Working Party invites medical testing laboratories to participate in this world leading program and welcomes feedback from all participants.

doi:10.1016/j.cca.2010.02.031

Symposium V

Therapeutic drug monitoring of immunosuppressant drugs by liquid chromatography–tandem mass spectrometry

P.J. Taylor, M.E. Franklin, C.-H. Tai, P.I. Pillans
Department of Clinical Pharmacology, Princess Alexandra Hospital, Woolloongabba, QLD 4102, Australia
Email: p.taylor1@uq.edu.au

Immunosuppressive drugs such as cyclosporine A, tacrolimus, everolimus and sirolimus require monitoring to provide optimal and individualized therapy for patients who have undergone solid organ transplantation. The methodology used by clinical laboratories for these drug analyses may impact on the quality of pharmacokinetic data provided to the transplant physician. The majority of laboratories use either liquid chromatography–tandem mass spectrometry (LC–MS/MS) or antibody-based immunoassays. While immunoassays are widely used for analysis of immunosuppressive drugs, there are several drawbacks to their use. Firstly, these methods tend to suffer from over-estimation in results, due to non-specific binding (to varying degrees) of metabolites with the assay antibody and may also be influenced by parameters such as hematocrit. Secondly, some immunoassays have been shown to have poor accuracy and precision at the critical lower end of the therapeutic range.

Most of the measured immunosuppressive drugs are neutral in nature and would appear unsuited to the ionization processes of LC–MS/MS. However, ionization of these compounds can be achieved by the addition of modifiers to the mobile phase which promote adduct formation, such as ammonium acetate. The use of successive (tandem) mass analysers provides for high selectivity and sensitivity, which is required for the measurement of the more potent drugs (i.e. tacrolimus, sirolimus and everolimus) and simplifies the chromatographic separation. Additionally, simultaneous measurement can be performed, making this technique highly suited to the clinical requirements for monitoring these drugs.

The aims of this presentation are to provide an overview of therapeutic drug monitoring of immunosuppressive drugs using LC–MS/MS instrumentation, to illustrate the robustness and reliability of such methods and to provide a critical comparison with immunoassays.

doi:10.1016/j.cca.2010.02.032

Symposium V

Performance of an UPLC-TOF MS method for comprehensive urine drug screening in 4 routine clinical chemistry laboratories sharing common libraries

Michael Lee
Chemical Pathology Laboratory, Department of Clinical Pathology, Tuen Mun Hospital, Tuen Mun, NT, Hong Kong
Email: lhk366@ha.org.hk

The discontinuation of world-wide support of the Bio-Rad REMEDi® Drug Profiling System (DPS) has necessitated its replacement in 4 Hong Kong hospitals. In collaboration with laboratories in Denmark and the United Kingdom, a method for comprehensive urine drug screening was developed using liquid chromatography and time-of-flight mass spectrometry. The method was assessed and validated by a parallel run study against REMEDi® DPS using 1000 routine patient samples and a com parison study against well established methods. To share a common library, a study on the method transferability was performed. To ensure the long-term harmonization between systems, round robin comparisons using patient samples and external quality assessment materials were regularly conducted. For a system to handle more than 300 requests for toxicology screening per months, the design of within laboratory quality system which should cover both analytical and result review algorithm is critical to assure the robustness and facilitate the troubleshooting of the system.

doi:10.1016/j.cca.2010.02.033

Symposium VI

Use of derivatisation for LC–MS/MS analysis in the clinical laboratory

Alan L. Rockwood[1,2], Mark M Kushnir[1]
[1] *ARUP Laboratories, University of Utah, Salt Lake City, UT, USA*
[2] *Department of Pathology, University of Utah, Salt Lake City, UT, USA*
Email: rockwoal@aruplab.com

Derivatization is the modification of the chemical structure of an analyte, generally to enable or improve the suitability of an analyte for separation or detection in chemical analysis. Derivatization has been widely applied to a number of analytical techniques, including, among others, chromatography and mass spectrometry. Among the more common uses are to modify a target compound, to improve its volatility, thermal stability, and compatibility with stationary phases in gas chromatography. However, as liquid chromatography–mass spectrometry (LC–MS and LC–MS/MS) has become more popular in recent years, derivatization has largely fallen out of favor. Indeed, one of the attractions of LC–MS is that derivatization is often unnecessary, thus simplifying the sample preparation process, lowering costs, and improving throughput. Nevertheless, as we and others have found, it is unwise to abandon derivatization altogether; and derivatization remains a useful tool to be applied when the advantages outweigh the disadvantages. The most common uses of the derivatization in LC–MS are for improving the ionization efficiency, sensitivity and (in some cases) specificity of analysis. Disadvantages often include more laborious sample preparation requirements, greater risk of contamination or procedural errors, and (in some cases) reduced analytical specificity. In this presentation we discuss advantages that may be gained through the use of derivatization, along with a number of the drawbacks that often accompany derivatization. The advantages and disadvantages of derivatization will be illustrated by practical applications from our laboratory or the literature.

doi:10.1016/j.cca.2010.02.034

Symposium VI

Development of a reference MS/MS method for plasma creatinine

R.N. Dalton, C. Turner
WellChild Laboratory, King's College London, Evelina Children's Hospital, London SE1 7EH, UK
Email: neil.dalton@kcl.ac.uk