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Brief Communication

Giant Cell Formation in Rat Hepatocytes under Stress of Cypermethrin and Beta-Cyfluthrin

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ABSTRACT

Pyrethroids are greatly in use these days therefore can contaminate ecosystem and living forms therein. Present investigation reveals the toxic potential of two type-II pyrethroids, cypermethrin and beta-cyfluthrin at the level of giant cell formation through histological examination in liver of albino rats. It has been observed that both these experimental compounds cause giant cell formation in the liver of treated animals with beta-cyfluthrin having an edge over cypermethrin, probably due to difference in their chemical structures.

Keywords: Albino rats, Beta-cyfluthrin, Cypermethrin, Giant cells, Liver, Pyrethroids, Toxicity

INTRODUCTION

Use of pesticides and their designing has increased greatly, pertaining to increased global food demands as well as genetically modified resistance development in various pest species. Pyrethroid pesticides are an integral part of various pest eradication programmes worldwide and find their use both in domestic and large-scale field purposes as considered comparatively safer[1-4]. It is with reason, many new synthetic analogues have been added to market from time being. On contrary to their broad spectrum use by virtue of low photostability and non-target toxicity, they can disturb various ecological balances existing on this planet[3, 5-7]. Hepatocytic toxicity of two broadly used type-II pyrethroid pesticides, cypermethrin and beta-cyfluthrin, has been assessed in the present investigation, focusing on giant cell formation through histological analysis. Beta-cyfluthrin has been designed from cypermethrin by introduction of a fluorine atom at position 4 of phenyl ring in its structure (Figures 1 and 2).

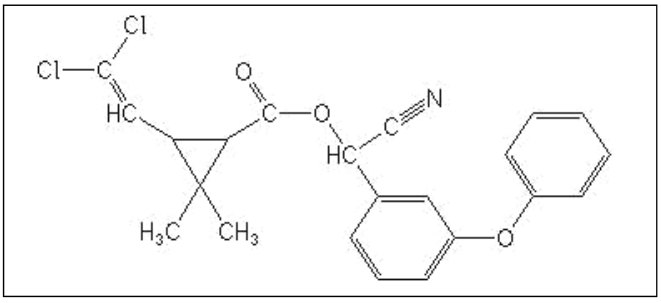

Figure 1: Structure of cypermethrin

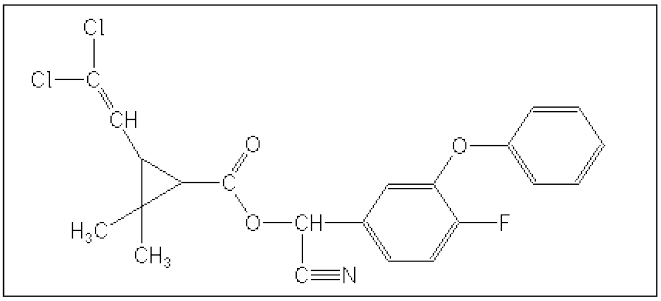

Figure 2: Structure of beta-cyfluthrin

MATERIALS AND METHODS

The present study was conducted on 75 female albino rats, *Rattus norvegicus* (Wistar), selected from an inbred colony. Animals selected were of about 2 weeks in age and 100 ± 20 g in weight. They were kept under appropriate temperature and light conditions, provided with standard rat pellet feed and water *ad libitum*. After 1 week of acclimatisation to laboratory conditions, these rats were divided into three sets having equal number of rats, that is 25. Experimental compounds, cypermethrin and beta-cyfluthrin (technical grades of approximately 95% purity, obtained from Bayer India Ltd., Mumbai), were orally administrated to these rats as per acute (1/10th of LD_{50} for 1 day) and sub-acute (1/10th of LD_{50} for 7, 14, 21 and 28 days) doses. All the three sets, one corresponding to control and others two for cypermethrin and beta-cyfluthrin, respectively, were subdivided into five subsets each comprising of five rats. LD_{50} for cypermethrin and beta-cyfluthrin (Finney, 1971) came out to be 416.98 and 354.8 mg/kg b.wt., respectively[1-2]. Respective doses were administrated to rats and sacrificed at predetermined time intervals (Table 1). The liver tissue was excised out, washed in physiological saline, cut into small pieces, fixed in Carnoy's fixative[9] for 4 h, dehydrated, embedded, sectioned (5µ sections) and finally stained with haematoxylin and eosin 10). These sections were then observed at 400 and 1,000× and appropriate locations were photographed.

Table 1: Dose administration schedule of the experimental compounds, cypermethrin and beta-cyfluthrin to experimental albino rats

Type of dose	Days of treatment	Type of Treatment	Dose (mg/kg/b.wt)
Acute	1	Control	–
		Cypermethrin	41.70
		Beta-cyfluthrin	35.48
Sub-acute	7	Control	–
		Cypermethrin	5.96
		Beta-cyfluthrin	5.07
	14	Control	–
		Cypermethrin	2.98
		Beta-cyfluthrin	2.53
	21	Control	–
		Cypermethrin	1.99
		Beta-cyfluthrin	1.69
	28	Control	–
		Cypermethrin	1.50
		Beta-cyfluthrin	1.27

RESULS AND DISCUSSION

Incidence of hypertrophy and giant cell formation has been found in a dose-dependent manner, which is more in beta-cyfluthrin intoxication in comparison with cypermethrin (Plates 1–11; giant cells have been shown up with the help of arrows).

Mammalian liver is important in maintaining body homeostasis as it plays a central role in many vital body functions, such as macromolecular metabolism, storage and redistribution of nutrients, xenobiotic detoxifying and elimination and others[2, 11-12].

Type-II pyrethroids including both these two experimental compounds have been well known for their hepatotoxic potential and disrupt structural as well as functional hepatic architecture in mammals. Hepatocytes are the main working engines of a mammalian liver. In an adult mammal, liver cells rarely divide under normal conditions but retain the property of massive proliferation under stress conditions, undergoing polyploidy. Polyploidy condition protects hepatocytes of genetic damage and maintains

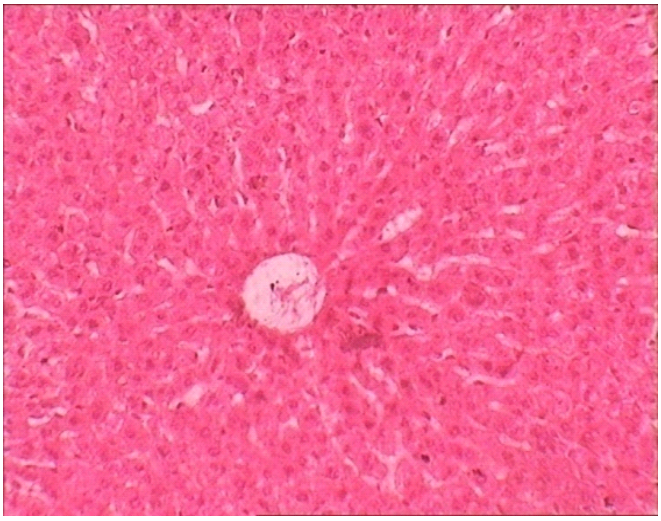

Plate 1: Histo-architecture of albino rat liver from control set (400×)

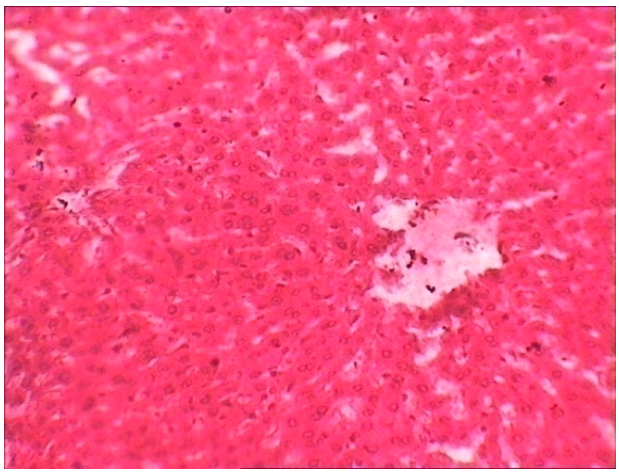

Plate 2: Histo-architecture of albino rat liver following acute (1 day) cypermethrin intoxication (400×)

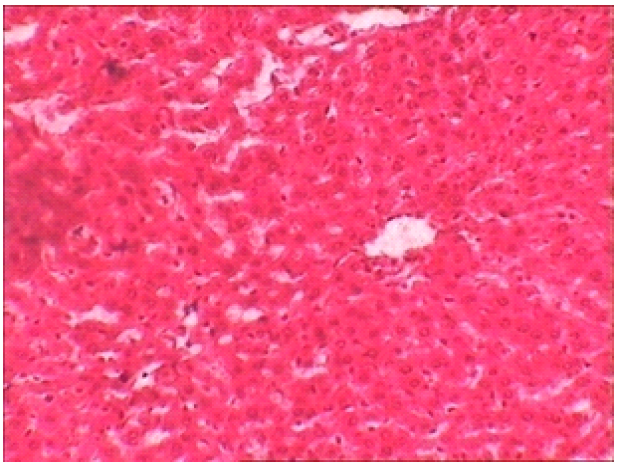

Plate 3: Histo-architecture of albino rat liver following acute (1 day) beta-cyfluthrin intoxication (400×)

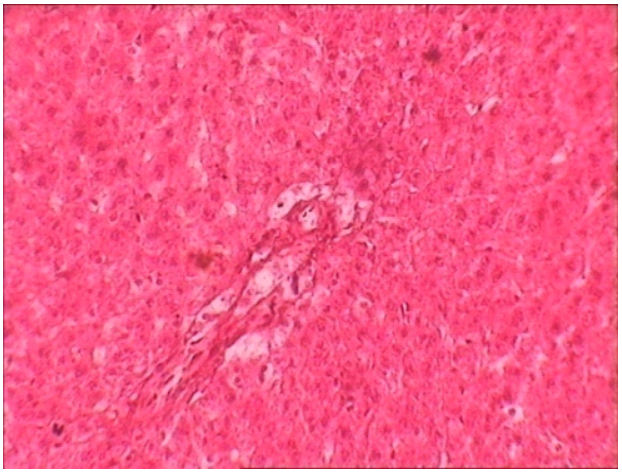

Plate 4: Histo-architecture of albino rat liver following sub-acute (7 days) cypermethrin intoxication (400×)

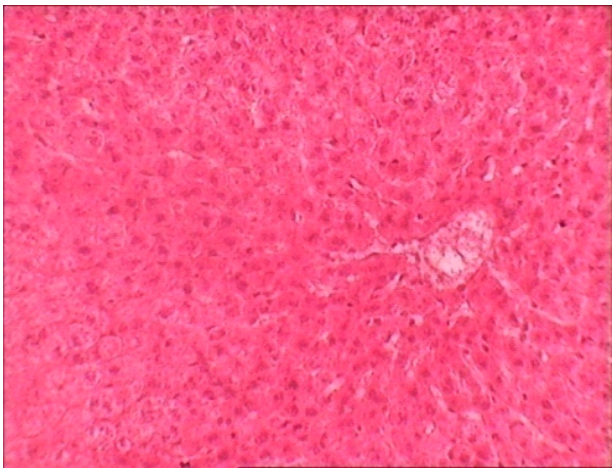

Plate 5: Histo-architecture of albino rat liver following acute (7 days) beta-cyfluthrin intoxication (400×)

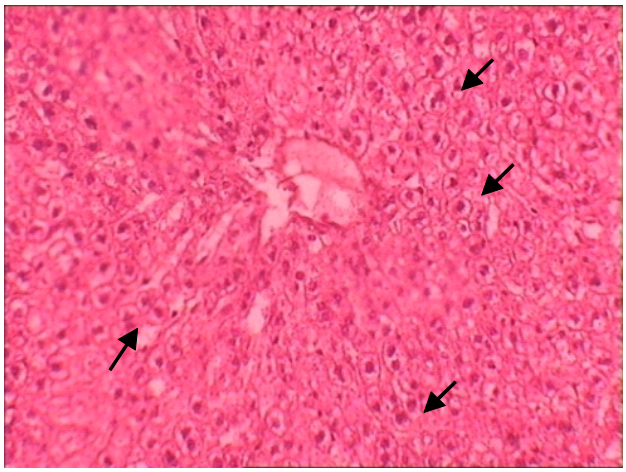

Plate 6: Histo-architecture of albino rat liver following acute (14 days) cypermethrin intoxication (400×)

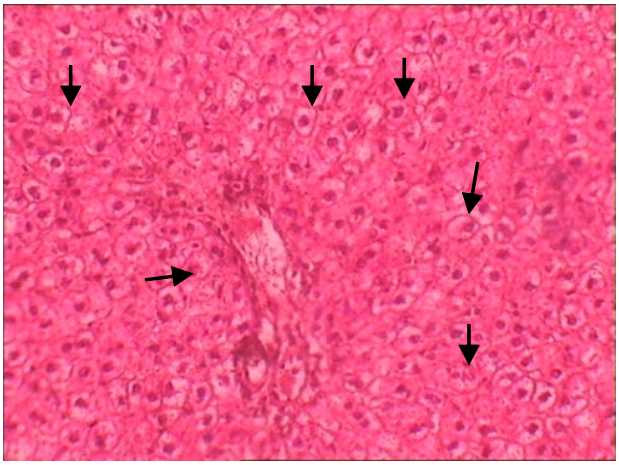

Plate 7: Histo-architecture of albino rat liver following acute (14 days) beta-cyfluthrin intoxication (400×)

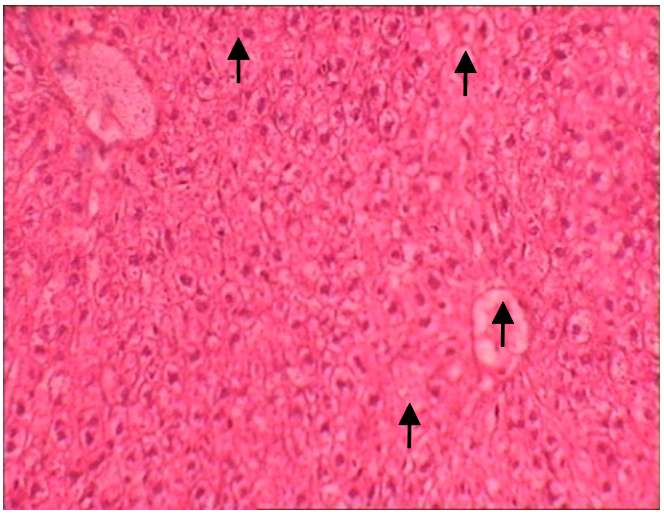

Plate 8: Histo-architecture of albino rat liver following acute (21 days) cypermethrin intoxication (400×)

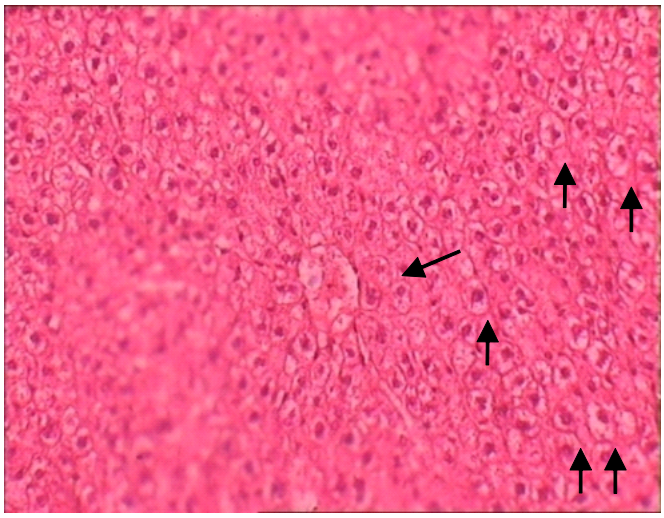

Plate 9: Histo-architecture of albino rat liver following acute (21 days) beta-cyfluthrin intoxication (400×)

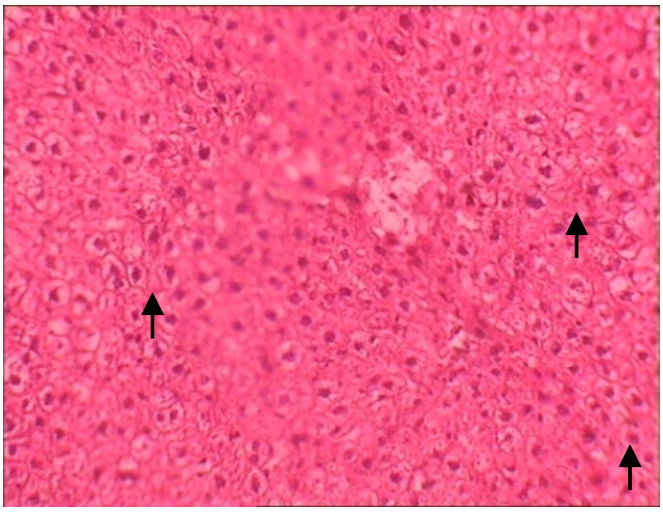

Plate 10: Histo-architecture of albino rat liver following acute (28 days) cypermethrin intoxication (400×)

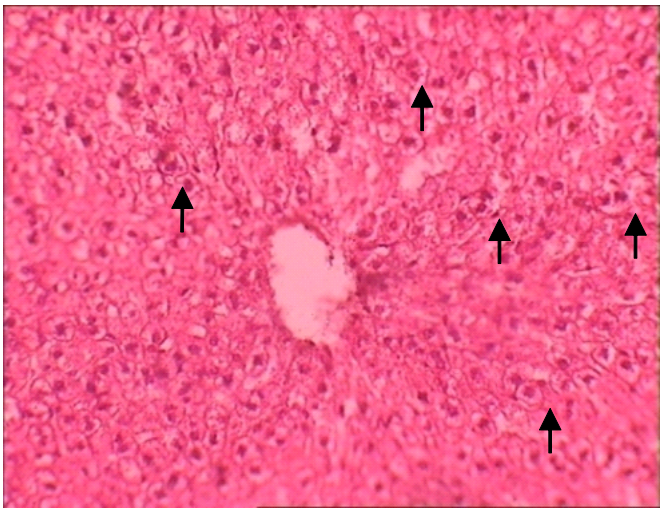

Plate 11: Histo-architecture of albino rat liver following acute (28 days) beta-cyfluthrin intoxication (400×)

its functionality under oxidative stress by increase in number of working genes as by replicating and also enhances the working capacity of cells to meet instant energy demands and to detoxify and eliminate the xenobiotic as well. Polyploidy is also associated with hypertrophy, the increase in cell volume[1-2,4, 11, 13].

Giant cell formation as observed in the present study may be a consequence of hypertrophy which in turn is a consequence of polyploidy condition under stress of experimental pyrethroids. Polyploidy, is associated with altered DNA function and type-II pyrethroids including both these experimental compounds are well capable of causing chromosomal as well as DNA damage and altering cell cycles, which may lead to variety of consequences up to tumour promotion. Tumour promotion, in turn, is a very complex process having various mysterious and multistep pathways. But initially, carcinogenesis induces nuclear enlargement which is generally associated with increase in DNA content and is evident in this study as presence of giant cells under stress of experimental pyrethroids[1, 13-16].

Further, giant cell formation is more pronounced in case of beta-cyfluthrin than cypermethrin probably due to structural differences in their chemistry. Beta-cyfluthrin is more recent pyrethroid product than cypermethrin and has been designed by modifying basic cypermethrin structure at the level of addition of fluorine group to position 4 of phenyl ring in beta-cyfluthrin, which seems to be responsible for this enhanced toxicity as C–F bond is one of the strongest bonds and difficult to break[2].

These signs of giant cell formation points out towards the mutagenic potential of these compounds to non-target organisms with a possibility of cancer initiation and promotion.

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