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The effects of drugs on experimental hepatic capillariasis in mice

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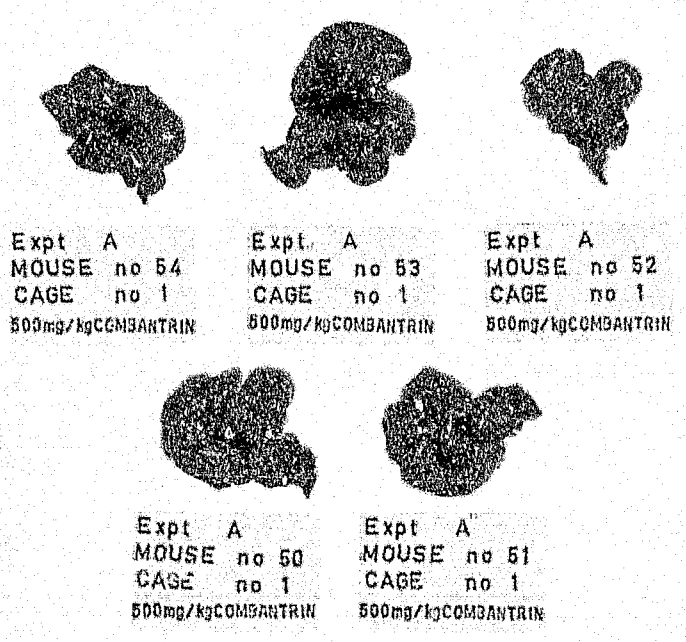

FIGURE 52 Livers from Mice Dosed with 500 mg/kg Pyrantel (Combantrin ®)

Scale bar indicates 25 mm

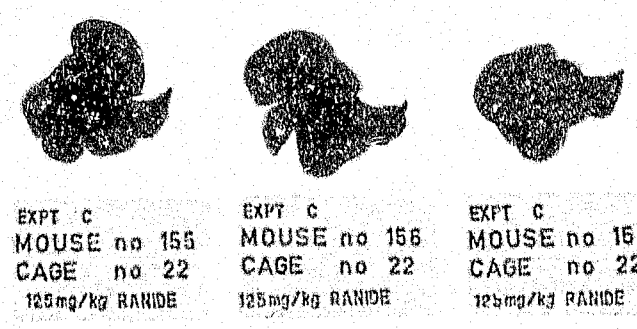

FIGURE 53 Livers from Mice Dosed with 125 mg/kg Rafoxanide (Ranide ®)

Scale bar indicates 25 mm

4.2 Scanning Electron Microscopy (SEM)

Examples of electron microscopic observations are given in Figures ' - 58. All the photographs of the worms are shown at the same magnification (x 1 000) and, therefore, direct comparisons may be made.

The control picture (Figure 54) shows the worm as having an area with pores and an area without. The cuticle is slightly wrinkled. The control worm measures approximately 55 µm in diameter. However, it must be stated that the preparation of specimens for SEM is known to cause shrinkage and that normal variation is considerable.

Figure 55 is of a mebendazole (Vermox ®) treated worm and reveals considerable vacuolisation of the worm's surface and collapse of the worm's body. The diameter of this specimen is approximately 47 µm. The picture of a worm treated with albendazole (Valbazen ®) (Figure 56) indicates that the drug may have caused enlargement of the pores, but no vacuolisation or other distortion can be observed. This specimen has a diameter of approximately 49 µm. Figure 57 of an oxfendazole (Systamex ®) treated worm, shows pores which are more enlarged that those of the control; and additional convolution of the tegument, which might be a drug-induced effect. This worm measures approximately 56 µm in diameter. Figure 58 shows a febantel (Rintal ®) treated worm. The diameter of this specimen is approximately 46 µm. There appears to have been some lengthwise shrinkage in this specimen, the surface of which is considerably obscured by a black deposit. The deposit may be an artifact caused by preparation, although all specimens were treated identically.

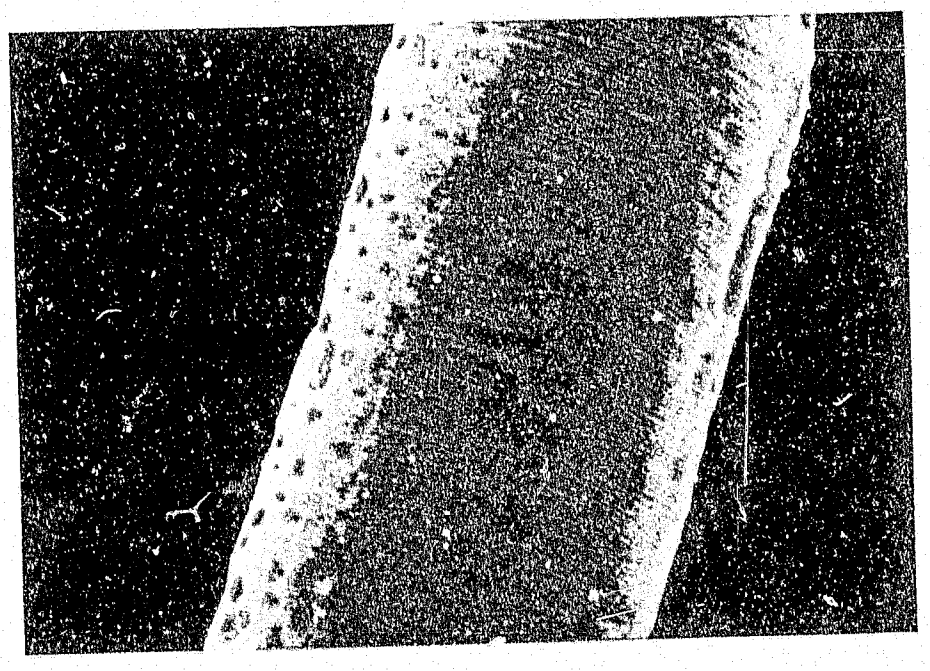

FIGURE 54 Scanning Electron Micrograph of a C. hepatica Worm from an untreated Mouse host (x 1 000)
(Note Slightly wrinkled cuticle and area of small pores)

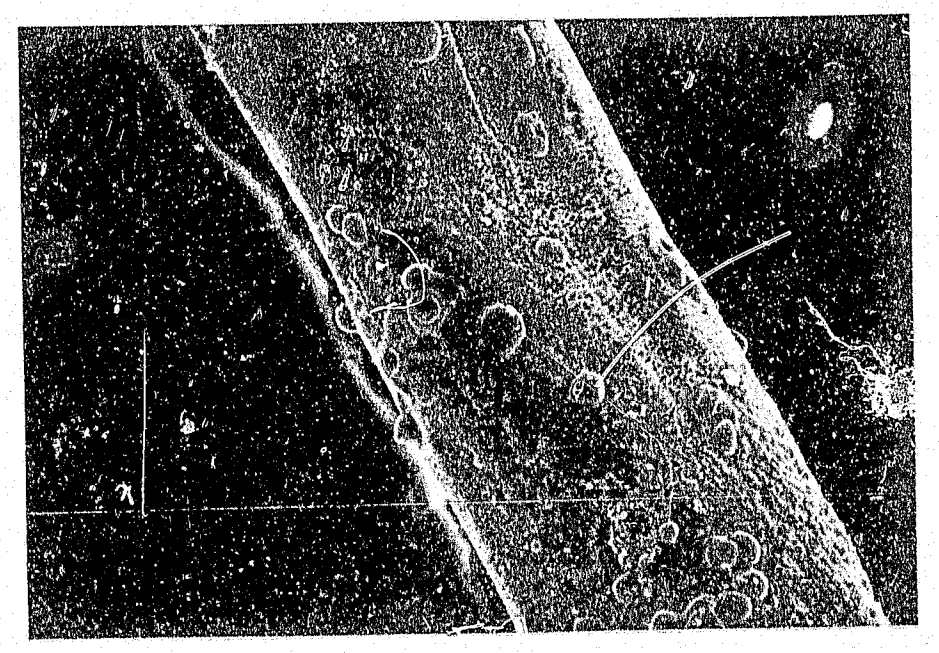

FIGURE 55 Scanning Electron Micrograph of a C. hepatica Worm from a Mouse Dosed with 3.13 mg/kg Mebendazole (Vermox ®) (x 1000)
(Note extensive vacuolisation and collapse of the worm body)

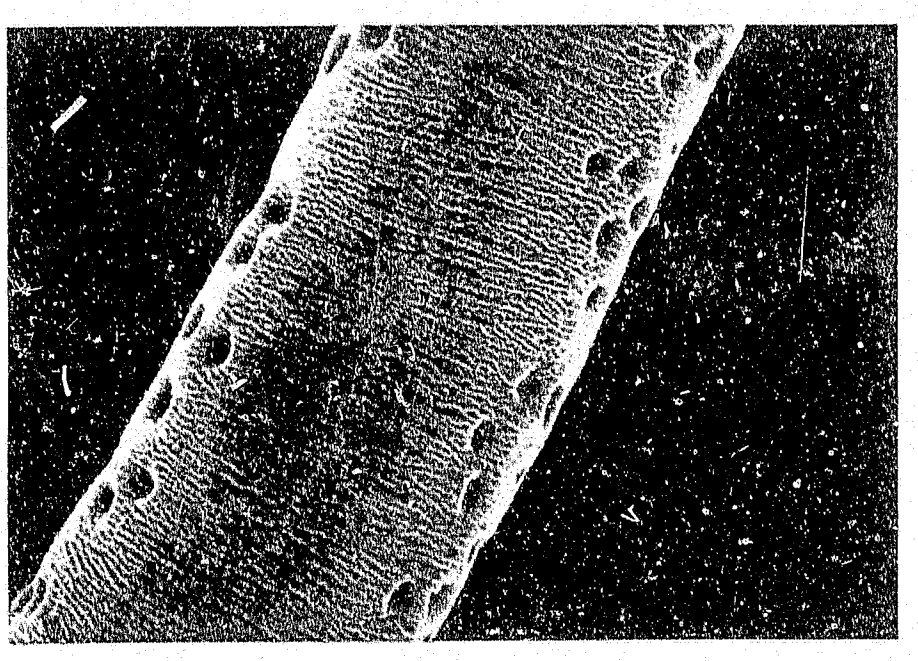

FIGURE 56 Scanning Electron Micrograph of a C. hepatica Worm from a Mouse Dosed with 30.0 mg/kg Albendazole (Valbazen ®) (x 1 000)
(Note enlarged pores)

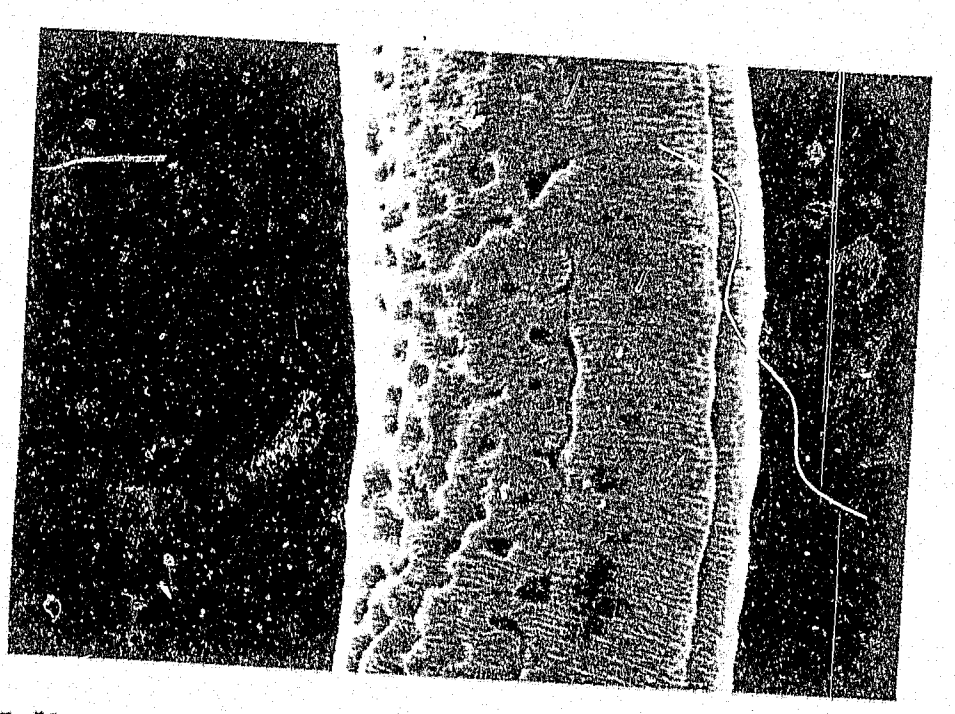

FIGURE 57 Scanning Electron Micrograph of a C. hepatica Worm From a Mouse Dosed with 12.5 mg/kg Oxfendazole (Systamex ®) (x 1 000)
(Note enlarged pores and cuticular convolution)

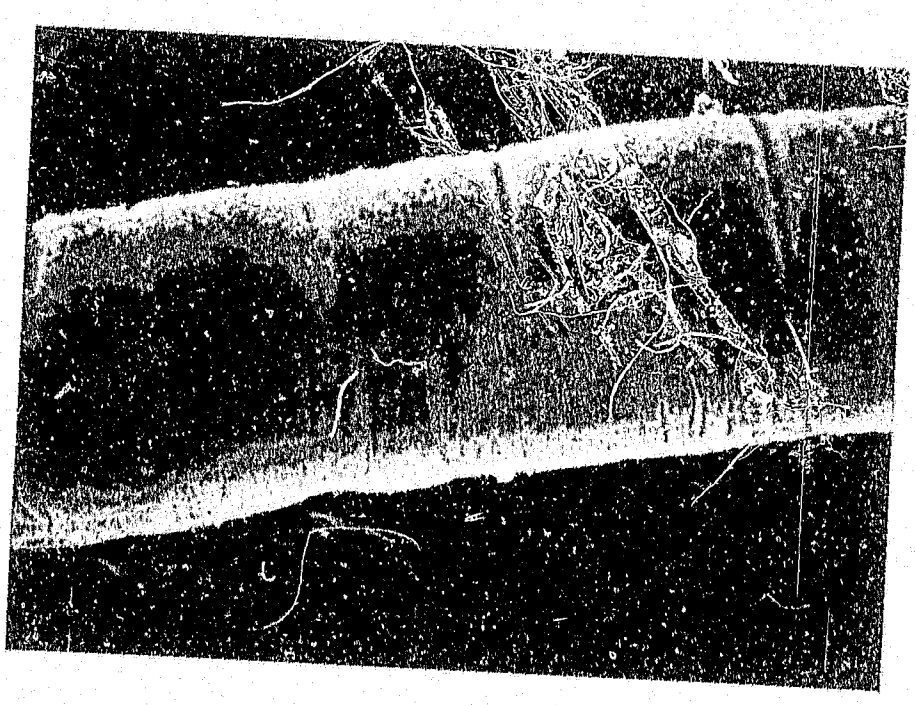

FIGURE 58 Scanning Electron Micrograph of a C. hepatica Worm from a Mouse Dosed with 30.0 mg/kg Febantel (Rintal ®) (x 1 000)
(Note lengthwise shrinkage)

5. DISCUSSION

5.1 Analysis of Material

In order to evaluate the effectiveness of the drug treatments, it was necessary to obtain an estimate of the number of C. hepatica eggs in both the treated and control animals. As the eggs are deposited in the liver of the host, but are immune to normal digestive processes in their unembryonated state, they may be released from the liver by the artificial digestion technique used in this work. This was first proposed by Matsusaki (1951) and was modified by Vollerthun et al. (1974). This technique relies on a combination of pepsin and hydrochloric acid being mixed with the liver tissue and stirred at 37.5°C for a period sufficient to digest the liver tissue and any fibrotic masses which are present, thus leaving the C. hepatica ova free in solution.

Once the eggs have been freed from the liver tissue, an estimate of their numbers needs to be made. The method employed by all the above authors was that of the McMaster counting chamber. This technique relies on the fact that many eggs and larvae float in certain salt solutions, while the debris (in this case liver particles) sink. The eggs float to lie immediately below the upper glass of the chamber, which is etched with a square 1 cm x 1 cm and can be examined by means of a microscope. The width between the two glass plates of the chamber is 0.15 cm, thus the volume of liquid being examined is 0.15 ml, and hence the total number of eggs per gram of liver may be extrapolated (Ministry of Agriculture, Fisheries and Food, 1971). The accuracy of this technique is sometimes called into question, but Dunn (1978), although accepting the limitations of this

method, states that counts of, for example, 500 and 2 000 eggs/g, respectively, or 2 000 and 10 000 eggs/g, respectively, represent valid results; whereas counts of 500 and 800 eggs/g or 2 000 and 3 000 eggs/g are not considered to be different. As one is looking for gross differences in egg counts between treated and untreated groups of mice after attempting to treat C. hepatica infection, this technique is considered to be valid.

Although this technique was satisfactory, it proved to be laborious when large numbers of animals were involved. With this in mind, it was felt that it might be possible to distinguish between successful and unsuccessful treatments on the basis of a difference between the liver weights of various dosed groups, as compared to their respective control group(s). In this type of experiment where each group is to be compared to the control, a multiple comparison procedure (i.e. between the treatment groups) is not required, but one does wish to know which treatments are most strikingly different from the control. For these reasons, the Dunnett's test for multiple comparisons with a control was used (Dunnett, 1964).

The use of the liver weights in the Dunnett's test, as described above, is only a valid representation of the number of eggs present, if there is a linear relationship between the liver weight and the number of eggs present in that liver. Figure 59 shows that there is a linear relationship between the weight of the mouse liver and the number of eggs per gram of liver. A linear regression analysis gives a correlation coefficient of 0.3499, which is significant at the one per cent level, thus showing that the linear relationship is a good fit for these data.

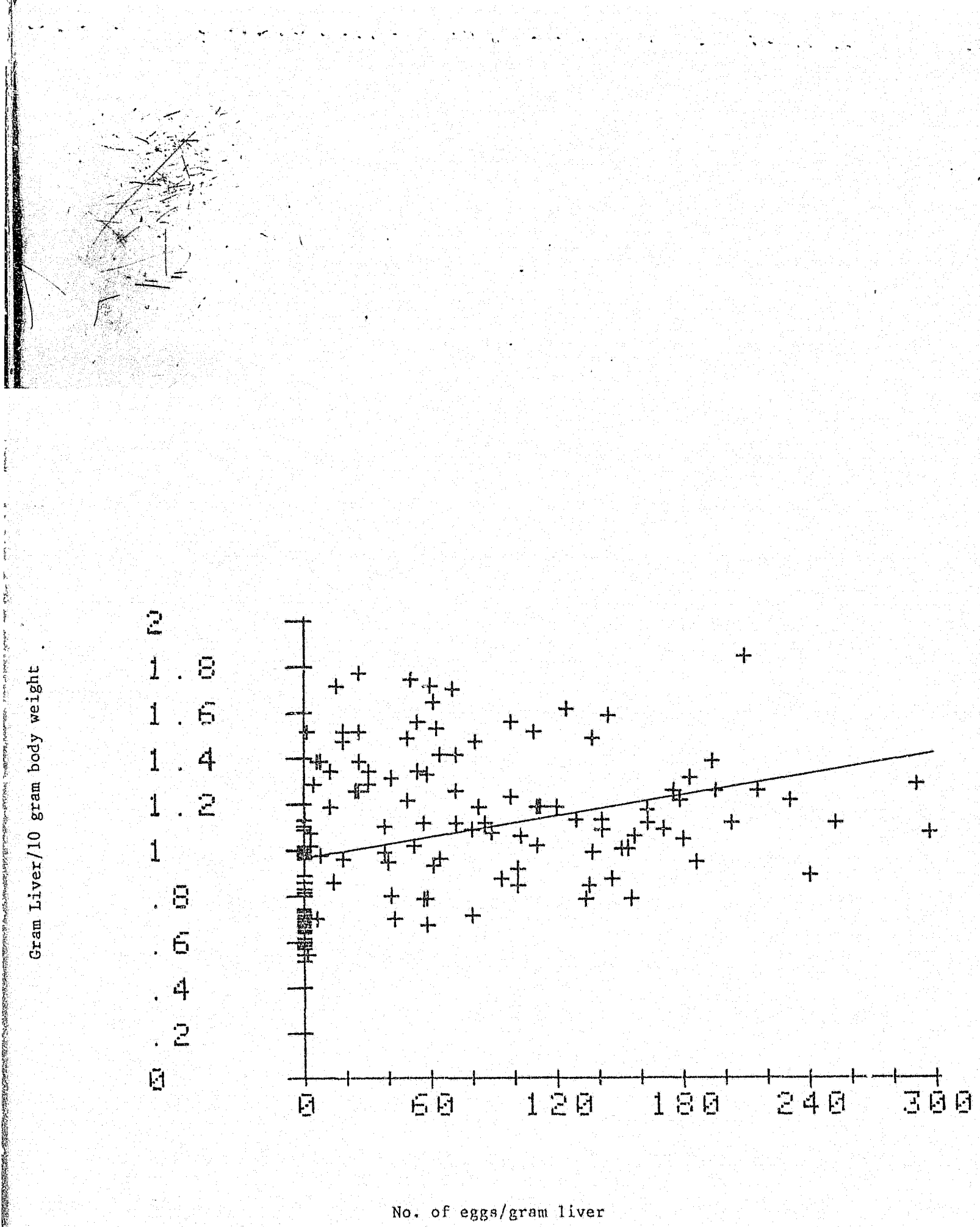

FIGURE 59 Graph to show the Linear Relationship between Mouse Liver Weight and the Number of Eggs per gram of Liver

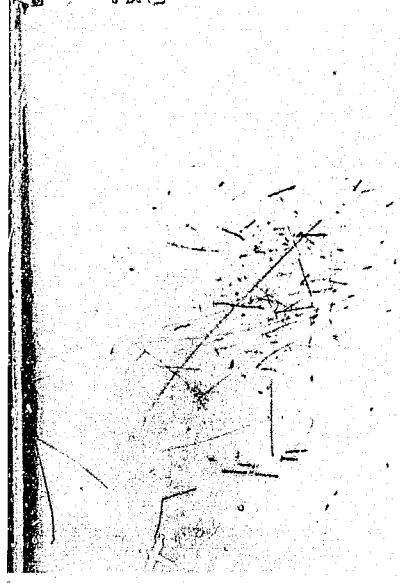

FIGURE 59 Graph to show the Linear Relationship between Mouse Liver Weight and the Number of Eggs per gram of Liver

The Dunnett's test was applied to the mouse liver weights, but because of the linear relationship between liver weight and egg numbers, the result of the Dunnett's test is a true reflection of the number of C. hepatica ova present in the liver. It may, therefore, be suggested that in pilot experiments (where high doses of drugs are used to determine their potential effectiveness against C. hepatica) the Dunnett's test, when used for liver weights, provides a good indication of the effectiveness of a drug. This would then obviate the necessity for laborious egg counting procedures in these initial stages of an investigation.

5.2 Chemotherapy

This study has revealed four anthelmintics which have good efficacy against the deposition of C. hepatica eggs in mice. The lowest dose-levels at which these compounds achieved more than 99 per cent reduction in deposition of eggs in the mouse liver, are given below in Table 7.

Of these four compounds, only mebendazole is at present marketed in South Africa as a preparation for human use. The remaining three compounds are at present available only for veterinary use. It should be noted that only in the case of mebendazole does the total experimental dose fall within the manufacturer's recommended dose range.

TABLE 7 Lowest Effective Dose Against C. hepatica

DRUG	EXPERIMENTAL		MANUFACTURER'S RECOMMENDED DOSE (mg/kg)
	DOSE LEVEL (mg/kg)	TOTAL DOSE GIVEN (mg/kg)	
Albendazole (Valbazen ®)	30.0	150	3.8 - 7.5
Febantel (Rintal ®)	30.0	150	5.0 - 20.0
Mebendazole (Vermox ®)	3.13	15.63	8.6 - 17.1
Oxfendazole (Systamex ®)	12.5	62.5	5.0

These results confirm the finding of Lämmler and Grüner (1976) for mebendazole. Working with M. natalensis, they determined the reduction in C. hepatica ova deposition to be 89.5 per cent at 3.12 mg/kg and 99.98 per cent at 6.25 mg/kg.

In the work recorded here, a reduction of 99.7 per cent was seen at 3.13 mg/kg, and 100 percent reduction at 6.25 mg/kg. In both Lämmler and Grüner's (1976) study and the present investigation, the drug was administered for the same period i.e. from days fourteen to eighteen of the experiment. Mebendazole is, therefore, considered to be the most effective anthelmintic tested to date for the prevention of egg deposition by C. hepatica.

As the drug was administered from days fourteen to eighteen post inoculation with C. hepatica eggs, the drug presumably either: prevents the worms from reaching maturity; or causes their death; or whilst allowing the worms to reach full maturity, prevents egg production. I would postulate that the worms are generally killed by the drug. The evidence available to support this statement is simply that, when dissecting livers to obtain specimens for SEM, it was noted that there were very few worms present in successfully treated livers, whereas they were abundant in untreated controls.

Little was previously known about anthelmintic treatment for C. hepatica infection but in the light of the results reported here, it would seem that patients suspected of suffering from C. hepatica infestation should be treated with mebendazole as soon as possible. However, treatment should not be withheld if the disease has progressed past the first few weeks, as Lämmler et al. (1974) showed that egg production proceeds until about day seventy of the infection. Of course, if there is any possibility of subsequent reinfection with embryonated C. hepatica eggs, then treatment should be given immediately in order to minimise further liver damage. In the human cases cited in the literature, the therapy given was largely supportive, as the nature of the disease was generally diagnosed long after the onset of illness.

Mebendazole has emerged over the last decade or so as an extremely effective broad spectrum anthelmintic, in a range of hosts. The human preparation of the drug is used for single and mixed infections of both nematodes and cestodes. The following are but a few selected examples of the effectiveness of mebendazole.

It has been utilized with success against Syngamus trachea in both turkeys and cock-pheasants (Thienpont et al., 1973; Schricke et al., 1973) and in cock-pheasants against Capillaria contorta in the oesophagus and Capillaria obsignata and Capillaria caudinflata in the intestine (Schricke et al., 1973). Mebendazole has been found to be highly effective agianst Trichinella spiralis. When used in mice, six doses at 7.5 mg/kg were given and deemed effective (McCracken et al., 1982). Mebendazole has been rated as highly effective against Strongyloides ratti and Strongyloides stercoralis, strongyloidiasis being one of the major human intestinal nematode infections (Grove, 1982). In a trial involving Indian school children, Kan (1983) showed that although mebendazole did not result in a complete parasitological cure, it reduced the egg burden in T. trichiura infections. This is of interest as this parasite is in the same family as C. hepatica. Mebendazole is a most useful anthelmintic drug, and treatment of C. hepatica infection may now be included in its range of uses.

The scope of this work did not include investigation of the effects of any of the drugs tested on the granulomas formed by the deposition of C. hepatica ova in liver tissue. It is possible that treatment with the same, or different drug, may reduce the liver damage. For example, Mehlhorn et al. (1982) have demonstrated that praziquantel (here shown to have a small, but insignificant, effect on egg deposition by C. hepatica) does cause regression of liver granulomas caused by Schistosoma mansoni. If a drug could be found to do this in the case of C. hepatica infection, it would obviously be of further aid in the treatment of this disease.

5.3 Scanning Electron Microscopy (SEM)

SEM seems to have become a popular method of visually determining the effects of anthelmintics on various parasites. For example, the effects of praziquantel on schistosomes has been clearly demonstrated (Becker et al., 1980; Mehlhorn et al., 1981; Mehlhorn et al., 1982; Mehlhorn et al., 1983). The effects of the same drug on cestodes have likewise been revealed by SEM (Becker et al., 1981; Conder et al., 1981). In the same way Blazek (1981) demonstrated the effects of two drugs in bovine cysticercosis. In all these examples, the general picture is one of tegumental shrinkage and vacuolisation.

Studies such as those mentioned above have not been performed on C. hepatica. Wright (1974 and 1978) appears to have been the only author to have attempted SEM on C. hepatica. He showed the cuticle to be highly wrinkled and folded over the spicule sheath of C. hepatica.

The SEM examination by the present author of C. hepatica worms treated with albendazole, febantel, mebendazole and oxfendazole revealed the general picture of tegumental shrinkage and vacuolization. The greatest degree of vacuolization was seen in the mebendazole-treated worms. This was the most successful drug against C. hepatica. It is not known what mechanism causes these effects, but Probert et al, (1982) treated Monezia expanza with oxfendazole and showed tegumental distortion and vacuolization; they suggest that the drug acts on the metabolism of the worms, causing starvation-like conditions and hence autophagy. Whatever the mechanism(s), these preliminary results would seem to show that the drugs tested do have a visible effect on the external appearance of the C. hepatica worms.

APPENDIX A

DETAILS OF ANTHELMINTICS USED

DETAILS OF ANTHELMINTICS USED

APPENDIX A

ACTIVE COMPONENT	REGISTERED TRADE-NAME	SUPPLIER	FOR USE IN:	ACTS ON:	TOTAL RECOMMENDED DOSE (mg/kg)
Albendazole[1]	Valbazen	Smith-Kline	Cattle, Sheep	Roundworm, Lungworm, Tapeworm, Liver fluke	3.8 - 7.5
Amoscanate[1]	-	Ciba Geigy	Man	Hookworm, Schistosomes	Not Available
Febantel[1]	Rintal	Bayer	Cattle, Sheep Goats, Cats, Dogs, Poultry, Ostriches	Roundworm	5 - 20
Mebendazole	Vermox	Janssen	Man, Dogs, Cats	Nematodes, Cestodes	8.6 - 17.1
Niclosamide[1,2]	Lintex	Bayer	Sheep, Goats Calves	Tapeworm	50
Oxamniquine	Vansil	Pfizer	Man	S. mansoni	60
Oxfendazole[1]	Systamex	Coopers	Sheep, Goats	Roundworm, Lungworm, Tapeworm	5
Oxyclozanide[1]	ICI Liver Fluke Remedy	ICI	Cattle, Sheep, Goats	Liver fluke	10
Piperazine[1] adepate	Ascaradina	Panvet	Horses, Pigs, Poultry	Roundworm	200 - 300
Piperazine citrate	Rid	WDC	Man	Threadworm, Roundworm	22
Piperazine[1] dihydro-chloride	Wazine	Salsbury	Pigs, Horses	Ascarids, Pinworm, Nodular worm	100 - 200
Praziquantel	Droncit	Bayer	Man, Dogs Cats	Tapeworm	5
Pyrantel	Combantrin	Pfizer	Man	Roundworm, Threadworm, Hookworm	10
Rafoxanide[1]	Ranide	MSD	Sheep, Cattle	Liver fluke, Wireworm, Nasal worm	7.5 - 15

1 Donated

2 Also available as Yomesan ® for man

APPENDIX B

RESULTS OF PILOT EXPERIMENTS

EXPERIMENT A1

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Mebendazole (Vermox ®)	6.25	1	26	36	38	3.25	1.63	1	1	0	0.7	0.4	
		2	26	35	35	2.78	1,39	0	0	0	0	0	
		3	26	33	36	3.65	1.83	0	0	0	0	0	99.9
		4	26	34	37	1.98	0.98	0	0	0	0	0	
		5	26	30	33	2.62	1.10	1	0	0	0.3	0.3	
	12.5	6	27	38	41	2.79	1.40	0	0	0	0	0	
		7	23	36	38	2.71	1.36	0	0	0	0	0	
		8	27	34	32	1.84	0.92	0	1	0	0.3	0.3	99.9
		9	27	35	35	3.09	1.55	0	0	0	0	0	
		10	27	34	35	2.25	1.13	0	1	0	0.3	0.3	
	25.0	11	28	39	40	2.08	1.04	0	0	0	0	0	
		12	28	39	41	2.66	1.33	0	0	0	0	0	
		13	28	31	33	2.92	1.46	0	0	1	0.3	0.2	99.9
		14	28	35	36	2.10	1.05	1	0	0	0.3	0.3	
		15	28	34	34	2.10	1.05	0	0	0	0	0	
Control		21	29	32	35	5.99	3.00	193	174	177	181.3	60.5	
		22	29	37	41	4.46	2.23	225	239	209	224.3	100.6	
		23	29	36	40	4.71	2.36	260	279	253	264.0	112.1	-
		24	29	35	38	4.67	2.34	496	505	518	506.3	216.8	
		25	29	34	28	5.52	2.76	305	314	321	313.3	113.5	

EXPERIMENT A

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Pyrantel (Combantrin ®)	500	50	1	35	37	2.58	1.29	57	52	60	56.3	43.7	
		51	1	38	46	5.13	2.57	589	615	556	586.0	228.5	
		52	1	30	23	2.10	1.05	106	105	107	106.0	101.0	57.3
		53	1	29	38	5.42	2.71	336	344	304	328.0	121.0	
		54	1	30	31	3.84	1.92	177	181	164	174.0	90.6	
	250	55	2	33	38	6.55	3.28	57	57	53	49.0	15.0	
		56	2	36	41	6.37	3.19	237	229	246	237.3	74.5	
		57	2	37	39	3.90	1.95	308	294	282	294.7	151.1	68.4
		58	2	35	38	5.03	2.52	253	234	260	249.0	99.0	
		59	2	34	36	3.00	1.50	149	132	137	139.3	92.9	
	125	60	3	31	35	4.40	2.20	167	159	147	157.7	71.7	
		61	3	30	33	4.06	2.03	106	115	122	114.3	56.3	
		62	3	35	39	4.15	2.08	215	216	208	213.0	102.7	75.6
		63	3	35	41	6.16	3.08	199	186	214	199.7	64.8	
		64	3	26	30	2.19	1.10	40	50	35	41.7	38.1	
Praziquantel (Droncit ®)	200	65		31									
		66	4	38									
		67	4	27	A L L D I E D								
		68	4	27									
		69	4	33									
	100	70	5	34	37	4.34	2.17	369	345	346	353.3	162.8	
		71	5	34	44	5.77	2.89	424	465	450	446.3	154.7	
		72	5	37	43	4.77	2.39	586	595	624	601.7	252.3	16.1
		73	5	38	49	5.43	2.72	650	635	622	635.7	234.1	
		74	5	31	33	3.49	1.75	589	620	596	601.7	344.8	

(Continued) . . . .

EXPERIMENT A (Continued)

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Praziquantel (Droncit ®) (Continued)	50	75	6	28	34	5.14	2.57	70	62	66	66.0	25.7	
		76	6	34	42	7.15	3.58	187	182	194	187.7	52.5	
		77	6	32	37	3.09	1.55	211	190	228	209.7	135.7	73.4
		78	6	32	35	4.49	2.25	135	147	152	144.7	64.4	
		79	6	30	33	3.24	1.62	132	138	149	139.7	86.2	
Control		80	7	40	47	4.41	2.21	415	413	403	410.3	186.1	
		81	7	38	38	5.04	2.52	920	894	936	916.7	363.8	
		82	7	39	45	5.91	2.96	554	532	540	542.0	183.4	-
		83	7	29	34	4.00	2.00	453	465	438	452.0	226.0	
		84	7	34	37	4.30	2.15	888	856	894	879.3	409.0	
Piperazine citrate (Rid ®)	500	85	8	28	35	4.48	2.24	674	629	657	650.3	290.3	
		86	8	32	41	4.70	2.35	552	543	570	555.0	236.2	
		87	8	34	45	4.68	2.34	428	423	409	420.0	179.5	9.1
		88	8	29	38	4.18	2.09	492	522	536	516.7	247.2	
		89	8	40	47	5.42	2.71	786	804	768	786.0	290.0	
	250	90	9	31	36	4.25	2.13	165	177	184	175.3	82.5	
		91	9	39	46	4.93	2.47	188	170	169	175.7	71.3	
		92	9	33	36	3.14	1.57	153	139	147	146.3	93.2	59.7
		93	9	33	35	3.56	1.78	317	289	298	301.3	169.3	
		94	9	27	33	4.86	2.43	333	324	328	328.3	135.1	
	125	95	10	35	40	5.02	2.51	448	432	444	441.3	175.8	
		96	10	33	34	3.63	1.82	183	159	194	178.7	98.4	
		97	10	41	47	5.67	2.84	178	627	660	655.0	231.0	28.4
		98	10	27	30	2.91	1.46	364	375	384	374.3	257.3	
		99	10	35	38	4.78	2.39	498	526	537	520.3	217.7	

EXPERIMENT B

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Oxyclozanide (ICI Liver Fluke Remedy ®)	85.0	100	11	34	37	5.13	2.57	19	20	25	21.3	8.3	
		101	11	28	32	3.92	1.96	75	76	79	76.7	39.1	
		102	11	29	34	4.13	2.07	108	96	105	103.0	49.9	65.8
		103	11	35	33	4.85	2.43	30	40	36	35.3	14.6	
		104	11	32	33	4.82	2.41	55	46	50	50.3	20.9	
	170	105	12	32	34	4.25	2.13	55	62	48	55.0	25.9	
		106	12	29	33	5.06	2.53	52	45	62	53.0	20.9	
		107	12	31	36	5.49	2.75	78	72	69	73.0	26.6	47.6
		108	12	31	31	3.96	1.98	134	140	156	143.3	72.4	
		109	12	33	39	5.32	2.66	156	142	163	153.7	57.8	
	340	110	13	33	35	4.84	2.42	15	16	14	15.0	6.2	
		111	13	26	31	5.00	2.50	15	14	15	14.7	5.9	
		112	13	29	34	5.12	2.56	4	3	3	3.3	1.3	93.1
		113	13	36	DIED								
		114	13	29	33	4.50	2.25	7	17	19	17.7	7.9	
Albendazole (Valbazen ®)	125	115	14	32	35	2.64	1.32	1	0	1	0.7	0.5	
		116	14	29	27	2.30	1.15	0	0	0	0	0	
		117	14	40	44	3.23	1.62	0	0	0	0	0	99.8
		118	14	41	45	3.21	1.61	0	0	0	0	0	
		119	14	36	36	2.95	1.48	1	0	0	0.3	0.2	
	250	120	15	32	34	2.31	1.16	1	0	0	0.3	0.3	
		121	15	30	33	2.64	1.32	0	1	0	0.3	0.3	
		122	15	30	30	2.32	1.16	0	0	0	0	0	99.7
		123	15	26	28	1.97	0.98	0	0	0	0	0	
		124	15	25	26	1.57	0.79	1	0	0	0.3	0.4	

(Continued) . . . .

EXPERIMENT B (Continued)

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Albendazole (Valbazen ®) (Continued)	500	125	16	29	31	2.13	1.07	0	0	0	0	0	
		126	16	22	29	1.43	0.72	0	0	0	0	0	
		127	16	25	32	1.87	0.94	0	0	1	0.3	0.3	99.6
		128	16	29	32	2.03	1.02	2	0	2	1.3	1.3	
		129	16	31	33	2.31	1.12	0	0	0	0	0	
Control		130	17	32	34	4.19	2.10	209	195	210	204.7	97.7	
		131	17	35	38	5.38	2.69	243	228	256	242.3	90.1	
		132	17	27	32	4.98	2.49	132	124	148	134.7	54.1	-
		133	17	25	28	4.83	2.42	118	127	113	119.3	49.4	
		134	17	33	37	4.06	2.03	193	186	211	196.7	96.9	
Piperazine adepate (Ascaradina ®)	125	135	18	36	43	4.36	2.18	235	258	232	241.7	110.9	
		136	18	24	30	3.55	1.78	238	214	226	226.0	127.3	
		137	18	38	40	4.84	2.42	420	454	416	430.0	177.7	0
		138	18	30	32	3.63	1.82	248	257	264	256.3	141.2	
		139	18	27	35	5.07	2.54	147	169	152	156.0	61.5	
	250	140	19	35	39	6.29	3.15	374	396	411	393.7	125.2	
		141	19	38	43	5.29	2.65	364	378	389	377.0	142.5	
		142	19	35	40	4.32	2.16	306	287	321	304.7	141.1	0
		143	19	38	44	6.55	3.28	300	290	319	303.0	92.5	
		144	19	35	40	5.54	2.77	336	342	321	333.0	120.2	
	500	145	20	37	42	4.69	2.35	390	372	385	382.3	163.0	
		146	20	41	47	4.65	2.13	390	426	415	410.3	192.6	
		147	20	34	29	4.51	2.26	216	239	208	221.0	98.0	0
		148	20	38	40	4.84	2.42	427	413	392	410.7	169.7	
		149	20	27	27	2.63	1.32	324	350	331	335.0	254.8	

EXPERIMENT C

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Rafoxanide (Ranide ®)	62.5	150	21	37	39	3.03	1.52	192	201	216	203.0	134.0	
		151	21	34	37	2.51	1.26	27	26	34	29.0	23.1	
		152	21	31	33	3.08	1.54	89	95	102	95.3	61.9	60.9
		153	21	36	43	2.91	1.46	113	97	106	105.3	72.4	
		154	21	37	38	3.39	1.70	65	67	74	68.7	40.5	
	125	155	22	35	44	3.51	1.76	72	81	66	73.0	41.6	
		156	22	38	42	3.22	1.61	34	33	39	35.3	22.0	
		157	22	30	DIED								58.6
		158	22	24	DIED								
		159	22	26	29	2.53	1.27	194	185	178	185.7	146.8	
	250	160	23	31									
		161	23	34									
		162	23	37	A L L D I E D								
		163	23	35									
		164	23	31									
Niclosamide (Lintex ®)	125	165	24	38	45	3.56	1.78	279	287	266	277.3	155.8	
		166	24	31	DIED								
		167	24	33	44	4.98	2.49	646	631	612	629.7	252.9	
		168	24	39	46	5.12	2.56	204	227	236	222.3	86.8	9.5
		169	24	41	51	5.36	2.68	309	316	331	318.7	118.9	
	250	170	25	30	37	3.68	1.84	243	262	252	252.3	137.1	
		171	25	36	DIED								
		172	25	34	41	3.86	1.93	162	162	156	160.0	82.9	20.0
		173	25	28	33	2.90	1.45	362	349	331	347.3	239.5	
		174	25	28	34	3.00	1.5	114	127	136	125.7	83.8	

(Continued) . . . .

EXPERIMENT C (Continued)

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Niclosamide (Lintex ®) (Continued)	500	66	26	40	37	3.76	1.88	103	105	98	102.0	52.3	60.2
		67	26	36	33	2.84	1.42	96	108	96	100.0	70.4	
		68	26	41	39	3.26	1.63	172	157	166	165.0	101.2	
		69	26	38	37	6.05	3.03	144	155	169	156.0	51.6	
		70	26	37	35	4.17	2.09	128	136	124	129.3	62.0	
Control		180	27	31	35	3.87	1.94	392	377	410	393.0	203.1	-
		181	27	38	42	4.73	2.37	606	624	589	606.3	256.4	
		182	27	29	32	3.21	1.61	234	247	263	248.0	154.5	
		183	27	42	45	3.61	1.81	195	184	216	198.3	109.9	
		184	27	31	34	4.28	2.14	255	269	277	267.0	124.8	
Febantel (Rintal ®)	62.5	185	28	24	25	1.43	0.72	0	0	0	0	0	99.9
		186	28	36	39	2.56	1.28	0	1	0	0.3	0.3	
		187	28	32	35	1.81	0.91	0	0	0	0	0	
		188	28	30	35	1.87	0.97	0	0	0	0	0	
		189	28	32	35	3.21	1.61	0	0	1	0.3	0.2	
	125	191	29	28	37	2.11	1.16	2	1	0	1.0	0.9	99.8
		192	29	30	31	1.72	1.00	0	0	0	0	0	
		194	29	32	35	2.51	1.05	0	1	0	0.3	0.3	
		62	29	45	42	2.31	0.86	0	0	0	0	0	
		63	29	37	36	2.00	1.26	0	1	1	0.7	0.5	
	250	195	30	31	40	2.34	1.17	0	0	0	0	0	99.9
		196	30	29	34	2.05	1.03	0	0	0	0	0	
		197	30	34	40	2.18	1.09	0	1	0	0.3	0.3	
		198	30	27	31	1.42	0.71	0	0	1	0.3	0.5	
		199	30	32	39	2.39	1.20	0	0	0	0	0	

EXPERIMENT D

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Piperazine dihyro-chlorideride (Wazine ®)	125	203	32	40	42	2.82	1.41	72	89	84	81.7	57.9	
		204	32	36	29	3.27	1.64	246	231	220	232.3	142.1	0
		205	32	30	DIED								
		206	32	40	DIED								
		207	32	32	DIED								
	250	208	33	38	42	5.00	2.50	322	297	281	300.0	120.0	
		209	33	34	33	3.08	1.54	192	211	185	196.0	127.3	
		210	33	37	39	5.80	2.90	419	391	378	396.0	136.6	0
		211	33	43	42	4.84	2.42	364	382	356	367.3	151.8	
		212	33	27	DIED								
	500	214	34	42	45	4.85	2.43	398	376	365	379.7	156.6	
		215	34	39	44	5.17	2.59	422	449	411	427.3	165.3	
		216	35	34	36	5.74	2.87	396	413	439	416.0	144.9	0
		217	35	29	35	4.16	2.08	334	350	325	336.3	161.7	
		218	35	26	DIED								
Oxfendazole (Systamex ®)	56.25	224	38	33	40	4.31	2.16	0	0	0	0	0	
		225	38	32	39	2.99	1.45	0	0	0	0	0	
		226	38	29	33	3.63	1.82	0	0	0	0	0	
		227	37	42	41	2.78	1.39	0	0	0	0	0	100
		228	38	36	42	3.36	1.68	0	0	0	0	0	

(Continued) . . . .

EXPERIMENT D (Continued)

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Oxfendazole (Systamex ®) (Continued)	112.5	229	39	32	35	2.23	1.12	0	0	0	0	0	
		230	39	28	31	1.84	0.92	0	0	0	0	0	
		231	39	30	35	2.97	1.49	0	0	0	0	0	100
		232	39	27	34	2.91	1.46	0	0	0	0	0	
		233	39	29	33	2.41	1.21	0	0	0	0	0	
	225	234	40	39	40	3.87	1.94	0	0	0	0	0	
		235	40	40	42	3.35	1.68	0	0	0	0	0	
		241	41	44	44	2.62	1.31	0	0	0	0	0	100
		200	42	32	36	3.12	1.56	0	0	0	0	0	
		202	42	36	43	2.76	1.38	0	0	0	0	0	
Control		51	46	35	38	5.41	2.71	182	214	190	195.3	72.2	
		52	46	36	37	5.31	2.66	225	239	246	236.7	89.1	
		53	46	43	45	4.82	2.41	219	197	234	216.7	89.9	-
		54	46	37	39	4.92	2.46	255	274	281	270.0	109.8	
		55	46	34	37	5.38	2.69	198	213	224	211.7	78.7	

EXPERIMENT E

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT, INITIAL	BODY WEIGHT, FINAL	LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS 1	2	3	$\bar{x}$	NO.EGGS/ g LIVER x 10^4	% REDUCTION
Amoscanate	125	250	1	35	36	6.27	3.14	654	670	642	655.3	209.0	
		251	1	36	40	3.00	1.50	122	111	107	113.3	75.6	
		252	1	31	39	5.52	2.96	312	325	336	324.3	109.6	20.2
		253	1	33	36	3.90	1.95	378	361	358	365.7	187.5	
		254	1	37	38	4.12	2.06	480	493	471	481.3	233.7	
	250	255	2	38	46	5.02	2.51	426	439	418	427.7	170.4	
		256	2	36	40	5.92	2.96	312	329	333	324.7	109.7	
		257	2	36	40	4.77	2.39	251	268	273	264.0	110.7	26.3
		258	2	43	45	5.16	2.58	629	591	580	600.0	232.6	
		259	2	37	43	5.35	2.68	336	351	359	348.7	130.3	
	500	260	3	30	DIED								
		261	3	33	DIED								
		262	3	30	DIED								
		263	3	37	35	4.41	2.21	484	471	467	474.0	215.0	0
		264	3	32	33	3.52	1.76	508	525	533	522.0	296.6	
Control 1 (Placebo for Amoscante)		265	4	44	48	6.07	3.04	589	617	568	591.3	194.8	
		266	4	31	36	3.82	1.91	450	439	431	440.0	230.4	
		267	4	40	36	4.99	2.50	482	497	477	435.3	194.5	-
		268	4	38	43	4.66	2.33	469	474	490	477.7	205.0	
		269	4	33	37	4.54	2.27	429	460	451	446.7	196.8	

(Continued) . . . .

EXPERIMENT E (Continued)

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Oxamniquine (Vansil ®)	125	275	6	34	39	4.41	2.21	284	297	274	285.0	129.3	
		276	6	25	34	5.01	2.51	234	249	252	245.0	97.8	
		277	6	30	36	5.12	2.56	156	174	168	166.0	64.8	0
		278	6	27	35	3.36	1.68	135	131	140	135.3	80.6	
		279	6	26	36	4.70	2.35	192	184	181	185.7	79.0	
	250	280	7	30	35	3.78	1.89	150	156	148	151.3	80.1	
		281	7	28	36	3.63	1.82	198	184	177	186.3	102.7	
		282	7	36	34	2.42	1.21	96	104	89	96.3	79.6	1.3
		283	7	27	33	4.13	2.07	138	150	133	140.3	68.0	
		284	7	35	39	5.20	2.60	122	97	111	110.0	42.3	
	500	285	8	34	35	5.13	2.57	210	204	232	215.3	84.0	
		286	8	36	DIED								
		287	8	32	36	5.51	2.76	180	160	176	172.0	62.4	3.1
		288	8	26	DIED								
		289	8	30	DIED								
Control 2 (Gum tragacanth for Oxamniquine)		290	9	33	36	5.92	2.96	180	189	193	187.3	62.3	
		291	9	30	34	5.62	2.81	210	216	227	217.7	77.5	
		292	9	31	37	6.29	3.15	231	217	222	223.3	71.0	-
		293	9	34	38	5.66	2.83	222	198	204	208.0	73.5	
		294	9	28	40	5.68	2.84	258	265	271	264.7	93.2	

APPENDIX C

RESULTS OF LOW-DOSE EXPERIMENTS

EXPERIMENT F

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Febantel (Rintal ®)	1.25	310	1	34	36	2.85	1.43	81	79	83	81.0	56.8	
		311	1	28	31	5.35	2.68	95	90	98	94.3	35.3	
		312	1	32	36	4.72	2.36	91	96	104	97.0	41.1	0
		313	1	30	34	5.75	2.88	64	67	75	68.7	23.9	
		314	1	28	33	3.96	1.98	96	90	88	91.3	46.1	
	2.50	315	2	38	40	4.44	2.22	131	126	124	127.0	57.2	
		316	2	35	35	5.20	2.60	73	69	64	70.3	27.1	
		317	2	36	37	4.95	2.48	141	132	129	134.0	54.1	0
		318	2	39	42	5.97	2.99	162	153	149	154.7	51.8	
		319	2	38	38	4.77	2.39	120	112	115	115.7	48.5	
	5.00	325	4	31	36	3.37	1.69	64	72	67	67.7	40.2	
		326	4	33	40	4.86	2.43	48	42	39	43.0	17.7	
		327	4	34	36	4.00	2.00	151	142	138	143.7	71.8	0
		328	4	36	43	5.70	2.85	60	67	70	65.7	23.0	
		329	4	36	39	6.51	3.26	68	57	60	61.7	18.9	
	10.0	330	6	30	33	3.53	1.77	4	6	7	5.7	3.2	
		331	6	32	34	4.21	2.11	10	12	14	12.0	5.7	
		332	6	34	37	3.78	1.89	7	7	5	6.3	3.4	87.9
		333	6	41	42	4.65	2.33	11	10	9	10.0	4.3	
		334	6	34	37	3.24	1.62	5	7	7	6.3	3.9	
Oxfendazole (Systamex ®)	1.25	335	7	32	36	3.96	1.98	73	78	75	75.3	38.1	
		336	7	34	39	6.69	3.35	183	164	178	175.0	52.3	
		337	7	37	38	3.65	1.83	37	35	26	32.7	17.9	0
		338	7	35	38	5.05	2.53	169	153	175	165.7	65.6	
		339	7	35	38	3.60	1.80	102	92	84	92.7	51.5	

(Continued) . . . .

EXPERIMENT F (Continued)

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Oxfendazole (Systamex ®) (Continued)	2.50	340	8	37	40	6.97	3.49	180	169	178	175.7	50.4	
		341	8	38	42	5.55	2.78	114	127	132	124.3	44.8	
		342	8	36	39	5.42	2.71	79	72	68	73.0	26.9	0
		343	8	31	34	2.85	1.43	39	46	46	43.7	30.6	
		344	8	40	43	4.90	2.45	123	138	135	132.3	54.0	
	5.00	345	9	32	35	4.12	2.06	22	24	27	24.3	11.8	
		346	9	36	38	4.59	2.30	54	49	57	53.3	23.2	
		347	9	38	39	3.85	1.93	75	78	70	74.3	38.6	15.7
		348	9	36	38	5.33	2.67	126	137	142	135.0	50.7	
		349	9	35	34	3.16	1.58	31	24	33	29.3	18.6	
	10.0	350	13	34	37	4.96	2.48	32	30	35	32.3	13.0	
		351	13	32	32	3.27	1.64	11	13	14	12.7	7.8	
		352	13	35	36	3.49	1.75	14	14	12	13.3	7.6	67.0
		353	13	31	34	3.85	1.93	32	27	26	28.3	14.7	
		354	13	32	35	3.96	1.98	26	27	23	25.3	12.8	
Control		355	14	40	38	5.10	2.55	70	78	83	77.0	30.2	
		356	14	35	38	5.69	2.85	72	66	78	72.0	25.3	
		357	14	28	37	5.50	2.75	127	145	138	136.7	49.7	-
		358	14	29	37	4.89	2.45	84	87	74	81.7	33.4	
		359	14	34	38	4.53	2.27	63	68	78	69.7	30.8	

(Continued) . . . .

EXPERIMENT F (Continued)

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Albendazole (Valbazen ®)	1.88	360	15	32	36	4.65	2.33	78	71	69	72.7	31.3	
		361	15	36	40	4.91	2.46	94	96	101	97.0	39.5	
		362	15	36	39	5.87	2.94	57	68	51	55.3	18.9	20.5
		363	15	29	33	2.66	1.33	24	29	32	28.3	21.3	
		364	15	38	41	4.53	2.27	54	49	58	53.7	23.7	
	3.75	365	16	34	39	5.73	2.87	59	48	56	54.3	19.0	
		366	16	33	35	4.20	2.10	38	43	45	42.0	20.0	
		367	16	38	42	5.31	2.66	71	63	66	66.7	25.1	41.1
		368	16	33	36	4.38	2.19	36	27	32	31.7	14.5	
		369	16	34	38	3.72	1.86	37	42	40	39.7	21.3	
	7.50	370	17	37	37	3.18	1.59	21	24	18	21.0	13.2	
		371	17	37	38	4.12	2.06	18	21	23	20.7	10.0	
		372	17	36	38	4.87	2.44	14	12	11	12.3	5.1	78.7
		373	17	32	35	4.48	2.24	10	11	14	11.7	5.2	
		374	17	24	27	4.04	2.02	6	5	5	5.3	2.6	
	15.0	375	18	38	37	4.77	2.39	14	11	12	12.3	5.2	
		376	18	34	36	4.95	2.48	0	1	2	1.0	0.4	
		377	18	36	37	4.18	2.09	1	0	1	0.7	0.3	91.8
		378	18	33	36	3.73	1.87	3	5	6	4.7	2.5	
		379	18	33	36	4.37	2.19	13	13	10	12.0	5.5	

EXPERIMENT H

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Febantel (Rintal ®)	15.0	455	1	31	32	2.23	1.12	7	7	5	6.3	5.7	
		456	1	30	34	2.46	1.23	11	12	9	10.7	8.7	
		457	1	30	31	2.00	1.00	1	0	1	0.7	0.7	90.2
		458	1	29	32	3.00	1.50	7	6	6	6.3	4.2	
		459	1	30	31	1.95	0.98	10	8	7	8.3	8.5	
	30.0	460	2	31	33	1.97	0.99	0	0	0	0	0	
		461	2	30	31	2.00	1.00	0	0	0	0	0	
		462	2	30	31	2.08	1.04	1	0	0	0.3	0.3	99.9
		463	2	29	29	1.77	0.89	0	0	0	0	0	
		464	2	32	33	2.23	1.12	0	0	0	0	0	
	60.0	465	4	34	36	2.55	1.28	0	0	0	0	0	
		466	4	34	35	2.09	1.05	0	0	0	0	0	
		467	4	29	31	1.86	0.93	0	0	0	0	0	100
		468	4	31	32	2.02	1.01	0	0	0	0	0	
		469	4	27	30	1.78	0.89	0	0	0	0	0	
Oxfendazole (Systamex ®)	12.5	470	6	31	33	3.19	1.60	0	0	0	0	0	
		471	6	30	32	2.43	1.22	1	0	0	0.3	0.3	
		472	6	31	31	2.32	1.16	0	0	0	0	0	99.8
		473	6	29	32	3.25	1.63	0	1	0	0.3	0.2	
		474	6	31	32	2.99	1.50	0	0	0	0	0	
	25.0	475	7	36	36	2.87	1.44	0	0	0	0	0	
		476	7	33	35	3.20	1.60	0	1	0	0.3	0.2	
		477	7	29	30	1.98	0.99	0	0	0	0	0	99.9
		478	7	31	33	2.40	1.20	0	0	0	0	0	
		479	7	30	33	4.01	2.01	1	0	0	0.3	0.2	

(Continued) . . . .

EXPERIMENT H (Continued)

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGC COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Oxfendazole (Systamex ®) (Continued)	50.0	480	8	26	30	1.82	0.91	0	0	0	0	0	100
		481	8	27	29	2.11	1.06	0	0	0	0	0	
		482	8	29	32	2.16	1.08	0	0	0	0	0	
		483	8	26	29	2.47	1.24	0	0	0	0	0	
		484	8	27	31	2.48	1.24	0	0	0	0	0	
Control		485	9	29	35	4.66	2.33	123	157	131	137.0	58.8	-
		486	9	29	31	3.48	1.74	108	111	97	105.3	60.5	
		487	9	31	32	4.50	2.25	147	138	154	146.3	65.0	
		488	9	27	29	3.43	1.72	69	77	83	76.3	44.5	
		489	9	29	31	4.28	2.14	114	114	127	118.3	55.3	
Albendazole (Valbazen ®)	30.0	490	13	30	33	3.24	1.62	0	0	1	0.3	0.2	99.8
		491	13	30	32	3.10	1.55	0	0	0	0	0	
		492	13	30	31	2.94	1.47	0	0	0	0	0	
		493	13	33	33	2.98	1.49	0	0	0	0	0	
		494	13	28	31	2.48	1.24	0	1	0	0.3	0.3	
	60.0	495	14	26	32	2.62	1.31	0	0	0	0	0	100
		496	14	31	33	2.48	1.24	0	0	0	0	0	
		497	14	28	30	1.98	0.99	0	0	0	0	0	
		498	14	30	33	2.17	1.09	0	0	0	0	0	
		499	14	24	28	1.95	0.98	0	0	0	0	0	
	120	500	15	28	35	2.44	1.22	0	0	0	0	0	100
		501	15	29	31	2.16	1.08	0	0	0	0	0	
		502	15	30	32	2.08	1.04	0	0	0	0	0	
		503	15	32	33	2.48	1.24	0	0	0	0	0	
		504	15	27	30	1.69	0.85	0	0	0	0	0	

EXPERIMENT J

DRUG	DOSE mg/kg x5	MOUSE NO.	CAGE NO.	BODY WEIGHT g		LIVER WEIGHT g	WT/Mc MASTER g x 10^{-4}	EGG COUNTS				NO.EGGS/ g LIVER x 10^4	% REDUCTION
				INITIAL	FINAL			1	2	3	$\bar{x}$		
Control		555	1	40	41	3.25	1.63	178	163	159	166.7	102.3	
		556	1	41	46	4.71	2.36	129	138	134	133.7	56.7	
		557	1	39	40	3.79	1.90	119	127	132	126.0	33.2	-
		558	1	32	35	2.80	1.40	75	78	87	80.0	57.1	
		559	1	39	41	2.97	1.49	131	123	126	126.7	85.0	
Mebendazole (Vermox ®)	3.13	560	2	40	41	3.01	1.51	0	0	0	0	0	
		561	2	41	46	3.43	1.72	0	1	0	0.3	0.2	
		562	2	40	39	2.48	1.24	1	1	0	0.7	0.6	99.7
		563	2	40	41	2.26	1.13	0	0	0	0	0	
		564	2	32	39	2.96	1.48	0	1	0	0.3	0.2	
	6.25	565	3	48	46	3.18	1.59	0	0	0	0	0	
		566	3	35	38	2.14	1.07	0	0	0	0	0	
		567	3	35	38	2.14	1.07	0	0	0	0	0	
		568	3	48	47	2.91	1.46	0	0	0	0	0	100
		569	3	37	37	2.46	1.23	0	0	0	0	0	
	12.5	570	4	34	33	1.73	0.87	0	0	0	0	0	
		571	4	45	50	3.31	1.66	0	0	0	0	0	
		572	4	35	39	2.63	1.32	0	0	0	0	0	100
		573	4	38	39	2.31	1.16	0	0	0	0	0	
		574	4	38	41	2.56	1.28	0	0	0	0	0	

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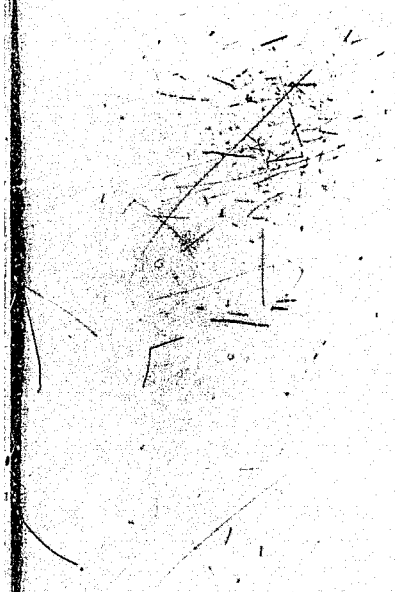

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