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Worker Reentry Research for Carbosulfan Applied to California Citrus Trees

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Carbosulfan [FMC 35001; 2,3-dihydro-2,2-dimethyl-7-benzofuranyl [(di-*n*-butylamino)thio]methylcarbamate] was applied to citrus trees at a rate of 1.7 kg of active ingredient $(18.7\ hL)^{-1}\ ha^{-1}$. The 0-day dislodgeable foliar carbosulfan residue was 1.2 ± 0.2 $\mu g/cm^2$, and it dissipated with a half-life of 3.7 ± 0.5 days. The maximum amounts of carbofuran and 3-hydroxycarbofuran found on the foliage were 0.16 and 0.03 $\mu g/cm^2$, respectively; net dissipation half-lives were 8.1 ± 2.6 and 12 ± 3 days, respectively. The maximum amounts of carbosulfan, carbofuran, and 3-hydroxycarbofuran found in the dry mobile grove dust were 46, 45, and 4 ppm, respectively. Half-lives for dissipation were 2–4 days for carbosulfan and 9 ± 3 days for carbofuran. Dermal dose–cholinesterase response curves for the three carbamate compounds were obtained for rats, and these data were used to calculate safe residue levels on foliage. A 7-day reentry interval was proposed for California citrus.

Carbosulfan [FMC 35001; Advantage; 2,3-dihydro-2,2-dimethyl-7-benzofuranyl [di-*n*-butylamino)thio]methylcarbamate] shows promise as a potentially useful insecticide for the control of citrus thrips in California. In addition to residue data needed to establish tolerances on and in citrus fruit for consumer protection, data on foliar and soil dust residues were needed to protect agricultural workers who reenter treated groves and come into prolonged and extensive contact with the treated foliage as during tree pruning and harvesting operations. The causes and effects of the citrus reentry problem and approaches to its minimization were reviewed by Gunther et al. (1977). Reported here are the residue data relevant to worker safety for carbosulfan and its two alteration products, carbofuran and 3-hydroxycarbofuran, after treatment of orange, lemon, and grapefruit trees with Advantage 2.5EC insecticide formulation. In addition, dermal dose–cholinesterase (ChE) response data were generated for the three carbamate compounds found as dislodgeable foliar residues. The ChE response data were used to calculate safe residue levels on foliage and, in conjunction with the dislodgeable residue data generated in this study, to calculate a safe reentry interval for California citrus.

Data on the decomposition of carbosulfan in aqueous and nonaqueous media, degradation in soils, metabolism in corn and cotton plants, and alteration in the stomach of rats have been reported by Fukuto and co-workers (Umetsu et al., 1979, 1980, 1981a,b; Clay et al., 1980; Nishioka et al., 1981; Umetsu and Fukuto, 1982a,b). An analytical method for carbosulfan residues in plants, soil, and water has been reported by Leppert et al. (1983).

EXPERIMENTAL SECTION

Treatment and Sampling. Mature orange, lemon, and grapefruit trees were located on the University of California Citrus Research Center, Riverside, CA. Treatments were made with a Kinkelder machine equipped with an air tower. Advantage 2.5EC, 2.5 lb of active ingredient (AI)/gal of emulsifiable concentrate formulation, was provided by FMC Corp. The insecticide was applied at a rate of 1.5 lb of AI $(200\ gal)^{-1}\ acre^{-1}$ [1.7 kg $(18.7\ hL)^{-1}\ ha^{-1}$] on May 31, June 7, and June 21, 1982, to orange, grapefruit, and lemon trees, respectively. Trees were oversprayed at the same rate 21 days later on June 21, June 28, and July 12, 1982, respectively.

Fifteen rows of six orange trees each were treated, and three subplots of five rows each were established. Fourteen rows of six lemon trees each were treated, and three subplots of four rows were established. Six rows of fourteen grapefruit trees each were treated, and three center rows

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were each designated as subplots. For each subplot, eight trees located in the middle of the subplot were selected for sample collection purposes.

A 40-leaf-disk sample was collected with a mechanical leaf punch by excising 5 2.54-cm diameter disks from each of 8 trees such that each octant position around the tree was represented by 5 disks in the composite sample (Gunther et al., 1973). Two samples were collected from each of the three replicate subplots at each sampling interval. A soil dust sample was collected by vacuuming through a 23 × 55 cm, 100-mesh screen as described by Spencer et al. (1977) from one octant from each of eight trees such that all octant positions were represented in the composite sample. One sample was collected from each of the three replicate subplots at each sampling interval. The mean amounts of dust collected for each sample were 73 ± 32 g for the orange grove and 101 ± 20 g for the grapefruit grove.

Processing. *Dislodgeable Residues.* The specific procedure, which was a variation of the method of Iwata et al. (1977), was provided by FMC Corp. (Fullmer, 1981). The wash solution was a pH 8, 0.025 M, phosphate buffer containing 0.004% (w/v) Aerosol OT wetting agent (75% dioctyl sodium succinate). A 40-leaf-disk sample was shaken in an 8-oz, screw-cap jar with 50 mL of wash solution for 10 min on a reciprocating shaker. The wash solution was decanted into a separatory funnel. The sample was washed 2 more times with 50 mL of solution and a 10-min shake each time. To the combined wash solution, 30 g of NaCl and 1 mL of 4% aqueous dodecyl sodium sulfate were added. The aqueous solution was extracted 3 times by using 50 mL of CH_2Cl_2 and a 1-min shake each time. Each CH_2Cl_2 extract was passed successively through a funnel containing Na_2SO_4 and into a flask. The Na_2SO_4 was rinsed with 10 mL of CH_2Cl_2. The combined CH_2Cl_2 extract was taken just to dryness by using a rotary evaporator. The residue was dissolved in acetone for gas chromatographic (GC) analysis for carbosulfan, carbofuran, and 3-hydroxycarbofuran.

All field samples were processed into CH_2Cl_2 solutions within 2 h after collection. On the same day, the residues were transferred into acetone solutions, which were then stored in a freezer to await analysis. Mean storage time and standard deviation prior to both carbosulfan and carbofuran analyses were 6 ± 5 days, and the maximum storage time was 20 days. Mean storage time prior to the more involved 3-hydroxycarbofuran analyses was 35 ± 20 days, and the maximum storage time was 60 days.

Soil. The procedure was provided by FMC Corp. (Fullmer, 1981). To 10 g of soil dust (≤100 mesh) 40 mL of 9:1 (v/v) methanol–(pH 8) 0.025 M phosphate buffer was added. The mixture was shaken for 20 min on a reciprocating shaker and was filtered through a Büchner funnel. The soil was rinsed with 10 mL of the methanol–buffer mixture. The extract was transferred to a separatory funnel with the use of 50 mL of water, and 5 g of NaCl was added. The combined mixture was extracted 3 times with 50 mL of CH_2Cl_2 and a 1-min shake each time. Each CH_2Cl_2 extract was passed successively through a funnel containing Na_2SO_4 and into a flask. The combined CH_2Cl_2 extract was taken just to dryness by using a rotary evaporator. The residue was dissolved in acetone for GC analysis for carbosulfan, carbofuran, and 3-hydroxycarbofuran.

All field samples were processed into CH_2Cl_2 solutions within 2 h after collection. On the same day, the residues were transferred into acetone solutions, which were then stored in a freezer to await analysis. Mean storage time prior to both carbosulfan and carbofuran analyses was 6 ± 5 days, and the maximum storage time was 17 days. Mean storage time prior to the 3-hydroxycarbofuran analyses was 75 ± 34 days, and the maximum storage time was 106 days.

Analytical Standards. Carbosulfan, carbofuran, 3-hydroxycarbofuran, and 3-ethoxycarbofuran were provided by FMC Corp., Agricultural Chemicals Division, Middleport, NY. The carbosulfan was stablized with epoxidized soybean oil (Kronox-S).

Derivatization. Conversion of 3-hydroxycarbofuran to its 3-ethoxy derivative for GC analysis was described by Nelsen and Cook (1980). After completion of the analyses for carbosulfan and carbofuran, the acetone solvent was removed. The residue was refluxed for 30 min with 20 mL of absolute ethanol and 0.1 mL of concentrated aqueous HCl solution. The cooled mixture was transferred to a separatory funnel with 50 mL of water. After addition of 5 mL of 10% $NaHCO_3$ solution to neutralize the acid, the mixture was extracted twice with 50 mL of CH_2Cl_2 and a 1-min shake each time. Each CH_2Cl_2 extract was passed successively through a funnel containing Na_2SO_4 and into a flask. The Na_2SO_4 was rinsed with 25 mL of CH_2Cl_2. The CH_2Cl_2 was removed, and the residue was dissolved in acetone for GC analysis. Neutralization of the acid was done to prevent trace amounts of acid from being carried through the procedure. Trace amounts of acid getting on the GC column destroyed the ability to analyze the carbosulfan in other sample extracts.

Analysis. Quantification was by GC analysis by using a Hewlett-Packard nitrogen–phosphorus thermionic detector. A 30 cm × 2 mm i.d. glass column packed with a 5% OV-101 on 80–100-mesh UltraBond 20M was used with a nitrogen flow rate of 30 mL/min. Injector and detector temperatures were 200 and 250 °C, respectively. For carbosulfan, carbofuran, and 3-ethoxycarbofuran, column temperature were 190, 160, and 180 °C, respectively. Corresponding retention times were 2.8, 1.2, and 1.0 min, respectively. All standard curves were linear and passed through the origin in the 1–5-ng range in which all measurements were made.

Fortifications. Leaf washes prepared from orange leaves were fortified with 400, 40, and 4 μg of compound, which corresponds to foliar residues of 1.0, 0.1, and 0.01 $\mu g/cm^2$, respectively. Respective mean recoveries for three replicate samples were 110 ± 5, 118 ± 3, and 94 ± 4% for carbosulfan, 102 ± 3, 98 ± 3, and 97 ± 7% for carbofuran, and 101 ± 3, 96 ± 6, and 97 ± 7% for 3-hydroxycarbofuran. Grove soil dust (≤100 mesh) derived from an Arlington fine sandy loam were fortified at 1, 5, 10, and 50 ppm. Respective mean recoveries for three replicate samples were 66 ± 2, 91 ± 4, 88 ± 4, and 86 ± 2% for carbosulfan and 108 ± 1, 93 ± 3, 98 ± 3, and 97 ± 3% for carbofuran. Dust fortified at 1 and 5 ppm of 3-hydroxycarbofuran gave recoveries of 82 ± 1 and 90 ± 1%, respectively. Residue data for field samples were not corrected for recoveries based on the satisfactory recoveries obtained above.

Dermal Toxicity. Dermal dose-ChE response studies were conducted according to the procedure of Knaak et al. (1980) by using analytical samples of carbosulfan (stabilized), carbofuran, and 3-hydroxycarbofuran. In this procedure, the hair on the backs of 220–240-g male Sprague-Dawley rats is first removed by clipping. The test compound is then applied in 1.0 mL of acetone to a 25-cm^2 area of the exposed skin. Four to five dose levels were used for each compound with four animals at each dose level. Eight control animals were used in each study. Animals were sacrificed after 24 h of exposure, and the ChE activity

Table I. Description of the Lines Drawn in Figures 1-3

compound	citrus	treatment[a]	slope	intercept, μg/cm²	correlation coefficient	half-life, days	data omitted[a]
carbosulfan	orange	initial	−0.159	0.94	−0.990	4.4	day 21
		overspray	−0.189	1.2	−0.993	3.7	
	grapefruit	initial	−0.202	1.4	−0.979	3.4	
		overspray	−0.233	0.91	−0.976	3.0	
	lemon	initial	−0.166	1.5	−0.987	4.2	
		overspray	−0.211	1.1	−0.980	3.3	
carbofuran	orange	initial	−0.066	0.043	−0.992	10.5	
		overspray	−0.062	0.067	−0.924	11.2	day 1
	grapefruit	initial	−0.118	0.041	−0.960	5.9	day 1
		overspray	−0.150	0.055	−0.994	4.6	
	lemon	initial	−0.094	0.073	−0.988	7.4	day 1
		overspray	−0.244	0.17	−0.999	(2.8)	days 10, 14, 17, 21
			−0.079	0.052	−0.977	8.8	days 1, 3
3-hydroxycarbofuran	orange	initial	−0.060	0.020	−0.904	12	
		overspray	−0.016	0.022	−0.872	43	days 1, 3
	grapefruit	initial	−0.094	0.031	−0.960	7	day 1
		overspray	−0.064	0.029	−0.986	11	day 1
	lemon	initial	−0.058	0.017	−0.984	12	
		overspray	−0.044	0.027	−0.962	16	day 1

[a] For the overspray treatments, 21 days elapsed is day 0.

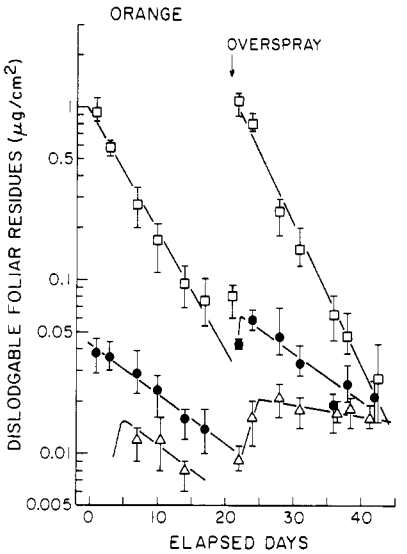

Figure 1. Dislodgeable foliar residues of carbosulfan (□), carbofuran (●), and 3-hydroxycarbofuran (△) after treatment of orange trees with Advantage 2.5EC insecticide formulation at 1.5 lb of AI (200 gal)$^{-1}$ acre^{-1}. Each datum point is the mean value obtained from six replicate field samples, and the vertical lines show the range of values found.

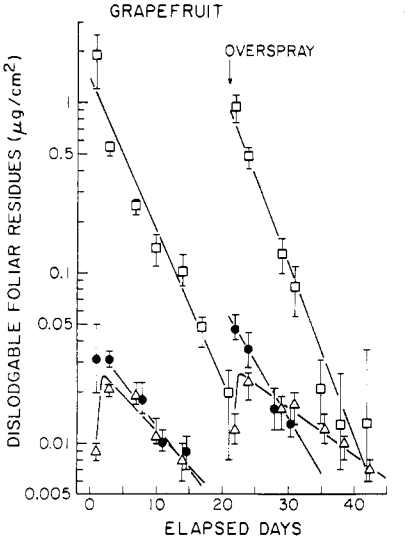

Figure 2. Dislodgeable foliar residues of carbosulfan (□), carbofuran (●), and 3-hydroxycarbofuran (△) after treatment of grapefruit trees with Advantage 2.5EC insecticide formulation at 1.5 lb of AI (200 gal)$^{-1}$ acre^{-1}. Each datum point is the mean value obtained from six replicate field samples, and the vertical lines show the range of values found.

in the red blood cells was determined by using an automated procedure (Knaak et al., 1978).

RESULTS AND DISCUSSION

The proposed use of carbosulfan as a foliar spray for pest control purposes on California citrus required to acquisition of residue data relevant to agricultural workers entering treated groves. Past episodes indicating illnesses caused by ChE inhibition have been attributed exclusively to residues of organophosphorus insecticides. However, since carbosulfan and its degrdation product, carbofuran, are carbamate compounds capable of ChE inhibition, data on residue dissipation from citrus foliage and mobile, orchard soil dust were obtained. These data give an understanding of the levels and dissipation trends of the toxic compounds present after field application of a commercial formulation at its maximum label rate. The understanding of residue behavior then allows for safer field use of the insecticide. A discussion and an example of the use of dislodgeable foliar residue data and dermal dose–ChE response data for calculating a reentry interval for the organophosphorus insecticide, chlorthiophos, applied to citrus were presented by Iwata et al. (1982).

Dislodgeable Foliar Residues. Citrus trees were sprayed at a rate of 1.5 lb of AI (200 gal)$^{-1}$ acre^{-1} and were oversprayed 3 weeks later at the same dosage. Residue data are shown in Figures 1, 2, and 3 for oranges, grapefruits, and lemons; the surface area of both sides of the leaf disks was used. In the cases of carbofuran and 3-hydroxycarbofuran, residue levels at any particular time are a net result of both compound formation and loss. Thus, the lines shown in Figures 1–3 are drawn only to enable the reader to see the trend exhibited by the overall residue data. Table I gives the mathematical descriptions of the drawn lines.

All six residue dissipation curves for carbosulfan were in good agreement with each other. The mean 0-day residue based upon the extrapolated curve was 1.2 ± 0.2 μg/cm², and the mean residue half-life was 3.7 ± 0.5 days.

Table II. Description of the Lines Drawn in Figures 4 and 5

compound	citrus grove	treatment[a]	slope	intercept, ppm	correlation coefficient	half-life, days	data omitted[a]
carbosulfan	orange	initial	−0.409	51		1.7	
		overspray	−0.183	22		3.8	day 3
carbofuran	orange	initial	−0.069	17	−0.963	10	
		overspray	−0.053	24	−0.958	13	
	grapefruit	initial	−0.123	21	−0.996	5.6	
		overspray	−0.094	33	−0.990	7.4	

[a] For the overspray treatments, 21 days elapsed is day 0.

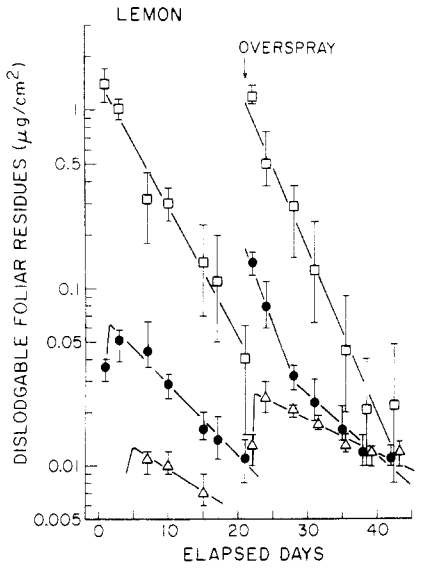

Figure 3. Dislodgeable foliar residues of carbosulfan (□), carbofuran (●), and 3-hydroxycarbofuran (△) after treatment of lemon trees with Advantage 2.5EC insecticide formulation at 1.5 lb of AI (200 gal)$^{-1}$ acre^{-1}. Each datum point is the mean value obtained from six replicate field samples, and the vertical lines show the range of values found.

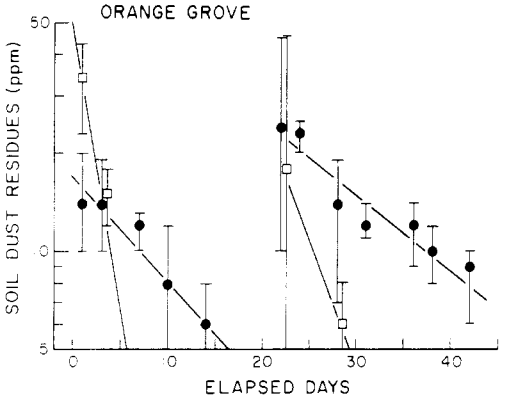

Figure 4. Residues of carbosulfan (□) and carbofuran (●) in the mobile soil dust beneath orange trees sprayed with Advantage 2.5EC insecticide formulation at 1.5 lb of AI (200 gal)$^{-1}$ acre^{-1}. All 3-hydroxycarbofuran residues were below the 3-ppm detectable limit. Each datum point is the mean value obtained from three replicate field samples, and the vertical lines show the range of values found.

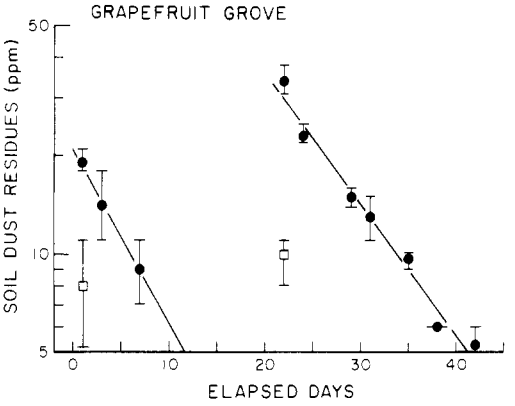

Figure 5. Residues of carbosulfan (□) and carbofuran (●) in the mobile soil dust beneath grapefruit trees sprayed with Advantage 2.5EC insecticide formulation at 1.5 lb of AI (200 gal)$^{-1}$ acre^{-1}. The maximum amount of 3-hydroxycarbofuran residue found was 4 ppm. Each datum point is the mean value obtained from three replicate field samples, and the vertical lines show the range of values found.

The overall data, wherein 3-day residues were greater than 1-day residues, indicate that carbofuran and 3-hydroxycarbofuran were being formed on the leaves. Residues of both compounds remained relatively low, however. The maximum amounts found were 0.16 μg/cm^2 carbofuran at 1-day postapplication and 0.03 μg/cm^2 3-hydroxycarbofuran at 3 days postapplication. The net, mean half-life for carbofuran residue dissipation was 8.1 ± 2.6 days. The net, mean half-life for 3-hydroxycarbofuran residue dissipation was 12 ± 3 days; one aberrant value of 43 days was omitted.

The abiotic formation of 3-hydroxycarbofuran on dusty leaf surfaces first noted by Fullmer (1981) and the well-documented formation of oxygen analogues from organophosphorus insecticides show that dry soil exposed to sunlight and oxidants in air can produce interesting chemical changes in insecticide residues.

Soil Dust Residues. Residues of mobile dust (≤100 mesh) were collected from around the perimeter of the sprayed trees near the skirt. These are the residues that have been suggested (Gunther et al., 1977) as being available to workers who agitate the soil surface during their assigned labors. Although some illnesses are believed to have been caused by residues on soil dust, no method has yet been developed to set at a safe level. Residue data were obtained here for potential future use. The U.S. Environmental Protection Agency (EPA) guidelines for registering pesticides in the United States (*Fed. Regist.*, 1982) do not require pesticide residue data for soil unless there is substantial exposure of workers to the soil. Residue data for carbosulfan, carbofuran, and 3-hydroxycarbofuran obtained after treatment of orange and grapefruit trees at a rate of 1.5 lb of AI (200 gal)$^{-1}$ acre^{-1} are shown in Figures 4 and 5. Soil dust samples were not collected from the lemon grove. Table II gives the mathematical description of the lines drawn in Figures 4 and 5 to show the trend in the residue levels.

The maximum carbosulfan level found was 46 ppm in a 1-day sample, and the soil dust residue dissipated with a half-life of 2–4 days. The maximum carbofuran level found was 45 ppm in the same 1-day sample. The carbofuran dissipated with a half-life of 9 ± 3 days. No 3-hydroxycarbofuran was found above the 2–3-ppm detectable limit in the dust collected from the orange grove. Trace amounts were found in the soil dust collected from

Table III. Calculation of Safe Residue Levels ($\mu g/cm^2$) on Citrus Tree Foliage Using the Results of Dermal Dose-ChE Response Curves and Field Reentry Studies according to Knaak et al. (1980)

insecticide or alteration product	slope of dose-response curve[a]	ED_{50}, $\mu g/cm^2$, of total body surface[b]	relative toxicity[c]	safe level on foliage, $\mu g/cm^2$[d]
carbofuran	1.12	6.6 ± 0.4	2.8	0.3
carbosulfan	1.35	7.8 ± 0.4	3.3	0.3
3-hydroxy-carbofuran	1.95	34.4 ± 0.3	14.3	1.3
parathion	1.3	2.4 ± 0.3	1.0	0.09[e]

[a] Values for the three carbamate compounds were calculated from the data used to construct Figure 6. Data were subjected to the log-probit analysis procedure of Finney (1972). [b] ED_{50} in $\mu g/cm^2$ multiplied by 25 cm^2 (treated area) and divided by 325 cm^2 (total surface area of the rat). [c] ED_{50} of the compound under investigation divided by the ED_{50} of parathion, a reference compound for which actual field safety information is available. [d] Relative toxicity multiplied by the established safe level of parathion, which was determined by actual reentry studies. [e] Spear et al. (1977).

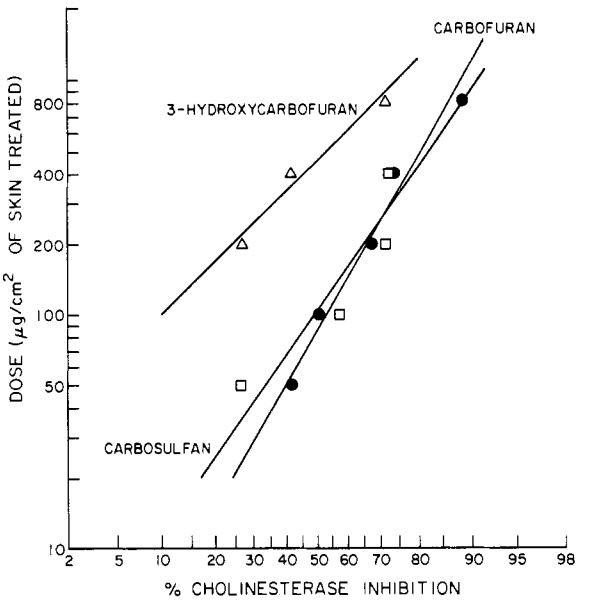

Figure 6. Percent red blood cell ChE inhibition in rats sacrificed 24 h after treatment of 25 cm^2 of skin surface with carbosulfan, carbofuran, or 3-hydroxycarbofuran.

the grapefruit grove. The maximum level found was 4 ppm.

Dermal Toxicity. Dermal dose–ChE response studies in the rat provide a useful procedure for assessing the toxicity of insecticide residues on foliage relative to field standards as indicated by Knaak et al. (1980). The results of the studies conducted with carbosulfan, carbofuran, and 3-hydroxycarbofuran are given in Figure 6. Carbosulfan and carbofuran are equivalent in toxicity because their ED_{50} values ($\mu g/cm^2$) and the slopes of their dose–response curves are similar, while 3-hydroxycarbofuran is approximately one-fifth as toxic, as indicated by its ED_{50} value.

Calculation of Allowable Residues on Foliage. Parathion, with a field-established safe level of 0.09 $\mu g/cm^2$ of foliage (Spear et al., 1977), was used as the insecticide standard for computing safe levels for carbosulfan and its alteration products in Table III. The ED_{50} values in the table are expressed in terms of total body surface area (325 cm^2), while in Figure 6, the ED_{50} values are in terms of the treated skin area (25 cm^2). The safe levels were determined to be 0.3 $\mu g/cm^2$ of foliage for both carbosulfan and carbofuran, while the safe level for 3-hydroxycarbofuran was 1.3 $\mu g/cm^2$ of foliage.

Because carbosulfan is converted on the leaf surface to carbofuran and 3-hydroxycarbofuran, a safe level must be established for total toxic carbamate residues rather than just for individual compounds. This was accomplished in Table IV by using a procedure similar to that used by Knaak and Iwata (1982) for toxic organophosphorus residues and in Table V according to the U.S. EPA guideline for registering pesticides in the United States (*Fed. Regist.*, 1982). The procedure in Table IV used the dislogeable residue data in $\mu g/cm^2$ of foliage for oranges from Figure 1 on days 1, 3, 7, and 10. The residue data for 3-hydroxycarbofuran were converted to carbosulfan toxicity equivalents by multiplying the residues ($\mu g/cm^2$) by a relative toxicity number (0.227). The relative toxicity number is defined as the ED_{50} of carbosulfan (7.8 ± 0.4) divided by the ED_{50} of 3-hydroxycarbofuran (34.4 ± 0.3). The carbosulfan equivalents of 3-hydroxycarbofuran are then added to the sum of the residues of carbosulfan and carbofuran. This quantity was then divided into the figure for total carbamate residues and multiplied by the safe level for carbosulfan. By this procedure the safe level for total carbamate residues at days 1, 3, 7, and 10 were obtained by taking into consideration the reduction in toxicity of the residues as the level of 3-hydroxycarbofuran increased. According to the calculations, it is safe to reenter and work 7 days after application of carbosulfan since, at 7 days, the total carbamate residue (0.31 $\mu g/cm^2$) has decreased to the calculated safe level for the carbamate mixture (0.31 $\mu g/cm^2$).

Table V also uses the residue data for oranges in Figure 1. The ratios for the three carbamate compounds at 1, 3, 7, and 10 days after spraying were calculated and used to determine the predicted ED_{10} value (in $\mu g/cm^2$) in the rat for total carbamates from the individual ED_{10} values as indicated. The individual ED_{10} values were obtained from the equations that described the dose–ChE response curves in Figure 6. The no effect level (NOEL, in $\mu g/kg$) was then

Table IV. Calculation of Safe Levels ($\mu g/cm^2$) Based on the Total Carbamate Residues of Carbosulfan on Citrus Tree Foliage

days after spraying	dislodgeable foliar residues, $\mu g/cm^2$[a] carbosulfan (CS)	carbofuran (CF)	3-hydroxy-carbofuran (HCF)	total carbamate (A)	toxic equivalents, (CS + CF) + (HCF × RT)[b] (B)	safe level for CS + CF + HCF mixture, (A/B) × SL for CF, $\mu g/cm^2$[c]
1	0.94	0.038	<0.01	0.99	0.98	0.30
3	0.58	0.036	<0.01	0.63	0.62	0.30
7	0.27	0.029	0.012	0.31	0.30	0.31
10	0.17	0.023	0.012	0.21	0.19	0.32

[a] Values are those used to construct Figure 1. [b] RT (relative toxicity) is the ED_{50} of CS divided by the ED_{50} of HCF. This RT differs in definition from that given in Table III. [c] SL (safe level) is 0.3 $\mu g/cm^2$ as found for CF (Table III), the most dermally toxic of the three carbamate compounds.

Table V. Calculation of Reentry Intervals according to U.S. Environmental Protection Agency (1981) Guidelines with a Slight Modification[a]

days after spraying	compound ratio,[b] CS:CF:HCF	NOEL,[c] μg kg^{-1} day^{-1}	AEL,[d] μg kg^{-1} day^{-1}	total dose,[e] μg/h	reentry level,[f] μg/cm^2
1	94:3.8:1	1224	122	1068	0.21
3	58:3.6:1	1209	121	1059	0.21
7	22.5:2.4:1	1197	120	1050	0.21
10	14.2:1.9:1	1200	120	1050	0.21

[a] Modification involves taking into account all toxic residues present on the foliage and using a total toxic residue curve. [b] Ratios calculated from values used to construct Figure 1. [c] No effect level (NOEL) calculated from data from dermal dose–ChE response curve. NOEL = $ED_{10}(25\ cm^2)/(0.23\ kg/day)$. Predicted $ED_{10} = [P_1/ED_{10,1} - P_2/ED_{10,2} + \ldots + P_N/ED_{10,N}]^{-1}$, where P = proportion of component in mixture (Finney, 1972). ED_{10} values were extrapolated from Figure 6. ED_{10} values for CS, CF, and HCF were 11.5, 6.24, and 98.8 μg/cm^2, respectively. [d] Allowable exposure level (AEL) = NOEL/SF. Safety factor (SF) = 10. [e] Total dose = (AEL)(body weight, 70 kg)/(duration, 8 h/day). [f] From total dose, reentry level was determined from the graph of whole-body dermal dose (μg/h) vs. dislodgeable foliar residues (ng/cm^2) from the data of Popendorf and Leffingwell (1982). Total dose was divided by 5.1, the k_d for citrus; derivation was based on the area of only one side of the leaf.

determined by dividing the predicted ED_{10} (25 cm^2) by the weight of the rat in kg/day. The allowable exposure level (AEL) was determined by dividing the NOEL by 10 (safety factor). Total dose was determined by multiplying the AEL by body weight in kg and dividing by the duration of exposure in h/day. The reentry level was obtained from a graph developed by Popendorf and Leffingwell (1982) relating whole-body dermal dose (μg/h) to dislodgeable foliar residues (ng/cm^2). The total dose was divided by 5.1, the k_d for citrus, to give the reentry level for leaf residues on only one side of the leaves. Division of these levels by two as suggested by Poppendorf and Leffingwell (1982) for residues on two sides of the leaves was not deemed necessary because a safety factor of 10 was used to calculate the allowable exposure level (AEL). The values (0.21 μg/cm^2, Table V) indicate that it is safe to reenter 10 days (0.21 μg/cm^2, Table IV) after application of carbosulfan.

The first procedure was patterned after the method of Knaak and Iwata (1982) and used parathion as a field standard because a carbamate standard was not available. The use of parathion as a standard most likely exaggerates the toxicity of carbosulfan. However, the second procedure, an EPA procedure that does not make use of a field standard, gave similar reslts (10 vs. 7 days). The EPA procedure makes use of a calculated AEL. The AEL was determined by using the ED_{10} values from the dermal dose–ChE response curve developed 24 h after application of the carbamates. Although maximum ChE inhibition might have occurred earlier, the 24-h time interval was selected because it was convenient for collection and analysis of blood samples.

On the basis of the data, a 7-day reentry time was selected as being sufficient to protect the health of workers. As with any newly established reentry interval, monitoring of the workplace and the health of the workers is desirable during the first year of use. If no injuries are observed or reported, 0.3 μg/cm^2 then becomes a field standard for carbosulfan. For other regions that grow citrus and have significantly different environmental factors, a locally generated dermal dose–dislodgeable foliar residue correlation and/or dislodgeable residue dissipation curve can be used.

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