Development of an Ultra-performance Liquid Chromatography Technique Coupled with Mass Spectrometry for the Measurement of Tacrolimus in Micro-samples of Whole Blood, and its Application on a Pharmacokinetic Trial

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Abstract

Objective: The aim was to develop a rapid, specific, sensitive and accurate chromatographic technique coupled with mass spectrometry for the measurement of tacrolimus (CAS 104987-11-3) in micro-samples of whole blood, and its application on a pharmacokinetic pilot trial.
Methods: A fast gradient was designed in an ultra-performance liquid chromatography, and coupled with a mass spectrometer for the quantification of tacrolimus in 100 µl samples of EDTA whole blood. Multiple reaction monitoring was used for the measurement of tacrolimus (m/z^{+1} 821.49→768.35 Th) and sirolimus as internal standard (m/z^{+1} 931.69→864.39 Th). The method was validated according to Mexican regulatory guidelines. Twenty-four young healthy male volunteers with similar hematocrit values participated in the pharmacokinetic trial; an oral single dose of one 5 mg tacrolimus capsule was administered and kinetic profiles were described since 0 h until 24 h post-dose.
Results: Method showed to be accurate, precise and linear over the range from 1 to 80 ng/ml, having an absolute recovery of 94 %. Molecule was stable for two months at –70 °C, and heparin interfered with its quantification. Total run-time is around 1.5 min. Mean maximum blood concentration was 32.63 ± 1.74 ng/ml, and was reached at 1 h post-dose; elimination half-life was 14.18 ± 5.71 h.
Conclusions: Method developed is not time-consuming, inexpensive, and sensitive enough for its application during pharmacokinetic trials, and can be suitable for therapeutic drug monitoring in transplanted patients. Pharmacokinetic data obtained in Mexican population are quite similar to previously reported in international literature.

Key words

- CAS 104987-11-3
- Immunosuppressive agents
- Mass spectrometry
- Tacrolimus, measurement in whole blood, pharmacokinetics
- Ultra performance liquid chromatography

Arzneimittel-Forschung (Drug Research) 2007;57(10)659–664