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2,826,530

SYNERGISTIC INSECTICIDAL COMPOSITIONS COMPRISING AN O,O-DI-ALKYL THIOPHOSPHATE-4-METHYLUMBELLIFERONE

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9 Claims. (Cl. 167—33)

(Granted under Title 35, U. S. Code (1952), sec. 266)

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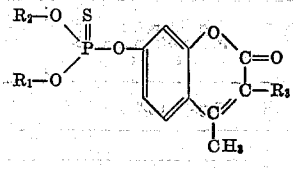
We hereby dedicate the invention herein described to the free use of the People in the territory of the United States.

This invention relates to insecticides, in particular to the so-called "organic phosphate" insecticides, such as parathion.

These organic phosphates are known to be toxic to warm-blooded animals in that they will lower the cholinesterase content of the blood by absorption through the skin, by inhalation or by oral ingestion.

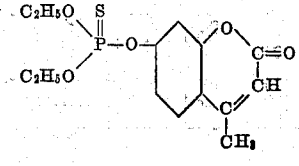
The present invention accomplishes an increasing of the toxic action to insects by including certain non-toxic materials which are themselves not insecticides but which act as synergists when mixed with the organic phosphates in an amount ranging about from .025% to .05% of the synergist to 1/10 thereof, that is, .0025% to .005%, respectively, of the organic phosphate. These synergists are 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl] benzene (known as sulfoxide) and the alphaisopropylpiperonyl ester of chrysanthemum monocarboxylic acid. In this manner it is possible to use the organic phosphates at a sufficiently low concentration as to be relatively non-toxic to warm-blooded animals and yet obtain a mixture of high insecticidal potency.

The invention is applicable to a number of organic phosphates which may be generally described by the formula:

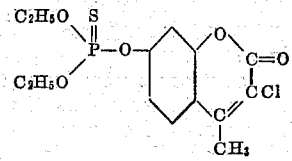


wherein R_1 and R_2 are identical alkyl radicals selected from the group consisting of methyl and ethyl, and R_3 is a member of the group consisting of hydrogen and chlorine. Examples of such phosphates and their structural formulae are:

O,O-diethyl O-4-methylumbelliferone thiophosphate

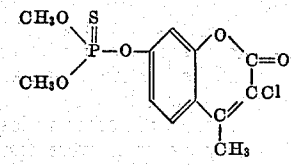


O-(3-chloro-4-methylumbelliferone) O,O-diethyl thiophosphate



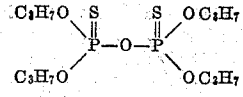
and

O-(3-chloro-4-methylumbelliferone) O,O-dimethyl thiophosphate

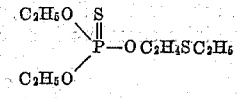


These compounds were tested in admixture with a variety of synergists and when compared with other phosphates, also tested in admixture with a variety of synergists, it was found that the combination of each of the said compounds with each of 1,3-methylenedioxy-4-[2-(octylsulfinyl)propyl]benzene or alphaisopropylpiperonyl ester of chrysanthemum monocarboxylic acid as a synergistic agent gave highly superior results. The data on these tests are given in Tables I to V, inclusive, hereinafter. Some of the other phosphates tested and their structural formulae are given hereafter:

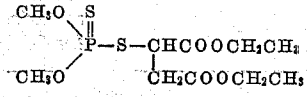
Tetrapropyl dithiopyrophosphate



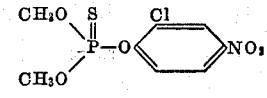
O,O-diethyl O-(2-ethylmercapto)ethyl thiophosphate



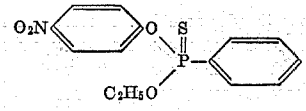
O,O-dimethyl dithiophosphate of diethyl mercaptosuccinate



O-(2-chloro-4-nitrophenyl) O,O-dimethyl thiophosphate



O-ethyl O-p-nitrophenyl benzenethiophosphonate



Tests reported herein were made with the human body louse, *Pediculus humanus humanus* (Deg.), as the test insect, the chemical mixtures being used as cloth impregnants and as powders.

In the impregnation tests the mixtures were dissolved in acetone at the desired concentration and 0.7 ml. of the test solution was added by pipette to circular cloth patches 1.5 inches in diameter. The treated patches were suspended on pins and allowed to dry for about an hour, after which each pad was placed in a 50-ml. beaker and 20 adult lice (10 of each sex) introduced. For testing, the beakers were held in an incubator at 30° C. and mor-

tality records were made after 24 hours. For aging, the treatments were held indoors at room temperature.

In the powder tests, the mixtures were applied to small balbriggan cloth patches and the insects were confined on the treated cloth. Examinations were made at various time intervals to determine their toxicity to the insects. The powders were handled and aged in the same manner as the cloth impregnants.

Tests against body lice were conducted to determine the immediate and residual effectiveness of certain of the organic phosphates when mixed with 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl]benzene as the synergist. Preliminary tests were run with the organic phosphates at several low concentrations in order to select dosages that would show synergistic action of the 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl]benzene.

Each organic phosphate was tested at a range of three concentrations, alone and combined with the synergist. A ratio of 1 part of the organic phosphate toxicant to 10 parts of the synergist was used in these tests, although synergism was evident with other ratios. In a second series of tests the phosphates were tested for residual effect at a concentration of 0.005 percent alone and combined with 0.05 percent of the synergist. In these tests 1-hour knock-down records were taken in the initial exposures and 24-hour exposure tests were conducted twice weekly for 3 weeks.

In the first series of tests, the results of which are shown in Table 1, the synergist caused remarkable increases in the effectiveness of both phosphates. An 0.005 percent concentration of the toxicant alone caused only 20 and 10 percent knock-down and 0 and 10 percent kill in 24 hours, while with the synergist the knock-down and kill were 100 and 90, and 100 and 70 percent, respectively. Half this concentration of the toxicant was completely ineffective in both cases, but when combined with the synergist, the knock-down and kill were 100 and 85, and 100 and 60 percent. The synergist namely, 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl]benzene(sulfoxide), alone at 0.05 percent was completely ineffective. The other synergist, namely, the alpha-isopropylpiperonyl ester of chrysanthemum monocarboxylic acid, alone at .05% was similarly substantially complete ineffective.

Table 1.—Results of beaker tests with umbelliferone phosphate compounds at low concentrations alone and combined with a synergist, 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl]-benzene. (Ratio of toxicant to synergist 1:10; 20 adult lice (10 of each sex) exposed for 24 hours.)

Toxicant	Percent concentration		Percent knock-down [1] and mortality after 24 hours	
	Toxicant	Synergist	Knock-down	Mortality
O,O-diethyl O-4-methylumbelliferone thiophosphate	0.005	0.05	100	90
	.0025	.025	100	85
	.001	.01	5	0
	.005		20	0
	.0025		0	0
	.001		0	0
O-(3-chloro-4-methylumbelliferone) O,O-diethyl thiophosphate	.005	.05	100	70
	.0025	.025	100	60
	.001	.01	15	15
	.005		10	10
	.0025		15	5
	.001		0	0
Check—untreated			0	0

[1] Knock-down also includes those listed as dead.

Seventeen other materials acted as synergists for the O,O-diethyl O-4-methylumbelliferone thiophosphate, O-(3-chloro-4-methylumbelliferone) O,O-diethyl thiophosphate, and O-(3-chloro-4-methylumbelliferone) O,O-dimethyl thiophosphate. 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl]benzene was included as a standard of comparison. The toxicants were tested at concentrations of 0.005, 0.0025, and 0.001 percent, alone and in combination with each synergist at a ratio of 1:10. The results of the tests are presented in Table 2. As can be seen, all the synergists increased the toxicity of the phosphates.

Further tests were conducted with a concentration of 0.005 percent of the phosphate and 0.05 percent of each synergist to determine the residual effectiveness of the materials. Results of these tests are presented in Table 3. All 17 synergists increased or prolonged the residual action of umbelliferone esters of thiophosphoric acid to a remarkable degree.

Table 2.—Effectiveness of certain umbelliferone esters of thiophosphoric acid at different concentrations in combination with various synergists. (Ratio of synergist to toxicant 10:1; 20 adult lice (10 of each sex) exposed for 24 hours.)

Item No.	Synergist: Name	Percent knock-down and kill (combined) at indicated concentrations								
		O,O-diethyl O-4-methylumbelliferone ester			O-(3-chloro-4-methylumbelliferone) O,O-diethyl ester			O-(3-chloro-4-methylumbelliferone) O,O-dimethyl ester		
		0.005%	0.0025%	0.001%	0.005%	0.0025%	0.001%	0.005%	0.0025%	0.001%
1	N-Isobutylhendecenamide	100	100	0						
2	Piperonyl butoxide	100	100	0	100	100	0	100	95	10
3	1,2-methylenedioxy-4-[2-(octylsulfinyl)-propyl] benzene	100	100	25	100	100	0	100	100	0
4	Chrysanthemummonocarboxylic acid, alpha-allylpiperonyl ester	100	100	35	100	100	0			
5	N-2-ethylhexylbicyclo[2.2.1]-5-heptene-2,3-dicarboximide	100	100	30				100	100	50
6	n-Propyl isome	100	95	70	100	35	0			
7	1,2-methylenedioxy-4-[2-(octylsulfonyl)-propyl] benzene	100	90	0	100	75	0	100	95	0
8	Propionic acid, p-(alpha, alpha-dimethyl-benzyl) phenyl ester	90	90	0						
9	Propionic acid, p-cyclohexylphenyl ester	100	70	10						
10	Propionic acid, 2,4-di-tert-butyl-6-isopropylphenyl ester	100	30	0						
11	alpha-Propylpiperonyl acetate	100	100	50						
12	Chrysanthemummonocarboxylic acid, alpha-propylpiperonyl ester	100	100	100	100	95	5	100	100	0
13	Chrysanthemummonocarboxylic acid, 4-(3,4-methylenedioxyphenyl)-sec-butyl ester	100	100	90						
14	Chrysanthemummonocarboxylic acid, alpha-ethylpiperonyl ester	100	100	90	100	100	20	100	100	10
15	5-butyl-5-ethyl-2-(3,4-methylenedioxyphenyl)-m-dioxane	100	100	90	100	100	10	100	100	70
16	Fencholic acid, alpha-allylpiperonyl ester	100	100	70	100	100	25	100	100	55
17	Chrysanthemummonocarboxylic acid, alpha-isopropylpiperonyl ester	100	100	100	100	95	0	100	100	25
	Toxicant alone	15	0	0	15	0		90	10	0

Table 3.—Residual effectiveness of certain umbelliferone esters of thiophosphoric acid at 0.005 percent in beaker tests in combination with 0.05 percent of various synergists. (Twenty adult lice (10 of each sex) exposed 24 hours.)

Synergist Item No.[1]	Percent knock-down and mortality (combined) on indicated day after treatment											
	O,O-diethyl O-4-methylumbelliferone thiophosphate											
	Initial	4	6	8	13–14	18	21	23	26	28	32	38
1	100	95	75	80	55							
2	100	100	95	100	100	100	100	100	75			
3	100	100	100	100	95	100	100	100	95			
4	100	100	100	100	95	95	100	100	70			
5	100	65										
6	100	100	100	100	100	30						
7	100	100	100	100	100	80	100		95	100	80	20
8	90	95	80	80								
9	100	25										
10	100	15										
11	100	30										
12	100	100	100	100	100	40						
13	100	100	100	100	100	80	100		90	40		
14	100	100	100	95	100	45						
15	100	100	100	100	100	100	95		100	85	70	25
16	100	100	100	100	95	20						
17	100	100	100	100	100	60						
Toxicant (alone)	15											

	O-(3-chloro-4-methylumbelliferone) O,O-diethyl thiophosphate							
	Initial	13	15	19	22	26	29	33
2	100	100	100	95	95	100	55	55
3	100	100	100	100	100	95	45	
4	100	100	95	70	25			
6	100	100	95	55				
7	100	100	100	100	100	100	95	75
12	100	100	100	85	80	90	55	20
14	100	100	100	65	60			
15	100	100	100	100	100	100	95	80
16	100	100	95	80	50			
17	100	100	100	85	75	90	25	
Toxicant (alone)	15							

	O-(3-chloro-4-methylumbelliferone) O,O-dimethyl thiophosphate						
	Initial	1	9	13	20	23	27
2	100	100	100	100	100	100	75
3	100	100	100	90	90	25	
5	100	100	90	20			
7	100	100	100	100	95	100	85
12	100	100	100	100	95	45	
14	100	100	100	80	20		
15	100	100	100	100	100	85	25
16	100	100	100	40			
17	100	100	100	95	55		
Toxicant (alone)	90	20					

[1] Names of compounds are given in Table 2.

Six other phosphates were selected for tests similar to those above, using 1,2-methylenedioxy-4-[2-octylsulfinyl)propyl]-benzene as the synergist. The phosphates were tetraethyl dithiopyrophosphate, tetrapropyl dithiopyrophosphate, O,O-diethyl O-(2-ethylmercapto)ethyl thiophosphate, O,O-dimethyl dithiophosphate of diethyl mercaptosuccinate, O-(2-chloro-4-nitrophenyl) O,O-dimethyl thiophosphate, and the O-ethyl O-p-nitrophenyl benzenethiophosphonate. The minimum effective concentration of these materials, alone and in combination with the synergist, are shown in Table 4.

The residual effectiveness of the various synergistic materials with the phosphoric acid esters when applied to cloth has been clearly demonstrated. When applied as powders, these materials also have a remarkable residual effectiveness, as shown in Table 5.

Table 4.—Results of beaker tests with selected phosphate compounds at low concentrations alone and combined with a synergist, 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl]benzene. (Ratio of toxicant to synergist 1:10; 20 adult lice (10 of each sex) exposed for 24 hours.)

Toxicant	Percent concentration		Percent knock-down [1] and mortality after 24 hours	
	Toxicant	Synergist	Knock-down	Mortality
Tetraethyl dithiopyrophosphate	0.0001	0.001	100	85
	.00005	.0005	25	15
	.00001	.0001	0	0
	.0001		95	70
	.00005		20	0
	.00001		0	0
Tetrapropyl dithiopyrophosphate	.0005	.005	100	55
	.00025	.0025	35	15
	.0001	.001	0	0
	.0005		80	35
	.00025		40	15
	.0001		0	0
O,O-diethyl O-(2-ethylmercapto)-ethyl thiophosphate	.0005	.005	95	60
	.00025	.0025	5	5
	.0001	.001	0	0
	.0005		55	25
	.00025		15	10
	.0001		0	0
O,O-dimethyl dithiophosphate of diethyl mercaptosuccinate	.001	.01	100	85
	.0005	.005	35	15
	.00025	.0025	5	0
	.001		70	40
	.0005		20	5
	.00025		0	0
O-(2-chloro-4-nitropheny) O,O-dimethyl thiophosphate	.001	.01	90	65
	.0005	.005	10	0
	.00025	.0025	0	0
	.001		50	20
	.0005		0	0
	.00025		0	0
O-ethyl O-p-nitrophenyl benzenethiophosphonate	.001	.01	90	55
	.0005	.005	25	10
	.00025	.0025	0	0
	.001		40	10
	.0005		0	0
	.00025		0	0
Check—untreated			5	5

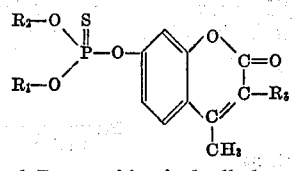
[1] Knock-down includes those also listed as dead.

Table 5.—Residual effectiveness of O,O-diethyl O-4-methylumbelliferone thiophosphate at 0.025 percent in combination with 0.25 percent of synergist, applied as powders (Pyrax) to cloth patches. (Average of two tests with 20 lice in each test, exposed for 24 hours.)

Synergist	Percent knock-down and kill (combined) on indicated days				
	Initial	3	5	7	10
Piperonyl butoxide	100	98	98	68	30
1,2-methylenedioxy-4-[2-(octylsulfinyl)-propyl]benzene	100	100	100	100	98
1,2-methylenedioxy-4-[2-(octylsulfonyl)-propyl]benzene	100	100	100	100	85
Chrysanthemummonocarboxylic acid, alpha-allylpiperonyl ester	100	98	93	58	25
Alpha-Propylpiperonyl acetate	100	50			
Chrysanthemummonocarboxylic acid, alpha-propylpiperonyl ester	98	60			
Chrysanthemummonocarboxylic acid, alpha-ethylpiperonyl ester	100	98	88	85	48
Chrysanthemummonocarboxylic acid, alpha-tert-butylpiperonyl ester	100	100	98	73	53
5-butyl-5-ethyl-2-(3,4-methylenedioxyphenyl)-m-dioxane	100	30			
Fencholic acid, alpha-allylpiperonyl ester	100	85	60		
Chrysanthemummonocarboxylic acid, alpha-isopropylpiperonyl ester	100	98	85	75	33
Chrysanthemummonocarboxylic acid, alpha-amylpiperonyl ester	98	70			
Chrysanthemummonocarboxylic acid, alpha-butylpiperonyl ester	100	70			
Chrysanthemummonocarboxylic alpha-(2-methylallyl)piperonyl ester	100	98	83	60	
Alpha-Cyclohexyl-piperonyl acetate	100	93	68		
None (toxicant alone)	75	33	33	13	
Control (Pyrax alone)	3	0	0	0	0
Control (untreated)	3	0	0	0	0

We claim:

1. An insecticide comprising a mixture containing as a toxicant an organic phosphate having the formula



wherein R_1 and R_2 are identical alkyl radicals selected from the group consisting of methyl and ethyl, and R_3 is a member of the group consisting of hydrogen and chlorine and, as a synergist therefor, a member selected from the group consisting of 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl] benzene and the alpha-isopropylpiperonyl ester of chrysanthemum monocarboxylic acid, said toxicant and synergist being present in the proportions of about from .0025% to .005% of toxicant to .025% to .05%, respectively, of the synergist.

2. The insecticide of claim 1 wherein the synergist is 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl] benzene.

3. The insecticide in claim 1 wherein the toxicant is O,O-diethyl O-4-methylumbelliferone thiophosphate and the synergist is 1,2-methylenedioxy-4-[2-(octylsulfinyl)-propyl] benzene.

4. The insecticide of claim 1 wherein the toxicant is O-(3-chloro-4-methylumbelliferone) O,O-diethyl thiophosphate and the synergist is 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl] benzene.

5. The insecticide of claim 1 wherein the toxicant is O-(3-chloro-4-methylumbelliferone) O,O-dimethyl thiophosphate and the synergist is 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl] benzene.

6. The insecticide of claim 1 wherein the synergist is the alpha-isopropylpiperonyl ester of chrysanthemum monocarboxylic acid.

7. The insecticide of claim 1 wherein the toxicant is O,O-diethyl O-4-methylumbelliferone thiophosphate and the synergist is the alpha-isopropylpiperonyl ester of chrysanthemum monocarboxylic acid.

8. The insecticide of claim 1 wherein the toxicant is O-(3-chloro-4-methylumbelliferone) O,O-diethyl thiophosphate and the synergist is the alpha-isopropylpiperonyl ester of chrysanthemum monocarboxylic acid.

9. The insecticide of claim 1 wherein the toxicant is O-(3-chloro-4-methylumbelliferone) O,O-dimethyl thiophosphate and the synergist is the alpha-isopropylpiperonyl ester of chrysanthemum monocarboxylic acid.

References Cited in the file of this patent

UNITED STATES PATENTS

2,458,656	Synerholm	Jan. 11, 1949
2,486,445	Synerholm	Nov. 1, 1949
2,493,927	Prill	Jan. 10, 1950
2,624,745	Schrader	Jan. 6, 1953

OTHER REFERENCES

Hoffman et al.: J. Econ. Ent. (February 1954), vol. 47, No. 1, pp. 72–76.

King: Chemicals Evaluated as Insecticides, U. S. Dept. Agr. Handbook 69, p. 115, Item No. 20, 337, May 1954.