

Anthelmintic activity of thiabendazole, cambendazole, mebendazole and haloxon against strain M-2 Haemonchus and other gastric nematodes in lambs.

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The effective action of thiabendazole against a wide variety of nematode parasites of various animals was first reported by Brown et al. (1961). One oral dose of 50 milligrams per kilogram in sheep was reported to remove more than 95 per cent of the worms belonging to the genus Haemonchus (Gordon, 1961; Drudge and Szanto, 1963; Lyons et al., 1967) However, Drudge et al. (1964) first reported the development of a strain of H. contortus resistant to thiabendazole given at the dose rate of 44 milligrams. per kilogram. Other investigators, including Conway (1964), Santos and Franco (1967), Smeal et al. (1970) and Theodorides et al. (1970) confirmed observation that the earlier recommended dose of thiabendazole was insufficient in controlling certain strains of H. contortus in sheep.

Certain strains of parasitic nematodes exhibit a cross-resistance to various benzimidazole anthelmintics. Theodorides et al. (1970) first reported that six thiabendazole-resistant strains of H. contortus were cross resistant to parbendazole, a benzimidazole compound related chemically to thiabendazole. Kates et al. (1973) also demonstrated that the thiabendazole-resistant strain of H. contortus was resistant to combendazole, another benzimidazole compound.

The purpose of the present study was to compare the anthelmintic activity of the benzimidazole compounds, thiabendazole, cambendazole, mebendazole, and an organic phosphorus compound, haloxon against a thiabendazole-

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resistant strain of H. contortus and other species of nematodes in the abomasum of sheep.

Materials and methods

Thirty mixed-bred Suffolk lambs were chosen for this experiment from a Woodford County flock because a test (Lyons et al., 1969) showed the animals were infected with a thiabendazole-resistant strain M-1 of H. contortus as well as other species of nematodes. The lambs were allotted to 5 groups of 6 lambs each, based on body weight and worm egg count on feces. Treatment of the various groups was as follows:

- Group 1 : Thiabendazole was administered at a dose rate of 50 milligrams per kilogram of body weight.
- Group 2 : Cambendazole was administered at a dose rate of 20 milligrams per kilogram of body weight.
- Group 3 : Mebendazole was administered at a dose rate of 10 milligrams per kilogram of body weight.
- Group 4 : Haloxon was administered at a dose rate of 50 milligrams per kilogram of body weight.
- Group 5 : Untreated group.

Individual doses of the appropriate anthelmintics were administered to the treated lambs as aqueous drenches by a plastic syringe equipped with a plastic tube. Five days posttreatment all lambs were necrosied for residual worm counts.

At necropsy, the abomasum was dissected from the omasum, and the omasal and pyloric opening were tied. Each abomasum was opened and the contents were emptied into a plastic container. The mucosal surface was rinsed 3 times with tap water. Forty per cent formaldehyde was added to each container at the rate of 50 milliliters per liter of contents to preserve for subsequent sampling and worm enumeration. To ensure complete recovery of the nematodes, the walls of the abomasum were digested in artificial gastric juice. These digests were preserved with formadehyde at the foregoing rate and added to the respective content collections.

The numbers of worm in the abomasum were estimated from replicated small samples. These were taken at the rate of one 50-milliliter for each liter of preserved content. The worms were identified into species under a compound microscope.

Results

According to worm count data (Table 1), There was no removal activity by thiabendazole against mature H. contortus. Low removal activity (28 and 56 per cent) against this species was also found for cambendazole and mebendazole, respectively. However, 100 per cent removal of H. contortus was recorded for haloxon.

Two species of Ostertagia, O. circumcincta and O. trifurcata were presented in these lambs. Thiabendazole was highly effective (96 to 100 per cent) and statistically significant for the removal of mature O. circumcincta and O. trifurcata of both sexes, but it was less effective (74 per cent) against fourth stage larvae of Ostertagia. Cambendazole was also significantly effective (92 to 99 per cent) against the mature stages of both Ostertagia species and 100 per cent for the fourth stage larvae. Mebendazole was 94 per cent effective against Ostertagia females, 69 to 85 per cent against Ostertagia males, and was totally ineffective against fourth stage larvae of this species. Haloxon was 96 per cent effective against both Ostertagia females and O. circumcincta males. This anthelmintic was less effective (76 per cent) against O. trifurcata males and totally ineffective against fourth stage larvae of Ostertagia.

Thiabendazole, cambendazole, mebendazole and haloxon were all highly effective (100 per cent) against mature T. axei.

Table 1. Anthelmintic activity of thiabendazole, cambendazole, mebendazole and haloxon in lambs (6 lambs per group). Controlled test worm collection data.

Parasite	Untreated Group			Treated Group			
	Average Number	Min. - Max. Number	Number of Lamb infected	Average Number	Min. - Max. Number	Number of Lamb infected	Removal (Per Cent)
<u>Haemonchus contortus</u> (mature)	10.7	1-36	6	38.0	4-154	6 ^a	0
<u>Ostertagia spp.</u> (4th stage)	26.7	0-60	4	6.7	0-40	1 ^a	74
<u>Ostertagia spp.</u> (female)	856.7	40-2, 040	6	26.7	0-80	3 ^d	96
<u>Ostertagia circumcincta</u> (male)	536.7	140-1, 140	6	20.0	0-120	1 ^d	96
<u>Ostertagia trifurcata</u> (male)	43.3	20-120	6	0	0	0 ^d	100
<u>Trichostrongylus axei</u> (mature)	13.3	0-60	2	0	0	0 ^a	100
Total (Average per cent)	1,500			80.1			(94)

a - Not significant at the 5 per cent level.

b - Significant at the 5 per cent level.

c - Significant at the 1 per cent level.

d - Significant at the 1 per cent level.

Per cent removal =

Average number of worms in controls minus average number of worms in treated lambs × 100

Average number of worms in controls

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Table 1--Continued

Parasite	Treated Group			
	Average Number	Min. - Max. Number	Number of Lamb infected	Removal (Per cent)
			Cambendazole (20 mg./kg.)	100
<u>Haemonchus contortus</u> (mature)	7.7	0-26	5 ^a	28
<u>Ostertagia</u> spp. (4 th stage)	0.1	0-500	30 ^c	100
<u>Ostertagia</u> spp. (female)	6.7	0-40	1 ^d	99
<u>Ostertagia circumcincta</u> (male)	6.7	0-40	1 ^d	98
<u>Ostertagia trifurcata</u> (male)	3.3	0-20	1 ^d	92
<u>Trichostrongylus axei</u> (mature)	0	0	0 ^a	100
Total (Average per cent)	26.7			(98)

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Table 1 -- Continued

Parasite	Treated Group			
	Mebendazole (10 mg./kg.)			
	Average Number	Min. - Max. Number	Number of Lamb infected	Removal (Per Cent)
<u>Haemonchus contortus</u> (mature)	4.7	1-7	6 ^a	56
<u>Ostertagia spp.</u> (4 th stage)	43.3	0-80	5 ^a	0
<u>Ostertagia spp.</u> (female)	46.7	0-200	3 ^b	94
<u>Ostertagia circumcincta</u> (male)	80.0	0-380	4 ^a	85
<u>Ostertagia trifurcata</u> (male)	13.3	0-60	2 ^b	69
<u>Trichostrongylus axei</u> (mature)	0	0	0 ^a	100
Total (Average per cent)	193.3			(87)

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Table 1—Continued

Parasite	Treated Group		
	Average Number	Min.—Max. Number	Number of Lamb infected Removal (Per Cent)
<u>Haemonchus contortus</u> (mature)	0	0	0 ^d 100
<u>Ostertagia spp.</u> (4th stage)	76.7	0—220	5 ^a 0
<u>Ostertagia spp.</u> (female)	26.7	0—60	4 ^a 96
<u>Ostertagia circumcincta</u> (male)	20.0	0—60	3 ^b 96
<u>Ostertagia trifurcata</u> (male)	10.0	0—40	2 ^b 76
<u>Trichostrongylus axei</u> (mature)	0	0	0 ^a 100
Total (Average per cent)	133.4		(91)

Discussion

A high level of efficacy (91 to 98 per cent) against the gastric nematodes was observed for thiabendazole, cambendazole and haloxon and a reduced level for mebendazole.

The data indicated that thiabendazole at the dose rate of 50 milligrams per kilogram of body weight was totally ineffective in removing mature H. contortus. This is a definite manifestation of resistance to thiabendazole. The latter situation was reported for certain strains of H. contortus in many parts of the world. Drudge et al. (1964) first reported the development of a strain H. contortus in Kentucky resistant to repeated doses of thiabendazole at the dose rate of 44 milligrams per kilogram of body weight. Furthermore, thiabendazole-resistant strains of H. contortus were reported in Arkansas (Conway, 1964), Mississippi (Knight et al., 1967), Brazil (Santos and Franco, 1967), Australia (Smeal et al., 1970), and New Mexico and Oregon (Theodorides et al., 1970).

Evidence is also accumulating that certain strains or isolates of parasitic nematodes are cross-resistant to various benzimidazole anthelmintics. Theodorides et al. (1970) first demonstrated that thiabendazole-resistant strains of H. contortus (5 strains from sheep and 1 strain from Angora goats) were all cross-resistant to parbendazole at the dose rates of 20 and 40 milligrams per kilogram of body weight. Moreover, Kates et al. (1973) found that the thiabendazole-resistant population of H. contortus in sheep was resistant to cambendazole at the therapeutic dose rates of 20 and 30 milligrams per kilogram of body weight.

The data in the present study indicated that the Haemonchus strain M-2 was cross-resistant to other benzimidazole anthelmintics, such as cambendazole and mebendazole. This was evident in the efficacies of 25 to 56 per cent for cambendazole and mebendazole against mature Haemonchus at dose rates of 20 and 10 milligrams per kilogram of body weight, respectively. The results, therefore, confirm those of previously cited authors that certain strains of H. contortus are cross-resistant to various benzimidazole anthelmintics. However, this benzimidazole

-resistant strain of Haemonchus was highly susceptible (100 per cent) to haloxon, an organic phosphorus compound.

Efficacies of thiabendazole, cambendazole and haloxon against mature Ostertagia females, O. circumcincta males and T. axei was favorable (96 to 100 per cent removal). Other investigators, including Armour et al. (1962), Drudge and Szanto (1963), Baker and Douglas (1965), Lyons et al. (1967), Hoff et al. (1970) and Gibbs and Gupta (1972) also reported similar results against these species of nematodes.

Summary

Anthelmintic activities of thiabendazole at the dose rate of 50 mg: per kg., cambendazole at the dose rate of 20 mg. per kg. mebendazole at the dose rate of 10 mg. per kg. and haloxon at the dose rate of 50 mg. per kg. were determined by controlled test method against Haemonchus contortus strain M-2 and other gastric nematodes in 30 mixed-bred Suffolk lambs.

Thiabendazole was highly effective (96 to 100 per cent) against mature Ostertagia circumcincta, O. trifurcata and Trichostrongylus axei, but it was less effective (74 per cent) against fourth stage Ostertagia. There was no removal activity of thiabendazole against mature H. contortus.

Cambendazole was highly effective (92 to 100 per cent) against mature O. circumcincta, O. trifurcata, T. axei and fourth stage Ostertagia. Mature H. contortus was partially removed (28 per cent) by this anthelmintic.

Mebendazole was highly effective (94 to 100 per cent) against mature T. axei and Ostertagia females. Less effective action was recorded against the other species, ranging from 85 per cent for O. circumcincta males, 69 per cent for O. trifurcata males to 56 per cent for mature H. contortus.

Haloxon was highly effective (96 to 100 per cent) against mature H. contortus, O. circumcincta males, Ostertagia species females and T. axei, whereas it was less effective (76 per cent) against O. trifurcata males.

The data indicated that H. contortus strain M-2 was resistant to thiabendazole and other benzimidazole anthelmintics - cambendazole and mebendazole.

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สรุป

การศึกษาประสิทธิภาพของไทอาเบนดาโซล, แคมเบนดาโซล, มีเบนดาโซล และ ฮาดีอากซอนต่อ Haemonchus strain M-2 และพยาธิตัวกลมในกระเพาะอื่นๆ ในแกะ ศึกษาประสิทธิภาพของยาถ่ายพยาธิไทอาเบนดาโซลในขนาด 50 มก. ต่อ กก. แคมเบนดาโซลในขนาด 20 มก. ต่อ กก. มีเบนดาโซลในขนาด 10 มก. ต่อ กก. และ ฮาดีอากซอนในขนาด 50 มก. ต่อ กก. โดยวิธี Controlled Test ต่อ Haemonchus contortus strain M-2 และพยาธิตัวกลมในกระเพาะอื่นๆ ในแกะ

ไทอาเบนดาโซลมีประสิทธิภาพสูง (96 ถึง 100%) ในการขับตัวแก่ Ostertagia circumcincta, O. trifurcata และ Trichostrongylus axei แต่มีประสิทธิภาพน้อย (74%) ในการขับตัวอ่อนระยะที่ 4 ของ Ostertagia ไทอาเบนดาโซลไม่มีประสิทธิภาพในการขับตัวแก่ H. contortus เลย

แคมเบนดาโซลมีประสิทธิภาพสูง (92 ถึง 100%) ในการขับตัวแก่ O. circumcincta, O. trifurcata, T. axei และตัวอ่อนระยะที่ 4 ของ Ostertagia ยานี้ขับตัวแก่ H. contortus ได้เพียงบางส่วน (28%)

มิเบนดาโซลมีประสิทธิภาพสูง (94 ถึง 100%) ในการขับตัวแก่ T. axei และ Ostertagia ตัวเมีย ยานี้มีประสิทธิภาพน้อยในการขับพยาธิชนิดอื่น ๆ โดยขับ O. circumcincta ตัวผู้ได้ 85% O. trifurcata ตัวผู้ได้ 69% และขับตัวแก่ H. contortus ได้ 56%

ฮาล็อกซอนมีประสิทธิภาพสูง (96 ถึง 100%) ในการขับตัวแก่ H. contortus, O. circumcincta ตัวผู้ Ostertagia species ตัวเมียและ T. axei แต่ยานี้มีประสิทธิภาพน้อย (76%) ในการขับ O. trifurcata ตัวผู้

ผลจากการทดลองแสดงให้เห็นว่า H. contortus strain M-2 ต่อยาต่อไทอาเบนดาโซล และยาถ่ายพยาธิเบนซิมิดาโซลอื่น ๆ ได้แก่ แคมเบนดาโซลและมีเบนดาโซล.