

likely that selection for reduced cuticular penetration may also account for a portion of the observed resistance in larvae.

We expect that studies in progress in this laboratory will provide the necessary qualitative and quantitative information on the nature of the resistance factors involved. We believe, however, that the information so far obtained on resistance to propoxur and cross-resistance to fenitrothion is of major importance in mosquito control and in malaria eradication strategies in particular, since both compounds are considered as front line substitutes against DDT and dieldrin resistant anophelines.

**Table 2** Effect of Synergists on the Toxicity of Various Compounds to Propoxur-selected *Anopheles albimanus*

Insecticide and dose (p.p.m.)	Synergist and dose (p.p.m.)	Percentage mortality	
		Insecticide alone	Insecticide + synergist
Propoxur 100	pb*	10	9
Propoxur 500	pb	10	7
Propoxur 700	pb	10	19
Carbaryl 30	pb	10	13
Carbaryl 50	pb	10	25
Malathion 2	TPP†	10	56
Parathion 0.175	pb	10	94
Methyl parathion 0.4	pb	10	93
Fenitrothion 0.3	pb	10	76
Fenthion 0.05	pb	10	95
Dichlorvos 0.2	pb	10	40
Paraoxon 0.2	pb	10	0
Paraoxon 1	pb	10	80
Paraoxon 0.2	TBPT‡	20	0
Paraoxon 1	TBPT	20	80
DDT 1	DMC§	10	76

\* Piperonyl butoxide.

† Triphenyl phosphate.

‡ Tributyl phosphorothioate.

§ 1,1-bis-(p-chlorophenyl) ethanol.

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## Acceptability of Daily *l*-Tetramisole by Pound Dogs infected with *Dirofilaria immitis*

THIENPONT *et al.*<sup>1</sup> reported on the anti-helminthic potency of a new synthetic drug named tetramisole which, when given in a single dose, was effective against many of the intestinal and pulmonary nematodes of fourteen mammalian species. In the absence of any information on the host's reaction to tetramisole given for 30 to 40 days, an experiment was designed with the primary objective of testing the acceptance of daily doses of the drug by dogs from pounds. A secondary objective was to detect any therapeutic activity against adult *Dirofilaria immitis*.

Three pound dogs, weighing 40–50 pounds and aged 1–2 yr, were used. Each had a *D. immitis* microfilaraemia, with pre-treatment concentrations of (A) 83, (B) 105 and (C) 5 microfilariae/20 mm<sup>3</sup> of blood respectively. Each was given one 50 mg tablet of tetramisole, directly or in a meatball, daily from Monday to Friday for 3 weeks, after which the dose was increased to one 100 mg tablet for the next 3 weeks. Four days after the last 100 mg dose, each dog was given a single dose at the rate of 9 mg per pound body weight.

The dogs were killed by intravenous injection of barbiturates 16 days after the last administration of drug and body cavities and viscera examined for worms. The great vessel leading to the heart was clamped off and the heart and lungs removed as a block. All chambers of the heart, the pulmonary artery, as well as all the dissectible branches of the arterial tree were opened in the search for adult heartworms. A gross examination for pathological changes was performed on all organs and principal tissues.

There were no unusual problems of drug acceptability with any of the three tetramisole regimens used. Dead worms were found in all dogs, often in the second order pulmonary arteries. All worms removed were placed in tissue culture fluid so that any movement could be observed, but none was seen. The microfilariae concentrations just before necropsy were: (A) 29; (B) 0; and (C) 0/20 m<sup>3</sup> of blood.

In the conditions of this limited experiment, there is clear evidence that tetramisole can be given to pound dogs at low concentrations for extended periods. Indications against the therapeutic use of tetramisole as a microfilaricide and as an adulticide were not observed clinically. More study is needed to determine the minimum effective concentration of tetramisole to destroy both microfilariae and adults of *D. immitis*.

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## Rational Design of Degradable Insecticides

I HAVE used a sterically based hypothesis of the mode of action of aryl insecticides, including DDT<sup>1</sup>, to predict possible structures of new compounds, the synthesis<sup>2</sup> of which has been directed at finding insecticides with low mammalian toxicity and which, because of their inherent chemical instability, would readily degrade. Insecticidal activity has been studied