



E-ISSN: 2278-4136  
P-ISSN: 2349-8234  
JPP 2019; SP4: 95-97

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**(Special Issue- 4)**  
**National Seminar**  
**“Role of Biological Sciences in Organic Farming”**  
**(March 20, 2019)**

## Effect of monocrotophos (an organophosphate) on liver of albino rat – Histochemical and biochemical studies

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### Abstract

Six groups of female albino rats (each of 125-150 gms) were taken for experimental work. 1/5<sup>th</sup> of LD<sub>50</sub> dose (14 mg/kg body weight) of monocrotophos was administered by intragastric intubation to groups TI, TII and R for 15 days, 30 days, 30 days with recovery period of 15 days respectively. Other three groups were kept as corresponding controls for all the treated groups and were fed on normal diet. Blood samples were collected from all groups for estimation of levels of GOT, GPT, alkaline phosphatase and acid phosphatase. For histochemical studies, liver was collected from various groups at the end of the experiment and fixed in Bouin fluid and then processed for staining with haematoxylin-eosin. In rats of control group, the sections of liver revealed normal histoarchitecture showing hexagonal hepatic lobules with central and portal veins as well as sinusoids with polyhedral Kupffer cells. The treated groups TI & TII, showed vacuolation of hepatocytes, widening of portal tract and sinusoids and various necrotic changes in the histoarchitecture along with increased level of GOT, GPT, alkaline and acid phosphatases in blood serum. As these enzymes are known to be the marker enzymes of the liver, so their rise in blood serum is indicative of hepatic injury. In rats of R group, recovery was observed at both histochemical as well as biochemical level.

**Keywords:** Monocrotophos, Organophosphate, Pesticide, Liver, GOT, GPT, Phosphatases

### Introduction

Monocrotophos [3 hydroxy-N-methyl-cis-crotonamide dimethylphosphate], an organophosphorous insecticide is widely used as an effective crop protectant. It has both systemic and contact properties and has been used against a wide range of insects including mites, boll worms, sucking insects, leaf eating beetles and other larvae on variety of crops [1]. The toxicity of the insecticidally active organophosphorous compounds to mammals and insects is primarily attributed to their ability to inhibit acetyl cholinesterase (AChE) [2, 3]. Though all organophosphates are neurotoxins, but at the same time, they damage the membranous integrity of organs such as in liver, evidenced by histopathological studies and changes in phosphatases and hepatic biomarkers such as serum aminotransferases [4, 5]. Various processes of metabolism and detoxification are catalyzed by these hepatic enzymes. Alkaline phosphatase is known to control the movement of substances across membrane, whereas acid phosphatase is capable of catalyzing the hydrolysis of numerous phosphate esters at acidic pH. The aminotransferases GOT (glutamate – oxaloacetate transaminase) and GPT (glutamate – pyruvate transaminase) function at the junction between metabolism of proteins and carbohydrates [6] and are recognized as the most specific liver marker enzymes. All these enzymes are located in various membranous compartments of liver cells and integrity of these membranes play a vital role in the metabolism of these insecticides, but a very little attention has been paid on the toxic stress laid on the intactness of these cell structures and cellular organelles after treatment with organophosphates [7-9]. The present investigations were, therefore, made to throw light on the histological changes in the liver and biochemical changes in level of its marker enzymes in blood serum of female albino rat after exposure to monocrotophos for various durations.

### Materials and Methods

LD<sub>50</sub> of monocrotophos (MCP) was standardized on the basis of the dose calculated by

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Janardhan *et al.* [10] and was found to be 14 mg/kg body weight. Adult female albino rats of Wistar strain in proestrous phase of estrus cycle weighing 100-150 gm were obtained and divided into three groups TI, TII and R groups (8 rats in each group). 1/5<sup>th</sup> of LD<sub>50</sub> value of monocrotophos i.e. 2.8 mg/kg body weight was administered for 15 days to TI group and for 30 days to TII group. To the rats of R group, the same dose was given for 30 days and then the rats were kept on normal conditions i.e. without monocrotophos for 15 days. Another three group CI, CII and CIII (8 rats in same phase of estrus cycle in each group) were kept as corresponding controls for all the treatment groups. All the animals were kept on the commercial standard diet and tap water *ad libitum*. The weight of animals were recorded weekly.

At the end of treatment period, blood samples were collected from all groups for serum formation for estimation of levels of GOT, GPT, alkaline phosphatase and acid phosphatase and then the wistar rats were sacrificed by cervical dislocation. The thoracic cavity was cut opened to take out the liver in all the groups. The extraneous material was removed and liver was washed in saline. For histopathological studies, small pieces of liver were fixed in Bouin for 24 hours and processed for paraffin wax embedding according to the standard technique. The paraffin sections were cut at 5-7  $\mu$  thickness and later on subjected to Delafield Haematoxylin – Eosin Technique [11].

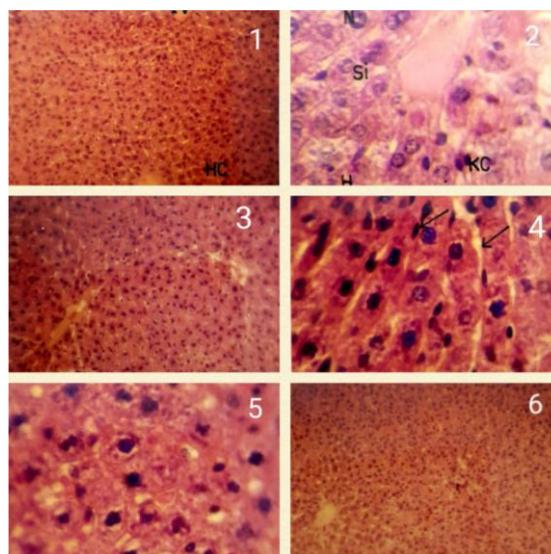
## Results and Discussion

In control rats, which remained without any treatment, the light microscopic observations showed a clear and fine hepatic cellular structure. Nuclear structures were well intact, with fine nuclear chromatin and well intact nuclear membrane (Pmgs. 1&2). Whereas liver of rats exposed to monocrotophos for 15 days (TI) (Pmgs. 3&4) and 30 days (TII) (Pmg. 5) showed many histopathological changes in both necrotic as well as less affected hepatic cells. There were marked necrotic effects on the liver cord disarray, shrinkage of hepatocytes, pyknosis of nuclei, granulated cytoplasm, rupture in cell membranes and vacuolization of hepatocytes. The prominent effects were evident on the membranous integrity of various organelles [4, 12-17]. These alterations in the impairment of microcirculation in the histoarchitecture may be responsible for fundamental insufficiency of organ. Vacuolation of hepatocytes could be explained on the basis that MCP might have manifested its toxic effects primarily by the generation of more oxidative stress on the body which might have lead to the production of increased number of free radicals leading to significant increase in lipid peroxidation and thus caused damage to the various membranous components of the cell. Alkaline phosphatase, an enzyme responsible for the movement of substances across membranes, and acid phosphatase, an intracellular enzyme, showed a significant elevation (Table) in activity in the blood serum of rats of TI and TII groups. Similar findings were reported by some other workers [18-21] in rats, buffalo calves, rats and fish respectively. The elevated levels of phosphates may indicate an increase in the rate of phosphorylation and transport of molecules across the cellular membrane and it was reported that the pesticides cause significant increase in the cellular damage which enhanced the activity of phosphatases [15-18].

During present studies, significant elevation in serum transaminases was also observed in TI and TII groups and this increase perpetuated till the end of the study i.e. it was

observed in R group also though less marked than TI and TII groups (Table). Moreover, the increase in serum GOT was more pronounced than serum GPT in the monocrotophos treated rats. This observed increase in activities of both these transaminases is in conformity with the results of other workers following monocrotophos intoxication in rats [17-18, 22-24]. The rise in aminotransferases during present studies might be due to hepatic dysfunction as these enzymes are considered to be the potential marker enzymes of liver. This if further supported by the documentation of Murphy (1980) [25] who stated that although, damage to any particular organ cannot be cited as a cause of increased levels of aminotransferases in rodents, liver being the primary organ involved in activation and/ or detoxification of OP esters, is expected to be damaged which could be the source of these enzymes in plasma. An increase in number of Kupffer cells was also observed during present studies which might be due to the fact that MCP induced the immunological defense mechanism in liver.

Keeping the monocrotophos treated rats on recovery for 15 days after 30 days treatment in R group resulted in normalizing the hepatic histoarchitecture quite appreciable (Pmg. 6). The recovery might be due to revival of reduced enzymatic activity responsible for detoxification of toxic agents in the liver of treated rats. Though some disturbances in levels of phosphatases and aminotransferases still prevailed (Table), but were of very nominal order. Hence the workers who get exposed to organophosphorous sprays are required to take a brief period of rest to cope up with the any kind of abnormality and to minimize the danger of intoxication from organophosphorous pesticides including monocrotophos intoxication.



### Explanation to figures.

#### Histopathology of liver

**Pmg. 1:** T.S. control liver showing cords of hepatic cells (HCL), sinusoids (Si) and intralobular vein (IV). B/HE.

**Pmg. 2:** T.S. control liver showing cords of hepatic cells (HCL), nuclei (N), nucleoli (n), sinusoids (Si), Kupffer cells (KC) and intralobular vein (IV). B/HE.

**Pmg. 3:** T.S. liver of TI group showing disruption of hepatic with congestion of blood vessels. B/HE.

**Pmg. 4:** T.S. liver of TI group showing contraction of hepatocytes, widening of sinusoids (arrow) and increase in number of Kupffer cells (arrow). B/HE.

**Pmg. 5:** T.S. liver of TII group showing pyknosis of nuclei and vacuolization of hepatic parenchyma. B/HE.

**Pmg. 6:** T.S. liver of R group showing normal hepatic lobule with intralobular vein. B/HE

**Table 1:** Effect of Monocrotophos on biochemical values in serum of female albino rats in proestrus phase of estrous cycle

Parameters	2.8 mg/kg body weight monocrotophos/day					
	15 days treatment (TI)		30 days treatment (TII)		15 days recovery (R)	
	Contl	Exptl	Contl	Exptl	Contl	Exptl
Alkaline phosphatase	82.13 ± 6.28	86.18 ± 5.43*	82.97 ± 7.98	87.54 ± 8.12*	81.30 ± 6.13	82.24 ± 7.49*
% Change	(+) 4.93%		(+) 5.50%		(+) 1.15%	
Acid phosphatase	25.38 ± 2.90	27.93 ± 3.47*	24.16 ± 6.72	30.49 ± 4.52**	25.51 ± 4.20	26.14 ± 3.78
% Change	(+) 10.04%		(+) 26.20%		(+) 2.46%	
SGOT	38.53 ± 4.62	44.52 ± 6.17*	38.37 ± 5.67	49.29 ± 7.25**	38.62 ± 6.81	45.02 ± 5.32*
% Change	(+) 15.54%		(+) 28.45%		(+) 16.57%	
SGPT	48.07 ± 7.98	51.95 ± 8.20**	48.29 ± 9.15	52.75 ± 9.10***	47.51 ± 7.21	50.16 ± 6.98*
% Change	(+) 8.07%		(+) 9.23%		(+) 5.57%	

The values are expressed as Mean ± S.D. (n=6)

\*P<0.05; \*\*p<0.01; \*\*\*p<0.001, when the values are compared with respective controls.

### Acknowledgements

The authors are grateful to the Chairman, Department of Zoology, Panjab University, Chandigarh (India) for providing necessary laboratory facilities and to University Grants Commission, New Delhi, for financial help.

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