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INTERACTION OF HEPATIC SCHISTOSOMIASIS MANSONI AND HEPATOTOXIC INSECTICIDES ADMINISTRATION: V: CHANGES IN TOTAL LIPID AND LIPID FRACTIONS IN LIVER

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ABSTRACT

The effects of oral administration of aldicarb (carbamate) and decis (pyrethroid) to normal healthy or bilharzial mice were studied. The acute (LD_{50}) as well as sublethal dose (1/10 LD_{50}) were tested and changes in liver lipogram (Total lipid, phospholipid, cholesterol and triglycerides) under different conditions was investigated.

Marked increases were noticed in total lipid with concomitant reductions in phospholipids and cholesterol and triglycorides contents in liver of acute treated-mice with both insecticides. These effects were more pronounced in bilharzial-infected mice. Similar pattern of changes was observed in case of single sublethal (1/10 LD_{50}), however, the magnitude of such changes depended on the stage of the disease. The possible factors interferring with lipid metabolism under such condition Conditions were discussed.

INTRODUCTION

In Egypt, a quite percentage of pepulation in rural areas are infected with schistosomiasis. According to the estimate carried out in 1985, the population at risk of infection in Egypt is about 33 million persons (WHO, 1985). In such rural areas where the disease became endemic, another health problem of insecticides pollution have to be occurred. The risk of human exposure to such insecticides has been also recognized (Fouda, 1983; Hagras, 1984).

For evaluation of the effects of the interaction between insecticide administration and S. mansoni infection, many investigations have been conducted by the present author, including studies on toxicity and other enzymatic changes (El-Elaimy, et al., 1988a,b,c). In continuation to the previous investigation, the present study was carried to evaluate the influence of such interaction on lipid metabolism.

Lipid metabolism has been studied under the influence of a variety of insecticides, thus, Singlevich, et al., (1972) showed that DDT or chlorocyclozine produced an increase in hepatic triglyceride levels. This increase was enhanced by simultaneous administration of ethanol. The authors also reported that the histological findings showed that DDT or chlorocyclozine but not ethanol caused fatty infiltration of the liver. In a similar investigation, the tissue analysis indicated the presence of DDT, DDD and DDE in all lipid fraction in liver of rats recieved oral doses of 3.5 mg/kg for 3 days(Kuz, et al., 1972). The levels of blood cholesterol, B-lipoprotein and total

lipid were found to be higher in rabbits treated with cholesterol plus DDT than in animals recieved cholesterol alone (Ludkaneva & Rodionov, 1973) Increased liver weights and lipids were also reported to occur in rats fed DDT or arochlor 1242. The structural changes induced by subchronic administration of dieldrin including dilation, congestion of sinusoids, necrosis and finally lipid accumulation (Hurket, 1978).

Organophosphates, were also reported to interfere with lipid metabolism, Buchet, et al., (1974) found that the inhibition of diglyceridase activity by esters of such compounds can not prevented by monoglycerides. Also, Civen, et al., (1977) suggested that the inhibition of adrenal cholesterol esterification and hydrolyses was due to their inhibition of adrenal steroidogenesis.

Other insecticides have been also reported to cause disturbances in lipid metabolism, as carbamate (Kuz, et al., 1972; Makhija & Pawary, 1975; Cecil, et al., 1974) and pyrethroids (El-Elaimy et al., 1988). However, these effects were superficially examined.

MATERIAL AND METHODS

Animals:

Male albine mice (18-20 gm) were used during experimentation. Chow and water were freely available ad.-libitum.

Insecticides used:

Aldicarb and decis are two insecticides belonging to carbamate and pyrethroid respectively. The active ingradient of such compounds were 100% for aldicarb and 95% for decis. The LD_{50}'s Aldicarb and Decis were 0.9, 30 mg/kg for normal healthy mice and were 0.5, 10 mg/kg for bilharzial mice as obtained from the lethal mortality curves constructed in a previous investigation (El-Elaimy, et al., 1988a).

Experimental Design:

Experiment (I): Effect of single sublethal doses:

For this experiment 60mice 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 group:** 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, treated and other infected 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 mice 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 the disease).

iii. **Treated group:** 20 mice were divided into two equal batches (10 mice for each insecticide). The two batches were administered with LD_{50} of each insecticide and were decapitated 24 hr 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 posttreatment at each stage.

Methods:

The total lipid and other lipid fractions in liver were estimated according to methods of Knight, et al., (1972) for total lipid, methods for cholesterol, phospholipids and for triglycerides are C.F. Varley, (1980).

In chronic bilharzial mice (60 day-old-infection) only total lipids showed to be accumulated in liver, however, the other lipid fractions were markedly decreased. Such effects were potentiated when the bilharzial-mice recieved the corresponding acute dose (bilharzial LD_{50}), thus higher percentage values for the elevation in total lipid or reduction in the other lipid fraction were recorded in infected-treated animals.

In an attempt to study the effects of such insecticides on bilharzial-mice during different stages of the disease (stages of infection), similar changes were observed in the liver lipogram, however, the magnitude of such changes depended to large extent on the stage of the disease (figures 1-4) whereas gradual increases in total lipid or reductions in the lipid fractions were noticed with the development of the disease.

Principally, in the normal animals there exists a continuous interchange of fat between the fat depots and liver (a triglyceride cycle). Triglycerides is stored in adipose tissue and acts as a large energy reserve, which can be made available when required by enzymatic hydrolysis to fatty acids and glycerol. Fat is then transported in the form of non-esterified fatty acids from the depots to the liver via the blood stream, in which it is resynthesized to triglycerides complexed with protein to form lipoprotein and is secreted into the blood stream almost certainly by the endoplasmic reticulum (Rees and Valerie, 1963). The same authors also reported that a large number of chemical substances when administered to laboratory animals like rats, they will produce

acute liver injury. In some cases the necrosis is associated with the accumulation of fat as in carbon tetrachloride (CCl_4) and dimethyl nitrosamine poisoning.

In another hypothesis, the fatty liver may results from an inhibition of the secretion of triglycerides synthesized in the liver. This could also be attributed to be due to either an impairment of the triglyceride secreting mechanism in liver of poisoned animals (Recknagel and Lombardi, 1961) and/or to a reduced synthesis of the protein necessary for the formation of lipoprotein, the vehicle which transports triglyceride from the liver (Robinson and Seakins, 1962).

Fatty liver infiltration may also be a physiologic response to an increase in lipid metabolization from peripheral fat, similar in this respect to what occur during starvation or may result from several disturbances of lipid transport and metabolism in a variety of disease states. Excessive lipid parenchymal cells may arise from one or more of three sources: 1) dietary sources. 2) peripheral fat depots and 3) hepatic synthesis. Lipid supply is inereased when hepatic oxidation of fatty acids or lipoprotein synthesis are reduced. (Cecil and Loeb, 1975).

In several conditions, liver infiltration may be associated with severe derangement of liver function. This is particular the case when fat accumulation is due to intoxication injuries causing decreased fatty acid oxidation or impaired lipoprotein synthesis as in phosphorus poisoning (Verzar & Laszt, 1936), alcoholism (Lieber and Spritz, 1965) and antibiotic (tetracycline) administration (Tahani, et al., 1980).

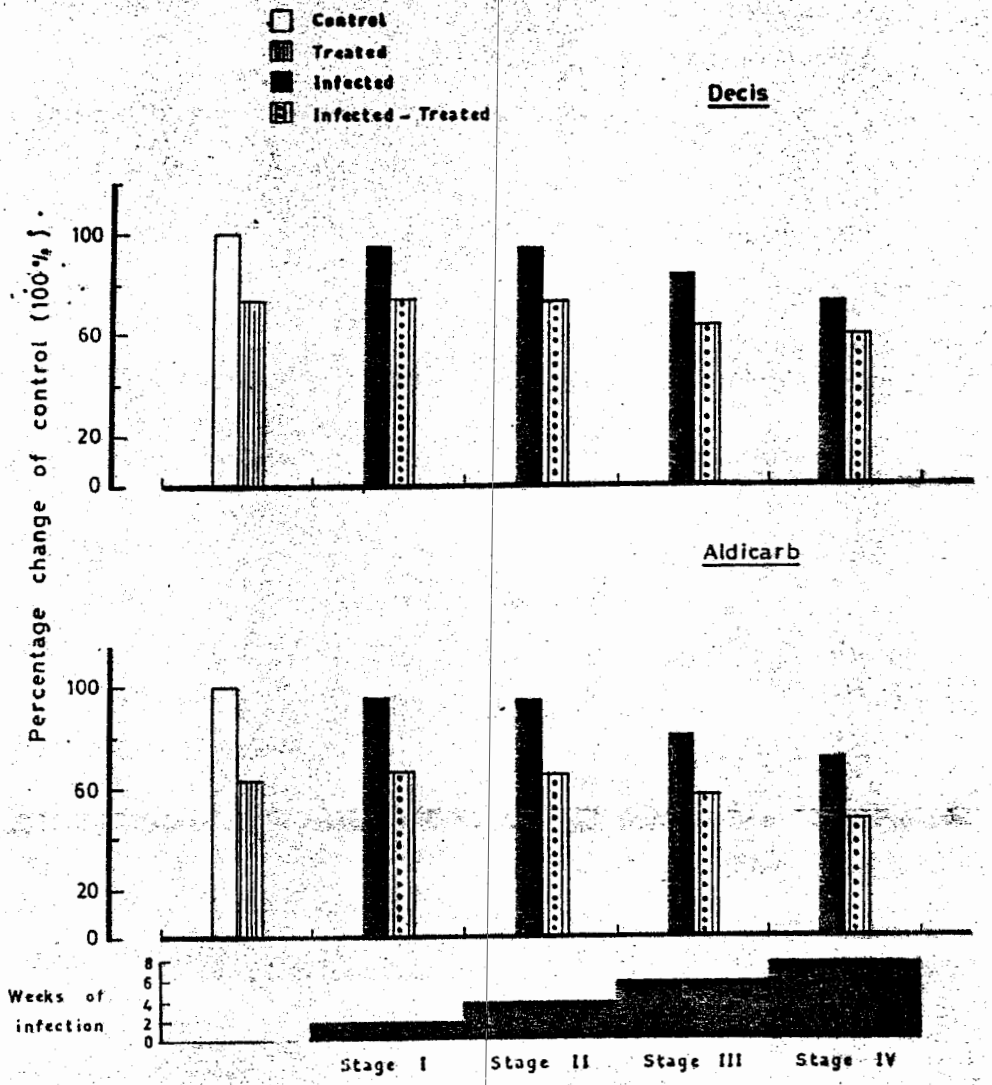

Fig.(1):Effect of oral administration of acute LD_{50} dose of Decis and Aldicarb on liver DNA content in normal and bilharzial infected albino mice .
(During different stages of infection) .

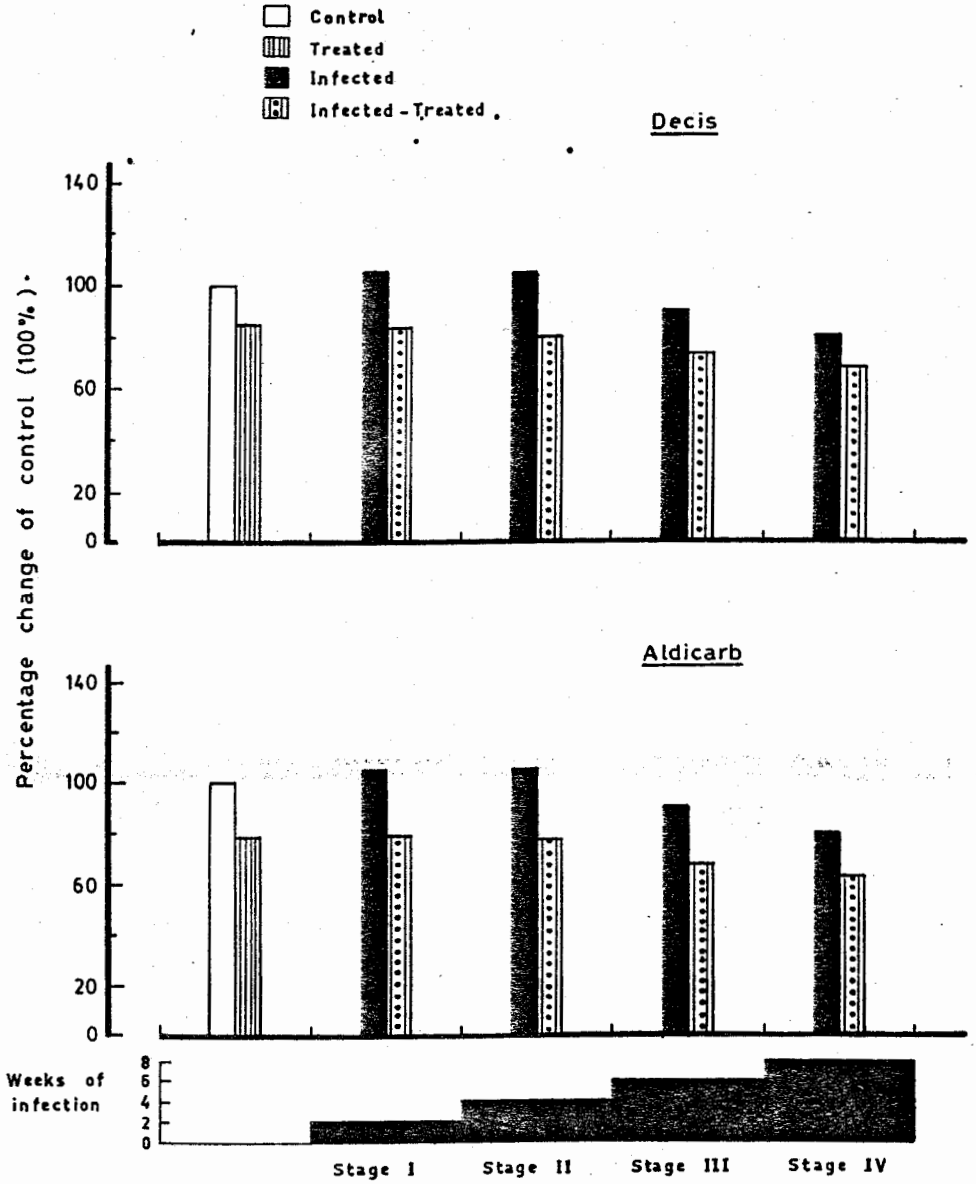

Fig.(2): Effect of oral administration of acute LD_{50} dose of Decis and Aldicarb on liver RNA content in normal and bilharzial infected albino mice.
(During different stages of infection).

Lipid abnormalities characterizing S. mansoni infection included, decreased plasma total and esterified cholesterol and phospholipids (Ghanem, et al., 1970; Gabr, et al., 1973; Mousa, et al., 1976; Gillet, et al., 1976). Although hypolipidemia seem to be a feature in schistosomiasis as the amounts of total lipids, triglycerides and free fatty acids have been reported to decrease (El-Kharbotly, et al., 1965; Gabr, et al., 1973; Mousa, et al., 1976). Some other studies revealed increased levels (Ghanem, et al., 1970b). In general lipid abnormalities are more pronounced patients with decompensated rather than in compensated hepatosplenic schistosomiasis (Gillet and Carvallio, 1978). In a recent study, Abdel Rahman and El-Sahly, (1988), found that lecithincholesterol acetyltransferase (LCAT) exhibited reduction in its activity together with reduction in B-lipoprotein in serum of patients with hepatosplenic schistosomiasis. The author also indicated that the low cholesterol ester recorded in schistosomal hepatic fibrosis is mainly due to impaired intravascular synthesis reflecting decreased hepatic synthesis of LCAT. They have also attributed the abnormalities encountered in hepatic schistosomiasis to the decreased LCAT activity recorded therein. These suggestions may be attributable in part to the lipid abnormalities recorded in our investigation. The severity of some of these abnormalities may be draw back to the potentiation effect of the insecticide administered.

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الملخـــص العربـــى

التفاعل بين مرضى الكبد البلهارسى (مانسونى)
والتسمم الكبدى ببعض المبيدات الحشرية
٥ ـ التغيرات التي تحدث في الدهون الكلية ومشتقاتها في الكبد

في هذا البحث تم دراسة مدى تأثير تناول مبيد الأليديكارب (مبيد من مجموعة الكرباميت) أو الديسيز (مبيد من نوع البيروثرويد) على محتوى الكبد من الدهون المختلفة (الدهون الكلية الفسفوليبيدات ، الكلوليسترول ، والجليسريدات الثلاثية) وذلك في الفئران السليمة والمصابـــه بمرض الكبد البلهارسى .

تم اعطاء فئران التجارب (المايس) كل من المبيدين عن طريق الفم على مستويين من الجرعات وهى الجرعة الحادة (LD 50) ، الجرعة تحت الحادة (1/10 LD 50) وذلك بالنسبة للفئران السليمة والفئران المعدية بسركاريا البلهارسيا من نوع المانسونى (٣٠ سركاريا لكل فأر)

سجلت النتائج زيادة ملحوظة فى المحتوى الكبدى من الدهون الكلية وذلك فى الفـــــئران السليمة بعد تناول الجرعة الحادة أو الجرعة تحت الحادة وقد صاحبت هذه الزيادة نقصا ملحوظـا فى باقى مشتقات الدهون (الفسفولبيدات) الكلوليسترول والجليسريدات الثلاثية) .

أوضحت الدارسة أيضا أن تناول نفس هذه الجرعات فى الفئران المصابة بالبلهارسيا بسـبب حدوث تغيرات مشابهة للسابقة ـ الا أنها ذات نسبة مئوية أكبر ـ وتتوقف مثل هذه النسبة عـلى مراحل المرض المختلفة .

وقد نوقشت مثل هذه التغيرات فى ضوء الأبحاث السابقة .