B165 Enantiomeric Purity Determination With HPLC-UV/Optical Rotary Detection

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After attending this presentation, attendees will 1)understand the theory and practice governing UV and optical rotary measurements made on drug substance pure enantiomers and enantiomeric mixtures; 2) review the application of HPLC with UV and optical rotary detection to the mea- surement of enantiomeric form and/or purity in forensic casework involving several different drug substances; and 3) implement a low cost approach for the determination of enantiomeric form and/or purity in bulk drug substances or drug formulations.

This presentation will impact the forensic community and/or humanity by providing a general, reliable, and low cost approach for the determination of enantiomeric purity in bulk drug substances and drug for- mulations.

For chiral drug substances, the enantiomeric form (*d*, *l*) and purity may have important implications in forensic casework. Enantiomeric drug pairs frequently exhibit varying pharmacological and toxicological effects in the body, which may result in differing legal classifications and/or pre- scribed uses for the two enantiomers in the pair. For example, the *l*-isomer of methorphan (levomethorphan) is under DEA schedule, whereas the *d*- isomer (dextromethorphan) is an unscheduled pharmaceutical drug. For methamphetamine, both the *d*- and *l*-isomers are under DEA schedule, and both isomers also have legitimate pharmaceutical uses. The determination of enantiomeric form and purity may also provide information on the syn- thetic route or source for some illicit drugs.

In this work, the determination of enantiomeric form and purity for a variety of drug substances based on HPLC analysis with in series UV and optical rotary detectors is presented. The principle is simple, and is based on the linear relationships which exist for both the UV signal (signal pro- portional to the total concentration of *d*- and *l*-isomers) and optical rotary signal (signal proportional to the net excess of *d*- or *l*- isomer). Calibration curves based on the ratios of the optical rotary and UV signals for the pure and mixed enantiomers are shown to be linear, and reliable for the deter- mination of enantiomeric purity in bulk drug substances and drug formula- tions. Examples from actual forensic casework including methorphan, selegiline, ephedrine, and pseudoephedrine are presented. Applications involving the determination of enantiomeric purity for amphetamine in a prescription drug formulated with a 3:1 enantiomeric ratio, and for methamphetamine will also be presented.

The major advantages to this approach are: 1) No chiral separation is necessary allowing the use of previously developed achiral HPLC assays. This also precludes the need to purchase multiple chiral columns for dif- ferent drug substances. 2) The measurement of bulk drug purity or drug formulation potency can be made at the same time. 3) The cost of the optical rotary detector is relatively low (ca. $25 K). Disadvantages include the limited sensitivity of the chiral detector, making this approach unsuitable for the analysis of drug substances in bodily fluids in clinical and toxicological investigations, or for drug substances with very low specific rotations.

Enantiomeric Purity, Optical Rotary Detection, Drugs and Drug Formulations

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