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Toxicological Report of Orally Administered Piroxicam on the Uteri and Ovaries of Sprague-Dawley Rats

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ABSTRACT

Piroxicam is a non-steroidal anti-inflammatory drug that is effective in treating pain and inflammation in the body. The safety profile of Piroxicam is influenced by episodic and sporadic abuse, in addition to adverse pharmacological reactions. The aim of the study is to investigate the effect of Piroxicam on the uterus and ovaries of female Sprague-Dawley rats. Twenty female rats were used and divided into four groups each (A-D: n-5) and received 0,10,20 and 40 mg/kg of Piroxicam orally for 28 days, then euthanized and the following were assessed: histological damage to the ovary and uterus, possible changes in some hormonal level, and oxidative stress levels. Piroxicam significantly suppressed the levels of SOD and CAT, and increased the level of MDA in rats. Piroxicam showed an irregular pattern in the level of Progesterone, LH, and Estrogen. Uterine sections showed mild to severe infiltration of the endometrial stroma by inflammatory cells, while ovarian sections showed moderate to mild vascular congestion in the ovaries. Results showed that chronic use of Piroxicam produces a deleterious effect on the histoarchitecture of the ovaries and uterus, as well as changes in hormone levels and oxidative stress.

***Keywords:** Piroxicam, Oxidative stress, Uterus, Ovary, Hormonal milieu.*

Introduction

Infertility in women can be caused by factors such as age, smoking, alcohol consumption, being overweight, eating disorders, sexually transmitted infections, exposure to chemicals, mental stress, ovulation disorders, problems in the uterus, and fallopian tubes, and drugs. The misuse of drugs also contributes to infertility [1]. Such drugs include Piroxicam, dextromethorphan, marijuana, and cocaine. This study focuses on the contribution of Piroxicam to infertility. Piroxicam is a nonsteroidal anti-inflammatory drug that is effective in treating fever, pain, and inflammation in the body [2]. A vast body of clinical experience has been used to establish a safety profile because it has been in use for years. An anthology of adverse drug occurrences was examined, with data derived from both published case records and a database of Piroxicam-related adverse events recorded by physicians and pharmacists during their own time. The safety profile indicates that negative medication responses are rare and typically mild. The most common side effects of Piroxicam are neurological, cardiovascular, and gastrointestinal problems, which are frequently dose related [3]. The safety profile of Piroxicam is influenced by both episodic and sporadic abuse, in addition to adverse pharmacological reactions. In fact, research on spontaneous adverse event reporting revealed that abuse appeared to be the most significant hazard. There is no indication that the well-known pharmacokinetic polymorphism associated with Piroxicam is linked to any clinically meaningful safety risks when used for short-term treatment [4].

Materials and Methods

Drugs

The pure substance of Piroxicam was purchased from Care-Yard Pharmaceuticals, Iwo, Osun State with batch numbers MP21230. The manufacturing date is February 2024, Expiry date is Jan 2027, and it was manufactured by McCoy Pharma Pvt Ltd, Maharashtra, India.

Experimental Animals

Twenty female Sprague- Dawley rats with weighing of 180- 300 g were purchased from the Anatomy department of Bowen University, Nigeria, and identified by a Zoologist. The rats were housed in the University's Anatomy department animal house in industrial cages at room temperature. They were fed with rodent pellet diet and water within this period of acclimatization for fourteen days. The rats were divided into 4 groups. Each group contains five rats (A-D). The experimental design consisted of a control group, a low dose group, a medium dose group and a high dose group, each receiving 0, 10, 20 and 40 mg/kg of Piroxicam respectively for 28 days.

The rats were euthanized one day after the experiment using 1ml of ketamine and were then pinned to a slab, and their bodies were perfused with distilled water to prevent tissue autolysis, followed by careful dissection and harvest of the ovaries and uterus. The tissues were divided into two groups: a group used for histological analysis fixed in Bouin's fluid. The other group was used for biochemical analysis, which was immediately homogenized with 1ml of phosphate buffer, poured into a specimen bottle, and placed on ice and prepared for further analysis.

Ethical Approval

Ethical approval was obtained from the Central Research Committee on Ethics regarding the use of human and experimental models for research (BCRC/ANA/02/022).

Measurement of LH, FSH and Progesterone

Serum concentrations of follicle-stimulating hormone (FSH), luteinizing hormone (LH) and progesterone were measured with a two-site chemiluminescence (sandwich) immunoassay using two antibodies specific for the intact FSH molecule. LH concentrations were determined using a two-site chemiluminescent immunoassay by Bayer Diagnostics. The serum progesterone assay was also a competitive chemiluminescent immunoassay [5].

Uterine and Ovarian Homogenate for Antioxidant Activities

The ovaries and uteri were washed in ice-cold 1.15% KCl solution, blotted and weighed. They were then homogenized with 0.1 M phosphate buffer (pH 7.2). The tissues were placed in a mortar and laboratory sand was added. This was crushed using a pestle. The resulting homogenate was centrifuged at 2500 rpm for 15 minutes. The supernatant was decanted and stored at -20°C until analysis. Superoxide dismutase (SOD) was assayed by its ability to inhibit the auto-oxidation of epinephrine, determined by the increase in absorbance at 480 nm. The enzyme activity was calculated by measuring the change in absorbance at 480 nm for 5 min [6]. Catalase (CAT) activity was assayed calorimetrically at 620 nm and expressed as µmoles of H_2O_2 [7]. consumed per minute per mg of protein. Malondialdehyde (MDA), an index of lipid peroxidation, was determined using the method from a previous study. The supernatant was removed and the absorbance was read at 532 nm. MDA was calculated using the molar extinction coefficient for MDA-TBA complex of 1.56 × 105 M-1cm-1 [8].

Statistical Analysis

Statistical analysis was performed using GraphPad software version 9.5 for windows. Numerical data obtained from the experiment were expressed as mean ± SD (standard deviation). The differences were compared for statistical significance using one-way analysis of variance (ANOVA) and post hoc Tukey's tests. Differences were considered significant at $p<0.05$.

Results

Effect of Orally Administered Piroxicam on the Body Weight of Female Sprague-Dawley Rats

There was an increase in the body weight of the control group, but a dose-dependent decrease in the body weight of the low dose and the medium dose (Table 1).

Table 1: Effect of Orally Administered Piroxicam on the Body Weight of Female Sprague-Dawley Rats

Group	Before Administration (g)	After Administration (g)	% Weight Difference
Control	196.20 ± 0.19	201.20 ± 0.09	2.5%
Low Dose	217.80 ± 0.42	216.60 ± 0.72	0.6%
Medium Dose	260.75 ± 0.44	252.50 ± 1.62	3.2%
High Dose	272.09 ± 0.81	269.41 ± 0.50	1.0%

Values are mean ± standard error of the mean (SEM); n=5, *p‹0.05

Effect of Orally Administered Piroxicam on the Weight of the Ovaries and Uteri of Female Sprague-Dawley Rats

There was a dose-dependent decrease in the weight of the ovaries and uteri of female Sprague-Dawley rats, with significance in the medium and high doses, when compared to the control group (Table 2).

Table 2: Effect of Orally Administered Piroxicam on the Weight of the Ovaries of Female Sprague-Dawley Rats

Group	Ovaries (g)	Uterus (g)
Control	0.08 ± 0.02	0.40 ± 0.38
Low Dose	0.06 ± 0.01	0.36 ± 0.10
Medium Dose	0.02 ± 0.27^{ab}	0.32 ± 0.04^{ab}
High Dose	0.02 ± 0.02^{ab}	0.26 ± 0.05^{abc}

Values are expressed as mean ± standard error of the mean (SEM).
[a]p‹0.05 significantly different compared to the control.
[b]p‹0.05 significantly different compared to the low dose.
[c]p‹0.05 significantly different compared to the medium dose.

Effect of Orally Administered Piroxicam on the Hormones of Female Sprague-Dawley Rats

In the values of luteinizing and progesterone, dose dependent decreases were recorded when treatments groups were compared to control, however, an irregular pattern was seen in the estrogen levels as there was a increase in medium dose when dose was compared to low dose (Table 3).

Table 3: Effect of Orally Administered Piroxicam on the Hormonal Parameters of Female Sprague-Dawley Rats

Group	Luteinizing Hormone (mg/ml)	Progesterone (mg/ml)	Estrogen (mg/ml)
Control	0.03 ± 0.02	0.47 ± 0.01	1.58 ± 0.02
Low Dose	0.02 ± 0.01	0.63 ± 0.03[a]	1.16 ± 0.04[a]
Medium Dose	0.02 ± 0.01	0.41 ± 0.04[b]	1.48 ± 0.02[b]
High Dose	0.02 ± 0.01	0.21 ± 0.04[abc]	1.02 ± 0.02[abc]

Values are expressed as mean ± standard error of the mean (SEM).
[a]p‹0.05 significantly different compared to the control.
[b]p‹0.05 significantly different compared to the low dose.
[c]p‹0.05 significantly different compared to the medium dose.

Effect of Orally Administered Piroxicam on the Oxidative Stress Markers of the Ovaries of Female Sprague-Dawley Rats

In the MDA values, a dose dependent increase was recorded when the treatment groups were compared to control with reverse seen in the SOD and CAT levels as decrease were recorded when treatment groups were compared to control in both ovaries and uteri (Table 4).

Table 4: Effect of Orally Administered Piroxicam on the Oxidative Stress Markers of the Ovaries of Female Sprague-Dawley Rats

OVARIES			
Group	**Malondialdehyde (mU/mL)**	**Superoxide Dismutase (mU/mL)**	**Catalase (mU/mL)**
Control	418.68 ± 2.44	190.23 ± 2.04	262.93 ± 3.11
Low Dose	462.80 ± 1.25[a]	161.70 ± 3.00[a]	204.43 ± 2.33[a]
Medium Dose	479.52 ± 2.82[ab]	155.29 ± 2.66[ab]	167.24 ± 2.25[ab]
High Dose	332.58 ± 0.33[abc]	105.19 ± 0.43[abc]	107.48 ± 3.00[abc]
UTERI			
Group	**Malondialdehyde (mU/mL)**	**Superoxide Dismutase (mU/mL)**	**Catalase (mU/mL)**
Control	307.85 ± 2.92	291.88 ± 2.64	335.90 ± 2.04
Low Dose	331.20 ± 2.29[a]	256.34 ± 3.22[a]	311.81 ± 2.59[a]
Medium Dose	429.71 ± 2.87[ab]	218.27 ± 2.55[ab]	260.21 ± 1.96[ab]
High Dose	486.93 ± 3.03[abc]	155.71 ± 1.97[abc]	204.41 ± 0.97[abc]

Values are expressed as mean ± standard error of the mean (SEM).
[a]p‹0.05 significantly different compared to the control.
[b]p‹0.05 significantly different compared to the low dose.
[c]p‹0.05 significantly different compared to the medium dose.

Haematoxylin And Eosin Staining Result And Analysis Of The Ovaries And Uteri Of Female Sprague-Dawley Rats For Each Group

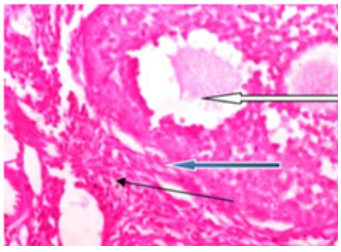

Plate 1

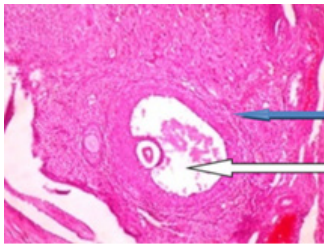

Plate 2

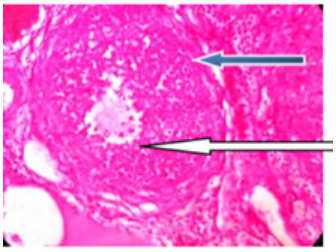

Plate 3

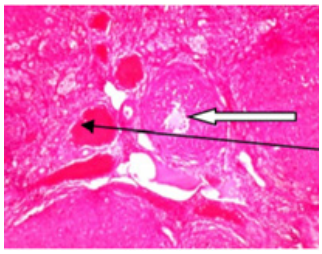

Plate 4

Plate 1 (control) *showing normal antral follicles (white arrow) with normal theca cells (blue arrow) within the ovarian cortex. The ovarian stroma appears normal with normal connective tissues (slender arrow).*

Plate 2 (low dose) *showing some normal antral follicles (white arrow) with normal theca cells (blue arrow) within the ovarian cortex.The ovarian stroma shows mild vascular congestion.*

Plate 3 (medium dose) *showing normal antral follicles (white arrow) with normal theca cells (blue arrow) within the ovarian cortex.The ovarian stroma shows mild vascular congestion.*

Plate 4 (high dose) *with ovarian stroma showing severe vascular congestion (slender arrow).*

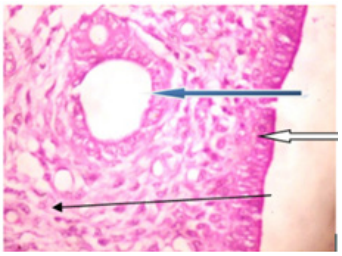

Plate 5

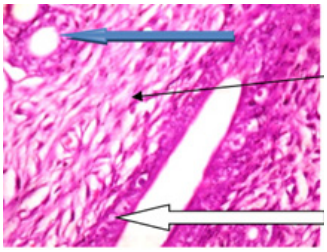

Plate 6

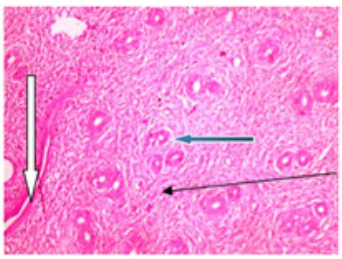

Plate 7

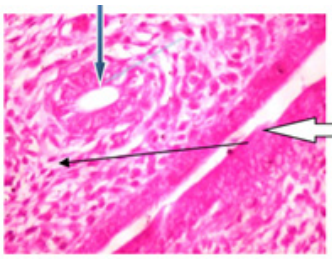

Plate 8

Plate 5 (control) *shows normal endometrium epithelial layer (white arrow), and normal endometrial glands (blue arrow).*

Plate 6 (low dose) *shows normal endometrium epithelial layer (white arrow), normal endometrial gland (blue arrow), and mild infiltration of the endometrial stroma by inflammatory cells (slender arrow).*

Plate 7 (medium dose) *shows endometrial gland hyperplasia (blue arrow) and severe infiltration of the endometrial stroma by inflammatory cells (slender arrow).*

Plate 8 (high dose) *shows severe infiltration of the endometrial stroma by inflammatory cells (slender arrow).*

Discussion

It has been documented that various consumables, such as food, medicinal plants, and medications, especially when overdosed, might cause organ failure, hormonal disruption, and even affects pregnancy and pregnancy outcomes. Drug-induced infertility, whether irreversible or reversible, remains a significant clinical problem that has not yet been resolved [9]. Many commonly used medications can be harmful to the gonads as shown in a study [10]. This study investigated the potential effect of Piroxicam on the histology of ovaries and uterus in female Sprague-Dawley rats, as well as on hormonal levels and oxidative stress. Piroxicam is a nonsteroidal anti-inflammatory drug that is effective in treating fever, pain, and inflammation in the body. In this study, Piroxicam caused a significant decrease in the hormonal milieu (Estrogen, Progesterone, Luteinizing hormone) when the treatment group was compared to the control group of female Sprague-Dawley rats. The significant increase observed in the level of MDA in the ovaries and uteri of treatment groups in the female rats, with a significant decrease in the levels of SOD and CAT, may be a clear indication that Piroxicam induced oxidative stress on the ovaries and uterus. A decrease in CAT could be attributed to an increase in MDA, a byproduct of lipid peroxidation that can cross-link and deactivate a variety of membrane-bound enzymes [11]. The decrease in cellular enzymes SOD observed in this study for female Sprague-Dawley rats of the uteri and ovaries is indicating oxidative stress [12]. It is evident that CAT and SOD form a mutually beneficial defense team. Piroxicam generated significant oxidative stress, which may fail the body's innate mechanisms and cause ovarian damage. Furthermore, this study shows that Piroxicam significantly decreases the body weight when the treatment was compared to the control groups, as well as a decrease in the weight of the ovaries and uteri when the control was compared to the treatment groups, which may serve as a sign of infertility. The histological plates in this study reveal the harmful effects of Piroxicam in causing congestion in the lumen of the uterus and vascular congestion in the ovaries, which may indicate pelvic congestion syndrome as stated in a study [13].

Conclusion

In conclusion, this study shows that Piroxicam has a dangerous effect on the hormonal milieu of female Sprague-Dawley rats. Piroxicam also caused oxidative stress levels to increase in both the ovaries and the uteri. The histological structure of the organs was also affected in a dose-dependent manner. The frequent use of Piroxicam in female adolescents has become very rampant, especially among females of reproductive age. This study shows how the administration of Piroxicam was harmful to female rats, this can lead to discouraging the reckless consumption of the drug as an over-the-counter medication so that healthier reproductive systems can be maintained.

Acknowledgement

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Conflicts of Interests

The authors declare that they have no conflict of interest.

Author Contributions

- Adebajo AO was responsible for study conceptualization, first draft preparation, manuscript preparation, manuscript revision.
- Ayoade OH was responsible for manuscript preparation, manuscript revision.
- Ojo JH was responsible for manuscript preparation, manuscript revision, preparation of diagrams.
- Oladipo JO was responsible for manuscript preparation, manuscript revision.
- Ajisegiri OM was responsible for study conceptualization, first draft preparation, manuscript preparation, manuscript revision.
- Akpan UU was responsible for analysis of the bench work and manuscript preparation
- All authors read and approved the final version of the paper.

References

1. Schifano N, Chiappini S, Mosca A, Miuli A, Santovito MC, et al. Recreational drug misuse and its potential contribution to male fertility levels' decline: a narrative review. Brain Sci. 2022; 12: 1582.
2. Alhaji SA. Piroxicam: source for synthesis of central nervous system (CNS) acting drugs. Cent Nerv Syst Agents Med Chem. 2017; 17: 135-140.
3. Sadeq OR. Piroxicam-induced hepatotoxicity. Biomed J Sci & Tech Res. 2018; 2: 2601–2606.

4. Lozupone M, Berardino G, Mollica A, Sardone R, Dibello V, et al. ALZT-OP1: an experimental combination regimen for the treatment of Alzheimer's disease. Expert Opin Investig Drugs. 2022; 31: 759–771.
5. Adebajo O, Adebajo P, Ojo H, Ayoade O, Ulasi P, et al. Role of ascorbic acid in ameliorating dextromethorphan-induced testicular toxicity in Sprague-Dawley rat model. J Pharm Sci Drug Discov. 2024; 3: 1–8.
6. Arirudran DB, Kumar DG, Aslam M. Pharmacological effects of Trigonella foenum-graecum L. seeds on cardiovascular and antioxidant stress-related disease. Int J Aquat Sci. 2021; 12: 2630–2642.
7. Panjamurthy K, Manoharan S, Ramachandran CR. Lipid peroxidation and antioxidant status in patients with periodontitis. Cell Mol Biol Lett. 2005; 10: 255–264.
8. Adebajo OA, Adebajo PK, Ayoade OH, Akpan UU, Ojo JH, et al. Ameliorative role of virgin coconut oil on tramadol-induced nephrotoxicity in Sprague-Dawley rats. Asian J Res Med Med Sci. 2024; 6: 24–30.
9. van der Spoel AC, Jeyakumar M, Butters TD, Charlton HM, Moore HD, et al. Reversible infertility in male mice after oral administration of alkylated imino sugars: a nonhormonal approach to male contraception. Proc Natl Acad Sci U S A. 2002; 99: 17173–17178.
10. Zhou Y, Jin Q, Xu H, Wang Y, Li M. Chronic nanoplastic exposure induced oxidative and immune stress in medaka gonad. Sci Total Environ. 2023; 869: 161838.
11. Sharma P, Jha AB, Dubey RS. Oxidative stress and antioxidative defense system in plants growing under abiotic stresses. In: Handbook of Plant and Crop Stress. 4th ed. Boca Raton, FL: CRC Press; 2019. p. 93–136.
12. Ibrahim MA, Albahlol IA, Wani FA, Tammam AA, Kelleni MT, et al. Resveratrol protects against cisplatin-induced ovarian and uterine toxicity in female rats by attenuating oxidative stress, inflammation and apoptosis. Chem Biol Interact. 2021; 338: 109402.
13. Ignacio EA, Dua R, Sarin S, Harper AS, Yim D, et al. Pelvic congestion syndrome: diagnosis and treatment. Semin Intervent Radiol. 2008; 25:361–368.