Research Paper

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Changes in Liver Enzymes Following Multigenerational Exposure in Albino Rats

Zoology

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ABSTRACT

Male and female albino rats were orally fed with quinalphos at dose concentration of 1mg/kg b.wt for three generations. Rats were divided into two groups i.e. control fed with peanut oil and treated fed with quinalphos for a period of six weeks in each generation to assess the alterations in the level of phosphatases and transferases in blood plasma. In male rats the ACP increased in treated rats of F0 generation whereas AKP increased in treated rats F0, F1 and F2 generation. The concentration of AST also increased in treated rats of F0 and F1 generation however the ALT increased in F0 and F2 generation. In female rats, ACP and ALP increased in F0 and F1; AST in F0 and ALT in F0 and F1 generation. Therefore the pesticide affects the basic liver enzymes when given for long term period hence altering the liver function.

Introduction

Phosphatases are important and critical enzymes in the biochemical process and are responsible for detoxificiation processes. Phosphatases catalyse the hydrolytic cleavage of phosphoric acid ester and are designated either acid or alkaline phosphatases according to their pH optima (Bergmeyer, 1974). Raised value of acid phosphatase in serum indicates diseases accompanied by increased osteoblast activity or involvement of the liver. The increase in alkaline phosphatase activity represents the functional status of different vital organs like testes, ovary and liver. Phosphatases are involved in many different processes that require mobilization of phosphate ions or dephosphorylation as part of anabolic, catabolic or transfer processes. Phosphatase enzymes act by hydrolyzing phosphomonoester bond and liberating free inorganic phosphate (Kaur and Dhanju, 2004). Measurement of acid phosphatases used almost exclusively in diagnosis and control of therapy of prostatic carcinoma (Bergmeyer, 1974). The rise in serum alkaline phosphatase and acid phosphatase levels indicate tissue damage and subtle disturbance in hepatic dysfunctions and biliary secretions of animals (Rahman *et al.,* 2000). Female albino rats when treated with organophosphates methyl parathion, monocrotophos and dimethoate exhibited increased activity of phosphatases in plasma (Kaur and Dhanju, 2005). Quinalphos is widely used pesticide these days against caterpillars on fruit trees, cotton, vegetables and peanuts; scale insect on fruit trees and pest complex on rice. Hence the present study was designed to analyze the effect of quinalphos on liver enzymes in blood plasma of male and female albino rats for three generation.

Material and methods

The multigeneration study was conducted on albino rats weighing 100-110g obtained from Guru Angad Dev Veterinary and Animal Sciences University (GADVASU), Ludhiana. The rats were maintained in laboratory under standard conditions of temperature (25±2°C) providing them laboratory pelleted feed and water *ad libitum.* The rats were acclimatized to new quarters for one week before starting the treatment. The experimental protocol met the National guidelines on the proper care and use of animals in the laboratory research. This experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC).

Technical grade (active ingredient) of Quinalphos procured from Sigma-Aldrich Laborchemikalien GmbH, West Germany; having 95 percent purity was used for the present studies. Adequate dilutions were made with peanut oil to achieve the test concentrations of 1 mg/kg corresponding to 1/100 of the LD_{50}. Rats were divided into two groups. One group was intubated orally with dose of quinalphos (1 mg/kg b.wt) disolved in peanut oil, daily for six weeks, simultaneously same amount of peanut oil was also administered orally to other group of rats called control. In each generation rats were paired to obtain the subsequent generation and similarly the parental rats were sacrificed after weaning of the pups. The animals were mildly anaesthetized using chloroform and the blood was collected directly from heart in heparinized vials. Plasma was separated from blood by centrifuging the blood at 2000 rpm (rotations per minute) for 15 minutes at 4°C. The supernatant was used for estimation of biomolecules viz. urea and creatinine. Phosphatases were estimated by method of Bessey *et al.* (1946) and Transferases were estimated by method of Reitman and Frankel as described by Bergmeyer (1974).

Results and discussion

The enzyme activity was estimated from the blood plasma of control and treated rats and is expressed in U/L. The ACP concentration of male rats of F0 generation in treated (65.60±6.65 U/L) group was significantly higher ($p \leq 0.05$) in comparison to the control (52.61±5.37 U/L) rats of F0 generation. However, the ACP concentration of control and treated group was non-significantly different in F1 and F2 generation. The ALP concentration of treated rats in F0 (370.78±26.99 U/L), F1 (421.00±41.11 U/L) and F2 (347.28±36.57 U/L) generation was significantly more ($p \leq 0.05$) in comparison to the concentration of ALP of control rats in F0 (370.78±26.99 U/L), F1 (421.00±41.11 U/L) and F2 (347.28±36.57 U/L) generation (Table 1).

The activity of AST in treated male rats of F0 (20.50±0.83 U/L) and F1 (12.78±1.79 U/L) generation was significantly more ($p \leq 0.05$) in comparison to the activity of AST in control rats of F0 (14.78±1.13 U/L) and F1 (10.44±0.89 U/L) generation. However, the activity of control rats in F2 generation was comparable to that of treated rats of F2 generation. The enzyme activity of ALT in control male rats in F0 (55.70±2.10 U/L) and F2 (50.65±1.16 U/L) generation was significantly less ($p \leq 0.05$) than the activity of ALT in treated male rats of F0 (62.83±3.56 U/L) and F2 (58.46±4.61 U/L) generation, whereas the activity of ALT in treated male rats of F1 generation was comparable to the control rats of F1 generation (Table 27).

The concentration of ACP in treated female rats of F0 (78.85±15.72 U/L) and F1 (71.45±19.69 U/L) generation was significantly increased ($p \leq 0.05$) as compared to the concentration of ACP in control rats of F0 (48.39±6.61 U/L) and F1 (36.74±1.28 U/L) generation. The concentration of ACP in control and treated rats was comparable to each other in F2 generation. While estimating the concentration of ALP in treated female rats it was found that the enzyme was significantly increased ($p \leq 0.05$) in F0 (338.06±24.35 U/L) and F1 (387.17±46.68 U/L) generation whereas the concentration in control rats was significantly less in F0 (213.17±25.92 U/L) and F1 (212.94±30.48 U/L) generation. Significant difference ($p \leq 0.05$) was observed in the concentration of AST in control (12.78±0.99 U/L) and treated (22.94±1.83 U/L) rats of F0 generation. However, the concentration of AST in female rats of treated groups of F1 and F2 generation was comparable to the control rats of F0 and F1 generation (Table 2).

Quinalphos had caused an elevation in the activity of ACP in the

present study. Increase in the ACP level is an indicator of tissue damage since acid phosphatase is a lysosomal enzyme and stimulated in case of eminent tissue damage (Duggal, 1998). The increase in serum AKP enzyme represents the functional status of liver. The increase or decrease of enzyme activity is related to intensity of cellular damage. So increased levels of AKP in serum suggest that quinalphos causes hepatic damage and pathogenesis may be through the generation of free radicals. Similar increase in levels of acid phosphatase and alkaline phosphatase was noticed by Duggal (1998) in female albino rats fed pyrethroid fenevalerate and by Kaur (2003) in female albino rats given organophosphate methyl parathion, dimethoate and monocrotophos. This rise in serum AKP levels seems to indicate a possible subtle disturbance taking place in hepatic dysfunctions and biliary secretions of animals (Zimmerman, 1978, Srivastava *et al.,* 2006).

The increased levels of aminotransferases in plasma of rats in present study may indicate their enhanced metabolic activity, perhaps to meet the stress induced by prolonged exposure to the pesticide (Kaur and Dhanju 2004). Increased transaminase activity is probably the consequence of quinalphos induced pathological changes in liver causing hepatic damage. Change in enzyme activity in general may be related to intensity of cellular damage (Muthuviveganandavel *et al.,* 2008). Similar increase in enzyme activity of ALT and AST had also been observed in plasma of organophosphate treated female rats (Kaur, 2003).

Quinalphos treatment at dose concentration of 250 micrograms/kg/day for 26 days to Wistar strain rats resulted in increased level of serum transaminases (Ray *et al.,* 1987). Siddiqui (2004) studied toxicological and immunological effects of subacute exposure of 8 to10 week old cockerels to quinalphos and reported an increase in plasma transaminase viz. AST and ALT. QP at dose concentration of 0.5, 1.5, 2, 3, 4.5 mg/kg body weight) was administered orally to pregnant rats from day 6-15 of gestation. At 3 and 4.5 mg/kg/day, quinalphos produced significant increase in hepatic alanine amino transferase (ALT), serum ALT, serum aspartate amino transferase (AST) (Srivastava and Raizada 1999).

Table 1:-Effect of quinalphos on concentration (U/L) of acid phosphatase, alkaline phosphatase, aspartate amino transferase and alkaline amino transferase in plasma of male rats of F0, F1 and F2 Generation as compared to control group.

Generation male	Group	Enzymes (U/L)			
		ACP	ALP	AST	ALT
F0	Control	52.61±5.37	261.94±18.54	14.78±1.13	55.70±2.10
	Treated	65.60±6.65*	370.78±26.99*	20.50±0.83*	62.83±3.56*
F1	Control	58.21±4.42	265.50±15.88	10.44±0.89	64.43±0.92
	Treated	62.96±7.33	421.00±41.11*	12.78±1.79*	66.50±7.13
F2	Control	64.47±6.06	270.94±14.54	12.72±2.17	50.65±1.16
	Treated	57.29±7.13	347.28±36.57*	12.94±2.03	58.46±4.61*

All the values are mean ±SE values of 6 animals in each group

***Significant difference at (p≤0.05) as compared to control**

Table 2:-Effect of quinalphos on concentration (U/L) of acid phosphatase, alkaline phosphatase, aspartate amino transferase and alkaline amino transferase in plasma of female rats of F0, F1 and F2 Generation as compared to control group.

Generation female	Group	Enzymes (U/L)			
		ACP	ALP	AST	ALT
F0	Control	48.39±6.61	213.17±25.92	12.78±0.99	39.51±2.06
	Treated	78.85±15.72*	338.06±24.35*	22.94±1.83*	60.99±3.28*
F1	Control	36.74±1.28	212.94±30.48	12.28±0.71	57.31±2.59
	Treated	71.45±19.69*	387.17±46.68*	13.61±2.86	66.39±5.25*
F2	Control	57.24±10.49	280.78±18.60	12.33±2.70	48.12±2.57
	Treated	47.91±5.18	283.33±13.75	11.28±2.15	50.19±5.10

All the values are mean ±SE values of 6 animals in each group

***Significant difference at (p≤0.05) as compared to control**

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