

## TRIALS WITH RAFOXANIDE\*

### 7. EFFICACY AGAINST *FASCIOLA HEPATICA*, *HAEMONCHUS PLACEI* AND *BUNOSTOMUM PHLEBOTOMUM* IN CATTLE

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#### SUMMARY

Anthelmintic efficacy studies involving 49 cattle either naturally or artificially infested with *Fasciola hepatica* are described. Some of the animals were also artificially infested with *Haemonchus placei* and *Bunostomum phlebotomum*.

At dosage rates of 3,75 and 5,0 mg/kg live mass rafoxanide was 64,6 and 92,6 per cent effective respectively against adult naturally acquired infestations of *F. hepatica*.

At 7,5 and 10,0 mg/kg it was 37,9 and 55,7 per cent effective against 42 day old liver fluke.

At 7,5 mg/kg it was 100, 87,4 and 94,6 per cent effective against mature *F. hepatica*, fourth stage *H. placei* and adult *B. phlebotomum* respectively.

#### INTRODUCTION

The anthelmintic efficacy of rafoxanide (3'-chloro-4'-p-chlorophenoxy)-3,5-diiodosalicylanilide against *Fasciola hepatica* in sheep<sup>1 2 4 6 10</sup> and cattle<sup>3 7 8</sup> has been described by several authors. Its activity against *Fasciola gigantica*<sup>13 14</sup> and *Haemonchus placei*<sup>13</sup> in cattle has also been recorded.

The present paper describes anthelmintic efficacy trials against natural and artificial infestations of *F. hepatica* and artificial infestations of *H. placei* in cattle. Because of the excellent efficacy obtained against adult *Gaigeria pachyscelis* in sheep<sup>6</sup> it was decided to include *Bunostomum phlebotomum* in one of the experiments.

#### GENERAL MATERIALS AND METHODS

A strain of *F. hepatica*, originally obtained from a naturally infested bovine has been maintained at our laboratory in sheep and *Lymnaea columella* since 1969. Metacercariae from these snails, harvested and counted on cellulose strips were used for artificial infestation of the cattle.

Some of the cattle were infested orally with the larvae of *H. placei* and percutaneously with those of *B. phlebotomum*, both of which have been maintained in pure culture in calves raised under worm-free conditions.

The rafoxanide was administered intra-ruminally as a 2,5% preformed suspension either by means of a trochar and cannula or by means of a stomach tube.

At autopsy the liver fluke and nematodes were recovered and counted by methods already described<sup>6</sup>.

#### EXPERIMENT 1

##### Materials and Methods

Thirteen, nine-month-old, Africander type calves were each infested with 400 metacercariae of *F. hepatica* and allocated to three groups.

Forty-two days after infestation five calves were treated with rafoxanide at 7,5 mg/kg and five at 10,0 mg/kg live mass. All the calves were slaughtered 47 to 49 days after treatment.

##### Results

The ranked fluke burdens are summarized in Table 1.

Table 1: EXPERIMENT 1: THE EFFICACY OF RAFOXANIDE AGAINST 42-DAY OLD *F. HEPATICA*

Controls	Numbers of <i>F. hepatica</i> recovered	
	Treated at 7,5 mg/kg	Treated at 10,0 mg/kg
171	22	4
177	40	32
208	157	65
	170	109
	188	202
185	115	82
% Eff	37,9	55,7

Rafoxanide at 7,5 and 10,0 mg/kg was 37,9 and 55,7% effective respectively against six-week-old *F. hepatica*.

##### Discussion

Immature liver fluke in cattle are not as susceptible to the effects of rafoxanide as are fluke of the same age in sheep.

Presidente and Knapp<sup>8</sup> recorded a mean efficacy of

\* RANIDE: Reg. Trade Mark of MSD (PTY) LTD, Merck Sharp & Dohme International, Division of Merck & Co., Inc., Rahway, N.J., U.S.A.

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58,8% against 42- to 47- day old *F. hepatica* in calves drenched at either 7,5 or 10,0 mg/kg live mass. In the present experiment these dosage levels resulted in efficacies of 37,9 or 55,7 per cent. In contrast a dosage level of 7,5 mg/kg resulted in a mean efficacy of 88,9% against 42 day old *F. hepatica* in sheep<sup>6</sup>.

This difference in efficacy is probably due to the slower growth rate of *F. hepatica* in cattle when compared with that in sheep<sup>12</sup>, thus resulting in smaller and less susceptible immature fluke in the former host species at the time of treatment.

## EXPERIMENT 2

### Materials and Methods

Seventeen, 18- month old Africander type cattle were selected on faecal examination from a herd naturally infested with *F. hepatica* and running in the Cradock district of the Cape Province.

Six of these animals were treated with rafoxanide at 3,75 mg/kg and six at 5,0 mg/kg live mass. The remaining five were slaughtered as untreated controls at the Cradock abattoir on the following day and the treated animals were transported to the laboratory where they were slaughtered 16 or 17 days later.

On counting, the liver fluke were divided into two populations consisting of individuals above or below 10 mm in length.

### Results

The numbers of *F. hepatica* recovered from the treated and control animals are summarized in Table 2.

Table 2: EXPERIMENT 2: THE EFFICACY OF RAFOXANIDE AGAINST A PATENT FIELD INFECTION OF *F. HEPATICA*.

Bovine No.	Numbers of <i>F. hepatica</i> recovered		
	< 10 mm	> 10 mm	Total
<b>Untreated controls</b>			
36	24	240	264
48	76	921	997
186	51	353	404
187	56	353	409
195	59	438	497
Mean	53	461	514
<b>Treated at 3,75 mg/kg</b>			
37	23	287	310
41	5	62	67
45	24	292	316
50	1	89	90
188	100	198	298
194	7	2	9
Mean	27	155	182
% Eff	49,1	66,4	64,6
<b>Treated at 5,0 mg/kg</b>			
31	21	19	40
32	10	0	10
39	8	3	11
43	16	17	33
190	13	4	17
197	43	76	119
Mean	18	20	38
% Eff	66,0	95,7	92,6

At 3,75 mg/kg rafoxanide was 49,1% effective against fluke less than 10 mm in length and 66,4% effective against larger fluke. At 5,0 mg/kg these efficacies increased to 66,0 and 95,7% respectively.

### Discussion

The results obtained in this experiment are in marked contrast to those obtained against both natural and artificial infestations of *F. gigantica* in cattle<sup>13 14</sup>. Rafoxanide at a dosage level of 2,5 mg/kg live mass resulted in efficacy of 98,4% against an adult natural infestation of *F. gigantica*<sup>14</sup> and a dose rate of 3,75 mg/kg in efficacy of 98,1% against 98-day old fluke<sup>33</sup>.

## EXPERIMENT 3

### Materials and Methods

Nineteen, four-month-old Sussex x Africander bull calves were each infested with 400 metacercariae of *F. hepatica*. They were also infested percutaneously on a single occasion with 2930 infective larvae of *B. phlebotomum* and on 12 consecutive days with doses of 270 to 310 larvae of *H. placei* administered orally.

Eleven of the calves were treated with rafoxanide at 7,5 mg/kg live mass when the *F. hepatica* were 101 days old (mature), the *B. phlebotomum* 52 days old (adult worms) and the *H. placei* 3 to 14 days old (fourth stage worms). All the calves were slaughtered 21 to 24 days later.

### Results

The ranked worm burdens of the control and treated calves are summarized in Table 3.

Table 3: EXPERIMENT 3: THE EFFICACY OF RAFOXANIDE AGAINST ARTIFICIAL INFESTATIONS OF MATURE *F. HEPATICA*, FOURTH STAGE *H. PLACEI* AND ADULT *B. PHLEBOTOMUM*.

Number of helminths recovered					
<i>F. hepatica</i>		<i>H. placei</i>		<i>B. phlebotomum</i>	
Controls	Treated	Controls	Treated	Controls	Treated
23	0	365	25	4	0
33	0	810	31	7	0
34	0	1 051	44	8	0
56	0	1 087	83	31	0
58	0	1 122	104	34	0
77	0	1 246	146	42	0
88	0	1 292	154	75	1
88	0	1 591	166	93	2
	0		200		4
	0		227		5
	0		309		7
57	0	1 071	135	37	2
% Eff	100,0		87,4		94,6

Rafoxanide dosed at 7,5 mg/kg live mass was 100, 94,6 and 87,4% effective against adult *F. hepatica* and *B. phlebotomum* and fourth stage *H. placei* respectively.

The numbers of *F.hepatica* and *B.phlebotomum* recovered from the untreated controls were disappointingly small when compared with the numbers used for infestation. The efficacy obtained against both these species, however, was so high that large worm burdens in the control animals were not required.

The efficacy against fourth stage *H.placēi* is less than that obtained against fourth stage *H.contortus* in sheep<sup>6</sup>, but whether this is a difference in host or parasite response cannot be determined from the present experiment. The results against adult *B.phlebotomum* closely resemble those against adult *G.pachyscelis* in sheep<sup>6</sup>.

The above results further confirm the efficacy of rafoxanide against some of the important haematophagous parasites of sheep and cattle. Taken in conjunction with the effect against the larvae of *Oestrus ovis*<sup>9</sup> and *Gedoelestia hässleri*<sup>11</sup> they must lead to speculation as to the effect of this compound against other bloodsucking internal and external parasites.

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## REFERENCES

1. ARMOUR J. & CORBA J. 1970 The anthelmintic activity of rafoxanide against immature *Fasciola hepatica* in sheep. *Vet. Rec.* 87 : 213
2. CAMPBELL N.J. & HOTSON I.K. 1971 The anthelmintic efficiency of clixonide and rafoxanide against *Fasciola hepatica* and *Haemonchus contortus* in sheep. *Aust. vet. J.* 47 : 5
3. CAMPBELL N.J. & RICHARDSON NARELLE J. 1972 A controlled test of oxyclozanide and rafoxanide against *Fasciola hepatica* in calves. *Vet. Rec.* 91 : 647
4. CAMPBELL W.C., OSTLIND D.A. & YAKSTIS J.J. 1970 The efficacy of 3,5-diiodo-3'-chloro-4'-(p-chlorophenoxy)-salicylanilide against immature *Fasciola hepatica* in sheep. *Res. vet. Sci.* 11 : 99
5. HORAK I.G., LOUW J.P. & RAYMOND S.M. 1971 Trials with rafoxanide 3. Efficacy of rafoxanide against the larvae of the sheep nasal bot fly *Oestrus ovis*, Linne, 1761. *Jl S. Afr. vet. Ass.* 42 : 337
6. HORAK I.G., SNIJDERS A.J. & LOUW J.P. 1972 Trials with rafoxanide 5. Efficacy studies against *Fasciola hepatica*, *Fasciola gigantica*, *Paramphistomum microbothrium* and various nematodes in sheep. *Jl S. Afr. vet. Ass.* 43 : 397
7. KNAPP S.E. & PRESIDENTE P.J.A. 1971 Efficacy of rafoxanide against natural *Fasciola hepatica* infections in cattle. *Am. J. vet. Res.* 32 : 1289
8. PRESIDENTE P.J.A. & KNAPP S.E. 1972 Anthelmintic effect of rafoxanide against immature *Fasciola hepatica* in calves. *Am. J. vet. Res.* 33 : 1603
9. RONCALLI R.A., BARBOSA A. & FERNANDEZ J.F. 1971 The efficacy of rafoxanide against the larval stages of *Oestrus ovis* in sheep. *Vet. Rec.* 88 : 289
10. ROSS D.B. 1970 Treatment of experimental *Fasciola hepatica* infection of sheep with rafoxanide. *Vet. Rec.* 87 : 110
11. SNIJDERS A.J. & HORAK I.G. 1972 Trials with rafoxanide 4. Efficacy against the larvae of the oestrid fly *Gedoelestia hässleri* in the blesbuck (*Damalisca dorcas phillipsi* Harper, 1939). *Jl S. Afr. vet. Ass.* 43 : 295
12. SNIJDERS A.J. & HORAK I.G. 1973 Unpublished data
13. SNIJDERS A.J., HORAK I.G. & LOUW J.P. 1971 Trials with rafoxanide 2. Efficacy against *Fasciola gigantica* in cattle. *Jl S. Afr. vet. Ass.* 42 : 253
14. SNIJDERS A.J., LOUW J.P. & SERRANO F.M.H. 1971 Trials with rafoxanide 1. *Fasciola gigantica* in cattle in Angola. *Jl S. Afr. vet. Ass.* 42:249

## Bovine Leukemia - Cause Identified

After more than a decade of attempts by local and foreign scientists to determine the cause of bovine leukemia, American scientists have tentatively shown that a C-type virus is the causal agent. (Most viruses associated with other forms of leukemia are similarly classified by structure as C-type viruses).

The work, a co-operative project between the National Animal Disease Center, Ames (Iowa) and the University of Wisconsin, Madison, was facilitated by the use of a short-term lymphocyte technique developed by University researchers. Earlier attempts at identifying the agent responsible for this disease were hampered by difficulties experienced in establishing cell cultures from tumours or white blood cells of affected animals and the inability to link previously isolated viruses with bovine leukemia.

Further progress in this study will be greatly facilitated by a recently developed laboratory method for growing the virus in monolayer cell cultures of tissue from leukemic cattle. Large-scale concentration and purification of the virus will ensure a continuous supply of the virus, in contrast to the previously used lymphocyte culture technique.

Until the scientists can demonstrate tumour production by the candidate virus in lymph tissue of cattle, the above results are to be regarded as tentative. Thus far, studies have already shown the ability of this virus to produce tumours in sheep... a species in which leukemia rarely occurs.

"Agricultural Report" Washington D.C. Agricultural Counsellor (Scientific); Embassy of South Africa; February 1975

## STILLBIRTHS IN SWINE

It has been reported by sources in the U.S. that sows with blood hemoglobin of less than 9 mg/100 ml gave birth to more stillborn pigs than females showing normal hemoglobin readings. The injection of 500 mg of iron dextran or the addition of 100 ppm of iron sul-

phate to the ration prior to parturition reduces the herd stillbirth rate to less than 5%.

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