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Environmental Monitoring and Support Laboratory
U.S. ENVIRONMENTAL PROTECTION AGENCY
Las Vegas, Nevada 89114

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This work was performed under
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BIOLOGICAL TRANSPORT OF CURIUM-243 IN DAIRY ANIMALS

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ABSTRACT

Lactating cows and goats were used to examine the biological transport of curium-243 in dairy animals. After either single oral or intravenous nuclide doses were administered, samples of milk, urine, blood, and feces were taken over a 144-hour collection period, and the curium concentrations were determined by gamma counting. Gastrointestinal uptake of curium was estimated to be 0.02 and 0.006 percent of the oral dose for cows and goats, respectively. The cumulative percentage of oral dose transported to milk and urine was 4.6×10^{-4} and 1.9×10^{-3}, respectively, for a cow and 2.7×10^{-4} and 1.6×10^{-4}, respectively, for goats. Plasma concentrations of curium decreased rapidly following all intravenous injections.

The average percentage of injected curium transferred to milk, urine, and feces was 2, 8, and 1 percent, respectively, for a cow and 2, 5, and 5 percent, respectively, for goats. All animals were sacrificed one week after dosing. Bovine bone retained the greatest fraction of the administered dose and the next highest was the liver. However, in all three intravenously dosed goats the liver contained the greatest amount of curium. Nuclide deposition in bone and liver was essentially equal for two of the three orally dosed goats while the skeleton contained the most curium in the other animal. Comparisons are presented between curium-243 and americium-241 transport in dairy cows.

INTRODUCTION

In assessing the potential transport of curium in a terrestrial ecosystem, it is particularly important to establish the metabolic retention of curium in those domestic animals maintained as a source of food for the human population. Milk and milk products form a direct link in man's food supply and a significant percentage of beef comes from cows and bulls discarded from dairy herds.

Low gastrointestinal absorption values, e.g., <0.05 percent of dose (Hamilton, 1947) and 0.04 percent of dose (Sullivan and Crosby, 1975) have been reported following the administration of curium to laboratory rats. Several studies have also been reported on curium transport following intravenous doses. In the case of beagle dogs, Lloyd et al., (1974) have shown that intravenously injected curium was excreted primarily in the urine. These investigators injected five beagles with approximately 2.6 microcuries (μCi) curium citrate per kilogram (kg) and noted that the average urinary curium excretion 1 day after injection was about 5 times as great as the average nuclide loss in the feces. Tissue concentrations 1 week after injection revealed that approximately 39 and 37 percent of the curium dose had been retained in the canine liver and bone, respectively. Following intravenous nuclide doses to lactating Suffolk sheep, McClellan et al., (1962) noted that while plutonium-239 and americium-241 both reached peak concentrations in the milk 7 hours after injection, the peak milk concentrations for curium-244 occurred slightly earlier at the 4- to 7-hour period. Both americium and curium were cleared more rapidly from the plasma, and their subsequent transfer to milk was greater than was observed for plutonium.

Results on curium metabolism in dairy animals have been reported at the Nevada Applied Ecology Group meetings (Sutton et al., 1977; Patzer et al., 1977). Information from these two reports, as well as some additional data

from the same experiments, has been incorporated into this summary document. The overall objectives of this investigation were (1) to establish the gastrointestinal uptake of curium, (2) to determine the amount of activity transported to milk, (3) to examine the plasma clearance rate of curium, (4) to quantify the excretion characteristics of curium in urine and feces, and (5) to establish the tissue deposition pattern of curium in dairy animals. In pursuing the objectives, samples of blood, milk, urine and feces were taken from groups of cows and goats after the animals had received either oral or intravenous doses. Tissue collections were made at time of sacrifice.

METHODS AND MATERIALS

The study was conducted in two phases at the Nevada Test Site farm. Six lactating goats, between 1 and 3 years of age and confined to individual metabolism stalls, were used in the initial phase. Three of these goats received acute oral doses of curium-243 (200 μCi per animal), and the other three goats received single intravenous curium-243 doses of 20.8 μCi per animal. Both intravenous and oral doses were in the chloride form. Intravenous doses were citrate-buffered and were administered by jugular venipuncture. Oral doses were placed in gelatin capsules containing cellulose fiber and administered using a balling gun. No intravenous or oral dose adjustments were made for individual variations in animal weight. Composite daily collections of milk, urine and feces were sampled from each goat over a 144-hour period after dosing. Blood samples were also taken during this period.

The animals were catheterized with in-dwelling, inflatable urinary catheters and the urine was allowed to drain through polyethylene tubing into plastic bottles at the rear of each stall. Fecal pellets were collected in a modified tray. The goats were milked by hand twice daily and single blood samples were taken by jugular venipuncture. All urine, milk and fecal collections were weighed and then combined (a.m. + p.m.) into respective 24-hour composites for each animal. Fecal collections were manually mixed. Respective composites of milk and urine were shaken thoroughly in plastic containers. Weighed subsamples were then taken from the respective composites

and placed in individual 200-ml aluminum cans with formaldehyde added as preservative. Blood samples were centrifuged and the plasma and cells separated using disposable pipettes. The packed cells were washed two times with physiological saline. Samples of plasma and cells were then individually diluted with distilled water and formaldehyde was added as a preservative.

In the second phase of this study, two Holstein dairy cows, average weight 666 kg, were used, and the same procedures as the caprine experiment were followed. The first animal was given a single oral dose (39.6 mCi) of curium-243 chloride, and the second animal received 1.12 millicuries (mCi) of citrate-buffered curium-243 chloride in a single intravenous injection. As before, the oral dose was placed in a gelatin capsule and administered using a balling gun. The intravenous dose was administered by jugular venipuncture. The cows were each catheterized for urine collections, and a grid-covered pan, lined with polyethylene sheeting, was used to collect the feces. Milk was collected with individual bucket milkers twice daily, and the 24-hour composite sampling was conducted for milk, urine and feces. A Hobart mixer was used to mix the large fecal collections. Daily blood samples were also taken from both cows.

Cows and goats were sacrificed 7 days after dosing (Table I) using intravenously administered euthanasia solution. Extensive precautions were taken in the sacrifice area (Nevada Test Site farm) to reduce any possibility of cross-contamination during tissue collection. Organs and tissues were removed from the partially exsanguinated animals within approximately 60 minutes of sacrifice. Extraneous tissue (adipose tissue or muscle associated with bone samples) was discarded, and the required sample, plus formaldehyde, was sealed in 200-ml aluminum cans. Total weights were taken on most organs so that the percentage of administered dose retained by a specific tissue or organ could be calculated. When total weight was not practical (for muscle, bone, blood, etc.), total curium-243 content was based on extrapolated organ weights using the respective percentage of body weight reported by Davis et al., (1975), Smith and Baldwin (1974) and Matthews et al., (1975). Curium concentrations from the femur (diaphysis and epiphysis) and sternum were averaged to estimate the osseous retention values.

Table I

BACKGROUND INFORMATION ON THE EIGHT DAIRY ANIMALS DOSED WITH CURIUM

Animal Number	Curium Dose	Animal Weight (kg)	Sacrifice Time Post-treatment (days)	Average Daily Output During Experiment (kg)		
				Milk	Urine	Feces
Cow 256	single oral dose (39.6 mCi) of curium-243 chloride	596	7	8.7	7.6	10.7
Cow 344	single intravenous dose (1.12 mCi) of citrate-buffered curium-243 chloride	736	7	12.7	17.8	20.2
Goat 1	single oral dose (200 μCi) of curium-243 chloride	37.5	7	1.3	1.0	0.8
Goat 2	single oral dose (200 μCi) of curium-243 chloride	35.5	7	1.2	0.9	0.7
Goat 3	single oral dose (200 μCi) of curium-243 chloride	49.5	7	1.5	1.3	0.8
Goat 4	single intravenous dose (20.8 μCi) of citrate-buffered curium-243 chloride	52.0	7	1.5	1.4	0.9
Goat 5	single intravenous dose (20.8 μCi) of citrate-buffered curium-243 chloride	39.0	7	0.9	0.8	0.3
Goat 6	single intravenous dose (20.8 μCi) of citrate-buffered curium-243 chloride	33.0	7	1.1	1.0	0.6

Gamma counting was considered the most feasible analytical technique for use in conjunction with these experiments. Curium-243 concentrations in the sample material were determined by counting the 228 and 278 KeV gamma rays that occur, respectively, in 7.3 and 11.2 percent of the disintegrations. Samples were counted in 200-milliliter aluminum cans using a NaI(Tl) detector and pulse height analyzer. For samples with low (1 picocurie per gram) curium-243 concentrations, 400-minute counting times were used. Checks were made for gain shifts and changes in efficiency with an aliquot of the dosing solution. Backgrounds were taken before, during and after each series of counts to confirm that contamination of the counting chamber had not occurred. Various spiked standards (feces, milk, urine, plasma, blood cells, distilled water and agar) were also prepared. The amount of curium added (spike) was based on (1) the supplier's value for the stock solution and on (2) the calculated concentration range (percentage of dose per gram) likely to occur in milk, urine, etc., throughout the project. The curium-243 stock material was obtained from Oak Ridge National Laboratory and contained curium-244 as a major impurity (as of May 1975; 55.9 atom % curium-243 and 42.1 atom % curium-244).

After assaying the samples by direct counting methods, radiochemical analyses (LFE Corporation, Richmond, California) were performed (1) on a portion of the quality assurance samples, (2) on sets of samples that demonstrated considerable between-animal or within-animal variability and (3) on samples that contained less than 500 femtocuries (fCi) of curium-243 per gram of material. These radiochemical assays were conducted for total curium concentration (curium-243 plus curium-244) using alpha spectrometry. Curium-242 was used as a tracer. In order to extract values for curium-243 from the total curium concentrations, i.e., radiochemical assays, it was assumed that both isotopes had been metabolized in the same way. The decay-corrected isotopic ratio present in the dosing solution was therefore assumed to be the same (decay-corrected) isotopic ratio encountered in the sample material.

RESULTS AND DISCUSSION

Approximately 0.02 percent of the oral curium dose was absorbed from the bovine gastrointestinal tract. Of this relatively small amount, approximately 9 percent and 2 percent were subsequently transported to bovine urine and milk, respectively. Curium uptake in orally dosed goats was estimated to be 0.006 percent of the administered nuclide. Five percent of this absorbed amount was then transported to caprine urine and less than 4 percent was recovered in the milk. At time of sacrifice (160 hours after dosing), 89 percent of the absorbed nuclide was recovered in the bovine carcass and approximately 88 percent of the absorbed curium was retained in the caprine carcass. The abovementioned findings for the orally dosed animals are summarized in Table II. Carcass retention values used in this table were derived by summing the curium recovered in bone, liver, kidney, lung, spleen, heart, gonads, thyroid, muscle and plasma for the individual animals.

The percentages of dose contained in plasma, milk, urine and feces for the orally dosed animals are shown in Tables III and IV. Values are given for each collection interval and for the total transport to milk, urine and feces during the 144-hour collection period. For the orally dosed cow (Table III), peak curium output in the feces occurred between the 48- and 96-hour collection periods. Plasma values were highest at 24 hours and remained elevated through the 48-hour period. Nuclide transport to milk and urine reflected these plasma values and, in the case of milk, a peak plateau was noted between 48 and 72 hours. The nuclide transport to urine increased to a peak at 48 hours and then gradually declined throughout the remainder of the collection period. Total nuclide transport to bovine milk and urine was 0.0005 and 0.002 percent of the administered oral dose, respectively. The mean peak curium transport to caprine milk (Table IV) occurred at the 72-hour collection period. However, two of the three goats had a distinctive peak

Table II

GROSS ESTIMATE OF CURIUM TRANSPORT IN DAIRY ANIMALS FOLLOWING A SINGLE ORAL CURIUM-243 DOSE

	Cow 256		Goat 1		Goat 2		Goat 3	
	% of Oral Dose	% of Absorbed Dose	% of Oral Dose	% of Absorbed Dose	% of Oral Dose	% of Absorbed Dose	% of Oral Dose	% of Absorbed Dose
Milk (144 h)	4.6×10^{-4}	2.0	6.2×10^{-4}	8.4	6.1×10^{-5}	1.3	1.1×10^{-4}	1.8
Urine (144 h)	1.9×10^{-3}	8.5	2.7×10^{-4}	3.7	3.4×10^{-4}	7.0	3.5×10^{-4}	5.6
Feces* (144 h)	88.9	1.0	116	2.9	111	2.9	100	2.9
Carcass (160 h)	2.0×10^{-2}	88.9	6.1×10^{-3}	84.7	4.3×10^{-3}	88.7	5.5×10^{-3}	89.4
Estimated** G.I. Uptake	2.3×10^{-2}	-	7.2×10^{-3}	-	4.9×10^{-3}	-	6.2×10^{-3}	-

*Curium excretion in feces should eventually approach 100 percent of dose following nuclide ingestion. Calculations for goats 1 and 2 (% of oral dose) exceed 100 percent due to inaccuracies associated with fecal determinations. Values for % of absorbed dose are based on observed nuclide transport to feces for intravenously dosed animals.

**Gross summation composed of (1) the total transport (144 h) to milk and urine, (2) recovered activity estimate for each carcass (160 h) and (3) the extrapolated amount of absorbed curium-243 returned to the gastrointestinal tract.

Table III

PERCENTAGE OF ORAL CURIUM-243 DOSE NOTED IN BLOOD PLASMA, MILK, URINE AND FECES FOR ONE DAIRY COW DURING THE 144-HOUR SAMPLING PERIOD

Time After Dosing	Plasma*	Milk	Urine	Feces
8 h	-	1.38×10^{-6}	1.06×10^{-5}	-
15 h	3.00×10^{-4}	-	-	-
24 h	4.15×10^{-4}	2.19×10^{-5}	2.17×10^{-4}	4.43
48 h	3.66×10^{-4}	1.32×10^{-4}	7.11×10^{-4}	16.3
72 h	1.53×10^{-4}	1.41×10^{-4}	3.93×10^{-4}	32.6
96 h	7.84×10^{-5}	7.42×10^{-5}	2.84×10^{-4}	27.4
120 h	4.31×10^{-5}	5.33×10^{-5}	1.91×10^{-4}	8.04
144 h	3.81×10^{-5}	3.51×10^{-5}	1.36×10^{-4}	4.14×10^{-3}
Total	-	4.60×10^{-4}	1.94×10^{-3}	88.8

*Extrapolated values

Table IV

MEAN PERCENTAGE OF ORAL CURIUM-243 DOSE NOTED IN BLOOD PLASMA, MILK, URINE AND FECES FOR THREE DAIRY GOATS DURING THE 144-HOUR SAMPLING PERIOD

Time After Dosing	Plasma*	Milk	Urine	Feces
8 h	3.64×10^{-5}	1.69×10^{-6}	2.08×10^{-5}	-
24 h	-	2.01×10^{-5}	1.59×10^{-4}	13.8
48 h	-	5.06×10^{-5}	7.03×10^{-5}	84.0
72 h	-	1.73×10^{-4}	2.06×10^{-5}	10.1
96 h	-	8.66×10^{-6}	1.84×10^{-5}	1.20
120 h	-	5.77×10^{-6}	1.37×10^{-5}	1.12×10^{-1}
144 h	-	5.96×10^{-6}	1.33×10^{-5}	1.00×10^{-2}
160 h**	6.34×10^{-6}	-	-	-
Total	-	2.66×10^{-4}	1.59×10^{-4}	109.2

*Extrapolated values, limited data available.
**Approximate time of sacrifice.

curium transport to milk by the 48-hour period. In all three goats the peak nuclide transport to urine and feces occurred 24 and 48 hours after dosing, respectively. Limited information on the amount of curium present in caprine plasma is also shown in Table IV.

Curium concentrations decreased rapidly in the plasma of all intravenously dosed animals (Table V). Approximately 1 percent of the injected nuclide was present in the plasma 8 hours after dosing. While further declines were not as dramatic, analysis of the 144-hour collections from the cow and goats revealed that 0.09 percent of the respective doses remained in the plasma. A rapid plasma clearance rate for curium has also been reported in sheep (McClellan et al., 1962).

Bovine plasma extrapolations (to percentage of dose per total plasma) were based on the assumption that whole blood would be 8 percent of the body weight and subsequently that plasma represented 60 percent of the whole blood. Caprine plasma was calculated at 55.9 ml per kg of body weight (Klement et al., 1955). Multiple samples of bovine and caprine blood analyzed by both the direct counting and radiochemistry techniques indicated that the major fraction of whole blood curium was occurring in the plasma. In spite of some fluctuation in the percentage distribution, approximately 90 percent of the whole blood curium was noted in the plasma fraction and approximately 10 percent of the whole blood nuclide content was recovered in the cellular portion.

Tables VI through XI present a comparison of the mean curium transport to milk, urine and feces for all treatment groups. Values are expressed as both a percentage of the dose recovered per total collection and as the percentage of dose per gram of milk, urine or feces. Where the respective tables show a blank at an early post-dosing time (8 hours through 24 hours), it indicates a slight alteration in the sampling schedule.

Nuclide transport to milk, urine and feces was basically similar between the orally dosed cow and the orally dosed goats. Curium concentrations reached a peak in bovine milk 48 hours after dosing and at 72 hours after dosing in caprine milk. Without the one unexplainably high milk value

Table V

MEAN PERCENTAGE OF CURIUM DOSE REMAINING IN BOVINE AND CAPRINE PLASMA FOLLOWING ACUTE INTRAVENOUS INJECTIONS OF CITRATE-BUFFERED CURIUM-243 CHLORIDE

Time post injection	% of Dose per Total Plasma*		% of Dose per Gram of Plasma	
	Cow	Goats	Cow	Goats
8 h	9.20×10^{-1}	1.23	2.61×10^{-5}	4.68×10^{-4}
16 h	1.21	5.75×10^{-1}	3.41×10^{-5}	2.58×10^{-4}
24 h	9.55×10^{-1}	4.54×10^{-1}	2.70×10^{-5}	1.91×10^{-4}
48 h	7.41×10^{-1}	3.18×10^{-1}	2.09×10^{-5}	1.33×10^{-4}
72 h	5.09×10^{-1}	2.32×10^{-1}	1.45×10^{-5}	9.76×10^{-5}
96 h	2.23×10^{-1}	6.11×10^{-2}	6.23×10^{-6}	2.40×10^{-5}
120 h	1.43×10^{-1}	6.33×10^{-2}	4.03×10^{-6}	2.40×10^{-5}
144 h	9.87×10^{-2}	8.82×10^{-2}	2.80×10^{-6}	3.85×10^{-5}

*Extrapolated values

(goat 1 at 72 hours), the mean peak concentration would have occurred in caprine milk 48 hours after dosing (2.31×10^{-8} percent of dose per gram) with a peak plateau from the 24-hour to 72-hour collection period. The mean total curium transport to caprine milk would also have been reduced to 1.06×10^{-4} percent of oral dose (instead of 2.66×10^{-4} as shown in Table VI) if the high 72-hour value for goat 1 had not been included with values for goats 2 and 3. However, multiple sampling and the results from two assay techniques produced no direct evidence of contamination and Tables II, IV, VI and VII include the higher-than-expected 72-hour milk value for goat 1. Total curium excretion in the urine was somewhat greater for the orally dosed cow than for the orally dosed goats (Table VIII). Peak nuclide concentrations occurred at 48 hours in bovine urine and at 24 hours in caprine urine (Table IX). Curium excretion in bovine feces was greatest between the 48-hour and 96-hour collection periods and reached a distinct peak in caprine feces 48 hours after nuclide ingestion (Table X and XI).

Similarities in curium transport to milk, urine and feces (between the cow and the goats) were also noted after intravenous dosing. The average percentage of injected curium transferred to milk, urine and feces was 2, 8 and 1 percent, respectively, for the cow and 2, 5 and 5 percent, respectively, for goats. Peak curium concentrations were found in the milk and urine of all intravenously dosed animals during the initial 8-hour collection period. The peak nuclide concentration was found in bovine feces 24 hours after nuclide injection, and the fecal concentrations subsequently declined throughout the remainder of the collection periods. In caprine feces the peak nuclide concentration was not reached until the 120-hour period. Curium excretion was mainly urinary for the cow, but in the case of intravenously dosed goats the total nuclide excretion was equally divided between urine and feces (Tables VIII, X and XII). The goats were excreting a somewhat greater quantity of feces (increasing daily fecal weight) toward the end of the collection period but, as shown in Table XI, the curium concentration (percentage of dose per gram) maintained somewhat of a peak plateau from 48 hours to 144 hours after curium injection.

Table VI

MEAN PERCENTAGE OF CURIUM DOSE TRANSFERRED TO MILK DURING THE 144-HOUR COLLECTION PERIOD

Time After Dosing	Oral Dose		Intravenous Dose	
	Cow	Goats	Cow	Goats
8 h	1.38×10^{-6}	1.69×10^{-6}	4.91×10^{-1}	8.07×10^{-1}
24 h	2.19×10^{-5}	2.01×10^{-5}	4.11×10^{-1}	5.09×10^{-1}
48 h	1.32×10^{-4}	5.06×10^{-5}	4.29×10^{-1}	3.29×10^{-1}
72 h	1.41×10^{-4}	1.73×10^{-4}	3.30×10^{-1}	1.87×10^{-1}
96 h	7.42×10^{-5}	8.66×10^{-6}	1.79×10^{-1}	1.74×10^{-1}
120 h	5.33×10^{-5}	5.77×10^{-6}	8.93×10^{-2}	8.99×10^{-2}
144 h	3.51×10^{-5}	5.96×10^{-6}	5.80×10^{-2}	6.41×10^{-2}
Total	4.60×10^{-4}	2.66×10^{-4}	1.99	2.16

Table VII

MEAN PERCENTAGE OF CURIUM DOSE TRANSFERRED PER GRAM OF MILK

Time After Dosing	Oral Dose		Intravenous Dose	
	Cow	Goats	Cow	Goats
8 h	7.25×10^{-10}	2.73×10^{-9}	7.46×10^{-5}	1.59×10^{-3}
24 h	7.81×10^{-9}	1.87×10^{-8}	5.71×10^{-5}	6.12×10^{-4}
48 h	2.06×10^{-8}	2.31×10^{-8}	3.54×10^{-5}	2.88×10^{-4}
72 h	1.64×10^{-8}	1.29×10^{-7}	2.44×10^{-5}	1.81×10^{-4}
96 h	7.65×10^{-9}	5.45×10^{-9}	1.36×10^{-5}	1.09×10^{-4}
120 h	4.72×10^{-9}	5.10×10^{-9}	7.32×10^{-6}	8.66×10^{-5}
144 h	3.03×10^{-9}	2.56×10^{-9}	5.09×10^{-6}	5.61×10^{-5}

Table VIII

MEAN PERCENTAGE OF CURIUM DOSE TRANSFERRED TO URINE DURING THE 144-HOUR COLLECTION PERIOD

Time After Dosing	Oral Dose		Intravenous Dose	
	Cow	Goats	Cow	Goats
8 h	1.06×10^{-5}	2.08×10^{-5}	3.23	2.08
24 h	2.17×10^{-4}	1.59×10^{-4}	1.68	9.94×10^{-1}
48 h	7.11×10^{-4}	7.03×10^{-5}	9.64×10^{-1}	3.94×10^{-1}
72 h	3.93×10^{-4}	2.06×10^{-5}	8.55×10^{-1}	2.95×10^{-1}
96 h	2.84×10^{-4}	1.84×10^{-5}	6.46×10^{-1}	2.92×10^{-1}
120 h	1.91×10^{-4}	1.37×10^{-5}	4.58×10^{-1}	2.92×10^{-1}
144 h	1.36×10^{-4}	1.33×10^{-5}	3.50×10^{-1}	2.07×10^{-1}
Total	1.94×10^{-3}	3.16×10^{-4}	8.18	4.55

Table IX

MEAN PERCENTAGE OF CURIUM DOSE TRANSFERRED PER GRAM OF URINE

Time After Dosing	Oral Dose		Intravenous Dose	
	Cow	Goats	Cow	Goats
8 h	7.50×10^{-9}	4.62×10^{-8}	8.28×10^{-4}	6.86×10^{-3}
24 h	6.77×10^{-8}	2.10×10^{-7}	1.20×10^{-4}	1.32×10^{-3}
48 h	1.29×10^{-7}	6.74×10^{-8}	5.81×10^{-5}	5.00×10^{-4}
72 h	6.34×10^{-8}	3.07×10^{-8}	5.81×10^{-5}	3.56×10^{-4}
96 h	3.46×10^{-8}	1.71×10^{-8}	3.73×10^{-5}	2.84×10^{-4}
120 h	1.87×10^{-8}	1.03×10^{-8}	2.30×10^{-5}	2.29×10^{-4}
144 h	1.28×10^{-8}	9.88×10^{-9}	1.74×10^{-5}	1.47×10^{-4}

Table X

MEAN PERCENTAGE OF CURIUM DOSE TRANSFERRED TO FECES DURING THE 144-HOUR COLLECTION PERIOD

Time After Dosing	Oral Dose		Intravenous Dose	
	Cow	Goats	Cow	Goats
8 h	-	-	7.34×10^{-3}	3.54×10^{-3}
24 h	4.43	13.8	3.61×10^{-1}	6.94×10^{-2}
48 h	16.3	84.0	3.21×10^{-1}	6.94×10^{-1}
72 h	32.6	10.1	2.95×10^{-1}	5.54×10^{-1}
96 h	27.4	1.20	2.05×10^{-1}	9.28×10^{-1}
120 h	8.04	1.12×10^{-1}	1.43×10^{-1}	1.13
144 h	4.14×10^{-3}	1.00×10^{-2}	9.82×10^{-2}	1.14
Total	88.8	109.2	1.43	4.52

Table XI

MEAN PERCENTAGE OF CURIUM DOSE TRANSFERRED PER GRAM OF FECES

Time After Dosing	Oral Dose		Intravenous Dose	
	Cow	Goats	Cow	Goats
8 h	-	-	2.30×10^{-6}	4.17×10^{-5}
24 h	1.58×10^{-3}	2.61×10^{-2}	2.30×10^{-5}	3.01×10^{-4}
48 h	3.79×10^{-3}	1.01×10^{-1}	1.79×10^{-5}	1.60×10^{-3}
72 h	3.11×10^{-3}	1.81×10^{-2}	1.49×10^{-5}	1.56×10^{-3}
96 h	1.72×10^{-3}	1.45×10^{-3}	9.55×10^{-6}	1.54×10^{-3}
120 h	6.09×10^{-4}	1.31×10^{-4}	6.55×10^{-6}	1.72×10^{-3}
144 h	2.45×10^{-7}	2.07×10^{-5}	4.66×10^{-6}	1.70×10^{-3}

Table XII

RELATIVE EXCRETION OF CURIUM IN URINE AND FECES FOLLOWING SINGLE INTRAVENOUS DOSES
(Values Expressed as a Mean Percentage of the Total Curium-243 Transported to both Urine and Feces over the 144-Hour Collection Period)

Time Post-Injection	Cow			Goats		
	% of Total Excretion Recovered in Urine & Feces	% of Total Excretion Recovered in Urine	% of Total Excretion Recovered in Feces	% of Total Excretion Recovered in Urine & Feces	% of Total Excretion Recovered in Urine	% of Total Excretion Recovered in Feces
24 h	55.0	51.1	3.8	35.4	34.5	0.9
48 h	13.4	10.0	3.3	12.1	4.3	7.8
72 h	12.0	8.9	3.1	9.5	3.3	6.1
96 h	8.8	6.7	2.1	13.1	3.2	9.9
120 h	6.2	4.7	1.5	14.9	3.1	11.8
144 h	4.6	3.6	1.0	15.0	2.3	12.7
Total	100	85.0	14.8	100	50.7	49.2

There was some suggestion of a species difference in the relative nuclide deposition between liver and bone. Bovine skeleton was the major deposition site following both intravenous and oral curium doses (Table XIII). However, in all three intravenously dosed goats, the liver contained the greatest amount of curium. Nuclide deposition in bone and liver was essentially equal for two of the three orally dosed goats while the skeleton contained the most curium in the other animal. These comparisons refer to total organ content only since the liver contained the greatest nuclide concentration (curium per gram of tissue) in all groups (Table XIV). Initial deposition of curium has been reported to occur primarily in the liver of laboratory rats (Hamilton, 1947). In the case of dogs, more curium was retained in the skeleton than in the liver 2 weeks after nuclide inhalation (McClellan et al., 1972). Intravenously dosed dogs (Lloyd et al., 1974) retained more curium in the liver 6 days post-injection but by the thirteenth day, bone had become the primary retention site.

Tables XV, XVI, XVII and XVIII present some comparisons between the metabolism of curium-243 and americium-241 in Holstein dairy cows. Following intravenous injections, nuclide transport to milk, urine and feces was quite similar with a dramatic decline in urinary nuclide excretion after the first 24 hours (Table XV). Liver contained the greatest concentration of both nuclides (Table XVI) approximately 1 week after the respective intravenous doses. Similarities were also noted in nuclide transport to edible bovine products after oral dosing (Table XVII) and the relative nuclide deposition, expressed as a percentage of absorbed dose, was nearly identical following nuclide ingestion.

MEAN PERCENTAGE OF CURIUM DOSE RETAINED
IN DAIRY ANIMALS AT TIME OF SACRIFICE

	Oral Dose		Intravenous Dose	
	Cow	Goats	Cow	Goats
Bone	1.09×10^{-2}	3.10×10^{-3}	58.6	18.7
Liver	6.92×10^{-3}	1.73×10^{-3}	29.1	37.2
Kidney	5.23×10^{-4}	1.13×10^{-4}	2.95	1.57
Lung	3.33×10^{-4}	8.70×10^{-5}*	1.38	7.31×10^{-1}
Muscle	1.03×10^{-3}	2.25×10^{-4}	3.17	4.86
Spleen	1.09×10^{-4}	1.78×10^{-5}*	7.50×10^{-1}	8.84×10^{-2}
Heart	2.53×10^{-4}	1.90×10^{-4}	7.50×10^{-1}	3.13×10^{-1}

*Based on two animals

Table XIV

MEAN PERCENTAGE OF CURIUM DOSE RETAINED
PER GRAM OF TISSUE

	Oral Dose		Intravenous Dose	
	Cow	Goats	Cow	Goats
Diaphysis	6.84×10^{-8}	6.67×10^{-7}	3.35×10^{-4}	7.37×10^{-3}
Epiphysis	8.01×10^{-8}	8.34×10^{-7}	4.22×10^{-4}	6.41×10^{-3}
Sternum	1.61×10^{-7}	1.86×10^{-6}	6.39×10^{-4}	8.14×10^{-3}
Liver	6.62×10^{-7}	1.89×10^{-6}	2.54×10^{-3}	4.23×10^{-2}
Kidney	3.13×10^{-7}	6.33×10^{-7}	9.91×10^{-4}	1.08×10^{-2}
Lung	6.89×10^{-8}	1.36×10^{-7}*	2.16×10^{-4}	1.30×10^{-3}
Muscle	3.75×10^{-9}	1.13×10^{-8}	9.38×10^{-6}	2.66×10^{-4}
Spleen	5.76×10^{-8}	1.22×10^{-7}*	2.92×10^{-4}	9.54×10^{-4}
Heart	7.96×10^{-8}	2.50×10^{-7}	2.09×10^{-4}	1.62×10^{-3}
Thyroid	2.65×10^{-8}	--**	1.04×10^{-4}	1.69×10^{-3}
Adrenal	3.13×10^{-8}	--**	2.49×10^{-4}	9.04×10^{-4}
Mammary Gld.	1.06×10^{-7}	2.50×10^{-7}	2.39×10^{-4}	3.33×10^{-3}
Gonads	4.95×10^{-8}	--**	1.43×10^{-4}	1.46×10^{-3}

*Based on two animals
**Limited data available

Table XV

COMPARISON OF CURIUM-243 AND AMERICIUM-241 TRANSPORT TO MILK, URINE AND FECES IN HOLSTEIN DAIRY COWS. (Values Expressed as a Percentage of the Respective Intravenous Doses)

Time post-injection	Curium-243*			Americium-241**		
	Milk	Urine	Feces	Milk	Urine	Feces
24 h	0.902	4.91	0.368	1.41	3.25	1.09
48 h	0.429	0.964	0.321	0.470	0.887	0.454
72 h	0.330	0.855	0.295	0.281	0.540	0.296
96 h	0.179	0.646	0.205	0.229	0.328	0.201
120 h	0.089	0.458	0.143	0.167	0.291	0.152
Total	1.93	7.83	1.33	2.56	5.30	2.19

*Values from one cow given an intravenous dose (1.12 mCi) of citrate-buffered curium-243 chloride.

**Average values from two cows each given an intravenous dose (0.96 mCi) of citrate-buffered americium-241 chloride (Sutton *et al.*, 1978).

Table XVI

COMPARISON OF CURIUM-243 AND AMERICIUM-241 RETENTION IN HOLSTEIN DAIRY COWS APPROXIMATELY ONE WEEK AFTER RECEIVING SINGLE INTRAVENOUS DOSES. (Values Expressed as a Percentage of Dose per kg of Tissue).

Tissue	Curium-243*	Americium-241**
Diaphysis	3.35×10^{-1}	3.05×10^{-1}
Epiphysis	4.22×10^{-1}	6.07×10^{-1}
Sternum	6.39×10^{-1}	6.79×10^{-1}
Liver	2.54	3.82
Kidney	9.91×10^{-1}	1.15
Muscle	9.38×10^{-3}	1.93×10^{-2}
Lung	2.16×10^{-1}	2.64×10^{-1}
Spleen	2.92×10^{-1}	2.71×10^{-1}
Heart	2.09×10^{-1}	2.88×10^{-1}

*Values from one cow given an intravenous dose (1.12 mCi) of citrate-buffered curium-243 chloride.

**Average values from two cows each given an intravenous dose (0.96 mCi) of citrate-buffered americium-241 chloride (Sutton *et al.*, 1978).

Table XVII

TRANSPORT OF ORALLY ADMINISTERED AMERICIUM-241 AND CURIUM-243 TO EDIBLE BOVINE PRODUCTS

Nuclide Dose	No. of Animals	% of Dose Secreted in Milk (Cumulative)	% of Dose/liter of Milk at Peak Concentration	Time of Sacrifice	% of Dose in Liver	% of Dose/g of Liver	% of Dose in Muscle (Skeletal)	% of Dose/g of Muscle
Americium chloride 41.7 mCi/animal acute dose (Sutton *et al.*, 1978)	2	4.4×10^{-4}	8.6×10^{-6}	2 animals sacrificed 8 days post-treatment	4.1×10^{-3}	4.3×10^{-7}	9.6×10^{-4}	3.6×10^{-9}
Curium chloride 39.6 mCi/animal acute dose	1	4.6×10^{-4}	2.0×10^{-5}	1 animal sacrificed 7 days post-treatment	6.9×10^{-3}	6.6×10^{-7}	1.0×10^{-3}	3.8×10^{-9}

Table XVIII

RELATIVE DEPOSITION OF CURIUM-243 AND AMERICIUM-241 IN HOLSTEIN DAIRY COWS ONE WEEK AFTER RECEIVING SINGLE ORAL DOSES. (Values Expressed as a Percentage of the Absorbed Dose*)

	Curium-243	Americium-241	
	Cow 256	Cow 281	Cow 269
Bone	48.1	40.7	41.2
Liver	30.4	30.5	31.4
Muscle	4.5	7.9	6.5
Kidney	2.3	3.4	2.2
Spleen	0.5	0.6	0.6
Gonads	0.005	0.003	0.005
Thyroid	0.004	0.005	0.003

*Gastrointestinal uptake of curium in cow-256 was estimated to be 2.3×10^{-2} percent of the oral dose; uptake of americium (Sutton *et al.*, 1978) was estimated to be 1.4×10^{-2} and 1.2×10^{-2} percent of the oral dose for cows 281 and 269 respectively. Both nuclides were given as chlorides.

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