Validated Microemulsion Liquid Chromatography-Fluorescence Method for the Quantification of Duloxetine and its Two Main Metabolites in Plasma: Application to Clinical Pharmacokinetic Studies

Abstract: Background: Duloxetine (DL) is a selective serotonin and norepinephrine reuptake inhibitor. The drug is used in the treatment of major depression, anxiety, pain related to diabetic peripheral neuropathy and stress urinary incontinence.

Objective: This study described, for the first time, the development and validation of a highly selective and sensitive microemulsion liquid chromatography-fluorescence (MELC-FL) method with low environmental pollution and without extraction steps for the simultaneous quantification of DL, and its two main metabolites; 5-hydroxy-6-methoxy duloxetine (5-HDL) and 4-hydroxy duloxetine glucuronide (4- HDLG) in plasma.

Methods: The studied analytes and methyl paraben (an internal standard) were detected using excitation and emission wavelengths of 280 and 340 nm, respectively. The analysis was performed on Water Symmetry C18 analytical column (100 Å, 150 mm x 3.9 mm, 5 µm) by directly injecting the plasma after appropriate dilution with microemulsion mobile phase. Total analytical run time was 4 min.

Results: The MELC-FL method was statistically validated according to the FDA guidelines for bioanalytical methods for linearity, accuracy, precision, specificity, robustness, and stability. Linear calibration plots were achieved in the ranges of 25-1200 ng/mL for DL and 50-1500 ng/mL for 5-HDL and 4-HDLG ($r^2 > 0.997$) in rat plasma. The intra- and inter- assay precisions and accuracy were acceptable. The overall recoveries of DL and its two main metabolites from rat plasma were between 97.12% and 103.12% with an RSD value between 0.34% and 4.57%.

Conclusion: The present study supports the possible use of the microemulsion mobile phase in LC as a “greener ” mobile phase. The developed method offered an advantage in the form of direct analysis of biological samples after appropriate dilution with eco-friendly microemulsion mobile phase, which decreased the possibility of sample loss during analysis. The developed assay was successfully applied in a pharmacokinetic study and it established the applicability of the method for the determination of concentration-time profiles of DL and its two main metabolites in rat plasma after systemic administration.

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