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The Effect of Cordycepin on Tsetse-Borne *Trypanosoma vivax* Infections

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Abstract

1. A preliminary field trial is reported of Cordycepin treatment of 12 cases of tsetse-induced *T. vivax* in sheep.
2. The toxicity of Cordycepin is shown to be slight.
3. The indication, so far, is that Cordycepin is ineffective in curing tsetse-induced *T. vivax* infection in sheep.

Introduction

In the treatment of African cattle trypanosomiasis, drug resistance has diminished, if not eliminated, the effectiveness of Antrycide and Ethidium, two of the only three established cattle trypanocides. Exclusive reliance on the third, Berenil, is potentially hazardous, and effective drugs, preferably of novel chemical type, are urgently required in order to counter the possible threat of Berenil-resistance (cf. MACLENNAN & JONES-DAVIES, 1967).

Cordycepin (3′-deoxyadenosine) (CUNNINGHAM, HUTCHINSON, MANSON & SPRING, 1951) is an antitumour antibiotic resembling Puromycin and Puromycin aminonucleoside, both of which have trypanocidal properties. Cordycepin similarly was found to be an active trypanocide (WILLIAMSON, 1966) especially on *Trypanosoma congolense,* but further examination of its activity demanded much larger amounts of material, which was kindly made available by the Microbial Products Section of the Microbiological Research Establishment, Porton Down, U.K. Earlier results were then reassessed on a larger scale (WILLIAMSON, 1972), and although activity on fly-transmitted strains of *T. vivax* or *T. congolense* was not expected to be of a high order, experiments of this type were felt to be useful in view of the novel character of the drug and of its activity in laboratory infections of rats and mice.

Accordingly, a preliminary trial of Cordycepin was conducted with tsetse-induced *T. vivax* infections of sheep.

Materials and Methods

Twelve clean sheep were purchased from the Mangu market on the Bauchi plateau; this area is known to be tsetse-free. Blood smears were made daily and were certified free of trypanosomes. Blood was also taken from the jugular vein and inoculated into rats; these failed to become infected. All the sheep were dewormed before use.

The tsetse flies used were virgin male and female *Glossina tachinoides* that had emerged from wild pupae collected by the Institute's staff at the Yankari Game

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Reserve of the North Eastern State. The newly-emerged flies were repeatedly fed on a sheep heavily infected with *T. vivax* (strain 36/15) until the majority of the sampled dissected flies showed that 90% or more of the flies in each batch were infected. These flies were then fed once, on clean sheep, numbers 71, 72 and 73 for trial I, and numbers 76, 84 and 85 for trial II, respectively; about 100–180 flies were used for feeding on each sheep. Blood, obtained from the tail and ear veins of the sheep, was examined daily and the parasitaemia observed.

All the sheep started showing trypanosomes 5–6 days after infection. The parasitaemia was then allowed to build up for a further 5–7 days before the administration of the drug.

Cordycepin (Batch 4) was administered to the sheep as a ground-up suspension in a small volume of 1% gum acacia (BDH) in water. (Gum acacia was used because Cordycepin 4 has a low solubility in water.) The injections were given subcutaneously in the neck of the sheep. Two dose regimens were used, 50 mg/kg and 25 mg/kg body weight. Control sheep received subcutaneous gum acacia alone.

Blood parasitaemia after the drug administration was examined daily and any signs of drug toxicity (such as loss in weight) were looked for.

Results

The results of these trials are summarized in the table below.

Table. Cordycepin trials in tsetse-induced *T. vivax* infection of sheep

Sheep No.	Drug dose (mg/kg)	Change in body weight (lb)	Parasite-free for (days)	Days of parasitaemia	Day of death after treatment
		Trial I			
71	50	(40–33)	3	(4–9)	9
72	25	(32–37)	2	(3–13)	13
73	Control	(35–33)	–	(2–10)	10
		Trial II			
76	50	(30–21)	3	(4–11)	11
85	25	(33–31)	2	(3–13)	13
84	Control	(28–30)	–	(2–14)	14

Toxic symptoms were observed at the two dosages given as indicated in the table above. There was a little swelling due to the depot of the drug, but the surrounding area did not become inflamed or oedematous.

Although the number of animals used for the Cordycepin trial is small (6 sheep in the first two trials, and a repeat with another 6 sheep that gave an identical result with the first two batches), there is every indication that the drug is ineffective in curing tsetse-induced *T. vivax* infection. There was only a brief disappearance of trypanosomes from the blood for only 2–3 days after the drug administration. This might mean that only a few trypanosomes are resistant to the drug.

These findings has been confirmed by another pharmaceutical firm's private

investigation in the United Kingdom (pers. Comms. J. WILLIAMSON, July 1972).

Although these initial results are disappointing, they suggest that further exploitation of adenine-nucleoside-type drugs as 'cattle' trypanocides may be profitable, especially in view of the central importance of adenine in the metabolism of African trypanosomes (WILLIAMSON, 1969, 1970).

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