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Toxic Effects of Monocrotophos (an organophosphate) on Histoarchitecture of Liver – Histopathological Studies

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Abstract

Four groups of Wistar rats were taken for experimental work. $1/5^{th}$ of LD_{50dose} (14 mg/kg body weight) of monocrotophos was administered by intragastric intubation to groups TI, TII and R for 15 days, 30 days, and 30 days with recovery of 15 days respectively. Corresponding controls for all the three groups were fed on normal diet. For histopathological studies, liver was collected from various groups at the end of the experiment and the technique of microtomy was used for the preparation of slides. In control group rats, the liver tissue revealed normal histology showing well defined nucleus with nucleolus, hepatocytes arranged in linear cords between central vein and portal triads. In groups TI and TII, conspicuous necrotic changes including liver cord disarray, shrinkage of hepatocytes, pyknosis of nuclei, granulated cytoplasm, rupture in cell membranes and vacuolization of hepatocytes were observed. Group R showed a lot of recovery at histological level as compared to TI and TII groups.

INTRODUCTION

Monocrotophos [3 hydroxy-N-methyI-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]. A few workers[4,5] reported effect of some pesticides on activity through phosphorylation of the active serine hydroxyl group situated in

the active centre of acetyl cholinesterase thus making the enzyme non available to hydrolyze acetylcholine (ACH) into acetic acid and choline. This results in the accumulation of acetylcholine at all sites of cholinergic transmission, hereby causing continuous stimulation of the muscle or nerve fiber, resulting eventually in the exhaustion and tetany[6]. The toxic effects of organophosphorous insecticides on the neuronal functions and structure have been investigated by many workers, but the cytotoxicity of these insecticides on the liver has been assessed to a very little extent[4,7-9]. Various processes of metabolism and detoxification are catalyzed by hepatic enzymes[10]. These 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[11-13]. The present investigations were, therefore, made to throw light on the histological changes in the liver of female albino rat after exposure to monocrotophos for various durations.

MATERIAL AND METHODS

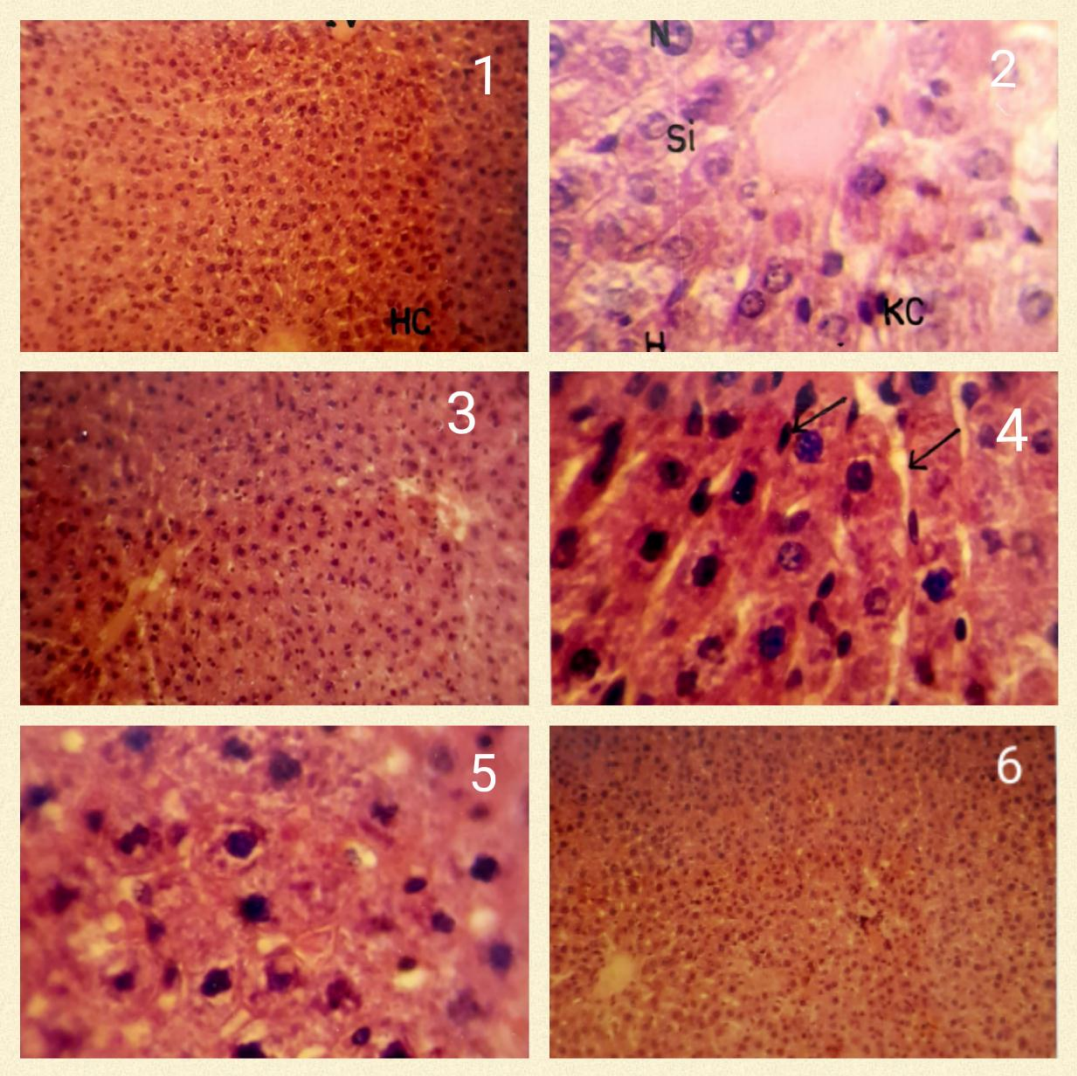
LD_{50} Monocrotophos was standardized on the basis of the dose calculated by Janardhan *et al*[14] and was found to be 14 mg/kg body weight. Adult female albino rats of Wistar strain in proestrous phase of estrus cycle weighing 100-150 gm were obtained and divided into three groups TI, TII and R groups (8 rats in each group). $1/5^{th}$ of LD_{50} 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, the 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 hrs. and processed for paraffin wax embedding according to the standard technique. The paraffin sections were cut at 5-7 µ thickness and later on subjected to Delafield Haematoxylin – Eosin Technique[15].

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. Whereas liver of rats exposed to monocrotophos for 15 days (TI) and 30 days (TII) 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. To the best of my knowledge, only a few reports are available in the literature on the toxic impact of organophosphorous insecticide on the histological studies of liver in mammals. Fatty degenerative changes were observed by Hanafy *et al*[13] in liver of rats treated with tamaron. During present studies vacuoation of parenchymal cells and congestion of central and portal blood vessel along with sinusoids were also observed. Similar observations were reported due to malathion toxicity in rats[9], dichlorvos poisoning in buffalo calves[16] and chlorpyrifos toxicity in rats[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. An increase in number of Kupffer cells was also observed during present studies which might be due to the fact that MCP induced the immunolgical 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. The recovery might be due to revival of reduced enzymatic activity responsible for detoxification of toxic agents in the liver of treated rats. 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 moncrotophos intoxication.



Histopathology of liver

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.

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