particular as stated (Olcese (1985 in male hamsters). As well as, confirmed [15] the capacity property to cross the placenta barrier milk which may prevent and delay the development of testis in infants and in turn adversely affects the installation of testicular and sperm at puberty, indicating that exposure to fluoxetine cross the placenta and during lactation could affect testosterone and testicular weight in addition to installation epididymis and spermatheca, sperm production and fertility in males at puberty [18]. These results are consistent with results of which showed a decrease in the weight of the seminal vesicle in sperm count. Agrees with Bataineh, and Daradka [17] which confirms the effect of the drug on the testis, epididymis and spermatheca, where led to significant low sperm count and low weights as the impact on fertility and birth number. While, [16] find the effects of exposure to sexual behaviour and FLX testis, epididymis and spermatheca in born in male rats, that there was no moral change in the gonads, testosterone concentration, testis weight, epididymis, seminal vesicle and the pituitary gland and the superiority of fluoxetine in reducing depression leading to infertility [9].

Ovary:
The presence of bleeding fabric-full Graf vesicle deformation and developing follicles that turned each into vesicles where the egg is fully decomposed led to filling the blanks fabric use decomposition result of flx to polycystic ovarian vesicular ovarian cysts. Also, appeared outside and lack of yellow body ovarian characterized by an accumulation of algribet bags and an increase in the thickness of tissues and a number of small bags ranging from (6-10) or more bags and diameter (4.7 mm) surrounded by layers of follicle cells bloated the sacculated-vesicular.

Oviduct:
The damage was less so still watching cells lining her vertical ciliaryintact despite some deformation and the disappearance of her eyelashes and muscle layer coated with the emergence of inflammatory cells and analyses led to the emergence of gaps in the fabric.

Uterus:
Uterus lack of muscle layer thickness increase uterine glands container class that some garbled installation resulting in a narrow uterine cavity with vertical epithelial lined. These results are consistent with the results of both emphasized the negative impact of the drug on the reproductive endocrinology [3]. (How antidepressants to treat depression in women with PCOS) reasons for its occurrence genetic predisposition, hormonal
imbalance, stress and reflected the influence of fluoxetine on sex hormones of ovarian estrogen and hormone stimulus to the growth of follicles (FSHr), catalyst for growth hormone yellow body (LHr) indicating that this was due to the influence of downsize to inflammation on the ovary which impact on ovulation and fertilization rate. and contradict us opinion [8] reported no fertility treatment sower property on the contrary confirms [9] that use of the drug has led to improve sexual fears. As indicated by [19] as found in the treatment group of infertility caused by depression drug fluoxetine pregnancy ratio in the treatment group 14 times higher than the control group and a Gynecol [10] opinion stating that, many women of childbearing age to take the property, despite the negative impact on the function of gonad these results confirm that taking fluoxetine has a negative effect on fertility and reproductive system in the born in mice hence, there must be further study to investigate the effect of treatment with the drug’s long-term fertility.

**Secondly, treatment and herbal extract:**

Generally, it was noted the return to normal tissue completely natural composition approach emerged healthy testicle installation and the sperm pipe density increased and sperm but enumerate more than normal. Also, returned to normal epididymis filled up with sperm as sound sound popping spermatheca. Ovarian appeared slim installation completely disappeared the bags inside and outside the ovary and follicles developing increased as good had Graf vesicle composition. As well as, the corpus luteum also appeared on both of the oviduct and uterine sound installation also, due to the characteristics and advantages of the herbs used where the volatile oils of anise to increase total protein and triglycerides, glucose concentration of some ions of the plasma has an effect similar to estrogen and named this compound dianethole or phytoanethole or plant estrogen and therefore not recommended for use during pregnancy of estrogenic effect [29] and has an impact in facilitating the delivery and regulation of the menstrual cycle [25,27]. concluded that doses (43 mg, 68 mg/kg BW) of anise on the male rats resulted in a marked improvement in the ability to procreate, and that explains the impact of treatment on sperm, perhaps through hormonal regulation via the pituitary gland axis. Mahood [25] mentioned that the dose 200/400 mg/kg of anise stimulate ovulation which led to stimulate progesterone synthesis in and a resulting inhibition of the LH surge. The extracted oil of aniseed plant reduces signs of PCOS in ovarian tissue helps LH secretion in mice. Albinine is the most active element in the anise and represents 85% of essential oil. Therefore, the effectiveness of estrogen due to a albinine (dianethole, photoanethole), while dopamine is effective in inhibiting prolactin secretion. Estrogenic effect was anithol on the reproductive system of female rats, others very few notes appear, such as increasing the weight of the ovary to the uterus. Increased ovarian weight in this study may be attributed to the incentive effects of anithol granule cells in the ovary where it stimulates the follicle addo and accelerate the processes of maturation in different stages of liposome. In addition to increasing the duration of blood and metabolic rates. However, can be attributed the significant increase in the weight of the uterus to the direct impact on anithol split cells [27].

Mahood [25] pointed out that, the use of 200/400 milligram/kg of extracted oil of aniseed caused a significant increase in ovarian weight. He said that compounds in the extract of anise promotes proliferation of oxygen in the tissues, and increase ovarian weight due to a rise in the number of small and medium-sized sacs (vesicles) and cut the darn small and medium-sized sacs apparently influence the ovary of aniseed high antioxidant polyphenolic compounds. Many studies confirmed that cinnamon has no effect in the treatment of pathological conditions affecting the female reproductive system, used when bleeding in the uterus after childbirth and fertility treatments, infertility in women and men, inflammation and fibrosis of uterus, ovarian abscesses, delayed menstruation, pain and taken in India after birth as pregnancy and due to the presence of a turbine in its essential oils [32]. Also, proven Kort (2014) through its study that cinnamon supplementation improves menstruation, and can be an effective option to treat some women with PCOS. Flax (Flax Seed) is helping to organize the androgen levels in women with Polycystic ovaries, and increase fertility [20]. In addition the extract of of Palm pollen contains astroginih materials that have a role in motivating a members, more than the total number of hovers and focus all of the hormone tstitiron, Palm pollen has the qualities that enabled him to resist infections and increase immunity. In addition, it contains a substance similar to the estrogen Estradiol. As well as, its ability to stimulate the ovaries so that estrogen affects the process of ovulation events as a result of its impact on the effectiveness of the hormones (Follicl Hormon Stimulating (FSH) hormone LH (Luteinizing Hormon (LH))). The Palm pollen contain estrogen which regulates stem cell formation process of male reproductive tissues and hovers, who during the astrogin receptors of the male reproductive system. Ring led to an increase in moral level of hormones (prolactin, LH, FSH). Also, found that the ring contains a Galactotogue is a factor that stimulates the secretion of milk and dairy glands of ductal nursing through breastfeeding to regularly increase der milk plant seed oil also ring estrogenic effects, the pattern may influence by increasing prolactin Hormone receptors and thus increase the growth lactic glands. aldisogneyen material found in the ring as raw material synthesis and preparation of sex hormones artificially. components Steroidal sapogenin steroid SOAP found in fenugreek seeds are also photosynthetic prokaryotes of steroidal hormones such as estrogen formation wallbrogistron walsteroidat anti-inflammatory such as [31,3].
Nigella sativa:

*Nigella sativa* is effective in reversing tissue damage induced by ischemia in ovaries. Thymoquinone is the major active component derived from *Nigella sativa*. Methotrexate is a folic acid antagonist widely used in clinic. The result show that Administration of thymoquinone reversed histological changes of methotrexate significantly. We suggest that thymoquinone use may decrease the destructive effects of methotrexate on testicular tissue of patients using this agent. [4,1]

*Prunus armeniaca* L (apricot), rich in carotenoids and vitamins, is a potent natural antioxidant. We hypothesized that an apricot-rich diet might ameliorate the detrimental effects of low-dose x-rays on testis tissue. The protective effects were prominent when the diet was maintained throughout the time course and were partially protected when the diet was initiated after exposure. The natural antioxidant activity of apricot ameliorates the delayed detrimental effects of low-dose irradiation on testis tissue. The high total antioxidant capacity of the apricot deserves further investigation [5].

Transverse sections (T.S.) of Testicular of male rate for control group

**Fig. 1:** Seminiferous tubules circular shape and show a clear interface between them and the fabric and surrounded by a layer of fibrous connective tissue (arrow) (H & E; x40).

**Fig. 2:** Alanabyib sperm glass show where the sperm inside the cavity (arrow) (H & E; x 100)

Transverse sections (T.S.) of Testicular of male rate for treatment group

**Fig. 3:** A sharp secession in Alanibbat (shares) and deformation seminiferous tubules and the widening distances (arrow) (H & E; x100)

**Fig. 4:** Integration and deformation germ cells and analyzed and epithelial cell death Hanfsal class The aneurysm (arrow) (H & E; x400)
Fig. 5: Anfsal connective tissue of the wall tubules and analyze the cells Ledge (arrow) and deformation Mmaady to cell death (arrow) (H & E; x400)

Fig. 6: Hemorrhage sharp Alanibbat wall between sperm and necrosis and cell death and decomposition Alespermat (arrow) and analyze the cells from the wall Srtola Alagnebh (arrow) (H & E; x400)

Fig. 7: Severe deformation in the wall of epithelial and deformation and increase the thickness of the epithelium and the decomposition of the inner layer and the separation of neighbor Internal Anibbat (arrow) (H & E; x400)

Fig. 8: The presence of bloody nominated Anbibat between sperm and peel off the wall in Alanibiat and analyzed x100 germ cells and the death of sperm (arrow) (H & E; x400)

Fig. 9: Existence between recession bloody Anbibat sperm and peel off the wall in Alanibiat and analyze the cells Srtola (arrow) (H & E; x400)

Fig. 10: Analyzes the wall of death Anibbat sperm germ cells initial decomposition cells Ledge between Alanibbat and death Alespermat and detachable Sertoli cells) (arrow) (H & E; x400)
Transverse sections (T.S.) of Testicular of male rats for treatment group

**Fig. 11:** Distort the shape Alagneb sharp and death in Htnkerz cell nuclei (arrow) (H & E; x400)

**Fig. 12:** Analyze and cell death and decomposition Alespermat sharp and deformation of the germ layers (arrow) (H & E; x400)

Transverse sections (T.S.) of Testicular of male rats for treatment group

**Fig. 13:** Necrosis nuclei and cell death and change the thickness of the epithelial layer and the separation of germ) (arrow) (H & E; x400)

**Fig. 14:** Sharply nominated bloody Alanyibat between sperm separation and change the shape of epithelial tubules) (arrow) (H & E; x400)

Transverse sections (T.S.) of the epididymis of male rats for control group

**Fig. 15:** Cross-sections appear in the form of a circular or oval clips) (arrow) (H & E; x 40)

**Fig. 16:** line the Btalaiah simple vertical or columnar of false normal) (arrow) (H & E; x 100)
Transverse sections (T.S.) of the epididymis of male rats for treatment group

Fig. 17: Tail of the epididymis appear distorted clips and variable formats (arrow) (H & E; x 400)

Fig. 18: Louhz lack of epithelial thickness of the culvert and increase grained positive Alraiqh pigmentation in cells and increase the membrane thickness of the grass-roots and its ability to pigmentation and free of sperm. (arrow) (H & E; x 400)

Transverse sections (T.S.) of the epididymis of male rats for treatment group

Fig. 19: Also found deformation Btalaiah channel and crash Bhafta brush border and is full Tjoifaa fluid secretory and cellular remnants and abnormal sperm (arrow) (H & E; x 400)

Fig. 20: Irregular thickness of the channel and the disintegration of epithelial Btalaiah and not to discriminate cells limits and the cavity is filled with remnants of cellular and animals is natural. (arrow) (H & E; x 400)

Transverse sections (T.S.) of Seminal vesicle of male rats for control group

Fig. 21: Seminal vesicle wall consists of external charge of connective tissue- 21- containing elastic fibers and thin casing of smooth muscle consists of a circular layer of the inside and outside of the long (arrow) ((H & E; x 400)

Fig. 22: Mucous layer be bent and many Alantinaat where tucks subdivided into primary and secondary (arrow) ((H & E; x 100)
Transverse sections (T.S.) of Seminal vesicle of male rat for control group

Fig. 23: Vertical glandular epithelial simple contain little of the basal cells, which is based on the basement membrane. (arrow) (H & E; x 100)

Fig. 25: Semen shows clearly within the lumen of the vesicles (arrow) (H & E; x 100)

Transverse sections (T.S.) of Seminal vesicle of male rat for treatment group

Fig. 26: Palace mucosal folds class overlooking the cavity and increase the thickness of the special class, which has been (arrow) (H & E; x 400)

Fig. 26: Associated lack of high mucous layer Bahoislat sperm (arrow) (H & E; x 400)

Transverse sections (T.S.) of Seminal vesicle of male rat for treatment group

Fig. 27: Small size of the mucous layer and the size of the nuclei and the lack of vesicles value and content of granular cells (arrow) (H & E; x 400)

Fig. 28: Nominated limited lymphocytes mucous and lack of limited materials secretory cavity seminal vesicles (arrow) (H & E; x 400)
REFERENCES


