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Effects of Sulpiride on the Reproductive System of Male Rats after Puberty

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ABSTRACT

Sulpiride is an antipsychotic drug commonly used in humans to mitigate the effects of stress by selectively targeting central dopaminergic receptors. During male rat puberty, neurotransmitter systems, including the dopaminergic system, undergo significant development, playing a crucial role in the release of gonadal hormones and the regulation of reproductive function. The present study aimed to investigate the effects of sulpiride on reproduction parameters in adult male rats. This study used 30 adult male rats with an average body weight of 250-300g and an average age of 90-95 days. The rats were randomly divided into three groups of 10 each. Group 1 (G1) received 10 mg/kg sulpiride, Group 2 (G2) received 25 mg/kg sulpiride, and the control group (G3) received normal saline, all administered via gavage. This study evaluated hematological (testosterone, luteinizing hormone, prolactin, and Follicle-stimulating hormone) and histopathological parameters (spermatogenesis, seminiferous tubules, and total sperm count). The histopathology result of the testes from treated rats revealed significant histological changes. In G1, the seminiferous tubules exhibited destruction, with disrupted spermatogenesis and reduced numbers of sperm in the lumen. These changes were more pronounced in G2, which received the higher dose of sulpiride (25 mg/kg). In contrast, the control group (G3) displayed normal histological structures and spermatogenesis. Hormonal analysis showed a significant decrease in testosterone and luteinizing hormone (LH) levels in G2 compared to G1 and G3. The hematological results for blood serum showed that the concentration of the hormone prolactin was also significantly increased in G2 treated with 25 mg/kg sulpiride as compared with G1 and G3; the concentration of follicle-stimulating hormone (FSH) levels did not differ significantly across groups. Sperm motility and concentration were significantly reduced in G2 compared to G1 and G3, accompanied by a significant increase in the percentage of abnormal and dead sperm. Histological findings further confirmed severe destruction of the seminiferous tubules in G2 compared to G1 and the control group. In conclusion, administering sulpiride at concentrations of 10 mg/kg and 25 mg/kg in adult male rats caused significant structural and functional defects in the seminiferous tubules of the testes.

Keywords: Follicle-stimulating hormone, Luteinizing hormone, Male rat, Prolactin, Sulpiride, Testosterone

INTRODUCTION

Sulpiride is primarily marketed as an antipsychotic treatment and acts as a selective antagonist of dopaminergic receptors (Mohameda et al., 2010). In rodents, treatment by sulpiride has been shown to produce behavioral effects, such as anti-aggressive actions, and to induce ovulation in female rats (Martín-López et al., 1993; Ali, 2024).

The administration of sulpiride in rats has been associated with a significant increase in serum prolactin concentration. Hyperprolactinemia, caused by elevated prolactin levels, diminishes gonadotropin secretion, reduces gonadotropin-releasing hormone (GnRH) secretion, and impairs luteinizing hormone (LH) responses to GnRH (Jafarpour et al., 2019). Hyperprolactinemia causes infertility in mice due to its effect on the release of GnRH (Zheng et al., 2020). The regulated release of hypothalamic GnRH ensures the normal functioning of the hypothalamo-hypophysio-gonadal axis through the secretion of gonadotropins and testosterone in the systemic circulation, necessary for spermatogenesis, maturation of spermatozoa, and reproductive behavior (Nira et al., 2008). Studies have shown that dopamine antagonists synapse on GnRH terminals in the median eminence, where dopamine application inhibits GnRH release (Okamura et al., 2013; Al-Mousawe and Ibrahim, 2024). The hypothalamus secretes GnRH, which stimulates the pituitary gland to release follicle-stimulating hormone (FSH) and luteinizing hormone (LH; Smith, 2012; Ali and Najlaa, 2023). GnRH influences serum testosterone concentration and can inhibit testicular development and spermatogenesis over time (Pan et al., 2023). Male fertility in animals is regulator by two adenohypophysial hormones, including follicle-stimulating hormone (FSH), and luteinizing hormone (LH), through testosterone synthesis in Leydig cells and its aromatization to estradiol in Sertoli cells (Wang et al., 2021; Ramya et al., 2023). Regulation of gonadotropin-releasing hormone (GnRH) release ensures proper functioning of the hypothalamic-pituitary-gonadal axis by releasing

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gonadotropins and testosterone into the systemic circulation, which is necessary for reproductive behavior, spermatogenesis, and sperm maturation (Acevedo-Rodriguez et al., 2018; Pan et al., 2024). The testes are the primary reproductive organ in males, responsible for sperm production and the synthesis of testosterone, a key male hormone (Pan et al., 2024). There is growing global concern regarding the impact of persistent organic pollutants on reproductive health. Various environmental toxicants have been shown to adversely affect spermatogenesis in both rodents and humans, leading to reduced sperm count, abnormal sperm morphology, and diminished semen quality (Guerrero-Limón et al., 2024). The present study aimed to evaluate the effects of sulpiride on hormone levels, sperm parameters, and testes in male rats.

MATERIALS AND METHODS

Ethical approvals

The animal experimentation was approved by the Ethical Clearance Committee of the College of Veterinary Medicine, Tikrit University, under registration number Tu. Vet. 28 (2024). This study was conducted from February to April 2024 at the animal house of the College of Veterinary Medicine, Tikrit University, Tikrit, Iraq.

Animals and treatment

The study included 30 adult male rats, with an average body weight ranging from 250 to 300 g and an average age of 90 to 95 days (from February to April of 2024). The animals were randomly divided into three groups, each consisting of 10 male rats. Five rats were housed in standard plastic cages measuring 46×28×13 cm, under controlled conditions of lighting, ventilation, and temperature (20-25℃). To maintain hygiene, the cage floors were coated in sawdust and replaced two or three times a week. Food and water were provided ad libitum, and artificial lighting was maintained. Group 1 received a daily oral dose of 10 mg/kg sulpiride (Solarbio Life Science, China), Group 2 received 25 mg/kg sulpiride, and Group 3 (control) received normal saline. Treatments were daily administered by gavage for four weeks (Mereu et al., 1983).

Blood collection

Within 24 hours after the completion of the treatment, blood samples (0.5 mL) were collected from the tail vein of all rats (experimental and control groups) to measure serum concentrations of testosterone, prolactin, FSH, and LH. Blood collection was performed under anesthesia. Anesthesia was induced using isoflurane via a vaporizer in a chamber with 3-5% isoflurane for five minutes, and maintenance was achieved with 1–3% isoflurane via a nose cone. The isoflurane concentration was adjusted based on continuous monitoring of the respiratory rate. Sedation was confirmed by a toe pinch before the procedure (Charlès et al., 2023).

Collection of testes and spermatozoa

The testes and epididymis from three male rats in each group were collected. The left testis was collected for histological study, while the right testis and epididymis were frozen at -20°C for the evaluation of sperm parameters.

Sperm parameters

Evaluation of sperm characteristics

After the treatment period, the epididymis tail was removed and placed in a Petri dish containing 10 ml of normal saline at 37℃. The cauda of the epididymis was incised into pieces (at least 200 slices), and the sperm were discharged (Tajik and Hassan, 2008; Naji et al., 2022).

Sperm motility was assessed by placing a drop of liquefied semen on a microscope slide, covering it with a coverslip, and observing it under a microscope at ×400 magnification. The motile and immotile spermatozoa in different fields of view on the slide were counted. A total of 200 spermatozoa were counted, and the mean of the counts for each sample was calculated (Khan, 2022).

Sperm vitality was estimated by assessing the integrity of the cell membrane. The percentage of live sperm was determined by dye exclusion to identify sperm with intact cell membranes. One drop of sperm was mixed with two drops of 1% eosin solution on a clean microscope slide. After 30 seconds, three drops of 10% nigrosine solution were added to the slide and mixed. One drop of the sperm-eosin-nigrosine mixture was placed on a clear slide, and a smear was prepared. The slides were air-dried and counted for sperm under a microscope to count the unstained (live) and stained (dead) cells (Khan, 2022).

Sperm concentration was determined using a 100 µm deep hemocytometer (Neubauer chamber). The sperm were diluted 1:10 with a diluent containing 50 g of sodium bicarbonate (NaHCO3), 10 ml of formaldehyde solution (36%-

40%) [v/v], 0.25 g of trypan blue, and 1000 ml of distilled water. The hemocytometer sides were filled with sperm suspension and covered by a cover slide; the sperm were counted in twenty-five small squares of the chamber (Naji et al., 2022).

To identify and count sperm shape abnormalities, a fine epididymal sperm suspension was prepared and stained with 0.2 ml of 1% eosin in water. A drop of the stained suspension was placed on a clean microscope slide and allowed to dry. The slide was inspected for abnormalities in the shape of the sperm head and tail. A total of 1000 spermatozoa were examined per animal according to the method introduced by Bairy and Shivananda (2001), and abnormalities were expressed as the total number of abnormal spermatozoa per 1,000 spermatozoa (Khan, 2022; Naji et al., 2022).

Histological study of the testis

After the treatment period, three male rats from each group were sacrificed by cervical dislocation. The left testis was excised and cleared of the attached fat and connective tissue for histological study.

Histological sections were prepared following Luna's (1968) method, as described below: Specimens were immediately fixed in 10% buffered neutral formalin for 48 hours. After fixation, the specimens were washed with water. The specimens passed through ascending grades of ethanol (70%, 80%, 90%, 96%, and 100%). Tissues were cleared by immersing them in xylene. Specimens were immersed in a mixture of xylene and paraplast wax at 54-56°C in an electric oven for 15 minutes, followed by transfer to melted paraffin for 2-3 hours with periodic replacement of the paraffin. The tissue blocks were placed in fresh, melted paraffin to solidify and encase the tissues. Paraffin blocks were trimmed and sectioned into 5-10 µm thick slices using a microtome. Tissue sections were mounted on glass slides using Mayer's albumin. Sections were stained according to the method of Bancroft and Stevens (1982), and paraffin was removed from sections using xylene in two 10-minute steps. The sections were rehydrated through descending ethanol concentrations and washed with distilled water. The sections were stained with hematoxylin for 15 minutes, washed with tap water for 10 minutes, and then washed with distilled water. The sections were put in Eosin stain for 2-7 minutes and then washed with tap water. The sections were passed through ascending concentrations of ethanol (70%, 80%, 90%, 100%, and 100%). The slides were then placed in xylene for 2 minutes. The slides were removed from xylene, a mounting medium (Balsam) was placed over the sections to harden them, and a cover glass was applied. Finally, the histological sections were examined under a light microscope to assess the histological changes in the sections prepared from the testes of the treated and control animals.

Statistical analysis

The analysis of data was performed using the Statistical Analysis System (SAS, Version 9.1). Differences between groups were assessed using one-way and two-way ANOVA. The least significant difference (LSD) test was applied to determine statistical significance at $p < 0.05$ (SAS, 2010).

RESULTS

Serum hormonal profiles of testosterone and prolactin

The serum hormonal profiles for testosterone, prolactin, LH, and FSH are shown in Table 1. Testosterone and LH concentrations were significantly decreased in Group 2 (25 mg/kg sulpiride) compared to the control group ($p < 0.05$). Conversely, prolactin concentration was significantly increased in Group 2 compared to the control group ($p < 0.05$). However, no significant differences were observed in FSH concentrations across all groups ($p < 0.05$).

Semen evaluation

Sperm count

As shown in Table 2, sperm count was significantly reduced in Group 2 (25 mg/kg sulpiride) compared to Groups 1 (10 mg/kg sulpiride) and 3 (control group, $p < 0.05$).

Sperm motility

Sperm motility was significantly decreased in Group 2 (25 mg/kg sulpiride) compared to Groups 1 and 3 ($p < 0.05$, Table 2).

Sperm abnormality

Sperm abnormalities and the proportion of dead spermatozoa were significantly higher in Groups 2 (25 mg/kg sulpiride) compared to Groups 1 and 3 ($p < 0.05$, Table 2).

Table 1. Hormone concentrations (ng/ml) in the blood of male rats

Groups	Number of sample rats	Follicle-stimulating hormone	luteinizing hormone	Testosterone	Prolactin
G1 (10 mg/kg Sulpiride)	6	56.60 ± 1.04^{a}	28.03 ± 1.03^{b}	0.77 ± 0.6^{b}	18.03 ± 0.23^{b}
G2 (25 mg/kg Sulpiride)	6	55.07 ± 1.13^{a}	18.25 ± 0.99^{c}	0.63 ± 0.8^{a}	20.13 ± 0.73^{a}
G3 (normal Saline)	6	53.65 ± 0.71^{a}	34.96 ± 1.78^{a}	1.45 ± 0.5^{c}	11.76 ± 0.55^{c}

^{abc} Means that a different capital superscript letter in the same column are significantly different ($p < 0.05$)

Table 2. Characteristics of sperm obtained from the epididymis tail of rats

Groups	Sperm Motility (%)	Concentration ($\times 10^4$/ml)	Sperm abnormality (%)	Dead sperms (%)
G1 (10 mg/kg Sulpiride)	80.66 ± 0.6^{b}	20.21 ± 2.5^{b}	11.10 ± 0.32^{b}	12.40 ± 0.43^{b}
G2 (25 mg/kg Sulpiride)	70.05 ± 0.55^{c}	18.55 ± 1.18^{c}	17.40 ± 0.48^{a}	15.62 ± 0.28^{a}
G3 (normal Saline)	85.92 ± 1.33^{a}	23.24 ± 1.53^{a}	9.91 ± 0.55^{c}	8.11 ± 0.56^{c}

^{abc} Means that a different capital superscript letter in the same column are significantly different ($p < 0.05$).

Histological study of the testis

The histological examination of seminiferous tubules is presented in Figures 1-3. In the control group (Group 3), the seminiferous tubules were healthy and appeared normal (Figure 1). In Group 1 (10 mg/kg sulpiride), partial destruction of the seminiferous tubules was observed (Figure 2). The damage was more severe in Group 2 (25 mg/kg sulpiride), where extensive destruction of seminiferous tubules was noted (Figure 3).

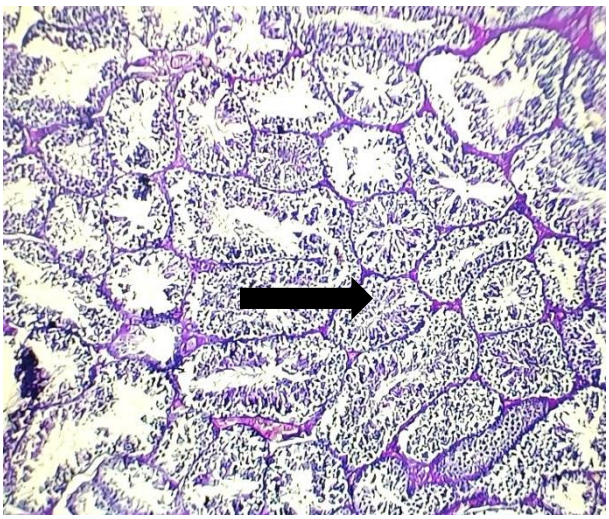

Figure 1. The normal seminiferous tubules of male rats in the control group (black arrow). ×100 H&E staining

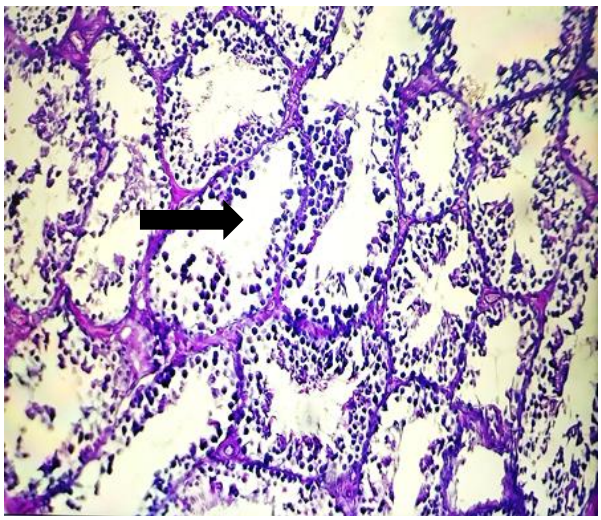

Figure 2. The mild seminiferous tubules degeneration of male rats treated with 10 mg/kg sulpiride (black arrow). ×100 H&E staining

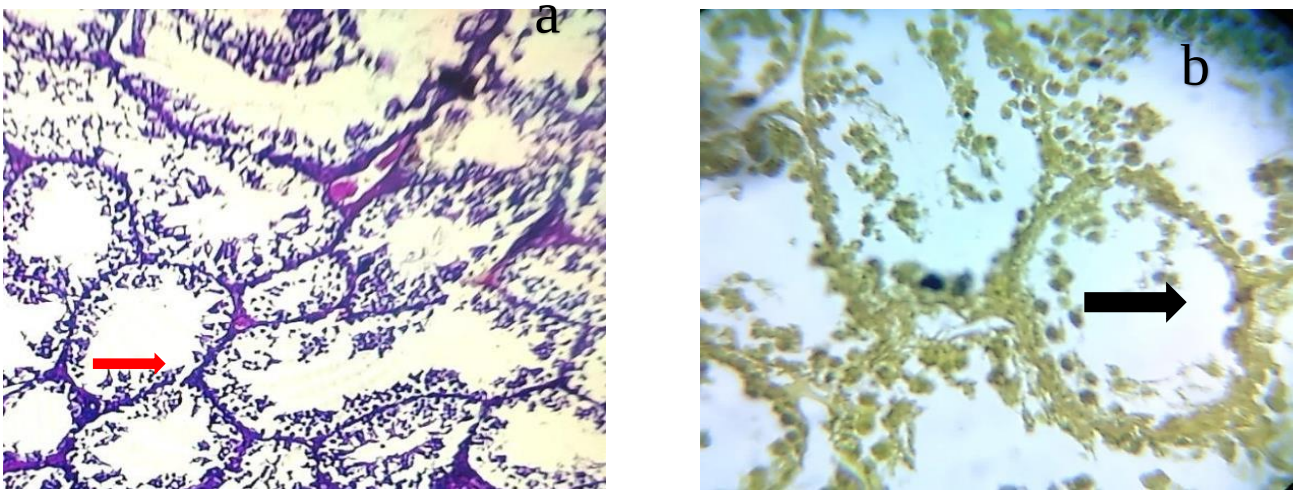

Figure 3. The increasing destruction of seminiferous tubules of male rats (red and black arrows) treated with 25 mg/kg sulpiride. **a**: ×100 H&E staining, **b**: ×400 H&E staining

DISCUSSION

The findings of this study revealed significant decreases in testosterone and luteinizing hormone (LH) concentrations, alongside increased prolactin levels in male rats treated with sulpiride (10 mg/kg and 25 mg/kg). These results align with previous studies reporting elevated serum prolactin and reduced testosterone and LH levels following sulpiride administration (Amiri et al., 2020; Zheng et al., 2020). The mechanism behind this effect involves sulpiride-induced stimulation of prolactin secretion from the pituitary gland, as previously demonstrated in Brown‑Norway rats (Zheng et al., 2020). Mahmoodi and Babaei (2021) similarly observed a significant reduction in testosterone levels in sulpiride-treated rats, corroborating the present study's findings. Taketa et al. (2011) reported that sulpiride treatment at higher doses (100 mg/kg) significantly increased prolactin levels, which aligns with the present study, where male rats were exposed to sulpiride in G1 (10 mg/kg) and G2 (25 mg/kg). Also, the results of this study are in agreement with the increasing levels of prolactin, where male rats were exposed to sulpiride (40 and 120 mg/kg, Zheng et al., 2020). Additionally, Ahmadi et al. (2015) demonstrated that sulpiride (40 mg/kg) acts on hypothalamic tuberoinfundibular dopaminergic neurons, increasing prolactin release in mice, consistent with the present findings. Ahmadi et al. (2013) reported the sulpiride treatment (40 mg/kg) in male mice due to a significant increase in serum prolactin levels found in the treated mice which were along with a significant decrease in LH and testosterone levels, which aligns with the findings of the present study. Elevated prolactin inhibits gonadotropin-releasing hormone (GnRH) secretion from the hypothalamus, leading to reduced LH secretion via negative feedback regulation, as also reported by Miki et al. (2016). In line with this study, Anderson et al. (2008) reported that chronic hyperprolactinemia induced by sulpiride (40 mg/kg) acts to suppress LH pulse in rats. Moreover, the findings of this study align with those of Szukiewicz (2024) which showed that hyperprolactinemia lowers the secretion of gonadotropin-releasing hormone, thereby decreasing the release of pulsation LH, and to a lesser degree, the FSH level in mammals. However, FSH concentrations remained unchanged, consistent with prior studies that reported no significant changes in FSH levels following sulpiride administration (Jafarpour et al., 2019). Jafarpour et al. (2019) who reported increased serum prolactin concertation and no changes in concertation of FSH when treatments used sulpiride (4 mg/kg) in male rats.

The results of sperm parameters align with findings that low dopamine levels increase sperm motility and viability through the stimulation of the D2 receptor, while higher levels of dopamine decrease sperm motility (Semet et al., 2017). The present study reported a significant reduction in sperm motility, viability, and concentration rates in rats administered sulpiride, along with a significant increase in sperm abnormalities and dead sperm. These findings are consistent with results reporting a significant decrease in sperm viability, motility, and count, as well as an increase in abnormal sperm, observed in treatment groups administered sulpiride (40 mg/kg, Ahmadi et al., 2012; 2015).

The histological study revealed the destruction of seminiferous tubules in rats receiving sulpiride. The extent of destruction significantly increased as the dose of sulpiride increased compared to the control group. These results align with the findings reported by Jafarpour et al. (2019). Vieira et al. (2013) also reported that treatment of male rats with sulpiride (25 mg/kg) caused changes in the volume and histopathology of the seminiferous tubules, such as an increased proportion of abnormal seminiferous tubules, as well as increased percentages of abnormal sperm head morphology and immobile sperm. Mahmoodi and Babaei (2021) reported that sulpiride (4 mg/kg) administration led to the destruction and disruption of the epithelium of seminiferous tubules, and increased interstitial space of the testicular tissue. Their findings are in agreement with the present study. Amiri et al. (2020) reported that sulpiride (4 mg/kg) administration led to a significant decrease in the number of spermatogenic cells (spermatogonia and spermatocytes) in seminiferous tubules, consistent with the results of the present study.

CONCLUSION

In conclusion, sulpiride (10 mg/kg) treatment negatively affects the male reproductive system, with these harmful effects increasing in severity with higher doses of sulpiride (25 mg/kg) treatment. Further researches are needed to focus on the sperm DNA damage during the use of sulpiride for treatment.

DECLARATIONS

Availability of data and materials

The data supporting the findings of this study are available upon reasonable request from the corresponding author.

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Competing interests

The authors declare that there is no conflict of interest.

Author's contributions

Ali Aziz Abd conducted the research, secured resources, prepared materials, and reviewed the manuscript. Qusia Saleh Jumma interpreted the findings and contributed to the experimental design. Oday Alawi Al-Juhaish performed statistical analyses and contributed to editing the manuscript. All authors have read and approved the final version of the manuscript before publication in the present journal.

Ethical considerations

This paper was originally written by the authors and has not been published elsewhere. The authors checked the text of the article for plagiarism index and confirmed that the text of the article is written based on their original scientific results.

REFERENCES

Acevedo-Rodriguez A, Kauffman AS, Cherrington BD, Borges CS, Roepke TA, and Laconi M (2018). Emerging insights into hypothalamic-pituitary-gonadal axis regulation and interaction with stress signaling. Journal of Neuroendocrinology, 30(10): e12590. DOI: https://www.doi.org/10.1111/jne.12590

Ahmadi A, Sadr khanlou RA, and Salami S (2012). Evaluation of sperm quality, maturation and DNA integrity in adult mice treated with sulpiride. Tehran University Medical Journal, 70(4): 205-211. Available at: DOI: http://tumj.tums.ac.ir/article-1-120-en.html

Ahmadi A, Saderkhanlou R, Salami S, and Mahmoudian S (2013). Evaluation of the effect of sulpiride as an atypical antipsychotic drug on the serum levels of prolactin, LH, FSH and testosterone in adult male rats. Studies in Medical Sciences, 23(6): 577-583. Available at: http://umj.umsu.ac.ir/article-1-1563-en.html

Ahmadi A, Sadrkhanlou RA, and Ahmadi A (2015). Role of sulpiride administration in sperm quality and relationship to male fertility and in vitro fertilization embryonic development. Journal of Arak University of Medical Sciences, 17(10): 1-11. Available at: http://jams.arakmu.ac.ir/article-1-3103-en.html

Ali AA (2024). Impact of sulpiride and PMSG hormone treatment on estrus and number of resulted offsprings in female rats. Assiut Veterinary Medical Journal, 70(138): 84-89. Available at: https://avmj.journals.ekb.eg/article_376645.html

Ali AA and Najlaa SI (2023). Induction of oestrus by Sulpiride and measurement of estrogen hormone in Iraqi Awassi Ewes during the out of breeding season. The Indian Veterinary Journal, 100(12): 15-18. Available at: https://epubs.icar.org.in/index.php/IVJ/article/view/146476

Al-Mousawe A and Ibrahim N (2024). Diagnosis of pregnancy in Iraqi Awassi ewes through progesterone hormone measurement and ultrasonography following induction of fertile estrus with sulpiride. Egyptian Journal of Veterinary Sciences, 55(4): 945-953. DOI: https://www.doi.org/10.21608/ejvs.2023.238362.1629

Amiri S, Babaei-Balderlou F, and Najafi G (2020). Evaluation of the effect of dopamine D2 receptor antagonist on the spermatogenesis process in rats under physical or psychological stress and their offspring. Qom University Medicine Sciences Journal, 14(6): 18-30. DOI: https://www.doi.org/10.29252/qums.14.6.18

Anderson GM, Kieser DC, Steyn FJ, and Grattan DR (2008). Hypothalamic prolactin receptor messenger ribonucleic acid levels, prolactin signaling, and hyperprolactinemic inhibition of pulsatile luteinizing hormone secretion are dependent on estradiol. Endocrinology, 149(4): 1562-1570. DOI: https://www.doi.org/10.1210/en.2007-0867

Bairy I and Shivananda PG (2001). Seroprevalence of HIV in Manipal. Indian Journal of Medical Sciences, 55(5): 257-262. Available at: https://pubmed.ncbi.nlm.nih.gov/11641917

Bancroft JD and Stevens A (1982). The haematoxylins. Theory and practice of histological techniques. Longman Group., London, pp. 109-122. Available at: https://www.scirp.org/reference/referencespapers?referenceid=2109030

Charlès L, Agius T, Filz von Reiterdank I, Hagedorn J, Berkane Y, Lancia H, Uygun BE, Uygun K, Cetrulo CL, Randolph MA et al. (2023). Modified tail vein and penile vein puncture for blood sampling in the rat model. Journal of Visualized Experiments, 196: e65513. DOI: https://www.doi.org/10.3791/65513

Guerrero-Limón G, Zappia J, and Muller M (2024). A realistic mixture of ubiquitous persistent organic pollutants affects bone and cartilage development in zebrafish by interaction with nuclear receptor signaling. PloS One, 19(3): e0298956. DOI: https://www.doi.org/10.1371/journal.pone.0298956

Jafarpour FM, Karami M, and Jalali NM (2019). Interaction of sulpiride with morphine in induction of male rat infertility. Journal of Basic and Clinical Pathophysiology, 7(2): 6-11. DOI: https://www.doi.org/10.22070/jbcp.2019.4722.1120

Khan I (2022). Sperm quality parameters and oxidative stress: Exploring correlation in fluoride-intoxicated rats. Journal of Human Reproductive Sciences, 15(3): 219-227. DOI: https://www.doi.org/10.4103/jhrs.jhrs_65_22

Luna LG (1968). Manual of histological staining method of Armed Forces Institute of Pathology, 3rd Edition. New York, U.S.A. pp. 123-147.

Mahmoodi H and Babaei-Balderlou F (2021). Effect of sulpiride on translocator protein (TSPO) gene expression and histomorphometric indices in the testis of rats under physical or psychological stress. Iranian Journal of Endocrinology and Metabolism, 22(5): 444. Available at: http://ijem.sbmu.ac.ir/article-1-2769-en.html

Martín-López M, Puigcerver A, Vera F, and Navarro JF (1993). Sulpiride shows an anti-aggressive specific effect after acute treatment in male mice. Medical Science Research, 21: 595-596. Available at: https://pascal-francis.inist.fr/vibad/index.php?action=getRecordDetail&idt=4893863

Miki K, Sasaki H, Kido M, Takahashi H, Aoki M, and Egawa S (2016). A comparative study on the efficacies of gonadotropin-releasing hormone (GnRH) agonist and GnRH antagonist in neoadjuvant androgen deprivation therapy combined with transperineal prostate brachytherapy for localized prostate cancer. BMC Cancer, 16(1): 708. DOI: https://www.doi.org/10.1186/s12885-016-2737-8

Mereu G, Casu M, and Gessa GL (1983). Sulpiride activates the firing rate and tyrosine hydroxylase activity of dopaminergic neurons in unanesthetized rats. Brain Research, 264(1): 105-110. DOI: https://www.doi.org/10.1016/0006-8993(83)91125-3

Mohameda GG and Solimanb MH (2010). Synthesis, spectroscopic, and thermal characterization of sulpiride complexes of iron, manganese, copper, cobalt, nickel, and zinc salts. Antibacterial and antifungal activity. Spectrochimica Acta. Part A, Molecular and Biomolecular Spectroscopy, 76(3-4): 341-347. DOI: https://www.doi.org/10.1016/j.saa.2010.03.016

Naji IQ, Wadee SA, and Hameed BK (2022). Adverse effects of aspirin on hormonal and histopathological changes in male rats. International Journal of Health Sciences, 6(S3): 8252-8264. DOI: https://www.doi.org/10.53730/ijhs.v6nS3.7814

Nira BJ, Christopher R, LaPensee Elizabeth W, and LaPensee (2008). What can we learn from rodents about prolactin in humans?. Endocrine Reviews, 29(1): 1-41. DOI: https://www.doi.org/10.1210/er.2007-0017

Okamura H, Tsukamura H, Ohkura S, Uenoyama Y, Wakabayashi Y, and Maeda K (2013). Kisspeptin and GnRH pulse generation. Advances in Experimental Medicine and Biology, 784: 297-323. DOI: https://www.doi.org/10.1007/978-1-4614-6199-9_14

Pan J, Liu P, Yu X, Zhang Z, and Liu J (2024). The adverse role of endocrine-disrupting chemicals in the reproductive system. Frontiers in Endocrinology, 17(14): 1324993. DOI: https://www.doi.org/10.3389/fendo.2023.1324993

Pan F, Du H, Tian W, Xie H, Zhang B, Fu W, Li Y, Ling Y, Zhang Y, Fang F, and Liu Y (2023). Effect of GnRH immuno-castration on immune function in male rats. Frontiers in Immunology, 13: 1023104. DOI: https://www.doi.org/10.3389/fimmu.2022.1023104

Ramya S, Poornima P, Jananisri A, Geofferina IP, Bavyataa V, Divya M, Priyanga P, Vadivukarasi J, Sujitha S, Elamathi S et al. (2023). Role of hormones and the potential impact of multiple stresses on infertility. Stresses, 3(2): 454-474. DOI: https://www.doi.org/10.3390/stresses3020033

Semet M, Paci M, Saïas-Magnan J, Metzler-Guillemain C, Boissier R, Lejeune H, and Perrin J (2017). The impact of drugs on male fertility: A review. Andrology, 5(4): 640-663. DOI: https://www.doi.org/10.1111/andr.12366

Smith JT (2012). The role of kisspeptin and gonadotropin inhibitory hormone in the seasonal regulation of reproduction in sheep. Domestic Animal Endocrinology, 43(2): 75-84. DOI: https://www.doi.org/10.1016/j.domaniend.2011.11.003

Szukiewicz D (2024). Current insights in prolactin signaling and ovulatory function. International Journal of Molecular Sciences, 25(4): 1976. DOI: https://www.doi.org/10.3390/ijms25041976

Tajik P and Hassan-Nejad LM (2008). Assessment of epididymal sperm obtained from dromedary camel. Iranian Journal Veterinary Research Shiraz University, 9(1): 46-50. Available at: https://sid.ir/paper/85599/en

Taketa Y, Yoshida M, Inoue K, Takahashi M, Sakamoto Y, Watanabe G, Taya K, Yamate J, and Nishikawa A (2011). Differential stimulation pathways of progesterone secretion from newly formed corpora lutea in rats treated with ethylene glycol monomethyl ether, sulpiride, or atrazine. Toxicological Sciences: An Official Journal of the Society of Toxicology, 121(2): 267-278. DOI: https://www.doi.org/10.1093/toxsci/kfr062

Vieira ML, Dos Santos AH, Silva LS, Fernandes GS, Kiss AC, Moreira EG, Mesquita S, and Gerardin DC (2013). Lactational exposure to sulpiride: Assessment of maternal care and reproductive and behavioral parameters of male rat pups. Physiology and Behavior, 122(2): 76-83. Available at: https://pubmed.ncbi.nlm.nih.gov/24021925

Wang HQ, Zhang WD, Yuan B, and Zhang JB (2021). Advances in the regulation of mammalian follicle-stimulating hormone secretion. Animals, 11(4): 1134. DOI: https://www.doi.org/10.3390/ani11041134

Zheng C, Luo Y, Chen Y, Chen D, Shao, C, Huang D, and Sun Z (2020). Oral exposure of sulpiride promotes the proliferation of Brown-Norway rat prostates. Experimental and Therapeutic Medicine, 19(4): 2551-2562. DOI: https://www.doi.org/10.3892/etm.2020.8521