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CONFERENCE

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TITLE

Determination of Moxifloxacin used as Positive Controls for QT Prolongation in Human Plasma by LC-MS/MS

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ABSTRACT

Novel Aspect: Simple LC-MS/MS method for moxifloxacin in human plasma offering excellent reproducibility showed by both validation and incurred sample reanalysis results.

Introduction

Moxifloxacin is a synthetic fluoroquinolone antibiotic agent and has been used for the treatment of acute exacerbation of chronic bronchitis and community-acquired pneumonia and present an admirable safety profile that is not matched by any other antibiotic group. Moxifloxacin is also frequently used as a positive control in QTc prolongation studies. We report here the development and validation of a simple and reliable LC-MS/MS assay for the quantification of gemifloxacin in human plasma. The excellent reproducibility and reliability of the method has been shown with incurred sample reanalysis (ISR) results.

Methods

Moxifloxacin and its deuterated internal standard were extracted from 50 µL human plasma by a liquid-liquid extraction using MtBE as the extraction solvent. After centrifugation, the supernatant was evaporated to dryness and reconstituted for injection onto the LC/MS/MS system. Liquid chromatography was performed on a Luna C8 column (50x2mm, 5µm, Phenomenex) with gradient elution on Shimadzu LC-10A pumps and CTC autosampler. The retention time of the analyte was 2.3 min. MS/MS detection and quantitation was performed on a Sciex API4000 tandem mass spectrometer under positive turboionspray ionization.

Preliminary results

The assay was validated over a range of 25 to 5000 ng/mL in human plasma. Validation data showed intra- and inter-day precision (%CV) of 1.4 to 9.8% and 3.0 to 10.1%, respectively, and intra- and inter-day accuracy (%RE – relative error from the nominal values) of -10.2 to 5.5 and -5.5% to 1.6 %, respectively. The method showed slight ion enhancement, and selective with no interference peaks observed at the retention time of the analyte. Analyte stability in human plasma was evaluated under conditions of room temperature bench-top storage, freeze/thaw cycles, following long-term storage at -20°C, and in solvent at room temperature and in freezer. The analyte showed to be stable under all conditions evaluated. The assay has been applied to support several clinical studies. Incurred sample reanalysis (ISR) reproducibility assessment for a clinical study showed excellent results – 99% of the ISR samples met the acceptance criteria.