K57 Paper Spray Mass Spectrometry for Rapid Drug Screening From Dried Blood Spots

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After attending this presentation, attendees will understand the emerging technique of paper spray mass spectrometry and its application in forensic toxicology as an effective, rapid, and simple screening technique for illicit drugs, pharmaceuticals, and their metabolites.

This presentation will impact the forensic science community by providing data demonstrating paper spray's potential to be highly useful to forensic toxicology. As a screening tool, it can effectively expedite and simplify existing procedures for identifying drugs and drug metabolites in biofluids, allowing for higher sample throughput and faster turnaround times.

Paper spray ionization is able to extract analytes and generate gaseous ions directly from dried blood spots and other biofluids at toxicologically relevant concentrations with no sample preparation and minimal solvent usage. Whole blood samples were dried directly onto Whatman™ 31ET Chromatography Paper (although robustness has been proven using other types of paper), which was cut to fit an in-house designed cartridge. With the cartridge placed in front of the inlet to a mass spectrometer, a small amount of solvent (20µL-40µL) was applied to the back of the paper. While most of the large biological molecules are left behind, undissolved in the solvent (typically 95% methanol with 0.01% acetic acid), the soluble analytes are extracted and traveled with the solvent front by capillary action though the paper. Once the solvent had completely wet the paper, a high voltage of 3kV-4kV was applied, inducing an electrospray at the paper's tip. As the charged droplets from the electrospray travel toward the inlet of the mass spectrometer, the solvent evaporates, generating gaseous analyte ions, which then enter the mass spectrometer.

The present study utilized a Thermo Scientific™ TSQ Vantage™ triple quadrupole mass spectrometer operated in Selected Reaction Monitoring (SRM) mode to investigate paper spray's detection limits and selectivity for 154 toxicologically relevant drugs and drug metabolites. Detection limits for the targets were determined by spiking known amounts of the targets into drug-free human blood. Positive identification of a drug or metabolite was achieved when both a qualifier and quantifier SRM transition for the target were present at a predetermined intensity and the ratio between the two transitions was within ±25% of the expected value. The detection limits achieved by direct dried blood spot analysis by paper spray were compared to screening cut-off levels specified by an area toxicology laboratory. These cut-off values ranged from 1ng/mL to 30,000ng/mL, depending on the target compound. Representative analytes spiked into whole blood from the following classes of drugs have already been detected at levels below the desired screening cutoff: anticonvulsants, anesthetics, cocaine and its metabolites, sedatives, benzodiazepines, analgesics, and amphetamines.

Selectivity of the method was assessed by compiling a list from DrugBank and the Human Metabolome Database of drugs and metabolites of drug origin with the same nominal mass as the target compounds. The potential for these compounds to yield false positive results was assessed based on their expected abundance and ionization efficiency relative to the target compound, as well as their MS/MS spectra. In nearly all cases, the selectivity of paper spray MS/MS was adequate. Some cases of interference were identified; however, in nearly all cases, the interferences were closely related structural isomers from the same compound class, such as morphine and hydromorphone.

The data collected on the achievable detection limits and selectivity indicate that paper spray is a promising method for quickly screening for a large number of drugs and drug metabolites in blood.

Paper Spray Mass Spectrometry, Toxicology, Dried Blood Spots

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