RESEARCH NOTE

LACK OF *IN VITRO* EFFECT OF IVERMECTIN ON *PLASMODIUM FALCIPARUM*

Peter Nasveld[1], Bruce Russell[1,2], Barbara Kotecka[1] and Karl Rieckmann[1]

[1]Australian Army Malaria Institute, Gallipoli Barracks, Enoggera, QLD, Australia; [2]Armed Forces Research Institute of Medical Sciences, Department of Entomology, Bangkok, Thailand

Abstract. The *in vitro* activity of ivermectin was assessed against the K1 isolate of *Plasmodium falciparum*. The mean IC_{50} and IC_{90} of ivermectin were 8.0 and 35.0 µg/ml, respectively. These results indicate that ivermectin has a very low activity against *P. falciparum in vitro.*

Ivermectin is a macrocyclic lactone originally isolated from an actinomycete. It is active at very low concentrations against a wide variety of parasites and is routinely used for treating onchocerciasis, filariasis and intestinal strongyloidiasis. During a filariasis treatment program in the Solomon Islands, it was observed that the incidence of malaria seemed to decrease in groups treated with ivermectin (Turner P, 1998; personal communication).

The observed reduction in malaria may be due indirectly to the insecticidal action of ivermectin on malaria vectors (Iakubovich *et al*, 1989; Tesh and Guzman, 1990) and/or directly due to an antiparasitic effect on *Plasmodium falciparum*. Activity of ivermectin against *P. falciparum* seems unlikely, as GABA receptors (the main target of ivermectin) are absent. This assumption is supported by Lariviere *et al* (1989) who noted that ivermectin at doses of 0.2 mg/kg had no effect on malaria parasites in onchocerciasis patients. However, ivermectin has also been found to be active against some bacteria (Burg and Stapley, 1989) which have no GABA receptors. This activity against bacteria may suggest that ivermectin has other, unidentified activities which may have bearing on *Plasmodium* sp.

Correspondence: Dr Bruce Russell, Department of Entomology, USAMC-AFRIMS, 315/6 Rajvithi Rd, Bangkok 10400, Thailand.
Tel: 66 (0) 2644 5777; Fax: 66 (0) 2246 8832
E-mail: russellbm@thai.amedd.army.mil

The aim of this study was to determine if ivermectin has an antiparasitic effect on *P. falciparum in vitro*.

The *in vitro* activity of ivermectin was assessed against the K1 isolate of *P. falciparium* by the radioisotopic method of Desjardins *et al* (1979), with minor modification. Serial dilutions of ivermectin, dissolved in 100% methanol were added to the wells of microtiter plates and dried overnight. The wells were subsequently inoculated with 90 µl of a 2.2% suspension of parasitized cells (0.5% parasitemia and 90% rings) and 10 µl of [^{3}H] hypoxanthine. The final ivermectin concentrations in the RPMI 1640 culture medium varied between 0.01 and 1,000 µg/ml. The microculture plates were incubated for 48 hours at 37ºC in a 5% O_2, 5% CO_2 and 90% N_2 gas mixure. The amount of [^{3}H] hypoxanthine incorporated by *P. falciparum* was measured and used as an index of parasite growth inhibition. The IC_{50} and IC_{90} were defined as the drug concentrations that inhibit 50% and 90% of isotope incorporation by the parasites relative to the drug-free control wells. The concentration-response data were analyzed by nonlinear regression analysis. Each test were replicated 12 times.

The mean IC_{50} and IC_{90} of ivermectin were 8.0 and 35.0 µg/ml, respectively. Okonkwo *et al* (1993) treated onchocerciasis patients with ivermectin 0.15 mg/kg with a resultant mean blood plasma level of 0.056 µg/ml (Cmax). This plasma concentration is about 625-fold less than the IC_{90} for ivermectin against the K1 *P.*

falciparum isolate. It can be reasonably concluded that ivermectin has a very low activity against *P. falciparum*. Therefore, the reduction in malaria observed by Turner (Personal communication) is unlikely to be due to a direct antiparasitic action of ivermectin against *P. falciparum.*

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