Ultrasound assisted dispersive liquid-liquid microextraction coupled with high performance liquid chromatography designated for bioavailability studies of felodipine combinations in rat plasma

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Abstract:

Felodipine (FLD), a calcium channel antagonist, is commonly prescribed for the treatment of hypertension either with Metoprolol (MET) or Ramipril (RAM) in two different drug combinations. FLD has high plasma protein binding ability affecting its extraction recoveries from plasma samples. Hence, a specific ultrasound assisted dispersive liquid-liquid microextraction (UA-DLLME) method coupled with HPLC using photodiode array detector was developed and validated for the simultaneous determination of FLD, MET and RAM in rat plasma after oral administration of these combinations. The factors affecting UA-DLLME were carefully optimized. In this study, UA-DLLME method could provide simple and efficient plasma extraction procedures with superior recovery results. Under optimum condition, all target drugs were separated within 13 min. The validation procedures was carried out in agreement with US-FDA guidelines and shown to be suitable for anticipated purposes. Linear calibration ranges were obtained in the range 0.05–2.0 mg mL⁻¹ for FLD and MET and 0.1–2.0 mg mL⁻¹ for RAM with detection limits of 0.013–0.031 mg mL⁻¹ for all the studied drug combinations. The %RSD for inter-day and intra-day precisions was in range of 0.63–3.85% and the accuracy results were in the range of 92.13–100.5%. The validated UA-DLLME-HPLC method was successfully applied for the bioavailability studies of FLD, MET and RAM. The pharmacokinetic parameters were calculated for all the investigated drugs in rats after single-dose administrations of two different drug combinations. Although FLD was bioequivalent in the two formulations, a small increase in plasma levels of MET and RAM was found in the presence of FLD.

Keywords:

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