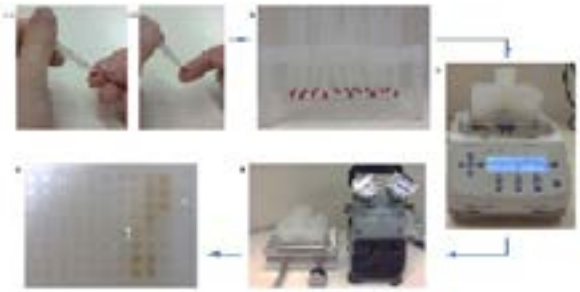
Marianne Fillet, Insights in Analytical Electrochemistry, 3:2
DOI: 10.21767/2470-9867-C1-001

Marianne Fillet

University of Liege, Belgium

Analytical strategies for sensitive quantitation of drugs and biomarkers from low blood sample volumes

In bioanalysis, samples are often available in limited volumes. For example, pharmacokinetic studies on rodents only provide a few dozen microliters of material at a time. In this context, analytical techniques requesting the smallest sample volume possible while keeping a high sensitivity are therefore preferred. To meet these requirements, LC miniaturization (micro- and nano-LC) presents undeniable advantages such as a small injection volume (down to 0.1 µL), low peak dispersion and reduced flow rates, both favorable to MS sensitivity. The concept of the 3Rs (refine, reduce, replace) is widely followed for *in vivo* testing, with the aim of reducing the use of animals. In the context of pharmacokinetic or toxicokinetic studies, 3Rs principle is mainly carried out by reducing the sampling volume to perform serial collection on the same animal over the whole study, while preserving animal health and welfare. This evolution requires the development of robust sampling and analytical approaches that handle very small sample volumes. In this presentation, we will discuss on one hand the potential of Dried Blood Spot (DBS) and Volumetric Absorptive MicroSampling (VAMS) compared to classical micro-Solid Phase Extraction (SPE) for the quantitation of hepcidin, chosen as model peptide, in blood samples. This low-concentration peptide was analysed by miniaturised liquid chromatography coupled to tandem MS (LC-Chip-MS/MS) to reach the appropriate sensitivity. On the other hand, a quantitative method was also developed and subsequently validated for the poorly soluble drug itraconazole (ITZ) using VAMS and ultra-high performance liquid chromatography (UHPLC) coupled to tandem mass spectrometry (MS). A proof of concept study showed that the optimized method is applicable to test the bioavailability of drug formulations containing ITZ. To compare the performance of the sample preparation methods, protocols were carefully optimized using the Design of Experiment (DoE) methodology. A special attention was also paid to phospholipid removal (PR) using 96 well-plates. Since whole blood is probably one of the most complex biological matrices than can be analyzed, matrix effect was expected to occur during blood analysis, especially when using a specific sample preparation technique. Matrix effects were thus carefully investigated and quantified.



Biography

Marianne Fillet completed Master's degree in Pharmaceutical Sciences at the University of Liège in 1993 and PhD in 1998 from the same university. She was a Post-doctoral Researcher at FRS-FNRS (National Funds for Scientific Research). She worked as the Professor at the University of Liège and the Head of the Laboratory for the Analysis of Medicines during the year 2010. She is now the Director of the CIRM (Centre for Interdisciplinary Research on Medicines). Her research activity includes: development of analytical methods for drug assays (synthetic drugs and drugs coming from the biotechnology) by HPLC, CE coupled with UV, LIF or MS; discovery and quantification of new disease biomarkers in biological fluids by proteomic and metabolomic approaches and enantiomeric separation of chiral compounds: fundamentals and applications. He has H index of 35 with citations 3302 and 134 publications in peer reviewed journals with cumulative impact factor of 465.8.

marianne.fillet@ulg.ac.be