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STUDY OF THE EFFECT OF MORPHINE AND GENISTEIN ON TESTOSTERONE HORMONE AND TESTICULAR TISSUE AT DIFFERENT PERIODS IN MALE LABORATORY MICE *MUS MSCULUS* L

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Abstract:

This experiment was conducted to find out the therapeutic effect of genistein as an antioxidant and anti-inflammatory in reducing the negative effects caused by morphine on the level of testosterone hormone and testicular tissue. 48 male laboratory mice divided into four groups were used. Each group included 12 mice, and the control group injected 0.1 M of normal saline. The morphine group was injected at a concentration of 20 mg/kg, and the genistein group was injected at a concentration of 25 mg/kg. Finally the morphine and genistein group that was injected with morphine at a concentration of 20 mg/kg for 15 days, and then injected with genistein at a concentration of 25 mg/kg for 15 days; Mice were injected once daily subperitoneally and divided into three periods (five, ten and fifteen days after injection). The results of the statistical examination showed a significant decrease in the morphine group in a period of 5 days, the morphine and Genistein group and the Genistein morphine group after 10 days, and the results showed a significant decrease at the probability level ($P<0.05$)) for the second treatment compared with other treatments during the fifteen days of injection .The results of the histological examination showed the presence of some histopathological changes compared to the control group, where the results of the histological examination of the testicles five days after the injection showed the presence of necrosis in the seminiferous tubules, the decomposition of the primary sperm, and after ten days of the injection there was a lack of spermatogenesis with no development in animal production. The primary spermatozoa and the occurrence of necrosis in the seminiferous tubules and hyperpigmentation of the sperm cells, while the tests showed fifteen days after the injection the presence of severe necrosis of the spermatogenetic tissue and the complete loss of sperm production with the loss of development of the primary spermogenic cells

Keywords: Morphine ; genistein , testosterone hormone , testies tissue, histological changes

INTRODUCTION

Morphine belongs to the class of opiates, which are known as a group of medicinal compounds that have been frequently used in recent decades for therapeutic purposes or for ecstasy purposes. Ancient civilizations, such as those in Egypt, Greece, and Mesopotamia, wrote accounts of the opium poppy plant. which dates back to more than 4000 BC, which indicates that Neanderthals used it(Lima et al,2021)Friedrich Serturner, a German scientist, named the drug morphine after the Phoenician deity of dreams, Morpheus, and it was first isolated from opium in 1806. (Lee et al., 2020)

As research on the negative consequences of morphine has grown, it has been shown that abusing opiates produces free radicals, lipid peroxidation, and reactive oxygen, which are important in cell death through fat oxidation of exposed cells and can also lead to addiction and dependency (Ghasemi-Esmailabad et al., 2022). Morphine can also be harmful to one's sexual health because it has been linked to hormonal imbalance and hypogonadism in long-term users of both sexes. Men may have

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infertility due to weakened sperm or testicular functioning or indirectly from the testicular-pituitary axis, which controls the release of sex hormones (David and Kirby, 2022). It was wise to look for novel approaches to lessen the damaging consequences of morphine on those who get addicted to its usage in terms of their sexual health.

Throughout history, medicinal plants have been used to obtain chemical compounds that can bind to estrogen receptors and use them to prevent negative effects on the organism. Di-phenolic obtained from vegetable origins such as soybeans, peanuts, green peas, chickpeas, and alfalfa(Hameed Hassan et al,2016)

Because of its structural and functional similarities to estrogen, the chemical compound genistein, which is derived from beans and other legumes, is also known as a phytoestrogen. It interacts with estrogen receptors in various parts of the body, including the testes, and has a positive impact on reproductive activity by altering behavior. Sexuality, the structure and operation of the reproductive system, and enhanced gonadotropin-stimulating hormone production (Prihantoko et al., 2020).

Research indicated the role of genistein in inhibiting the formation of free radicals, lipid peroxidation and nitric oxide, as it has antioxidant properties and is considered an anti-inflammatory for cancerous diseases and non-alcoholic fatty liver disorders (Liu et al., 2017), as indicated by the study (Lecante et al.,2022) to the role that genistein plays in improving sperm functions, as it is of great benefit in treating cases of sexual weakness and sperm abnormalities when used in certain concentrations

MATERIALS AND METHODS

2-1: Experimental animals

Forty-eight male laboratory mice, *Mus musculus L*, belonging to the L/BALB strain, aged between 10–12 weeks and weighing 20–25 g were bred in the animal house of the Qurna College of Education-University of Basrah and kept in plastic cages covered with sawdust in controlled environmental conditions. Animals were freely access to feed and water (Aubaeed et al., 2020).

2-2: Experimenta design

The animals were divided into four groups, and each group included 12 mice, as follows: 1: The control group: received 0.1 M normal saline as an injection.; 2: the morphine group: these rats were injected with morphine at a dose of 20 *M*g/kg; 3: Genistein group: males of this group injected at a concentration of 25 mg/kg in; 4: A combination of morphine and genistein was injected with morphine at a concentration of 20 mg/kg for 15 days and then injected with genistein at a concentration of 25 mg/kg for 15 days ((Al-Salashur et al. 2019: Kuthati et al, 2021) Mice were injected once per day in the sub peritoneal membrane for 15 days and divided into three periods (five, ten and fifteen days after injection). At the end of each period, mice were anesthetized with chloroform and blood was drawn directly from the heart through a sterile 1 ml syringe, part of which was used for blood analysis. On the blood serum and its use in biochemical analysis, the testis was isolated for the purpose of histological study.

2-3 Measuring testosterone hormone level in the blood

Testosterone levels were measured using the method (Tietz, 1995), according to the competitive enzyme immunoassay.

2-4 Euthanasia and Histological examination

mice were anesthetized with ketamine/xylazine (3/1). Animals sacrificed, testes and ovary organs were immediately removed and dehydrated with graded concentrations of alcohol for embedding in paraffin. Thereafter paraffin-embedded tissues were sectioned on a microtome (Leica, Wetzlar, Germany) into 5-7-µm coronal sections, and they were mounted into silane-coated slides. The sections were stained with hematoxylin and eosin (H&E) according to genera protocol(Kathim and Al –Aitte ,2022) .

2-5 Statistical analysis

The results were statistically analyzed using an analysis test Analysis of Variance ANOVA)Analysis of Variance. The significance between averages was tested (ANOVA).List using the least significant difference test . At Significant Difference (L.S.D.).Using the program, $P < 0.05$. level of significance, Statistical Package for the Social Sciences (SPSS ver. 19).

RESULTS

3-1 The effect of treatments on sex hormones(testosterone hormones)

Table(1) shows a significant effect at the probability level ($P<0.05$) of the treatments during the different injection periods on testosterone levels, as the results showed a significant decrease ($P<0.05$) in the fourth treatment than the rest of the other treatments during the five-day period of the injection. The results of the current study also showed that there was a significant decrease at the probability level ($P<0.05$)) for the second and fourth treatments over the first and third treatments during a ten-day period of injection.The results showed a significant decrease at the probability level ($P<0.05$)) for the second treatment compared with the other treatments during a period of fifteen days from the injection, and the third treatment showed a significant increase compared with the first and fourth treatments, and the first and fourth treatments did not show any significant differences between them Below the probability level $P < 0.05$.

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When comparing the effect of the periods on the treatments in (Table 1), the results showed a significant decrease at the level of probability (P<0.05) in the second treatment during a period of fifteen days of injection, compared with two periods of injection of five and ten days of the experiment. The results showed a significant increase at the level of Probability (P<0.05)) in the fourth treatment during the ten and fifteen days of injection compared with the five-day injection period of the experiment under the same probability level.

Table (3) Explains the effect of treatment with morphine and genistein on the concentration of testosterone (average ± standard error n=8).

Type / Treatment	Testosterone *mg* |dl		
Time	5day	15 day	10 day
Treatment 1	^{a} ± 0. 6$3.7$	±0.9$3.5^{b}$	^{a} ±0. 7$3.8$
Treatment 2	± 0.8$3.1^{a}$	±0.9$1.21^{b}$	±0.8$2.36^{a}$
Treatment 3	^{a} ± 0.6$3.9$	^{a} ±1.1$4.8$	^{a} ±0.7$4.4$
Treatment 4	± 0.5$1.5^{b}$	±0.7$2.9^{a}$	2.5^{a} ±0.5

a, b The difference of letters indicates a significant presence at the probability level (P<0.05)

3-2 Effect of morphine and genistein on testicular tissue

3-2-1 control group

The results of microscopic examination of the testes of mice in the control group showed that they consist of seminiferous tubules that contain within them the cells that form spermatogonia, primary spermatocytes, and spermatides, as shown in Fig(1).

3-2-2 morphine group

The results of the histological examination of the testes of mice injected with morphine at a concentration of 20 mg/kg revealed some histopathological changes compared to the control group. The lysis and thickening of the thickened nuclei of primary spermatids as in the figure(2,3)

The results showed that ten days after the injection, there was a lack of spermatogenesis with no development in the production of primary sperm, and the occurrence of necrosis in the seminiferous tubules, hyperpigmentation of sperm cells, hyperplasia of the tubules, and narrowing of the seminal ducts as in the figure(4,5)

Whereas, fifteen days after the injection, the tests showed severe necrosis of the spermatogenetic tissue and complete loss of sperm production with loss of development of primary spermogenic cells and loss of normal tissue features of seminiferous tubules with degeneration and necrosis of secondary spermogenic cells with separation or The divergence of the adjacent seminiferous tubules as a result of degeneration and loss of intertubules, the accumulation of fatty droplets within the seminiferous tubule, hyperplasia and hyperplasia of the seminiferous tubules, as in the figure(6,7,8).

3-2-3 Genistein group

The results of the histological examination of the testes of mice injected with genistein at a concentration of 25 mg/kg showed the presence of some pathological changes compared to the control group. Normal condition and seminiferous tubules in normal condition, as in Figure (9,10)

While the ten-day period of injection showed the normal appearance of the testes, as it was observed that the sperms were normal and the tubules appeared in a normal manner with the presence of slight hyperplasia in a part of the sperm-generating tissue as in the figure (11)

Fifteen days after the injection, it also showed the appearance of seminal tubules and the production of sperm in a normal manner with the appearance of slight necrosis of the spermatogenetic tissue and cloudy degeneration of the cytoplasm as in Figure (12).

3-2-4 morphine & genistein group

The results of the histological examination of the testes of mice injected with morphine at a

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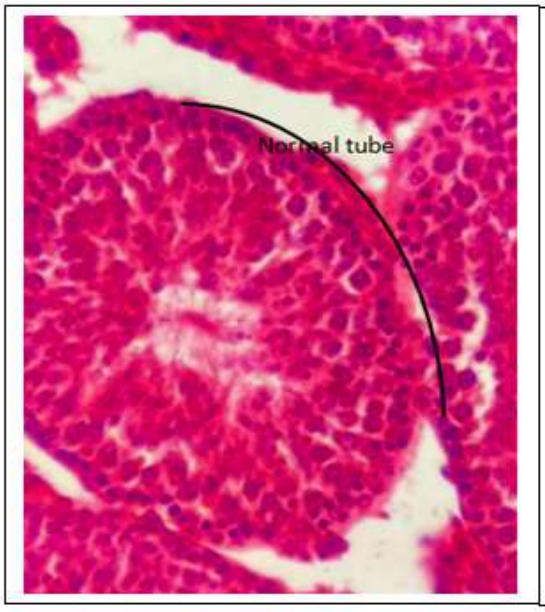
concentration of 20 mg/kg and treated with genistein at a concentration of 25 mg/kg showed a slight improvement in the shape and organization of spermatogenetic cells in the seminiferous tubules, with the presence of some pathological cases that still appear in the seminiferous tubules, which included degeneration Spermogenic tissue with rupture in some sperm-generating cells, degeneration in some primary sperms, accumulation of fat droplets within the tissue, severe necrosis of part of the spermatogenetic tissue, decreased production of sperm, and separation of the adjacent seminiferous tubules as in the figure(13,14).

Ten days after the injection, there was a noticeable improvement in the shape and organization of the sperm-producing cells in the seminiferous tubules and the appearance of the tubules in a normal manner, with some pathological cases that still appear in the seminiferous tubules, which included the presence of slight necrosis in some sperm-generating cells and the separation of the adjacent seminiferous tubules Leydig cells degeneration and necrosis(15,16).

While the results of the tests showed a clear improvement in the histological parameters of the seminiferous tubules treated with genistein after fifteen days of injection by observing the appearance of the seminiferous tubules naturally and the production of normal sperm and cells in the tissue Leydig in a normal state with the appearance of some pathological changes that were represented With the separation of the basal cells that generate sperm, noting that there is no necrosis, degeneration or exudation as in the figure(17, 18).



Figure(1) A cross section of the seminiferous tubule in the testes of the control group showing the normal growth stages of the sperm , H&E, 4X.

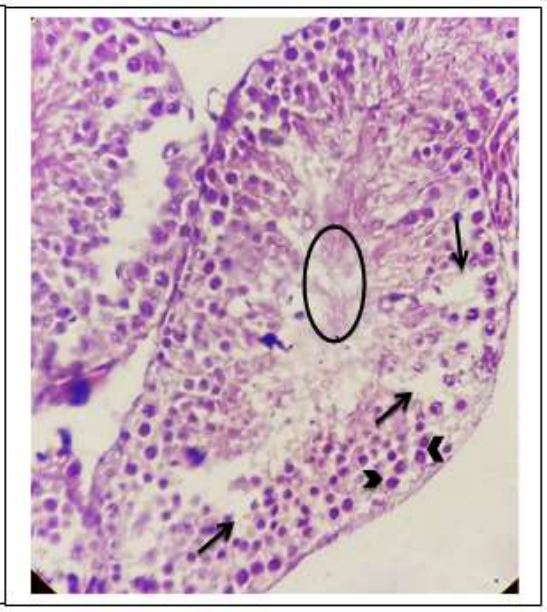


Figure (2) a section of the testes of mice injected with morphine during a five-day injection period necrosis of cells (black arrow) ,Sperm lysis(Circle),thickened nuclei (arrowhead),H&E,10X

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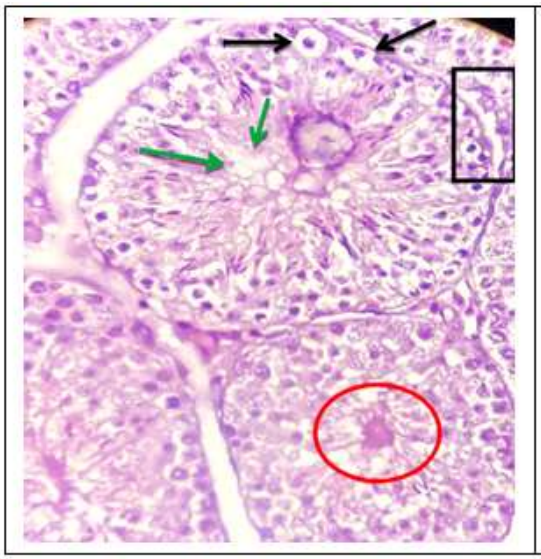

Figure (3) A section of the testes of mice injected with morphine during the five-day injection period shows: fatty droplet accumulation (green arrow), cytoplasmic rupture (black arrow), seminiferous tubule detachment (black square), sperm degeneration (red circle).H&E, 40X.

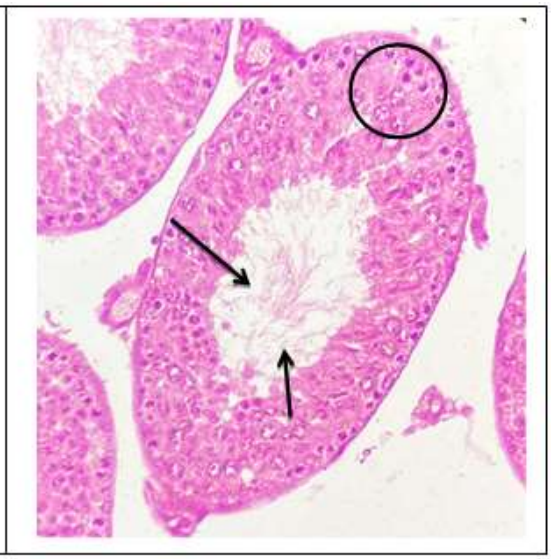

Figure (4) A section of the testes of mice injected with morphine during a ten-day injection period showing: decreased spermatid differentiation (circle) and decreased sperm production development(arrow),H&E,10X.

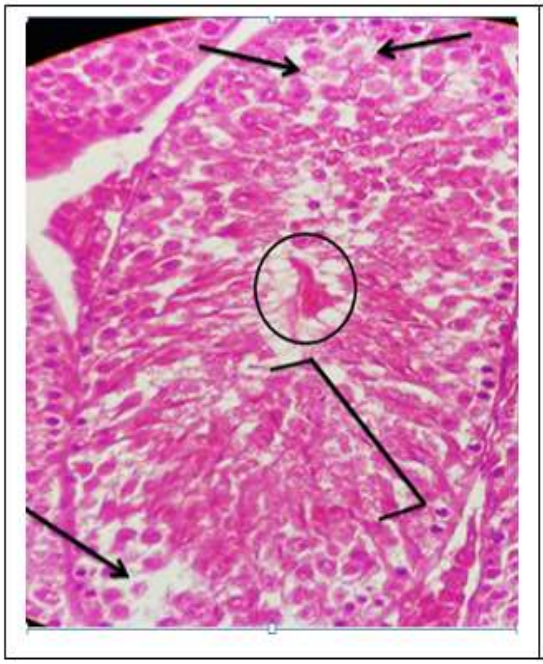

Figure (5) a section of the testes of mice injected with morphine during a ten-day injection period showing: cell necrosis (black arrow), hyperpigmentation of sperm cells (circle), hyperplasia and narrowing of the seminiferous tubule ducts (straight line).H&E,40X .

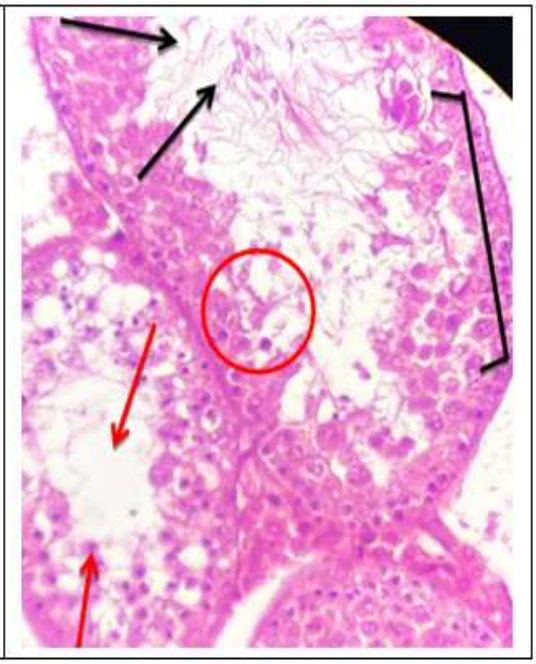

Figure (6) a section of the testes of mice injected with morphine during a fifteen-day injection period, showing: severe necrosis of the sperm-generating tissue (arrow), loss of normal tissue features of seminiferous tubules (straight line), complete loss of sperm production (red arrow), Degeneration and necrosis of secondary sperm-producing cells (red circle)H&E,40X.

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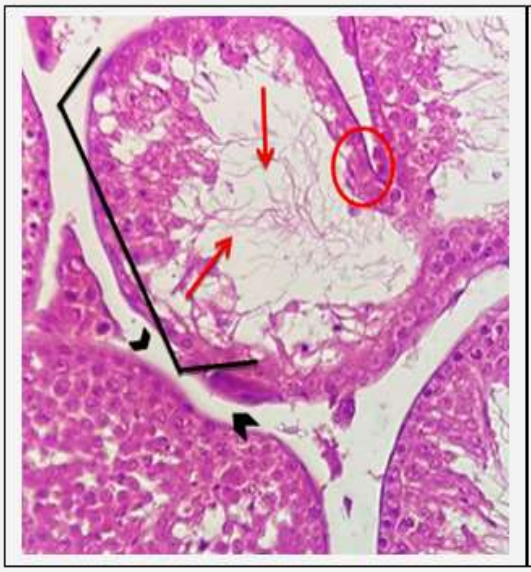
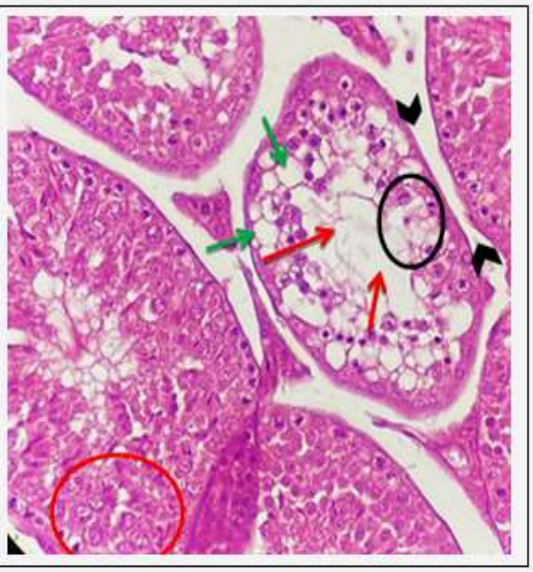
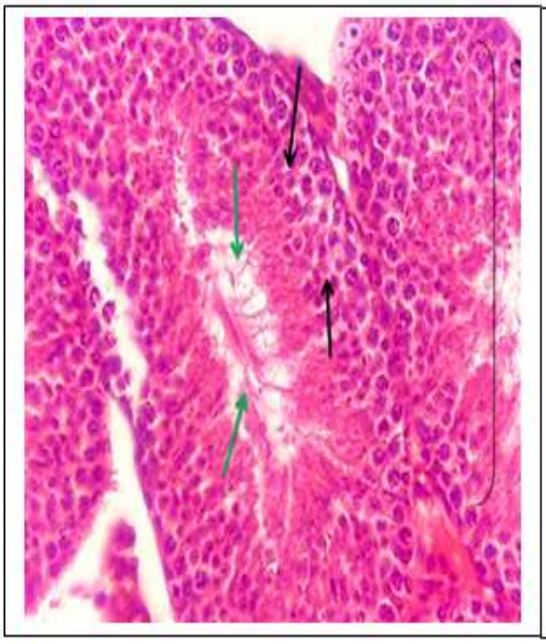


Figure (7) A section of the testes of mice injected with morphine during a fifteen-day injection period shows:Decreased sperm production (red arrow), degeneration and necrosis of the spermogenic epithelium (red circle), loss of normal tissue features of the seminiferous tubules (rectal line) H&E, 10X.



Figure(8) Tests of mice injected with morphine during a fifteen-day injection period showing: lipid droplet aggregation (green arrow), loss of spermatogonial development (black circle), tubule detachment (arrowhead), hyperplasia and hyperplasia (red circle), loss of sperm (red arrow)H&E,10X.



Figure(9) A section of the testes of mice injected with genistein during a five-day injection period shows: Normal spermatogenesis (black arrow), normal sperm (green arrow),H&E, 10X.

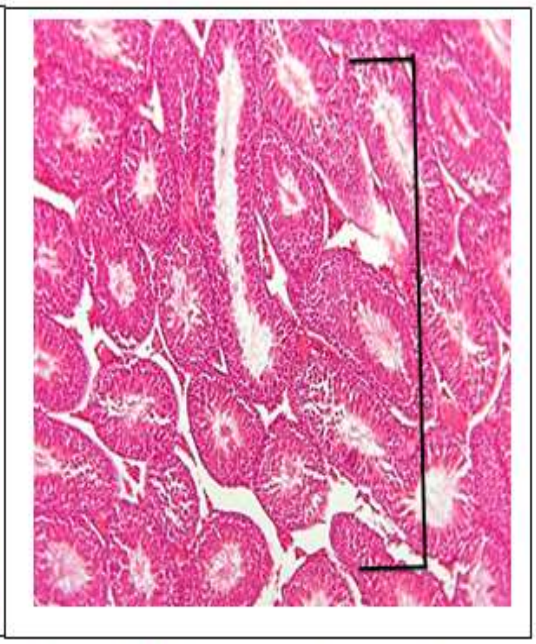


Figure (10) Section of testes of mice injected with genistein during a five-day injection period showing normal tissue parameters in a cross-section of the testes. H&E,4X.

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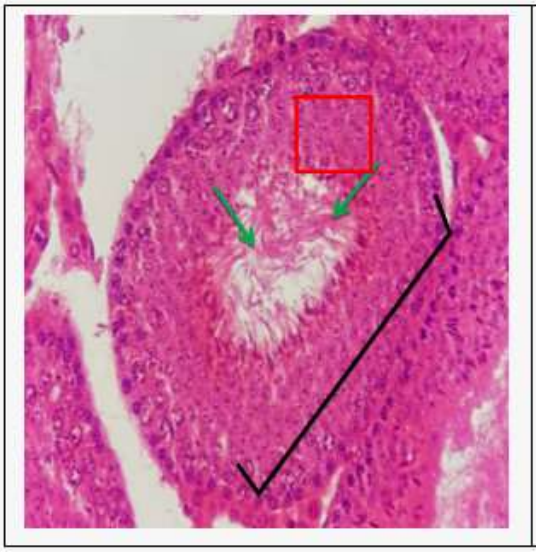


Figure (11) Section of testes of mice injected with genistein during a ten-day injection period showing: normal sperm (green arrow), normal features of seminiferous tubules (straight line), slight hyperplasia of primordial spermatozoa ,H&E, 10X.

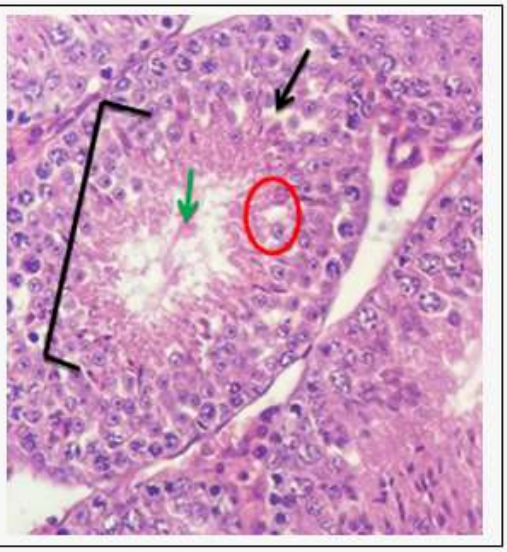
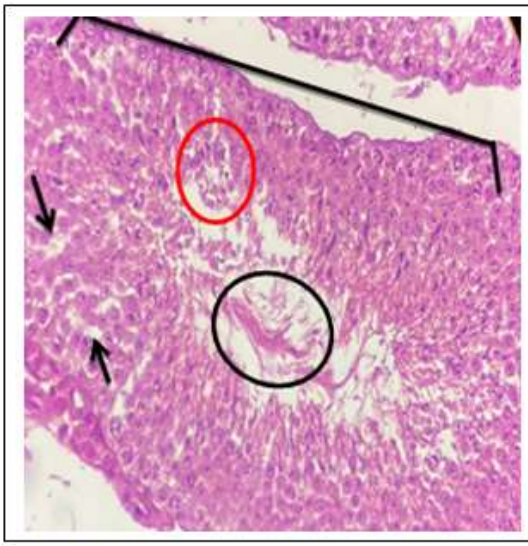
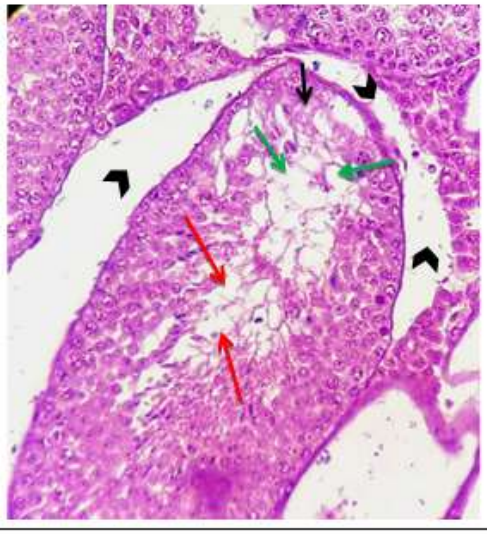


Figure (12) Section of testes of mice injected with genistein during a fifteen-day injection period shows: normal sperm (green arrow), normal features of seminiferous tubules (straight line), simple necrosis (black arrow), cytoplasmic degeneration (red circle).H&E, 40X.



Figure(13) Section of testes of mice injected with morphine and genistein during a five-day injection period showing: Spermogenic tissue degeneration (red circle), eruption of some spermatogenetic cells (black arrow), hyperpigmentation of sperm cells (black circle), H&E, 10X.



Figure(14) Section of the testes of mice injected with morphine and genistein during a five-day injection period shows: accumulation of intra-tissue fat droplets (green arrow), necrosis of spermatid tissue (black arrow), decreased sperm production within the seminiferous tubule (red arrow), detachment of adjacent seminiferous tubules (arrow head) , H&E. 10X.

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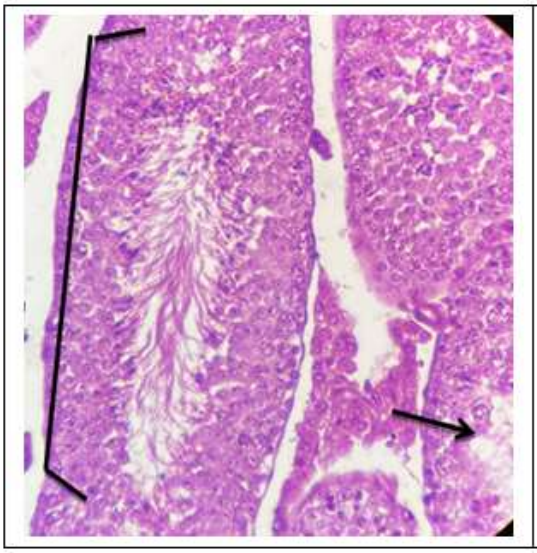

Figure (15) A section of the testes of mice injected with morphine and genistein during a ten-day injection period shows: necrosis of the sperm-generating tissue (black arrow), the seminiferous tubules are normal (straight line), H&E, 10X.

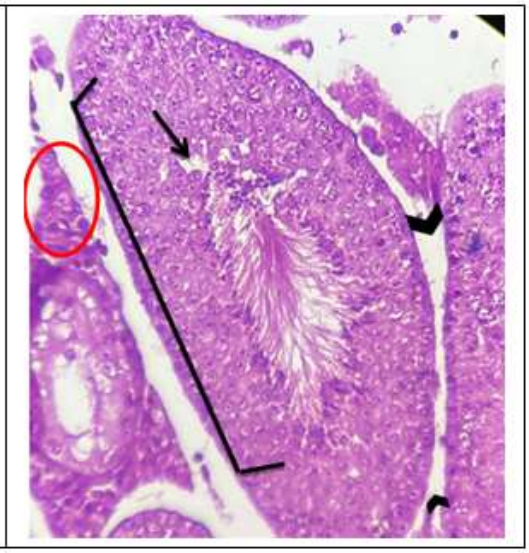

Figure (16) Section of the testes of mice injected with morphine and genistein during a ten-day injection period shows: necrosis of the spermogenic tissue (black arrow), Leydig cell degeneration (red circle), detachment of the adjacent seminiferous tubules (arrowhead), normal seminiferous tubules (straight line), H&E,10X.

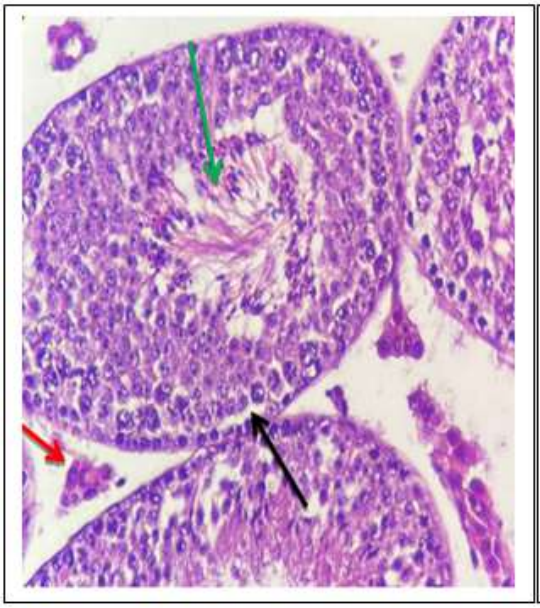

Figure (17) Histological section of the testes of mice injected with morphine and genistein during a fifteen-day injection period showing: basal cell detachment (black arrow), normal sperm production (green arrow), normal cells in tissue containing Leydig cells (red arrow), H&E, 10X.

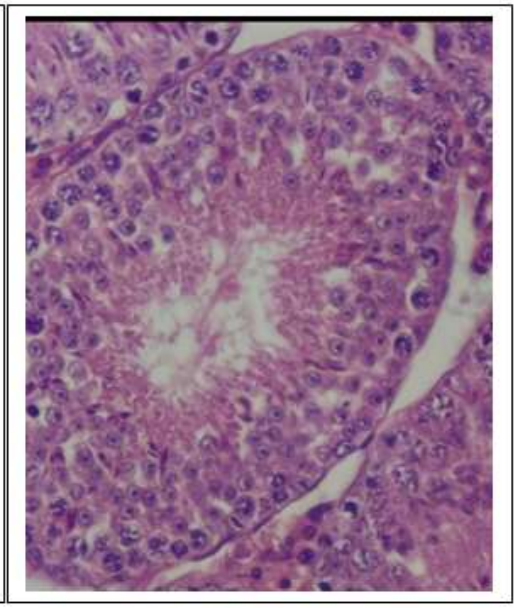

Figure (18) Histological section of the testes of mice injected with morphine and genistein during a fifteen-day injection period showing a normal-looking semitubule H&E, 40X.

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DISCUSSION

4-1 Effect of morphine on testosterone hormone

The results of the study of the level of testosterone hormone in the blood serum of a group of male laboratory mice injected with morphine at a concentration of 20 mg/kg showed a significant decrease ($P<0.05$)) in the level of serum testosterone during the ten and fifteen days of injection periods compared with the control group, while it showed The injection period of fifteen days significantly decreased ($P<0.05$) compared with the period of five and ten days, and the reason for this was due to:The use of opiates, such as morphine, may have a direct effect on GnRH because they bind to opioid-μ receptors in the hypothalamus, which inhibit the secretion of GnRH-stimulating hormone, which in turn prevents the activation of proteins needed to produce GnRH. LH and FSH, impairing the ability of Leydig cells to function and lowering testosterone levels (Coluzzi et al, 2018; Moghaddam et al, 2019). The seminiferous tubules that are involved in sperm maturation are activated and blood testosterone levels are regulated by luteinizing hormone. The pituitary gland follicle-stimulating FSH (Gottumak et al, 2013 ;Duha, 2017) and FSH secretion is inhibited when morphine is used. This reduces testosterone synthesis in testes of laboratory mice (David et al, 2022). According to the study, a decrease in testosterone levels is caused by morphine. It inhibits the ability of Leydig cells to produce testosterone, which reduces the level of testosterone in the blood as a result (Jamshidi et al, 2022). Dopamine, a neurotransmitter released from below The hypothalamus is a hormone that plays an important role in suppressing prolactin-producing cells (Sharma et al, 2022). Dopamine synthesis is significantly slowed down by the use of morphine. This increases the production of prolactin by the anterior pituitary gland, which inhibits the release of kisspeptin, and this inhibits the stimulation and release of GnRH, Skorupskaite et al, 2014 ;Drobnis Grattan et al, 2017) which inhibits the secretion of LH and FSH, which are responsible for stimulating the production of testosterone. Also, morphine inhibits the functions of the liver and kidneys, which negatively affects the metabolism of the hormone prolactin, increasing its concentration inside the body (Zhang et al, 2022).

The hypothalamus, hypothalamus, testes, and tonsils contain opioid -μ receptors, so morphine directly affects Leydig cells in the testis. By contacting these receptors in the testicular tissue, which leads to the inhibition of testosterone secretion. Vicente et al, 2016 ;Fabbri et al, 1988;Jafarpour et al, According 2019;Moinaddin et al, 2021).
to previous studies conducted, the use of opioids has a significant impact on the mental health of users, causing lower quality of life, depression and anxiety. It affects the secretion of sex hormones, which causes low levels of testosterone in the body and causes hypogonadism (Zhang et al.2022).

The acetylcholinesterase enzyme may be affected by morphine. This may interfere with the transmission of nerve signals, which may affect the release of LH and FSH, which slows down the production of testosterone by Leydig cells (Haratian et al, 2021) .As the STAR gene is expressed, StAR, a protein that controls steroidogenesis, is built. Which plays a critical role in the process of testosterone production by transporting cholesterol from the outer mitochondrial membrane to the inner membrane in Leydig cells, where the P450 enzyme complex stimulates the conversion from cholesterol to Progneolone, activating testosterone synthesis, and the use of morphine leads to inhibition of the expression of this Protein, which inhibits this evening, thus lowering the concentration of testosterone in the serum.(Jana et al, 2010 :Jamshidi et al, 2022).

The results of the current study are in agreement with the studies of (Jamshidi et al, 2022) and (David et al, 2022 Jalili) and Moinaddini et al, 2021 (Ajdary et al,2021; Bai et al, 2020;Salahshoor et al, 2018) and (Yilmaz et al, 1999) who recorded a significant decrease in testosterone concentration when morphine was injected with different concentrations and for different periods.

4-2 Effect of genistein on testosterone hormone

The results of the current study showed a significant increase in the level of testosterone when injected with genistein, the third treatment showed a significant increase in the concentration of testosterone during the injection period of fifteen days compared with the control group, while the third treatment did not show a significant difference during the different injection periods, and the fourth treatment showed A significant improvement in the concentration of testosterone during the fifteen-day injection period, as no significant differences were recorded compared to the control group, while the ten and fifteen injection periods showed a significant increase compared to the five-day injection period of the experiment, which could be due to

ESR estrogen receptors are found throughout the body, with higher concentrations located in the hypothalamus, pituitary gland, testes, ovaries and uterus, where estrogen hormones bind to them

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causing varying effects on the hormones and functions of the reproductive organs (Pelletier et al, 2000 et al, 2006 ;Rago et al,2018).

Genistein injection works as a plant estrogen inside the body, as it binds to estrogen receptors (ERS) in the hypothalamus (Le Maire et al, 2010). Thus activates the production of GnRH hormone, which in turn stimulates the pituitary gland to secrete hormones LH and FSH that travel to the testicles and cause the activation of Leydig cells, which produce testosterone, and increase its concentration inside the body. (Ran et al, 2001 ; Xiong et al, 2022 ;Selvage et al, 2004).

Or perhaps genistein raises the level of plant estrogen, which can bind to estrogen receptors in the pituitary gland, thereby activating LH and FSH synthesis. As a result, the level of these hormones in the blood increases, and this stimulates the production of testosterone in the testicles (Banik et al, 2013).

Leydig cells and sperms are protected from damage by free radicals, reactive oxygen and lipid peroxidation thanks to genistein, which also increases their quantity and preserves their original structure. And helps it to produce testosterone (Luo et al, 2020).The expression of the mRNA of the STAR gene, which in turn enhances the gene expression of the steroidogenic protein StAR, is activated by the use of genistein. In Leydig cells, this triggers the testosterone synthesis pathway, which increases the serum testosterone level. Luo et al, 2020 : Xiao et al, 2019).Antioxidants can protect testicular cells from oxidative damage (Mathur et al, 2011).

Histopathological changes

The results of the current study showed that injecting morphine into male mice during the five-day injection period of the experiment caused pathological histological changes represented by the presence of necrosis in the seminiferous tubules, lysis of primary sperm, and thickening of the nuclei of the protozoan cells, while the ten-day injection period of the experiment showed similar changes For a period of five days with loss of primary sperm production, hyperpigmentation of sperm cells, hyperplasia of the tubules and narrowing of the seminal ducts, while the period of fifteen showed changes similar to periods of five and ten with an increase in the extent of necrosis, loss of histological features, degeneration and separation of adjacent tubules from each other This is due to the use of morphine causes necrosis of cells, which may be due to the fact that the composition of the testicles is significantly changed by morphine, which affects the germ cells that make up the mature sperm, and due to the fact that morphine stimulates the production of free radicals by promoting lipid peroxidation and this leads To cause disruption of germ cell differentiation, changes in the lipid structures of cells, cell division, necrosis and lysis of animal Primary spermatogonia and its degeneration, and the separation of the connective vesicles of the adjacent seminiferous tubules (Houston et al, 2018), as well as changes in cell nuclei and degeneration due to the influence of free radicals, reactive oxygen and oxide that interact with components of DNA causing significant negative effects on purine and pyramidine bases. And deoxyribose, which is the backbone of DNA, which may cause significant changes in the nucleus of cells and the gradual decomposition of the nucleus, its thickening and change of shape, which is punished by nucleolysis in its last stages and the occurrence of cell death (Zhu et al, 2012), as well as the cause of hyperplasia and enlargement in the tubules. The reason for this may be that hyperplasia in the testes of the studied mice is a form of inflammation that occurs due to the harmful effects of morphine, as it causes hormonal imbalances that cause cell proliferation, which causes an increase in the size of the injected testes (Jamshidian et al, 2019).

Morphine also causes the decomposition and loss of sperm, which may be due to the decrease in the production of testosterone from the cells producing it in the testes, causing the loss of mature sperm (Banik et al, 2013) or nitric oxide is frequently produced when using morphine. testicles; As nitric oxide binds to receptors on mitochondrial membranes, causing activation of oxidative stress, the mitochondrial membrane in sperm cells is impaired and cytochrome C is released, which in turn leads to caspase activity. 3- Which activates the programmed death of sperm cells, which leads to a decrease in their number when taking morphine (Ertzgaard et al, 2017).The accumulation of fat droplets inside the seminal tubule, which is due to the increase in the concentration of fat inside the body due to morphine impeding the metabolism of fat inside the body, which causes the accumulation of fat inside the body's organs (Chahkandi et al, 2015). According to studies, the use of morphine affects the membrane transport system in the mitochondria of cells Which negatively affects the membrane changes in mitochondria, which reduces the process of ATP formation and thus changes the energy-dependent protein synthesis process and thus the utilization of fats in the process of lipoprotein formation is reduced, which may lead to the accumulation of fat in the form of droplets inside the cytoplasm of cells (Holmquist, 2009).Loss of development of primary spermatozoa due to the fact that the parietal seminiferous tubules differentiate very quickly through the effect of lipid peroxide on weakening the cytoplasmic bonds that connect the

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cells among themselves, causing their release from the seminiferous tubules (Ghoneim et al, 2014) or it may occur Inhibition of mature sperm production by the possible binding of morphine to opioid receptors present in testicular tissue, affecting Sertoli and Leydig cells according to (Jafarpour et al, 2019).

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