

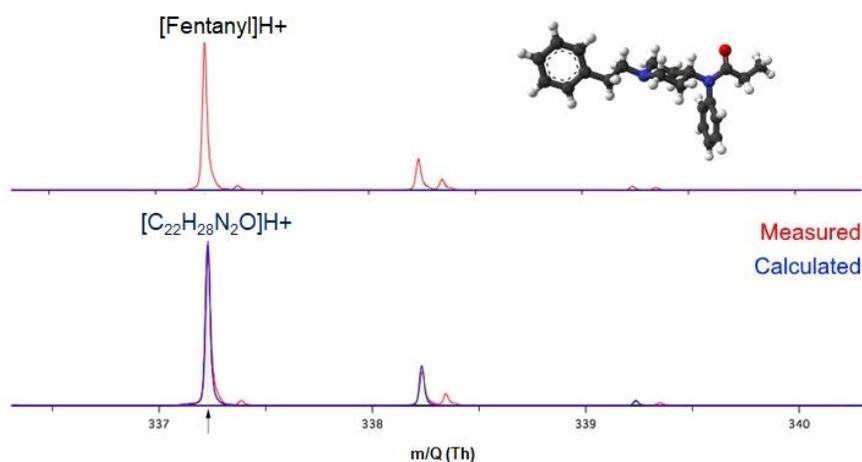
# Rapid, sensitive detection of fentanyl by thermal desorption PTR-MS

*A method for unambiguous identification of trace fentanyl in a complex matrix*

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Widespread opioid abuse causes hundreds of thousands of fatalities worldwide every year. The synthetic opioid fentanyl is frequently mixed with heroin to create an intense, euphoric high. Because fentanyl can be a hundred times more potent than heroin, this mixing greatly increases the rate of fatal overdoses. Fentanyl can cause an overdose at concentrations as low as a few to hundreds of ng/ml in the blood. Detection and identification of trace

quantities of fentanyl in forensic or biological samples demands very sensitive methods capable of resolving fentanyl within potentially complex backgrounds. This note demonstrates the ability of the TOFWERK Vocus 2R proton transfer reaction time-of-flight mass spectrometer (PTR-TOF) to rapidly identify trace quantities of fentanyl in solution and from the surface of a filter with no sample pre-treatment or separation step.



*Figure 1. Measured spectrum (red) and calculated isotope distribution (blue) of pure fentanyl analyzed by thermal desorption (TD) coupled to a TOFWERK Vocus 2R PTR-TOF. A water solution containing 10 ng of fentanyl was injected into the TD system at room temperature and programmatically heated to 200°C. The vapor was diluted into a 500 ml/min flow of clean air and sampled directly into the Vocus 2R. Soft ionization by proton transfer reaction ionization yielded the protonated fentanyl ions. Exact mass combined with isotopic pattern analysis enables molecular composition assignment with high confidence.*

## Thermal Desorption PTR-MS

Low-vapor-pressure street drugs are commonly analyzed by thermal desorption of a swabbed sample into a detector. In the first experiment, an aqueous solution was injected onto the glass surface of a thermal desorption oven, delivering 10 ng of fentanyl to a Vocus 2R PTR-TOF. PTR ionization of the fentanyl molecule in the Vocus reaction cell produced protonated ions with limited fragmentation.

As depicted in Figure 1, the composition of the main mass spectral peak was determined by a molecular formula search based on the observed exact mass of the peak. The experimentally determined exact mass is within 2.8 ppm of the mass of protonated fentanyl,  $C_{22}H_{28}N_2O \cdot H^+$ . This identification was evaluated by comparison of the measured isotopic pattern to the theoretical distribution (lower panel), and the agreement of the two supported the molecular fentanyl assignment.

### Collision Induced Dissociation

The identification was further evaluated by structural analysis based on controlled collision induced dissociation (CID) in the ion lenses immediately after the Vocus reaction cell (CID, Figure 2). With this procedure it was possible to intentionally induce the formation of fragment ions, which are structurally unique to fentanyl. During analysis, conditions were scanned from the standard Vocus settings, where only protonated fentanyl was observed, to higher collisional energies, which produced fragment ions detected at 105.070 Th ( $C_8H_9^+$ ) and at 188.144 Th ( $C_{13}H_{18}N^+$ ), corresponding to

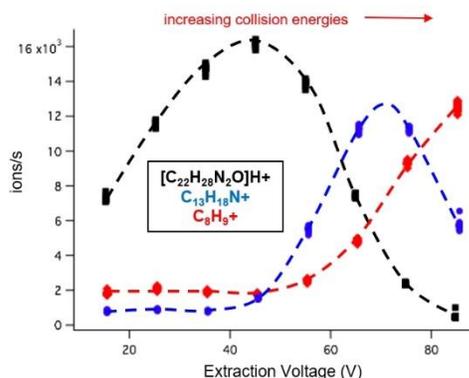


Figure 2. Confirmation of fentanyl molecular identification by collision induced dissociation (CID) in the Vocus 2R PTR-TOF. The extraction voltage after the Vocus reaction cell was increased to induce molecular fragmentation via energetic collisions. The recorded fragmentation pattern provides information about the molecule structure as in MS/MS techniques. At higher collisional energies the parent ion corresponding to protonated fentanyl ( $C_{22}H_{28}N_2O \cdot H^+$ ) is fragmented into  $C_{13}H_{18}N^+$  and  $C_8H_9^+$  ions, matching fentanyl fragments from MS/MS databases, thus confirming fentanyl identification.

known fentanyl fragments from MS/MS databases.

### Analyzing a Swab

These results demonstrate the confident detection of fentanyl deposition on the clean glass surface of the thermal desorption oven, but the real world is more challenging, requiring detection of traces of fentanyl in complex mixtures. To simulate a complicated real-world sample, 10 ng of fentanyl were deposited on uncleaned filter paper. The sample was then placed on the thermal desorption oven for online detection with the Vocus 2R PTR-TOF. Figure 3 shows an example spectrum. The high mass resolving power of the Vocus 2R ( $M/\Delta M = 15000$ ) enables separation of

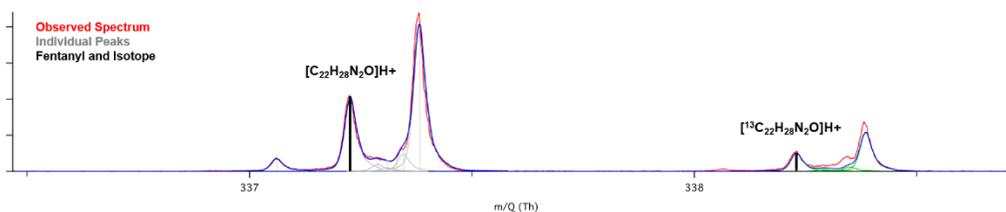


Figure 3. Measured thermal desorption PTR-TOF spectrum (red) of trace fentanyl on uncleaned filter paper and calculated isotope distribution of protonated fentanyl ion (black). The peak corresponding to protonated fentanyl ( $C_{22}H_{28}N_2O \cdot H^+$ ) and its first order isotope are clearly present with expected abundances, confirming fentanyl identification. The high mass resolving power of the Vocus 2R ( $M/\Delta M = 15000$ ) enables separation of these fentanyl-related peaks from other ions peaks originating from the uncleaned filter, thus providing robust identification of fentanyl even in a complex sample.

fentanyl ion peaks from interferences that are present near both the parent and first order isotope ion peaks. Without such separation power, the presence of interfering ions would hinder or prevent fentanyl identification and quantification.

Single digit nanogram detection limits were achieved under clean desorption conditions. Faster desorption rates for example from a swab desorber would result in even lower detection limits.

## Conclusion

The combination of the Vocus 2R PTR-TOF and a thermal desorption system allows real-time detection, identification, and quantification of trace amounts of fentanyl from a swab without any sample preparation or preconcentration step. Exact mass analysis is validated by isotopic pattern matching and structural analysis by CID. The high mass resolving power of the Vocus 2R is critical to separate the fentanyl peaks from background interferences.

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