B174 A Confirmatory Method for the Analysis of 30 Fentanyl Analogs Using Gas Chromatography/Mass Spectrometry (GC/MS)

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Learning Overview: After attending this presentation, attendees will understand the results of various optimizations in GC to improve resolution between fentanyl standards and the importance of accurate reporting of seized drugs.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by providing an optimized GC/MS method that can identify 30 fentanyl analogs with improved resolution. The overall run time of 22.33 minutes is practical for forensic use of large amounts of seized-drug casework.

Forensic drug chemists are responsible for reporting the composition of commonly seized drugs. The recent opioid epidemic has resulted in many commonly seized drugs such as heroin, cocaine, and marijuana being observed laced with fentanyl and fentanyl analogues. The Centers for Disease Control and Prevention (CDC) reported in 2016 that opiate related drugs make up 66% of drug related deaths and fentanyl is an increasing source of these drug related overdose deaths.[1,2] The fentanyl epidemic includes fentanyl analogues that are being synthesized in clandestine laboratories, some of which are still not considered illegal due to lag time for legislation. The potency of each analogue varies; fentanyl is estimated to be one 100 times more potent than morphine while an analogue such as carfentanil is estimated to be 10,000 times more potent than morphine.[3] In order to report the presence of fentanyl, drug chemists take steps involving initially performing a qualitative presumptive test. This first test is critical for efficiency but only detects drug classes.[4] The next step is to perform a validated confirmatory test to identify the analyte(s) of interest. Drug chemists typically use gas chromatography/mass spectrometry (GC/MS) to identify drugs.

A confirmatory method for the analysis of 30 fentanyl analogues using GC/MS has been developed. The fentanyl standards included in optimizing this method were fentanyl, crotonyl, acetyl fentanyl, butyryl fentanyl, para-fluorofentanyl, meta-fluorofentanyl, ortho-fluorofentanyl, cis-3-methyl fentanyl, trans-3-methyl fentanyl, para-fluorobutyryl fentanyl, meta-fluorobutyryl fentanyl, ortho-fluorobutyryl fentanyl, acryl fentanyl, valeryl fentanyl, isobutyryl fentanyl, carfentanil, ocfentanil, cyclopropyl fentanyl, alfentanil, sufentanil, remifentanil, W-15, 4-ANPP, para-methoxybutyryl fentanyl, thiofentanyl, β-hydroxythiofentanyl, α-methyl fentanyl, β-methyl fentanyl, and furanyl fentanyl. This method utilized a gas chromatograph outfitted with two FID detectors and coupled with a single quadrupole mass spectrometer to improve resolution between fentanyl standards utilizing a split injection with a split ratio of (10:1). The preferred GC/MS conditions used an initial temperature of 60°C with an initial hold time of 1.00 minute, the first ramp rate at 30°C/min to 250°C, and then a second ramp rate at 4°C/min to 300°C with a final hold time of 2.50 minutes. The inlet temperature was 280°C and the injection volume was 1 μL. This development also investigated the employment of complementary dual columns. The primary column employed was comprised of a 5% diphenyl: 95% dimethyl polysiloxane stationary phase (30 m x 0.25 mm x 0.25 μm), the other two columns utilized for analysis were a 5% diphenyl: 95% dimethyl polysiloxane column optimized for amines (30 m x 0.25 mm x 0.5 μm) and a trifluoropropylmethyl polysiloxane column (30 m x 0.25 mm x 0.25 μm). The columns were compared using calculated linear retention indices. Both columns with a 5% diphenyl: 95% dimethyl stationary phase behaved similarly, with resolution between fentanyl standards remaining preserved using both columns. The column with a trifluoropropylmethyl stationary phase provided complementarity data for standards containing fluorine compounds that originally had elution times overlapping with non-fluorinated compounds using the primary column. The validation process of this method included three sets of six serial dilutions of each standard run on five different days. Stock solutions of mixtures were analyzed as well.

The development of a confirmatory method using GC/MS for the analysis of fentanyl analogues has provided contributory insight for the implementation of a split method, an intricate oven temperature ramp rate, and results from atypical columns for the use of drug analysis. The procedure can be utilized to accurately identify 30 different fentanyl analogues. The method results can be used as a reference using linear retention indices as well as retention times.

Reference(s):

1. Rob Portman, Tom Carper, "Combatting the Opioid Crisis: Exploiting Vulnerabilities in International Mail," *Permanent Subcommittee on Investigations* (2017): 1-95.
2. David Guerrieri, Emma Rapp, Markus Roman, Henrik Druid, Robert Kronstad, "Postmortem and Toxicological Findings in a Series of Furanylfentanyl-Related Deaths," *Journal of Analytical Toxicology* 41 (2017): 242-249.
3. Nektaria Misailidi, Ioannis Papoutsis, Panagitoa Nikolaou, Artemisia Dona, Chara Spiliopoulou, Sotiris Athanaselis, "Fentanyls continue to replace heroin in the drug arena: the cases of ocfentanil and carfentanil," *Forensic Toxicology* 36 (Spring 2018): 12-32.
4. Morgan Philp, Shanlin Fu, "A review of chemical 'spot' tests: A presumptive illicit drug identification technique," *Drug Testing and Analysis* 10 no. 1 (Spring 2018): 95-108.

Forensic Drug Chemistry, Fentanyl Analogs, Gas Chromatography/Mass Spectrometry