B190 Separation of Fentanyl Analogues, Homologues, and Positional Isomers by Ultra High-Performance Liquid Chromatography (UHPLC)

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After attending this presentation, attendees will be familiar with methods of separation for fentanyl analogues, homologues, and positional isomers, using UHPLC.

This presentation will impact the forensic science community by enhancing the collective expertise in the separation of fentanyl-related compounds using UHPLC. Positional isomers, which have the same mass and similar structure, are particularly difficult to separate using gas and liquid chromatographic methods.

Fentanyl is a Schedule II narcotic opioid that is an agonist at the μ-opioid receptor. While it mimics the effects of morphine, it is structurally different and is 50-100 times more potent. Some analogs of fentanyl, such as carfentanil, can be thousands of times more potent. Given their higher potency, there is a higher risk of overdosing. This poses a significant threat to opioid users and users of street drugs. Many street drugs, most commonly heroin, are being laced with fentanyl or its derivatives, leading to a significant public health problem. Derivatives of fentanyl are designed to avoid legal prosecution, as they are not scheduled. One of the main issues in the field of forensic drug analysis is that they are being produced faster than they can be identified.

Derivatives of fentanyl, including positional isomers, have substituents of varying degrees of polarity, hydrophobicity, and size. The substituents of the derivatives are expected to interact differently with different stationary phases and modes of chromatography. The particular challenge lies in separating the positional isomers, as they have the same substituents attached to different locations on the molecule.

A total of 12 fentanyl derivatives, including positional isomers, were subjected to analysis by UHPLC-time of flight/mass spectrometry. A variety of different 150mm x 2.1mm x2.7μm columns (SPP C18, SPP PFP, SPP Phenyl-Hexyl, and Hydrophilic Interaction Liquid Chromatography (HILIC)) were used in both the Reversed Phase Chromatographic (RPC) and HILIC modes and results were compared. The mobile phase conditions were optimized for each column to obtain the best possible separation.

For RPC, gradient conditions were preferred while for HILIC, isocratic conditions were utilized. Varying performance was found when analyzing positional isomers on different columns. For example, when using the C18 column, despropionyl para- and ortho-fluorofentanyl were separated with a resolution better than 1. Isomers such as ortho- and meta-fluorofentanyl were not separated, resulting in overlapped peaks.

These results both enhance the collective forensic knowledge and may aid forensic laboratories dealing with the influx of fentanyl-related cases by facilitating the identification process. This methodology may also aid in helping in the scheduling of fentanyl derivatives.

Fentanyl, Positional Isomers, UHPLC-TOF/MS

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