P R E F A C E

Intensive research in the field of plant protection and pest control has been going on throughout the world. As a result, various types of pesticides are being prepared, and their biological activities are being studied everyday. Of these, organophosphorus compounds is a class in which quite a large number of compounds have been synthesised and examined as effective insecticides. Owing to the wide diversity in their activities, these organophosphorus pesticides have won epoch-making popularity for use in field as potential pest controlling agents.

The work embodied in this thesis is related to the investigation of some cyclic organophosphorus compounds with reference to their insecticidal and chemical properties, besides their structural elucidations by chemical analyses and spectroscopic methods.

At the outset, in Chapter-1, an introduction of the organophosphorus pesticides has been presented. The pioneer researches of Prof. Schrader in Germany and of Prof. Saunders in England just prior to the second world war stimulated a great deal of advancement in this field, and by this time thousands of organophosphorus compounds have been discovered. Substances with a great variety of pesticidal properties have

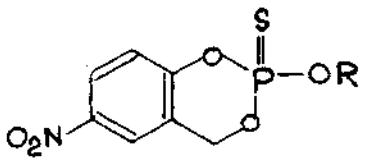
been found among the organophosphorus compounds with insecticidal, acaridical, nematocidal, fungicidal, herbicidal and rodenticidal properties. These organophosphorus compounds exhibit varying range of biological activities on the target. Thus compounds with short to prolonged residual activity, broad spectrum insecticidal activity and high selectivity in action are known. Examples of a few representative compounds of above descriptions are given. An interesting and by far the most important property of the organophosphorus insecticides is their antiesterase activity. The behaviour of esterases and their substrate-specificity and the inhibitory action of organophosphorus insecticides to the enzyme activity have been discussed comprehensively. The persistence or the disappearance of these compounds in the medium is related to their decomposition and hydrolysis and is very important in view of health hazard, environmental polution, etc. The hydrolysis of organophosphorus compounds and the mechanism involved therein are also discussed.

In 1961, O-tolyl saligenin cyclic phosphate (2-O-tolyloxy-4H-1,3,2-benzodioxaphosphorin-2-oxide) was discovered as a biologically active metabolite of phosphate triesters of O-Cresol (TOCP).

Chapter-2 of this dissertation has been devoted to a short review on saligenin cyclic phosphorus esters with special emphasis on salithion (2-methoxy-4H-1,3,2-benzodioxaphosphorin-2-sulphide), an organophosphorus insecticide having a unique cyclic structure, discovered by Prof. Eto and his co-workers in 1963. Salithion, a broad spectrum insecticide, was commercialized by Sumitomo Chemical Co. of Japan in 1968. Since then several saligenin cyclic phosphorus esters have been synthesised and examined for insecticidal activity. These esters are phosphates, phosphorothiolates, phosphoramidates, phosphonates and their thiono-analogs. The investigations on activity-structure relationship of these esters have revealed that the biological activities of these compounds are greatly influenced by the exocyclic substituents on phosphorus atom and also by substituents in benzene and heterocyclic rings. The specificity of saligenin cyclic phosphorus esters in the biological activity relates to their selectivity in enzyme inhibition. Therefore the compounds have different types of biological properties including insecticidal, fungicidal, nematocidal, antiesterase, synergistic, systemic and others.

It has been reported by Eto and co-workers that 2-methoxy-6-nitro-4H-1,3,2-benzodioxaphosphorin-2-sulphide (ED-8) was obtained as a paste after purification through silicic acid column chromatography and found to have about sixty times less insecticidal activity compared to salithion. However, it has

been observed by us that the BD-8 is a solid (m.p. 34°C) and has about 1.5-2 times greater oral insecticidal activity to Periplaneta americana than malithion. These observations have impelled us to undertake a systematic investigation on some 6-nitro-saligenin cyclic alkyl/phenyl phosphorothionates of the following general formula, where R is $-CH_3$, $-C_2H_5$,



$-n-C_3H_7$, $-n-C_4H_9$, $-iso-C_3H_7$, $-iso-C_4H_9$, $-C_2H_4OCH_3$, $-C_2H_4OC_2H_5$ or $-C_6H_5$ (phenyl) groups.

Chapter-3 of this thesis deals with the work related to the synthesis and structure determination of these compounds. All these nine compounds have been examined for alkaline hydrolysis, antiesterase activity in human blood plasma as well as housefly-head preparation and oral toxicity to cockroaches and rats.

It has been found that the methoxy compound shows greater insecticidal activity than malithion and other compounds to cockroaches; iso-propoxy homologue shows about 1.5-2 times less insecticidal activity than malithion; where as the phenoxy derivative is non insecticidal. All compounds are less toxic

to rats than malithion. Iso propoxy compound is most stable in alkaline hydrolysis; but all the compounds of this class have greater hydrolysis constant value than that of malithion. It has been observed that for all compounds except phenoxy one, the acetylcholinesterase of housefly-head homogenate (HFAChS) is more inhibited than that of human blood plasma (AChS). The methoxy compound is most toxic to HFAChS, but the iso-propoxy compound is least toxic to AChS.

The structures of all compounds have been established by chemical analyses, UV, Mass, IR and ^{1}H NMR spectral data. Mass fragmentation processes and the splittings in ^{1}H NMR signal at δ = 5.4 ppm of (β-methoxy) ethoxy and (β-ethoxy) ethoxy compounds are entirely different from those of other alkoxy compounds; ether type oxygen in exocyclic side chain plays an important role in this class of organophosphorus compounds.

* * *