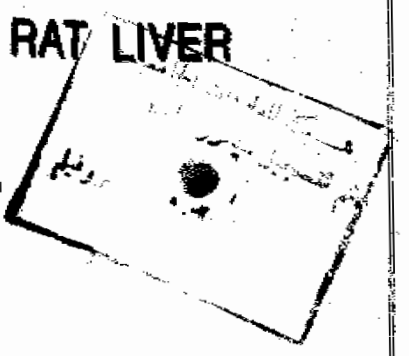
EFFECTS OF METHOMYL AND AMMONIUM NITRATE ON THE HISTOLOGY AND HISTOCHEMISTRY OF THE RAT LIVER



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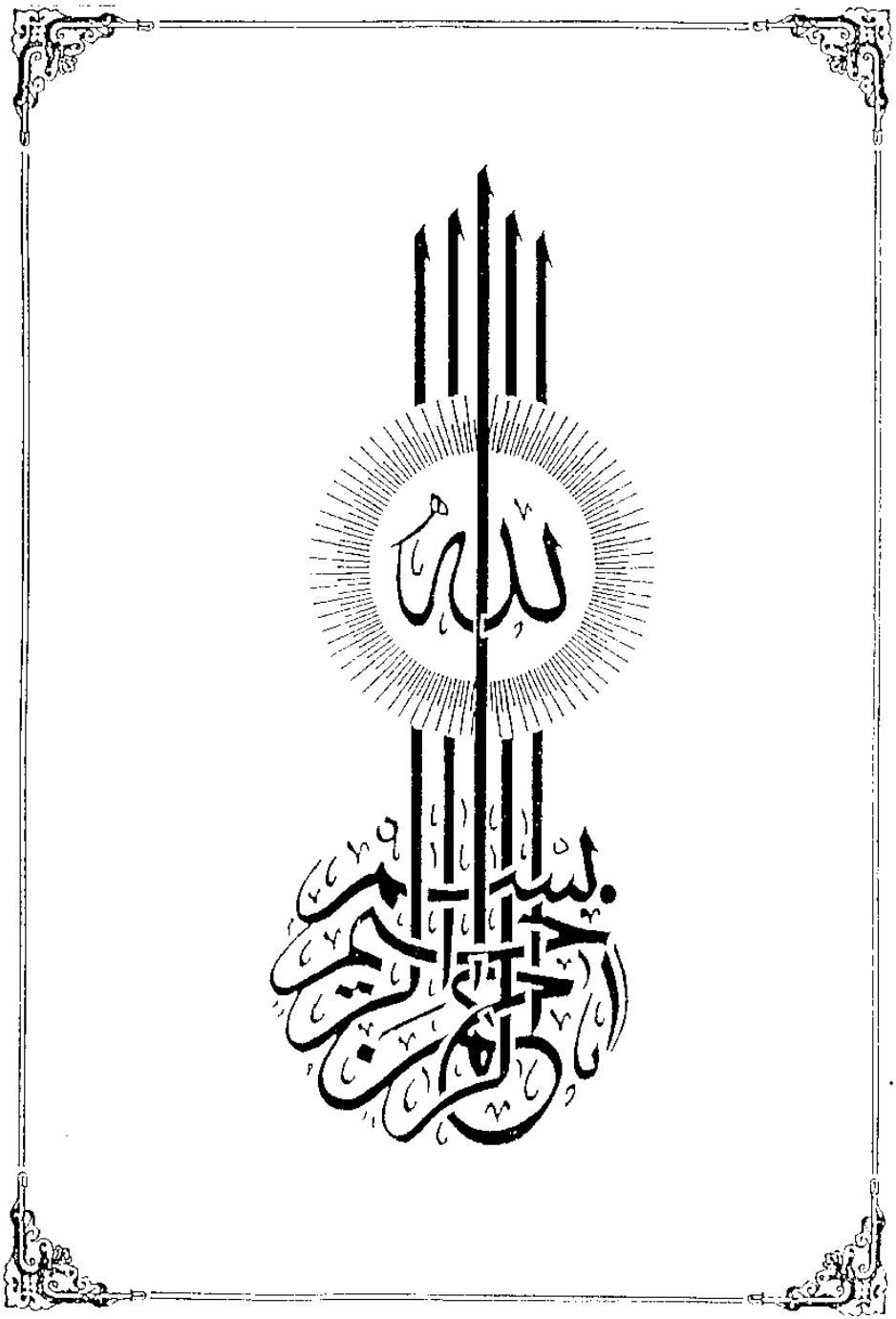


INTRODUCTION

The recent years have witnessed a marked increase in the application of agrochemicals, including pesticides, fertilizers, and growth promotors , attempting to increase the food resources, improve their quality, as well as serving various prophylactic purposes.

It is true that such agrochemicals have contributed positively to the above mentioned goals, but nonetheless, it is equally true that, in many instances, they have created tremendous serious environmental pollution , commonly reflected as considerable health problems.

Thus, it can be stated that agrochemicals evoke both useful and harmful consequences in life matters. In view of the postulation offered by Metcalf and Mckelvey (1976) in this respect; "The question, whether to use or not to use the agrochemicals in a particular situation, is of prime concern to all human beings". This trend necessitates deep and thorough investigations to assess and evaluate the possible hazards of such chemicals to the living organisms including man, benifical animals and plants.

AIM OF THE WORK

Bearing the previously listed introductory remarks in mind, the present work was planned to examine the possible adverse effects of such chemicals on the body organs.

For this purpose, two different varieties of these materials have been considered in the present investigation, namely; the insecticides-represented by the carbamate one "methomyl" - and the soil plant nitrogen fertilizer "ammonium nitrate" .

As a target organ, one of the essential mammalian body organs, i.e. the liver, was to be applied for these expermentations. The liver is well known to play a major role in the metabolism as well as detoxifying the vast majority of drugs and chemicals in the body (Cohen,1982).

To accomplish these purposes, the work constituted the following main aspects:

1-Estimation of the lethal doses of both chemicals: "methomyl" and "ammonium nitrate" , and accordingly, the selection of the appropriate doses for the present experiments.

2-Detection of the signs of poisoning (external or clinical symptoms) in either cases of treatment.

3- General histology of the liver for the sake of comparison.

4- Histopathological features induced in this organ consequent to the application of the two tested chemicals.

5-Some essential histochemical parameters including: General carbohydrate, lipids, total proteins, nucleic acids (DNA & RNA) and sites of acid phosphatase activity.

It is hoped that the results which could be achieved from this investigation would be of some value in enlightening the proper use and safety measures in the application of such chemicals. Besides, they could urge the necessity of creating certain remedies for any deleterious consequences which might arise under the influence of these materials.

REVIEW OF LITERATURE

Methomyl:

Among agrochemicals, pesticides have received a special attention by those who are much concerned about the environmental pollution.

Unluckily, pesticides produce their effects , not only on their intended targets, but they also act as potential hazards for health in general.

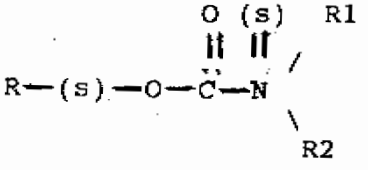
Nowadays, it is well realized that several pesticides have affected wildlife in a considerably adverse manner (Carson, 1962). Nonetheless, the continuing intensive trend toward chematization of the agriculture has led to the manufacture and production of large amounts of various kinds of pesticides, being introduced year after year into the environment.

Such chemicals find their way into the atmosphere, soil, water, food products and eventually enter the bodies, thus deleteriously affecting man and his useful animals as well as the whole wildlife, as elucidated by Duggan et. al. (1967), Casarett et.al. (1968), Kraybill (1969), New York Academy of Sciences (1969), Riad (1971), Deichman (1973),

Pimental (1973), Hayes (1975), Brown (1978), El- Banhawy et al. (1984, 1986-a&b) and El- Banhawy, et. al. (1993).

Pesticides are commonly categorized according to their chemical composition into three main groups :
(I) Inorganic compounds, (II) pesticides of vegetative, bacterial and fungal origin, and (III) Organic copmpounds comprising organochlorine and organophosphorous materials, as well as derivatives of carbamic acid .... etc. (Hayes, 1975) .

Carbamate insecticides first appeared in (1953), when United States Scientists introduced one of these compounds under the name "Carbaryl" with the commerical name (Sevin). However, the general chemical formula of carbamates is



(Kuhr and Dorough, 1976).

Other examples of the carbamates are: Methomyl (lannate), Carbofuran (Furadan), Methiocarb (mesurol), Metal Kamate (bux), Pirimicarb (pirimor), Propoxur (baygon), Aldicarb (temik), Dimetan and Pyrolan (Hayes, 1975).

One of the most effective impacts of carbamate compounds on the biological parameters of the body is their

inhibition of cholinesterase enzyme. This malfunction is brought about by carbamolation of the esteratic site of the acetyl cholinesterase. This enzyme has a vital function in the neural activities of the organism (Kolbzen et.al., 1954). This inhibitor process was elucidated by Winteringham and Fowler, (1966) in a way strictly analogous to its phosphorylation by organic phosphorous compounds. Once acetylcholinesterase is carbamolated or phosphorylated, it is unable to deesterify acetylcholine, which thus accumulates at the nerve synapses, leading to the development of considerable nervous disorders.

However, one of the well known carbamates is methomyl which is the insecticide of choice in the present experiments. It has the trade mark 'Lannate', with the chemical name (S- methyl- N- (methyl carbamoyl) oxythioacetimidate).

Methomyl was postulated by some investigators to be very effective against aphids and other sucking insects as well as various kinds of vegetations comparable to other insecticides. At the present time , this insecticide has been recommended by the "Environmental Protection Agency" to be applied for insect control on 13 crops, including

tobacco, sweet corn, tomatoes, cabbage, cauliflower, broccoli, and head lettuce (Harvey et.al., 1973).

Laboratory studies, carried out by Harvey and Pearse (1973) on soils, treated with [^{14}C] methomyl, indicated that methomyl, degrades rapidly to [^{14}C] carbon dioxide as an end product. Those researchers have also followed the metabolic fate of methomyl in tobacco, corn and cabbage in the laboratory and green house. The results which they had achieved, implied that treatment with radiolabelled methomyl (S-methyl [1-^{14}C] N-[(methyl carbamoyl) oxy] thioacetimidate), had rapidly degraded the compound to [^{14}C] carbon dioxide and [1-^{14}C] acetonitrile, which were eventually volatilized from the plant tissues.

In the same above communication, it was inferred that when rats were administered [^{14}C]- labelled Methomyl, it was rapidly eliminated as; one part carbon dioxide, three parts acetonitrile (expelled in the expired air) and one part as urinary metabolites.

Concerning the possible noxious impacts of methomyl on experimented animals, El-Kashory (1984) marked that it had caused an increase in the liver/body weight of mice in

particular. She also illustrated certain histopathological consequences in the liver of those treated mice, symptomized essentially by the development of haemosidrin granules, besides other signs of degeneration.

The influence of methomyl was also followed in the mammalian kidney by some researchers amongst whom was El-Kashory (1984) who found that it had caused an increase in the kidney/body weight ratio. Also, Kaplan and Sherman (1977) recorded the appearance of vacuolation in the epithelial cells of the proximal convoluted tubules as well as tubular hypertrophy of the proximal convoluted tubules in the rat kidneys.

The impacts of methomyl- on inverebrate creatures- were also investigated by some workers (Metwally et. al., 1978). The most serious histological consequnces were noticed in such cases in the body wall and midgut of the larvae of the cotton leaf worm (*Spodoptera littoralis*). Some parts of the epidermis and its basement membrane were destroyed together with the appearance of vacuoles between the epidermal cells.

Sevin, which is another carbamate , was reported by Riad (1971) to cause vacuolation of the hepatic cells of mice

when given in even low doses, while the high doses had made such cells exhibiting severe signs of variable kinds of degeneration. In both cases, the sinusoidal spaces were obviously widened in those liver cells.

El- Gendi (1974) examined the adverse influence of Carbaryl which is also a carbamate compound)- on the lung, heart, liver and kidneys of mice. The liver cells exhibited cloudy swelling, vacuolar degeneration, focal infiltration of lymphocytes as well as acute congestion of the blood vessels. The kidney tissues were also marked by the same researcher to suffer from similar consequences especially vascular congestion and hydropic degeneration of the kidney tissues.

In a research paper submitted by Evdokimov et. al. (1980), they elucidated that the application of a variety of carbamates, including carbaryl, tri-allate, zineb, thiram, and metiram (carbamates) had induced specific pathological lesions in the livers of mice, fowls, rabbits, sheep, swines and calves. These lesions were reflected in the form of dystophy, necrobiosis and gastroenteritis. They added that the extent of such lesions were mainly dependent

on the type and dose of the pesticide as well as the duration of their action.

Other insecticides, namely DDT (an organophosphorous compound) was found by Laug et. al. (1950) to cause an obvious enlargement of the rat hepatic cells, besides noticeable nuclear and cytoplasmic destruction.

Parathion, which is an organophosphorous compound was noticed by Assal and Kamel (1964) to bring about hypertrophy of the hepatocytes in addition to dilation of the hepatic blood vessels in the treated rats. The widened sinusoids were markedly engorged with red blood corpuscles.

Diazinone (another organophosphorous insecticide) was pointed out by Sastry and Sharma (1980) to produce vacuolation, rupture of the cell membranes and hypertrophy of the nuclei of the hepatocytes of the teleost fish *Ophiocephalus punctuatus* .

In (1984), El- Banhawy et al, submitted a communication indicating that the application of "dimethoate" (an organophosphorous insectiside) had resulted in prominent signs of impairment of the histological organization of the

intestine of the earth worm *Allolobophora caliginosa* besides distinct necrosis of its lining ciliated columnar cells.

Two years later, El- Banhawy et al, (1986-b) followed the pathological impacts of the organophosphcrous insecticide (cyolane) on the lining epithelial cells of the teleost fish *Clarias lazera* Consequently, they presented distinct lesions in the various regions of the ileal villi. Precisely, their cellular limitations appeared ill- defined, the ground cytoplasm was noticeably vacuolated, the nuclei were quite pyknotic and many cells were distinctly necrotic.

From the histochemical point of view, the effects of insecticides on the main histochemical indices have also been followed up in the livers of some animal types. In this respect, Sherief (1984) noticed that the glycogen contents were prominently increased in the rat liver cells under the effect of the acute dose (LD_{50}) of methomyl.

From another angle, El-Beih et. al. (1991) elucidated that the polysaccharide substances were slightly decreased in the hepatic cells of guinea pigs post - methomyl application for one week. This decrease became more distinct in the same cells when the period of insecticidal application was extended to two weeks.