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Effect of Acute Dose and Subchronic Dose of Cyfluthrin (Synthetic Pyrethroid –Solfac 050EW) on Serum Phosphatase Level of Swiss Albino Mice

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ABSTRACT

Higher tropical level of the ecosystem may be affected directly and indirectly by the continuous and persistence use of synthetic pyrethroids. Human health may also be adversely affected by the accidental exposure of these synthethic pyrethroid at the workplace and their presence in the environment. Cyfluthrin is a broad spectrum synthetic type II pyrethroid insecticide and acaricide which is used in public health situations, and for domestic pests.Toxic effect of sub chronic and acute dose exposure of a synthetic pyrethroid, Cyfluthrin under the trade name Solfac 050EW, on the serum phosphatase, i.e. Acid phosphatase(ACP) content and Alkaline phosphate(ALP), were observed in this study. Oral administration of sub-chronic dose of Cyfluthrin (Solfac 050 EW) for 15 days and 30 days showed significant decrease in Acid phosphatase(ACP) content and Alkaline phosphate(ALP) content as compared to control group. For acute studies (double the recommended dose), after oral administration of Cyfluthrin after 3 hrs, 24 hrs and 15 days of the treatment, a highly significant decrease in content of ACP and ALP was observed as compared to control group. The present study suggests that Cyfluthrin (Solfac 050EW) shows significant toxic effects on serum phosphatase level of Swiss Albino Mice indicating the effect on metabolic activity.

Keywords: Synthetic Pyrethroid, ALP, ACP, Solfac 050 EW

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INTRODUCTION

Cyfluthrin is a synthetic type-2 pyrethroid insecticide. The original compound was isolated from the flower of chrysanthemum.[1] The insecticide properties of pyrethrins are obtained from ketoalcoholic esters of Chrysanthemic and Pyrethroic acids [2].These are strongly lipophilic and rapidly penetrate many insects and paralyze their nervous system [3]. Due to its versatility it has become a useful active ingredient in the manufacture of many insecticides[4].Pyrethrins affect the nervous system of insects by causing multiple action potentials in nerve cell by delaying the closing of an ion channel [5].

A nonsystemic synthetic pyrethroid, Cyfluthrin is used in the control of chewing and sucking insects. Although primarily used in agriculture, Cyfluthrin is also used in public health situations, and for domestic pests. Early reports have shown that Cyfluthrin exhibits low toxicity to mammals due to rapid metabolism and excretion; however laboratory animals exposed to very high dosages of the compound had exhibited the same toxic effect observed in insects [6]. Although Cyfluthrin is an irritant to human skin, especially facial skin, it is not considered to have high dermal toxicity[7]. Zang et al[8] reported that cyfluthrin and β-cyfluthrin are moderate antiandrogenic chemicals and they elicit antiandrogenic effects at least partly by antagonizing Androgen Receptor. Cyfluthrin triggers inflammatory reaction in the kidneys of female rats, and an irreversible damage to the sciatic nerves.[9]

Some of these enzymes, like aminotransferase and phosphatase group, can constitute good molecular bioindicators for oxidative stress and can also indicate the magnitude of response in populations chronically exposed to contaminants such as metals and other xenobiotics [10]. These enzymes are involved in a variety of metabolic activities such as permeability, growth and cell differentiation, protein synthesis, absorption and transport of nutrients, gonadal maturation, and steroidogenesis [11].Two important phosphatases are Acid Phosphatase (ACP) and Alkaline phosphatase (ALP), both differing in their sub cellular distribution. ALP activity was found to be highly concentrated in plasma membrane enriched fraction, where as ACP is associated with lysosomes. These enzymes are found virtually in all tissues of vertebrates, but show in general, high activity in the liver, a major organ for xenobiotics uptake and enzymatic transformation of ROS [12] and eventually leak to blood. Acid Phosphatase(ACP E.C.3.1.3.2) is hydrolytic in nature and helps in the autolysis of the cell after its death[13].It could be used as indicator for studying cell mortality due to intoxication(Mandal ,2010).Alkaline phosphatase (ALP E.C.3.1.3.1)is also responsible for transphosphorylation. The study of the activity levels of ALP and ACP was carried out to measure the effect on metabolic activity by observing variation in enzyme levels after exposure to acute level of Cyfluthrin (Solfac 050 EW).

MATERIALS AND METHODS

Swiss Albino mice were housed in an air cooled room and a colony was maintained. Mice were fed on standard mice feed (mixed seeds and pellets) and water was given *ad libitum*. For all the present studies adult male mice (4-6 weeks old) were used. Animals were divided into two groups:

Group I (Control I): Animals were given distilled water as vehicle orally.

Group II (Acute): Animals were given high dose dissolved in distilled water orally and was given once. The dose administered to the animals was calculated according to the concentration of cyfluthrin recommended (8 ml in 1000 litre) for use in field sprays which came out to be 1.6 μl in 100 μl of distilled water – double of the recommended dose. Autopsy was conducted after 3 hrs, 24 hrs, and 15 days after the dose administration.

Group III (Control II): Animals were given distilled water as vehicle orally daily.

Group IV (Subchronic): Animals were given low doses dissolved in distilled water orally continuously for 1 month. The dose administered to the animal was calculated according to the concentration and it came out to be 0.2 μl in 100 μl of distilled water – one fourth of the recommended dose. Autopsy was conducted after 15 days and 30 days.

Quantitative biochemical estimation of Alkaline Phosphatase (ALP) marker for bone destruction, Acid Phosphatase (ACP) the lysosomal enzyme activity were estimated by using ALP and ACP kit (Accurex). Accurex Autozyme Alkaline Phosphatase is based on kinetic method using p-nitrophenyl phosphate (p- NPP). Accurex Autozyme Acid Phasphatase is based on kinetic method using α-naphthylphosphate. Blood samples were collected, centrifuged and supernatant serum was collected and ALP and ACP content at each autopsy interval was estimated. These parameters are sharp indicators of any type of injury or damage in liver cells.

The experimental protocol was approved by Institutional Animal Ethical Committee (IAEC) of International College for Girls, Jaipur with CPCSEA Registration No1689/PO/a/13/CPCSEA.

RESULT & DISCUSSION

On the acute dose administration the value ALP in experimental animal decrease significantly ($p<.001$) as compared to control at all the autopsy interval, that is, 3 hrs, 24 hrs and 15 days. The value of ACP at acute dose decreased significantly at autopsy interval 3hrs ($p<.001$), 24 hrs ($p<.05$) and 15 days ($p<.001$) in experimental group as compared to control.(Table 1)

Table I: Effect of Acute Dose of Cyfluthrin (Synthetic Pyrethroid –Solfac 050EW) on Serum Phosphatase Level of Swiss Albino Mice.

Phosphatase	Autopsy Interval					
	3 Hours		24 Hours		15 Days	
	Control	Experimental	Control	Experimental	Control	Experimental
ACP IU/L	3.833 ±.17	2.733 ±.12***	3.503 ±.22	3.1 ±.15*	3.666 ±.14	2.233 ±.14***
ALP IU/L	175 ±2.89	121.66 ±3.84***	203.33 ±2.90	112 ±2.60***	218.33 ±4.41	94 ±2.08***

Significance in relation to control,* p<0.05, ** p<0.01, *** p<0.001

Sub chronic dose showed significant (p<.001) decline in ALP concentration in experimental group as compared to control at autopsy interval of 15 days and 30 days. Sub chronic dose also exhibited declining trend in ACP concentration in experimental group as compared to control at autopsy interval of 15 days(p<.001)and 30 days(p<.001). (Table 2)

Table II: Effect of Sub Chronic Dose of Cyfluthrin (Synthetic Pyrethroid –Solfac 050EW) on Serum Phosphatase Level of Swiss Albino Mice.

Phosphatase	Autopsy Interval			
	15 Days		30 Days	
	Control	Experimental	Control	Experimental
ACP IU/L	3.733 ±.17	1.733 ±.12***	3.633 ±.17	2.533 ±.12*
ALP IU/L	193.33 ±1.85	80 ±2.8***	202.33 ±1.85	83.33 ±1.86***

Significance in relation to control,* p<0.05, ** p<0.01, *** p<0.001

Acid posphatase seem to be an important index for the examination of the integrity of the lysosomal membrane and are responsible for the tissue damage and necrosis of hepatic tissue. Cytoplasmic cellular enzymes, such as alkaline phosphatase (ALP) membrane bound indicator of type II cell secretary activity or the lysosomal enzyme â-glucuronidase, an indicator of phagocytic activity, can also be used as sensitive markers of cellular integrity and cellular toxicity induced by pathological conditions.[14]

Acid phosphatase (ACP) and alkaline phosphatase (ALP) activities may be inhibited or accelerated by various insecticides, Dalela et.al. [15],Bhatnagar et.al. [16], Deshpande et.al. [17]. Decrease in ACP and ALP

activities may be due to the uncoupling of phosphorylation by the insecticide; Deshpande et.al. [17]. The activities of these enzymes are usually raised in acute hepatotoxicity or mild hepatocellular injury, but tend to decrease with prolonged intoxication due to damage in liver[18,19].

The decrease level of ALP might be attributed to the loss of ALP from plasma membrane into the extracellular fluid[20] and the reduction in concentration or total absence of specific phospholipids required by this membrane bound enzyme to express its full activity [21] under the interaction of xenobiotic/metal with plasma membrane, or due to inhibition of the enzyme activity at the cellular/molecular level [22] and inactivation of the enzyme molecule in situ [23] by the binding of xenobiotic/ metal to ALP directly. ALP catalyses the hydrolysis of organic phosphates at alkaline pH. ALP activity gives an indication of possibility of liver diseases [24]. Probable damage to the plasma membrane of the liver may be the reason for the reduced ALP activity in the liver. Decline in ALP activity may result from fall in the rate of synthesis of glycogen caused by lowered metabolic demands and electrolytic imbalance due to tissue overhydration [25].Decrease in ALP may reflect a change in endoplasmic mass known to occur in the cell membrane [26]. Since it also function in the conversion of energy compounds NADPH to NAP [27]. Therefore, decline ALP activity could result in biosynthesis shift and energy metabolism pathway of the exposed organism[28].

ACP catalyses the removal of phosphoryl group from a phosphate ester in an acidic medium. It is found throughout the body[24]. However, damage to tissues including liver, kidney, heart, red blood cells etc. causes a decrease in tissue level of ACP [29]. The decrease in the ACP activity was observed lends credence to liver dysfunction [30]. Alkaline phosphatase is a membrane bound enzyme found at bile pole of hepatoctyes and also found in pinocytic vesicle and Golgi complex. It is present on all cell membranes where active transport occurs, and hydrolase and transphosphorylase in function. It is often employed to access the integrity of plasma membrane [22] since it is localized predominantly in the microvilli of the bile canaliculi, located in the plasma membrane. Decrease in ALP activity may be taken as an index of hepatic parenchymal damage and hepatocytic necrosis [31]. Inhibition of ALP reflects alteration in protein synthesis and uncoupling of oxidative phosphorylation [32].

CONCLUSION

The present study suggests that Cyfluthrin (Solfac 050EW) shows significant toxic effects on serum phosphatase of Swiss Albino Mice.

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