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A REVIEW ON THE TOXICITY OF FENPROPATHRIN (SYNTHETIC PYRETHROID) ON DIFFERENT ANIMAL MODELS

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ABSTRACT

Synthetic pyrethroids are most extensively used pesticides for pest management across the world compared to other classes of pesticides due to its great efficacy, ease of degradability and less toxicity to humans and other animals. Fenpropathrin is a type II synthetic pyrethroid with an alpha cyano moiety and is most commonly used in agriculture, horticulture, household and veterinary medicines to manage ecto-parasites such as ticks, fleas, moths, cockroaches and vegetable pest. It is a non-systemic insecticide mainly applied on fruits, vegetables and crops and behaves as a contact toxin and acts on the nervous system by initiating numerous action potentials which cause delay in closure of sodium ion channels leading to convulsions, paralysis and finally the death of insects. Acute and sub-chronic doses of fenpropathrin administration led to variations in physiology, histology and several biochemical and neurological parameters indicating toxic effects on fishes, insects and mammals. Toxic symptoms of fenpropathrin exposure include irritation of eyes and skin, numbness, oxidative stress, headache, fatigue, dizziness, vomiting, sensation of tingling, diarrhea and unusual facial sensation. This article provides information and an overview of the possible toxicity of fenpropathrin at different dose levels in the experiments conducted by scientists during the last ten years in different animal models, suggesting restricted and judicious usage of fenpropathrin

Keywords: Synthetic pyrethroid; Fenpropathrin; Insecticide; Animal model; Toxicity; Non systemic

INTRODUCTION

Pesticides are toxic substances that kill pests, create economic damage to the environment and are dangerous to domestic animals and humans. The widespread use of pesticides raises numerous concerns regarding their negative impacts on human and animal health. When pesticides are released into the environment, they travel through several pathways before entering the body of humans and domestic animals, altering their internal endocrinology **[1]**. There are different types of pesticides such as insecticides, fungicides, herbicides, larvicides, acaricides, miticides, rodenticides, molluscides, pheromones and plant growth regulators etc. which are widely used across the world.

Synthetic pyrethroids are one of the largely used insecticide and currently account for around 30% of all pesticides used worldwide **[2]**. These insecticides are chosen over organochlorine, organophosphorus, and carbamate insecticides because of their high efficacy at low concentrations, greater stability to photochemicals, ease of degradation by microbes, and minimal human and animal toxicity **[3]**. Pyrethroids are modified derivatives of pyrethrins, a naturally occurring chemical that is extracted from *Chrysanthemum cinerariaaefolium.* There are two classes of pyrethroids on the basis of their chemical structure, exposure symptoms, target location and toxicological effects, type I and type II. Type I is less toxic than type II in depolarizing the nerves of insects.

Fenpropathrin (α-cyano-3-phenoxybenzyl-2, 2, 3, 3-tetramethylcyclo propane carboxylase) is a type II synthetic pyrethroid that is used in agriculture, veterinary medicines and household purposes. It is light stable pyrethroid which was firstly synthesized in 1971 **[4]**. Fenpropathrin is sparingly soluble in water but exhibits high solubility in organic solvents such as DMSO, ethanol, saline and corn oil. Exposure of fenpropathrin to light and air results in oxidation and loss of activity. Possible exposure to fenpropathrin might occur through the diet i.e. food and water, through handling or while using the product. It is a highly toxic chemical, especially if exposed to skin and toxic if inhaled. Several harmful side effects of fenpropathrin. are irritation of eyes and skin, numbness, headache, fatigue, dizziness, vomiting, sensation of tingling, diarrhea and unusual facial sensation. Fenpropathrin residues could be found in many fruits and vegetables such as grapes, apples, peaches, citrus fruits, cucumbers, sweet peppers, cabbage, tomatoes and beans **[5]**. Fenpropathrin is marketed under numerous brands such as: Meothrin, Dannitol, Herald, Fenpropatrina, Ortho Danitol, Fenpropatrin, Rody and Fenpropanate.

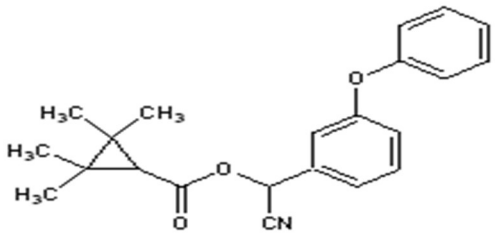

Figure 1: Structure of fenpropathrin

Mode of action:

Synthetic pyrethroids such as fenpropathrin primarily affect the nervous system of insects by disrupting neuronal function. Pyrethroids delay the closure of voltage-dependent sodium channels in neurons, which depolarizes the neuron and impairs the nervous system's ability to transmit nerve signals resulting in subsequent clinical repercussions. Type II pyrethroids (Fenpropathrin) is distinguished by initial pawing and burrowing, salivation and choreoathetosis. Sequence of its symptoms are Excitation (A normal action potential is converted into double or continuous discharge in nerve) followed by Convulsions (Muscles contract and relax fastly and create uncontrollable vibrations in the body) then Paralysis (Complete loss of muscle function) and finally Death of organism **[6]**.

Applications of Fenpropathrin: They are usually used in agricultural fields to control a broad range of insects and mites in fruits and vegetables for the control of mosquitoes, cockroaches and beetles in homes, control of flies and mites on dogs and cats, used in veterinary medications and also used for spraying on horticulture crops to control insects and mites **[7]**.

Risk to terrestrial organisms

For earthworms fenpropathrin presents the least risk, while birds, pollinators, mammals and insects are at high risk of exposure to fenpropathrin. Earthworms may get contact with fenpropathrin when it enters the soil following spray treatments of fenpropathrin. Exposure of fenpropathrin to foraging bees may be through spray droplets during application or through contact exposure by residues present on the surface of leaves. Bees can also be exposed through oral exposure by pollen and nectar polluted by direct spray and the principal route of exposure for birds and mammals is ingestion of food contaminated with fenpropathrin spray droplets **[8]**.

Environmental fate of fenpropathrin:

Fenpropathrin enters the environment through two routes: the soil and surface water. It is

easily broken down in shallow water under the influence of sunlight or the activities of soil bacteria. The rate of deterioration is determined by the quality of the soil. Fenpropathrin is intended to remain in the soil rather than leech into groundwater. It can also persist in sediments. Fenpropathrin does not accumulate in organism tissues and does not spread far from its original location **[9]**.

TOXICITY IN DIFFERENT ANIMAL MODELS

I. Insects:

A study was conducted by Rugno *et al* (2021) on the effects of fenpropathrin on *C. cubana* using various exposure methods revealed that topical exposure was the most harmful, followed by residual and ingested exposure **[10]**. Rasuli *et al.* (2017) estimated the medial lethal doses of fenpropathrin in honey bees. Fenpropathrin LC_{50} values for 72, 48, and 24 hours were 2.9, 3.8, and 5.7 ppm, respectively. The results showed that fenpropathrin produced the highest amount of toxicity when compared to the other insecticides. Fenpropathrin was also responsible for 90% of deaths **[11]**. Fenpropathrin's sublethal effects as well as the functional response in *Cryptolaemus montrouzieri* were evaluated by Palyari *et al.* (2016) and it was resulted that fenpropathrin at LC_{20} showed the greatest theoretical predation as compared to other pesticides treatments while at LC_{30} it had a reduced functional response curve in *Cryptolaemus montrouzieri* **[12]**.

The sublethal effects of various concentrations of fenpropathrin, including LC_{10} (1.63 g a.i./ml), LC 20(2.63 g a.i./ml), and LC_{30}(3.70 g a.i./ml), on the amount of prey consumed by *Scolothrips longicornis* females and their offspring were estimated by Pakyari *et al.* (2015). According to the findings, fenpropathrin had a significant impact on the amount of prey that were consumed by female thrips and the prey consumption by thrips larvae was negatively influenced by fenpropathrin treatment in the progeny of treated females **[13]**. The LC_{50} values of fenpropathrin on honeybees at 24 h (0.54 ppm) and 48 h (0.29 ppm) was recorded by Rasuli *et al.* (2013) and it was observed that honeybees had a high degree of oral toxicity to fenpropathrin, therefore it should not be used on blooming crops **[14]**.

The toxicity of different commercial insecticides, including fenpropathrin, on *C. carnea* was investigated by Nasreen *et al.* (2007). Administration of 750 ppm fenpropathrin by the egg immersion technique on *C. carnea* eggs resulted in hazardous effects on exposed and later life stages of *C. carnea*. When the first, second, and third stages of an instar were treated with

fenpropathrin, the death rates were 95%, 92%, and 70%, respectively. The death rates for pupae stages were reported to be the highest when treated with fenpropathrin **[15]**. Effect of fenpropathrin on the functional action of predatory thrips was studied by Li *et al.* (2006) and it was found that utilising half the required amount of fenpropathrin, i.e. 500 mg per litre, rather than the recommended dose of 1,000 mg per litre caused a change in the functional activity of the thrips. Fenpropathrin had the highest degree of toxicity, which reduced predatory thrimp predation and resulted in substantially differing death rates **[16]**.

II. Fishes:

The effects of two pesticides, fenpropathrin and paclobutrazol on zebrafish were studied simultaneously by Wang *et al*. (2020). The results show that the pesticides' acute toxicity ranges from 0.0029 to 0.16 mg a.i. L^1 for fenpropathrin and 13.16 to 23.43 mg a.i. L^1 for paclobutrazol. The toxic effects of fenpropathrin were found to be more severe in juvenile zebra fishes, whereas the toxic effects of paclobutrazol were found to be more severe in larval zebra fishes. When compared to the untreated group, the majority of single and combination therapies significantly affected activities such as CYP450, T-SOD, and Cu/Zn-SODCAT activity, but it was greatly enhanced at the low dose of the combination therapy. Pesticides, both alone and in combination, harmed zebrafish embryos, according to data on mRNA and the quantity of 17 genes linked with cellular death, the endocrine system, oxidative stress, and the immune system **[17]**. To measure the pesticide residues in fish found in Chilika Lake in India, a study was conducted by Nag *et al.* (2020) during the summer and autumn seasons. The results showed that fenpropathrin with a concentration of 0.17 ug/g, has been found throughout *P. indicus* body particularly in liver and gills. Fish poisoning was induced by fenpropathrin, which has also been reported to be hazardous to human health **[18]**.

Rahman *et al*. (2020) determined the effects of using fenpropathrin as a toxin in fish when fishes were administered with 0.065 mg/liter of fenpropathrin for 2 to 10 days. Results showed that, owing to the high toxicity of fenpropathrin, the number of zooplankton steadily decreased after exposure. Important characteristics such as short duration of toxicity, low price, ease of application and no risk of further hampering the pond's production capability demonstrated that fenpropathrin can be used as a killer for food fish in the northwest side of Bangladesh; however, fenpropathrin also causes harmful effects on public health due to eating fish that were killed by fenpropathrin. As a result, the

demand for fenpropathrin as a toxicant for food fish should be restricted **[19]**. A study was conducted by Khater *et al.* (2018) to measure the mean concentration of fenpropathrin in *C. gariepinus* and *P. clarkia* during the autumn of 2017 and 2018 in Tal-Haween and El-Shabakat water samples, respectively from Muweis canal in Europe. The results showed that elevated levels of fenpropathrin were found in *C. gariepinus* and *P. clarkia* and the mean concentration of fenpropathrin in water was found to be 0.009 mg/l, whereas the concentration in fishes were less than 0.1 mg/kg. Fenpropathrin concentrations were more than the suggested international acceptable levels in both water samples and fish, indicating that fenpropathrin may provide a cancer risk to regional populations that consume toxic fishes **[20]**.

The acute toxicity of Fenpropathrin at LC_{50} for 24 hours in shrimp juveniles (*Metapenaeus monoceros*) was observed by Shoaib *et al.* (2015). The experimental results indicated that fenpropathrin LC_{50} for 24 h was 0.26 ppb, indicating that shrimp juveniles were susceptible to fenpropathrin **[21]**. *A.mossulensis* was administered sub-lethal dose of fenpropathrin at 24, 48, 72, and 96 h LC_{50} for 15 days in *A.mossulensis* were administered by Banaee *et al.* (2014). Various biochemical parameters were evaluated and it was discovered that 1.25, 5.50, and 12.6 g/L fenpropathrin administration raised the activities of AST, ALP, and LDH. MDA and lipid peroxidation values were similarly elevated. Total protein level, antioxidant level, CPK, AChE activity, and AST level were lowered in the fish as compared to the control group. Mortality was not found when subjected to sub lethal concentration of fenpropathrin and control group. Following changes were seen in fish after exposure to high concentrations (5.50 and 12.60 g/L) of fenpropathrin: swimming in a vertical manner, rise in aberrant behaviour, loss of hunger, swimming on the surface of the water and increased mucus production. It can be inferred that when a sublethal dosage was administered to *A. mossulensis,* substantial changes in its behaviour and metabolic parameters were detected, suggesting these alteration can be probable factors for the survival rate of *A. mossulensis* **[22]**.

Administration of LC_{50} 0.0014 ppm fenpropathrin in *A.dispar* by Shoaib *et al* .(2013) resulted in significant responsiveness of fish juveniles, high mortality ratesand low total protein content in *A.dispar* muscle tissue, indicating protein synthesis impairment and essential physiological conditions of fish juveniles. Their low LC_{50} value indicates that

fenpropathrin has a toxic impact on fish even when exposed for a short period of time (24 h) and if exposed for a longer period of time, there is a strong possibility that fenpropathrin will cause negative effects in people through consumption of hazardous fish **[23]**. The acute toxicity and deleterious effects of diazinon, iprodione, fenproparthrin, and myclobutanil on Chinese bleak was investigated by Yeom *et al.* (2006). Results showed that fenpropathrin LC_{50} values (0.003 mg L^{-1}) at 96-h was the most toxic pesticide among the other pesticides and fenpropathrin poisoning is extremely harmful for fish **[24]**.

III. Mammals:

The effects of long-term fenpropathrin exposure on intestinal absorption and drug gliquidone barrier in male rats were investigated by Xu *et al*. (2022). Male rats were divided into two groups: the control group, which received corn oil and the fenpropathrin-treated group. In male rats, 3 mg per kg of fenpropathrin was dissolved in corn oil and a volume of 1 ml per kg body weight was delivered in the stomach by gavage technique every day for two weeks. A chamber study was also conducted and the results suggested that fenpropathrin might increase gliquidone transport in the intestine. Intestinal absorption of fluorescein was seen significantly elevated in rats treated with fenpropathrin through gavage method. Additionally, fenpropathrin treatment induced structural damage to the intestine, a decrease in the expression of proteins of tight junctions in intestinal tissue, a decrease in SOD, an increase in intestinal MDA and an increase in the production of inflammatory markers. Fenpropathrin treatment in Caco cells led to a decrease in tight junction protein expression, an increase in gliquidone transport and an increase in reactive oxygen species. Fenpropathrin also reduced the expression of UCP -2 and PPAR - in Caco -2 cells and intestinal tissue, while increasing the expression of p-P38.The above findings suggested that fenpropathrin treated groups can produced oxidative stress and can impair the intestinal barrier by affecting the expression of the P38/P38/PPAR-/UCP-2 protein, consequently increasing gliquidone intestinal absorption **[25]**.

Wu *et al*. (2021) examined the impact of autophagy and oxidative stress on astrocytes in fenpropathrin-induced Parkinson-like damage in mice. Fenpropathrin (0.0854 mg/kg body weight) was administered for 6 months using stereotactic injections. Results suggested that fenpropathrin increased ROS in astrocytes leading to oxidative stress, which lowered CDK5 expression and inhibited autophagy **[26]**.

Manglani *et al*. (2020) conducted a study to determine the median fenpropathrin lethal dose in Wistar rats. Oral doses of fenpropathrin were administered at concentrations of 15, 30, 45, 60, and 75 mg per kg of body weight after being dissolved in corn oil. Animals were monitored for 96 hours in order to calculate the median lethal dose and to estimate toxicity. The results were evaluated and it was shown that the median lethal dose of fenpropathrin in male Wistar rats was 52mg per kg body weight, and 48 mg per kg body weight in female Wistar rats. Fenpropathrin oral dose of 10 mg per kg body weight did not cause any toxicity or behavioural changes, therefore it may be considered as the NOAEL (No Observed Adverse Effect Level) **[27]**. Jiao *et al*. (2020) investigated the toxic effects of fenpropathrin as well as its underlying mechanism for disrupting the dopaminergic system *in vivo* and *in vitro* in mice. Animals were divided into two groups: the control group, which received DMSO and the fenpropathrin-treated group. Fenpropathrin (6.1 µg/g of brain weight) was dissolved in DMSO and a volume of 1.092 mg/ml of Fenpropathrin and DMSO were injected for 24 weeks into the right side of stratum of mice through the stereotaxic injection. The result revealed that fenpropathrin causes dopaminergic neuron cellular death *in vivo*. Furthermore, fenpropathrin increases the production of reactive oxygen species, decrease in locomotory functions and a decrease in the amount of tyrosine hydroxylase protein compared to the control group, leading to the conclusion that fenpropathrin treatment initiates dissipation of dopaminergic neurons and partially mimics the pathologic features of Parkinson's **[28]**.

The impacts of fenpropathrin on kidney function and the levels of proinflammatory cytokines such as interleukin 1 beta and tumour necrosis factor in a mouse model were studied by Jaremek *et al*. (2020). Fenpropathrin at a dose of 11.9 mg/kg was given to mice every day for 28th day and on the 29th day. Blood samples were taken to estimate the amount of serum creatinine and the animal was killed to obtain the kindey for estimation of tumour necrosis factor and interleukin 1 beta using the ELISA assay. It was resulted that fenpropathrin has a minimal impact on kidney function and increases interleukin 1 beta levels in mouse kidney, which supports the idea of the drug's effects on immunotoxicity and nephrotoxicity in non-target animals **[29]**. Administration of fenpropathrin (7.09 mg per kg body weight) for 15 days in male rats were recorded by Zeid *et al*. (2020). The result showed that

fenpropathrin treatment significantly reduced serum glutathione levels while significantly increasing blood levels of catalase, superoxide dismutase, 8 hydroxy 2 deoxyguanosine and malondialdehyde. Furthermore, fenpropathrin treatment significantly raised hepatic CYP1A1 mRNA expression as well as spatial computable general equilibrium (SCGE) indices in treated rats' whole blood, spleen, and liver tissues **[30]**. The neurotoxicity of fenpropathrin administered for 60 days at an oral dose of (15 mg/kg) was studied in rats by Elhakim *et al*. (2020). Results indicated diminished memory, deficits in sensory motor functions and decreased exploration. Dopamine, acetylcholinesterase, antioxidant, Bcl-2 and interleukin 10 levels were reduced, whereas nitric oxide, Caspase-3, tumour necrosis factor, myeloperoxidase, and malondialdehyde levels were increased. Rats also showed signs of encephalopathy **[31]**.

Oral intoxication of fenpropathrin (7.06 mg/kg body weight) for 60 days in male rats were studied by Zeid *et al*. (2019). Results showed that the fenpropathrin significantly reduced RBC counts, MCHC, HCT, Hb content, phagocytic index, phagocytosis percentage, IgM levels and serum lysozyme activity. In addition, fenpropathrin causes a considerable increase in platelet count, leukogram, IL6 serum levels, and tumour necrosis factor alpha. Spleen tissues from the fenpropathrin-treated group revealed significant shrinkage and lymphoid depletion, as well as apoptosis. Furthermore, significant shrinkage of the thymus cortex, portrayal of the medulla and cortex and depletion of multifocal lymphocytes was seen **[32]**. Mohamed *et al*. (2019) estimated the toxicity of fenpropathrin on the reproductive system of rats. Oral administration of 15 mg/kg fenpropathrin to rats for 60 days resulted in decreased levels of LH (leutenizing hormone), FSH (follicle stimulating hormone) and TES (serum testosterone) and increased levels of TBARS (thiobarbituric acid reactive substances), indicating oxidative stress. Furthermore, it was demonstrated that fenpropathrin significantly degenerate the structure of testicular tissue, character of sperm, status of antioxidants andhormonal level of sex due to mitochondrial initiation path of apoptosis in rats spermatogonial cells and fenpropathrin's DNA impair effect **[33]**.

The effect of fenpropathrin on the dose response relationship for *in vivo* motor function, memory and antioxidant activities in mice brain was studied by Iwanicka *et al*. (2016). Intraperitoneal injections of fenpropathrin at doses of 0.5 LD_{50} (11.9), 0.25 LD_{50} (5.95) and 0.1 LD_{50} (2.38) mg/kg daily for 28 days were given to mice. The results

showed that the mice receiving the highest dosage had significantly lower locomotor activity. Even though fenpropathrin did not affect memory, mice's mobility decreased after 7 and 14 days when lower doses were used. The direct inhibition of enzymes by fenpropathrin may be responsible for the decrease in SOD activity in mouse brains, while the increased values of SOD may be due to the higher free radical production when oxidative stress is initiated by fenpropathrin. Reduced glutathione accessibility may have contributed to the loss of GPx function, and fenpropathrin-induced dopaminergic system damage manifested behaviorally as a decrease in movement activity **[34]**. A study was conducted by Zhang *et al*. (2010) to evaluate fenpropathrin poisoning through intragastric technique and postmortem dispersion of fenpropathrin in rabbits. Six rabbits were poisoned with fenpropathrin and promptly dissected. Various samples were taken, including peripheral blood, cardiac blood, kidney, liver, and bile and microscopic investigations were performed on them. The results suggested that symptoms of fenpropathrin poisoning appeared two to three hours after the drug was administered. Deaths were reported 48 hours after intoxication. Fenpropathrin was found in all samples except urine and the research and postmortem distribution information from fenpropathrin poisoning can be used for forensic identification **[35]**.

Abdou *et al*. (2010) studied the effects of fenpropathrin on hepatic cytochrome P450 and the Michaelis-Menten kinetics of metabolic processes mediated by liver cytochromes in rats. For CYP1A, 2C, 2D, and 3A activities, metabolic processes such as ethoxyresorufin O-deethylation, tolbutamide hydroxylation, bufuralol 1'-hydroxylation, and midazolam 4-hydroxylation were investigated. Rats were administered 2 mg per kg and 6.6 mg per kg of fenpropathrin orally for up to 5 days. Fenpropathrin did not inhibit CYP2C or 3A, but it was the most effective inhibitor of CYP1A and cytochrome P450, with a Ki value of 3.71 for CYP1A, which might result in considerable aggregation of multiple compounds. In a rare situation, the resulting aggregation may cause deadly toxicities **[36]**. A study was conducted by Iwanicka *et al*. (2020) to determine whether bilateral clasping of carotid arteries (BCCA), a representation of ischemia, in combination with fenpropathrin influenced memory in various tests such as passive escape task and recent spatial memory in the Y maze, locomotion activity and locomotion control on rotarod in mice. Fenpropathrin (23.8 mg/kg) was administered intraperitoneally to mice.

When compared to the control group, fenpropathrin significantly reduced latency in the passive escape task. There was no significant difference between groups in terms of locomotor activity, Y maze, or movement coordination. As a result, it was determined that fenpropathrin should be used with caution in the presence of an elderly population due to the risks of ischemia, which was capable of causing significant memory loss in mice **[37]**. Samia *et al*. (2008) determine the effects of repeated exposure of fenpropathrin administration on different serum biochemical tests, blood images, protein levels, sperm characteristics, and their residual levels in various tissues and organs. Male rats were orally given fenpropathrin of 0.076 and 0.76 mg/kg body weight (i.e. 1/1000 and 1/100 LD_{50}) everyday for 10 consecutive weeks collectively with control and the results shows that both the amounts of LD_{50} shows less concentration of haemoglobin, erythrocyte numbers and packed cell volume with the remarkably higher number of leukocytes and significant rise in the activities of ALT, AST, creatinine and urea amount. The treated ones showed hypoalbuminaemia, hypoproteinaemia and a low albumin-to-globulin ratio. Semen testing of treated rats reveals a considerably decreased motility % with fewer sperm density and fenpropathrin residues were located in numerous organs such as the heart, lungs, liver, spleen, testis, kidneys and brain **[38]**. Mansour *et al*. (2008) examined the toxicity of various pesticides (abamectin, carbosulfan, fenpropathrin, methomyl and profenofos) and their combinations on rats. Individual and combination LD_{50} dosages of abamectin, carbosulfan, fenpropathrin, methomyl and profenofos (33.3, 50.0, 11.8, 1.9, and 17.9 mg kg body weight.) respectively were given to rats for 28 days. The results showed that there was a significant drop in body weight, kidney weight, and an increase in liver weight during the therapy. Treatment led to increased ALT and AST while lowering AChE. While fenpropathrin and all pesticide combinations increased blood total protein levels, rats treated with all pesticide combinations also had a rise in creatinine levels, constriction of Bowman's capsule and injury to the renal epithelial lining **[39]**.

Effect of structure activity relationship of various pyrethroid insecticides (Allethrin; Bifenthrin; Cismethrin; Cyfluthrin; Cyhalothrin; Cypermethrin; Deltamethrin; Fenpropathrin; Fenvalerate; Permethrin and Tefluthrin) on the rats sodium channels were recorded by Choi *et al*. (2006). Fenpropathrin along with all other compounds was used at a concentration of 100μM to estimate the

relative potencies of pyrethroids. It was found that Nav1.8 (sodium voltage) channels were most sensitive to fenpropathrin while being in the resting state and fenpropathrin was also most effective against the Nav1.8 sodium channel in terms of both resting and use-dependent alterations Adittionally tail currents decreased with first-order kinetics in the presence of allethrin, cismethrin, permethrin, fenvalerate, fenpropathrin, tefluthrin, and bifenthrin **[40]**. Administration of fenpropathrin (10% EC) to male albino rats for 90 days at doses of 5.916, 2.958, and1.479 mg/kg body weight were evaluated by Bhelonde *et al*. (2006) The results revealed that after seven week, fenpropathrin doses of 5.916 and 2.598 mg/kg body weight had a significant impact on the rats' increased body weight, indicating that the chemical may have effects on feed consumption and weight gain at substantially higher concentrations **[41]**.

Table 1: An overview of some recent findings on the toxicity of fenpropathrin in various animal models

Animal Model	Fenpropathrin Experimental dose	Duration	Observations	Ref.
Fish	0.0029, 0.16 mg / l	96 h	Influence on mRNA, cellular apoptosis, endocrine system, oxidative stress and immune system.	[17]
Fish	0.17 ug/g	Summer and autumn of 2012 - 2016	Detection of Fenpropathrin residues in *P. indicus* (fish) entire body and specially in the organs such as liver and the gill.	[18]
Fish	0.065 mg/l	2 – 10 days	Use of fenpropathrin as a killer for fish was done.	[19]
Fish	0.1mg/kg	Autum 2017 – summer 2018.	Fenpropathrin amount in fishes were higher than the recommended international admissible limits so can be a potential cancer risk.	[20]
Rat	3 mg/kg	2 weeks	Structural damage of intestine, Decrease in the expression of proteins of tight junctions in intestinal tissue. Production of inflammatory marker, SOD and MDA levels were increased. Increase gliquidone transport in the intestine and elevation in the intestinal absorption of fluorescein.	[25]
Mice	0.0854 mg/kg	6 months	Influence on oxidative stress, Inhibition of autophagy and induced Parkinson like damage.	[26]
Rat	10 ,15, 30, 45, 60 and 75mg/kg	96 h	Medial lethal dose estimated in male rat was 52 mg/kg body weight and in female rat was 48 mg/kg body weight.	[27]
Mice	6.1 µg/g	24 weeks	Increase in the production of reactive oxygen species, decrease in locomotory functions, decrease in the amount of tyrosine hydroxylase protein, dissipation of dopaminergic neurons and partially mimics the pathologic features of Parkinson's.	[28]
Mice	11.9 mg/kg	28 days	Influence on kidney function and increase in interleukin 1 beta levels.	[29]
Rat	7.09 mg per kg	15 days	Influence on hepatic CYP1A1 mRNA expression and SCGE indices in treated rats' whole blood, spleen, and liver tissues. Reduction in serum glutathione levels and increase in blood levels of catalase, superoxide dismutase, 8 hydroxy 2 deoxyguanosine, and malondialdehyde.	[30]
Rat	15 mg/kg	60 days	Influence on memory, sensory motor functions and decreased exploration. Dopamine, acetylcholinesterase, antioxidant, Bcl-2, and interleukin 10 levels were reduced. Nitric oxide, Caspase-3, tumour necrosis factor, myeloperoxidase and malondialdehyde levels were increased.	[31]
Rat	7.06 mg/kg	60 days	Reduction in RBC counts, MCHC, HCT, Hb content, phagocytic index, phagocytosis percentage, IgM levels and serum lysozyme activity. Shrinkage of spleen tissue and depletion of multifocal lymphocytes.	[32]
Mice	15 mg/kg	60 days	Degeneration of the structure of testicular tissue, Decreased levels of LH, FSH and TES and increased levels of TBARS.	[33]

CONCLUSION

The present review provides evidence of the toxicity of fenpropathrin in different animal models. Variable fenpropathrin concentrations resulted in developmental toxicity that also led to death in several animal models. Fenpropathrin's effects are dose and time dependent. It alters a number of biochemical, haematological and neurological parameters whether taken alone or in combination. The review also sheds light on fenpropathrin's mechanism of action. The harmful impact of this pyrethroid has been extensively documented in several animal models, indicating that its usage should be limited so that non-target individuals are not affected. Farmers and workers should also be made aware of the possible risks of fenpropathrin on human health so that they can use it judiciously and wear protective equipment while working with pesticides.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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