

EFFICACY OF SYSTEMIC ADMINISTRATION OF IVERMECTIN AGAINST TSETSE FLIES

by

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Summary — A preliminary evaluation of the systemic insecticidal efficacy of ivermectin against *Glossina palpalis palpalis* was carried out in guinea pigs and a goat. The killing effect starts at a concentration of 2 mg/kg and all tsetse flies died within 5 day after being permanently fed on a 10 mg/kg treated goat.

Ivermectin may be a promising systemic drug against tsetse flies and it would be worthwhile to continue both efficacy trials and toxicological studies in cattle.

KEYWORDS : Tsetse Flies; *Glossina palpalis palpalis*; Trypanosomiasis; Ivermectin; Systemic Insecticides.

Introduction

Eight major avermectins have been isolated from a newly described actinomycete, *Streptomyces avermitilis* (Burg *et al.*, 1979). One of them has been selected for commercial use and is known as ivermectin or 22,23-dihydroavermectin B₁. This drug, as well as other avermectins, appears to be a very potent broad-spectrum anthelmintic agent, affecting most of the important immature and mature roundworms of the intestinal and respiratory tracts of domestic livestock (Egerton *et al.*, 1979; 1980). Efficacy against some filarial parasites has also been observed following oral or parenteral administration of the drug (Campbell, 1982).

The insecticidal activity of the drug could be established against beetles and flies (Ostlind *et al.*, 1979) and the avermectins have been recognised as new promising insecticides, acaricides and nematocides in agriculture (Putter *et al.*, 1981), as well as in veterinary medicine, where they show a high efficacy against parasitic mites, lice (Barth & Sutherland, 1980) and ticks (Centurier & Barth, 1980).

Numerous papers have since been published on ivermectins' activity against flies parasitising directly or indirectly man and his livestock (Meyer *et al.*, 1980; Miller *et al.*, 1981; James *et al.*, 1980; Lyons *et al.*, 1980; etc.). We are not aware of reports mentioning an activity of ivermectin against *Glossina spp.*

Trypanosomiasis is still a major constraint to development of livestock in a large part of Africa south of the Sahara. The disease is mainly transmitted by *Glossina* larvae bearing insects belonging to the family of Diptera. One can state that all former and present control measures such

as bush clearing, wildlife destruction, insecticides application by ground-spray or aerial spray, trapping etc., have failed on the long run for different reasons: impractical, too expensive, insufficient result, unethical etc. For this reason other control measures are investigated. In the present study, experiments carried out with several broad-spectrum antiparasitic drugs on guinea pigs and a goat provided evidence that high doses of ivermectin administered by subcutaneous injection were highly effective against tsetse flies sucking on these animals.

Material and methods

Tsetse flies

Glossina palpalis palpalis (originally from Kaduna, Nigeria, but bred as an autonomous strain at the laboratory since 1974) were used in all experiments. Flies are held in standard PVC-cages, measuring 16 × 10 × 7 cm, containing 20 flies each. The colony is maintained at 24.5 °C and 85 per cent R.H. in climatic chambers (Weiss 14'/+17/uk) and has a 4 days a week feeding regimen on guinea pigs.

Evaluation of the systemic efficacy of ivermectin

Efficacy in guinea pigs

In order to obtain a general idea about a possible effect of ivermectin against tsetse flies, 6 different concentrations, being respectively 1, 2, 4.5, 6, 8.5 and 10 mg/kg (mpk) of a commercially available preparation of ivermectin (Merck Sharp & Dohme; 1 per cent solution), were administered as single subcutaneous injections into 2 female albino inbred guinea pigs each. The average weight of these 12 animals was 608 g.

Flies emerging 2 days after the inoculation were fed permanently (7 days a week) on those guinea pigs. Their survival was compared with controls held on untreated animals. Seventy-seven females and 85 males were fed once on the 10 mpk treated guinea pig. Fully engorged flies were retained and were fed afterwards on untreated animals. A second unit, containing 10 day old flies from our stock colony, were fed on the same 10 mpk treated guinea pig 2 days post inoculation.

Efficacy in goat

Ten mpk ivermectin was injected subcutaneously into a goat of 32 kg weight. Flies emerging on consecutive days were fed permanently on the goat, in order to determine the efficacy period of one single application of ivermectin. Survival was compared with controls fed on an untreated goat. Again, one small unit of teneral was fed once on the treated goat and was held afterwards on an untreated one.

A 2 × 2 G-test (with Williams' correction; Sokal & Rohlf, 1981), was used to determine the statistical significance of the influence of ivermectin upon the survival of *G. p. palpalis*.

Results

Efficacy in guinea pigs

Figure 1 gives the survival course over a 25 days period. Data are summarized in table 1. Ivermectin influenced the survival of *G. p. palpalis*. The effect started at a concentration between 1 mpk (threshold level; $G_{adj} = 1.38$) and 2 mpk (tenfold anthelmintic dose; $G_{adj} = 45.94$) and raised with increasing dosage. All flies died as early as on the 15th day post emergence (female flies) and on the 22th day (males) at 10 mpk ivermectin. Older flies, aging 10 days before being fed on the 10 mpk treated guinea pig, were affected likewise though not so intensively as the teneral. One single feeding on the 10 mpk treated guinea pig sufficed to influence survival markedly. Generally male *G. p. palpalis* were found to be slightly more susceptible to ivermectin than females: 184 of the 499 females (37 per cent) survived after 25 days of ivermectin treatment, whereas only 129/435 males did so (30 per cent) ($G_{adj} = 4.20$).

Efficacy in goat

The first group of teneral was fed on day 2 post inoculation and died as early as on the 5th day post emergence (fig. 2a). The last group of teneral was fed on day 16 post inoculation and died after 8 days. The group of teneral with one single ivermectin bloodmeal on day 3 post inoculation died after 4 days (fig. 2b).

Further observations are being made in order to determine the efficacy period of one single injection of ivermectin.

All flies before dying, showed a progressive paralysis, firstly reducing the flight movements, finally affecting the legs. Blood digestion seemed to be hampered as well, since the flies remained fully engorged after having taken a bloodmeal from an ivermectin treated animal. The tsetse flies finally died with a markedly swollen abdomen. The apparent action of ivermectin on the flies' nervous system corroborates earlier findings (Campbel, 1981). Signs of drug toxicity at the 10 mpk level were not observed in both the goat and guinea pigs.

TABLE 1
Relationship between different concentrations of ivermectin (mg/kg or mpk) and survival of *G. p. palpalis* after 25 days

	Females		Males	
	Number	Survivors after 25 days	Number	Survivors after 25 days
Controls	80	74 (93 %)	80	74 (93 %)
Ivermectin (mpk) :				
1	80	77 (96 %)	80	76 (95 %)
2	50	34 (68 %)	50	23 (46 %)
4.5	42	22 (52 %)	30	7 (23 %)
6	80	29 (36 %)	60	11 (18 %)
8.5	80	10 (13 %)	40	2 (5 %)
10	50	0 (on day 15)	50	0 (on day 22)
1 × 10 mpk	77	8 (10 %)	85	3 (8 %)
10 day old flies (controls)	20	19 (95 %)	20	14 (70 %)
10 day old flies on 10 mpk	40	4 (10 %)	40	7 (18 %)

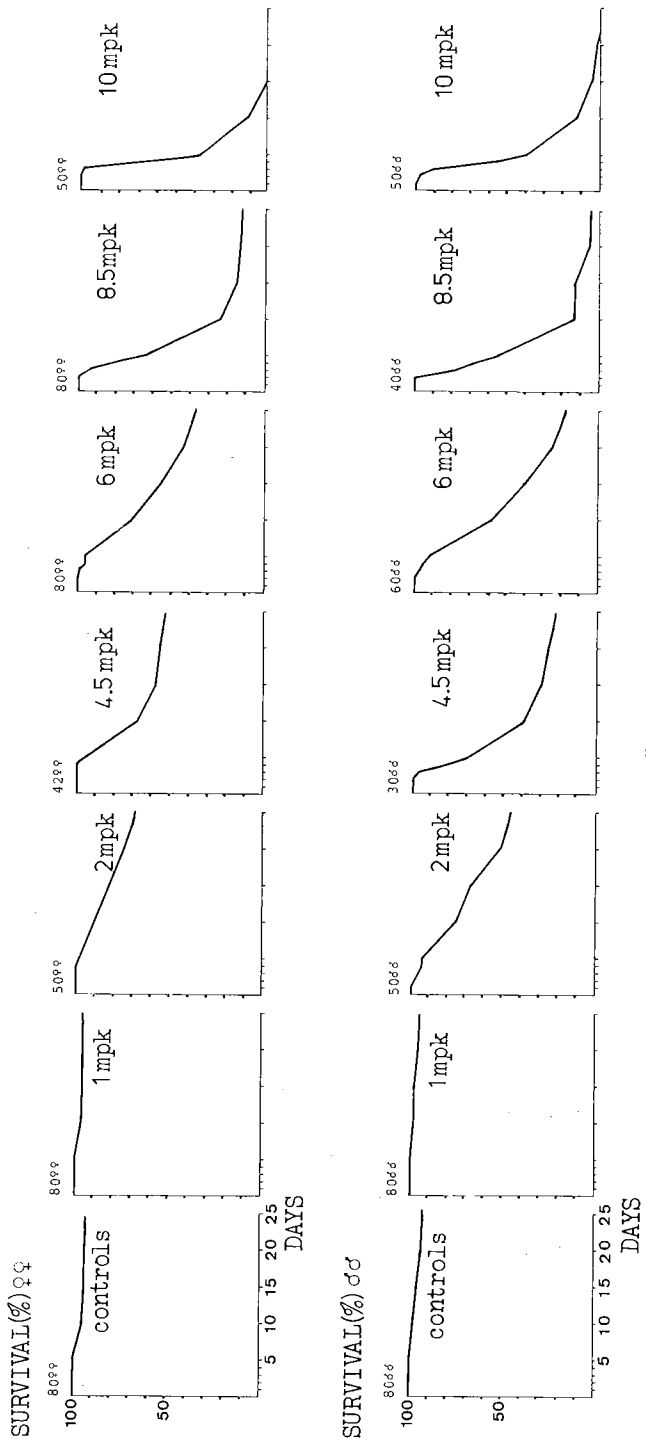


Figure 1 a.

Survival course of general *G. p. palpalis* being fed on ivermectin treated guinea pigs over a 25 day period. The initial number of flies are indicated above each diagram. The dosage ivermectin is expressed in mg/kg (mpk).

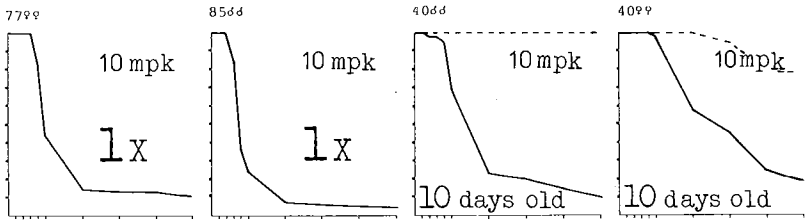
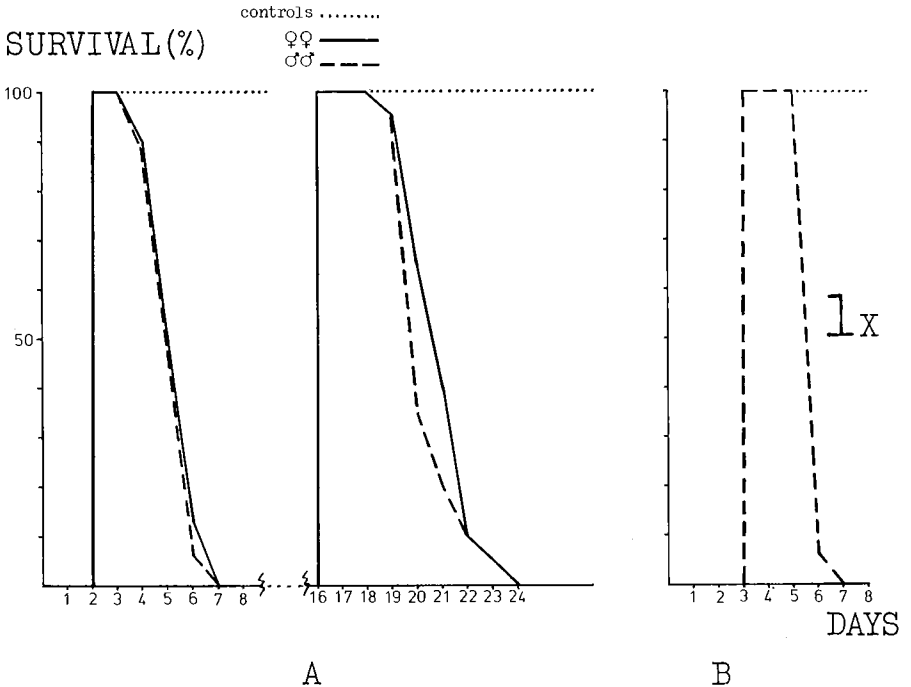


Figure 1 b.
 Influence on survival of one single bloodmeal taken from a 10 mpk treated guinea pig
 Visualizing the survival course of flies, aging 10 days before being fed
 during 25 days on the 10 mpk treated guinea pig.



Figures 2 A and B.

- A. Survival course of teneral *G. p. palpalis* being fed permanently on a 10 mpk treated goat. The first group (containing 39 females and 51 males) was emerged on day 2 post inoculation, the last group (20 females and 20 males) on day 18.
- B. Survival course of 33 males being fed *once* on day 3 post inoculation. Controls were fed on an untreated goat.

Discussion

As it appears from these preliminary experiments ivermectin is active against tsetse flies sucking on animals previously treated with the drug. One single bloodmeal with ivermectin already affected the flies' life expectancy. The effect started at a concentration between 1 and 2 milligramme pro kilo and was absent at the usually recommended dose of 0.2 milligramme pro kilo. Although the experimental activity was excellent, the at least tenfold higher dosage rate compared to the usually recommended dose to treat endo- and ectoparasites of animals, might constitute a serious financial constraint.

Tsetse flies have a very slow reproduction rate, which has sometimes seasonal bindings in many parts of Africa; they also have a very marked preference for their hosts. Thus, it might be possible to decrease sensibly the *Glossina* population in a given area by injections of ivermectin with intervals depending on local conditions. The high activity against many other parasites will enhance at the same time the physical condition of the animal.

Generally it can be concluded that ivermectin might be a promising drug against tsetse flies. Further efficacy trials and toxicological studies in cattle should be initiated.

Efficacité de l'administration systémique d'ivermectine contre les glossines.

Résumé — Les auteurs ont évalué l'effet systémique d'ivermectine chez des cobayes et une chèvre contre *Glossina palpalis palpalis*. Un effet léthal est constaté à partir d'une concentration de 2 mg/kg et toutes les mouches tsétsé meurent dans les 5 jours après avoir été nourries sur une chèvre ayant reçu 10 mg/kg d'ivermectine.

L'ivermectine pourrait donc constituer un insecticide systémique très prometteur contre les mouches tsétsé. Des études supplémentaires portant sur l'efficacité et l'effet toxicologique chez le bétail sont fortement recommandées.

Werking van systemisch toegediende ivermectine tegen tsetse-vliegen.

Samenvatting — De systemische insecticide werking van ivermectine tegen *Glossina palpalis palpalis* werd nagegaan in cavia's en bij een geit. Sterfte ontstaat vanaf een dosis van 2 mg/kg en alle tsetse vliegen waren dood binnen de 5 dagen nadat zij permanent gevoed werden op een geit met 10 mg/kg ivermectine.

Ivermectine zou dus een zeer interessant systemisch middel tegen tsetse-vliegen kunnen zijn. Het is aangewezen de efficiëntie verder na te gaan bij runderen en toxicologische studies uit te voeren.

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