The efficacy of furazolidone against experimental infections with *Trypanosoma evansi* in camels and mice in Sudan: comparisons with quinapyramine and suramin

B. H. Ali 1  
T. Hassan 1  
K. H. Malik 2

In the present study, an attempt has been made to assess the therapeutic effectiveness of the nitrofuran drug, furazolidone, which is known to be effective against a variety of bacteria (e.g. Campylobacter, Salmonella and *E. coli*), and protozoa (e.g. Giardia, *Coccidia* and *Trichomonas*). Brief notes on the effect of this drug against *T. evansi* in mice have been published recently (1, 13), and these studies seem to indicate that this drug, at rather high doses (320 and 160 mg/kg; orally) is useful in treating mice experimentally infected with *T. evansi*. Lower doses were ineffective. These findings led us to evaluate this drug in the natural host of the parasite, the camel. The results obtained were compared with those obtained after conventional therapy with quinapyramine and suramin.

**MATERIALS AND METHODS**

**Animals**

Ten healthy camels (Camelus dromedarius) of both sexes, weighing 160-320 kg and ranging from 3-7 years old were purchased from the Khartoum area (known to be free from trypanosomiasis), and kept in a fly-proof house. They were given sorghum grains, hay and water *ad libitum*. The animals were numbered 1 through 10, and were divided into three groups: Group I (n=5 to 10), Group II (n=6 to 7) and Group III (n=10).

Healthy white albino mice (locally bred) of both sexes, weighing 20-25 g were used. They were kept in clean plastic cages and allowed free access to drinking water and pelleted diet. They were divided at random into six groups designated I to VI.

**T. evansi**

A local strain was isolated from naturally infected camels in the Gadarmballa region of the southeastern Sudan, an area where camel trypanosomiasis is prevalent. The parasite was maintained in albino white...
mice by syringe passage. Trypanosomes were separated from blood of infected mice showing a high parasitaemia using the method described before (2). Each experimental mouse received 500,000 parasites intraperitoneally while each experimental camel received 1 million parasites.

**Experimental infection**

(a) Camels

(i) Six camels (no. 1 to 6) were infected with trypanosomes (Day 1) and then treated orally with furazolidone (12 mg/kg for 5 days) after one week.

(ii) Three camels (no. 7 to 9) were infected but not treated.

(iii) One camel (no. 10) was kept as an uninfected control.

(b) Mice

(i) 5 mice were kept as uninfected untreated controls.

(ii) 5 mice were each infected with trypanosomes (Day 1).

(iii) 5 mice were each infected as above (Day 1) and treated with an oral dose of furazolidone (320 mg/kg) on Day 8.

(iv) 5 mice were each infected as above (Day 1) and treated with an oral dose of furazolidone (320 mg/kg) on Day 22.

(V) 5 mice were given furazolidone at a dose of 320 mg/kg orally.

(VI) 5 mice were infected as above (Day 1) and treated subcutaneously with quinapyramine (2 mg/kg) on Day 8.

**Treatment with furazolidone**

Furazolidone of particle size 5 μm (Furazolidon®, Orphahell, The Netherlands) was administered orally to camels at a dose rate of 12 mg/kg for 5 days as recommended by the British Pharmacopoeia (Veterinary), 1977, for susceptible infections in mammals. The drug was given to mice at a dose of 320 mg/kg as recommended by Zhang (13). In both species, the drug was given 7 days after infection when parasitaemia was high.

**Treatment with quinapyramine and suramin**

After the experiment with furazolidone, the camels remained infected (see below) so it was decided to see if quinapyramine or suramin would be effective in reducing parasitaemia. Quinapyramine salt (supplied by May & Baker Laboratories) was given subcutaneously to camels (no. 1 to 6) at a dose rate of 5 mg/kg. For comparison, 5 mice were given the drug at a dose rate of 2 mg/kg subcutaneously. Suramin (Naganol®, Bayer, Germany) was administered to camels at a dose rate of 25 mg/kg (iv) as recommended by the manufacturer. No sign of interactions between the administered drugs were noted in mice or camels.

**Histopathological methods**

Small pieces of heart, lung, liver, kidneys, spleen and lymph nodes of selected mice in each group were fixed in 10 p. 100 v/v formal saline and cut at 5 μm thickness, and stained with haematoxylin and eosin.

**RESULTS**

**Effect of furazolidone on trypanosomiasis in mice**

Some of the results of this experiment are shown in table I. In infected untreated mice (Group II), the trypanosomes appeared in blood within 12 h, disappeared in one mouse within 31 days, relapsed in 3 mice and never disappeared in one mouse. In mice treated with furazolidone one or three weeks after infection with T. evansi, the parasites disappeared from the blood three to seven days after treatment. The blood remained free from the trypanosomes for four weeks following which parasitaemia recurred. Furazolidone treatment in uninfected mice (Group V) did not cause obvious adverse effects, and the animals were killed at day 30.

**Histopathological findings in mice**

In infected untreated mice (Group II) there was some evidence of hepatic damage manifested by focal necrosis, haemosiderin deposition, and infiltration of the portal tract by mononuclear cells. There was also congestion and haemorrhage in the spleen, kidney and lungs. In Groups III, IV and VI only slight congestion was seen in the spleen and hearts of mice nos. 13, 17, 26 and 27. No obvious histopathological findings could be seen in mice in Groups I and V.

**Effect of furazolidone on camel trypanosomiasis**

As shown in table II, furazolidone (10 mg/kg liveweight for 5 days) was not effective in removing the parasite.
TABLE I The effect of furazolidone (320 mg/kg orally) and quinapyramine (12 mg/kg)* on mice experimentally infected with T. evansi (500,000 trypanosomes).

<table>
<thead>
<tr>
<th>Group</th>
<th>Onset of parasitaemia (h)</th>
<th>Trypanosome disappeared from blood (day)</th>
<th>Fate of mice at day</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>6</td>
<td>30 (killed)</td>
<td>30 (killed)</td>
</tr>
<tr>
<td>II</td>
<td>12</td>
<td>31</td>
<td>40 (died)</td>
</tr>
<tr>
<td>III</td>
<td>12</td>
<td>3 (after treatment)</td>
<td>30 (killed)</td>
</tr>
<tr>
<td>IV</td>
<td>12</td>
<td>3 (after treatment)</td>
<td>30 (killed)</td>
</tr>
<tr>
<td>V</td>
<td>12</td>
<td>30 (killed)</td>
<td>30 (killed)</td>
</tr>
<tr>
<td>VI</td>
<td>12</td>
<td>3 (after treatment)</td>
<td>30 (killed)</td>
</tr>
</tbody>
</table>

* Relapsing parasitaemia. ** Trypanosome never disappeared.

from the blood stream. Monitoring the infection by the diagnostic methods mentioned before, parasitaemia remained for at least one month.

Effect of quinapyramine and suramin on trypanosomiasis

Following the failure of furazolidone in eliminating T. evansi infection in camels, an attempt was made to cure the infection with quinapyramine at the recommended dose of 5 mg/kg. Following the same procedure for diagnosis used before, it was found that the treatment was only effective in removing the parasite from the blood for periods ranging from 5 to 21 days. Relapses then occurred. Infected mice (Group VI) given the drug at a dose of 2 mg/kg were apparently cured for a period of two months, following which relapses occurred in four out of five mice. Another attempt was made to treat the experimental infection in camels with the therapeutic dose of suramin (25 mg/kg). This dose removed the parasite from the blood for up to 16 days. Three to five days after the recurrence of parasitaemia, 3 of the camels died and the rest were slaughtered.
TABLE II The effect of furazolidone (12 mg/kg for 5 days orally) on camels experimentally infected with Trypanosoma evansi (10⁶ parasites).

<table>
<thead>
<tr>
<th>Group</th>
<th>Camels</th>
<th>Onset of parasitaemia (h)</th>
<th>Trypanosome disappeared from blood (day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (infected treated)</td>
<td>1</td>
<td>12</td>
<td>Never disappeared</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>II (infected untreated)</td>
<td>7</td>
<td>12</td>
<td>Never disappeared</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>III (uninfected untreated control)</td>
<td>10</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

DISCUSSION

Several drugs have been tried against T. evansi infections in camels and other domestic and laboratory animals (2, 4, 5, 7, 11, 12). More recently furazolidone has been shown to possess a remarkable efficacy against T. evansi in mice comparable to that of quinapyramine (1). Therefore it was of interest to try the drug in infected camels. The dose which was effective in mice (320 mg/kg) was too high and probably toxic to camels. Lower doses were not attempted because it has been shown to be ineffective as trypanocidal drugs in mice (13). It was shown previously that camels are susceptible to furazolidone toxicity at doses which are apparently harmless in other animals (2, 8), seems to indicate that camels are particularly susceptible to the toxic effects of trypanocidal drugs. The reason for this particular susceptibility of camels is not known with certainty. It may possibly be due to a deficiency in the liver metabolizing capacity of camels, in particular the absence of some important drug metabolizing enzymes in this species, or to the biotransformation of these drugs into toxic metabolites. Experiments are in progress in this laboratory to study some drug metabolizing enzymes in the camel.

It is known that T. evansi is becoming more resistant to suramin especially when the drug is used regularly in the field (4). Quinapyramine is practically no longer commercially available. Recently it has been shown that isometamidium chloride eliminates T. evansi from experimentally infected camels for periods of only 3 weeks or less (2). Thus the research for effective and safe anti-trypanosomal drugs must continue. Considering the great economic significance of camels in tropical countries, the importance of the search for such drugs cannot be over-emphasized.

ACKNOWLEDGEMENTS

This study was made possible, partially by financial support from May & Baker, England. Thanks are due to Messrs A. Abdel WAHID and Ali HAMID for their assistance.


The efficacy of furazolidone against experimental Trypanosoma evansi infection was studied in camels and mice. The criteria for assaying the anti-trypanosomal effect of furazolidone included quinapyramine and suramin were effective only in removing the protozoan from the blood stream for up to 21 days. Repeated treatment with these drugs may, therefore, be necessary. With furazolidone, however, repeated treatment is not without some risk due to its known cumulative toxic properties.

The observation that mice were not affected either clinically or histopathologically by furazolidone at a dose rate of 320 mg/kg, while the same drug and diminazine aceturate and isometamidium chloride all affect camels adversely at doses which are apparently harmless in other animals (2, 8), seems to indicate that camels are particularly susceptible to the toxic effects of trypanocidal drugs. The reason for this particular susceptibility of camels is not known with certainty. It may possibly be due to a deficiency in the liver metabolizing capacity of camels, in particular the absence of some important drug metabolizing enzymes in this species, or to the biotransformation of these drugs into toxic metabolites. Experiments are in progress in this laboratory to study some drug metabolizing enzymes in the camel.

It is known that T. evansi is becoming more resistant to suramin especially when the drug is used regularly in the field (4). Quinapyramine is practically no longer commercially available. Recently it has been shown that isometamidium chloride eliminates T. evansi from experimentally infected camels for periods of only 3 weeks or less (2). Thus the research for effective and safe anti-trypanosomal drugs must continue. Considering the great economic significance of camels in tropical countries, the importance of the search for such drugs cannot be over-emphasized.
examination of blood and tissue for *T. evansi* and the clinical and pathological changes seen in some selected tissues. In infected mice furazolidone at a single oral dose of 320 mg/kg liveweight produced complete elimination of the parasite from the blood stream for four weeks. At this dose no toxic effects were seen in the treated mice. Quinapyramine at a single subcutaneous dose of 2 mg/kg liveweight produced similar effects.

In infected camels furazolidone at an oral dose of 10 mg/kg liveweight for five days did not remove the protozoon from the blood stream. Treatment of the same infected camels with quinapyramine (5 mg/kg liveweight subcutaneously), and four weeks later by suramin (25 mg/kg liveweight intravenously), removed the parasite from the blood for periods up to 21 days, following which relapses occurred.

The study indicated that despite the anti-trypanosomal effect of furazolidone in mice, it was found ineffective against *T. evansi* in camels when given at doses tolerated by this species. Key words: Dromedary - Experimental infection - *Trypanosoma evansi* - Mouse - Furazolidone - Quinapyramine - Suramin - Sudan.

### REFERENCES


