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Research Article

STUDY OF DELTAMETHRIN ASSOCIATED HEPATOTOXICITY AND NEPHROTOXICITY IN *SWISS ALBINO* MICE

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Abstract: Present study was conducted to assess hepatotoxicity as well as nephrotoxicity of low dose oral exposure of deltamethrin in 90 *Swiss Albino* male mice. The pesticide dissolved in groundnut oil was administered through oral route for 15, 30 and 60 days at three dose levels of 0.5mg/kg b.wt., 1.0 mg/kg b.wt. and 1.5 mg/kg b.wt. after completion of experimental trials , mice were sacrifices and liver as well and renal tissues were examined for histopathological alterations. As deltamethrin isd a lipophilic synthetic pyrethroid, the accumulation in liver and kidneys has led to various toxicological effects in the tissues in terms of congestion of renal blood vessel, necrosis of hepatic tissues and degeneration of Bowman's capsule.

Keywords: *Deltamethrin, Mice, Tissue, Degeneration*

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Introduction

Synthetic pyrethroids are the most commonly used class of pesticides now-a-days replacing organophosphates and organochlorines class. Delatamethrin is an alpha-cyanopyrethroids having potent insecticidal effect [1] and is thus most intensely used in agriculture and households. The indiscriminant usage, however, has led to various adverse health effects in all living organism *viz*., genotoxicity, immunotoxicity, reproductive toxicity, neurotoxicity *etc*, biochemical alterations in liver and kidney specific parameters [2]. Liver tissue has a tendency to accumulate greater concentration of pyrethroid metabolites as it is considered to be a major site of pyrethroid metabolism [3].Deltamethrin, due to its lipophilic nature has tendency to get accumulated in fat rich tissues such as liver, adipose and kidneys.The aim of this study is to determine the hepatotoxixity as wells as nephrotoxicity in *Swiss Albino* male mice after low dose long duration exposure of deltamethrin through oral route. The doses used in the study were in the multiples of maximum residual limit (MRL) values of deltamethrin found in various food products i.e. 0.5 mg/kg for chicken fat, 0.3 mg/kg for chicken muscle[4]. The highest dose of deltamethrin was 1/30th of the LD50 of the pesticides. Oral LD50 for deltamethrin in mice is reported to be 30-50 mg/ kg body weight [5].

Material and Methods

In this study, 90 *Swiss Albino* male mice were exposed to daily dose of deltamethrin dissolved in groundnut oil at the dose rate of 1.5 mg/kg b.wt., 1 mg/kg b.wt. and 0.5 mg/kg b.wt., each for 15, 30 and 60 days through oral route [Table-1].

Table-1 *Treatment schedule of mice and experiment design*

Pesticides	Groups	Doses	Number of mice		
			15 days	30 days	60 days
Negative Control	I	Groundnut oil	6	6	6
Positive Control	II	Cyclophosphamide	6	6	6
	III	(1.5 mg/kg)	6	6	6
Deltamethrin	IV	(1.0 mg/kg)	6	6	6
	V	(0.5 mg/kg)	6	6	6
		Total	30	30	30
		Grand Total			90

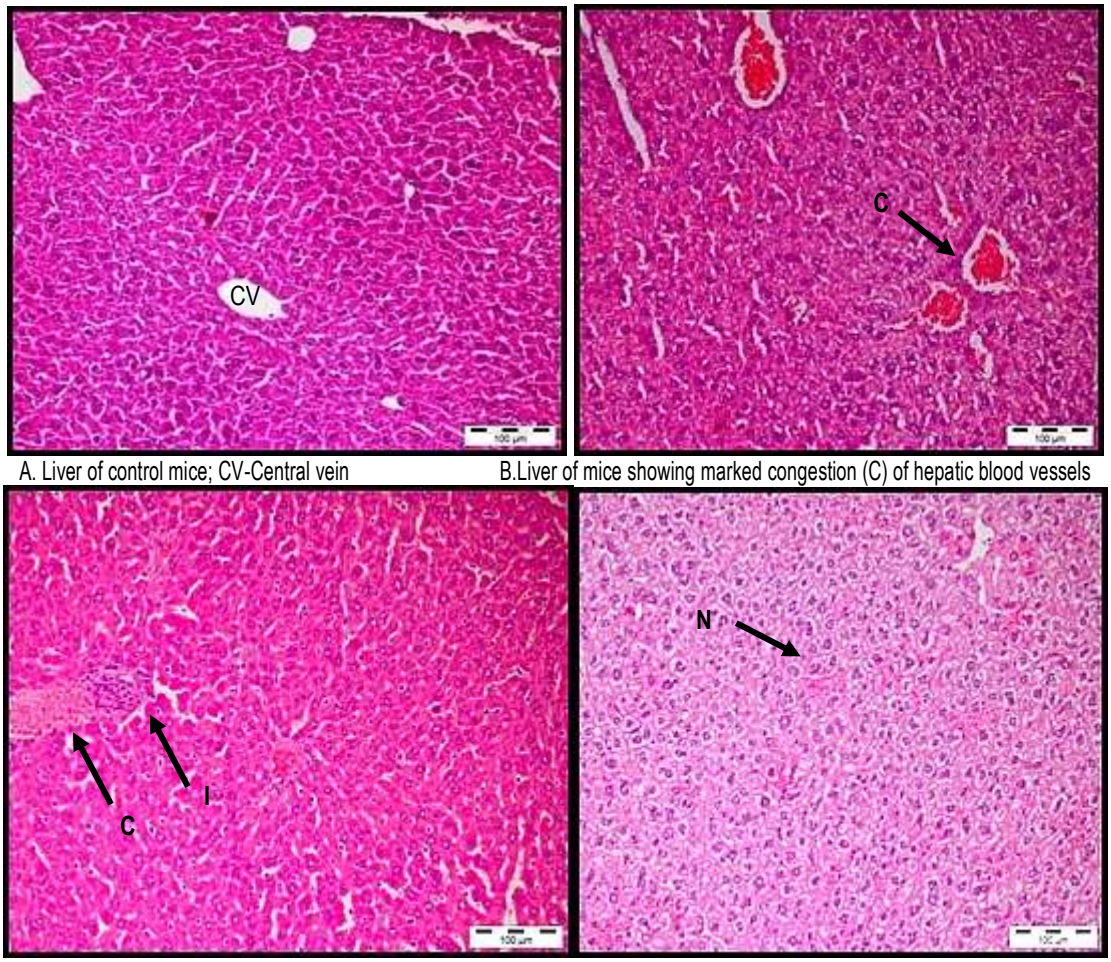
Mice were kept under controlled conditions of temperature (22 ± 1°C) and humidity (60 ± 5%). They were provided with ad libitum pelleted feed (Ashirwad industries, Chandigarh, India) and drinking water. A twelve-hour day and night cycle were maintained. Animals were administered daily dose of deltamethrin [Table-1], dissolved in groundnut oil through oral route. The experimental protocol met the national guidelines on the proper care and use of animals in the laboratory research. The Institutional Animal Ethics Committee (IAEC) approved the experimental protocol. Technical grade Deltamethrin with 98.50% purity was obtained from Kilpest India Limited, Bhopal, India. The three doses of deltamethrin used in the study were 0.5, 1.0 and 1.5 mg/kg bwt/day. The highest dose of deltamethrin was 1/40th of the LD50 of the pesticides. Mice were sacrificed after 24 hr of completion of trial period (15/ 30/ 60 days) under ketamine (100 mg/kg body weight) and xylazine (10 mg/kg body weight) anaesthesia, intraperitoneally. The sections of tissues from the vital organs of mice i.e. liver and kidneys were taken and stained with haematoxylin and eosin to visualize the histopathological changes caused due to exposure of mice to the pesticides.

Results

The histological examination revealed the degenerative change in all the tissues studied at all the dose and duration of exposure to the pesticide. The changes were more or less dependent upon the dose of pesticide as well as the duration of exposure to pesticide. Since the main site of deposition and metabolism of these pesticides are liver and kidney, therefore, the alteration caused in the hepatic and renal tissues in this study have considerable association with the pesticide exposure.

Liver

Tissue sections of control animals showed normal architecture of liver as observed under light microscope after staining with Hematoxylin and Eosin [Fig-1A]. On exposure to deltamethrin for 15 days, granular degeneration of liver was observed at dose 1(1.5 mg/kg bwt). Milder degree of hepatic necrosis was also seen at dose 2 (1 mg/kg bwt) of deltamethrin exposure. At dose 3 (0.5 mg/kg bwt), mild to severe necrosis was observed.



A. Liver of control mice; CV-Central vein B.Liver of mice showing marked congestion (C) of hepatic blood vessels

C. Liver of mice showing congestion (C) and infiltration (I) of mononuclear cells D. Liver of mice showing necrosis (N)

Fig-1 H & E stained section (20 X) of liver of Control (A), 1.5 mg/kg bwt (B), 1 mg/kg bwt (C) and 0.5 mg/kg bwt (D) after 60 days of deltamethrin exposure

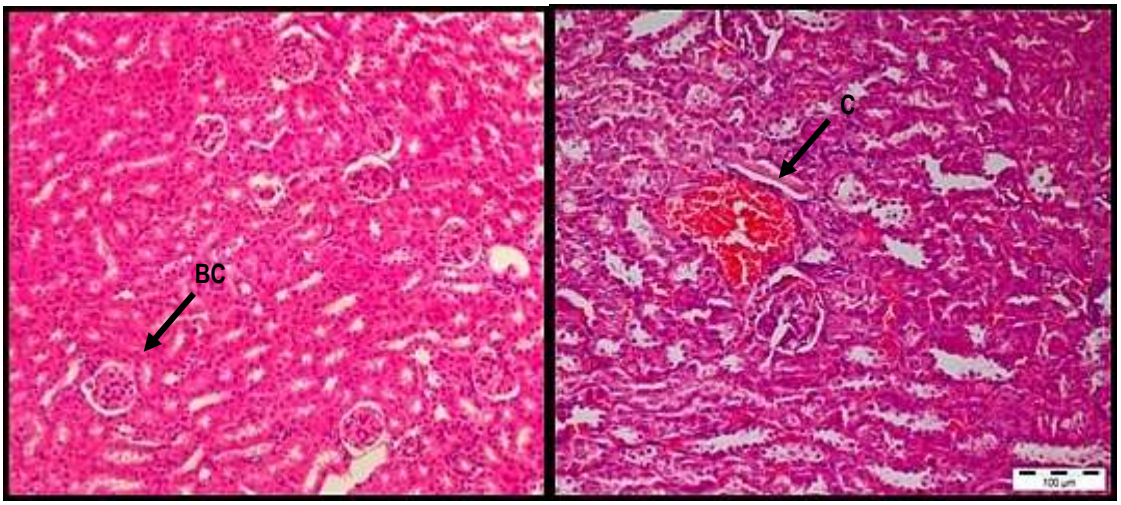
At 30 days of exposure to deltamethrin, haemorrhages were seen at dose 1 and dose 2 of deltamethrin whereas at dose 3, marked infiltration of mononuclear (MN) cells was observed. Focal degeneration, hemorrhages and congestion in liver were seen at 30 days of exposure to deltamethrin. Fatty degeneration was observed in liver along with knuckling associated with advancement of lesions. At 60 days of exposure, the changes were more severe. Marked congestion of hepatic blood vessels was observed at dose 1 [Fig-1B]. Congestion and infiltration of mononuclear cells was found at dose 2 [Fig-1C] of deltamethrin whereas focal necrosis was seen at dose 3 [Fig-1D]. There was abundance of congestion and hypertrophy of hepatocytes which led mainly to the appearance of vacuoles in the cytoplasm.

Kidneys

The section of the kidneys of the control animal showed normal histoarchitecture (2A). In the present study, kidneys of exposed individuals exhibited changes in their histology in comparison to control. Prominent changes included shrinkage of glomerulus and dilation of tubular lumen. Vacuolization, desquamation and hyaline degeneration of tubular epithelium was also observed. At 15 days exposure, mild congestion and vacuolar degeneration was observed. At 30 days of exposure marked congestion and hemorrhages of the renal blood vessels was seen. At 60 days post exposure, the congestion was very much marked at dose 1 of deltamethrin [Fig-2B]. Infiltration of mononuclear cells along with congestion was observed at dose 2 and 3 [Fig-2C] and [Fig-2D].

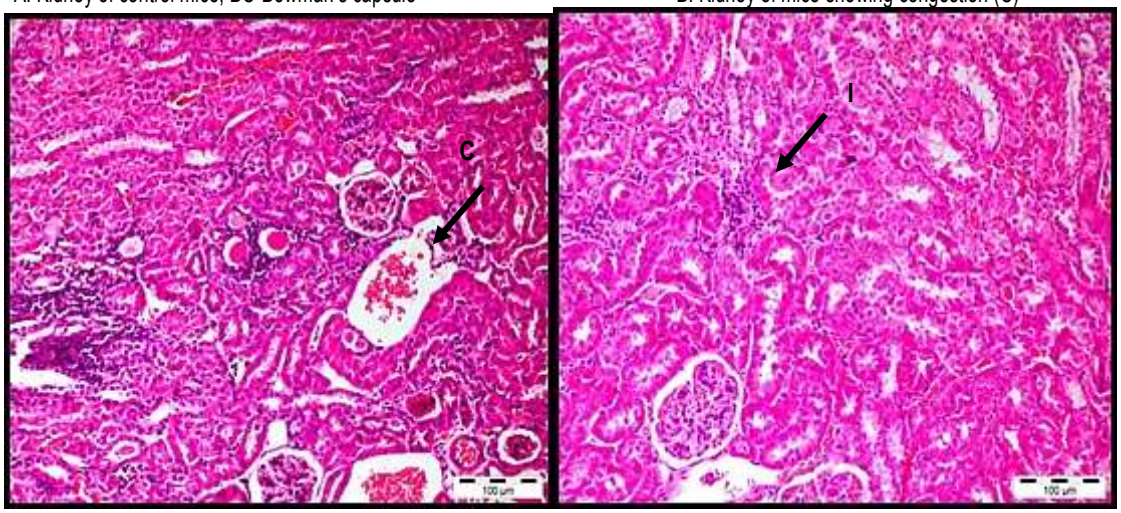
Discussion

Histopathological examination of tissues from vital organs of mice revealed various alterations on exposure to deltamethrin. These changes were dependent on the dose of the deltamethrin administered as well as the duration of exposure. Even the lowest dose of deltamethrin (0.5mg/kg bwt) and the shortest exposure period (15 days) were able to induce these histopathological alterations. Also, these changes are in agreement with the studies conducted in the past on histopathology of deltamethrin [6]. According to some reports, liver was found to accumulate a greater concentration of deltamethrin metabolites since it is a major site of pyrethroid metabolism [3]. Because of this reason, the hepatotoxicity caused on exposure to deltamethrin is much marked as the dose and duration of exposure increases. It should be noted that the cumulative effect of these pyrethroids, which can change the function of certain targets, should be taken seriously in light of the effects obtained following exposure of organisms to low doses accumulated during life. The hepatotoxicity of deltamethrin in present study suggests that intense liver damage occurred at 30 and 60 days of exposure. Once deltamethrin is introduced into the body it begins to set in target tissues due to its lipophilic properties. As one of the most toxic pyrethroid, deltamethrin is not fully metabolized or detoxified completely in the body and so it creates serious problems due to accumulation of its residue specifically in the lipophilic tissues. Similarly, in case of histopathological study of kidneys, results in present study are consistent with those observed by Tos-Luty, *et al*., (2001) [7] wherein it was observed that treatment of mice with deltamethrin intragastrically at the dose of 25mg/kg bwt/d for 28 days caused hypertrophy of Bowman's capsule, parenchymal degeneration and shrinkage of bowman's capsule. Thus, the dose used in present study (1/25 times the dose used in earlier study) was also found to cause significant renal damage on deltamethrin exposure. This showed low dose long term potential of deltamethrin to cause nephrotoxicity in mice. Congestion of blood vessels of kidneys in present study was consistent with the findings of [8] who found similar changes at higher dose of deltamethrin (15 mg/kg bwt/d) for 30 days. This dose was 15 times higher than the dose used in present study. These results are also consistent with the work of [6, 9]. A number of studies have demonstrated nephrotoxicity of deltamethrin in mammalian and non-mammalian species [10].



A. Kidney of control mice; BC-Bowman's capsule

B. Kidney of mice showing congestion (C)



C. Kidney of mice showing infiltration (I) of MN cells and congestion (C)

D. Kidney of mice showing infiltration (I) of MN cells

Fig-2 H&E stained section (20X) of Kidney of Control (A), 1.5 mg/kg b. wt (B), 1.0 mg/kg b. wt (C) and 0.5 mg/kg b. wt (D) after 60 days of deltamethrin exposure

Deleterious effect of the combination of endosulfan and cypermethrin were also reported by Raj, *et al*., (2013) [11] in terms of hepatic and medullary congestion, leading to mild pathological change in liver and kidney tissues, which was also observed by Manna, *et al*., (2004) [12]. These findings were in agreement with those observed in cypermethrin toxicity in rats by Grewal, *et al*., (2010) [13] and Muthuviveganandavel, *et al*., (2008) [14]. Degeneration in the epithelial cells of renal tubules, dilation of glomerular capillaries, degeneration of glomerulus, intracytoplasmatic vacuoles in the epithelial cells with hypertrophied cells and narrowing of the tubular lumen were observed in the kidney tissues of fish exposed to deltamethrin [15]. In a study conducted by Sharma, *et al*., (2016) [2], hepatic as well as renal damage was revealed by significantly altered biochemical levels of certain liver and kidney specific parameters in *Swiss albino* male mice following oral exposure to deltamethrin which is in support to hepatic and renal damage observed in this study through histopathological examination.

Conclusion

The findings of the present study on histopathological examination of vital organs of mice after low dose long term exposure to deltamethrin even at lowest dose level of 0.5 mg/kg b.wt. are in agreement with the studies conducted earlier. However, the doses used in this study were many times lower than those used in the earlier studies. So, these finding are important in understanding that the low doses of deltamethrin have the tendency to cause significant damage to liver and kidneys and their exposure for long term may prove fatal due to resulted liver and kidney failure.

Application of research: The results of the present study highlight the fact that even the lowest dose of deltamethrin closer to MRL of deltamethrin in various food products can cause histotoxic effects and thus are applicable in formulating newer guidelines of pesticides usage in the forthcoming time.

Research Category: Hepatotoxicity and Nephrotoxicity

Abbreviations: MRL- Maximal residual limit, LD50- lethal dose 50, IAEC-Institutional Animal Ethical Committee, MN – mononuclear cells

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Study area / Sample Collection: School of Public Health and Zoonoses

Breed name: Laboratory Animal- *Swiss Albino* Mice

Conflict of Interest: None declared

Ethical approval: Ethical approval taken from Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, 141004, India
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