Comparative activity of anthelmintic drugs, mebendazole, praziquantel and albendazole against *Hymenolepis diminuta* in experimentally infected rats

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GALAL (M.), CHIN (S. R.). Comparaison de l'action de différents anthelminthiques (mébendazole, praziquantel et albendazole) contre *Hymenolepis diminuta* chez des rats expérimentalement infectés. *Rev. Elev. Méd. vét. Pays trop.*, 1987, **40** (2) : 147-150.

Des rats expérimentalement infectés avec *H. diminuta* ont été traités par voie orale avec trois anthelminthiques, administrés soit en dose unique, soit en tiers de dose 3 jours consécutifs. Le praziquantel (250 mg/kg ou 83 mg/kg/j 3 fois) et l'albendazole (800 mg/kg ou 167 mg/kg/j 3 fois) ont totalement éliminé les vers, alors que le mébendazole (500 mg/kg ou 167 mg/kg/j 3 fois) ne les a que partiellement éliminés, avec une efficacité de 76 p. 100. Parmi ces 3 anthelminthiques, il n'a pas été relevé de différence significative d'efficacité entre les différents dosages pour chaque traitement. Aucune toxicité n'est apparue chez les rats traités. *Mots clés* : Rat - Helminthose - *Hymenolepis diminuta* - Anthelminthique - Mébendazole - Praziquantel - Albendazole - Infection expérimentale.

INTRODUCTION

H. diminuta is primarily a rat tapeworm but man is occasionally infected, because the intermediate host is found in human food like rice and flour.

A large number of anthelmintic drugs are available and used in the treatment of various helminths including nematodes, trematodes and cestodes. These drugs are used in different methods of administration and different doses, depending on the type of helminths and the host.

GUPTA *et al.* (4) have demonstrated significant cestodicidal activity in 3 - 5 - dibromo - 2 - chlorosalicyanilide - 4 - isothiocyanate (CDRI Compound 77-6) and compared its efficacy with the known anticestode drugs, niclosamide and praziquantel in rats. In the same species, praziquantel has been claimed to be rapidly effective against *Hymenolepis nana*, immobilizing the worms in 10 minutes after the drug administration (7). Mebendazole is known to be active against the larval and adult stages of several cestodes (2).

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CAVIER and ROSSIGNOL (3) studied the taenicidal properties of albendazole, mebendazole, niclosamide and praziquantel in experimentally infected mice and found that praziquantel and niclosamide have similar taenicidal properties.

Now are reported the comparative efficacy of mebendazole, praziquantel and albendazole against experimental infection of rats with *H. diminuta*, using single and divided oral doses for 3 consecutive days, 30 days after infection.

MATERIALS AND METHODS

Definitive and intermediate hosts

Albino rats (*Rattus norvegicus*) of both sexes and aged 6-8 weeks were used as the definitive hosts. They were obtained from breeding stock in the Division of Laboratory Animal Resources, Institute for Medical Research, Kuala Lumpur, Malaysia, fed Gold coin rodent feed and had free access to water. Male and female rats were separated in group cages, each containing no more than 4 rats.

Flour beetles (*Tribolium castaeneum*) (Fig. 1) were obtained from the animal house feed store of the Institute for Medical Research and used as the intermediate hosts. One hundred male and female adult beetles were starved for 48 hours.

Parasite eggs

Eggs of *Hymenolepis diminuta* were obtained from the gravid segments of *H. diminuta* (Fig. 2) found in rats (*Rattus rattus diordii*) trapped from the Division of Laboratory Animal Resources, Division of Malaria and Institute for Medical Research Hostel. The gravid segments of *H. diminuta* were scratched smoothly onto filter paper in a petridish. The starved beetles were allowed to feed on the eggs of *H. diminuta* for 72 hours.

After 14 days, the infected beetles were dissected and mature cysticercoids (Fig. 3) were obtained.

Sources of anthelmintic drugs

Mebendazole human commercial formula (SUNWARD Chemical Ind Co. SDN BHD, Johore Bahra) was provided in form of tablets. Each tablet contained 100 mg mebendazole.

Praziquantel was used as the commercial veterinary formulation, Droncit® (Bayer Leverkusen) with each tablet containing 50 mg of praziquantel.

Albendazole was used as the commercial human formulation, Zentel®(Smith Kline and French Laboratories, Australia) with each tablet containing 200 mg of albendazole.

Treatment of infected rats

Five cysticercoids were suspended in normal saline and given to each rat by stomach tube after the rat was anesthetized with ether.

At 30 days post infection, rats were divided at random into four groups. Each group containing 12 male and female rats was divided into two subgroups of 6 rats each. Subgroup (a) was given a single dose of mebendazole at a dose rate of 500 mg/kg body weight and subgroup (b) was given the same amount of mebendazole at 167 mg/kg/day for 3 days. Subgroup (c) was given a single dose of praziquantel at 250 mg/kg body weight, and subgroup (d) was given the same amount of the drug at three equal doses of 83 mg/kg/day. Subgroup (e) was given a single dose of albendazole at 800 mg/kg body weight and subgroup (f) was given the same amount of albendazole at three equal daily doses of 267 mg/kg/day. Each drug was suspended in 10 millilitres of water and given to rats by stomach tube.

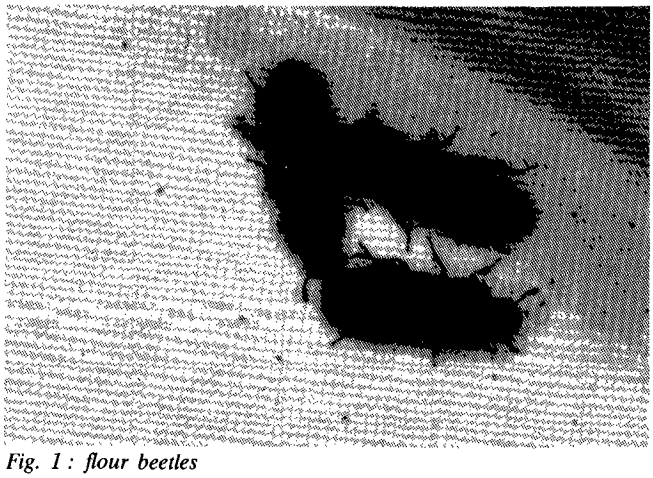

Fig. 1 : flour beetles

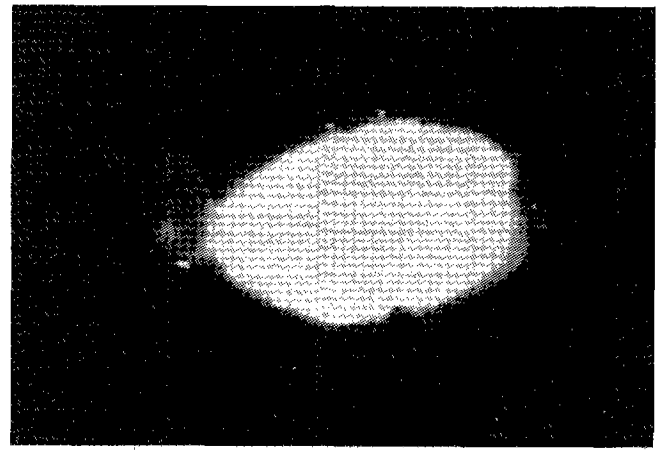

Fig. 2 : egg of Hymenolepis diminuta.

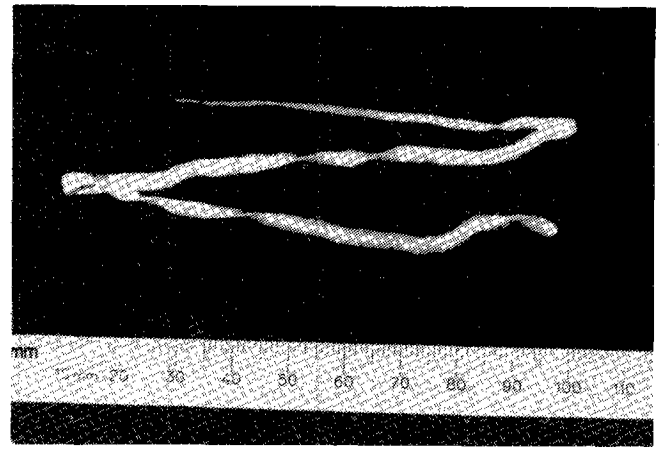

Fig. 3 : cysticercoids.

The control groups containing 12 rats of both sexes were divided into two subgroups and given normal saline by the same technique.

Recovery of worms

Six days post-treatment, the rats were sacrified using chloroform and the intestine was dissected and normal saline was pumped into it, using a 20 ml disposable syringe to wash out all the tapeworms into a petridish.

RESULTS AND DISCUSSION

The efficacy of mebendazole, praziquantel and albendazole against *Hymenolepis diminuta* infection in rats is shown in tables I, II and III.

TABLE I Number of **Hymenolepis diminuta** *recovered from control and mebendazole-treated rats at 30 days after infection.*

Treatment	Dose (mg/kg)	No. of rats in each group	No. of Cysti-cercoides per rat	Average No. of worms per rat	Efficacy of treatment
Control	—	6	5	5	—
Mebendazole Subgroup (a) Subgroup (b) (*)	 500 167	 6 6	 5 5	 1.2 0.8	 76 p. 100 83 p. 100

(*) Dose was given daily for 3 consecutive days.
All rats were necropsied 6 days after treatment.

TABLE II Number of **Hymenolepis diminuta** *recovered from control and praziquentel-treated rats at 30 days after infection.*

Treatment	Dose (mg/kg)	No. of rats in each group	No. of Cysti-cercoides per rat	Average No. of worms per rat	Efficacy of treatment
Control	—	6	5	5	—
Praziquentel Subgroup (c) Subgroup (d) (*)	 250 83	 6 6	 5 5	 — —	 100 p. 100 100 p. 100

(*) Dose was given daily for 3 consecutive days.
All rats were necropsied 6 days after treatment.

TABLE III Number of **Hymenolepis diminuta** *recovered from control and albendazole-treated rats at 30 days after infection.*

Treatment	Dose (mg/kg)	No. of rats in each group	No. of Cysti-cercoides per rat	Average No. of worms per rat	Efficacy of treatment
Control	—	6	5	5	—
Albendazole Subgroup (e) Subgroup (f) (*)	 800 207	 6 6	 5 5	 — —	 100 p. 100 100 p. 100

(*) Dose was given daily for 3 consecutive days.
All rats were necropsied 6 days after treatment.

This investigation has shown that the three drugs have definite anticestodal activity. However, the efficacy of the drugs differed. Mebendazole at 500 mg/kg body weight had a lower activity than praziquantel (250 mg/kg) and albendazole (800 mg/kg). The efficacy of mebendazole was found to be 76 p. 100. This supports the results of other investigators (1, 6). On the other hand, praziquantel and albendazole completely eliminated the worms from the host rats with 100 p. 100 efficacy. Albendazole has also been used as an anthelmintic against liver fluke, and lung and gastro-intestinal round worms in cattle, sheep and other laboratory animals (5).

It has been suggested that mebendazole destroys the microtubules of cestodes with consequent blocking of the transport of nutrients especially the blocking of glucose uptake (8, 9).

Praziquantel has been claimed to be rapidly effective *in vivo* against *Hymenolepis nana*, immobilizing the worms in 10 minutes after the drug administration (7).

The three drugs are effective in the treatment of *H. diminuta* infection in rats when given at single doses and it was found that there was no significant difference between single and divided doses of any of the three drugs used, according to the number of worms recovered as compared to controls.

The three drugs were used at high dose levels and were found be safe. The conclusion is drawn because no toxic symptoms developed in any of the treated rats. Nevertheless, it is preferable to use albendazole in the treatment of *Hymenolepis* infection because of its high activity and economy.

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Experimentally *Hymenolepis diminuta* infected rats were treated orally with single and equal divided doses of the three anthelmintic drugs 30 days after infection. Praziquantel (250 mg/kg and 83 mg/kg/day for 3 consecutive days) and albendazole (800 mg/kg and 267 mg/kg/day for 3 consecutive days) completely eliminated the worms, while mebendazole (500 mg/kg and 167 mg/kg/day for 3 consecutive days) partially eliminated the worms with an efficacy of 76 p. 100. Among the three anthelmintic drugs, there was no significant difference in efficacy between treatment with single and divided doses. No toxicity developed in treated rats. *Key words* : Rat - Helminthiasis - *Hymenolepis diminuta* - Anthelmintic - Mebendazole - Praziquantel - Albendazole - Experimental infection.

Se trataron ratas infectadas por *Hymenolepis diminuta* con tres antihelmínticos administrados por vía oral sea a dosis única, sea a tercera dosis durante 3 días consecutivos. El praziquantel (250 mg/kg o 83 mg/kg/día 3 veces) y el albendazole (800 mg/kg o 167 mg/kg/día 3 veces) eliminaron totalmente los helmíntos mientras que el mebendazole (500 mg/kg o 176 mg/kg/día 3 veces) no los eliminaron más que parcialmente, con una eficacia de 76 p. 100. No se observó una diferencia significativa de eficacia entre los diferentes modos de administración para cada tratamiento. No apereció ninguna toxicidad en las ratas tratadas. *Palabras claves* : Rata - Helmintosis - *Hymenolepis diminuta* - Antihelmíntico - Mebendazole - Praziquantel - Albendazole - Infección experimental.

REFERENCES

1. BARRET-CONNOR (E.). Recent advances in the treatment of common intestinal helminths. *Am. J. Gastroent.*, 1975, **63** : 105-116.

2. CAMPBELL (W. C.), McCRACKEN (R. O.), BLAIR (L. S.). Therapy of hydatid disease. *J. Am. med. Ass.*, 1974, **230** (6) : 825-831.

3. CAVIER (R.), ROSSIGNOL (J. F.). Comparative study of tenicidal properties of albendazole, niclosamide and praziquantel in experimentally infected mice. *Annls pharm. fr.*, 1982, **40** : 351-355.

4. GUPTA (S.), KATYAR (J. C.), SEN (A. B.), DUBEY (S. K.), SINGH (H.), SHARMA (S.), HIER (R. N.). Anticestodes activity of 3 - 5 dibromo - 2 - chloro - Salioglanilide. *Helminthologia*, 1980, **54** : 271-273.

5. THEODORIDES (V. J.), GYURIK (R. J.), KINGSBURY (W. D.), PARISH (R. C.). Anthelmintic activity of albendazole against liver fluke, tapeworms, lung and gastro-intestinal round worms. *Experientia*, 1976, **32** : 702-703.

6. THIENPONT (D.), VANPARIJS (O.), HERMANS (L.). Anthelmintic activity of mebendazole against cycticercus fasciolaris. *J. Parasit.*, 1974, **60** : 1052-1053.

7. THOMAS (H.), CONNERT (R.). The efficacy of praziquantel against cestodes in animals. *Z. ParasiKde.*, 1977, **52** : 117-127.

8. VAN DEN BOSSCHE (H.). The molecular basis of anthelmintic action in biochemistry of parasitic and host-parasites relationship. Amsterdam, Netherland, North-Holland Publishing Company, 1976. Pp. 553-572.

9. VERHEYEN (A.), VANPARIJS (O.), BORGERS (H.), THIENPONT (D.). Scanning electron microscopic observation of *Cysticercus fasciolaris (Taenia taeniaeformis)* after treatment of mice with mebendazole. *J. Parasit.*, 1978, **64** : 411-425.