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Impairment Of Hepatic And Renal Enzyme Activities During λ -Cyhalothrin Intoxication In Albino Mice

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ABSTRACT

*Lambda **λ** -cyhalothrin (trade name Karate) is a pyrethroid insecticide, widely used to control insect pests in agriculture, public health, and homes and gardens. Pyrethroids are synthetic chemical analogues of pyrethrins, which are naturally occurring insecticidal compounds produced in the flowers of chrysanthemums (Chrysanthemum cinerariaefolium). Insecticidal products containing pyrethroids have been widely used to control insect pests in agriculture, public health, and homes and gardens. The aim of this study was to establish hepatic and renal toxicity of the most common, new-generation, type II pyrethroid Lambda cyhalothrin. After determining the oral LD50 (24mg/kg body weight) we assessed the hepatotoxicity and renal toxicity in albino mice following sub lethal doses of Lambda (1/5th of LD50 4.8 mg/kg bw) orally for 10, 20 and 30 consecutive days. The assessment was based on hepatic marker enzymes AST, ALT. Mice treated with lambda cyhalothrin showed a significant increase in aminotransferase (AST and ALT) in liver and kidney tissues.*

Key words: Biochemical parameters, synthetic pyrethroid, glutamate dehydrogenase, Lambda

INTRODUCTION

Nowadays, the overall pattern of pesticides use has been changed considerably in comparison with the past while the hazards of using such chemicals have been accentuated by the sharp rise in their use in agriculture, industry, and by householders **Giovanni Annuzzia *et.al.*, 2009; Gray *et.al.*, 1995; Gloyn *et.al.*, 2009.** The insecticides used earlier are now getting replaced by the recently developed fourth-generation broad spectrum synthetic pyrethroids like cypermethrin and Lambda cyhalothrin, as they are more effective for the purpose. For the last few decades, pyrethroid pesticides have strengthened their place in the pesticide market for several uses. This enhanced use, however, affects more and more nontarget species **(Rana *et.al.* 2008; Fetoui *et.al.* 2009)**

Pyrethroids may be classified into two large groups **(Hussain *et.al.* 2012; Hites, 2004)** type I pyrethroids (e.g. allethrin, permethrin) lack a cyano moiety. Type II pyrethroids (e.g. deltamethrin, fenvalerate and cyhalothrin) have a cyano group in the α-position. In recent years, the use of synthetic pyrethroids has increased due to their obvious advantages. Lambda-cyhalothrin is one of the newer synthetic pyrethroid insecticides with effective immediate and persistent activity against a large variety of arthropods harmful both to human and animal health and to vegetal production. These types of halogenated and lipophilic compounds are generally recognized as potent neurotoxicants, characterized by high insecticidal properties and low mammalian toxicity (**International FH, 2003)**.

MATERIAL AND METHODS

Chemical Substance

Lambda cyhalothrin, a synthetic pyrethroid has been considered for this toxicology study. The effective dose 4.8 mg/kg/day given orally in corn oil vehicle for 10, 20 and 30 days below their acute LD_{50} level of intoxication according to their body weight. The mouse oral LD_{50} for Lambda cyhalothrin is 24 mg/kg body weight.

Experimental Animal

Albino mice of 30±5g were selected from an inbred colony for the experimentation. The mice were maintained in the laboratory at 26˚C ± 1˚C temperature in separate cages. They were provided food pellets and clean water for survival.

Experimental protocol

1/5th of LD50 has been taken as experimental dose which was divided equally according to experimental protocol i.e. divided by experimental days viz. 10, 20 and 30. The albino mice were divided in two sets viz. control (without treatment), λ-cyhalothrin treated. Further, experimental set was divided in three sub-sets- 10days, 20days, and 30days. The control and experimental animals after a stipulated period (*i.e.* on 11th, 21st and 31st day) were sacrificed and the tissues were quickly isolated, cleaned in physiological saline and processed immediately for microscopic analysis under ice-cold conditions. The tissues were also quickly isolated and were kept in deep freezer at -80°C and used for biochemical analysis.

Biochemical studies

Experimental rats of control and experimental sets were taken and tissues liver and kidney was excised out for further biochemical estimations. Autopsy was done as per experimental protocol on specified days as 11, 21 and 30. The estimations of aspartate transaminase (AST) and alanine transaminase (ALT) in liver and kidney were done by the method of **Reitman and Frankel (1957).**

Statistical analysis

Statistical significance between the control and experimental data were subjected to analysis of variance (ANOVA) together with Dunnett's test ($P<0.05$).

Results and Discussions

As regards to the results of the biomarker enzymes, alanine aminotransferase (ALT) and aspartate aminotransferase (AST), chronic intoxication of lambda cyhalothrin showed gradual increase in each of ALT and AST enzymes of albino mice. The results are tabulated in Table-1 & 2.

The increase is with increased treatment from 10 days to 30 days in the tissues liver and kidney of albino mice.

Alanine aminotranferease (AlAT) and Aspartate aminotransferase (AAT) are enzymes located in liver cells that leak out into the general circulation when liver cells are injured. These two enzymes were previously known as the SGPT (serum glutamic-pyruvic transaminase) and the SGOT (serum glutaic-oxaloacetic transaminase). These two transaminase enzymes may be reported on lab slips with both their new names and previous names or by their newer names only. AlAT and AAT are present in highest concentrations in cells from the liver, heart, skeletal muscles and red blood cells.

Liver is a target organ and primary site of detoxification and is generally the major site of intense metabolism and is therefore prone to various disorders as a consequence of exposure to the toxins of extrinsic as well as intrinsic forms. Liver plays important role in metabolism to maintain energy level and structural stability of body **(Guyton and Hall, 2002).** It is also site of biotransformation by which a toxic compound has been transformed in less harmful form to reduce toxicity **(Hodgson, 2004).** However, this will damage the liver cells and produce hepatotoxicity. Alanine transaminase (ALT) is an enzyme that helps metabolize protein. When the liver is damaged, ALT is increased in liver and released in the bloodstream. Aspartate transaminase is the mitochondrial enzyme, predominantly found in the liver, skeletal muscles and kidneys. Alanine transaminase is a cytosolic enzyme, which is more specific for the liver than aspartate transaminase. Increased levels in liver are the result of treatment and indicative of toxic liver necrosis **(Poli *et al*., 1987).** In the present investigation marked increase in liver ALT and AST under stress of pesticides has been observed.

The increase in transaminase activity in the liver is indicative of liver damage that occurs due to formation of reactive oxygen species and reactive intermediates after the treatment of pesticides **(Bandyopadhyay *et al.*, 1999).**

Aspartate and alanine aminotransferases are present both in mitochondria and cytosolic fractions of animal **(Walton and Cowey, 1982)**. In protein metabolism aminotransferases catalyze the transfer of the amino group from an amino acid to a keto acid; new amino and keto acids are formed in the process **(Murray *et al.*, 2007)**. The activities of these aminotransferases were shown to be altered in tissues under several pathological conditions **(Varshneya *et al.*, 1983; Paul *et al.*, 1984)**. Elevated AST and AlAT activities can be considered as an index of gluconeogenesis **(Knox and Greengard, 1965; Murray *et al.*, 2007)**.

Table 1: Changes in Aspartate aminotransferase (µ moles of pyruvate formed/ mg protein/hr) levels in different tissues of control and Lambda cyhalothrin treated albino mice.

Tissues	Control	10 Days	20 Days	30 Days
Liver				
Mean	1.448	1.554	1.658	1.799
S D	±0.0240	±0.0212	±0.0540	±0.0206
PC		(7.320)	(14.502)	(22.859)
Kidney				
Mean	0.228	0.243	0.254	0.269
S D	±0.2527	±0.124	±0.243	±0.200
PC		(6.578)	(11.403)	(17.982)

Values are mean of six individual observations
±SD-Standard Deviation; PC - Percent Change over control

One Way Anova

Source of Variation	DF	Liver	Kidney
		Mean Squares	Mean Squares
Between Groups	3	0.134*	0.002*
Within Groups	20	0.001	0.0009
Total	23		

All the values are Significant at P<0.05

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Table 2: Changes in Alanine amino transferase (µ moles of pyruvate formed/mg protein/hr) levels in different tissues of control and Lambda cyhalothrin treated albino mice.

Tissues	Control	10 Days	20 Days	30 Days
Liver				
Mean	1.527	1.749	1.842	1.960
S D	±0.1320	±0.1378	±0.1158	±0.1617
PC		(14.538)	(20.628)	(28.356)
Kidney				
Mean	0.461	0.517	0.532	0.568
S D	±0.0667	±0.0582	±0.0574	±0.0543
PC		(12.147)	(15.401)	(23.210)

Values are mean of six individual observations

±SD-Standard Deviation; PC - Percent Change over control

One Way Anova

Source of Variation	DF	Liver	Kidney
		Mean Squares	Mean Squares
Between Groups	3	0.2020*	0.1132*
Within Groups	20	0.0190	0.00428
Total	23		

All the values are Significant at P<0.05

Fig: 1. Changes in Aspartate aminotransferase (µ moles of pyruvate formed/mg protein/hr) levels in different tissues of control and Lambda cyhalothrin treated Albinomice

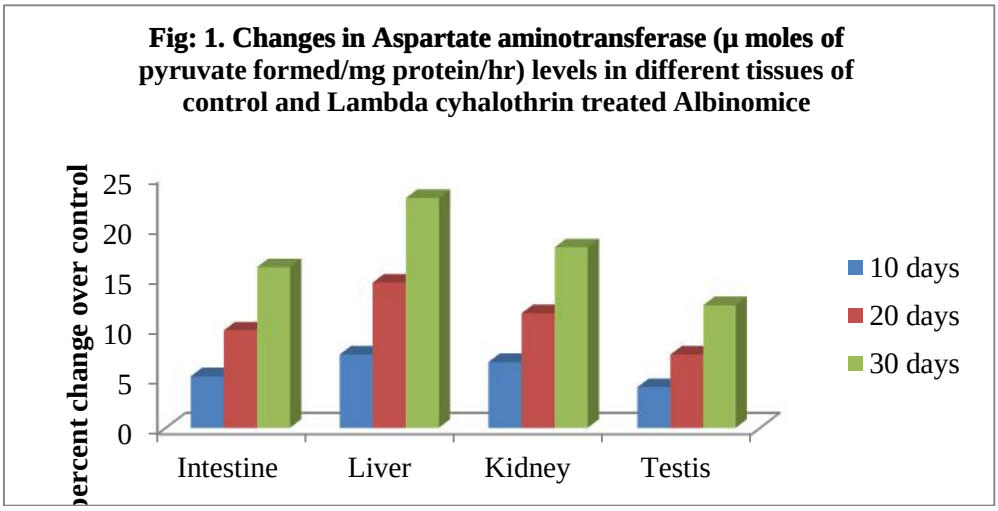
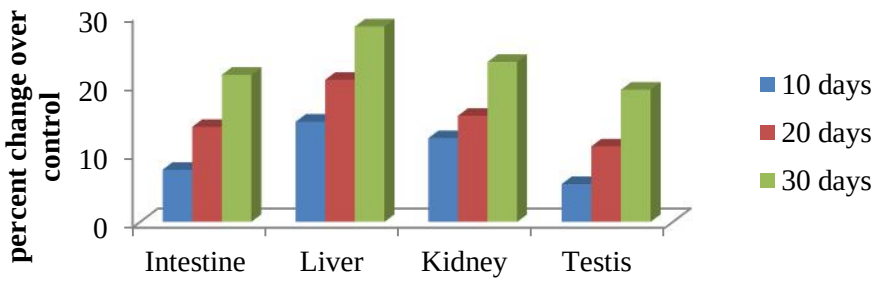


Fig: 2. Changes in Alanine amino transferase (µ moles of pyruvate mg protein/hr) levels in different tissues of control and Lambda cyhalothrin treated Albino mice



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