B68 Profiling Reaction Intermediates and By-Products in Illicit Synthetic Drug Samples Using Direct Analysis in Real Time (DART®) and an Ion Trap Mass Spectrometer

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After attending this presentation, attendees will better understand the detection of impurities present in synthetic drugs for the purpose of sourcing the drug being analyzed. Attendees will be aware of a method being developed for this purpose based on DART® ionization coupled with an ion trap mass spectrometer.

This presentation will impact the forensic science community by demonstrating a new approach for sourcing synthetic drugs. DART®-ion trap Mass Spectrometry (MS) is a rapid technique and the Tandem Mass Spectrometry (MS/MS) capabilities can determine the presence of minority components in samples that are primarily synthetic drugs.

Profiling of excipients has been previously used to source "cut" drugs. Characterization of impurities in methamphetamine samples can be an effective tool to determine the synthetic pathway used to make the drug. Typically, these profiling approaches have been conducted with Gas Chromatography/Mass Spectrometry (GC/MS). The goal of this work is to explore rapid drug sample profiling using DART® MS and to focus on contaminants in newer synthetic drugs. Recently seen designer drugs, such as the synthetic cannabinoids, are produced through multi-step reactions that are significantly more involved than methamphetamine production. Clandestine facilities are unlikely to have rigorous quality control and may contain some amount of impurities due to insufficient sample clean-up. These containments (even when present at low levels) are likely to originate from intermediate products in the multi-step reaction and could potentially be used to source the synthetic batch from which the drug came.

Using DART® to profile the impurities in these samples imparts the advantage of a fast and simple analysis with little sample preparation. The use of an ion trap capable of MS/MS analysis will allow detection of impurities present at low concentrations in a sample with large amounts of the drug product. This type of analysis allows for isolation of a known impurity ion and further fragmentation of that ion to yield a selective signal with high sensitivity.

Initial validation experiments were performed using an IonSense® DART® source coupled with a Thermo™ LTQ XL™ ion trap mass spectrometer. Diphenhydramine was used as an uncontrolled analog drug. The synthesis reaction was conducted using a commonly employed pathway and fractions from various points in the reaction were analyzed. Several reaction intermediates were observed in the final product and identified using MS/MS. Current work is focused on the synthesis of alkyl indoles, which are intermediate products used to make the naphthylindole class of synthetic cannabinoids (i.e., JWH-018, AM-2201). Additionally, a flow system was constructed and coupled with the DART® source for real-time analysis of the reaction products during synthesis.

Near-future work will focus on several areas: (1) determining the relative dynamic range of the DART®-ion trap instrument; (2) comparing this parameter with GC/MS analysis; and, (3) analyzing actual illicit synthetic drugs. The purity of clandestine synthetic drugs is likely to be relatively high, such that any signal from minority contaminants may be masked by the signal from the drug itself. The initial goal is to determine at what level the minority components can be determined in the presence of overwhelming signal for the majority component. The signal-to-noise for low-level contaminants is significantly enhanced through the use of MS/MS. The levels of

minority components determined using DART®-MS/MS will be compared with the signal achieved using GC/MS. Finally, actual synthesized cannabinoids will be tested to determine if the presence of reaction intermediates or byproducts can be determined in these samples.

DART®, Impurity Profiling, Synthetic Cannabinoids