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Oral and Dermal Toxicity of MSMA to New Zealand White Rabbits, *Oryctalagus cuniculus*

M. T. W. Jaghabir,[1] A. Abdelghani,[2] and A. C. Anderson[2]

[1]Department of Community Medicine, University of Jordan, Amman, Jordan and [2]Department of Environmental Health Sciences, Tulane University, 1430 Tulane Avenue, New Orleans, Louisiana 70112

The 14 day LD_{50} of monosodium methanearsonate (MSMA) for New Zealand white rabbits was estimated to be 102 mg MSMA/kg body weight. The average size of the rabbit dermal irritant patch tests was 1.0, indicating that MSMA is a mild irritant to intact skin.

Relatively little work has been done on the toxicity of organic arsenicals, especially the herbicide monosodium methanearsonate (MSMA). However, in an initial scientific review of MSMA/DSMA by the EPA (1975), the following observations were reported: Ansar 529, containing MSMA (32.21%) had a LD_{50} of 1.8 g/kg as MSMA in albino rats. The same results (1.8 g/kg as MSMA) were found for Ansar 170 containing 51.55% MSMA. Moderate gastritis was observed in the animals prior to death. Cattle had an LD_{50} of 250 mg MSMA/kg of body weight compared to 1.8 g/kg as MSMA in albino rats. Thus, species variation in tolerance can be demonstrated by the acute oral studies.

The EPA review (1975) reported a dermal study carried out on 6 adult male rabbits. The clipped skin areas of the rabbits were exposed to doses of MSMA for a 24 hour period. The animals were observed for a period of 2 weeks for signs of toxicity following the exposure. The dermal LD_{50} value was found to be between 2 and 4 g/kg.

MATERIALS AND METHODS

Adult male New Zealand White (NZW) rabbits, weighing 2.5-3.0 kg, were placed in separate cages and observed for a period of 2 weeks to ensure their acclimatization to the laboratory environment.

Send reprint requests to A. A. Abdelghani, Sc.D. at the Tulane University address.

Based on the mortality data from a preliminary study, oral doses of 30, 60, 100, 125 and 150 mg MSMA/kg respectively, were selected. One dose was given to each group of 4 rabbits. An additional group of 4 rabbits served as controls.

The rabbits were given the designated dose of MSMA orally, using rubber mouth blockers, gastric tubes and syringes. The dose was followed by 10 mL of distilled water pushed through the gastric tube to ensure that the whole dose was received. Rabbits were observed for mortality for 14 days, and the percent mortality was calculated and plotted vs. MSMA dose, to obtain the LD_{50}.

These studies assessed the dermal irritation effect of MSMA, utilizing the method described by Draize et al. (1944). The dermal test, however, was conducted on intact skin according to the Organization for Economic Cooperation and Development (OECD).

RESULTS AND DISCUSSION

Following the administration of MSMA, rabbits exhibited a variety of the following signs of toxicity: constipation, diarrhea, oligouria, generalized weakness and loss of appetite. The duration and the severity of these signs was related to the oral dose.

All of the rabbits dosed with 60 mg MSMA/kg showed severe milky diarrhea. Changes in the color and amount of urine were also observed. Rabbits treated with 30 or 60 mg/kg showed brownish discoloration of the urine, which was more pronounced in the groups receiving higher doses. Reduction in urine volume was observed in all the dosed groups.

All rabbits showed general weakness and reduction of activity and loss of appetite. None of the signs described above were observed in the control group.

These signs of toxicity resemble those reported by Selby et al. (1977), who stated that mono and disodium methanearsonate can be sources of intoxication for domestic animals. Clinical symptoms and histological findings are similar to those caused by the inorganic forms of arsenic and include gastroenteritis, diarrhea, lower blood pressure and electrocardiogram (ECG) changes.

The cumulative percent mortality of rabbits following oral administration of MSMA is shown in Table 1.

The acute oral LD_{50} for NZW rabbits was estimated to be 102 mg MSMA/kg body weight.

Table 1. Cumulative percentage mortality of rabbits following oral administration of MSMA

Dose (mg/kg	Cumulative Percentage of Mortality
0.0	0.0
30.0	0.0
60.0	25.0%
100.0	50.0%
125.0	75.0%
150.0	100.0%

The data indicate that NZW rabbits are more sensitive to MSMA than other species, such as Sprague-Dawley albino rats, which have an LD_{50} of 1.8 g MSMA/kg (EPA, 1975), snowshoe hares, with an LD_{50} of 173 mg MSMA/kg (EPA, 1975) and cattle with an LD_{50} of 230 mg MSMA/kg (EPA, 1975). The difference in LD_{50} could be due to various factors, including species variation, sex, age, physiological condition of the animals, the method of administration of the dose and environmental conditions, as well as type of diet, temperature and humidity (Hodgson and Galheries, 1980).

The scores of MSMA irritation to intact rabbit skin was obtained from a scale of weighted scores recommended by Draize (1944). The average score of the 12 patches tested on 3 rabbits was 1.0, indicating that MSMA is mildly irritating to the skin. Organic arsenic compounds like those used to treat trypanosomiasis are capable of causing dermatitis as a side effect (Neujean et al., 1948).

The results of this study, however, did not rule out possible dermal effects which include forms of hyperkeratosis, hyperpigmentation and depigmentation, since these changes are generally observed after prolonged exposure to arsenic. It is estimated that several years of exposure to approximately 1 mg of arsenic per day could give rise to dermal effects (WHO, 1981).

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