

Determination of dronedarone and debutyldronedarone in plasma by HPLC-UV

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Introduction: Dronedarone (D) is a newer antiarrhythmic drug approved for use in selected types of cardiac arrhythmias. Due to the risk of severe side effects, the use of D must be carefully supervised, and TDM may be a useful tool for monitoring pharmacotherapy. The aim of the study was to develop and validate of a method for the determination of D and debutyldronedarone (DBD) in plasma using HPLC with UV detection.

Methods: A simple HPLC-UV isocratic system (Spectra Physics) with a manual injector (50 μ L loop) was applied. The separation of compounds was performed at ambient temperature on Supelcosil LC-CN column (150x4.6 mm, 5 μ m) protected with Supelguard LC-CN precolumn. The mobile phase was a mixture of: CH₃OH:CH₃CN: H₂O:0.5M KH₂PO₄ (170 : 85 : 237 : 7.8 (v/v)) + 0.1 mL 85% H₃PO₄ pumped with the flow rate of 1.8 mL/min. Bepridil (BEP), which is not currently used as a drug, was selected as the internal standard. *Tert*-butyl methyl ether (3 mL volume) was chosen as the extraction reagent for alkalized plasma sample (0.4 mL). The analytical wavelength was 290 nm.

Results: No significant interference with biological matrix was observed in described chromatographic conditions. DBD, BEP and D were eluted at retention times of 4.1, 5.3 and 6.1 min, respectively. The obtained extraction yield was: 68.45-84.56% for DBD, 74.55-92.71% for BEP and 70.85-87.16% for D. The method has been validated according to EMA guidelines in the range of 10-1000 ng/mL for both D and DBD. For intraassay, the mean inaccuracy ranged from -12.54% to +5.44% for D and from -12.23% to +8.22% for DBD and imprecision ranged 2.37-10.95% for D and 3.79-17.26% for DBD. For interassay, the inaccuracy was from -1.86% to +6.76% for D and from -6.85% to +10.22% for DBD; the imprecision ranged 2.11-13.65% for D and 2.79-13.79% for DBD.

Conclusions: The developed method can be successfully used in routine laboratory analyses, both for TDM and pharmacokinetic studies. It can be recommended to laboratories equipped with basic HPLC apparatus as an economical alternative to the LC-MS/MS technique.

Key words: HPLC-UV, Bioanalysis, Dronedarone, Debutyldronedarone