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INTERACTION OF HEPATIC SCHISTOSOMIASIS MANSONI AND HEPATOTOXIC INSECTICIDES ADMINISTRATION: IV: EFFECTS ON LIVER NUCLEIC ACIDS CONTENTS

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ABSTRACT

The effects of induced intoxication with two insecticides (aldicarb or decis) on normal healthy and S. mansoni infected mice were studied. The acute (LD_{50}) and sublethal doses of each compound were tested and the alterations of liver nucleic acids (RNA, DNA) were recorded.

The data obtained herein indicate that oral administration of either sublethal (1/10 LD_{50}) or acute doses (LD_{50}) of both insecticides to normal or bilharzial infected mice, caused remarkable reductions of RNA & DNA contents in liver. however, such reductions were more pronounced in bilharzial than in healthy mice under the same dose level and the severity of these effects in case of acute doses was found to be depended on the stage of the infection.

The reduction in liver nucleic acids contents was attributed to either higher catabolic rates or disturbance of the nucleic acids syntnesizing system.

INTRODUCTION

In spite of recognizing the tremendous problem of pesticides and its international impact as environmental contaminants, yet, they are still representing a very real necessity for eradication of undesired pests and disease vectors. The extremely wide spread use together with the misuse of such insecticides, constitute a very serious health problem all over the world, specially in the developing counteries (Davies, 1977; El-Sabae and Soliman, 1982).

Accordingly, the risk of human exposure to such biocides has been recognized. Thus poisoning or even mortalities with lower percentage have been reported to occur in human exposed to organochlorines (Guzelian, et al., 1980), polychlorinated biphenyls (Fishbein, 1974; Hirayama, 1976), carbamates (Leavitt, et al., 1982) organophosphates (Hagras, 1984) and pyrethroids (Fouda, 1983 and Mahmoud, 1983).

What increased the risk of these hazards, is that; such pollutants are intensively sprayed in rural areas, wherein large segment of population are infected with Schistosomiasis However, it is estimated that the population at risk of infection in Egypt is about 33 million persons (WHO, 1985).

To simulate the interaction of the two problems in our laboratory, a series of investigations were planned by the authors (El-Elaimy, et al., 1988 a,b,c). In these investigations, S. mansoni infected mice were exposed to different dose levels of insecticides; aldicarb (carbamate) or decis (pyrethroid) which are currently and widely used in agricultural protection purposes in Egypt. This paper concerned with effect of such interaction on nucleic acids metabolism in liver.

In this respect, insecticides have been implicated to interfere with nucleic acids metabolism (Chung, et al., 1967; Sharma, et al., 1976; Gupta and Paul, 1978 and El-Nabi, 1989). In their experiment, Chung, et al., (1967) cultured Hela S cells in the presence of various levels of p.p DDT and dieldrin. They found that both agents inhibit DNA, RNA and protein synthesis as assessed by the rates of incorporation of isotopic precursors of these macromolecules. In a recent study, administration of dimethoate (O.P) to mice caused depletion of both nucleic acids contents in liver and testis (El-Nabi, 1989).

Similar effects on nucleic acid contents were reported in case of bilharzial infected liver (Shawky, et al., 1964; Salwa, et al., 1981) which were attributed to the disturbance in enzymes interfereing with the nucleic acid metabolism (Auradalla, et al., 1975; El-Merzabani, et al., 1977).

MATERIAL AND METHODS

Experimental Animals:

A total number of 150 male albino mice of 8-10 weeks old were used. Chow and water were freely available ad. libitum during experimentation.

Schistosoma mansoni infection:

The individual mice were exposed by tail immersion technique (Olivier and Stirewalt, 1982) to 30 cercariae of S. mansoni shed by laboratory infected Biomphalaria alexandria snails.

Insecticides used:

Two insecticides widely used in Egypt, Aldicarb (carbamate) of technical grade 100% and decis (pyrethroid) of technical grade 95% purity were tested in the present study. Different dilutions were prepared using corn oil.

The LD_{50}'s of such insecticides were 0.9, 0.5 mg/kg (aldicarb) and 30, 10 mg/kg (decis) for normal healthy and bilharzial mice (60 day-old infection) respectively as obtained from the lethal mortality curves constructed in a previous study (El-Elaimy, et al., 1988a).

Groups and treatments:

Experiment (I): Effect of single sublethal doses:

for this experiment, 60 mice were used and divided into the following groups:

i. **Control group:** 10 healthy mice were saved as control.

ii. **Treated group:** 20 mice (10 for each insecticide) were treated orally at a time with single sub-lethal dose (1/10 LD_{50}) of each compound.

iii. **Infected:** 10 mice (60 day-old infection).

iv. **Infected-treated group:** 20 mice (10 mice for each compound) at the same stage of infection as group iii, were orally treated at a time with 1/10 LD_{50} (bilharzial LD_{50}).

Animals of control; infected and other treated groups were simultaneously decapitated 24 hr after insecticide administration.

Experiment (II): Acute effect study (LD_{50}'s):

Animals of this experiment (90 mice) were divided as follows:

i. **Control group:** 10 healthy wice were taken as control.

ii. **Infected group:** 20 mice infected at a time with 30 cercariae/ head and then batches of five

animals were decapitated at 2, 4, 6, 8 weeks post-infection (4 stages of this disease).

iii. **Treated group:** 20 mice were divided into two equal batches (10 mice for each insecticide). The two batches were orally administered LD_{50} of each insecticide and were decapitated 24hr post-treatment.

iv. **Infected-treated group:** 40 bilharzial infected (similar to group ii) were divided equally (20 mice for each compound). At the same stages as group ii, 5 animals were orally treated with LD_{50} of each compound (Bilharzial LD_{50}'s) and were decapitated 24 hr post-treatment at each stage.

Methods:

The nucleic acid contents in liver tissue homogenate were determined using the methods of Glick (1966) for RNA and Ceriotti (1955) for DNA and the protein content was also determined using the method described by Lowry, et al. (1951).

Data were statistically analysed and the significance of the difference between averages was tested using Student "t" test (Hill, 1971).

RESULTS

The data presented in table (I) showed that single sublethal dose (1/10 LD_{50}) of both decis or aldicarb induced slight but significant reductions in the liver nucleic acids (RNA and DNA) contents, 24 hr. after administration. Similar but moderate reductions were also observed in both nucleic acids contents in liver homogenate from bilharzial infected mice (60 day-old infection). However, when groups of bilharzial mice at the same stage of infection, were orally treated with doses equivalent to 1/0 LD_{50} (bilharzial LD_{50}) of each insecticide, higher percentage reductions of the liver nucleic acids were recorded in such groups. This indicates the higher susceptibility of infected mice towards insecticide intoxication.

It seems also from the results obtained that the depletion of liver nucleic acids as affected by acute (LD_{50}) insecticides administration was related to the stage of the disease (Figures 1,2). Thus gradual increasing reduction of both RNA and DNA contents were observed with development of the disease.

DISCUSSION

The interference of insecticides with nucleic acids metabolism (RNA, DNA) in mammalian tissues have been superficially examined. However, in an investigation carried out by Chung, et al., (1967), they showed that DDT and dieldrin were able to alter the rate of DNA-RNA and protein synthesis.

Table 1: Effect of single sublethal dose (1/10 LD_{50}) of Decis or Aldicarb on liver nucleic acid contents in normal and bilharzial infected albino mice (60 days-old infection with 30 cercariae/head).

Parameter	Normal Av.±SD.	Normal-Treated Av. ± SD.	% Diff.	Infected Av.± SD.	% Diff.	Infected-Treated Av. ± SD.	% Diff.
		Decis					
RNA	90.71±5.10	81.12±2.51**	-10.57	68.40±3.32**	-24.59	61.15±2.15**	-32.58
DNA	25.60±1.81	22.10±2.13*	-13.67	19.30±1.31**	-24.61	16.31±1.18**	-36.29
		Aldicarb					
RNA	90.71±5.10	76.13±3.11**	-16.07	68.40±3.32	-24.59	58.22±4.15**	-35.81
DNA	25.60±1.81	20.11±2.15**	-21.45	19.30±1.31	-24.61	14.12±2.20**	-44.84

1/10 LD_{50} = dose of normal mice = 3 mg/kg (D.); 0.09 mg/kg (Al.)

1/10 LD_{50} = dose of infected mice=1 mg/kg (D.); 0.05 mg/kg (Al.).

Units expressed as mg/gm protein.

** highly significant ($P < 0.01$).

* significant ($P < 0.05$).

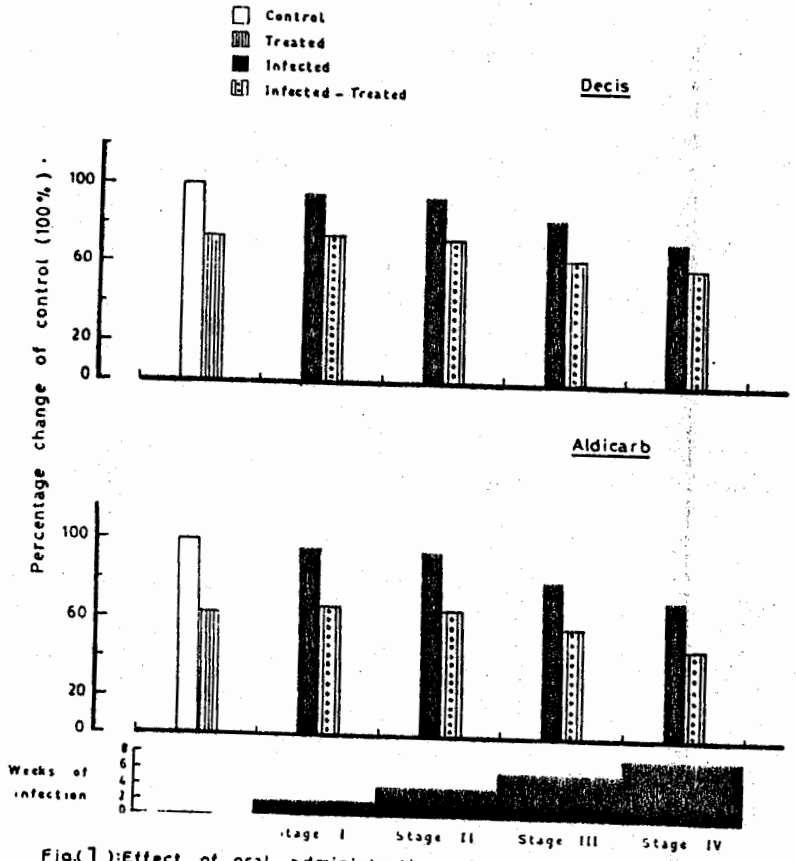

Fig.(1): Effect of oral administration of acute LD_{50} dose of Decis and Aldicarb on liver DNA content in normal and bilharzial infected albino mice. (During different stages of infection).

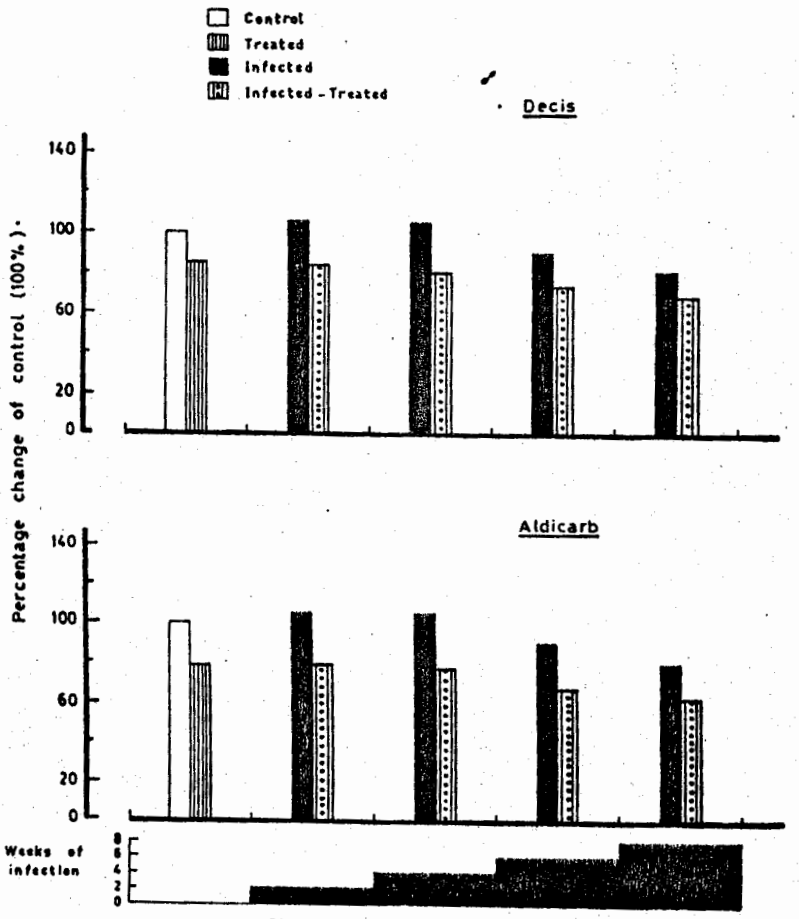

Fig.(2): Effect of oral administration of acute LD_{50} dose of Decis and Aldicarb on liver RNA content in normal and bilharzial infected albino mice. (During different stages of infection).

Also, in ducks fed on various dietary levels of dieldrin, reduction in liver protein, deoxyribonucleic acid and ribonucleic acid contents were recorded (Sharma, et al., 1976). Moreover the effect of dieldrin on the de novo RNA purine synthesis from formate were slight, while mirex inhibited the synthesis of both RNA purines (Walker, et al., 1977). The same author reported also that dieldrin inhibited the in vitro incorporation of thymidine, uridine and L-Leucine into DNA, RNA and protein respectively. Similar results were further recorded in cultured Hela S cells in the presence of various levels of p,p DDT and dieldrin (Chung, et al., 1967). Metasystox, an organophosphorus insecticide was able to induce a significant decrease in DNA in all brain regions, however, the RNA level decreased only in the cerebellum (Tayyabe, et al., 1981).

The reduction observed in liver nucleic acids (RNA and DNA) recorded in the present study was further confirmed by the author in another investigation, whereas reduction in liver nucleic acids accompanying by elevation in liver nucleases activities in rogor intoxicated mice (El-Nabi, 1989). Thus it would be plausible to interpret the present data along the same line as in our previous investigation wherein such reductions were attributed to the enhancement of catabolism of nucleic acids in liver of intoxicated animals.

Another suggestions have been also reported by Gale, et al., (1971) and Martin and Lewis (1979). They have provided indirect evidence that captan inhibits the synthesis of nucleic acids and this was attributed to at least two possible

mechanisms, one being the direct interaction of captan with nucleic acid synthesizing system to cause the inhibition. The alternative explanation was speculated to be inhibition by captan to the uptake or phosphorylation of labelled precursors by the cells. These suggestions were further confirmed by Dillwith and Lewis (1980) who recorded inhibition in DNA polymerase B activity in isolated bovine liver nuclei, thus it was concluded that captan inhibited DNA synthesis by acting directly on DNA polymerase catalyzed reactions rather than by causing a nonspecific or indirect effect on the nuclear system.

Acid ribonuclease (RNase), acid phosphatase and alkaline phosphatase are directly or indirectly involved in nucleic acids metabolism by controlling the nucleotides in cell. Fritzson (1967) also claimed that 5'-NT enzyme may have some relations to the growth of cells. Thus, its role in the catabolism of DNA and RNA is therefore suggested. In this respect we may suggest that any factors which affect such enzymes would indirectly influence the nucleic acid metabolism. This is true in our study if we considered the disturbance of such enzymes by different insecticides administration (El-Elaimy et al., 1988c) and in case of schistosomiasis (Saleh, et al., 1976; El-Merzabani, et al., 1977; Abdel Salam, 1983; Al-Sharkawi, 1985 and El-Elaimy et al., 1988c).

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الملخص العربي

التفاعل بين مرضى الكبد البلهارسى (مانسونى)
والتسمم الكيدى ببعض المبيدات
٤ - التأثيرات التى تحدث فى المحتوى الكيدى من الأحماض النووية

يهدف هذا البحث الى دراسة مدى تأثير الأحماض النووية (الدانا ، الرانا) فى كبد حيوانات التجارب (المايس) السليمة والمصابة بمرض الكبد البلهارسى .

استخم لذلك نوعين من المبيدات وهما مبيد الألديكارب وينتمى لمجموعة الكرباميت ومبيد الديسيز وينتمى الى مجموعة البيروثرويد .

تم اختيار مدى تأثير كل من المبيدين على المحتوى الكبدى للأحماض النووية على مستوى الجرعة الحاده (LD 50) والجرعة تحت الحادة (1/10 LD50) .

أوضحت النتائج التى سجلت فى هذه الدراسة أن التسمم المحدث بأى من المبيدين السابقين سواء على مستوى الجرعة الحادة أو تحت الحادة يتسبب فى نقص بسيط فى محتوى كبد الفئران السليى من المرانا والرانا لو أن هذا النقص كان ذات مغزى احصائى .

أما بالنسبة للفئران المصابة بمرض الكبد البلهارسى فقد أظهرت النتائج نقصا كبيرا فى المحتوى الكبدى من الأحماض النووية . وقد وجد أيضا بأن النقص فى الأحماض النووية يعتمد على تركيز الجرعات المعطاه وكذلك على مراحل المرض المختلفة .

وقد نوقشت العوامل المختلفة والتى يحتمل أن تتدخل فى احداث خلل فى تخليق هذه الأحماض النووية .