Editorial

Wide spread use of LC–MS in bioequivalence studies

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Mass spectrometry has made tremendous advancement during the last decade. This progress has led to revolution in the analysis of small and large molecules. LC–MS analysis employed for qualitative and quantitative determination of drugs and their metabolites in biological fluids plays a significant role in the evaluation and interpretation of bioequivalence, pharmacokinetic, and toxicokinetic studies. The quality of these studies, which are often used to support regulatory filings, is directly related to the quality of underlying bioanalytical data. It is therefore important that the guiding principles for the validation of theses analytical techniques be established and should be followed uniformly across the academia and pharmaceutical community.[1] The US FDA guidance on analytical method validation, in one form or another, has been adopted universally as a standard procedure for validating bioanalytical assays used for pharmcokinetic, bioavailability, and bioequivalence studies intended for regulatory submission.[2]

Before the first bioanalytical method validation workshop, there was lack of uniformity in conducting validation of bioanalytical methods and submission of data to regulatory agencies. The bioanalytical validation workshop in 1990 was the first major workshop dedicated to investigating and harmonizing procedures in method validation. The workshop was cosponsored by the American Association of Pharmaceutical Scientists (AAPS), the US FDA, the International Pharmaceutical Federation (FIP), the Health Protection Branch (HPB), and the Association of Analytical Chemists (AOAC). The conference focused on the requirements for bioanalytical method validation procedures to establish reliability of the analytical method, parameters to ensure acceptability of analytical method performance, method development (prestudy validation), and method application (in–study validation). The workshop defined important parameters for method validation e.g. accuracy, precision, selectivity, sensitivity, reproducibility, limit of quantification as well as addressing "how to" evaluate and determine these parameters. It was also clarified that it is not essential to have 100% recovery, but it is important that the recovery be reproducible. One of the most important outcomes of the first workshop was that it defined "the acceptance criteria for a run". The recommendations of the first workshop were well received within the scientific community. These recommendations did not become did not become official until the draft guidance on bioanalytical method validation was published in January 1999 by the US FDA with the intention of seeking public opinion prior to finalizing the guidance. The second bioanalytical method validation workshop was cosponsored by the AAPS and the US FDA in January 2000 a year after the draft guidance went into effect and ten years after the first workshop took place. The main advances occurred in the field of mass spectrometry. Two issues were addressed in relation to LC–MS;[1] interference from substances that are physico–chemically similar to the analyte (e.g. metabolites, endogenous compounds, interference from matrix components unrelated to the analyte (matrix effect).[2] In the case of LC–MS–MS based procedures, appropriate steps should be taken to ensure the lack of matrix effects throughout the application of the method, especially if the nature of the matrix changes from the matrix used during method validation.[3] Different type of validation was defined, namely: partial validation, cross validation, and full validation.[2]

MS ranks among the most powerful analytical techniques, with important applications in the biomedical area. Its mode of detection is not only highly selective but also sensitive. MS can be utilized for the quantitative analysis of a great variety of compounds. Quantitative MS assays in biological fluids are now available for a significant number of drugs. MS analysis depends on the formation and separation in vacuo of ionized drug molecules. Separation of the ions can be achieved in various ways. MS analysis in conjunction with highly efficient separations (LC–MS, LC–MS–MS, and GC–MS) can be performed with electron impact ionization.[3] The future challenges of LC–MS include the following:[1]

i. Regulatory compliance based bioanalytical processing as per 21 CRF part II.

ii. New developments in metabolomics and proteomics.

iii. New and different approaches for high throughput screening, lead optimization, lead screen, lead hit and lead validation of new chemical entities.

iv. Advanced and latest chromatographic separation theory.

v. Bioanalytical method development, pre–validation and full validation report template.

vi. Advanced tandem technology based bioanalysis.

vii. Laboratory information management system (LIMS) through bioanalytical data compilation and maintenance.

viii. Electronic based bioanalytical data system for submission to international regulatory agencies i.e. electronic submission.

ix. Application of LC–MS in diagnostics for future diseases in human.

Our ability to study the physical and biological world has become closely linked to the capabilities of our instrumentation. As instrumentation improves, so do our abilities to make observations.

The evolution of mass spectrometry instrumentation and drug discovery have become intertwined, so that many of the advances in the instrumentation have arisen because of a demand for throughput, sensitivity, or a need to perform chemical analysis with respect to a given pharmacological problem. This symbiosis appears destined to continue and should provide many fruitful benefits for both mass spectrometry instrumentation and drug discovery. Although many evolutionary changes have been forecasted, it is possible, perhaps even likely, that the most important innovations have yet to be recognized or devised.[1]

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Conflict of interest

The author declares no conflict of interest.

References

1. Ahmed T, Rohatagi S. Application of LC-MS in Supporting PK/PD Studies During Drug Discovery and Development. *Journal of Pharmacy Research*. 2012;5(5):2514–2526.
2. Shah VP. The history of bioanalytical method validation and regulation: Evolution of a guidance document on bioanalytical methods validation. *AAPS J*. 2007;9(1):E43–E47.
3. Gao J, Li Q. Application of modern analytical techniques for monitoring drug concentration in biological samples. *Asian Journal of Drug Metabolism and Pharmacokinetics*. 2004;4(3):189–198.