Toxicologic Evaluation of Diisopropyl Methylphosphonate and Dicyclopentadiene in Cattle

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Abstract. Diisopropyl methylphosphonate (DIMP), and dicyclopentadiene \([3a,4,7,7a\text{-tetrahydro-4,7-methyanoindene}]\) (DCPD), were found as contaminants of groundwater in Colorado. Since there was a potential for cattle to be exposed to these chemicals by drinking well water, a study of their effects was initiated. Eight-to-ten week old calves were given a single dose of either DIMP at 62.5, 125, 250, 500 and 1000 mg/kg of body weight (b.w.) or DCPD at 250, 500, 1000 or 2000 mg/kg of b.w. The calves given DIMP developed tympanitis and ataxia, followed by depression, prostration, and death within two hr after dosing. A slight but significant increase in activated partial thromboplastin time was the only change observed in any of the clinical pathologic parameters. The only gross pathologic changes were acute gastroenteritis with hemorrhages in calves given 1000 mg/kg of b.w. Mild signs of intoxication, ataxia and excess salivation, were observed in calves given 250 mg of DCPD/kg of b.w. At higher doses, these signs were intensified; in addition, calves fell and, while prostrate, exhibited running movements and tonic, clonic spasms. The severity of the signs observed increased as the dose of DCPD increased. All calves given 2000 mg/kg of b.w. and one calf given 1000 mg/kg of b.w. died before seven days after dosing. The only clinical pathologic changes found were increased serum levels of creatine phosphokinase, glutamic-oxalacetic transaminase, and glutamic pyruvic transaminase. The only consistent gross pathologic change was congestion in a variety of tissues in calves given 2000 mg/kg of b.w. A variety of histologic changes were observed in tissues from calves treated with both chemicals. However, these changes were not consistent for any one dose level and were not dose dependent. DIMP was slightly toxic for calves, since no signs of intoxication were observed at doses less than 1000 mg/kg of b.w.
mg/kg of b.w. DCPD exerted detrimental effects on calves at 250 mg/kg of b.w. and was classified as moderately toxic.

Between 1943 and 1957, a variety of chemical wastes were stored in unlined ponds at the Rocky Mountain Arsenal in Colorado by the U.S. Department of Defense. This has resulted in some groundwater contamination by certain of these chemicals (Anonymous 1975); one was diisopropyl methylphosphonate (DIMP), a byproduct of the nerve gas isopropylmethylphosphonofluoridate or sarin. Another chemical was dicyclopentadiene [\(3a,4,7,7a\)-tetrahydro-4,7-methyanoindene] (DCPD). The cyclic dienes are used extensively by the agricultural chemical industry in the manufacture of organochlorine pesticides (Kinkeak et al. 1971). DIMP is slightly toxic in mice and rats given a single oral dose; the LD_{50}’s were 1041 and 1363 mg/kg of b.w. for male and female mice, respectively, and 1125 and 826 mg/kg of b.w. for male and female rats, respectively (Dacre and Hart 1975). Application of DIMP to either abraded or intact skin of albino rabbits at doses of 200, 632, and 2000 mg/kg of b.w. caused deaths, 0 of 4, 1 of 4 and 3 of 4, respectively. Subacute-toxicity feeding studies in dogs for 14 days with dietary levels of 150, 500 and 1500 ppm and in rats for 90 days with dietary levels of 300, 1000, and 3000 ppm failed to produce any evidence of toxicity (Dacre and Hart 1975). DCPD is moderately toxic in mice and rats given a single oral dose; the LD_{50}’s were 190 and 250 mg/kg of b.w. for male and female mice, respectively, and 520 and 378 mg/kg of b.w. for male and female rats, respectively (Hart and Dacre 1975). Application of DCPD to the skin of albino rabbits at doses as high as 2.0 mg/kg of b.w. produced only minimal skin irritation and no signs of systemic intoxication (Hart and Dacre 1975).

Since there was no information available on the effects of either of these chemicals on livestock and because of the potential for cattle to be exposed by drinking well water, studies were initiated on the toxicological effects of DIMP and DCPD in this species.

Materials and Methods

Chemicals: Technical DIMP, greater than 99% purity and DCPD, 95% purity (provided by the U.S. Army Medical Bioengineering Research and Development Laboratory of Fort Detrick, MD) were used in this study.

Animals: Thirty-six calves about two weeks old and of mixed breed and sex were purchased at local auctions. The calves were housed at the Veterinary Toxicology Laboratory, and the experiments were started when they were 8 to 10 weeks old. During the acclimatization period, the calves were vaccinated against blackleg and malignant edema (Clostridium Chauvoei-Septicum Bacterin, Haver-Lockhart Laboratories, Shawnee, KA) and were given an oral vaccine for protection against enteric viral and bacterial infections (IDS Scourvac, Norden Laboratories, Lincoln, NE). Thiabendazole (Thibenzone, Merck and Co., Inc., Rahway, NJ) was administered to control internal parasites. The calves were fed a pelleted calf feed, and hay was provided ad libitum.

Treatment and Sampling Schedule: Calves were divided into nine groups of four animals (two males, two females) each. Dosage schedules were established in preliminary studies with 5 to 10-day-old calves. The DIMP was given at 62.5, 125, 250, 500 and 1000 mg/kg of b.w. in single oral doses. The DIMP was placed in gelatin capsules, which were administered with a balling gun. The DCPD was given at 250, 500, 1000 and 2000 mg/kg of b.w. as a single oral dose via gastric intubation. In both studies, blood and urine samples were collected at 1 and 12 days before