AN ALTERNATIVE LIQUID CHROMATOGRAPHY-MASS SPECTROMETRIC METHOD FOR THE DETERMINATION OF AZITHROMYCIN IN HUMAN PLASMA AND ITS APPLICATION TO PHARMACOKINETIC STUDY OF PATIENTS WITH MALARIA

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Abstract. A simple, sensitive, selective and reproducible method based on high performance liquid chromatography-electrospray ionization-tandem mass spectrometry (LC/MS) was developed for the determination of a macrolide antibiotic azithromycin in human plasma. The internal standard (roxithromycin) was separated from azithromycin on a Hypersil Gold C_{18} column, with retention times of 10.71 and 13.67 minutes, respectively. The mobile phase consisted of a mixture of 20 mM ammonium acetate buffer (pH 5.2), acetonitrile and methanol (50:40:10, v/v/v), running through the column at a flow rate of 0.3 ml/minute. Chromatographic analysis was carried out at 25ºC. Sample preparation was by liquid-liquid extraction with a mixture of 7:3 (v/v) diethylether:dichloromethane. The precision of the method based on within-day repeatability and reproducibility (day-to-day variation) was below 5% (% coefficient of variations: % CV). Good accuracy was observed for both intra-day and inter-day assays. The limit of quantification was acceptable at 0.5 ng using 200 µl plasma samples. The mean recoveries for azithromycin and the internal standard were greater than 85%. The method was applied successfully to the investigation of the pharmacokinetics of azithromycin when given in combination with fosmidomycin as oral doses of 750 mg twelve hourly for 3 days in 5 Thai male patients with acute uncomplicated falciparum malaria.

Key word: azithromycin, chromalographic analysis, pharmacokinetic malaria

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