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Effects of Cyfluthrin on Biochemical and Histopathological Alterations in Liver of *Swiss Albino* Mice

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ABSTRACT

In recent past pesticide poisoning and related diseases have gained considerable attention. Cyfluthrin is a type II synthetic pyrethroid pesticide. Its versatility makes it a useful active ingredient in the manufacturing of many pesticides. In the present study cyfluthrin has been evaluated for its acute hepatotoxicity in *Swiss albino* mice. For acute hepatotoxicity acute low (0.32 g/kg b.wt), acute medium (0.64 g/kg b.wt) and acute high (1.28 g/kg b.wt) doses of cyfluthrin were orally administered once daily for 30 consecutive days and mice were necropsied after 30 days of treatment. Biochemical estimations of ALP, SGPT, and SGOT together with histopathological studies were carried out. Acute treatment of cyfluthrin for 30 days resulted in significant increase in liver weight ($p<0.05$). Significant increase in activity of ALP, SGPT and SGOT ($p<0.001$) levels were also observed. A variety of pathological lesions in liver were observed in acute treatment. In conclusion present results suggest that cyfluthrin is hepatotoxic to *Swiss albino* mice.

KEY WORDS: Hepatotoxicity; Liver; Histopathology; ALP; SGOT; SGPT, Pyrethroid

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INTRODUCTION

Pyrethroid insecticides have achieved widespread agricultural and environmental applications due to their strong insecticidal properties and they are one of the most frequently used classes of pesticides as they are safer than organophosphates, organochlorines and carbamates. The mighty role of pesticides to farmers surely merits appreciation but their widespread use is associated with serious health hazards to various non-target organisms[1,2]. Pyrethroids are widely used as pest control agents in a wide array of indoor and outdoor applications, including medicinal, veterinary and agricultural scenario and are the synthetic derivatives of natural pyrethrins with greater potency and environmental stability[3]. Because of their low acute human toxicity, sold under the trade names Baygon and Solfac pyrethroids are widely used to control insects like ants, silverfishes, cockroaches, grain beetles, flies and mosquitoes in and around homes[4] .Recently, pyrethroids account for about 25% of the total pesticidal market[5,6].Most synthetic pyrethroids are safer than organophosphates, organochlorines and carbamates, although some are toxic to the nervous system still many different pyrethroids are being used today. Pyethroids are subdivided into two groups according to their chemical structures – type-I pyrethroids are devoid of a 'cyano'moiety at the α-position while type-II pyrethroids have α-cyano moiety. Action of these two classes is primarily on the sodium channels of nerve. While type-I produces repetitive neuronal discharge and prolonged negative after potential, type-II pyrethroids produce even longer delay in sodium channel inactivation leading to persistent depolarization of the nerve membrane[7] .Cyfluthrin [Cyano (4-fluoro-3-phenoxyphenyl) methyl3-(2, 2-dichloroethenyl)-2, 2dimethylcyclopropanecarboxylate] a type II synthetic pyrethroid is the active ingredient of non systemic insecticides primarily used for the control of chewing and sucking insects and also in public health situations[8] .This compound, alike other similar synthetic pyrethroids, is a neurotoxin. Early studies have demonstrated the neurotoxic, genotoxic, immunotoxic, reproductive, and endocrine effects of SPs in mammalian and non-mammalian species[9, 10, 11, 12]. Furthermore, despite having teratogenic effects, there is no evidence of mutagenic, carcinogenic and genotoxic effects[13]. In addition to nervous system effects, moderate eye or skin irritation, and paresthesia , allergic skin reactions and mucous membrane irritation of the nose, throat and upper respiratory tract, have also been reported[14] . Still more researches are needed to evaluate the toxic effects of cyfluthrin. Hence the present work has been planned to evaluate its hepatotoxic potential in *Swiss albino* mice.

MATERIALS AND METHODS

Chemicals

Solfac 050 EW, a formulated product containing 5% w/w cyfluthrin was used for the study.

Experimental animal

Swiss albino mice originally obtained from the Indian Veterinary Research Institute, Bareilly (U.P.) were bred in an animal house under controlled conditions of temperature (25±3 ^{o}C) and light (12 hours light and 12 hours darkness). The animals were given pelleted standard mice feed obtained from the Hindustan Lever Limited, Chandigarh, India. Tap water was provided *ad libitum*.

Mode of administration

To study the effect of acute toxicity of cyfluthrin in male mice, the required amount of cyfluthrin dissolved in distilled water was administered orally once daily with the help of a micropipette of 10 L capacity.

Experimental design

To study the effect of acute toxicity of cyfluthrin, 6 animals each of treated and control groups were sacrificed simultaneously at 30 days after treatment with low, medium and high dose. Blood and serum samples were collected for biochemical studies. Blood was collected by making cut on vein of tail using a clean and sharp blade. Liver was removed quickly, weighed and processed for biochemical and histopthological studies. For all autopsies mice were sacrificed by cervical dislocation. The liver weight was also recorded.

Histological examination

Liver removed from the mice was fixed in Bouin's solution , dehydrated in alcohol series, and embedded in mixture of paraffin and bees wax (3:1) for histological procedure[15]. The sections were examined for histopathological changes after staining with hematoxylene and eosin.

Biochemical parameters

Serum alkaline phosphatase (ALP) activity was measured by using commercially accessible kits (Sigma Pvt. Ltd.) and optical density was measured at 405 nm. The serum glutamate oxaloacetate transaminase (SGOT) and the serum glutamate pyruvate transaminase (SGPT) activities were estimated according to International Federation of Clinical Chemistry (IFCC) method.

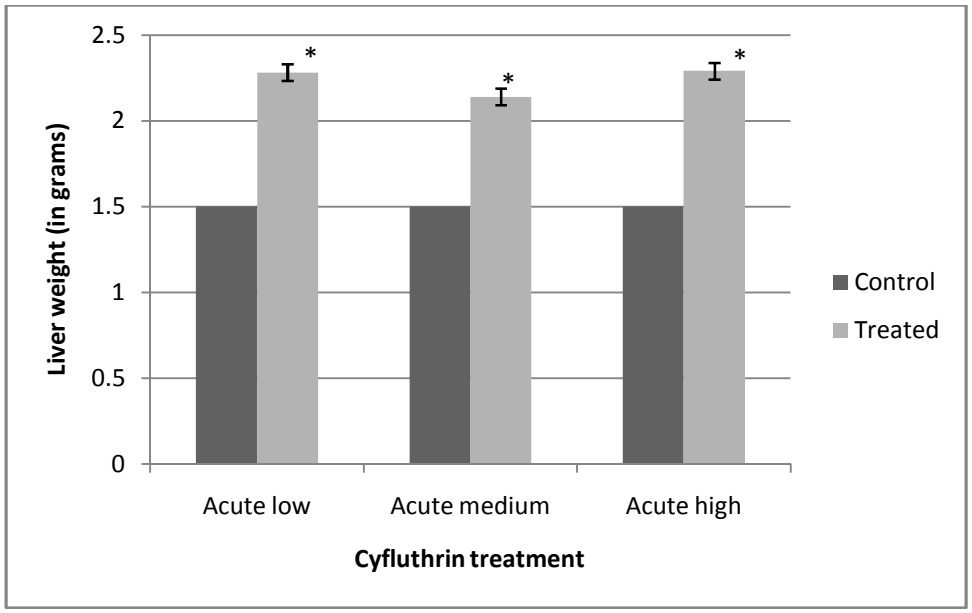
Statistical analysis

The results obtained in the present study were expressed as mean ± SEM (standard error of mean). The statistical differences between various groups were analysed by the students's *t* -test and the significance was observed at the $p>0.05$, $p<0.05$ and $p<0.001$ level.

RESULTS

Effect of cyfluthrin on liver weight

Liver weights increased at all the post treatment intervals in dose dependent manner with respect to acute low, medium and high dose of cyfluthrin (Fig. 1).



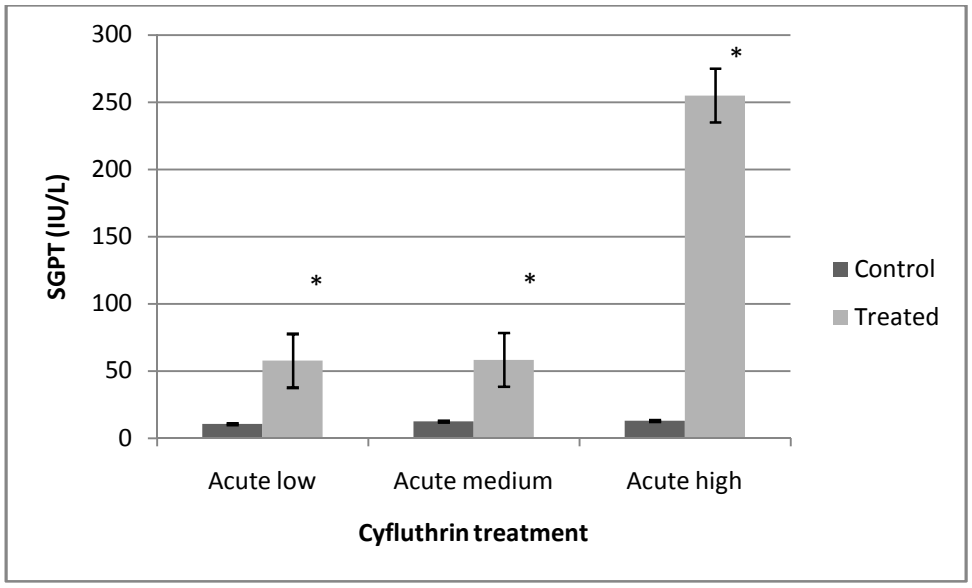
*All values are significant at P<0.05(P='t' test).

Fig.1. Effect of acute (low, medium, high) dose of cyfluthrin on liver weight of *Swiss albino* mice

Biochemical observations after acute treatment with low, medium and high dose of cyfluthrin

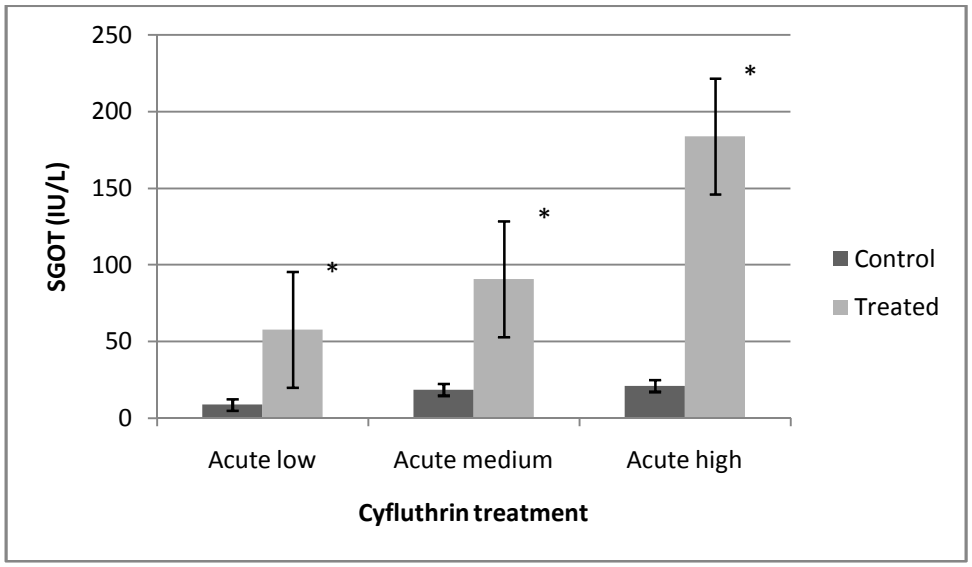
After 30 days of acute treatment with low, medium and high dose of cyfluthrin levels of SGPT, SGOT and ALP activities were found to be increased in dose dependent manner as compared to that

of control. Maximum increase in SGPT and SGOT activities level was found at high dose (Fig. 2, 3, 4).



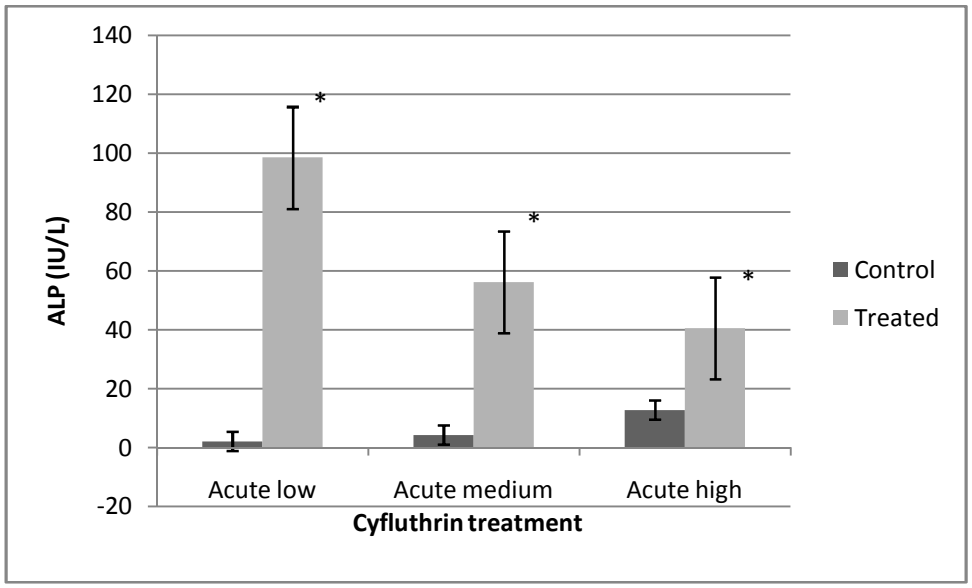
*All values are significant at P<0.001(P='t' test)

Fig. 2. Effect of acute (low, medium and high) dose of cyfluthrin on SGPT in serum of *Swiss albino* mice.



* All values are significant at P<0.001(P='t' test).

Fig. 3: Effect of acute (low, medium and high) dose of cyfluthrin on SGOT in serum of *Swiss albino* mice.



*All values are significant at P<0.001(P='t' test).

Fig. 4. Effect of acute (low, medium and high) dose of cyfluthrin on ALP in serum of Swiss albino mice.

Histopathological observations after acute treatment with low, medium and high dose of cyfluthrin

After 30 days of acute treatment with low dose 0.32 g/kg b.wt histopathological examination in liver revealed nucleus to be normal but with congested sinusoidal spaces (Fig. 5). Nuclear hypertrophy and binucleated hepatocytes were observed at some places. Treatment with medium dose caused foamy appearance of hepatocytes, condensed nuclei, anucleated hepatocytes and enlarged cell sizes with pycnotic nuclei (Fig. 6). High dose treated liver showed increased sinusoidal spaces, condensed nuclei and enlarged hepatocytes with hydropic degeneration together with cytoplasmic vacuolization (Fig. 7).

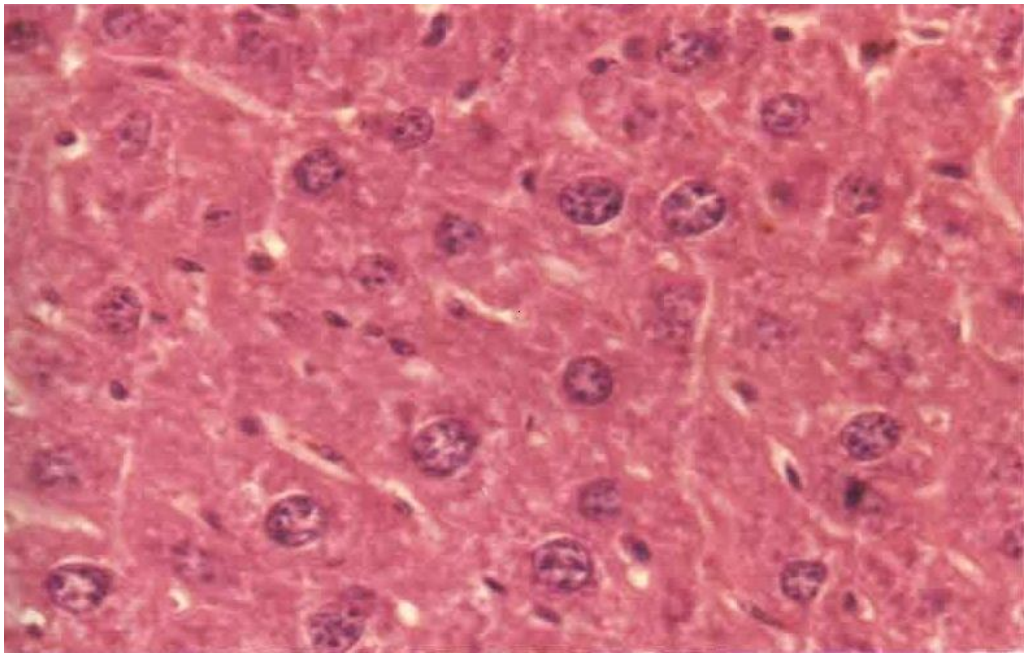


Fig. 5: Photomicrograph of a section of liver showing normal hepatocytes with usual arrangements of hepatic cords and sinusoids (Control) 400X

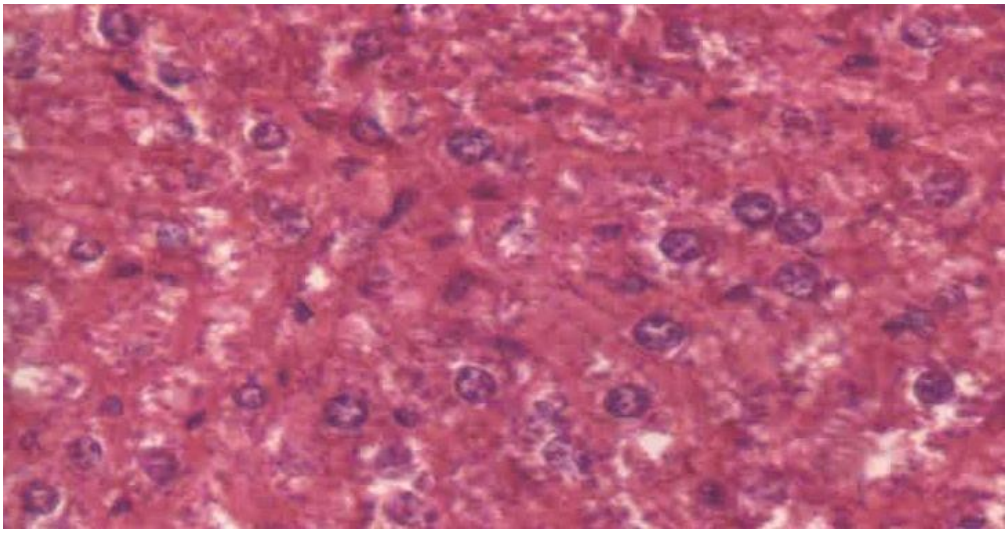


Figure 6: Photomicrograph of a section of liver showing anucleated and necrotic hepatocytes (acute 30 days low dose) 400X

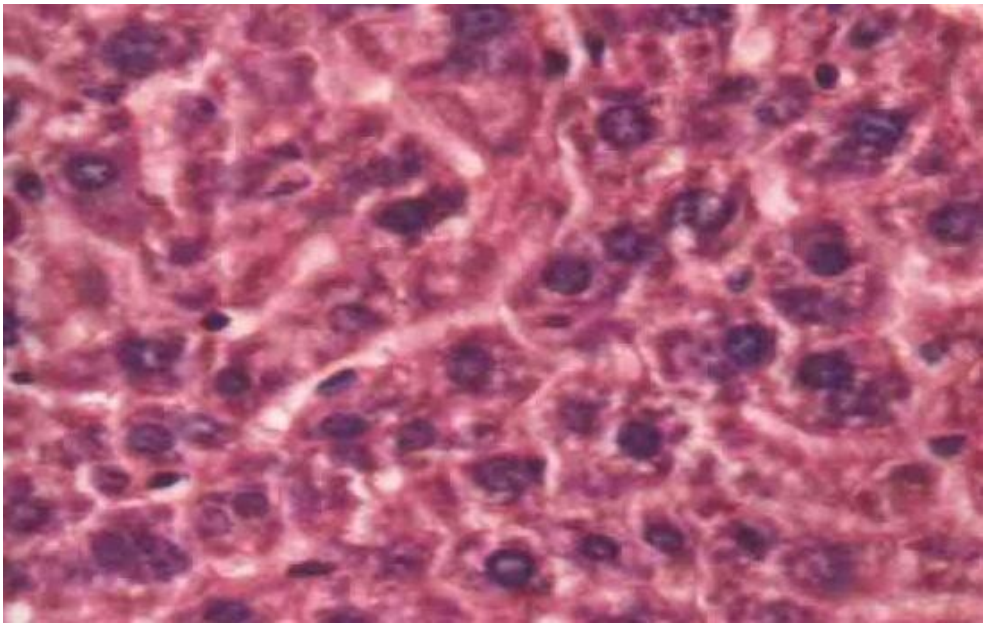


Figure 7: Photomicrograph of a section of liver showing nuclear hypertrophy and hydropic degeneration (acute 30 days medium dose) 400X

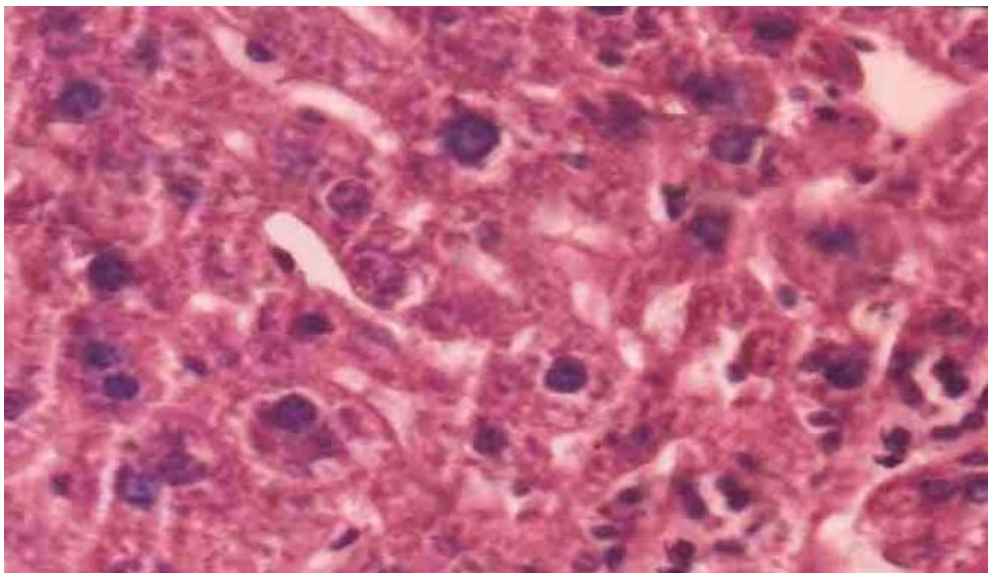


Figure 8: Photomicrograph of a section of liver showing nuclear hypertrophy and hydropic degeneration, enlarged hepatocytes increased sinusoidal spaces, pycnotic nuclei are also seen (acute 30 days high dose) 400X

DISCUSSION

Man in his living environment ingests, inhales and absorbs many chemicals that can impose stress on numerous biochemical mechanisms. Chemical induced liver injury resulting from the acute

exposures can produce marked alterations of the entire liver structure with degenerative and proliferative changes.

In the present investigation significant increase in liver weight was observed after acute low, medium and high dose treatment with cyfluthrin. Findings of present investigation agree with the studies of other workers with different pesticides on mammals as well as on birds. Changes in liver weight after cyfluthrin intoxication are frequently associated with hydropic changes of hepatocytes and hypertrophy of hepatocytes[16]. Significant increase in liver weight is also an indicator of hepatocellular proliferation under stress of beta-cyfluthrin and may have increased due to excessive cell division. Increase in liver weight after pesticide intoxication could be due to adaptive mechanism of liver [17, 18, 19, 20].

Functional importance of ALP in animals has been demonstrated by many workers. The enzyme is associated to check the possibility of bone disease or liver disease. In acute low treatment the increase in the activity of the ALP probably indicates that pesticide has a stimulatory effect on cell growth and proliferation. Other reason for the increase in the enzymatic activity may be due to improper functioning of the liver, bile ducts or gallbladder system [21]. Acute intoxication with cyfluthrin low, medium and high doses caused a very highly significant increase in ALP activity in the hepatic tissue of treated *Swiss albino* mice in the present undertaken investigation which may be due to increase in liver weight or it may be due to hepatocyte damage (necrosis) as evident in the present study.

Dose dependent increase in SGPT and SGOT activity observed in the present study may be due to injury to parenchymal cells, the enzyme (GOT) and (GPT) gain entrance into the serum and consequently their concentration rises markedly in hepato-cellular diseases. The results of undertaken study revealed that metabolism in liver is affected by cyfluthrin administration. Various types of dose dependent degenerative changes noticed in the nuclei of hepatocytes such changes observed are common in the animals exposed to various types of pesticides. Our results corroborate with the findings of [22] who also observed marked hepatotoxicity after Beta-cyfluthrin acute and sub acute treatment in form of altered hepatosomatic index and histochemical alterations. Degenerative changes and inflammatory infilteration in liver and kidney of albino rats after treatment with high dose of α-cypermethrin has been reported [23]. Toxicological studies of deltamehtrin, alphacypermethrin and choloropyrifos [24, 25] on albino rats are also reported to cause paranchymatous degenerative changes in the hepatocytes as in our study.

To conclude, the exposure of *Swiss albino* mice to different doses of cyfluthrin caused alterations to biochemical indices as well as histopathology of the liver. Hence the pesticide is toxic at even low acute dose of 0.32 g/kg b.wt.

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