24/7 fully automated therapeutic drug analysis for research projects by LC/MS/MS

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Background

Simplifications in LCMS instrumentation have made MS a viable option for clinical research (specificity, accuracy, and reduced reagent costs). The ability to support various analysis methods on a single system is a key feature. Automation is an essential function in aiming for a better quality of results and better comfort for the users. However, lately, the automation of biological sample extraction, directly coupled to LCMS, has proven to be a challenge in the field.

Method

A collaboration between the University Medical Center Göttingen (UMG) and Shimadzu Corporation was built to jointly develop and validate multiple analytical methods for therapeutic drugs, using a fully automated platform. The purpose is the development and the validation of a unified methods set for LCMS, for 24/7 therapeutic drug analysis, with a single system configuration.

The evaluated analytical system was a fully automated platform, from Shimadzu Corporation, composed of CLAM-2040 automation module, coupled to Nexera(TM)X2 UHPLC and LCMS-8060NX(TM) LCMSMS. HL-7 interface standards were used for bidirectional communication between LIS (Dedalus, Germany) and the CLAM-LCMSMS. Target applications were Antibiotics, Direct Oral Anticoagulants, Antiepileptics, Neuroleptics, Antidepressant drugs (SSRI), Tricyclic Antidepressants, and Benzodiazepines (7 methods). All methods use similar analytical conditions. The fitness for purpose for 24/7 use was evaluated by requesting measurements for all methods in random alternance.

Results

All validations results were within the acceptance criteria. Individual methods validations include isobars resolution (above 1), calibration accuracy (85-115%), method repeatability (RSD below 15%), day to day intermediate precision (RSD below 15%), mobile phase stability (RT deviation below 2% after 2 weeks), LLOQ confirmation (S/N above 10 and RSD below 15%), absence of carryover confirmation (blank to LLOQ area ratio below 20%) and ring trial analysis (accuracy 85-115%). Also, repeated measurements for all methods in random alternance showed results within the acceptance criteria (accuracy 85-115% and RSD below 15%).

Conclusion

This strategy proved its fitness for purpose. The fast LCMS methods which can alternate smoothly, and the automated sample extraction enable robust therapeutic drug analysis with a high throughput and at low cost, without compromising the user comfort. **For research use only.**

Key words

24/7; automated; TDM; analysis; RUO; LCMS