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Plasmodium berghei: lack of antimalarial activity of an analogue of folate precursor, 2,4-diamino-6-hydroxymethylpteridine in a mouse model.

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Abstract

It was earlier hypothesized that the malarial parasite may convert precursors of folate analogues to synthesize de novo inhibitors toxic to itself, but not to the mammalian cell. It was suggested that one such analogue, 2,4-diamino-6-hydroxymethylpteridine (DAP) may be converted to aminopterin (AMP), a known dihydrofolate reductase inhibitor. In the present study, we evaluated the ability of DAP to inhibit proliferation of Plasmodium berghei NK65 in mice, with(out) folinic acid rescue. Cumulative dosages of DAP ranging from 0.1 to 20mg/kg bw. administered either orally or intraperitoneally showed no suppression of parasite growth, or gave mild activities that were not statistically significant (P>0.05). Our findings do not seem to support the hypothesis of selective de novo metabolism of DAP to AMP by the malarial parasite.

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