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Determination of Free Cyclosporine A with a LC-MS/MS Method: Application to C2 Monitoring in Rabbits

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SUMMARY. Cyclosporine A (CsA) is a cyclic peptide widely used as an immunosuppressant. Therapeutic drug monitoring (TDM) of CsA is becoming mandatory for transplant patients who received CsA therapy in the routine clinical practice because of large individual variability, dose-related toxicity and the risk of acute rejection. In this study, a rapid, sensitive, and selective LC-MS/MS method was developed and validated for the quantitative analysis of free CsA (fCsA), a better indicator for the prediction of efficacy and safety of CsA-based therapy. Following ultrafiltration for fCsA, chromatographic separation was performed on an Agilent Zorbax SB-C18 column (100 mm x 2.1 mm, 3.5 μm) with acetonitrile and 0.1 % ammonium hydroxide in water (85:15, v/v) as the mobile phases. The compounds were quantified by positive electrospray ionization tandem mass spectrometry. Selectivity, linearity, accuracy, precision, recovery, and stability were evaluated during method validation. The validated method was applied to a single blood concentration measurement 2 h after CsA administration (C2) measurement study of fCsA after an oral administration of a single 15 mg/kg intravenous dose of CsA to six rabbits.

KEY WORDS: Cyclosporine A, LC-MS/MS, Therapeutic drug monitoring.

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