TOXICITY OF SOME ORGANOPHOSPHORUS INSECTICIDES TO MAMMALS

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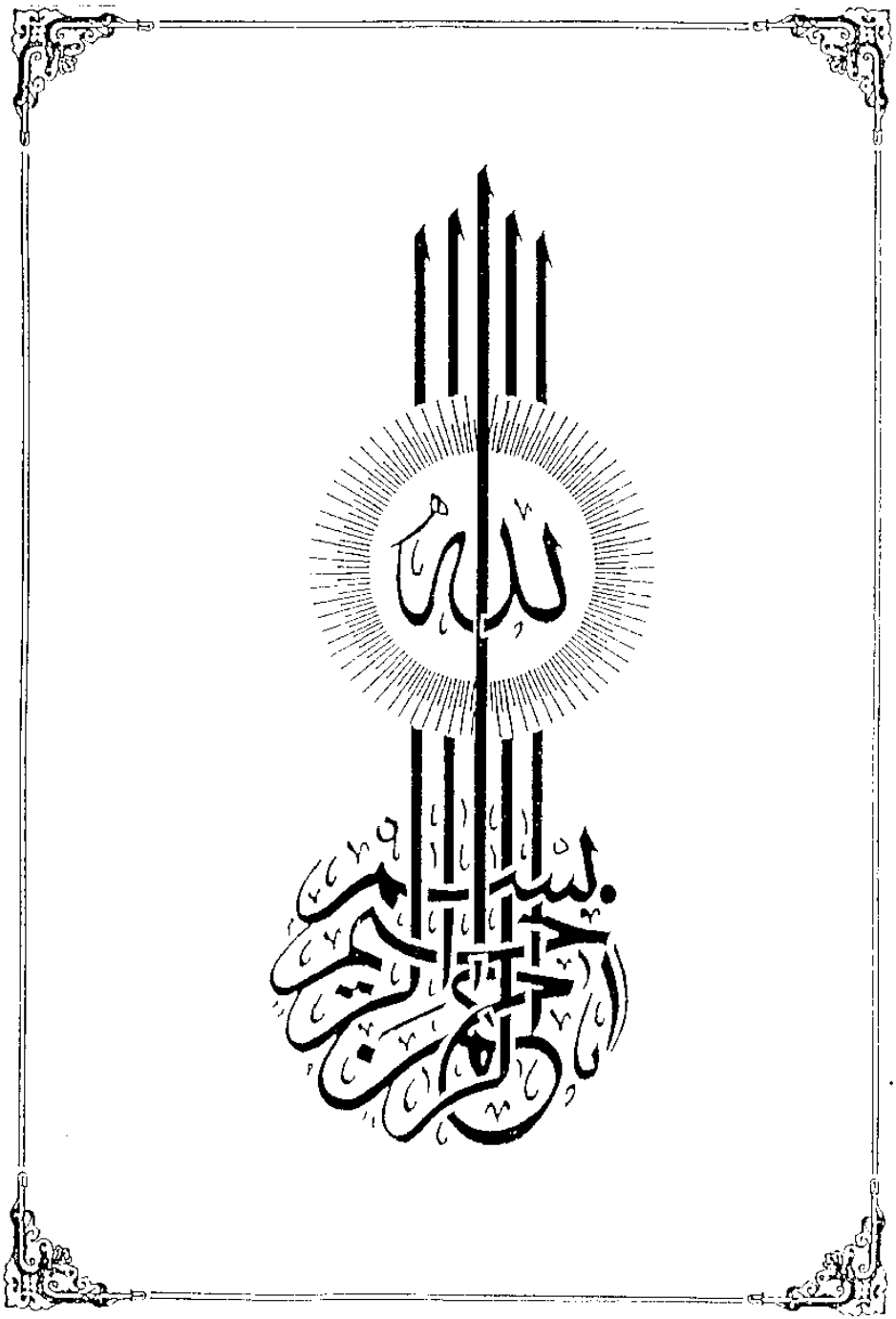

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C O N T E N T S

I. INTRODUCTION

Over the past twenty-five years a voluminous literature has accumulated in the field of pesticides, particularly, the organophosphorus(OP) insecticides. The administration of such compounds resulted in detrimental hazardous effects, not only on plants but also on animals. Also, emphasis has been directed towards evaluating the diverse effects exerted by residues of these insecticides.

To elucidate the high mammalian toxicity and the relatively long persistence of the organophosphorus insecticides, inhibition of cholinesterase enzyme activity in vivo is one measure of the potential toxicity of such chemicals. The primary concern of this work, is to throw some lights on the toxicity of two organophosphorus insecticides, Cyolane and Phosvel, on mice. These materials have been widely used over the last 5 years against cotton pests in the country.

On the cellular level, histopathological studies as well as cholinesterase enzyme activity were carried out. Determination of biological activity of residues on clover and maize plants were also established.

II. General Review of Literature

Determination of pesticide residues on plants:

Organophosphorus pesticides, in general, are becoming increasingly important for their comparatively persistence on sprayed plants. Numerous reports on determination and estimation of insecticide residues have already been published in the respective scientific literature. Among others, are studies conducted by Bluman(1964) who reported that the mean recoveries of Phosdrin residues in fruits and vegetables ranged from 91.6% to 95.9% when using the enzyme inhibition spectrophotometric procedure.

Leuck et al.(1969) reported that Phosvel, its O-analogue were diminished in whole corn plants or in the ears throughout the sampling periods. A year later Leuck et al. stated that residues of phosvel were determined to be 0.84,1.73 and5.28 ppm at the 42-day posttreatment sampling period at the three rates of application used.

On the other hand, Lindquist et al.(1965) found that Bidrin was quite persistence when applied as a foliary spray on cotton seedlings. Moreover, they stated that the material rapidly penetrated excised leaves and cotyledons of intact plants.

In 1966 , Shaw and others, studied the disappearance of Bidrin residues from alfalfa. They found that when Bidrin was administered on plants at the rate of 0.5 lb/acre, it decreased from 43 to 0.19 ppm in 21 days on dried alfalfa. On contrary, degradation declined from 46 to 0.42 ppm;when Bidrin was applied at 0.1 lb/acre on the green alfalfa.

Struble and McDonald(1973) stated that straw harvested 63 days after application of Chlorpyrifos on wheat plants contained only 0.003 ppm of the parent compound. They further stated that the oxygen analogue could not be detected.

A test conducted by Young and Bowman(1966) revealed that a linear residue disappearance of Gardona has been determined. In addition, they reported that the initial deposits were directly proportional to the rate of applications.

Westlake et al. (1970) determined the residual activity of Azodrin on and in Valencia oranges and citrus pulp cattle food prepared from the treated fruit. The rates of spray were 10 lb/ acre of the technical grade Azodrin as a full volume spray and I lb/ acre as a low volume spray. The residue half life (RL_{50}) for low volume spray was 13 days while that of the full volume spray was 16 days with an initial deposit 10 ppm. Whereas that for the low volume spray was about 4 ppm on a rind basis.

Toxicity of pesticides to mammals and insects:

Toxicology of organophosphorus insecticides has prompted extensive investigations, because of their established value and their widespread use as agricultural insecticides.

Bagatell et al.(1969) found that extensive damage to the epithelium of all organs had resulted in cantharidin poisoned rats. Also, they noticed injury to the cell membrane as early as 5,10 and 15 minutes after poison injection. However, no significant differences were observed in phospholipid and cholestrol contents.

At the same year, when Boyd and Dobs feeding, male albino rats, monuron at the LD_{50} rate, noticed that the autopsy had revealed local irritated gastroenteritis accompanied by degenerative changes in the liver and kidneys,in addition to a stress reaction and loss of weight with significant alterations in water content of most body organs.

When ninety-eight pesticides and two DDT metabolites were administered, by either oral or dermal routes, to Sherman strain adult rats, Gaines(1969) reported that the pesticides showed greater toxicity to the animal by the oral route, but only fenitrothion, merphos, mevinephos, isolan and omite were more toxic by the dermal route.

Toxicity and residual activity of insecticides were carried out by Polles and Payne (1970). They evaluated seventeen insecticides on Curculio caryae(Hor). Monocrotophos and carbofuran were the only compounds showing residual activity, after one and five days. However, relative toxicities of the insecticides were similar.

In 1971 , Sherman et al, studied the comparative toxicity of four halogenated organophosphorus insecticides on chicks and Japanese quail. They found no difference in susceptibility between sexes of the quail. Except for the higher dose, 800 ppm, little inhibition of cholinesterase activity was detected.

Studies on Cholinesterase inhibitors:

Cholinesterases can be characterized by several means, of which, histochemical techniques can disclose the cells or parts of cells in which the enzyme activity is localized.

Holmstedt(1971) has reviewed various colorimetric methods for the determinatin of cholinesterase levels both in normal and parathion- poisoned persons. He also reviewed and discussed the correlation between the histochemical localization and the function of neuronal cholinesterase.

In addition, enzymatic methods for the determination of submicrogram quantities of organophosphate insecticides

as well as studies on cholinesterase inhibition have been reported.

James et al.(1969) testing representatives of each of three classes of pesticides on the acetyl cholinesterase and aliesterase activity in serum, brain and liver microsomes of rats fed on diets with various levels of casein found that parathion inhibited liver and brain acetylcholin esterase to a greater extent at the 0% casein level than at the higher levels. However, inhibition of brain and serum aliesterase by banol was negligible at all casein levels.

Karloge and Poulsen in Mcfarland and Lacy(1968) demonstrated that acute poisoning of chickens by parathion, given orally , caused a decrease in cholinesterase activity in the brain to about 10% of the normal.

In 1973, Khoo and Sherman concluded that halogenated organophosphorus pesticides used, were slightly more toxic to Boettcherisca peregrina (Robineau-Desvoidy), after injection than after topical application. In addition, they found that head cholinesterase inhibition was more rapid and that maximum inhibition was also reached earlier by the former than by the latter application.

The acute anticholinesterase toxicity in ducks and Japaneese qualil was studied by Mcfarland and Lacy(1968).

Both suggested that the acute signs of parathion toxicity were directly related to the parasympathominitic effect of increased acetylcholine produced by the anticholinesterase activity of the insecticide.

Namba(1971) stated that the acute poisoning by organophosphorus compounds in man was due to blocking of cholinergic transmission as a result of acetylcholinesterase inhibition. The manifestation, mainly, involved the parasympathetic nerves, the neuromuscular junction and the central nerve synapses, but to a lesser extent the cholinergic sympathetic nerves.

Histopathological changes in different organs of mammals as affected by pesticides:

For an evaluation of the pesticide pathological potency and histochemical changes, a series of work was carried out by many investigators.

Aldridge and Johnson(1971) reported that many of the organophosphorus pesticides produced a so called" dying-back" process in which the long axons were mostly affected.

The toxicity exhibited by one of organophosphorus compounds has been elucidated as early as 1930. In which year , Smith et al. and Smith and Elvove (in Ezell and Adkins,Jr.1971) had reported that the organic phosphate

chemical, triorthocresyl phosphate(TOCP) was able to induce flacid paralysis in the extremities of man, accompanied by demyelination of peripheral nerves.

In 1953 , Barnes and Denz showed that several organophosphorus materials, bis-monoisopropylamino fluorophosphine oxide(mipafox), diisopropyl fluorophosphonate(DFP) and tri-orthocresyl phosphate(TOCP) were able to show demyelination in the spinal cord and peripheral nerves of the tested animals.

Cavanagh 1964, demonstrated the damage of peripheral nerve fibres and their endings as the result of tri-O-cresyl phosphate poisoning of cats. He further indicated that the damage was selective to large-diameter and long fibres.

Demyelination as refered to it by Ezell and Adkins, Jr.(1971) is :" a state in which the myelin sheath around the nerve fiber is lost or destructed". They further divided this condition into two groups, primary and secondary demyelinations. They reported that the first condition occurs before the nerve fiber is affected, while the latter condition occurs after the fiber degenerates. They further demonstrated, in an electron microscope study the induction of demyelination in TOCP- treated mature white

leghorn chicken hens. They stated that daily loss of weight, beginning within the second day after treatment followed by ataxia on the twelveth day was an end result of the dosages given .

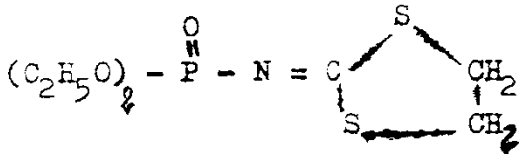
On the histological level, the same authors observed splitting of the myelin lamellar unit as a first change sign in the myelin sheath structure.

In 1974, Papadimitrion et al., reported a variety of nuclear changes directly correlated with the dose of toxin, lypsin, administered on the murine liver.

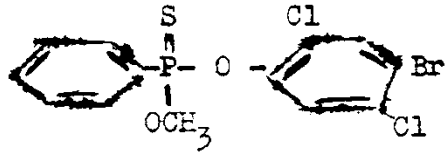
III. General Materials and Methods

Two organophosphorus insecticides, Cyolane containing not less than 25.0% of 2-(diethoxyphosphinylimino)1,3-dithiolane and Phosvel having 30% active ingredient O-(4- bromo-2,5- dichlorophenyl) O- methyl phenyl phosphonothioate. Were used in the present investigation . The former insecticide is characterized by its ability to penetrate the leaves on which it is sprayed. in addition, it has a comparatively long residual action.

However, Phosvel has also proved its activity as a fungicide as well as its broad spectrum to control economically important insect pests.



Cyolane



Phosvel

A. Colorimetric determination of pesticides:

Various techniques had been developed for the micro determination of posticides, specially the organophosphorus insecticides. At the present investigation, the method reported by Getz and Watts(1964) was adopted. The basis