

## **Long Abstract**

### **Paper Spray Ionization - Tandem Mass Spectrometry for Quantification of Prescription Drugs in Oral Fluid**

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Paper Spray (PS) is an ambient ionization technique used with mass spectrometry (MS) for rapid analysis from complex matrices. Briefly, the procedure includes drying a sample onto a piece of triangular shaped paper, placing the paper in front of the MS source, wetting the paper with solvent, and applying a high voltage using a copper clip which generates ions via electrospray-like mechanisms (Fig 1). PS seeks to remove the need for complex sample preparation (e.g., SPE) as well as time consuming and expensive chromatographic separations (e.g. LC and GC), but still relies on MS for specificity, particularly enhanced with multiple stages of mass analysis (MS/MS). PS-MS/MS allows for the analysis of drugs and small molecules in biofluids, e.g. whole blood, plasma, urine and oral fluid. Applications include point of care diagnostics, roadside drug testing, pharmaceutical metabolite studies and many more. Presented here is a rapid method for the detection of prescription drugs and their metabolites in oral fluid.

Experiments were performed with a Thermo Fisher Quantum Max triple quadrupole mass spectrometer. Opiates and opioids, benzodiazepines, and tranquilizers were detected in positive ion mode via multiple reaction monitoring, selecting two fragments per drug to increase the specificity of the analytical signal. Less than 10  $\mu$ L of oral fluid spiked with stable isotopic internal standards was spiked onto triangular shaped filter paper. Methanol: water 95/5, doped with 0.1% of formic acid constituted the solvent system. Analytes were detected in less than 3 min.

All tested compounds were selectively detected down to the ng/mL range. A more complete study of analytical figures of merit is ongoing.

This PS-MS/MS methodology allows for straightforward analysis of intact oral fluid, which is applicable for point-of-care screening and confirmatory drug testing, especially when coupled with automated interfaces for paper preparation such as are available from Prosofia, Inc. PS-MS/MS significantly lowers sample volume requirements for oral fluid testing in comparison to chromatographic assays, and reduces turnaround times for quantification of target drugs. Both aspects are of key importance for clinical applications, considering that a large volume of oral fluid can be difficult for many patients to provide, and that routine screening of patients' biological fluids may be required, e.g. in pain management. PS methodology may be easily adapted to other biological matrices however, oral fluid testing is beneficial for both the patients and clinicians because it is less invasive and more difficult for the patient to tamper with the sample.

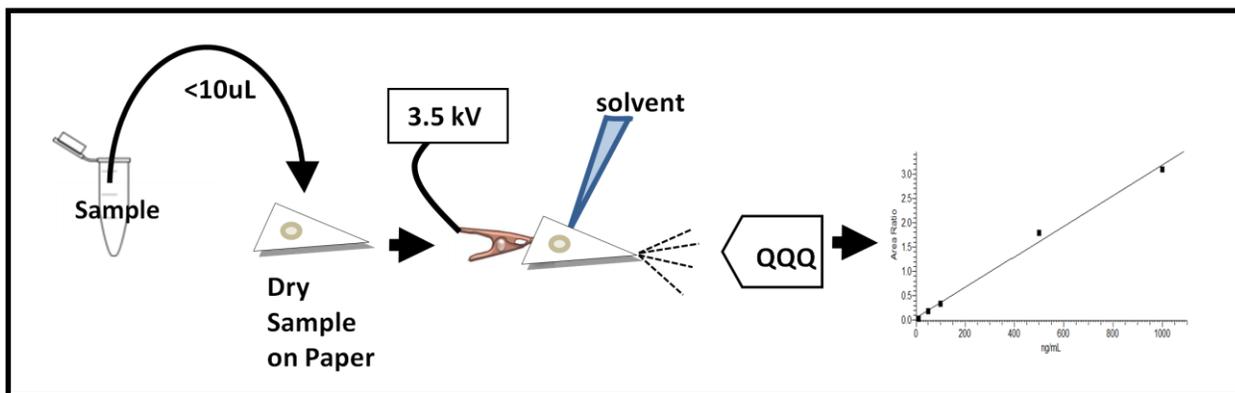


Figure 1: PS-MS/MS methodology outline from sample to quantitative results.