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Assessment and implications of the quality of some chloroquine products from Nigeria and Thailand

O. SHAKOOR AND R. B. TAYLOR

School of Pharmacy, The Robert Gordon University, Schoolhill, Aberdeen AB10 1FR

Chloroquine (CQ) is a synthetic antimalarial agent and is regarded as one of the safest and cheapest antimalarials, when used at recommended dosage. It is the drug of choice for treatment of infections caused by all sensitive strains of malaria inducing parasites despite considerable resistance to it (Slater, 1993).

There is growing concern about the availability of substandard CQ products to the general public in Nigeria and Thailand, where self-medication with the drug is common practice. Such products have therapeutic as well as social and economic implications. There is little discussion based on objective information on the reasons for such products being available and the majority of literature reports assume the products to be counterfeit (ten Ham, 1993). The alternatives of drug decomposition and poor manufacturing contributing to substandard CQ being available has been paid little attention. This study, therefore, aimed to generate such data and assess the possible implications of the use of substandard CQ products.

A total of 40 Samples of CQ products were obtained for analysis from Nigeria and Thailand, where they were purchased from both pharmacy and non-pharmacy outlets. For this analysis an assay method was developed which was capable of simultaneously determining the drug and its manufacturing precursors and major decomposition products. Such a method has not previously been reported and would allow a possible assessment of the reasons for any compromised quality detected.

The method used was adapted from a previously published one (Taylor *et al*, 1990) and validated for the current work. It was found that adjustment of SDS increased and TBA reduced retention of the analytes. The final concentrations of these agents chosen resulted in adequate resolution with acceptable analysis times. In Figure 1 peak 5 is CQ and the remaining peaks are the possible drug-related impurities included.

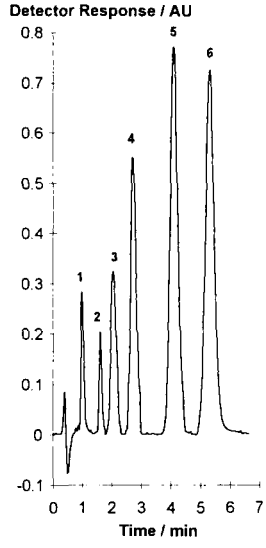

Figure 1. Separation achieved with chromatographic conditions: C_{18} column 100 x 2mm ID with 3μm particles; solvent of acetonitrile-20 mmolL^{-1} aqueous phosphate buffer (50-50) pH 2.0, with 200 mmolL^{-1} sodium dodecysulphate (SDS) and 10 mmolL^{-1} tetrabuylammonium bromide (TBA); flow rate 0.5 mLmin^{-1}; UV detection at 254 nm.

A summary of the results of the CQ sample analysis is presented in Table 1, where BP (1993) limits for CQ content were applied. In addition, it was found that the majority of substandard samples (86%) were obtained from non-pharmacy outlets, a result which supports the frequently held contention that such vendors are more likely to supply poor quality products. The poor quality products uncovered in this study that were either marginally above or below BP limits appear to be so, on balance, due to inadequate rather than fraudulent manufacturing. Even with the products with no active ingredient there was no additional evidence to suggest counterfeiting. These results highlight the difficulty of detecting a good counterfeit.

Table 1. CQ sample analyses - BP (1993) limits applied.

Total tested	Within	Below	Above	No drug
40	66 %	5 %	18 %	13 %

It is clear that the use of products with no CQ will lead to treatment failure and in addition, may be a factor in the selection pressure for drug-resistant organisms. Both outcomes are undesirable and have profound public health implications.

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Taylor, R.B. *et al* (1990), *J Chromatogr*, **527**, 490-497.
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