K17 Capillary Electrophoresis and Capillary Electrochromatography Mass Spectrometry for Chiral Drug Detection

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After attending this presentation, attendees will understand some principles of how chiral drugs can be separated and detected using capillary electrochromatography – time-of-flight mass spectrometry (CEC-TOF-MS).

This presentation will impact the forensic science community by discussing one of the novel chiral separation techniques called capillary electrochromatography mass spectrometry (CEC-MS).

Worldwide issues with poisoning and death from clandestine drug manufacturing make it important to develop methods that can not only detect low levels of drugs but also determine their chirality. In this way, law enforcement can better track users and victims of these products. In addition, the field of chiral toxicology has become increasing important as researchers and practitioners recognize the importance of defining the precise role structure – reactivity relationships play in drug activity. As a result, a large amount of research has been conducted in the analysis of chiral drugs. The goal of this project is to develop methods to detect these drugs using Capillary Electrophoresis (CE) and Capillary Electrophoresis Mass Spectrometry (CE-MS) techniques.

Trace detection of pharmaceutical compounds typically employs several analytical techniques, including gas chromatography-mass spectrometry (GC-MS), and liquid chromatography-mass spectrometry (LC-MS). For chiral separations, these techniques may utilize specific stationary phases or may require derivation to diastereisomers. Capillary electrophoresis can be a powerful alternative for the separation of neutral and chiral drugs through the use of guest-host reactions and micellar-solute interactions. It is proposed that CE-MS with an electrospray ionization (ESI) source would be a useful technique for separating and analyzing this class of drugs. Capillary electrophoresis-mass spectrometry has a number of important advantages for toxicological analysis including low sample consumption and the potential for highly efficient chiral analysis. Generally electrophoretic techniques are restricted to the analysis of charged molecules. However, in the past 20 years, a variety of electrophoresis techniques have been developed which are suitable for the detection of neutral and chiral drugs including micellar electrokinetic capillary electrophoresis (MEKC) and capillary electrochromatography (CEC).

Proper identification of unknown drugs is a critical issue in forensic drug analysis. While capillary electrophoresis with UV, electrochemical or fluorescence detection can be used to presumptively determine the presence of a particular compound, for absolute identity of trace levels of these compounds, mass spectrometry coupled to chromatography is necessary. While a number of useful procedures have been developed for the detection and screening of compounds by capillary electrophoresis/mass spectrometry, to date applications involving neutral or chiral drug detection by MEKC procedures have been problematic. These samples require separation via a detergent or cyclodextrin based pseudo-stationary phase that can be incompatible with electrospray ionization methods that require volatility. One potential solution for this issue is to operate the CE-MS system in a partial filling mode to avoid spraying the reagent into the spectrometer. However, the issues of timing of the capillary filling and the potential instability of a bimodal buffer make this a difficult technique.

Alternatively, capillary electrochromatography (CEC) can be used. This procedure is a novel technique which permits the detection of neutral compounds by combining the high efficiency of CE with outstanding selectivity of HPLC. In CEC, the capillary column is packed with an HPLC type stationary phase. Separation occurs via sample partitioning between the packed stationary phase and an electrodriven mobile phase. An efficient way to produce this stationary phase is through in-situ polymerization into a so called polymer monolith2. When coupled to mass spectrometry, the procedure has been shown to provide efficient and sensitive detection of drugs and their metabolites in biological fluids.

In this study, monolithic CEC-MS will be developed and compared with partial filling MEKC for the application of chiral drug detection in complex matrices. The CEC stationary phase will be developed by bonding chiral selectors onto the silica inner wall of a capillary or through attachment of these selectors to carbon chains on acrylate monomers. In this way CEC-MS can be developed as a powerful technique for chiral toxicology as well as other applications in pharmacological analysis.

Capillary Electrochromatography, Mass Spectrometry, Chiral Drug Detection

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