Carter

MRID:

DATA EVALUATION RECORD

(1) CHEMICAL: Trichlorfon

(2) TYPE OF FORMULATION: Technical

(3) CITATION: Carter, M.K., and Maddux, B. 1974. Interaction of dichlorvos and anticholineterases on the in vitro inhibition of human blood cholineterases. Toxicol. Appl. Pharmacol. 27:456-463

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(6) TOPIC: This study has information pertinent to discipline toxicology, topic biochemistry. It relates to none of the Proposed Guidelines data requirements.

(7) CONCLUSION: The concentrations of trichlorfon that caused 50% inhibition of human plasma and erythrocyte cholinesterase were $1.1x10^{-7}$ and $3.1x10^{-6}$ M, respectively. The corresponding concentrations for dichlorvos, a possible metabolite of trichlorfon, were $3.0x10^{-8}$ and $4.7x10^{-7}$ M, respectively.
CORE CLASSIFICATION: Not applicable

(8) MATERIALS AND METHODS: Trichlorfon in the form of Dipterex, obtained from Chemagro Corp., and dichlorvos in the form of Vapona, obtained from Shell Chemical Co., were used. Other chemicals with anticholinesterase activity (carbaryl, chlorpromazine, crotoxyphos, dimecron, malaoxon, malathion, mevinphos, para-oxon, parathion, and physostigmine) were also tested. All but dimecron were described as being "of analytical grade."

Cholinesterase (ChE) activity and inhibition were measured using a manometric technique (Augustinsson. 1957. In Glick, D., ed. Methods of Biochemical Analysis. Wiley-Interscience, New York. Vol. 5, pp 1-63). Acetylcholine chloride (5 mM for RBC, 10 mM for plasma) was used as the substrate. Stock solutions of the inhibitors were made using propylene glycol unless they were water soluble. The last "several" dilutions were made in water and the last in buffer solution.

The I_{50} values (the molar concentrations of a compound that inhibits the enzyme 50%) for all compounds using RBC

or plasma ChE were determined from log-probit-percentage inhibition plots. In the experiments where combinations of dichlorvos and the various agents to be tested were used, concentrations of the individual compounds that would result in "an approximate I_{15} - I_{45}" were selected. Every time a compound was tested, dichlorvos was also tested and the effect of the combination of the two agents was determined. Statistical significance was reported to have been determined with Student's t-test, with a probability (p) of 0.05 used as the level of significance.

(9) REPORTED RESULTS: The I_{50} values for dichlorvos and trichlorfon with plasma and erythrocyte cholinesterase derived from log-probit-percentage inhibition plots are listed below.

I_{50} (M)	Plasma ChE	Erythrocyte ChE
Dichlorvos	3.0×10^{-8}	4.7×10^{-7}
Trichlorfon	1.1×10^{-7}	3.1×10^{-6}

The combination of 10^{-7} M trichlorfon plus 10^{-8} M dichlorvos produced a 40% inhibition in the plasma ChE activity, compared to the "calculated" 46% inhibition. The combination of 5×10^{-7} M trichlorfon with 1.7×10^{-7} M dichlorvos produced a 42% inhibition in the erythrocyte ChE activity, compared to the "calculated" 51% inhibition.

Similar effects were observed with the combination of dichlorvos with the other anticholinesterase chemicals tested with the exception of chlorpromazine. This combination inhibited erythrocyte ChE, but not plasma ChE more than expected.

(10) DISCUSSION: The procedures used in this study were adequate and the I_{50} values reported may be assumed to be valid. However, the authors presented no data to indicate whether the differences between the observed and "calculated" inhibition cuased by the pesticide combinations were statistically significant. Furthermore, they reported neither how they derived their "calculated" inhibition value for the combinations, nor the slopes of the inhibition curves for each chemical. It is, therefore, impossible to determine whether their "calculated" values have any validity.

(11) TECHNICAL REVIEW TIME: 6.5 hours