# Automated Substance Identification using Proton-Transfer-Reaction Mass Spectrometry (PTR-MS): Exemplary Analysis of a New Psychoactive Substance Blend

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## Abstract

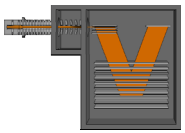
**P**roton-**T**ransfer-**R**eaction **M**ass **S**pectrometry (**PTR-MS**), which was already introduced to the scientific community in the 1990's, has quickly evolved into a **well-established technology** for **a broad range of application fields [1]**. A relatively new area of application for PTR-MS is the field of **safety and security**, i.e. the detection of **chemical warfare agents, toxic industrial compounds, explosives, new psychoactive substances (NPS), illicit and prescribed drugs**.

However, until now this very sensitive and selective method for real-time gas analysis is mostly used as tool in scientific research and to a negligible extend for automated detection. However, here we want to present a new method which can be used for substance identification with a high level of confidence and can easily be automated prospectively [2]. The working principle is demonstrated using the example of the analysis of new psychoactive substances (NPS).

This current work emphasizes the use of **PTR-MS as a broad-based and highly selective analytical drug detection technology [3]**.

Furthermore we provide details about the performance data of the latest PTR-MS instrument generation as well.

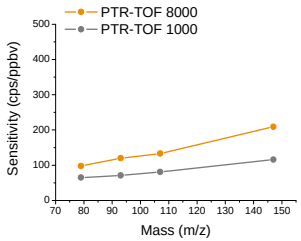
## Compactness and Performance

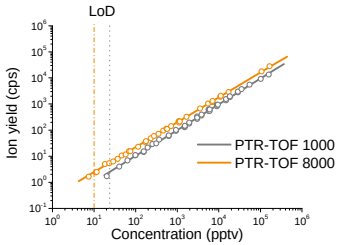


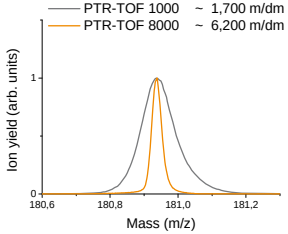
PTR-TOF 1000

The **figures below** show important performance data of the **compact and lightweight PTR-TOF 1000** (see the schematic figure to the left) and the **PTR-TOF 8000**: the m/z dependent **sensitivities**, **linearity** from about 100 ppbv down to the respective **LoDs** (dichlorobenzene isotopes) and **mass resolving powers** (for trichlorobenzene).

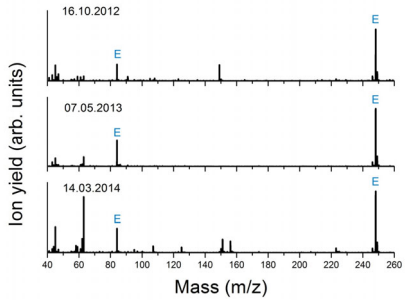
These two PTR-MS instruments which are both based on a time-of-flight mass spectrometer should satisfy the varying demands depending on the field of application (e.g. size and weight vs. instrumental performance), which generally cannot be combined in one single device. Therefore in 2014 we introduced a new device, the compact **PTR-TOF 1000**. Its prototype originated from a collaborative project with the **University of Innsbruck**. The requirement of this project was to invent an instrumentation which can be installed in an aircraft for airborne measurement campaigns. It had to be resistant against vibrations, variable pressures and changing temperature in the cabin. The prototype was already successfully applied in a **NASA campaign** [4].




## Product variability and „EPH crisis“ [5]



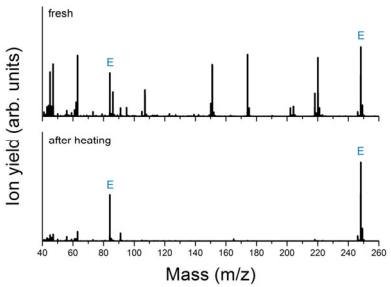

**Ethylphenidate (EPH)** is a NPS which is formed as a byproduct of the prescribed drug **methylphenidate** (aka **Ritalin®**). Therefore its effects are well known and it is available in many countries without being banned for several years. Therefore we wanted to analyze its **product variability** and purchased several batches of EPH from an online vendor between 2012 and 2014.

In the **figure to the left** the mass spectra of three batches which have been bought in **2012**, **2013** and **2014** are depicted resulting from proton transfer reaction with $H_3O^+$ reagent ions. The letter **"E"** marks the peaks identified as originating from EPH. The results demonstrate that the sample from **2013** seems to be the one with the **highest purity** possible synthesized under very pure condition. The other two batches, however, show varying residual impurities at higher mass range. Therefore it can be assumed that **different synthetic methods** have been used for these two samples.

The „EPH crisis“ describes the fact that in December 2013 one online vendor after the other reported a **supply bottleneck** of EPH, which is an indication that most vendors are reselling the drugs from a wholesale lab. In January 2014 the vendor from whom we got our samples offered a „homemade“ EPH which he had synthesized in his own lab. Since customers reported negative reactions, like **headaches** and **extreme burning sensation** in the nose, we bought a batch during this period to analyze it.

In the **figure to the right** mass spectra of the EPH sample during the „**EPH crisis**“ are shown. Obviously this batch has by far the highest level of impurities (**upper panel**) which haven`t appeared for the other samples (**see above**). The impurities seem to be very volatile residuals from the synthesis which disappear when the sample has been left at 80°C under the fume hood over night (**lower panel**).

The results seem to match with the announcments of the vendors and indicate that this batch has been synthesized in a semi-professional lab. Possibly these impurities are even the reason for the negative experiences reported on the Internet forums.




## Automated identification of new psychoactive drugs with SRI-TOF-MS

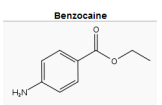
In the recent past **new psychoactive substances (NPS)** or so called "**designer drugs**" have flooded the drug market. These legal kind of drugs are getting increasingly attractive as an alternative to illegal drugs (e.g. cocaine, heroine), since these NPS are created by combining different active ingredients to simulate the effects of illegal drugs. However, they are generally supplied as blends which have a varying composition depending on the vendor and even on the batch. Consequently, the confident identification of these ingredients is an analytical challenge. **Synthacaine** is one of the most popular blended NPS which should imitate **cocaine** and is sold without any information about its chemical composition.

We demonstrate how **S**elective-**R**eagent-**I**onization-**T**ime-**o**f-**F**light **M**ass **S**pectrometry (**SRI-TOF-MS**) can be used as a powerful tool for sampling, detecting and identifying chemicals which are combined to NPS blends within about **30s** by switching the operation parameters rapidly.

First we gain a mass spectrum of the blend`s headspace using $H_3O^+$ as reagent ions. The dominant mass peaks could be identified as protonated **benzocaine**, an anesthetic responsible for the cocaine- like numbness feeling, and **methiopropamine**, a stimulant and a structural analogon to methamphetamine (see the chemical structures **below left**).

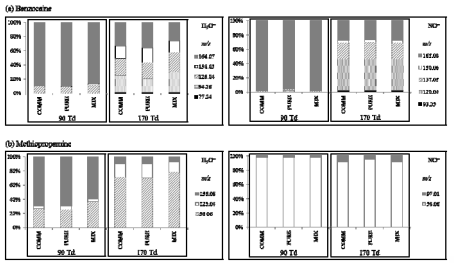
Since the information about the exact mass isn't sufficient, we change the E/N (reduced electric field strength) in the PTR-MS drift tube to facilitate an unambiguous identification of the substance based on the comparison of the product ion branching ratios to those from the pure compounds (see figure at the **bottom left**). Additionally, we switched the reagent ions in the case of synthacaine to $NO^+$ to compare the branching ratios with the one of the pure compounds to receive even more information about the identity of the substances.

The results have recently been published in M. Lanza et al [2].

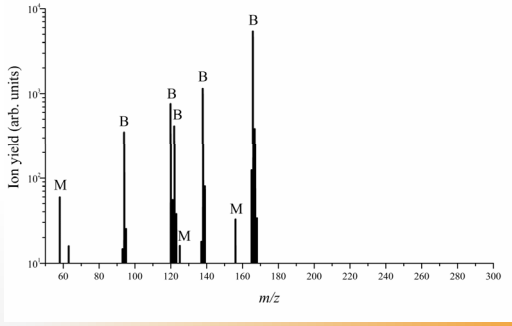




$H_3O^+$



Comparison of the branching ratios of **benzocaine** and **methiopropamine** in the commercial blend of synthacaine (COMM), the pure compounds and a self-made 1:1 mixture of benzocaine and methiopropamine (MIX) using $H_3O^+$ and $NO^+$ as reagent ions at two characteristic E/N values. This information is essential for a rapid and confident identification of unknown matrices (e.g. drugs) within few seconds.

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