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A rapid LC-MS/MS Method for the Quantification of Cyclosporine A in Rabbit Whole Blood and Plasma

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***SUMMARY*. A sensitive and selective liquid chromatography-tandem mass spectrometry method for the determination of cyclosporine A (CsA) was developed and validated in rabbit whole blood and plasma. After addition of cyclosporine D (CsD) as internal standard, a simplified extract procedure with diethyl ether was employed for the sample preparation. Chromatographic separation was performed by an Agilent Zorbax SB-C18 column (100 × 2.1 mm, 3.5 μm). The mobile phase was acetonitrile-0.1% ammonium hydroxide in water (85:15 v/v) delivered at a flow rate of 0.4 mL/min. The calibration curve for CsA in rabbit whole blood was linear over the tested concentration range of 4.0-512.0 ng/mL with a correlation coefficient of 0.9985. Calibration plots were over the range of 1.0-200.0 ng/mL for CsA in rabbit plasma and showed linearity with a correlation coefficient of 0.9978. For inter-day and intra-day tests, the precision (RSD) for the entire validation was less than 10%, and the accuracy was within the range 91.43-108.52%. The developed method was successfully applied to therapeutic drug monitoring of CsA in rabbits following single intravenous injection dose of 15 mg/kg. The low volume of blood or plasma needed (200 μL), simplicity of the extraction process, short run time (1.5 min) and low injection volume (10 μL) make this method suitable for quick and routine analysis.**

KEY WORDS: Cyclosporine A, LC-MS/MS, Plasma, Rabbit, Whole blood.

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