

INFLUENCE OF COMPOUND 16.842 ON HOOKWORM INFECTIONS

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Compound 16.842 was tried with three different groups of patients in order to evaluate its tolerancy, and efficacy as well, with a view of using the drug in mass campaigns against hookworm.

Group I, used for a preliminary trial, consisted of 38 patients attending an out-patient clinic, and living either in the out-skirts or in the various urban areas of the city of R.o de Janeiro, including some inmates of an orphanage.

Group II, a field trial, was carried out in two farms, where the drug was administered both to the positive cases (124) and to the rest of the population (nearly 90%).

Group III, a field trial was also carried out in a small town where nearly 40% of the total population was treated with the Compound.

Tolerability was considered rather satisfactory, mainly among the patients receiving two single doses (50-150mg), according to the age, 4 — 6 weeks apart). These results suggest that 2-4 courses of therapy within a shorter span of time should be the ideal for a mass treatment campaign.

Efficacy varied from 26.6% to 76.2% parasitological cure in the various groups, with a wide range of variation also in the percent of mean reduction of eggs for hookworm.

The drug showed also some effect against *Ascaris lumbricoides* giving cure rates between 10.5% and 35.7% in the various groups, with a percentage reduction in mean egg counts of 27% to 83.3% according to the various groups.

It was concluded that Compound 16.842 possesses a marked effect on hookworm and a mild effect on *A. lumbricoides*. The findings indicate the need for more accurate studies to determine the most efficient schedules of treatment and the real value of the drug, as compared to other antihelminthics against the two parasites under study.

Intestinal helminthiasis have been known to constitute a major Public Health problem in Brazil for many decades, if not for centuries. Among these helminthic diseases, (Figs. I-A and B), hookworm infection, for obvious reasons (high prevalence, wide distribution and under certain circumstances, a high degree of morbidity, in terms of impairment, disability and even death) has deserved special attention from the Public Health Service authorities, mainly at the Federal level.

Mass campaigns aiming at the control of hookworm infection were organized on three different occasions. At the present time, most of the activities concerning the control of intestinal helminthic infections are under the responsibility of the "Departamento Nacional de Endemias Rurais", an agency of the Ministry of Health. A branch of that department, the "Instituto Nacional de Endemias Rurais" is in charge of special investigation and research of the various endemic rural diseases. In ad-

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dition to wide scale surveys to determine the prevalence of these diseases, the value of the different diagnostic techniques is appraised. Regarding the intestinal helminthic diseases, pilot-projects for clinical trials of antihelminthic drugs are carried out as well as studies to evaluate the result of the control measures. Studies on other angles of the problem (practicability, cost, etc.) are also made.

Due to the high prevalence of associated intestinal helminthic infections found all over the country, control measures must always be selected and conducted with a view of attacking the greatest possible number of those endemic parasitic diseases not only through mass treatment, but also through environmental sanitation, health education, etc.

The main purpose of this paper is to present the observations made on the use of a new drug (Compound 16.842) which, according to previous experiences, has been found to be effective against hookworm infection in various parts of the world.

MATERIAL AND METHODS

Compound 16.842 is a colorless, tasteless and inodorous powder derived from the mustard oil; acute and chronic toxicity studies in animals failed to reveal significant physiopathological changes directly attributable to drug toxicity. Animal experiments showed that Compound 16.842 is specially effective against *Ankylostoma* and *Ascaris*, with relative efficacy against *Cestodes*.

The patients selected for the therapeutic trials may be divided into three groups:

I-A and I-B) — Preliminary trials. 38 were patients (8 to 62 years of age) attending an out-patient clinic. Their residence was either in the suburbs or the various areas of the city of Rio de Janeiro. Some of them were inmates from an orphanage.

II-A and B) — Field trials in rural areas. In two farms (Figs. II-A and B) of the municipality of Sumidouro (about 100 miles from the city of Rio de Janeiro) stool examination revealed 124 positive cases.

(44.2% of the total population). In these two places several other helminthic diseases, including schistosomiasis mansoni are highly prevalent. Besides treatment for the positive cases, mass treatment was provided for the rest of the population. Ten positive cases, for different reasons, did not receive any course of treatment.

III — Field trials: (in a semi-rural community.) 298 patients were positive for hookworm at the first stool examination, representing 43% of the 693 people submitted to stool examinations; 134 of these patients received treatment. These people live in the semi-rural town of Sumidouro (about 1000 inhabitants), a locality which has some of its streets paved, a public swimming pool, and is partially served by a sewage system and water supply. (Fig. III).

Table I shows the data regarding age and sex for the three groups.

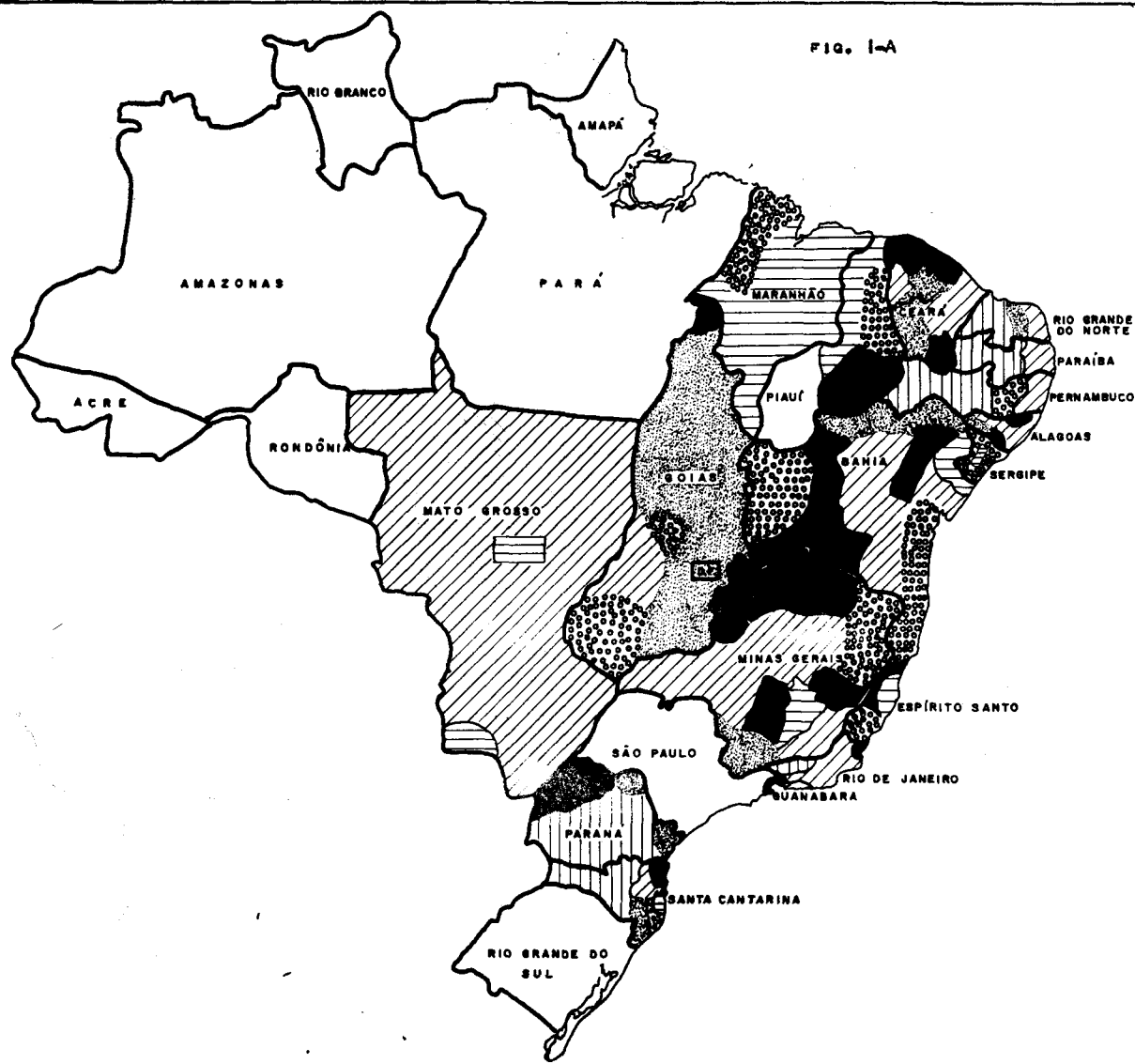
All of the patients in group I had the diagnosis established by the results of stool examinations, using the sedimentation method (Hoffman et al. technique), (7) while all of those in group II and III were examined by the MIFC § technique, a modification of the Sapero et al. technique, (Table II). In both groups, the stools of almost all patients were submitted to a counting method, Barbosa technique (1). The hookworm burden was low in the three groups. Nevertheless, it was higher in group I (Table III).

The general health status of all patients was rather satisfactory although those of group I, II and part of group III, lived in a very unhealthy environment. 286 people of group II lived in 48 houses of which only 8 had tap water and 15 had latrines. Children and most of the adults go bare-foot as a rule. Table IV shows the hematological findings as well as the results of serum protein and iron determination in 60 random positive patients of group II (farms.) The results of these studies reveal a mild hypochromic anemia in most of those patients as well as minor changes in the biochemical results.

In the town of Sumidouro itself, most of the adults wear shoes while only a few children do so, at least as a habit.

§ Coutinho's modification of the MIF technique.

FIG. 1-A



HOOKWORM INFECTION

Infection by *Ancylostoma duodenale*, and, more frequently by *Necator americanus*, is widespread in Brazil, according to the coproscopic surveys.

ANCILOSTOMÍASE

A INFECÇÃO PELO ANCYLOSTOMA DUODENALE, É MAIS FREQUENTEMENTE PELO NECATOR AMERICANUS, É LARGAMENTE DIFUNDA NO BRASIL. DE ACÓRDO COM OS LEVANTAMENTOS COPROSCÓPICOS EFETUADOS ENTRE ESCOLARES, FALTANDO ENTRETANTO DADOS MAIS COMPLETOS SOBRE A PREVALÊNCIA DESSA PARASITOSE EM ALGUNS DOS ESTADOS DO BRASIL.

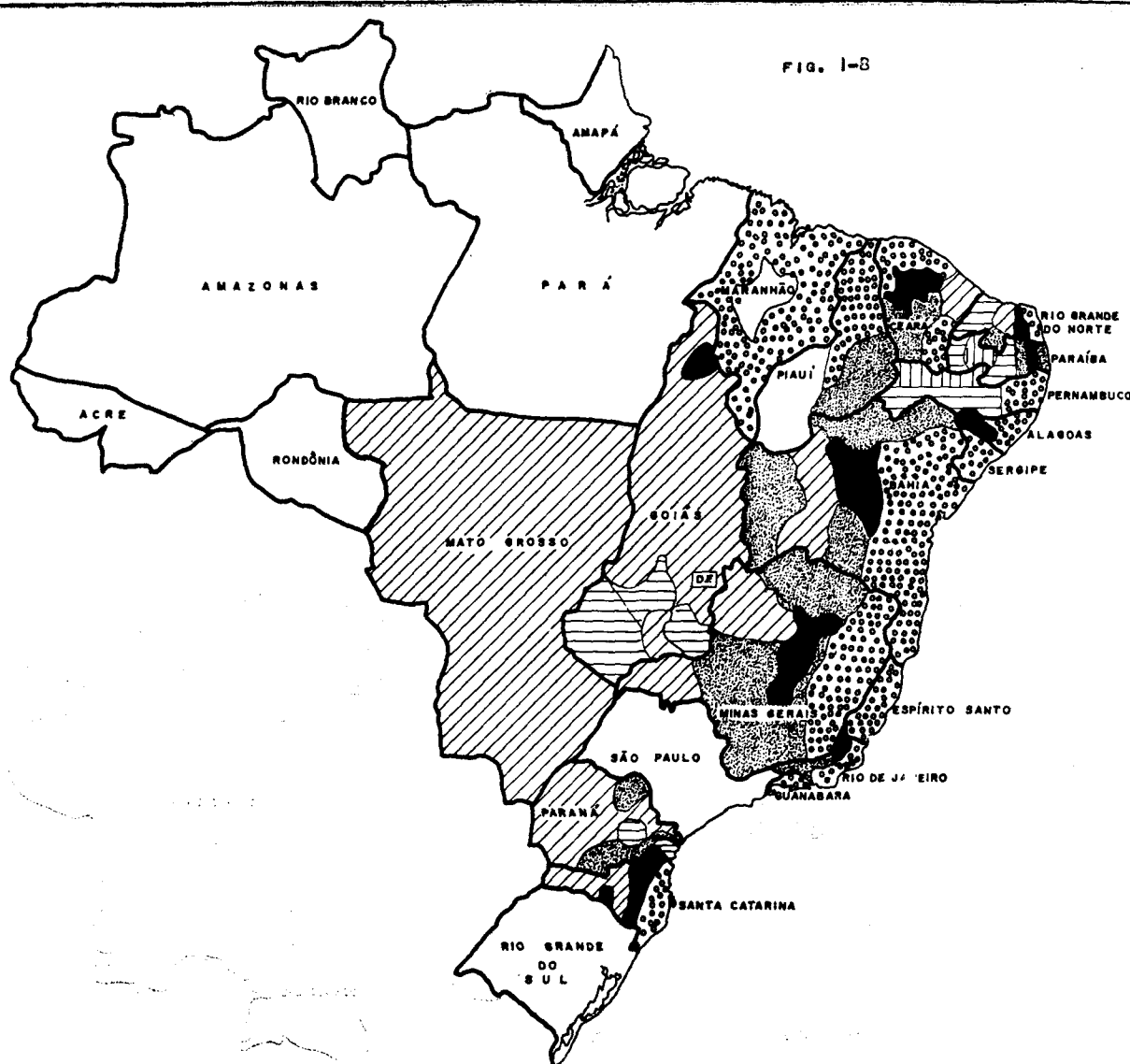
	UNDER ABAIXO DE		30 %
	30	A	40 %
	40	A	50 %
	50	A	60 %
	60	A	70 %
	70	A	90 %
	Not DADOS	NÃO	avaliáveis disponíveis

FIG. 1-8

INTESTINAL HELMINTHIASIS
(EXCEPT HOOKWORM INFECTION)

Infection by intestinal Helminthiasis (*Ascaris lumbricoides*, *Trichuris trichiura*, *Strongyloides stercoralis* and *Enterobius vermicularis*) is widespread in Brazil, according to the coproscopic surveys.

Available data on the incidence of *Strongyloides stercoralis* and *Enterobius vermicularis* are not however, as complete as those on the other intestinal helminths, mainly because the surveys are based on the sedimentation of stools.



	30	A	50 %
	50	A	70 %
	70	A	80 %
	80	A	90 %
	90	A	95 %
	95	A	100 %
	NOT		AVAILABLE

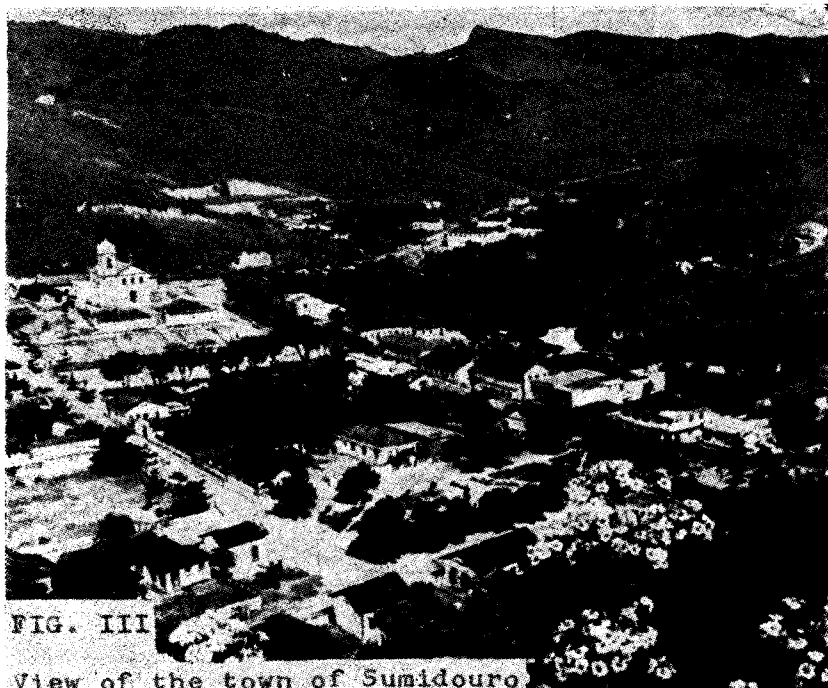


FIG. III

View of the town of Sumidouro

The treatment regimen used was as described in Table V.

To those of group I, the drug was given by a "sanitary" guard or an assistant nurse, while in the cases of groups II and III, it was always given by the medical doctor in charge of the study. In these two last groups, the Compound was administered to a large part of the population regardless whether the person was infected or not. As shown in Table VI, a few patients found negative before the treatment became positive after the first dose and even after the second course of therapy. The parents of the children and the adults themselves were properly instructed to communicate any untoward symptoms to the local Public Health Medical Doctor or to the Health Educator of the project. A record of all complaints of the patients was kept. Stool examinations were repeated by the same techniques already mentioned around the 30th day after the first course and again 30 days after the second dose.

COOPERATION OF THE PATIENTS

Cooperation was rather satisfactory in group I, while in group II, 10 refused the

first treatment, 23 the second treatment and four refused both treatments. Besides that, 33 did not receive the 1st treatment due to pregnancy, difficulty of ingestion of the capsules, problems of age, change of residence etc. Because of the same reasons 27 did not receive the second treatment; and 29 did not receive both treatments, which means that 33 patients did not receive any treatment.

In group III, the cooperation of the population was even worse, as 339 refused to take the drug; 121 failed to take the drug for various other reasons. 233 received the first treatment and 151 the second; 147 people were given both treatments.

TOLERABILITY

Table VII shows the side effects observed in the patients of the three groups. There were variations in the incidence and spectrum of side effects, according to the groups and the schedules as follows:

1) Side effects as a rule were more severe and more frequent after the first dose than after the second (group II).

2) Side effects were more intense and more frequent with a single dose schedule (200-300mg, according to the weight.)



Fig. II A: A view of a dwelling on farm A (Boa Vista)



Fig. II B: Picture of a typical farm dweller on farm B (Pamparrão)

TABLE I
DISTRIBUTION OF CASES ACCORDING TO AGE, SEX AND COLOUR

		GROUP I	GROUP II	GROUP III
		AGE (years)	2 — 6 7 — 14 > 14	13 25
SEX	MALE FEMALE	11 27	72 52	157 141
COLOUR	WHITE BLACK MESTIZOES	27 — 11	81 34 9	257 34 7

than with the fractionated schedule (100 to 300 mg, 2-3 times at 12 hour intervals).

3) The most common side effects with all schedules were: (Table VII)

Diarrhea appeared as the most frequent side effect among the patients of group II — both after the first and the second treatment and only as the third or fourth side-effect among the patients of groups I and III. Since all the patients of group II were given a glass of milk as they ingested the drug, in a population not used to drinking milk, the difference in the incid-

ence of diarrhea between the two groups could be traced to this fact.

Vomiting was perhaps the most common among the objective side effects in all groups — since it ranked second in group II, both after the first and second treatment, second in schedule I-A, third in group I-B, and first in group III.

Nausea, a subjective side effect, was very common with variations which may be explained by differences in the psychological behavior of the patients, under the conditions of the treatment of the various

TABLE II
RESULTS OF STOOL EXAMINATIONS IN THE VARIOUS GROUPS

GROUP	HELMINTH		Technique employed
	Hookworm	A. lumbricoides	
I A B (Preliminary trials)	26 12	6 3	HOFFMAN et al.
II A B (Field trials (rural))	24/ 85* or 28.2% 100/195* or 51.2%	42/ 85 or 49.4% 98/195 or 50.3%	MIFC
III (Field trials — semi rural)	298/693* or 43.1%	341/693 or 49.2%	MIFC

* Positives/examined.

T A B L E I I I
W O R M B U R D E N (E G G C O U N T S)

GROUPS	NUMBER OF POSITIVE CASES HOFFMANN* — MIFC**		NUMBER OF EGGS (BARBOSA TECHNIQUE)					
			HOOKWORM			A. LUMBRICOIDES		
	HOOKWORM	A. LUMBRICOIDES	RANGE	TOTAL	MEAN 3*	RANGE	TOTAL	MEAN
I A*	22	6	0-21800 6 cases	22456	1020	10200 — 14400	24420	4070
B	16	3	200 8 cases	2800	195	2400 — 3200	5600	1866
II**	51	39	0-420 51 cases	3978	78	0-1840 39 cases	9648	247,2
III**	118	73	0-417 118 cases	21423	181,5	5-3772	53343	730

3* Negative cases (0) on egg counts were considered as zero in establishing the mean when eggs were found by the qualitative methods.

TABLE IV

SUMMARY OF SOME HAEMATOLYGHICAL AND BIOCHEMICAL FINDINGS IN 60 PATIENTS FROM THE RURAL AREA (GROUP II)

FINDINGS	RANGE	MEAN	TOTAL
RED CELLS (mil/mm ³)	3,0 — 5,2	4,34	260,4
Hb (g%)	8,1 — 14,9	11,8	710
HAEMATOCRIT (%)	27 — 50	37,3	2240
EOSINOPHILS (%)	2 — 47	16,3	980
TOTAL SERUM PROTEIN (49 cases) (g%)	5,8 — 8,5	6,9	340,7
ALB.	3,2 — 4,8	4,1	205,9
GLOB.	2,2 — 3,7	2,8	142,0
SERUM IRON yg% (37 cases)	50 — 237	125,4	4642

TABLE V

SCHEDULES TRIED WITH COMPOUND 16.842 IN THE TREATMENT OF HOOKWORMS AND ASCARIS LUMBRICOIDES

GROUPS	PATIENTS DISTRIBUTION ACCORDING		TOTAL DOSE (mg)	REGIME
	AGE (Years)	WEIGHT (kg)		
I A	> 15	—	300	100 mg 3 times at 12 hours interval
	10-15	—	200	100 mg twice " " " "
	5-10	—	100	50 mg twice " " " "
I B	—	> 40 kg	300	Single dose
		≤ 40 kg	200	" "
II and III	> 15	—	150	Single dose repeated 4-6 weeks later
	10-15	—	100	" " " " " "
	5-10	—	50	" " " " " "
	2-5	1.5mσ/kg of body weight	—	" " " " " "

TABLE VI

STOOL EXAMINATIONS SPECIALLY CONSIDERING POSITIVITY OF HOOKWORM

	NUMBER AND % OF INITIALLY POSITIVE CASES		N.º AND % OF HOOKWORM POSITIVE CASES ONLY AFTER THE 1st. TREATMENT	N.º AND % OF HOOKWORM POSITIVE CASES ONLY AFTER 2nd. TREATMENT	POSITIVE HOOKWORM EGG COUNTS/NEGATIVE MIFC
	HOOKWORM	A.L.			
II A	24/85 (28,2%)	44/85 (51,7%)	6/66 (9%)	4/67 (5,9%)	5/30 (16,6%)
II B	100/195 (50%)	97/195 (49,7%)	17/76 (25%)	9/67 (13,4%)	6/66 (9%)
III	298/693	341/693 (40,3%)	0/74	12/107 (11,2%)	2/118* (1,6%)

* Barbosa Technique was performed almost exclusively in positive cases to MIFC technique.

groups and sub-groups. The mildness of this manifestation could be due, in groups III and specially in II, to the "buffering" effect of milk taken with the drug.

Dizziness, also a subjective symptom, ranked third in the patients of group II and I-A — while in group I-B it ranked first and in group III, second.

Headache was most frequent among the patients who took a high single dose (group I-B) while in all the other groups it was much less frequent.

Another side effect worth discussing was abdominal pain (as a rule, more intense in the epigastric area) which always ranked 4th or 5th, with the exception of group I-A, whose patients did not report this side effect.

A comparative analysis of the side-effects in a group of 60 parasited and non-parasited patients showed no difference statistically significant between the two groups.

What must be said about these side effects is that at least dizziness was less frequent with Compound 16.842, than with tetrachloroethylene which according to the different authors using the drug, is known to produce that manifestation in more

than 50% of the population treated, at least in Brazil (2).

EFFICACY

The results of the stool examinations by the Hoffman et al. technique (on the 8th, 15 and 28-30 days) shown in Table VIII, demonstrate that in 13 out of 22 cases of group I-A, eggs were not present in stools, the parasitological cure rate being 54.5%. If we consider only the results following the last examination (28-30 days) the cure rate increased to 85.4% (19 cases out of 22). In group I-B the total cure rate was 26.6% according to the last stool examination performed on the 15th day after treatment. According to the results of the first stool examination on the 8th day, the cure would be 53.3%.

In group II (Table IX) disappearance of eggs from the stools was observed in 14 out of 42 cases submitted to examination 25-30 days after the first treatment (33.3%) while the same fact was observed in 27 out of 59 cases (45.7%) subjected to stool examination 25-30 days after the second treatment. (MIFC technique).

Regarding the cases of Sumidouro, Table IX shows that the cure rate was higher

than that observed in group II, in the small group of patients already analysed for this presentation (64.8% after the first treatment and 60.5% after the second course of therapy, according to MIFC technique).

Table VIII also shows the results obtained through the counting technique (Barbosa). The test was positive only in 6 cases of group I-A and in 5 of group I-B. The mean egg counts were 1.020 and 175 eggs respectively. After the last treatment, the egg counts were positive in two and six cases respectively, with mean egg counts of 2 and 80. The mean egg count dropped from 1020 to 6 (99.4%) after the last treatment, while in group B it dropped from 175 to 80.

Table IX shows the results of the counting techniques in groups II and III. Regarding group II, the mean egg count was 78 before treatment. It went up to 248 after the first treatment, with a mean percent reduction of 32.4%, considering that 33.3% of the cases presented parasitological cure.

In group III, the results of the counting technique refers to 25 cases before and after the first treatment. The mean egg count which was 274 (0-2140) dropped to 98.2 (0-390) which means a reduction of 64.1%; after the second treatment, mean egg count was 150.

The results concerning groups II and III refer to followed-up positive hookworm cases, whether or not receiving any of the treatment courses, as the trial was designed for mass treatment. If only the results of followed-up cases which received treatment are considered, parasitological cure in the farms is 36.6% (14 out of 38) after the first course of treatment and 45.9% (21 out of 46 cases) after the second treatment. In the town of Sumidouro, 24 out of 33 followed-up after the first treatment showed parasitological cure (72.7%); this percentage dropped to 55.3% (24/38) after the second treatment. (Table X).

The probability of re-infection in the group II-A is not to be disregarded, a fact which seems to be enhanced by the lower cure rate observed after the second treatment in relationship to that observed after the first treatment.

Regarding the effect of the drug on *Ascaris lumbricoides*, (Table XI) the number of cases in group I was too small

for conclusions, while in group II and III the results are as follows:

After the first treatment, 21 out of 79 (26.5%) showed parasitological cure while only 9 out of 64 (14%) showed cure after the second course of therapy (MIFC technique).

Considering the reduction of egg counts, the average number of eggs which was 247 before treatment (0-1840) went up to 316 after the first treatment (0-1190) and went up again to 487 (0-1953) after the second treatment. The mean percent reductions were 27% and 34.6% respectively after the first and the second treatment. As far as the effect of Compound 16.842 on *Ascaris lumbricoides*, the data of the town of Sumidouro shows results of only a few cases — with 10.3% and 22.2% of negativations after the first and the second treatment respectively. The mean percent reduction was 43.8% and 47.3% respectively, in the same situations.

It has to be mentioned that all these patients continued to live in the same unhealth environment where the rate of prevalence of hookworm infection was, as mentioned before, respectively 28.5% and 51% with an average of 44.1%, in the two farms and 43% in the town.

DISCUSSION

Compound 16.842 appears to be a promising drug against hookworm and with mild action against *Ascaris lumbricoides*. Since the drug is, as rule, well tolerated, with the observation that the second dose is followed by milder side effects than the first one, it is possible to use it either in higher single doses or in courses of therapy of 2-4 consecutive days. Another important problem to be considered is related to the species or even strains of the parasites, mainly regarding hookworm. Our studies, in order to determine the species of hookworm present in the two rural areas and in the town of Sumidouro have not yet been successful, but in the two other subgroups the prevalent species was *Necator americanus* with a few cases in which both species, *Necator* and *Ancylostoma duodenale*, were associated.

At this stage, it was not possible to compare the value of the drug with other

antihelmintics which are known to be effective against both hookworm and *Ascaris lumbricoides*, since previous work on those drugs which showed significant cure rates utilized other techniques for counting eggs. It has been, however, our experience in Brazil that, the Stoll technique (11) always gives higher counts than the Barbosa technique; nevertheless, the later gives results which are more reproduceable than those of the Stoll technique.

COMMENTS ON OTHER DRUGS FOR THE TREATMENT OF HOOKWORM

A. Trying to compare Compound 16.842 to tetrachloroethylene, we may see in Tables XII-A and XII-B, that a single dose of the later gave 92% of cures in patients living in healthier environments, treated in our out-patient clinics, while using the same schedule it gave 0% of cures in a group of 20 patients with a higher mean egg count living in a rural and unhealthy environment. (Camillo-Coura et al, unpublished data.)

Regarding tolerance to tetrachloroethylene, we may see in Table XII-C that dizziness and drowsiness were more frequent with tetrachloroethylene than with Compound 16.842. In part, the relatively high incidence of side effects among the patients treated with Compound 16.842 might result from the fact that the patients themselves or their parents were informed in advance to call the local doctor in case of any trouble. Another fact is that the drug was given to several people at the same occasion and this seems to cause psychological factors which may predispose patients to complain of symptoms which have been described by others and which can be real or imaginary. Another observation, made by the doctor in charge of the trials, is that the intensity of the side effects was in fact milder with Compound 16.842 than with tetrachloroethylene, (in the given doses).

B. Bephenium hydroxynaphtoate

An analysis of the data of Table XIII shows that Bephenium hydroxynaphtoate always gave poor cure rates, except when a 5.0g schedule for 3 days, among cases of low density infections with hookworm, was given. (3, 9).

C. Trichlorophenol piperazine (CI-416 Parke Davis)

Table XIV shows that 1-2 day courses of therapy always gave low cure rates. Side effects were very frequent with longer courses which, nevertheless, gave higher cure rates. (4).

D. Thiabendazole

Thiabendazole (25 mg/kg/d for 3 days) in 39 cases of low density hookworm infection gave 63% of cures. Side effects were very mild (Table XV). Analysis on the effect of this drug on other helminths is under way. (unpublished data)

OTHER COMMENTS

Other facts revealed from this study, mainly from those carried out in the rural areas, are the variations found in the results of stool examinations and egg counts — such as: a) Failure to detect eggs before treatment followed by their detection only after a first treatment; b) increase in the number of eggs after a first and even a second treatment 24-40 days later; c) Failure to detect eggs in the same sample of stools, by the MIFC technique, followed by their detection by the sedimentation technique. It is known that these controversial findings may occur mainly in cases of light infection. On the other hand, one must consider the possibility of an increase in the number of eggs, due to the evolution of a recent reinfection (previous or post-treatment) mainly among patients living in highly endemic areas — or to normal fluctuations on the oviposition. This last fact may either favor any given drug or hamper the results of therapy.

The explanation for the discrepancies observed in some of the above results (efficacy) are being explored and will perhaps be found only after more accurate studies are performed. New trials are forecast, examining at least three different samples of stools and by having the patient submitted to more frequent post treatment stool examinations using the most reliable techniques. The trials should be conducted under different conditions i.e., while one group would continue to live in the same previous sanitary conditions, another group would have these environmental

T A B L E V I I

SIDE EFFECTS OBSERVED AMONG THE PATIENTS OF THE 3 GROUPS TREATED WITH COMPOUND 16.842

SIDE EFFECT	GROUP I		GROUP II		GROUP III	
	A. 3 single doses 12 — 12 hs. (22 cases)	B. One single dose (16 cases)	1st Treatment (220 cases)	2nd Treatment (176 cases)	1st Treatment (189 cases)	2nd Treatment (21 cases)
Dizziness	2 (8.6%)	8 (50%)	42 (19%)	19 (10.8%)	32 (16.8%)	3 (11.1%)
Drowsiness	— —	— —	3 (1.3%)	9 (5.1%)	9 (4.7%)	1 (3.7%)
Nausea	10 (43%)	6 (37.8%)	22 (10%)	7 (3.9%)	15 (7.9%)	4 (14.8%)
Vomiting	6 (26%)	7 (43.7%)	57 (25.8%)	32 (18.6%)	45 (23.8%)	7 (25.9%)
Headache	2 (8.6%)	9 (56%)	16 (7.2%)	17 (9.7%)	— —	— —
Abdominal pain	— —	3 (18%)	13 (5.9%)	1 (0.5%)	4 (2.1%)	— —
Diarroea	2 (8.6%)	6 (37.8%)	65 (29.5%)	44 (25%)	26 (13.7%)	2 (7.4%)
Asthenia	— —	— —	15 (6.8%)	1 (0.5%)	— —	— —
Lipotimia	— —	— —	— —	— —	1 (0.5%)	— —
Meteorism	— —	— —	3 (1.3%)	— —	— —	— —
Association of two or more side ef- fects	7 (31.8%)	15 (93.3%)	83 (37.7%)	27 (15.3%)	30 (15.8%)	1 (3.7%)
NIHIL	13 (56.6%)	— —	74 (33.6%)	82 (46.5%)	93 (49.1%)	16 (58.5%)

TABLE VIII

EFFECT OF COMPOUND 16.842 UPON HOOKWORM INFECTION (GROUP I)

GROUP I	BEFORE TREATMENT			FOLLOWING FIRST CONTROL (8th DAY)			FOLLOWING SECOND CONTROL (15th DAY)			FOLLOWING THIRD CONTROL			TOTAL N.° CASES NEG. IN ALL STOOL TESTS N/T
	N.° OF CASES TREATED	TOTAL N.° OF EGGS*	MEAN EGG COUNTS	N.° OF CASES OBSERV- ED N/T **	TOTAL N.° OF EGGS	MEAN EGG COUNTS	N.° OF CASES OBSERV- ED N/T **	TOTAL N.° OF EGGS	MEAN EGG COUNTS	N.° OF CASES OBSERV- ED N/T **	TOTAL N.° OF EGGS	MEAN EGG COUNTS	
A	22	22.456 (6 cases)	1.020 (0-21.800)	13/21 (51%)	2482	310 (0-1800)	16/21 (76.2%)	600	120 (0-600)	19/22 (85.4%)	6	2 (0-6)	13/22 (54.5%)
B	16	2.800 (5 cases)	175 (0-800)	9/16 (56.2%)	1180	168 (0-1000)	8/15 (53.3%)	2200	80 (0-1200)				6/16 (26.6%)

* Only 6 out of 22 cases found positive for Ancylostomidae by the Hoffman Technique were positive by the sedimentation count method (Barbosa).

** Negative/treated and followed up.

T A B L E IX
EFFECT OF COMPOUND 16.842 ON HOOKWORM INFECTION (GROUPS II AND III)

GROUP	POSITIVE CASES	EGG COUNTING (BARBOSA TECHNIQUE)									
		BEFORE TREAT.		AFTER 1st. TREATMENT			AFTER 2nd. TREATMENT				
		TOTAL NUMBER	MEAN	TOTAL NUMBER	MEAN	MEAN % OF REDUCTION	C/T *	TOTAL NUMBER	MEAN	MEAN % OF REDUCTION	C/T *
II A + B	124 (114 treated)	3978 (67 cases)	78 (0-420)	12771 (49 cases)	248 (0-1127)	32.4%	14/42 (33.3%)	4029 (48 cases)	83.9 (0-380)	69.6%	27/59 (45.7%)
III	268 (134 treated)	6871 (25 cases)	274 (0-2140)	2456 (25 cases)	98.2 (0-390)	57.5%	24/37 (64.8%)	4613 (24 cases)	150 (0-1633)	57.6%	26/43 (60.5%)

C/T — cured/treated

TABLE X

COMPARISON OF RESULTS OF THERAPY WITH COMPOUND 16.842 ON HOCKWORM INFECTION (GROUPS II AND III), IN FOLLOWED-UP PATIENTS*

GROUP	NUMBER OF CASES FOLLOWED UP	TOTAL CURES (TREATED AND NOT TREATED FOLLOWED-UP)				CURES (TREATED AND FOLLOWED-UP)			
		AFTER 1st. COURSE		AFTER 2nd. COURSE		AFTER 1st. COURSE		AFTER 2nd. COURSE	
		C/T**	%	C/T	%	C/T	%	C/T	%
II A	1st. course: 16 2nd. course: 23	5/16	31.2	8/23	34.7	5/13	38.4	4/16	25.3
B	1st. course: 26 2nd. course: 36	9/26	34.3	19/36	52.8	9/25	34.3	17/30	56.6
III	1st. course: 37 2nd. course: 43	24/37	64.8	26/43	60.5	24/33	72.7	21/38	55.3

* according to Mifc Technique

** cured/treated

T A B L E X I

EFFECT OF COMPOUND 16.842 ON ASCARIS LUMBRICOIDES

GROUP	NUMBER OF EGGS BEFORE TREATMENT			EXAM. AFTER 1st. TREATMENT				AFTER 2nd. TREATMENT			
	TOTAL	RANGE	MEAN	TOTAL NUMBER	MEAN	MEAN % REDUCTION	C/T*	TOTAL	MEAN	MEAN % REDUCTION	C/T
I A	22420 (6 cases)	0-14400	4070	600	100 (0-600)	83.3%	2/6 (33.3%)	—	—	—	—
B	5600 (3 cases)	0-3200	2800	10300	3600 (600-9000)	54%	0/3				
II	9648 (39 cases)	0-1840	247.2	9827 (31 cases)	319 (0-1190)	27%	21/79 (26.5%)	19975 (41 cases)	487 (0-1953)	34.6%	9/64 (14%)
III	53343 (73 cases)	5-3772	730	7432 (19 cases)	391 (0-1574)	43.8%	2/19 (10.5%)	21766 (19 cases)	1145 (-8667)	47.3%	3/18 (22.2%)

* Cured/Treated.

T A B L E X I I I

BEPHENIUM HYDROXYNAPHTHOATE IN THE TREATMENT OF OUT-PATIENTS WITH HOOKWORM INFECTION

PRESENTATION OF DRUG	SCHEDULE		LOW INFECTION DENSITY			HIGH INFECTION DENSITY				
	DAILY DOSE	DAYS OF TREATMENT	STOOL EXAM. BEFORE TREATMENT NUMBER OF EGGS/ML STOOL (STOLL TECHNIQUE)		PERCENTAGE OF EGG REDUCTION	N/T*	STOOL EXAM. BEFORE TREATMENT NUMBER OF EGGS/ML STOOL (STOLL TECHNIQUE)		PERCENTAGE OF EGG REDUCTION	N/T*
			RANGE	MEAN			RANGE	MEAN		
MICROPELLETS	2.5 g	1	100-2000	773	59	11/29	7800-13800	10800	85	0/2
	2.5 g	2	200-1080	1080	60	8/31	0- 6400	6400	87.5	0/1
	2.5 g	3	100-2000	800	74	7/11	3000-18000	8000	44	1/3
GRANULES	2.5 g	1	100-2500	1038	56	8/29	3000-44300	11544	55	0/11
	2.5 g	3	400-1200	925	77	1/4	4000- 5600	4800	85	0/2
	5.0 g	3	100-900	514	85	6/7	—	—	—	—

* Negative/treated

T A B L E X I V

TRICHLOROPHENOL PIPERAZINE (CI-416), IN THE TREATMENT OF OUT-PATIENTS WITH HOOKWORM INFECTION

PRESENTATION	SCHEDULE		DAYS OF TREATMENT	NUMBER OF PATIENTS	STOOL EXAM. BEFORE TREATMENT (STOLL TECHNIQUE)		PERCENTAGE OF EGG REDUCTION		
	DAILY DOSE				RANGE	MEAN	100	99-75	74-50
DRAGEES	2-3 g (adults)	A	4	62	200-48300	2321	74.2	8.1	8.1
	0.5-2 g children) 3-5 g	B	1	50	200-76700	5380	54	20	14
SOFT GELATIN CAPSULES	20-30 mg/kg	C	2	10	300-11200	2100	50	10	10
	50 mg/kg	D	1	25	300-10500	1908	20	4	8
	50 mg/kg	E	2	9	100-8300	1570	44	—	—
	50 mg/kg	F	4	7	200-2800	800	85	—	—
	80 mg/kg	G	3	5	200-2000	840	100	—	—
	100 mg/kg	H	2	9	900-2000	1544	55.5	44	—
	2-4 g	I	2	10	500-1500	840	80	10	10
	50 mg/kg	J	1 + 2*	19	900-2900	1715	63.1	—	26.3
	2-4 g	K	2 + 1**	4	200-1700	900	75	—	25

* Seven days after

** Ten days after

conditions changed, wearing of shoes included, besides health education.

Finally it must be pointed out that, since this trial deals almost exclusively with *Necator americanus*, the relatively low cure rates obtained may be due to the fact that that species of hookworm is more resistant to therapy than *Ancylostoma duodenale* — a fact mentioned by Hsieh et al. (8), among patients treated with Bephenium.

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S U M Á R I O

Os autores ensaiam um novo antihelmíntico, Composto 16.842, em 3 grupos de pacientes de modo a testar sua eficácia, tolerância e a possibilidade de seu emprego em campanhas de massa contra ancilostomíase. O primeiro grupo, em que se empregou a droga em ensaio preliminar, consistiu de um grupo de 38 pacientes de ambulatório do Serviço e de um orfanato no Estado da Guanabara. No grupo II administrou-se o medicamento a toda a população de duas fazendas no município de Sumidouro e no grupo III incluiu-se grande parte da população da pequena cidade de Sumidouro.

A tolerância foi satisfatória, principalmente nos pacientes que receberam 2 doses de 50 a 150 mg com intervalos de 4 a 6 semanas e os resultados obtidos sugerem que 2 a 4 cursos de tratamento num menor período de tempo são ideais para tratamento em massa.

A cura parasitológica variou de 26,6% a 76,2% nos vários grupos, com grande variação também nos percentuais de redução média do número de ovos de ancilostomídeos nas fezes.

Observou-se efeito contra *Ascaris lumbricoides*, com índices de cura de 13,5 a 35,7% nos vários grupos.

Concluem os autores que o Composto 16.842 tem seu lugar no tratamento da infecção por ancilostomídeos e que são necessários maiores estudos para determinar os esquemas terapêuticos mais eficientes.

REFERENCES

1. BARBOSA, F. S. — Morbidade na Esquistossomose. (A thesis) 176, pp. Recife, 1965.
2. CAMILLO-COURA, L. ET AL — Ensaio sobre a terapêutica antihelmíntica com sais de piperazina, tetrachloretileno e hidroxinoftoato de befenio. Paper presented to the IX Brazilian Congress of Medicine, Rio de Janeiro, July, 1962.
3. CAMILLO-COURA, L. ET AL — O hidroxinaftoato de befenio no tratamento de algumas parasitoses intestinais humanas. O Hospital, 69: ... 981-989, 1966.
4. CAMILLO-COURA, L. ET AL — Therapeutical trials with a new antihelmintic-trichlorophenol piperazine (CI 416) on hookworm, *Ascaris lumbricoides*, and *Trichuris trichiura*. J. Bras. Med. Trop., I, I, 57-64, 1967.
5. COUTINHO, J.O. — Nota sobre modificações do MIFC na conservação de fezes para pesquisa de cistos e protozoários. Arc. Fac. Hig. e Saúde Publ. Univ. S. Paulo, 10 (1-2), 1956.
6. FERREIRA, L. F. — O exame parasitológico das fezes — estudo comparativo de principais técnicas. O Hospital, 70: 347-368, 1966.
7. HOFFMANN, W. A. ET AL — The sedimentation-concentration method in Schistosomiasis mansoni: Puerto Rico, J.P. Health, Trop. Medicine, 9: 283-291, 1934.
8. HSIEH-CHEN HSIEN ET AL — The treatment of hookworms, *Ascaris lumbricoides*, and *Trichuris* infections with Bephenium hydroxynaphtoate. J. Trop. Med. Hyg. 9: 496-499, 1960.
9. RODRIGUES DA SILVA, J. ET AL — O hidroxinaftoato de Befenio no tratamento da ancilostomíase, ascariíase e tricuriase. J. Bras. Med. 6: .. 270-288, 1962.

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10. SAPERO, J. J. & LAWLESS, D. K. — The "MIF" stain preservation technique for the identification of intestinal protozoa. *Am. J. Trop. Med. Hyg.* 2, 4: 613-619, 1953.
11. STOLL, N. R. — An effective method of counting hookworm eggs in feces. *Am. J. Hyg.* 3: 59-70, 923.