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Research Article

Clinico-haematological and histopathological features of the Swiss albino mice *Mus musculus* L. in response to chronic cypermethrin exposure

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Abstract: Cypermethrin is one of the widely used broad-spectrum pyrethroid insecticides because of their high insecticidal activities and lower mammalian toxicity. But indiscriminate and unregulated uses of this insecticide in agriculture and public health in Bangladesh have led to drastic effects on many non-target species including man. Using 0.1 to 0.25 LD_{50} dose equivalents, 25 healthy male mice were divided randomly into five groups *viz*., T0 (control), T1, T2, T3 and T4, each comprising five animals, which received intraperitoneally 0.0, 0.10, 0.15, 0.20, and 0.25 mL cypermethrin kg^{-1} body weight $week^{-1}$ respectively for 28 days. Clinical signs and behavioural manifestations were monitored throughout the experiment, and vital haematological parameters and histopathological features were analyzed in the end. Compared to the control mice, repeated cypermethrin exposure elicited characteristic symptoms like decrease in feed intake, hind limb jerking, laboured breathing, lesions, body weight loss, necrosis, startle response, haemorrhages, eye discharge and oedema in the experimental mice. Owing to cypermethrin mediated oxidative stress on haematological profile, decreases in TEC, DLC, TTC, ESR and Hb concentration, but increases in TLC and lymphocytes, accompanied by lymphocytic infiltrations, congestion of vessels as well as inflammation of various tissues account for the degenerative changes in the hepatic and renal tissues. The present findings imply that cypermethrin is hazardous, which can affect the well-being of the non-target organisms including agricultural, industrial and household human workers who are liable to get cypermethrin toxicosis following its repeated dermal or aerial exposure, leading to anaemia and/or hepatic and renal failure.
Keywords: *Mus musculus*, cypermethrin, clinical signs, haematological profile, histopathology, hepatic and renal tissues.

INTRODUCTION

Since its first synthesis in 1974, cypermethrin has been one of the widely used broad-spectrum pyrethroid insecticides because of their high insecticidal activities and considerably lower mammalian toxicity [1]. It is very effective in the control of many pest insect species in agriculture, animal breeding and households [2-3]. It behaves as a fast-acting neurotoxin and is known to cause free radical-mediated tissue damage in mice [4]. It is moderately persistent in soil with a field degradation half-life (DT_{50}) of 69 days [5] and is classified as Class II category of moderately hazardous chemicals [6].

In spite of their low toxicities, persistence of pyrethroid insecticides in mammalian tissues may be dangerous [7]. Cypermethrin acts as a neurotoxin and suppresses immune system in mammals [3, 8], as manifested by various clinical and/or behavioural abnormalities [9-12]. Apart from this, cypermethrin toxicosis results in severe alterations in haematological profiles of rodents [13-18]. Moreover, several studies have demonstrated that cypermethrin has hepatotoxic [19-22] and nephrotoxic [23-26] potentials in mice and rats. Indiscriminate and unregulated uses of cypermethrin in agriculture and public health in Bangladesh have led to drastic effects on many non-target species including man [27-28]. This led to design the present investigation, the aim of which was to address the effects of sub-acute but chronic cypermethrin exposure on the Swiss albino mice model in terms of clinico-haematological and histopathological endpoints.

MATERIALS AND METHODS

Test animals

Adult 2-3 week-old male Swiss albino mice *Mus musculus* L. (Rodentia: Muridae), each weighing 30±3g were collected from the Animal Rearing Facilities, Jahangirnagar University, Bangladesh. The mice were maintained in steel cages (45cm × 30cm × 30cm) with sawdust bedding for a week to acclimatize to laboratory conditions of 28±4° C, 75±11% RH and 8:16 hrs light: dark regime. To ensure proper hygiene,

sawdust was replaced once a week. Water and poultry feed (National Feed Mills Limited, Gazipur, Bangladesh) were supplied *ad libitum*. In compliance with the standard animal ethical guidelines of the University, 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 to June 2013.

Test chemical

Technical grade cypermethrin (99% purity; *cis: trans* isomeric ratio of 40: 60), trade name Caught-10 EC, manufactured by Tag Rose Chemicals India Ltd, was procured from ACI Formulations Ltd, Dhaka, Bangladesh.

Experimental design

Twenty five healthy male mice were divided randomly into five groups (T0-T4), each comprising five animals. Group T0 served as the control and received distilled water, while for groups T1-T4, 0.10, 0.15, 0.20 and 0.25 $mLkg^{-1}$ body weight of cypermethrin (equivalent to approximately 0.1 to 0.25 LD_{50} doses) were injected intraperitoneally per mouse every week for 28 consecutive days. Clinical signs, haematological profile and histopathological abnormalities were analyzed to determine cypermethrin toxicosis in the experimental mice as follows:

Clinical signs

Clinical signs and behavioural manifestations thereof were recorded everyday by direct observations of some parameters such as feed intake, eye discharge, hind limb jerking, breathing, loss/gain in body weight, oedema, salivation, seizures, startle response and death In addition, internal haemorrhages, gross lesions and necrosis were noted from postmortem specimens (see Histopathology below).

Haematology

At the end of the exposure period of four weeks, blood samples were drawn aseptically from saphenous vein under restrained condition without anaesthesia [29] and were collected in heparinized 70mL microhaematocrit capillary tubes into vials, each containing an anticoagulant of 0.5mL EDTA. The peripheral blood cell indicators assessed were: total erythrocyte (RBC) count (TEC, $\times 10^6$ cells/mm^3), total leucocyte (WBC) count (TLC, $\times 10^3$ cells/mm^3), differential leucocyte count (DLC, which included numbers of basophils, eosinophils, lymphocytes, monocytes and neutrophils per 100 cells), total thrombocyte count (TTC, $\times 10^4$ cells/mm^3), erythrocyte sedimentation rate (ESR, mm/hr) and haemoglobin concentration (Hb, g/dL) were determined according to the standard methods [30], using an automated haematology analyzer (Mythic-22, China).

Histopathology

After end of the exposure period of 28 days, mice in each group were sacrificed by placing them in anaesthetic jar containing cotton wools soaked in chloroform. Complete anaesthesia was considered accomplished when the pedal movements and eyelid reflex disappeared and the animals became recumbent while still breathing. Detailed postmortem examinations were conducted by opening up of belly of the mice, gross lesions and internal haemorrhages were noted, and liver and kidneys were fixed in 10% formalin. For histopathological examinations standard procedures were followed [31]. 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 analyses

Clinical and behavioural symptoms were recorded by direct observations designated as absent (×) or present (√). The mean ±SD values for haematological data were analyzed using SPSS for Windows (version 15.0). Total variation present in a set of data were estimated by one-way analysis of variance (ANOVA), followed by Fisher's least significant difference (LSD) tests [32]. P-values of ≤ 0.05 were regarded as statistically significant.

RESULTS AND DISCUSSION

Clinical manifestations

Control mice remained highly energetic with voracious appetite and furry throughout the experiment. Although cypermethrin did not elicit death, salivation and seizures in the experimental mice, characteristic symptoms such as decrease in the feed intake (data not shown), hind limb jerking, laboured breathing, lesions, loss in body weight (data not shown), necrosis and startle response were manifested by different doses of the insecticide. Notably, haemorrhages, eye discharge and oedema were observed only at higher doses of cypermethrin (Table 1).

Haematological profile

Peripheral blood cell indicators in response to cypermethrin administration in the experimental mice

are presented in Tables 2 and 3. Total erythrocyte count (TEC) reduced significantly (P<0.001) from around 6 million per mm^3 in the control (T0) to about 3 million per mm^3 in the highest dose (T4) over a period of four weeks. Total leucocyte count (TLC), on the other hand, increased significantly from around 16 to 26 thousand per mm^3 (P<0.001) but total thrombocyte count (TTC) decreased significantly from about 930 to 730 thousand per mm^3 (P<0.001). Other two vital blood parameters *viz*., erythrocyte sedimentation rate (ESR) and haemoglobin (Hb) concentration were also found to decrease significantly from about 4 to 3 mm/hr and from around 16 to 11 g/dL, respectively (P<0.001). All components of the differential leucocyte count (DLC) were also found to reduce significantly (P<0.001) except lymphocytes, which increased significantly (P<0.001) from 74% to over 90% in a dose-dependent manner (Table 3).. So, in a nut-shell, majority of the haematological parameters were found to decrease, whereas WBC and lymphocytes were increased by the repeated cypermethrin exposure in *M. musculus*, which correspond to the adverse clinical manifestations such as laboured breathing, lesions, haemorrhage and oedema.

Table 1: Cypermethrin-exposed clinical manifestation in the male albino mice *M. musculus*

Clinical and behavioural signs	T0	T1	T2	T3	T4
Death	×	×	×	×	×
Decrease in feed intake	×	√	√	√	√
Eye discharge	×	×	×	×	√
Haemorrhage	×	×	×	√	√
Hind limb jerking	×	√	√	√	√
Laboured breathing	×	√	√	√	√
Lesions (internal organs)	×	√	√	√	√
Loss in body weight	×	√	√	√	√
Necrosis	×	√	√	√	√
Oedema	×	×	×	×	√
Salivation	×	×	×	×	×
Seizures	×	×	×	×	×
Startle response	×	√	√	√	√

T0, T1, T2, T3 and T4 refer to 0.00 µL (control), 0.10mL, 0.15mL, 0.20mL and 0.25mL cypermethrin kg^{-1} body weight of mice, respectively; ×= absent; √= present.

Table 2: The peripheral blood cell indicators affected by cypermethrin exposure in the male albino mice *M. musculus*

Haematological Parameters	Treatment Groups					F-values
	T0	T1	T2	T3	T4	
TEC ($\times 10^6$ cells/mm^3)	5.59 ± 0.24^a	3.74 ± 0.21^b	3.93 ± 0.11^c	2.71 ± 0.32^d	2.85 ± 0.08^e	149.84***
TLC ($\times 10^3$ cells/mm^3)	15.56 ± 0.38^a	18.51± 0.27a	21.53 ± 0.20^b	21.50 ± 0.30^c	25.80 ± 0.03^a	283.76***
TTC ($\times 10^4$ cells/mm^3)	93.16 ± 0.48^a	73.37 ± 0.51^b	72.80 ± 0.22^c	73.48 ± 0.30^d	72.92 ± 0.91^e	1384.94***
ESR (mm/hr)	3.72 ± 0.22^a	4.59 ± 0.16^b	4.40 ± 0.22^c	3.30 ± 0.12^d	2.89 ± 0.11^e	85.84***
Hb concentration (g/dL)	15.80 ± 0.33^a	12.26 ± 0.13^b	12.52 ± 0.24^c	11.54 ± 0.25^d	10.56 ± 0.30^e	290.68***

Values are mean ±SD; TEC= total erythrocyte (RBC) count; TLC= total leucocyte (WBC) count; TTC= total thromocyte (platelet) count; ESR= erythrocyte sedimentation rate; Hb= haemoglobin; T0, T1, T2, T3 and T4 refer to 0.00 µL (control), 0.10mL, 0.15mL, 0.20mL and 0.25mL cypermethrin kg^{-1} body weight of mice, respectively; F-values are at 4, 20 df; ***= P<0.001; superscripts in dissimilar letters in each row differ significantly by LSD tests at P<0.05.

Table 3: Differential leucocyte count (DLC) influenced by cypermethrin exposure in the male albino mice *M. musculus*

Differential leucocyte count (DLC)	Treatment Groups					F-values
	T0	T1	T2	T3	T4	
Basophils (%)	1.24± 0.25[a]	0.68± 0.20[b]	0.76 ± 0.18[c]	0.94 ± 0.17[a]	0.98 ± 0.18[a]	5.99*
Eosinophils (%)	1.06± 0.09[a]	1.06± 0.09[a]	1.16± 0.21[a]	1.24± 0.15[b]	0.78± 0.08[a]	9.54*
Lymphocytes (%)	74.00± 0.38[a]	84.25± 0.24[b]	84.90± 0.18[c]	85.05± 0.21[d]	90.38± 0.26[e]	2649.69***
Monocytes (%)	4.44± 0.36[a]	1.18± 0.15[b]	1.24± 0.05[c]	1.10± 0.34[d]	0.84± 0.23[e]	176.62***
Neutrophils (%)	17.66± 0.22[a]	13.40± 0.32[b]	12.76± 0.48[c]	12.22± 0.08[d]	8.67± 0.10[e]	808.49***

Values are mean ±SD of 5 replicates; T0, T1, T2, T3 and T4 refer to 0.00 µL (control), 0.10mL, 0.15mL, 0.20mL and 0.25mL cypermethrin kg^{-1} body weight of mice, respectively; F-values are at 4, 20 df; *= P<0.05; ***= P<0.001; superscripts in dissimilar letters in each row differ significantly by LSD tests at P<0.05.

Histopathology of liver

In the untreated control mice, the transverse section of liver showed usual structures of the hepatocytes with normal central vein, Kupffer cells and sinusoids (**Plate** 1.C). Whereas in 0.1 $mLkg^{-1}$ treatment group (T1), shrunken portal vein, haemosiderin in hepatocytes, Kupffer and epithelial cells, binucleated hepatocytes, fibrous central and portal veins; haemorrhage and dilated sinusoids were salient features (**Plate** 1.1). In 0.15 $mLkg^{-1}$ treatment group (T2), haemorrhage accompanied by dilated sinusoid, degenerated hepatocytes, congested central and portal veins, cell debris and vacuolation were common (**Plate** 1.2). In the next higher dose T3, necrotic hepatocytes and congested portal vein, fibre-deposited central vein and inflammatory cell infiltration (**Plate** 1.3) and in T4, haemorrhage and inflammatory cell infiltration, increased number of mononuclear cells, fibre-deposited portal vein accompanied by cell debris, enucleated cells and necrotic hepatocytes were diagnosed (**Plate** 1.4). These histopathological changes in the hepatic tissues clearly demonstrate toxicosis of the pyrethroid insecticide in the experimental mice.

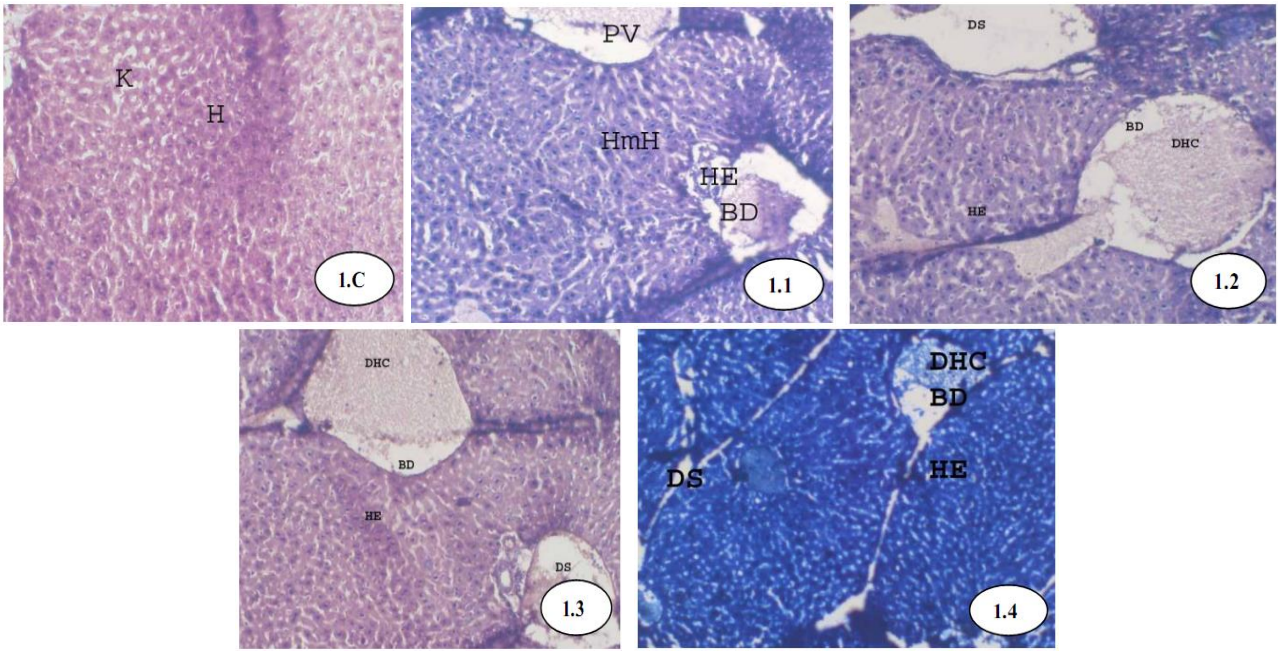

Plate 1 Transverse sections of liver of cypermethrin treated mice after 28 days. Slides for the control (T0) and treatment groups (T1-T4) are designated by 1.C, 1.1, 1.2, 1.3 and 1.4, respectively (200×).
Abbreviations: BD= bile duct; DHC= degenerated hepatocytes cells; DS= dilated sinusoid; H= hepatocytes;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

Histopathology of kidney

The transverse section of the kidney cells in untreated mice revealed normal arrangements of Bowman's capsule, glomerulus, urinary pulp, distal and proximal convoluted tubules and podocytes (**Plate** 2.C). In contrast, various doses of cypermethrin treatments

induced the following exposure-dependent symptoms in the experimental mice: In 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 (**Plate** 2.1). In 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 were noticed (**Plate** 2.2). While 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, vacuolated tubule and degenerated Bowman's capsule were salient features in T3 (**Plate** 2.3). In 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, shrinkage of proximal tubule, increased number of podocytes and haemorrhage were common (**Plate** 2.4)

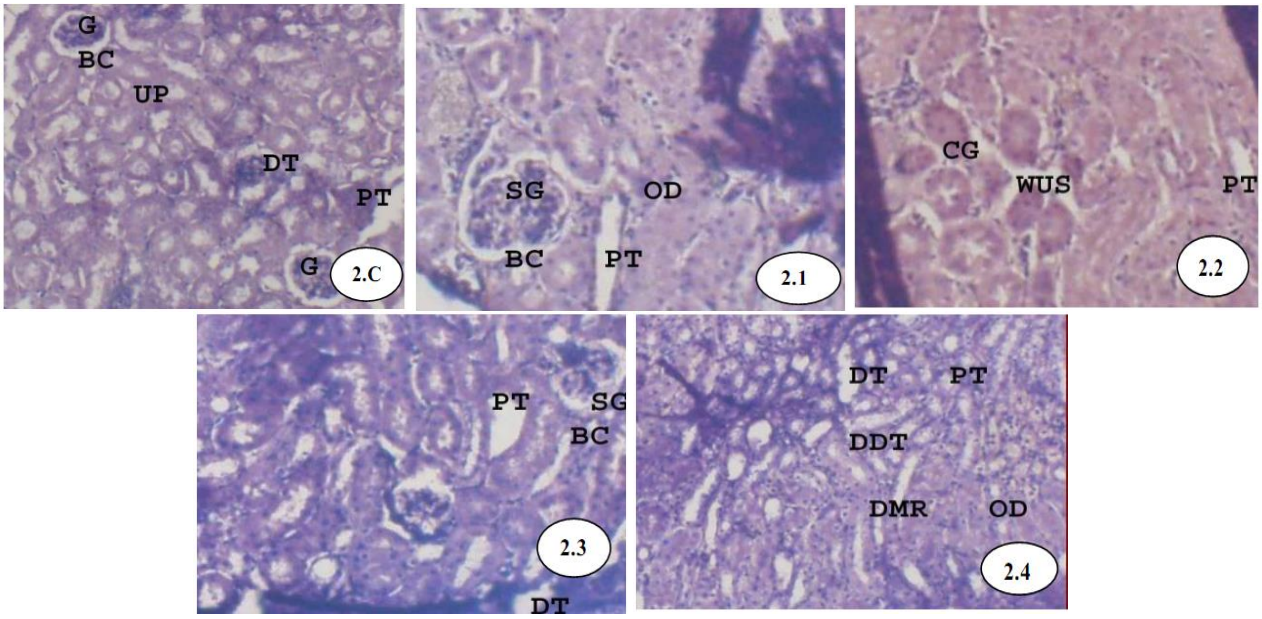

Plate 5 Transverse sections of kidney of cypermethrin treated mice after 28 days. Slides for the control (T0) and treatment groups (T1-T4) are designated by 2.C, 2.1, 2.2, 2.3 and 2.4, respectively (200×).
Abbreviations: BC= Bowman's capsule; CG= congested glomerulus; DDT= dilated distal tubule; DMR= dilated medullary ray; DT= dilated tubule; G= glomerulus; OD= oedema; PT= proximal convoluted tubule; SG= shrunken glomerulus; UP= urinary pulp; VT= vacuolated tubule; WUS= widened urinary space.

Cypermethrin toxicosis elicits a host of clinical and behavioural changes in mice and rats. Thus oral and inhalation exposure of this insecticide in rodents were indicative of an action on the central nervous system that consisted of salivation, ataxia, splayed gait and hyper-excitability to auditory stimuli, tremors, convulsions and choreoathetosis [33]. An oral dose of 5 $mgkg^{-1}day^{-1}$ of cypermethrin for 30 days in female albino rats *Rattus norvegicus* induced intermittent diarrhoea, decreased feed intake, and thick eye discharge, whereas a higher dose of 20 $mgkg^{-1}day^{-1}$ displayed mild to moderate toxicosis with diarrhoea, decreased feed intake, loss of body weight, dyspnoea, ataxia, eye discharge, salivation and death of two rats after displaying lack of coordination and signs of tremors [9]. In addition, nervous signs, gross lesions, bloat, congestion of lungs, heart, brain, pulmonary haemorrhage and degenerative changes in the liver and kidneys; loss of body weight, hind limb extensor tone followed by recovery, burrowing behaviour, abnormal jerking of the hind limbs, increased startle response, salivation, somnolence and seizures, laboured breathing, gasping and death at higher doses were recorded in Sprague Dawley rats [10]. Loss of body weight, soft faeces, frequent diarrhoea and occasional death were the most prominent clinical signs of cypermethrin poisoning in Wister rats [11]. In contrast, oral administration of cypermethrin at 103.72 $mgkg^{-1}$ body weight had no significant changes in behaviour of Wister rats [12]. The aforesaid findings corroborate nicely with the present results in terms of decreased feed intake, limb jerking, laboured breathing, lesions on various organs, loss in body weight, necrosis and startle response, haemorrhages, eye discharge and eodema, although the used doses did not elicit death, salivation and seizures in the experimental mice.

Cypermethrin-induced alterations in blood profiles in rodents have been shown to be dose-, species- as well as mode of administration-dependent.

In ~200g rats, for example, oral cypermethrin of 40, 80 and 120 $mgkg^{-1}$ body weight for 21 days resulted reduction in TEC, TLC, DLC, PCV (packed cell volume) and Hb concentration [13]. Whereas oral cypermethrin of $25mgkg^{-1}$ body weight on male rats for 90 days resulted in significant decrease in body weight gain and significant reduction in PCV and WBC [14]. Chronic use of cypermethrin led to a series of haematological, biochemical, reproductive and pathological changes including damages of hepatic and renal tissues in rodents, sheep, rabbit, chicken and fishes [15]. In male adult Swiss albino mice, cypermethrin at 15 $mgkg^{-1}$ body weight resulted in TLC decrease from 9.3 to 9.0 $\times 10^3/mm^3$, lymphocytes from 78.1 to 60.0%; neutrophils from 17.9 to 15.0%; monocytes from 4.6 to 3.0% but no change for eosinophils [16]. Again, albino mice fed 32.26 $mgkg^{-1}$ body weight to alpha cypermethrin 8 $hrsday^{-1}$ for 13 wks led significant decrease in RBC, PCV and Hb concentration but with insignificant increase in WBC, leading to anaemia [17]. While oral administration of both acute (300 $mgkg^{-1}$ body weight for a day) and sub-chronic (10.7 $mgkg^{-1}$ body weight for 7, 14, 21 and 28 days) doses of cypermethrin gave rise to significant decline in TEC and Hb concentration but insignificant decrease in PCV, ESR, TLC and DLC [18]. The present results are in well agreement with those of [13, 17 and 18] but differed from those of [14 and 16] because both TLC and lymphocytes were found to increase, leading to gross lesions, necrosis and eodema in our treated mice.

Apart from cypermethrin, however, effects of organochlorine and organophosphate insecticides and some other pyrethroid insecticides on rodent blood parameters have be assessed. Similar to this report, endosulfan [34], chlorpyrifos [35], deltamethrin [36] and lambda-cyhalothrin [37] declined RBC count and Hb content but elevated WBC. In contrast, however, there are reports where chlorpyrifos [38] and three pyrethroids *viz*., 0.02% imiprothrin, 0.03% d-phenothrin and 0.01% d-transallethrin [39] increased RBC and Hb, but decreased WBC in the experimental rodents.

Oral administration of cypermethrin at 60, 150, 300 $mgkg^{-1}$ body weight for 28 days in rats induced vacuolar degeneration, enlargement of sinusoids, degeneration of hepatic cords and hepatocytes, vacuole formation, increase in Kupffer cells and significant increase in apoptotic index of liver [19]. Rats subjected to daily administration of cypermethrin (12 mg/kg^{-1} body weight) doses for 30 days by gavages was found to induce histopathological damage and genomic DNA fragmentation, leading to liver and kidney injuries [20]. Wister rats exposed to acute and sub-acute doses of 0.1 LD_{50} cypermethrin for 1, 7, 14, 21 and 28 days resulted in hepatocytes vacuolization, nuclear polymorphism, eccentric nuclei, karyolysis, karyorrhexis and sinusoidal dilation [21]. Swiss albino mice exposed to 0.5% cypermethrin in inhalation chamber showed time-dependent changes in lung and liver tissues, causing liver injury due to necrosis, significant reduction in hepatocytes, widening of sinusoids and fibrosis [22]. The present results lend support to the above findings with respect to cypermethrin poisoning in hepatic tissues in *M. musculus* under study.

Adult albino mice exposed to dermal application of cypermethrin at 30 $mgkg^{-1}$ body weight daily for 6 weeks resulted in congestion of vessels and marked lymphocytic infiltration in the kidneys [23]. Whereas 0.1 LD_{50} cypermethrin in albino rats for 6 weeks showed many histopathological alterations in kidney cortex, for example, renal tubules lost their characteristics, degeneration of glomeruli, congestion of renal blood vessels, and intertubular spaces were infiltrated by inflammatory leucocytes [25]. In addition, a number of studies revealed simultaneous damages in both hepatic and renal tissues in the cypermethrin treated rats and mice. Thus oral doses of 5 and 20 $mgkg^{-1}day^{-1}$ for 30 days in female albino rats *Rattus norvegicus* induced disorganization of hepatic laminae, increase in sinusoids, and necrosis of hepatocytes, in addition to hemorrhage and sloughing off renal epithelial cell in the convoluted tubules, shrinkage of glomeruli, and necrosis of renal tubules [9]. Further cypermethrin at 5, 7.5 and 10 $mlkg^{-1}$ body weight resulted in enlarged sinusoidal spaces, vacuoles in hepatocytes, leucocytic infiltration, congestion of blood vessels with hemorrhage, shrinkage of glomeruli, necrosis of renal tubules, dilation of blood vessels, severe congestion of renal glomeruli and hemorrhage in renal tissues [24], and prolonged chronic doses of cypermethrin at $10mgkg^{-1}$ body weight day^{-1} for 45 and 60 days produced necrosis of hepatocytes, cytoplasmic vacuolation, bile duct hyperplasia, mononuclear cellular infiltration, glomerular atrophy accompanied by necrosis of tubular epithelium cells, cytoplasmic vacuolation and cellular infiltration in the Swiss albino mice [26. Aside from these reports, degenerative changes induced by chlorpyrifos on hepatic tissues [40-41], those by cypermethrin on ovarian tissues [42] and those by permethrin on hepatic and renal tissues [43] in rats have been reported. Other than liver and kidney tissues, however, cypermethrin-induced histopathological changes in brain tissues in female rats [44] and testicular tissues in mice [45] have also been documented. In contrast, however, no noticeable changes in the behaviour and brain and colon tissues, accompanied by mild histopathological changes in liver and kidneys at the highest combined doses of endosulfan and cypermethrin (207.50 $mgkg^{-1}$ body weight) were reported in Wister rats [12]. The present histopathological observations corroborate with the findings of [9, 20, 24-26] who observed cypermethrin-mediated severe degenerative changes in the hepatic and renal tissues of rats and mice as in our study. Taking these findings in consideration, it is obvious that cypermethrin and other such synthetic pyrethroids cause hazardous effects on non-target organisms including

humans through inhalation and direct contact. Therefore, serious efforts and awareness are required to monitor and reduce the insecticide induced health hazards in third world countries like Bangladesh.

CONCLUSIONS

The observed histopathological changes in the hepatic and renal tissues may be explained in terms of cypermethrin induced oxidative stress on haematological profiles, accompanied by lymphocytic infiltrations, congestion of vessels as well as inflammation of various tissues which account for the degenerative changes in liver and kidneys in the experimental mice. The present findings therefore imply that the insecticide is hazardous, which can affect the well-being of the non-target organisms including agricultural, industrial and household human workers who are liable to get cypermethrin toxicosis following its repeated dermal or aerial exposure, leading to anaemia and/or hepatic and renal failure. Limited and specific applications of the insecticide may therefore be carried out only at recommended doses. However, further studies are needed to explore the mechanism(s) underlying the role of the major metabolite(s) of the pyrethroid insecticide under study.

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