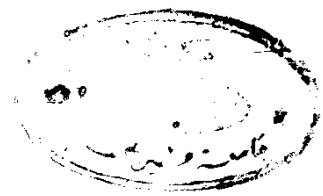
HISTOPATHOLOGICAL, HISTOCHEMICL AND ULTRASTRUCTURAL STUDIES ON THE EFFECTS OF DIMETHOATE ON THE GASTROINTESTINAL MUCOSA AND LIVER OF RAT



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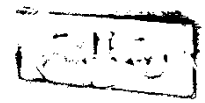

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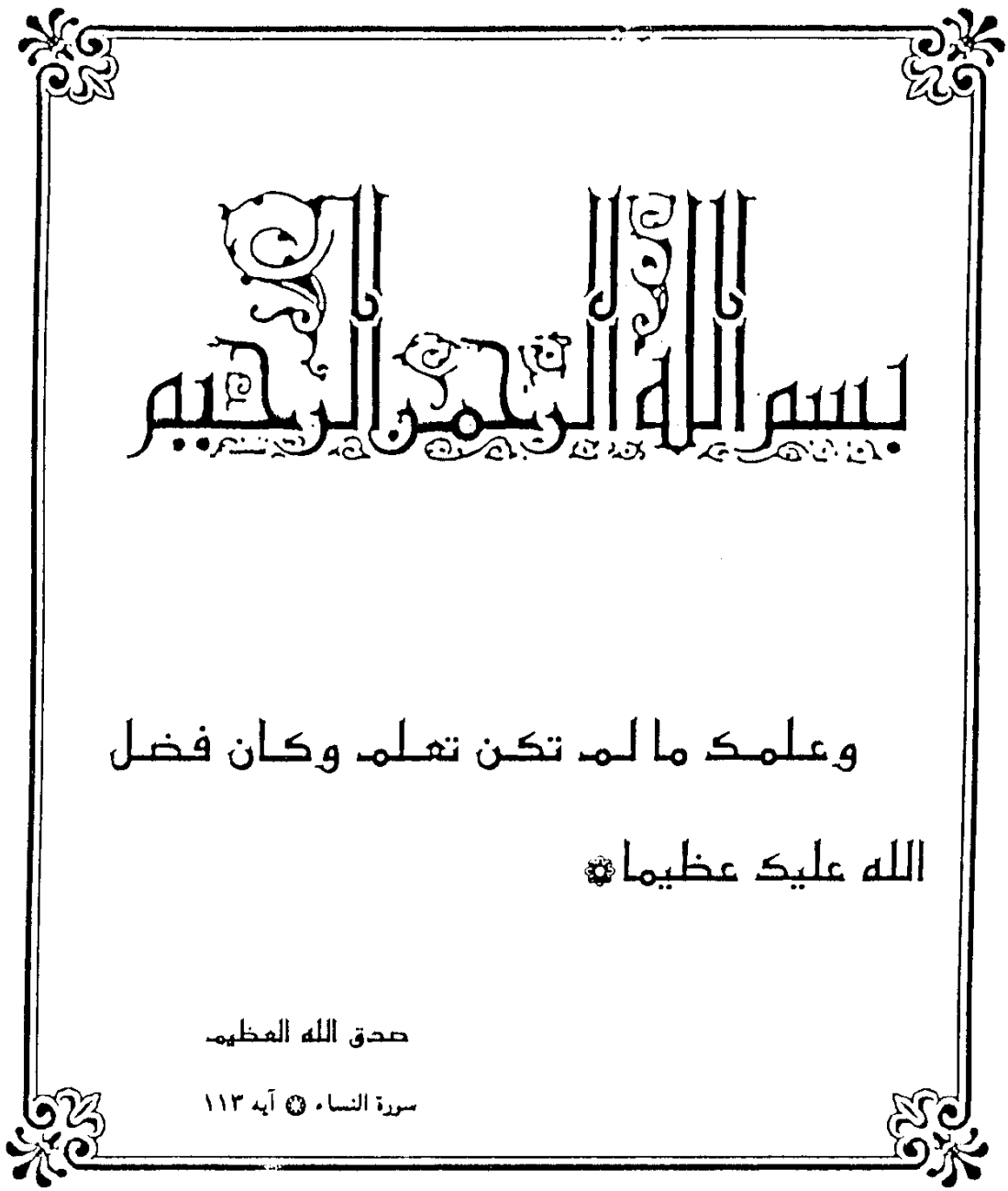

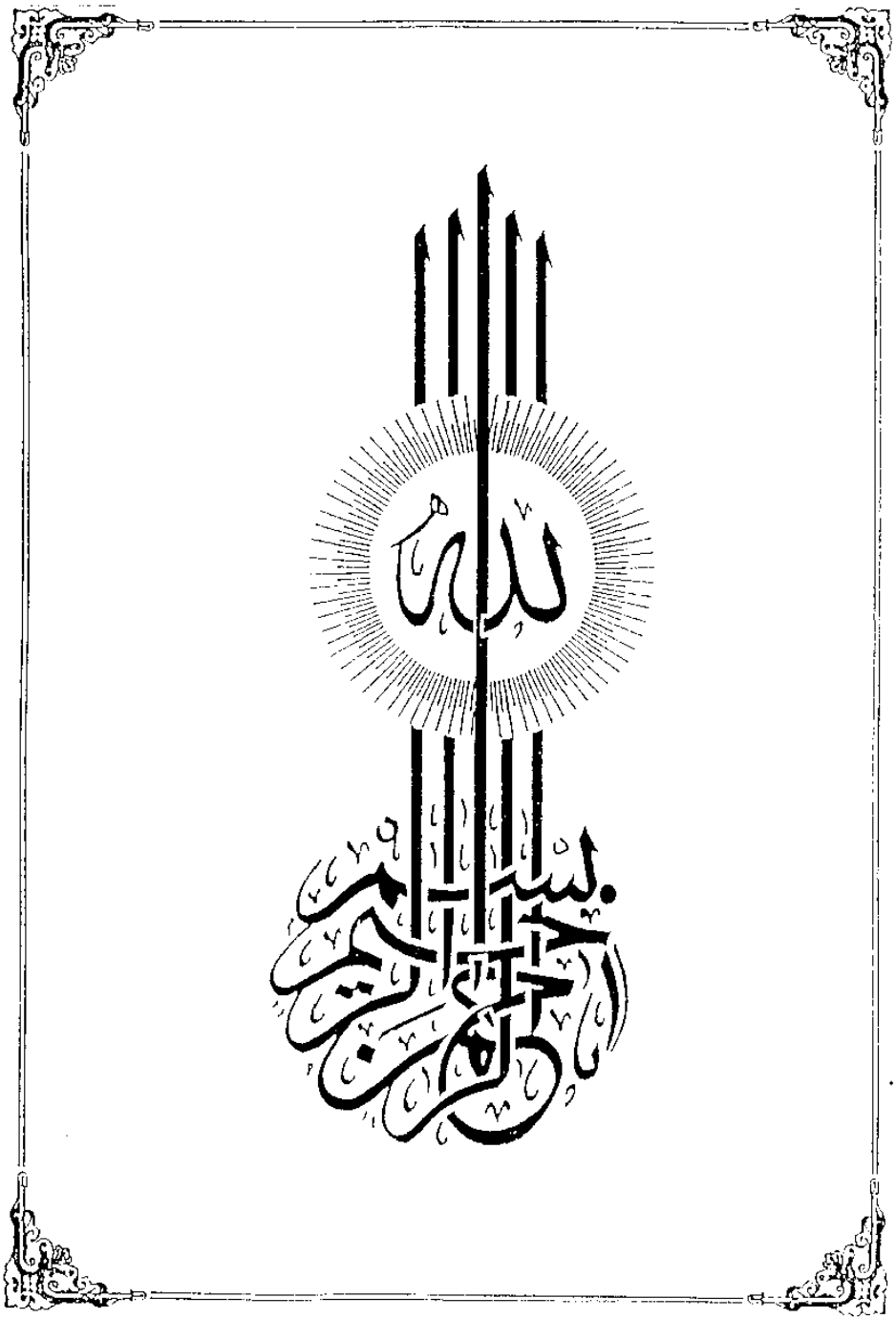

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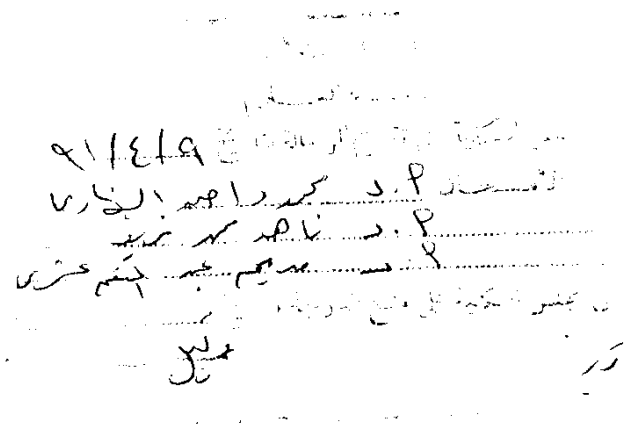


Contents

Introduction

INTRODUCTION

The importance of insecticides has steadily increased; being extensively used as herbicides, defoliants, and fungicides. But unfortunately, their hazardous (toxic) effects have also progressively increased and widely spread. Thus, it is not strange that these compounds are now encountered among the major factors incriminated for environmental pollution creating a serious and pressing problem for mankind in many parts of the world.

Now, there is considerable evidence that man and his domestic animals - do - regularly ingest small amounts of the applied insecticides which - in the long term - will, most probably, induce deleterious responses in their constituent cells and tissues (Durham et al. 1965; Howland, 1975; Whorton et al. 1977 and Cremlyn, 1978). This has led some counteries to minimize - to a great extent, or even to stop completely, the application of some insecticides which have been proved to exert pronounced dangerous impacts.

However, many areas including our country - do not presumably seem to do without the application of these chemical compounds for the ***ereadication*** of the prevailing pests and insects. Bearing this in mind, a strong need has sprung for illustrating and evaluating the serious consequences of these substances on the body organs in a detailed manner, both from the structural (histologic) and (histochemical points of view), which are of great relevance to the functional activities of the whole body in general.

AIM OF THE WORK

With reference to the above recorded introductory information, studies on the effects of insecticides on animal cells and tissues are urgently and badly needed to draw attention to their hazards, aiming to establish certain safety measures regarding their application and to call for the importance of providing effective means of cure and remedy of affected organs.

To achieve these goals, the present work was planned to include the following aspects :

- Determination of the LD50 of a selected insecticides, which is now of common use in our country, namely the organophosphorus insecticide "**dimethoate**" as a start point in this investigation.
- Histological survey of some target body organs for the sake of comparison and illustration of the magnitude of any injurious responses as a consequence of insecticidal application.

In this respect, the stomach, ileum and liver of a representative mammal, the white rat, have been selected for this investigation.

- Histopathological profile of the affected organs in animals subjected to the action of dimethoate.
- Follow up of some basic histochemical aspects both before and after insecticidal usage. These criteria included, carbohydrate groups, total proteins, general lipids, acid phosphatse, cytochrome oxidase, succinic dehydrogenase and lactic dehydrogenase.
- Detailed study - at the ultrastructural level - of the principal component cells of the chosen organs to demonstrate the depth of such hazardous alterations.

RIVIEW OF THE LITERATURE

As previously cited in the introductory remarks, the modernization of agricultural operations, and the rapid growth of industrial activity has led to much activity in the manufacture and ultilization of insecticides, pesticides and herbicides. These chemicals ultimately find their way into the rivers and lakes along with the garbage from the agricultural and industrial sources as well as forest lands.

In this respect, several publications have been presented elucidating that the application of chemical pesticides - on a large scale - had indeed greatly improved crop production, but has nonetheless, exerted serious hazards to man and his domestic animals (Barnes,1953, Davignon et al. 1965, Durham et al. 1965, Kamada, 1971, Miyamoto, 1971, Paccagnelle et al. 1971, Richou - Bac and Cumont,1971, Fishbein, 1972, Spynu et al. 1973, Banhawy et al. 1984, 1986(a) & 1986(b)and Banhawy and Mohran, 1991).

Synthesized insecticides commonly fall into two main categories :

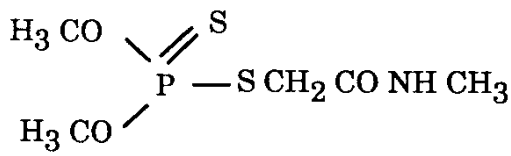
Organochlorine and Organophosphorus ones. However, the latter ones have been goining more popularity and wider application particularly in our country for some reasons which are beyond the scope of the present investigation.

Nevertheless, one of these organophosphorus compounds - which is utilized on a large scale in Egypt in the present time is ***"dimethoate"***.

This insecticide has been chosen to be the core of the present investigation to test its possible deleterious effects on the body organs; which would be presumobly reflected in their functional activities.

The chemical name, of dimethoate is (O, O - dimethyl S- N -methyl carbamoyl methyl).

Phosphorodithiodate and is diagramtically represented as follows :



According to Mengle and Ceside (1985), dimethoate is an anticholinesterase agent having a wide practical application in the fields of plant protection.

Krueger et al. (1960) and Schrader (1963) postulated that this compound has long been considered as a selective insecticides owing to its relatively low mammalian toxicity compared to the toxicity it exerts on insects. In general, such effects are attributed to its inhibitory influence on the activity of acetylcholinesterase (AhE), the enzyme which is mainly involved in the nerve transmission processes (Plimer, 1982). The properties of this enzyme and its relation to insecticidal treatment were dealt with by Met-calf and March (1950) in their investigations on bees, flies and mice.

However, the inhibitory responses of cholinesterase in treated animals was also elucidated by Palpp and Bigley (1961) to be brought about by other insecticides such as parathion.

Sites of accumulation of insecticides - in general - were investigated by Tewari and Harplani (1977). In their experimentation on white rats- given a lethal dose of some organophosphorous insecticides (e.g. ethyl parathion,

malathion,etc...) - they postulated that those insecticides showed marked tendency towards accumulation in the body fat for a long time though a small amount of it was excreted through urine. Along the same line, Dauterman et al.,(1959) found - in their investigation on the metabolism of dimethoate in rat and cow that about 40% of the water - soluble dimethoate metabolites were excreted as carboxylic acid derivatives.

Dimethoate toxicity (in its pure form) - compared with technically manufactured commercial material - was investigated by Casida and Sanderson (1963) who came to the conclusion that technical dimethoate varied in its acute oral LD50 from about 215 to 350 mg/kg, whereas the highly purified material gave values of about 550 mg for male and 650mg. per kg. for female rats.

Nonetheless, measurements of acute toxicity of the pure, laboratory grade, technical grade dimethoate and also formulations technical grade dimethoate were also determined for several birds and mammals by Sanderson and Edson (1964) and Tucker and Crabtree (1970) who recorded that the acute oral toxicity of these dimethoate varieties was lower in mammals in comparison with birds.

However, in a report offered by both FAO and WHO, in 1967, it imptied that the acute oral LD50 of technical domethoate - for male rats - ranged from 180 to 325 mg/kg body weight Later, in a test carried out by Khera (1979), he postulated that LD50 of commercial technical dimethoate, marked as Cygon 4E and containing 47.3% pure dimethoate and 52.7% unknown ingredients, was 300mg/kg. body weight.

The ability of vertebrate tissues to degrade dimethoate in vitro was investigated by Uchida et al. (1964), who declared that dimethoate was rapidly degraded in rat liver - but to a much lesser extent in the other rat tissues.

Concerning the toxic effects of dimethoate on the body tissues, Talukdar et al. (1985) speculated that the toxicity varied greatly with the species concerned as well as its mode of administration.

In this regard, dimethoate was elucidated by Gibel et al. (1973) and Reuber (1984), to act as a carcingenic agent in rats and mice when applied at high doses for long periods of time.

From the histopathological point of view, the impects of the organophosphorus insecticides in particular - on various body organs of various animals species have been the target of investigations by many researchers including Laug et al. (1950), Metcalf (1955), Yamasaki and Narahashi (1957), Assal and Kamel (1964), Matsumura and O'Brien (1966), Boyd and Chen (1968), Banhawy (1974), Anees (1976), Sastry and Malik (1979), Sastry and Sharma (1981) and Banhawy et al. (1974, 1984 and 1986 b).

The histopathological alterations induced by two sublethal concenterations of the organophosphorus insecticide diazinon, on the stomach and intestine in the fresh water teleost fish ***ophiocephalus punctatus*** - was studied by Sastry and Sharma, (1981). According to these authors, the only visible alterations produces in such cases were mainly

symptosized by some erosion of the mucosa in the stomach and intestine, also a few villi were deteriorated and the nuclei of their component cells were reduced in volume.

In 1968, Boyd and Chen postulated that when young albino rats were given a lethal dose of lindane, they manifested marked degenerative changes in the gastrointestinal tract, kidney and liver, especially when death was delayed for some days.

Later, in 1979, Sastry and Malik described abvious erosion of the gastric mucosa and intestine in the fresh water fish ***Channa Punctatus*** exposed to a sublethal concentration of the organophosphorus insecticide dimecron.

The effects of 3 organophosphorous compounds, namely dimethoate, diazinon and methyl parathion on the fish water teleost ***Channa Punctatus*** was inspected by Anees (1976). Accordingly, he listed certain deleterious alterations comprising muscular atrophy beside, necrobiosis, cytoplasmic vacuolation and cytoplasmic granulation in the component cells of various parts of the intestine.

Rather recently, Banhawy et al. (1986b) follwed the pathological effects of the organophosphorus insecticide cyolane on the lining epithelial cells of the teleost fish ***Clarias Lazera***. They detected distinct lesions in the various regions of the ileal villi. Precisely, their cellular limitations appeared ill - defined, the ground cytoplasm noticeably vacuolated, the

nuclei suffered from obvious pyknosis and many cells were distinctly necrotic.

Dimethoate was also tested for its pathological impacts in the intestine of the earth warm ***Allolobophora caliginosa*** by Banhawy et al. (1984), in which case it was observed to induce certain responses symptomized mainly by obvious histopathological disturbances including prominent destructive histological organization and distinct necrosis of the ciliated columnar lining cells; some of which were highly demolished.

The liver has also been a target organ for detecting its structural responses to insecticidal application. In a publication forwarded by Laug et al. (1950), they mentioned that DDT caused obvious enlargement of hepatic cells in the liver of rat, beside obvious nuclear and cytoplasmic distruction (Khattab et al., 1972).

In the same organ, Assal and Kamel (1964) elucidated that parathion poisoning caused hypertrophy of the hepatocytes and dilatation of the hepatic blood vessels especially the central veins. Also, the hepatic sinusoids were widened, much enlarged and engorged with red blood corpuscels.

Besides, in 1981, Sastry and Sharma demonstrated vacuolation in the cytoplasm and rupture of the cell membranes in addition to hypertrophy of the nuclei of the hepatocytes of the teleost fish ***Ophiscephalus punctuatus*** treated with diazinone.

The impacts of insecticides on the main histochemical indices have also