conferenceseries.com

J Chromatogr Sep Tech 2018, Volume 9
DOI: 10.4172/2157-7064-C1-041

7th World Congress on

Mass Spectrometry

June 20-22, 2018 | Rome, Italy

Transformation of clinical transporter biomarkers: Characterization and quantification using high resolution mass spectrometry

Ragu Ramanathan
Pfizer Inc., USA

Rapidly advancing drug transporter biomarker sciences suggest that selected endogenous compounds, detectable in human plasma and urine, may serve as biomarkers for specific transporters. Among them, coproporphyrin isomers, CP-I and CP-III, bile acids (BAs), and N1-methylnicotinamide (NMN) have been evaluated as possible candidate biomarkers for organic anion transporting peptides (OATP) and renal organic cation transporting (OCT)/multidrug and toxin extrusion proteins (MATEs), respectively. Successful bioanalysis of transporter biomarkers require suitably labelled reference standards, internal standards, appropriate matrices and careful assessment of assay robustness, sensitivity, selectivity, precision, accuracy and biomarker stability. Over the last five years, bioanalytical quantification using liquid chromatography coupled with high resolution mass spectrometry (LC-HRMS) has evolved as an alternative to the conventional methods using LC coupled with triple quadrupole mass spectrometry (LC-MS/MS). Currently, platforms, based on the Orbitrap and time-of-flight (TOF) technologies, are used for LC-HRMS or LC-MS/HRMS analysis. Advantages of liquid chromatography-high resolution mass spectrometry (LC-HRMS) analysis include reduced upfront of the required method development, and rich data accumulated for post-acquisition data mining, which provide information neglected in conventional LC-MS/MS analysis or interrogation for biomarkers discovered post data acquisition. In this presentation, the researchers present singly- ([M+H]+) and doubly-charged ([M+2H]2+) precursor ions of CP-I/CP-III respectively at m/z 655.3 and 328.1 to evaluate high-resolution MS (TOF-MS) for untargeted and MS/HRMS for targeted quantification data on a high-speed triple TOF 6600 LC-MS/MS system. The highly selective and sensitive CP-I/CP-III assay developed offers options for earlier characterization and clinical safety projections for OATP1B1/3-mediated drug-drug interactions (DDIs) along with pharmacokinetic analyses of an NCE as part of first-in-human clinical studies. N1-methylnicotinamide (NMN) is a polar molecule with a [M+H]+ at m/z of 137 and requires hydrophilic interaction chromatography (HILIC) for separation from numerous endogenous interferences. Relatively complex pool of circulating bile acids (BAs), requires separation of multiple isomeric components before MS/HRMS for targeted quantification.