CAPSULES
preliminary notes and applications from Bioanalytical Systems, Inc.

WR 238,605 SUCCINATE (ANTIMALARIAL)

Purpose

Determination of the antimalarial N4-[2,6-dimethoxy-4-methyl- 5-[(3-trifluoromethyl)phenoxy]-8-quinolinyl]-1,4- pentanediamine (WR 238,605 succinate, F1) in plasma.

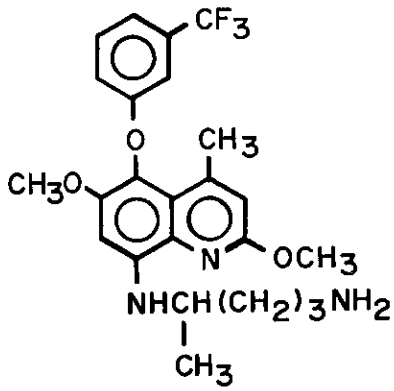

Figure 1. Structure of WR 238,605 succinate.

Primaquine is the standard treatment for cases of malaria caused by the protists *Plasmodium falciparum* and *P. vivax.* However, primaquine may show toxic side effects. WR 238,605 succinate appears to be more potent and less toxic. Studies in rhesus monkeys, for example, suggested that this drug was 12 times more effective than primaquine. A rapid and accurate method for determining levels of WR 238,605 succinate in plasma was needed for pharmacokinetic studies.

Reference

Rapid and Sensitive Quantitative Analysis of the New Antimalarial N^4-[2,6-Dimethoxy-4-Methyl-5-[(3-Trifluoromethyl)Phenoxy]-8-Quinolinyl]-1,4-Pentane diamine in Plasma by Liquid Chromatography and Electrochemical Detection, J.M. Karle and R. Olmeda, J. Chromatogr. 424 (1988) 347-356.

Conditions

Detector: BAS LC-44 Amperometric Detector
Electrode: BAS Glassy Carbon
Potential: +0.95 V vs Ag/AgCl
Column: 4 µm, C 18 reverse-phase, 100 x 8 mm
Mobile Phase: 300 mL water, 9 mL 85% phosphoric acid, 6.8 g sodium acetate and 700 mL methanol.
Flow rate was 4 mL/min.
Detection Limit: 1 ng/mL plasma (S/N = 4)
Validated Range: 5 - 1000 ng/mL plasma

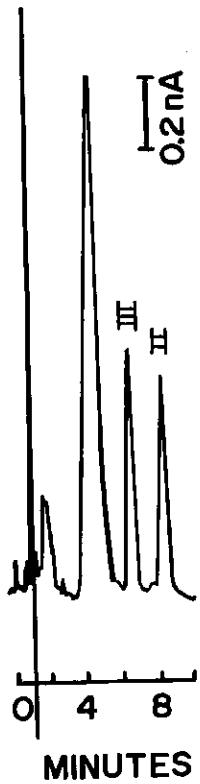

Figure 2. Chromatogram of plasma from a dog given an oral dose of WR 238,605 (II) 9 hours previously. III = internal standard. The large peak is an impurity from a previous sample.

Sample Preparation

Plasma samples were treated with acetonitrile to precipitate proteins, vortexed and centrifuged. The supernatants were loaded onto disposable cyano columns, washed with water and methanol, then eluted with mobile phase. Injection volume was 100-200 µL.

Notes

A representative chromatogram of plasma from a dog given an oral dose of WR 238,605 succinate is presented in F2.

The antimalarials mefloqine, quinine, chloroquine, primaquine, halofantrine, pyrimethamine and proguanil were found not to interfere with the above assay.

Extraction efficiency was 80%.

Electrochemical detection of WR 238,605 succinate provided a 6-fold lower detection limit than was possible with UV detection at 254 nm.

The determination of WR 238,605 succinate presented in this report can be duplicated utilizing the BAS 400 Liquid Chromatograph or the BAS 200 Problem Solver.

The information in this publication is supplied as a service to our customers. Performance of the methodology has not necessarily been verified by BAS technical staff.