

Clinical research and toxicology

Paper spray mass spectrometry simplifies and expedites turnaround of drug toxicity screening

King's College London aims to investigate its use in emergency department applications

Summary

Forensic researchers from King's College London (KCL) are using cutting edge equipment from Thermo Fisher Scientific to carry out critical research relating to the detection of drugs in human samples with suspected acute drug toxicity. A partnership between the university, Guy's and St Thomas' NHS Foundation Trust, and Thermo Fisher Scientific is exploring the potential for faster analysis of blood samples from patients presenting with acute drug toxicity to the emergency department (ED). The research could pave the way for new, routine methods of acute drug toxicity detection and quantification in the hospital that ultimately may improve health outcomes for individuals presenting to the emergency department.

Specifically, KCL researchers are utilizing novel paper spray mass spectrometry (PS-MS) technology from Thermo Fisher, the [Thermo Scientific™ VeriSpray™ PaperSpray ion source](#), to investigate the stability of drugs in dried matrices and validate its utility in more efficiently quantifying drugs in samples from patients presenting to the ED with minimal to no sample preparation. During proof-of-concept testing, the research team has processed hundreds of samples for pre-validation and method optimization, and currently has more than 500 human plasma samples exhibiting acute drug toxicity stored for future analysis with an ongoing sample collection of approximately 20 samples per month.



Figure 1. VeriSpray PaperSpray ion source for mass spectrometry attached to a TSQ Altis mass spectrometer

Preliminary results shared at The International Association of Forensic Toxicologists (TIAFT) 2023 annual meeting in Rome, Italy, showed that the researchers have been able to achieve good linearity for 6 drugs across a range of concentrations. To offer an alternative to the current clinical management of acute drug toxicity, which is based on self-reporting and treating the clinical features, the KCL team is optimizing the process to enhance accuracy, working toward the potential implementation of PS-MS into the clinic.

Introduction

Acute recreational drug toxicity is a common reason for emergency department presentation. Although the mortality rate associated with these presentations is low in the UK, they can lead to significant morbidity and prolonged hospitalization.¹

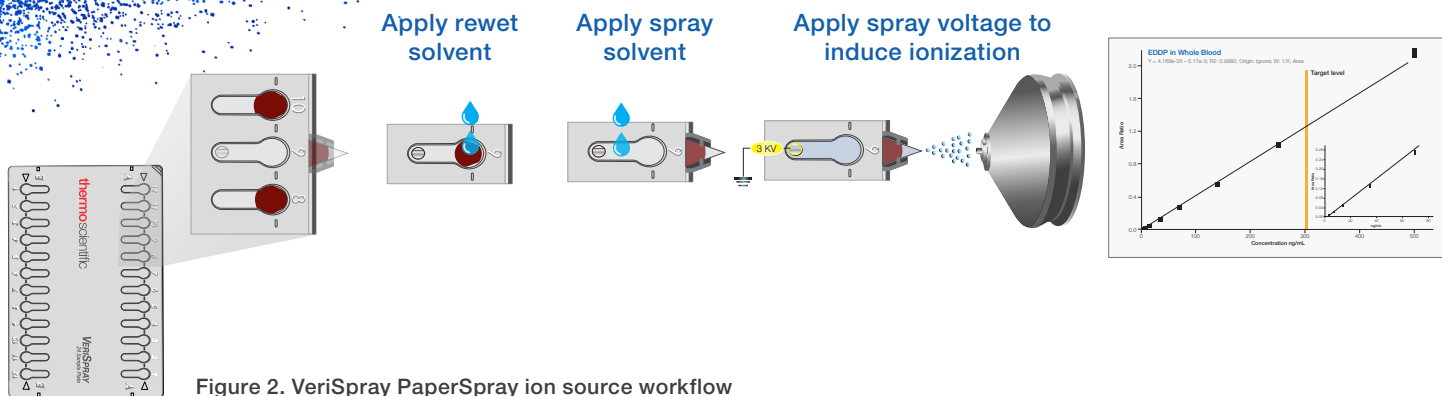
Further, those with acute drug toxicity presenting to the ED are not always able to tell clinicians what substances they have taken or may have been exposed to, leading to uncertainty in the

drug(s) involved. Toxicology screening with confirmatory liquid chromatography mass spectrometry (LC-MS) techniques is not routinely undertaken in these individuals because results are not available within a timeframe which would influence treatment. Therefore, techniques which offer fast detection and quantification of the drugs involved in these presentations could be an important advantage in the management of these patients. Researchers at King's College London are focused on advancing research that may help meet this need by identifying methods for faster turnaround of blood sample analysis enabling clinicians to be promptly advised of the drugs involved and inform treatment.

To support this research, Thermo Fisher installed a VeriSpray PaperSpray ion source system at KCL, Franklin-Wilkins Building, Waterloo Campus in November 2022.² Alongside the novel VeriSpray ion source, the installation included the latest generation, high-sensitivity Thermo Scientific™ TSQ Altis™ Plus Triple Quadrupole mass spectrometer in the research laboratory (Figure 1).

“I am delighted that this translational healthcare research using sophisticated mass spectrometry is being supported by this important agreement with Thermo Fisher and my colleagues at King's College London and Guy's and St Thomas' NHS Foundation Trust, which we anticipate will have international impact.”

—Dr. Vincenzo Abbate, Reader in Bioanalysis, King's Forensics



The VeriSpray ion source utilizes a paper spray ionization technique that offers a new method of analyzing samples of biological fluids, such as blood, to identify and quantify the concentration of analytes within a sample. The VeriSpray ion source applies a rewetting solvent to the sample that has been spotted and dried onto the paper. A high voltage is then applied, ionizing the sample molecules which enter the mass spectrometer.

Using archived human samples, the team is testing the equipment's ability to identify and quantify the drugs, both when they are a pure substance and when they are present in samples of blood. The researchers are also investigating the applicability of using this technique to provide fast and accurate measurements with small samples of blood, to confirm its viability for hospital use.

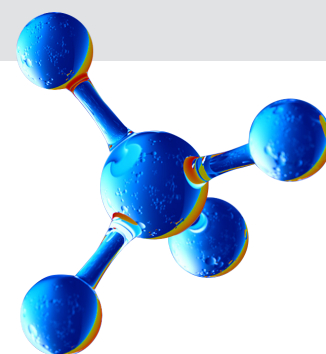
Winning combination: Minimal sample preparation, high-throughput and ease-of-use

With the VeriSpray ion source, the sample is eluted off a paper substrate directly to the mass spectrometer—requiring minimal sample preparation and eliminating the need for a liquid chromatography (LC) step. This allows researchers to go from sample collection straight to analysis quickly and easily. The system is designed for ease of use, allowing students and other beginners to operate it effortlessly.

The VeriSpray PS-MS plate loader magazine can be loaded with 10 cartridge plates at once, so 240 samples can be run, unattended, in 8 hours (Figure 2). The machine runs the samples sequentially and autonomously, with each run taking just 1–2 minutes. The system will also allow a single cartridge plate or even a single sample to be run if time is critical. This capability makes the system more efficient and provides better throughput than other drug-checking solutions, leading to faster results.

PS-MS offers many advantages compared to other clinical methods such as LC-MS

- **Rapid:** Analysis is performed in 1–2 minutes. It has direct sample analysis capability and does not require chromatography-based separation or lengthy sample preparation/cleanup.
- **Efficient:** The sampling device is disposable, streamlining processes as a result of reduced labware cleaning requirements and solvent/reagent use.
- **Quantitative:** The technique provides trace amount, quantitative results for highly toxic drugs such as fentanyl.
- **Accurate:** The sample is compared against deuterated internal standards for accurate quantification.
- **Easy to use:** Removal of the LC system translates to reduced training needs and leads to additional cost-savings.
- **Clean:** Each sample is run on a different sample spot, removing the risk of cross-contamination.
- **Sustainable:** The process uses less chemicals and solvents, making for a more environmentally friendly approach.



Evaluating methods for drug toxicity screening at the bedside

The benefit of VeriSpray PS-MS compared to traditional LC-MS technologies for toxicological identification of drug analytes is that the lengthy, multi-step workflow that often posed a roadblock to adoption in a clinical setting is eliminated. LC-MS methods work well for surveillance and large sample processing. However, LC-MS does not allow for fast results, which delays critical treatment for patients exposed to toxic substances who need immediate care. Leveraging the innovative VeriSpray PS-MS technique from Thermo Fisher, KCL researchers are working to streamline the traditional sample preparation and targeted analysis process, making drug toxicity screening at the bedside a possibility in the future.

VeriSpray PaperSpray ion source offers a fast turnaround time for high-throughput screening, and it would allow clinicians to run a single sample from a patient to expedite analysis and identification of the drug or substances present. As one of the first commercial systems that allows PS-MS to be put into practical use, VeriSpray PS-MS allows for routine analysis with the intent to standardize the workflow in laboratories around the world, removing manual steps and reducing the opportunity for human errors to be introduced in multi-step processes.

Empowering tomorrow's scientists

VeriSpray PS-MS is highly adaptable, making it ideal for future drug testing requirements, particularly as new psychoactive substances (NPS) are developed and misused. These NPS can easily be added to the test panel over time to keep screening processes current. With the [Thermo Scientific™ Tox Explorer™ Collection](#), which currently has a SRM library of over 2,000 drugs, researchers and clinicians have access to a dynamic and flexible panel of identified drugs capable of expansion with future findings and advancements.

Today's young scientists, whether training to become the next generation of toxicologists, studying in a post-graduate program, or beginning a career in industry, will benefit from the ease-of-use that VeriSpray PS-MS offers compared to more complex LC-MS instruments.

Conclusion

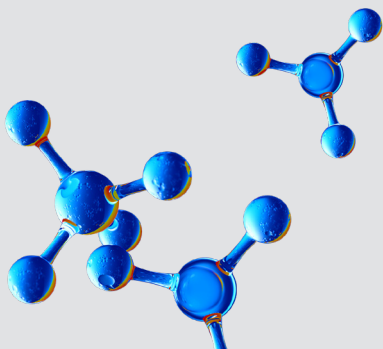
The research done by King's College London is the first step in looking at the potential of VeriSpray PS-MS to facilitate EDs in delivering point-of-care testing for individuals with acute drug toxicity. By having rapid drug screening completed closer to the individual—within the same hospital and even the same floor, hospitals can avoid the lengthy process of sending samples to specialty laboratories at a separate site. With broader adoption, this accessibility could reduce the waiting time for results from multiple days to minutes, greatly improving healthy outcomes.

References

1. [Toxicology in the emergency department: what's new?](#)
2. [Thermo Fisher Scientific collaboration offers potential for faster, more efficient analysis of samples from drug toxicity patients](#), March 9, 2023.

“The ease of use of the VeriSpray PS-MS has the additional benefit of enabling students to gain valuable instrument training regardless of their skill level. Through hands-on experience, students can quickly and effectively develop their expertise in the ever growing field of ambient mass spectrometry and carry this knowledge forward as they progress in their careers.”

—Stefania Boccuzzi, PhD Student, King's Forensics





Acknowledgement

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