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EFFECTS OF SIX FASCIOLICIDES AGAINST *Fascioloides magna* IN WHITE-TAILED DEER

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Abstract: Thirty-three white-tailed deer (*Odocoileus virginianus*) of various ages, both sexes, and in good physical condition were captured for anthelmintic evaluation of six compounds against the large American liver fluke, *Fascioloides magna.* Based on fluke mortality, hexachlorophene administered at the rate of 12 to 26 mg/kg of body weight was lethal to 5 of 10 mature flukes in seven deer. Nitroxynil at 11 to 24 mg/kg inhibited egg production, but did not kill mature flukes in eight deer. Rafoxanide at 12 to 25 mg/kg killed 6 of 8 (75%) immature flukes in eight deer, but was not effective against 17 mature flukes. Clioxanide at 16 to 38 mg/kg, diamphenethide at 255 to 280 mg/kg, and hexachloroethane at 463 to 629 mg/kg were not effective against *F. magna* in four, two and four deer, respectively. There was no indication that treatment with fasciolicides at the higher dose rates was more efficacious than at the lower dose rates.

Detection of fluke eggs in the feces was a reliable method for diagnosing the presence of mature *F. magna* in deer prior to treatment, but was not reliable for measuring fasciolicidal activity of all compounds tested.

INTRODUCTION

The white-tailed deer (*Odocoileus virginianus*) is a natural definitive host of the large American liver fluke, *Fascioloides magna.*[9,20] The mature flukes in the liver are enclosed in fibrous capsules which connect to the biliary system by afferent and efferent ducts, allowing passage of eggs in the feces. With suitable environmental conditions and an intermediate snail host, the life cycle can be completed.

Fascioloides magna is commonly found in sheep and cattle that share pastures with infected deer in areas where suitable intermediate snail hosts are present.[5,6,11,14,20] In these animals, the fluke normally does not complete the life cycle. Infection in sheep is usually fatal before the fluke matures[5,9,20] and is rarely detected by fecal examination. In cattle, mature flukes are isolated in closed capsules that do not connect to the biliary system. Eggs do not pass out in feces except in occasional cases of severe hepatic damage.[8] Infection in cattle is therefore difficult to diagnose by fecal examination.

In the United States, *F. magna* and *Fasciola hepatica,* the common liver fluke of sheep and cattle, are annually responsible for 1-1.5 million bovine liver condemnations,[1] resulting in an economic loss to the cattle industry. Anthelmintic therapy against *F. hepatica* in cattle and sheep has been extensively investigated,[2,3,12,17,21,22] whereas efficacy of anthelmintic therapy against *F. magna* in cattle has been reported only once.[8] In a parallel study, using deer,[7] oxyclozanide was reported to be efficacious against mature *F. magna.*

The purpose of this work was to investigate experimental treatment of *F. magna* infections in white-tailed deer as a possible method of control. The six anthelmintics tested have been shown to

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be efficacious against *F. hepatica* in livestock, but efficacy against *F. magna* had not been investigated. The white-tailed deer was used in these experiments, because it is a common definitive host and mature infections can be diagnosed by fecal examination. Even though prepatent infection is not demonstrable by fecal examination, activity against immature *F. magna* also could be tested because of the high prevalence of infection in deer from this area.[6,10]

MATERIALS AND METHODS

Thirty-three deer were live-trapped by means of a drop net[16] or immobilized with succinylcholine chloride and Cap-Chur equipment[1] on the Welder Wildlife Refuge, Sinton, and the P. H. Welder Ranch, Victoria, Texas. Deer collected on the Ranch were transported to the Refuge in an enclosed horse trailer. The deer consisted of five males and 28 females, ranging between 8 months and 7 years in age, and between 27.3 and 50.0 kg in weight. They were aged according to tooth eruption and wear of the lower molars.[18]

A fecal sample was collected from the rectum and examined for fluke eggs using a modified sedimentation technique.[19] A negative result did not rule out the possibility of immature fluke infection and each deer was treated with one of the fasciolicides on the day it was captured.

Clioxanide,[2] diamphenethide,[3] hexachloroethane,[4] hexachlorophene,[5] and rafoxanide[6] were administered as a single oral drench at the recommended dose rates for cattle and sheep. Nitroxynil[7] was administered as a subcutaneous injection. The chemical compounds, dose rates used, number of deer with patent infections, and total deer per group are shown in Table 1. At least one deer with a patent infection was included in each group. After treatment, deer were held in a 0.4 ha enclosure where their food consisted of natural grasses, supplemented with kernel corn.

The deer were killed from 1 to 40 days after treatment, weighed, and examined within one hr of death. Fecal samples were collected from each deer and examined for fluke eggs. The liver of each animal was removed, cut into 5 mm slices, and examined for flukes or lesions. The sliced liver was washed in warm water and the sediment examined for complete flukes, decomposing flukes and fluke eggs. Flukes were examined under 4X magnification, sectioned, stained with hematoxylin and eosin, and examined for eggs in the uteri. Decomposition of the specimens was the criterion used for indicating fluke mortality.

During this same time period, 129 deer were collected from the same areas by shooting.[6] A similar postmortem examination was conducted on these animals.

RESULTS

Fecal Examination

Fluke eggs were detected in 15 of 33 (45%) deer in these experiments (Table 1). Deer with patent infections were distributed among the seven treatment groups. At the time of necropsy, 10 of 15 (67%) deer with patent infections had fluke eggs (positive) in their feces. Eggs were not recovered at necropsy from 2 of 3 deer with positive feces and treated with hexachlorophene at 12 to 26 mg/kg, and from 3 of 4 deer with positive feces and treated with nitroxynil at 11 to 24 mg/kg. At necropsy, there was a direct correlation between the disappearance of eggs in feces and death of mature flukes in those deer treated with hexachlorophene, but not with nitroxynil.

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[1] Palmer Chemical and Equipment Company, Inc., Douglasville, Georgia.
[2] Tremerad; supplied by Parke, Davis and Company, Ann Arbor, Michigan.
[3] Coriban; supplied by William Cooper and Nephews, Chicago, Illinois.
[4] Hexachoethane Drench, William Cooper and Nephews, Chicago, Illinois.
[5] Bisophene; William Cooper and Nephews, Chicago, Illinois.
[6] Supplied by Merck, Sharpe, and Dohme, Rahway, New Jersey.
[7] Trodax; supplied by Hess and Clark, Ashland, Ohio.

TABLE 1. Effects of Six Fasciolicides Tested Against **Fascioloides magna** in 33 White-tailed Deer.

Fasciolicide*	Dose Rate in mg/kg (mean)	No. of Treated Deer	Experimental days (mean)	No. of Deer Passing Eggs		No. of Deer with Mature Flukes at Necropsy	Total Mature Flukes Recovered	Total Dead	%	No. of Deer with Immature Flukes at Necropsy	Total Immature Flukes Recovered	Total Dead	%
				At Treatment	At Necropsy								
Clioxanide	16-38 (27)	4	12-27 (21)	1	1	1	2	0	0	3	3	0	0
Diamphenethide	255-280 (268)	2	6-8 (7)	1	1	1	2	0	0	1	3	0	0
Hexachloroethane	463-629 (540)	4**	12-21 (12)	3	3	3	11	0	0	2	2	0	0
Hexachlorophene	12-26 (17)	7	4-25 (14)	3	1	3	10	5	50	1	1	0	0
Nitroxynil	11-24 (16)	8**	4-26 (14)	4	1	4	12	0	0	2	2	1	50
Rafoxanide	12-25 (16)	8	6-40 (22)	3	3	3	17	0	0	7	8	6	75
Total Treated		33		15	10	15	54	5	9	16	19	7	37
***Field collected		129		—	—	88	323	0	0	47	69	0	0

* Administered as an oral drench, with the exception of nitroxynil which was a subcutaneous injection.

** One deer died during experiment and death was not attributed to treatment.

*** Deer collected from same areas over same period as treated animals.

Postmortem Examination

Examination of the livers from deer which had eggs in their feces at time of treatment revealed that all 15 (100%) had live or dead mature flukes contained within fibrous capsules (Table 1). Immature flukes also were present within hepatic parenchyma in seven of these deer. Of the 18 deer without eggs in feces at time of treatment, none had mature flukes and nine had immature flukes.

In the seven deer treated with hexachlorophene, 5 of 10 (50%) dead mature flukes and one live immature fluke were recovered. Twelve live mature flukes were recovered from deer treated with nitroxynil; fluke eggs were not evident in the uteri of these flukes. One of 2 immature flukes was dead in deer treated with nitroxynil. In the eight deer treated with rafoxanide at 12 to 25 mg/kg, 6 of 8 (75%) dead immature flukes and 17 live mature flukes were recovered. There was no indication that treatment with compounds at higher dose rates was more efficacious than at lower dose rates.

Hexachloroethane at 463 to 629 mg/kg, clioxanide at 16 to 38 mg/kg, and diamphenethide at 255 to 280 mg/kg, were not effective against eight immature or 15 mature *F. magna* in four, four, and two deer, respectively. Dead flukes were not recovered from these animals or from the 129 untreated deer containing 392 flukes also examined from the study areas during the experimental period. Toxicosis associated with anthelmintic treatments was not evident in any of the 33 deer.

DISCUSSION

Although there were no untreated controls in this experiment, dead or decomposing flukes were not found among the 69 immature and 323 mature flukes in the 129 untreated deer collected from the study areas during the experiments (Table 1). The use of white-tailed deer is useful for testing fasciolicidal activity against *F. magna,* because dead flukes are not usually found in untreated deer, and detection of mature flukes by finding eggs in feces is reliable. Postmortem examination is essential to evaluate efficacy of anthelmintics against *F. magna*, especially immature flukes.

Based on fluke mortality, hexachlorophene was moderately efficacious (50%) against mature flukes. The other compounds were not effective against mature *F. magna.* All compounds tested in these experiments have been used for the successful treatment of mature *F. hepatica* infections in sheep and cattle at similar dosages reported here,[2,3,12,17,21,22] but the parasite relationship of *F. magna* is different between cervine and bovine hosts. Flukes are not in the bile ducts and this may account for the reduced efficacies in deer. Relatively few fasciolicides will kill immature *F. hepatica* in livestock because the chemicals do not concentrate around the immature *F. hepatica* in hepatic parenchyma as they do around mature *F. hepatica* in the bile ducts.[4] The activity of the chemicals may also be reduced in the presence of blood, presumably by protein binding.[4] Perhaps these findings help explain the reduced efficacies of the compounds tested against *F. magna.*

Foreyt and Todd[7] reported 100% efficacy of oxyclozanide against 17 mature *F. magna* in eight white-tailed deer. This presently is the only fasciolicide known to be efficacious against mature *F. magna* in cervine hosts.

Rafoxanide at 12 to 25 mg/kg was lethal to 6 of 8 (75%) immature migrating *F. magna* in eight treated deer (Table 1), indicating its potential against immature flukes. Data collected by this laboratory indicate that *F. magna* matures in seven or more months in deer but can remain in the immature migrating state for at least 12 months.[9] Under such conditions, the time of treatment in deer would not be critical in order to kill the fluke before it matures and passes eggs into the environment. Rafoxanide has been shown to have stronger activity against mature *F. hepatica* than immature forms in cattle,[13,15] but was 100% effective at 10 and 15 mg/kg against immature and mature *F. magna* in cattle.[5]

Nitroxynil had an inhibitory effect on egg production of *F. magna* in deer, but did not kill the flukes. Eggs were not

evident in the uteri of flukes in deer killed 17, 18, and 20 days after treatment. Although the fluke was not killed, the potential for transmission was temporarily eliminated. The duration of this inhibition is not known, but similar reports have not been made for *F. hepatica* in cattle.[2]

Although these experiments were designed to investigate chemical control of *F. magna* in domestic ruminants, control of flukes in deer by chemotherapy also needs to be examined as deer herds become more intensively managed and confined, and as the use of block or pelleted feeds, containing protein, mineral supplements, vaccines, and anthelmintics become more feasible. This may be especially true in areas where deer can be easily fed or during times of the year when deer congregate. Anthelmintic control of *F. magna* infection in white-tailed deer or other definitive hosts could theoretically reduce the infection in domestic animals.

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