increased at a faster rate when fruits approached the ripe stage. All varieties attained almost the same percentage, about 90% of dry matter when ripe.

The protein content at the green stage as shown in Table I is the highest and it is twofold higher than the concentration of the ripe stage (dry weight basis). There is no significant difference in the protein content of the three varieties studied with the same stage.

Amino acid compositions of the three varieties are given in Table II. In all varieties there are identical patterns of amino acid composition and 17 amino acids were detected. The protein-rich green stage contained the highest concentration of amino acids with more glutamic acid, aspartic acid, lysine, leucine, alanine, and serine than the other two stages of maturity. The data in Table II show that total and free amino acids concentrations are considerably different in the three varieties for the three stages of maturity. This seems to be associated with the protein contents of the three stages of development (Table I). The data also show for the three varieties at the yellow and completely ripened stages that glutamic acid, aspartic acid, lysine, leucine, proline, and glycine were present at high concentrations.

The concentrations of essential amino acids in the protein hydrolysates for the two stages of development where date is mostly consumed (yellow and ripened) differ significantly in the two stages for the three varieties. They total to approximately 1125, 1059, and 674 mg per 100 g of dry date for Khastawi, Khadhrawi, and Zahdi, respectively, at the yellow stage as compared to 604, 529, and 511 mg per 100 g of dry date at the ripe stage.

At the yellow stage lysine was the predominant essential amino acid for the three varieties followed by leucine, while at the ripe stage lysine was predominant in the variety Zahdi and leucine was predominant for the varieties Khastawi and Khadhrawi. The data show that Khastawi is higher in the essential amino acids than Khadhrawi and Zahdi. The difference between Khastawi and Zahdi is very significant at the yellow stage and becomes less at the ripe stage.

For most amino acids the concentration is higher at the yellow stage than the ripe stage and also the varieties (Khastawi and Khadhrawi) are significantly higher than Zahdi. From these results it can be concluded that date fruits are not very poor in protein and amino acid composition and that the highest concentration of amino acids, for the two stages in which dates are generally eaten, is in the yellow stage.

LITERATURE CITED

Al-Aswad, M. B., *J. Food Sci.* **36**, 1019 (1971).
Al-Rawi, N., Markakis, P., Bauer, D. H., *J. Sci. Food Agric.* **18**, 1–2 (1967).
Ashmawi, H., Aref, H., Hussein, A. A., *J. Sci. Food Agric.*, 626 (Oct 7, 1956).
Auda, H., Mirjan, J., Al-Wandawi, H., Report No. B-26, Nuclear Research Institute, Tuwaitha, Baghdad, Iraq, 1974.
Bidwell, C. L., Sterling, W. F., *Ind. Eng. Chem.* **17**, 147 (1925).
Globbelaar, N., Pollard, J. K., Steward, F. C., *Nature (London)* **175**, 703 (1955).
Koch, F. C., McMeekin, T. L., *J. Am. Chem. Soc.* **46**, 2066 (1924).
Mondino, A., Bongiovanni, G., *J. Chromatogr.* **52**, 405 (1970).
Ragab, M. H. H., El-Tabey Shehata, A. M., Sedky, A., *Food Technol.* **10** (Sept, 1956).
Rinderknecht, H. J., *Food Sci.* **24**, 298 (1959).

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Long-Term Exposure of Swine to a [14C]Dichlorvos Atmosphere

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Young swine have been exposed for 24 days to an atmosphere containing between 0.10 and 0.15 μg of [*1-vinyl*-14C]dichlorvos per l. of air. As in feeding experiments with the same labeled compound, the 14C content varied widely among different tissues, but none contained dichlorvos. The relative specific activities of isolated key intermediates are compatible with the degradation pathway postulated by Page et al. [Page, A. C., DeVries, D. M., Young, R., Loeffler, J. E., *Toxicol. Appl. Pharmacol.* **19**, 378 (1971); Page, A. C., Loeffler, J. E., Hendrickson, H. R., Huston, C. K., DeVries, D. M., *Arch. Toxicol.* **30**, 19–27 (1972)] which proceeds from dichlorvos after cleavage of the P–O–vinyl bond and dechlorination through a hypothetical symmetrical two-carbon intermediate to glycine and serine, and from there through well-established metabolic pathways to other naturally occurring tissue constituents.

Besides its application in various areas of animal husbandry, dichlorvos (2,2-dichlorovinyl *O,O*-dimethyl phosphate) is also used extensively in the NO-PEST Insecticide Strip from which dichlorvos is released.

Short-term pulmonary administration of 32P-labeled dichlorvos to pigs has shown that dichlorvos is degraded under these conditions by cleavage at the oxygen atom bonding the vinyl group to the dimethyl phosphate moiety (Loeffler et al., 1971). This is the same pathway as experimentally found after gastric or intestinal infusion of [32P]dichlorvos (Loeffler et al., 1972), and as the one which has to be postulated to account for the results with [*1-vinyl*-14C]dichlorvos after intestinal infusion and after single or multiple oral administration to swine (Page et al., 1971).

Work with rodents (Hutson et al., 1971a,b) has confirmed that in short-term experiments even at much higher than normal use concentrations the degradation pathway of inhaled and of orally administered dichlorvos was independent of the route of application and that the metabolism in the rat proceeded essentially in the same way as in swine.

Prolonged feeding of dichlorvos to swine did not change the degradation pathway from that seen after a single oral

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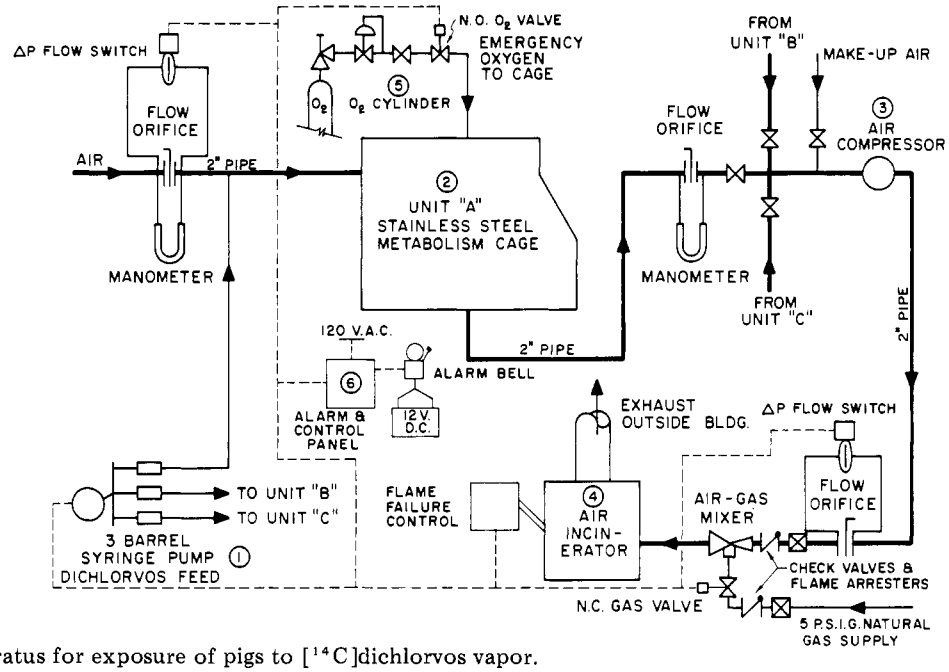

Figure 1. Apparatus for exposure of pigs to [^{14}C]dichlorvos vapor.

dose. Similarly, no such change was seen after infusion of dichlorvos into the duodenal loop of pretreated or naive swine. In spite of these results from oral treatments, there was still the possibility to consider that a different degradation pathway might come into play after prolonged exposure of animals to vapors of dichlorvos.

Pigs were, therefore, exposed for 24 days to an atmosphere of [*1-vinyl*-^{14}C]dichlorvos to determine the key metabolites and their sequence of formation.

EXPERIMENTAL CONDITIONS

The synthesis of [*1-vinyl*-^{14}C]dichlorvos has been reported (Burton, 1971). Two batches with radiochemical purities of 97 and 99% were mixed with nonradioactive, high purity dichlorvos dissolved in ethyl acetate to give a solution with a specific activity of 1.95 μCi/mg and a concentration of 0.144 mg/ml.

Air-tight metabolism cages were constructed of stainless steel. They were equipped with an air inlet manifold with six ports distributed evenly close to the roof, an air outlet in the floor, air sampling ports, a thermometer, a glass observation window, and a removable front and side panel to allow access to the feeding trough and to the containers in which excreta were collected. These cages were part of a specially designed system for continuous exposure of animals to radiolabeled dichlorvos in air. Figure 1 shows a schematic drawing of the whole system.

A three-barrel motor-driven syringe pump fitted with three 250-μl gas-tight microsyringes delivered the [^{14}C]-dichlorvos solution via 0.01-in. i.d. Teflon tubing into 2-in. diameter, 4-ft long galvanized iron pipes which were kept at 45 ± 5°C by an externally applied electrical heating tape. These pipes served as air inlets to the three cages. The rate of delivery was set to give a concentration of about 0.1 mg of dichlorvos per m^3 of air under the airflow conditions used.

Air was drawn through the cages from the suction side of a positive displacement air compressor (Model 1022 V1036Z72X, Gast Manufacturing Company, Benton Harbor, Mich.) at a rate of 135 ft^3 per cage per hr, providing about three air changes per hour, and a slight negative pressure inside the cages. After addition of make-up air to fit the capacity (600 ft^3/hr) of the compressor, the exhaust air was mixed with natural gas, incinerated, and exhausted to the outside of the building. Calibrated differential manometers connected across the orifices in the inlet and outlet lines of the cages served to monitor the air flow. Electrical differential pressure switches were set to activate an emergency oxygen supply to the cages if the air flow should drop below 100 ft^3/cage per hr and simultaneously activate an alarm signal. Additional precautions were taken to stop delivery of [^{14}C]dichlorvos in case of power failure or malfunction of the system and to prevent natural gas from backing up into the cages in case the incinerator failed to work.

Animals used were two male and one female Yorkshire Landrace cross pigs weighing about 20 kg and caged individually at the start of the experiment. Feed was standard pig mash supplied by Dawes Laboratories (Chicago, Ill.). The animals were fed once a day in the morning and received feed and water ad libitum for the duration of the experiment.

ANALYTICAL METHODS AND RESULTS

The ^{14}C content of the air in the cages was monitored daily in the morning before feeding. Fifty liters of air was drawn from one of the sampling ports through 50 ml of ethyl acetate in a glass impinger (Ace Glass No. 7542). Aliquots of the ethyl acetate solution were counted in a Packard liquid scintillation counter (Potter et al., 1973b). Periodically, air samples were also analyzed by GLC for dichlorvos and dichloroacetaldehyde content using *n*-hexane instead of ethyl acetate as the solvent when sampling for dichloroacetaldehyde (Schultz et al., 1971).

After taking the daily air samples, dichlorvos delivery was interrupted for 1 hr to permit opening of the cages for removal of excreta and replenishing feed and water. The total ^{14}C content of feces samples was determined by a packed-tube combustion and liquid scintillation counting of the $^{14}CO_2$ (Potter et al., 1973b). Urine samples were counted directly. Data are summarized in Table I. Data on feces refer to samples as they were collected daily. Quantitative collection of feces was not always possible during the course of the experiment. Accumulated remnants were collected after termination. The ^{14}C content of these is not included in Table I since they had been exposed to the [^{14}C]dichlorvos vapor in the cages for unknown and variable periods of time. Spot checks of leftover drinking water were made by direct liquid scintillation counting. Carbon-14 content of these samples

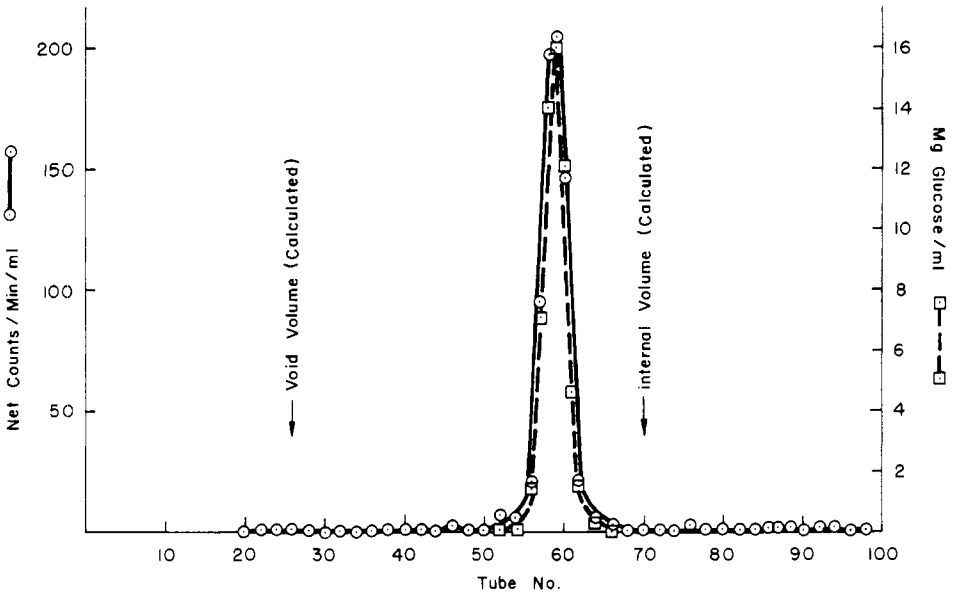

Figure 2. Sephadex G15 column of hydrolyzed glycogen (bed volume 570 ml).

Table I. Summary of Data on Experimental Conditions During 24 Days of Exposure of Pigs to [*1-vinyl*-^{14}C]Dichlorvos in Air

	Pig number and sex			
	233, female	236, male	238, male	Mean
Weight at day 0, kg	23.2	22.4	20.8	22.1
Weight at day 24, kg	30.0	31.2	28.6	29.9
Weight gain, kg	6.8	8.8	7.8	7.8
^{14}C in air, μg/l.[a]	0.101[b]	0.119[b]	0.152[b]	0.124
Dichlorvos in air, μg/l.	0.092[c]	0.114[c]	0.144[c]	0.117
Dichloroacetaldehyde in air, μg/l.	<0.004	<0.004	<0.004	
Urine, l.	56.2	28.8	15.1	33.4
^{14}C equivalents in urine, mg	21.3	21.5	18.1	20.3
Feces, kg	3.6	4.2	4.3	4.0
^{14}C equivalents in feces, mg	9.5	9.1	11.3	10.0

[a] Expressed as micrograms of dichlorvos equivalents per liter of air. [b] Average of 24 determinations. [c] Determination by GLC. Average of 11 determinations.

varied between 0.14 and 0.67 ppm equivalents of dichlorvos with an average of 0.39 ppm.

Twenty-four days after the start of the experiment, delivery of [^{14}C]dichlorvos was discontinued and the cages were purged with air for 12 hr. The animals were killed by electrocution. Samples of blood, liver, and lungs for determination of specific metabolites were immediately frozen in small portions in liquid nitrogen. Samples of these and other tissues for determination of total ^{14}C were stored at −20°C until analyzed by packed-tube combustion and liquid scintillation counting of the $^{14}CO_2$ (Potter et al., 1973b). Results are listed in Table II. The mean recovery of control samples of tissues fortified at a level of 1 ppm with [^{14}C]dichlorvos was 94.7% (standard deviation 3.0%).

Table II. Range of Total ^{14}C Content of Tissues Expressed as ppm Equivalents of Dichlorvos

Mean ppm equiv.	Tissue
0.2-0.4	Brain, subcutaneous fat
0.4-0.6	Blood, gastrocnemius muscle, quadriceps muscle, mesenteric fat, spiral colon, thyroid, heart
0.6-0.8	Bladder, duodenum, lungs, salivary gland, spleen, stomach, carcass, femur
0.8-1.0	Adrenals, kidneys, pancreas
1.0-1.2	Gallbladder
2.4-2.6	Liver

Cholinesterase activity was determined by the pH stat method (Boyer, 1967) on blood samples obtained immediately before the start of the experiment and again just before euthanization. Results were within the normal range of variability in pigs, and are listed in Table III.

Analysis for [^{14}C]dichlorvos and [*demethyl*-^{14}C]dichlorvos was performed on quick frozen blood and lung samples by chromatography on microgranular cellulose (Loeffler et al., 1971). At a sensitivity limit of 3 ng/g, neither one of these two compounds could be detected.

Glycogen was isolated from quick frozen liver by the method of Roe and Daily (1966). The specific activity was 12 dpm/mg at a purity of 88% based on a semimicro Glucostat assay. The material was hydrolyzed for 3 hr in 1 *N* HCl and, after neutralization, chromatographed on Sephadex G-15. Glucose distribution in the fractions coincided with the distribution of radioactivity (Figure 2).

Further confirmation of the nature of the isolated compound was obtained by preparing the osazone. It had a mp of 207°C dec; reported 207°C dec. Anal. Calcd: C, 60.32; H, 6.19; N, 15.63. Found: C, 60.7; H, 6.2; N, 15.7. The specific activity of the osazone was 6.93 dpm/mg, equivalent to a specific activity of 13.8 dpm/mg for glucose.

Glycine and serine were isolated from quick frozen liver after acid hydrolysis by repeated ion exchange chromatography (Hirs et al., 1954) and were purified as the 5-nitronaphthalene-1-sulfonate and the 4-hydroxyazobenzene-4'-sulfonate (Stein and Moore, 1949), respectively.

Table III. Cholinesterase Activity of Blood in Pigs before and after Their Exposure to Dichlorvos Vapor for 24 Days and of Control Pigs

Dichlorvos treated pigs	Acetylcholine hydrolyzed, mmol/min			
	Plasma		Red blood cells	
	Day 0	Day 24	Day 0	Day 24
Pig no. 233	1.30	1.47	0.67	0.71
Pig no. 236	2.12	2.10	0.88	*a*
Pig no. 238	1.40	1.44	0.94	0.77
Control pigs				
Pig no. 235	2.19	3.00	0.94	0.87
Pig no. 237	1.53	1.52	0.57	0.56

[a] Blood clotted.

Glycine was isolated by ion exchange of the sulfonate salt on Dowex 50-X8, H^+ form, and elution with 2 *N* ammonia. After recrystallization from aqueous ethanol, it gave a single ninhydrin-positive spot on TLC, reacted with *o*-phthalaldehyde (Curzon and Giltrow, 1954), and co-chromatographed with authentic glycine. The decomposition point was 233°C; reported mp 233°C dec. Anal. Calcd: C, 32.0; H, 6.71; N, 18.66. Found: C, 31.8; H, 6.8; N, 17.9. The specific activity was 266 dpm/mg.

Serine was isolated by ion exchange chromatography of a solution of its salt in 0.5 *N* acetic acid on Dowex 1-X8, acetate form, and elution with the same solvent. After recrystallization from aqueous ethanol, it gave a single ninhydrin-positive spot on TLC and cochromatographed with authentic serine. The decomposition point was 225°C; reported mp 228°C dec. Anal. Calcd: C, 34.28; H, 6.71; N, 13.32. Found: C, 34.1; H, 6.7; N, 13.2. The specific activity was 186 dpm/mg.

RNA and DNA were isolated from quick frozen liver by the method of Kirby (1968). The protein content of the isolated material, as determined by the method of Lowry et al. (1951) with bovine serum albumin as standard, was found to be 14% for RNA and 2.7% for DNA. Reaction with diphenylamine and with orcinol showed absence of cross-contamination. The specific activity of RNA was 19.6 dpm/mg while that of DNA was 10.5 dpm/mg.

Adenine and ribose were isolated from RNA by acid hydrolysis and chromatography on Sephadex G-15 by the procedure of DeBersaques (1967). After purification of the adenine containing fraction by TLC on cellulose powder, the ratios of absorbance were 0.41 and 0.78 for 280/260 nm and 250/260 nm, respectively. Absorbance ratios of authentic adenine at the same wavelengths were 0.37 and 0.76, respectively. The isolated compound cochromatographed on TLC with authentic adenine. Only one uv-absorbing spot was found. The specific activity of isolated adenine (based on uv absorption at 262.5 nm) was 90.2 dpm/mg. The ribose containing fraction from the Sephadex G-15 chromatogram was further purified by mixed-bed ion exchange chromatography on Dowex 50-X8, H^+ form, and Dowex 1-X8, OH^- form, and by paper chromatography of the ribose containing fraction on Whatman 3MM. After elution with water the radioactive ribose cochromatographed with authentic ribose on a cellulose thin layer in two different solvent systems. Treatment of the TLC's with aniline–phthalate reagent gave a single colored spot at the R_f value of authentic ribose. Based on colorimetry with orcinol (Schneider, 1957), the specific activity was found to be 19.2 dpm/mg.

Tissue lipids from quick frozen liver and lung samples were extracted and separated in different classes as reported (Page et al., 1972b). Liver with a total lipid content of 4.2% contained an amount of ^{14}C equivalent to 0.11 μg of dichlorvos per g of tissue. The specific activity of the total lipid was 11.2 dpm/mg. The corresponding data for lung tissue were 1.9% total lipid, ^{14}C equivalent to 0.03 μg/g, and a specific activity of 7.3 dpm/mg.

Table IV. Percent of Total Lipid ^{14}C in Different Lipid Classes

Lipid class	Liver	Lung
Phospholipids	93	39
Mono- and diglycerides, free sterols, free fatty acids	2	47
Triglycerides	4	11
Sterol esters	2	3

Table V. Percent of Total [^{14}C]Phospholipid in Different Phospholipid Classes

Phospholipid class	Liver	Lung
Unidentified[a]	9	0
Lysophosphatidylcholines	6	26
Phosphatidylcholines and -serines	58	60
Phosphatidylethanolamines	27	14

[a] Behaves similarly to partially degraded phosphatidylethanolamines.

The percentage distribution of ^{14}C in four lipid classes is shown in Table IV. Phospholipids were further separated by TLC. The percent of ^{14}C content in the fractions obtained is listed in Table V.

Cholesterol was isolated as described (Page et al., 1972b). The specific activity of cholesterol from liver was 2.8 dpm/mg; that from lung was 4.3 dpm/mg.

DISCUSSION

It was technically not possible in a long-term experiment to restrict the [^{14}C]dichlorvos uptake by the animals to inhalation as had been done in the short-term inhalation studies. The whole animal had to be exposed to a [^{14}C]dichlorvos atmosphere and, therefore, received the compound not only by inhalation but also by absorption through the skin and, to a small degree, orally. For example, the drinking water could absorb dichlorvos from the air during the 24 hr before it was replaced with fresh water. Secondly, it appeared technically impossible to separate, with any meaningful degree of precision, expired $^{14}CO_2$ from [^{14}C]dichlorvos at the large volumes and high rate of air flow which were necessary for the well-being of the animals. A material balance could, therefore, not be reported. A third compromise was necessitated because the long-term feeding studies had been carried out with pregnant sows and not with young pigs. Although the use of pregnant sows for this experiment was possible in principle, the practical difficulties and the cost of equipment and radioactive material made this quite impractical. Therefore, the data on ^{14}C content of different tissues and on the specific activities of key metabolites obtained in this experiment can be compared only approximately with those reported from feeding studies.

The data show large variations in the ^{14}C content of different tissues similar to those reported (Potter et al., 1973a) to occur after oral treatment. The isolation of key metabolites in pure form showed that glycine, as in the feeding experiments (Page et al., 1972a,b) had the highest specific activity, 9 μCi/mol (266 dpm/mg), followed closely by serine with 8.8 μCi/mol (186 dpm/mg). Further conversion of glycine to adenine at 5.5 μCi/mol (90.2 dpm/mg) and nucleic acids follows known pathways of intermediary metabolism. Although choline was not isolated from phospholipids in this experiment because of the small amount of labeled material available, the large percentage of the total ^{14}C-labeled lipid in the liver in the phospholipid fraction makes it likely that most of the radioactivity resides in the choline and/or serine moiety

of these compounds. If one arbitrarily assumes an average mol wt of 800 for the total liver lipids, one finds a specific activity of about 3.3 μCi/mol (9.2 dpm/mg) in line with the conclusions drawn above. The pathway from serine to carbohydrates as expected dilutes the specific activity considerably; glucose and ribose have 1.1 and 1.3 μCi/mol (13.8 and 19.2 dpm/mg, respectively), and an even lower specific activity of 0.6 μCi/mol (3.6 dpm/mg) is found in acetate-derived cholesterol.

The relative specific activities of the isolated compounds fall into an order which is compatible with the pathway postulated (Page et al., 1971, 1972a) leading from dichlorvos after cleavage of the P–O–vinyl bond and dechlorination via a hypothetical symmetrical two-carbon intermediate, to glycine and serine. At the glycine stage the carbon on the 1 position of the vinyl group has undergone a dilution of about 5×10^4 and proceeds from here with relatively little additional dilution through the metabolic pools of the other naturally occurring tissue constituents. There is no indication that a degradation pathway develops after prolonged exposure of animals to dichlorvos vapor which would differ measurably from that found to occur during short-term inhalation, gastric or intestinal infusion, and single and multidose oral ingestion of dichlorvos.

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LITERATURE CITED

Boyer, A. C., *J. Agric. Food Chem.* **15**, 282–286 (1967).
Burton, W. B., *J. Agric. Food Chem.* **19**, 869–871 (1971).
Curzon, G., Giltrow, J., *Nature* **173**, 314–315 (1954).
DeBersaques, J., *J. Chromatogr.* **31**, 222–223 (1967).
Hirs, C. H. W., Moore, S., Stein, W. H., *J. Am. Chem. Soc.* **76**, 6063–6065 (1954).
Hutson, D. H., Blair, D., Hoadley, E. C., Pickering, B. A., *Toxicol. Appl. Pharmacol.* **19**, 378–379 Abstr. (1971a).
Hutson, D. H., Hoadley, E. C., Pickering, B. A., *Xenobiotica* **1**, 593–611 (1971b).
Kirby, K. S., *Methods Enzymol.* **12B**, 87–92 (1968).
Loeffler, J. E., DeVries, D. M., Young, R., Page, A. C., *Toxicol. Appl. Pharmacol.* **19**, 378 Abstr. (1971).
Loeffler, J. E., Kirkland, V. L., DeVries, D. M., Collins, R. D., Young, R., Page, A. C., Biological Sciences Research Center, Shell Development Company, Modesto, Calif., unpublished work, 1972.
Lowry, O. H., Rosebrough, N. J., Farr, A. L., Randall, Rose J., *J. Biol. Chem.* **193**, 265–275 (1951).
Page, A. C., DeVries, D. M., Young, R., Loeffler, J. E., *Toxicol. Appl. Pharmacol.* **19**, 378 Abstr. (1971).
Page, A. C., Loeffler, J. E., Hendrickson, H. R., Huston, C. K., DeVries, D. M., *Arch. Toxicol.* **30**, 19–27 (1972a).
Page, A. C., Tocco, D. J., Huston, C. K., Hendrickson, H. R., Loeffler, J. E., Biological Sciences Research Center, Shell Development Company, Modesto, Calif., unpublished work, 1972b.
Potter, J. C., Boyer, A. C., Marxmiller, R. L., Young, R., Loeffler, J. E., *J. Agric. Food Chem.* **21**, 734–738 (1973a).
Potter, J. C., Loeffler, J. E., Collins, R. D., Young, R., Page, A. C., *J. Agric. Food Chem.* **21**, 163–166 (1973b).
Roe, J. H., Daily, R. E., *Anal. Biochem.* **15**, 245–250 (1966).
Schneider, W. C., *Methods Enzymol.* **3**, 680–682 (1957).
Schultz, D. R., Marxmiller, R. L., Koos, B. A., *J. Agric. Food Chem.* **19**, 1238 (1971).
Stein, W. H., Moore, S., *Biochem. Prep.* **1**, 9–22 (1949).

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Fate of Croneton (2-Ethylthiomethylphenyl *N*-Methylcarbamate) in Rats

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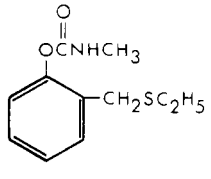
The fate of Croneton, 2-ethylthiomethylphenyl *N*-methylcarbamate, was determined in rats following both single oral or dietary exposure to the ^{14}C-carbonyl- and ^{14}C-ring-labeled insecticide. Greater than 95% of the [^{14}C]Croneton equivalents was excreted in the urine or as a combination of $^{14}CO_2$ (47%) and urinary products (41%) 72 h after a single oral dose. The feces contained 2–7% of the dose. A similar excretion pattern was observed during a 7-day feeding period. The principal urinary metabolites were Croneton sulfoxide (23–28% of the dose), phenol sulfoxide (20–23%), phenol sulfone (9–25%), and Croneton sulfone (3–11%) after a single oral dose and similar in the long term study. The carbamates were excreted primarily as free metabolites while the phenolic constituents were eliminated as acid labile conjugates. The 24-h acute oral LD_{50} values of Croneton, Croneton sulfoxide, and Croneton sulfone to mice were 71, 59, and 282 mg/kg, respectively.

Croneton, 2-ethylthiomethylphenyl *N*-methylcarbamate (Bay Hox 1901), is an experimental plant systemic insecticide with excellent aphicical properties. One of its principal projected uses is the control of these insects on vegetable, fruit, and cereal crops. Croneton is highly toxic to aphids, LD_{50} of 5 mg/kg, while the mammalian oral toxicity is rather low, with an LD_{50} of 411 mg/kg to rats (Bayer Information Bulletin E.1-715/29 359, 1974).



Croneton

The potential use of Croneton on food and feed crops

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