RESEARCH NOTE

LACK OF IN VITRO EFFECT OF IVERMECTIN ON PLASMODIUM FALCIPARUM

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Abstract. The in vitro activity of ivermectin was assessed against the K1 isolate of Plasmodium falciparum. The mean IC50 and IC90 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.

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. falciparum 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 [3H] 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% O2, 5% CO2 and 90% N2 gas mixture. The amount of [3H] hypoxanthine incorporated by P. falciparum was measured and used as an index of parasite growth inhibition. The IC50 and IC90 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 IC50 and IC90 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 IC90 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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**REFERENCES**


