B191 Using Quadropole Time-Of-Flight (qTOF) Liquid Chromatography/Mass Spectrometry (LC/MS) to Distinguish 2- and 3-Furanyl Fentanyl and Other Fentanyl-Related Compounds

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After attending this presentation, attendees will better understand the analysis of 2- and 3- furanyl fentanyl and the importance of being able to separate and identify positional isomers.

This presentation will impact the forensic science community by providing LC/MS methodology capable of separating and identifying heroin, fentanyl, fentanyl-related compounds, and common adulterants.

The presence of fentanyl and fentanyl-related compounds in drug evidence has been on the rise recently. Two of these fentanyl-related compounds include 2-furanyl fentanyl(N-(1-phenethylpiperidin-4-yl)-N-phenylfuran-2-carboxamide), known colloquially as furanyl fentanyl, and 3-furanyl fentanyl (N-(1-phenethylpiperidin-4-yl)-N-phenylfuran-3-carboxamide). Differing only by the attachment site of the furanyl ring, these two compounds are difficult to distinguish chemically. Effective November 29, 2016, 2-furanyl fentanyl was placed into Schedule I federally; however, because 3-furanyl fentanyl was not specified in the final order, distinguishing between these two positional isomers is essential during analysis.[1]

The separation and identification of these two positional isomers can be accomplished via conventional Gas Chromatography (GC) methods. Standard screening conditions on the Gas Chromatography/Mass Spectrometry (GC/MS) provides a 0.1-minute separation between the isomers; however, the mass spectra of the two compounds have a very similar fragmentation pattern, with the most obvious difference being the presence of the 212m/z ion in the mass spectrum of 2-furanyl fentanyl. Thus, using standard GC/MS methods for identification of these compounds is not considered reliable as the similarities in mass spectra and slight drifts in retention time make their identification difficult. Gas Chromatography coupled with Vapor Phase Infrared Detection (GC-IRD) can provide confirmatory data to distinguish between the two positional isomers as it is apparent that the difference in site attachment of the furanyl ring leads to response differences in the Infrared (IR) fingerprint region.

LC/MS is an alternative methodology for both the separation and the identification of 2- and 3-furanyl fentanyl. Using this method, 2- and 3-furanyl fentanyl are baseline resolved from each other with a calculated resolution of 4.01 between the two compounds. The qTOF LC/MS also provides the exact mass of the analytes. Note that the positional isomers have the same molecular formula and therefore the same exact mass, thus requiring column separation to detect the presence of a mixture of 2- and 3-furanyl fentanyl or to distinguish which positional isomer is present. Confirmatory structural information was obtained through the subsequent fragmentation of each analyte's precursor ion. With an applied collision energy of 30eV, 2- and 3- furanyl fentanyl have similar fragmentation patterns. Therefore, using the combination of the chromatographic separation, molecular weight, and fragmentation patterns, the presence of 2-furanyl fentanyl and 3-furanyl fentanyl can be confirmed in a mixture.

Other fentanyl-related compounds may also present similar analytical challenges, such as their existence at low concentrations in drug evidence. To compensate for these difficulties, the LC/MS methodology was extended to include heroin and a variety of fentanyl-related compounds.

Reference(s):

1. United States Drug Enforcement Administrator. Final Order. Schedules of Controlled Substances: Temporary Placement of Furanyl Fentanyl Into Schedule I, 21 CFR Part 1308. *Federal Register 81*, no. 229 (November 29, 2016): 85873.https://www.gpo.gov/fdsys/pkg/FR-2016-11-29/pdf/2016-28693.pdf.

Furanyl Fentanyl, Fentanyl, LC/MS

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