Anthemintic Efficacy of Milbemycin D against *Toxocara cati* and *Ancylostoma tubaeforme* in Domestic Cats

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**ABSTRACT.** Anthelmintic efficacy of milbemycin D was evaluated against *Toxocara cati* and *Ancylostoma tubaeforme* in domestic cats. Twelve cats naturally infected with each nematode species were allocated among 2 groups of 6 animals each, and milbemycin D was orally administered to the 2 groups of cats in doses of 0.05 mg/kg and 0.1 mg/kg body weight, respectively. In all the cats infected with *T. cati*, fecal egg counts decreased followed by their disappearance from the feces and 2–35 worms were excreted into the feces after the medication in both doses of 0.05 mg/kg and 0.1 mg/kg. At postmortem of these medicated groups, no worms were detected from 4 cats of each group, but 1 and 2 immature worms were recovered from the other 2 cats respectively. In the cats infected with *A. tubaeforme*, fecal egg counts decreased followed by the disappearance from the feces and 2–62 worms were excreted into the feces in all the cats of the 2 groups, no nematodes remaining at postmortem. These results indicate that milbemycin D is fully effective against *T. cati* and *A. tubaeforme* in cats in a dose of 0.05–0.1 mg/kg.—**KEY WORDS:** *Ancylostoma tubaeforme*, anthemintic, cat, milbemycin D, *Toxocara cati*.


Milbemycin D, one of milbemycins, is a compound of 16-membered lactone structure, which is produced through a fermentation product of the actinomycete *Streptomyces hygroscopicus* subsp. *aurolacrimosis* [12, 13]. Although the compound corresponds to macrolides in structure, it has no antibacterial activity but has anthelmintic (nematocidal) and arthropodic activities; for instance, milbemycin D has been proved to have excellent prophylactic and therapeutic efficacy against canine dirofilariosis [10, 11] and against *Toxocara canis* and *Ancylostoma caninum* infections of dogs [4, 7–9], respectively. However, its anthelmintic effect on feline intestinal nematodes has not been fully elucidated.

In the present study, we investigated the anthelmintic efficacy of milbemycin D against feline intestinal nematodes, *Toxocara cati* and *Ancylostoma tubaeforme*

**MATERIALS AND METHODS**

**Drug:** Milbemycin D used was a 1% (W/W) powder formulation in lactose, supplied by Sankyo Co., Ltd., Tokyo, Japan.

**Animals:** Twenty three domestic cats, 18 females and 5 males, weighing 0.9–3.7 kg, naturally infected with either or both species of *T. cati* and *A. tubaeforme* were used for the present study. One of the 23 cats was coincidentally infected with the two species of nematodes.

**Experimental design:** Twelve cats infected with each nematode species were allocated among 2 groups of 6 animals each. The two groups were medicated with milbemycin D in doses of 0.05 mg/kg and 0.1 mg/kg body weight, respectively.

Fecal examinations were carried out by McMaster’s method to determine the number of eggs per day (EPD) for 3 consecutive days. After confirming the persistent oviposition of parasites, milbemycin D was orally administered to the cats in a dose of 0.05 mg/kg or 0.1 mg/kg on day 3. EPD values were continuously determined for 7 days after medication, and a qualitative fecal examination by the flotation method using saturated NaCl solution was also employed when no eggs were detected by McMaster’s method.

In addition, nematode worms excreted into the feces of the medicated cats were collected and counted every day.

All the animals were autopsied on day 7 after medication. At postmortem, the small intestine was cut into 4 parts: the duodenum and 3 equally long parts of the jejumum and ileum. Each part of the intestine was opened and carefully examined for remaining parasites.

When infection with other species of helminths than *T. cati* and *A. tubaeforme* was observed,
efficacy of milbemycin D against these species was also examined.

Clinical findings of the medicated cats were carefully observed every day to evaluate the adverse effects of the anthelmintic.

RESULTS

Efficacy against *T. cati*: All the cats infected with *T. cati* persistently passed their eggs into the feces for 3 days before medication with milbemycin D.

In the group medicated with milbemycin D in a dose of 0.05 mg/kg, fecal egg counts decreased and then no eggs became to be detected not only by McMaster's method but also by the flotation method 3-7 days after treatment in all the cats. Two to 6 *T. cati* worms were excreted into the feces of each cat. At postmortem, 1 and 2 specimens of *T. cati* were recovered from the upper part of the jejunum and ileum of 2 cats respectively, although no worms were detected from the other 4 cats. All the remaining nematodes were immature (Table 1 and Fig. 1).

In the group medicated in a dose of 0.1 mg/kg, results were almost the same as in the group in a dose of 0.05 mg/kg: EPD values decreased followed by the disappearance of eggs from the feces 2-5 days after treatment, and 2 to 35 *T. cati* worms were excreted into the feces of all the cats. At postmortem, 1 and 2 immature *T. cati* specimens were obtained from the upper part of the jejunum and ileum of 2 cats, respectively, whereas no worms were detected from the other 4 cats (Table 1 and Fig. 2).

Efficacy against *A. tubaeforme*: Eggs of *A. tubaeforme* were persistently detected for 3 days before medication in all the cats.

After administration of milbemycin D in both doses of 0.05 mg/kg and 0.1 mg/kg, fecal egg counts decreased until no eggs were detected by either McMaster's method or the flotation method on day 2-5 after treatment. The worms were excreted in all the cats, ranging from 2 to 62 in number. No remaining worms were observed in any of the cats at postmortem. Milbemycin D was completely efficacious in both dosages of 0.05 mg/kg and 0.1 mg/kg.

![Fig. 1. Fluctuation of eggs per day (EPD) and the number of excreted and remaining worms in cats infected with *Toxocara cati* and medicated with milbemycin D in a dose of 0.05 mg/kg body weight. Arrows (→) show the oral administration of milbemycin D. Black dots (●) on X axis indicate that eggs were no longer detected by both McMaster's method and the flotation method, and broken lines (---) indicate that cats did not defecate.](image)

Table 1. Efficacy of milbemycin D against *Toxocara cati* and *Ancylostoma tubaeforme*

<table>
<thead>
<tr>
<th>Helminth species</th>
<th>Dose (mg/kg)</th>
<th>No. of cats used</th>
<th>Range Average Total</th>
<th>No. of worms excreted</th>
<th>No. of worms remaining</th>
<th>Range Average Total</th>
<th>Efficacy rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>T. cati</em></td>
<td>0.05</td>
<td>6</td>
<td>2-6</td>
<td>4.2</td>
<td>25</td>
<td>0-2</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>0.1</td>
<td>6</td>
<td>2-35</td>
<td>9.5</td>
<td>57</td>
<td>0-2</td>
<td>0.5</td>
</tr>
<tr>
<td><em>A. tubaeforme</em></td>
<td>0.05</td>
<td>6</td>
<td>2-62</td>
<td>14.0</td>
<td>84</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0.1</td>
<td>6</td>
<td>2-22</td>
<td>7.2</td>
<td>43</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

a) Total in 6 cats used in each experimental group.
b) Efficacy rate (%) = \( \frac{\text{No. of worms excreted}}{\text{No. of worms excreted + No. of worms remaining}} \) × 100.
c) All collected from the upper part of jejunum and ileum.
against *A. tubaeforme* (Table 1 and Figs. 3 and 4).

**Efficacy against other species of helminths:** One cat was infected with *Physaloptera* sp. in addition to *A. tubaeforme*. Although no eggs of *Physaloptera* had been detected by fecal examinations, one worm of this species was excreted into the feces after administration of milbemycin D in a dose of 0.1 mg/kg. No remaining worms were detected in the stomach at postmortem.

Cestode infections were observed in 5 cats: 3 with *Spirometra erinacei*, 1 with *Dipylidium caninum* and 1 with *Taenia taeniaeformis*. These cats were medicated with milbemycin D in a dose of 0.05 mg/kg or 0.1 mg/kg, but no efficacy was recognized against the cestode species at all (Table 2).

**Adverse effects:** No noticeable adverse effects were observed in any of the medicated cats in the course of study.

**DISCUSSION**

Two kinds of anthelmintics of macrolide structure, milbemycin D and ivermectin, have been manufactured for veterinary use [2]. These two anthelmintics are very similar in their molecular structure and show relatively similar anthelmintic spectra. Both milbemycin D and ivermectin have been proved to have excellent activity to immature precardiac stages of *Dirofilaria immitis* parasitizing in the muscle of dogs in doses of 1 mg/kg [10, 11] and 6 µg/kg [5, 6], respectively, and are now widely used for prophylaxis of canine dirofilariasis.

Concerning the efficacy against intestinal nematodes of dogs, milbemycin D has been reported to be effective against *T. canis* and *A. caninum* in a lower dose of 0.05-0.1 mg/kg [4, 7-9] than that against immature *D. immitis*; but ivermectin needs a much higher dosage against the intestinal nematodes than that against immature *D. immitis* [1]. Therefore, it is considered that milbemycin D has an advantage to be able to deworm *T. canis* and *A. caninum* when prophylaxis of dirofilariasis is done.

Of canine intestinal nematodes, *A. caninum* is much more susceptible to milbemycin D than *T.
canis, because the drug can almost always completely deworm A. caninum but not always deworm completely T. canis in a dose of 0.05–0.1 mg/kg [4, 7–9]. In feline practice, milbemycin D has been evaluated only against Toxascaris leonina to be effective in doses of 0.05 mg/kg and 0.1 mg/kg although immature worms remained in 1 of the 3 cases after medication in a dose of 0.05 mg/kg [3], corresponding to the results against T. canis [4, 7–9].

The results in the present study were similar to those in the reports [3, 4, 7–9] mentioned above: Milbemycin D was effective against T. cati and A. tubaeforme in doses of 0.05 mg/kg and 0.1 mg/kg with remainings of immature T. cati worms in some cases. All these findings indicate that the anthelminthic effect of milbemycin D is almost the same each in the roundworm species T. canis, T. cati and T. leonina and in the hookworm species A. caninum and A. tubaeforme.

The present study also revealed that milbemycin D was effective against Physaloptera sp. Consequently, the agent has a possibility to show excellent anthelminthic efficacy against various species of nematodes in the alimentary tract as well as against immature D. immitis, although it is not effective against cestodes as observed in the previous [4, 8, 9] and the present evaluations. Milbemycin D is expected to be successfully used not only in canine but also in feline practices.

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REFERENCES


Table 2. Efficacy of milbemycin D against other helminth species than Toxocara cati and Ancylostoma tubaeforme

<table>
<thead>
<tr>
<th>Species</th>
<th>Cat No.</th>
<th>Dose (mg/kg)</th>
<th>Total No. of worms excreted</th>
<th>Total No. of worms remaining</th>
<th>Efficacy rate(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physaloptera sp.</td>
<td>18</td>
<td>0.1</td>
<td>1</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>0.1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>0.1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>0.1</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Dipylidium caninum</td>
<td>7</td>
<td>0.1</td>
<td>0</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>Taenia suisaeformis</td>
<td>16</td>
<td>0.05</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

a) Cat No. corresponds to that in Figs. 2–4.

b) Efficacy rate (%) = \[ \frac{\text{Total No. of worms excreted}}{\text{Total No. of worms remaining}} \times 100. \]
MILBEMYCIN AGAINST INTESTINAL NEMATODES


