Applications of supercritical fluid chromatography for chiral metabolite separations in drug metabolism and pharmacokinetics environment

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In recent years, interest has expanded to perform chiral separations by supercritical fluid chromatography (SFC) which is proven to be superior to conventional liquid chromatography in separating structurally related compounds, such as diastereoisomers and enantiomers. Several examples will be described for separation of multiple stereoisomers in biological samples, confirming SFC to be a powerful tool for stereoisomeric resolution for drug metabolism and pharmacokinetics (DMPK) applications. Two of these examples are summarized below: Gradient UPLC methodologies have previously been applied to separate a drug development compound and its six polyoxygenated metabolites (M2-M6 and M13), supporting numerous non-clinical and clinical PK studies. However, each of these metabolites exists in different stereoisomeric forms, resulting in 14 separate species. Initial attempts at developing UPLC methodologies were not capable of adequately separating these complex species; separation was unsuccessful using chemical derivatization, chiral and conventional reversed-phase liquid chromatography. The application of SFC is described herein to separate this complex mixture of 14 stereoisomeric metabolites; these data provided important data on which species circulate in human. SFC in combination with chemical derivatization was proven superior for separation of four diastereomeric species of another drug development compound. This method was fully validated and applied to evaluate potential in vivo chiral conversion in pooled clinical and preclinical samples.

Biography
Hermes Licea Perez is a Senior Scientific Advisor and Technology Leader in Department of Bioanalysis, Immunogenicity & Biomarkers at GlaxoSmithKline, USA. He has been recently selected as GSK Fellow for his scientific contribution to the analytical community at GSK. He has completed his Master of Science degree in Chemistry at Moscow State University and a PhD degree at Stockholm University. His PhD research was focused on “Quantification of haemoglobin adducts of industrial chemicals under the supervision of Prof. Siv Osterman-Golkar”. His interests at GlaxoSmithKline include method development and validation of pharmaceutical drugs and metabolites in biological matrices using techniques such as protein precipitation, Solid Phase Extraction (SPE), Liquid Liquid Extraction (LLE), and chemical derivatization (chiral and achiral) for LC (or SFC)-MS/MS detection.

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