Filip Cuyckens, J Chromatogr Sep Tech 2016, 7:5(Suppl)
http://dx.doi.org/10.4172/2157-7064.C1.015

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Macro and micro-scale methods using large volume injections and heart-cutting 2D-LC for ultrahigh sensitivity bioanalysis

Analytical sensitivity can be a critical parameter in the study of absorption, distribution, metabolism and excretion (ADME) of a drug in development. Microdosing, microtracer, microsampling studies and inhalation or intranasal delivery studies are typical examples where sensitivity can be a bottleneck. Often only a small fraction of the available sample is being analyzed which provides an opportunity to improve sensitivity using a larger fraction. A widely applicable online pre-concentration approach was developed for very large volume injections of biological samples. Due to the high selectivity of radioactivity and mass spectrometry detection, a very high increase in sensitivity was obtained despite the biological background. When combining the latter approach with heart-cutting 2D-LC, the sensitivity gain can also be obtained in cases where selectivity (e.g., UV detection) is a bottleneck. The compound(s) of interest are trapped on a short column in between the 1st and 2nd dimension separation enabling the selection of orthogonal conditions in the 2nd dimension independent of the first dimension. The same heart-cutting 2D-UPLC methodology was also scaled down to a micro-scale setup using IonKeyTM technology. The gradually decreasing column dimensions applied in this setup allow the combination of large volume injections with micro-LC/MS sensitivity for bioanalysis. All the approaches discussed will be illustrated on real life samples from different matrices and containing drugs and metabolites with a wide variety in polarity. The injection of 18 mL of blood, 100 mL of urine 2D-LC analysis with attogram/mL limit of quantification with radioactivity detection, comparison of sample analysis of a human microtracer study with results obtained with accelerator mass spectrometry (AMS) and micro-2D-LC Ionkey MS analysis of midazolam and its 1'-hydroxy metabolite in plasma are some of the examples that will be presented.

Biography

Filip Cuyckens is a Scientific Director and a Fellow at Janssen R&D in Beerse, Belgium. He is responsible for Analytical Sciences in the Pharmacokinetics, Dynamics and Metabolism (PDM) department. He has earned a Pharmacist degree in 1998, a degree in Industrial Pharmacy in 2002 and a PhD in Pharmaceutical Sciences in 2003. He has (co)authored more than 50 publications, is a member of the Associate Editorial Board of *Rapid Communications in Mass Spectrometry* and Board Member of the Belgian Society for Mass Spectrometry.

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