ENANTIOMERIC RESOLUTION, IDENTIFICATION, AND QUANTITATION OF CHIRAL ILLICIT DRUGS USING SFC APCI MS/MS

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Illicit drugs can include active ingredients from bona fide registered pharmaceuticals having therapeutic uses or active ingredients that are banned from all use under various international conventions or national laws. Many of the illicit drugs occur as optical isomers with different psychotropic activities. The enantiomeric purity and impurity profile in the drugs can provide valuable intelligence to the law enforcement to determine the synthetic route as well as the manufacturing practice for the illicit drugs. It is therefore important to develop a rapid, reliable, and sensitive analytical method for the separation, identification, and quantitation of chiral illicit drugs.

Widely accepted as the technique of choice for chiral separation, supercritical fluid chromatography (SFC) has found its use in many stages of pharmaceutical industry, from discovery to development. On average, SFC is 3-10 times faster than normal phase HPLC for chiral separations due to the low viscosity and high diffusivity of supercritical CO_2, the main mobile phase used in SFC. The co-solvent used in SFC, most commonly alcohols, also enables a facile coupling between SFC and MS detectors. However, the SFC chiral applications in forensic arena are limited in scope. This is, at least in part, due to the limitations in instrument design that prevents the low level detection often required in forensic applications.

Presented here are examples of chiral separation, identification, and quantitation of illicit drugs using SFC APCI MS and SFC APCI MS/MS. Methadone, 3, 4-methylenedioxy amphetamine, hexobarbital, and tetramisole were chosen as the representative illicit drugs in this study. Chiral columns of different size particles (5 µm and 3 µm) and lengths will be evaluated with respect to the chromatographic efficiency and speed of analysis. The interface between SFC and MS and the choice of ionization will be evaluated. Quantitative analyses including limit-of-detection (LOD), limit-of-quantitation (LOQ), linearity, calibration curve, precision, accuracy, reproducibility, stability and recovery will be presented and compared with those obtained from HPLC and CE. Key system attributes that need to be addressed to enable fast analysis with high detection sensitivity will also be discussed.