B179 Gas Chromatography (GC) With Tandem Cold Electron Ionization/Mass Spectrometric (Cold EI/MS) Detection and Vacuum Ultraviolet (VUV) Detection for the Comprehensive Analysis of Fentanyl Analogs

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Learning Overview: After attending this presentation, attendees will understand unique benefits of gas chromatography (GC) coupled with cold electron ionization mass spectrometric (cold EI-MS) and vacuum ultraviolet (VUV) detection as a rapid and reliable analytical technique for the analysis of emerging drugs, specifically fentanyl analogs.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by investigating an alternative analytical technique that will greatly modernize analysis. This will allow for more rapid analysis, thus aiming to reduce the backlog challenge which impinges many forensic laboratories. The combination of these two complementary detectors in tandem with the high resolving power of the gas chromatograph allows for higher confidence in sample identification by the presence of retention times, enhanced molecular ions with fragmentation, and complementary VUV detection. Additionally, the research aims to demonstrate the value of ultraviolet detection in the gas phase for the analysis of emerging drugs.

GC with electron ionization (GC/MS) is widely used in examination of emerging drugs. While providing predictable and extensive fragmentation patterns, its hard ionization technique yields little or no molecular ions for certain analytes, leading to uncertainty in identification. Conversely, GC coupled with cold EI/MS is based on cooling the molecules emerging from the GC in supersonic molecular beams. The cool molecules have a higher chance of surviving as molecular ions following ionization. In addition to an enhanced molecular ion, the fragmentation pathways are like those obtained using classical EI, enabling the use of established libraries.

Mass spectra generated from GC/MS with both EI and cold EI ionization cannot reliably discriminate between positional isomers, especially when substitution occurs on the benzene ring. UV spectra generated from GC/VUV can distinguish between positional isomers, including those having identical MS spectra. UV detection in the gas phase probes primarily the electronic transitions found in single bonds ($\sigma \rightarrow \sigma^*$) as well as the electronic transitions of double bonds ($\pi \rightarrow \pi^*$), resulting in discernable spectral patterns. These patterns are related to the individual structure of the compound, which may be quickly and accurately identified by a spectral reference library. The high specificity of each spectra not only allows for positional isomer differentiation but for peak deconvolution as well.

GC with flame ionization detection (FID) is also commonly employed in forensic analysis for both screening and quantitation but lacks specificity due to its inability to determine the components under the peak. Conversely, VUV detection allows for quantitation and identification under the peak using deconvolution capabilities, therefore providing for high specificity.

The present study investigates the efficacy of GC interfaced to both cold EI/MS detection and VUV detection by the means of a flow splitter for the simultaneous qualitative and quantitative analysis of twenty-four fentanyl analogues, including seven sets of positional isomers. For 23 analogues, enhanced molecular ions were obtained which were confirmed by MS/MS experiments. The cold EI/MS spectra exhibited similar MS fragments (other than the molecular ion) to those obtained by EI/MS. All the fentanyl related compounds exhibited unique VUV spectra and were successfully identified by a reference library containing hundreds of entries. The repeatability of the interface was demonstrated with both short term (run to run) and long term (day to day) studies further emphasizing accuracy of identification. Stability of the interface is further exhibited through linearity studies using VUV detection for all fentanyl related compounds over a concentration range of 390 PPB to 200 PPM. Additionally, the quantitation value of the interface is exhibited using simulated samples.

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