

Exploring Rapid, Sensitive and Reliable Detection of Trace Explosives Using Paper Spray Mass Spectrometry (PS-MS)

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Abstract: In this publication we work towards providing fast, sensitive and selective analysis of explosive compounds collected on swabs using paper spray mass spectrometry. We have (a) increased the size of the paper spray substrate to 1.6 × 2.1 cm for compatibility with current practise in swabbing for explosive material; (b) developed a method for determining a successful extraction of analyte from the substrate to reduce false negative events; and (c)

expanded the range of analytes that can be detected using paper spray to include the peroxide explosive HMTD, as well as nitroglycerine (NG), picric acid (PA) and tetryl. We report the development of a 30 s method for the simultaneous detection of 7 different explosive materials using PS-MS with detection limits below 25 pg, as well as detection of HMTD at 2500 pg, showing an improvement on previously published work.

Keywords: Explosives · Paper Spray · Mass Spectrometry

1 Introduction

An increase in the threat level associated with terrorist activities has prompted the development of new analysis techniques, and concomitant methods for rapid detection of trace amounts of explosive materials. Several techniques are available, including chemiluminescence [1–4], thermo-redox [3–6], surface acoustic wave [4, 7, 8], chemical reagents [9], spectroscopy methods [4, 10–13], mass spectrometry (MS) and ion mobility spectrometry (IMS) [4, 14–31].

Thermal desorption (TD) coupled with IMS is the most common technique used in recognised “high-risk” areas to screen passengers and their personal belongings including luggage. This combination of techniques utilises the high vapour pressures of common explosives (e.g. trinitrotoluene) to thermally desorb the explosive materials from the swab, allowing these materials to become ionised using atmospheric pressure chemical ionisation (APCI) before being separated and detected using IMS [15, 32–34]. The popularity of TD-IMS arises from its portability, high sample throughput, ease-of-use and set-up. However, successfully using IMS as a detection technique is sample dependent, as poor peak resolution often results in unresolvable background and analyte peaks, giving rise to false positives. This lack of selectivity can be overcome through using gas chromatography (GC) which provides separation of materials prior to detection. However, using GC increases the analysis time from a few seconds to several minutes making it unsuitable for this specific application [14, 15]. TD-IMS also requires the sample to be introduced in vapour form. Whilst this is not a problem for explosives such as nitrotoluenes and nitroglycerine de-

rivatives, others such as 1,3,5-trinitro-1,3,5-triazinane (RDX), hexamethylene triperoxide diamine (HMTD) and 1,3,5,7-tetranitro-1,3,5,7-tetrazocane (HMX) have been found to have inefficient desorption processes due to their lower vapour pressures and thermal instability [15, 16, 35, 36]. The wide range of vapour pressures and thermal labilities of the explosive materials make developing a universal method using TD difficult; optimising experimental conditions for one material would result in a decrease in sensitivity for another. Therefore, development of a non-temperature dependent sample introduction technique and coupling it to an instrument that enables the simultaneous detection of multiple analytes without compromising the sensitivity of the analysis, may help compensate or eliminate some of the issues currently associated with TD-IMS.


Mass spectrometry based methods offer versatility as there is a wide range of ionisation sources currently available, namely direct ionisation and ambient mass spectrom-

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etry techniques, that enable rapid analysis with minimal sample preparation [37]. Several ambient ionisation techniques have been used for explosive detection [38], desorption electrospray ionisation (DESI) [17, 18, 20, 37, 39, 40], direct analysis real time (DART) [25, 27, 41], desorption atmospheric pressure chemical ionisation (DAPCI) [42], dielectric barrier discharge (DBDI) [21] and low-temperature plasma (LTP) [26]. Recently, paper spray-mass spectrometry (PS-MS) [43] has been successfully applied to explosives detection [30, 31]. This technique, which has been extensively developed for drug detection in blood spots [44] and a variety of other matrices, including fingerprint samples [45], offers the potential for a fast analysis method with high levels of sensitivity. The traditional analysis methods for PS-MS use a triangular piece of paper onto which the sample is collected [43]. PS-MS has been shown to be versatile, enabling analytes to be measured directly from different substrates, including leaves [46], medical swabs [47] and probes (e.g. needles) [48]. Thus, it follows that the technique could be adapted for fast explosive screening directly from a swab. In this publication, we consider the optimal solvent systems required for rapid, simultaneous detection of multiple explosive compounds.

Tsai *et al.* [30, 31] have applied PS-MS for explosives detection for TNT, RDX, HMX and PETN with sensitivities of 1, 0.5, 0.06 and 0.1 ng, respectively. Bain *et al.* [29] also reported detection of these compounds using swab touch ionisation, which follows a similar principle to paper spray. In this publication we have (a) developed a novel method for determining a successful extraction of analyte from the substrate to reduce false negative events; (b) increased the size of the paper spray substrate for compatibility with current practise in swabbing for explosive materials [49] and (c) expanded on the range of analytes that can be detected using paper spray to include the peroxide explosive HMTD, as well as nitroglycerine (NG), picric acid (PA) and tetryl. We report the development of a 30 s method for the simultaneous detection of 7 different explosive materials using PS-MS with detection limits in the pg range.

2 Experimental Section

The PS-MS source was built in-house and utilises the Thermo Nanospray Flex™ Ion Source casing. This was coupled with a Thermo Scientific™ Q Exactive™ Hybrid Quadrupole-Orbitrap™ mass spectrometer (Thermo Scientific, Bremen, Germany). Data was acquired using Xcalibur 2.10 software (Thermo Scientific, Bremen, Germany). The paper spray substrate was Whatman grade 1 chromatography paper, cut into a triangular (1.6 × 2.1 cm, b × h). Aluminium foil and a glass slide were used for the analysis to prevent contamination of the source and consequent carry-over effects, as shown in Figure 1.

Explosive standards were prepared from certified reference materials (Kinesis, St Neots, UK). Chloramphenicol

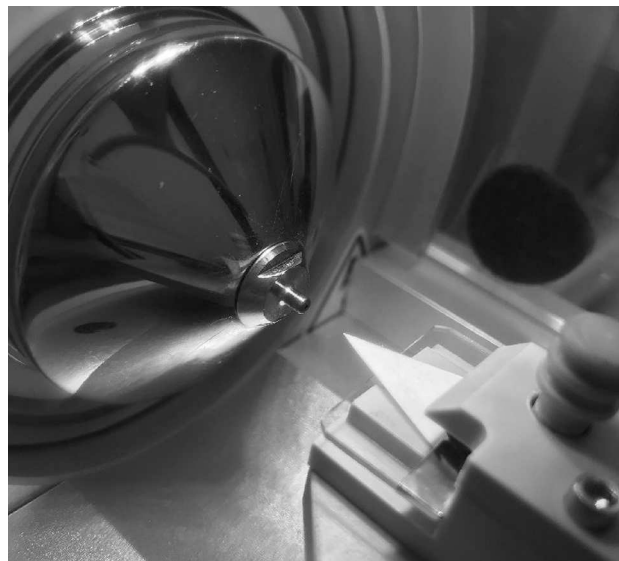


Figure 1. Paper spray source (right) coupled with Thermo Scientific™ Q-Exactive Plus Orbitrap™ (left).

(CAM) was obtained from Sigma Aldrich (Poole, UK). Optima™ LC-MS grade solvents (methanol (MeOH), acetonitrile (ACN), isopropanol (IPA) and water) were used to prepare all solutions and solvent mixtures (Fischer Scientific, Loughborough, UK). The analytes targeted in this work, their corresponding monoisotopic mass and commonly formed adducts are listed below in Supplemental Data Table 1. HMTD, which forms positive ions, was optimised separately from the other analytes, known to form negative ions.

The mass spectrometer parameters (capillary temperature, spray voltage and S-lens RF level) for negative ion mode were optimised using a solution containing 100 ng/mL of TNT, RDX, HMX, PETN, tetryl, NG and PA. The solution was prepared in 50:50 (%v/v) MeOH:ACN with 10 mM $\text{NH}_4\text{Ac}/\text{NaCl}$ and infused into the electrospray (ESI) source using a syringe pump set to 5 $\mu\text{L}/\text{min}$ flow rate. Because of the two additives added to the solutions, several adducts can potentially be formed (see Supplemental Data Table 1) giving more peaks for substance identification. Optimal parameters were chosen based on the sum of the peak intensities for all adducts detected. Optimised parameters for detection of explosives in negative ion mode using ESI was a 90 °C capillary temperature, a 4 kV applied voltage and a S-lens RF level of 80.

Optimisation of the paper spray parameters was performed and included optimisation of (a) the composition and (b) volume of the spray solvent, (c) spray solvent additives and (d) applied voltage.

In PS-MS, there is a phenomenon that happens relatively infrequently (~2% of measurements) in which a measurement is set up, but analytes do not reach the mass spectrometer, we refer to this as a “failed spray”. This can be caused by many factors, including bending of the paper

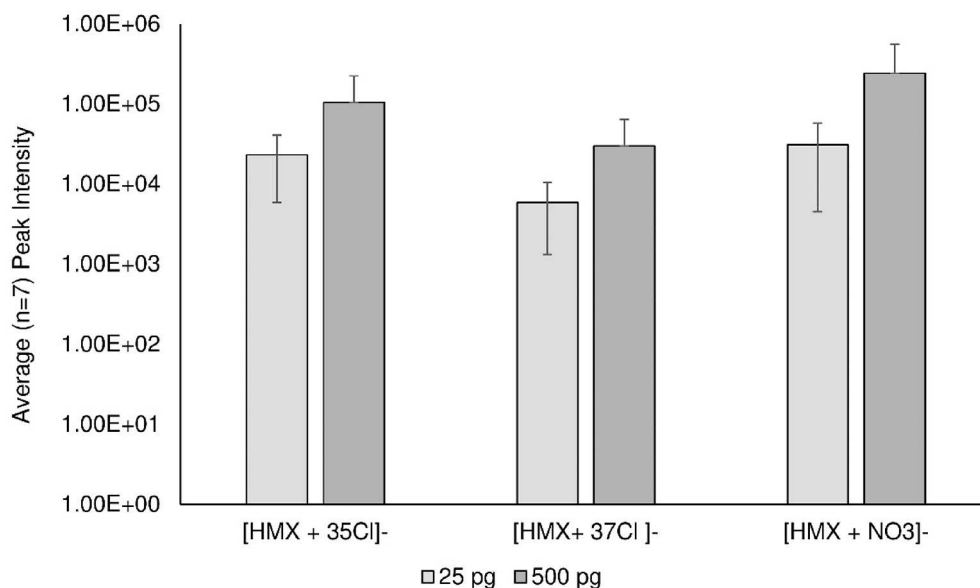


Figure 2. Average (n = 7) peak intensity for the three main HMX adducts observed at low (25 pg) and high (500 pg) mass.

substrate or poor alignment with the mass spectrometer interface. Failed sprays are undesirable for explosive screening applications as they may lead to false negative events; where an explosive that has been picked up on a swab is not detected. To indicate that material had been successfully extracted from the paper swab three compounds, (chloramphenicol (CAM), 2,4-dinitrotoluene (DNT) and paracetamol) selected for their ability to ionise well in negative ion mode, were investigated to act as an internal standard and thus monitor the efficacy of the spray.

3 Results & Discussion

3.1 Paper Spray Method Optimisation – Negative Ions

The effect of the composition of the spray solvent on the observed intensity of relevant analyte ions is presented in the supporting material, Supplemental Data Figure 1. In contrast to Tsai *et al.* [31] we adopted 100% MeOH with 1 mM of $\text{NH}_4\text{NO}_3/\text{NaCl}$ because it produced the highest peak intensities across this expanded range of analytes. The spray solvent additive was reduced from 1 mM $\text{NH}_4\text{NO}_3/\text{NaCl}$ to 0.1 mM $\text{NH}_4\text{NO}_3/\text{NaCl}$ to prevent ionisation suppression as a result of the high salt content and this resulted in an increase in analyte signals, as presented in Supplemental Data Figure 2.

The volume of spray solvent was optimised due to the area of the paper spray substrate here being an order of magnitude larger than in previous work [30,31]. Spray solvent volumes of 20, 50 and 100 μL were tested. It was found that, for a 30 s acquisition, 50 μL of spray solvent produced the highest peak intensities from all the analytes

of interest as shown in Supplemental Data Figure 3. Voltages between 1 and 5 kV in increments of 0.5 kV were tested and 2 kV was found to yield the highest peak intensity for all analytes in negative ion mode, as shown in Supplemental Data Figure 4.

Supplemental Data Table 1 shows the percentage distribution of each adduct ion formed using the optimised paper spray method, based on a 250 pg of standard (average of n = 5 replicates). Detection of multiple adducts can be used to confirm detection of a particular explosive compound. For example, Figure 2 shows that for either 25 or 500 pg of HMX, three adduct signals are detected in each replicate measurement and that in most cases, the relative intensity of each adduct ion is repeatable.

3.2 Introduction of Internal Standard

As mentioned in the experimental section, the use of an internal standard was investigated as a spray monitoring tool to reduce false negative events. Paracetamol, DNT and CAM were investigated as candidate internal standards due to their known ability to form negative ions [50–52]. DNT in particular was investigated as a potential internal standard due to its chemical similarity with TNT. However, internal standards of DNT (500 pg) and paracetamol (5 ng) did not produce abundant ion signals for any identified adducts (see Supplemental Data Table 1) using negative ion method.

Both 500 pg and 2500 pg CAM produced signals corresponding to $[\text{M}-\text{H}]^-$ and $[\text{M}+\text{NO}_3]^-$. The RSD of 5 replicate measurements is reduced from 105% at the lower mass of CAM to 42% at the higher mass. A T-test was performed on

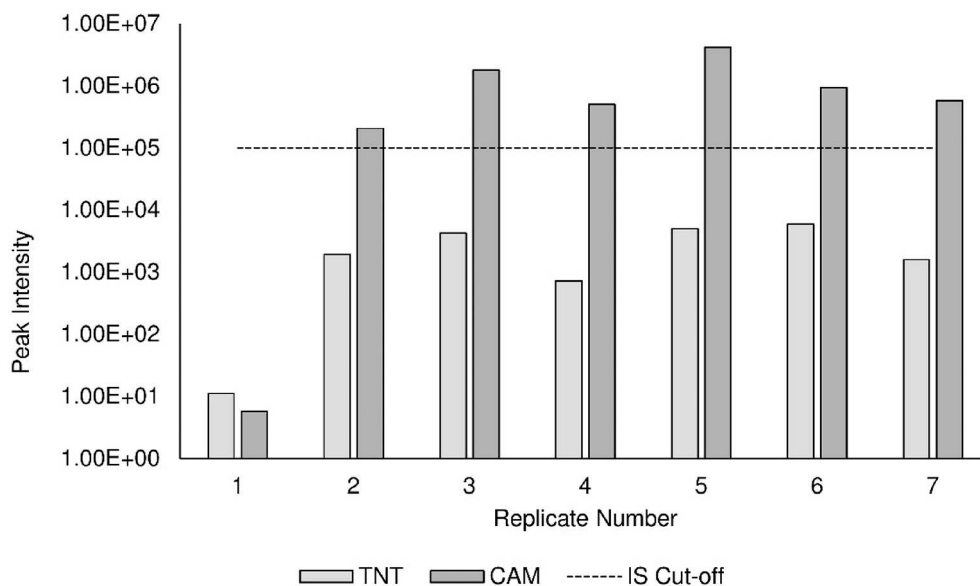


Figure 3. Peak intensities measured for TNT (50 pg) and CAM (2500 pg) using the paper spray method developed for the detection for explosives in negative ion mode. The dashed line shows the proposed cut-off level ($1e5$) for the internal standard to be used to determine failed sprays.

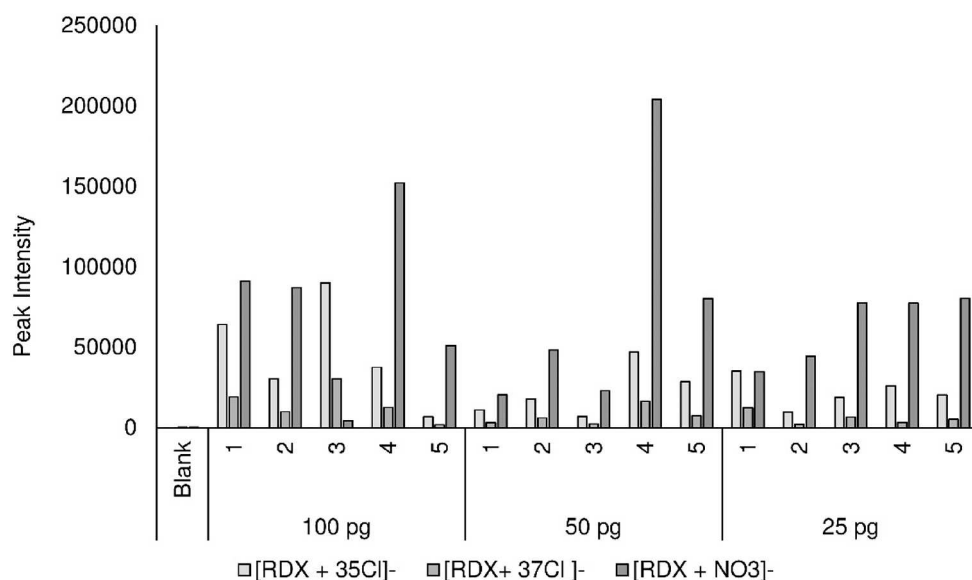


Figure 4. Measured peak intensity for RDX at 25, 50 and 100 pg measured using the paper spray method developed for the detection of explosives in negative ion mode.

500 pg explosive standards with and without the addition of the internal standard to test for ion suppression of the analyte due to the preferential ionisation of the internal standard. At $\alpha=0.05$, T_{calc} was 0.506 and at 6 degrees of freedom T_{crit} is 2.447 for a two-tailed test $T_{\text{calc}} < T_{\text{crit}}$ and therefore the null hypothesis is accepted. This would suggest that addition of CAM as an internal standard did not result in ion suppression of the analytes of interest. Figure 3 shows that when a spray fails (i.e. due to poor alignment),

the intensity of the peaks measured for 2500 pg of chloramphenicol falls below 1×10^5 counts, and the signal observed for 50 pg TNT drops appreciably. Therefore we propose the use of a 2500 pg CAM standard with an acceptance threshold of 1×10^5 counts (based on the sum intensity of CAM peaks as specified in Supplemental Data Table 1) as a spray monitoring tool.

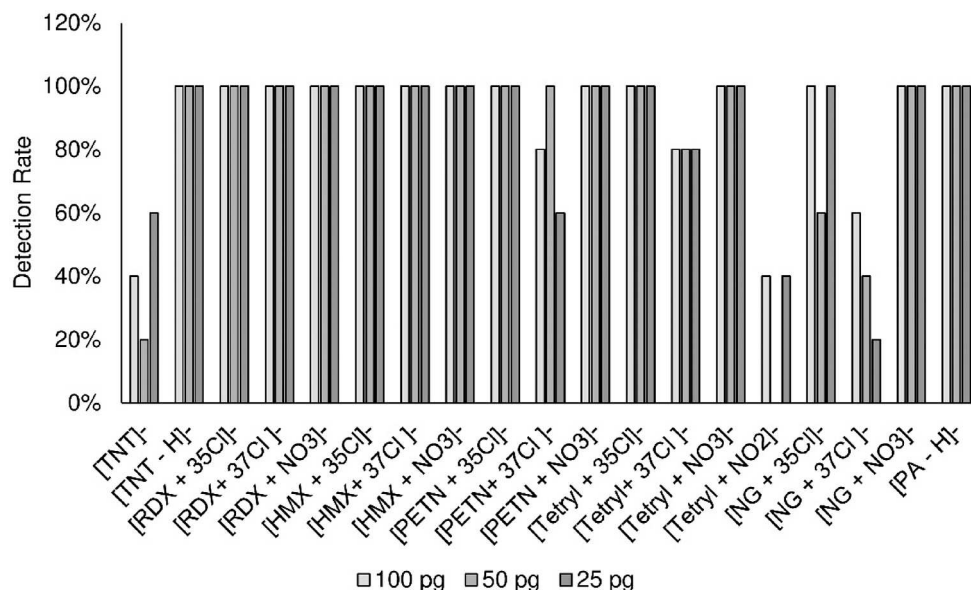


Figure 5. Detection rate based on 5 measurements of each adduct formed at 100, 50 and 25 pg of analytes in negative ion mode using paper spray mass spectrometry.

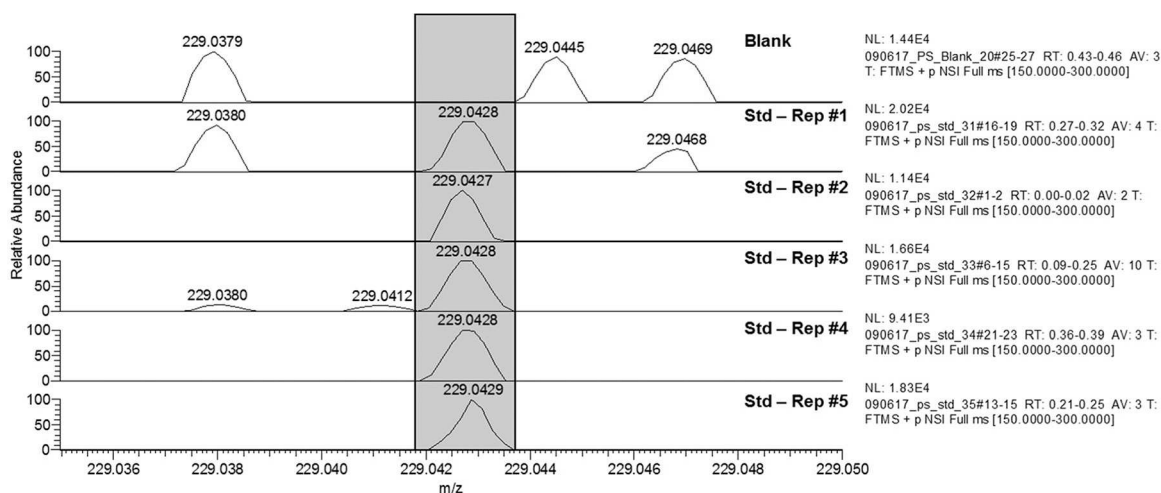


Figure 6. Example spectra showing the HMTD signal $[HMTD-2H+Na]^+$ in blank measurements (top spectrum) and 5 replicate standard measurements using PS-MS. 2500 pg of HMTD were deposited on the substrate for analysis (5 μ L of 500 ng/mL).

3.3 Application to Low Mass Explosive Standards

Standards were prepared at 100, 50 and 25 pg and analysed with the paper spray method described above. Figure 4 shows the measured peak intensities for each of the detected adducts of RDX after application of the internal standard cut-off defined above. This demonstrates the sensitivity of the method developed here, where at 25 pg, every RDX adduct is detected. Supplemental Data Figure 5 shows the corresponding data for the other explosive compounds. Each of the explosive materials were systematically detected in all 5 replicate measurements (based on the

most abundant adducts), showing the possibility of detection down to 25 pg in each case. The detection rate of each adduct being monitored (Supplemental Data Table 1) was found to vary (Figure 5) for the different analytes. For RDX and HMX there are 3 peaks corresponding to NO_3 , ^{35}Cl and ^{37}Cl adducts that are systematically detected in all replicates at all masses, which can be used to aid identification. For PETN, tetryl and NG only the NO_3 adduct was consistently detected. For TNT and PA, only $[M-H]^-$ peak was consistently detected.

3.4 Detection of HMTD in Positive Ion Mode

The detection of HMTD using paper spray was demonstrated using the optimised solvent composition and spray solvent volume determined already for the negatively ionising analytes. The applied voltage was increased to 3.5 kV and mass spectra were acquired in positive ion mode. HMTD was detected at m/z 229.0431 ([HMTD-2H+Na]⁺), as shown in Figure 6. We believe this is the first time that peroxide explosives have been successfully detected using paper spray mass spectrometry and the data here supports the possibility of analysing both positive and negative analytes from the same sample.

4 Conclusions

A rapid (30 s) and sensitive (LOD < 25 pg) method for the simultaneous detection of explosive materials (TNT, RDX, HMX, PETN, tetryl, NG and PA) in negative ion mode was developed and optimised using PS-MS. Addition of additives aids identification by the production of multiple adduct peaks, in particular for HMX, RDX, PETN, tetryl and NG. Optimisation of the method included the addition of chloramphenicol as a spray monitoring tool to prevent false negatives. We also report, for the first time, on the detection of HMTD (2500 pg) using this method.

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FULL PAPER



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Exploring Rapid, Sensitive and Reliable Detection of Trace Explosives Using Paper Spray Mass Spectrometry (PS-MS)

