

A rapid MCM-41 dispersive micro-solid phase extraction coupled with LC/MS/MS for quantification of ketoconazole and voriconazole in biological fluids

ABSTRACT

A rapid dispersive micro-solid phase extraction (D-SPE) combined with LC/MS/MS method was developed and validated for the determination of ketoconazole and voriconazole in human urine and plasma samples. Synthesized mesoporous silica MCM-41 was used as sorbent in D-SPE of theazole compounds from biological fluids. Important D-SPE parameters, namely type desorption solvent, extraction time, sample pH, salt addition, desorption time, amount of sorbent and sample volume were optimized. Liquid chromatographic separations were carried out on a Zorbax SB-C18 column (2.1 × 100 mm, 3.5 μm), using a mobile phase of acetonitrile:0.05% formic acid in 5 mM ammonium acetate buffer (70:30, v/v). A triple quadrupole mass spectrometer with positive ionization mode was used for the determination of target analytes. Under the optimized conditions, the calibration curves showed good linearity in the range of 0.1–10,000 μg/L with satisfactory limit of detection (0.06 μg/L) and limit of quantitation (0.3 μg/L). The proposed method also showed acceptable intra- and inter-day precisions for ketoconazole and voriconazole from urine and human plasma with RSD ≤ 6.5% and good relative recoveries in the range 84.3–114.8%. The MCM-41-D-SPE method proved to be rapid and simple and requires a small volume of organic solvent (200 μL); thus it is advantageous for routine drug analysis.

Keyword: Dispersive micro-solid phase extraction; Ketoconazole; LC/MS/MS; MCM-41; Voriconazole