

Histopathological Effects of Monosodium Methanearsonate (MSMA) on New Zealand White Rabbits (*Oryctolagus cuniculus*)

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Monosodium Methanearsonate (MSMA) is an herbicide commonly used for grass control (especially Johnson grass) along secondary road way rights-of-way. Three groups of adult male New Zealand white rabbits (NZW) weighing 2.5-3.0 kg were given 5, 10 or 20 mg MSMA/kg orally for 40 days to monitor potential histopathology resulting from organic arsenic exposure. Primary lesions included hepatic cellular degeneration, periportal inflammation, renal tubular nephrosis, interstitial nephritis and vascular hyperemia. The severity of lesions varied with dose.

Relatively little work has been done on the effect of organic arsenicals, especially MSMA in mammals. The clinical manifestations and histological findings of organic arsenic toxicity in animals seem to be similar to those induced by inorganic forms of arsenic. The main effects include gastritis, diarrhea, electrocardiograph changes and a drop in blood pressure (Selby, et al. 1977). The LD₅₀ of MSMA was found to be: 1800, 250 and 102 mg/kg for albino rats, cattle and NZW rabbits respectively (EPA 1975, Dickenson et al., 1972, Jaghabir et al. 1988).

Four out of five cattle succumbed to the toxic effects of MSMA on the renal tubules following a total oral dose of 100 mg MSMA per kg of body weight, administered over a period of ten days. Signs of toxic nephrosis and hemorrhage were observed in all five animals (Dickenson et al., 1972).

The objective of this study was to investigate the histopathological effects of MSMA by using New Zealand white rabbits as a test species. Low doses of MSMA over relatively short exposure times were used to

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simulate conditions that could prevail in an environmental exposure along sprayed roadsides. The potential health effects of arsenic from MSMA on rabbits is an important consideration requiring study, since wild rabbits might be exposed to arsenicals via grazing on grass treated with MSMA. Samples of treated Johnson grass at recommended levels of 4.0161 MSMA/acre taken 10 hours after treatment showed an absorbed concentration of 810 mg MSMA/kg (Mason, et al., 1979). Kaplan, et al. (1979) reported that rabbits normally consume about 200 grams of grass per day.

MATERIALS AND METHODS

Adult male NZW rabbits, weighing 2.5-3.0 kg each, were placed in separate cages and observed for 2 weeks prior to the study to ensure their acclimatization to the laboratory environment.

The rabbits were given the designated dose of MSMA orally. Rubber mouth blockers, gastric tubes and syringes were utilized for the dose administration. The dose was followed by 10 ml of distilled water through the gastric tube to ensure that the whole dose was received.

Rabbits were exposed daily to MSMA for 40 days as follows: Group A (four rabbits) dosed at 5 mg MSMA/kg; Group B (two rabbits) dosed at 10 mg MSMA/kg, and Group C (two rabbits) dosed at 20 mg MSMA/kg. At the conclusion of 40 days of daily exposure, rabbits were sacrificed, necropsied, and tissue sections from the liver and kidney were taken for microscopic examination. Tissues were fixed in 10% formalin, cleared in ethyl alcohol, processed by automatic tissue processor, paraffin embedded, sectioned and stained with Harris Hematoxylin and Eosin.

Group D (two rabbits) was used as a control. These rabbits were maintained on an MSMA-free diet of rabbit chow throughout the duration of the experiment. Rabbits were sacrificed at the end of 40 days. Tissues were processed as in the exposed group.

RESULTS AND DISCUSSION

At necropsy, the digestive tract looked hyperemic and overdistended. Intestinal walls were fragile, and the kidney was swollen. The liver showed intense peripheral hyperemia. These findings were observed in all animals in Groups A, B and C.

Table 1. The primary pathological lesions in liver and kidney tissue of rabbits following forty days of exposure to an oral dose of 5, 10, 20 mg MSMA/kg, respectively

Animal Group	MSMA Dose mg/kg	Liver		Kidney	
		Hepatocellular Degeneration	Periportal Inflammation	Interstitial Nephritis	Tubular Nephrosis
A-1	5	3*	2	2	2
A-2	5	2	3	2	2
A-3	5	2	2	1	1
A-4	5	2	2	1	1
B-1	10	3	2	2	3
B-2	10	4	2	2	4
C-1	20	3	3	3	2
C-2	20	4	4	4	2
D-1	0	1	1	1	1
D-2	0	1	1	1	1

*Numerical values represent a subjective rate of 1+ to 4+, with 1+ indicating normal and 4+ indicating the most severe lesions noted in the eight sections examined.

Primary lesions included hepatic cellular degeneration, periportal inflammation, renal tubular nephrosis, interstitial nephritis and vascular hyperemia.

Table 1 shows primary lesions resulting from 40 days continuous exposure to 5, 10, or 20 mg MSMA/kg, respectively. The most severe lesions were found in rabbits exposed to 20 mg/kg, and the mildest were in those exposed to 5 mg/kg dose of MSMA. No lesions were observed in the controls.

The microscopic changes in both liver and kidney were mild to moderate, and appeared reversible. The hepatic changes were diffuse, and would compromise function more than the multi-focal renal lesion. This could explain the fast and more efficient elimination of arsenic in liver compared to kidney over two weeks of clearance as indicated in a companion study.

Similar pathological lesions were reported by Exon et al., (1974), where toxic hepatitis was present in all eight rabbits necropsied at seven to twelve weeks of exposure to MSMA (1.5 mg arsenic/kg/day).

Dickenson (1972) reported multiple foci of coagulative necrosis in the liver, with marked diffuse nephrosis in all five yearling white-faced cattle exposed to 10 mg/kg/day of MSMA for a period of ten days.

The findings of this study indicate that MSMA can result in tissue damage and pathological lesions in NZW rabbits at relatively low doses.

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