RESEARCH ARTICLE AGROBIOLOGICAL RECORDS
ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)

ALLETHRIN INDUCED TOXICOPATHOLOGICAL ALTERATIONS IN ADULT MALE ALBINO RATS

Quratulain Mujahid [1,2], Ahrar Khan [1,3,*], M. Kashif Saleemi [1], M. Farhan Qadir [1,4], Absar Ahmad [2], Waseem Ejaz [5], Tahir Zahoor Chohan[6], Shahla Mujahid [7], and Jahangir Mujahid [8]

[1]Department of Pathology, University of Agriculture, Faisalabad, Pakistan; [2]Para Veterinary Institute Karor Lal Eason, University of Veterinary and Animal Science, Lahore, Layyah Campus, Pakistan; [3]Shandong Vocational Animal Science and Veterinary College, Weifang, China; [4]College of Veterinary Medicine, Shanxi Agricultural University, Jinzhong, China; [5]University of Veterinary and Animal Sciences, Lahore, Pakistan;
[6]ALP PARC, Islamabad, Pakistan; [7]Health Department Punjab; [8]Fatima Memorial Hospital, Lahore, Pakistan

*Corresponding author: ahrar1122@yahoo.com

ABSTRACT

This study was designed to investigate the allethrin induced toxico-pathological changes in adult male albino rats. A total of 60 adult male albino rats were divided randomly into 4 equal groups. Group A served as control. Groups B, C and D were administered orally Allethrin @ 0.5, 1.0 and 1.5g/kg body for 14 experiment days, respectively. Dullness, erected hairs, alopecia, less response towards feed and water, watery droppings, tremors, convulsions and coma were more prominent signs in treated groups. Feed intake and body weight decreased in all treated groups. Mortality was recorded in group C and D. The total erythrocyte and leukocyte counts, hemoglobin concentration and packed cell volume decreased significantly ($P \leq 0.05$) in all allethrin treated groups as compared to the control group. Histopathologically, kidneys exhibited condensed nuclei, necrotic tubules and congested renal parenchyma. In liver, vacuolar degeneration in nucleus and cytoplasm was observed. Micro nucleated lymphocytes were also evident in group D treated with the highest dose of allethrin. In conclusion, allethrin induced dose and time dependent toxico-pathological effects in adult male albino rats.

***Keywords*:** Allethrin, Albino rats, Toxico-pathology and Genotoxicity.

Article History (2020-0722) || Received: 07 Jul 2020 || Revised: 28 Sep 2020 || Accepted: 22 Oct 2020 || Published Online: 16 Jan 2021

1. INTRODUCTION

Mosquito borne diseases like Dengue and Malaria are major public health threat faced by developing countries (Naz et al. 2019). The later disease is endemic in most of the countries and one million deaths occur annually due to malaria worldwide (Idowu et al. 2013; Gul et al. 2019). About 30,000 people only in Punjab in 2011 has been affected by dengue (Khan et al. 2012).

The use of insecticides is the most widely used control method to kill mosquito. Among various insecticides, pyrethroids contribute about 25% of all and are utilized in the market for over and above 40 years (Shafer et al. 2005; Caloni et al. 2016). Pyrethroids are being used extensively because they have more efficacy against many insects and are also less toxic, hydrophobic and biologically degradable (Dorman and Beasley 1991). They act selectively blocking sodium channels and cause their metabolic degradation (Narahashi 1996).

Synthetic compounds like pyrethroid results in increased stress and its high amount in the household dust contaminate the environment (Colt et al. 2004). Humans are exposed to these insecticides with mixers, loaders, greenhouses, atmosphere, workers, and applicators (Hernandez-Valero et al. 2001). Exposure can also be occurred through ingestion, inhalation, dermally and orally. Particularly, in developing countries their extensive use has caused severe ecological contamination and health dangers and results in increased counting of acute and chronic cases of animal and human poisoning along with harm to other non-targeted entities (Chedik et al. 2017; Guéniche et al. 2020). It is well known for neurotoxicity but it can have hepatotoxic, immunosuppressive, carcinogenic, anti-progestagenic and estrogenic effects as well (Gupta et al. 2013).

Different biochemical and physical disorders include the fall in reproductive efficiency, oxidative damage, poor erythropoiesis, and genotoxic effects (Hussien et al. 2013). In recent years, more considerations are given to

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)

pyrethroid toxicity in animals because animals being exposed to these insecticides exhibited behavioral changes as well as other obvious pathological changes (Khan et al. 2009).

Like allethrin and resmethrin (Mortein Coil-Neurotoxins) which are the pyrethroid insecticides, their toxicity is a matter of great importance because their use is growing day by day in household pest management. The relationship between abnormal exposure and several biological responses were determined by toxico-pathological studies (Antunes-Kenyon and Kennedy 2007) as the sub-lethal and chronic exposure because histopathological changes and these changes indicate occurrence of pollutants in different organs and tissues (Bernet et al. 1999). Thus, current study was designed to investigate the responses of allethrin in albino rats for the assessment of safety by using micronucleus assay technique.

2. MATERIALS AND METHODS

2.1. Rats housing and feed

A total of 60 adult albino rats were procured from National Institute of Health Sciences and were kept in cages under standard management conditions. Ad-libitum water and basal feed with 16% protein was offered to the different groups. After three days of acclimatization period rats were divided into four groups A to D having 15 rats in each group.

2.2. Experimental design

Sixty of adult male albino rats were divided into four groups' i.e. A, B, C and D having 15 rats in each group. Three levels of allethrin (0.5, 1.0 and 1.5g/kg) were administered only once at day 14 of the experiment. Group A served as control while group B received allethrin @ (0.5g/kg BW), group C @ (1.0g/kg BW) and group D (1.5g/kg BW) respectively. The feed intake and body weight of different experimental groups was recorded on daily and weekly basis, respectively.

2.3. Parameters Studied

Rats were monitored twice a day on daily basis to observe the change in behavioral responses and categorized based on severity into very mild (+), mild (++), moderate (+++) and severe (++++). Rats mortality was recorded during the whole length of the experimental trial. Numbers of rats died during whole period of 42 days were calculated. Feed intake per rats was calculated on daily basis in the treatment groups. Body weight of each rat was measured on weekly basis.

2.4. Hematological parameters

Six rats from each group were randomly selected and killed humanely on day 21 of the experiment and blood was collected with Na_2EDTA; for the estimation of TEC and TLC following the method of Khan (2008). Hematocrit was dogged by micro hematocrit for determination of PCV and hemocytometer method was used for the Hb concentrations respectively, in different groups (Benjamin 1978).

2.5. Micronucleus Assay

Blood was obtained by venipuncture technique and collected in heparin vacutainers. Lymphocytes were cultured by adding 0.5ml of whole blood to 4.5 ml of RPMI 1640 medium containing 15% heat-inactivated FBS, L-glutamine and 1% PenStrep (penicillin and streptomycin). Lymphocyte culture was stirred by incubating the samples at 37°C for 72 hours after addition of 1% of phytohemagglutinin. Forty-four hours later 6µg/ml (final concentration) of cytochalasin B (Surralles et al. 1994) was added to the cultures to arrest cytokinesis. The cultures were harvested after 72 hours of incubation by centrifugation at 200g for 8 minutes. The samples were then treated with a hypotonic solution of 0.075 M KCl at 4°C for 2 to 3 minutes. A methanol acetic acid solution (3:1, v/v) was gently added after centrifugation. The cells were resuspended in a small volume of fixative and dropped onto clean slides. The slides were prepared in triplicates. The slides were finally stained with 10% Giemsa stain (in PBS) for 10 minutes. The numbers of binucleated cells with micronuclei (BNMN) were counted under the microscope (500 per replicas).

2.6. Gross and Histopathological Studies

Formalin fixed samples of liver and kidneys collected from each group were processed for histopathological examination by using routine method of dehydration in ascending grades of ethanol, clearing in xylene and stained with hematoxylin and Eosin (Hassein et al. 2012).

2.7. Statistical Analysis

Data collected from the experiment was subjected to the statistical analysis by applying 2-Factor factorial. The means of the different groups were compared by using Duncan multiple range (DMR) test. The level of significance was $P \leq 0.05$.

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)

3. RESULTS

3.1. Physical Parameters

Clinical signs (Table 1) including dullness, depression, erected hairs, alopecia, tremors, convulsions, coma and watery droppings were present in all treated groups. However, the signs were mild in the group treated with 0.5g/kg allethrin, all signs were moderate while coma was more prominent with dose 1.0g/kg allethrin than all the other groups. Same signs were seen in group treaded with highest dose of allethrin with varying degree shown in Table 1. Acute mortality was observed in treated groups. There was no mortality in control group. Mortality of rats administered different doses of allethrin was 25, 50 and 50% in groups B, C and D, respectively.

Table 1: Clinical signs displayed by Allethrin treated rats

Signs	Groups		
	B	C	D
Dullness	++	+++	++++
Erected hairs	+++	++++	++++
Alopecia	+	++	++++
Tremors	++	++++	+++
Convulsions	+	+	++++
Coma	+++	++++	++
Watery droppings	+	++	+++
Decreased feed intake	+	++	+++
Decreased body weight	+	++	+++

Groups B, C and D received Allethrin @ 0.5, 1.0 and 1.5g/kg once for day 14th of experiment. Group A was kept as control and no signs were observed.

3.2. Feed Intake and Body Weight

All the treatment groups were offered ad-libitum feed throughout experiment. Feed intake was decreased with increasing dose of allethrin. Maximum decrease was observed in D group. Feed intake of group B and C was lower throughout experiment (Fig. 1). There was increase in body weight of all groups significantly up to two weeks of experiment. At day 14 of experiment, significant decrease in body weight of group B, C and D was observed. Body weight of group D was less than all other groups throughout experiment. Body weight in group B was not much decreased than control group**.** From third- and fourth-week post treatment all groups again started to gain weight (Table 2).

Table 2: Body weights (g) of mice fed with different doses of allethrin for 6 weeks

Groups	Experimental Days						
	1st	7th	14th	21st	28th	35th	42nd
A	168.6±10.0a	173.6±18.0a	200.9±9.9a	211.5±20.0a	217.5±19.9a	224.5±21.3a	227.5±23.3a
B	175.1±12.1a	181.1±23.1a	208.9±20.7ab	196.4±19.8a	185.5±19.3a	196.7±21.7a	215.0±22.1a
C	170.4±15.0a	179.5±27.0a	216.4±26.9b	190.6±24.8ab	178.50±2.1a	190.5± 3.5a	208.0±1.4a
D	179.4±15.6a	197.3±25.6a	236.9±28.2b	185.1±25.6b	173.0±12.7a	185.0±9.9a	200.0±5.6a

Values (Mean±SD) in each column following different letters are statistically significant (P≤0.05).

3.3. Hematological Parameters

The total erythrocyte count, packed cell volume and hemoglobin concentration fluctuated in allethrin treated groups (Table 3). At day 21 of experiment, total erythrocyte counts (TEC) was significantly decreased in group treated with highest dose of allethrin (Table 3). Whereas, an increase in the number of red blood cells was observed in allethrin treated group C. At 42-day total erythrocyte count was not significantly different in all treated groups as compared to control. However, total leukocyte count decreased significantly throughout experiment in comparison to control at days 21 and 42.

3.4. Genotoxicity (Formulation of Micronuclei)

Incidence of micronucleated lymphocytes was found in all treated groups than control group. Micronucleated lymphocytes were more evident in group D (0.81%) treated with higher dose of allethrin as compared with groups treated with low doses i.e., group C (0.60%) and group B (0.41%). In non-treated control (group A), there was also 0.30% micronucleated lymphocytes.

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)

3.5. Pathological Observations

Microscopically, liver of rats in group D exhibited slight vacuolation in nucleus at day 21 of experiment whereas the liver architecture and cells remained normal (Fig. 2). At day 42 of experiment mild cellular infiltration and fatty change was present in the hepatic parenchyma (Fig. 3). In present study, kidneys showed condensation of nucleus and cytoplasm was strongly stained that is indication of necrosis in rats of D group. Protein rich fluid was also present in the lumen of tubules with inflammatory changes at 21 day of experiment (Fig. 4). At day 42 an increase in the necrotic changes of the renal tubules, pyknotic nucleus in some cells and tubular degeneration were present in the renal parenchyma (Fig. 5).

Table 3: Erythrocyte indices and leukocytic counts in allethrin treated albino mice in contrast to control mice

Parameters/Days	Groups			
	A	B	C	D
Total erythrocyte count ($\times 10^{12}$/µL)				
21	5.91±0.24	5.36±0.35c	6.91±0.44a	1.96±0.28d
42	4.43±0.70b	5.51±0.09a	4.64±0.17b	4.58±0.60b
Hemoglobin Concentration (g/dl)				
21	15.42±0.50a	13.70±1.06b	16.97±1.05a	15.27±1.43c
42	12.32±1.73b	14.45±0.38a	12.25±0.29b	11.80±1.71b
Packed cell volume (%)				
21	35.60±6.08ab	30.45±3.81b	36.97±2.38a	10.47±2.07c
42	28.02±4.10b	34.92±0.42a	27.97±0.24b	27.97±0.24
Total leukocyte count ($\times 10^{9}$/L)				
21	12.57±3.12a	15.30±3.56a	4.45±0.72b	3.62±0.17b
42	7.87±2.74a	8.50±3.53a	7.22±0.33a	7.37±3.10a

Values (Mean±SD) with different alphabets in a row differ significantly (P≤0.05). Group B to D were administered with allethrin @ 0.5, 1.0 and 1.5g/kg, respectively. Group A was kept as control.

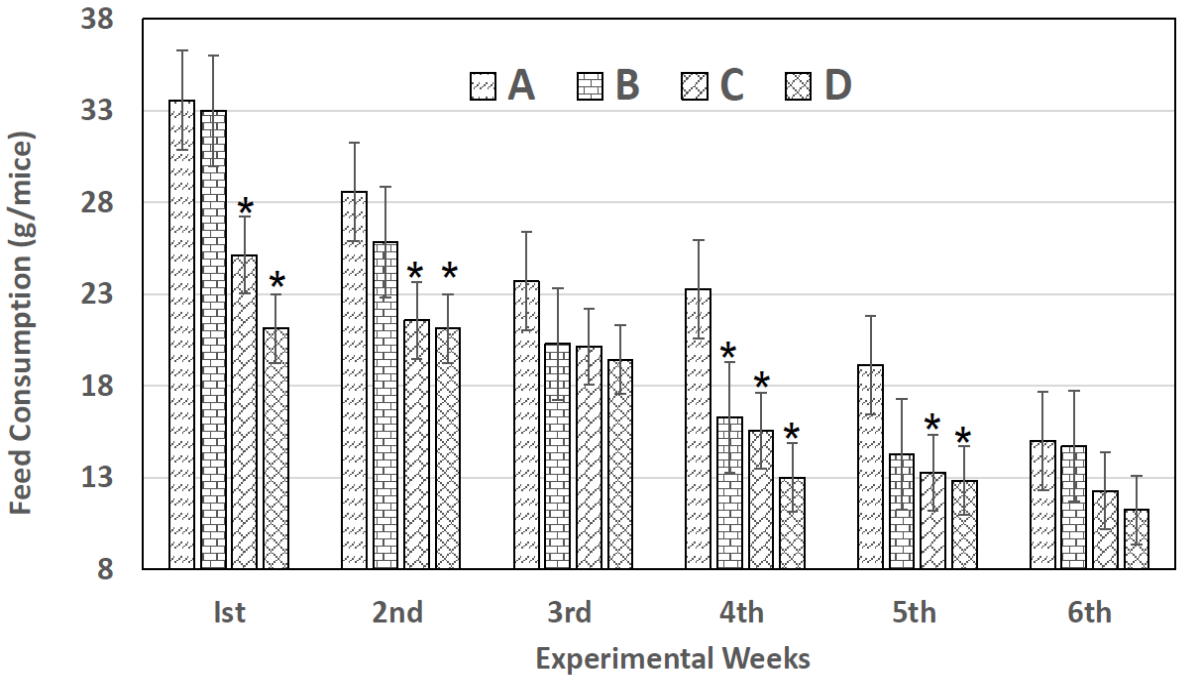

Fig. 1: Feed intake (g/mice/day) fed with different doses of allethrin for 6 weeks. In every column, bars (Mean±SD) following asterisk differ significantly (P≤0.05) than that of control group. Group A (Control) = No treatment; groups B, C and D were with Allethrin @ 0.1, 0.5 and 1.5mg/kg. respectively.

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)

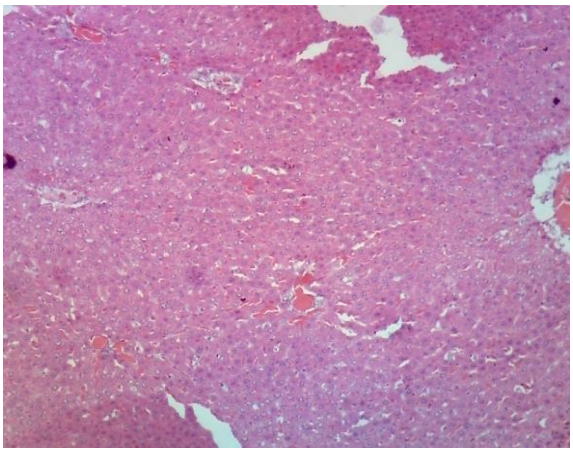

Fig. 2: Photomicrograph of liver of rats administered with allethrin 1.5g/kg BW at 21 day. showing slight change of vacuolation in nucleus, otherwise liver architecture and cells normal. H & E stain; 100X.

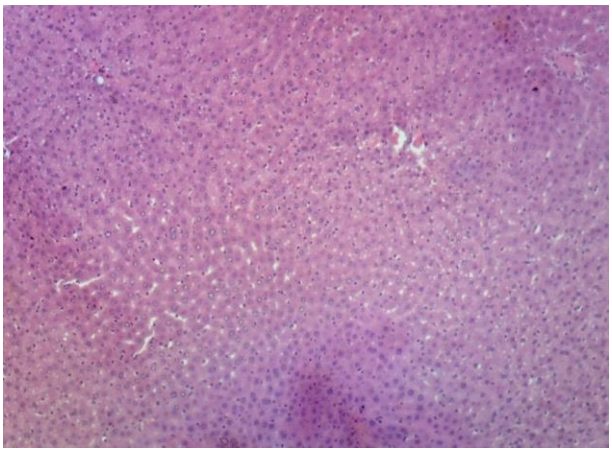

Fig. 3: Photomicrograph of liver of rats at 42 day (allethrin 1.5g/kg BW) showing vacuolar change in the cytoplasm and inflammatory reaction. H & E stain; 100X.

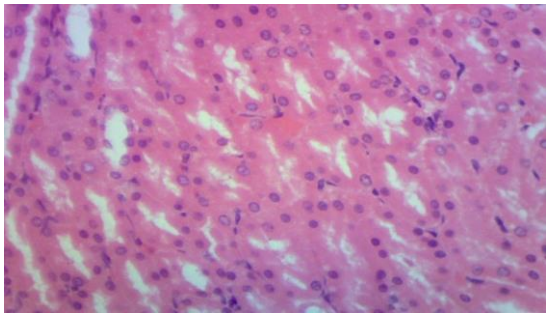

Fig. 4: Photomicrograph of kidney of rats at 21 day administered with allethrin 1.5g/kg BW showing condensation of the nucleus. H & E stain; 400X.

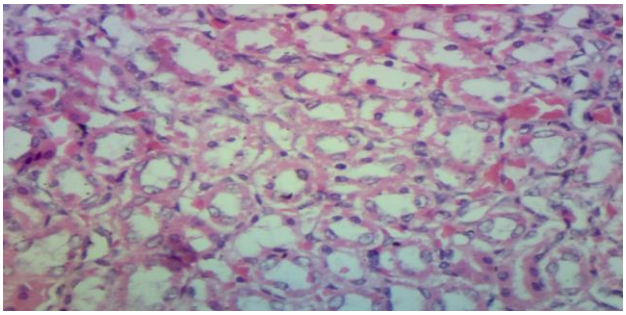

Fig. 5: Photomicrograph of kidney of mice at 42 day administered with allethrin 1.5 g/kg BW showing more necrotic changes in tubules and congestion in renal parenchyma. H & E stain; 400X.

4. DISCUSSION

Allethrin exposure is one of the most common and important public health risks in almost all regions of the world. Pyrethroids toxicity in animals is also considerable because it causes behavioral alterations and other pathological changes (Khan et al. 2009). Allethrin has ability to accumulate in different surfaces thus it can be present in household dust and can contaminate environment (Colt et al. 2004). Allethrin is found in almost all mosquito repellents and has therapeutic potential to control the spread of mosquito borne diseases like dengue and malaria which are responsible for million deaths annually in whole world (Idowu et al. 2013).

Nervous excitability observed in this study can be due to oxidative stress which causes lipid peroxidation of neuronal plasma membrane and production of lethal free radicals. Oxidative stress can cause various diseases by damaging the cellular components like cell membrane, fatty acids, proteins, RNA and DNA (Zhu et al. 2020). Similar hyper-excitability symptoms have also been reported previously in broiler chicks by Mashkoor et al. (2013). It has also been observed in last decades in mammals that toxicity is induced by production of free radicals (Zini et al. 1993). Reduction in hematological parameters in present study could be due to bone marrow depression as a consequence of allethrin toxicity. Increase in erythrocyte count could result from polycythemia and decrease in hemoglobin and red blood cells count has also been previously reported in rats (Anonymous 1988; Institoris et al. 1999). The cause of change in hematological values might be due to the toxic effect on hematopoietic system which is responsible for such alterations in hematological parameters. Mansee (1998) and Shakoori et al. (1992) also reported decreased hematological parameters in rats. The alteration in hematological parameters might have occurred due to direct depression of bone marrow (Iteire et al. 2017).

Srivastava et al. (2012) studied the genotoxic effect of allethrin in albino mice. They said that allethrin is a kind of pyrethroid having extensive use in the houses to control mosquitoes. Their study showed that it has mutagenic effect as well as neurotoxic effect in the target species. They checked genotoxic effect of allethrin by using

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)

micronuclei induction assay and chromosomal aberration. Chromosomal abnormality and induction of micronucleus in mice bone marrow cells were increased significantly after administration of allethrin at dose rate of 25 and 50mg/kg BW. Using DNA alkaline unwinding assay, allethrin induced DNA damage was evaluated in mouse liver. They measured the level of 8 hydroxy 2 deoxy guanosine and confirmed that it has pro-oxidant potential. It has been confirmed by their study that gene p51, p53 and GADD45 mediated DNA damage. They completed that allethrin has pro-oxidant and genotoxic effect on albino mice.

In addition to above changes, mild changes in activities of liver has been reported after allethrin intoxication in male rats (Srivastava et al. 2006). The changes observed in present study could be due to lipid peroxidation because of reactive oxygen species generation (Vinoth et al. 2016; Sukmawati et al. 2019). According to Garba et al. (2007) kidneys showed proteinaceous casts within ducts and interstitial mononuclear cellular infiltration after allethrin intoxication in rats.

Conclusion: Allethrin induced clinico-hemato-pathological alterations in adult male albino rats, which may be due to toxic effect on hematopoietic system which is responsible for such alterations in hematological parameters or microscopic changes in adult albino rats. So, Allethrin being active ingredients of mosquito coils and other repellents is used extensively in houses to kill mosquitoes and can be harmful for human health if used more than needed. It is recommended to burn the coils only for two hours prior to enter the room and put it off when sitting or sleeping in that area to reduce the harmful effects described in this manuscript.

Author's Contribution: Research plan was conceived and guided by AK and MKS. Study was executed by QM, MFQ, AA, WE, SM and JM. Manuscript was written by QM, MFQ and TZC. All authors read and approve the final version of the manuscript.

ORCID

Quratulain Mujahid https://orcid.org/0000-0003-2818-7607
Ahrar Khan https://orcid.org/0000-0001-5492-4266
M. Kashif Saleemi https://orcid.org/0000-0002-2329-7228
M. Farhan Qadir https://orcid.org/0000-0002-0712-436X
Absar Ahmad https://orcid.org/0000-0003-2564-7241
Waseem Ejaz https://orcid.org/0000-0002-5549-6803
Shahla Mujahid https://orcid.org/0000-0001-6491-4774
Jahangir Mujahid https://orcid.org/0000-0003-3234-6930

REFERENCES

Anonymous 1989. US Environmental Protection Agency. Pesticide Fact Sheet Number, 199: Cypermethrin. US Environmental Protection Agency Office of Pesticide Programs, Registration Division, Washington, DC, USA.

Antunes-Kenyon S, Kennedy G and Bureau MP, 2007. Methoprene: A review of impact of insect growth regulator methoprene on non-target aquatic organisms in fish bearing waters. Massachusetts Pesticide Bureau, Department of Food and Agriculture.

Benjamin 1978. Outline of Veterinary Clinical Pathology, 3rd Ed. The Iowa State University Press, Ames, Iowa, USA.

Bernet D, Schmidt H, Meier W, Holm PB and Wahli T, 1999. Histopathology in Fish: Proposal for a protocol to assess aquatic pollution. Journal of Fish Diseases 22: 25-34.

Caloni F, Cortinovis C, Rivolta M and Davanzo F, 2016. Suspected poisoning of domestic animals by pesticides. Science of The Total Environment 539: 331-336. https://doi.org/10.1016/j.scitotenv.2015.09.005

Chedik L, Bruyere A, Le Vee M, Stieger B, Denizot C, Parmentier Y, Potin S and Fardel O, 2017. Inhibition of human drug transporter activities by the pyrethroid pesticides allethrin and tetramethrin. PLoS ONE 12: e0169480. https://doi.org/10.1371/journal.pone.0169480

Colt JS, Lubin J, Camann D, Davis S, Cerhan J, Severson RK, Cozen W and Hartge P, 2004. Comparison of pesticide levels in carpet dust and self-reported pest treatment practices in four US sites. Journal of Exposure Science & Environmental Epidemiology_14: 74-83.

Dorman DC and Beasley VR, 1991. Neurotoxicology of pyrethrin and the pyrethroid insecticides. Veterinary and Human Toxicology 23: 238-243.

Garba SH, Adelaiye AB and Msheli LY, 2007. Histopathological and biochemical changes in the rats kidney following exposure to a pyrethroid based mosquito coil. Journal of Applied Science and Research 3: 1788-1793.

Guéniche N, Bruyere A, Vée ML and Fardel O, 2020. Implication of human drug transporters to toxicokinetics and toxicity of pesticides. Pesticide Management Science 76: 18-25. https://doi.org/10.1002/ps.5577

Gul ST, Khan A, Saleemi MK, Ahmad M, Zahoor A, Naseem MN and Hussain R, 2019. Immuno-toxicological effects of allethrin (Active ingredient in mosquito repellent coils) in BALB/c mice following oral administration. Pakistan Veterinary Journal 39: 256-260. http://dx.doi.org/10.29261/pakvetj/2019.036

ISSN: 2708-7182 (Print); ISSN: 2708-7190 (Online)

Gupta G, Chaitanya RK, Golla M and Karnatai R, 2013. Allethrin toxicity on human corneal epithelial cells involves mitochondrial pathway mediated apoptosis. Toxicology in Vitro 27: 2242-2248.

Hernández-Valero MA, Bondy ML, Spitz MR and Zahm SH, 2001. Evaluation of Mexican American migrant farmworker work practices and organochlorine pesticide metabolites. American Journal of Industrial Medicine 40: 554-560.

Hussien HM, Abdou HM and Yousef MI 2013. Cypermethrin induced damage in genomic DNA and histopathological changes in brain and haematotoxicity in rats: The protective effect of sesame oil. Brain Research Bulletin 92: 76-83. https://doi.org/10.1016/j.brainresbull.2011.10.020

Idowu ET, Aimufua OJ, Ejovwoke YO, Akinsanya B and Otubanjo OA 2013. Toxicological effects of prolonged and intense use of mosquito coil emission in rats and its implications on malaria control. Revista de Biología Tropical 61: 1463-1473.

Institoris L, Undeger U, Siroki O, Nehez M and Desi I, 1999. Comparison of detection sensitivity of immuno- and genotoxicological effects of subacute cypermethrin and permethrin exposure in rats. Toxicology 137: 47-55. https://doi.org/10.1016/s0300-483x(99)00081-5

Iteire KA, Igbigbi PS and Oyibororho O, 2017. Toxicological effects of pyrethroids insecticide on the spleen and bone marrow of adult Albino rats. Nigerian Journal of Basic and Applied Sciences 27: 143-150. https://doi.org/10.4314/njbas.v25i2.15

Khan A, 2008. Veterinary Clinical Pathology. University of Agriculture Press, Faisalabad, ISBN: 969-8237-22-4.

Khan A, Faridi HA, Ali M, Khan MZ, Siddique M, Hussain I and Ahmad M, 2009. Effects of cypermethrin on some clinico-hemato-biochemical and pathological parameters in male dwarf goats (*Capra hircus*). Experimental and Toxicologic Pathology 61: 151-160. https://doi.org/10.1016/j.etp.2008.07.001

Khan S, Khan A, Khattak FS and Naseem A, 2012. An accurate and cost effective approach to blood cell count. International Journal of Computer Applications 50: 18-24.

Mansee AHM, 1998. Persistence of cypermethrin and permethrin and their effects on rat blood hematological characteristics. Journal of Agricultural and Marine Sciences 3: 35–39.

Mashkoor J, Khan A, Khan MZ, Abbas RZ, Saleemi MK and Mahmood F, 2013. Arsenic induced clinico-hemato-pathological alterations in broilers and its attenuation by vitamin E and selenium. Pakistan Journal of Agricultural Sciences 50: 131-138.

Narahashi T, 1996. Neuronal ion channels as the target sites of insecticides. Pharmaxology and Toxicology 79: 1-14. https://doi.org/10.1111/j.1600-0773.1996.tb00234.x

Naz M, Rehman N, Ansari MN, Kamal M, Ganaiea MA, Awaad AS and Alqasoumi SI, 2019. Comparative study of subchronic toxicities of mosquito repellents (coils, mats and liquids) on vital organs in Swiss albino mice. Saudi Pharmaceutical Journal 27: 348-353. https://doi.org/10.1016/j.jsps.2018.12.002

Shafer TJ, Meyer DA and Crofton KM, 2005. Developmental neurotoxicity of pyrethroid insecticides: critical review and future research needs. Environmental Health Perspectives 51: 123-136. https://doi.org/10.1289/ehp.7254

Shakoori AR, Aslam F and Sabir M, 1992. Effect of prolonged administration of insecticide (cyhalothrin/karate) on the blood and liver of rabbits. Folia Biologia 40: 91–99.

Srivastava A, Srivastava MK and Raizada RB, 2006. Ninety-day toxicity and one-generation reproduction study in rats exposed to allethrin-based liquid mosquito repellent. Journal of Toxicological Science 31: 1-7. https://doi.org/10.2131/jts.31.1

Srivastava AK, Srivastava PK, Al-Khedhair AA, Musarrat J and Shukla Y, 2012. Allethrin induced genotoxicity and oxidative stress in swiss albino mice. Mutation Research 747: 22-28. https://doi.org/10.1016/j.mrgentox.2019.503116

Sukmawati Y, Arisanty D, Tofrizal A and Amir A, 2019. Vitamin E ameliorates testicular histological features and androgen binding protein levels in testicle of rats induced by allethrin. Journal of Advanced Veterinary and Animal Research 6: 486–491. https://doi.org/10.5455/javar.2019.f372

Surralles J, Xamena N, Creus A, Catalan J, Norppa H and Marcos R, 1995. Induction of micronuclei by five pyrethroid insecticides in whole blood and isolated human lymphocyte cultures. Mutation Research 341: 169-184.

Vinoth K, Mani VM and Ali AL, 2016. protective effect of pomegranate peel extract on mosquito coil smoke exposed alveolar damage in male Wistar rats. International Journal of Science and Humanities 2: 417–430.

Zhu Q, Yang Y, Zhong Y, Lao Z, O'Neill P, Hong D, Zhang K and Zhao S, 2020. Synthesis, insecticidal activity, resistance, photodegradation and toxicity of pyrethroids (A review). Chemosphere 254: Article # 126779. https://doi.org/10.1016/j.chemosphere.2020.126779

Zini A, Lamirande E and Gagnon C, 1993. Reactive oxygen species in semen of infertile patients: levels of superoxide dismutase- and catalase-like activities in seminal plasma and spermatozoa. International Journal of Andrology 16: 183-188.