Metabolism of Xenobiotics in Ruminants

Dieldrin Recycling from the Blood to the Gastrointestinal Tract

Robert M. Cook

1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-*endo-exo*-5,8-dimethanonaphthalene-(HEOD), the major component of dieldrin, is recycled from the blood to the gastrointestinal tract of ruminants. The common bile and pancreatic ducts of goats and sheep, the bile ducts and pancreatic ducts of calves, and the parotid salivary ducts of all species were cannulated. Intravenously administered HEOD was readily secreted in saliva, bile, and pancreatic juice and readily detected in rumen fluid. HEOD probably entered the gut in saliva from the submaxillary, sublingual, and buccal glands and in the gastric and intestinal secretions. These data suggest that there is a significant entry of HEOD from the blood to the gut.

Contamination of animal food products with chlorinated hydrocarbon pesticides presents a serious problem in animal agriculture. Once livestock become contaminated with chlorinated pesticides, the elimination of these pesticides by the animal is a very slow process. In cases of severe contamination, it may take more than 1 yr before the pesticide is eliminated. Because of the slow excretion rate of chlorinated pesticides, this laboratory began fundamental studies of the behavior of dieldrin in ruminants to obtain information that might be applied to the problem of increasing the rate of dieldrin excretion by cattle. During the course of these studies it was discovered that dieldrin is recycled from the blood to the gastrointestinal tract in ruminants. This communication presents the results of those experiments.

EXPERIMENTAL PROCEDURE

The insecticide dieldrin consists of not less than 85% 1,2,-3,4,10,-10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-*endo-exo*-5,8-dimethanonaphthalene (HEOD). All HEOD employed in this study was greater than 99% pure and was a gift from Shell Chemical Co. (New York). All chemicals used were reagent grade or Nanograde (Mallinckrodt). Analyses for HEOD were performed using a Varian Aerograph Model 1520 gas chromatograph, equipped with a tritium foil electron capture detector. Analytical columns were 5 ft x 1/8 in. stainless steel packed with 60/80 mesh HMDS-treated Chromosorb W containing either 5% QF-1 or 5% silicone DC-11. Routine analysis utilized a column temperature of 180° to 190° C. The carrier gas was high purity nitrogen and the flow rate was 30 to 40 ml per min.

Blood, rumen fluid, saliva, bile, and pancreatic juice were prepared for analysis according to the method used by Crosby and Archer (1966) for blood, except that hexane was used instead of pentane.

Indwelling polyethylene or silastic cannulae were placed in veins and ducts, from which samples were injected or withdrawn. Except for calves, all animals were fitted with rumen fistulae. Experiments were conducted 1 to 2 months after installing rumen fistulae and 1 to 2 days after cannulating blood vessels and the various ducts. HEOD was dissolved in corn oil or ethanol for i.v. administration, and was dissolved in ethanol or acetone for intraruminal administration. Intravenous injections of 20 to 50 mg of HEOD were optimum for most experiments. HEOD at this level could be readily measured in the samples, yet did not produce toxicity symptoms.

RESULTS AND DISCUSSION

In an initial experiment to study the rate of HEOD absorption from the rumen, it was observed that even though HEOD rapidly appeared in jugular vein blood when added to the rumen, the concentration of HEOD in rumen fluid remained fairly constant for 2 days (Figure 1). This suggested that HEOD reentered the rumen. Subsequent experiments were conducted to determine if HEOD, when injected into jugular vein blood, appeared in rumen fluid. Results of one of these studies are presented in Figure 2. HEOD was found in rumen fluid 2 hr after being injected into the jugular vein.

Experiments were next conducted to determine how HEOD moved from the blood to the rumen. The most logical explanation was that HEOD is excreted by the salivary glands. In one experiment 750 mg of HEOD were injected into the jugular vein of a sheep. The animal went into convulsions within a few minutes, began excess salivation, and died within 40 min. HEOD levels in saliva and rumen fluid were extremely high 30 min after treatment. The concentrations for blood, saliva, and rumen fluid were 5800, 2600, and 2600 ppb, respectively.

There also appeared to be a rumen clearance of HEOD. The right ruminal vein of a 35 kg sheep was cannulated and 100 mg of HEOD was injected into the jugular vein. There was a fifteen-fold difference in HEOD concentrations in rumen vein and jugular vein blood 30 min after administering HEOD.

Dairy Department, Michigan State University, East Lansing, Mich. 48823

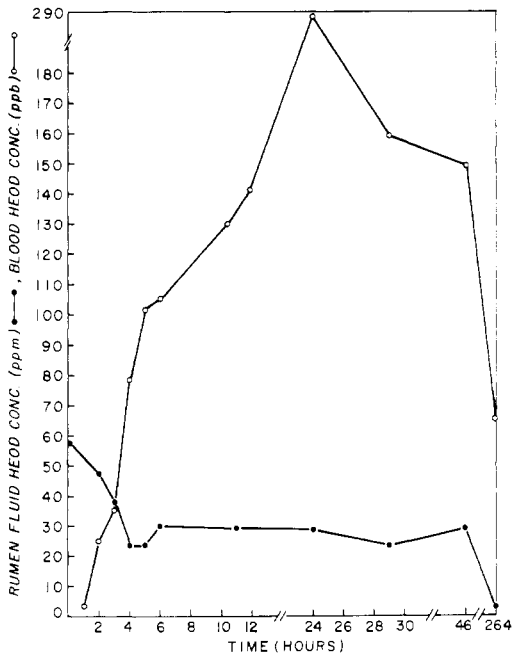

Figure 1. Concentration of HEOD in jugular blood (○—○—○) and rumen fluid (●—●—●) after addition of 500 mg of HEOD to the rumen of a 56-kg wether goat

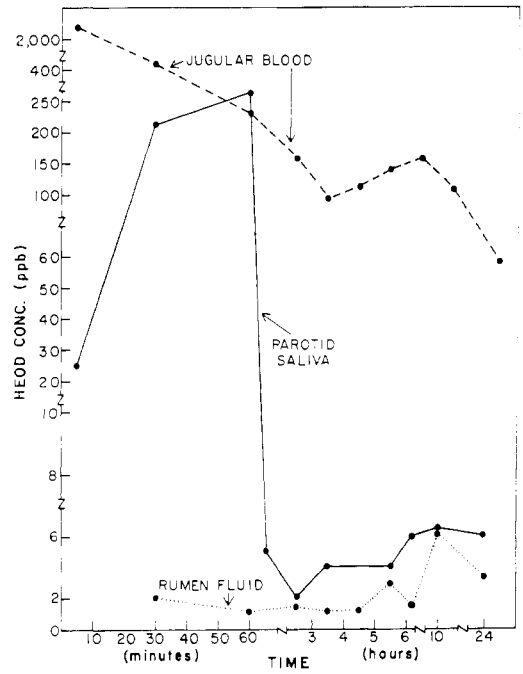

Figure 3. Concentration of HEOD in blood, parotid saliva, and rumen fluid after injecting 50 mg of HEOD into the jugular vein of a 34-kg sheep

The levels of HEOD in jugular blood remained four- to ten-fold greater than in rumen vein blood for 19 hr.

HEOD was secreted in the saliva rapidly after being injected into the jugular vein, reached a peak at 1 hr, and small amounts were secreted from 24 hr (Figure 3).

HEOD is excreted in the bile plus pancreatic juice from goats and sheep. The data from an experiment with a goat is shown in Figure 4. HEOD could be detected in bile plus pancreatic juice 30 min after injecting the pesticide into the jugular vein. The concentration of HEOD in bile approached that in the blood after 10 hr. In this experiment, HEOD was readily secreted by the parotid salivary glands and was also present in rumen fluid.

Sheep and goats have a common bile and pancreatic duct. However, the bile duct and pancreatic duct are separate in the calf. Experiments were, therefore, conducted with calves to determine whether HEOD is excreted by the pancreas and in the bile. When 50 mg of HEOD were injected into the jugular vein of 100 kg calves, the average HEOD concentration over a

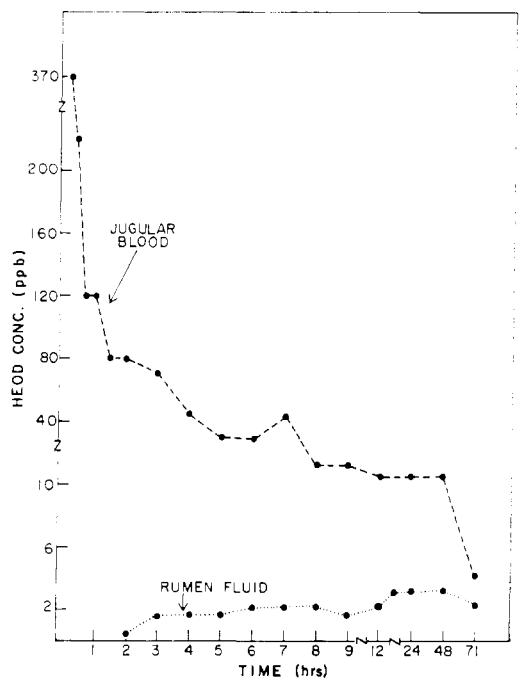

Figure 2. Levels of HEOD in blood and rumen fluid after injecting 50 mg of HEOD into the jugular vein of a sheep

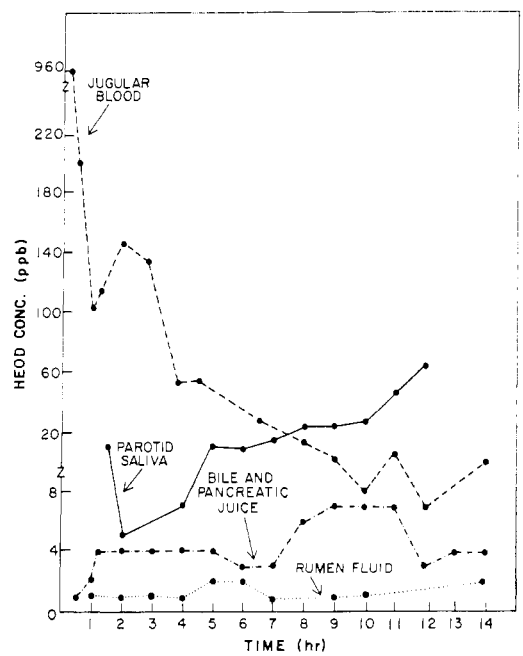

Figure 4. Concentration of HEOD in blood, parotid saliva, rumen fluid, and bile and pancreatic juice after injecting 20 mg of HEOD into the jugular vein of a goat

24-hr period was 10.6 and 2.6 ppb for bile and pancreatic juice, respectively. Also, the flow rates over the 24-hr collection period average 0.57 and 0.32 ml per min for bile and pancreatic juice, respectively.

This work demonstrates that HEOD enters the gastrointestinal tract *via* the saliva, bile, and pancreatic juice and probably *via* a rumen clearance. It is also very probable that HEOD is secreted in the gastric juice and the intestinal juice, particularly by the mucous secreting cells. Total saliva was not collected over a long time period. However, HEOD in the total saliva that was collected was ten-fold higher than in parotid saliva. The data suggest that the sublingual and submaxillary salivary glands are more active than the parotid glands in HEOD secretion. Several investigators have shown that chlorinated hydrocarbon pesticides are excreted in bile in rats (Heath and Vandekar, 1964; Jensen *et al.*, 1956; Morsdorf *et al.*, 1963; Weikel, 1956). Although the amount of biliary excretion was not rigorously studied, Heath and Vandekar (1964) suggested that the excretion of dieldrin in the bile may be high.

The total entry of HEOD from the blood to the gastrointestinal tract of ruminants may be of major significance, particularly in cases of acute poisoning. Under such stress conditions, salivation is markedly increased and secretion of bile and other fluids into the stomach and intestine may be increased. When a small amount of HEOD is injected into the blood stream, this pesticide is also readily detected in saliva, bile, pancreatic juice, and rumen fluid. Consequently, the reentry of HEOD into the gastrointestinal tract suggests that an ingested adsorbent for HEOD could be an effective antidote when administered several hours after poisoning occurs.

ACKNOWLEDGMENT

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