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Protective Effects of Curcumin Against Haloperidol-Induced Reproductive Toxicity in Male Wistar Rats: Hormonal, Spermatological, and Histopathological Assessment

Mohammed A. Aboktifa[1*] and Kamal. J. Awni[2] and Adnan M. Jasim[1] and Noor Al Huda Hussein Al-ramahi[3]

[1]Department of Physiology, Biochemistry and Pharmacology, College of Veterinary Medicine, AL-Qasim Green University, Babylon,51013 Iraq. [2]Department of Dialysis Technique, Balad Technical Institute, Middle Technical University, Iraq. [3]Department of Physiology, Biochemistry and Pharmacology College of Veterinary Medicine, University of Al-Qadisiyah, Al-Diwaniyah, Iraq.

ABSTRACT

The relationship between hormonal imbalances and psychotropic drugs at a pathophysiology level remains unclear. The study was aimed to determine whether curcumin, a polyphenolic antioxidant, and phenylalanine can safeguard male Wistar rats from reproductive issues. We randomly assigned 40 male Wistar rats into five groups: a negative control group, G1 receiving haloperidol at a dosage of 1 mg/kg/day, G2 receiving curcumin at a dosage of 200 mg/kg/day, G3 receiving phenylalanine at a dosage of 200 mg/kg/day, and G4 also receiving phenylalanine at a dosage of 200 mg/kg/day. There were no significant variations in serum levels of prolactin among the groups, while giving haloperidol to G1 resulted in testosterone levels to reduce from 224.25 ng/dL to 111.00 ng/dL. Combined treatment with curcumin (G2) brought testosterone levels back to the highest level ever recorded (296.00 ng/dL). The triple combination (G3) was able to keep FSH and LH levels similar to their baseline levels. Histopathological examination showed that haloperidol treatment caused structural impairment and atrophy of the germinal epithelium in approximately 70% of seminiferous tubules. In contrast, curcumin (G2) and the combined treatment (G3) considerably restored testicular spermatogenesis and architecture. The study concluded that curcumin, particularly when combined with phenylalanine, revealed a notable protective effect against reproductive harm induced by haloperidol. These findings indicated that curcumin may ameliorate the adverse effects that drugs of antipsychotic on male fertility by protection testosterone levels and the structural integrity of the testes.

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E-mail addresses:
mohammed.aboktifa@vet.uoqasim.edu.iq

ORCID: 0000-0003-3095-5564

* Corresponding author
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INTRODUCTION

Male infertility has only recently begun to gain significant clinical and scientific recognition, despite being primarily attributed to factors such as reduction in sperm count, abnormal sperm ejaculation, decreased sperm motility, and structural abnormalities of sperm morphology [1,2]. Notably, idiopathic

infertility continues to represent a substantial proportion of male infertility cases, accounting for approximately 30%–40% of diagnoses. An increasing volume of research has demonstrated that numerous contributing factors play a role, including physiological variables such as age, body weight, and overall body composition [3]. Additional contributing factors include pathological conditions such as metabolic disorders and inflammatory processes [1,2]. Psychological influences including trauma and chronic stress, lifestyle-related behaviors such as smoking, excessive alcohol consumption, and substance abuse, as well as environmental exposures to toxins and heavy metals, all of which have been shown to significantly impact male reproductive fertility [4]. Among the most significant and detrimental contributors to male infertility is oxidative stress, which compromises sperm function and impairs germ cell development. Increase reactive oxygen species (ROS) leading to decline in defense capacity of antioxidant this called oxidative stress, such imbalance occur, ROS causes damage in all biological macromolecules, including lipids, proteins, DNA and RNA [5].

Methods of treatment for infertility, such as traditional therapy and surgical intervening, this revealed important clinical advantages and depict the primary options of treatment available today [6]. The new and effective drugs for reproductive dysfunction become very important. Medicinal plants play an important role in covering a broad spectrum of reproductive health conditions, these natural ingredients explained marked biological benefits, especially to toxicity reduction and a decrease in adverse effects [7].

Curcumin is wide proven as one of the most important polyphenolic compounds derived from turmeric [8]. Chemical structure of curcumin possesses three biologically active functional groups, contained two phenolic groups and a diketone group [9]. Curcumin is subject to a variety of chemical and biological transformations, encompassing degradation, hydrolysis and N-attack reactions (reversible and irreversible), as well as hydrogen donation reactions, all of them can finally play to its oxidation. Due to its antioxidant properties, curcumin has expressed a wide range of therapeutic benefits [10]. Curcumin functions as a potent scavenger of ROS, in effect neutralized harmful free radicals such as superoxide anion radicals, nitrogen dioxide radicals and hydroxyl radicals. In addition, it has been confirmed to suppress lipid peroxidation across numerous animal model studies.

Recent examinations into health of male reproductive system have highly evaluated the effects of different compounds, including its potential toxicity. In particular, administration of curcumin at doses ranging from 100 to 400 mg/kg was found to provide rebuild antioxidant activity of testicular enzyme, especially SOD and GPx, while simultaneously reducing markers of lipid peroxidation (MDA) [11]. As well, this treatment significantly improved sperm count, motility, and viability, as well as testicular histological integrity in male rats that had been exposed to lead acetate at dosing 50 mg/kg over a 35-day period.

Several experimental studies on animals have showed that curcumin may enhance sperm quality and mitigate hormonal imbalances through its different pharmacological mechanisms. Additionally, curcumin may be considered as a potent cytoprotective agent via the regulation of apoptotic and cell survival signaling pathways [12]. So that curcumin may improve testicular function and support reproductive system fertility by enhancement biological pathways.

MATERIALS AND METHODS

Animals:

Total of forty animals (male rats) were used in this experiment with body weight of 180-220 g and 8-10 weeks of age;

housing: four male rats/ container; twelve hours' light/dark cycle; standard food of animal's chow and water ad libitum and acclimation: seven days prior to treatment initiation. All procedures were conducted in accordance with institutional animal ethics committee (IACUC) guidelines.

Ethical approval:

The design and methodology of this study were cautiously examined and approved to meet the animal welfare ethical criteria set by the Research Ethics Committee of at Al-Qasim Green University in certificate number qgec/88/2026.

Experimental design of the study:

Animals were divided randomly to five groups (each group 8 rats) built on homogeneity of body weight. Control group (negative) received distilled water orally only, G1 (positive control) administered haloperidol (1 mg /kg/day intraperitoneally), G2 (curcumin 200 mg/kg/day orally+ haloperidol 1 mg /kg/day), G3 Phenylalanine (200 mg/kg/day orally) + Curcumin (200 mg/kg/day) + Haloperidol (1 mg/kg/day), and G4 Phenylalanine (200 mg/kg/day) + Curcumin (200 mg/kg/day) + Haloperidol (1 mg/kg/day)

Table 1. The treatment groups

Group	Name	Treatment
C	Negative Control	Vehicle only (normal saline)
G1	Positive control (haloperidol-treated)	Haloperidol (1 mg/kg/day)
G2	Curcumin + Haloperidol	Curcumin (200 mg/kg/day) + Haloperidol (1 mg/kg/day)
G3	phenylalanine +Curcumin + Haloperidol	Phenylalanine (200 mg/kg/day) + Curcumin (200 mg/kg/day) + Haloperidol (1 mg/kg/day)
G4	Phenylalanine + Haloperidol	Phenylalanine (200 mg/kg/day) + Haloperidol (1 mg/kg/day)

Note: Doses are indicative; investigators should adjust based on validated protocols and pilot data. haloperidol vehicle is normal saline. Treatment duration: 28 days (4 weeks).

Statistical Analysis

Data were statistically processed using the Microsoft Statistical Package (SPSS), through which an independent T-test was applied to assess differences between group means, with statistical significance established at a threshold of $P<0.05$.

RESULTS

Measurement of serum prolactin concentrations across all experimental groups revealed no intergroup statistically significant differences, with all groups assigned the same letter designation (a). The untreated control animals had a mean prolactin level of 1.68 ± 0.47 ng/mL, while those receiving haloperidol

alone (G1) recorded a slightly higher concentration of 2.84 ± 1.17 ng/mL. A numerically elevated mean was observed in the G2 group treated with curcumin and haloperidol (2.02 ± 0.69 ng/mL), though this did not reach statistical significance. Animals in the G3 group receiving phenylalanine combined with curcumin against haloperidol yielded a mean of 2.39 ± 0.63 ng/mL, whereas administration of group Phenylalanine + Haloperidol returned a significant elevation of prolactin value comparable to the control to 3.35± 0.87 ng/mL.

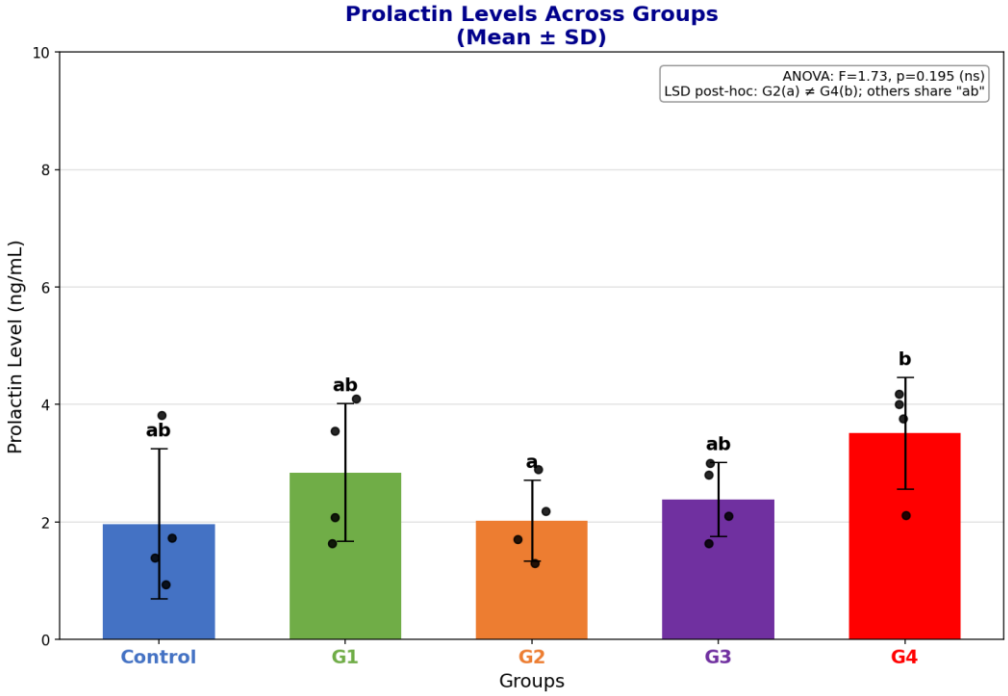

Fig. 1. Prolactin Levels Across Groups

Concentrations of serum FSH revealed a marked increase in treated groups, the most pronounced elevation seen in animals that received combination haloperidol and phenylalanine. The animals in control group kept a basal level of FSH (4.17 ± 0.29 mIU/mL) (a), showing the lowest value between all treated groups. Treatment of haloperidol alone (G1) was illustrated a more than twofold elevation to (1.75 ± 0.60 mIU/mL), even though concomitant treatment with haloperidol with curcumin (G2) produced a compared increase of (2.62 ± 0.91 mIU/mL). The triple-combination group G3 recorded a mean of (4.28 ± 0.41 mIU/mL). (G4) phenylalanine with haloperidol showed a significant decrease in serum of FSH.

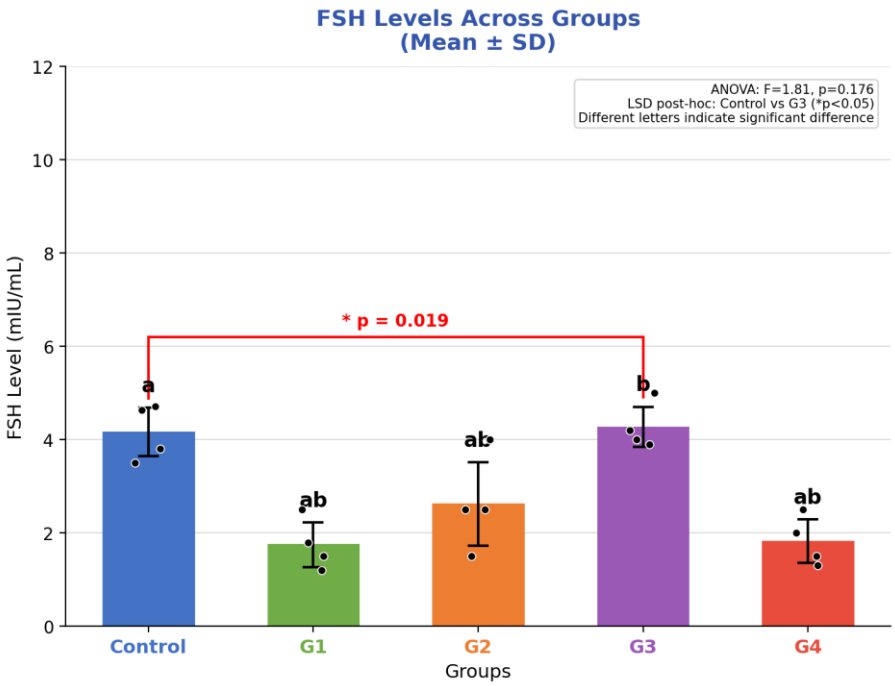

Fig. 2. FSH Levels Across Groups

Serum concentrations of LH proof that the most significant disruption of hormone was with the co-administration of haloperidol and curcumin. While, animals in control group sustained a mean LH level of (2.08 ± 0.77 mIU/mL), this value close to (G1) (at 0.97 ± 0.02 mIU/mL), suggest that haloperidol alone did not effectively disrupt LH secretion. As well, the G3 of triple combination restored a mean concentration of (2.53 ± 0.66 mIU/mL) (a), which was almost indiscernible from the untreated controls. On the other hand still has no a significant difference as compared with (G1,G4).

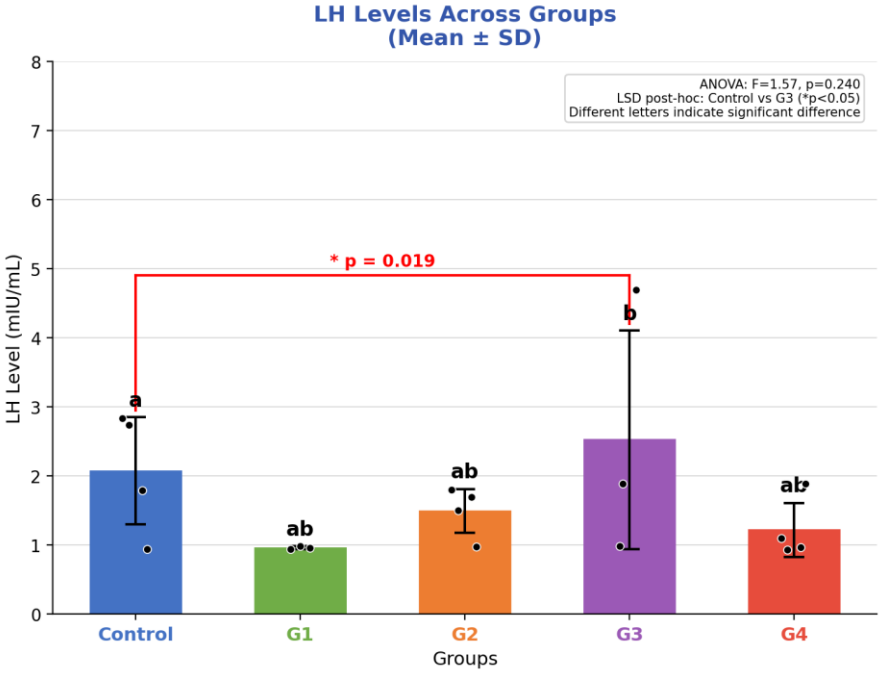

Fig. 3. LH Levels Across Groups

Serum testosterone concentrations displayed considerable variability across groups, The control animals recorded a mean testosterone level of 224.25 ± 152.58 ng/dL (ab), while animals receiving haloperidol alone (G1) showed a reduced mean of 111.00 ± 59.25 ng/dL (ab), The G2 group (Curcumin + Haloperidol) exhibited the highest mean testosterone concentration among all groups at 296.00 ± 23.39 ng/dL (b), Analysis identified G2 as significantly higher than both G3 (Phenylalanine + Curcumin and Haloperidol 78.50 ± 23.01 ng/dL, and G4 (Phenylalanine + Haloperidol appear asignificant reduction in serum testosterone to recorded mean value 38.50 ± 8.06 ng/dL.

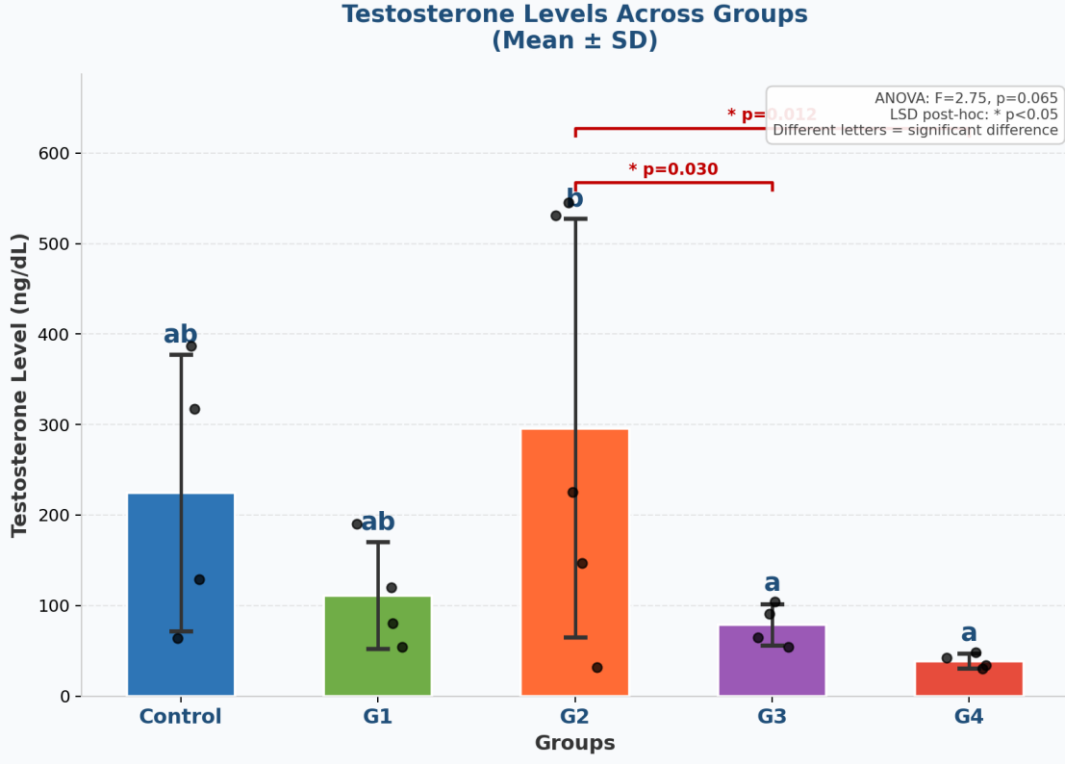

Fig. 4. Testosterone Levels Across Groups

Analysis of serum estrogen concentrations revealed that the control animals exhibited a mean estrogen level of 229.8 ± 52.80 pg/mL, while animals administered haloperidol alone (G1) reached 278.0 ± 35.02 pg/mL. The co-treatment of curcumin with haloperidol (G2) yielded a mean of 174.0 ± 29.4 pg/mL, whereas phenylalanine combined with haloperidol and curcumin (G3) produced the highest recorded concentration at 234.3 ± 49.3 pg/mL. In contrast, the G4 group demonstrated a notably reduced estrogen level of 251.8 ± 51.5 pg/mL. The significant depletions in G4 implication that the simultaneous administration of all three agents' phenylalanine with haloperidol may decrease secretion or biosynthesis of estrogen.

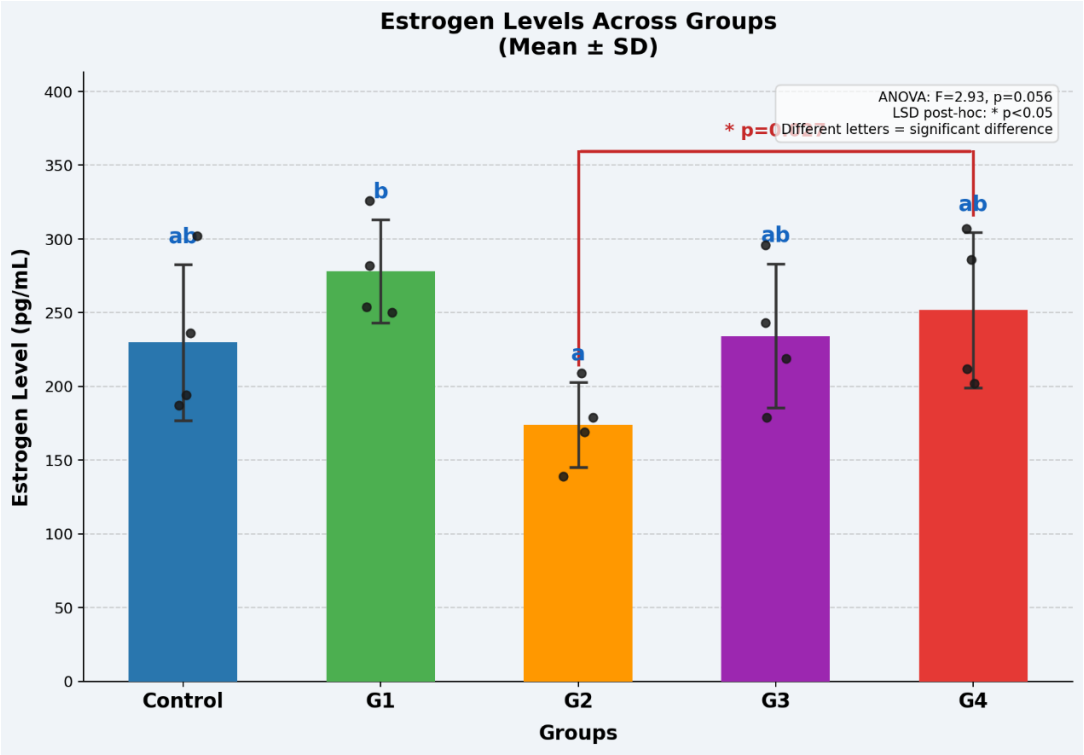

Fig. 5. Estrogen Levels Across Groups

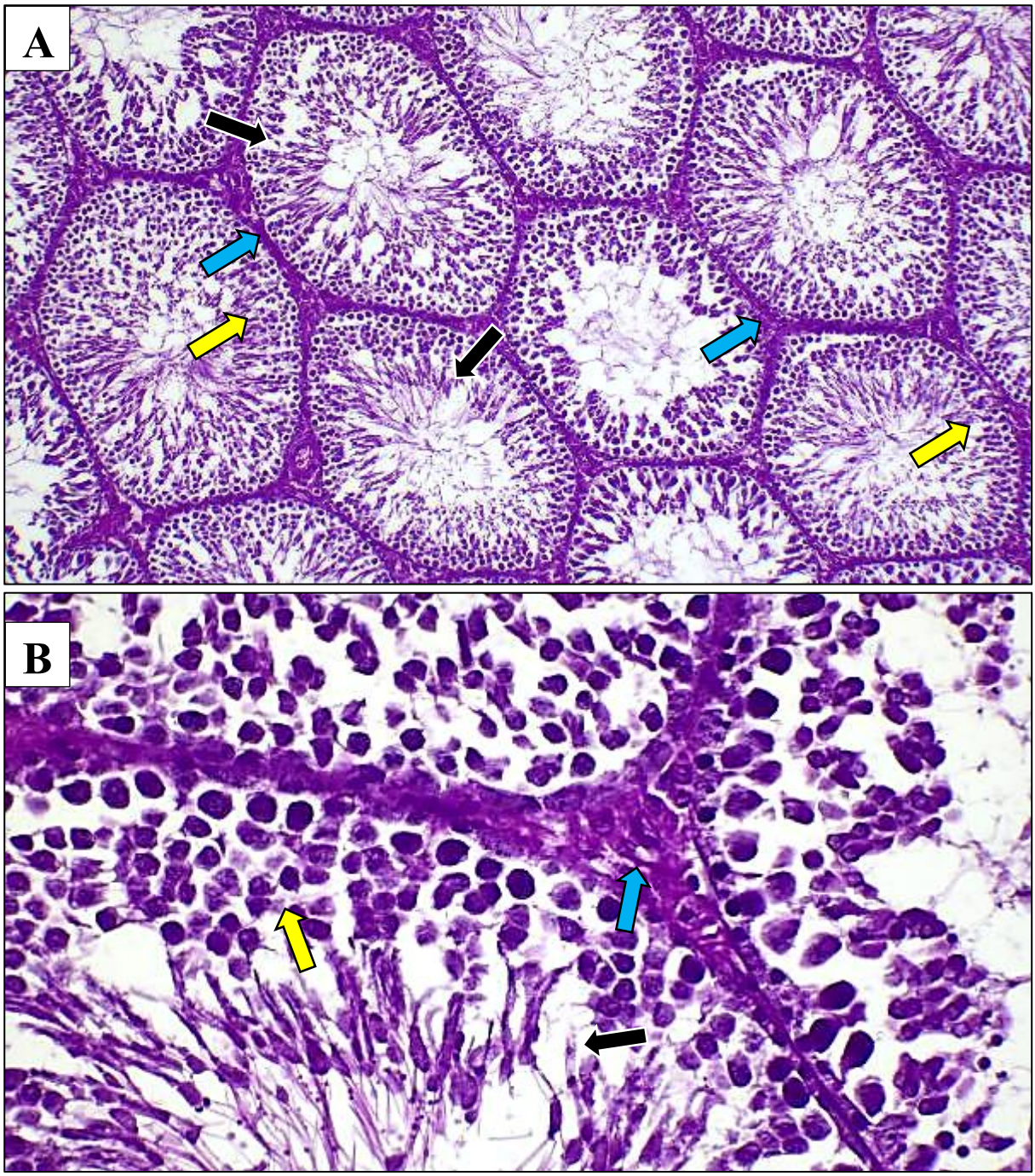

Fig. 6. Shows of rat testis in control negative group.

A and B/ Histological architecture of testicular tissue is normal. Leydig cells (blue arrows) are apparent within the interstitial tissue among seminiferous tubules. The develop seminiferous tubules (black arrow) display an organized germinal layer (yellow arrow) with distinct stages of spermatogenesis. **H&E. A: 100x and B: 400x.**

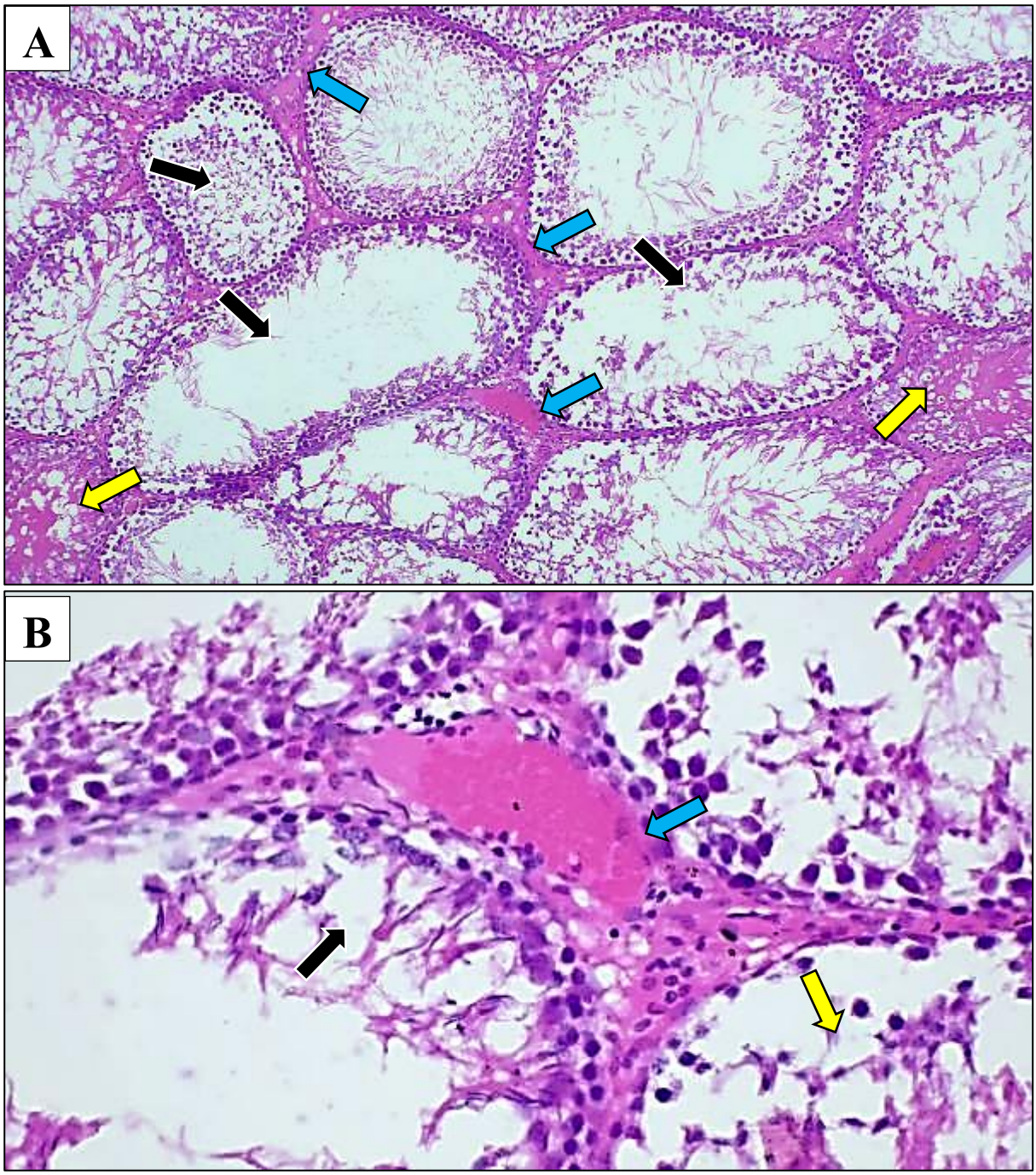

Fig. 7. Shows of rat testis in control positive group.

A and B/ Histological examination of the seminiferous tubules revealed a clear thinning of the germinal epithelium (black arrow), resulting from toxicity effects of haloperidol on spermatogenesis. Histopathological altering was prescribed around 70% of the seminiferous tubules contrast with the negative group. Furthermore, full structure disruption (yellow arrow) of several seminiferous tubules was seen, invariable with severe toxicity gonads lesions induced by haloperidol. In particular, a development of the interstitial tissue (blue arrow) was visible in the areas between the effect tubules. **H&E. A: 100x and B: 400x.**

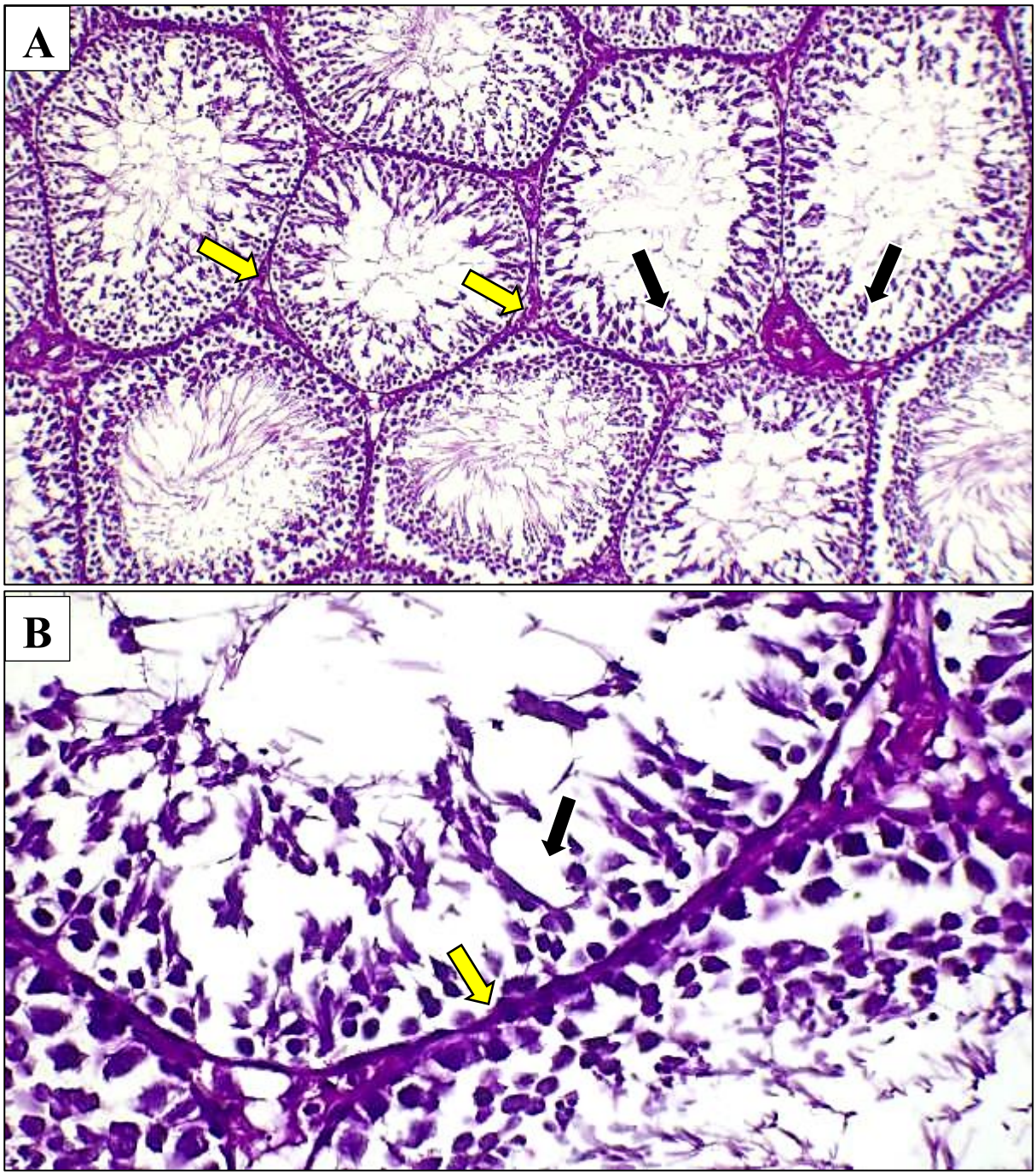

Fig. 8. Shows of testis of rat in Curcumin treated group.

A and B/ Histopathological investigation of the seminiferous tubules revealed mild pathological alterations (black arrow), nomination a protecting action of curcumin against toxicity induced by haloperidol on spermatogenesis. just minimal alterations (yellow arrow) were recorded in a restricted number of examined tubules. In addition, the interstitial tissue between the seminiferous tubules (yellow arrow) showed mostly sustained, displayed near-normal histopathological features when compared with the positive group. **H&E. A: 100x and B: 400x.**

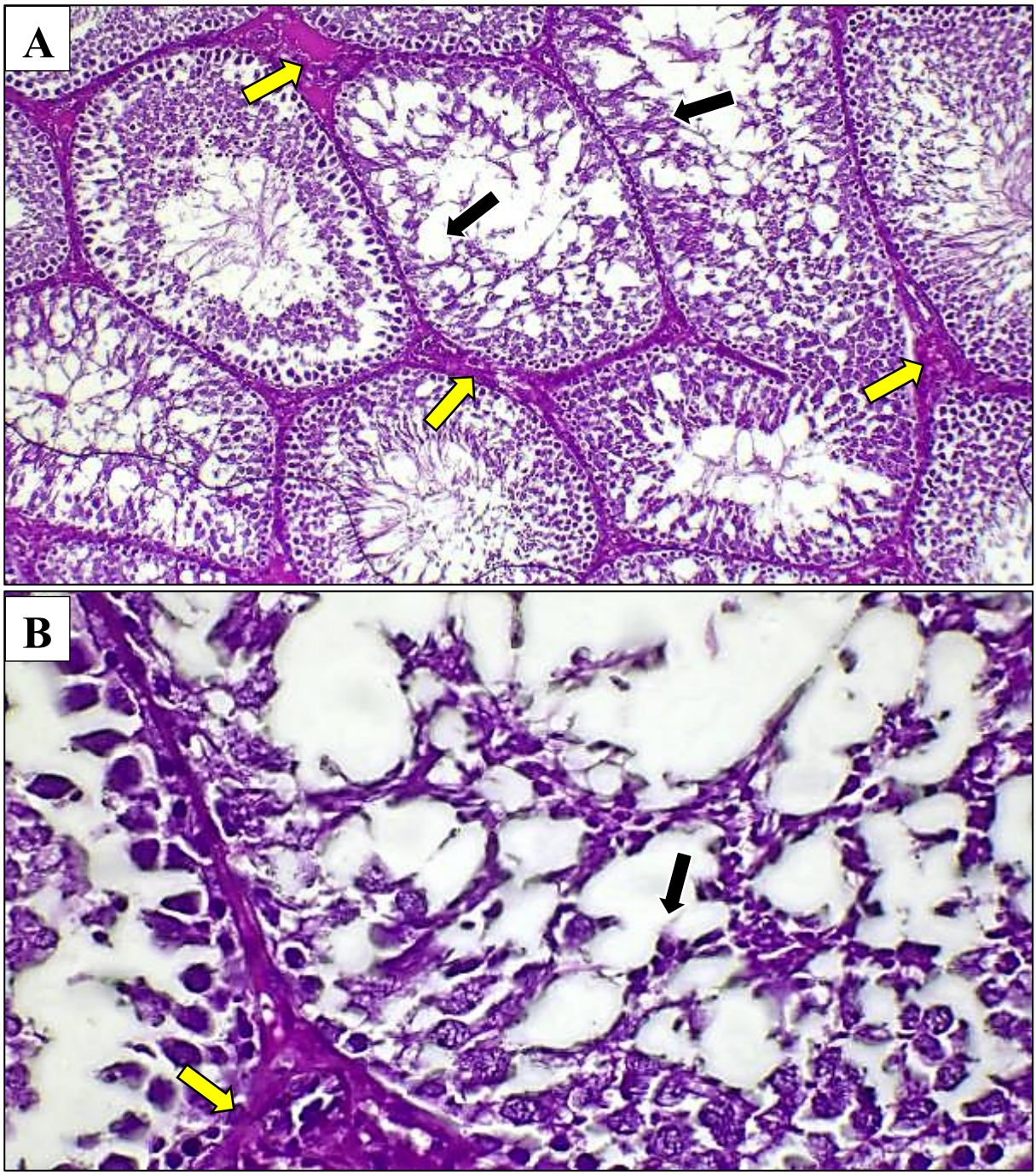

Fig. 9. Shows of rat testes in group treated with Phenylalanine.

A and B/ histopathological examination of the seminiferous tubules exhibited moderate alterations (black arrow), show a partial protection of phenylalanine against toxicity induced by on spermatogenesis. Though, these changes were more definite compared with the group treated with curcumin. In addition, shows expansion of the interstitial tissue between the seminiferous tubules (yellow arrow) related to the negative control and curcumin-treated groups, despite to a lesser level than that respected in the positive control group. **H&E. A: 100x and B: 400x.**

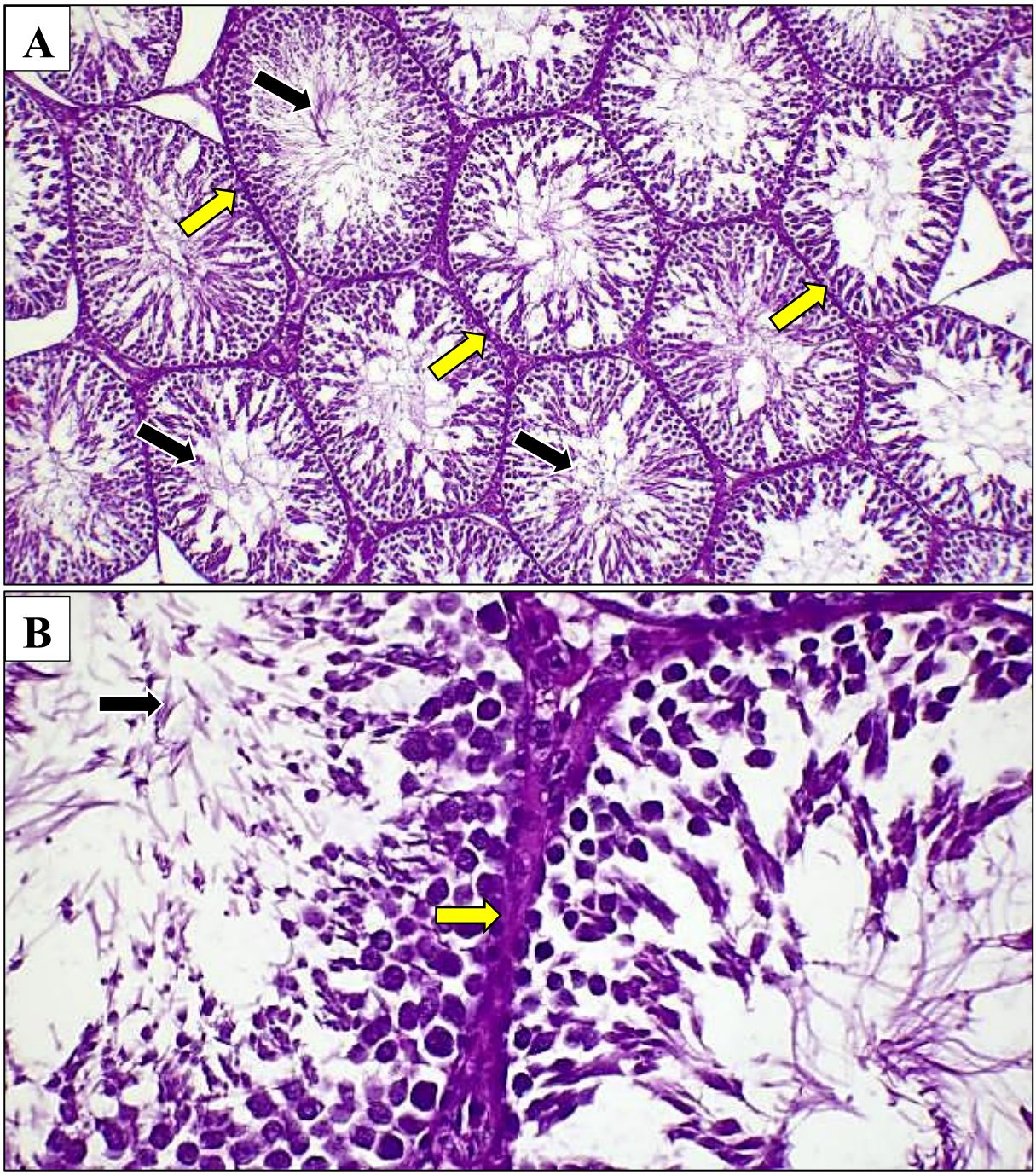

Fig. 10. Shows of rat testes of group treated by Curcumin and Phenylalanine.

A and B/ The normal histological architecture of the testicular tissue was preserved. The seminiferous tubules (black arrow) exhibited a typical structural organization, with clearly identifiable stages of spermatogenesis, indicating the effective protective role of the combined curcumin and phenylalanine treatment against haloperidol-induced cytotoxicity. Furthermore, the interstitial tissue between the seminiferous tubules (yellow arrow) appeared well maintained, demonstrating near-normal histological features compared with the positive control group. **H&E. A: 100x and B: 400x.**

DISCUSSION

The present study examined the effects of haloperidol (1 mg/kg/day), alone or combined with curcumin (200 mg/kg/day) and/or phenylalanine (200 mg/kg/day), on serum reproductive hormones in rats over 28 days. Major results showed no significant

prolactin differences despite rises with curcumin+haloperidol; higher FSH across treated groups than controls; mostly unchanged LH except elevation with curcumin+haloperidol; markedly increased testosterone from curcumin+haloperidol compared to phenylalanine+haloperidol or the triple mix; and lower estrogen in the triple combination relative to haloperidol alone or phenylalanine+haloperidol.

No significant intergroup differences in serum prolactin suggest haloperidol's expected hyperprolactinemia via dopamine D2 receptor blockade was not pronounced here, possibly due to dose, duration, or strain-specific factors. The numerical rise with curcumin+haloperidol (7.76 ng/mL) lacks statistical power but aligns with antipsychotics' pituitary effects without curcumin mitigation [13]. Also, data indicate that the blood-brain barrier effectively limits access to the brain of circulating PRL. [14].

FSH elevations (control 3.42 mIU/mL to ~8-9 mIU/mL in treated groups) indicate potential germ cell loss or Sertoli cell stress from haloperidol-induced toxicity, consistent with antidopaminergic disruption of the hypothalamic-pituitary-gonadal axis. LH remained stable except in curcumin+haloperidol (elevated), suggesting curcumin may counteract haloperidol's Leydig cell suppression in some contexts, though not fully protective [15].

Combination administration of Curcumin plus haloperidol produced high level of testosterone 296 ng/dL, significantly above phenylalanine plus haloperidol at 78.5 ng/dL, supposing curcumin has antioxidant effect preserve leydig function against atrophy induced by haloperidol. Levels by haloperidol alone reduced 111 ng/dL vs. control 224 ng/dL, comparable studies of testicular toxicity; the triple combo's low (38.5 ng/dL) imply at phenylalanine intervention [16]. Levels of estrogen lowered significantly in triple combination treatments 196 pg/mL vs. 278 pg/mL haloperidol alone, possibly through muffled biosynthesis, contrasting peak of phenylalanine with haloperidol (282.5 pg/mL). This conforms with curcumin's modulation of steroidogenic enzymes like Aldo-Keto reductase 1C2 (AKR1C2), reduction androgen to estrogen change [17].

Curcumin shows protective potential against haloperidol's reproductive disruptions, especially testosterone preservation via anti-oxidative mechanisms, supporting its use in mitigating antipsychotic side effects [18].

Data available shows that curcumin had a protection effect for health of male reproductive against injury induced by drug, according to its different effects in attenuating inflammation and oxidative stress, these produce healthy reproductive male through using pharmacological interference [19].

On histological pathological examination of treated groups, in positive group (haloperidol) showing the seminiferous tubules demonstrated a pronounced thinning of the germinal epithelium, reflecting the cytotoxic effects of haloperidol on spermatogenesis with consistent with severe gonadotoxic injury induced by haloperidol.

Haloperidol, a first-generation typical antipsychotic, exerts profound cytotoxic effects on male reproductive tissue through multiple converging pathways by (1) seminiferous tubule damage (2) germ cell exfoliation and (3) leydig cell atrophy [20,21].

Cytotoxicity of haloperidol mediated by oxidative stress by depletes superoxide dismutase (SOD) and glutathione (GSH) while elevating malondialdehyde (MDA), indicating severe lipid peroxidation of sperm membrane phospholipids so the results as shows in figure (1) corresponding with [21].

Several researches showed that increased prolactin levels caused by antipsychotics lead to a decrease in testosterone levels, resulting in reduced sexual function. [22,23].

Curcumin (Curcuma Longa Linn), the active component of turmeric, has been shown to be effective in ameliorating several stress and drug-induced disorders in rats and humans [24].

Curcumin has been thoroughly researched for its activity against inflammation and oxidative stress which are especially significant to male infertility, as oxidative stress significantly contributes to DNA damage and sperm malfunction [2].

In combination treated group haloperidol with curcumin revealed protective effects of curcumin, so it is recognized for its effect on balance of hormone and plays important role in the male reproductive system. It increased testosterone and has a necessary effect on the endocrine system. Leydig cells are cells of endocrine that govern testosterone production, spermatogenesis, and health of male reproductive.

Enhancement of curcumin for activity of the enzymes of steroidogenic cells [25]. Also, our results comply with [26] that pointed the beneficial effect of curcumin. L-Phenylalanine, an essential aromatic amino acid and catecholamine precursor, could theoretically mitigate haloperidol toxicity via dopaminergic modulation, antioxidant capacity, protein synthesis support, and neuroendocrine stabilization as reported by [27, 28], therefore the result of phenylalanine group shows protective effect of phenylalanine against haloperidol-induced cytotoxicity on spermatogenesis. The triple combination of curcumin and phenylalanine treatment against haloperidol-induced cytotoxicity exhibited a typical structural organization, with clearly identifiable stages of spermatogenesis, this results due to synergistic effect of combination therapy.

Haloperidol causes cell death in spermatogenesis by causing oxidative stress, hormonal imbalance, and cytotoxic effects of on spermatogenesis. This shows up in histopathology results. Curcumin strongly fights toxicity effects by working as an antioxidant, and an anti-inflammatory. It also restores testicular histology and function. Phenylalanine's function is mechanistically conceivable as a dopaminergic precursor, and antioxidant activity [21].

CONCLUSION

The conclusion of this study indicated that curcumin may ameliorate the adverse effects of antipsychotic on male fertility by protection testosterone levels and the structural integrity of the testes.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest associated with this study.

REFERENCS:

1. Agarwal A, Rana M, Qiu E, AlBunni H, Bui AD, Henkel R. Role of oxidative stress, infection and inflammation in male infertility. Andrologia. 2018;50(11): e13126. https://doi.org/10.1111/and.13126
2. Agarwal A, Virk G, Ong C, du Plessis SS. Effect of oxidative stress on male reproduction. World J Mens Health. 2014;32(1):1-17. https://doi.org/10.5534/wjmh.2014.32.1.1
3. Katz DJ, Teloken P, Shoshany O. Male infertility - The other side of the equation. Aust Fam Physician. 2017;46(9):641-646. https://doi.org/10.1097/01.NPR.0000390435.13252.5a

4. Kalender S, Apaydin FG, Kalender Y. Testicular toxicity of orally administrated bisphenol A in rats and protective role of taurine and curcumin. Pak J Pharm Sci. 2019;32(3):1043-1047. https://pubmed.ncbi.nlm.nih.gov/31278718/
5. Samavarchi Tehrani S, Mahmoodzadeh Hosseini H, Yousefi T, et al. The crosstalk between trace elements with DNA damage response, repair, and oxidative stress in cancer. J Cell Biochem. 2019;120(2):1080-1105. https://doi.org/10.1002/jcb.27617
6. Jiang D, Coscione A, Li L, Zeng BY. Effect of Chinese Herbal Medicine on Male Infertility. Int Rev Neurobiol. 2017;135:297-311. https://doi.org/10.1016/bs.irn.2017.02.014
7. Aly, M.A., et al., Protective effect of nanoencapsulated curcumin against boldenone-induced testicular toxicity and oxidative stress in male albino rats. Egyptian Pharmaceut J. 2021;20(1): p. 72-8. https://doi.org/10.4103/epj.epj_53_20
8. Nair A. Chemistry of turmeric. In: Gopi S, editor. The Chemistry and Bioactive Components of Turmeric. Cambridge: Royal Society of Chemistry. 2020;Pp.30–52. https://doi.org/10.1039/9781788015936
9. Roney M, Huq AKMM, Rullah K, Zamri NB, Mohd Aluwi MFF. Curcumin, a bioactive compound of Turmeric (Curcuma longa) and its derivatives as α-amylase and α-glucosidase inhibitors. Cell Biochem Biophys. 2025;83(1):53-71. https://doi.org/10.1007/s12013-024-01477-5
10. RinaIkhar, Sabale P, Kadam P. A Review on Synthesis and Biological Activity of Curcumin and Curcumin Derivatives. Asian J. Chem. Sci. 2021;10(4):7-23. https://doi.org/10.9734/ajocs/2021/v10i419099
11. Wu H, Ye N, Huang Z, Lei K, Shi F, Wei Q. Dietary curcumin supplementation relieves hydrogen peroxide-induced testicular injury by antioxidant and anti-apoptotic effects in roosters. Theriogenology. 2023;197:46-56. https://doi.org/10.1016/j.theriogenology.2022.10.038
12. El-Sherbiny HR, Fathi M, Samir H, Abdelnaby EA. Supplemental dietary curcumin improves testicular hemodynamics, testosterone levels, and semen quality in Baladi bucks in the non-breeding season. Theriogenology. 2022;188:100-107. https://doi.org/10.1016/j.theriogenology.2022.05.020
13. Zamani Z, Zar, S, Sadrkhanlou R, Ahmadi A, Movahed E. Chlorpromazine-Induced Hyperprolactinemia on Rat's Uterus. Iranian Biomed J. 2015;19(4):226–232. https://doi.org/10.7508/ibj.2015.04.006
14. Simpkins J. W. Effects of haloperidol and prolactin secreting tumors on cerebrospinal fluid concentrations of prolactin in the female rat. Life Sci. 1992;51(4):295–301. https://doi.org/10.1016/0024-3205(92)90088-7
15. Mohamadpour M, Noorafshan A, Karbalay-Doust S, Talaei-Khozani T, Aliabadi E. Protective effects of curcumin co-treatment in rats with establishing chronic variable stress on testis and reproductive hormones. Int J Reprod Biomed. 2017;15(7):447-452. https://pubmed.ncbi.nlm.nih.gov/29177247/
16. Imanishi M, Yoneyama M, Takagi S, Takeuchi M. Collaborative work to determine an optimal administration period and optimal parameters for detection of effects on male fertility in rats--male reproductive toxicity study of haloperidol. J Toxicol Sci. 1995;20(3):297–307. https://doi.org/10.2131/jts.20.297

17. Ide H, Lu Y, Noguchi T, Muto S, Okada H, Kawato S, Horie S. Modulation of AKR1C2 by curcumin decreases testosterone production in prostate cancer. Cancer Sci. 2018;109(4):1230–1238. https://doi.org/10.1111/cas.13517
18. Bishnoi M, Chopra K, Rongzhu L, Kulkarni SK. Protective effect of curcumin and its combination with piperine (bioavailability enhancer) against haloperidol-associated neurotoxicity: cellular and neurochemical evidence. Neurotox Res. 2011; 20(3): 215–225. https://doi.org/10.1007/s12640-010-9229-4
19. Tarlan M, Moradi S, Heidarizade N, Tavallaei O, Khazayel S, Farzaei MH, Echeverría J. The protective role of curcumin in mitigating drug-induced toxicity in male reproductive system. Front Pharmacol. 2025;16:1620732. https://doi.org/10.3389/fphar.2025.1620732
20. Kohge S, Hagi S, Utsumi H, Takegawa K, Takagi S, Nagaoka T, Takeuchi M, Hanada S. Collaborative work to evaluate toxicity on male reproductive organs by repeated dose studies in rats 6). 2- and 4-weeks administration study of haloperidol. J Toxicol Sci, 2000;25(SpecialIssue):71-77. https://doi.org/10.2131/jts.25.specialissue_71
21. Dincer B, Bulent Yazici A, Cinar I, Toktay E, Selli J, Cadirci E, Bayraktutan Z, Yazici E. Antipsychotics Induced Reproductive Toxicity by Stimulating Oxidative Stress: A Comparative in Vivo and in Silico Study. Chemist Biodivers, 2023. 20(5), e202201190. https://doi.org/10.1002/cbdv.202201190
22. Meaney AM, Smith S, Howes OD, O'Brien M, Murray RM, O'Keane V. Effects of long-term prolactin-raising antipsychotic medication on bone mineral density in patients with schizophrenia. British J Psychiat. 2004;184(6):503-8. https://doi.org/10.1192/bjp.184.6.503
23. Bostwick JR, Guthrie SK, Ellingrod VL. Antipsychotic-induced hyperprolactinemia. Pharmacotherapy. 2009;29(1):64–73. https://doi.org/10.1592/phco.29.1.64
24. Sookram C, Tan M, Daya R, Heffernan S, Mishra RK. Curcumin prevents haloperidol-induced development of abnormal oro-facial movements: possible implications of Bcl-XL in its mechanism of action. Synapse. 2011;(8):788-94.
25. Ungurianu A, Zanfirescu A, Margină D. Regulation of Gene Expression through Food-Curcumin as a Sirtuin Activity Modulator. Plants (Basel). 2022;11(13):1741. https://doi.org/10.3390/plants11131741
26. Tarlan M, Moradi S, Heidarizade N, Tavallaei O, Khazayel S, Farzaei MH, Echeverría J. The protective role of curcumin in mitigating drug-induced toxicity in male reproductive system. Front Pharmacol. 2025;16:1620732. https://doi.org/10.3389/fphar.2025.1620732
27. Dong Y, Bai Y, Liu G, Wang Z, Cao J, Chen Y, Yang, H. The immunologic and antioxidant effects of L-phenylalanine on the uterine implantation of mice embryos during early pregnancy. Histol Histopathol. 2014;29(10):1335–1342. https://doi.org/10.14670/HH-29.1335.
28. Beganović-Petrović A, Mornjaković Z, Cosović E, Alicelebić S, Susko I. Haloperidol i njegovi nezeljeni efekti na reproduktivni sistem [Haloperidol and its side effects on the reproductive system]. Med Arh. 2006;60(2):83-6. https://pubmed.ncbi.nlm.nih.gov/16528922/