TOXICITY OF CACODYLIC ACID SILVICIDE IN CATTLE

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SUMMARY

Since cacodylic acid, a pentavalent organic arsenical, is widely used as a herbicide and silvicide, the potential for chronic poisoning of cattle does exist. In this study, five cattle were subjected to a chronic oral exposure of cacodylic acid over a six week period. The dosage for the first three weeks was 10 mg./kg./day, followed by 20 mg./kg./day for the second three weeks. Examination of tissues at necropsy indicated acute enteritis, hepatic degeneration and irreversible renal tubular degeneration. Liver and kidney arsenic concentrations were elevated above control values but not into a range of values generally considered to have diagnostic significance. Accumulation of arsenic in hair was progressive, and values achieved were considerably above those recorded at the beginning of the period.

INTRODUCTION

Cacodylic acid and the Sodium salt (sodium cacodylate) have found usage as therapeutic agents. In addition, cacodylic acid is widely used as a herbicide and as a silvicide in precommercial thinning of forests. Under these circumstances, cattle, as well as wild grazing animals, are exposed to treated areas, and a potential for poisoning does exist.

The oral LD_{50} of cacodylic acid in rats has been reported to be 1800 mg./kg. body wieght (5). The oral LD_{50} in rats of a herbicide preparation containing 46.0% cacodylic acid, 8.3% triethanolamine cacodylate, plus inert ingredients has been reported to be 2000 mg./kg. body weight (2). In 1969 this particular preparation was used as a silvicide in an area in north central Washington where cattle were found dead, apparently from arsenic poisoning. This provided a stimulus for further study of the lethality of cacodylic acid.

Cacodylic acid contains arsenic in the pentavalent form. Pentavalent arsenic is considered less toxic than the trivalent form; apparently there is less binding to sulfhydryl groups. It is possible that the pentavalent form may be converted to the trivalent form within the animal body and accumulate in various tissues. Sodium cacodylate is reported to be converted to cacodylic oxide. The arsenic is liberated as inorganic arsenic, which is very slowly excreted in the urine. After oral ingestion, inorganic arsenic is likely to be freed rapidly by the action of acid gastric juice (3).

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More recent research (4) tends to indicate that oral cacodylic acid intake does not result in tissue arsenic accumulation but, rather, in complete excretion in the urine. The metabolic fate of cacodylic acid remains to be fully described.

The purpose of this study was to determine the lethal dose in cattle of a commercial cacodylic acid silvicide. Both gross and microscopic pathology were considered, as well as arsenic accumulation in various tissue.

MATERIALS AND METHODS

The product utilized[a] contained 50% diemthylarsinic acid (cacodylic acid) plus inert ingredients. The material was administered orally to cattle (1 heifer, 4 steers) by use of gelatin capsules. A rather low beginning dosage level was selected in an effort to gain information concerning chronic toxicity of the silvicide. Cattle were treated daily at a level of 10 mg./kg./day. Control samples of hair and liver were analyzed by neutron activation analysis (6)[b] prior to the beginning of the treatment period. The dosage level of 10 mg./kg./day was continued for three weeks. At the end of this period, a liver biopsy sample was taken for arsenic determination; a hair sample was also removed at this time. A second three-week period followed with a doubling of the dosage to 20 mg./kg./day; hair and liver samples were removed at the end of this period. The third three-week period completed the study; the dosage was increased to 30 mg./kg./day during the final period. At the conclusion of the experiment, all animals were necropsied, and tissues were examined for gross and microscopic lesions of significance. Hair and tissue samples from all treated animals were assayed for arsenic content.

[a]Silvisar 510, The Ansul Company, Marinette, Wisconsin.

[b]Nuclear Radiation Center, Washington State University, Pullman, Washington.

RESULTS

The results of tissue arsenic analysis are presented (Table 1). The 4 steers (Nos. 2, 6,128,131) and 1 heifer (No. 1) survived the first three-week period (10 mg./kg./day dosage rate) with minimal difficulty. All three exhibited a rather persistant diarrhea by the end of the second week, but appetite was unimpaired. At the end of the fifth week, heifer No. 1 exhibited a pronounced anorexia and weight loss; administration of cacodylic acid to this animal was discontinued. This heifer ultimately appeared to recover completely from the effects of the silvicide. On the 35th day steer No. 131 died. Steer No. 128 died on the 42nd day.

Steers Nos. 2 and 6 were judged to be in such poor physical condition (severe depression, inability to rise, atonic rumen and complete inappetence) at the end of six weeks (3 weeks at 10 mg./kg./day, plus 3 weeks at 20

TABLE 1: Tissue Arsenic Residues (in ppm) From Cattle Receiving Silvisar 510

(50% Cacodylic Acid)

Tissue	Control (Steer 33)	Heifer #1	Steer #2	Steer #6	Steer #131	Steer #128
Kidney	0.280	0.777	5.554	11.940	7.592	10.070
Liver (beginning)	0.017	0.227	0.179	0.082	0.211	0.061
(21 days)	0.088	3.090	3.711	2.492	3.800	2.777
(end)	1.171	-----	4.236	3.177	2.606	3.312
Muscle (intercostal)	0.031	0.096	4.056	3.427	3.711	4.007
Abomasum (mucosa)	0.049	0.008	9.174	14.940	12.414	13.092
Brain	0.033	0.076	1.273	1.272	1.208	1.332
Bone	0.071	0.005	0.424	1.264	0.887	1.317
Hair (beginning)	3.176	2.040	0.980	1.010	0.861	3.186
(10 days)	3.301	4.270	2.555	2.041	2.771	4.772
(21 days)	2.976	6.144	5.099	2.488	4.008	5.137
(30 days)	3.331	6.617	6.985	5.752	5.808	6.332
(35 days)	3.476	19.220	7.752	10.630	7.527	9.078
(48 days)	4.002	32.850	15.720	12.930	-----	22.319

mg./kg./day) that both were euthanized at this point, and tissues were removed for arsenic determination and histopathologic examiniation. Acute enteritis, and hepatic and renal degeneration were the primary pathologic changes observed. The acute enteritis was of a mild nature; the lamina propria was infiltrated with lymphocytes and a few macrophages. Lipid vacuoles appeared in most hepatic parenchymal cells, with some lymphocytic infiltration into periportal spaces. The proximal renal tubules were swollen, granular and contained considerable debris in the lumen. Primary cause of death, assuming the animals had been permitted to die, would have been renal tubular degeneration. Histopathologic examination of tissues from steers Nos. 128 and 131 revealed similar lesions.

Three steers (Nos. 2,6,126) and one heifer (No. 1) each received a total dose of 630 mg. of cacodylic acid per kg. of body weight. Steer No. 131 received a total dose of 525 mg. of cacodylic acid per kg. of body weight.

DISCUSSION

Four of the five animals were able to survive for a period of six weeks, during which time 630 mg. of cacodylic acid had been administered per kg. of body weight. Severe renal tubular degeneration was observed at necropsy. Tissue arsenic concentrations were not elevated to values normally associated with arsenic toxicity, and, therefore, would be of little assistance in any diagnosis of cacodylic acid poisoning. This is contrary to the results observed in an earlier study with a closely related compound, MSMA (monosodium acid methanearsonate), where elevated body tissue arsenic concentrations of diagnostic significance were observed (1). However, an increase in arsenic content of the hair paralleled the exposure to cacodylic acid. Therefore, characteristic tubular damage accompanied by increased arsenic content of the hair could be indicative of chronic cacodylic acid toxicity.

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