B18 The Development of a Characterization Scheme for Emerging Synthetic Phenethylamines

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After attending this presentation, attendees will be familiar with the development of a characterization scheme that can be used to assign new synthetic phenethylamine analogs according to structural class. The scheme is based on mass spectral data and uses isotope patterns, neutral losses, and mass defects to define the structural class.

This presentation will impact the forensic science community by providing a tool that can be used to screen emerging analogs to determine the likely designer drug class. While this initial work focuses on synthetic phenethylamines, similar characterization schemes can be developed for other designer drug classes.

The identification of synthetic designer drugs by conventional Gas Chromatography/Mass Spectrometry (GC/MS) methods is challenging due to the high degree of structural similarity among members of a given class. For example, the 2C-phenethylamines consist of a core 2,5-dimethoxyamphetamine structure, but compounds within this series differ in the position and identity of substituents on the aromatic ring. Such modifications to the core structure create compounds that have similar psychoactive effects but may not be regulated under current legislation. As a result, new analogs rapidly appear on the market to circumvent current legislation and no reference standards are immediately available to aid in the identification.

The objective of this study was to develop a characterization scheme to assign emerging analogs to a designer drug class such that more resources can be focused on definitive identification, as necessary. This initial study uses synthetic phenethylamines as the model class to develop such a characterization scheme. A set of 2C-phenethylamines that included alkyl, halogen, and nitro substitutions on the aromatic ring was analyzed by Gas Chromatography/Time-Of-Flight/Mass Spectrometry (GC/TOF/MS). This high-resolution instrument uses electron ionization, insuring that the fragmentation patterns obtained are similar to those obtained by the more conventional GC/MS instruments currently used. Further, the exact mass of each molecular (when detected) and fragment ion is determined from which elemental formulas can be assigned with a high degree of confidence.

To begin developing a suitable characterization scheme, the mass spectral data for each 2C-phenethylamine were probed to identify common features. These features included isotope patterns, neutral losses, and mass defects of characteristic ions. Isotope patterns in the mass spectra were used to identify the presence of chlorine and bromine. Neutral losses from each molecular ion were determined and losses common to all 2C-phenethylamines in the training set were identified. These losses included CH_3N, C_2H_6N, and C_2H_6NO, which were measured as neutral losses of 29 Da, 44 Da, and 60 Da, respectively, from the molecular ion. Finally, the Kendrick mass defect of the fragment ion remaining after each neutral loss was calculated. For example, for the loss of $CH_3N\bullet$, the Kendrick mass defect filter based was defined as 85.96 mDa ± 0.7224 mDa, at the 95% confidence level.

The characterization scheme was then applied to a prediction set containing additional 2C-phenethylamines, other synthetic phenethylamines, and synthetic cathinones, which are structurally similar to the phenethylamines. Spectra for the test set were interrogated first for isotope patterns and, second, for the characteristic neutral losses previously identified. For those test set compounds that displayed the targeted neutral losses, the Kendrick mass

defect of the remaining fragment ion was calculated and tested against the previously developed filter. Overall, the characterization scheme showed promise for initial screening of 2C-phenethylamines, despite some false positives and negatives.

This presentation will demonstrate the characterization scheme in the form of a flow-chart and further discuss the development and application of the scheme for the characterization of 2C-phenethylamines.

Synthetic Phenethylamine, High-Resolution MS, Mass Defect