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Therapeutic efficacy evaluation of anthelmintics activity of albendazole and ivermectin drench formulations in donkeys in Darfur, Sudan

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ABSTRACT

The therapeutic efficacies of albendazole and ivermectin drench formulation at the manufacturer's recommended dose were evaluated in a controlled trial in Nyala town, South Darfur State, Sudan. The study involved 24 donkeys naturally infected with gastrointestinal nematodes; they were divided into four groups of equal size. Albendazole was administered orally once at a dose rate of 10 mg/kg body mass, or twice, 14 days apart at dose rate of 10 mg/kg body mass. Ivermectin was administered orally as a single dose at 200 µg/kg body mass. Treatment efficacy was based on the mean faecal egg count reduction 14 days post treatment. A faecal egg count reduction of 100% was found after treatment with albendazole and ivermectin. In addition efficacy percentages of albendazole and ivermectin against immature and adult nematodes were as follows: *Trichostrongylus axei* 67.09% and 100%, *Parascaris equorum* 100% and 100%, *Oxyuris equi* 100% and 100%, *Strongylus* sp. 98.4% and 100%; and small strongyles 100% and 100%. Albendazole single and twice and ivermectin with the single dose showed moderate efficacy (33%, 59.08% and 62.71%, respectively) against larvae found in the cranial mesenteric artery aneurisms. No adverse reactions were observed in treated donkeys during the experiment period.

Key words: albendazole, donkeys, gastrointestinal nematodes, ivermectin

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Introduction

Albendazole is not used in equines, and there is a paucity of data available in the literature on toxic or side effects in these species (GOKBULUT et al., 2005). A higher metabolic capacity, first-pass effects and lower absorption of benzimidazoles in donkeys decrease bioavailability and efficacy compared to ruminants (GOKBULUT et al., 2005). High intestinal concentrations could be effective against gastrointestinal nematodes that inhabit the gut lumen, but very low plasma concentrations of albendazole may not be effective against migrating fourth larval stages of large strongyles or lung worms. Repeated dosage regimes of albendazole or co-administration with metabolic inhibitors could be used to treat migrating larval or tissue stages of strongyles and lungworms in donkeys (GOKBULUT et al., 2005).

The effect of repeated early-season albendazole (EYSKER et al., 1986) and oxfendazole (EYSKER et al., 1989) treatments was evaluated. The results of these studies invariably showed reduction in faecal egg output after the first treatment but the poor effect of later treatments. Apparently the repeated use of one Benzimidazole within one grazing season is of little prophylactic value (EYSKER et al., 1989a). An important aspect of the epidemiology of cyathostomins infection in equids is the occurrence of inhibited development.

Ivermectin is today an elixir in the world of parasite chemotherapy, in equines. SERI et al. (2005) reported that the efficacy of ivermectin when used as an intramuscular injectable formulation, at a dose rate 200 μg/kg body mass, against arterial stages of *Strongylus vulgaris* was only 69.23%.

The aim of this study was to investigate the therapeutic efficacy of albendazole on a single or repeated dose regimen as an anthelmintic in donkeys harbouring natural gastrointestinal worm infestation and to compare the obtained results with that of ivermectin.

Materials and methods

Experimental animals. In this study we utilized 24 male donkeys (3-10 years). Before starting the study, animals were examined to prove infestation with gastrointestinal helminth parasites. The animals were kept at the premises of the Department of Clinical Studies, Faculty of Veterinary Science, University of Nyala. They were provided with tap water and allowed to graze freely in pasture.

Experimental drugs. The following drug formulations and trade marks were used as experimental drugs: Albendazole suspension, Albendex 25 mg/mL (Avico®, Jordon); Ivermectin drench, Avimec liquid (Avico®, Jordon).

Experimental design. The animals were allocated into four groups and penned according to treatment groups. The first three groups were treated and the last group

remained untreated as a control group. The animals in the three treatment groups received treatment as follows:

Albendazole treated group 1 (ABZT1) received a single oral dose of Albendazole at the manufacturer's recommended dose of 10 mg/kg body weight.

Albendazole treated group 2 (ABZT2) received two oral doses of Albendazole 14 days apart, at the manufacturer's recommended dose of 10 mg/kg body weight.

Ivermectin treated group (IVMT) received a single oral dose of ivermectin drench at the manufacturer's recommended dose of 200 μg/kg body weight.

Then donkeys were monitored for possible adverse or unwanted reactions for 2 hours after administration of each drug.

The experiment extended for 21 days. Faecal samples were collected at 0 (before treatment), 1, 3, 7, 14, and 21 days post treatment. Necropsy of the animals was done at day 21 post treatment for all donkeys.

Animals were euthanized for worm recovery as described by REINECKE and LE ROUX (1972). After the donkeys were euthanized, the thoracic and abdominal cavities were opened by making an incision along the ventral line of the animal and the left half of the thorax and the abdominal wall was removed. The organs from the thoracic and the abdominal cavities were removed from the carcass. The different organs from the gastro-intestinal tract were then isolated by tying double ligatures around the gut to separate it in the stomach, small intestine, caecum, colon and rectum. The contents of the different organs were removed and then sieved through a 150 mm sieve to obtain residue samples. The residues preserved in 10% formalin. Residue samples of ingesta were examined macroscopically. Nematodes present were placed in a specimen bottle containing 10% formalin. Helminths were identified at a later stage by placing them on a glass slide, examining them microscopically and classifying them according to LICHTENFELS (1975).

The anthelmintic efficacy of albendazole was estimated using a faecal egg count reduction test (FECR) for helminths burden. The arithmetic mean of the egg count and helminths burden were calculated to determine the mean percentage reduction within each group, according to the following formula:

$$\text{FECR \%} = \frac{\text{Pre-treatment EPG - Post-treatment EPG}}{\text{Pre-treatment EPG}} \times 100$$

A modified McMaster technique (ANONYM., 1986) was used to count the egg per gram (epg) of faeces.

Results

The results of mean egg per gram of faeces and the range in addition to the reduction percentage of egg per gram of faeces for the three treated groups from day zero to day 21 are presented in the Tables 1, 2 and 3.

Table 1. Mean faecal egg counts (± SD) and reduction percentage for albendazole-treated donkeys

Days	Arithmetic mean (epg)	Range	Reduction%
0	3621.43 ± 3583.05	500-10400	-
1	1221.43 ± 1526.94	200-4500	66.27%
3	21.43 ± 39.34	50-100	98.25%
7	0	0	100%
14	0	0	100%
21	0	0	100%

Table 2. Mean faecal egg counts (± SD) and reduction percentage for albendazole twice-treated donkeys

Days	Arithmetic mean (epg)	Range	Reduction %
0	2462.50 ± 2137.50	1300-4500	-
1	1250.00 ± 574.46	900-2100	49.24%
3	100.00 ±141.42	0-300	92%
7	0	0	100%
14	0	0	100%
21	0	0	100%

Table 3. Mean faecal egg counts (± SD) and reduction percentage for ivermectin-treated donkeys

Days	Arithmetic mean (epg)	Range	Reduction %
0	783.33 ± 625.03	50-1900	0
1	1683.33 ± 1586.72	0-3500	-114.89%*
3	16.67 ± 40.82	0-100	99.01%
7	0	0	100%
14	0	0	100%
21	0	0	100%

Here please note the increase in epg count following death of nematode and expulsion of worms with faeces.

On day 3, Albendazole showed reduction of 97.13% egg per gram count (EPGC), while albendazole with the two doses showed 98.90%. In ivermectin treated group 98.94% of egg per gram count (EPGC) was reported. All three groups reported 100% reduction of egg per gram of faeces on day 7 and till day 21 when animals were euthanized.

Table 4. Summary of harvested worms from control and animals treated with albendazole (ABZT1) drench at necropsy

Organs examined	Control	Albendazole	
		No.	Reduction %
Cranial mesenteric artery			
Strongylus vulgaris	303	203	33.00
Stomach			
Gastrophilus sp.	349	273	21.78
Habronema sp.	291	147	49.48
Trichostrongylus axei	79	26	67.09
Small intestine			
Parascaris equorum	25	0	100.00
Strongyloides westeri	31	10	67.74
Caecum			
Gastrophilus sp.	3151	59	98.13
Strongylus sp.	841	157	81.33
Cyathostomum sp.	6012	0	100.00
Colon and rectum			
Strongylus sp.	6800	109	98.40
Cyathostomum sp.	37660	701	98.14
Oxyuris equi	3151	0	100.00

The results of post-mortem findings are presented in the Tables 4, 5 and 6 for the three groups. Albendazole showed efficacy of 97.13% at single dose while albendazole at the two doses showed 98.90%, but the efficacy against L4 *Strongylus vulgaris* found in the cranial mesenteric arteries was 33% for albendazole and 59.08% for albendazole twice, as shown in Fig. 1. On the other hand, ivermectin showed 62.71% efficacy against L4 *Strongylus vulgaris*. As shown in Fig. 2., albendazole failed to remove *Gastroophilus* larvae from the stomach of the donkeys.

Table 5. Summary of harvested worms from control and animals treated with albendazole twice (ABZT2) at necropsy

Organs examined	Control	Albendazole twice	
		No.	Reduction %
Cranial mesenteric artery			
Strongylus vulgaris	303	124	59.08
Stomach			
Gastrophilus sp.	349	393	(12.61)
Habronema sp.	291	24	91.75
Trichostrongylus axei	79	0	100.00
Small intestine			
Parascaris equorum	25	0	100.00
Strongyloides westeri	31	0	100.00
Caecum			
Gastrophilus sp.	3151	0	100.00
Strongylus sp.	841	0	100.00
Cyathostomum sp.	6012	50	99.17
Colon and rectum			
Strongylus sp.	6800	54	99.21
Cyathostomum sp.	37660	0	100.00
Oxyuris equi	3151	0	100.00

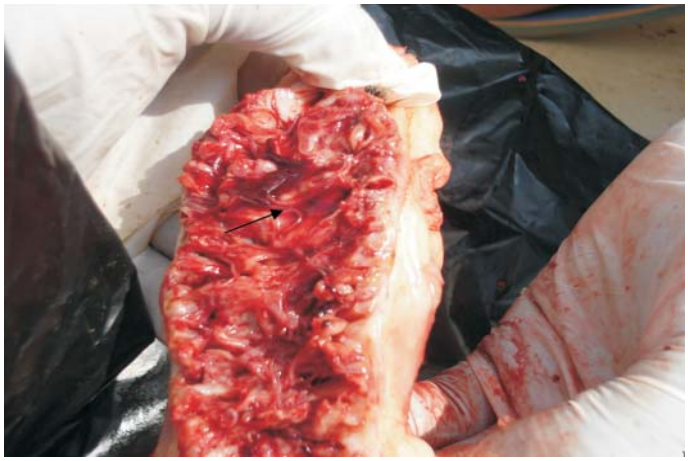

Fig. 1. Larvae of *Strongylus vulgaris* in cranial mesenteric artery removed from albendazole treated donkey

Table 6. Summary of harvested worms from control and animals treated with ivermectin (IVMT) drench at necropsy

Organs examined	Control	Ivermectin	
		No.	Reduction %
Cranial mesenteric artery			
Strongylus vulgaris	303	113	62.71
Stomach			
Gastrophilus sp.	349	0	100.00
Habronema sp.	291	2	99.31
Trichostrongylus axei	79	0	100.00
Small intestine			
Parascaris equorum	25	0	100.00
Strongyloides westeri	31	0	100.00
Caecum			
Gastrophilus sp.	3151	0	100.00
Strongylus sp.	841	10	98.81
Cyathostomum sp.	6012	0	100.00
Colon and rectum			
Strongylus sp.	6800	500	92.65
Cyathostomum sp.	37660	0	100.00
Oxyuris equi	3151	0	100.00

Fig. 2. Larvae of *Gastroophilus* in a stomach removed from albendazole treated donkey

Discussion

Horse strongylids are known to be resistant to Benzimidazoles (BZ) and tetrahydropyrimidines (KAPLAN, 2002, 2004), while the only case of resistance in cyathostomins to microcyclic lactones was reported in a donkey in the UK (TRAWFORD et al., 2005).

The therapeutic efficacy of albendazole in donkeys in this study, in both groups of animals treated either with the single or repeated dose regimen, was 100% reduction in (epg) count on day 7 post treatment. KUZMINA and KHARCHENKO (2008) obtained a similar result at day 10 post treatment in horses treated with albendazole at a dose rate of 5 mg/kg body weight in Ukraine to control *Strongylus* sp.

Following post-mortem, albendazole administered at a single dose resulted in low efficacy of 49.48% against *Habronema* sp.*,* and *Trichostrongylus axei* 67.09%, *Strongyloides westeri* 67.74%; but expressed high efficacy against *Parascaris equorum* 100%; and 81.33%, 98.40% for *Strongylus* sp. present in the caecum, colon and rectum respectively; *Cyathostomum* sp. 100% 98.14% for the caecum, colon and rectum respectively. This result may be explained by the justification of GOKBULUT et al. (2005) who stated that, a higher metabolic capacity, first-pass effect and lower absorption of benzimidazoles in donkeys decrease bioavailability and efficacy compared to ruminants, this explanation also justify the increase in efficacy when we used the double dose for the second group in this study.

Albendazole at a single and multiple dose regimen showed efficacy of 21.78% and 12.61% against *Gastrophilus* sp. Albendazole at two doses 14 days apart showed the following efficacy percentages against: *Habronema* sp. 91.75%; *Trichostrongylus axei* 100%; *Parascaris equorum* 100%, *Strongyloides westeri* 100%*; Strongylus* sp. in the caecum, colon and rectum 100%, 99.21% respectively. *Cyathostomum* sp. in the caecum, colon and rectum 99.17% and 100% respectively; and 100% for *Oxyuris equi.* These results are in agreement with that obtained by KUZMINA and KHARCHENKO (2008) in Ukraine.

Besides the strongylid nematodes, eggs of *Parascaris equorum, Oxyuris equi, Strongyloides westeri* and *Habronema* sp. were found in faecal samples a day before treatment. No eggs of these nematodes were found in horse faeces on the 10th and 14th days after treatment with both drugs.

In this study, ivermectin showed 100% faecal egg count reduction on day 7, which is in agreement with SERI et al. (2005), who reported the same result when using ivermectin injectable formulation intramuscularly at a dose rate of 200 μg/kg body weight in donkeys in the Sudan. The efficacy against *Habronema* sp. was 99.31% this result is in close agreement with that reported in horses by HERD and DONHAM (1984), who showed 1-2

intramuscular doses of ivermectin at 200 μg/kg were highly effective against *Draschia* sp. and *Habronema* sp., while DIPIETRO (1982) revealed 100% efficacy. When ivermectin was given intramuscularly to donkeys at a dose rate of 200 μg/kg, the efficacy was 100% against larvae of *Gastrophilus* sp. (SERI et al., 2005), and this result is in agreement with the results obtained in this study. Ivermectin successfully (100%) removed *P. equorum* from the small intestine when given orally as a paste formulation at 200 μg/kg. Ivermectin totally eliminated the passage of *P. equorum* in the naturally infected horses (COBRA et al., 1986). In the case of *T. axei,* ivermectin (100%) eliminated *T. axei* from the small intestine of donkeys when used at dose rate of 200 μg/kg in intramuscular formulation (SERI et al., 2005). In this study, *Strongylus* sp. were 98.81% eliminated from the caecum and 92.65% from the colon and rectum, which is in close agreement to the cases reported by SERI et al. (2005) of 100% when they used ivermectin injectable formulation intramuscularly for donkeys at a dose rate of 200 μg/kg, which may be attributed to the route of administration that affects the bioavailability of the drug in this study.

Cyathostomum sp. were 100% eliminated from both the caecum and colon in this study, and this result also is in agreement with that obtained by SERI et al. (2005). COSTA et al. (1998) when utilizing ivermectin at the same dose rate of 200 μg/kg for equine in Brazil as a paste formulation, reported efficacy of 100% against *Oxyuris equi*, and the same result was also obtained in this study. In this study, ivermectin expressed moderate efficacy of 62.71% against *Strongylus vulgaris* larvae which were found in the cranial mesenteric arteries. This result is to be considered in the same range with that reported by COSTA et al. (1998) and SERI et al. (2005) who reported 67.8%, 69,23% respectively.

The effect of albendazole against larval stages was lower than against adult worms; this low effect is mainly the result of the limited efficacy of albendazole against larval stages (DRUDGE et al., 1984).

Conclusion

A single or repeated oral dose (14 days apart) of albendazole drench formulation administered at a dose rate of 10 mg/kg body mass was highly efficient against naturally acquired infections of adult *Cyathostomum* sp., *Strongylus* sp., *Trichostrongylus axei, Parascaris equorum*, *Oxyuris equi* and *Strongyloides westeri* gastrointestinal nematodes in donkeys. Neither albendazole nor ivermectin drench formulation used in this study were able to remove L4 larvae of *Strongylus vulgaris* from the cranial mesenteric artery. These findings suggest that further research might be warranted into the use of new dosage regimens of albendazole or ivermectin drench formulation as an equine anthelmintic and to control *Strongylus vulgaris* in the cranial mesenteric artery.

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SAŽETAK

Učinkovitost pripravaka albendazola i ivermektina u preporučenoj dozi istražena je u kontroliranom pokusu provedenom na magarcima u gradu Nyala u južnom Darfuru u Sudanu. Istraživanje je obuhvatilo 24 magarca prirodno invadirana želučanocrijevnim oblićima. Magarci su bili ravnomjerno raspoređeni u četiri skupine te peroralno liječeni albendazolom u dozi od 10 mg/kg tjelesne mase jednokratno ili dvokratno u razmaku od dva tjedna. Ivermektinom su liječeni peroralno i to jednokratno u dozi od 200 mg/kg tjelesne mase. Ljekovit učinak bio je određen na temelju smanjenja broja jaja u izmetu dva tjedna nakon liječenja. Dokazano je bilo 100%-tno smanjenje broja jaja nakon liječenja obama pripravcima. Učinkovitost je bila dokazana i postmortalnom parazitološkom pretragom i to prebrojavanjem nezrelih i odraslih oblića. U liječenih životinja ustanovljeno je 67,9% manje nezrelih te 100% manje odraslih oblića *Trichostrongylus axei*. Stopostotna učinkovitost bila je dokazana za nezrele i za zrele obliće *Parascaris equorum*, *Oxyuris equi* te male strongilide. Nešto manja učinkovitost (98,4%) bila je dokazana za nezrele obliće *Strongylus* sp. Kombinacija jednokratnoga i dvokratnoga davanja albendazola s jednokratnim davanjem ivermektina pokazala je prosječno dobru učinkovitost (33%, 59,08% i 62,71%) protiv ličinki u aneurizmama na području kranijalne mezenterijske arterije. U magaraca nisu bile primijećene nikakve nuspojave nakon primjene lijekova.

Ključne riječi: albendazol, magarci, želučanocrijevni oblići, ivermektin