Separations Sciences coupled to Mass Spectrometry for the Analysis of Complex Samples: Challenges and Opportunities

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With the introduction in the late nineties of atmospheric pressure ionisation, and in particular electrospray (ESI), liquid chromatography coupled to tandem mass spectrometry (LC-MS) has become a key analytical technique where molecular ions are selected and fragmented, often by collisional induced dissociation (CID). This is the basis of highly specific assays that are widely used in drug discovery and development, toxicology, doping control, etc. and enables applications such as proteomics and metabolomics. However, comprehensive qualitative and quantitative analysis of complex biological samples suffers from several constrains such as: limited sample throughput, large number of analytes, large chemical space, isomeric and isobaric analytes, lack of standards and high concentration dynamic range of analytes calling for advanced and integrated analytical workflows. High resolution mass spectrometry and in particular data independent acquisition (DIA) has become a straightforward way to monitor analytes expression in complex systems using various chromatographic setup including RPLC, HILIC and supercritical fluids chromatography. Due to the nature of ESI, annotating of mass spectra becomes also essential for features reduction but remains a challenging problem for quantitative analysis due to the multiple processes occurring during ionization. While ESI is largely applied for the detection of functionalized compounds the use of atmospheric pressure photoionization (APPI) has mainly been described with dopants for the analysis of compounds lacking of functional groups. With APPI depending on the ionization conditions either radical cation or protonated ions can be formed selectively for a large polarity range. Radical cation precursors can further be fragmented by collision induced dissociation and the spectra showed numerous fragments common to that observed in EI spectra enlarging the use of MS libraries.

The integration of ion mobility spectrometry, based on the shape of the charged analytes, with mass spectrometry (IMS-MS) enables an additional separation dimension, in particular for isobaric and isomeric analytes. Open port port probe (OPP) offers are better alternative to flow injection analysis (FIA) for the development of fast assays also in combination with IMS..

Beside workflows, ionisation control and data analysis optimization instrumental development are essential to obtain more molecular information in a single LC-MS analysis. Furthermore, electron induced dissociation or electron capture dissociation (ExD) and photodissociation (UVPD) extend the possibility for sensitive analyte identification and quantification, combined with IMS.