International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 16s,2025
https://theaspd.com/index.php

Ameliorative Potential Of Alcoholic Ginseng Extract On Ibuprofen-Induced Reproductive Toxicity In Male Rats

Shelan Abd AlSalam Hamad[1] , Siham Agmee Wadee[2] , Wasan Sarhan Obaid[3]
[1,2,3]Department of Pharmacology , College of Veterinary Medicine, Tikrit University, Tikrit , Iraq
sa230019pve@st.tu.edu.iq

Abstract
The therapeutic benefits of ginseng (Panax ginseng) have attracted an abundance of interest. So, this investigation was aimed to study the effect of alcoholic Ginseng extract against Ibuprofen induced reproductive dysfunction in male rat. This investigation was carried out from August 24 to September 26, 2024, in the animal house of Veterinary Medicine College at Tikrit University. Seventy (70) adult, seemingly healthy Albino male rats were acquired from the Veterinary Medicine College's animal house at Tikrit University. The results showed that the Testosterone and FSH concentrations were normal in all groups and there were no significant differences (P≤0.05) between groups.On the other hand, significant (P≤0.05) differences were found in the concentration of LH, where the highest concentration was in the fourth group, which took Ibuprofen for 30 days (15.493 ± 0.591) compared to the control group (14.556 ± 1.008), while the treated groups did not show significant differences (P≤0.05) compared to the control group. Sperm motility, sperm life, sperm dead, abnormal sperm and Sperm counts in Ibuprofen (30 days) group and Ibuprofen (10 days) group showed significant (P≤0.05) differences compared to the control group. In the treated groups and ginseng group showed non-significant (P≤0.05) differences compared to the control group. Coenzyme Q10 activity in Ibuprofen (10 days) group showed significant (P≤0.05) elevated compared to the control group. while, in the treated groups and ginseng group showed non-significant (P≤0.05) differences compared to the control group. The Carnitine levels in all groups showed non-significant (P≤0.05) differences compared to the control group. Histological examination of rats dosed with both dimethyl sulfoxide and ibuprofen for 10 and 30 days revealed some histological changes, including hemolyzed blood vessels, reduced spermatogonia, and decreased sperm count. However, after using ginseng extract to treat and prevent the harmful effects of ibuprofen, it was found that seminiferous tubules were containing the different stages of spermatogenic development, and most spermatogenic cells were improved. Its concluded that the alcoholic extract of ginseng roots shows a protective and therapeutic effect on sex hormones and spermatogenesis cells, and improves spermatogenesis.
keywords: *Panax ginseng, Ibuprofen, testis, FSH, LH.*

INTRODUCTION

Fertility issues have traditionally been treated using herbal treatments. As early as 200 A.D., there is proof that herbal medicines were used to improve both male and female fertility. Special herbs and plant extracts that are thought to benefit the reproductive organs, hormonal system, and sex drive are used to make these herbal fertility medicines. Both men and women who want to improve their chances of getting pregnant take them, as do couples who are having trouble conceiving [1, 2, 3]. Numerous research have revealed that many victims have tried to enhance their libido, sexual function, and fertility by using herbal remedies like ginseng, maca, or dang gui [4,5]. One typical Eastern Asian plant that is used as a tonic to slow down the aging process is ginseng [6]. Ginseng saponin, which is made up of several ginsenosides, is the main active component of ginseng. As of right now, about 30 ginsenosides have been found [7]. Male infertility can be effectively treated with it. It has been demonstrated to stimulate sexual activity, spermatozoa production, and testicular expansion in animals [8]. In rats, ginseng reduces oxidative stress, which raises antioxidant capacity and decreases lipid peroxidation [9]. Analgesic exposure has been linked to adverse endocrine and reproductive effects in fetuses, according to mounting data in recent years [10]. However, no comprehensive research has examined how mild analgesics affect the human pituitary-gonadal axis. Ibuprofen is particularly intriguing in this regard due to its growing popularity among the general public and, in particular, among professional athletes [11]. Because of its extensive usage as a nonsteroidal anti-inflammatory medicine (NSAID) and its well-established pharmacological effects on the reproductive and endocrine systems, ibuprofen was included in the analysis [12]. According to new research, ibuprofen may affect male fertility by interfering with the hypothalamic-pituitary-testicular axis,

which can result in disorders like compensatory hypogonadism that impair sperm quality and testosterone production [13]. Ibuprofen is a crucial NSAID to research in relation to male reproductive health because of these special effects [14]. so, this investigation was aimed to study the effect of alcoholic Ginseng extract against Ibuprofen induced reproductive dysfunction in male rat

MATERIALS AND METHODS

Ibuprofen

Was obtained from General Company for the Manufacture of Pharmaceuticals and Medical Appliances Samarra Iraq.

Panax ginseng roots extraction

The roots of Panax ginseng were purchased from the Baghdad, Iraq, market. To get rid of any contaminants, properly wash the ginseng roots in distilled water. After that, thoroughly dry the roots in the shade for five to seven days at room temperature until they are entirely dry. cleaned the dried roots to get rid of any dirt or debris that could have remained. Using a grinder, grind the cleaned roots into a fine powder. 200 milliliters of 99% ethanol were added to a round-bottom flask that contained 20 grams of powdered ginseng roots. To improve extraction efficiency, the mixture was left to stand for 24 to 72 hours while being shaken periodically. Use a filter sieve to separate particles and contaminants from the solution when the soaking time is over. To eliminate the alcohol and concentrate the flavonoids, use a rotary evaporator to concentrate the filtrate at a low temperature of about 40–50°C. After that, the extract was applied to nylon bags and allowed to dry at room temperature.

Animals

This investigation was carried out from August 24 to September 26, 2024, in the animal house of Veterinary Medicine College at Tikrit University. From the animal house of the Veterinary Medicine College at Tikrit University, seventy (70) mature male Albino rats that appeared to be in good health were acquired. The creatures are 8–10 weeks old and weigh between 200 and 250 g, with an average of 225 g. Standard cages made of plastic measuring 46*28*13 cm were used to house the animals. They were maintained in an atmosphere that was suitable for them (20–25 C)°.

General Experimental Design

The animals that used in current study were divided into 7 groups, and each group contain 10 rats, as following:

- G1: control group received normal saline (orally) for 30 days.
- G2: rats received dimethyl sulfoxide (DMSO) (orally) daily for 30 days.
- G3: rats received Ibuprofen (120mg/kg) (orally) daily for 10 days.
- G4: rats received Ibuprofen (120mg/kg) daily for 30 days.
- G5: rats received ginseng extract (20mg/kg) (orally) daily for 30 days.
- G6: rats received Ibuprofen (120mg/kg) for 10 days and followed by ginseng extract (20mg/kg) daily for 20 days.
- G7: rats received Ibuprofen (120mg/kg) and ginseng extract (20mg/kg) daily for 30 days.

Measurements

- **Testosterone**: Sandwich-ELISA is an ELISA technique used by the ELISA Kit (SUNLONG, China) to measure the amount of testosterone in serum and plasma.
- **Follicle-stimulating hormone (FSH)**: Sandwich-ELISA is an ELISA technique used by the ELISA Kit (SUNLONG, China) to measure the amount of FSH in serum and plasma.
- **luteinizing hormone (LH)**: Sandwich-ELISA is an ELISA technique used by the ELISA Kit (SUNLONG, China) to measure the amount of LH in serum and plasma.
- **Carnitine:** Sandwich-ELISA is an ELISA technique used by the ELISA Kit (SUNLONG, China) to measure the amount of Carnitine in serum and plasma.
- **Coenzyme Q10:** Sandwich-ELISA is an ELISA technique used by the ELISA Kit (SUNLONG, China) to measure the amount of Coenzyme Q10 in serum and plasma.

Histological study

Rat testis pieces were taken, fixed with 10% formalin, paraffin-processed, cut with a rotary microtome to a thickness of six micrometers, and stained with Hematoxylin and Eosin (H&E) histological stains [15,16]. Through the use of an Optica microscope (Italy), sections were inspected.

Statistical analysis

The Data of sexual hormones were analyzed by using a program called Minitab (statistical program). The difference between the experimental group's means was analyzed by ANOVA.

RESULTS & DISCUSSION

Table (1) shows the levels of some sexual hormones in male rats and in all study groups. Testosterone concentrations were normal in all groups and there were no significant differences (P≤0.05) between groups, as it reached 21.172 ± 0.692 in the dimethyl sulfoxide group and the third ibuprofen group (21.593 ± 1.133), which did not show significant differences (P≤0.05) compared to the rest of the groups and the control group (22.130 ± 0.377). FSH concentrations were normal in all groups and there were no significant differences (P≤0.05) between groups, as it reached 11.549 ± 0.392 in the dimethyl sulfoxide group and the third ibuprofen group (11.908 ± 1.183), which did not show significant differences (P≤0.05) compared to the rest of the groups and the control group (11.711 ± 1.178). On the other hand, significant (P≤0.05) differences were found in the concentration of LH, where the highest concentration was in the fourth group, which took Ibuprofen for 30 days (15.493 ± 0.591) compared to the control group (14.556 ± 1.008), while the treated groups did not show significant differences (P≤0.05) compared to the control group.

Table (1): the levels of some sexual hormones in male rats and in all study groups

Groups	Testosterone (IU/L)	FSH (IU/L)	LH (IU/L)
G1	22.130 ± 0.377 a	11.711 ± 1.178 a	14.556 ± 1.008 bc
G2	21.172 ± 0.692 a	11.549 ± 0.392 a	14.109 ± 0.863 c
G3	21.593 ± 1.133 a	11.908 ± 1.183 a	14.981 ± 0.808 ab
G4	21.686 ± 1.229 a	12.392 ± 1.013 a	15.493 ± 0.591 a
G5	22.052 ± 0.880 a	11.967 ± 1.295 a	15.152 ± 0.446 a
G6	21.739 ± 1.473 a	11.884 ± 0.802 a	14.091 ± 0.451 c
G7	21.301 ± 0.508 a	12.190 ± 0.701 a	14.100 ± 0.747 c
P- value	0.528 ns	0.864 ns	0.01**

Our experiment demonstrated that male rats' usage of ibuprofen increased their LH levels. This idea is supported by our data from the ex vivo trials, which show that ibuprofen's direct anti-androgenic activity was the cause of the observed increase in LH. This is in line with a prior study that found that men who volunteered to take acetylsalicylic acid, another NSAID, in combination with human chorionic gonadotropin (hCG), a hormone that mimics LH, had lower levels of steroidal hormones than controls who were exposed to hCG but not the analgesic [17]. According to the current study's findings, ginseng also improved serum sexual hormones (FSH and LH). Ginsenoside, the triterpenoid saponin that is the active component of ginseng, shares structural similarities with steroid hormones. Because ginseng has a lot of steroid receptors (androgen receptors) in the male reproductive tract, genital organs, and spermatozoa, this component of ginseng may be linked to improved sexual function and reproductive behavior [18]. Other researchers have reported similar findings about ginseng's benefits, explaining that it acts on steroid receptors to increase testosterone synthesis and, indirectly, libido Matsumoto [19].

Sperm properties

Table (2) showed some sperm properties in male rats and in all study groups. Sperm motility percentage in Ibuprofen (30 days) group (48±5.70) and Ibuprofen (10 days) group (72±2.74) showed significant (P≤0.05) reduced compared to the control group (89±4.18). while, in the ginseng group (88±2.74) showed non-significant (P≤0.05) differences compared to the control group. In the treated groups, sperm motility showed significant (P≤0.05) reduced compared to the control group but there is improved compared to Ibuprofen groups. Sperm life percentage in Ibuprofen (30 days) group (35.2±4.63) and Ibuprofen (10 days) group (52.2±4.92) showed significant (P≤0.05) reduced compared to the control group (84±8.63).

while, in the ginseng group (82±9.46) showed non-significant (P≤0.05) differences compared to the control group. In the treated groups, sperm life showed significant (P≤0.05) reduced compared to the control group but there is improved compared to Ibuprofen groups. Sperm dead percentage in Ibuprofen (30 days) group (64.8±9.63) and Ibuprofen (10 days) group (47.8±4.92) showed significant (P≤0.05) elevated compared to the control group (16±3.63). while, in the ginseng group (18 ± 4.46) showed non-significant (P≤0.05) differences compared to the control group. In the treated groups, sperm life showed significant (P≤0.05) elevated compared to the control group but there is improved compared to Ibuprofen groups. Abnormal sperm percentage in Ibuprofen (30 days) group (19.6±3.85) and Ibuprofen (7 days) group (13 ±1.0) showed significant (P≤0.05) elevated compared to the control group (7.6±2.074). while, in the treated groups and ginseng group (8.2±2.39) showed non-significant (P≤0.05) differences compared to the control group. Sperm count percentage in Ibuprofen (30 days) group (10.2±1.483) and Ibuprofen (10 days) group (17.8±2.164) showed significant (P≤0.05) reduced compared to the control group (31.4±2.103). while, in the ginseng group (28.0±5.147) showed significant (P≤0.05) reduced compared to the control group. In the treated groups, sperm count showed significant (P≤0.05) reduced compared to the control group but there is improved compared to Ibuprofen groups.

Table (2): the feature of sperm in studied groups

Groups	Sperm Motility %	Life Sperm	Dead Sperm	Abnormal Sperm	Sperm count
G1	89±4.18 a	84±8.63 a	16±3.63 e	7.6±2.074 c	31.4±2.103 a
G2	56±4.18 d	65±2.74 d	35±2.74 c	11.4±1.140 b	20.8±3.582 d
G3	72±2.74 c	52.2±4.92 e	47.8±4.92 b	13 ±1.0 b	17.8±2.164 e
G4	48±5.70 e	35.2±4.63 f	64.8±9.63 a	19.6±3.850 a	10.2±1.483 f
G5	88±2.74 a	82±9.46 ab	18 ± 4.46 e	8.2±2.39 c	28.0±5.147 b
G6	77±2.74 b	76.8±4.15 c	23.2±4.15 d	8.8±1.643 c	24.8±3.667 c
G7	75±3.54 bc	79.8±3.35 bc	20.6±3.71 de	8 ±2.35 c	23.1±3.324 c
P-value	0.00004	0.0008	0.0008	0.002	0.0007

Ibuprofen's effects on sperm parameters were demonstrated in the current study using rats as an experimental model. In both groups, Ibuprofen can lower the percentage of fast spermatozoa motility, according to the sperm motility assessment. Aspirin, a non-steroidal inhibitor of cyclo-oxygenase (COX), has been shown to have detrimental effects on sperm motility. These findings were consistent with those of Ekalou et al. (20). Similar outcomes were also noted by Ekalou et al. following a 90-day aspirin treatment. The decrease in sperm viability and count could be the consequence of apoptosis or necrosis, which were brought on by pharmacological treatments, particularly in the high dose group in the later stages. In the current investigation, ginseng treatment proved efficient in increasing sperm motility and morphology. Dahlberg (21) noted that sperm motility and fertility are connected, with human sperm motility being identified as the most significant factor in fertility. It was reported by Morgentaler et al. (22) that sperm morphology affects fertility. According to Choi et al. (23) ginseng root will promote the morphology and motility of epididymal sperm, but it won't alter the concentration of sperm in male rats. The high concentration of active ingredients in ginseng root, including saponins, phenolic compounds, alkaloids, polyacetylene, and polysaccharides, was noted by Shin et al. (24) as having a significant impact on reproductive efficacy. (25) noted that ginsenoside, a compound found in ginseng root that resembles steroid hormones in composition, is one of the chemicals that encourage sexual activity. Ginsenoside will cause male rats' anterior pituitary glands to secrete more LH (26).

Coenzyme Q10 & Carnitine

Table (3) showed the levels of some parameters in male rats and in all study groups. Coenzyme Q10 activity in Ibuprofen (10 days) group (7.879 ± 1.949) exhibited significant (P≤0.05) differences when compared to control (4.193 ± 0.661). while, in the treated groups and ginseng group (7.987 ± 0.714) showed non-significant (P≤0.05) differencesu compared to the control group. The Carnitine levels in Ibuprofen (30 days) group (2857±90.2) exhibited non-significant (P≤0.05) differences when compared to control (3174 ±100.4). while, in the treated groups and ginseng group (38 30±120.4) exhibited non-significant (P≤0.05) differences when compared to control.

Table (3): the activity of Coenzyme Q10 & Carnitine in studied groups

Groups	Coenzyme Q10 (mg/L)	Carnitine (mg/ L)
G1	4.193 ± 0.661 ab	3174 ± 100.4 a
G2	3.769 ± 0.327 b	1841 ± 80.7 a
G3	7.879 ± 1.949 a	3665 ± 105.7 a
G4	5.464 ±1.835 ab	2857 ± 90.2 a
G5	7.987 ± 0.714 a	38 30 ±120.4 a
G6	7.056 ± 0.663ab	3689 ± 106.9 a
G7	7.792 ± 1.137a	2237± 85.04 a
P- value	0.05 *	0.05 *

Same letters mean there are non-significant (P≤0.05) differences. Where, different letters mean there are significant (P≤0.05) differences. NSAIDs are used primarily for their anti-inflammatory, anti-fever, and pain-relieving properties, but they also have other therapeutic effects. Without taking into account their toxic effects and contraindicated instances, they are mostly available as over-the-counter medications (27). NSAID use has been linked to a number of pathological situations, particularly when used over an extended period of time, and has been shown to significantly alter Coenzyme Q10 (28). According to the results of the current investigation, ginseng consumption did not significantly alter urea levels. By decreasing gentamicin accumulation in the renal tubule, P. ginseng extract has been demonstrated to be useful in preventing kidney damage. An evaluation of P. ginseng's nephroprotective effect on gentamicin-induced nephropathy revealed improvements in renal function assessment indicators (29). Given that CoQ10 is a potent antioxidant, this validates the findings of the current study that ginseng can raise the levels of Carnitine and Coenzyme Q10 in mice, which in turn improves the properties of the testicles and tissues. CoQ10 scavenges lipid peroxidation products during free radical reactions (31) and prevents the production of ROS (30).

Histological study

Control group

The parenchyma of testis had Crowded Seminiferous tubules, each lumen of tables had Spermatogonia which are resting on the basement membrane (B.M) and other spermatogenic stages of development, the interstitial connective tissue had blood vessels surrounding the Leydig cells (fig: 1).

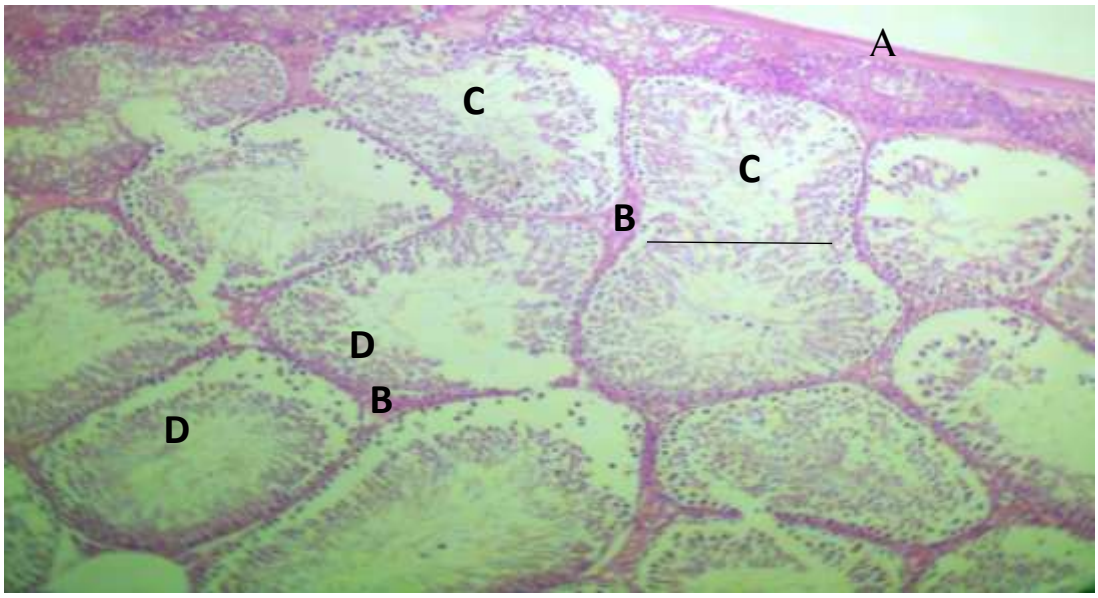

Fig (1): Histological section from the testis of the rat (G1) shows : Parenchyma of Testis , capsule (A) . Interstitial connective tissue (B) crowded seminiferous tubule (C) spermatogenic developments (D) (H&E X10).

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 16s,2025
https://theaspd.com/index.php

Dimethyl sulfoxide (DMSO)

The Capsule of testis was formed by dense Collagen fibers with fibroblasts, Subcapsuler blood vessels were present Containing hemolyzed blood. The lumen of seminiferous tubules had small size spermatogonia resting on basement membrane. great size primary Spermatocyte and smaller size with double rows of Secondary Spermatocyte. Spermatid were seen in small groups and the center of each seminiferous tubule had spermatozoa (fig: 2).

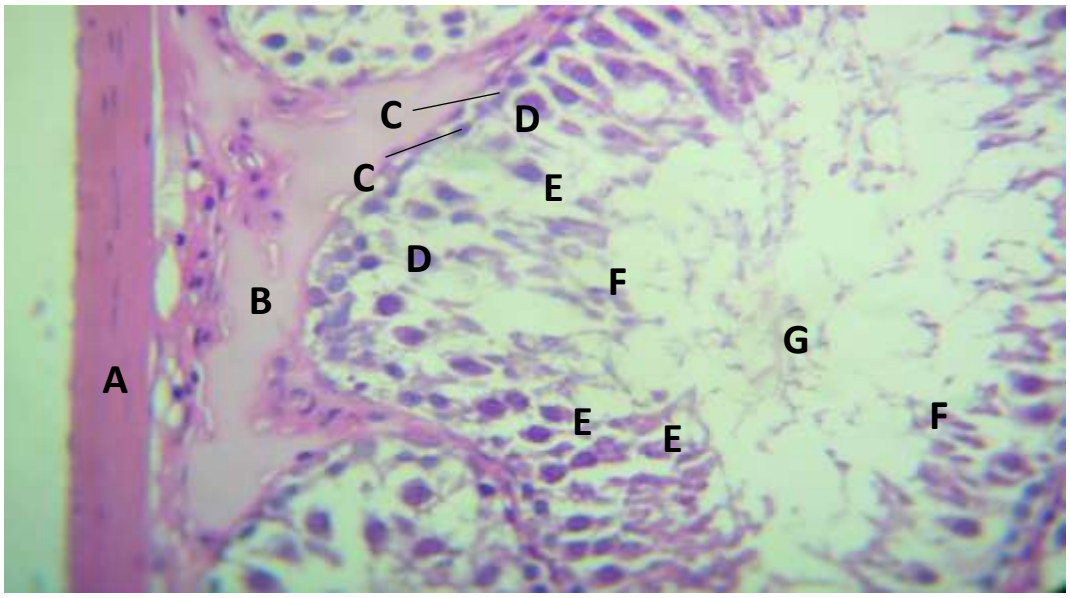

Fig (2) Histological section from the testis of the rat (G2) shows : Capsule of testis formed by dense Collagen bundle (A) . Subcapsuler hemolyzed blood (B) . spermatogonia (C). hypertrophied primary spermatocyte (D). secondary spermatocyte (E). Spermatide (F) spermatozoa (G) (H & E X40).

Ibuprofen (10 days) group

Seminiferous tubules had spermatogonia resting on the basement membrane primary and secondary Spermatocytes were present and small size of spermatids in Clusters were evident near the center of seminiferous tubules. Spermatozoa were seen in the center of seminiferous tubules, leydig cells were present in the interstitial connective tissue in small groups (fig: 3).

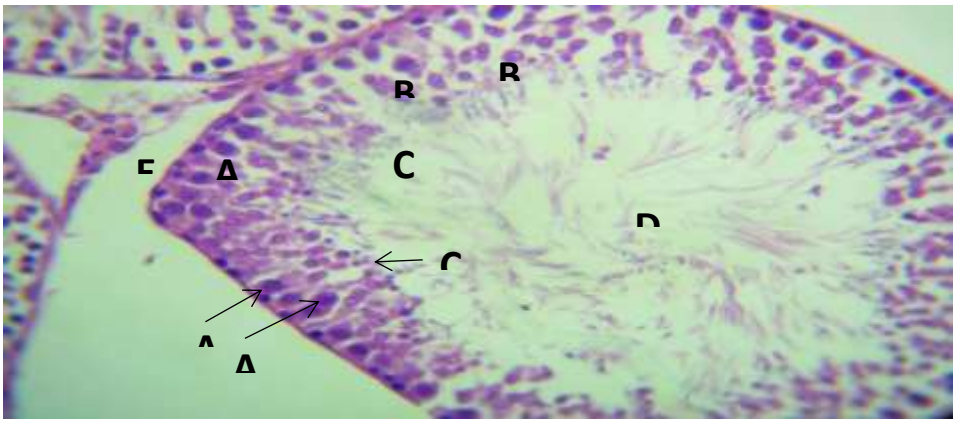

Fig (3): Histological section from the testis of the rat (G3) showed Seminiferous tubules, primary

Ibuprofen (30 days) group

Seminiferous tubules were demonstrated occupied win spermatogonia, row of Primary Spermatocytes, 2-3 rows of Secondary Spermatocytes and groups of spermatids. The center of seminiferous tubules had Spermatozoa, appeared as flame like toward the Sertoli cells which are resting on basement membrane. Groups of leydig cells were located in the interstitial connective tissue (fig: 4).

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 16s,2025
https://theaspd.com/index.php

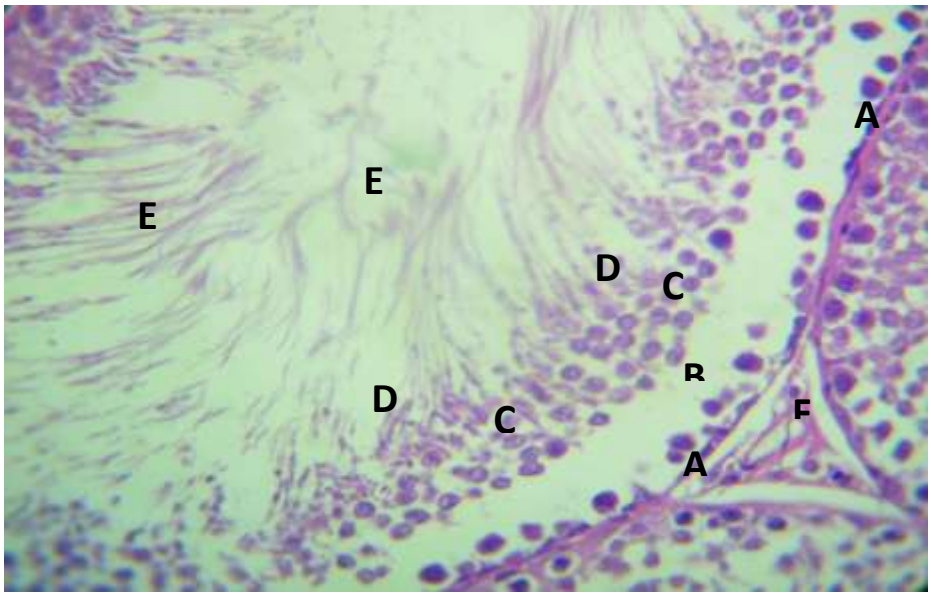

Fig (4): Histological section from the testis of the rat (G4) shows : seminiferous tubule basement membrane (A). primary spermatocyte (B). groups of secondary spermatocyte (C). Clusters of spermatide (D). Flame like spermatozoa (E). Lydig cells (F). (H&E X40).

Ginseng (30 days)

The Capsule of testis was formed by dense Collagen fibers, there was many Spermatogenic cells surrounded by collagen bundle, Great Cavities of seminiferous tubule had degenerated spermatogonia and other cells of Spermatocytes were absent homogenized odema were present inside the lumen of Certain seminiferous tubules (fig: 5).

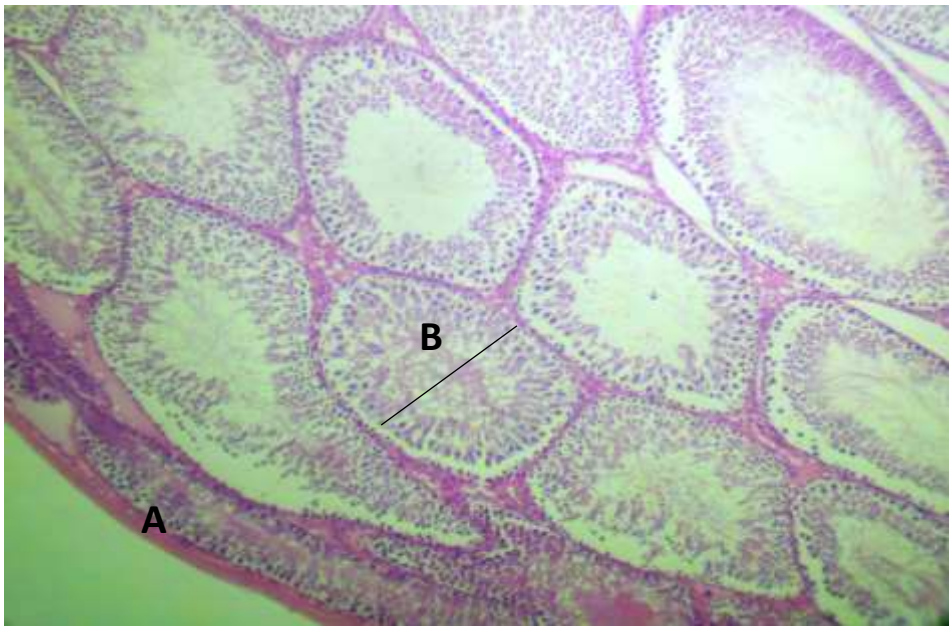

Fig (5): Histological section from the testis of the rat (G5) showed Capsule of testis formed by Collagen bundle (A).(H & E X10).

Ibuprofen (10 days) and ginseng (20 days)

The testicular tissue was Coated with Capsule of Collagen bundles, the parenchyma of testis was occupied with crowded seminiferous tubule which had different stages of Spermatogenic development, the interstitial connective tissue had groups of leydig Cells with blood capillaries (fig: 6).

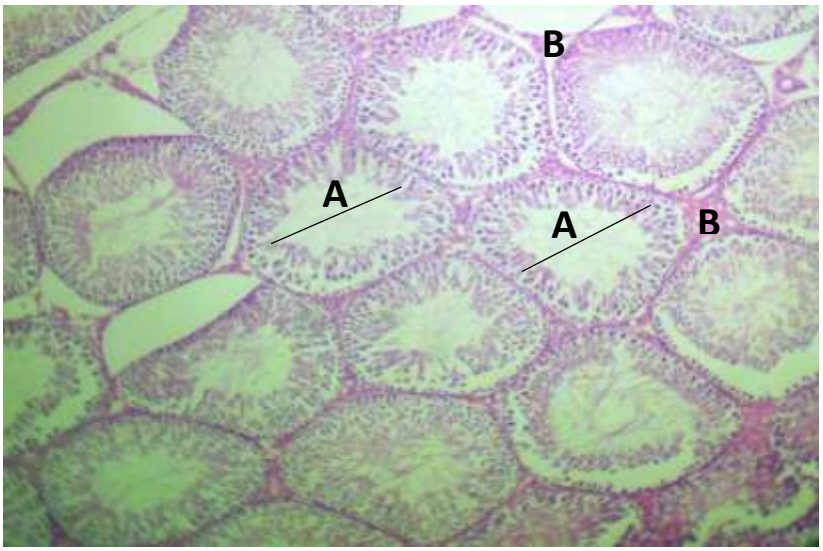

Fig (6): Histological section from the testis of the rat (G6) showed parenchyma of testis, Crowding of seminiferous tubules, with different stages of spermatogenic development (A). Interstitial connective tissue with blood Capillaries (B) Leydig cells (C) (H&E x10).

Ibuprofen + ginseng together (30 days)

Seminiferous tubules were containing the different stages of spermatogenic development. Primary spermatocytes in certain tubules appeared atrophied and secondary spermatocytes were abundant and intermingled with spermatids. Scanty of spermatzoa were seen in the certain seminiferous tubules. The blood vessels in the interstitial connective tissue were engorged with hemolyzed blood in the form of pools-like with presence of small fat droplets in lumen of basement cavity (fig: 7).

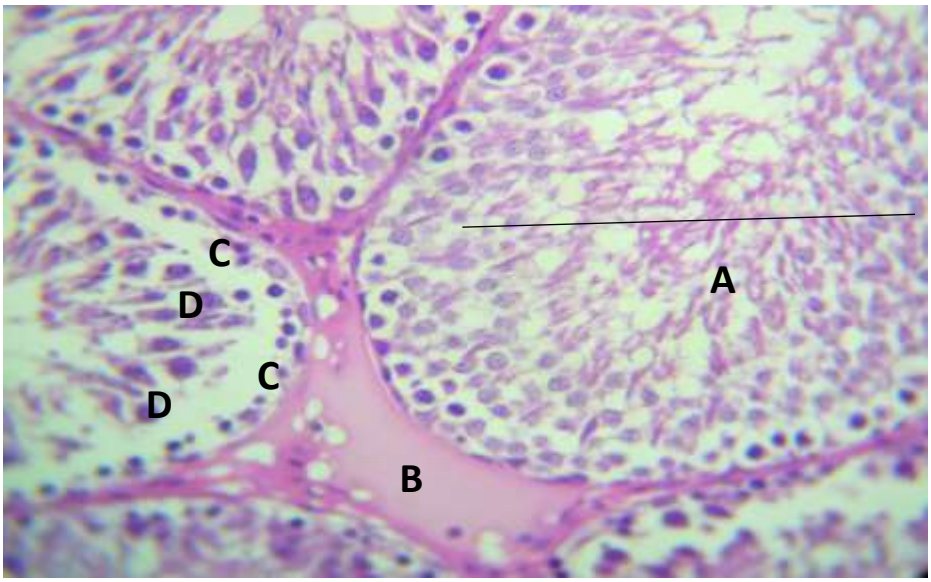

Fig (7): Histological section from the testis of the rat (G7) showed Seminiferous tubules, spermatogenic development (A). hemolyzed blood with small droplets of fat (B). Atrophy of primary spermatocytes (C). Hypertrophy of secondary Spermatocyte (D) (H&E X40).

The histological analysis of rats given ibuprofen and dimethyl sulfoxide for 10 and 30 days showed various histological alterations, such as hemolyzed blood vessels, fewer spermatogonia, and a lower sperm count. Seminiferous tubules were found to contain the various phases of spermatogenic development, and the majority of spermatogenic cells were improved when ginseng extract was used to cure and prevent the negative effects of ibuprofen. Ibuprofen has been shown in several studies to have a remarkable dual effect

on both Leydig and Sertoli cells. This makes it the NSAID with the most extensive endocrine-disturbing qualities found in males to date, considering all chemical classes. Only on Leydig cells have prior ex vivo investigations on adult testis indicated antiandrogenicity (32,33,34). The study found that the interstitium widened with a large gap between cut parts of the seminiferous, which was in agreement with the findings of Halawa and Nagwa (35). Numerous seminiferous tubules displayed apparent hypocellularity at every stage, along with symptoms of nuclear pyknosis, cell degeneration, and loss of germ cells. In several areas of the section, cell membranes were visible, although seminiferous tubular epithelium appeared to be separated from the basement membrane. Hyaline material was deposited in the interstium, and numerous dilated, clogged blood vessels were visible. On the other hand, According to the current study, ginseng root extract effectively improves and shields testicular tissue from the harmful effects of ibuprofen. Ginseng has been demonstrated in subsequent research to enhance the number of sperm in both people and animals. Rats given ginseng have shown an enhanced rate of spermatogenesis by activation of the testicular cAMP-responsive element modulator (CREM) (36) and elevation of glial cell-derived neurotrophic factor (GDNF) production in Sertoli cells (37). Ginsenosides (0.01 mg/ml) have also been demonstrated to promote sperm development in vitro, according to Chen et al. (38). In the other study, it was discovered that via modifying the expression of Fas/Fas-L, Korean red ginseng (300 mg/kg) taken every other day for four weeks might prevent rats from experiencing spermatogenesis impairment caused by zearalenone (39).

CONCLUSIONS

Based on the results of the current study, the alcoholic extract of ginseng roots shows a protective and therapeutic effect on sex hormones and spermatogenesis cells, and improves spermatogenesis. This may be due to its presence of active substances that play a role as antioxidants.

Conflict of interest

The authors declare that there are no conflicts of interest.

Ethics and institutional animal care and use committee (IACUC):

The research methodology and protocols were reviewed and approved by the scientific committee of Veterinary Medicine Collage, university of Tikrit, Salah Alden-Iraq (TU.VET.30) in compliance with animal welfare ethical measures prior to any experiments being conducted.

Acknowledgment

The authors are grateful to the University of Tikrit /College of Veterinary Medicine for all the facilities to achieve this study.

REFERENCES

1. Kashani L., Akhondzadeh S. Female Infertility and Herbal Medicine. Journal of Medicinal Plants. 2017; 16(61): 1-7.
2. Sarhat, E.R., Wadi, S.A., Mahmood, A.R. Effect of ethanolic extraction of moringa oleifera on paraoxonase and arylesterase enzyme activity in high fat diet-induced obesity in rats. Research Journal of Pharmacy and Technology, 2018, 11(10): 4601–4604
3. Akbaribazm M., Nader G., Mohsen R. Female infertility and herbal medicine: An overview of the new findings. Food Sci Nutr. 2021; 9(10):5869–5882.
4. SayranSS, ER Sarhat.Effects of Ethanolic MoringaOleifera Extract on Melatonin, Liver and Kidney Function Tests in Alloxan-Induced Diabetic Rats Indian Journal of Forensic Medicine & Toxicology.2019;13(4):1015-1019.
5. Hussain I. Hussain, Elham M. Mahmood, Saif Kamil, Huda A. Hameed, Samira AH. Abdulla.Chloroquine Induced Lesions in the Visceral Tissues of Albino Mice.Bahrain Medical Bulletin,2024; 46(3): 2313— 2317
6. Bo-Hyon Y., Young Sik C., SiHyun C., Byung S. L., Si Kwan K., Seok K. (2018). Effects of Ginseng on Fertility. Biomed J Sci & Tech Res. 11(1): 8234-8237.
7. Saleh, N.I.S.; Wadee, S.A. Minimizing the side effects of Doxorubicin Induced Hepatotoxicity by using alcoholic extract of Date Palm in adult rats .Revista Bionatura 2023;8 (2) 63. http://dx.doi.org/10.21931/RB/CSS/2023.08.04.03.
8. Sarhat, E., Wadi, S. A., Sedeeq, B., Sarhat, T. R., Jasim, N. Study of histopathological and biochemical effect of Punica granatum L. extract on streptozotocin -induced diabetes in rabbits. Iraqi Journal of Veterinary Sciences, 2019; 33(2): 189-194. doi: 10.33899/ijvs.2019.125523.1045
9. Srinivasu M, Singh S, Ahmad A, Pathak A. Effect of enrofloxacin and ciprofloxacin on oxidative stress in rats. Journal Of Veterinary Pharmacology And Toxicology. 2022;21(1):80-2.
10. Kristensen DM., Séverine M., Pierre G., Laurianne L., Tania S., Katharina M M. (2016). Analgesic use - prevalence, biomonitoring and endocrine and reproductive effects. Nat Rev Endocrinol 12**, 381–393.**
11. Elham M. Mahmood, Maryam T. Tawfeq , Siham A. Wadee.Histological and Biochemical Study of The Effect of Fexofeadine on Salivary Gland in Rats. Georgian Medical News.2024;2 (347):38-40.

12. Esteves S.C. Peter H., Filippo M U., Carlo A., Leen A., Christopher L R., Hermann M B., Niels J., Allan A P., Manuela S., Daniele S. APHRODITE criteria: addressing male patients with hypogonadism and/or infertility owing to altered idiopathic testicular function. Reprod Biomed. 2024; 48(4):103647.
13. Intesar J. Mohammed, Sarhat ER, Siham A. Wadee, and Salwa M. Al-Shiakhani Histological and Biochemical Evaluation of the Effect of Desloratadine Drug in Parotid Gland Tissues. ANB. MED. J. 17(2):72—77, 2021.
14. Wan-Ting H., Jen-Hung W., Dah-Ching D. Ibuprofen use and male infertility: Insights from a nationwide retrospective cohort study. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2025; 307: 128-133.
15. Mahmood, E.M., Sarhat, E.R., Tawfeq, M.T., Wadee, S.A. Histological and biochemical study of the effect of fexofenadine on salivary gland in rats. Georgian Medical News, 2024, 347(2), 38–40
16. Hameed, B.K., Hameed, M.A., Hussein, H.M., Wadee, S.A. Histological Study of Antibiotic Effect on Liver, Kidney and Breast Muscle in Poultry. Egyptian Journal of Veterinary Science(Egypt), 2025, 56(1), pp. 39–46.
17. Conte D, et al. Aspirin inhibits androgen response to chorionic gonadotropin in humans. Am J Physiol. 1999; 277: E1032–E1037.
18. Solakidi, S., Psarra, A.G., Nikolaropoulos, S. andSekeris, C.E., 2005. Estrogen receptors α and β(ERα and ERβ) and androgen receptor (AR) inhuman sperm: Localization of ERβ and AR inmitochondria of the midpiece. Hum. Reprod., 20:3481-3487.
19. Travison, T.G., Morley, J.E., Araujo, A.B., O'Donnell,A.B. and McKinlay, J.B., 2006. The relationshipbetween libido and testosterone levels in agingmen. J. Clin. Endocr. Metab., 91: 2509-2513.
20. Ekaluo UB, Ikpeme EV, Udokpoh AE. Sperm head abnormality and mutagenic effects of aspirin, paracetamol and caffeine containing analgesics in rats. Int J Toxicol. 2012;7:6–11.
21. Dahlberg B. Sperm motility in fertile men and males in infertile units: in vitro test. Arch Androl. 2008;20:31-34
22. Morgentaler A, Alper MM, Harris DH et al. Sperm morphology and in vitro fertilization outcome : a direct comparison of World Health Organization and strict criteria methodologies. Fertil Steril. 1995;64(6):1177- 1182
23. Choi H J, Han H S, Park J H, Son J H, Bae J H, Seung T S and Choi C (2013) Antioxidantive, phospholipase A2 inhibiting, and anticancer effect of olyphenol rich fractions from Panax ginseng C. A. Meyer. J. Korean Soc. Agric. Chem. Biotechnol. 46, 251- 256.
24. Shin J G, Park J W, Pyo J K, Kim M S and Chung M H (1990) Protective effects of aginseng component, maltol (2-methyl-3-hydroxy-4-pyrone), against tissue damages induced by oxygen radicals. Korean J. Ginseng Sci. 14, 187-190.
25. Solakidi S, Psarra A M, Nikolaropoulos S and Sekeris C E (2015) Estrogen receptor alpha and beta (ER alpha and ERbeta) and androgen receptor (AR) in human sperm: localization of ERbeta and AR inmitochondria of the midpiece. Hum. Reprod. 20, 3481 – 3487.
26. Tsai S C, Chiao Y C, Lu C C and Wang P S (2013) Stimulation of the secretion of LH by Ginsenoid Rb1 in rats. Chin. J. Physiol. 46(1), 1-7
27. Choo S, Nuelle JA. NSAID Use and Effects on Pediatric Bone Healing: A Review of Current Literature. Children. 2021;8(9):821.
28. Bally M, Dendukuri N, Rich B, Nadeau L, Helin-Salmivaara A, Garbe E, et al. Risk of acute myocardial infarction with NSAIDs in real world use: bayesian meta-analysis of individual patient data. Br Med J. 2017;357.
29. Lee YK, Chin YW, Choi YH. Effects of Korean red ginseng extract on acute renal failure induced by gentamicin and pharmacokinetic changes by metformin in rats. Food Chem Toxicol. 2013; 59: 153--9.
30. Sohet FM, Neyrinck AM, Pachikian BD, de Backer FC, Bindels LB, Niklowitz P, et al. Coenzyme Q10 supplementation lowers hepatic oxidative stress and inflammation associated with diet-induced obesity in mice. Biochem Pharmacol. 2009;78(11):1391-400.
31. Tsuneki H, Sekizaki N, Suzuki T, Kobayashi S, Wada T, Okamoto T, et al. Coenzyme Q10 prevents high glucose-induced oxidative stress in human umbilical vein endothelial cells. Eur J Pharmacol. 2007;566(1-3):1-10.
32. Burd NA, et al. Effect of a cyclooxygenase-2 inhibitor on postexercise muscle protein synthesis in humans. Am J Physiol Endocrinol Metab. 2010;298:E354–E361.
33. Desdoits-Lethimonier C, et al. Human testis steroidogenesis is inhibited by phthalates. Hum Reprod. 2012;27:1451–1459.
34. Markworth JF, Vella LD, Figueiredo VC, Cameron-Smith D. Ibuprofen treatment blunts early translational signaling responses in human skeletal muscle following resistance exercise. J Appl Physiol (1985) 2014;117:20–28.
35. Halawa H., Nagwa E. Evaluation of Melatonin Effect on Ibuprofen Induced Renal and Testicular Toxicity in Adult Male Albino Rats. The Egyptian Journal of Forensic Sciences and Applied Toxicology. 2012; 12(2):125-144.
36. Yang WM, Park SY, Kim HM, Park EH, Park SK, Chang MS. Effects of Panax ginseng on glial cell-derived neurotrophic factor (GDNF) expression and spermatogenesis in rats. Phytother Res. 2011;25:308–11.
37. Park WS, Shin DY, Kim R, Yang WM, Chang MS, Park SK. Korean ginseng induces spermatogenesis in rats through the activation of cAMP-responsive element modulator (CREM) Fertil Steril. 2007;88:1000–2.
38. Chen JC, Chen LD, Tsauer W, Tsai CC, Chen BC, Chen YJ. Effects of Ginsenoside Rb2 and Rc on inferior human sperm motility in vitro. Am J Chin Med. 2001;29:155–60.
39. Cho ES, Ryu SY, Jung JY, Park BK, Son HY. Effects of red ginseng extract on zearalenone induced spermatogenesis impairment in rat. J Ginseng Res. 2011;35:294–300.