

## Research Note

### THE EFFICACY OF MK-401 (4-AMINO-6 TRICHLOROETHENYL-1,3-BENZENEDISULFONAMIDE) AGAINST *FASCIOLA HEPATICA* IN CATTLE UNDER PUERTO RICAN CONDITIONS<sup>1</sup>

Fascioliasis is one of the important parasitic diseases affecting cattle<sup>2</sup>. An accurate determination of the loss to the cattle industry due to fascioliasis is not easy. However, the amount of direct loss due to condemnation of infested livers at time of slaughter can be estimated. USDA records reveal that the livers of 32% of cattle killed at the 9 slaughterhouses on the island during 1976 were condemned because of fluke infestation<sup>3</sup>. This represents a direct loss to the livestock industry of over a million dollars. Other direct losses, such as death from fascioliasis, cost of medicines and treatment are harder to estimate. Losses due to indirect causes such as poor feed conversion and low quality meat are also difficult to determine.

Control of fascioliasis is directed towards the destruction of the intermediate host snail, *Lymnaea cubensis*, and its habitat<sup>4</sup>. Flat and poorly drained pasturelands, very common in Puerto Rico, permit water to accumulate during the rainy season. Mild ambient temperature, combined with high rainfall and humidity, makes control of fascioliasis in pastures extremely difficult. In addition, the ability of the snails to undergo cryptobiosis or aestivation is a problem not easy to solve.

No effective chemotherapeutic agent to control fascioliasis is available at present. Hexachlorethane<sup>5</sup>, the only drug approved by the FDA for the treatment of fascioliasis, was withdrawn from the market because insufficient data on the safety and efficiency of the drug was furnished by the manufacturer. Albendazole<sup>6</sup>, the only flukicide being considered for new drug approval by the Food and Drug Administration, is effective only against mature liver-flukes.

<sup>1</sup> Manuscript submitted to Editorial Board June 25, 1981.

<sup>2</sup> De León, D. D., Ritchie, L., and Chiriboga, J., 1971. Programa de *Fasciola hepatica* en Puerto Rico. First Report, January 1970 to April 1971, PRNC-148.

<sup>3</sup> Frame, A. D., Bendezú, P., Mercado, H., Otiniano, H., Frame, S. J., and Flores, W., 1979. Increase of bovine fascioliasis in Puerto Rico as determined by slaughterhouse surveys, J. Agric. Univ. P. R. 63 (1): 27-30.

<sup>4</sup> Chiriboga, J., De León, D., and Rodríguez-Frías, J., 1980. Epidemiology of *Fasciola hepatica* infestation in dairy cattle at Dorado, Puerto Rico, J. Agric. Univ. P. R. 64: (1) 93-106.

<sup>5</sup> Anon., 1980. Hexachlorethane being distributed illegally, JAVMA 177: 398.

<sup>6</sup> Anon., 1980. Two states may receive Albendazole, JAVMA 177: 1080.

MK-401 (4-amino-6-trichloroethenyl-1,3-benzenedisulfonamide), a new drug developed by Merck, Sharp and Dohme, is reported to be effective against mature and immature *F. hepatica* worms and has a large margin of safety<sup>7</sup>. It was thought worthwhile to assess the efficacy and safety of MK-401 when given at different dosages to calves artificially infected with *F. hepatica* and raised under the typical management conditions of Puerto Rico.

A total of 20 Holstein-Friesian and Brown Swiss male and female calves, approximately 3 to 5 months old, were brought to the dairy farm at the Gurabo Experiment Substation, University of Puerto Rico. The calves were identified, weighed, and given "Levamisole" to expel the gastro-intestinal parasites.

The 20 calves were randomly allotted to 4 groups of 5 calves each and given orally 500 to 600 *F. hepatica* metacercariae in sealed gelatin capsules. Two months later, Group I Control was given placebo orally and Groups II, III, and IV were given MK-401 *per os* at 3, 6, and 12 mg/kg bodyweight, respectively.

At 3 weeks after administration of the drug, all the calves were weighed and slaughtered. The livers were isolated and identified. The bile ducts were dissected, and the liver-flukes were collected and counted. The livers were cut into small pieces of 7.5 to 10.0 cm and placed in a pail containing warm physiological salt solution. After 30 minutes, the liver fragments were removed from the pail and disposed of. The physiological saline solution was filtered through a sieve. The flukes were collected, counted, and preserved in a 70% alcohol solution. The gall bladders were emptied in individual beakers and the eggs of *F. hepatica* were collected and allowed to develop.

Also a section of the duodenum, where the bile duct enters, was removed. Both ends of the section were tied and examined for adult *F. hepatica*. Carcass remains were doused with creoline solution and buried deeply under the ground.

At 3 mg/kg bodyweight, MK-401 was less effective against *F. hepatica*, as indicated by the presence of 1 to 16 8-week-old flukes in the liver of the treated calves. At 6 and 12 mg/kg bodyweight, the drug had a 100% efficacy against *F. hepatica*. No adverse reaction was observed in the experimental calves after the drug was administered. MK-401 had no

<sup>7</sup> Mrozik, H., Bochis, R. J., Eskola, P., Matzuk, A., Waksmunski, F. S., Olen, L. E., Schwartz-Kopf, G., Grodski, A., Linn, B. O., Lusi, A., Wu, M. T., Shunk, C. H., Peterson, L. H., Milkowski, J. D., Hoff, D. R., Kulsa, P., Ostlind, D. A., Campbell, W. C., Riek, F. R., and Harmon, R. E. New fasciolicides with benzenesulfonamide structures, Abstr. of Papers 173rd Nat. Meet. Am. Chem. Soc., New Orleans, March 20-25, 1977, MEDI-15.

ovicidal property on *F. hepatica*. The eggs collected from the gall bladders of the treated calves developed and released miracidia.

Necropsy revealed that the calves given placebo had 19 to 120 immature and mature liver-flukes.

*Delfín de León*

*Rubén Quiñones*

*Department of Animal Industry*