

Use of proton transfer reaction time-of-flight mass spectrometry for the analytical detection of illicit and controlled prescription drugs at room temperature via direct headspace sampling

B. Agarwal¹, F. Petersson^{1,2}, S. Jürschik^{1,2}, P. Sulzer², P. Watts³, C. A. Mayhew³, C. Lindinger², L. Märk² and T. D. Märk^{1,2}

¹ Institut für Ionenphysik und Angewandte Physik, Universität Innsbruck, Technikerstr. 25, 6020 Innsbruck, Austria

² IONICON Analytik GmbH, Eduard-Bodem-Gasse 3, 6020 Innsbruck, Austria

³ School of Physics and Astronomy, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK



IONICON
ANALYTIK

Abstract

Starting in the 1990s Proton-Transfer-Reaction Mass Spectrometry (PTR-MS) nowadays is a well established technology in fields like **environmental research**, **atmospheric chemistry**, **food and flavor science**, etc. [1] because of its great sensitivity, **ultra-low detection limits**, **response times in the 100 ms** regime, the possibility of **real-time quantification** and many more advantages. However, recent developments in the last few years (high resolution time-of-flight mass spectrometers, switchable reagent ions, etc.) paved the way for several new fields of application. In PTR-MS a hollow cathode ion source produces H_3O^+ ions from distilled water at extremely high purity levels (over 99%), i.e. no mass filter is needed after the ion source to purify the primary ions. Alternatively with the so-called SRI (switchable reagent ions) feature, also O_2^+ or NO^+ can be utilized as primary ions. Subsequently the reagent ions enter a drift tube where the trace compounds get ionized either via proton transfer (H_3O^+) or via charge transfer (O_2^+ , NO^+) and are finally analyzed with either a quadrupole mass filter or a high resolution time-of-flight mass analyzer. This setup provides several advantages like detection limits in the **ppqv range** [2], mass resolving power of up to **8.000 $m/\Delta m$** [3], separation of isomers, etc.

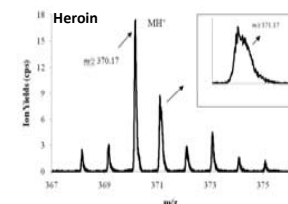
Here we will present first results from investigations of **illicit, prescribed and designer drugs**. The latter ones were investigated in their pure forms and admixed in different concentrations to common drinks.

Category	Drugs	Chemical Formula	m/z
Common drugs	Heroin	$\text{C}_{21}\text{H}_{23}\text{NO}_5$	370.17
	Cocaine	$\text{C}_{17}\text{H}_{21}\text{NO}_4$	304.15
	Codeine	$\text{C}_{18}\text{H}_{21}\text{NO}_3$	300.16
	Morphine	$\text{C}_{17}\text{H}_{19}\text{NO}_3$	286.14
	Ecstasy (MDMA)	$\text{C}_{11}\text{H}_{15}\text{NO}_2$	194.12
Designer drugs	Dimethocaine	$\text{C}_{16}\text{H}_{26}\text{N}_2\text{O}_2$	279.20
	2C-D	$\text{C}_{11}\text{H}_{17}\text{NO}_2$	196.13
	Ethcathinone	$\text{C}_{11}\text{H}_{18}\text{NO}$	178.12
	4-Fluoroamphetamine	$\text{C}_9\text{H}_{12}\text{FN}$	154.10
"Rape" drugs	1,4-Butanediol	$\text{C}_4\text{H}_{10}\text{O}_2$	91.07
	gamma-Butyrolactone	$\text{C}_4\text{H}_6\text{O}_2$	87.04

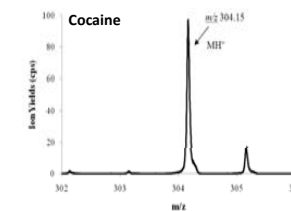
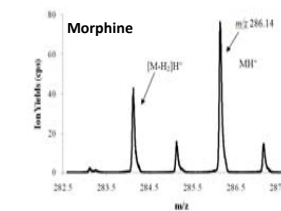
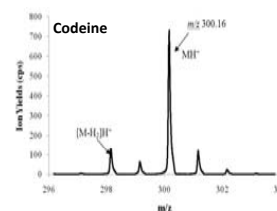
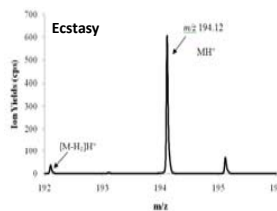
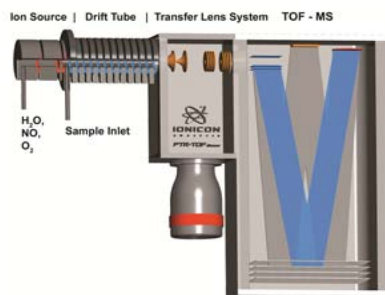
Illicit and Prescription Drugs

The table on the left represents an overview over all drugs studied by us.

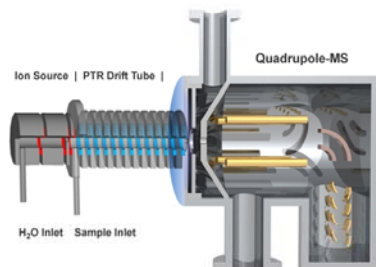
Below and on the right parts of the mass spectra obtained from the most common illicit and prescription drugs are shown. It can be easily seen that all substances lead to a rather high ion yield already at room temperature, although they are known to possess low vapor pressures. This once more underlines the fact that PTR-MS is an extremely sensitive technique for trace gas analysis. Additionally we performed so-called E/N studies (dependence of the ratio between the protonated parent ion and the fragment ion yields to the reduced electric field strength in the drift tube) for all mentioned molecules (not shown here). As e.g. cocaine and heroin show a rather constant ratio in the investigated E/N range (85 to 225 Td), ecstasy (MDMA) has a highly interesting branching ratio and therefore fragments completely different even at small E/N changes. Furthermore, for MDMA, the most dominant ion seen is the protonated parent ion (194.12 m/z). Quite surprisingly we also observed an ion at 212.12 m/z, which is either due to an addition of water onto the protonated parent or formed through stabilization of the initial complex ($\text{M}\cdot\text{H}_3\text{O}^+$), i.e. the association of H_3O^+ with the MDMA.



PTR-TOF 8000



HIGH SENSITIVITY PTR-MS

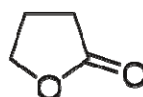
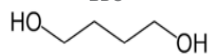


Experimental Setup

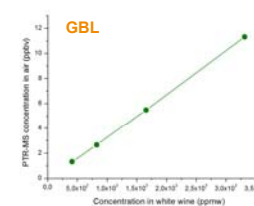
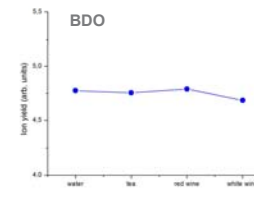
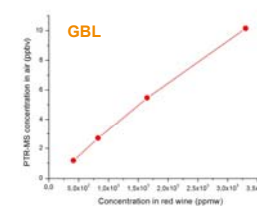
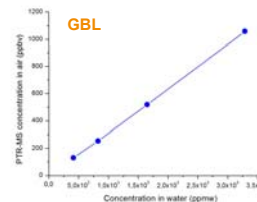
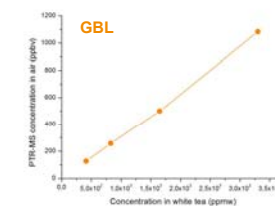
For the headspace measurements of the illicit and prescription drugs we utilized a PTR-TOF 8000 (see above for a schematic view) because of its high mass resolution (to separate the "real signal" from background impurities). Small amounts of samples (about 50 mg each) were put into glass vials at room temperature. Charcoal-filtered air was drawn through these vials and subsequently analyzed by the PTR-TOFMS.

For the detection of the "rape drugs" admixed to common drinks we coupled a quadrupole based high sensitivity PTR-MS (left) with our recently introduced direct aqueous injection system (DAI) [4]: quantities of about 1 mL of the liquid samples were drawn up into a syringe and consequently injected into a heated carrier airstream, which was finally partly guided into the PTR-MS instrument for analysis.

1,4-Butanediol ($\text{C}_4\text{H}_{10}\text{O}_2$)
BDO



gamma-Butyrolactone ($\text{C}_4\text{H}_6\text{O}_2$)
GBL



"Liquid Ecstasy"

As there are drugs which are predominantly consumed highly diluted in liquids, we extended our headspace studies to GBL and BDO (for chemical compositions see the figures on the far left) traces mixed in different concentrations into plain water, tea, red and white wine. Both substances are metabolized in the human body to gamma-hydroxybutyric acid ("liquid ecstasy") and are therefore frequently abused as recreational drugs (in lower doses) or so-called "rape drugs" (in higher doses). With the DAI system coupled to PTR-MS we were able to detect both substances in all above-mentioned liquids with great linearity down to concentration levels far below the activation threshold for effects in human beings. On the left the results of these measurements are displayed (linearity at different concentrations, starting with 1 mL in a 300 mL glass, which is the typical dose for recreational use for GBL and one concentration level in different liquids for BDO).

Acknowledgement

We wish to gratefully acknowledge that this work was partially supported by the Leopold Franzens Universität, Innsbruck, the European Commission (via a Marie Curie IAPP project, GA 218065; FP and S.J.), Brussels and the FFG, Wien. CAM and PW wish to acknowledge the EPSRC (EP/E027571/1) that in part supported this work.

References

- R. S. Blake, P. S. Monks, A. M. Ellis; Chem. Rev., 109 (3) (2009), 861-896.
- A. Jordan, S. Haidacher, G. Hanel, E. Hartungen, J. Herbig, L. Märk, R. Schottkowsky, H. Seehauser, P. Sulzer, T. D. Märk, Int. J. of Mass Spec., 286 (2009), 32-38.
- A. Jordan, S. Haidacher, G. Hanel, E. Hartungen, L. Märk, H. Seehauser, R. Schottkowsky, P. Sulzer, T. D. Märk, Int. J. of Mass Spec., 286 (2009), 122-128.
- S. Jürschik, A. Tani, P. Sulzer, S. Haidacher, A. Jordan, R. Schottkowsky, E. Hartungen, G. Hanel, H. Seehauser, L. Märk, T. D. Märk, Int. J. of Mass Spec. 289 (2010), 173-176.