POLYCHLORINATED BIPHENYL: AN ENVIRONMENTAL CONTAMINANT ACTS AS AN INSECTICIDE SYNERGIST

Abstract

Bioassay experiments with houseflies demonstrated that the polychlorinated biphenyl preparation known as Arochlor 1254 is a powerful synergist for the carbamate insecticide carbaryl. The mechanism of synergism is unknown, but probably does not involve the inhibition of microsomal oxidase which is usually responsible for insecticide synergism.

In recent years the widely used plasticizers known as polychlorinated biphenyls (PCB) have become recognized as DDT-like environmental contaminants (1). As with DDT and other chlorinated insecticides, PCB are environmentally persistent, subject to biological magnification, and are inducers of the microsomal enzyme systems which detoxify insecticides and metabolize steroids (1,2). Some PCB, particularly materials containing small amounts of chlorine, are toxic to mammals and insects (3). The potential health hazard of these materials has been emphasized by recent work which demonstrated that prior exposure of ducklings to PCB increased their susceptibility to duck hepatitis virus (4).

In the present report data are presented on a hitherto undescribed property which further relates PCB to insecticides. Tests with Arochlor 1254, a PCB preparation containing 54% chlorine, demonstrated that the material is a powerful synergist for the carbamate insecticide carbaryl against the housefly. Since nonpersistent insecticides such as carbaryl are widely used as replacements for the persistent chlorinated insecticides, any environmental contaminant which increases its toxicity is a potential complicating factor in the development of this and similar short residual insecticides.

In this research houseflies were bioassayed by exposure to films of 1:5 (w:w) combinations of carbaryl and PCB and the toxicity of the combinations was compared to that of carbaryl only. We also tested 1:5 combinations of carbaryl and piperonyl butoxide, a standard insecticide synergist. In other experiments we measured the effect on the toxicity of carbaryl to houseflies after prior exposre to PCB or piperonyl butoxide. We also determined the effect of exposure to the 2 synergists

on oxidative metabolism of several insecticide chemicals by houseflies under in vivo conditions.

Carbaryl and piperonyl butoxide were technical grade samples available in the laboratory (5). Arochlor 1254, was used as supplied by the manufacturer (6). GLC analysis confirmed its identity as a typical, multicomponent PCB preparation (7).

Flies tested were an insecticide susceptible strain (Orlando Regular) and a strain (Orlando DDT) highly resistant to chlorinated insecticides and possessing a low tolerance to carbaryl and other carbamate insecticides. The origin and resistance spectra of the strains have been described previously (8).

Pint glass jars were coated on the inner surface with measured amounts of the test chemicals. A water supply and food were placed in each jar, 20 flies of mixed sexes were introduced, and the jars were covered with cheesecloth and held 24 hours at which time mortality determinations were made. All experiments were replicated and LC_{50} values in micrograms per jar of carbaryl were estimated by computer analysis of the data.

Results of the toxicity tests (Table 1) revealed that the PCB preparation was highly active as a synergist for carbaryl. It increased the toxicity of the insecticide in the several tests by factors of 11- to 82-fold. With piperonyl butoxide, the degree of synergism was similar, ranging from 15- to 68-fold. Thus, PCB is approximately as active as piperonyl butoxide as a synergist for carbaryl. The degree of synergism was usually greater when flies were exposed simultaneously to carbaryl and the synergists, but was still significant when flies were exposed to the insecticide after preexposure to PCB or piperonyl butoxide. As

is usual in synergism experiments, the increase in toxicity was greater with the resistant than with the susceptible strain.

Differences occurred in the time required for response of treated flies to PCB-carbaryl combinations as compared with piperonyl butoxide-carbaryl combinations. In tests with Orlando Regular flies, exposure to combinations of 1000 ug/jar each of carbaryl and synergist resulted in more rapid knockdown when piperonyl butoxide was employed (50% in 2 hours) than when PCB was the synergist (50% in approximately 6 hrs.). After 24 hr preexposure to the synergists, the time required for response to carbaryl upon subsequent exposure was decreased to 1 hour for piperonyl butoxide and 1.25 hours for PCB. These results suggest that there may be differences in the mechanism by which the 2 compounds cause synergism.

It is thought that piperonyl butoxide owes its synergistic activity to its ability to inhibit microsomal oxidative enzymes (9). PCB, on the other hand, would not be expected to act as synergists in the same way since they are considered to be microsomal inducers rather than inhibitors (1).

To measure the effect of the synergists on microsomal oxidation we exposed Orlando DDT flies to films of PCB or piperonyl butoxide at a rate of 1,000 ug/jar for 24 hours and then to the cyclodiene insecticides, aldrin and heptachlor at the sublethal dose of 10 ug/jar for 4 hours. Subsequent GLC analyses (7) revealed (Table 2) that exposure of flies to PCB resulted in an increase in the amounts of aldrin oxidized to dieldrin and heptachlor oxidized to h. epoxide to 146 and 153% of control values, respectively. Exposure to piperonyl butoxide resulted in a reduction in oxidase activity of 28 to 50% for the 2 substrates. The results provide evidence that the mechanisms of synergism of PCB and piperonyl butoxide must differ since their effects on the microsomal enzyme system appear to be opposite in nature.

The possible significance of these findings is only speculative at present. If synergism related to PCB occurs with other insecticides and with mammals as well as with insects, then unintentional exposure due to environmental contamination might render nontarget organisms more susceptible than expected to certain pesticides. Thus, PCB may increase the already high level of danger associated with the use of many insecticides. Indeed, such a mechanism might explain some of the epidemics of poisoning that have occurred in farm workers exposed to apparently "safe" concentrations of certain highly toxic insecticides (10).

REFERENCES AND NOTES

1. R. W. Risebrough, P. Rieche, D. P. Peakall, S. G. Herman, M. N. Kriven, Nature 220, 1098 (1968).

2. D. C. Holmes, J. H. Simmons, J. O'G. Tatton, Ibid. 216, 227 (1967), R. W. Risebrough in Chemical Fallout, M. W. Miller and G. G. Berg, Eds. (Thomas, Springfield, Ill. 1969), p. 5.

3. W. F. Von Oettingen, U. S. Publ. Health Serv. Publ. No. 414, 306 (1955), E. P. Lichtenstein, K. R. Schulz, T. W. Fuhremann, T. T. Liang, J. Econ. Entomol. 62, 761 (1969), D. B. Peakall, J. L. Lincer, BioScience 20, 958 (1970).

4. M. Friend, D. O. Trainer, Science 170, 1314 (1970).

5. Carbaryl is 1-naphthyl methylcarbamate, piperonyl butoxide is a-[-(2-butoxy-ethoxy)ethoxy]-4,5-methylenedioxy-2-propyltoluene.

6. We thank Monsanto Chemical Co., St. Louis for the sample of Arochlor 1254 used in these experiments.

7. Gas chromatographic analyses were performed on a Micro-Tek Model 160 chromatograp equipped with a Ni^{63} detector. The 1/8" I.D. x 10' column contained 2% SE-30 and 3% QF-1 on Chromosorb W HP, 80/100 mesh. Column temperature was 209°C and detector temperature was 260°C. Dieldrin and heptachlor epoxide, the metabolites of aldrin and heptachlor, respectively, were identified by cochromatography with authentic standards and by standard tlc methods.

8. F. W. Plapp, R. F. Hoyer. J. Econ. Entomol. 61, 768 (1967).

9. J. E. Casida, Agr. Food Chem. 18, 753 (1970). MONS 049255

10. Personal communication, Nov. 1970 from Marion Moses, R.N., Rodrigo Terronez Memorial Clinic, Delano, Calif.; testimony of T. H. Milby, M.D., Chief, Bureau of Occupational Health and Environmental Epidemiology, Cal. Dept. Public Health, presented 9 Dec. 1970 before California. Assembly Committee on Agriculture.

11. I thank G. Hold for assistance with the bioassays and W. H. Vance for

GLC assays. Approved as Technical Article _____ by the Director, Texas Agricultural Experiment Station and supported in part by USDA Regional Research Project, S-73.

Table 1. Toxicity of carbaryl and carbaryl:synergist combinations to susceptible (Orlando Regular) and resistant (Orlando DDT) houseflies.

Treatment	Orlando Regular		Orlando DDT	
	Carbaryl LC_{50} (ug/jar)	Increase in toxicity	Carbaryl LC_{50} (ug/jar)	Increase in toxicity
Carbaryl only	1386	-	4402	-
Carbaryl:PCB 1:5	96	14 X	54	82 X
Carbaryl:Piperonyl butoxide 1:5	37	37 X	65	68 X
PCB for 24 hrs, then carbaryl	80	17 X	384	11 X
Piperonyl butoxide for 24 hours, then carbaryl	94	15 X	174	25 X

*Calculated as quotient of response of flies to carbaryl divided by response of flies to indicated carbaryl:synergist combination.

Table 2. Microsomal oxidase activity in Orlando DDT flies untreated and after exposure to PCB or piperonyl butoxide.

Treatment	Aldrin Epoxidase*		Heptachlor epoxidase*	
	% substrate Converted to dieldrin	Activity as % of control	% substrate Converted to h. epoxide	Activity as % of control
Control	11.4	100	34.6	100
PCB @ 1000 ug/jar	16.7	146	52.8	153
Piperonyl butoxide @ 1000 ug/jar	5.7	50	24.8	72

*Calculated from GLC scans by totaling recovery of substrate and product and then calculating the % conversion. Results are averages of duplicate or triplicate assays.