Toxicity of Endosulfan After Repeated Oral Administration to Rats

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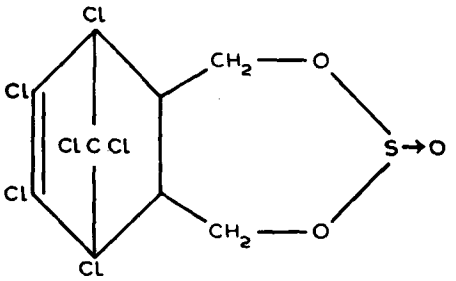
Endosulfan, an insecticide of the cyclodiene group, has a widespread use for the crop protection in the field of agriculture (MARTIN, 1964 and MILLER, 1965). The toxicity of the material has been recently reviewed by MAIER-BODE (1968) and GUPTA and GUPTA (1976b). Since the material is a chlorinated hydrocarbon, concern has been expressed over the possible repeated low level exposure to the chemical which is likely to enter human and animal system either directly or as environmental pollutant. It is, therefore, considered desirable to study the effects of repeated oral doses of endosulfan on organ weights, and histopathological alterations in various organs of male albino rats.

MATERIALS AND METHODS

Industrial Toxicology Research Centre colony bred male albino rats weighing 154-160 g were used. They were given commercial diet ad libitum and had free access to water. Technical grade endosulfan having the following structural formula, received throught the courtesy of NCL, poona, India, was used for this study.



Rats were divided into three groups, having 8 animals each. First and second groups received 5.0 and 10.0 mg/kg endosulfan orally in peanut oil daily for 15 days. The third group served as control and received peanut oil alone. The animals were examined daily for any signs of toxicity and mortality was noted. The body weights were determined initially and at the 15th day of the experiment before they were sacrificed. At the termina-

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TABLE 1

BODY AND ORGAN WEIGHT OF MALE RATS AFTER ORAL DOSES OF ENDOSULFAN DAILY FOR 15 DAYS

Doses mg/kg day	Initial body weight	% gain in body weight	Liver	Kidneys	Lungs	Testes	Small Intestines	Brain	Adrenals[a]
			Absolute organ weight (g)						
0.0 (Control)	160	30	7.47	1.82	1.80	2.19	6.62	1.80	56.4
5.0	158	29	8.62[b]	1.75	1.62	2.27	6.45	1.77	54.8
10.0	154	9	6.40[c]	1.40[b]	1.42[b]	1.50[c]	5.48[b]	1.60	47.4[b]
			Relative organ weight (g/100 g body weight)						
0.0 (Control)			3.59	0.88	0.87	1.05	3.18	0.87	27.11
5.0			4.23[b]	0.86	0.79	1.11	3.16	0.87	26.86
10.0			3.90	0.83	0.85	0.89[c]	3.26	0.95	28.21

a mg

Values are means of 8 animals except in group 3 receiving 10 mg/kg/day where 3 rats died due to toxicity. Figures marked with asterisks differ significantly from those of controls: [b] $P > 0.05$; [c] $P > 0.001$.

tion of the experiment, the animals were sacrificed with ether anaesthesia. The organs were examined for gross pathological changes,and liver, kidneys, lungs, small intestine, brain and adrenals were removed and weighed. Pieces of these tissues were fixed in 10% neutral formalin. Liver pieces were also fixed in Bouin's fluid for histochemical demonstration of glycogen. Lungs were fixed by injecting 1 to 2 ml 10% formalin through trachea prior to their removal from the body. All the tissues were processed in a routine way for histopathological studies. Paraffin sections cut at 5 μ were stained with haematoxylin and eosin and with PAS (MCMANUS and MOWRY, 1965).

RESULTS AND DISCUSSION

The mean values of body weights, absolute and relative organ weights of male rates given endosulfan orally daily for 15 days are given in Table 1. There was no mortality in the group receiving 5 mg/kg endosulfan. Liver weight was significantly increased. No significant change in body weight, absolute and relative organ weights of kidneys, lungs, testes, small intestine, brain and adrenals was observed. The increase in liver weights observed in this study confirms our previous reports as well as those of other investigators that such an increase in liver weight could be due to an adaptive mechanism, not necessarily reflecting the toxic effects of insecticides (FITZHUGH et al., 1971, GUPTA, 1976, and GUPTA, 1976a). Since the increased liver weight was also associated with pathological changes, the possibility of this dose level being toxic can not be ruled out. At higher dose (10 mg/kg), three rats died, one on 5th, 2nd on 7th and 3rd on 12th day of treatment. Body weight and absolute organ weights were significantly low when compared with controls, but no change in relative organ weights was observed, except in testes which registered a significant decrease in weight. The distinct changes in body weight and organ weights of rats given 10 mg/kg endosulfan could probably be due to the toxic effects of endosulfan. On autopsy, most of the organs were normal except for the liver and kidneys which were markedly congested.

The histological pattern of liver of control rats presented normal architecture, whereas the liver of rats treated with endosulfan (5 mg/kg) for 15 days showed moderate dilatation of sinusoids around central veins. Minute areas of focal necrosis, comprising of few degenerated hepatocytes and mononuclears, were seen throughtout the section. Kupffer cell hyperplasia and moderate degree of bile duct proliferation was also evident. At higher dose (10 mg/kg) dilatation and congestion of central veins and sinusoids were more prominent and fairly bigger areas of focal necrosis with marked inflammatory reaction were noticed. In some of the hepatic lobules hepatocytes in the vicinity of central veins showed nuclear pleomorphism and rounded vacuoles in the cytoplasm (Figures 1 and 2). Kupffer cells markedly hypertrophied and bile duct proliferation was seen throughout the

sections. Such hepatic changes have also been reported following single and repeated exposure to several other pesticides (KIMBROUGH et al., 1972).

Kidneys, lungs and testes of rats given endosulfan (5 mg/kg) for 15 days showed almost similar pattern to that seen in the sections of control rats. However, rats receiving higher dose (10 mg/kg) showed marked congestion and focal degenerative changes in the epithelial lining of kidney tubules (Figure 3). Lung tissue revealed focal inflammatory areas particularly in the sub-

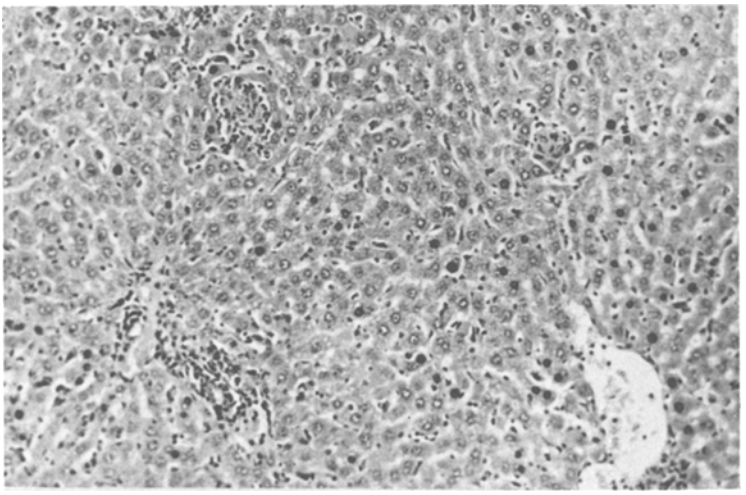

Fig. 1. Liver from a rat treated with endosulfan (10 mg/kg), showing areas of focal necrosis and Kupffer cell hyperplasia, H&E x 150.

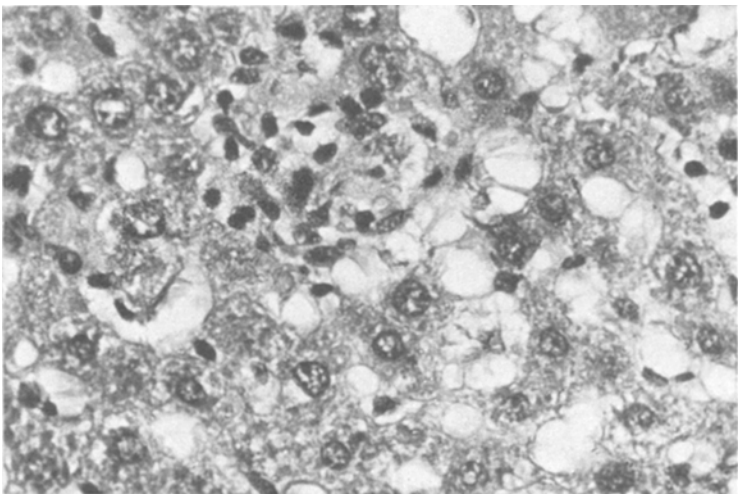

Fig. 2. Liver from a rat treated with endosulfan (10 mg/kg), showing rounded vacuoles in the hepatocytes, H&E x 600.

pleural regions. These areas were comprised of lymphocytes, plasma cells and numerous histocytes. Some of the alveoli showed dilatation; bronchioles and blood vessels appeared normal (Figure 4). The sections of testes showed marked degererative changes in the seminiferous epithelium of tubules. Nearly one-third of the tubules in a section were devoid of spermatogenic elements and were lined by a single layer of cells consisting of Sertoli cells and few spermatogonia. Interstitial tissue was oedematous, however, Leydig cells and blood vessels did not show

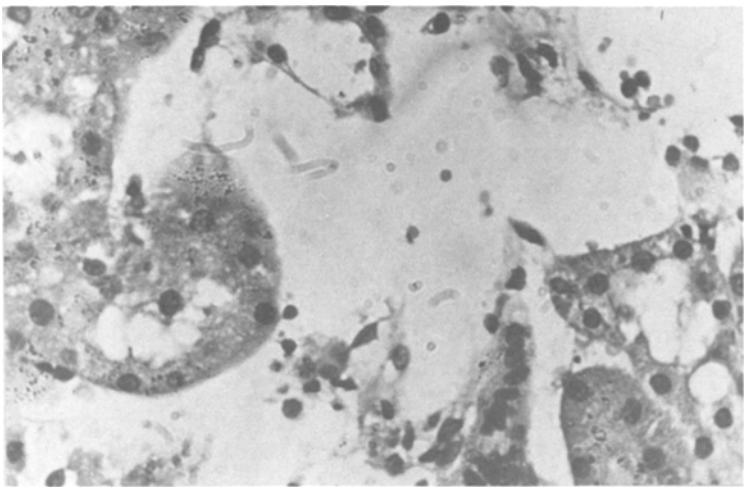

Fig. 3. Kidney section from a rat treated with endosulfan (10 mg/kg), showing necrosis of tubular epithelium. H&E x 600.

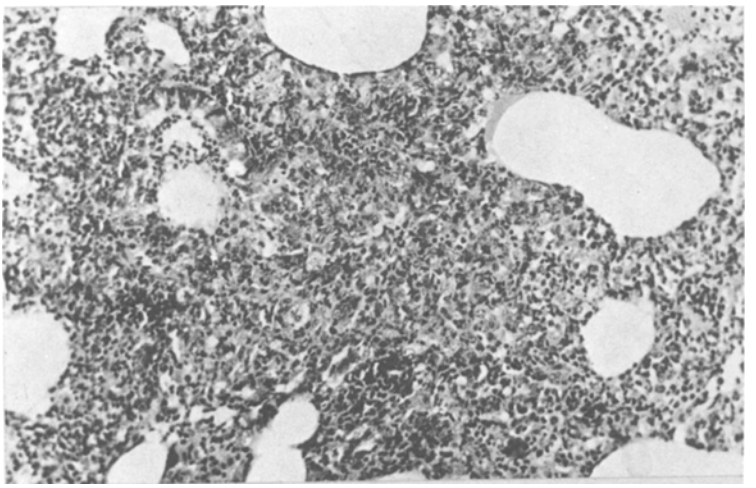

Fig. 4. Lung section from a rat treated with endosulfan (10 mg/kg), showing dilated alveoli and inflammatory reaction around them. H&E x 150.

any appreciable change (Figures 5 and 6). No pathological changes were observed in brain, small intestine and adrenals of rats receiving 5 or 10 mg/kg endosulfan. In contrast, various isomers of DDT are known to produce damage of adrenals cortex of dog (HART el al., 1973). Liver glycogen as demonstrated histochemically was not significantly changed with either of the treatment. The endosulfan produced marked histopathological changes of various tissues which confirms this level as a toxic level. Similar histopathological changes in various organs have been reported after acute or chronic exposure to DDT or endosulfan in various species of animals (KIMBROUGH et al., 1972, GUPTA and CHANDRA, 1975). The mechanism of such a change in the present experiments needs further investigations.

Fig. 5. Testis from a control rat showing normal pattern of testicular tissue. H&E x 150.

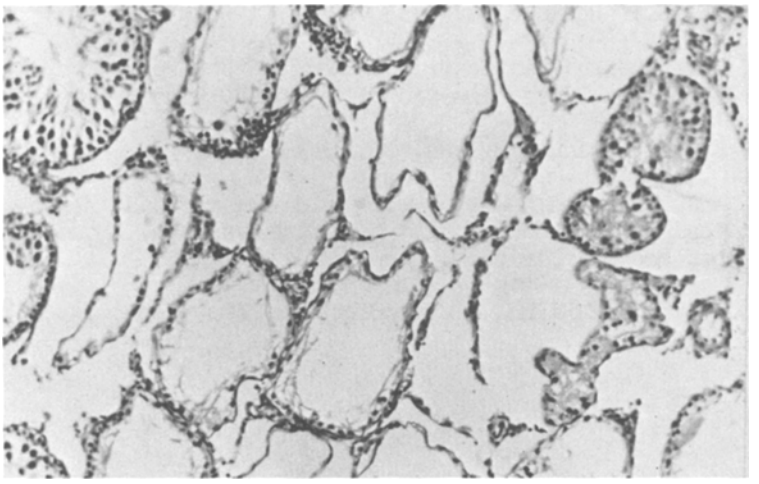

Fig. 6. Testis from a rat treated with endosulfan (10 mg/kg), showing degenerated, seminiferous tubules lined by a single layer of cells. H&E x 150.

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