Toxicity of the Arsenical Herbicide Monosodium Acid Methanearsonate in Cattle

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SUMMARY

The study was conducted to determine the toxicity of monosodium acid methanearsonate (MSMA) in cattle. A total of 5 cattle was treated with solutions of MSMA. Of the 5 cattle, 4 succumbed to the toxic effects of the compound on the renal tubules after they were given a total dosage of 100 mg. of MSMA per kilogram of body weight (10 mg./kg./day for 10 days) or less. Arsenic residues as high as 64 p.p.m. were found in kidney with a minimal content in liver of 27 p.p.m. Toxic nephrosis and hemorrhagic gastritis were seen in all cattle; lesions in liver were variable and were absent from other tissues studied.

Monosodium acid methanearsonate, a widely used organic herbicide, is sometimes used in precommercial thinning of forests. Since cattle often were grazed in areas where MSMA was used, the question of toxicity of the agent to cattle arose. The median lethal dose (LD_{50}) in cattle is not known, but according to one report,[a] repeated doses of 10 mg./kg. produced poisoning in cattle. In this instance, poisoning was considered to have occurred when any sign of abnormal function or behavior was observed.

The oral LD_{50} in mice and in rats are 1,800 and 700 mg./kg., respectively; 120 ml. of MSMA solution is considered sufficient to kill a 68-kg. man.[4]

Monosodium acid methanearsonate contains arsenic in the pentavalent form. Pentavalent organic arsenic is considered less toxic than is the trivalent inorganic form; apparently, the former is less binding to sulfhydryl groups.[1] The pentavalent form, however, may be converted to the trivalent form in the animal body. There is almost no information on the breakdown of MSMA in animal tissues. The fate is presumed to be similar to that of cacodylic acid; namely, unchanged in urinary excretion.

Materials and Methods

Two preparations of MSMA were used: one contained 44.9% MSMA in an aqueous solution plus other ingredients, primarily a dye,[b] and the other contained only 59% MSMA in an aqueous solution.[c] In both preparations, the total arsenic content was 21%. These were administered orally to cattle, using gelatin capsules. A total of 7 yearling white-faced cattle were used; 2 were used as controls (1 steer and 1 heifer), 3 were treated with the dye-containing solution (2 steers and 1 heifer), and 2 were treated with the aqueous solution (1 steer and 1 heifer). Weights ranged from 118 to 217 kg. at the start of the project (Table 1).

A rather small dose was initially given to

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[a] Palmer, J. S., College of Veterinary Medicine, Texas A&M University, College Station, Texas: Personal communication, March 20, 1970.

[b] Glowon Tree Killer, Key Chemicals, Inc., Anacortes, Wash.

[c] Ansar 170 HC, The Ansul Company, Marinette, Wis.

gain information on chronic toxicity of the herbicide. Cattle were treated each day at the dosage level of 10 mg. of MSMA per kilogram of body weight per day. The dosage level of 10 mg./kg./day was continued for 3 weeks; at the end of this period, a hepatic biopsy sample was obtained for arsenic determination. During the 2nd 3-week period, the dosage was doubled to 20 mg./kg./day, and biopsy of liver was done at conclusion of this segment. The 3rd 3-week period completed the study of chronic toxicity; the dosage was increased to 30 mg./kg./day during the final period.

TABLE 1—Test Procedure

Cattle							
No.	Age (mo.)	Sex	Body weight (kg.)	MSMA formulation	Daily dose (mg./kg.)	Duration of treatment (days)	Disposition
3	13	Steer	216	44.9% with dye	10	10	Died, day 10
4	13	Heifer	167	44.9% with dye	10	10	Recovered
5	12	Steer	177	44.9% with dye	10	10	Killed, day 12
12	14	Steer	211	59.0% aqueous	10	8	Died, day 8
15	9	Heifer	118	59.0% aqueous	10	8	Died, day 16
126	14	Steer	209	.... (control)	....	....	Killed, day 12
124	15	Steer	217	.... (control)	....	....	Killed, day 10

At the conclusion of the 9-week experiment, remaining cattle were killed and necropsied, and tissue sections from liver, kidney, brain, and abomasum were examined for gross and microscopic lesions of significance. Hair and tissue samples from all cattle were assayed for arsenic content at the end of the treatment period; hair samples were also assayed at the start of the treatment period. Duplicate analyses were done on all samples, using neutron activation analysis[3,d] and a spectrophotometric method.[2,e]

Results

The procedure as outlined was not completed because the cattle were unable to tolerate the MSMA solution (preparation 1) at the lowest dosage rate for more than 10 days. At this point, 1 steer (No. 3) died, and treatment was stopped on the other 2 (1 steer and 1 heifer). All 3 cattle had developed severe diarrhea by the 7th day of treatment, along with dehydration and body weight loss; these were the first clinical signs of poisoning. Steer 5 became more lethargic and was unable to rise by day 12; this steer was killed (overdose of sodium pentobarbital). Heifer 4 had signs of recovery by this time and was observed each day after treatment was ended. The heifer apparently recovered.

Evidence of gross pathologic changes were seen in kidney and abomasum of steers 3 and 5. Kidneys were markedly swollen. On cut surface of the kidney, medulla appeared darkened, even hemorrhagic, whereas little change was seen in the cortex (Fig. 1). There was hemorrhagic gastritis characterized by mucosal erosion and ulceration and intense hyperemia. A large amount of blood was admixed with abomasal contents.

Results of microscopic examination of abomasum from steers 3 and 5 indicated marked hemorrhagic gastritis. Multiple foci of coagulative necrosis having a midzonal distribution were in the liver of

Fig. 1—Cut surface of kidney of steer 3 which was given 10 mg. of monosodium acid methanearsonate per kilogram per day and died on day 10. Notice hemorrhage in the cortex.

[d] Nuclear Radiation Center, Washington State University, Pullman, Wash.

[e] Washington State Division of Health, Wenatchee, Wash.

TABLE 2—Tissue Arsenic Residues (p.p.m.) in Cattle Given Monosodium Acid Methanearsonate (44.9% Solution with Dye)

Tissue*	Steer No. 3			Steer No. 5			Control (steer 126)
	Before treatment	Neutron activation analysis	Spectrophotometric analysis	Before treatment	Neutron activation analysis	Spectrophotometric analysis	Neutron activation analysis
Kidney cortex	N.D.	57.9	64.2	N.D.	26.7	23.2	0.25
Liver	N.D.	27.0	24.9	N.D.	27.4	30.3	0.82
Brain	N.D.	1.8	1.7	N.D.	2.6	1.7	0.05
Bone (rib)	N.D.	4.9	N.D.	N.D.	2.5	N.D.	0.03
Muscle (intercostal)	N.D.	10.3	N.D.	N.D.	7.4	N.D.	0.02
Abomasum (mucosa)	N.D.	N.D.	N.D.	N.D.	14.2	17.7	0.02
Hair (top of back)	2.7	3.3	N.D.	1.1	1.4	N.D.	0.81

* All tissue samples were obtained at necropsy following treatment period, except for hair samples.
N.D. = not done.

steer 3. In steer 5, lesions were not seen in liver or brain. Both steers, however, had marked diffuse nephrosis. It was concluded that renal tubular degeneration was the cause of death of steer 3 and ultimately would have been the cause of death of steer 5.

Tissue arsenic concentrations are recorded (Table 2) for steers 3 and 5; results from both the neutron activation analysis and spectrophotometric method are given. Agreement between the 2 methods was quite satisfactory. Sample of liver was withdrawn from heifer 4 on May 10; the hepatic arsenic content was 7.2 p.p.m.

In steer 12 and heifer 15, given preparation 2 (aqueous solution of 50% MSMA) at the dosage rate of 10 mg. of MSMA per kilogram of body weight per day, diarrhea was evident by day 5. This diarrhea represented the first clinical sign of toxicity. Steer 12 died on the 8th day of treatment. Heifer 15 survived until day 16, even though treatment was discontinued on the 8th day. Gross and microscopic pathologic changes were quite similar to those described for steers 3 and 5. The tissue arsenic concentrations for liver and kidney are given (Table 3).

Discussion

Of the 3 cattle in the 1st group given MSMA (10 mg./kg./day), 2 died from apparent kidney failure—1 steer (No. 3) after 10 days of treatment and the 2nd steer (No. 5) 2 days later. The latter steer was not given MSMA on days 11 or 12, but kidney damage was apparently irreversible.

The hepatic arsenic concentrations for both steers were similar (27 p.p.m.); however, the changes in renal arsenic concentrations were different. After treatment was discontinued in steer 5, the renal arsenic concentration decreased to a value less than the concentration in the liver. It is assumed that the steer was able to remove arsenic from the kidney rather rapidly. Nevertheless, toxic nephrosis was the apparent cause of death. The phenomenon could have diagnostic significance, since organic pentavalent arsenicals are assumed to produce higher renal tissue concentrations than hepatic tissue concentrations in poisonings. Cattle could conceivably deplete the arsenic content in the kidney rather rapidly to a value below that of the liver and perhaps below the value having diagnostic significance, but succumb to irreversible tubular damage.

TABLE 3—Tissue Residues (p.p.m.) in Cattle Given Monosodium Acid Methanearsonate (59% Aqueous Solution)

Tissue*	Spectrophotometric assay		
	Steer 12	Heifer 15	Steer 124
Liver (necropsy sample)	17.7	1.6	0.7
Kidney (necropsy sample)	45.8	3.5	1.1

* All tissue samples were obtained at necropsy following treatment period.

The results obtained by using an aqueous solution of MSMA (preparation 2) were essentially the same as those obtained with the commercial dye-containing product (preparation 1). Toleration of the 10-mg./kg./day dosage was quite similar.

A total dose of 80 to 100 mg./kg. was fatal to 4 of 5 cattle used in the present experiment. Clinical signs of poisoning (diarrhea and anorexia) were evident in all 5 cattle when a total dose of 50 to 70 mg./kg. had been given.

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