EFFECTS OF 2-DIETHYLAMINOETHYL 2,2-DIPHENYLPENTANOATE (SKF 525A) ON INSECTICIDAL POTENCY

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2-DIETHYLAMINOETHYL 2,2-diphenylpentanoate (SKF 525*A*) is well known to prolong the actions of a variety of drugs in mammals[1], and we have therefore investigated the effects of the compound on the toxicity to insects of pyrethrins and other insecticides, comparing its effects with those of the pyrethrin synergist 'piperonyl butoxide' (PB)[2,3]. SKF 525*A* has been administered to mammals in the form of its water-soluble hydrochloride, but when injected the hydrochloride proved inconveniently toxic to the test insects, and if applied externally could be expected to penetrate only slowly through the insect cuticle; hence we dosed the insects externally with SKF 525*A* in the form of the free base, which, like PB, was then non-toxic at the doses used.

In a series of qualitative tests, lesser mealworm beetles, *Alphitobius laevigatus* (F.), were dosed topically between the hind coxæ[4] with a solution of SKF 525*A* or PB, and 5–10 min. later with a solution of insecticide on the neck[5]. Separating the applications reduced the risk of chemical reaction between the basic SKF 525*A* and those insecticides that were acidic, before they had penetrated into the insect. 7 μgm. of SKF 525*A* or PB were applied in 0·07 μl. of solution in refined (odourless) kerosene, and an appropriate dose of insecticide in 0·025 μl. of solution in a heavier refined petroleum oil, Shell 'Risella 17'. Applications of insecticide without SKF 525*A* or PB were made comparably, with a dose of oil solvent on the other site. Use of the two different oil solvents enabled the two techniques of dosage to be used in conjunction. In additional qualitative tests, houseflies, *Musca domestica* L., were dosed topically[4] with pyrethrins or malathion, mixed with SKF 525*A* or PB, in solution in refined kerosene. Effects were determined by percentage of beetles paralysed 4 days after dosage (approximating to final mortality) and percentage of flies dead 24 hr. after dosage. The results, shown in Table 1, indicate a joint-action spectrum for SKF 525*A* qualitatively similar to that for PB; reduction by PB of the insecticidal activity of malathion in flies has been noted previously[6].

Table 1. EFFECTS OF SKF 525*A* AND PB ON THE TOXICITIES OF CERTAIN INSECTICIDES

Insecticide	*A. laevigatus*		*M. domestica*	
	SFK 525*A*	PB	SKF 525*A*	PB
Pyrethrins	+	+	+	+
Allethrin	+	+		
Barthrin	+	+		
Malathion	(−)	−	−	−
2-*n*-Valeryl 1,3-indandione	+	(+)		
2-*sec*butyl 4,6-dinitrophenol	0	0		
DDT	0	0		
γ-BHC	0	0		
Dieldrin	0	0		

+, Considerable synergism; (+), slight synergism; 0, no effect; (−), slight antagonism; −, considerable antagonism.

The synergistic effects of SKF 525*A* and PB on the pyrethrins were compared quantitatively. The synergist was used in mixture with the pyrethrins, in solutions in refined kerosene. The volume was 0·07 μl. per beetle, applied between the hind coxæ[4]; and 0·05 and 0·10 μl. per male and female fly respectively, applied dorsally on the thorax[4]. Factors of synergism[3,7] were determined, each the ratio of the ED_{50} for pyrethrins in the absence of synergist to that in the presence of synergist at 10 times the dose of pyrethrins. With SKF 525*A* the factor was 1·8 for the beetles and 2·5 for the flies; with PB the factor was 3·2 for the beetles and 15 for the flies. SKF 525*A* was less synergistic than PB.

Neither 2,2-diphenylpentanoic acid nor 2-diethylaminoethanol affected the toxicity of pyrethrins. Other congeners of SKF 525*A* are being investigated.

In mammals SKF 525*A* depresses the metabolism, especially oxidative metabolism, of numerous drugs, thereby increasing[1] or decreasing[8] their effectiveness according as the metabolic products are more or less active than the drugs themselves. In the present work SKF 525*A* depressed the effect of malathion, which is oxidized in the cockroach, *Periplaneta americana*, to the more insecticidal malaoxon[9]. O'Brien[10] mentions that SKF 525*A* failed to reduce the action on the cockroach and the housefly of certain organo-phosphorus insecticides with more insecticidal oxidation products, but does not state the conditions in his experiments. In the present work SKF 525*A* was found to increase the effectiveness of pyrethrins, which, like related pyrethroids, are metabolized in insects to less insecticidal compounds not as yet identified, though chromatographic evidence[11] indicates that they could be oxidation products. The influence of PB on the toxicities was qualitatively similar to that of SKF 525*A*. Thus the findings reported here are in general accord with other evidence[12] that PB and other 3,4-methylenedioxyphenyl compounds synergize pyrethrins in insects by depressing oxidative detoxification.

In mammals SKF 525*A* depresses drug metabolism brought about by the liver microsomes[1]; a scheme has been put forward[10] to account for the apparently low specificity of the enzyme systems involved. The present results suggest that there may be in insects systems analogous to those inhibited by SKF 525*A* in the liver microsomes of mammals.

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