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Fatal intoxication related to two new arylcyclohexylamine derivatives (2F-DCK and 3-MeO-PCE)

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Abstract

Continuous development and rapid turnover of drug market of new psychoactive substances (NPS) make it difficult to obtain up-to-date analytical methods for efficient detection of intoxication cases with new substances: no analytical data and no previously published concentration values in biological samples are indeed available. In this context, we aim to report the first fatal case involving two newly emerging arylcyclohexylamine derivatives (a group of dissociative ketamine-based substances): 2-fluoro-deschloroketamine (2F-DCK) and 3-methoxyeticyclidine (3-MeO-PCE). A 42-year-old man was found dead at his home with three plastic bags of “research chemicals” powders near him. Comprehensive screenings of drugs and toxic compounds as well as more selective assays (performed using NMR, HS-GC-FID, LC-MS/MS and LC-HRMS methods) allowed (1) to identify the three unknown powders, 2F-DCK, 3-MeO-PCE, and 5-methoxy-*N,N*-dimethyltryptamine (5-MeO-DMT, a hallucinogenic tryptamine-related NPS), with purity above 95%, and (2) to determine peripheral blood (1780, 90, and 52 µg/L), urine (6.1, 6.3, and 2.2 mg/L), bile (12, 3.5, and 1.7 mg/L), and vitreous humour (1500, 66 and 155 µg/L) concentrations of 2F-DCK, 3-MeO-PCE and 5-MeO-DMT, respectively. In addition, toxicological results also revealed recent use of cannabis, cocaine, and amphetamine by the victim, and hair analysis draw pathway of addiction (including experiments with various other NPS) for several months before death. This fatality was considered as the consequence of respiratory depression in a poly-drug user due to a “cocktail effect” of concurrent intakes of 2F-DCK (mainly), 3-MeO-PCE, 5-MeO-DMT, amphetamine, and cocaine. In addition, this case report provides analytical data that could support subsequent toxicological result interpretation in forensic cases involving such arylcyclohexylamine derivatives.

Keywords: Forensic, New Psychoactive Substances, Arylcyclohexylamine derivatives, Intoxication, 2F-DCK, 3-MeO-PCE, hair

Introduction

Detection of illicit or legal drugs in biological samples is the basis of analytical toxicology performed in a forensic situation. One of the major challenges for toxicologists all over the world consists in the continuous development of new psychoactive substances (NPS). Indeed, the rapidly changing NPS landscape makes it difficult to obtain up-to-date analytical methods for efficient NPS detection in bulk form, biological samples, and even more in *post-mortem* matrices [1]. NPS encompass a large range of narcotic or psychotropic drugs (*i.e.* stimulants, synthetic cannabinoids, benzodiazepines, opioids, hallucinogens and dissociatives) widely available as alternatives to many of the more traditional and common drugs of abuse (DOA). At the end of 2019, the European Monitoring Centre for Drugs and Drug Addiction has monitored more than 790 NPS, 53 of which were reported for the first time in Europe in 2019 [2].

This analytical challenge is amplified in cases related to NPS belonging to a somewhat minor NPS group and, even more, in cases of a newly emerging NPS which is still barely used and, consequently, sparsely reported in the literature (no or only few biological concentration or metabolism data are available). In European countries, NPS seizures are dominated by cathinone derivatives and synthetic cannabinoids, which together accounted for 64% of all seizures reported in 2018: 36% for cathinone derivatives and 28% for synthetic cannabinoids [2]. In contrast, even if recreational use of ketamine has gained popularity, especially in Asia (India, China) [3], new arylcyclohexylamine derivatives (NADs), a group of dissociative ketamine-based substances (methoxetamine, 3-methoxyphencyclidine, ...), still represent only a small part of the European NPS landscape. Indeed, conventional arylalkylamines and NADs concerned only 7% of NPS seizures in European Union in 2018 [2] and only 8% of identified NPS (between 2008 and April 2017) in France. Notwithstanding, obtained by slight chemical modification on ketamine scaffold, several new NDAs, *e.g.* 2-fluoro-deschloroketamine (2F-DCK) or 3-methoxyeticyclidine (3-MeO-PCE), with similar or more potent effects than ketamine, are emerging worldwide and have forensic concerns [4-6]. However, to the best of our knowledge, no fatality case involving these NADs has been yet reported in the literature. Here, we report a fatal case related to 2F-DCK and, to a lesser extent, 3-MeO-PCE use, documented with analytical data in various *post-mortem* biological samples.

Case history

A 42-year-old Caucasian man (165 cm, 61 kg) was found dead on his bed at home. He was seen living 24 hours before and his medical history included depressive disorders, history of drug abuse, and suicide attempts. Several drug tablets (alprazolam, tramadol, loxapine, lorazepam and quetiapine) were found near the **victim**, together with three plastic bags of “research chemicals” powders labeled “2F-DCK”, “3-MeO-PCE”, and “5-MeO-DMT” (5-methoxy-*N,N*-dimethyltryptamine, a hallucinogenic NPS belonging to the tryptamine group), respectively.

Two days later, autopsy findings were not specific (no external lesions other than non-specific injuries on the legs, congestion of internal organs and pulmonary oedema) and the coroner concluded to a death related to a non-specific asphyxia syndrome that could be of toxic origin. Biological samples (peripheral and cardiac blood, urine, vitreous humor, bile, gastric content, and brown hair sample) were maintained at - 20°C until analyses (except hair sample which was maintained at room temperature) and sent to a forensic toxicology laboratory together with the three powder samples.

Material and methods

Powder analysis

A **liquid chromatography with high-resolution mass spectrometry detection** (LC-HRMS) method (see below) was used to identify 2F-DCK, 3-MeO-PCE, and 5-MeO-DMT in the three powder samples found close to the victim. However, in order to confirm the absence of other compounds, such as synthesis impurities, and to check the purity of each powder, a nuclear magnetic resonance (NMR) analysis was performed as described previously [7-9]. The NMR spectra were recorded on AVANCE 300 (Bruker Biospin, France) operating at 300 MHz equipped with a 5 mm quadruple nucleus probe (QNP) probe at 295 K, and ¹H spectra were recorded with 64 scans, a 32-K time-domain data points with 4800 Hz spectral width, an acquisition time of 3.42 s, a relaxation delay of 2 s and a flip angle of 30°. The Free Induction Decays (FIDs) were transformed (0.3 Hz broadening) and the baseline was corrected. After thin manual grinding of the three powder samples using a mortar, 7.5 mg of each one were dissolved in 600 µL of methanol-D₄ and the ERETIC (Electronic REference To access In vivo Concentrations) method was then used for the determination of absolute concentrations of 2F-DCK, 3-MeO-PCE, and 5-MeO-DMT. ERETIC consisted of a digitally generated Gaussian peak (calibration was performed using a reference sample of 15 mg of caffeine in 600 µL of CDCl₃ and a sample of 10 mg of the same substance in 600 µL of CDCl₃ was used as control) inserted into the spectrum of a sample by the software after processing the FID. With ERETIC,

the peak area value gives directly information about the concentration of protons and the sample purity [10].

Biological sample analysis

Hair sample pre-treatment consisted in a decontamination step using 2 x 2-min baths in water, followed by 2 x 1-min baths in dichloromethane. Between the different decontamination steps, the hair strand was dried using absorbent paper and the last dichloromethane decontamination solutions were dried under nitrogen and kept for analysis. It is of note that in our practice, in order to assess external contamination issues (especially in *post-mortem* situations), the second dichloromethane wash bath solution is analyzed and the obtained result is compared with the concentration measured in the hair sample (when the ratio wash bath/hair is higher than 0.1, possibility of external contamination is considered). Then, the decontaminated hair strand was segmented in four sections from root to tip: three 1-cm length hair sections (S1, S2 and S3) and a remaining hair section from 3 cm to the tip (5 cm) (S4). Each hair section was cut into small pieces (< 1 mm): 20 mg were soaked in 500 μ L of methanol for 12 hours at 60 °C. After centrifugation, 100 μ L of the supernatant were added to 100 μ L of the internal standard mixture (methyl-clonazepam at 1.25 mg/L and β -hydroxy-ethyltheophyllin at 16 mg/L in methanol), then evaporated, and reconstituted using 100 μ L of ammonium formate buffer 5 mM, pH 3 and acetonitrile in 0.1 % formic acid (87/13, v/v) [9,10-14].

Comprehensive screenings of drugs and toxic compounds in biological samples were performed using (i) a liquid chromatography with tandem mass spectrometry detection (LC-MS/MS) method and (ii) a LC-HRMS method consisting in untargeted data acquisition (full scan) and targeted identification (using a homemade database of more than 1700 substances including more than 650 NPS or metabolites – feb 2020). The following quantification was performed using analytical reference standards, as previously reported [8,12]. Criteria used for identification of the targeted compounds included 3 mDa as exact mass error of the precursor ion as well as product ions, and +/- 0.25 min as the tolerance in retention time for the precursor ion. More selective assays for alcohols and several classes of therapeutic drugs, DOA or other toxicants were carried out in liquid biological samples with various *ad-hoc* dedicated methods using immunoassays, headspace gas chromatography with flame ionization detection (HS-GC-FID), LC-MS/MS and LC-HRMS.

The 3 identified NPS (2F-DCK, 3-MeO-PCE and 5-MeO-DMT) were quantified using a dedicated LC-HRMS method (XEVO G2-XS QTOF, Waters, Manchester, UK) [8]. Briefly, after addition of 100 μ L of the aforementioned internal standard mixture, 100 μ L of liquid biological sample or hair extract were diluted in 400 μ L of 3% 5-sulfosalicylic acid and

subsequently centrifuged at 4 °C for 14 min at 32000 g. Seventy-five µL of the supernatant were then injected into the chromatographic system consisting of two binary solvent manager LC pumps, a sample manager autosampler, and a column manager oven Acquity (Waters). The on-line extraction step was performed using an OASIS HLB column (30 x 2.1 mm, 20 µm) (Waters) and the mobile phase consisted in 0.2 % ammonium solution (A1) and 100% methanol (B1). Loading of the sample was performed with 0% B1 at a flow rate of 2.0 mL/min for 0.5 min. Injection in the chromatographic system occurred at 0.5 min: valve switch and back-flushing for 13.5 min using the chromatographic separation mobile phase. During this injection step, the flow (A1 and B1) was as follows: 0.5 min, 0% B1, flow rate of 2.0 mL/min; 1.0 min, 0% B1, flow rate of 0.2 mL/min; 5 min, 100% B1, flow rate of 0.2 mL/min; 14 min, 100% B1, flow rate of 2.0 mL/min. At 14 min, after a new switch to initial valve position, the initial conditions were achieved at 14.2 min. The chromatographic separation was then performed using an ACQUITY HSS C18 column (150 x 2 mm, 1.8 µm, Waters) in an oven at a temperature of 50 °C, and mobile phases including ammonium formate buffer 5 mM, pH 3 (A2) and acetonitrile in 0.1 % (v/v) formic acid (B2); a flow rate of 0.4 mL/min was used. The initial concentration of the mobile phase B2 (3 %) was held until 0.5 min, increased to 30% at 4.2 min, to 50% at 9 min, then to 100 % at 9.5 min, and finally held until 14 min. Mass spectrometry data were acquired using a XEVO G2-XS QTOF (Waters) instrument controlled with MassLynx 4.1 software. Mass spectrometric conditions were as follows: positive electrospray ionization interface (ESI+), ion spray voltage of 20 V, nitrogen as desolvation gas and argon as collision gas, source temperature at 140 °C and desolvation temperature at 500 °C with a desolvation gas (nitrogen) flow rate of 900 L/h. Conditions for the time of flight mass spectrometer scan mode were as follows: scan range 100-1000 m/z at 6 eV (low energy) and 50-1000 m/z with a collision energy ramp from 10-40 eV (high energy). Calibration was performed using 2F-DCK, 3-MeO-PCE or 5-MeO-DMT spiked blood specimens in the concentration range of 10 to 3000 µg/L and three independent internal quality control samples (25, 500, and 2000 µg/L) were analyzed together with the *post-mortem* samples.

The validation procedure of this assay complied with both the French Analytical Toxicology Society (SFTA) and international recommendations for the validation of new analytical methods and acceptance criteria for the validation of new analytical methods used in single case studies of uncommon analytes [15-18], including linearity, limit of detection (LOD), lower and upper limits of quantification (LLOQ and ULOQ), accuracy, precision, and matrix effects. Calibration curves (n=6), estimated using 1/x weighted quadratic regression, were considered acceptable if the coefficient of determination (r^2) was at least 0.95 The LOD was defined as the

lowest concentration with presence of two transitions and a signal-to-noise ratio of at least 3. The LLOQ was the lowest concentration with presence of two transitions together with an intra-assay precision CV% and a relative bias both lower than 20%. Inter-day CV and bias were assessed using six replicates of independent spiked samples at 3 concentration levels, and ion suppression phenomenon was studied following the experimental system previously proposed by Antignac *et al.* [19].

Results

NPS powders

LC-HRMS together with NMR spectroscopy were applied for identification and characterization of the three powder samples collected close to the **victim**. 2F-DCK, 3-MeO-PCE, and 5-MeO-DMT were detected using both LC-HRMS (identification criteria for 2F-DCK, 3-MeO-PCE, and 5-MeO-DMT are presented in Table 1) and NMR (Figure 1). No significant organic impurity was detected in these powders using both LC-HRMS and NMR. In addition, using the ERETIC method, NMR analysis revealed a 2F-DCK, 3-MeO-PCE or 5-MeO-DMT content over 95% in each powder (the remaining 5% consist putatively in inorganic compounds).

Biological samples

Positive results in biological samples are reported in Table 2. It is of note that blood and urine samples were negative for ethanol (and urinary ethylglucuronide < 0.1 mg/L) and none of the drugs found near the **victim** (alprazolam, tramadol, loxapine, and quetiapine) was detected in liquid biological samples except lorazepam.. These three NPS were subsequently quantified in blood (LOD: 5 µg/L, LLOQ: 10 µg/L, ULOQ: 3000 µg/L, inter-day CV and bias < 14%, $r^2 \geq 0.97$ for each calibration curve; **additional validation data are provided in supplementary material**) and other liquid biological samples after adequate dilution. In hair, LOD and LLOQ were 25 and 100 pg/mg, respectively, and hair calibration curves were built and validated in the range of 100-5000 pg/mg for the three NPS (**additional validation data are provided in supplementary material**). It is of note that a hair external contamination issue can be considered in the present case, but was certainly not of paramount importance as no significant drug concentration was detected in the second dichloromethane wash bath solution.

Discussion and conclusion

On a toxicological point of view, this fatality is dominated by (and probably related to) NPS positive results, especially NADs (2F-DCK and 3-MeO-PCE). These NPS are commonly perceived as ketamine-like dissociative substances and are believed to act as relatively selective non-competitive antagonists at the ionotropic NMDA glutamatergic receptor [20]. The affinity of NAD for this receptor is strongly correlated with the clinical potency in producing feelings of detachment and dissociation from self and the environment [21]. Accordingly, the current rise of new NAD is challenging. Indeed, NAD-related intoxication cases usually exhibit enhanced clinical effects owing to a regular increase in receptor binding affinity and mainly a greater lipophilicity than ketamine [5,22].

Comparatively to ketamine, 2F-DCK is more lipophilic due to the replacement of the chlorine group by a fluorine [20]. Nevertheless, there is currently no clear pharmacological or toxicological information about 2F-DCK because of its newness. In Hong Kong, 2F-DCK appears to be mainly consumed **through inhalation and** reported doses ranged from 87.5 to 330 mg [5]. On internet forums, users reported that 2F-DCK has a similar potency and same dissociative effects (including anesthesia and analgesia without loss of consciousness) as ketamine [6]. Clinical effects including neurological (agitation, delirium, abnormal behavior, and convulsions) and cardiovascular effects (hypertension, tachycardia) were reported in a poisoning outbreak in Hong Kong (report of 20 intoxication cases confirmed by urine 2F-DCK detection) [5]. **It is obvious that the effects of a 2F-DCK overdose are broadly similar to those of a ketamine overdose. Although excessive cardiovascular stimulation (elevated heart rate and blood pressure) is observed in ketamine overdose cases, the cause of fatality is more commonly attributed to dose-dependent respiratory depression, particularly when the drug is used together with other CNS suppressants.** There are only few reported 2F-DCK concentrations in biological samples in the literature. Five urine concentrations (21.7, 56.2, 213, 21.7, 105, and 919 $\mu\text{g/L}$) were reported following 2F-DCK intoxication cases which occurred in March and April 2020 in Taipei, Taiwan [23]. 2F-DCK blood concentrations (5, 30, 200, 220, and 480 $\mu\text{g/L}$) were reported in 5 Danish drivers suspected of driving under the influence of drugs in 2020 and 2F-DCK hair concentrations were also reported (2 cm-length hair segments, from proximal to distal: 7, 31, and 34 pg/mg) in one case [4].

In the present case, 2F-DCK observed concentrations in biological samples appear high (*e.g.* 2F-DCK blood concentration is four times higher than the higher previously published one). These results support the hypothesis of a lethal dose intake of 2F-DCK. **Furthermore, given that the potency of 2F-DCK is similar to, or slightly higher than, that of ketamine, these results could thus be compared to those observed in fatalities related to ketamine. In this way, in a**

retrospective study (2000-2019) of sixty-eight Australian cases in which self-administered ketamine was a mechanism contributory to death, the median blood ketamine concentration was 0.2 mg/L (0.02-6.9 mg/L) and other drugs were detected in 95.5% of cases [24]. In a mixed drug fatality involving ketamine and ethanol (173 mg/dL), a ketamine blood concentration of 1.8 mg/L was reported [25]. Nevertheless, there is very few reports of mono-intoxication with ketamine: a high blood ketamine concentration of 27 mg/L was reported in a case of homicide for homosexual ends [26], a ketamine blood concentration of 3.8 mg/L was reported in an unusual homicide caused by chronic ketamine poisoning [27], and a ketamine concentration of 1.8 mg/L was observed in femoral blood of a 26-year-old man [28] that is very similar to the 2F-DCK observed concentration in peripheral blood (1.78 mg/L) of the present case.

Additionally, the observed 2F-DCK hair concentrations are high, in the ng/mg range, in agreement with the hypothesis of repeated 2F-DCK intakes by the victim for several months. Dissociative drugs are rarely consumed alone and most NAD users are poly-users [5]. Accordingly, our results (Table 2) suggest recent intakes by the victim of two other NPS (3-MeO-PCE and 5-MeO-DMT) and DOA (cannabis, amphetamine, and cocaine).

3-MeO-PCE is another NAD related to eticyclidine, which exhibits slightly more potent hallucinogenic effects than phencyclidine (PCE) [29,30]. Even if published analytical methods for 3-MeO-PCE detection in biological samples are available [31,32], no 3-MeO-PCE concentration value in biological samples is available in the literature. As a consequence, observed 3-MeO-PCE concentrations in the present case (90, 6305, 3500, and 66 µg/L in peripheral blood, urine, bile, and vitreous humor, respectively) can only be cautiously compared to 3-MeO-PCP (3-methoxyphencyclidine, another NAD, analogue of phencyclidine) previously reported concentrations. 3-MEO-PCP blood concentrations ranging from 49 to 350 µg/L in non-fatal intoxication cases, of 380 µg/L in a fatal mono-intoxication, and ranging from 50 to 3200 µg/L in fatal mixed drug intoxication cases are reported in the literature [33-36]. The 3-MeO-PCE blood concentration found in the present case (90 µg/L) appears to be in the lower range of observed 3-MEO-PCP blood concentrations in non-fatal and fatal cases.

5-MeO-DMT is a powerful tryptamine naturally-occurring hallucinogen, 4 to 10 times more potent than dimethyltryptamine (DMT), a non-selective 5-HT agonist. 5-MeO-DMT can be found in several plants (*e.g.* major ingredient of South American *Virola* snuffs and *Ayahuasca* beverage) and in high concentrations in *Bufo alvarius* toad venom [37,38]. In a fatal intoxication case following the ingestion of 5-MeO-DMT in an *Ayahuasca* preparation, observed concentrations were 1880, 1200, 9810, and 9590 µg/L in heart blood, peripheral blood, bile,

and urine, respectively [39]. Considering the lower 5-MeO-DMT concentration values (52, 2190, 1740, and 155 µg/L in peripheral blood, urine, bile, and vitreous humor, respectively) we observed in the present case, 5-MeO-DMT can be considered as contributive to the death, but probably to a lesser extent than that of 2F-DCK.

Lastly, *post-mortem* blood results also indicate recent use by the victim (close to the death or some hours before) of cannabis, cocaine, and amphetamine. From a forensic point of view, a recent consumption of cocaine and amphetamine **needs also to be considered because of** their well-known cardiotoxicity. All in all, this fatality can be considered as related to a mixed drug intoxication involving 2F-DCK (mainly), 3-MeO-PCE, 5-MeO-DMT, amphetamine, and cocaine.

In hair, the 3-MeO-PCE and 5-MeO-DMT concentration values, ranging from 1610 to 3610 pg/mg and from 1990 to 3390 pg/mg, respectively (i) are the first reported ones for these two NPS to the best of our knowledge, and (ii) probably support the hypothesis of repeated 3-MeO-PCE and 5-MeO-DMT intakes for several months, in an identical way than for 2F-DCK. Hair analysis also revealed the presence of 7 NPS in addition to 2F-DCK, 3-MeO-PCE, and 5-MeO-DMT: two other arylcyclohexylamines [3-MeO-PCP and diphenidine (1,2-diphenylethyl)-piperidine], two new synthetic benzodiazepines (etizolam and flualprazolam), a synthetic cannabinoid [4F-MDMB-BINACA (methyl 2-[1-(4-fluorobutyl)-1H-indazole-3-carboxamido]-3,3-dimethylbutanoate)], a benzofuran analogue of amphetamine [X-APB (6 or 5-(2-aminopropyl)benzofuran)], and another stimulant that is a fluorinated derivative of phenmetrazine [3-FPM (3-Fluorophenmetrazine)]. Repeated intakes of conventional DOA as well as of pharmaceutical drugs during the past months were also concluded from hair analyses. Overall, the victim's hair analysis draws a clear pathway of addiction (including experiments of various NPS) for several months before death.

In conclusion, on the basis of drug packages found near the **victim** and toxicological results, the present fatal case was considered as the consequence of **respiratory depression** in a poly-drug user due a “cocktail effect” of concurrent intakes of 2F-DCK (mainly), 3-MeO-PCE, 5-MeO-DMT, amphetamine, and cocaine. This first report of a fatal case involving two emerging NAD, 2F-DCK and 3-MeO-PCE, will help future toxicological result interpretation in forensic case investigations involving such NAD.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Ethical approval

This article does not contain any studies with human participants or animals that would have been performed by the authors.

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Table and Figure legends

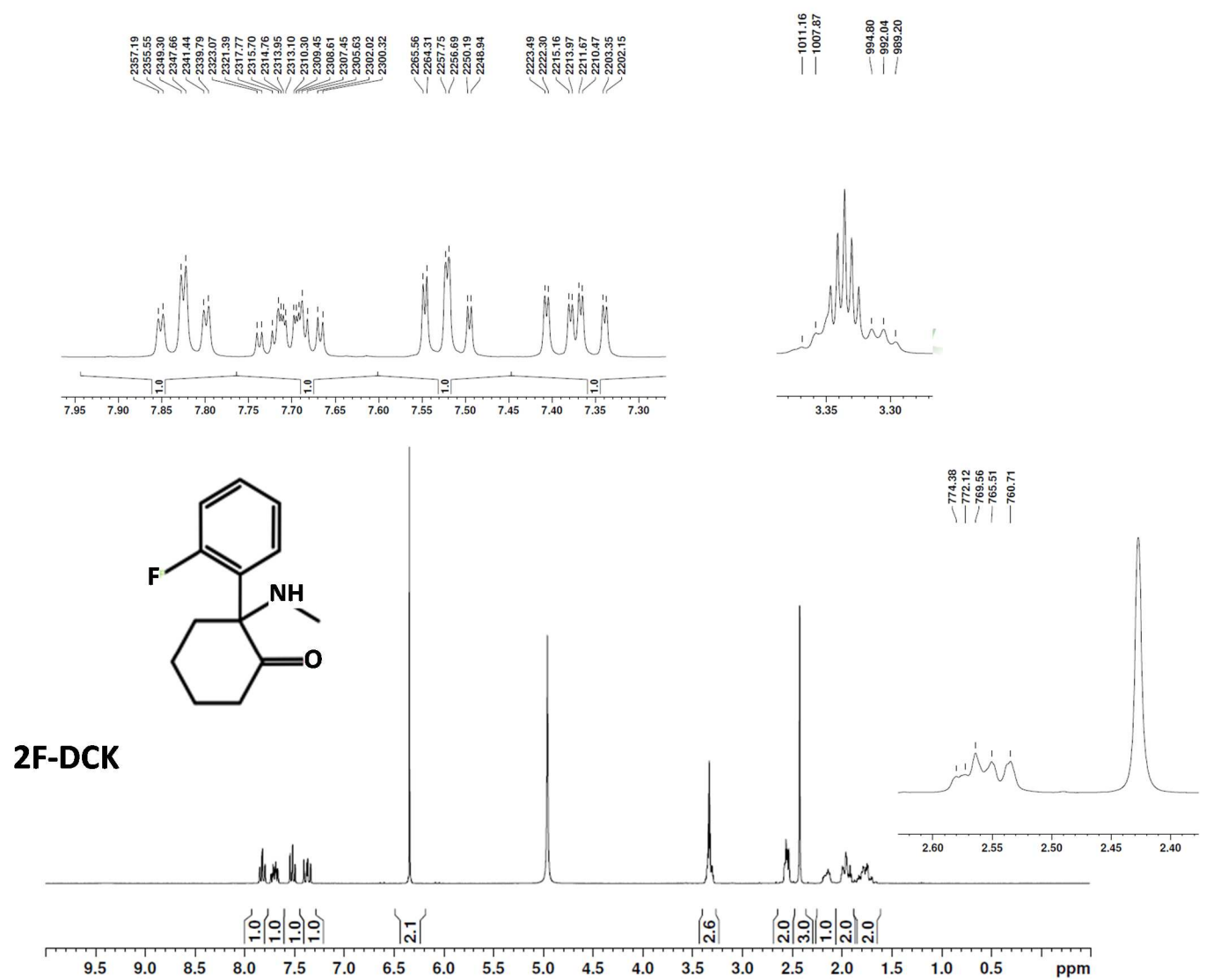
Figure 1: 2F-DCK, 3-MeO-PCE and 5-MeO-DMT chemical structure and ¹H-NMR (300 MHz, MeOD) analysis of the 3 powders including signals related to (A) **2F-DCK** [δ 7.82 (td, J = 7.9, 1.6 Hz, 2H), 7.70 (dddd, J = 8.3, 7.2, 5.3, 1.7 Hz, 2H), 7.52 (td, J = 7.8, 1.2 Hz, 2H), 7.37 (ddd, J = 11.8, 8.3, 1.2 Hz, 2H), 3.39 – 3.27 (m, 5H), 2.64 – 2.48 (m, 4H), 2.43 (s, 6H), 2.25 – 2.06 (m, 2H), 2.06 – 1.88 (m, 4H), 1.88 – 1.64 (m, 4H)], (B) **3-MeO-PCE** [δ 7.48 (t, J = 8.0 Hz, 1H), 7.28 – 7.20 (ddd, J = 7.8, 1.9, 0.7 Hz, 1H), 7.19 (t, J = 2.1 Hz, 1H), 7.07 (ddd, J = 8.3, 2.4, 0.7 Hz, 1H), 3.88 (s, 3H), 2.76 (d, J = 12.3 Hz, 2H), 2.69 (q, J = 7.4 Hz, 2H), 2.02 – 1.56 (m, 5H), 1.53 – 1.25 (m, 3H), 1.18 (t, J = 7.3 Hz, 3H).], (C) **5-MeO-DMT** [δ 7.28 (dd, J = 8.8, 0.4 Hz, 1H), 7.17 (s, 1H), 7.09 (d, J = 2.3 Hz, 1H), 6.82 (dd, J = 8.8, 2.4 Hz, 1H), 3.86 (s, 3H), 3.33 – 3.23 (m, 2H), 3.21 – 3.05 (m, 2H), 2.85 (s, 6H).], together with other signals presumably related to powder excipients.

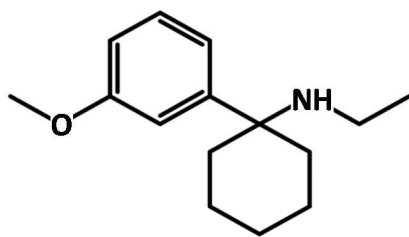
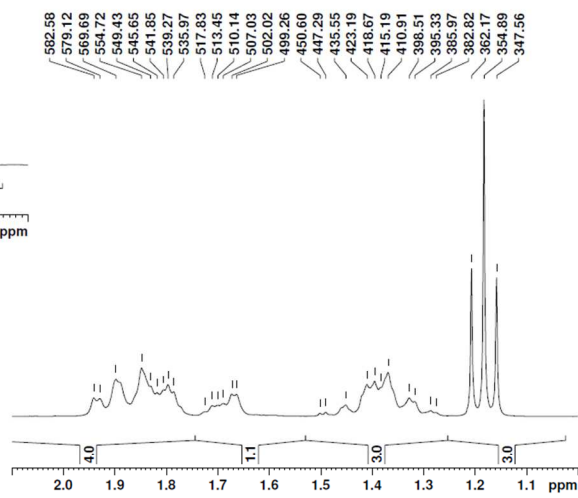
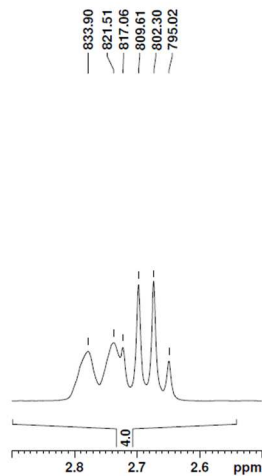
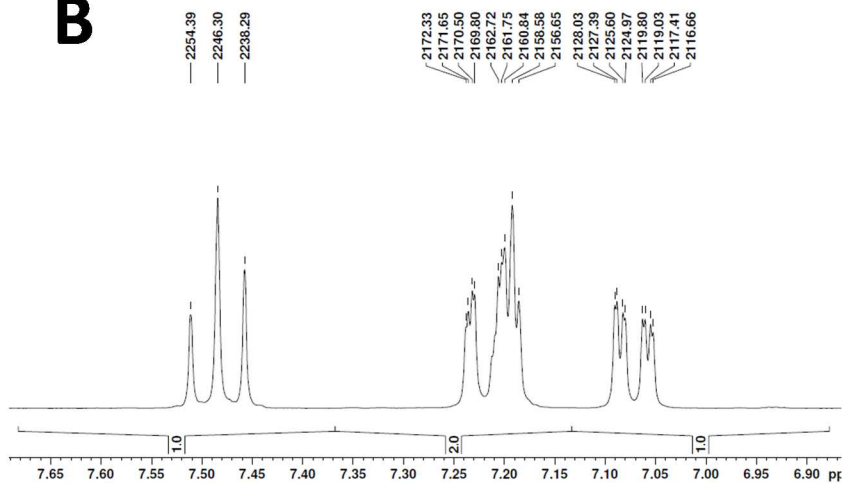
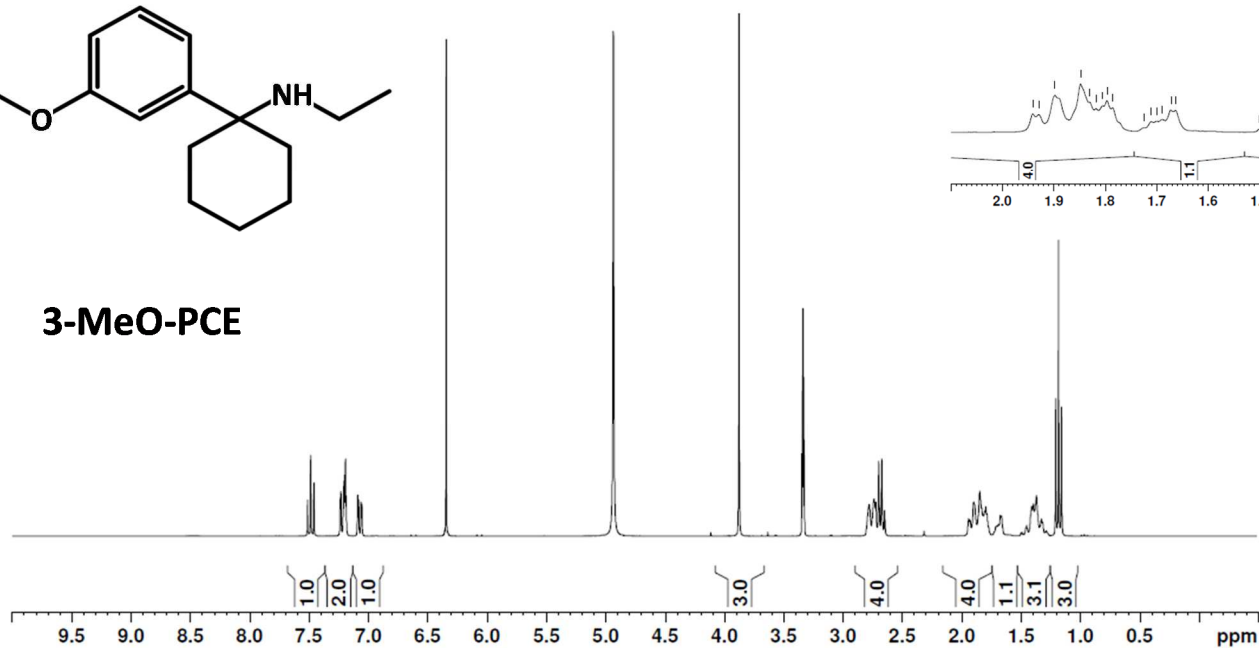
Table 1: LC-HRMS-related identification criteria for 2F-DCK, 3-MeO-PCE and 5-MeO-DMT.

Table 2: Results of the toxicological investigations in biological samples [liquid samples concentration in $\mu\text{g/L}$; in bold: NPS; nd: not detected; nt: not tested; *S1 to S4 hair concentrations in pg/mg ; 2F-DCK: 2-fluoro-deschloroketamine; 3-MeO-PCE: 3-methoxyeticyclidine; 5-MeO-DMT: 5-methoxy-*N,N*-dimethyltryptamine; 3-MeO-PCP: 3-methoxyphencyclidine; 4F-MDMB-BINACA: methyl 2-[1-(4-fluorobutyl)-1H-indazole-3-carboxamido]-3,3-dimethylbutanoate; X-APB: 6 or 5-(2-aminopropyl)benzofuran; 3-FPM: 3-Fluorophenmetrazine].

Figure 1

A



B**3-MeO-PCE**

C

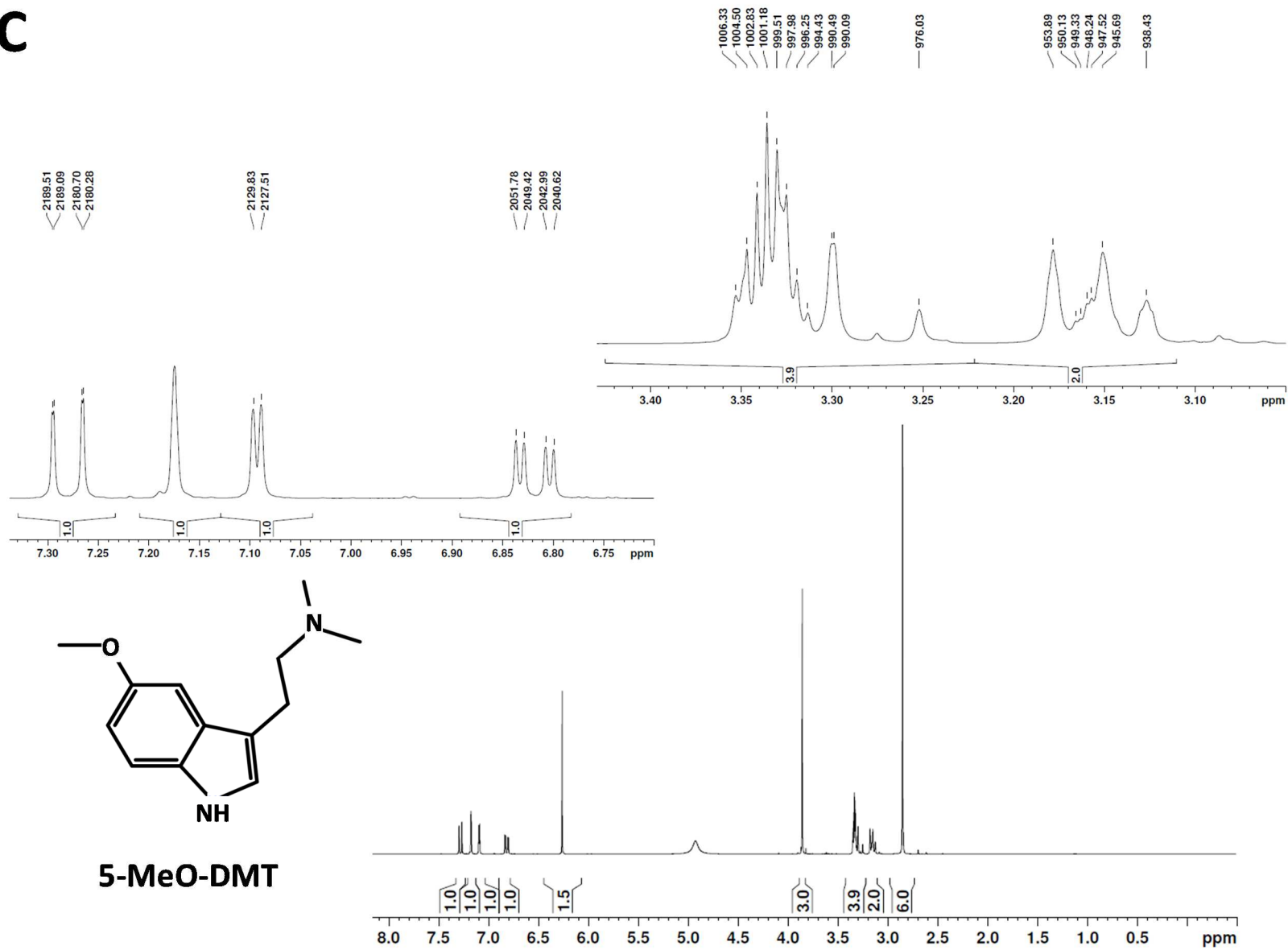


Table 1.

	Name	Formula	[M+H+]	RT (min)	Main fragment ions
2F-DCK	2-fluoro-deschloroketamine	C ₁₃ H ₁₆ FNO	222.128	4.13	109.04 ; 163.09 ; 191.09 ; 204,12
3-MeO-PCE	3-methoxyeticyclidine	C ₁₅ H ₂₃ NO	234.185	5.67	121.06 ; 189.13 ; 81.07
5-MeO-DMT	5-methoxy- <i>N,N</i> -dimethyltryptamine	C ₁₃ H ₁₈ N ₂ O	219.149	4.06	58.07 ; 174.09 ; 161.08 ; 189.07

Table 2

Compound	Peripheral blood	Urine	Bile	Vitreous humour	Hair (detection in at least one hair section)	
					Also present in blood and/or urine	Only detected in hair
2F-DCK	1780	6106	12200	1500	4410, 4860, 5080, 4330*	3-MeO-PCP Diphenidine Etizolam Flualprazolam 4F-MDMB-BINACA X-APB 3-FPM Cannabidiol, Cannabinol Benzocaine Quetiapine Loxapine (and metabolites) Acetaminophen Tramadol (and metabolites) Clozapine Diazepam (and metabolites)
3-MeO-PCE	90	6305	3500	66	1610, 3600, 3410, 3610*	
5-MeO-DMT	52	2190	1740	155	1990, 3030, 3160, 3390*	
THC	9.4	nd	nt	nt	+	
THC-COOH	24	+	nt	nt	nt	
THC-OH	1.1	nd	nt	nt	nt	
Amphetamine	27	970	43	nd	+	
Cocaine	nd	+	nd	+	+	
BZE	2.5	787	32800	+	+	
EME	9.8	32	8400	+	+	
Levamisole	+	+	nd	+	+	
Lorazepam	nd	7.5	186	nd	+	