LC-MS Method Development for the Identification of Route Specific MDMA Impurities

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After attending this presentation, attendees will have an understanding of the benefits of using LC-MS instrumentation over GC-MS for impurity profiling of amphetamine impurities.

This presentation will impact the forensic science community by demonstrating the simple extraction techniques possible with LC-MS instrumentation.

MDMA, 3,4-methylenedioxymethamphetamine, is a Schedule 1 psychoactive hallucinogenic stimulant commonly found in "Ecstasy" tablets or referred to as "Molly." By analyzing the organic by-products, or impurities, in MDMA tablets, it is possible to identify the synthetic route used to prepare the sample. Two of the most common methods of synthesis are the reductive amination of MDP-2-P and the Leuckart reaction. The differentiation between these two synthetic routes can aid investigators in the identification of the manufacturer of the sample and to compare tablets from multiple drug seizures.

In the past decade, several GC-MS techniques have been developed to analyze MDMA tablets and to identify common route specific impurities. It is hypothesized that LC-MS will be more suitable for this research due to its increased sensitivity and ability to analyze more polar compounds without derivatization. The aim of this research was to develop a simplified method for the extraction and identification of 11 previously identified route specific MDMA impurities using dry extraction techniques and LC-MS instrumentation. By only identifying the impurities selected, this method is able to focus on the impurities, typically found at low concentrations, which indicate these two popular synthesis routes. In order to achieve this aim, an LC-MS method was designed to identify the compounds and several extraction methods were evaluated for the optimal extraction of the compounds of interest from simulated tablet matrices.

Of the impurities chosen, 8 were indicative of the reductive amination route. These compounds were: N-cyclohexylacetamide, 3,4-methylenedioxyamphetamine (MDA), p-methoxymethamphetamine (PMMA), N-(1,3-benzodioxol-5-yl-methyl)-N-methylamine, 3,4-methylenedioxyacetophenone, 3,4-methylenedioxypropiophenone, methyl piperonylate, and 3,4-methylenedioxyethylamphetamine (MDEA). The remaining 3 were indicative of the Leuckart reaction. These compounds were: N-ethylamphetamine, N-formylmethamphetamine, and N,1,7,7-tetramethylbicyclo-[2.2.1]-heptan-2-amine. In addition to the impurities that were analyzed, the LC-MS method was designed to identify MDMA and caffeine in order to ensure that the presence of the primary ingredient and a popular additive would not inhibit the identification of the analytes of interest. Benzylmethylamine was used as an internal standard.

The LC-MS method developed for the identification of the analytes of interest was able to qualitatively identify all compounds at concentrations above 2µg/mL and identify all amphetamine analytes at concentrations above 1 ng/mL. All analytes were positively ionized and baseline separated.

Three dry extraction methods were utilized for the extraction of the compounds of interest from tablets. The compounds of interest were extracted from 4 different common excipients: cornstarch, d-lactose, d-sorbitol, and microcrystalline cellulose. The extraction solvents were methanol, 0.05 N hydrochloric acid in methanol, and 0.1% trifluoroacetic acid (TFA) in methanol. Percent area ratios were used to determine the percent recovery of each method and these results were compared to the percent recoveries obtained from a previously optimized liquid-liquid extraction method. When extracted from cornstarch, the liquid-liquid extraction had the highest average percent recovery for all compounds at 58 %. Of the three dry extraction methods, the methanolic hydrochloric acid had the highest average percent recovery at 52% where the methanolic TFA had 48% and the methanol had 42%. When the percent recoveries for the individual analytes are compared, the data shows that the methanolic hydrochloric acid was the optimum extraction method for a majority of the analytes, but lower recoveries for MDMA and caffeine drastically reduced the overall average.