B195 High-Sensitivity Drug Analysis With Optical Isomer Resolution Using Mixed Chiral Selectors

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The goal of this presentation is to discuss the application of mixed chiral selectors to the separation of drugs and their optical isomers using highly sensitive Capillary Electrophoresis/Mass Spectrometry (CE/MS) in approximately 20 minutes.

This presentation will impact the forensic science community by describing how to use this rapid and highly sensitive method to separate and identify isomers of commonly encountered drugs of abuse such as amphetamine and methamphetamine.

The separation of drug isomers is essential since scheduling and sentencing could vary based on which isomer of a compound is present in a sample. Several techniques are currently used for the separation and detection of optical isomers including Gas Chromatography/Mass Spectrometry (GC/MS), Capillary Electrophoresis/Ultraviolet (CE/UV), and Liquid Chromatography/Mass Spectrometry (LC-MS). The drawbacks of these techniques are the use of expensive chiral columns (GC/MS and LC/MS), derivatization of the sample (GC/MS), and low sensitivity and specificity (CE/UV). To address these deficiencies, a highly sensitive CE/MS technique has been developed for the separation and detection of drugs and their optical isomers in about 20 minutes using only 1 nanoliter of the solution. The technique is faster and is almost 1,000x more sensitive than current GC/MS and LC/MS techniques. In addition, it provides base-line separation of the optical and positional isomer in one run. The superior properties of this technique are due to three unique characteristics of this design: (1) the new CE/MS uses a porous tip for interfacing CE to MS. A porous tip allows narrow capillaries (<20µm-i.d.) to be interfaced to MS allowing maximum sensitivity under electrospray ionization without introducing any dead volume and consuming only one nanoliter of the sample solution; (2) the use of 18-crown-6 as a complexation reagent in the CE background electrolyte — the sensitivity of the amine-containing compounds are enhanced due to high ionization efficiency of the complexes; and, (3) the addition of the chiral selector (+)18-crown-6-tetracarboxylic acid not only allows for higher sensitivity but also separation of the optical isomers of compounds containing primary amines; however, the optical isomers of secondary amines such as methamphetamine were not baseline separated. To separate all amines, (+)18-C-6-TCA was mixed with several types of cyclodextrins (α-, β-, γ-cyclodextrin) to examine the optimum background electrolyte for CE/MS analysis drugs and their optical isomers. Using a mixture of (+)18-C-6-TCA and β-cyclodextrin was found to baseline separate (±)-amphetamine and (±)-methamphetamine mixture in less than 20 minutes. To speed up the analysis, this recently developed ultrafast CE-MS is being applied to the analysis of drugs and their positional and optical isomers in approximately 60 seconds.

Using a background electrolyte containing both 18-C-6-TCA and cyclodextrin provides enhanced separation and sensitivity over a background electrolyte of the individual chiral selectors.

Drug, Chiral Separation, CE/MS