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Mobility of Avermectin B_{1a} in Soil

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Avermectin B_{1a} (AVM) was determined to be immobile in soil by three methods: sorption/desorption using a batch equilibrium technique, soil thin-layer chromatography, and soil column leaching using aged and unaged soil. From the sorption data from batch equilibrations of AVM with three soils, the K_{oc} (distribution constant normalized to the percent organic matter) for AVM was determined to be 4.76×10^3. When ascending chromatography was performed on TLC plates prepared with six different soils, average R_f values for AVM and 2,4-dichlorophenoxyacetic acid, a pesticide of known mobility, were determined to be 0.00 and 0.78, respectively. Also, AVM did not readily leach from four soils in soil column leaching studies.

Avermectin B_{1a} (AVM, Figure 1) is a macrocyclic lactone produced by the actinomycete *Streptomyces avermetilis* (Burg et al., 1979). It is effective in controlling different phytophagous pests of field crops, ornamentals, vegetables, and fruits (Putter et al., 1981) and in controlling fire ants (Lofgren and Williams, 1982), which are a serious problem in some areas of the southern United States. Abamectin (the commercial product containing AVM) is being developed for these purposes.

The contamination of surface water and groundwater by the agricultural use of pesticides and other chemicals is a major national concern. How tightly a compound binds to the soil of the area of use largely determines whether the pesticide is likely to leach into groundwater or be carried in runoff water into lakes and streams. Soil TLC studies performed with three soils show AVM to be immobile (Bull et al., 1984; Bull, 1985). To more firmly establish AVM's mobility characteristics in soil, additional studies were performed with AVM using three commonly used methods: (I) sorption/desorption of the chemical with soil using a batch equilibrium technique for determination of Freundlich and distribution constants, (II) soil thin-layer chromatography (TLC), and (III) soil column leaching of the chemical.

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MATERIALS AND METHODS

Chemicals. Three different preparations of AVM were used for these studies: [5-^{3}H]avermectin B_{1a} ([^{3}H]AVM) with a specific activity of 1.63 mCi/mg, 98+% radiopure; [3,7,11,13,23-^{14}C]avermectin B_{1a} ([^{14}C]AVM) with a specific activity of 16.4 μCi/mg, 99+% radiopure; and [^{3}H]AVM with a specific activity of 118 μCi/mg, 99+% radiopure. The syntheses of both [^{3}H]AVM and [^{14}C]AVM have been published [Chabala et al. (1981) and Ku and Hwang (1985), respectively]. The four ^{14}C-labeled pesticides, 2,4-dichlorophenoxyacetic acid-*carboxy*-^{14}*C* (2,4-D), Temik-*methylthio*-^{14}*C*, [U-^{14}C]mirex, and [ring-U-^{14}C]parathion, used as standards in the TLC study had specific activities of 4.48, 4.91, 7.25, and 7.42 mCi/mmol, respectively, and were obtained from Pathfinder Laboratories Inc., St. Louis, MO.

Soils. The six soils used in these studies (Table I) (silt loam from Three Bridges, NJ; loam from Riverside, CA; sand from Lakeland, FL; sand from Sanford, FL; Houston clay loam from Waco, TX; Lufkin sandy loam from College Station, TX) were nonsterile and were air-dried and sieved to pass a 35-mesh screen prior to use in all three studies. The soils were not classified by their soil taxonomies.

Equipment. Radioactivity contained in a liquid was quantified by direct liquid scintillation counting (LSC) on either a Model 460 or Model 4530 liquid scintillation counter from Packard Instrument Co., Inc., Downers Grove, IL. Radioactivity contained in a solid was quantified by LSC after conversion of the radioactivity to tritiated water with a Packard Tricarb Oxidizer, Model B306.

Autoradiography was performed with "blue-sensitive" medi-

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Table I. Properties of Test Soils[a]

geographic location	Three Bridges, NJ	Riverside, CA	Lakeland, FL	Sanford, FL	Waco, TX	College Station, TX
pH	7.5	6.7	7.5	5.6	6.6	7.5
organic matter, %	2.1	2.5	0.1	0.9	4.8	1.1
CEC, mequiv/100 g	12.5	12.3	1.5	2.1	39.2	8.7
bulk density, g/cm^3	1.12	1.23	1.73	1.57	1.30	1.42
H_2O retention, % at $^1/_3$ atm	30.3	17.8	1.20	2.30	34.7	15.0
mechanical anal., %						
sand	11.6	49.6	91.9	95.6	31.6	57.6
silt	61.6	35.6	5.6	1.6	37.6	27.6
clay	26.8	14.8	2.8	2.8	30.8	14.8
soil texture	silt loam	loam	sand	sand	clay loam	sandy loam

[a] Soil analyses were carried out by United States Testing Co., Inc., Memphis, TN.

cal X-ray film, Kodak SB-5, from Eastman Kodak Co., Rochester, NY.

HPLC was performed with a Model I Constametric pump from Laboratory Data Control, Division of Milton Roy Co., Riviera Beach, FL, and one of the following systems: system 1, Whatman Partisil 10/25 ODS-3 column (25 cm × 4.6 mm (i.d.), 10-μm particle size) with a mobile phase of acetonitrile, methanol, and water (56:18:26 (v/v/v)) at a flow rate of 1 mL min^{-1}; system 2, Zorbax ODS column (25 cm × 4.6 mm (i.d.), 5–6-μm particle size) with a mobile phase of methanol and water (85:15 (v/v)). Detection was by LSC of 1-mL fractions of the HPLC effluent collected by either a Model Frac-100 fraction collector from Pharmacia Fine Chemicals AB, Sweden, or a Model 328 fraction collector from ISCO, Inc., Lincoln, NE.

Batch Equilibrium. Four stock solutions of [^{3}H]AVM (1.63 mCi/mg, 98% radiopure) were prepared to contain 0.560, 2.92, 23.3, and 217 μg of [^{3}H]AVM/mL of methanol. The three soils used for this method were Houston clay loam from Waco, TX; sand from Lakeland, FL; and silt loam from Three Bridges, NJ. Duplicate 2-g aliquots of each soil were weighed into glass 50-mL round-bottom centrifuge tubes (glass adsorption of AVM was investigated in a preliminary experiment and was found to be insignificant under the conditions of this experiment). After 10 mL of 0.01 M $CaSO_4$ solution was added to and mixed with the soil, 20 μL of stock solution of the test compound was added to the sample. The samples were immediately capped and shaken by hand until well mixed. They were placed on a Burrell wrist action shaker and shaken at room temperature for 16 h to equilibrate. In a preliminary experiment, equilibrium was found to occur within 6 h under these same conditions. After the samples were centrifuged for 5–10 min at approximately 2000 rpm, the supernatant was removed and the concentration of [^{3}H]AVM in the supernatant was determined by LSC.

For the desorption step, fresh 0.01 M $CaSO_4$ solution, equal in volume to the supernatant removed in the sorption step, was added to the sample. As before, the samples were shaken for 16 h on the wrist action shaker and centrifuged, and the concentration of [^{3}H]AVM in the supernatant was determined by LSC. After the supernatant in each sample was replaced by 20 mL of methanol, the samples were again shaken for 16 h and centrifuged, and the extracted [^{3}H]AVM was quantified by LSC. For each soil, an HPLC radioprofile of the methanol extract of the soil was obtained for comparison with the stock solution using HPLC system 2.

The binding constants for AVM to soil were determined by using the Freundlich equation. The Freundlich equation, $x/m = Kc^{1/n}$, where x/m equals the of [^{3}H]AVM sorbed to the soil (μg/g), c equals the [^{3}H]AVM in solution (μg/mL), and K and n are constants, can be expressed as log [sorbed (μg/g)] = log $[K]$ + $(1/n)$ log [solution (μg/mL)]. The log [sorbed (μg/g)] vs log [solution (μg/mL)] was graphed and fitted with the best fit line. The Freundlich constants, K and n, were calculated from the intercept (at 1 μg/mL) and from the slope.

The distribution constant (K_d) at given concentrations was determined by using the formula K_d = [sorbed (μg/g)/solution (μg/mL)]. K_{oc} was determined by normalizing the distribution to the percent of organic carbon present in the soil. The percent organic carbon was calculated by dividing the percent organic matter by 1.724 (Hamaker and Thompson, 1972).

Soil TLC. The soil TLC technique used was similar to that of Ambrosi and Helling (1977). Two soils, Houston clay loam from Waco, TX, and Lufkin sandy loam from College Station, TX, which Bull et al. (1984) used for their soil TLC experiments, were included in the study as well as four additional soils. Soil TLC plates were hand-prepared by spreading a slurry of soil, $CaSO_4$, and water onto a 20 × 20 cm glass plate. For each plate, the slurry contained 60 g of soil, 3 g of $CaSO_4$, and 15–35 mL of water, depending on the soil type. The plates were air-dried at room temperature before use. Six TLC plates were prepared by using the six different soils listed in Table I.

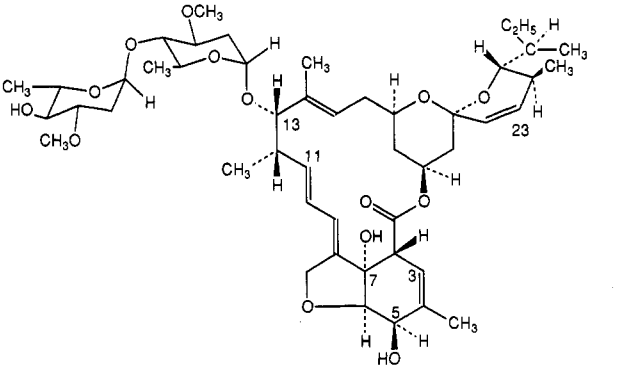

Figure 1. Structure of avermectin B_{1a} (AVM).

Carbon-14-labeled 2,4-D, Temik, mirex, and parathion were applied side by side with [^{14}C]AVM to the soil TLC plates and developed approximately 15 cm with water by ascending chromatography. The plates were visualized by autoradiography.

Soil Column Leaching. Samples of soil from Lakeland, FL (sand), College Station, TX (Lufkin sandy loam), Waco, TX (Houston clay loam), and Three Bridges, NJ (silt loam), were used to make the soil columns for the column-leaching experiments. Soil of each type was hand-packed "dry" into six glass columns measuring 51.5 × 4.2 cm. The glass columns contained a cotton plug to hold the soil and were packed to a height of approximately 38 cm with soil. Ten micrograms of [^{3}H]AVM (118 μCi/mg, 99+% radiopure) contained in 1 mL of methanol was applied onto four soil columns of each soil type. The other two soil columns were treated with 1 mL of methanol to serve as controls. Two centimeters of untreated soil was placed on top of each of the six soil columns to bring the height of the soil to 40 cm. The columns were wrapped with aluminum foil to prevent exposure to light. For each soil type, two of the treated soil columns and one untreated control were set aside to age for 29 days at ambient temperature. None of the soil columns were prewetted. During a period of 28 days, a total of 760 and 800 mL of water was applied to the top of the unaged and aged soil columns, respectively. The water was applied at a rate of 50–100 mL over a 2–3-day period.

At the end of the leaching period, the leachate, which had been collected from each column, was assayed for radioactivity by LSC. The soil column was extruded and sectioned into six segments. The segments were air-dried at ambient temperature, pulverized, and assayed for radioactivity by combustion analysis.

The leachate from each column was assayed for [^{3}H]AVM by HPLC radioprofile with HPLC system 1.

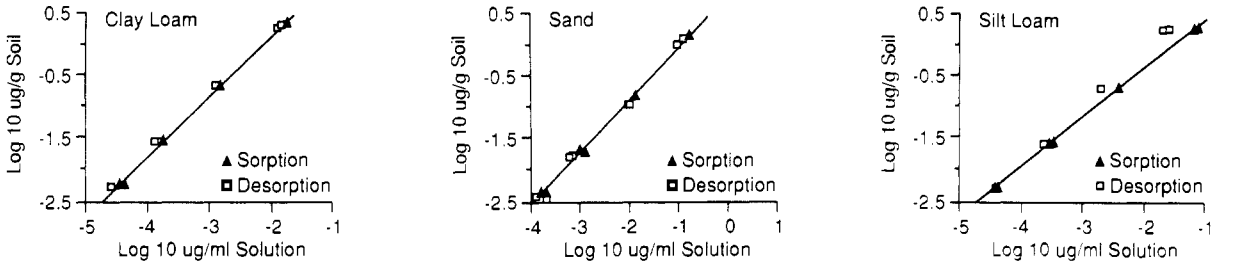

Figure 2. Batch equilibrium plots of sorption (▲, line) and desorption (□) of AVM with clay loam, sand (Lakeland), and silt loam.

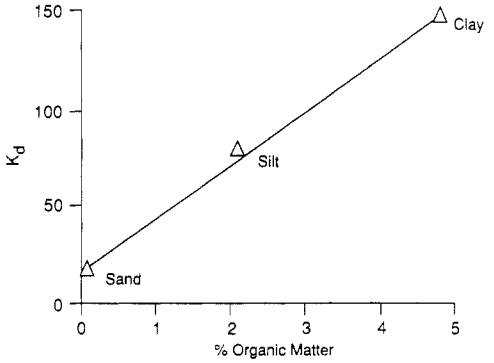

Figure 3. K_d vs percent organic matter.

Table II. Sorption Distribution and Freundlich Constants

	n	K	K_d (range)	K_{oc}
clay loam	1.0	134	147 (131–161)	5.3×10^3
sand (Lakeland)	1.2	6.99	17.4 (9.74–29.1)	3×10^4
silt loam	1.3	18.2	80.2 (30.2–144)	6.6×10^3

RESULTS AND DISCUSSION

Batch Equilibrium. Sorption isotherms were graphed for the three soils (Figure 2) by plotting duplicate assays as separate points (rather than averaged) to determine the best fit line. Two points were observed to be outliers and were not used; however, each isotherm had at least one point for all four concentrations. Freundlich constants, K and n (Table II), were calculated from the isotherms by using best fit line parameters determined by linear regression. Values for the distribution constant (K_d) were calculated at each concentration and then averaged (Table II). Only for clay loam does $n = 1.0$ so that K approximates K_d. For sand and silt loam, proportionally more AVM was sorbed at lower concentrations.

When the desorption data for each soil were plotted on the same graph as the sorption data (Figure 2), a hysteresis of some of the desorption data from the sorption data was observed for silt loam but not for the other two soils. When this happens, a pesticide's mobility is likely to be overestimated when only sorption data are used in the prediction (Bowman and Sans, 1985).

The organic matter content of soil is often an important factor in the sorption of nonionic chemicals (Hamaker and Thompson, 1972). Clay loam, sand (Lakeland), and silt loam were chosen for this study because the organic matter content of these three soils covered a wide range. When the percent organic matter of the three soils vs K_d (average) is graphed, the direct linear relationship between the organic matter of the soil and the sorption of AVM is exemplified (Figure 3). With K_d constants averaged over the concentration range investigated, K_{oc} values are 5.3×10^3, 3×10^4, and 6.6×10^3 for sorption with clay loam, sand, and silt loam, respectively. K_{oc} values for clay loam and silt loam, where the percent organic matter is 4.8 and 2.1%, respectively, are somewhat similar. However, for the sand soil, where the percent organic matter is 0.1%, the K_{oc} is 3×10^4. High K_{oc} values have been observed for other compounds when the organic matter of the soil is only a few tenths of a percent. It is speculated that, in some cases, the mineral phases of the soil make a significant contribution to the total adsorption (Hamaker and Thompson, 1972). To give more weight to the numbers where organic matter was the major influence for the sorption of AVM, K_{oc} was calculated from the data of the graph (Figure 3). When $x = 100\%$ organic matter, $y = K_{om}$ (distribution constant normalized to the percent organic matter). Calculated by this method, $K_{oc} = 4.76 \times 10^3$.

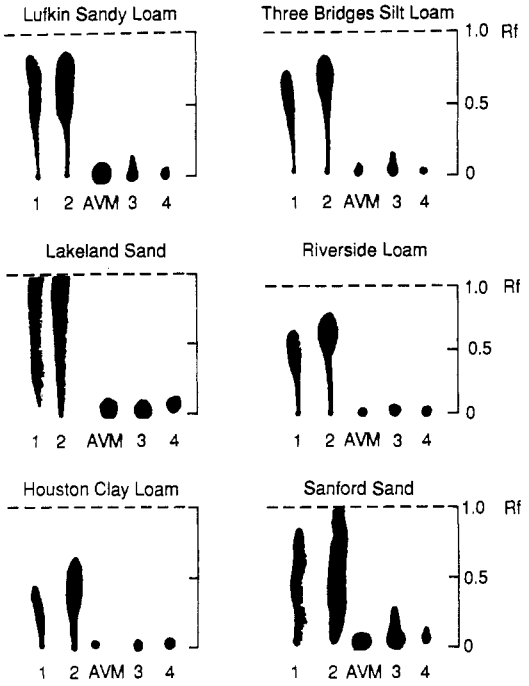

Figure 4. Autoradiographs of soil TLC: 1 = 2,4-D, 2 = Temik, 3 = parathion, 4 = mirex.

Average recovery of radioactivity from the batch equilibration system was 102%, ranging from 89.6 to 111%. Thus, desorption of the [^{3}H]AVM from the soil with the methanol was complete. Also, the [^{3}H]AVM was stable during the procedure as seen by comparison of the HPLC radioprofiles of the stock solution and the methanol extracts of the soil.

Kenaga (1980) reported that pesticides having a $K_{oc} > 1000$ are sorbed tightly to soil and are generally considered immobile. Therefore, AVM was determined to be an immobile pesticide by this method.

Soil TLC. Autoradiographs of the six soil TLC plates using soils from six different geographic locations (Table I) are presented in Figure 4. Average R_f values for AVM, mirex, parathion, Temik, and 2,4-D for the six soil TLCs

Table III. Distribution (%) of Radioactivity in Aged and Unaged Soil Columns

	sand (Lakeland)		sandy loam		clay loam		silt loam	
col portion assayed	unaged	aged	unaged	aged	unaged	aged[a]	unaged	aged
top to 6 cm	86.0	92.4	91.0	95.8	92.0	98.6	83.3	79.4
6–12 cm	6.2	3.5	6.5	1.3	0.8	0.0	9.2	4.7
12–18 cm	0.0	0.0	0.0	0.0	0.0	0.0	3.7	5.2
18–24 cm	0.0	0.0	0.0	0.0	0.0	0.0	0.7	2.8
24–30 cm	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7
30 cm to end	0.0	0.0	0.0	0.0	0.0	0.0	0.0[b]	0.8
leachate	7.8	4.1	2.5	2.9	7.2	1.4	3.1	6.4

[a] Data were generated from only one soil column. [b] One of the duplicate soil columns was only 30 cm long.

are 0.00, 0.00, 0.05, 0.88, and 0.78, respectively. Helling and Turner (1968) ranked the relative mobility of a number of pesticides by their R_f values from soil TLC. Pesticides of class 1 are immobile while those of class 5 are very mobile. R_f values for class 1 range from 0 to 0.09, whereas class 5 values range from 0.90 to 1.00. Helling and Turner reported that 2,4-D falls within class 4 (R_f range 0.65–0.89) for Hagerstown soil. The average R_f for 2,4-D in the six soils used in our study also placed 2,4-D in class 4. The other compounds were not evaluated by Helling; however, in our study, Temik was in class 4, and AVM, mirex, and parathion all fell within class 1. Even in the sand soils where the organic matter content is low, AVM remained immobile.

Soil Column Leaching. The average volume of leachate collected was 565 mL, ranging from 522 to 616 mL, with no significant differences between the different soils. The distribution of tritium in the soil columns and leachates is presented in Table III. The radioactivity in the leachates was determined by HPLC radioprofile to be composed mostly of unidentified polar degradates of the parent compound. It was not determined whether degradation of the [^{3}H]AVM occurred on the soil column, thus increasing mobility of the radioactivity, or whether the parent leached (or traveled through channels) into the water and degraded during storage or workup for analysis. However, the results from the aged and unaged soil columns were not significantly different, which suggests the latter to be the case.

Analysis of the soil column showed that most of the radioactivity remained in the top 6 cm of the soil column. This clearly indicates that AVM did not readily leach from the soil. Only the Three Bridges silt loam had radioactivity below 12 cm. However, it was observed that the Three Bridges soil did not pack properly. There was excessive shrinkage in one of the Three Bridges soil columns, which correlated with increased "leaching" of the radioactivity in that column. In another Three Bridges soil column, "uneven leaching" (radioactivity not occurring in decreasing levels as it descended the soil column (Table III, aged Three Bridges soil)) occurred. This could be explained if channeling existed in the upper third of the soil column. These observations lead us to conclude that the radioactivity below 12 cm in the Three Bridges soil was due to a channeling effect in the column packing rather than leaching, especially since a true leaching of AVM should have been more pronounced in the sandy soils.

The 760 or 800 mL of water applied to the columns over a period of 28 days was equivalent to approximately 22 and 23 in. of rain, respectively. These conditions were chosen to create a worst case situation where large volumes of water flow through the soil column and the soil remains water saturated. In a natural environment, when the soil begins to dry out, capillary action of the groundwater carries chemicals back toward the surface, thus decreasing leaching. Therefore, the column-leaching experiment represents a worst case situation (Hamaker, 1975).

CONCLUSIONS

All three methods showed AVM to be immobile in soil. An average K_{oc} value of 4.76×10^3 and the lack of movement on the soil TLC plates and soil columns indicate that AVM sorbed tightly to all six soils, including sands of low organic contents. The six soils selected for these mobility studies are from locations where abamectin may be used and typify the wide range of soil types found in the United States. Pesticides that are immobile in soil are considered unlikely to leach into groundwater or travel in runoff water into streams and lakes (Kenaga, 1980). Therefore, the field application of abamectin or its use in fire ant control should not pose a threat to surface or underground water resources.

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Environmental Fate of Ceftiofur Sodium, a Cephalosporin Antibiotic. Role of Animal Excreta in Its Decomposition

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The degradation of ceftiofur sodium, a wide-spectrum cephalosporin antibiotic, was studied in the urine and feces of cattle, in three soils, and in buffers of pH 5, 7, and 9. Photodegradation was also studied. Fortification of cattle feces with [^{14}C]ceftiofur showed that it was quickly degraded to microbiologically inactive metabolites. Sterilization of the cattle feces inhibited the degradation of ceftiofur, which suggests that microorganisms or heat-labile substances may be responsible for the degradation. The $t_{1/2}$ values of aerobic degradation of ceftiofur sodium in California, Florida, and Wisconsin soil were found to be 22.2, 49.0, and 41.4 days, respectively. Hydrolysis of ceftiofur, as measured by either HPLC or microbiological methods, was accelerated by increasing pH. The $t_{1/2}$ values at pH 5, 7, and 9 were 100.3, 8.0, and 4.2 days, respectively, at 22 °C and dramatically increased at 47 °C. The photodegradation of ceftiofur, as determined by HPLC and a microbiological method, showed that after initial degradation for several days the rate of degradation was minimal, probably due to a protective film formed from degradation products. A major role for feces in the degradation of ceftiofur was observed, although other pathways of degradation such as soil, light, and water were also important.

During the last 60 years, chemicals have dramatically improved the quality of life for humans. However, the world has witnessed a few cases of chemical hazard to the population that have changed our thinking about controlling pollution. Environmental contamination has become a topic of political debate. This is a justified concern, and environmental fate studies are a justifiable requirement for the registration of new chemicals. Animal health drugs intended for therapeutic use do not pose a threat similar to pesticides and other production chemicals due to their limited use in a rather controlled area. However, the question of environmental safety of an animal health drug has to be addressed because certain animal health drugs could have adverse effects on the environment as was recently demonstrated (Wall and Strong, 1987; Houston, 1987).

A recent symposium held at The Upjohn Co. (1988), Brook Lodge, Augusta, MI, highlighted the studies required to evaluate the safety of animal health drugs. Studies such as photolysis, hydrolysis, partition coefficients, and aerobic soil degradation similar to those used for pesticides are required.

This study was done to evaluate the environmental fate and impact of ceftiofur sodium (Figure 1; ^{14}C-labeled in the 2-position of the thiazole ring), a broad-spectrum antibiotic recently approved for the treatment of cattle for shipping fever (*Fed. Regist.* 1988). Ceftiofur sodium has been found to be quite effective against various pathogens of veterinary importance both in vitro and in vivo (Yancey et al. 1987).

We recently described the metabolism of [^{14}C]-ceftiofur sodium labeled in the 2-position of the thiazole ring in cattle and rats (Jaglan et al., 1989), which indicate that ceftiofur is metabolized and excreted. The drug is unusual in that after killing the bacteria in the cattle, it is readily degraded to microbiologically inactive products by substances or organisms in the feces, thus alleviating any environmental contamination concerns.

EXPERIMENTAL SECTION

Microbiological Assay. The standard cylinder plate method (AOAC, 1984) utilizing antibiotic medium 8 supplemented with 5.0 g/L agar, 0.45 g/L monobasic potassium phosphate, and 0.1% Tween 80 was used. *Micrococcus luteus* UC-130 (ATCC 9341) maintained as a frozen suspension over liquid nitrogen was the test organism. An inoculation of 0.08% (about 8×10^8

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