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EFFECT OF PROLNGED ADMINISTRATION OF LARVIN ON ALBINO RATS

BY

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SUMMARY

Prolonged oral administration (90 days) of larvin 80 DF to albino rats in doses 1/20 and 1/10 LD50 (19.91) and 39.80mg/kg b. wt.) resulted in a significant increase in Alanine aminotransferase (ALT). Aspartate aminotransferase (AST) and alkaline phosphatase activityes. Urea and creatinine concentrations were also significantly increased in treated rats as compared with those of control. Total lipids and cholesterol were significantly decreased. Histopathological examination showed degenerative changes and necrosis in liver, kidney, cardiac muscles, cerebrum and cerebellum. No haematological changes were observed.

INTRODUCTION

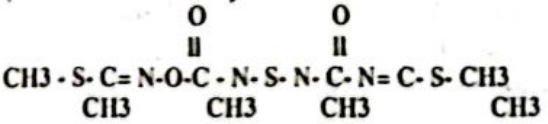
Larvin is one of the non phytotoxic thiodicarb insecticide, it is applied by spraying against lepidopterous pests resistant to synthetic pyrethroid and organophosphate (Allen et al., 1986). Durhan and Williams (1972); Collins et al., (1971) and Smalley et al., (1968) noticed that carboryl at 10000 ppm. impaired fertility in rats while Righer et al., (1987):; Murray et al., (1979): Dikshith et al., (1975): and Weil et al., (1972) mentioned that carbamets showed neither teratogenicity nor toxicity in experimental animals. Prolonged administration of pesticides leads to singnificant increase in biochemical constituents in blood and degenerative changes in liver, kidney and cardiac muscles Wilkinson (1970). Wacher and Coombs (1969), Clermont and Chalmers (1967). No available literatures dealing with the toxic effects resulted from the chronic contact with larvin in man and animals.

This experiment was designed to evaluate the expected harmfull effects of larvin 80 DF (thiodicarb) on albino rats as a guide to its relation to the human health.

MATERIAL AND MEHTODS

Insecticide:

Larvin 80 DF (Dimethyl N, N, {thiobis (methylimino) carbonyloxy) bis (ethanimidothioate}.



Was provided by unicarbid Co. in the form of wettable powder

Animals:

Thirty male albino rats (60-80 gram)maintained on pellet diet and watered ad-libitum were used. The animals were divided into 3 equal groups. the first group was given corn oil as solvent and kept as control, 2nd and 3rd groups were given larvin 1/20 and l/10 LD 50 (19.91 and 39.80 mg/kg b. wt.), respectively (Soliman and Aziza Amer, 1992) orally for 90 days. After 90 days, 2 blood samples were collected from each animal one on EDTA as anticoagulant for haematological examination and the other sample was used to obtain clear serum for determination of serum enzymatic activities, cholesterol and total lipid concentrations. The rats were killed and tissue samples (liver, kidney, lung, spleen, heart, brain, testes and epididymis) were taken for histopathological examination.

1- Haematological examination:

Haemoglobin concetration was determined according to Zijlstra (1960), erythrocytic and leucocytic counts according to Witnrobe (1967) and PCV according to Schalm et al., (1975).

2- Enzymatic activity:

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were determined according to Reitman and Frankel (1957). Alkaline phosphatase (ALP) activity was estemated according to Belfield and Goldberg (1971), urea (Hallett and Cook, 1971) and creatinine (Bartels, 1972).

3- Total lipid and cholesterol concentrations were determined according to (Girard et al., 1970 and Husdan et al., 1968).

4- Histopathological examination: Specimens from the liver, kidney, heart, lung, brain, testis and epididymis were fixed in formol saline 10%, and embedded in paraffine for histopathological examination according to Carleton et al., (1967).

RESULTS

The obtained results showed a singificant increase in the activity of ALT, AST and alkaline phosphatase and concentration of urea and creatinine. Total lipids and cholesterol were significantly decreased in treated rats than the control ones following oral administration of larvin in two doses (19.91 and 39.80mg/kg b. wt.) (Table 1).

The histopathological changes in the liver of the group receiving larvin 1/20 LD_{50}, revealed that some hepatocytes showed degenerative changes accompanied by mononuclear cells aggregated between the hepatocytes and around the central vein (Fig.1). These changes were more sever in the liver of the group receiving higher doses of larvin (1/10 LD_{50}) where the degenerative changes were seen in most of the hepatocytes accompanied by congestion of the central vein.

Kidney showed mild degeneration within some renal tubules, while in the group receiving the higher dose of larvin (1/10 LD_{50}), the same lesions were observed accompanied by congestion and haemorrhage. In addition, round cells aggregation were obvious between the renal tubules in the cortico-medullary junction.

Myocardial necrosis was observed in the heart of the rats receiving larvin (1/20 LD_{50}). Higher doses of insecticide, showed this change more agrevated and associated by congestion thrombosis of some croneries, and cuffing of others by mononuclear cells (Fig. 2).

Table (1): Effect of prolonged administration of larvin on liver function, kidney function, cholesterol and total lipids in rats.

Treatment	Liver function			Kidney function		Cholesterol mg%	Total lipid mg%
	AST u/l	ALT u/l	ALP u/l	Urea mg%	Creatinine mg%		
Control	125.0 ± 2.24	38.0 ± 1.22	28.64 ± 0.33	19.91 ± 0.53	1.204 ± 0.071	57.44 ± 0.23	310.66 ± 0.088
19.91 mg/kg b. wt. 1/20 LD50	163.6** ± 1.57	54.2* ± 1.80	47.74* ± 0.15	38.29** ± 0.65	2.16** ± 0.056	37.50** ± 0.22	214.80** ± 0.09
39.80 mg/kg b. wt. 1/10 LD50	182.0** ± 1.85	75.17** ± 1.19	67.76** ± 0.57	58.06** ± 0.53	3.808** ± 0.021	37.40** ± 0.024	213.46** ± 0.102

* = P < 0.05 ** = P < 0.01.

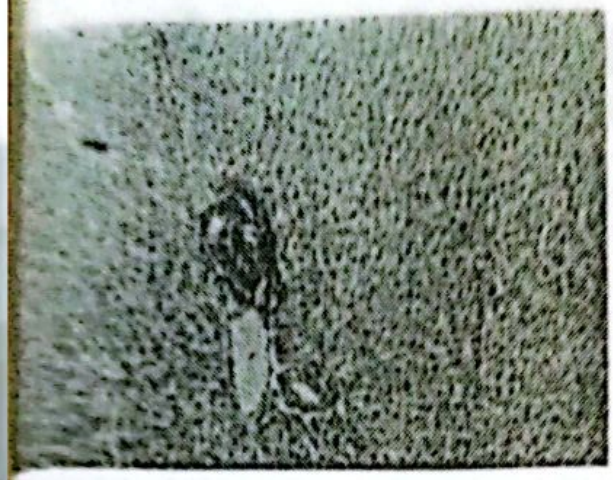


Fig. 2: Liver showing aggregating of mononuclear cells between the paranchyma and around the central vein (H & E X 50).

Fig. 3: Lung showing congestion of the pulmonary blood vessels and their surrounding by mononuclear cells H & E X 50.

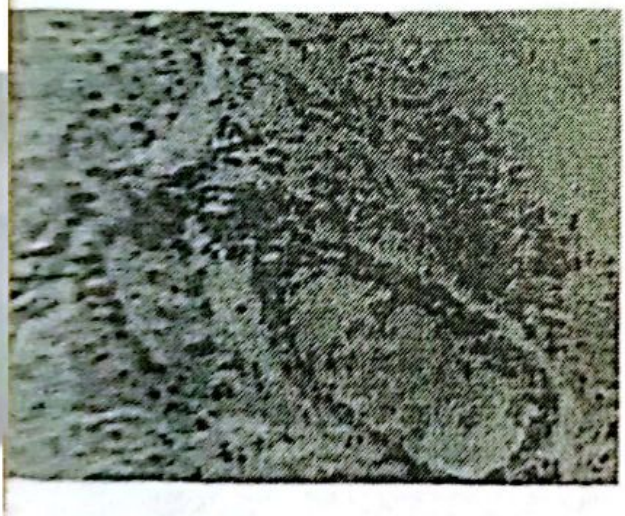


Fig. 2: Heart showing congestion of the coronory blood vessels and its cuffing with mononuclear cells H & E X 160.

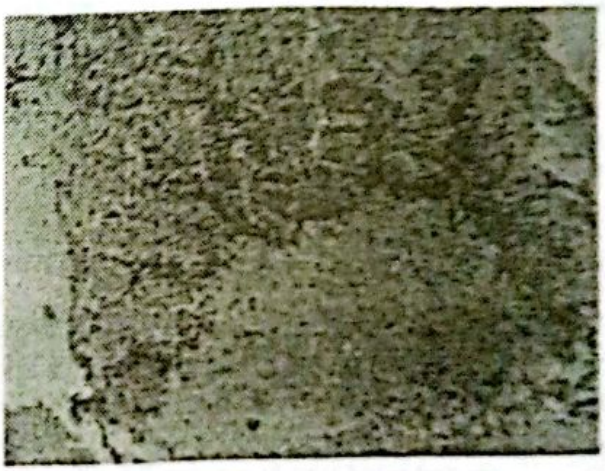


Fig. 4: Cerebrum showing focal necrosis H & E X 50.

Microscopical examination of lung from rats receiving 1/20 LD_{50} larvin, showed mild bronchitis. Administration of higher doses caused bronchitis and thickening of the alveolar wall. Most of the pulmonary blood vessels appeared congested and surrounded by mononuclear cells (Fig. 3) together with thrombosis.

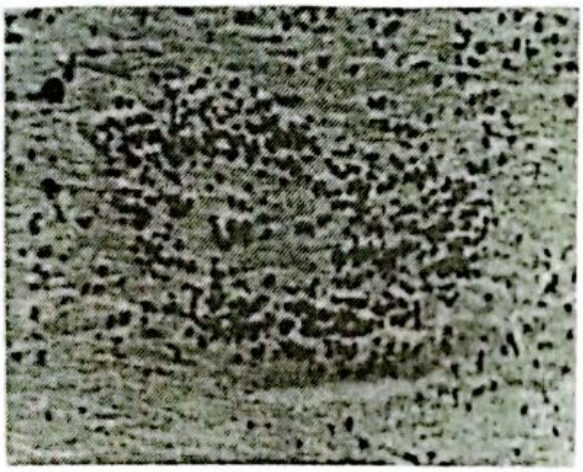


Fig. 5: Cerebrum showing focal gliosis H & E X 100.

Fig. 6: Cerebellum showing submenigial haemorrhages. H & E X 50.

The most obvious changes were observed in the brain. With low dose of larvin 1/20 LD50, the crebrum showed congestion, pericellular and perivascular oedema and focal necrosis (Fig. 4). Administration of high dose caused more agrevated chagnes beside the previous lesion. Focal and diffuse areas of gliosis were seen (Fig. 5) Submeningial congestion and haemorrhages were the most prominant changes seen in the cerebellum (Fig. 6) together with degeneration and necrosis of perkinjie cells (Fig. 7).

The histopathological changes of the testis were only detected in rats receiving larvin 1/10 LD50- These changes were congestion, necrosis of

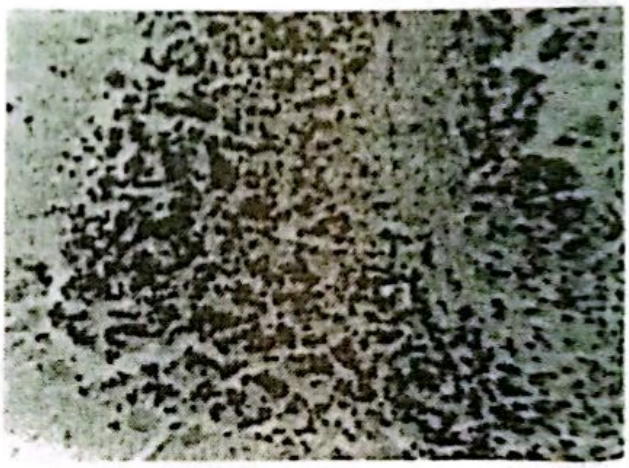


Fig. 7: Cerebellum showing necrosis of many of purkinjie cells. H & E stain X 100.

spermatozoa and spermatid accompanied by interstitial mononuclear cells aggregation around most of the epididymal blood vessels.

Table (2): Haematological picture in rats treated with larvin for 90 days.

Treatment	RBCs X 10^6	WBCs X 10^3	HB gm %	PCV
Control	6.55 ± 0.12	6.20 ± 0.07	14.38 ± 0.42	31.16 ± 0.47
19.91 mg/kg b. wt. (1/20 LD_{50})	7.50 ± 0.03	6.30 ± 0.05	15.23 ± 0.34	33.17 ± 1.55
39.80 mg/kg b. wt (1/10 LD_{50})	7.20 ± 0.10	6.10 ± 0.01	15.37 ± 0.17	33.33 ± 0.98

DISCUSSION

Prolonged administration of larvin for 90 days (19.91 and 39.80mg/kg b. wt.) resulted in a significant increase in activity of ALT, AST and alkaline phosphatase. These results were supported by the degenerative changes and necrotic change observed in the liver, kidney and cardiac muscle by our histopathological examination. As the ALT was found in higherst concentration in the liver and AST in heart muscle, skeletal muscle, brain, liver and kidney (Wroblewski, 1958), therefore, any damage of the previous tissues lead to an increase in the level of these enzymes in serum.

The same results were obtained by El-Sabbagh (1987) following prolonged adminisration of basagran and atrazine in rabbits. Wilkinson (1970), Wacher and Coombs (1969), and Clermont and Chalmers (1967) reported increase in enzymatic activities and degenerative changes in liver, kidney and heart muscles in rats following prolonged adminestration of pesticides.

The obtained significant increase in urea and creatinine concentration (Table 1) was attributed to the observed degeneration within some renal tubules in rats receiving larvin in doses of 19.91 and 39.80 mg/kg b. wt.

Total lipids and cholesterol concentration in serum of treated rats were significantly decreased, the same results also obtained by Aarsland et al., (1990) who reported that thiodicarboxylic acid (Tiadenol) administration in rats resulted in hepatomegaly and decrease triacylglcerols and cholesterol concentration due to increased the peroxisomal beta-oxidation, palmitoyl-Co A hydrolase and glycerophosphate acyltransferase, as well as decrease the carnitine palmitoyl-transferase.

No significant haematological changes were reported in treated rats. The same results also reported by Risher et al., (1987) and Dikshith et al., (1975) who reported no significant haematological changes in rats treated with aldicarb and carboryl.

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