

Compound Alpha: Comparison of 2 Fasciolicide Formulations in Cattle

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KEY WORDS: *Fasciola hepatica*, experimental fasciolicide, boluses, cattle

ABSTRACT

The efficacy of the 5-chloro-2-methylthio-6-(1-naphthylthio)1*H*-benzimidazole called compound alpha, formulated as boluses or suspension, was evaluated against adult *Fasciola hepatica* in cattle. Twenty-seven steers were infected, each with 600 metacercariae of *F. hepatica*. After 10 weeks of infection, the animals were divided into 3 groups of 9 animals each. Group 1 received boluses at 10 mg/kg p.o. Group 2 received an oral suspension of 10 mg/kg. Group 3 served as an untreated control. Efficacy was calculated on fluke reduction on the treated animals relative to the control. Results showed a 100% efficacy for both formulations.

INTRODUCTION

Fasciolosis is a disease that affects domestic livestock, particularly cattle and sheep, and occasionally human beings. Its control is generally carried out by the use of fascioli-

cide compounds. The fasciolicide activity of the 5-chloro-2-methylthio-6-(1-naphthylthio)1*H*-benzimidazole known as alpha¹ has been previously tested in sheep and cattle.²⁻⁵ However the drug formulated as a bolus preparation has never before been evaluated.

The aim of the present study is to compare the efficacy of compound alpha administered in either bolus or suspension form to cattle artificially infected with *Fasciola hepatica*.

MATERIALS AND METHODS

Animals

Twenty-seven, 4-year-old cross-bred steers weighing approximately 400 kg were used. They were born and located in a free-fluke area at the "GB" ranch in Querétaro, state of Querétaro (Central Mexico). The animals were fed green alfalfa and some commercial pelleted feed for cattle, water being supplied ad libitum.

Experimental Compound

Bolus formulation. Compound alpha was formulated as rapidly disintegrating boluses,

Table 1. Comparative Efficacy of Compound Alpha Formulated as Bolus or 10% Suspension Against Adult *F. hepatica* in Artificially Infected Steers.

Drug Formulation (10 mg/kg p.o.; 9 heifers/group)	Average EpG*		Number of Flukes Recovered			% Animals Excreting Eggs Before/After Therapy	% Efficacy
	Before Therapy Day 0	After Therapy Day 21	Total	Range	Mean (± SD)		
Bolus	111.4*	0.0*	0	0	0	100/0	100*
Suspension	87.6*	0.0*	0	0	0	100/0	100*
Untreated Control	109.8*	355.0†	1761	107–297	195.6 (±68.09)	100/100	—†

EpG = eggs per gram.

*Percentages of fluke or egg reduction with the same symbol are not statistically different ($P < 0.05$).

each containing 4.0 g of the drug. All ingredients were previously mixed and sieved in a No. 30 mesh that was compressed in a Carver-Press. They were prepared 2 days before administration on the basis of the exact weight of each steer.

Suspension formulation. Compound alpha was prepared as a 10% suspension formulated as previously described.⁶

Experimental Procedure

Prior to the experiment, fecal and serum samples from the steers were analyzed by the sedimentation test⁷ and the indirect enzyme-linked immunosorbent assay (ELISA) test⁸ to assure that they were really free of flukes. On Day 0, all steers were infected with 600 metacercariae of *F. hepatica* given orally in a gelatin capsule. They were raised in *Lymnaea cubensis* snails experimentally infected in our laboratory with miracidia from eggs collected from gallbladders of cattle sacrificed at the local slaughterhouse. When the flukes reached 10 weeks of age, the animals were divided into 3 groups of 9 animals each. Group 1 was treated with compound alpha in the form of rapid disintegrating bolus at a dose of 10 mg/kg body weight given orally with the aid of a baling gun for cattle. Group 2 was also treated with compound alpha at a dose rate of 10 mg/kg body weight, with a 50-mL plastic syringe. Group 3 remained as an untreated control.

Slaughter of Animals

Two weeks after the treatment of each group,

the steers were sacrificed. The livers were removed and carefully dissected to search for the flukes, as previously described.⁹

Efficacy

Percent efficacy was calculated by means of the formula previously reported¹⁰:

$$\% E = \frac{\text{No. of flukes in non-treated group} - \text{No. of flukes in treated group}}{\text{No. of flukes in non-treated group}} \times 100$$

In addition, the fluke length of the recovered parasites was obtained to determine the size distribution of the trematodes.

Statistical Analysis

To compare the number of flukes in each group, the non-parametric Wilcoxon rank sum test was used.¹¹

RESULTS

The results of the necropsy fluke counts are shown in Table 1.

Efficacy

The efficacy exerted for both groups was at very high level, eggs or flukes having been 100% removed. The average egg per gram for the untreated control was 109.8 before therapy and 355.0 after therapy. The fluke recovery for the untreated control group was 1761 trematodes (195.6 flukes per animal). An average of 32.6% of the challenge dose was recovered from each liver.

As expected, statistical differences were observed when comparisons on the efficacy of the treated groups versus the untreated control group were made ($P < 0.05$).

Fluke Size Distribution

Flukes generally ranged from a minimum of 107 and a maximum of 265. Here, 2 main peaks of size distribution are observed: one consists of 272 flukes (15.4%) measuring from 15 to 15.9 mm and the other of 319 flukes (18.1%) with a length between 20 to 20.9 mm. The smallest size of fluke recorded is 9.5 mm and the largest, 35 mm. (Figure 1).

Bolus Formulation

Table 2 shows the required ingredients to formulate compound alpha for a bolus presentation. All ingredients were easily obtained, no foreign materials being required to produce them.

DISCUSSION

The use of rapid disintegrated boluses is a common manner to formulate drugs that have a different way of administration.¹²⁻¹⁴ Information obtained from a survey conducted in Trikala (central Greece) reports that tablets and boluses were the most preferred anthelmintic formulation used by 96% of farmers, benzimidazoles and probenzimidazoles being the most broad-spectrum anthelmintics.¹⁵

The study demonstrates that compound alpha given either as a bolus or suspension at a dose rate of 10 mg/kg is highly and equally effective against adult *F. hepatica* in cattle. Like albendazole, compound alpha is transformed in 2 metabolites, sulphoxide and sulphone, the former being the active one.¹⁶ These metabolites, filtered in the portal system and taken to the liver, eliminate the liver flukes present.¹⁷ It is worth mentioning that the boluses were compressed into a small oblong form, thus being very handy to dose with the help of a baling gun. No esophageal injury or adverse effects

Table 2. Formulation of a bolus with the experimental compound alpha

Ingredients	Grams	%
1. Active ingredient	4	30.76
2. Sodium sulphate Lauril	0.065	0.5
3. Aerosil	0.065	0.5
4. Magnesium estearate	0.13	1
5. Avicel Ph 102	2.05	10.77
6. Avicel Ph 200	6.69	51.47
Total:	13	100

Boluses were directly compressed using a Carver-Press.

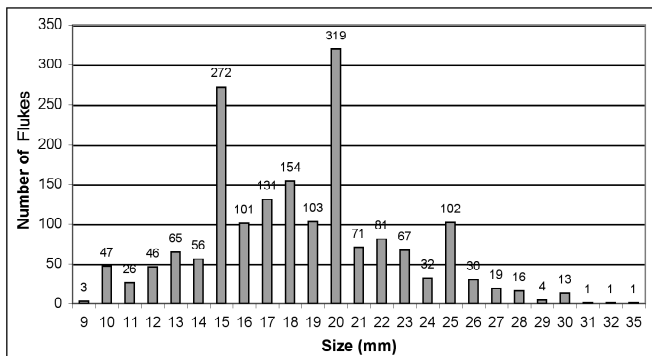


Figure 1. Fluke size distribution of the trematodes collected from the untreated control group

associated with the administration of the boluses were observed.

It is important to note that the effective dose established for compound alpha in cattle is 12 mg/kg p.o.¹⁸ and in this study, even though the fact that the dose used was lower, the efficacy exerted was equally effective. Nevertheless, further confirmation trials should be conducted to determine if 10 mg/kg is a dose to be administered for compound alpha in the future. On the other hand, the maximum tolerated dose of compound alpha is 180 mg/kg, which is 15 times larger than the recommended dose of 12 mg/kg. (Vera et al, unpublished data, May 2005). This safety margin far overtakes the safety index reported for the majority of fasciolicide drugs.^{19,20}

The measurement of the fluke length was carried out to determine if there were statistical differences between untreated or treated flukes since the latter produce

delayed development and thus a possible extension of the prepatent period, as has been demonstrated with triclabendazole.²¹ However, in our study it was not possible to do this since no flukes were recovered in the treated groups. With regard to the average of 32.6% of the challenge dose recovered from each liver, this percentage recovery is similar to that obtained by other authors.^{20,22}

CONCLUSION

Compound alpha dosed at 10 mg/kg p.o. and formulated either as a bolus or suspension is both a very safe and highly effective drug for the treatment of fasciolosis in cattle.

ACKNOWLEDGEMENTS

This study was partially supported by the projects: PAPIIT-DEGAPA, UNAM, IN214502-3, Mexico and CONACYT 34942-B, Mexico, and this study complies with the current laws of Mexico.

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