

Title: High Throughput LC/MS/MS Analysis of
Drugs and Their Metabolites
Author: G. McKay
Affiliation: PharmaLytics, Inc., A Drug Metabolism, Drug
Disposition Research Institute, University of
Saskatchewan, Saskatoon, SK, S7N 5C9.

Abstract

The enhanced chromatographic flexibility of high performance liquid chromatography makes it ideally suited to analysis of multiple analytes with widely different physical chemical properties. Thus in the case of drug and metabolite analysis where the physical chemical properties of the analytes may vary widely such a system is ideally suited. When this system is coupled to a mass spectrometer as a detection system it is possible to further enhance the selectivity of detection through the use of tandem mass spectrometry techniques. As a consequence high throughput analysis is possible where chromatographic resolution is sacrificed in lieu of analysis time and selectivity is maintained through a higher order detection system. Examples from the author's laboratory including a method for the analysis of the individual enantiomers of methylphenidate and a method for the analysis of selegiline and three of its metabolites will be given. The use of tandem mass spectrometry and multiple reaction monitoring of unique precursor product ion pairs illustrates the analytical power of such techniques and demonstrates analysis times of less than 2 minutes per sample while maintaining quantitative sensitivity of 5-2000 pg/mL. In order to successfully carry out such analysis it is essential that the metabolism, pharmacokinetics and limitations of the instrumentation be fully understood so as to preclude the generation of data artifactually influenced by potentially interfering analytes.

