High-Throughput Screening of Explosive Residues

Using a Thermal Extraction Ionization Source (TEIS) Coupled with a SCIEX QTRAP® 4500 System

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The rise of terrorism in recent years is a constant reminder that terror attacks remain a significant threat globally. The recurrence of these attacks underscores the pressing need for homeland security agencies to adopt detection platforms capable of rapidly screening trace levels of explosives with a high level of sensitivity and selectivity. Improvised explosive devices[1] (IEDs) are a prime example of threats that drive the need for improved chemical detection and screening capabilities. Currently, analytical security screening methods for the detection of illicit and explosive residues in public places rely on the combination of thermal desorption (TD) with ion mobility.[2] However, ion mobility suffers from lack of sensitivity and specificity, which often results in a high rate of false positives. In addition, confident identification cannot be achieved solely by measuring collisional cross section. As a result, there is a need to develop detection methods capable of reliably screening for trace explosives.

In this technical note, a thermal extraction ionization source (TEIS)[3] that operates with Thermal Desorption-Atmospheric Pressure Chemical Ionization (TD-APCI) is coupled with a SCIEX QTRAP 4500 System for the accurate identification of explosive residues without the need for chromatography. The combined system is shown to produce rapid and confident compound identification suitable for rapid security screening.

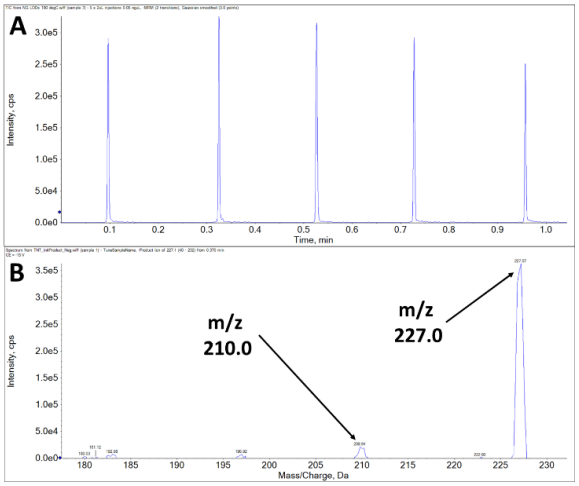
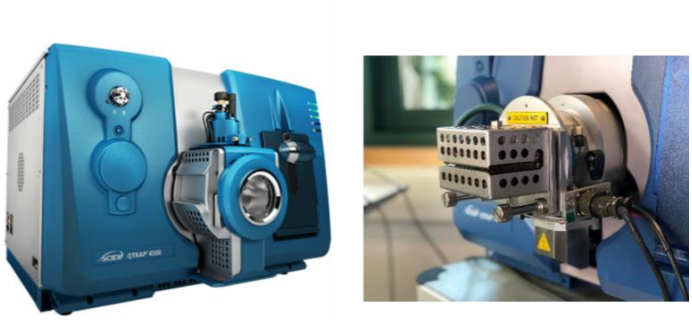


Figure 1: Extremely Fast and Reproducible Analysis of Trinitrotoluene (TNT) Using Direct Injection Analysis with the TEIS. A) Total Ion Chromatogram (TIC) showing 5 x 2 µL manual injections within a minute of 0.1 ng of trinitrotoluene (TNT) for the ion transition *m/z* 227.0/210.0, B) Product ion scan for $[TNT]^-$ ion at m/z 227.0.



Key Features of the TEIS Coupled to the QTRAP 4500 System for Real-Time Detection of Explosive Residues

- Rapid robust approach allows direct MS analysis of explosive residues without sample preparation or chromatography
- Direct sampling from fingerprint swabs enables confident residue detection within seconds
- Targeted MRM workflow allows sensitive explosive residues detection with higher selectivity and confidence in identification
- Additionally full scan MS/MS can be employed for even higher confidence
- Quantitation method described provides an estimate of the amount of unknown explosive residues transferred to a swabs
- Combination of the TEIS with QTRAP 4500 System for direct analysis is an ideal fit for screening and confirmation applications, providing high levels of sensitivity and robustness for residue detection

Methods

Sample Preparation: Pentaerythritol tetranitrate (PETN), ethylene glycol dinitrate (EGDN), nitroglycerine (NG), 2,4,6-trinitrotoluene (TNT), hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX), erythritol tetranitrate (ETN), octahydro-1,3,5,7-tetranitro-1,3,5,7-triazine (HMX) and pentaerythritol tetranitrate (PETN) were obtained from Accustandard Inc. (New Haven, CT). Standard solutions were obtained at 100 ng/µL and diluted in MeOH to create calibration solutions ranging from 0.0005 ng/µL to 1 ng/µL. Fingerprint depositions were created using an individual who handled a highly contaminated phone and then deposited their fingerprints onto glass slides, 90 consecutive times. Residues from the sixth fingerprint were selected for analysis and the glass slide was sampled using a sterile cotton swab prior to being introduced between the two hot plates of the TEIS.

Ionization Source: The Thermal Extraction Ionization Source (TEIS) was heated to 190 °C to volatilize the solvent injection (or analyte on a swab) and a sample pump was used to draw the gaseous molecules towards the ionization region with a flow of 25 L/min. A chloride adduct was used by introducing dichloromethane (methylene chloride) via a gas bubbler. The APCI needle voltage was controlled using the ESI spray voltage setting.

Sample Introduction: Using the injection port at the front of the top block for liquid standards, 2 µL of samples were injected via a microliter syringe. Residues from cotton swabs were inserted in the slot between the two heated blocks.

Mass Spectrometry: Analysis was performed on the SCIEX QTRAP 4500 system using Analyst® Software 1.6.3. Compound optimization was performed on each compound to determine the best source conditions for ionization. The explosive standards were analyzed using a targeted Multiple Reaction Monitoring (MRM) method and the compound dependent parameters were tuned for each fragment independently. The best two MRM transitions for each compound were selected and used for identification and quantification of the explosive residues in the study.

Data Processing: MultiQuant™ Software 3.0 was used for data processing. Using global integration parameters for all peaks within the run, the multiple fragments monitored were averaged together for each analyte calibration series. The integration parameters used are shown in Table 1.

Table 1. Global Integration Parameters.

Parameter	Setting
Quantitation Method	*IntelliQuan MQ4*
Min Peak Width	*3 points*
Min Peak Height	*500 cps*
Speak Split Factor	*8*
Gaussian Smooth Width	*3 points*
Noise Percentage	*80%*
Baseline Subtract Window	*2 min*

Development of a Strategy for High Throughput Detection of Explosive Residues

To get started with the analysis, the SCIEX QTRAP 4500 System was first calibrated by following the standard protocol using the Turbo V™ Source. Compound optimization was performed for each explosive compound in ESI mode. The Turbo V Source was then removed and substituted for the TEIS. The source temperature was set to 190˚C using the source controller and connected to a bubbler containing dichloromethane. Nitrogen was pumped through the bubbler at 0.1 sccm to create dichloromethane vapor at approximately 5 mM. The chloride adducts combine with the explosive compounds to form $[M+Cl]^-$ which aids detection. Using a chloride adduct improves the ionization efficiency of some explosives, but also provides additional information, such as the use of chlorine isotopes (^{35}Cl and ^{37}Cl), improving discrimination and identification confidence.

Figure 1A shows the typical signal response from the instrument in the form of a Total Ion Chromatogram (TIC) following five sequential 2 µL manual injections of 0.1 ng of trinitrotoluene (TNT), highlighting the speed of analysis possible and 2 of signal response from the instrument. All injections done for method development were performed using a manual, 2 µL direct injection, using a sterile glass syringe which contributed to some variance observed in peak responses. Figure 1B shows the resulting product ion scan for $[TNT]^-$ ion at m/z 227.0.

Generation of Calibration Curves

The MRM acquisition method used in this study allows quantitation of the explosive compounds through the detection of multiple fragment ions, meaning additional confidence in forensic analyte detection at low ng/µL concentration levels. To generate calibration curves, the series of calibrator solutions were manually injected for each of the explosive compounds. Two MRM transitions were monitored per explosive compound across five sequential 2 µL manual injections at each concentration. The manual injections were performed using a syringe via the front injection port. The linear dynamic range was evaluated across ~4 orders of magnitude with explosive residue amounts ranging from 0.001 to 2 ng.

Figure 2 shows the calibration curves (A and B) for NG and PETN and XIC (C) for NG using the MRM method. Peak areas were plotted as a function of ng amount of explosive residue to make the calibration curves compatible with residue testing. Good linear dynamic range was achieved across the targeted explosive compounds from manual injections. As seen in Figure 2, the calibration curves for both NG and PETN transitions are showing R^2 values greater than 0.993 and 0.999, respectively, even with the manual injection process. These results suggest that quantification of explosive residues using the TEIS with a SCIEX QTRAP 4500 System is feasible without the need for sample preparation. Good quantitation results were observed even with the manual injection process, suggesting workflow extensions such as autosampler.

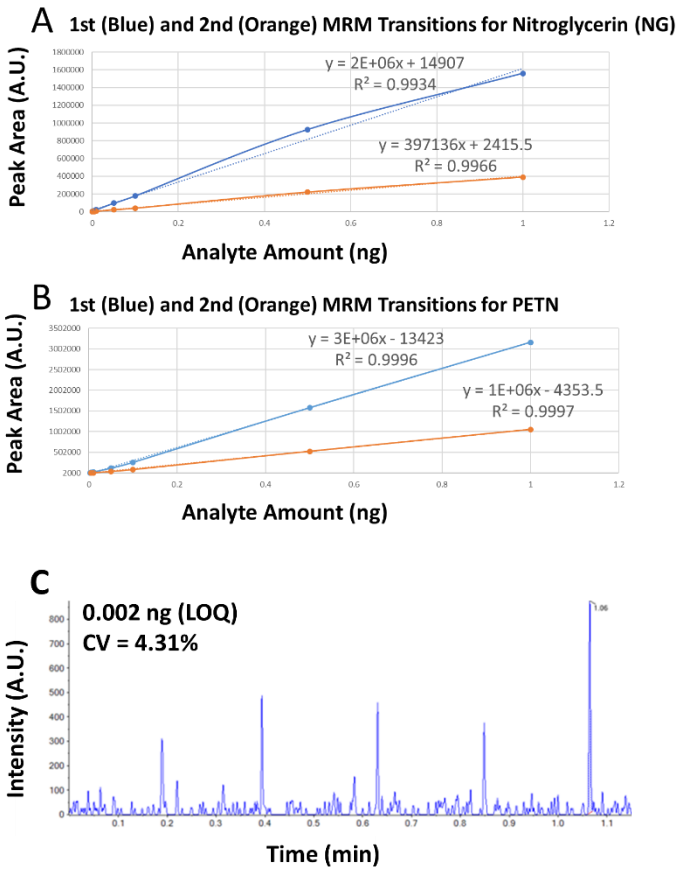


Figure 2: Good Linear Dynamic Range Achieved Across the Targeted Compounds Using MRM. Calibration curve for NG (A) and PETN (B) for both MRM transitions. (D) Extracted Ion Chromatogram (XIC) trace showing the five sequential 2 µL injections of NG at the LOQ (0.002 ng). Linear dynamic range averaged ~4 orders of magnitude, showing quantitation from 0.002 to 20 ng of explosives in 2 µL injections.

Accurate Identification and Quantitation of Unknown Explosive Residues

Following calibration curves generation, the capability of the instrument for screening and quantifying unknown explosive residues was tested by swabbing fingerprints from individuals known to have handled explosives. Explosives residue from the sixth fingerprint (on the glass slide surface) was sampled using a sterile cotton swab that was then placed in the slot between the two heated blocks on the TEIS. The entire process is shown in Figure 3. The MRM detection of the unknown explosive residues is nearly instantaneous as seen in Figure 3D. The analyte profile during thermal desorption was observed in real time using the Explore Mode in Analyst Software.

The positive identification of three explosive compounds (RDX, PETN and ETN) present in the fingerprint swab was confirmed through visualizing the MRM transitions used to specifically detect the explosive compounds (Figure 3D). The quantitative results of the targeted screen from the explosive swab residue is shown in Table 2. Using the linear regression equations for each of the two transitions used for the explosive compounds (computed in Figure 2) and the area value for each of the XIC peaks resulting from the TD profile, one can calculate the approximate amount of the explosive detected from the total signal area. Using the average value from both transitions, the amounts of RDX, PETN and ETN was found to be 0.029, 10.069 and 0.002 ng, respectively. The low amount of ETN is likely due to the breakdown of PETN.

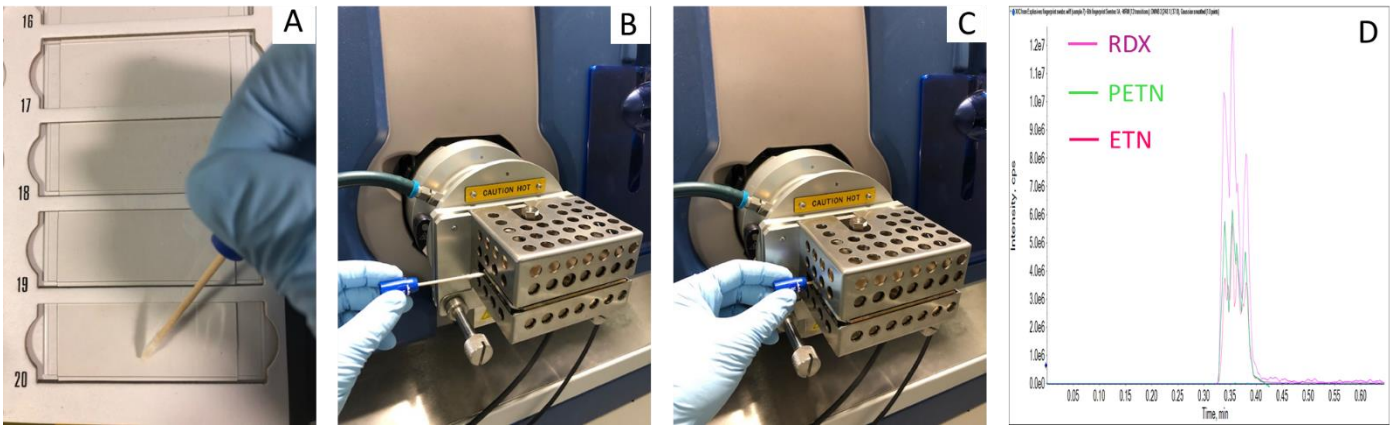


Figure 3: Process of Screening for Explosive Residues from Fingerprints on a Glass Surface Using the TEIS. A) Sampling of explosive residues on fingerprints using a sterile cotton swab on a glass slide, B) cotton swab of the fingerprints before insertion in the slot between the two heated blocks, C) introduction of the cotton swab containing explosive residues into the thermal desorption source for sample extraction, and D) data acquisition and real-time monitoring of the TD profile in Explore Mode in Analyst Software 1.6.3.

This quantitation method provides an estimate of explosive residues amounts on swabs used to sample fingerprints, taking into account the efficiencies in sample collection and desorption during the entire acquisition process. The use of MRM provided an additional level of confidence in compound identification, hence reducing the chance of false positive results. Overall the integration of the TEIS to the SCIEX QTRAP 4500 System enabled sensitive quantitation of low levels of explosive residues which improved selectivity and confidence in identification when compared to screening technologies such as ion mobility.

Table 2. Quantitative Results From the Swab Analysis of the Fingerprint Residue Using the SCIEX QTRAP 4500 System.

Sample ID	Explosive Transition ID	Averaged Area (N=2)	Linear Regression Equation	Calculated Amount (ng)
RDX	*257→62* *259→62*	*1.14E+04* *3.76E+03*	*y=633004x-5627.7* *y=202499x-2253*	*0.027* *0.030*
PETN	*351→62* *353→62*	*2.71E+07* *1.11E+07*	*y=3E+06x-13423* *y=1E+06x-4353.5*	*9.038* *11.101*
ETN	*337→62* *339→62*	*4.79 E+04* *8.77E+03*	*y=2E+06+1490* *y=397136x+245.5*	*0.002* *0.002*

Conclusions

A streamlined targeted approach for the detection and identification of explosive residues was developed and successfully applied to fingerprint analysis. The integration of the TEIS to the SCIEX QTRAP 4500 System enabled the rapid acquisition of MRM data for confident identification of explosive residues for rapid manual screening. The combination of precursor and product ion information using MRM transitions provides higher confidence in positive detection, hence reducing the rate of false positive results. This screening approach would significantly decrease consumable needs when compared to LC-MS approaches while greatly increasing laboratory throughput. In addition, the use of this optimized targeted method allowed confident identification of low levels of explosive residues from fingerprints.

Real-time visualization of results is performed using the Explore Mode in Analyst Software. Simultaneous visualization of the multiple MRM transitions provides additional confidence in the identity of the detected explosives. Using this direct analysis method, detection of low levels (sub ng) levels of RDX, PETN and ETN was achieved nearly instantaneously.

This approach demonstrates that thermal desorption with atmospheric pressure chemical ionization (TD-APCI) in combination with MS aligns well with current security screening requirements as a rapid sample introduction approach and shows potential for the direct analysis of a variety of security screening applications such as the detection of illicit drug residues from parcels, packages and fingerprints.

References

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4. For more information on the TEIS source, please visit www.msaltd.co.uk.

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