Chemotherapy of Gnathostomiasis

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OBJECTIVE: To continue to search for chemicals with chemotherapeutic activity against advanced third—stage larvae of *Gnathostoma spinigerum.*

BACKGROUND: These studies are a continuation of the work reported in previous years. Many antihelmintic drugs have been evaluated for possible chemotherapeutic activity against experimental *G. spinigerum* infections of mice with advanced third stage or migrating larvae. All drugs have been ineffective so far.

DESCRIPTION: Mice of the ICR strain were infected by oral administration of five advanced third—stage larvae of *G. spinigerum.* After infection for some days, the test drug or combination of drugs dissolved in distilled water was administered orally or parenterally in a predetermined regimen. Infected control mice were given distilled water orally. After completion of the treatment regimen, the mice were sacrificed at intervals and necropsied. Parasites were counted in the liver and/or body muscles and the results recorded.

The drugs tested during this reporting period were: Astiban (sodium antimony dimercapto—succinate), Lucanthone (Miracil D. or Nilodin) (1—methyl—4—diethylamino—ethylaminothioxanthone hydrochloride), Hycanthone (Etrenol) an active metabolite of Lucanthone, and Iodine in Lugol's solution.

PROGRESS: Drug screening tests on mice infected with *G. spinigerum* advanced third stage larvae gave the following results.

Astiban: This drug was administered last year in five daily oral doses of 640 mg/kg or with a single oral dose of 1920 mg/kg to gnathostome—infected mice without effect. This year an oral dose of 1920 mg/kg daily for two days was also found to be ineffective in significantly reducing the numbers of the larvae in treated mice. Therefore the drug appears to have no therapeutic effect on infected mice (Table 1).

Lucanthone: Gnathostome—infected mice were treated with two doses of 150 mg/kg/day for five days (ten doses). The results are shown in Table 2. This drug is judged to have no therapeutic value in the treatment of *G. spinigerum* infection.

Hycanthone: This drug was administered orally over a five day course using doses of 100, 200, 300, and 400 mg/kg. The results are shown in Table 3. There was no significant reduction in the number of gnathostome larvae in the treated mice. Therefore Hycanthone is considered to have no therapeutic effect on the infection.

Lugol's solution: The prescription of the solution was Iodine, two grams; Potassium iodide, four grams; and purified distilled water, 100 ml. An *in vitro* experiment of various dilutions of the solution (1: 1000 to 1: 20,000 or iodine solution equivalent of 1: 500 to 1: 10,000) on living *G. spinigerum* advanced third—stage larvae obtained from the experimentally infected mice caused the death of the larvae in ten minutes to four days compared with the control in distilled water where the larvae lived for eight days.

The screening tests on infected mice (average body weight of 25 grams per mouse) were done by oral administration of various doses of the solution containing iodine 40, 200, and 400 mg/kg (or iodine solutions in mice of 1:625, 1:125, 1:60) twice daily for five days. The results showed no therapeutic value on the infection (Table 4), and all five infected mice who received 400 mg/kg died of toxicity about six hours after the administration of the last dose.

The drug was also given by subcutaneous injection of Lugol's solution using a dose of 20 mg. iodine/kg body weight of the infected mouse or equivalent to about 1:1250 solution of iodine in the mouse body. The result is shown in Table 5. This dose of the drug by subcutaneous administration is judged ineffective.

SUMMARY: Oral administration of Astiban, Lucanthone, Hycanthone and Iodine in Lugol's solution and subcutaneous injection of iodine in Lugol's solution were ineffective in the chemotherapy of *Gnathostoma spinigerum* in experimentally infected mice. Further investigation on iodine in Lugol's solution given by subcutaneous injection is in progress and the combined therapy with Astiban and Ambiltar has shown a modest chemotherapeutic effect and will be investigated further (1).

REFERENCES:

1. Daengsvang, S., Yingyourd, P., Machimasatha, R., and Dharmasarathul, T,: SEATO Medical Research Laboratory Annual Report March 1974.

Table 1. Treatment of *Gnathostoma spinigerum* Infected Mice with Astiban Oral Administration

Astiban Drug Dose (mg/kg/day)	No. of Infected Mice Treated	Third–stage Larvae Found	Time of Necropsy (Days)*
1920**	30	90	20
Control	30	93	19

* Days after administration of last drug dose
** For two days

Table 2. Treatment of *Gnathastoma spinigerum* Infected Mice with Lucanthone Oral Administration*

Lucanthone Drug Dose (mg/kg/day)	No. of Infected Mice Treated	Third–stage Larvae Found	Time of Necropsy (Days)**
150	10	31	24
Control	5	16	24

* Two doses per day for five days
** Days after administration of last drug dose

Table 3. Treatment of *Gnathostoma spinigerum* Infected Mice with Hycanthone Oral Administration*

Hycanthone Drug Dose (mg/kg/day)	No. of Infected Mice Treated	Third–stage Larvae Found	Time of Necrospy (Days)**
100	15	45	4–27
Control	15	46	14–28
200	13	42	10–27
Control	15	46	14–28
300	15	45	4–40
Control	15	44	33–40
400	14	40	1–40
Control	15	44	33–40

* One dose per day for five days
** Days after last dose of drug

Table 4. Treatment of *Gnathostoma spinigerum* Infected Mice by Oral Administration of Iodine in Lugol's Solution*

Iodine Drug Dose (mg/kg/day)	No. of Infected Mice Treated	Third–stage Larvae Found	Time of Necropsy (Days)**
40	5	19	7
Control	5	20	3–7
200	5	16	17
Control	5	17	17
400	5	17	All mice died six hrs. after last dose

* Two doses per day for five days
** Days after last dose of drug

Table 5. Treatment of *Gnathostoma spinigerum* Infected Mice by Subcutaneous Injection in Iodine in Lugol's Solution*

Iodine Drug Dose (mg/kg/day)	No. of Infected Mice Treated	Third–stage Larvae Found	Time of Necropsy (Days)**
20	10	30	17
Control	5	16	17

* One dose daily for five days
** Days after the last dose