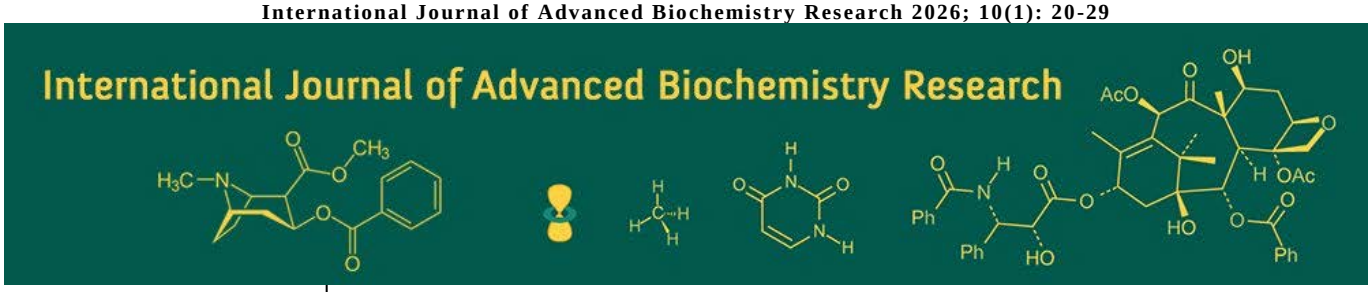

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Antioxidant Mediated Hepato-Renal Protection by *Punica granatum* Peel Extract in Fipronil-treated Rats

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Abstract
The present study was carried out to check the ameliorative effect of pomegranate peel extract (PPE) against fipronil-induced hepato-renal toxicity in male Wistar albino rats. A study was conducted for 45 days period in 4 groups of male Wistar albino rats with 6 animals in each group. Group I and III served as vehicle (distilled water) control and *Punica granatum* control. Group II animals were treated with fipronil @ 10 mg/kg b. wt. orally with distilled water. Group IV animals were treated with both fipronil and pomegranate peel extract @ 10 and 200 mg/kg b. wt. respectively for a period of 45 days using distilled water as a vehicle. Tissue pieces of liver and kidney were subjected for oxidative stress estimation, which revealed a significant increase ($P<0.05$) in the levels of lipid peroxidation (LPO) and decreased levels of superoxide dismutase, catalase, reduced glutathione and glutathione peroxidase in fipronil-treated rats. Grossly, the liver of fipronil-treated rats was congested and enlarged compared to other groups. Histopathological examination of liver sections of rats in the same group revealed moderate to severe degenerative changes in hepatocytes with loss of architecture, hepatic cords disruption, mononuclear cell infiltration, fatty changes and bile duct epithelial hyperplasia. In kidney section, severe degenerative changes were observed. Co-administration of *Punica granatum* (pomegranate peel extract) along with fipronil resulted in restoration of liver and kidney enzymes values and oxidative stress parameters near to normal ranges. Histologically, the architectural details of the liver and kidney were regained with minimal degenerative changes. The findings obtained through serum biochemical, oxidative stress estimation, gross and histopathological evaluation clearly revealed the ameliorative effects of *Punica granatum* (pomegranate peel extract) against fipronil-induced hepato-renal toxicity in male Wistar albino rats.

Keywords: Amelioration, fipronil, male Wistar albino rats, oxidative stress, *Punica granatum.*

Introduction
Pesticide (especially insecticides) use has gradually increased over the past few decades in both agricultural and non-agricultural areas, in the form of sprays, liquids, and powders, to get rid of rats, ticks, cockroaches, and other dangerous bugs (WHO. 1990) [67]. India is the leading producer of pesticides in Asia and ranks 12th on a global scale (Indira *et al*., 2007) [34]. Around 90,000MT of pesticides are used annually in India as an effective pest control management (Chauhan and Singhal, 2006). But indiscriminate and inappropriate use of these insecticides leads to excess leaching and surface runoff into aquatic ecosystems, which will hamper the non-target species and eventually disturb its food chain (David *et al.*, 2015) [21]. Over the past forty years, pesticides have found widespread use in horticulture and veterinary activities around the world. (De *et al.*, 2014) [22]. Through an ongoing cycle of evaporation and deposition, persistent pesticides that are applied in one part of the planet might spread through the air to other parts. (Koirala *et al.*, 2007) [40].
Fipronil is one among the group of "new generation" insecticide which differs from other groups of insecticides like pyrethroids (sodium channel blockers), organophosphates and carbamates (cholinesterase inhibitors) in their mode of action (Aajoud *et al.*, 2007) [1]. Being a broad-spectrum insecticide, fipronil is used in veterinary (Medleau *et al*., 2002) [45] households, topical pet care products, and agricultural practices to control ants, wasps, flies, cockroaches, termites, thrips, rootworms, weevils, fleas, ticks, and beetles (Badgujar *et al*., 2015) [15]. Fipronil causes hyperexcitation and mortality in insects by noncompetitively blocking glutamate-activated chloride channels and g-aminobutyric acid A receptors in the central nervous system. According to reports, the parent molecule is less harmful to fish,

birds, mammals, and insects than its sulfone metabolites and fipronil desulfinyl, a byproduct of photodegradation. (Hainzl *et al.*, 1998) [29]. The kidney and liver are the most vulnerable organs to pesticide toxicity and injury, and they are also key players in the biotransformation of pesticides. These tissues' vulnerability to pesticide stress results from a disruption in the equilibrium between the level of oxidative stress and antioxidant capacity. Most pesticides cause toxicity that results in cell and DNA damage from free radicals, and oxidative stress is a major contributing factor in this process. (John *et al.*, 2001) [35]. In addition to managing oxidant-antioxidant balance, oxidative processes play a crucial role in insecticide-induced tissue damage by preventing neutrophil infiltration and controlling inflammatory mediators. (Muniz *et al.*, 2008) [49]. Thus, measuring antioxidant indicators such as catalases, superoxide dismutase, glutathione peroxidase, and lipid peroxidase can assist in determining the extent of oxidative damage to the liver and kidney (Li *et al.*, 2003) **[41].** Estimation of biochemical parameters like liver enzymes (AST, ALT, Total Protein, Albumin, globulin levels) and renal enzymes (BUN, Creatinine) was also an effective indicator for determining the extent of toxic effects caused by pesticides such as fipronil in respective organs (Pimpao *et al.*, 2007) [52].

Herbal medicines are now widely used as complementary and alternative medicine in many developing countries (Anquez-Traxler, 2011) **[13].** Because of their low side effects and compatibility with physiological flora, herbal medications are used by almost 80% of the world's population (Pandy *et al.*, 2011) [51]. Pomegranate (*Punica granatum*) is one among them, and it has been widely used in traditional medicine for many years (Ajai Kumar *et al.*, 2005) [8], in which the peel extract of pomegranate has been reported to have higher antioxidant potential compared to other parts (Wang *et al.*, 2011) [66]. PPE enriched with polyphenolic compounds like (gallagic acid), flavonoids (catechins and quercetin), and anthocyanidin which are responsible for the natural antioxidant potential of pomegranate (Gil *et al.*, 2000) [28]. Protective effects of pomegranate peel on brain injury have been widely studied by (Belal *et al.*, 2020) [16]. The hepatoprotective and nephroprotective (Emam *et al.*, 2020) [25] actions of PPE have also reported. Hence, the current study aimed to investigate the toxic effects of fipronil on the liver and kidney of Wistar rats and to check the hepato-renal protective role of Pomegranate peel extract (PPE) in it.

Materials and Methods

Purchase of lab animals, fipronil and pomegranate peel extract

A total of 24 male Wistar albino rats used for this study were purchased from Sri Venkateshara Enterprises, Bangalore. The procured rats were randomly grouped and housed in standard polypropylene cages after two weeks of acclimatization. They were maintained at 25 ºC±1 ºC and a 12:12 hour interval light / dark cycle throughout the experimental period of 6 weeks by taking necessary precautions, and standard laboratory hygienic conditions by providing laboratory animal feed and water *ad libitum*. The Institutional Animal Ethical Committee (IAEC) approval was obtained prior to the commencement of the experiment (wide no 281/ go/ ReBi/ S/ 2000/CPCSEA/ CVSc/ TPTY/ 010/ Veterinary pathology/ 2023 dated: 08.05.2023).

Technical grade of fipronil (99% pure) with batch no. FIP92B5266 was procured from Gharda Chemicals Ltd., Mumbai. The *Punica granatum* (Pomegranate) peel extract product (Dadim LC23030077) was procured from Chemiloids Life Science Pvt. Ltd., Vijayawada, Andhra Pradesh.

Study design

The study was designed such that a total of 24 male Wistar albino rats were randomly assigned into four groups with six animals in each group as shown below.

a) Group 1 (Negative control) - six rats fed with ad libitum feed and distilled water.
b) Group 2 (Fipronil control) - six animals treated with fipronil @ 10 mg/kg b. wt. orally in distilled water for a period of 45 days.
c) Group 3 (*Punica granatum* control) - six animals treated with *Punica granatum* orally @ 200 mg/kg b. wt. for a period of 45 days.
d) Group 4 (Fipronil + *Punica granatum*) - six animals treated with both fipronil @ 10 mg/kg b. wt. and *Punica granatum* @ 200 mg/kg b. wt. orally in distilled water for a period of 45 days.

Animal parameters studies

Oxidative stress

Tissue pieces of liver and kidney were minced and homogenized in 0.05 M ice-cold phosphate buffer (pH 7.4) by using a Virtis homogenizer to make a 10% homogenate. 0.2 ml of the homogenate was used for lipid peroxidation assay (Yagi, 1976) [68]. The remaining part of the homogenate was mixed with 10% trichloroacetic acid in the ratio of 1:1, centrifuged at 5000 rpm for 10 min at 4 ºC and the supernatant was used for the estimation of Reduced glutathione (Moron *et al.*, 1979) [47]. The remaining part of the homogenate was further centrifuged at 15000 rpm for 60 min at 4 ºC and the supernatant obtained was used for estimation of Superoxide dismutase (Marklund and Marklund, 1974) [44], Catalase (Caliborne, 1985) [17] and Glutathione peroxidase (Rotruck *et al.*, 1973) [56] in liver and kidney of all rats in all groups.

Gross and histopathology

A detailed post-mortem examination was conducted on all the sacrificed rats in all the experimental groups. The gross lesions were recorded and representative tissue pieces from liver and kidney were collected and preserved in 10% neutral buffered formalin for histopathological studies. Fixed tissues were processed by the routine paraffin embedding technique. Sections of 5-6 (µ) thickness were cut and stained with the routine Hematoxylin and Eosin method (H&E) (Culling, 1974) [18].

Statistical analysis

By performing one-way ANOVA, the results were statistically analysed (Snedecor and Cochran, 1994) [61].

Results and Discussion

Oxidative stress

Lipid Peroxidation (LPO)

The mean LPO values in the liver of Group I to IV rats were 171.15, 352.18, 166.54, and 175.38 (nM of MDA/ g of tissue) respectively and are given in **Table 1.** In kidney, LPO values were 194.61, 517.8, 195.58 and 234.04

respectively which are given in Table 2. A significant increase (P<0.05) in the LPO values was observed in the kidney and liver of fipronil-treated rats compared to the control group. Ameliorated (Group IV) rats showed a significant decrease (P<0.05) in the LPO values compared to fipronil-treated rats. However, no significant difference was noticed in LPO values among *Punica granatum-treated* rats (Group III) compared to control rats (Group I). The present findings were in accordance with the results reported by earlier authors (Singh *et al.,* 2019) [60], (Albasher *et al*., 2020) [9] and (Elshony *et al.,* 2021) [24]. The increased LPO value might be due to alterations of lipid bilayer configuration in the cell membrane by reactive oxygen species (ROS) generated by fipronil, which in turn produces an excess of lipid peroxides (malondialdehyde) from the damaged membrane (Liu *et al.,* 1996) [43], (Scandalios, 2005) [57] and (Kanbur *et al.,* 2008) [36]. Hence, Malondialdehyde is a secondary product of lipid peroxidation, and is used as a marker of cell membrane damage (Esterbauer *et al.,* 1991) [26] and Pizzimenti *et al.,* 2013) [53].

Superoxide Dismutase (SOD)

The mean liver SOD values in the Group I to IV rats were 13.8, 7.7, 12.9, and 12.2 (U/ mg of protein) respectively, and are given in Table 1. In kidney, SOD values were 14.2, 6.4, 13.8 and 13.4 respectively, which are given in Table 2. A significant decrease (P<0.05) in the liver and kidney SOD values was observed in fipronil-treated rats compared to the control group. Ameliorated (Group IV) rats showed a significant increase (P<0.05) in the SOD values when compared to fipronil-treated rats.

Catalase

The mean values of catalase in liver of Group I to IV rats were 0.21, 0.08, 0.18, and 0.15 (nM of H2O2 decomposed/min/ mg of protein) respectively, and given in Table. 1. In kidney, CAT values were 0.18, 0.09, 0.16 and 0.15 respectively, which are given in Table 2. There was a statistically significant (P<0.05) decrease in the mean liver and kidney catalase value of fipronil-treated (Group II) rats when compared to control rats. Meanwhile, the mean catalase values of control and *Punica granatum-treated* (Group III) rats were not statistically significant. A Significant (P<0.05) increase was observed in *Punica granatum* ameliorated rats (Group IV) when compared to fipronil-treated rats.

Reduced glutathione

The mean liver GSH values in Group I to IV rats were 21.78, 11.49, 21.31, and 20.03 (µmoles GSH/g of tissue) respectively, and are given in Table. 1. In kidney, reduced glutathione values were 19.63, 12.93, 19.21 and 18.36 respectively, which are given in Table 2. Compared to *Punica granatum* ameliorative rats (Group IV) and control rats (Group I), there was a significant (P<0.05) decrease in the GSH values of fipronil-treated rats (Group II). Meanwhile, mean GSH values of *Punica granatum-treated* (Group III) and control rats were statistically insignificant.

Glutathione Peroxidase (GPx)

The overall mean liver GPx values in Group I to IV rats were 27.66, 13.69, 27.49, and 22.46 (U/mg of protein) respectively, and are given in Table. 1. In kidney, reduced glutathione values were 32.13, 19.08, 29.93 and 26.68 respectively, which are given in Table 2. There was a significant (P<0.05) decrease in GPx values of fipronil-treated rats (Group II) when compared to the control group (Group I). No significant difference was noticed between Punica granatum-treated (Group III) and control rats. A significant improvement was recorded in mean liver GPx values in the ameliorated rats (Group IV) compared to the fipronil-treated rats (Group II). In the current research, a significant (P<0.05) decrease in SOD, CAT, GPx, GST, and GSH was observed in the liver and kidney of fipronil treated animals when compared to corresponding controls. These findings were in agreement with (Mossa *et al.,* 2015) [48], (Badgujar *et al.*,2016) [14], (Kartheek and David, 2016) [37], (Singh *et al.,* 2019) [60], (Albasher *et al.,* 2020) [9] and (Elshony *et al.,* 2021) [24]. The decreased antioxidant enzymes activities in different organs in the current study might be due to fipronil-induced excessive generation of reactive oxygen species (ROS) and reduced cell defence mechanism.

Significant reduction in LPO values along with increased levels of SOD, CAT, GPx, GST, and GSH was observed in the *Punica granatum* ameliorated group (Group IV). The restoration of these values near to normal range in *Punica granatum* ameliorated rats might be due to anti- lipid peroxidation property of *Punica granatum* (Dkhil *et al.,* 2013) [23] and (AI-Gubory *et al.,* 2015) [10] and its antioxidant activity (Li *et al.,* 2006) [42], (Shabtay *et al.,* 2008) [58], (Moneim *et al.,* 2012) [46], (Hasan *et al.,* 2016) [30] and (Farideh *et al.,* 2017) [27].

Table 1: Mean and SE values of LPO, SOD, CAT, GSH and GPx in liver of rats of different experimental groups.

At the end of experimental Period (6thweek)				
Oxidative stress parameters in liver	**GROUP I**	**GROUP II**	**GROUP III**	**GROUP IV**
LPO (nM MDA/g of tissue)	171.15±0.76^{c}	352.18±1.26^{a}	166.54±1.63^{d}	175.38±0.84^{b}
SOD (U/mg of protein)	13.8±0.27^{a}	7.7±0.19^{d}	12.9±0.13^{b}	12.2±0.22^{c}
Catalase	0.21±0.03^{a}	0.08±0.01^{b}	0.18±0.02^{a}	0.15±0.01^{a}
Reduced glutathione (µmoles GSH/g of tissue)	21.78±2.34^{a}	11.49±1.77^{b}	21.31±1.50^{a}	20.03±1.85^{a}
Glutathione peroxidase (U/mg of protein)	27.66±0.73^{a}	13.69±0.40^{c}	27.49±0.45^{a}	22.46±0.82^{b}

Mean values with different superscripts differ significantly (P < 0.05), ANOVA, S.E - Standard Error.

Table 2: Mean and SE values of LPO, SOD, CAT, GSH and GPx in kidney of rats of different experimental groups.

At the end of experimental Period (6th week)				
Oxidative stress parameters in kidney	**GROUP I**	**GROUP II**	**GROUP III**	**GROUP IV**
LPO (nM MDA/g of tissue)	194.61±1.35^{c}	517.88±1.32^{a}	195.58±0.76^{c}	234.04±0.88^{b}
SOD (U/mg of protein)	14.2±0.18^{a}	6.4±0.23^{c}	13.8±0.25^{ab}	13.4±0.11^{b}
Catalase	0.18±0.01^{a}	0.09±0.01^{b}	0.16±0.01^{a}	0.15±0.01^{a}
Reduced glutathione (µmoles GSH/g of tissue)	19.63±0.66^{a}	12.93±0.46^{b}	19.21±0.25^{a}	18.36±0.72^{a}
Glutathione peroxidase (U/mg of protein)	32.13±0.37^{a}	19.08±0.32^{d}	29.93±0.73^{b}	26.68±0.08^{c}

Mean values with different superscripts differ significantly ($P < 0.05$), ANOVA, S.E - Standard Error.

Gross and histopathology

At the end of 6th week of experimental period, liver of fipronil treated rats (group II) showed paleness (Fig: 1). Whereas some of the *Punica granatum* ameliorated (group IV) rats showed slight paleness of the liver and most of the ameliorated rats regained almost normal appearance compared to fipronil treated rats. Histopathology of the liver of fipronil treated rats revealed congested and dilated blood vessels, sinusoidal congestion (Fig: 2), moderate to severe degenerative changes in hepatocytes with areas of loss of architecture, disruption of hepatic cords, dilated sinusoids, and atrophied hepatocytes with infiltration of MNC's (Fig: 3). Mild to moderate fibroblasts proliferation (Fig: 4), bile duct epithelial hyperplasia and proliferation of bile ducts (Fig: 5) along with mononuclear cell infiltration were observed in portal and periportal areas. In multi-focal areas, dilatation of sinusoids with haemorrhages, focal loss of hepatocytes with infiltration of MNCs, and mild to moderate fatty degenerative changes (Fig: 6) were conspicuous in the majority of rats whereas some rats showed the microvesicular type of fatty change. Perivascular infiltration of mononuclear cells, centrilobular necrotic changes (Fig: 7) and micronodule like lesions with fibroblasts and MNC's infiltrations were more evident by the end of 6th week of the experiment. These findings are in line with (De Oliveira *et al.,* 2012) [50], (Badgujar *et al.* 2016) [14], (da Cunha *et al.,* 2017) [19], (Abdel-Daim and Abdeen 2018) [4], (Kartheek and David 2018) [38] and (Anber *et al.*, 2021) [12]. The liver alterations in the present study might be due to free radicals produced by fipronil and its primary metabolite (fipronil sulfone) in the liver impairing mitochondrial respiratory function, membrane potential, and the electron transport chain complex (Das *et al.,* 2006) [20] leading to greater leakage of mitochondrial Ca2+ into the cytoplasm and stimulates proteases, phospholipases, and endonucleases, which disrupt cytoskeleton-plasma membrane connections and destabilize the liver's lipid bilayer structure. Ultimately, the histologic architecture of the liver becomes altered (Trump and Berzesky, 1992) [63].

Histopathological findings of liver in group IV rats were similar to that of group II with reduced intensity like mild sinusoidal congestion**,** mild infiltration of MNC's in portal and perivascular areas (Fig: 8) and mild degenerative changes in hepatocytes with regained architecture of hepatic cords near to normal appearance by the end of the 6th week of experiment was observed. Similar lesions with reduced intensity were observed in Punica granatum ameliorated rats (group IV) and this might be due to the hepatoprotective action of pomegranate peel extract (Ahmad *et al.,* 2016) [7], (Al-Shaaibi *et al.,* 2016) [11], (Ibrahim *et al.,* 2016) [33] and (Ramzy *et al.,* 2019) [54]. Punica granatum has oxygen free radical scavenging activity and antioxidant property, which helps to scavenge the excess free radicals generated due to fipronil toxicity in the liver (Moneim *et al.,* 2012) [46], (Shiban *et al.,* 2012) [59], Dkhil *et al.,* 2013) [23] and (Hasan *et al.,* 2016) [30].

Histopathology of kidney of the fipronil rats revealed severely degenerated and desquamated tubular epithelium with the presence of cellular debris in the renal tubules (Fig: 9), mild to moderate infiltration of fibroblasts in the interstitial spaces (Fig: 10), intertubular hemorrhages, congested and thickened blood vessels, perivascular edema and pockets of hemorrhages in the cortex and medullary region. Congested, degenerated, atrophied, and cystic glomeruli (Fig: 11) were more evident in all treated rats. The majority of the tubules lost their architectural details with complete distortion and loss of basement membrane (Fig: 34) accompanied by the presence of hyaline cast in some tubules. Moderate to severe infiltration of mononuclear cells in between the tubules and periglomerular spaces (Fig: 12) was more conspicuous in the majority of treated rats. The similar findings were observed by (Uzunhisarcikli *et al.,* 2003) [64], (Mossa *et al.,* 2015) [48], (Abdel Daim and Abdeen, 2018) [4], (Abdel Daim *et al.,* 2019) [5], (Khalaf *et al.,* 2020) [39], (Abou zeid *et al.,* 2021) [6], (Hossam El din *et al.,* 2022) [32] and (Soliman *et al.,* 2023) [62]. These kidney lesions might be due to the generation of oxygen free radicals by fipronil and its metabolite. Fipronil primarily modifies NADPH oxidase activity in the inner mitochondrial membrane, which results in alterations in the electron transport chain and lipid peroxidation in cell membrane. Fipronil also damages the cellular proteins, lipids, and DNA structure and causes complete histologic alterations of renal tissue (Walmsley and White, 1994) [65] and Abdel-Daim and Abdeen, 2018) [3].

Histopathological findings of kidney in group IV rats were similar to that of group II rats with reduced intensity like focal areas of mild renal tubular degenerative changes, mild haemorrhages (Fig: 13) and mild infiltration of MNC's in periglomerular spaces. The kidney regained its normal architecture near to the normal with slight variation in the size of the glomerulus by the end of experimental period**.** These reduced kidney alterations might be due to high polyphenolic compounds, particularly ellagitannins present in *Punica granatum,* which can easily pass through the mitochondrial membrane and decrease the production of excess free radicals that damage the renal tissue (Gil *et al.,* 2000) [28], (Rosenblat *et al.,* 2015) [55].

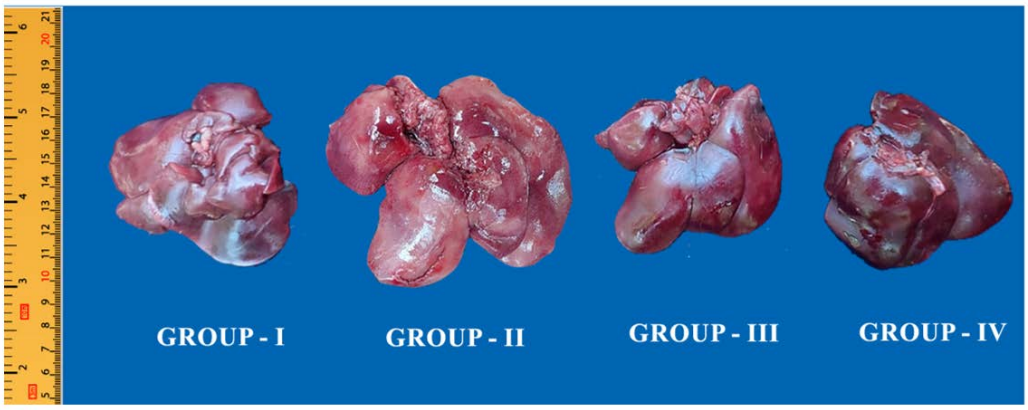

Fig1: Gross morphology of liver from different experimental groups at 6th week showing pale appearance in Group II compared to other groups.

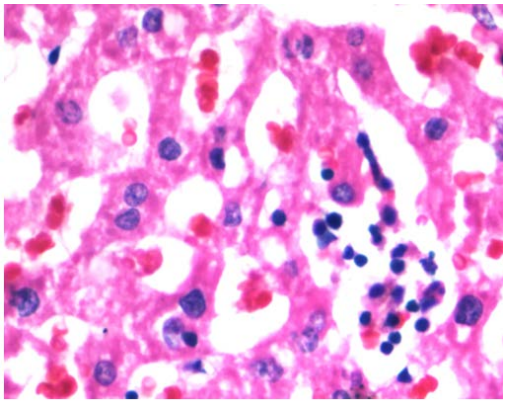

Fig 2: Liver section of Group II showing sinusoidal dilatation and congestion (H&E, ×100).

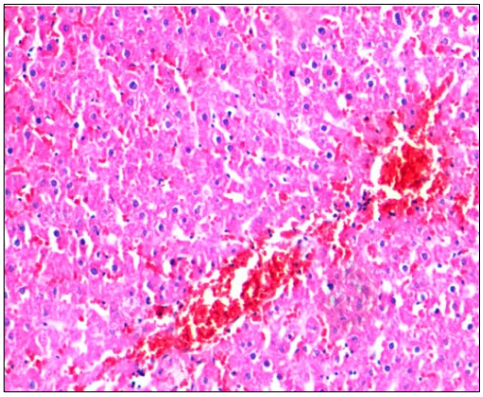

Fig 3: Liver section of Group II showing dilated sinusoids with atrophied hepatocytes and mononuclear cell infiltration (H&E, ×400).

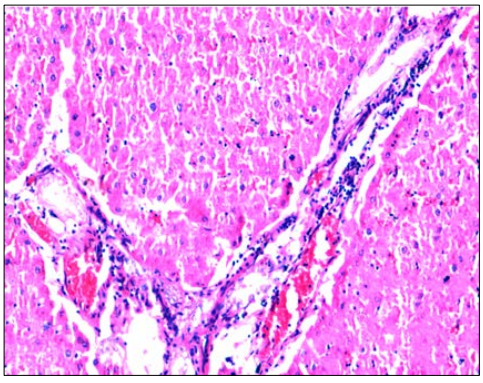

Fig 4: Liver section of Group II showing mild to moderate proliferation of fibroblasts and mononuclear cells in the portal area (H&E, ×100).

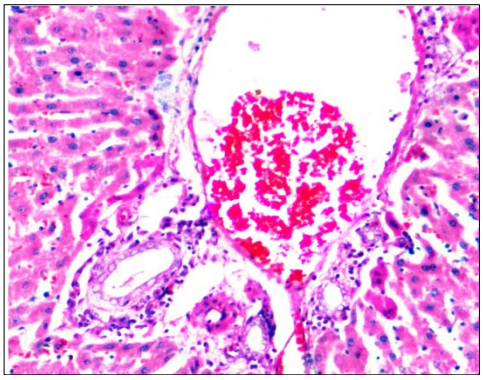

Fig 5: Liver section of Group II showing bile ductular hyperplasia and dilated, congested portal vein (H&E, ×100).

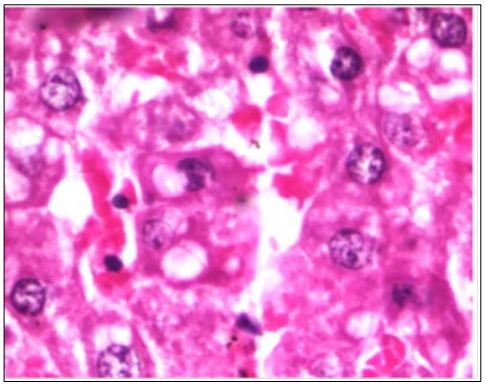

Fig 6: Liver section of Group II showing mild to moderate fatty degenerative changes (H&E, ×100).

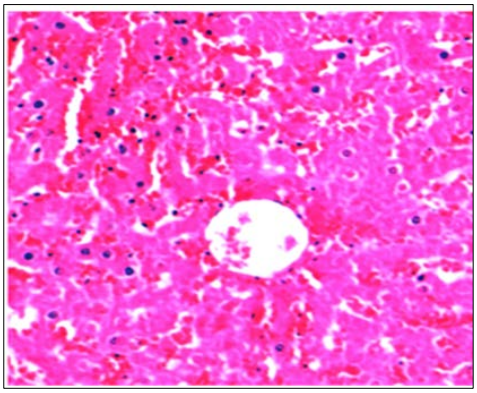

Fig 7: Liver section of Group II showing centrilobular necrotic changes (H&E, ×100).

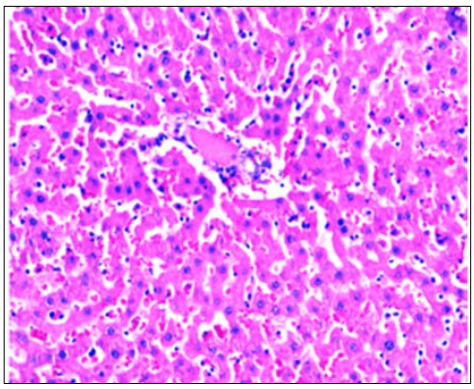

Fig 8: Liver section of Group IV showing mild sinusoidal congestion with normal appearance of the periportal area (H&E, ×100).

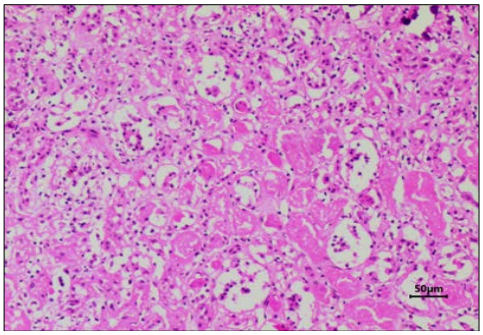

Fig 9: Kidney section of Group II showing degenerative and desquamative changes of renal tubular epithelium with hyaline cast formation within the renal tubules (H&E, ×100).

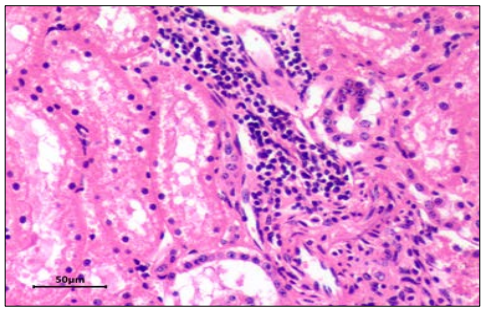

Fig 10: Kidney section of Group II showing severe infiltration of mononuclear cells with fibroblast proliferation in the intertubular space (H&E, ×200).

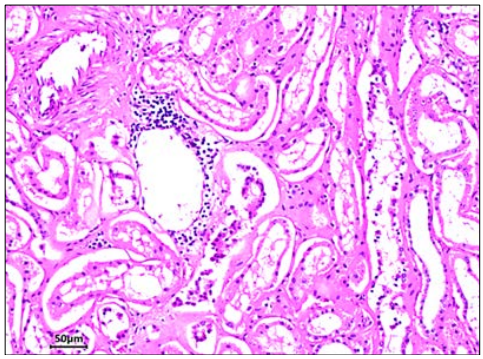

Fig 11: Kidney section of Group II showing atrophied glomeruli with periglomerular infiltration of mononuclear cells (H&E, ×100).

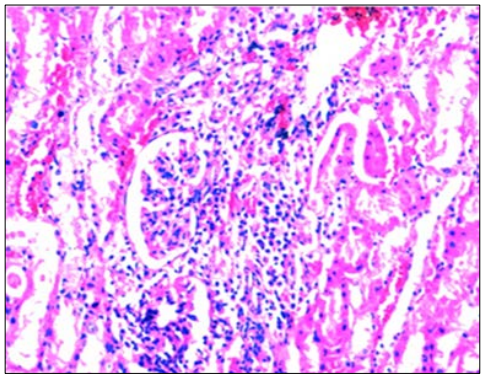

Fig 12: Kidney: Group II: Section showing moderate to severe infiltration of MNC's in periglomerular spaces and hyaline cast in renal tubule. H & E: x 100

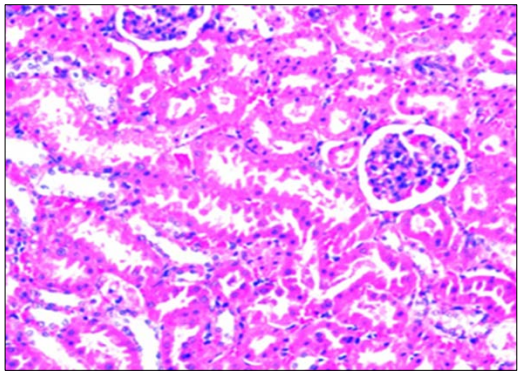

Fig 13: Kidney: Group IV: Section showing mild degenerative changes in renal tubules and mild hemorrhages in intertubular spaces. H & E: x100

Conclusion

The present investigation clearly demonstrates that sub-chronic exposure to fipronil induces marked hepato-renal toxicity in male Wistar albino rats, as evidenced by enhanced oxidative stress, and pronounced gross and histopathological lesions in the liver and kidney. Oral administration of Punica granatum peel extract (PPE) concomitantly with fipronil effectively mitigated these toxic effects by restoring hepatic and renal function markers, normalizing antioxidant defence systems, and markedly reducing lipid peroxidation. The substantial improvement in gross morphology and near-complete restoration of normal histoarchitecture of the liver and kidney further confirm the cytoprotective potential of PPE. Overall, the findings suggest that Punica granatum peel extract exerts significant hepato-renal cytoprotective and antioxidant effects against fipronil-induced toxicity, highlighting its potential as a natural therapeutic agent for managing pesticide-associated oxidative organ damage.

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