Estimating the Relative Toxicologic Potential of Each Pesticide in a Mixture of Residues on Foliage[1]

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In the treatment of crops with pesticides it is a fairly common practice to apply two or more materials during the growing season, sometimes simultaneously. At the time of reentry into the fields or orchards for thinning or harvesting the question of assessing blame to one or more material arises when any worker suffers adverse effects from exposure to the residues. Though absolute quantitation of the effect produced by each component of the mixture is not possible, it is indeed possible to estimate the relative contribution each pesticide could have made as long as each produces the same physiological effect. Some field data are available for use to illustrate the method.

APPLICATION OF PESTICIDES

In August and September 1970, 51 acres of Thompson seedless grapes near Fresno, California were treated with organic phosphate pesticides according to the following schedule:

Pesticide[2]	Field Number	Dates of Application	Active Ingredient Per Acre (lbs.)	Formulations Applied in 30 Gals. Water Per Acre
(Ethion	R 1	Aug. 27	1.60	25% W.P.
and	R 2 & R 3	Aug. 28		
Guthion)	R 4 & R 5	Aug. 31	1.90	50% W.P.
Zolone	R 1-R 3	Sept. 11	3.00	3#/gal. EC
	R 4 & R 5	Sept. 14		
Dibrom	R 1-R 5	Sept. 24	1.00	8#/gal. EC

1 The analysis upon which this publication is based was performed pursuant to Community Studies on Pesticides Contract No. 68-02-0719 with the Environmental Protection Agency.

2 Pesticides named in this paper, equivalent trade or generic names and the chemical names are as follows: Ethion or ethion 0,0,0',0'-tetraethyl S,S'-methylene bis phosphorodithioate; Guthion(R) or azinphosmethyl, 0,0-dimethyl S-4-oxo-1,2,3-benzotriazin-3 (4H)- ylmethyl phosphorodithioate; Dibrom(R) or naled, 1,2-dibromo-2,2-dichlorethyl dimethyl phosphate and Zolone(R) or phosalone, 0,0-diethyl S- [(6-chloro-2-oxobenzoxazolin-3-yl)methyl]phosphorodithioate.

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DISAPPEARANCE OF PESTICIDE RESIDUES

Leaf samples were taken before and at varying intervals after pesticide applications in order to determine the rate of disappearance of residues. Sampling was random with respect to plants in each field. Following removal by washing, residues remaining at the varying times were estimated by gas chromatographic analyses and a kinetic analysis of the data indicated first order losses with rate constants for pesticide disappearance, k, of 10.2×10^{-2}, 4.83×10^{-2} and 6.07×10^{-2} $days^{-1}$ for Ethion, Guthion and Zolone, respectively. Dibrom residues could not be detected four days after application and thus the pesticide was not further considered.

ESTIMATION OF RELATIVE TOXICOLOGICAL POTENTIAL

Workers entered the vineyards to harvest grapes on October 6 and were monitored for blood cholinesterase changes, relative to values obtained before entering the fields, that day, and again October 8 and October 12 by procedures under good quality control (SERAT and MENGLE 1973). There were depressions in the enzyme activities but at the time no quantitative assessment could be made of the pesticide or pesticides most likely responsible.

It is reported that Ethion and Guthion together, at levels of half the LD_{50}, potentiate the sum of the respective toxicities by some two-fold when administered to female white rats by intraperitoneal injection (DUBOIS 1962). Moreover, Zolone potentiates the toxic activity of both Ethion and Guthion when administered orally to female white rats (information kindly supplied by the manufacturer). From the data available, a potentiating factor of some 1½ to 2 fold was estimated. Data concerning potentiation following dermal exposure could not be found.

For initial calculations, considering each pesticide separately, the toxicologic potential, T, at any time is defined here as the ratio between the pesticide residue level on foliage and the dermal LD_{50} value. Only dermal values are considered here since, from a knowledgeable consensus of opinions, that mode of absorption is believed to be the major route of exposure to field workers. From the integrated expression for a first order loss of pesticide residue

$$\log P = \log Po - \frac{kt}{2.303} ,$$

where P is the residue level at time t after application, Po is the deposit level and k the specific rate constant. Then,

$$T = \frac{P}{LD_{50}} \quad \text{or} \quad \log T = \log \frac{Po}{LD_{50}} - \frac{kt}{2.303} .$$

Toxicologic potential, as defined, for each pesticide in a mixture of residues can thus be determined for any time after application as long as an LD_{50} value and the rate constant for pesticide disappearance are known. The kinetics of loss for all pesticides do not have to be of the same order, but for all cases of which we are aware, first order or pseudo first order kinetics prevail. For any pesticide whose disappearance is other than first order, an appropriate expression for P as a function of time must be used in the expansion of the basic equation for T.

Where potentiation exists, dividing the LD_{50} values for the respective pesticides by the potentiating factor allows a correction to be made. The correction is probably excessive when very low residue levels are existant because there are finite concentration limits beneath which a physiological effect cannot be measured.

In the field application mentioned above the deposit level of Ethion was 192 ppm; Guthion, 322 ppm and Zolone, 380 ppm as obtained by extrapolation of the first order decay lines to zero time. The values for dermal LD_{50} as determined on rabbits are, according to the manufacturers, 915 mg per kg for Ethion (tech.), at least 1500 mg per kg for Guthion (1 lb per gal. emulsion) and at least 1500 mg per kg for Zolone (3 lb per gal. emulsion). It is recognized that LD_{50} values should be measured on materials as they are expected to exist in the residues on foliage, but such values are not available.

Values of the toxicologic potential for the three pesticides were calculated with an assumption that they are mutually potentiating at factors of 1½ fold for each. This assumption may be less valid for Ethion, since the low levels of residues present at the time workers entered the fields may rule out its role as a potentiator.

Results are depicted in Fig. 1. For Ethion and Guthion, residues were extant for an average of 40 days after application at the time fields were entered while for Zolone the average time was 24 days. Accordingly, at the time fields were entered the toxicologic potentials are determined as 0.0053, 0.0467 and 0.0885 for Ethion, Guthion and Zolone, respectively. For this combination of the residues of 3 pesticides, relative to Ethion Guthion showed a toxicologic potential of 9 fold, while for Zolone it was 17 fold.

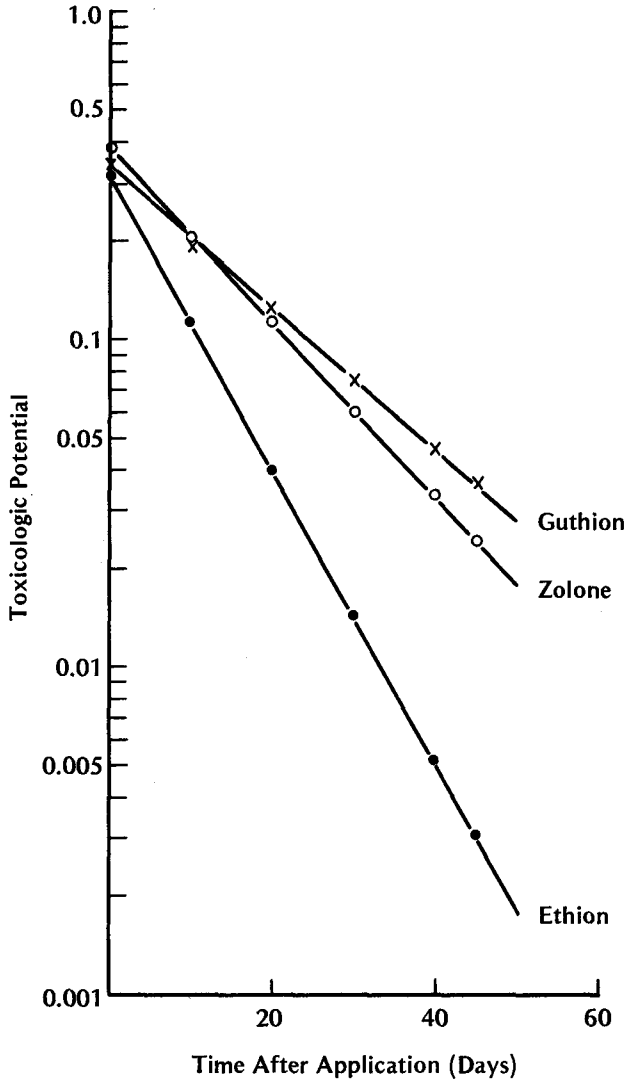

Fig. 1 Toxicologic potential of the residues of three pesticides in a mixture on grape foliage.

DISCUSSION

Due to the common practice of applying more than one pesticide simultaneously or over a short time period there is definite need to estimate the potential toxicity of each as a function of the age of the residues. Only estimates can be made but these should be subject to refinement from the values calculated above when better and standardized methods are used by those who will determine the level of residues on crops, the LD_{50} values and the degree of potentiation pesticides show at varying levels of absorption as would be expected from foliage at the times of reentry into treated fields.

Only a toxicologic potential has been calculated. For such purposes as the calculation of a reentry time (SERAT 1973) the inherent toxicity of each compound as it is to be used in the field, must be determined. Approximations, however, of a reentry time for a mixture of compounds of similar physiological activity can be made when the inherent toxicity of one component, the toxicologic potentials and the interdependent potentiating capacities of all are known.

The calculation of toxicologic potentials involves some known parameter of the toxicity of the pesticides. At present only LD_{50} values are available and these are determined on animals by procedures that seldom are the same for the different compounds. It is not assumed that the LD_{50} values used above are in the same relative proportion to those that might be observed in man, nor is it anticipated that the relative proportions are widely variant from those that might exist for man.

Though the results suggest that Zolone contributed most heavily to the cholinesterase loses observed, it must be remembered that at the 24 days (ave.) after application of Zolone when fields were entered there were residue levels averaging 89 ppm on the foliage, while for Guthion and Ethion at 40 days after application there were 47 and 3 ppm residue levels, respectively. In toxicologic potential Zolone would compare with Guthion at comparable residue age. It would appear that Ethion, per se, offered little if any contribution to the observed cholinesterase decreases. Its possible contribution in potentiating the effects of the other compounds, however, is not known.

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