B130 Characterization of Synthetic Phenethylamines Using High Resolution Mass Spectrometry (HRMS)

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After attending this presentation, attendees will understand the advantages of HRMS for the analysis of synthetic designer drugs, specifically synthetic phenethylamines. Attendees will learn how the mass defect obtained via HRMS can be used to characterize these compounds according to structural class.

This presentation will impact the forensic science community by providing a method to characterize unknown synthetic designer drugs according to structural class. This method is especially useful in the characterization of novel designer drug analogs for which no reference standard is yet available.

A number of different classes of synthetic designer drugs are known, including synthetic cannabinoids, phenethylamines, and cathinones. Compounds within each class often share a core structure and differ only in the position or identity of substituents. When a compound is regulated, a new analog often appears on the market. This analog exhibits similar psychoactive effects but because the structure is slightly different, the analog may not regulated under current legislation.

Samples submitted to the laboratory that may or may not contain controlled substances are analyzed by Gas Chromatography/Mass Spectrometry (GC/MS). This technique satisfies the Scientific Working Group for the Analysis of Seized Drugs recommendations, allowing definitive identification of controlled substances through a comparison of the mass spectrum obtained for the submitted sample to that of a reference standard. The GC/MS instruments used are typically configured with Electron Ionization (EI) and a single quadrupole mass analyzer (qMS). Electron ionization results in substantial fragmentation and the fragment ions observed can be used toward structural elucidation to identify the compound. The single qMS gives unit resolution, resulting in nominal mass data which is sufficient for identification of most controlled substances; however, synthetic designer drugs pose challenges that make definitive identification using GC/qMS difficult. First, isomers have the same nominal mass, making distinction by GC/qMS alone problematic. Second, because novel designer drug analogs appear on the market frequently, reference standards are often not immediately available, making identification challenging.

The objective in this research was to address the above issues by investigating the applicability of HRMS as a tool to aid in the identification and characterization of synthetic phenethylamines. Using HRMS, the accurate mass of each fragment ion is measured, providing additional understanding about the fragmentation pathway of the compound. This knowledge of the fragmentation behavior can be used to determine the compound structure with a high degree of certainty and therefore distinguish isomers. Further, accurate mass data is used to determine the mass defect of a compound, defined as the difference between the accurate and nominal mass. Compounds with similar core structure have similar mass defects. Thus, the mass defect can be used to determine the structural class of a new analog, which is useful in cases where no reference standard exists.

In this research, a set of synthetic phenethylamines from different subclasses (e.g., 2C and NBOMe) was investigated. Reference standards were prepared in methanol (1mg/mL) and analyzed in replicate by GC/qMS and by GC/Time-of-Flight (TOF) MS. Both instruments use EI; however, the TOF is a high-resolution mass analyzer, affording accurate mass data. For each standard, GC/qMS and GC/TOF/MS data were compared and showed similar fragmentation patterns. For example, characteristic fragment ions for 2C-E were observed at m/z 209Da, 180Da, and 165Da via GC/qMS and at m/z 209.1457Da, 180.1185Da, and 165.0947Da via GC/TOF/MS. The accurate mass data were used to confirm fragmentation pathways of the phenethylamines from which distinction of isomers such as 2C-E and 2C-G was possible.

For each standard within a subclass, the mass defects of the molecular ion and characteristic fragment ions were determined. From this, a range of mass defects representative of the core structure was calculated. For example, a mass defect range for the 2C subclass of 133.88±26.02mDa was determined based on the molecular ion for all 2C phenethylamines in the data set. An additional set of phenethylamine standards was used to evaluate the efficacy of the mass defect range for characterization. Successful classification was achieved despite the presence of some false positives and false negatives.

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This presentation demonstrates the utility of HRMS in the identification and characterization of synthetic phenethylamines, focusing on the potential of mass defect as a characterization tool.

Synthetic Designer Drugs, Mass Spectrometry, Mass Defect

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