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FIELD TRIALS OF PYRANTEL PAMOATE (COMBANTRIN) IN ASCARIS, HOOKWORM AND TRICHURIS INFECTIONS

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Summary

In a trial involving 185 school children, pyrantel pamoate (Combantrin) at a dose of 20 mg/kg body weight for 1-3 days was found to be very effective against the *Ascaris* and moderately effective against the hookworm, with mean cure rates ranging from 93.3-96.7% and 53.3-73.3% respectively.

No apparent action against the *Trichuris* was detected, a mean cure rate of between 34.2 and 46.1% being only slightly, but not significantly, better than the 33.8% cure for a placebo-treated control group.

Single and multiple doses of the suspension and tablet formulations of the drug were well tolerated. From the series of randomized and controlled trials conducted, we recommend that, in this area, the appropriate dose of the drug to use for treating ascariasis is 10 mg/kg per day for 1 day, and for infections which include hookworm, 20 mg/kg per day for 3 days.

Résumé

Dans un essai concernant 185 élèves, le pyrantel pamoate (Combantrin) à une dose de 20 mg/kg poids de corps pour 1-3 jours a été découvert d'être très efficace contre l'*Ascaris* et légèrement efficace contre le hookworm avec un taux moyen de guérissage de 93.3-96.7% et 53.3-73.3% respectivement.

Aucune action apparente est découverte contre le *Trichuris*, un taux moyen de guérissage

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entre 34.2 et 46.1% étant non pas meilleur que le 33.8% pour un groupe controlle et traite de placebo.

Des doses unique et multiple de suspension et des formations de comprimés de la drogue ont été bien tolérées. De la serie des essais contrôllés nous recommeandons que dans cet aspect, la dose convenable de la drogue à utiliser pour traiter ascariasis c'est 10 mg/kg per jour et pour les infections y compris le hookworm c'est 20 mg/kg per jour pendant trois jours.

Introduction

In two earlier studies we compared the anthelmintic efficacy of 1-, 2- and 3-day courses of pyrantel pamoate at a dose of 10 mg/kg per day with thiabendazole at a dose of 25 mg/kg body weight b.d. for 1 day and a 2-day regimen consisting of piperazine citrate (2-3 g/day) and bphenium (5 g/day) (Kale, 1977a, 1981). We found that pyrantel pamoate was very effective against *Ascaris* with percentage cures of 88.3-95.5%; moderately effective against the hookworm at the higher doses with average cures of 31.8, 56.8 and 59.6% and percentage reduction in egg counts of 61.1, 78.4 and 80.8% for the 1-, 2- and 3-day courses respectively.

The drug was adjudged ineffective against the *Trichuris*, the spontaneous negative conversion rate in the placebo-treated group being of the same magnitude as the pyrantel groups. There were a number of side-effects elicited on direct and specific questioning, particularly gastrointestinal, but these were generally very mild and of such short duration that it was considered justifiable, and a decision was taken to try higher doses of the drug, still well within the level re-

commended by the manufacturers, in order to determine whether its action, particularly against both the hookworm and the *Trichuris*, would be enhanced.

This paper is a report of a controlled field trial of single daily doses of pyrantel pamoate at 30 mg/kg body weight per day for 1–3 days.

Subjects and methods

The study was conducted at St Luke's Primary School, Lalupon, a rural town 25 km north-east of Ibadan, capital of Oyo State.

Subjects

Out of a total of 263 pupils whose stools were screened by the direct-smear method, 185 (70.3%) were found to be excreting the eggs of at least two of the three intestinal helminths, *Ascaris lumbricoides*, *Trichuris trichiura* and the hookworm. These 185 pupils (112 boys and 73 girls) aged 8–16 years were enrolled for the study.

Parasitology

A quantitative assessment of the load of infection with each of the helminths was made by the Stoll dilution egg-counting technique (Stoll, 1963). Two consecutive stool specimens were obtained from each pupil before treatment and duplicate egg counts conducted on each specimen. For each parasite the mean egg count per gm of faeces from the four results obtained was recorded as the pre-treatment infection load.

Single stool specimens, on which duplicate egg counts were made, were collected 2 weeks (Day 14) and 6 weeks (Day 42) after treatment to determine percentage cure (complete absence of eggs) and reduction in egg excretion.

Treatment

On the basis of the degree of infection with hookworm, the pupils were divided into three strata—light (500 e.p.g.), moderate (500–1000 e.p.g.) and heavy (>1000 e.p.g.). From each stratum, allocations were made at random into four groups and treatment given in the following manner:

Group A (45 patients) — pyrantel pamoate 20 mg/kg body weight as a single dose;

Group B (45 patients) — pyrantel pamoate 20 mg/kg body weight as a single dose, daily for 2 days;

Group C (45 patients) — pyrantel pamoate 20 mg/kg body weight as a single dose, daily for 3 days; and

Group D The placebo-treated control group (50 patients) — two yeast tablets daily for 3 days.

Pyrantel pamoate (Combantrin) was supplied in the form of chewable scored tablets each containing 125 mg base and as a suspension containing 250 mg of pyrantel base per 5 ml.

Side effects

The pupils were seen at the school on every day during and for 2 days after conclusion of treatment and questioned about side-effects of treatment.

Results

Parasitological

Pre-treatment. The infection rates in the study groups were 185 (100%) for *Ascaris*, 181 (97.8%) for hookworm and 150 (81.1%) for *Trichuris*.

The stratification on the basis of load of hookworm infection as measured by egg excretion, and the random allocation into treatment groups ensured adequate comparability of the groups as shown by the following pre-treatment mean egg counts for the four groups A, B, C and D respectively: *Ascaris*, 21796, 15884, 23789 and 20110; *Trichuris* 770, 882, 782 and 780; hookworm, 1298, 978, 938 and 1020.

Two pupils had *Strongyloides stercoralis* larvae in the stools and one had a few eggs of *Schistosoma mansoni*. *Entamoeba coli* cysts were seen in three stools.

Post-treatment. The percentage cure for *Ascaris* in all the three pyrantel groups was uniformly very high ranging between 88.8–97.8% with a mean value for the three groups of 93.7% as against a spontaneous negative conversion ('cure') of 8.0% in the control group. (Table 1).

The negative conversion ('cure') rate (NCR) for *Trichuris* in the three pyrantel-treated groups were roughly identical — ranging from 34.2–50.0% (mean 41.6%) and not significantly better than for the control group which had

TABLE 1. Showing the cure rate for *Ascaris trichuris* and hookworm with 1-, 2- and 3-day regimens of pyrantel pamoate at 20 mg/kg body weight per day and a control group

Helminth	Group A Pyrantel (20 mg/kg/day × 1 day)			Group B Pyrantel (20 mg/kg/day × 2 days)			Group C Pyrantel (20 mg/kg/day × 3 days)			Group D Control 2 yeast tabs daily × 3 days		
	Pre-treatment no. positive		Post-treatment no. cured	Pre-treatment no. positive		Post-treatment no. cured	Pre-treatment no. positive		Post-treatment no. cured	Pre-treatment no. positive		Post-treatment no. cured
	Day 0	Day 15	Day 42	Day 0	Day 15	Day 42	Day 0	Day 15	Day 42	Day 0	Day 15	Day 42
<i>Ascaris</i>	45	42 (93.3)*	42 (93.3)*	45	40 (88.8)*	44 (97.8)*	45	44 (97.8)*	43 (95.6)*	50	3 (6.0)*	5 (10.0)*
<i>Trichuris</i>	37	14 (37.8)	17 (45.9)	38	19 (50.0)	18 (47.4)	38	13 (34.2)	13 (34.2)	37	12 (32.4)	13 (35.1)
Hookworm	45	25 (55.6)	23 (51.1)	45	27 (60.0)	33 (73.3)	45	30 (66.7)	36 (80.0)	46	6 (13.0)	7 (15.2)

*Numbers in parentheses are percentages

mean NCR of 32.4–35.1% (mean 33.8%) (Table 1). The pattern and degree of fluctuation in the egg counts after treatment were similar and of the same magnitude in all the four treatment groups. Clearly pyrantel pamoate has no demonstrable activity against *Trichuris*.

Percentage cures for hookworm were: Group A, 53.3%; Group B, 66.6%; Group C, 73.3%; and Group D (control) 14.4%, indicating a dose-related effectiveness of pyrantel pamoate (Table 1). The percentage reduction in egg counts for the pyrantel-treated groups was 82.2, 81.4 and 86.1% for Groups A, B and C respectively, and for the control group, D, 8.7% (Table 2).

The two pupils with *S. stercoralis* larvae in pre-treatment stools fell into Groups A and C. The infections were very light and no symptoms attributable to them were elicited. Both cases were apparently 'cured' of the infection after treatment since no larvae were recovered in post-treatment stools.

The stool of the only pupil (Group C) with the occasional *S. mansoni* egg before treatment was negative for the parasite after the treatment on Day 15, but positive on Day 42. All three pupils with *E. coli* cysts (two in Group B and one in Group D) continued to excrete the parasite after treatment.

Side-effects

The frequency and severity of the side-effects of treatment, about 50% of which were volunteered, were proportional to the dose of pyrantel. All side-effects were transient, each episode lasting less than 12 h, and were well within tolerable limits. No side-effects were considered as severe in any of the patients. Gastrointestinal disturbances predominated with abdominal colic topping the list (Table 3). There were no differences in the frequency or severity of side-effects or the parasitological response to treatment between those who received the tablets and those given the oral suspension.

Discussion

This study confirms the effectiveness of pyrantel pamoate in the treatment of ascariasis, and its relative ineffectiveness against *Trichuris*.

Treatment group	Post-treatment interval	Reduction scales				Mean egg count/gm		Post-treatment egg count as % of pre-treatment egg count
		0*	1-24%	25-49%	50-74%	75-100%	Pre-treatment	
Pyrantel 20 mg/kg/day × 1 day n = 45	Day 15	6(13.3)†	2(4.4)†	1(2.2)†	4(8.9)†	32(71.1)†	296	22.8
	Day 42	2(4.4)	0(—)	0(—)	1(2.2)	42(93.3)	1298	12.9
Pyrantel 20 mg/kg/day × 2 days n = 45	Day 15	4(8.9)	0(—)	4(8.9)	6(13.3)	31(68.9)	246	25.2
	Day 42	2(4.4)	1(2.2)	2(4.4)	3(6.7)	37(82.2)	117	12.0
Pyrantel 20 mg/kg/day × 3 days n = 45	Day 15	1(2.2)	0(—)	2(4.4)	4(8.9)	38(84.4)	109	11.6
	Day 42	1(2.2)	0(—)	1(2.2)	6(13.3)	37(82.2)	151	16.1
Control 2 yeast tabs/day × 3 days n = 46	Day 15	28(60.9)	5(10.9)	4(8.7)	4(8.7)	5(10.9)	1100	107.8
	Day 42	30(65.2)	3(6.5)	2(4.3)	4(8.7)	7(15.2)	762	74.7

*No reduction.

†Numbers outside parentheses are the numbers of patients, and those within are the percentages.

TABLE 3. Showing frequency and severity of side-effects of treatment in four treatment groups*

Side-effect	Group A Pyrantel - 20 mg/kg/day × 1 day n = 45			Group B Pyrantel - 20 mg/kg/day × 2 days n = 45			Group C Pyrantel - 20 mg/kg/day × 3 days n = 45			Group D Yeast - 2 tabs/day × 3 days n = 50		
	Mild	Moderate	Total	Mild	Moderate	Total	Mild	Moderate	Total	Mild	Moderate	Total
Abdominal colic	9	3	12	9	5	14	8	6	14	3	1	4
Nausea	2	1	3	3	1	4	4	2	6	1	0	1
Vomiting	3	0	3	3	2	5	5	2	7	0	0	0
Diarrhoea	1	1	2	3	0	3	5	3	8	2	0	2
Dizziness	1	0	1	0	0	0	2	0	2	0	0	0
Weakness	0	0	0	1	0	1	3	0	3	2	1	3
Anorexia	1	0	1	2	0	2	2	0	2	1	0	1
Headache	2	0	2	0	1	1	2	1	3	1	1	2
Skin rash	0	0	0	1	0	1	1	0	1	0	0	0
Pruritus	0	0	0	0	0	0	1	0	1	0	0	0
Feverishness	0	0	0	0	0	0	1	0	1	1	0	1

*No side-effect was graded as severe.

Against hookworm, the predominant species of which has been repeatedly shown in this area to be *Necator americanus*, the proportion of patients cured with the dose used in this trial (20 mg/kg per day for 1–3 days) was substantially higher than earlier recorded with lower doses (10 mg/kg per day for 1–3 days) of the drug (Kale 1977a, 1981). Both formulations of the drug, even at the higher doses used, was well tolerated.

Summary of the three-part series

The three separate trials that make up this series were conducted, over a period of 2 years and 6 months under identical conditions and along the lines recommended by the W.H.O. Scientific Group on Principles for the Clinical Evaluation of Drugs (1968). To eliminate bias, conscious or otherwise, the laboratory team that examined the stools were unaware of the treatment group to which the patients, whose stools they examined, belonged and the doctor who administered treatment was different from the one who questioned the subjects about side-effects. The latter was unaware of the treatment schedules.

A standard and convenient method of quantifying egg output was used throughout the series *vis.* the Stoll dilution egg-counting technique, and repeated replicate observations were made on stool specimens.

All the subjects in the trials were school children aged 6–17 years and were selected from village schools so as to reduce to a minimum the possibility of indiscriminate self-medication with potent anthelmintics which may interfere with, and distort the results of such field-trials. Experience in most urban areas where myriads of patent medicine and chemists' shops abound has shown that self-medication, encouraged by intense advertising on the radio, television and in the press is quite rampant (Kale, unpubl. observ.). The drug was administered in the morning to all the subjects, after breakfast.

Our first two trials included groups treated with current standard drugs, and each trial in the series included a placebo-treated control group. The merit of this is clearly illustrated in the results obtained in respect of infection with *T. trichiura* where a substantial percentage of spontaneous 'cures' were recorded in the control groups (mean 40.9%) comparable to and of the same degree as the apparent 'cures' in the pyrantel-

treated groups (38.4%). In an uncontrolled trial, Katz *et al.* (1972) recorded 42.8% cure in eleven patients with trichuriasis treated with pyrantel pamoate at a dose of 20 mg/kg per day for 2 days, and concluded that the drug 'demonstrated partial activity against *Trichuris*'. However, the same group of workers in a subsequent trial also uncontrolled, obtained in nine patients a 0.0% cure against the same helminth, using the same dosage schedule. (Katz, Antunes & Zicker, 1973). More curiously, higher doses of 20 mg/kg per day for 3 days in thirteen patients and 20 mg/kg per day for 5 days in fifteen patients gave only 8.0 and 20% cures respectively, considerably lower than in the first trial. These workers' results suggest a lack of activity by pyrantel against *Trichuris*, a point that might have been further strengthened if the results of untreated or placebo-treated controls had been available.

To increase the precision of comparison between the various groups, the subjects in this series were allocated at random after stratification on the basis of pre-treatment hookworm egg count records. Table 4 which shows the pre-treatment load of infection with respect to the three helminths under study, reflects the degree of comparability of the various treatment groups. The results of the three control groups have been pooled.

We ensured that the sample size for each treatment group was adequate for significant differences to be determined, and taking cognisance of the intrinsic incubation period of the helminths, post-treatment examination of stools were limited to 6 weeks so that re-infections, to which our subjects were highly exposed, may not distort the results.

Owing to technological difficulties operating at the time we were unable to undertake coproculture and worm counts in order to identify the species of hookworm with which the subjects were infected. This would have been desirable for, in spite of the consensus of all previous reports and our consistent personal experience which have both established that *N. americanus* is the predominant species in this area, a change in the pattern and distribution of the species of hookworm or a local variation in the areas of study could not be ruled out.

Table 5 gives a summary of the cure rates achieved for each of the three worms with the various treatment regimens. It is concluded from these results that pyrantel pamoate is very effec-

TABLE 4. Showing the pre-treatment egg load 1 g* for *Ascaris*, hookworm and *Trichuris* in nine treatment groups

Treatment group	<i>Ascaris</i>			Hookworm			<i>Trichuris</i>		
	Range	Mean	Range	Range	Mean	Range	Range	Mean	
Pyrantel 10 mg/kg/day × 1 day	100- 34300	8990	100- 4000	100-3200	980	100-3200	100-3200	730	
Pyrantel 10 mg/kg/day × 2 days	200- 44000	10670	100- 5200	100-2800	770	100-2800	100-2800	580	
Pyrantel 10 mg/kg/day × 3 days	200- 97700	13840	100- 3200	100-3000	620	100-3000	100-3000	650	
Pyrantel 20 mg/kg/day × 1 day	800- 86300	21770	100-16800	100-4100	1300	100-4100	100-4100	770	
Pyrantel 20 mg/kg/day × 2 days	300- 81400	15880	100- 6300	100-4100	980	100-4100	100-4100	880	
Pyrantel 20 mg/kg/day × 3 days	200-210000	23790	100- 5100	100-4100	940	100-4100	100-4100	780	
Thiabendazole 25 mg/kg b.d. × 1 day	100- 32700	8350	100- 4200	100-3600	970	100-3600	100-3600	670	
Piperazine (2-3 g) plus Bephenium (5 g) daily × 2 days	900- 55500	10680	100- 9100	100-4300	760	100-4300	100-4300	850	
Yeast 2 tabs daily × 1-3 days	200-122100	11200	100- 3700	100-3800	790	100-3800	100-3800	810	

*Mean of replicated counts per g of faeces (Stoll technique) approximated to nearest 10.

TABLE 5. Showing cure rates for *Ascariis*, *Trichuris* and hookworm with various treatment regimens

Drug and dosage	<i>Ascariis</i>			<i>Trichuris</i>			Hookworm					
	No. positive pre-treatment	No. negative post-treatment (%)	Cured (%)	No. cured/No. treated† (%)	No. positive pre-treatment	No. negative post-treatment (%)	Cured (%)	No. positive pre-treatment	No. negative post-treatment (%)	Cured (%)	No. cured/No. treated† (%)	
Pyrantel												
10 mg/kg/day × 1	64	56.5	88.3	—	63	20.5	32.5	—	55	17.5	31.8	—
10 mg/kg/day × 2	56	53.5	95.5	16/16 (100)	31	12.5	40.3	0/3 (0.0)	44	25.0	56.8	3/21 (14.3)
10 mg/kg/day × 3	44	41.5	94.3	8/9 (88.9)	25	9.0	36.0	1/14 (7.1)	26	15.5	59.6	12/16 (75.0)
20 mg/kg/day × 1	45	42.0	93.3	—	37	15.5	41.9	—	45	24.0	53.3	—
20 mg/kg/day × 2	45	42.0	93.3	7/9 (77.8)	38	18.5	48.7	1/15 (6.7)	45	30.0	66.7	13/17 (70.6)
20 mg/kg/day × 3	45	43.5	96.7	10/11 (90.9)	38	13.0	34.2	0/14 (0.0)	45	33.0	73.0	8/15 (53.3)
Thiabendazole												
25 mg/kg b.i.d × 1 day	61	27.5	45.1	—	61	21.5	35.2	—	55	17.0	30.9	—
Piperazine 2-3 g plus												
Bephenium 5 g daily × 2	46	40.5	88.0	—	24	11.0	45.8	—	34	25.0	73.5	—
Bephenium 5 g daily × 3	—	—	—	2/8 (25.0)	—	—	—	1/19 (5.3)	—	—	—	1/20 (5.0)
Yeast, 2 tabs/day × 1-3	135	18.5	13.7	—	93	38.0	40.9	—	114	22.5	19.7	—

*Mean number of patients negative on days 15 and 42 post-treatment.

†Culled from Botero and Castano (1973) working in Colombia.

tive in ascariasis at all doses. A single dose of 10 mg/kg body weight for 1 day is as effective against the *Ascaris* as a combined regimen of piperazine (2-3 g) and bephenium (5 g) given daily for 2 days, with cures of 88.3 and 80.0% respectively. The percentage cure when all the results for the pyrantel groups are pooled is 90.2% (279/309).

All nine treatment regimens proved disappointing against the *Trichuris*. The pooled result for the pyrantel groups gives a cure rate of 38.4% (89/232) against 40.9% (38/93) for the control groups.

Against the hookworm, the results show that the cure rates for pyrantel was proportional to the dose, ranging from 31.8% for the lowest dose (10 mg/kg per day for 1 day) to 73.3% for the highest (20 mg/kg per day for 3 days). The best result for pyrantel (73.3%) is of the same magnitude as that for the piperazine-bephenium regimen (73.7%).

The results for the pyrantel groups suggest that repeated doses may be better than single doses. Thus 10 mg/kg per day for 2 days (total of 20 mg/kg) gave 56.8% cure while the same amount given as single dose (20 mg/kg per day for 1 day) gave 53.3%. (Table 5). But the differ-

ence is not statistically significant ($P > 0.05$).

The mean percentage reduction in hookworm egg counts showed the same dose-related trend as the cure rate, ranging from 53.5% in the group treated with 10 mg/kg per day for 1 day to 86.1% in the group treated with 20 mg/kg per day for 3 days. The piperazine-bephenium regimen (90.3%) was slightly but not significantly better than the best pyrantel regimen (86.1%) ($P > 0.05$) (Table 6).

Thiabendazole at a dose of 25 mg/kg b.d. for 1 day was rather disappointing against all the three helminths. This we attribute in part to the high frequency of vomiting which occurred in 32.8% of sixty-seven subjects. This must have interfered considerably with the absorption of the drug (Kale, 1977a).

To illustrate the geographical differences in response to treatment, we have reproduced, alongside our results in Table 5, the results obtained by Botero and Castano (1973) who treated 105 patients over the age of 14 years with doses of pyrantel, similar to those used by us. These workers' results do not show the same consistent dose-related trend in efficacy of the drug as in our series.

TABLE 6. Showing the mean percentage reduction in hookworm egg count with various treatment regimens

Drug and dosage	Mean count/gm pre-treatment	Mean count/gm post-treatment	Reduction (%)	No. of patients with >50% reduction in egg-count (%)*	
Pyrantel					
10 mg/kg/day × 1 day (n = 55)	979	455	53.5	33.6	(61.1)
10 mg/kg/day × 2 days (n = 44)	767	232	69.8	34.5	(78.4)
10 mg/kg/day × 3 days (n = 26)	619	181	70.8	21.0	(80.8)
20 mg/kg/day × 1 day (n = 45)	1298	227	82.5	39.5	(87.8)
20 mg/kg/day × 2 days (n = 45)	978	182	81.4	39.0	(86.7)
20 mg/kg/day × 3 days (n = 45)	938	130	86.1	42.5	(94.4)
Thiabendazole					
25 mg/kg b.d. × 1 day (n = 34)	969	612	36.8	30.0	(54.5)
Piperazine 2-3 g plus Bephenium 5 g daily × 2 days (n = 34)	761	74	90.3	30.0	(88.2)
Yeast 2 tabs/day × 1-3 days (n = 114)	786	778	1.0	22.0	(19.3)

*Mean number of patients for days 15 and 42.

Conclusion

For persons infected with only *Ascaris*, a single dose of pyrantel pamoate at 10 mg/kg body weight is adequate to eliminate all, or nearly all of the worms. The cost at current prices for a patient weighing 50 kg is roughly ₦0.50 (Nigerian naira) or U.S.\$0.85 (U.S. dollars).

For infections which include hookworm the recommended dose of pyrantel pamoate is 20 mg/kg body weight per day for 3 days. The cost for a 50 kg patient is about ₦3.00 or \$5.4.

Pyrantel pamoate has no apparent action against the *Trichuris* and where this helminth is the target of chemotherapy, we recommend the use of one of the broad-spectrum antihelmintics with proven anti-*Trichuris* activity. One is a mixture containing pyrantel pamoate and oxantel pamoate, marketed locally under the trade name *Combantrin plus* by Pfizer Ltd, Nigeria, (Kale, 1977b). The other is mebendazole (*Vermox*) produced by Janssen Pharmaceutica. (Pena Chavarria *et al.*, 1973).

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References

- Botero, D. & Castano, A. (1973) Comparative study of pyrantel pamoate, bephenium and tetrachloro-ethylene in the treatment of *Necator americanus* infections. *Amer J Trop. Med. Hyg.*, **22**, 45-52.
- Kale, O.O. (1977a) A comparative trial of the anthelmintic efficacy of pyrantel pamoate (Combantrin) and thiabendazole (Mintezol). *Afr. J. Med. Med. Sci.*, **6**, 89-93.
- Kale, O.O. (1977b) Anthelmintic efficacy of a mixture of pyrantel pamoate and oxantel pamoate. *Curr. Ther. Res* **22**, 802-806.
- Kale, O.O. (1981) Controlled comparative study of the efficacy of pyrantel pamoate and a combined regimen of piperazine citrate and bephenium hydroxynaphthoate in the treatment of intestinal nemathelminthiasis. *Afr. J. Med. Med. Sci.*, **10**, 63-67.
- Katz, N., Zicker, F., Chaves, A. & Antunes, C.M.F. (1972) Clinical trials with pyrantel pamoate in intestinal parasitoses. *Rev. Inst. Med. Trop. Sao Paulo.*, **14**, 212-221.
- Katz, N., Antunes, C.M.F. & Zicker, F. (1973) Clinical trials with pyrantel pamoate on intestinal helminths in urban and rural areas. *Rev. Inst. Med. Trop. Sao Paulo.*, **15**, 331-339.
- Pena Chavarria, A., Swartzwelder, J.C., Villarejos, V.M. & Zeledon, R. (1973) Mebendazole, an effective broad spectrum anthelmintic. *Amer. J. Trop. Med. Hyg.*, **22**, 592-595.
- Stoll, N.R. (1963) Dilution egg-counting technique for hookworm, *Ascaris*, *Trichuris* and other parasites. Report of C.C.T.A./W.H.O. African Conference on Ancylostomiasis, Brazzaville, August 1961. *Wld. Hlth. Org. techn. Rep. Ser.*, No. 255 Annex 2, 21.
- World Health Organization Scientific Group on Principles for Clinical Evaluation of Drugs. (1968) *Wld. Hlth. Org. techn. Rep. Ser.*, No. 403.

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