Rapid measurement of drug-drug interaction utilizing generic gradient ultra performance liquid chromatography and tandem mass spectrometry

A significant number of candidate medicines fall out of the development process due to toxicity, the latter (i.e., drug-drug interactions). In the discovery/development process, a large number of candidate medicines have been withdrawn from the market due to toxic events. These clinical trials are often due to drug-drug interactions or unpleasant "sideeffects" events. As part of the drug discovery and development process it is critical to evaluate the candidate drugs for possible toxicity. Drug-drug interactions or inhibition/reduction of metabolizing enzymes in the body. Failure to properly identify these potential toxic events can lead the compound being withdrawn from the market and significant loss in revenue.

The effect of a medicine on the major drug metabolizing enzymes, Cytochrome p450 (CYP450) isoenzymes, is a part of the lead candidate evaluation process and during development to determine potential drug interactions. These studies involve evaluating the effect of the candidate medicine on the drug metabolizing CYP450 enzymes by monitoring the changes in the concentrations of a set of probe substrate molecules. These assays are typically performed in vitro with the most recently by LC/MS/MS with analysis times in the 5-10 minute range.