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# The Potential Protective Role of Tiger Nut (*Cyperus esculentus*) Against Clomipramine-Induced Alterations in Sex Hormones and Testicular Tissue in Male Mice

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**Abstract**

Clomipramine (Clm.) is considered one of the most effective tricyclic antidepressant drugs. The present study focuses on the ability of the flavonoid extract of tiger nuts to reduce the damage caused by the drug. The study involved 48 male mice weighing 30 g ± 5 and divided into four groups of 12 mice for each group. The control group with no treatment, the G2 group treated with 200 mg/kg of flavonoid extract, and G3 treated with 50 mg of Clm. and the G4 group was treated with 50 mg Clm. + 200 mg/kg of extract. The treatment continues for 40 days. The results showed a significant ($P < 0.05$) increase in FSH, LH, and testosterone T, and in addition, an increase in semen quality and the sperm abnormalities decreased significantly ($P < 0.01$) in the G2 group, while the G3 group showed a significant ($P < 0.01$) decrease in hormone levels (FSH, LH, and T) and a decrease in sperm count and motility and an increase in sperm abnormalities compared to the control group. The G4 showed a significant ($P < 0.01$) increase in FSH, with no significant effect on LH levels, in addition to a decrease in T levels; also, there was an increase in dead sperm with a reduction in sperm motility and an increase in sperm abnormalities compared to the control group. The histological study displays a disruption in spermatogenesis, an interruption in sperm development, dense infiltration of inflammatory cells in the interstitial space between seminiferous tubules, tubular atrophy, and bleeding seen within or around seminiferous tubules in the Clm. group, while the damage is reduced in the G4 group. This indicates that C. esculentus improves testicular and sex hormonal function.

**Keywords:** FSH, Testosterone, LH, male reproductive system, fertility.

## 1. Introduction

Obsessive-compulsive disorder (OCD) is a prevalent and debilitating psychological condition. The database from ten countries, including Iraq, indicates that the combined lifetime prevalence of OCD is 4.1%. The 12-month prevalence of 3.0% indicates a notably persistent course of illness[1]. Clomipramine is a tricyclic antidepressant used to treat obsessive-compulsive disorder OCD, depression, and panic disorder[2]. Tricyclic Antidepressants (TCAs) are effective inhibitors of serotonin and norepinephrine reuptake and also block histamine H1 receptors, α1-adrenergic receptors, and muscarinic receptors[3]. Meta-analyses indicate that clomipramine may demonstrate greater efficacy than selective serotonin reuptake inhibitors (SSRIs)[4]. However, the administration of clomipramine is associated with adverse effects on male fertility, evidenced by decreased sperm count and motility, reduced serum levels of testosterone, FSH, and LH, as well as an increase in sperm abnormalities[5]. A researchers investigated the effect of Clomipramine on sexual dysfunction of male Sprague-Dawley rats dependent upon time and dosages, and they concluded that there was a significant decrease in the testosterone level at the end of 30 and 60 days of treatments. in testicular cell count after 30 days and further decrease at the end of 60

days. In all dosages, there was a considerable decrease in the percentage of rats mounted, intromitted, and ejaculated[6]. Moreover, a study demonstrated that clomipramine therapy at high doses can harm Spermatogenesis in addition to decreasing the diameter and thickness of seminiferous tubules[7]. Clomipramine has a genotoxic effect on medium and high doses of spermatocytes and liver cells by causing morphological sperm cell abnormalities and histological damage in hepatic cells[8]. *Cyperus esculentus L*., commonly known as tiger nut, chufa, atadwe, yellow nutsedge, and earth almond[9]. It is a tuberous plant that enhances and maintains the process of reproduction[10]. The physiological significance and nutritional advantages underscore the relevance of tiger nut. Phytochemicals such as flavonoids, alkaloids, lipids, and fatty acids, prevalent in plants, facilitate various metabolic processes and induce therapeutic and biological effects, including antioxidative, anti-inflammatory, cardioprotective, aphrodisiac, and antidiabetic properties, thereby enhancing overall well-being and health status. Furthermore, in other industries beyond the medical sector, such as pharmaceuticals, agriculture, and food, tiger nuts can be employed in the production of starch, animal feed, drinks, and biofuel, among others. Taking into account the substantial advantages and uses of tiger nut, Flavonoids have been thoroughly examined as prospective inhibitors for the therapy of malfunction in the male reproductive system, among other natural items[11]. So, our study aims to investigate the protective role of C. esculentus flavonoid extract to reduce the side effects of Clomipramine on sex hormones, semen quality, and testis.

## 2. Materials and Methods

### 2.1 Plant Extract Preparation

*Cyperus exculentus* dried tubers have been purchased from local markets in Wasit Province, particularly in the city of Al-Suwaira, and were ground with an electric grinder to make a fine powder. 250 grams of tiger nut tuber powder were used for the extraction process by Soxhlet equipment by using absolute solvent methanol for 8 hr at room temperature to obtain a crude alcoholic extract. The flavonoid content was isolated by adding 5% HCl/ethyl acetate to remove the aqueous layer, which comprises alkaloids and water-soluble compounds. The ethyl acetate layer, containing flavonoids and other phenolic substances, was subsequently isolated. The extract is poured into petri dishes to allow the solvent to evaporate in petri dishes, then stored at 4°C until used. Then the total flavonoid content was assessed by using the aluminum chloride colorimetric method.

### 2.2. Animal model and study design

A total of 48 male Swiss albino mice weighing 30±5 g were utilized in the current experiment and were kept under suitable environmental conditions of 20 ±2 °C in the animal house of the Pharmacy College/Al-Mustansiriyah University. They were fed on standard laboratory feedings. The animals were randomly divided into four groups and treated orally by gavage for 40 days as follows:

-Control groups G1: No treatment was administered.

-*Cyperus esculentus* group G2: Animals were treated with 200 mg/kg/day of tiger nut extract.

-Clomipramine group G3: animals were treated with a 50mg/day dosage of the drug.

-Combination group G4: animals were treated with 200mg/kg/day of extract and 50mg/day of drug.

### 2.3. Sample collection

At the end of the treatment period, the blood collected through cardiac puncture from each animal was used with disposable insulin syringes. Samples were deposited into Eppendorf tubes and permitted to coagulate. Serum was extracted following centrifugation at 3000 revolutions per minute (rpm) for 10 minutes, and subsequently, serum samples were preserved in a freezer at -18°C until used.

### 2.4. Sperm evaluation

After dissection of animals, the cauda epididymis of each side was isolated and immersed in one

ml of phosphate buffer saline at 37℃ in a Petri dish. Then, the tail of the epididymis was cut into small sections by microsurgical scissors to perform the microscopical examination on epididymal sperm evaluations[12]. The percentage of live sperm and their morphology were estimated as follows[13]. A drop of prepared sperm suspension mixed with a drop of 1% eosin stain and two drops of nigrosine stain. After that, the thin smear was left to dry, and one hundred spermatozoa were identified on each slide to determine the percentage of viable and morphologically abnormal spermatozoa. According to the protocol of Burgstaller et al.[14], sperm motility was measured as follows: a sperm suspension (50 µL) was placed over a warm (37℃) surface and covered with a cover slip. Several fields were examined under a light microscope to estimate the percentage of individual progressive motility of sperm.

### 2.5. Hormone assay and histopathological study

The determination of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels in serum was measured using a commercially available kit (Linear, Spain). Testosterone hormone levels were measured using a commercially available kit (Neogen, USA). Tissue of testes was preserved by immersion in 10% formalin for 28 hr, then washed and dehydrated with ascending concentrations (70, 80, 90, and 99%) of ethanol to be embedded in paraffin. After that, it was prepared and stained with Hematoxylin and Eosin (H&E) for routine histopathological evaluation[15].

### 2.6. Statistical analysis

The Statistical Packages of Social Sciences-SPSS (2019) program was used to detect the effect of different groups on study parameters. LSD (Least Significant Difference) and Duncan's test were used to significantly compare means in this study[16].

## 3. Results

Hormonal assay assessment showed FSH significantly ($p < 0.01$) elevated in the G2 group at 25.4 ± 1.41 mIU/mL compared to the G1 group at 17.05 ± 0.94 mIU/mL (**Figure 1**). In contrast, the G3 group showed a significant ($p < 0.01$) decrease in FSH level compared to the G1 group at 4.55 ± 0.61 mIU/mL. while the G4 showed a slight elevation in FSH level compared to the G1 group at 19.61 ±0.47 mlU/ml.

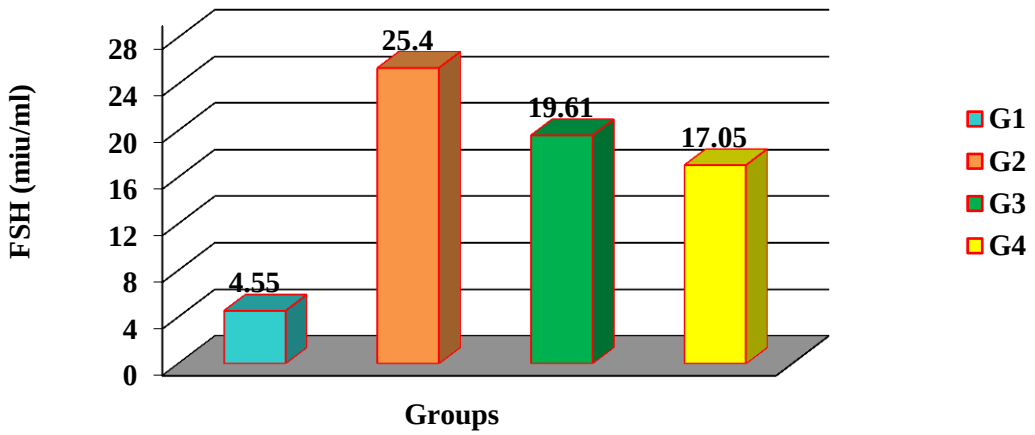


**Figure 1.** comparison between difference groups in Follicle Stimulating Hormone levels

Luteinizing hormone, LH was increased significantly ($P<0.05$) in the G2 group at 1.476±0.07mlU/ml compared to the G1 group at 1.312±0.05mlU/ml. The hormone levels decreased significantly ($P<0.05$) in the G3 group at 1.223±0.07mlU/ml compared to the G1 group at 1.312±0.05mlU/ml ($P<0.05$). Compared to the G1 at the same time, the hormone levels in the G4 group were slightly elevated compared to the G3 group and not significantly ($P<0.05$) affected compared to the G1 group at 1.36±0.05mlU/ml **(Figure 2)**.

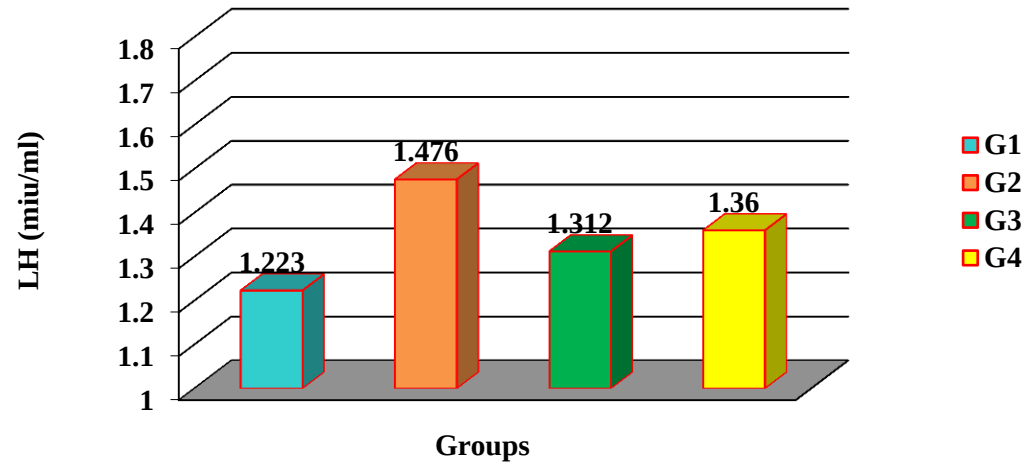


**Figure 2.** comparison between difference groups in Luteinizing Hormone level

Testosterone in the G2 group showed a significant ($p<0.01$) increase in the testosterone levels at 6.506±0.32 ng/ml compared to the G1 group ng/ml. On the contrary, the G3 group exhibits a reduction in testosterone level at 1.573±0.07ng/ml compared to the G1 group. However, in the G4 group, the levels of testosterone decreased significantly ($p <0.01$) compared to the G1 group at 2.39±0.06 ng/ml (**Figure 3**).

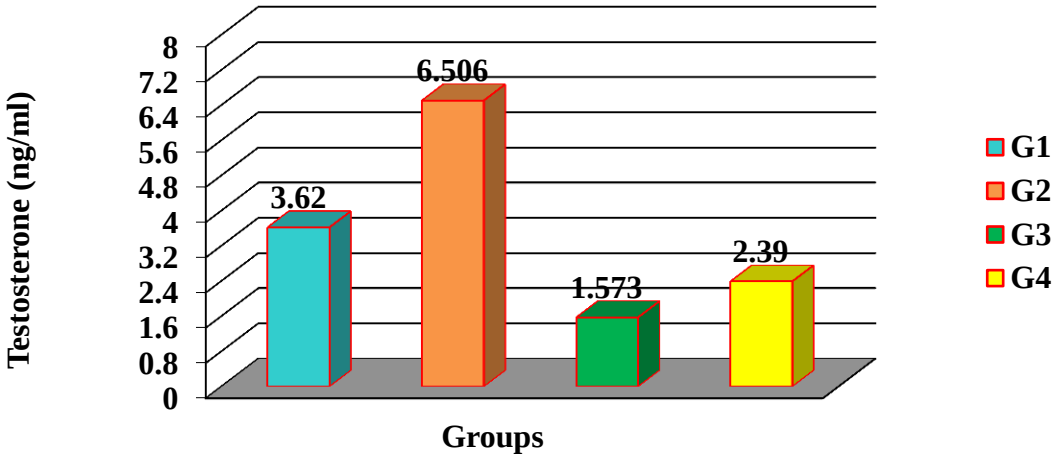


**Figure 3.** comparison between difference groups in Testosterone level

The dead sperm in the G2 group significantly ($p < 0.01$) decreased by 8.50 ± 0.56, and the motility 86.67 ± 1.41 significantly ($p < 0.01$) increased compared to the G1 group 73.67 ± 1.45, and at the same time there was a decrease in sperm abnormalities 10.00% ± 0.82. In the G3 group there was a significant ($p < 0.01$) increase in the dead sperm, 47.00 ± 1.93, and in the abnormalities, 30.83 ± 1.30, compared to the G1 group. The sperm motility of 63.00% ±1.73 significantly ($p <0.01$) decreased compared to the control group. The G4 showed an elevation in the dead sperm 18.83% ± 1.76 compared to the G1 group, and sperm abnormalities also elevated 19.50 ± 0.76, as shown in **Table 1.** The motility showed a significant ($p < 0.01$) difference compared to G1 57.00% ± 1.53.

**Table 1**.Comparison between semen parameters

| Groups | Means ±SE | | |
|---|---|---|---|
| | Viability (%) | Abnormality (%) | Motility (%) |
| G1 | 13.00 ±0.73 c | 13.50 ±0.84 c | 73.67±1.45 b |
| G2 | 8.50 ±0.56 d | 10.00 ±.82 d | 86.67 ±1.41 a |
| G3 | 47.00 ±1.93 a | 30.83 ±1.30 a | 63.00 ±1.73 c |
| G4 | 18.83 ±1.76 b | 19.50 ±0.76 b | 57.00 ±1.53 d |
| L.S.D. | 4.087 ** | 2.822 ** | 4.447 ** |
| P-value | 0.0001 | 0.0001 | 0.0001 |

Means having with the different letters in same column differed significantly. ** (P <0.01).

## 3.1 Histopathological finding

The G1 group showed no obvious signs of degeneration, atrophy, or inflammation **(Figure 4-a)**. The histopathological figure of seminiferous tubules showed a well-organized circular or oval structure that was lined with germinal epithelium, showing the full spermatogenic series: spermatogonia near the basement membrane. Primary and secondary spermatocytes in the middle layers. Spermatids and mature spermatozoa toward the lumen **(Figure 4-b)**. In contrast, the G2 group displayed a case of severe tubular damage with atrophy and marked luminal aspermia and severe macrovascular and microvascular degeneration of germ cells and severe thickening of testicular interstitium associated with hemorrhage and hemolysis. **(Figure 4-c)**. The G4 showed mild interstitial fibrosis with fibroblast activation and collagen deposition in interstitial tissue with little macrophage clearance of debris and degenerated cells; Leydig cells may proliferate (hyperplasia) **(Figure 4-d)**.

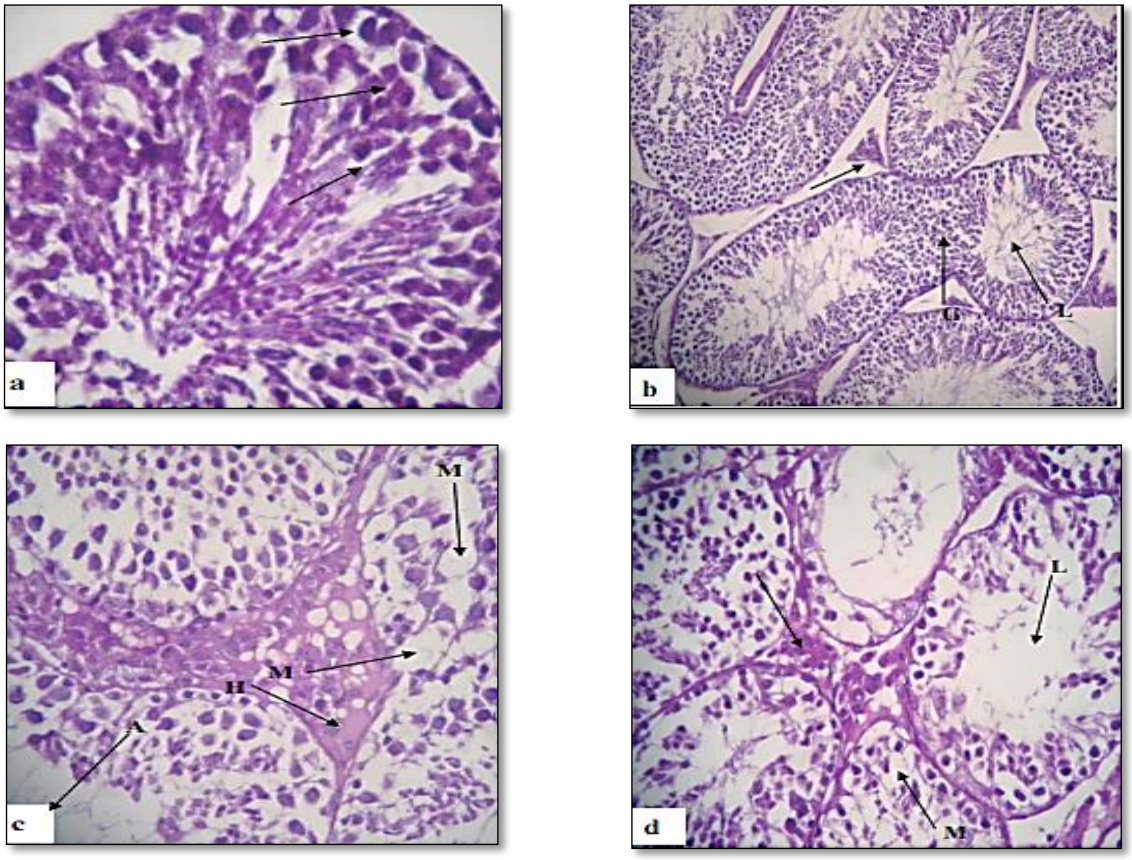


**Figure 4.** a.G1 shows no obvious signs of degeneration, atrophy, or inflammation. H&E stain.40x b. The G2 section of the seminiferous tubule shows normal layers of cells of germinal epithelium (G), normal lumina (L), and interstitial tissue. H&E stain. 40x**.** c**.** section of seminiferous tubules (G3) shows severe tubular damage with marked lumina aspermia (A), severe macrovacular degeneration of germ cells (M), and severe thickening of testicular interstitium associated with hemorrhage and hemolysis (H). H&E stain.40x**.** d**.** A section of seminiferous tubules (G4) shows severe oligospermia of germinal epithelium with microvascular degeneration (m), lumina aspermia, mild interstitial fibrosis with collagen deposition with cellular infiltration, and hyperplasia of interstitial cells. H&E stain.10x.

## 4. Discussion

In the current study, the results of hormones (follicle-stimulating hormone, luteinizing hormone, and testosterone) show a significant elevation in their levels and sperm motility in addition to a decrease in dead sperm and sperm abnormalities in the group treated with Cyperus esculentus flavonoids extract, and this is compatible with a study that investigates the effect of three different dosages of aqueous extract of tiger nuts on Sprague Dawley rat fertility, and they conclude that tiger nuts enhance spermatozoa production by elevating serum testosterone and vitamin C and E levels. Notable increases in spermatozoa production, as well as enlargement of interstitial spaces and blood vessels, were observed in the group administered 2000 mg/kg. Additionally, the width of seminiferous tubules increased, and the collagen fibers remained intact and well-preserved in the test groups[17].

Another study investigated the aphrodisiac potential of C. esculentus on male Wistar albino rats. The study concludes that the plant powder at different dosage increases the sex hormone levels of testosterone and follicle stimulating[18]. Flavonoids exhibit several roles, including immunological stimulation, anti-inflammatory properties, and antioxidative benefits. These characteristics render them possible inhibitors of male reproductive system disorder[19]. The natural polyphenolic antioxidants that positively influence testosterone production typically augment the expression of the steroidogenic acute regulatory protein (Star) gene in Leydig cells. The STAR protein enables the transport of the steroid precursor cholesterol into mitochondria, a critical rate-limiting step in androgen production[20]. Among many herbal products, flavonoids have been examined for the treatment of male reproductive system disorders such as testicular structural disruption, sperm quality decline, and spermatogenesis disturbance[21]. Flavonoids are amphipathic molecules that can enter the lipid bilayer of membranes, thus giving possible protection for the entire spermatozoa and acrosome membrane, blocking oxidative damage, and assuring the sperm acrosome reaction needed for fertilization[22]. The G3 group showed a significant decrease in hormone levels and motility and an increase in dead sperm and sperm abnormalities, a finding compatible with a study that assessed the impact of clomipramine on male fertility in rats. The results showed that clomipramine administration resulted in significant changes in testicular weight, sperm parameters, and hormonal biomarkers, including FSH, LH, and testosterone[6]. These results further support our investigation that clomipramine adversely affects male reproductive function by altering hormonal profiles. There are many mechanisms behind clomipramine-associated sexual dysfunction and hormonal reduction; one of them is that Clomipramine increases the serotonin level due to its selective serotonin reuptake inhibiting activity, thus producing sexual dysfunction[23]. Studies indicate that some serotonin reuptake inhibitors lower cholesterol level, which is a precursor for testosterone production; therefore, decreased testosterone levels can reduce the number of LH receptors, impairing the function of Leydig cells and subsequently reducing testosterone.[24] The cytotoxic effect's molecular mechanism of antidepressants is facilitated by disruptions in redox equilibrium (elevated generation of reactive oxygen species and reactive nitrogen species), inadequacy of enzymatic and non-enzymatic cellular defense mechanisms (glutathione system, nuclear factor-κB, and fibroblast growth factor 2-mediated pathways), and dysfunction of mitochondrial operations. The work presents, for the first time, evidence that antidepressant therapy may induce abnormalities in spindle apparatus formation and organelle distribution during in vitro cell division[25]. In the G4 group there is an increase in hormone levels and in sperm motility. Also, the dead sperm and sperm abnormalities were reduced compared to the G3 group, which means that C. esculentus can reduce the negative effect of the Clomipramine. This is similar to another study whose results were investigated on the effect of C. esculentus to reduce the side effects of long-term administration of antiretroviral drugs, and they conclude that tiger nut elevated FSH and testosterone levels.[26] Histopathological finding of testis tissue shows normal architecture of seminiferous tubules and the lumen full of mature spermatids and well-formed Leydig and Sertoli cells in the extract group, indicating the antioxidant status induced by plant extract. The

plant extract markedly influenced the weight of the entire reproductive tract, the volume and circumference of the testes, the length of the epididymis, the weight of the semen, and the size of the testes in mature experimental rabbits. Additionally, a study investigated the effects of intraperitoneally administered tiger nut extract on reproductive abnormalities induced by lead acetate[27]. Spermatogenesis is the process of sperm formation within the testis, and it is under the control of gonadotropic hormones (LH and FSH). Spermatogenesis involves the stimulation of Sertoli cells by FSH and the subsequent activation of testosterone production through Leydig cell stimulation by LH. Since any disturbance in their level leads to spermatogenesis disruption and sperm abnormalities[28], this is compatible with the testis tissue results of the G3 group. This finding is accurate with the study that investigated prolonged treatment of Clomipramine induced oxidative stress, inflammation, and structural alterations in the liver, heart, and testis, resulting in decreased sperm count and motility, an increase in abnormalities, and diminished serum levels of testosterone, FSH, and LH29. In the G4 group there is a reduction in tissue damage. The flavonoids quercetin and myricetin stand out among the secondary metabolites in tiger nuts. Quercetin, a flavonoid compound, at a dosage of 20 mg/kg, effectively improved testicular tissue and reduced germ cell apoptosis by reversing the vacuolation of the germinal epithelium, the detachment of germ cells from the basal lamina, and the shedding of immature germ cells in Wistar rats subjected to cadmium-induced testicular toxicity over a period of 4 weeks[27] and this is compatible with our study. Furthermore, the extract was shown to have somewhat improved the histopathological abnormalities in the experimental rat's testicles. The study concluded that the extract's antioxidant properties or its capacity to alter sex hormones might have been the cause of the noted improvement. According to the findings of the aforementioned studies, tiger nuts improve male reproductive parameters and protect them from injury, making them crucial for male reproductive health[30].

## 5. Conclusion

According to our study, clomipramine is a tricyclic antidepressant considered an effective drug in OCD and depression treatment. However, it is associated with several negative effects on sexual activity due to its mechanism of action, which leads to a decrease in sex hormones and affects semen quality and the testis tissue. In contrast, tiger nut (*Cyperus esculentus*) flavonoid extract showed an improvement in sex hormone levels and semen quality, and when it is combined with clomipramine treatment, it exhibits a therapeutic role by inducing high antioxidant activity, which leads to reduced tissue damage and increased hormone levels and sperm quality.

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No thanks

## Conflict of Interest

The authors declare that they have no conflicts of interest.

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## Ethical Clearance

Ethical approval 51 in 5/1/2025 was obtained by Al-Mustansiriyah University/Collage of Pharmacy**.**

## References

1. Stein DJ, Ruscio AM, Altwaijri Y, Chiu WT, Sampson NA, Aguilar-Gaxiola S, Al-Hamzawi A, Alonso J, Chardoul S, Gureje O, Hu C, Karam EG, McGrath JJ, Navarro-Mateu F, Scott KM,

Stagnaro JC, Torres Y, Vladescu C, Wciórka J, Xavier M, Kessler RC. Obsessive-compulsive disorder in the World Mental Health surveys. BMC Med. 2025 Jul 9;23(1):416. https://doi.org/10.21203/rs.3.rs-6090427/v1

2. StatPearls. Clomipramine. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK541006
3. DrugBank. Clomipramine (DB01242) [Internet].https://go.drugbank.com/drugs/DB01242
4. Pittenger C, Bloch MH. Pharmacological treatment of obsessive-compulsive disorder. Psychiatr Clin North Am. 2014;37(3):375–91. https://doi.org/10.1016/j.psc.2014.05.006
5. Friedrich ME, Akimova E, Huf W, Konstantinidis A, Papageorgiou K, Winkler D, 5. Drug-induced liver injury during antidepressant treatment : results of AMSP, a drug surveillance program. Int J Neuropsychopharmacol. 2016;19(4):pyv126. https://doi.org/10.1093/ijnp/pyv126
6. Devaangam SS, Satyanarayana S, Eswar Kumar K, Vivek B, Velmurugan C, Kumar A. Amantadine on clomipramine-induced sexual dysfunction in rats. Oman Med J. 2011;26(6):404–9. https://doi.org/10.5001/omj.2011.104
7. Karimi A, Etemadi E. Effect of clomipramine on spermatogenesis and hormones. J Isfahan Med School. 2018;36(481):575–80. https://doi.org/10.22122/jims.v36i481.10015
8. El-Fiky SA, Abou-Zaid FA, Farag IM, Fahmy MA, El-Fiky NM. Genotoxic effect of clomipramine hydrochloride. Asian Pac J Trop Dis. 2016;6(4):321–7. https://doi.org/10.1016/S2222-1808(15)61038-6
9. Sánchez-Zapata E, Fernández-López J, Pérez-Alvarez AJ. Tiger nut: composition and health. Compr Rev Food Sci Food Saf. 2012;11(4):366–77. https://doi.org/10.1111/j.1541-4337.2012.00211.x
10. Nwakanma A, Ekong M, Ngwuben I, Obumneme C, Idaguko C. Cyperus esculentus protects testis in rats. Int J Med Surg Sci. 2022;9:1–16. https://doi.org/10.32457/ijmss.v9i3.1924
11. Edo GI, Onoharigho FO, Jikah AN, Oloni GO, Samuel PO, Rapheal OA, Ikpekoro O, Akpoghelie PO, Agbo JJ, Ekokotu HA, Ugbune U, Ezekiel GO, Abere GA, Oghroro EEA, Ojulari AE, Okoronkwo KA, Owheruo JO, Akpoghelie EO. Cyperus esculentus (tiger nut): An insight into its bioactive compounds, biological activities, nutritional and health benefits. Food Chem Adv. 2023;3:100511. https://doi.org/10.1016/j.focha.2023.100511
12. Esteves SC, Miyaoka R, Agarwal A. Sperm retrieval techniques. Int Braz J Urol. 2011;37:570–83. https://doi.org/10.1590/S1677-55382011000400013
13. Agarwal A, Sharma RK, Gupta S, Boitrelle F, Finelli R, Parekh N, Shah R. Sperm vitality and necrozoospermia: diagnosis, management, and results of a global survey of clinical practice. World J Mens Health. 2021;40(2):228. https://doi.org/10.5534/wjmh.210149
14. Burgstaller SM, Auer KE, Rülicke T. Repeated in vivo sperm collection in mice. J Assist Reprod Genet. 2024;41:2537–46. https://doi.org/10.1007/s10815-024-03201-x
15. Bancroft JD, Gamble M. Theory and Practice of Histological Techniques. 6th ed. London: Churchill Livingstone/Elsevier; 2008.
16. SPSS. IBM SPSS Statistics 26 step by step. 16th ed. 2019. https://doi.org/10.4324/9780429056765
17. Osibemhe M, Musa S. Aphrodisiac potential of tiger nut powder. Sahel J Life Sci FUDMA. 2024;2:30–8. https://doi.org/10.33003/sajols-2024-0202-05
18. Ofem OE, Udonkang MI, Bassey IE, Okechi OO. Tiger nut improves fertility in rats. Trop J Nat Prod Res. 2023;7(12):4510–7. https://doi.org/10.26538/tjnpr/v7i12.4510.26538
19. Mishra R, Nikam A, Hiwarkar J, Nandgude TD, Bayas J, Polshettiwar SA. Flavonoids as potential therapeutics in male reproductive disorders. Future J Pharm Sci. 2024;10(1):100. https://doi.org/10.1186/s43094-024-00677-3
20. Martin L. Flavonoids and testicular steroidogenesis. Antioxidants. 2020;9(3):237. https://doi.org/10.3390/antiox9030237
21. Ye RJ, Yang JM, Hai DM, Liu N, Ma L, Lan XB, Niu JG, Zheng P, Yu JQ. Interplay between male reproductive system dysfunction and the therapeutic effect of flavonoids. Fitoterapia. 2020 Nov;147:104756. https://doi.org/10.1016/j.fitote.2020.104756
22. Osawe SO, Farombi EO. Quercetin and rutin ameliorate spermiotoxicity. Andrologia. 2018;50(5):e12981. https://doi.org/10.1111/and.12981
23. Shekar DS, Satyanarayana S, Veeresh Babu P, Vinayak K. Cyproheptadine and clomipramine-induced dysfunction. Int J Basic Clin Pharmacol. 2016;5(6):2227–32. https://doi.org/10.18203/2319-2003.ijbcp20162436

24. Zirkin BR, Papadopoulos V. Leydig cell formation and function. Biol Reprod. 2018;99(1):101–11. https://doi.org/10.1093/biolre/ioy059
25. Solek P, Mytych J, Tabecka-Lonczynska A, Sowa-Kucma M, Koziorowski M. Toxic effect of antidepressants on male reproductive cells. J Physiol Pharmacol. 2021;72(3). https://doi.org/10.26402/jpp.2021.3.06
26. Ogedengbe OO, Bature A, Fafure AA, Kehinde SO, Adekeye AO, Akintayo CO, Ajiboye BO, Adeeyo OA. Evaluation of Testicular Function and Structural Changes of Wistar Rats Following Antiretroviral Exposure: Protective Role of Cyperus Esculentus. Niger J Physiol Sci. 2023 Dec 31;38(2):201-209. https://doi.org/10.54548/njps.v38i2.9
27. Edo GI. Antibacterial and phytochemical analysis of Thevetia peruviana. Nat Resour Hum Health. 2022. https://doi.org/10.53365/nrfhh/146543
28. Hall JE, Hall ME. Guyton and Hall Textbook of Medical Physiology. 14th ed. Philadelphia: Elsevier; 2020.
29. El-Sheikh SMA, Eleiwa NZ, Khairy GM, Abd El Aziz RM, Metwally MMM, Galal AAA. Effect of sildenafil and clomipramine on tissues of male rats. Andrologia. 2021;53:e13983. https://doi.org/10.1111/and.13983
30. Zhang X, Tang Y, Lu G, Gu J. Quercetin and testicular injury. Nutrients. 2023;15(9):2231. https://doi.org/10.3390/nu15092231