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Controlled efficacy study of the bioequivalence of Strongid® C and generic pyrantel tartrate in horses

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Abstract

The bioequivalence of Strongid® C and generic pyrantel tartrate was determined in a controlled study using 30 horses with naturally acquired endoparasitic infections. Three horses were randomly allocated to each of ten replicates based on quantitative nematode and ascarid egg counts and fecal larvae culture results. Horses within each replicate were randomly assigned to one of three treatment groups. Horses in Treatment Group 1 received only oats; horses in Treatment Group 2 received generic pyrantel tartrate pellets (2.65 mg pyrantel tartrate kg^{-1}) mixed with oats; horses in Treatment Group 3 were fed Strongid® C pellets (2.65 mg pyrantel tartrate kg^{-1}) mixed with oats. Horses were treated daily for a 30 day continuous treatment period. At the termination of the study the horses were necropsied and endoparasites recovered, identified, and enumerated. In all instances, no significant difference ($P > 0.05$) in mean numbers of parasites recovered existed between horses treated with generic pyrantel tartrate and Strongid® C. Numbers of gastrointestinal parasites recovered from horses treated with generic pyrantel tartrate or Strongid® C were shown to be significantly different ($P < 0.05$) from numbers of gastrointestinal parasites recovered from non-treated controls for the large strongyles (*Strongylus vulgaris*, *S. edentatus*, and *Triodontophorus* spp.), small strongyles (*Cyathostomum* spp., *Cylicocyclus* spp., and *Cylicostephanus* spp.) and fourth-stage *Parascaris equorum*. Numbers of adult *P. equorum* recovered from horses treated with Strongid® C were also significantly different ($P < 0.05$) from those from non-treated controls. Numbers of adult *P. equorum* recovered from horses treated with generic pyrantel tartrate were not significantly different ($P = 0.0761$) from those from non-treated controls. The determination of bioequivalence was based upon the 95% confidence interval of the difference between the mean number of parasites recovered from horses treated with generic pyrantel tartrate and the mean number of parasites recovered from horses

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treated with Strongid® C. For all instances in which the numbers of parasites recovered from horses treated with either Strongid® C or generic pyrantel tartrate were significantly different from the numbers of parasites recovered from non-treated controls, bioequivalence was demonstrated.

Keywords: Horse; Pyrantel tartrate

1. Introduction

Pyrantel tartrate is an imidazothiazole derivative that belongs to the pharmacologic class of tetrahydropyrimidine anthelmintics (Roberson, 1988). Subsequent to the discovery that pyrantel tartrate was therapeutically effective in eliminating adult lumen-dwelling gastrointestinal parasites and prophylactically effective in preventing larval stages of gastrointestinal parasites from penetrating and damaging the mucosa of the gut when administered on a daily basis in the feed (Howes and Lynch, 1966), the anthelmintic was developed by researchers from Pfizer laboratories as a commercially available product for use in horses (Strongid® C, Pfizer, New York, NY) and swine (Banminth®, Pfizer, New York, NY).

An equine parasite control program utilizing Strongid® C is designed to provide a prophylactic method of parasite control during the time that horses are at risk of exposure to gastrointestinal parasitic infection. By killing ingested infective nematode larvae, prior to intestinal penetration and subsequent migration through visceral organs of the equine abdomen and thorax, pyrantel tartrate acts as a true prophylactic anthelmintic which prevents the establishment of potentially harmful gastrointestinal parasites in horses consuming Strongid® C daily. Strongid® C is recommended to be fed daily at a dose of 1 oz of the pyrantel tartrate-medicated, alfalfa–molasses-based pellet per 250 lb of body weight either as a top-dress or mixed in a daily grain ration. This feeding rate provides a daily dosage of 2.65 mg of pyrantel tartrate kg^{-1}.

Since the approval of Strongid® C, the introduction of a true prophylactic method of equine parasite control incorporating the continuous administration of a daily low level of an anthelmintic has gained recognition and acceptance, and has been implemented by all facets of the equine industry. An additional benefit provided by this method of equine parasite control is a reduction in the potential for transmission to horses housed together or grazing common pastures, owing to a decrease of contamination of premises and pasture with parasite ova. Strongid® C is the only product currently available and approved for use in horses in the USA in which pyrantel tartrate is continuously administered at daily low levels for prevention and control of common equine gastrointestinal endoparasites.

Few field or experimental studies have evaluated the therapeutic or prophylactic potential of continuously administered daily low levels of pyrantel tartrate to prevent the establishment of or eliminate previously established equine gastrointestinal endoparasites. Previous investigators have demonstrated the ability of pyrantel tartrate, administered continuously at daily low levels, to prevent infective third-stage larvae of *Strongylus vulgaris* from penetrating the intestinal mucosa, thus preventing further larval migration and resultant subsequent potential pathological consequences of verminous arteritis (US Department of Agriculture, 1990a). The prophylactic potential of Strongid® C to prevent the establishment of small strongyle populations has also been previously demonstrated (Bello and Lan-

ingham, 1992). Several brief communications have described significant reductions in fecal egg counts, over time, in horses consuming continuous daily doses of Strongid® C (Hackett et al., 1988; Daniels et al., 1989; Herd and Majewski, 1993; Slocombe and Lake, 1993; Craig et al., 1993). Recently, a small pilot study reported preliminary findings suggesting efficacy of Strongid® C, when administered continuously at daily low levels, against tapeworms in horses (Greiner and Lane, 1994).

The objective of this study was to determine the bioequivalence of Strongid® C and a generic pyrantel tartrate equivalent (Equi Aid CW®, Equi Aid Products, Inc., Phoenix, AZ) as an equine anthelmintic administered continuously at a daily low level to horses naturally infected with common equine gastrointestinal parasites.

2. Materials and methods

2.1. Animals, housing, and husbandry

Thirty horses representing various breeds, 8–24 months of age (mean 20 months), weighing 171–310 kg (mean 260 kg), were used in this study. Animals selected for use in the study received no previous anthelmintic treatment and harbored moderate to heavy naturally acquired parasite burdens as assessed by quantitative fecal egg counts. Horses were housed in an enclosed large animal research facility at the University of Illinois Veterinary Medicine Research Farm. An acclimation period, prior to treatment, extended over 30 days to permit the horses to acclimate to facilities and feed. Pens were thoroughly cleaned and fresh straw bedding was provided three times weekly. Manure was removed daily from each pen to eliminate the possibility of coprophagia and additional clean straw bedding added as necessary. All animals in the study received identical rations; each horse was individually fed 0.5 l of oats once daily and had free access to trace mineralized salt, fresh water, and alfalfa–grass hay ad libitum. Individual animal body weights were recorded once during the acclimation period and on Study Days 0, 10, 20, and 30. Body weights were used to calculate accurate dosages of generic pyrantel tartrate and Strongid® C pellets for each horse throughout the study.

2.2. Anthelmintics

Generic pyrantel tartrate pellets were manufactured and supplied by Equi Aid Products®, Inc., Phoenix, AZ. Each pound of pellets contained 4.8 g of pyrantel tartrate (10.58 g kg^{-1}) incorporated into a pellet carrier consisting of brewer's insolubles. Each pound of Strongid® C pellets contained 4.8 g of pyrantel tartrate (10.58 g kg^{-1}) incorporated into a pellet carrier consisting of alfalfa meal, wheat middlings, ground corn, and cane molasses.

2.3. Allocation and treatment

Prior to initiation of treatment, horses were rank ordered, first by *P. equorum* egg counts in descending order, second by the presence of patent large strongyle infections identified by fecal culture for third-stage larvae in descending order, and third by strongyle egg counts

in descending order. The first three horses in the ranked list were assigned to the first replicate, the second three horses to the second replicate, and so on, for a total of 30 horses assigned to ten replicates. Horses in each replicate were randomly assigned to treatment groups by use of computer-generated random numbers so that one horse from each treatment group was represented in each replicate. Each pen housed one replicate, with each replicate consisting of three horses representing one horse per treatment group. Horses allocated to Treatment Group 1 were untreated controls; each horse was fed 0.5 l of oats without any medicated pellets each day throughout the study. Horses allocated to Treatment Group 2 were fed generic pyrantel tartrate pellets; each horse received 1 oz of generic pyrantel tartrate pellets per 250 lb of body weight per day, providing a daily dosage of 2.65 mg of pyrantel tartrate kg^{-1}. Horses allocated to Treatment Group 3 were fed Strongid® C; each horse received 1 oz of Strongid® C pellets per 250 lb of body weight per day, providing a daily dosage of 2.65 mg of pyrantel tartrate kg^{-1}. Anthelmintics were fed once daily mixed into 0.5 l of oats. Consumption of oat–treatment mixtures was monitored for approximately 1 h after feeding and any remaining oats or pellets after 1 h were removed from the feed bucket. Remaining anthelmintic pellets were separated out, weighed, and recorded. Anthelmintic treatments were initiated on Treatment Day 0 and continued for 30 days.

2.4. Parasitological techniques

Throughout the study, anthelmintic activity against adult gastrointestinal nematodes was assessed by monitoring changes in quantitative fecal egg counts at 10 day intervals. Fresh fecal samples were collected from each horse on Study Days 0, 10, 20, and 30. Quantitative egg counts of nematode ova were determined by the modified McMaster technique (Whitlock, 1948). The more sensitive Wisconsin technique (Cox and Todd, 1962) was used to determine quantitative egg counts on fecal samples in which no parasite eggs were detected by the modified McMaster technique. Fresh fecal samples were cultured (Ivens et al., 1978) at 10 day intervals, larvae recovered utilizing the Baermann technique (Ivens et al., 1978), and third-stage strongyle larvae examined microscopically to differentiate between large and small strongyles with the aid of a taxonomic key (Georgi and Georgi, 1990).

Parasites recovered at necropsy were subsequently separated from gastrointestinal contents with the aid of a dissecting microscope and temporarily stored in 70% ethyl alcohol. To facilitate imaging of taxonomic detail sufficient for species identification, recovered parasites were cleared utilizing increasing concentrations of ethyl alcohol and immersed in lactophenol for 24 h prior to examination. Fourth-stage larvae and adult nematode parasites were identified to species with the aid of a taxonomic key (Lichtenfels, 1975).

2.5. Necropsy procedures

Horses were anesthetized with 2 g of thiamylal sodium (BIO-TAL®, Bio-Ceutic Laboratories, Inc., St. Joseph, MO) followed immediately by 20 mg of succinylcholine (Sucostrin®, Bristol–Meyers Squibb Co., Princeton, NJ), administered intravenously, and killed by captive bolt immediately followed by exsanguination. The abdomen was opened and double ligatures were placed around the cardia, pylorus, ileocecal junction, and the terminal

colon, to isolate each anatomical section of the gastrointestinal tract. The gastrointestinal tract was then removed in its entirety.

2.5.1. Stomach

The stomach was opened, contents were collected, and the mucosa was washed thoroughly over a 100 mesh screen with 150 μm or less apertures (USA Standard Testing Sieve, Fisher Scientific Co., Springfield, NJ). The combined contents and screened residue was collected and fixed in 10% buffered formalin. *Gasterophilus* spp. larvae that remained attached during the washings were recovered, fixed in 10% buffered formalin, and later identified to genus and species with the aid of a taxonomic key (Soulsby, 1982), and enumerated. The cleaned stomach wall was placed in 750 ml of 0.9% NaCl solution with 3.0×10^6 IU of procaine penicillin G (Pfi-Pen G®, Pfizer, New York, NY) and was incubated for 12 h at 37°C (98.6°F) to facilitate recovery of *Habronema* spp., *Draschia* spp., and/or *Trichostrongylus axei* located within the gastric mucosa. After incubation, each stomach was individually washed with warm water. The washings and the saline solution were screened through 100 mesh screens. The screened residue was fixed with 10% buffered formalin and parasites from the stomach digest as well as the stomach contents were subsequently recovered with the aid of a dissecting microscope, cleared, identified to genus and species, and enumerated.

2.5.2. Small intestine

The duodenum, jejunum, and ileum were opened, contents collected, and the mucosa was washed thoroughly over a 100 mesh screen. The combined contents and screened residue were collected and fixed in 10% buffered formalin. Adult ascarids and tapeworms were collected and fixed in 10% buffered formalin as the small intestine was opened. Parasites from the small intestine were subsequently recovered from the small intestinal contents with the aid of a dissecting microscope, cleared, identified to genus and species, and enumerated.

2.5.3. Cecum and colon

The cecum and colon were opened, contents collected, and the mucosa was washed thoroughly to remove all free parasites. The contents of the cecum, ventral colon, dorsal colon, and small colon, together with the washings of each portion, were mixed uniformly and the volumes of ingesta adjusted to either 20 l or 40 l. Two 5% aliquots of the combined washings were obtained and fixed in 10% buffered formalin. The remaining contents of each portion were then screened over 100 mesh screens for all mature large strongyles and pinworms, which were collected and fixed in 70% ethyl alcohol. The washed surfaces of each part of the cecum and colon were carefully examined for large strongyles attached to the mucosa. Large strongyles attached to the mucosa of the cecum and colon were recovered and fixed in 70% ethyl alcohol. These were subsequently cleared, identified to genus and species, and enumerated.

Recovered adult and immature fourth-stage small strongyles were subsequently separated from aliquots of the combined contents of the cecum and colon with the aid of a dissecting microscope. Because of the extremely large number of parasites in the original large intestinal 5% aliquots, it was necessary to prepare 20% subaliquots. Recovered parasites separated from the 20% subaliquots of the combined contents of the cecum and colon were

cleared, identified, and enumerated. The number of each parasite recovered from the subaliquots was then used to calculate the total number of parasites recovered from each animal at necropsy. Parasites such as ascarids found in abnormal locations in the gastrointestinal tract were considered removed by treatment (Drudge and Lyons, 1977; Duncan et al., 1988).

2.5.4. Mural transillumination

Mural transillumination for quantitation of encysted cyathostome larvae in horses was accomplished similar to a previously described technique (Reinemeyer and Herd, 1986). Uniform (52.8 cm^2), full thickness sections of tissue were taken from each horse at identical locations of the intestinal wall: the proximal portion of the right ventral colon, the distal portion of the right ventral colon, and the distal portion of the mid-cecum.

The cranial mesenteric artery was examined for evidence of verminous arteritis and the presence of viable fourth-stage larvae of *Strongylus vulgaris*. The area immediately beneath the parietal peritoneum of the right abdominal wall adjacent to the cecum was examined at necropsy for developing fourth-stage larvae of *Strongylus edentatus*.

2.6. Statistical methods

A normalizing logarithmic transformation of data was utilized to transform individual values and minimize large distribution violations as follows (Zar, 1984): logarithmic transformation ($\log_{10}(x+1)$). Efficacy of generic pyrantel tartrate and Strongid® C for specific genera and species of endoparasites recovered was calculated by comparing the $\log_{10}$ transformed geometric mean number of parasites found in the untreated animals to the $\log_{10}$ transformed geometric mean number of parasites remaining in the treated animals as follows (Duncan et al., 1988):

$$\text{Efficacy} = \frac{(\text{Geometric mean number of parasites in control animals} - \text{Geometric mean number of parasites in treated animals})}{\text{Geometric mean number of parasites in control animals}} \times 100$$

Efficacies were not determined for individual parasite species in which fewer than six control horses were infected.

Specific guidelines for statistical analysis were adopted from the Food and Drug Administration Bioequivalence Guideline (US Department of Agriculture, 1990b) and the World Association for the Advancement of Veterinary Parasitology (WAAVP) Guidelines for Evaluating the Efficacy of Equine Anthelmintics (Duncan et al., 1988). Both the parametric *t*-test and the nonparametric Mann–Whitney test were used independently to compare generic pyrantel tartrate and Strongid® C treatment groups using a statistical software program (SPSS/PC + ™, Version 5.0, SPSS, Inc., Chicago, IL). In addition, both generic pyrantel tartrate and Strongid® C treatment groups were compared separately with the non-treated controls to insure that the study had adequate sensitivity to detect differences when they actually occurred. For all comparisons the null hypothesis of no difference between the two populations was tested, with an appropriate non-directional, two-tailed alternative hypothesis at the significance level of $\alpha = 0.05$. In the event that both generic pyrantel

tartrate and Strongid® C were shown to be significantly different from the non-treated controls, the determination of bioequivalence was based upon the 95% confidence interval of the difference between the two population means (Conover, 1980).

Total numbers of encysted larvae counted by mural transillumination for each treatment group and total numbers of encysted larvae counted for each treatment group per anatomical site (distal mid-cecum, DMC; proximal right ventral colon, RVA; distal right ventral colon, RVB) were compared by the nonparametric Mann–Whitney test.

3. Results

Arithmetic mean number of parasites recovered at necropsy are summarized in Tables 1 and 2. Geometric mean number of parasites and efficacy based on geometric means are summarized in Tables 3 and 4. The results of this trial demonstrate that the daily administration of pyrantel tartrate to horses at a dose of 2.65 mg pyrantel tartrate kg^{-1} body weight is nearly 100% effective in eliminating adult *Strongylus vulgaris*, with efficacies of 100% and 99.39% for generic pyrantel tartrate and Strongid® C, respectively. Generic pyrantel tartrate was 89.01% effective in eliminating adult lumen-dwelling *Strongylus edentatus*, in contrast to a slightly higher efficacy of 93.32% demonstrated by Strongid® C. Both products were highly effective against adult *Triodontophorus* spp., with respective efficacies of

Table 1
Mean arithmetic number of large and small strongyles recovered at necropsy from horses treated with generic pyrantel tartrate and Strongid® C after continuous administration to naturally infected horses for 30 days

Parasite	Arithmetic mean no. of parasites recovered at necropsy		
	Controls Mean ± SD (range)	Generic Mean ± SD (range)	Strongid® C Mean ± SD (range)
Large strongyles			
Strongylus vulgaris	397 ± 1137 (0-3630)	0 ± 0 (0–0)	0 ± 1 (0–3)
Strongylus edentatus	122 ± 108 (0–289)	31 ± 58 (0–175)	13 ± 17 (0–45)
Triodontophorus spp.	4249 ± 8325 (0–27656)	51 ± 128 (0–405)	12 ± 37 (0–118)
Small strongyles			
Cyathostomum spp.	8717 ± 7126 (3–21916)	80 ± 132 (0–400)	10 ± 32 (0–100)
Cylicocyclus spp.	25232 ± 24024 (3–70065)	1290 ± 1535 (0–4700)	400 ± 591 (0–1800)
Cylicostephanus spp.	21471 ± 19655 (900–73362)	700 ± 901 (0–2900)	270 ± 343 (0–1200)
Fourth-stage larvae [a]	3430 ± 3585 (0–10377)	1160 ± 687 (0–2000)	900 ± 738 (100–2600)

[a] Includes fourth-stage larvae of *Cyathostomum* spp. and *Cylicocyclus* spp.
$n = 10$ for each treatment group.

Table 2
Mean arithmetic number of *Parascaris equorum*, *Oxyuris equi*, *Habronema* spp., and *Gasterophilus* spp. recovered at necropsy from horses treated with generic pyrantel tartrate and Strongid® C after continuous administration to naturally infected horses for 30 days

Parasite	Arithmetic mean no. of parasites recovered at necropsy		
	Controls Mean ± SD (range)	Generic Mean ± SD (range)	Strongid® C Mean ± SD (range)
Ascarids			
Adult *Parascaris equorum*	17 ± 27 (0–88)	1 ± 2 (0–5)	0 ± 0 (0–0)
Fourth-stage *P. equorum*	1 ± 1 (0–3)	0 ± 0 (0–0)	0 ± 0 (0–0)
Pinworms			
Adult *Oxyuris equi*	0 ± 0 (0–0)	1 ± 3 (0–8)	0 ± 0 (0–0)
Fourth-stage *O. equi*	1520 ± 2080 (0–6577)	390 ± 526 (0–1600)	190 ± 203 (0–500)
Stomach helminths			
Habronema spp.	194 ± 378 (7–1248)	94 ± 159 (0–466)	65 ± 88 (4–228)
Bots			
Gasterophilus spp.	298 ± 90 (187–484)	326 ± 135 (113–536)	330 ± 176 (19–547)

$n = 10$ for each treatment group.

99.58% and 99.90% for generic pyrantel tartrate and Strongid® C. Efficacies approached 100% for both generic pyrantel tartrate and Strongid® C in eliminating adult small strongyles, *Cyathostomum* spp., *Cylicocyclus* spp., and *Cylicostephanus* spp. Adult and immature ascarids were recovered from only five control horses at necropsy; however, for purposes of calculation of efficacy, at least six control horses were known to be infected with ascarids as assessed by allocation and pre-treatment quantitative egg counts. Strongid® C was 100% effective in eliminating both adult and fourth-stage *Parascaris equorum*. Generic pyrantel tartrate was 100% effective in eliminating fourth-stage *P. equorum* and 92.13% effective against adult ascarids. An insufficient number of infected non-treated control horses (fewer than six) precluded determination of efficacy calculations for the adult pinworm, *O. equi*. Efficacies for generic pyrantel tartrate and Strongid® C against fourth-stage *Oxyuris equi* were 82.63% and 80.37%, respectively. Pyrantel tartrate treatment had moderate activity against *Habronema* spp., with both products yielding efficacies near 59%. Removal of *Gasterophilus* spp. (0% and 13.91%) as well as fourth-stage small strongyle larvae (0% and 0%) was negligible for both generic pyrantel tartrate and Strongid® C, respectively.

Results of the Mann–Whitney test are illustrated in superscript form in Tables 3 and 4, and summarized in tabular form in Table 5. At the 5% significance level, results of the non-parametric Mann–Whitney test revealed a significant difference ($P < 0.05$) in parasites recovered at necropsy between the non-treated controls vs. horses treated with generic pyrantel tartrate and the non-treated controls vs. horses treated with Strongid® C for all large strongyles (*Strongylus vulgaris*, *S. edentatus*, and *Triodontophorus* spp.), all adult

Table 3
Geometric mean number of large and small strongyles recovered at necropsy and efficacy of generic pyrantel tartrate and Strongid® C after continuous administration to naturally infected horses for 30 days

Parasite	No. of parasites recovered at necropsy [a]			Efficacy [b] (%)	
	Controls Mean ± SD (range)	Generic Mean ± SD (range)	Strongid® C Mean ± SD (range)	Generic	Strongid® C
Large strongyles					
Strongylus vulgaris	24.56 ± 9.00 [a] (0–3630)	0 ± 0 [b] (0–0)	0.15 ± 0.55 [b] (0–3)	100	99.39
Strongylus edentatus	48.24 ± 5.80 [a] (0–287)	5.30 ± 5.92 [b] (0–177)	3.22 ± 4.62 [b] (0–44)	89.01	93.32
Triodontophorus spp.	587.71 ± 21.39 [a] (0–27,541)	2.47 ± 8.12 [b] (0–406)	0.61 ± 3.57 [b] (0–119)	99.58	99.90
Small strongyles					
Cyathostomum spp.	3436.16 ± 11.00 [a] (3–21877)	6.79 ± 13.00 [b] (0–397)	0.59 ± 3.00 [b] (0–99)	99.80	99.98
Cylicocyclus spp.	8259.38 ± 16.00 [a] (3–70794)	240.21 ± 21.00 [b] (0–4676)	86.01 ± 12.00 [b] (0–1818)	97.09	98.96
Cylicostephanus spp.	14493.39 ± 20.00 [a] (890–74130)	94.50 ± 25.00 [b] (0–2883)	122.25 ± 5.00 [b] (0–1201)	99.35	99.16
Fourth-stage larvae [c]	331.51 ± 56.00 [a] (0–10470)	544.88 ± 9.00 [a] (0–1994)	628.51 ± 2.00 [a] (99–2629)	0	0

[a] Means with the same letters in the same horizontal row are not significantly different ($P > 0.05$).
[b] Efficacy based on $\log_{10}$ transformed geometric means.
[c] $n = 10$ for each treatment group.

small strongyles (*Cyathostomum* spp., *Cylicocyclus* spp., and *Cylicostephanus* spp.), and fourth-stage *Parascaris equorum*. A significant difference in recovery of adult *P. equorum* at necropsy existed between the non-treated controls vs. horses treated with Strongid® C. A slightly non-significant difference in recovery of adult *P. equorum* at necropsy existed between the non-treated control horses vs. horses treated with generic pyrantel tartrate ($P = 0.0761$). No significant difference ($P > 0.05$) in numbers of parasites recovered at necropsy between treatment groups existed between horses treated with generic pyrantel tartrate and horses treated with Strongid® C for all parasites evaluated. Testing for differences between means of treatment groups using the *t*-test for independent samples yielded results identical to those of the Mann–Whitney test with one exception. The *t*-test for independent samples revealed a significant difference ($P = 0.037$) for adult *Parascaris equorum* between the non-treated controls vs. horses treated with generic pyrantel tartrate. No significant difference ($P > 0.05$) existed in numbers of parasites recovered at necropsy from non-treated controls and numbers of parasites recovered at necropsy from horses treated with either generic pyrantel tartrate or Strongid® C for fourth-stage *Oxyuris equi*, *Habronema* spp., and *Gasterophilus* spp.

Nonparametric confidence intervals for numbers of parasites recovered from horses treated with generic pyrantel tartrate vs. numbers of parasites recovered from horses treated with Strongid® were calculated for all cases in which both general generic pyrantel tartrate and Strongid® were shown to be significantly different from the non-treated controls (Table

Table 4
Geometric mean number of *Parascaris equorum, Oxyuris equi, Habronema* spp., and *Gasterophilus* spp. recovered at necropsy and efficacy of generic pyrantel tartrate and Strongid® C after continuous administration to naturally infected horses for 30 days

Parasite	No. of parasites recovered at necropsy [a]			Efficacy [b] (%)	
	Controls Mean ± SD (range)	Generic Mean ± SD (range)	Strongid® C Mean ± SD (range)	Generic	Strongid® C
Ascarids					
Adult *Parascaris equorum*	4.25 ± 5.16 [a] (0–88)	0.33 ± 0.86 [a,b] (0–5)	0 ± 0 [b] (0–0)	92.13	100
Fourth-stage *P. equorum*	0.69 ± 0.82 [a] (0–3)	0 ± 0 [b] (0–0)	0 ± 0 [b] (0–0)	100	100
Pinworms					
Adult *Oxyuris equi* [c]	0 ± 0 (0–0)	0.25 ± 0.99 (0–8)	0 ± 0 (0–0)	[c]	[c]
Fourth-stage *O. equi*	144.24 ± 36.15 [a] (0–6606)	25.06 ± 30.62 [a] (0–1584)	28.32 ± 18.05 [a] (0–500)	82.63	80.37
Stomach helminths					
Habronema spp.	63.16 ± 3.47 [a] (7–1,258)	26.25 ± 5.02 [a] (0–466)	25.55 ± 3.17 [a] (4–228)	58.45	59.55
Bots					
Gasterophilus spp.	286.47 ± 0.35 [a] (185–489)	296.37 ± 0.62 [a] (114–536)	246.63 ± 1.82 [a] (19–548)	0	13.91

[a] Means with the same letter in the same horizontal row are not significantly different ($P > 0.05$).
[b] Efficacy based on $\log_{10}$ transformed geometric means.
[c] Insufficient number of infected control animals to analyze statistically or calculate efficacy.
$n = 10$ for each treatment group.

6). As demonstrated by the inclusion of zero by the 95% confidence interval bounds, no difference between generic pyrantel tartrate and Strongid® treatment group means is apparent for all large strongyles (*Strongylus vulgaris, S. edentatus*, and *Triodontophorus* spp.) and all adult small strongyles (*Cyathostomum* spp., *Cylicocyclus* spp., and *Cylicostephanus* spp.). The calculated upper and lower nonparametric confidence interval bonds were both zero for *Parascaris equorum*. Confidence intervals were not calculated for immature ascarids, as no fourth-stage *P. equorum*, in either the generic pyrantel tartrate treated horses or Strongid® C treated horses, were recovered at necropsy.

3.1. Fecal egg counts

The effect of treatment on strongyle egg counts is illustrated in Fig. 1. Strongyle egg counts decreased rapidly following commencement of treatment in horses with either generic pyrantel tartrate or Strongid® C as compared with strongyle egg counts from non-treated control horses. At the first sampling period, Day 10, strongyle egg counts were reduced by 91% and 96%, respectively, in horses treated with either generic pyrantel tartrate or Strongid® C as compared with respective pre-treatment strongyle egg counts. Strongyle

Table 5
Summarized *P* values for the Mann–Whitney test of differences between treatment groups [a]

Parasite	Control vs. generic *P* value	Control vs. Strongid® C *P* value	Generic vs. Strongid® C *P* value
Large strongyles			
Strongylus vulgaris	0.0002*	0.0004*	0.3173
Strongylus edentatus	0.0206*	0.0194*	0.4344
Triodontophorus spp.	0.0020*	0.0006*	0.1643
Small strongyles			
Cyathostomum spp.	0.0004*	0.0001*	0.1110
Cylicocyclus spp.	0.0015*	0.0014*	0.1183
Cylicostephanus spp.	0.0003*	0.0002*	0.4012
Fourth-stage larvae [b]	0.1602	0.1728	0.3064
Ascarids			
Parascaris equorum	0.0761	0.0130*	0.1468
P. equorum, 4th stage	0.0129*	0.0129*	1.0000
Pinworms			
Oxyuris equi, 4th stage	0.1595	0.1415	0.6340
Stomach helminths			
Habronema spp.	0.2727	0.1617	0.5964
Bots			
Gasterophilus spp.	0.5452	0.4055	0.8206

[a] Non-treated controls ($n=10$). Generic pyrantel tartrate treated group ($n=10$). Strongid® C treated group ($n=10$).
[b] Includes fourth-stage larvae of *Cyathostomum* spp. and *Cylicostephanus* spp.
* $P<0.05$.

Table 6
Nonparametric (Mann–Whitney) confidence intervals [a,b]

Parasite	95% Confidence interval
Large strongyles	
Strongyles vulgaris	[0.000; 0.000]
Strongyles edentatus	[−0.860; 0.700]
Triodontophorus spp.	[0.000; 0.480]
Small strongyles	
Cyathostomum spp.	[0.000; 2.000]
Cylicocyclus spp.	[−0.360; 1.420]
Cylicostephanus spp.	[−2.000; 0.850]
Fourth-stage larvae	[−0.190; 0.520]
Ascarids	
Adult *Parascaris equorum*	[0.000; 0.000]
Fourth-stage *P. equorum*	[N/A] [c]

[a] Confidence intervals for the difference of means between generic pyrantel tartrate and Strongid® C treatment groups for all cases in which both treatment groups were significantly different ($P<0.05$) from non-treated controls.
[b] Based on $\log_{10}$ transformed geometric means.
[c] No variance exists for either the generic pyrantel tartrate or Strongid® C treatments, therefore all values in the sample empirical distribution are zero.

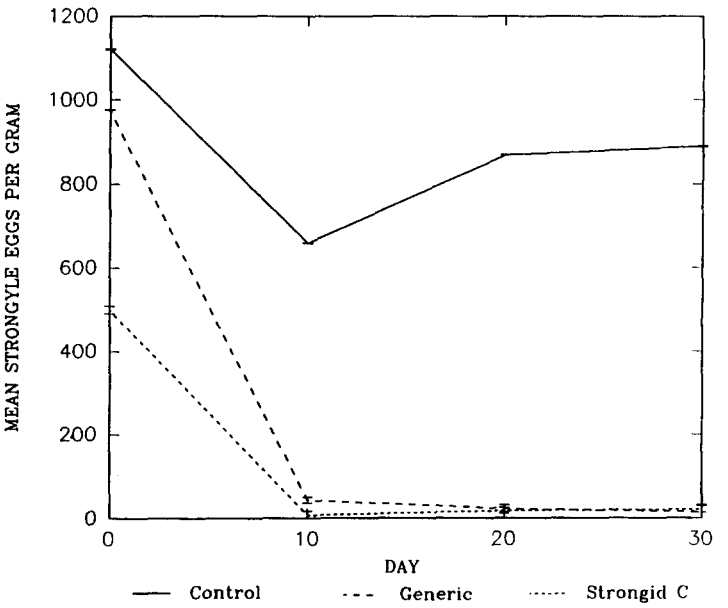

Fig. 1. Change in strongyle egg counts over time after treatment of naturally infected horses with generic pyrantel tartrate or Strongid® C compared with non-treated controls.

egg counts remained at reduced levels for the duration of the study for both anthelmintic treatment groups.

The effect of treatment on ascarid egg counts is illustrated in Fig. 2. Ascarid eggs counts were reduced by 100% at the first sampling period, Day 10, and remained negative for the duration of the study for all horses treated with either generic pyrantel tartrate or Strongid® C as compared with pre-treatment ascarid egg counts.

3.2. Culture of nematode larvae

Culture of nematode larvae from fresh fecal samples collected from non-treated control horses at each 10 day sampling interval yielded both small and large strongyle larvae. Small strongyle larvae recovered from cultures of fecal samples collected from non-treated control horses constituted 94.55% of the cultured larvae population, on average, throughout the duration of the study. Numbers of small strongyle larvae recovered from cultures of fecal samples from horses treated with generic pyrantel tartrate were reduced by 92.0%, 94.0%, and 96.7% on post-treatment Days 10, 20, and 30, respectively, as compared with pre-treatment numbers of small strongyle larvae. Numbers of small strongyle larvae recovered from cultures of fecal samples from horses treated with Strongid® C were reduced by 97.3%, 99.0%, and 99.2% on post-treatment Days 10, 20, and 30, respectively, as compared with pre-treatment numbers of small strongyle larvae. Culture of fecal samples from horses treated with generic pyrantel tartrate and Strongid® C groups at each 10 day interval failed to yield large strongyle larvae.

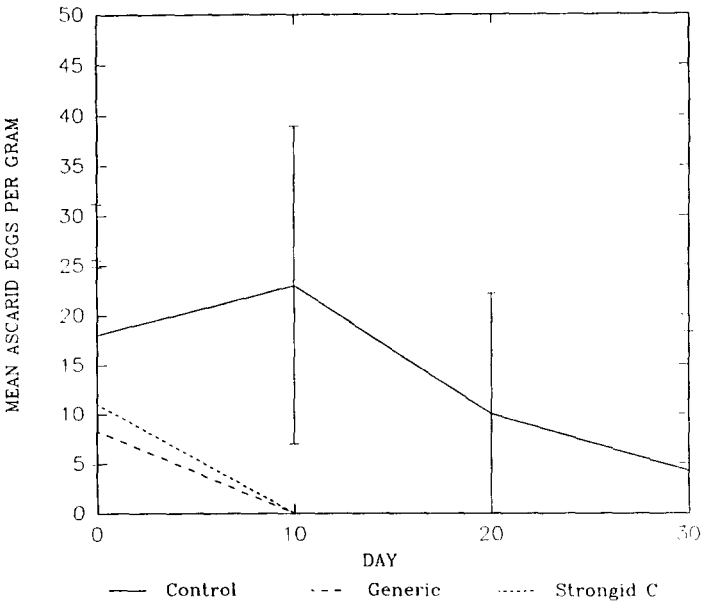

Fig. 2. Change in ascarid egg counts over time after treatment of naturally infected horses with generic pyrantel tartrate or Strongid® C compared with non-treated controls.

3.3. Mural transillumination

Mean numbers of encysted cyathostome larvae were greatest in all three anatomically studied locations (DMC, RVA, and RVB), in non-treated control horses compared with horses treated with generic pyrantel tartrate or Strongid® C (Table 7). Differences between treatment groups were not significant ($P > 0.05$) for total numbers of encysted larvae in all locations or for total numbers of encysted larvae for each anatomical location.

Table 7
Geometric mean numbers of encysted cyathostome larvae [a,b]

Treatment group	Location			Mean totals
	DMC	RVA	RVB	
Controls	87.09 ± 1.88 [a] (27–467)	25.91 ± 4.01 [a] (1–250)	41.66 ± 2.98 [a] (5–301)	168.82 ± 2.09 [a] (35–1023)
Generic pyrantel tartrate	43.66 ± 0.82 [a] (12–92)	27.84 ± 0.74 [a] (12–77)	24.70 ± 1.14 [a] (7–101)	99 ± 0.82 [a] (42–268)
Strongid® C	49.12 ± 1.04 [a] (12–109)	42.65 ± 1.40 [a] (6–119)	34.48 ± 1.09 [a] (12–88)	133.89 ± 0.99 [a] (31–315)

[a] Encysted cyathostome larvae counted per 52.8 cm^2 area.
[b] Means with the same letters in the same horizontal row are not significantly different ($P > 0.05$).
DMC, Distal mid-cecum; RVA, proximal right ventral colon; RVB, distal right ventral colon. $n = 10$ for each treatment group.

3.4. Other observations

All horses in the study had viable fourth-stage *Strongylus vulgaris* larvae present in the cranial mesenteric artery and visual evidence of verminous arteritis at this location. All but two horses, one horse in each of the non-treated control and Strongid® C treatment groups, in the study were noted to have viable fourth-stage *S. edentatus* larvae migrating in a retroperitoneal location adjacent to the cecum on the right abdominal body wall just beneath the parietal peritoneum. No adverse effects attributable to the feeding of pyrantel tartrate were noted in any animals in the generic pyrantel tartrate or Strongid® C treatment groups.

4. Discussion

The daily administration of pyrantel tartrate to horses at a continuous low level was highly effective in eliminating common gastrointestinal parasitic infections of horses, including adult large strongyles (*S. vulgaris*, *S. edentatus*, and *Triodontophorus* spp.), adult small strongyles (*Cyathostomum* spp., *Cylicocyclus* spp., and *Cylicostephanus* spp.), and adult and fourth-stage *P. equorum*. Moderate efficacy was demonstrated against fourth-stage *Oxyuris equi*, and *Habronema* spp., and little to no efficacy against *Gasterophilus* spp. and fourth-stage small strongyle larvae.

Bioequivalence was demonstrated by the 95% confidence interval of the difference between the means of gastrointestinal endoparasites recovered at necropsy from horses treated with generic pyrantel tartrate and horses treated with Strongid® C for all cases in which generic pyrantel tartrate and Strongid® C were each shown to be significantly different ($P < 0.05$) from non-treated controls, including the large strongyles (*S. vulgaris*, *S. edentatus*, and *Triodontophorus* spp.), adult small strongyles (*Cyathostomum* spp., *Cylicocyclus* spp., and *Cylicostephanus* spp.), and fourth-stage *P. equorum*. Numbers of adult *P. equorum* recovered at necropsy from horses treated with generic pyrantel tartrate were slightly non-significantly different ($P = 0.0761$) from numbers of adult *P. equorum* recovered at necropsy from non-treated control horses as evaluated by the nonparametric Mann–Whitney test. As assessed by the parametric *t*-test, the difference was significant ($P = 0.037$). Because the data are non-normally distributed, as evident by the existence of heteroscedasticity and large standard deviations, the results of the non-parametric method of analysis are more reliable and more powerful than those of the parametric method. Although the difference between non-treated control horses and horses treated with generic pyrantel tartrate by the Mann–Whitney test for numbers of recovered adult *P. equorum* was slightly non-significant ($P = 0.0761$), no significant difference exists ($P > 0.05$) between numbers of *P. equorum* recovered from horses treated with either generic pyrantel tartrate or Strongid® C. In addition, both ends of the 95% confidence interval fell on zero. This suggests the possibility that the difference between means of adult *P. equorum* recovered from horses treated with either generic pyrantel tartrate or Strongid® C may be equal to zero and the mean number of parasites recovered from each treatment group may be equal, thus implying that the null hypothesis of no difference between treatment group means cannot be rejected, suggesting bioequivalence.

Few controlled efficacy studies have evaluated the ability of pyrantel tartrate administered at a continuous low level to eliminate gastrointestinal endoparasites in horses. In two recent field studies conducted in Alabama and Wisconsin, extending over 534 days and 535 days for each trial, respectively, a total of 24 horses per study were necropsied at approximately 5, 11, 17, and 23 months after the initiation of daily treatment (US Department of Agriculture, 1990a). For both trials, pooled results of mares and foals for each trial yielded efficacies of 100% against *Strongylus vulgaris* and 100% against *Triodontophorus*, results essentially identical to those obtained in this study. Pooled results of mares and foals yielded efficacies of 98.9% and 100% against *Strongylus edentatus* for the Wisconsin and Alabama study, respectively. Results of this study yielded slightly lower efficacies of 89.01% and 93.32% against *Strongylus edentatus* for both groups of horses treated with either generic pyrantel tartrate or Strongid® C, respectively, than the Wisconsin or Alabama studies. This may be a reflection of a difference in duration of study periods, as, although lower efficacies were recorded for treated horses in this study, the difference was reflected equally in both the generic pyrantel tartrate and Strongid® C treatment groups.

Efficacies documented in this study against small strongyles are in agreement with those recorded in the Wisconsin and Alabama field studies (US Department of Agriculture, 1990a). Efficacies against the small strongyle species (*Cyathostomum* spp., *Cylicocyclus* spp., and *Cylicostephanus* spp.), as well as total adult small strongyle species, approached 100% in both the Wisconsin field study and this study.

Efficacy against fourth-stage small strongyle larvae in this study for both groups of horses treated with generic pyrantel tartrate or Strongid® C was 0%. These results are different from efficacy against fourth-stage small strongyle larvae noted in the Wisconsin study of 99.8% (US Department of Agriculture, 1990a). The most probable explanation may be related to the re-emergence of encysted small strongyles. It is possible that the observed fourth-stage small strongyle larvae recovered at necropsy from horses treated with either generic pyrantel tartrate or Strongid® C were previously encysted small strongyle larvae that recently emerged from the intestinal mucosa to resume development in the lumen of the gut. The therapeutic removal of adult small strongyles from the lumen of the gut may be a catalyst for termination of an arrested state of the encysted small strongyle larvae. In 1953, Gibson suggested that the inhibition of development may be due to the influence of mature parasites present in the lumen of the intestine, and consequently, when this influence was removed after the mature parasites have been eliminated by a dose of anthelmintic, the dormant larvae are able to leave the gastrointestinal mucosa and develop to maturity (Gibson, 1953). When these larvae reach maturity a new inhibitive influence would deter further larvae from leaving the gastrointestinal mucosa. This situation would persist until another dose of anthelmintic removed the new population of mature parasites. This process would be repeated each time a therapeutic dose of anthelmintic is administered, thus resulting in a gradual depletion of the encysted small strongyle larval reservoir in the gastrointestinal mucosa until finally, after multiple treatments, almost all the larvae will have developed into mature parasites and it would be expected that few, if any, larvae would remain in the mucous membrane. It is currently not clearly known whether the maturation of encysted small strongyle larvae is a manifestation of normal population turnover or if luminal adults actually influence tissue larvae to remain in situ (Reinemeyer, 1986).

If the hypothesis suggested by Gibson is accepted, it is theoretically possible for horses harboring encysted stages of small strongyles to eliminate all encysted larval cyathostomes if treatment with a continuous daily low level of pyrantel tartrate is of sufficient duration. Many thousand small strongyles may be encysted in the colonic mucosa and subsequently re-emerge over a variable period of time over the course of treatment. It is therefore likely that fourth-stage larvae would be continuously present in the lumen of the gastrointestinal tract of treated horses consuming a continuous daily low level of pyrantel tartrate. For those horses on a prophylactic parasite control program which incorporated the continuous daily low level administration of pyrantel tartrate, re-emerging larvae contacting the anthelmintic in the gastrointestinal lumen would be killed and subsequently removed by normal peristaltic action.

Activity of pyrantel tartrate against adult and fourth-stage ascarids was excellent, with efficacies of 92.13% and 100% for generic pyrantel tartrate, respectively, and efficacies of 100% against both adult and fourth-stage ascarids for Strongid® C. Both Alabama and Wisconsin field studies reported efficacies against adult and fourth-stage *P. equorum* of 100% (US Department of Agriculture, 1990a). A subsequent study (Ewert et al., 1992) also reported a high efficacy of 99.44% against fourth-stage *P. equorum* in a controlled study of experimentally infected pony foals treated daily with 2.64 mg of pyrantel tartrate kg^{-1} (Strongid® C, Pfizer, New York, NY). An efficacy of 92.13% against adult ascarids noted for horses treated with generic pyrantel tartrate was slightly lower than efficacies reported from both Wisconsin and Alabama field studies. This lower efficacy was influenced by the presence of five adult *Parascaris equorum* recovered at necropsy from one horse and two adult *P. equorum* recovered at necropsy from another horse, both in the generic pyrantel tartrate treatment group. As demonstrated in previous studies, it is likely that as the duration of treatment increases, efficacy would also increase, as all adult *P. equorum* would be expected to be eliminated, thus confirming observations of excellent efficacy against adult ascarids.

An insufficient number of *Oxyuris equi* adult parasites were recovered from control horses to draw conclusions accurately regarding efficacy or differences between control and treated animals. Continuous daily administration of a low level of pyrantel tartrate yielded a high efficacy of 99.4% against adult *O. equi* in the Wisconsin field study (US Department of Agriculture, 1990a). Efficacies noted against fourth-stage *O. equi* larvae of 82.63% and 80.37%, respectively, for horses treated with either generic pyrantel tartrate or Strongid® C were lower than the reported efficacies of 97% in both the Alabama and Wisconsin field studies (US Department of Agriculture, 1990a). Again, this may be a reflection of a difference in duration of study periods, as, although lower efficacies were recorded for treated horses in this study, that difference was reflected equally in both groups of horses treated with either generic pyrantel tartrate or Strongid® C.

Little to no efficacy was observed against *Habronema* spp. and *Gasterophilus* spp. in this study, similar to results of efficacy observed against these parasites in previous studies evaluating the therapeutic activity of pyrantel tartrate in horses (Cornwell and Jones, 1968; Lyons et al., 1974).

All horses in the study had viable fourth-stage larvae of *Strongylus vulgaris* present in the cranial mesenteric artery and visual evidence of verminous arteritis at this location. In addition, all but two horses were noted to have viable fourth-stage *S. edentatus* larvae

migrating in the area immediately beneath the parietal peritoneum of the right abdominal wall adjacent to the cecum. These findings confirm that the continuous daily low level administration of pyrantel tartrate (2.65 mg pyrantel tartrate kg^{-1}) is not effective against *S. vulgaris* and *S. edentatus* larvae undergoing migration in these locations at the time of treatment. Although not examined in this study, similar results would also be expected to be true in the case of fourth-stage *P. equorum* larvae migrating through visceral organs of the abdomen (liver) and thorax (lungs). The provision of a complete comprehensive parasite control program therefore requires horses that have previously been exposed to parasite challenges to be treated with a therapeutic purge dose of a larvicidal product, such as 200 μg of ivermectin kg^{-1} (Eqvalan®, Merck and Co., Rahway, NJ), to eliminate the migratory stages of immature large strongyles or ascarids, prior to placement on a prophylactic program utilizing a continuous daily administration of a low level of pyrantel tartrate.

As in previous reports, fecal egg counts were rapidly reduced by more than 90% as compared with pre-treatment egg counts after the initiation of treatment (Slocombe and Lake, 1993). The reduction of strongyle and ascarid fecal egg counts was similar to the immediate reduction seen within the first sampling period of 7 days in an earlier study in which a low level of pyrantel tartrate was fed daily to seven Arabian horses for 7 weeks (Daniels et al., 1989). A decrease in the number of adult large and small strongyles and ascarids recovered at necropsy from horses treated with either generic pyrantel tartrate or Strongid® C compared with non-treated controls confirmed the observed reduction in fecal egg counts as a measure of a decrease in the total parasite burden harbored by horses treated with a continuous daily low level of either generic pyrantel tartrate or Strongid® C.

Although mean numbers of encysted fourth-stage larvae were greatest in all three anatomically studied locations in non-treated control horses as compared with horses treated with either generic pyrantel tartrate or Strongid® C, the differences were not significant. There appears to be no convincing evidence that any modern anthelmintic has good efficacy at recommended dosages against encysted cyathostomes, nor do any anthelmintics have label claims against encysted third- or fourth-stage larvae within mucosal tissues of the cecum and colon (Herd, 1990). Although several larvicidal dosages of fenbendazole (7.5 mg $kg^{-1} \times 5$ days, 10 mg $kg^{-1} \times 5$ days, or 30 mg kg^{-1}; 60 mg kg^{-1} (Panacur®, Hoechst–Roussel, Somerville, NJ) (Duncan et al., 1977, 1980; Lyons et al., 1983)), oxfendazole (10 mg kg^{-1} or 50 mg kg^{-1} (Synanthic®, Syntex, West Des Moines, IA) (Duncan and Reid, 1978; Kingsbury and Reid, 1981)) and thiabendazole (440 mg $kg^{-1} \times 2$ days (Equizole® Suspension, Merck and Co., Rahway, NJ) (Hopfer et al., 1984)) have been reported to be successful in eliminating encysted cyathostome larvae, the accuracy of the method used to quantitate larval recoveries in those studies has been questioned and larvicidal efficacies reported in those trials may be inaccurate (Reinemeyer, 1986). A high dose of ivermectin (1.0 mg kg^{-1}; Eqvalan® Liquid, Merck and Co., Rahway, NJ) has also been demonstrated to have minimal effect on encysted equine cyathostomes (Klei et al., 1993). Recently reported, a new endectocide, moxidectin gel, appears to have activity against encysted stages of small strongyles. Efficacy of moxidectin against mural cyathostome larvae as determined by mural transillumination or digest was 58.9–71.7%, 85.1–95.2%, and 78.0–91.7% for animals treated with moxidectin 300 μg kg^{-1}, 400 μg kg^{-1} and 500 μg kg^{-1}, respectively (DiPietro et al., 1992).

Although this study demonstrated therapeutic bioequivalence of generic pyrantel tartrate compared with Strongid® C, additional evaluation would be required to demonstrate prophylactic bioequivalence. A prophylactic bioequivalence study would involve similar treatment groups utilizing parasite-free horses continuously exposed to infective parasitic larval challenges, accomplished either naturally by exposure to parasite-contaminated pastures or artificially by experimental infection. Only one prophylactic claim is made for the proprietary product Strongid® C, the prevention of *S. vulgaris* larval infections. A prophylactic bioequivalence study would be capable of demonstrating the potential of generic pyrantel to prevent intestinal penetration and subsequent migration by parasitic larvae of not only *S. vulgaris*, but *S. edentatus* and *P. equorum* as well; Strongid® C has no prophylactic label claims relative to the last two of these. A study to determine prophylactic bioequivalence would also permit evaluation of the prophylactic potential of pyrantel tartrate to prevent intestinal mucosal penetration and subsequent encystment by small strongyle larvae, a label claim also not currently available on the proprietary product, Strongid® C.

Horses on pasture that are maintained on a prophylactic parasite control program incorporating the continuous daily administration of a low level of pyrantel tartrate are protected against intestinal penetration and subsequent pathological consequences of not only large strongyle and ascarid infective larvae but small strongyle larvae as well, which are also capable of causing clinical or subclinical illness. Because encysted cyathostomes appear to be apparently minimally affected by contemporary anthelmintics, additional incentive to utilize control programs that prevent the accumulation of these potentially pathogenic encysted populations, such as the continuous daily administration of a low level of pyrantel tartrate, may be in order.

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References

Bello, T.R. and Laningham, J.E.T., 1992. Evaluation of daily pyrantel tartrate treatment of horses for prevention of intestinal penetration and development of small strongyle larvae resulting from experimentally induced infections. Equine Vet. Sci., 12: 280–286.

Conover, W.J. (Editor), 1980. Practical Nonparametric Statistics, 2nd edn. Wiley, New York, pp. 213–227.

Cornwell, R.L. and Jones, R.M., 1968. Critical tests in the horse with the anthelmintic pyrantel tartrate. Vet. Rec., 82: 483–484.

Cox, D.D. and Todd, A.C., 1962. Survey of gastrointestinal parasitism in Wisconsin dairy cattle. J. Am. Vet. Med. Assoc., 141: 706–709.

Craig, T.M., Scrutchfield, W.L. and Martin, M.T., 1993. Comparison of prophylactic pyrantel and suppressive ivermectin anthelmintic programs in young horses. Equine Pract., 15: 24–29.

Daniels, R.P., Hackett, G.E., Wickler, S.J. and McCormick, R.M., 1989. The anthelmintic efficacy of continuous feeding of pyrantel tartrate to horses. Proc. 34th Annual Meeting of the American Association of Veterinary Parasitologists, 16–18 July 1989. Orlando, FL, p. 27.

DiPietro, J.A., Paul, A.J., Lock, T.F., Ewert, K.M., Todd, K.S. and Aguilar, R., 1992. Efficacy of moxidectin gel in equids. Proc. 37th Annual Meeting of the American Association of Veterinary Parasitologists, 2–4 August 1992, Boston, MA, p. 51.

Drudge, J.H. and Lyons, E.T., 1977. Methods in the evaluation of antiparasitic drugs in the horse. Am. J. Vet. Res., 38: 1581–1586.

Duncan, J.L. and Reid, J.F.S., 1978. An evaluation of the efficacy of oxfendazole against the common nematode parasites of the horse. Vet. Rec., 103: 332–334.

Duncan, J.L., McBeath, D.G., Best, J.M.J. and Preston, N.K., 1977. The efficacy of fenbendazole in the control of immature strongyle infections in ponies. Equine Vet. J., 9: 146–149.

Duncan, J.L., McBeath, D.G. and Preston, N.K., 1980. Studies on the efficacy of fenbendazole used in a divided dosage regime against strongyle infections in ponies. Equine Vet. J., 12: 78–80.

Duncan, J.L., Arundel, J.H., Drudge, J.H., Malczewski, A. and Slocombe, J.O.D., 1988. World Association for the Advancement of Veterinary Parasitology (WAAVP) guidelines for evaluating the efficacy of equine anthelmintics. Vet. Parasitol., 30: 57–72.

Ewert, K.M., DiPietro, J.A., Sanecki, R., Walstrom, D.J. and Todd, K.S., 1992. The effect of daily administration of pyrantel tartrate on the development and larval migration of experimentally induced infections of *Parascaris equorum* in pony foals. Proc. 37th Annual Meeting of the American Association of Veterinary Parasitologists, 2–4 August 1992, Boston, MA, p. 49.

Georgi, J.R. and Georgi, M.E. (Editors), 1990. Parasitology for Veterinarians, 5th edn. W.B. Saunders, Philadelphia, PA, 412 pp.

Gibson, T.E., 1953. The effect of repeated anthelmintic treatment with phenothiazine on the fecal egg counts of housed horses, with some observations on the life cycle of *Trichonema* spp. in the horse. J. Helminthol., 27: 29–40.

Greiner, E.C. and Lane, T.J., 1994. Effects of the daily feeding of pyrantel tartrate on *Anoplocephala* infections in three horses: a pilot study. J. Equine Vet. Sci., 14: 43–44.

Hackett, G.E., McCormick, R. and Mendoza, L., 1988. Comparative efficacy and safety of pyrantel tartrate fed daily to horses for a year. Proc. 33rd Annual Meeting of the American Association of Veterinary Parasitologists, 17–18 July 1988, Portland, OR, p. 39.

Herd, R.P., 1990. Equine parasite control. Problems associated with intensive anthelmintic therapy. Equine Vet. Educ., 2: 41–47.

Herd, R.P. and Majewski, G.A., 1993. Comparison of Strongid C (daily) and Strongid P (every 4 weeks) in yearling thoroughbreds and Strongid C (daily) in barren and foaling mares. Proc. 38th Annual Meeting of the American Association of Veterinary Parasitologists, 17–20 July 1993, Minneapolis, MN, p. 30.

Hopfer, S.M., van Kruiningen, H.J. and Daniels, W.H., 1984. The elimination of equine strongyles and hematological and pathological consequences following larvicidal doses of thiabendazole. Vet. Parasitol., 14: 21–32.

Howes, H.L. and Lynch, J.E., 1966. Pyrantel tartrate, a new broad spectrum anthelmintic. I. Activity against intestinal parasites in laboratory animals. Proc. 41st Annual Meeting of the American Society of Parasitologists, 31 October–4 November 1966, San Juan, Puerto Rico, p. 48.

Ivens, V.R., Mark, D.L. and Levine, N.D., 1978. Principal parasites of domestic animals in the United States. Special Publications 52, 2nd edn. Colleges of Agriculture and Veterinary Medicine, University of Illinois at Urbana–Champaign, pp. 282–292.

Kingsbury, P.A. and Reid, J.F.S., 1981. Anthelmintic activity of paste and drench formulations of oxfendazole in horses. Vet. Rec., 109: 404–407.

Klei, T.R., Chapman, M.R., French, D.D. and Taylor, H.W., 1993. Evaluation of ivermectin at an elevated dose against encysted equine cyathostome larvae. Vet. Parasitol., 47: 99–106.

Lichtenfels, J.R., 1975. Helminths of domestic equids. Proc. Helminthol. Soc. Wash. (special issue), Vol. 42, 92 pp.

Lyons, E.T., Drudge, J.H. and Tolliver, S.C., 1974. Critical tests of three salts of pyrantel against internal parasites of the horse. Am. J. Vet. Res., 35: 1515–1522.

Lyons, E.T., Drudge, J.H. and Tolliver, S.C., 1983. Controlled tests with fenbendazole in equids: special interest on activity of multiple doses against natural infections of migrating stages of strongyles. Am. J. Vet. Res., 44: 1058–1063.

Reinemeyer, C.R., 1986. Small strongyles: recent advances. In: R.P. Herd (Editor), The Veterinary Clinics of North America. Equine Practice, Vol. 2. W.B. Saunders, Philadelphia, PA, pp. 281–312.

Reinemeyer, C.R. and Herd, R.P., 1986. Comparison of two techniques for quantitation of encysted cyathostome larvae in the horse. Am. J. Vet. Res., 47: 507–509.

Roberson, E.L., 1988. Antinematodal drugs. In: N.H. Booth and L.E. McDonald (Editors), Veterinary Pharmacology and Therapeutics, 6th edn. Iowa State University Press, Ames, pp. 882–927.

Slocombe, J.O.D. and Lake, M.C., 1993. Control of strongyles in ponies receiving a daily feed ration containing pyrantel tartrate (Strongid C®). Proc. 33rd Annual Meeting of the American Association of Veterinary Parasitologists, 17–20 July 1993, Minneapolis, MN, p. 31.

Soulsby, E.J., 1982. Textbook of Veterinary Clinical Parasitology. Lea and Febiger, Philadelphia, PA, p. 401.

US Department of Agriculture, 1990a. Freedom of Information Summary NADA 140-819. Department of Health and Human Services, Food and Drug Administration, Center for Veterinary Medicine, Rockville, MD, 19 pp.

US Department of Agriculture, 1990b. Bioequivalence guideline. Department of Health and Human Services, Food and Drug Administration, Center for Veterinary Medicine, Rockville, MD, 18 pp.

Whitlock, H.V., 1948. Some modifications of the McMaster helminth egg-counting technique and apparatus. J. Counc. Sci. Ind. Res., 21: 177–180.

Zar, J.H. (Editor), 1984. Biostatistical Analysis, 2nd edn. Prentice–Hall, Englewood Cliffs, NJ, 718 pp.