

# Simultaneous Determination of Chloroquine and Its Metabolite Desethyl Chloroquine in Human Plasma Using Liquid Chromatography Tandem Mass Spectrometry

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## Abstract

This study presents a liquid chromatography tandem mass spectrometry (LC-MS/MS) method for the simultaneous determination of chloroquine (CQ) and its metabolite desethyl chloroquine (DCQ) in human plasma. The method generally involved methanol protein precipitation and LC-MS/MS detection. The mass spectrometer was operated with positive electrospray ionization (ESI) source and the data acquisition was carried out in multiple reaction monitoring (MRM) mode. Quantification was performed by labeled isotope dilution method with matrix-matched calibration curves. Inter-batch accuracies were ranged from 90.2% to 109.8%. Both intra-batch and inter-batch precisions (relative standard deviation, RSD, %) of the analytes were no more than 15.0%. The recoveries were from 73.7% to 79.0%, and the limit of quantification (LOQ) was 1.0 and 0.5 ng/mL for CQ and DCQ, respectively. The linear ranges of CQ/DCQ were 1.0/0.5–500.0/250.0 ng/mL with the linear correlation coefficient  $R^2 > 0.999$ . No significant matrix effect was observed in this study. The carryover effect was significantly minimized by the addition of ethylene glycol in the reconstitution solution and the utilization of basic washing solution and repetitive fast washing gradient program. After optimization, the carryover effect was less than 20%. This method is in possession of sufficient resolution, high sensitivity as well as selectivity and convenient to be applied to the trace determination of CQ and DCQ in human plasma.

**Keywords:** Chloroquine, Desethyl chloroquine, Human plasma, Liquid chromatography tandem mass spectrometry

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