The detection of amodiaquine in blood after oral administration

We wish to reply to the recent publication by Salako & Idowu (1985) entitled *Failure to detect amodiaquine in the blood after oral administration*. We have reported a high performance liquid chromatographic method for the measurement of amodiaquine (AQ) in plasma. This method has permitted the measurement of plasma AQ after a 4 h intravenous infusion (Mihaly *et al.*, 1985). Using a modification of this method to give a lower limit of detectability of 5 ng ml⁻¹ for both AQ and desethylamodiaquine (AQm) we have measured the concentrations of both in plasma and urine. In addition, we have conducted a single dose study in seven healthy male Caucasians (aged 22–45 years) given 600 mg AQ orally after an overnight fast (Winstanley *et al.*, 1986). In contrast to the findings of Salako & Idowu (1985), we were able to measure plasma concentrations of AQ for up to 8 h after dosing. The drug became detectable at 0.25 h, and reached a peak concentration of 31.9 ± 3.1 ng ml⁻¹ (mean $\pm$ s.e. mean) at 0.5 ± 0.03 h. The mean apparent terminal half-life of AQ was 5.2 ± 1.7 h. Like Salako & Idowu (1985), we found much higher plasma concentrations of AQm than AQ. The peak AQm concentration was 181.4 ± 25.8 ng ml⁻¹, reached at 3.4 ± 0.8 h. Sampling continued until 96 h at which time no AQ was detectable, but the mean AQm concentration was 29.1 ± 8.4 ng ml⁻¹. We have also been able to detect AQ and AQm in red cells.

Since Salako & Idowu (1985) sampled blood at 0.5, 0.75, 1, 1.5 h and thereafter, it is surprising that they did not detect AQ in plasma. This could be due to one or more of the following reasons:

(a) The pharmacokinetics of AQ might differ markedly between Caucasians and Negroes. However in a separate study we have investigated the disposition of AQ in Thai subjects, and found no major differences from Caucasians.

(b) We have demonstrated that AQ is light sensitive (Mihaly *et al.*, 1985). No mention of this was made by Salako & Idowu (1985).

(c) The method described by Salako & Idowu (1985) is reminiscent of that of Churchill *et al.* (1985), which uses no internal standard and therefore provides little safeguard against failure of extraction of the compounds, or an indication when this has occurred.

While we agree with Salako & Idowu (1985) when they state that the pharmacokinetics of AQ differ markedly from those of chloroquine, we would question the statement that 'AQ . . . probably takes no part in the *in vivo* antimalarial effect after a single oral dose', since in our hands the plasma concentration of AQ exceeded the *in vitro* minimum inhibitory concentration against *Plasmodium falciparum* for 5 h after a 600 mg oral dose (Churchill *et al.*, 1985).

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