A202 Pharmaceutical Identifier Confirmation Via AccuTOF™ DART®

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The goal of the presentation is to show how pharmaceutical identity can be confirmed using tablet physical identifiers and mass spectrum from an Accurate Mass Time-Of Flight Mass Spectrometer, coupled with the Direct Analysis In Real Time ion source (AccuTOF™ DART®).

This presentation will impact the forensic science community by using physical identifiers and the AccuTOF™ DART® to confirm pharmaceutical identity that will eliminate the use of GC/MS and effectively reduce analysis time. This will prove helpful in laboratories with large backlogs and will simplify the confirmation process.

Pharmaceutical tablets are analyzed in a forensic-controlled substances laboratory on a daily basis and comprise a large amount of the casework. The current method for identifying pharmaceuticals at the Virginia Department of Forensic Science (VaDFS) begins with physical identification, using sources such as Ident-A-Drug, The Drug Identification Bible, and RxID software. Thin Layer Chromatography (TLC) is then utilized to screen for the presumptive identity of the pharmaceutical. Alternatively, the AccuTOF™ DART® is utilized for pharmaceutical screening at DFS and is the most definitive screening test. Finally, the tablet is analyzed using a Gas Chromatograph and Mass Spectrometer (GC/MS) to confirm the identity.

The AccuTOF™ DART® is composed of an ambient ion source coupled with an accurate mass time-of flight mass analyzer. The ambient ion source allows samples to be analyzed at atmospheric pressure requiring minimal sample preparation without extraction. The sample molecule is protonated via the DART® and enters the TOF mass analyzer. The mass of the protonated molecule is accurate to ± 5.0 mDa with a much higher resolving power than the nominal mass produced in a quadrupole MS. Higher ion source voltages cause fragmentation through collision-induced dissociation (CID), producing a spectrum similar to an electron ionization source.

This project seeks to investigate the confirmation of pharmaceuticals using the AccuTOF™ DART® after preliminary identification through tablet and capsule markings. The Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG) advises confirming the identity of pharmaceutical tablets through a Category B technique, such as physical identification, and a Category A technique, such as mass spectrometry. Differentiating between pharmaceuticals with the same molecular mass can be difficult when using the AccuTOF™ DART® because the same protonated molecule is produced. For example, codeine and hydrocodone have a molecular mass of 299 Da and will produce a protonated molecule with a mass of 300.160 Da on the AccuTOF™ DART®. By increasing the source voltage, unique ion fragments are expected to appear in the spectrum and will aid in distinguishing between drugs with identical protonated molecules. Cocaine and scopolamine have a molecular mass of 303 Da; when fragmented, cocaine will produce an ion with a mass of 182 Da and scopolamine will produce an ion with a mass of 138 Da. These unique fragments, along with others, differentiate cocaine and scopolamine. Reproducibility of spectra from one data file to another were experimentally determined and statistically evaluated to ensure accurate identification. For pharmaceuticals that do not have an obvious difference in ion fragments, Principal Components Analysis (PCA) was used for differentiation. PCA is a statistical analysis used to discriminate between similar data values. Linear Discriminant Analysis (LDA) was performed on the PCA plot to determine differences between data values. LDA models categorical data through linear combinations to determine differences. It provides an objective, measurable value to the PCA plot.

Results were obtained using DART® parameters of 275°C gas stream temperature, and Orifice one voltages of 30V and 90V. The 90V spectra provided different fragment ions and abundance values for pharmaceuticals with the same molecular mass, thus making it possible to differentiate between hydrocodone and codeine and, similarly, morphine and hydromorphone. A separate analysis was performed on the isomers of codeine: heterocodeine, hydrocodone, neopine, and pseudocodeine. All five were differentiated using PCA and LDA. Over 500 pharmaceutical tablets and capsules, collected from VaDFS casework, were analyzed and their pharmaceutical identifiers were accurately confirmed in this experiment. If the AccuTOF™ DART® spectrum identifies a different drug than what was indicated by the pharmaceutical identifiers, then the sample would be confirmed using the original analysis scheme with the use of GC/MS.

Using physical identifiers and the AccuTOF™ DART® to confirm pharmaceutical identity will eliminate the use of GC/MS and effectively reduce analysis time. This will prove helpful in laboratories with large backlogs and will simplify the confirmation process.

Pharmaceutical, DART®, Mass Spectrometry

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