

LC-TOF in Forensic Toxicology – A Critical Review on 5 Years Experience

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Liquid chromatography (LC) coupled to mass spectrometry (MS) has evolved as a standard tool in forensic toxicology. The usual triple stage MS provides a very high sensitivity and reliability for quantitative analyses but the sensitivity for screening analyses for unknown substances is limited. Therefore screening analyses are usually performed as target compound analyses with a large set of targeted substances providing selectivity by predefined selected reaction monitoring.

The use of single stage MS does usually not provide the required sensitivity or selectivity but by using time-of-flight MS (TOF) the acquisition of accurate masses allows high selectivity in various matrices without the need to define the set of targeted substances prior to analysis. From the experience with LC-TOF MS in the past 5 years we found this very useful for a wide range of forensic applications but it also has some limitations that the analyst must be aware of.

PRO: In our laboratory the Agilent LC-TOF MS has proved to be robust and very reliable and almost all analyses can be accomplished with only one generic method (Varian 100 x 2.0 mm Polaris C18-Ether 3 µm column, gradient elution system with 0.1% formic acid and acetonitrile), especially as the MS acquires all ions without the need to modify detector parameters. The selectivity of accurate mass and the sensitivity are sufficient for forensic relevant concentrations of low dosed compounds (e.g. fentanyl, buprenorphine, low dose benzodiazepines etc.) in biological matrices. We use the LC-TOF MS for general unknown screening analyses in various matrices (urine, blood, hair and post mortem materials) and it also allows accurate quantitation e.g. for routinely performed therapeutic drug monitoring and has been confirmed in numerous proficiency tests.

CONTRA: The selectivity of the accurate mass for detecting substances containing only "CHO" (like tetrahydrocannabinol) in biological matrices is not sufficient to detect even high concentrations. Also the high selectivity and sensitivity of triple stage MS is not achieved, e.g. in target compound analyses of trace amounts in hair samples.

CAVEAT: Accurate mass alone cannot be considered as proof of identity, even in combination with an isotopic pattern (except for halogenated compounds), as in complex biological matrices isobaric compounds may be (and are) present. At least retention time must be confirmed. Further identification by structure related fragmentation is only a limited option, as the collision induced dissociation (CID) in the source region of single stage MS is in many cases not versatile enough to yield significant fragments (with accurate mass).