Mass Spectrometric Analysis of Drugs Consumed in Drug Consumption Rooms in the City of Frankfurt

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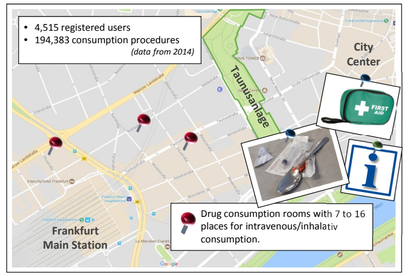
INTRODUCTION

The first drug consumption room in Frankfurt am Main was established in 1995 in an attempt to deal with the precarious situation in Germany's largest open drug scene near Frankfurt main station with about 200 deaths in public spaces at that time. These rooms intend to help relocate drug consumption from public areas to a controlled, hygienic and safe environment. These rooms are also seen as an important element to minimize drug-related health problems (e.g. infection risk) and promote contact of drug users with employees of drug help programs.

Since 2000, the 3rd Amendment of the German Narcotics Law serves as a legal foundation for drug consumption rooms, legalizing already existing institutions and enabling the start of new drug help projects. The six federal states where drug consumption rooms are established - Berlin, Hamburg, Hesse, Saarland, Lower Saxony and North Rhine-Westphalia - passed additional regulations for establishing and operating such institutions. While the German Narcotics Law explicitly prohibits the analysis of drugs from/for users ("Drug Checking"), the responsible authorities agreed on anonymous analysis of the drugs consumed in three consumption rooms around Frankfurt main station and a scientific evaluation of the findings in cooperation with the drug department of the City of Frankfurt.

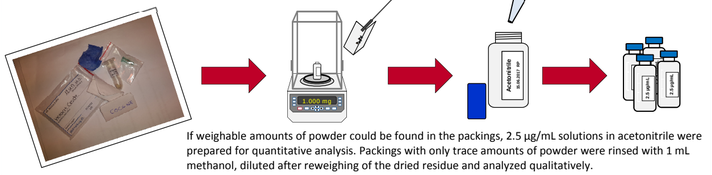


The main objective of the project is to gather information on the type and quality of the drugs used by these clients with a special focus on the prevalence of New psychoactive Substances (NPS) in street drugs.

Drug packing material and used filters were collected by the staff of the three consumption rooms an sent to our institute.

METHODS

Sample Preparation

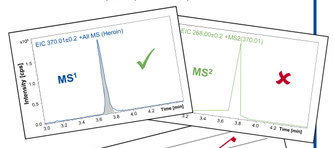


If weighable amounts of powder could be found in the packings, 2.5 µg/mL solutions in acetonitrile were prepared for quantitative analysis. Packings with only trace amounts of powder were rinsed with 1 mL methanol, diluted after reweighing of the dried residue and analyzed qualitatively.

Setting up a Quantitative Screening Approach

The original Toxtyper™ 2.0 approach was modified by adding about 200 compounds - mostly designer stimulants and synthetic opioids - and switching the ion source to ESI positive mode only to obtain more data points per peak. Due to data dependent acquisition in autoMS^n mode, including active exclusion of precursors, in contrast to other MS/MS approaches only MS^1 full scan data is available for quantitation.

To set up the quantitative part of the screening the linear range of each analyte has to be evaluated first. Therefore, the peak area ratio of the molecular ion of the compound and the corresponding deuterated internal standard (ISTD) was used (Cal_Slope_1). The upper (ULOQ) and lower limits (LLOQ) as well as the concentration of the calibration sample were added to a .csv-file linked to the DataAnalysis script of the method.

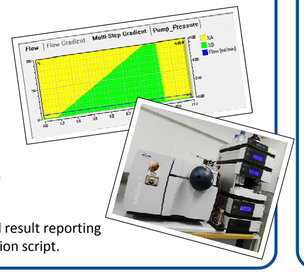


Analyte Name	ISTD	Slope	Intercept	LLOQ	ULOQ	Unit	Calibration Concentration	Quant m/z	Cal_Slope_1	Cal_Slope_2
Heroin	D9-Heroin	3.20E-02		1	120	Gew-%	50		3.20E-02	
Morphine	D3-6-Acetymorphine	1.02E-02		1	120	Gew-%	50		1.02E-02	
Codeine	D3-6-Acetymorphine	2.04E-02		1	120	Gew-%	50		2.04E-02	
6-Acetylcodeine	D9-Heroin	4.64E-02		1	120	Gew-%	50		4.64E-02	
6-Acetymorphine	D3-6-Acetymorphine	2.33E-02		1	120	Gew-%	50		2.33E-02	
.....										

This .csv-file is crucial for automated quantitative evaluation of screening results using an one-point-calibration. If marked as a calibrator, all qualitative findings in a sample were checked for an entry in the .csv-file and the area ratio of the compound and its assigned ISTD is recorded, subsequently. If marked as an unknown, all qualitative findings are checked for an calibration entry (Slope) and the calculated concentration is reported. Positive findings below or above the linear range were reported as '< cal_{Low}' or '> cal_{High}', respectively.

LC - MS^n Settings

LC-System: Dionex UltiMate 3000 LC-System
Eluent A: Water, 2 mM ammonium formate, 0.1% formic acid, 1% acetonitrile
Eluent B: Acetonitrile, 2 mM ammonium formate, 0.1% formic acid, 1% water
Column: Acclaim® RSLC 120 C18 2,2 µm 120A 2.1x100 mm
Total flow: 500 µL/min
Gradient: 1 % to 95 % B in 8 min; 11 min runtime
MS-System: Bruker amaZon speed™ ion trap
Ion source: ESI source, positive mode
Scan mode: UltraScan (70 - 600 Da at 32.500 Da/s), Auto MSn mode (n = 3)
Scheduled Precursor List to trigger data dependent acquisition of MS^2- and MS^3-spectra



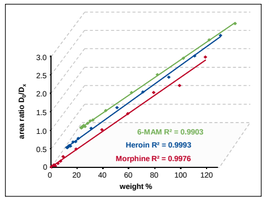
Data Evaluation and Reporting

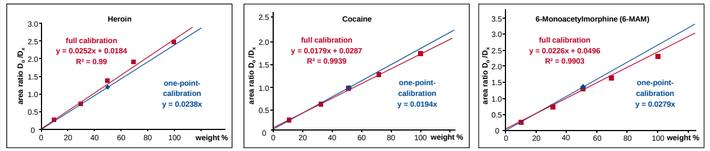
DataAnalysis 4.1 software package for automated data processing and result reporting according to the Toxtyper workflow including an automated quantitation script.

RESULTS

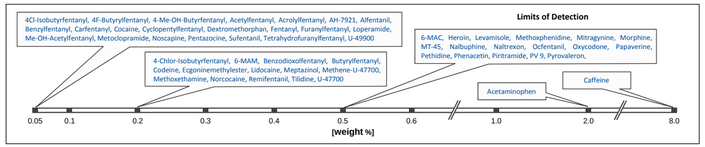
Method Development

Heroin and cocaine were supposed to be the most common drugs among this user group. So, linearity and limits of detection (LOD) for these drugs, poppy alkaloids, common extenders and degradation products were determined first. Regression coefficients (R^2) of calibration curves (1 to 120 wt.%) ranged from 0.9777 to 0.9993.
R^2 of the main drug analytes with corresponding isotope labeled standards were found to be higher than 0.99 and were in good agreement with data from respective one-point-calibrations.



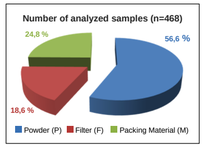


LODs were evaluated by analyzing standard solutions in decreasing concentrations and the lowest concentration automatically detected (n=3) was set as LOD.

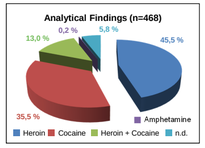


Analysis of Drug Samples

Up to now, the three drug consumption rooms sent in 409 different drug samples for analysis. Samples consisted of powder residues (P), syringe filters (F) or packing material (M) only, or varying combinations of the latter. Taking into account samples with multiple specimens, we analyzed a total of 468 different samples. As expected, heroin and cocaine were the drugs found most in this user group and the analytical findings of the powder samples were in good agreement with the information given by the user. Few samples labeled as cocaine or heroin only, were found to be a mixture of both or vice versa.



There was only one single amphetamine finding (labeled as "Speed") and 27 samples where no drugs could be found at all. In total, heroin could be detected in 213 specimens (P: n=158, F: n=24, M: n=31), cocaine in 166 specimens (P: n=83, F: n=34, M: n=49), and cocaine plus heroin in 61 specimens (P: n=17, F: n=25, M: n=19).



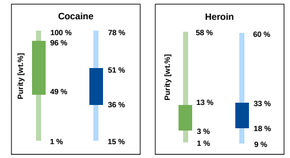
The analgesic phenacetin could be detected in 63 % of the cocaine specimen analyzed, 25 % of them containing levamisole as additional extender. Heroin samples were regularly extended with acetaminophen and caffeine. In addition, the opium alkaloids noscapine and papaverine as well as 6-MAM and 6-Monoacetylcodeine (6-MAC) were found in these samples.

In two packing materials the opioid fentanyl could be detected besides cocaine, phenacetin and levamisole. Unfortunately, there were no weighable amounts of powder preservable, so this is only a qualitative finding. One heroin powder contained 19 wt.% of the local anaesthetic drug ropivacaine.

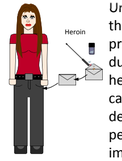
No NPS could be detected in the powders and materials analyzed up to now. Nevertheless, LODs of this approach shown above are suitable to detect further active ingredients like highly potent fentanyls.

Quantitative Results

We got 265 specimen with weightable amounts of powder, 158 heroin samples, 83 cocaine samples, and 17 cocaine/heroin samples, respectively. Cocaine concentrations ranged from 1 to 100 wt.%, with 50 % of the findings between 49 and 96 wt.%. Heroin conc. ranged from 1 to 58 wt.%, with 50 % of the findings between 3 and 13 wt.% (shown in green). Trace amounts of cocaine mostly found in powder mixtures were excluded in the figure on the right.
For comparison, the purity of seized cocaine and heroin according to data from the European Drug Report is shown in blue.



Heroin Samples with High Amounts of 6-MAM



Unsuspected findings were particular high amounts of 6-MAM in some of the heroin samples. We don't know if this is caused by insufficient production conditions or induced by environmental effects, e.g. humidity during distribution or storage. For further investigation, we packed a heroin sample (heroin x HCl: 53 wt.%) into a little paper envelope and carried it around in the trouser pocket for three weeks to monitor potential degradation. No significant degradation could be detected during this period of time, so the high 6-MAM concentrations probably derive from improper production processes.

CONCLUSION

As expected, cocaine and heroin are the most common drugs consumed in the three consumption rooms in this area of Frankfurt. Up to now, there were no unusual analytical findings apart from the detection of fentanyl in cocaine and ropivacain in heroin specimens.

The presented LC-MS^n approach allows automated identification and quantitative determination of the active ingredients and cutting agents of drug preparations with active ingredients contents down to 1 % by weight. If lower levels are expected and quantification is of interest, the dilution step during sample preparation can easily be adjusted to match the linear calibration range of the calibration. LODs are typically in the range of 0.5 to 0.05 wt.% which is of particular interest for detecting highly potent opioids like fentanyl derivatives potentially added to heroin preparations.

In addition to this study, this method has also been used in several forensic cases dealing with seized materials, ancient opioid samples and pills containing designer stimulants and synthetic cannabinoids.

The approach is not considered to be used in cases dealing with cutoff questions but it's a sufficient and easy-to-use method for qualitative analysis of all kinds of powders and materials and a valuable tool to asses the potential harm of such specimens.

ACKNOLEDGEMENTS

We would like to thank the staff members and users of the three drug consumption rooms for their collection of sample material and the City of Frankfurt for financial support of this ongoing study.

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