REAL-TIME ANALYSIS OF VAPOR PRODUCTS USING PROTON TRANSFER REACTION TIME-OF-FLIGHT MASS SPECTROMETRY (PTR-MS)

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Background

- PTR-MS is a soft chemical ionization technique that can simultaneously analyze and quantify a wide range of organic compounds, making it especially suitable for analysis of small molecules in vapor product aerosols as well as exhaled breath.
- Ionization occurs when proton affinity of the analyte is higher than that of the reagent ion.
- PTR-MS is a more sensitive technique compared to the offline methods traditionally used (collection of subsequent puffs, extraction of analytes from filter pad, derivatization, instrumental analysis), enabling quantitation of ppt concentrations.
- E-liquid can also be measured by PTR-MS by using a liquid calibration system, which evaporates the sample before introducing it to the instrument for ionization and detection.
- Online methods can be validated by adapting the ICH guidelines for accuracy, precision, linearity and range, Limit of Detection (LOD)/Limit of Quantitation (LOQ), specificity, and robustness.
- Real-time analysis enables insight into device dynamics that offline methods obscure.

Methods & Results

aerosol analysis

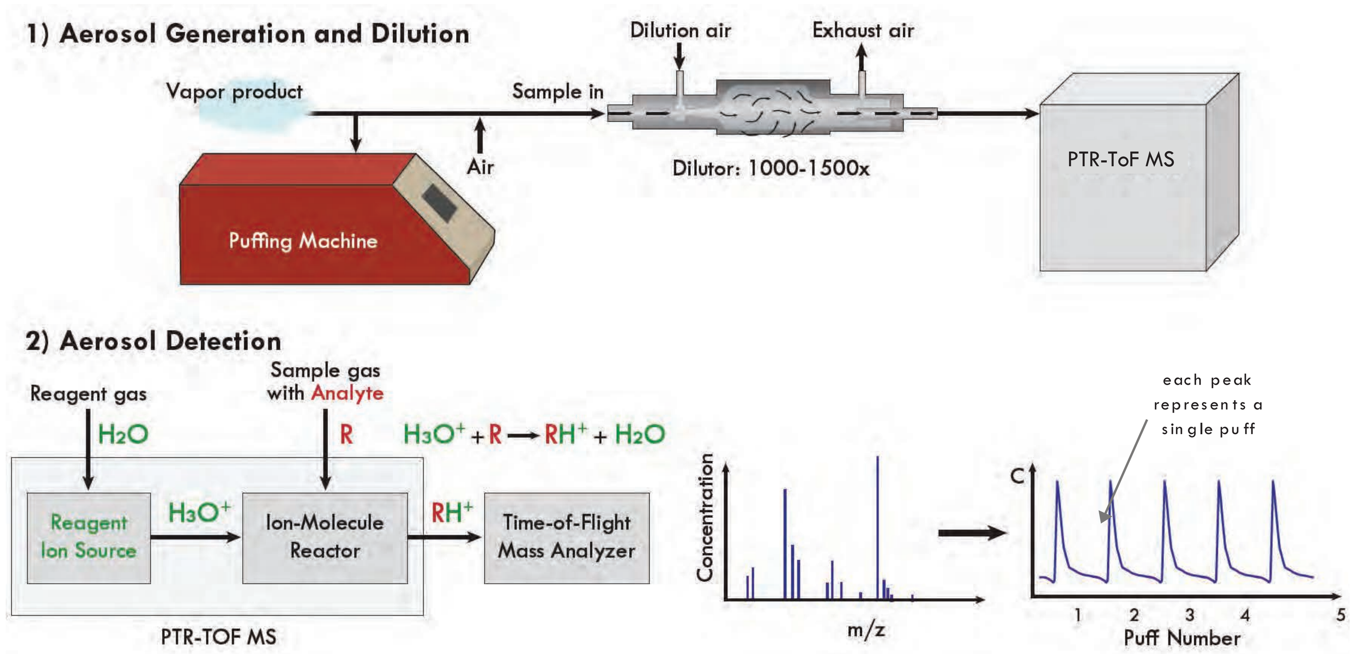

Figure 1. Sampling setup for chemical profiling of Volatile Organic Compounds (VOCs) in aerosol. Aerosol was diluted and vaporized prior to ionization by reagent gas and ToF detection.

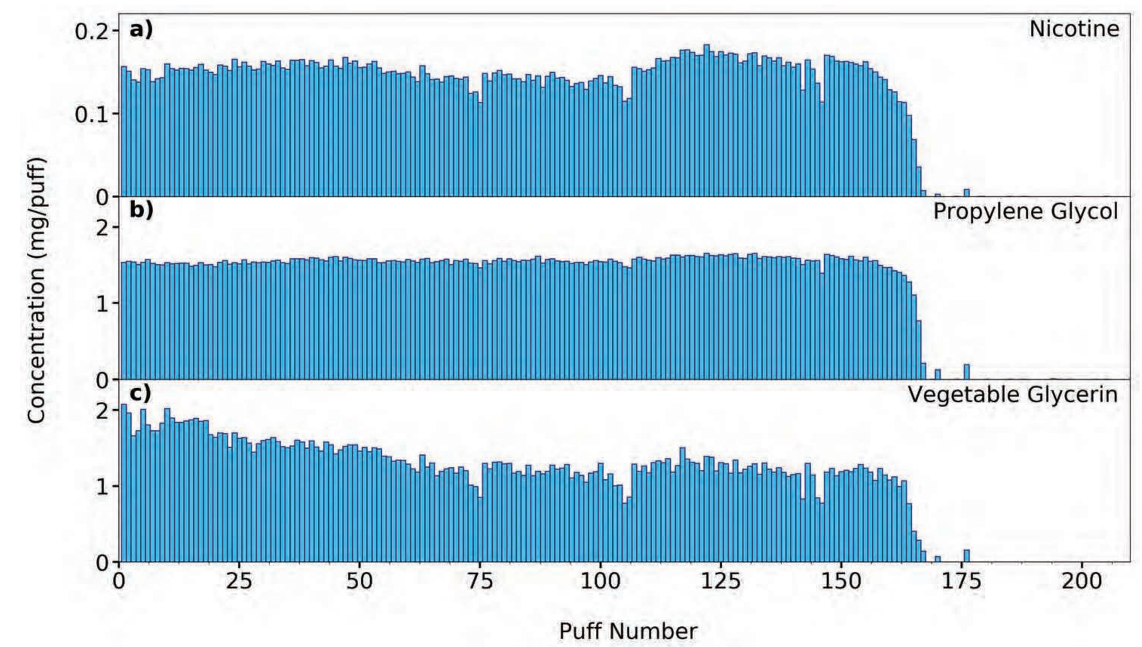

Figure 2. Primary constituents of Electronic Nicotine Delivery System (ENDS) aerosol are measured in a puff-by-puff manner. Each puff is analyzed individually in a time-series fashion. Concentrations (mg/puff) for a) nicotine, b) propylene glycol, and c) vegetable glycerin from first to last puff of a cig-a-like ENDS design with 4.5% w/w nicotine with H_3O^+ as primary ion.

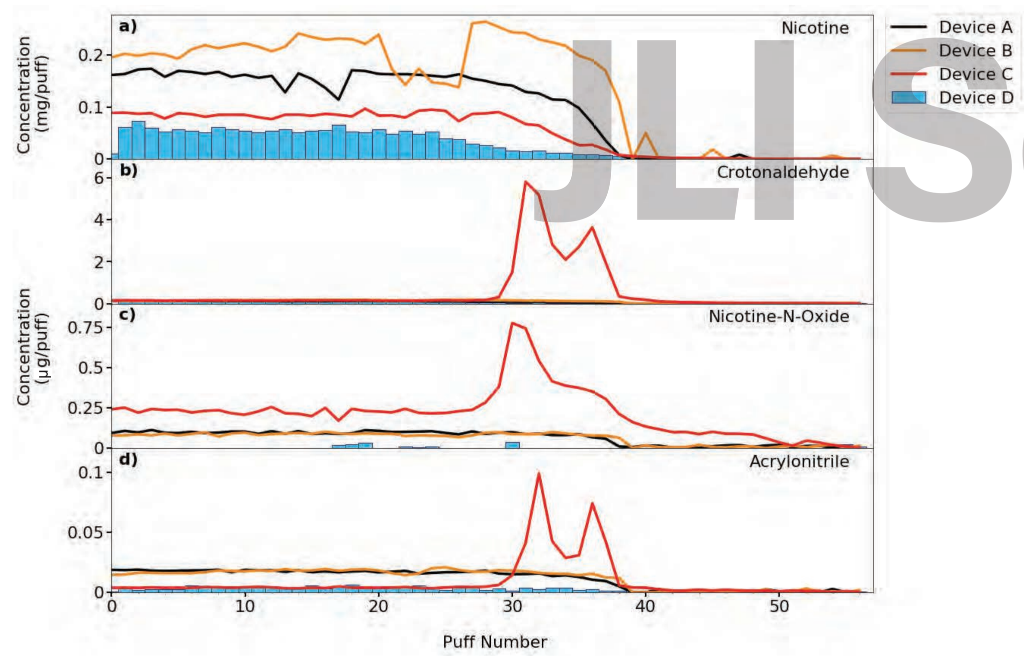

Figure 3. Puff-by-puff analysis enables deeper insight into device performance characteristics; such as chemical profile changes as the e-liquid depletes. Only the last 50 puffs for each device are shown here.

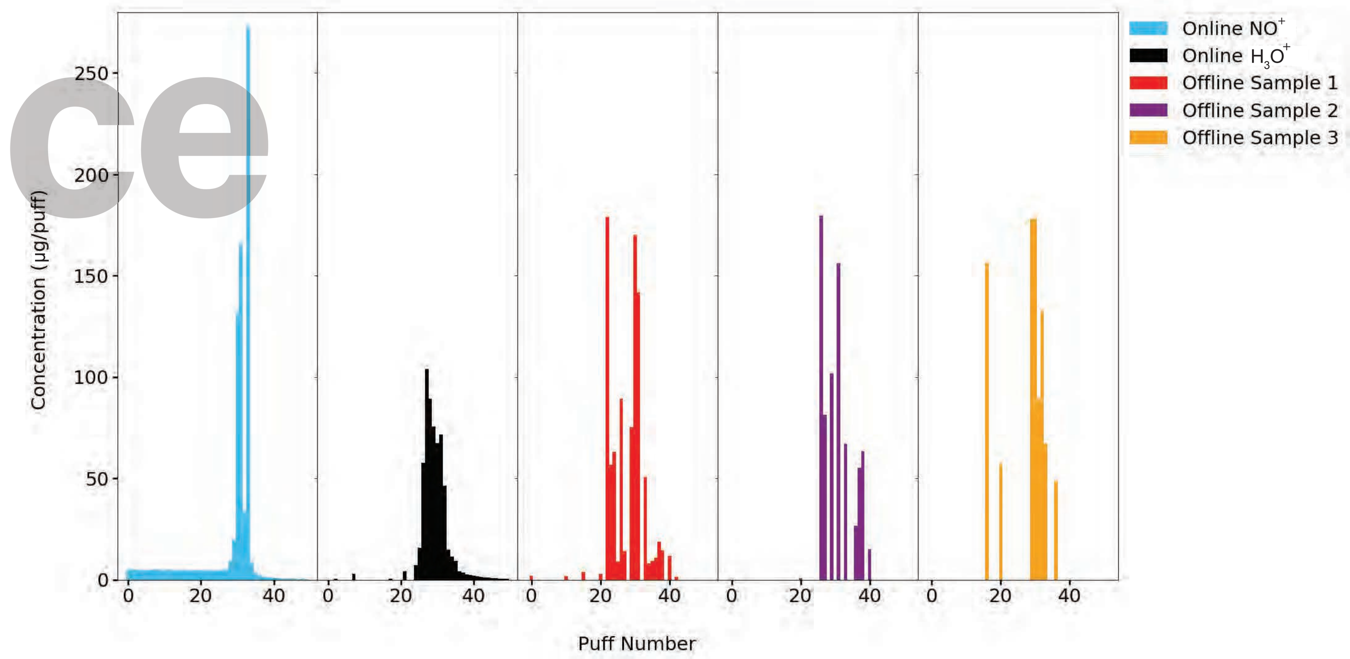

Figure 4. Comparison of acrolein measurements at end-of-liquid using PTR-MS and offline Gas Chromatography–Mass Spectrometry (GC-MS) methods. For GC-MS analysis, single puffs were collected individually using an impinger solution, then subsequently extracted before instrumental analysis. Two reagent ions were used for PTR-MS measurements to assess ionization differences. A spike in acrolein was observed using all methods, supporting PTR-MS as a viable method for this analysis.

e-liquid analysis

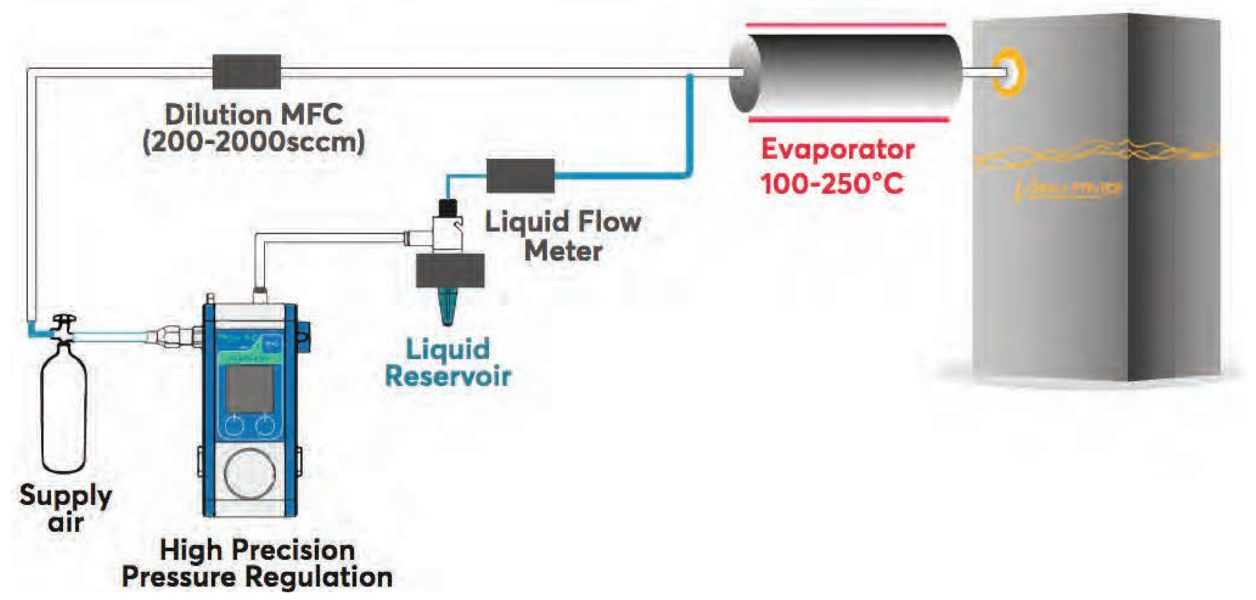

Figure 5. Sampling setup for chemical profiling of VOCs in e-liquid. The sample is introduced to the PTR-MS via a liquid calibration system (LCS) that evaporates the sample before ionization in the ion-molecule reactor and detection by Time-of-Flight mass analyzer. Calibrations are done by adjusting the liquid flow rate to introduce more or less sample. Figure provided by TOFWERK.

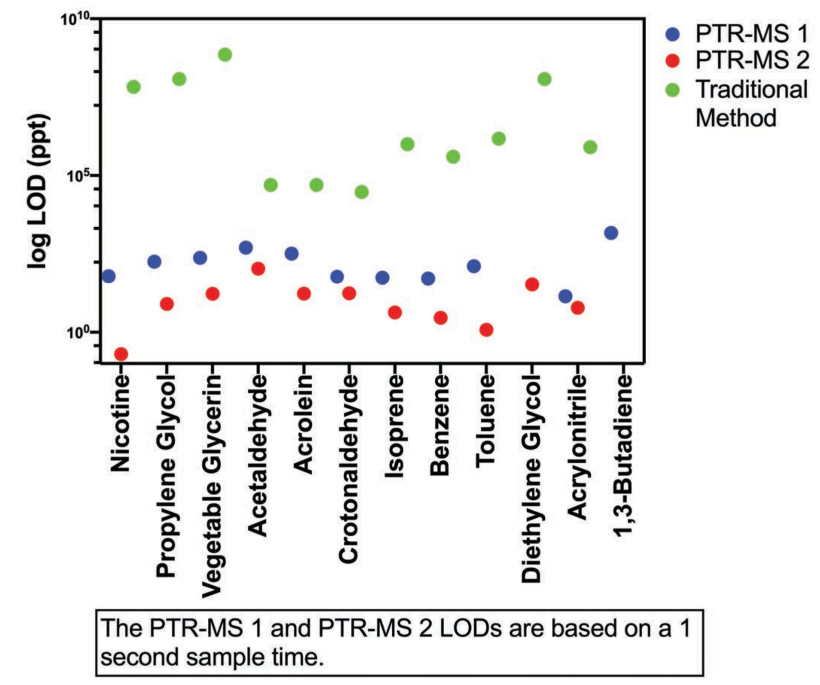

Figure 6. Limit of detection improvements in the characterization of HPHCs in e-liquid using PTR-MS compared to conventional offline methods using extraction, derivatization, and chromatographic separation for analysis.

Discussion

- PTR-MS enables puff-by-puff analysis, improves time resolution, and reduces resources required to analyze vapor product aerosols.
- Analysis of e-liquids can also be improved; online methods are faster and capture more analytes in a single acquisition method.
- Aerosol and e-liquid methods developed are qualitative and quantitative.
- PTR-MS methods can successfully be validated by following existing guidance on method validation.
- Tremendous improvement in the limit of detection makes it possible to analyze the chemistry of a single puff in real-time.
- This method is able to analyze a wide range of compounds simultaneously, eliminating the need to run multiple methods to capture all analytes of interest.
- Limitations of this technique include overlapping fragments of some molecules and a lack of isomer separation. These factors can make a clear assignment difficult, and they can be mitigated by employing different reagent ions or adding a fast gas chromatograph.

Further Reading:

• Blair et al. A Real-Time Fast-Flow Tube Study of VOC and Particulate Emissions from Electronic, Potentially Reduced-Harm, Conventional, and Reference Cigarettes. Aerosol Sci and Tech. 2015, 49, 816-827

• Breiev et al. An Online Method for the Analysis of Volatile Organic Compounds in Electronic Cigarette Aerosol Based on Proton Transfer Reaction Mass Spectrometry. Rapid Commun. Mass Spectrom. 2016, 30 (6), 691–697.