S Y N O P S I S

The work embodied in this dissertation is related to the investigation on some chloro/bromo/nitro saligenin cyclic phosphoramidothionates with reference to their synthesis, antifungal, insecticidal and anticholinesterase activities, toxicity and other properties besides structure elucidation by chemical analyses and spectroscopic methods; toxic effect of some pesticides on Spirogyra sp., their degradation period and residues study by chlorophyll assay method has also been presented.

Part I:

Part I of this dissertation deals with a brief introduction, organophosphorus fungicides, their reaction with cholinesterase and chemical hydrolysis, discovery of salithion, properties of salithion; also biological activities and structural relationship have been presented along with the aims and objectives of the present investigation.

Part II:

(i) Some 2-alkylamido-6-chloro/bromo/nitro-4H-1,3,2-benzodioxaphosphorin-2-sulphides have been prepared by the reaction of the corresponding phosphoramidothionate dichlorides with 5-chloro/bromo/nitrosaligenin. All compounds are white crystalline solid

(ii) The structure of the compounds have been determined by chemical analysis and IR, Mass and PMR spectra. The spectral data of the only four compounds are presented.

The common IR bands for the compounds: 1010 - 1030 cm^{1} (S), P-O-C (alkyl); 1235-1250 cm^{-1} (VS), P-O-C (aryl); 880-920 cm^{-1} (S), P-O-C (aryl); 1515 - 1520 cm^{-1} (S), asym.str. of nitro group; 1340 - 1345 cm^{-1} (S), sym.str. of nitro group; 800 - 820 cm^{-1}, P = S (I); 640 - 660 cm^{-1}, P = S(II). Neither of the two P = S bands shows any systematic shifts which reflect changes in the inductive properties of the substituents; this is not unexpected if they do indeed arise from mixed modes.

The compounds show parent molecular ion (M^{+}) peaks in the mass spectra. Fragmentation by loss of 'SH' radical is important; all compounds show an ion due to $(M - SH)^{+}$, and it is the base peak for all of the four alkylamidophosphorothionates. Finally the structure of the compounds has been settled by taking PMR spectra; for all compounds the endo-cyclic-CH_2-group gives eight lines in PMR spectra.

(iii) All phosphoramidothionates have some insecticidal activity, but their activities are less than that of the 2-methoxy-6-nitro-4H-1,3,2-benzodioxaphosphorin 2-sulphide (BD-8) and salithion except CL-12.

(iv) All compounds (CL-6, CL-12, CL-17, BR-6, BR-12, BR-17, BD-25, BD-31 and BD-34) are less toxic to rats than salithion and BD-8. However, the 2-N-N-diisobutyl-6-nitro-4H-1,3,2-benzodioxaphosphorin 2-sulphide (BD-25) compound have greater toxicity compared to other phosphoramidothionates.

(v) The results of rice seed germination studied indicate that none of the 2-alkylamido-6-chloro/bromo-4H-1,3,2-benzodioxaphosphorin 2-sulphides shows phytotoxicity upto 200 ppm. None of the 2-alkylamido-6-nitro-4H-1,3,2-benzodioxaphosphorin 2-sulphides shows phytotoxicity upto 500 ppm. However, some of the compounds (CL-6, BR-17 and BD-25) shows 90 percent germination at 200, 200 and 500 ppm respectively. Treatments of rice seeds with the compounds (CL-6, CL-12, BR-6, BR-12, BD-31 and BD-34) have no effect on germination; however, root and shoot growth have been drastically reduced. Among these compounds the CL-6, CL-12 and BR-6, BR-12 shows less decrease of the

root and shoot length than the BD-31 and BD-34 compounds. Phytotoxic properties of other compounds on rice seeds and plants have not yet been performed.

(vi) It has been observed that the 6-nitro saligenin cyclic phosphoramidothionates (BD-25, BD-31 and BD-34) shows more inhibition on goat plasma (ChE) than blow-fly head homogenate (HFAChE). These compounds show more acetylcholinesterase inhibition on goat plasma and blow-fly head homogenate than the 6-chloro/bromo saligenin cyclic phosphoramidothionates. Among the 6-chloro/bromo saligenin cyclic phosphoramidothionates, the CL-17 compound shows more inhibition on goat plasma and CL-12 compound on blow-fly head homogenate but the inhibition is less than that of 6-nitro saligenin cyclic phosphoramidothionates on both cases.

(vii) From the chemical hydrolysis studies it has been observed that in case of 6-chloro saligenin cyclic phosphoramidothionates the diisobutylamido compound (CL-6) is more stable than 2,6-dimethylmorpholino (CL-12) compound.

In case of 6-bromo saligenin cyclic phosphoramidothionates the hexamethylenimido compound (BR-17) is most stable to alkaline hydrolysis.

For 6-nitro saligenin cyclic phosphoramidothionates, the 2-6-dimethylmorpholino compound (BD-31) is most stable among the compounds.

In comparision to the 2,6-dimethylmorpholino 6-chloro/bromo/nitro - 4H-1,3,2-benzodioxaphosphorin 2-sulphides the BD-31 compound is most stable and the CL-12 compound is least stable.

(viii) The fungicidal activity studies (by growth inhibition) against P. oryzae, H. oryzae, A. solani and A. candida indicate that some of the compounds show good inhibitory effect on the growth of different fungi; however, compared to Hinosan some of the compounds show less inhibitory effect. Among the nine compounds, the 2(2,6-dimethylmorpholino)-6-bromo-4H-1,3,2-benzodioxaphosphorin 2-sulphide (BR-12) is most active against P. oryzae H. oryzae, A. solani and A. candida.

From the spore germination inhibition studies against A. niger, P. oryzae, and H. oryzae, it has been observed that all compounds are effective. The 2(2,6-dimethylmorpholino)-6-chloro-4H-1,3,2-benzodioxaphosphorin 2-sulphide (CL-12) is most active against A. niger, P. oryzae and H. oryzae. The activity of other compounds are also greater against the A. niger, P. oryzae and H. oryzae except BD-25, BD-31 and BD-34 against H. oryzae.

Protectant activity studies (*in vivo*) against *H. oryzae* on detached rice leaves by using six compounds (CL-6, CL-12, BR-6, BR-12, BD-31 and BD-34) indicate that the CL-12 and BR-12 compounds show more activity than the other compounds. Protectant activity studies for other compounds have not yet been performed.

(ix) Satisfactory correlation is obtained between the pED_{50} value (for *P. oryzae* at 72 hours) and the hydrophobic constant (π), Taff's steric parameter (E_s) of the exocyclic alkylamido group, and the Hammett constant (σ) of the chloro, bromo and nitro groups; the regression equation of nine compounds are given below:

$$pED_{50} = -2.261\,\sigma - 0.086\,E_s - 0.043\pi + 6.085 \ldots (E$$

$n = 9$, $S = 0.199$, $r = 0.971$, $F_{3,5} = 27.25$.

(x) The antifungal activity data justify further examination of these phosphoramidothionates as potential fungicides with special reference to the selectivity of their action. Whether the use of these compounds will protect the plants from diseases in the field remains to be studied.

In order to find out details of the chemical structure-biological activity relationship in these chloro, bromo and nitro saligenin cyclic phosphoramidothionates, we have to synthesize several new compounds in which the chloro, bromo and nitro groups are to be incorporated in different position of the aromatic ring, and to investigate their biological activities, anti-SH enzyme activities, and other toxicological properties, including delayed neurotoxicity in hens.

(xi) The toxic effect and degradation periods of phorate, Hinosan, Thiodan, Ripcord and Decis on Spirogyra sp. have been reported. Phorate is most toxic to Spirogyra sp. in 40 ppm concentration and the degradation period is 6 days. At 7th. day of the experiment, phorate totally decomposed and lost the toxic effect.

Among these five pesticides Decis is less toxic to Spirogyra sp. and after three days the compound decomposed and showed no toxic effect on Spirogyra sp.

The toxic effect of Hinosan, Thiodan and Ripcord on Spirogyra sp. is less than that of phorate but more than that of Decis.

By estimating the chlorophyll content, the residue and the rate of decomposition of these pesticides have been determined.