MSI Journal of
Medicine and Medical Research (MSIJMMR)

Histopathological Effects of Fipronil Sulfone Toxicity in Mice

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The authors declare that no funding was received for this work.

ABSTRACT: Fipronil sulfone, a major metabolite of the insecticide fipronil, has been found to possess greater toxicity than its parent compound. This study aims to investigate the histopathological effects of acute fipronil sulfone exposure in male mice. The research demonstrated significant tissue damage across several vital organs, including the testis, seminal vesicle, kidney, liver, and brain. Histological examination revealed marked alterations in tissue architecture, such as an increase in interstitial space, degeneration of seminiferous tubules, and neuronal damage. Histomorphometric analysis was performed using ImageJ software to quantify these tissue changes, highlighting the severity of the damage. Specifically, the testis exhibited disruption in spermatogenesis, with altered seminiferous tubules and a significant increase in interstitial space. The seminal vesicle showed signs of metaplasia and epithelial changes. Kidney tissues presented with increased Bowman's space and degeneration of renal tubules, while the liver exhibited glycogen accumulation, hepatocyte degeneration, and signs of apoptosis. Notably, the brain showed degenerative changes in hippocampal neurons. This is the first study to provide histopathological evidence of the toxic effects of fipronil sulfone on these organs. The results suggest that

OPEN ACCESS

Received: 01-February-2025
Accepted: 25-February-2025
Published: 04-March-2026

This article is published in the **MSI Journal of Medicine and Medical Research (MSIJMMR)**
ISSN 3049-1401 (Online)

The journal is managed and published by MSI Publishers.

Volume 3, Issue 1 (Jan-Apr), 2026

fipronil sulfone induces significant organ damage through mechanisms such as oxidative stress. Further studies are required to investigate the underlying molecular mechanisms and to assess the long-term risks posed by fipronil sulfone exposure.

Keywords: *Fipronil sulfone, histopathology, organ toxicity, ImageJ software, neurotoxicity, oxidative stress, spermatogenesis, seminal vesicle, kidney damage, liver toxicity*

1. Introduction

The extensive use of pesticides in modern agriculture has significantly improved crop yield and food security worldwide (Popp, Pető et al. 2013). However, their widespread and often uncontrolled application has raised serious concerns regarding environmental contamination and potential health hazards to humans and animals. Among various classes of pesticides, insecticides represent a major group used to control agricultural and domestic pests (Abubakar, Tijjani et al. 2020). While these chemicals are designed to target specific organisms, many exhibit unintended toxic effects on non-target species, including mammals. Continuous exposure through contaminated food, water, soil, and occupational handling has intensified the need to evaluate the safety profiles of both parent compounds and their metabolites (Lebelo, Malebo et al. 2021).

Fipronil is a broad-spectrum phenylpyrazole insecticide widely used in agriculture, veterinary medicine, and household pest control. It acts primarily by blocking gamma-aminobutyric acid (GABA)-gated chloride channels in the central nervous system of insects, leading to neuronal hyperexcitation and death. Although fipronil shows higher selectivity toward insects, increasing evidence indicates that it can also interact with mammalian GABA receptors (Rosa, Oliveira et al. 2024). Acute exposure in humans has been associated with symptoms such as nausea, dizziness, headache, seizures, and neurobehavioral disturbances. Furthermore, environmental persistence and bioaccumulation have increased concerns regarding its long-term ecological and biological impacts (Edo, Samuel et al. 2024). After entering biological systems, fipronil undergoes metabolic transformation, primarily through cytochrome P450-mediated oxidation, forming several metabolites. Among these,

fipronil sulfone is considered the predominant and most toxic metabolite. Studies have shown that fipronil sulfone exhibits a longer half-life, greater tissue persistence, and stronger binding affinity to mammalian GABA receptors compared to its parent compound. Experimental evidence suggests that this metabolite may exert enhanced neurotoxic, cytotoxic, and endocrine-disrupting effects. Additionally, recent in vitro investigations have indicated that fipronil sulfone induces oxidative stress, mitochondrial dysfunction, and apoptotic cell death in neuronal and hepatic cell lines. Despite these findings, the comprehensive in vivo effects of this metabolite on mammalian organs remain insufficiently explored (Choi, Cho et al. 2007).

Toxicological research has increasingly emphasized the importance of studying pesticide metabolites rather than focusing solely on parent compounds. Metabolites can sometimes be more biologically active, persistent, and harmful than the original chemical (Aliferis and Chrysayi-Tokousbalides 2011). In this context, fipronil sulfone represents a significant toxicological concern. It has been detected in various tissues, including liver, kidney, brain, and reproductive organs, suggesting its systemic distribution after exposure. However, limited data are available regarding the structural and histopathological alterations induced by acute exposure, particularly in male reproductive and neural tissues. Histopathological analysis provides valuable insight into the cellular and tissue-level consequences of toxic exposure (Shah, Wambaugh et al. 2010). Structural alterations such as cellular degeneration, necrosis, vacuolation, inflammation, and disruption of normal tissue architecture serve as critical indicators of organ toxicity. In reproductive organs, damage to seminiferous tubules and supporting cells may impair spermatogenesis and fertility. Similarly, alterations in renal corpuscles and tubular structures can compromise filtration and reabsorption functions of the kidney. Hepatic degeneration reflects impaired detoxification capacity, while neuronal damage in brain regions such as the hippocampus may lead to cognitive and behavioral deficits. Therefore, evaluating histopathological changes across multiple organs is essential to understanding the systemic toxicity of fipronil sulfone (Wang, Martínez et al. 2016).

Despite growing awareness of pesticide-associated health risks, there remains a scarcity of comprehensive in vivo studies examining the histopathological

consequences of fipronil sulfone exposure in mammals (Gibbons, Morrissey et al. 2015). Most available studies focus on biochemical or molecular endpoints, leaving a gap in knowledge regarding structural tissue damage. Furthermore, the reproductive and neurological implications of this metabolite require detailed investigation due to their critical role in overall health and species survival (Bundy, Davey et al. 2009). The present study was designed to address this research gap by examining the histopathological effects of acute fipronil sulfone exposure in male mice. Using standard histological staining techniques and histomorphometric analysis through ImageJ software, this research evaluates structural changes in the testis, seminal vesicle, kidney, liver, and brain. By providing systematic evidence of tissue-level alterations, the study aims to enhance understanding of the toxicological profile of fipronil sulfone and contribute to improved risk assessment strategies (Fu, Yu et al. 2025). The findings may offer valuable baseline data for future investigations exploring the molecular mechanisms, oxidative stress pathways, and long-term consequences associated with exposure to this pesticide metabolit

2. Materials and Methods

2.1 Experimental Animals

Healthy adult male albino mice (*Mus musculus*) were used in the present study. The animals were obtained from a certified breeding facility and housed in the Animal House under controlled laboratory conditions (Ihedioha, Ugwuja et al. 2012). The mice weighed approximately 30–40 g at the start of the experiment. They were maintained at a temperature of 25 ± 3°C with relative humidity of 40–60% under a 12-hour light/12-hour dark cycle. Standard rodent pellet diet and tap water were provided *ad libitum*. Prior to the initiation of the experiment, animals were acclimatized for two weeks to minimize stress-related variables. All experimental procedures were conducted in accordance with institutional ethical guidelines for the care and use of laboratory animals (Health 1985).

2.2 Experimental Design and Treatment

A total of sixteen mice were randomly divided into two equal groups (n = 8 per group):

Control Group: Animals received intraperitoneal injections of dimethyl sulfoxide (DMSO), which served as the vehicle.

Treatment Group: Animals received fipronil sulfone at a dose of 100 mg/kg body weight via intraperitoneal injection.

The selected dose represented approximately 55% of the calculated lethal dose (LD_{50}), ensuring acute toxicity without immediate mortality. The injection volume was standardized to 0.2 mL per animal. The dose of fipronil sulfone was calculated individually according to the body weight of each mouse to ensure accuracy and consistency (Hainzl, Cole et al. 1998).

2.3 Tissue Collection

Following the treatment period, the animals were anesthetized using ketamine hydrochloride and sacrificed humanely. A midline abdominal incision was made to expose internal organs. The liver, kidneys, brain, testes, and seminal vesicles were carefully excised, rinsed in phosphate-buffered saline (PBS) to remove blood residues, and immediately fixed in 10% paraformaldehyde prepared in PBS for histological examination (Douglas, Fitzgerald et al. 2019).

2.4 Histological Processing

After fixation for 24 hours, tissues were processed for routine paraffin embedding. Samples were dehydrated in ascending grades of ethanol (60%, 70%, 80%, 90%, and 100%), cleared in xylene, and infiltrated with molten paraffin wax. The tissues were then embedded in paraffin blocks and allowed to solidify. Using a microtome, 5 µm thick sections were cut and mounted onto clean glass slides. The slides were dried overnight at 37°C to ensure proper adhesion (Sompuram, McMahon et al. 2003). Before staining, sections were deparaffinized in xylene and rehydrated through descending grades of alcohol followed by washing in distilled water.

2.5 Histological Staining

To evaluate structural and cellular changes, three different staining techniques were employed:

Hematoxylin and Eosin (H&E) Staining: This routine stain was used to examine general tissue architecture and cellular morphology. Hematoxylin stained nuclei blue, while eosin stained cytoplasm and extracellular matrix components pink, enabling identification of degeneration, necrosis, and structural alterations.

Periodic Acid–Schiff (PAS) Staining: PAS staining was performed to detect glycogen content and basement membrane integrity. This stain helped assess glycogen accumulation in hepatocytes and structural changes in renal tubules and seminiferous tubules.

Masson's Trichrome Staining: Trichrome staining was used to evaluate connective tissue components and fibrosis. It differentiated muscle fibers, collagen deposition, and cytoplasmic elements, allowing detailed observation of tissue remodeling and degeneration (Dubuisson, Versele et al. 2022).

After staining, slides were dehydrated, cleared in xylene, and mounted using DPX mounting medium.

2. 6 Microscopic Examination and Morphometric Analysis

All stained sections were examined under a light microscope at different magnifications (10× and 40×). Photomicrographs were captured using a digital camera attached to the microscope. Histomorphometric analysis was performed using ImageJ software (NIH, USA). Parameters measured included interstitial space, seminiferous tubule diameter, epithelial height, renal corpuscle area, glomerular area, Bowman's space, and the number of degenerating hepatocytes and neurons. Measurements were recorded as mean ± standard error of the mean (SEM) (SUBHASH).

2.7 Statistical Analysis

Data obtained from morphometric measurements were analyzed using Microsoft Excel and GraphPad Prism software. Comparisons between control and treated groups were performed using Student's *t*-test. A *p*-value of less than 0.05 was considered statistically significant. This methodological approach allowed for

comprehensive evaluation of the histopathological effects of acute fipronil sulfone exposure on multiple organs in male mice (Abdelgadir, Al-Qudsi et al.).

3. Results

3.1 Testis

Histopathological examination of the testes from the fipronil sulfone-treated group revealed marked structural alterations compared to the control group. In control animals, the seminiferous tubules were compactly arranged with normal architecture, showing intact germinal epithelium and active spermatogenesis at different stages. The interstitial spaces were minimal, and Leydig cells appeared normal in distribution and morphology.

In contrast, mice exposed to fipronil sulfone exhibited significant degeneration of seminiferous tubules. The tubular architecture was disrupted, with noticeable disorganization of germ cells and impaired spermatogenic progression. A clear reduction in the number of spermatids was observed, indicating compromised spermatogenesis. The seminiferous tubules showed altered diameters, and the tubular lumen appeared enlarged in several sections. Additionally, a significant increase in interstitial space between tubules was noted, likely due to degeneration or reduction of interstitial (Leydig) cells. Morphometric analysis confirmed statistically significant changes in tubular diameter and interstitial space in the treated group compared to controls ($p < 0.05$). These structural abnormalities collectively indicate that acute exposure to fipronil sulfone adversely affects testicular integrity and may substantially impair male reproductive function.

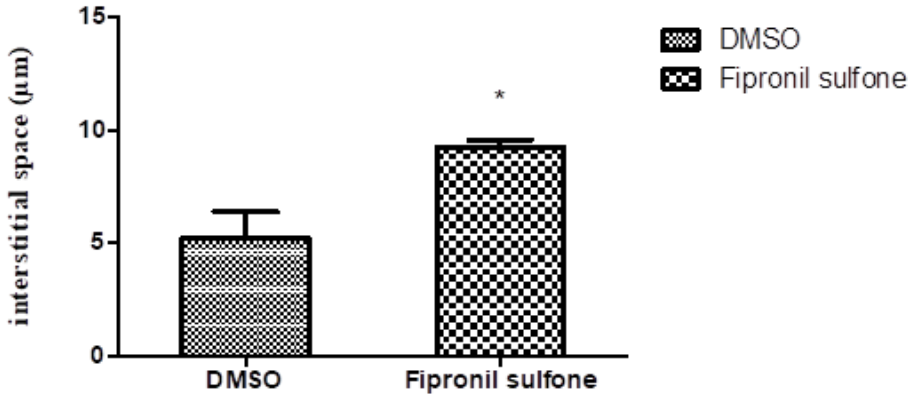

Fig 1. * shows significant increase in interstitial space (µm) of testis of fipronil sulfone group as compared to control group. Data expressed in Mean ± SEM, (P<0.05).

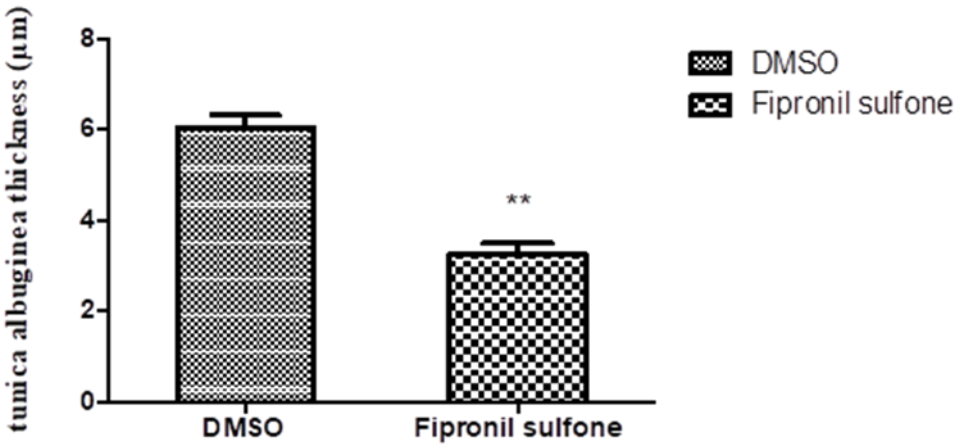

Fig 2: ** shows significant decrease of tunica albuginea thickness of testis fipronil sulfone group as compared to control group. Data expressed in Mean ± SEM, (P<0.05).

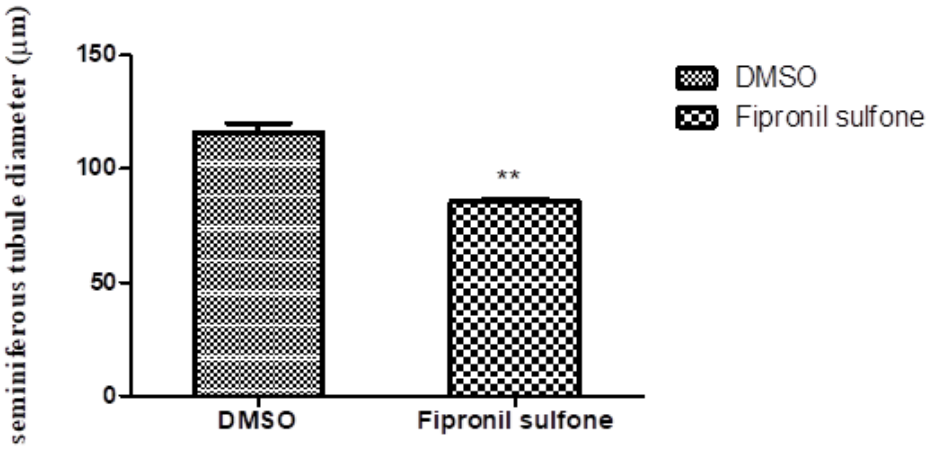

Fig 3. ** shows significant decrease in the tubule diameter of fipronil sulfone as compared to control group. Data expressed as Mean ± SEM, (P<0.05).

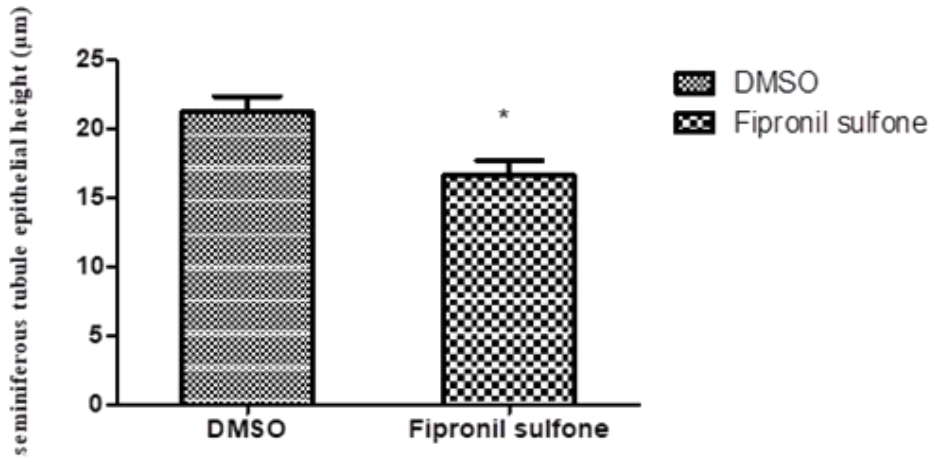

Fig 4. * shows significant decrease in the seminiferous tubules epithelial height of control group and F Sulfone. Data expressed in Mean ± SEM, (P<0.05).

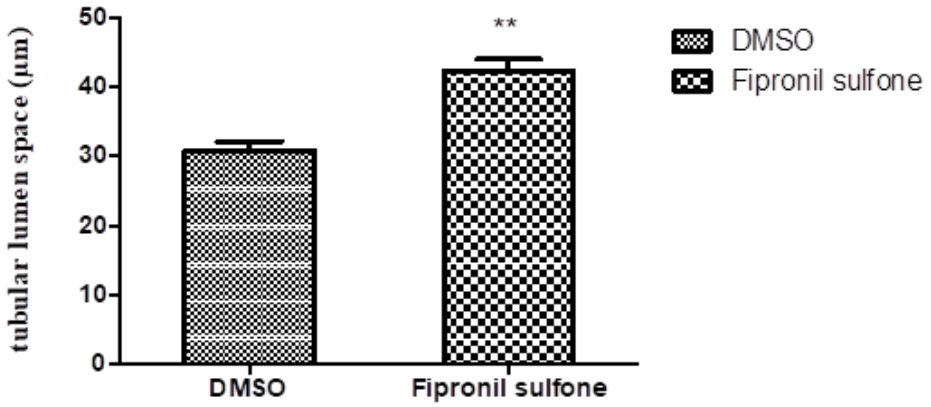

Fig 5. ** shows significant increase in the tubular lumen space of testis of fipronil sulfone group. Data expressed in Mean ± SEM, (P<0.05).

3.2 Seminal Vesicle

Histopathological evaluation of the seminal vesicle revealed noticeable structural differences between the control and fipronil sulfone-treated groups. In the control group, the seminal vesicles exhibited normal glandular architecture characterized by a highly folded mucosal lining and a complex, irregular lumen. The epithelium consisted of pseudostratified columnar cells with normal height and intact basement membrane. The muscular layer surrounding the gland appeared well organized, indicating normal secretory and functional activity.

In contrast, the treated group showed significant histological alterations. A marked increase in epithelial height was observed, which was confirmed by histomorphometric analysis ($p < 0.05$). The epithelial cells appeared altered in morphology, with evidence of metaplastic changes. Additionally, there was a noticeable reduction in epithelial folding, leading to a comparatively dilated and less complex lumen. These structural changes suggest disruption in the normal secretory function of the seminal vesicle. Since the secretory activity of the seminal vesicle is closely regulated by androgen levels and is essential for the production of seminal fluid components, such alterations may adversely affect male reproductive performance. The observed increase in epithelial height, along with reduced folding and luminal dilation, indicates that acute exposure to fipronil sulfone may impair normal glandular function and contribute to compromised reproductive health.

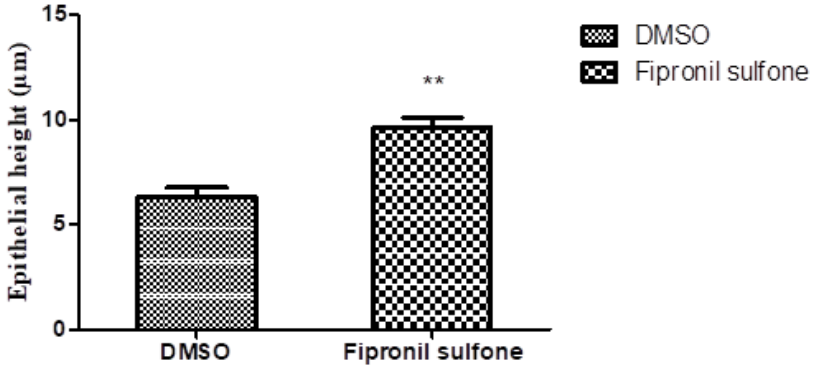

Fig 6: ** shows significant increase in the mean of seminal vesicle epithelial height of fipronil sulfone group as compared to control group. Data expressed in Mean ± SEM, ($P<0.05$).

3.3 Kidney

The kidney is a primary organ responsible for filtration, electrolyte balance, and excretion of metabolic waste products. Histomorphometric analysis revealed that exposure to fipronil sulfone resulted in a **significant decrease in renal corpuscle area** along with a **reduction in glomerular area**. These findings indicate structural shrinkage and distortion of the glomerulus, likely due to podocyte injury and necrosis. The reduction in glomerular size suggests compromised filtration capacity and impaired renal function. A notable feature in the treated group was the **significant enlargement of Bowman's space**. Expansion of Bowman's space generally occurs secondary to glomerular atrophy or shrinkage, reflecting pathological separation between the glomerular tuft and Bowman's capsule. This structural alteration is commonly associated with nephrotoxic injury and reduced glomerular filtration efficiency. Furthermore, degeneration of tubular epithelial cells was observed, particularly in the proximal convoluted tubules (PCTs). Loss of brush border integrity, tubular epithelial disintegration, and increased luminal space were evident. Since PCTs play a critical role in reabsorption of glucose, amino acids, and electrolytes, such degeneration may severely impair renal reabsorptive function. Hemorrhages, blood-filled spaces, and damage to medullary tubules further confirm extensive nephrotoxicity. Collectively, these alterations—decreased renal corpuscle area, glomerular shrinkage, increased Bowman's space, and tubular degeneration—clearly demonstrate that fipronil sulfone exerts significant nephrotoxic effects.

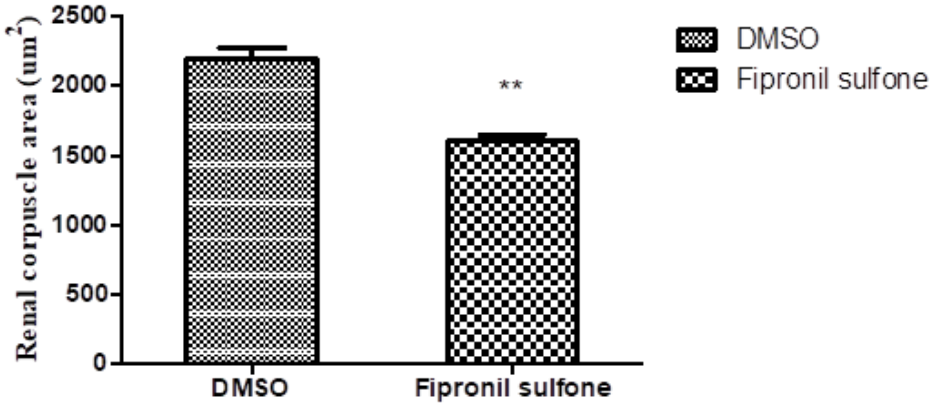

Fig 7. ** shows significant decrease Renal corpuscle area of the kidney in the F sulfone group with compared to control group. Data is expressed as Mean ± SEM, (P<0.05).

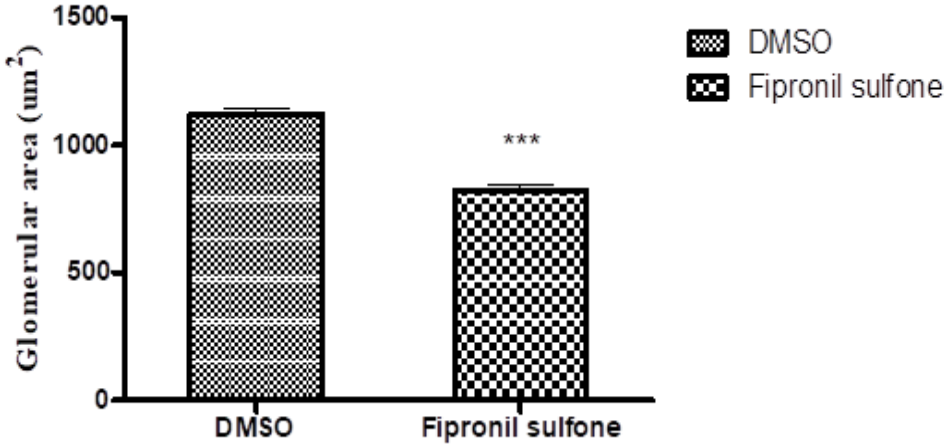

Fig 8: shows mean of Glomerular area in the F sulfone group as compared to control group. Data expressed in Mean ± SEM, (P<0,05).

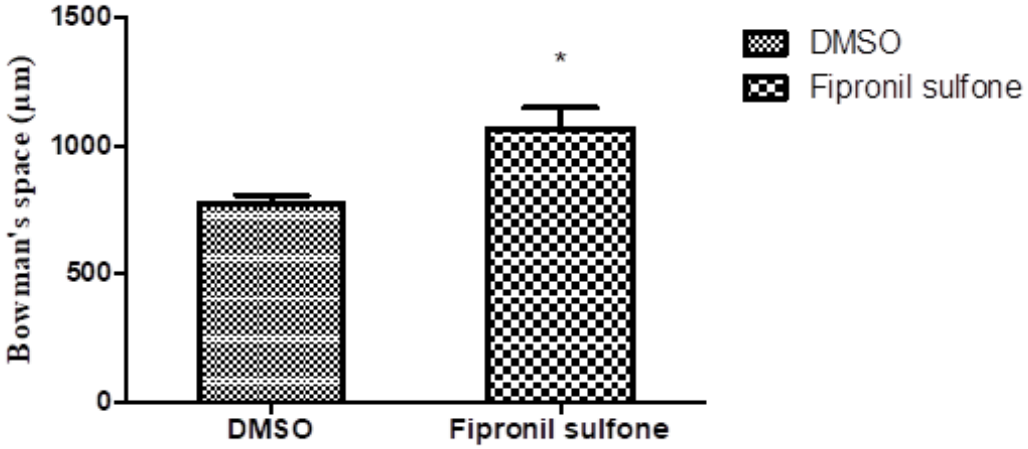

Fig 9. * shows significant increase in the Bowman`s space of nephron in the fipronil sulfone group with compared to control group. Values expressed in Mean ± SEM, (P<0,05).

3.4 Liver

The liver serves as the primary detoxification organ and is highly susceptible to chemical-induced injury. Histological examination of the control group revealed normal hepatic architecture, including intact hepatocytes arranged in cords radiating from the central vein and normal portal triads. In contrast, the treated group displayed marked disruption of hepatic cytoarchitecture.

Prominent histopathological findings included **tissue congestion and blood accumulation within the central vein**, indicating circulatory disturbance. Enlargement of the central vein was also observed, suggesting vascular stress and impaired hepatic microcirculation.

Hepatocytes in the treated group exhibited **cytoplasmic vacuolation, glycogen accumulation, and cellular enlargement**. Vacuolation may reflect lipid accumulation or hydropic degeneration, both indicative of metabolic disturbance. Glycogen accumulation suggests altered carbohydrate metabolism, potentially linked to mitochondrial dysfunction and impaired oxidative phosphorylation.

Nuclear abnormalities were prominent, including **pyknosis (nuclear condensation), karyorrhexis (nuclear fragmentation), and pericentric necrosis**, particularly around the central vein (zone III). This region is highly vulnerable to toxic injury because of its role in xenobiotic metabolism and relatively lower oxygen supply. The increased number of degenerated hepatocytes around the central vein further confirms localized hepatocellular damage. An increase in Kupffer cells around the central vein and portal areas was also noted, indicating activation of resident macrophages in response to tissue injury and inflammation. Overall, these findings demonstrate significant hepatotoxicity characterized by vascular congestion, metabolic disturbance, hepatocyte degeneration, and necrosis.

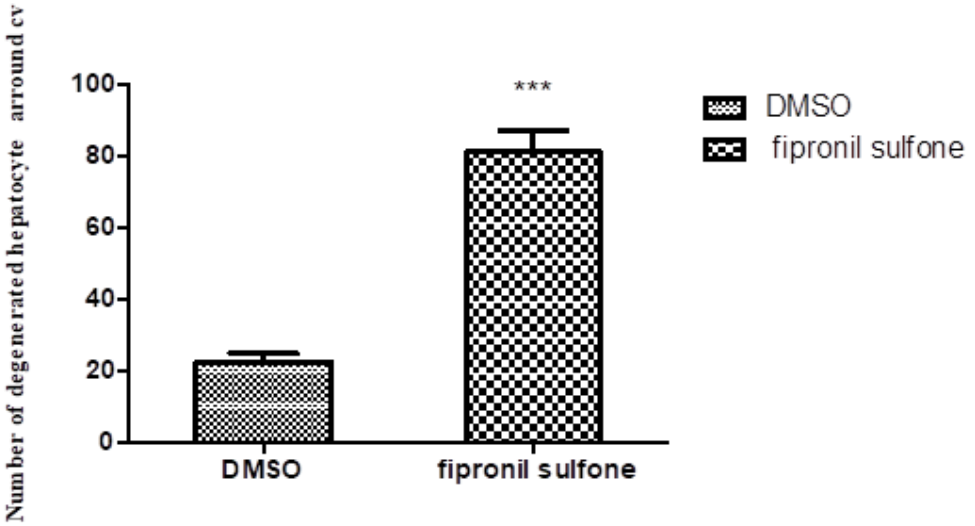

Fig 10. shows significant increase number of degenerated hepatocytes around the central vein (cv) in the fipronil sulfone group as compared to control group. Data expressed as Mean ± SEM, ($P<0.05$).

3.5 Brain

The brain, particularly the hippocampus, is highly sensitive to toxic insult due to its high lipid content and metabolic demand. The hippocampus plays a critical role in learning, memory consolidation, and cognitive processing. Histological analysis of the control group showed normal cytoarchitecture, well-organized pyramidal and granular layers, and intact neuronal morphology. In contrast, the treated group exhibited pronounced neurodegenerative changes. Hippocampal neurons showed **vacuolation, necrosis, and pyknosis**, indicating severe neuronal injury. Degeneration of pyramidal neurons in the cornus ammonis (CA) region and disruption of the dentate gyrus were evident. Loss of normal neuronal alignment and layer disorganization further demonstrated structural breakdown. Morphometric analysis confirmed a **significant increase in the number of degenerating neurons** in the treated group compared to control. Vacuolar changes suggest cellular edema and mitochondrial dysfunction, while necrosis reflects irreversible neuronal damage. These findings are consistent with oxidative stress–mediated neurotoxicity and GABA receptor interference associated with fipronil metabolites. Given the hippocampus' essential role in cognition, such structural damage may translate into functional deficits, including impaired memory and learning.

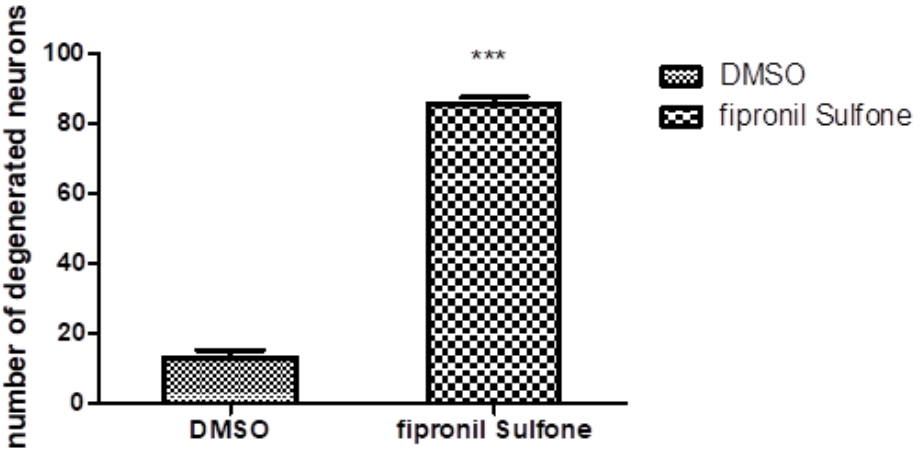

Fig 11. shows significant increase in the number of degenerating neurons of hippocampus in the fipronil sulfone group with compared to control group. values expressed as Mean ± SEM, ($P<0.05$).

4. Discussion

The present study provides comprehensive in vivo evidence that acute exposure to fipronil sulfone induces significant histopathological alterations in multiple organs of male mice, including the testis, seminal vesicle, kidney, liver, and brain. Fipronil sulfone, the major oxidative metabolite of Fipronil, is recognized for its longer half-life, greater tissue persistence, and stronger affinity for mammalian GABA-gated chloride channels compared to its parent compound. These characteristics likely contribute to the widespread tissue damage observed in the present investigation.

Reproductive organs showed pronounced structural disruption. In the testis, degeneration of seminiferous tubules, increased interstitial space, reduced tubular diameter, and impaired spermatogenesis were evident. Enlargement of the tubular lumen and reduction in germ cell populations indicate compromised spermatogenic activity. The increased interstitial space may reflect Leydig cell degeneration, which can impair testosterone synthesis and disrupt endocrine regulation of spermatogenesis. Similarly, the seminal vesicle exhibited epithelial hypertrophy, reduced mucosal folding, and metaplastic changes. Since seminal vesicle function is androgen-dependent, these alterations suggest possible endocrine-disrupting effects of fipronil sulfone. Collectively, these findings indicate that acute exposure may negatively affect male reproductive potential through both structural and hormonal pathways.

Renal histopathology revealed significant nephrotoxic effects, including decreased renal corpuscle and glomerular area, along with enlargement of Bowman's space. Glomerular shrinkage and increased capsular space are indicative of filtration impairment and structural atrophy. Degeneration of proximal convoluted tubules, loss of brush border integrity, and tubular dilation further suggest compromised reabsorptive function. Because renal tubular cells are highly metabolically active and vulnerable to oxidative stress, these findings support the hypothesis that fipronil sulfone induces nephrotoxicity through mitochondrial dysfunction and reactive oxygen species–mediated damage.

The liver, being the primary detoxification organ, exhibited marked hepatocellular injury. Observed changes included congestion of the central vein, glycogen accumulation, cytoplasmic vacuolation, nuclear pyknosis, karyorrhexis, and pericentric necrosis. The predominance of injury around the central vein (zone III) is consistent with toxicant-induced damage, as this region contains high concentrations of cytochrome P450 enzymes responsible for xenobiotic metabolism. Increased Kupffer cell activity further suggests an inflammatory response secondary to hepatocellular injury. These findings indicate that fipronil sulfone disrupts hepatic metabolic processes and induces degenerative and apoptotic changes.

Neurotoxicity was evident in the hippocampus, where neuronal vacuolation, necrosis, and layer disorganization were observed. The significant increase in degenerating neurons confirms structural brain damage. Given the hippocampus' central role in memory and learning, such alterations may have functional implications. The neurodegenerative effects are likely related to interference with GABAergic signaling and oxidative stress–induced mitochondrial damage, mechanisms previously associated with fipronil metabolites.

Overall, the consistent pattern of degeneration across highly perfused organs suggests systemic toxicity mediated by oxidative stress, mitochondrial dysfunction, and receptor-mediated neuronal hyperexcitation. This study fills an important gap by providing detailed histopathological evidence of fipronil sulfone toxicity in vivo. Further investigations focusing on molecular pathways, antioxidant defense mechanisms, and long-term exposure models are necessary to better understand the

full toxicological impact and to improve risk assessment strategies for this pesticide metabolite.

5. Conclusion

The present study provides clear and systematic evidence that acute exposure to fipronil sulfone produces significant multi-organ toxicity in male mice. As the principal and more persistent metabolite of Fipronil, fipronil sulfone demonstrated pronounced histopathological alterations in reproductive, renal, hepatic, and neural tissues. In the reproductive system, structural degeneration of seminiferous tubules, disruption of spermatogenesis, increased interstitial space, and epithelial alterations in the seminal vesicle indicate potential impairment of male fertility. Renal findings, including decreased renal corpuscle and glomerular area along with increased Bowman's space and tubular degeneration, confirm significant nephrotoxic effects that may compromise filtration and reabsorptive functions. Hepatic tissue exhibited congestion, glycogen accumulation, hepatocyte vacuolation, nuclear pyknosis, and pericentric necrosis, reflecting metabolic disturbance and hepatocellular injury. Moreover, pronounced degeneration of hippocampal neurons, characterized by vacuolation and necrosis, highlights the neurotoxic potential of this metabolite and suggests possible functional consequences for cognition and memory.

Histomorphometric analysis using ImageJ software quantitatively validated these structural changes, demonstrating statistically significant differences between control and treated groups. The widespread tissue damage observed across highly perfused organs suggests that fipronil sulfone exerts systemic toxicity, likely mediated through oxidative stress, mitochondrial dysfunction, and interference with GABAergic signaling pathways. In conclusion, this study establishes that acute exposure to fipronil sulfone results in substantial histopathological damage in multiple vital organs. These findings emphasize the toxicological importance of pesticide metabolites and underscore the need for further molecular, biochemical, and long-term studies to better understand the mechanisms of toxicity and to support improved risk assessment and regulatory evaluation of fipronil-based compounds.

References

1. Abdelgadir, E., et al. "Sub-acute Exposure of Fipronil Induces Biochemical and Histopathological Changes in the Liver, Kidney and Heart of Male Albino Rats."

2. Abubakar, Y., et al. (2020). Pesticides, history, and classification. Natural remedies for pest, disease and weed control, Elsevier: 29-42.

3. Aliferis, K. A. and M. J. M. Chrysayi-Tokousbalides (2011). "Metabolomics in pesticide research and development: review and future perspectives." 7(1): 35-53.

4. Bundy, J. G., et al. (2009). "Environmental metabolomics: a critical review and future perspectives." 5(1): 3-21.

5. Choi, I.-S., et al. (2007). "Multiple effects of bisphenol A, an endocrine disrupter, on GABAA receptors in acutely dissociated rat CA3 pyramidal neurons." 59(1): 8-17.

6. Douglas, A., et al. (2019). "Storage of blood clots for histological analysis: how long is too long in saline and paraformaldehyde?".

7. Dubuisson, N., et al. (2022). "Histological methods to assess skeletal muscle degeneration and regeneration in Duchenne muscular dystrophy." 23(24): 16080.

8. Edo, G. I., et al. (2024). "Environmental persistence, bioaccumulation, and ecotoxicology of heavy metals." 40(3): 322-349.

9. Fu, L., et al. (2025). "Transformation and transport: polyvinyl chloride microplastics modulate fipronil accumulation and toxicity in zebrafish."

10. Gibbons, D., et al. (2015). "A review of the direct and indirect effects of neonicotinoids and fipronil on vertebrate wildlife." 22(1): 103-118.

11. Hainzl, D., et al. (1998). "Mechanisms for selective toxicity of fipronil insecticide and its sulfone metabolite and desulfinyl photoproduct." 11(12): 1529-1535.

12. Health, N. I. o. (1985). Guide for the care and use of laboratory animals, National Academies.

13. Ihedioha, J. I., et al. (2012). "Reference values for the haemotology profile of conventional grade outbred albino mice (Mus musculus) in Nsukka, Eastern Nigeria." 9(2).

14. Lebelo, K., et al. (2021). "Chemical contamination pathways and the food safety implications along the various stages of food production: a review." 18(11): 5795.

15. Popp, J., et al. (2013). "Pesticide productivity and food security. A review." 33(1): 243-255.

16. Rosa, M. E., et al. (2024). "Recent advances on the influence of fipronil on insect behavior." 65: 101251.

17. Shah, I., et al. (2010). "Virtual tissues in toxicology." 13(2-4): 314-328.

18. Sompuram, S. R., et al. (2003). "A novel microscope slide adhesive for poorly adherent tissue sections." 26(2): 117-123.

19. SUBHASH, P. P. EFFECT OF ACETAMIPRID ON MALATHION INDUCED TOXICITY WITH SPECIAL REFERENCE TO MALE REPRODUCTIVE SYSTEM IN WISTAR RATS, MAHARASHTRA ANIMAL AND FISHERY SCIENCES UNIVERSITY.

20. Wang, X., et al. (2016). "Fipronil insecticide toxicology: oxidative stress and metabolism." 46(10): 876-899.