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# EFFICACY OF BENZIMIDAZOLES AGAINST LARVAL ANCYLOSTOMA CANINUM INFECTION IN MICE

Amongst the anthelmintic drugs, the benzimidazole derivatives have shown the widest spectrum of activity against nematode eggs and adult worms, liver flukes and cestodes. Benacil hydrochloride (1-phenoxyacetyl 2-methoxycarbonylaminobenzimidazole hydrochloride) and 4-chlorobenacil (4-chloro-1-phenoxyacetyl-2-methoxycarbonylaminobenzimidazole), benzimidazole derivatives, have a very wide spectrum of nematocidal activity in sheep, cattle, pigs, poultry and horses (Demidov N. V. et al., Abstracts, Asian Congr. Parasitol. Bombay: 35—36, 1978, Berezkina S. V. et al., Byull. VIGIS 28: 23—27, 1981, Nekipelova R. N. et al., Byull. VIGIS 28: 76—77, 1981, Lyubavin V. S., Byull. VIGIS 28: 73—74, 1981, Demidov N. V. and Solonenko I. G., Byull. VIGIS 28: 35—37 1981, Rustamova M. S. and Demidov N. V., Byull. VIGIS 28: 80, 1981, Berezkina S. V. and Solonenko I. G., Byull. VIGIS 28: 18—22, 1981). In view of this broad spectrum of nematocidal activity, we decided to investigate the efficacy of benacil hydrochloride and 4-chlorobenacil in mice infected with *Ancylostoma caninum* larvae which is zoonotically important in man for producing cutaneous and visceral larvae migrans (Beaver P. C., Exp. Parasitol. 5: 587—621, 1956, Indust. Med. Surg. 33: 319—322, 1964, Janssen P. A. J., Progress Research 18: 191—203, 1974, Little M. D. et al., Am. J. Trop. Med. Hyg. 32: 1285—1288, 1983). The test compounds were procured from Prof. N. V. Demidov, The All-union K. I. Skryabin Institute of Helminthology, Moscow, USSR. Infective *A. caninum* larvae were obtained from faecal samples of experimentally infected dog as per the methods of Sen et al. (Trans. Roy. Soc. Trop. Med. Hyg. 59: 684—689, 1965) and Ray et al. (J. Helminthol. 46: 357—362, 1972). For the evaluation of drugs, Swiss albino mice (18—22 g) were infected orally with 1000 larvae each. Fifteen days later, mice were divided into groups of five and treated with compounds in different dosage schedule for 5 consecutive days orally. For each experiment a separate infected control group without treatment was maintained. The mice were killed 5 days after the last dose of treatment, i.e. 25 days postinfection and viable larvae from various skeletal muscles and brain were recovered as described by Soh (J. Parasitol. 44: 515—519, 1958). The anthelmintic activity was evaluated by calculating the average number of larvae and the reduction of the recovery rate in treated groups as compared to corresponding control groups.

The results are summarised in Table 1. Benacil hydrochloride and 4-chlorobenacil at the dose of 5 × 400 mg/kg showed more than 99 % efficacy against larvae migrated in the muscles, whereas benacil hydrochloride at the same dose showed 97.22 % larval clearance in the brain region and 4-chlorobenacil showed 88.40 % clearance. Kessler and Stoye (Z. Tropenmed. Parasit. 22: 49—56, 1971) have reported 71.1 and 64.6 % efficacy of thiabendazole (3 × 200 mg/kg) and cambendazole (3 × 100 mg/kg), respectively, against *A. caninum* larvae in mice. Lammler et al. (Br. Vet. J. 126: 427—439, 1970) and Lammler and El-Gendi (Z. Parasitend. 58: 55—63, 1978) also demonstrated



significant activity of cambendazole (5 × × 50 mg/kg), mebendazole (5 × 200 mg/kg) and marked activity of thiabendazole, oxibendazole, parbendazole and fenbendazole at high dosage levels against *A. caninum* larvae in the muscles of *Mastomys natalensis*.

In conclusion, the results of the present studies showed that benacil hydrochloride and 4-chlorobenacil might be of value in the treatment of visceral and cutaneous larva migrans of abnormal host, such as man, and migrating larvae in the dog.

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Table 1. Efficacy of benacil hydrochloride and 4-chlorobenacil against larval *Ancylostoma caninum* infection in mice

| Anthelmintics | Site | Dose mg/kg body weight X 5 | Average number of larvae recovered per mouse mean ± S.E. | | Percentage reduction of larvae | No. of mice cured/treated |
|---|---|---|---|---|---|---|
| | | | Control group | Test group | | |
| Benacil hydrochloride | Muscles | 400 | 434.2 ± 43.74 | 0.8 ± 0.08 | 99.81 | 4/5 |
| | | 200 | 434.2 ± 43.74 | 7.4 ± 3.95 | 98.29 | 2/5 |
| | | 100 | 434.2 ± 43.74 | 103.6 ± 14.58 | 76.14 | 0/5 |
| | | 50 | 434.2 ± 43.74 | 281.8 ± 29.77 | 35.09 | 0/5 |
| | Brain | 400 | 22.6 ± 4.08 | 0.6 ± 0.24 | 97.22 | 2/5 |
| | | 200 | 22.6 ± 4.08 | 3.6 ± 1.43 | 84.07 | 0/5 |
| | | 100 | 22.6 ± 4.08 | 8.2 ± 2.93 | 63.71 | 0/5 |
| | | 50 | 22.6 ± 4.08 | 17.2 ± 3.55 | 23.89 | 0/5 |
| 4-chlorobenacil | Muscles | 400 | 365.4 ± 53.92 | 1.4 ± 0.97 | 99.61 | 3/5 |
| | | 200 | 365.4 ± 53.92 | 23.2 ± 6.63 | 93.65 | 1/5 |
| | | 100 | 365.4 ± 53.92 | 124.6 ± 15.12 | 65.90 | 0/5 |
| | | 50 | 365.4 ± 53.92 | 276.4 ± 36.97 | 24.39 | 0/5 |
| | Brain | 400 | 27.6 ± 4.62 | 3.2 ± 1.39 | 88.40 | 1/5 |
| | | 200 | 27.6 ± 4.62 | 8.8 ± 1.85 | 68.11 | 0/5 |
| | | 100 | 27.6 ± 4.62 | 13.2 ± 4.09 | 52.17 | 0/5 |
| | | 50 | 27.6 ± 4.62 | 20.4 ± 4.21 | 21.08 | 0/5 |