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Research Paper

CYPERMETHRIN-INDUCED CHANGES IN BODY MORPHOMETRICS AND HISTOPATHOLOGY OF LIVER AND KIDNEYS IN THE SWISS ALBINO MICE *MUS MUSCULUS* L.

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Abstract

Effects of cypermethrin, a synthetic pyrethroid insecticide having a fast-acting neurotoxin that causes free radical-mediated tissue damage in animals, on the body, liver and kidney weights as well as changes in the histopathology of hepatic and renal tissues in the Swiss albino mice *Mus musculus* L. have been assessed. Twenty five adult male albino mice of 2-3 weeks of age were divided equally into five groups where each 20g mice received the following treatments: distilled water only (T0, served as control); 0.10ml cypermethrin (T1); 0.15ml cypermethrin (T2); 0.20ml cypermethrin (T3); and 0.25ml cypermethrin (T4). Treatments were accomplished intraperitoneally each week for four consecutive weeks. During the experimental period, there were significant decreases between the initial and final body weights in the cypermethrin-treated mice but no abnormalities were observed in the control group. At the end of the 4th week, all the mice were sacrificed; their kidneys and liver were dissected out, weighed and preserved in 70% ethanol. The samples of liver and kidneys were processed for histological studies. Cypermethrin treatment exhibited severe histopathological changes in the hepatic and renal tissues accompanied by weight loss of the organs. Salient manifestations such as haemosiderin in hepatocytes, epithelial and Kupffer cells, dilated sinusoids, haemorrhage and vacuolation, necrotic hepatocytes and congested central and portal veins, inflammatory cell infiltration and increased number of mononuclear cells were diagnosed in liver sections. In kidney sections, on the other hand, oedema, congested or degenerated glomeruli, widened urinary spaces, dilated or vacuolated tubules, degenerated or eroded walls of Bowman's capsules, haemorrhages and inflammatory cell infiltrations, hyalinized areas and increased numbers of podocytes and mesangial cells were notable features. From these findings, it is postulated that cypermethrin and other synthetic pyrethroids might cause hazardous effects on mammals including human beings, and therefore, judicious applications of this insecticide should be assured while usiing them at agricultural field and household purposes.

Key words: Swiss albino mice, cypermethrin, morphometrics, histopathology, liver, kidneys.

INTRODUCTION

Cypermethrin is a broad spectrum pyrethroid insecticide which is marketed under the trade names, among others, Caught-100, Barricade, Basathrin, CCN52, Cymbush, Cynoff, Cypercopal, Cyperguard 25EC, Cyperkill, Cypermar, Demon, Polytrin, PP 383, Ripcord, Siperin, Stockade and Super which is classified as 'moderately hazardous' chemical belonging to Class II category [1]. It interacts with the sodium channels in nerve cells through which sodium enters the cell in order to transmit a nerve signal. These channels can remain open for up to seconds, compared to the normal period of a few milliseconds, after a signal has been transmitted. Cypermethrin also interferes with other receptors in the nervous system. The effect is that of long-lasting trains of repetitive impulses in sense organs. The insecticide is extensively used in Bangladesh to control insects in a wide variety of field crops including rice and vegetables [2].

Recent studies showed that indiscriminate and unregulated uses of insecticides like cypermethrin in agriculture and public health in Bangladesh have led to drastic effects on many non-target species including man [2, 3]. Symptoms of poisoning include abnormal facial sensations, dizziness, headache, nausea, anorexia and fatigue, vomiting and increased stomach secretion. Cypermethrin is also a skin and eye irritant. The toxic responses in all species were found to be qualitatively similar. The clinical signs observed after oral and inhalation exposure were indicative for an action on the central nervous system that consisted of salivation, ataxia, splayed gait and hyper-excitability to auditory stimuli, tremors, convulsions and choreoathetosis [4].

Several reports on cypermethrin toxicity in mice and rats reveal that the insecticide induces remarkable histopathological changes in various organs including liver, stomach, intestine, spleen, pancreas and kidneys [5, 6]. Its exposure has also been well documented in potentially sensitive subpopulations including pregnant women, infants and children [7]. Use of the insecticide has continuously been increasing since 1998 due to the phase out of older drugs like organophosphorus compounds [8]. Pyrethroid residues have been reported to cause epilepsy, liver and kidney dysfunction [9], somatic growth depression, neuritis and testicular cancer and produce dose-dependent decreases in motor activity of rats [10]. Since liver is associated with metabolism and elimination of toxicants from the body and kidney is associated with excretion, their histological parameters are considered to be the key points to elucidate toxicity of the insecticides on the experimental rodents [11, 12]. A recent study at Xuzhou Medical College in China showed that, in male rats, cypermethrin can exhibit a toxic effect on the reproductive system. These data suggested that cypermethrin can induce impairments of the structure of seminiferous tubules and spermatogenesis in male rats [13].

Apart from the aforesaid pyrerhroid poisoning in mice and rats, however, a number of other insecticides, for examples, organochlorine such as endosulfan [14, 15], organophosphate like chlorpyriphos and profenofos [16, 13, 12] have also been tested to assess their histopathological impacts on the experimental rodents. Taking these findings in consideration, the present investigation was designed to observe a detailed account of cypermethrin-induced changes in body, liver and kidney weights along with histopathological alterations in the tissues of liver and kidneys in the male Swiss albino mice under laboratory conditions.

MATERIALS AND METHODS

Insecticide

Technical grade cypermethrin (trade name Caught-100 EC; 99% pure; *cis: trans* isomeric ratio of 40:60) were purchased from a local pesticide shop situated at Kantakhali, Rajshahi, Bangladesh. The chemical was registered, formulated and repacked by The ACI Formulations Limited and manufactured by Tag Rose Chemicals India Limited (Diagram 1).

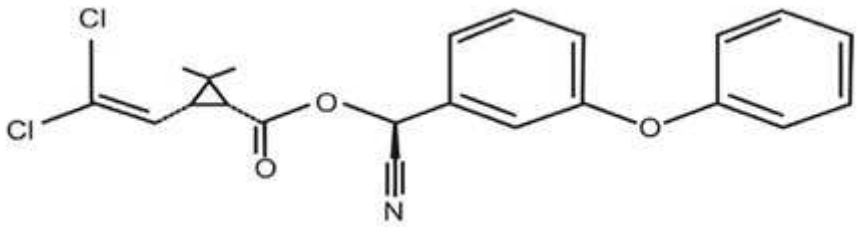

Diagram 1 Structural formula of cypermethrin (chemical name: Cyano (3-phenoxyphenyl) methyl 3-(2, 2-dichloroethenyl)-2, 2-dimethylcyclopropanecarboxylate; molecular formula: $C_{22}H_{19}C_{l2}NO_3$; molecular weight: 416.3; [1].

Test animals

Male Swiss albino mice *Mus musculus* L. (Rodentia: Muridae) of 2-3 weeks of age, each weighing 30±3 g were collected from Jahangirnagar University, Bangladesh. They were kept in iron cages (45cm × 30cm × 30cm) with sawdust bedding, which was replaced once a week. Water and poultry feed were supplied *ad libitum*. The mice were maintained at laboratory conditions (28±4° C; 75±11% RH and 8:16 hrs light: dark regime) throughout the period of the study. In compliance with the standard animal ethical guidelines the present study was carried out at the Genetics and Molecular Biology Laboratory, Department of Zoology, University of Rajshahi, Bangladesh, during the period from February 2013 to June 2013.

Experimental design

Twenty five healthy adult male albino mice were divided into five groups (T0-T4), each composed of five animals. T0 group served as the control while for groups T1-T4 various doses of cypermethrin were injected intraperitoneally at 5, 7.5, 10 and 12.5 ml/kg body weight of the mice for four consecutive weeks. Body, liver and kidney weights of the experimental mice were recorded and histological slides of the hepatic and renal tissues were prepared for microscopic examinations.

Morphometric parameters

Initial body weights of the control and treatment groups of mice were recorded at the beginning of the experiment. Then all the experimental mice were weighed after each week post-treatment just before sacrificing. The mice to be sacrificed were placed in a jar containing cotton wool soaked in diethyl ether. Complete anaesthesia was considered accomplished when the pedal movements and eye lid reflex disappeared and the animal became recumbent while still breathing. The belly of the mice was cut open to collect liver and kidneys which were weighed, gently rinsed in normal saline, fixed in 10% formalin and stored at 4°C for histopathology. Finally, percentages of liver and kidney indices were estimated as follows: liver or kidney weight ÷ body weight × 100 [12].

Histopathology

For histopathological examinations the procedures described by Sarker *et al*. [17] were followed. In brief, the preserved liver and kidney samples were washed in running tap water for a couple of hours, dehydrated in ascending grades of ethanol (30%-95%), cleared in xylol and embedded in paraffin wax (melting point 50-56° C). After solidification the wax blocks were cut at 5µm thickness using a rotary microtome at 200µm intervals and the small pieces of the ribbon were affixed on the slides. Finally, the slides with the sections were placed in descending grades of ethanol (95%-70%), rinsed in distilled water for 2-3 min and then double stained in haematoxylin (10-15 min) and aqueous eosin (5-10 min), followed by further rinsing in distilled water. The sections were then dehydrated in absolute alcohol for 5-10 min, further cleared in xylol, mounted in DPX (digital picture exchange) and covered with cover slips. Examinations of the slides were made by a light microscope (Zeiss, Germany) and microphotographs were taken at the Department of Genetic Engineering and Biotechnology, University of Rajshahi, Bangladesh, using an automated digital camera system (Olympus CH30/CH40, Japan).

Statistical analysis

Morphometric data on body, liver and kidney weights were analyzed using SPSS for Windows (version 15.0). Comparisons were made between experimental groups using one-way analysis of variance (ANOVA) followed by LSD (least significant differences) tests. P-values of less than 0.05 were regarded as statistically significant.

RESULTS

Morphometric parameters

Body weight: The body weight of mice in the control line (T0) increased gradually from around 27g to 31 g over a period of 28 days. In contrast, this parameter in the treated lines (T1-T4) decreased, apart from a minor fluctuation, from about 27g to 22g during the observation period. Thus Cypermethrin induced a gain in body weight of the untreated mice and the corresponding loss in the parameter of the treated mice significantly ($F_{4, 95}$ = 129.22; P<0.001; Table 1).

Liver weight: There was a slight increase in liver weight of the untreated mice, ranging from 2.50 g to 2.60g. Liver weight was also recorded in the treated mice in a dose-dependent manner; the decline was from 2.50g to 2.42g over a period of 28 days. This decline was also reflected in the percentages of liver indices values from approximately 8% in the control to about 5% in the highest dose. Although the decrease in liver weight in the experimental mice was statistically significant ($F_{4, 19}$ = 5.625; P<0.001; Table 1).

Kidney weight: The kidney weight of the control mice increased from 0.76g to 0.81g during the course of the experiment. Whereas kidney weight of the Cypermethrin-treated mice was found to decrease from 0.64g to 0.56g after the termination of the experiment. Thus the overall increase of kidney weight in the control line and decrease of the same in the treated line was significant ($F_{4, 19}$ = 6.283; P<0.001; Table-1).

Histopathology of liver

In untreated control group, the transverse section of liver showed usual structures of the hepatocytes with normal central vein, Kupffer cells and sinusoids (Plate 1.C.). Whereas at lower (0.1-0.15 ml/20 g) and higher (0.20-0.25 ml/20 g) doses of Cypermethrin-treatment for four weeks, the following histopathological abnormalities were recorded (summarized in Table 2):

Sections of control mice liver revealed that the hepatocytes arranged in strands with one or two spherical nuclei and eosinophilic cytoplasm. The sinusoids are occupied by Kupffer cells (Plate 1.C). Examination of liver of CYP-treated mice displayed apparent signs of degenerative changes. The normal structural organization of the hepatic lobules was impaired and the characteristic cord-like arrangement of the normal liver cells was lost. In addition, severe inflammatory leucocytic infiltrations were abundant. Such inflammatory infiltration is spread over several liver areas and around the blood vessels (Plate 1.1). Enlargement and congestion of blood vessels, especially veins were observed. The hepatocytes were clearly manifested by marked cytoplasmic vacuolization (Plate 1.2) and most cells showed nuclei with signs of karyolysis and pyknosis.

After 28 days of treatment with cypermethrin histopathological examination in liver revealed nucleus to be normal but with congested sinusoidal spaces (Plate 1.C). High dose treated liver showed increased sinusoidal spaces, condensed nuclei and enlarged hepatocytes with hydropic degeneration together with cytoplasmic vacuolization (Plate 1.4).

Nuclear hypertrophy and binucleated hepatocytes were observed at some places. The liver sections from treated mice showed moderate changes when compared with those from the control mice (Plate 1.C). These changes include the presence of more endothelial cells scattered among the hepatocytes and some vacuolation in the liver texture (Plate 1.1), showed rupture in some hepatocytes and dark stained hepatocytic nuclei indicating cell pyknosis (Plate 1.1, 1.2, 1.3 and 1.4). Some hepatocyes have shrinked nuclei (Plate 1.4).

Table 1: Effects of Cypermethrin on the relative body, liver and kidney weights (g) of the male Swiss albino mice

Parameters/ Treatments	1st Week	2nd Week	3rd Week	4th Week	F-Values
Body Weight					
T0	31.50±0.34[a]	34.46±0.50[b]	37.60±0.35[c]	38.62±0.38[d]	325.19***
T1	29.02±0.81[a]	27.24±0.61[b]	26.66±0.63[c]	26.34±0.63[d]	15.714***
T2	30.12±0.39[a]	28.84±0.39[b]	28.04±0.21[c]	27.84±0.09[d]	60.127***
T3	36.08±0.53[a]	35.00±0.59[b]	34.38±0.64[c]	34.12±0.68[d]	10.165***
T4	37.30±0.19[a]	36.06±0.21[b]	35.24±0.24[c]	34.44±0.40[d]	101.460***
Liver weight (Hepatosomatic index)					5.625*** (132.178***)
T0	-	-	-	2.60± 0.07[a] (6.7333±0.2[a])	
T1	-	-	-	2.42± 0.08[b] (9.1864±0.16[b])	
T2	-	-	-	2.50± 0.07[a] (8.9735±0.26[c])	
T3	-	-	-	2.42± 0.10[c] (7.0929±0.3[d])	
T4	-	-	-	2.36± 0.05[d] (6.8540±0.21[a])	
Kidney Weight (Renosomatic index)					6.283*** (5.194***)
T0	-	-	-	0.76± 0.05[a] (1.9156±0.1[a])	
T1	-	-	-	0.56± 0.08[b] (2.1257±0.34[a])	
T2	-	-	-	0.58± 0.04[c] (2.0814±0.15[a])	
T3	-	-	-	0.64± 0.09[d] (1.8740±0.2[a])	
T4	-	-	-	0.54± 0.05[e] (1.5674± 0.15[b])	

Values are mean ± SD; All F-values are at 4, 19 df; **= P<0.01; ***= P<0.001; superscripts in dissimilar letters in each column differ significantly by LSD tests at P<0.05.

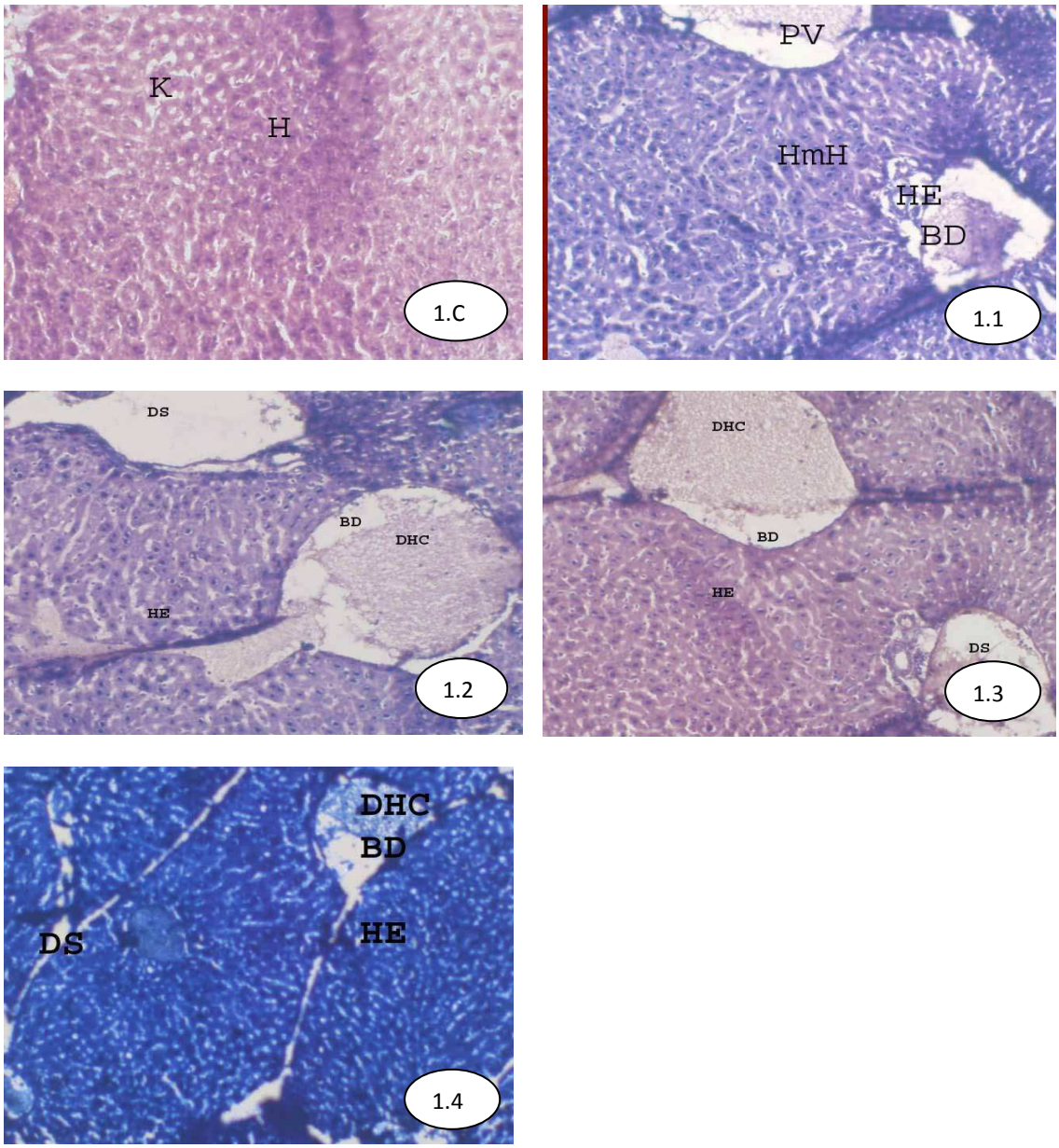

Plate 1 Transverse sections of liver of Cypermethrin treated mice after 28 days. Slides for the control (T0) and treatment groups (T1-T4) are designated by 1.C, 1.1, 1.2, 1.3 and 1.4, respectively (200×). **Abbreviations:** BD= bile duct; DS= dilated sinusoid; DHC= degenerated hepatocytes cells H= hepatocytes; HE= haemorrhage; HmH= haemosiderin hepatocytes; K= Kupffer cells; PV= portal vein.

Table 2: Major histopathological changes detected after Cypermethrin treatments in the Swiss albino mice

Treatment groups/ Organs	Major histopathological changes	Severity[1]
Liver		
T0	Usual structures of the hepatocytes with normal central vein, Kupffer cells and sinusoids	_
T1	Shrunken portal vein and haemosiderin in Kupffer cells; binucleated hepatocytes, haemosiderin in hepatocytes, fibrous central and portal veins; haemosiderin in epithelial cells; haemorrhage and dilated sinusoids	+
T2	Haemorrhage accompanied by cell debris, vacuolated and congested central vein; haemorrhage and dilated sinusoid; congested portal vein, cell debris and vacuolation; and congested area and dilated central vein	++
T3	Necrotic hepatocytes and congested portal vein; fibre deposited central vein; inflammatory cell infiltration and congested central vein; and fibrous tissue accompanied by inflammatory cell infiltration	+++
T4	Haemorrhage and inflammatory cell infiltration; increased number of mononuclear cells and dilated portal vein; fibre-deposited portal vein accompanied by cell debris and haemorrhages; and enucleated cells, necrotic hepatocytes and increased number of mononuclear cells	++++
Kidney		
T0	Normal arrangements of Bowman's capsule, glomerulus, urinary pulp, distal and proximal convoluted tubules and podocytes	_
T1	Oedema and congested glomerulus accompanied by widened urinary space; inflammatory cell infiltration and vacuolated tubules; dilated collecting duct, medullary ray and distal tubule, increased number of mesangial cells and degenerated glomerulus	+
T2	Dilated collecting ducts, vacuolated tubules, cell debris, congested glomerulus and widened urinary space; shrunken glomeruli, presence of inflammatory cell infiltration and hyalinized area; dilated tubule, eroded wall of Bowman's capsule and increased number of podocytes	++
T3	Haemorrhage accompanied by degenerated or congested glomerulus and widened urinary space; dilated proximal tubule and increased number of mesangial cells; inflammatory cell infiltration and dilated tubule; and vacuolated tubule and degenerated Bowman's capsule	+++
T4	Vacuolated distal tubule and haemorrhage; dilated collecting and proximal tubules and degenerated glomerulus; increased number of podocytes, large mononuclear cells and eroded wall of Bowman's capsule; and shrinkage of proximal tubule, increased number of podocytes and haemorrhage	++++

1_ = no change; += minor; ++=not severe; +++= severe; ++++=very severe.

Histopathology of kidney

The transverse sections of untreated control renal cells revealed normal arrangements of Bowman's capsule, glomerulus, urinary pulp, distal and proximal convoluted tubules and podocytes (Plate 2.C). In contrast, the Cypermethrin treatment induced the following exposure-dependent symptoms in the experimental mice (summarized in Table 2): Kidneys of all the

animals of the control as well as the experimental groups were paired structures located on the posterior abdominal wall, one on either side of the midline. The kidneys were reddish brown in color and were covered by a thin glistening capsule, which was not adherent to the surrounding tissues.

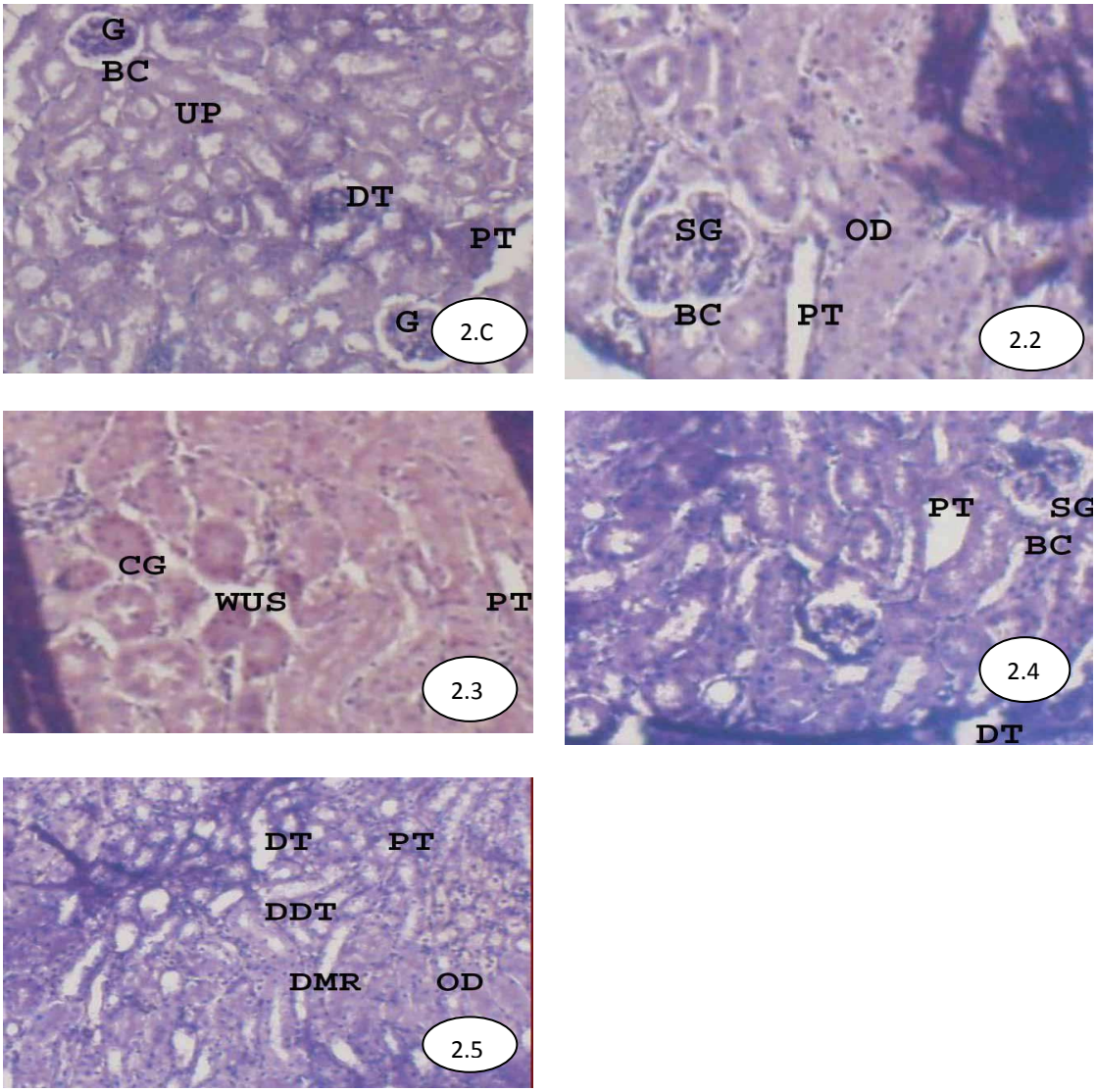

Plate 2 Transverse sections of kidney of Cypermethrin treated mice after 28 days. Slides for the control (T0) and treatment groups (T1-T4) are designated by 2.C, 2.1, 2.2, 2.3 and 2.4, respectively (200×). **Abbreviations:** BC= Bowman's capsule; CG= congested glomeruli; DDT= dilated distal tubule; DMR= dilated medullary ray; DT= dilated tubule; G= glomerulus; OD= oedema; PT= proximal convoluted tubule; UP= urinary palp; VT= vacuolated tubule; WUS= widened urinary space.

Sections from the kidneys of mice treated with cypermethrin as well as those from the controls were also examined (Plate 2.C, 2.1, 2.2, 2.3, and 2.4). Control group showed normal renal architecture. The histological changes observed in the kidneys after damage by toxins include changes in the tubules and in the interstitium. There is necrosis predominantly in the proximal tubules. Plate 2.C showed that kidney cortex consists of renal corpuscles and tubules. Renal corpuscles consist of Bowman 'capsule with double membrane with urinary space in between. Also, a tuft of glomerular capillaries is enclosed in Bowman's capsule. Renal tubules are of two types, proximal and distal tubules. Proximal tubules lined with low columnar epithelium and

have narrow lumen. Distal tubules possess wide lumen and lined by cuboidal epithelial. Even the kidneys showed marked hemorrhage and congestion in cypermethrin-treated animals as compared to normal histological examination of renal tissue in control mice. Animals treated with cypermethrin showed degeneration and deterioration of the cortical constituents. The epithelial linning of the renal tubules appeared with cloudy swelling and vacuolated cytoplasm with pyknotic nuclei. Intertubular leucocytic infiltrations were observed (Plate 2.1, 2.2, 2.3 and 2.4). A number of glomerular capillaries were suffering from severe signs of glomerular congestion, while others were completely damaged.

DISCUSSION

In this investigation, a detailed account of Cypermethrin treatment changes in body, liver and kidney weights, coupled with corresponding toxic effects of the pyrethroid insecticide in the liver and kidney tissues of male Swiss albino mice has been presented. The results of the current study revealed that there were significant decreases in body and liver weights in mice treated with Cypermethrin. In toxicological studies, however, organ and relative organ weights are important criteria for evaluation of organ toxicity [18]. The organ and relative organ weights may be increased or decreased depending on the nature and mode of action of the insecticide.

In earlier study [19, 20] observed bloat, haemorrhages in the stomach, intestine, and lungs, in both single dose and repeated dose toxicity studies of cypermethrin in rats. In crossbred calves, cypermethrin intoxication produced congestion and/or haemorrhages on the auriculoventricular groove of the heart, lungs, mucosal surface of the intestine, cortex of the kidney, and brain [21]. The histopathological changes in the lung and liver tissues of cypermethrin exposed mice have shown significant changes. Exposure of the mice to cypermethrin through inhalation induces significant time dependent changes in the histopathology of lung as well as liver tissue. Inhalation is a major route of exposure to air born pollutants such as the pesticides [22]. Lungs and liver are the organs which are at highest risk to the environmental pollutants especially the air born chemicals [23]. Cypermethrin has shown the carcinogenic effect in the lung tissues of mice. Exposure to cypermethrin caused a gradual distortion of normal structure of alveoli in the [19, 20] observed bloat, haemorrhages in the stomach, intestine, and lungs, in both single dose and repeated dose toxicity studies of cypermethrin in rats. In crossbred calves, cypermethrin intoxication produced congestion and/or haemorrhages on the auriculoventricular groove of the heart, lungs, mucosal surface of the intestine, cortex of the kidney, and brain [21]. The histopathological changes in the lung and liver tissues of cypermethrin exposed mice have shown significant changes. Exposure of the mice to cypermethrin through inhalation induces significant time dependent changes in the histopathology of lung as well as liver tissue. Inhalation is a major route of exposure to air born pollutants such as the pesticides [22]. Lungs and liver are the organs which are at highest risk to the environmental pollutants especially the air born chemicals [23]. Cypermethrin has shown the carcinogenic effect in the lung tissues of mice. Exposure to cypermethrin caused a gradual distortion of normal structure of alveoli in the lung. Cypermethrin also interferes with other receptors in the nervous system. The effect is that of long-lasting trains of repetitive impulses in sense organs [24]. Toxicants may also pass into the systemic circulation from the lungs and affect the other body parts especially the liver because the hepatocytes directly receive the chemicals from the blood [22]. Haemorrhages in the liver, kidneys, lungs, ventricles, and endocardium of male dwarf goats treated with high doses (0.8 and 1.6%) of cypermethrin were reported by Khan *et al*. [25].

The most consistent lesions in the liver of animals, of all treatment groups, were varying degrees of degenerative changes and vascular changes. In some areas, the degenerative changes extended up to necrotic changes. In the livers of the group III animals, Kupffer cell hyperplasia was pronounced. These findings were in agreement with those observed in cypermethrin toxicity in rats by [19, 20, 26, 27, 28 and 29]. All had conducted experiments in albino rats, but the dosage and route of administration of cypermethrin were different. In crossbred cow calves, cypermethrin intoxication produced moderate congestion of the sinusoids and hepatic

vasculature, and the hepatocytes showed tiny vacuoles along with increased granularity in the cytoplasm of the liver.

Cypermethrin induces dose dependent changes in the liver as well as in lungs. Cypermethrin also damaged the normal organization of liver tissues causing liver injury shown by necrosis, significant decrease in number of cells, widening of sinusoids and fibrosis. It possesses carcinogenic potential as it induced carcinogenesis in the lung tissues of mice, observed as significant hyperplasia, clumping of cells and necrosis. It also induced pulmonary edema, alveolitis and pulmonary fibrosis by the deposition of collagen. Exposure to cypermethrin for long time resulted in the development of skin tumor in the epidermis of mice. From these findings, we may conclude that cypermethrin and other pyrethroids cause hazardous effects in non-target organisms through inhalation exposure. So, the use of this insecticide should be controlled seriously. Husseina *et al.* [30] reported that Cypermethrin caused different histopathological changes in rat organs including ischemia and pyknosis of the cytoplasm of the neurons in the brain tissue. Long-term exposure to cypermethrin during adulthood is found to induce dopaminergic neurodegeneration in rats, and postnatal exposure enhances the susceptibility of animals to dopaminergic neurodegeneration if rechallenged during adulthood [31]. Cypermethrin induced necrosis, degeneration, and loss of striation in hearts, necrosis of hepatic cells, with degeneration, dilatation of sinusoids and dissociated remark cordons in livers, sloughing off epithelial cell, shrinkage of glomeruli, and necrosis of renal tubules in kidneys of mice [32]. A Study done by Al-Azizz [33] demonstrated also lung toxicity in pigeons upon exposure to different doses of cypermethrin. Because humans are at the top of the food chain, it is probable that detrimental residues of Cypermethrin may remain in the edible portion of the vegetable or plants and thus may affect human health and well-beings. Several reports demonstrate that exposure of Cypermethrin results in some histopathological changes in liver and kidney of human and other mammals that include mononuclear cell infiltration, congestion, enlargement of the veins and sinusoids, necrosis, increased number of Kupffer cells, cytoplasmic vacuolation and degenerative hepatocytes [6]. These are in good agreement with the present results on histopathological changes in the experimental mice.

Recent studies showed that indiscriminate and unregulated uses of insecticides like Cypermethrin in agriculture and public health in Bangladesh have led to drastic effects in many non-target species including man [2, 3]. Since the present treatments of albino mice with Cypermethrin clearly demonstrated decrease in body, liver and kidney weights as well as marked changes in the histopathology of hepatic and renal tissues, it could be possible that prolonged exposure to this insecticide in man may play a significant role in aggravating such diseases as chronic liver and renal failure. In addition, structural changes to hepatic and renal tissues such as haemorrhage, congestion, vacuolation and erosion may also lead to acute liver or kidney damages and/or carcinogenicity of the organs. The present results could thus be exploited as a potential biomarker of common insecticide toxicity in human beings.

CONCLUSIONS

The present findings clearly demonstrate that Cypermethrin is capable of inducing dose-dependent morphometric *i.e*. body, liver and kidney weights and their relative weights as well as histopathological changes in the liver and kidney of the exposed mice. According to these data, it is suggested that systemic insecticide like Cypermethrin exposure might cause hazardous effects, especially at high doses, to man and environment. For field and domestic uses of this insecticide, quantities and mode of usage need to be strictly monitored to minimize the possibility of its exposure to non-target organisms including human beings. This can be achieved through public health education to make people aware of the hazardous effects of this chemical. It is therefore recommended that great precautions are to be taken to minimize the harmful side effects of Carbofuran to the environment, especially to man, animals and agricultural products, aiming at avoiding environmental pollution. Moreover, recommended doses of the insecticide and precautionary measures like wearing of impermeable gloves and masks to reduce the risk of inhalation of spray should be implemented. Due attention also is to be paid for a delayed period of field application of this insecticide to avoid its possible adverse

effects to consumers, who should be warned of the potential risk of Cypermethrin contamination of food and drinking water in the country.

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