T. Sobolevsky, I. Prasolov, G. Rodchenkov

# Designer stimulants recently identified on black market

Antidoping Centre, Moscow, Russia

*Abstract*

Recently, designer stimulants have become a great concern due to their availability on the market as bath salts, plant feeders *etc*. We have ordered several preparations over the Internet, and six substances were identified: mephedrone (methylmethcathinone), flephedrone (fluoromethcathinone), fluoroamphetamine (2 isomeric compounds), methylamphetamine (3- or 4-substituted), and methylenedioxypyrovalerone.

Forensic urine samples (samples provided to our laboratory by local drug enforcement body for investigation) were also analyzed and many of them were found to contain these designer stimulants. Some metabolic products were tentatively identified for mephedrone, flephedrone and methylenedioxypyrovalerone. In these urine samples the parent drugs were always detectable.

*Introduction*

Following the designer steroids synthesized with the purpose of getting around the regulations of drug enforcement bodies, the designer stimulants have become a concern as well. Recently Perrenoud *et al*. reported the detection of 4-methyl-2-hexanamine, a stimulant analog of tuaminoheptane [1]. During 2009 we detected this compound, also known as 1,3-dimethylpentylamine or 1,3-dimethylamylamine, as a component of several so-called "social stimulants" which are available over-the-counter in Russia. However, at present the range of stimulants is much wider and includes various amphetamine and cathinone derivatives. They might be sold over the Internet as bath salts, scrubs or plant feeders and usually have a statement on the package "not for human consumption". Nevertheless, recreational drug users do understand its intended mode of administration.

Most publications related to the identification of designer stimulants belonging to the cathinone class have appeared in 2009–2010 [2-6], indicating the increasing popularity of these "legal" (that is, *not controlled*) stimulants among the drug abusers.

*Materials and Methods*

**Sample preparation**

*Powders*: 5 mg of specimen were extracted with 1 ml of methanol in ultrasonic bath. Upon centrifugation, 5 µl of the solution were taken to dryness under nitrogen and reconstituted in 100 µl of ethyl acetate.

*Urine*: To 3 ml of urine 1 ml of carbonate buffer (3M, pH 10.1) and 2 g $Na_2SO_4$ were added followed by extraction with 5 ml of diethyl ether. Ethereal extract was taken to dryness under nitrogen and reconstituted in 100 µl of ethyl acetate.

**Instrumental parameters**

Samples were analyzed on an Agilent MSD 5973, under the conditions as follows.

Electron ionization, 70 eV; fullscan data acquisition (*m/z* 50-500).

Interface temperature: 280°C; ion source and quadrupole temperature: 230°C and 150°C.

Column: Rxi-1ms, 12 m × 0.2 mm × 0.33 µm.

Temperature program: 110°C (2 min), ramp 15°C/min to 300°C (4 min).

Injection: split, 2 µl at 1:20.

*Results and Discussion*

In 2009 we have obtained through the Internet various "party powders", "herbal highs" *etc.* and 6 compounds were identified as a result. The identification was done based on GC-MS electron ionization data and comparison to the literature available at the moment [2–4]. These include methylenedioxypyrovalerone (MDPV), 4-methylmethcathinone (mephedrone), fluoromethcathinone (flephedrone, either *meta*- or *para*-substituted), fluoroamphetamines (two isomers detected), and methylamphetamine (either *meta*- or *para*-substituted, *i.e.* not ortetamine). Several preparations occasionally contained other ingredients like hordenine, caffeine and lidocaine or synthesis by-products.

During the last year we were also receiving forensic urine samples from a local drug enforcement body. These samples were collected from persons who were seized in a condition of presumptive drug intoxication. Each sample was analyzed, and some of them revealed the presence of the abovementioned drugs and/or their metabolites.

We have found that fluoroamphetamines, methylamphetamine and methylenedioxypyrovalerone might be monitored as parent drugs, though the latter is slightly metabolized to the products tentatively identified as MDPV-ketone and hydroxymethoxypyrovalerone (<5%). Flephedrone mostly has its *β*-oxo moiety reduced, with parent compound being less abundant

but well detectable (<50%). Unlike flephedrone, mephedrone shows different metabolic pattern: its main metabolite is hydroxylated at the tolyl methyl group. *N*-desmethyl metabolites of both flephedrone and mephedrone are low (<5%). Our findings are in agreement with the published data [5]. The electron ionization mass spectra of the studied designer stimulants and their tentative metabolites are presented in **Fig. 1**.

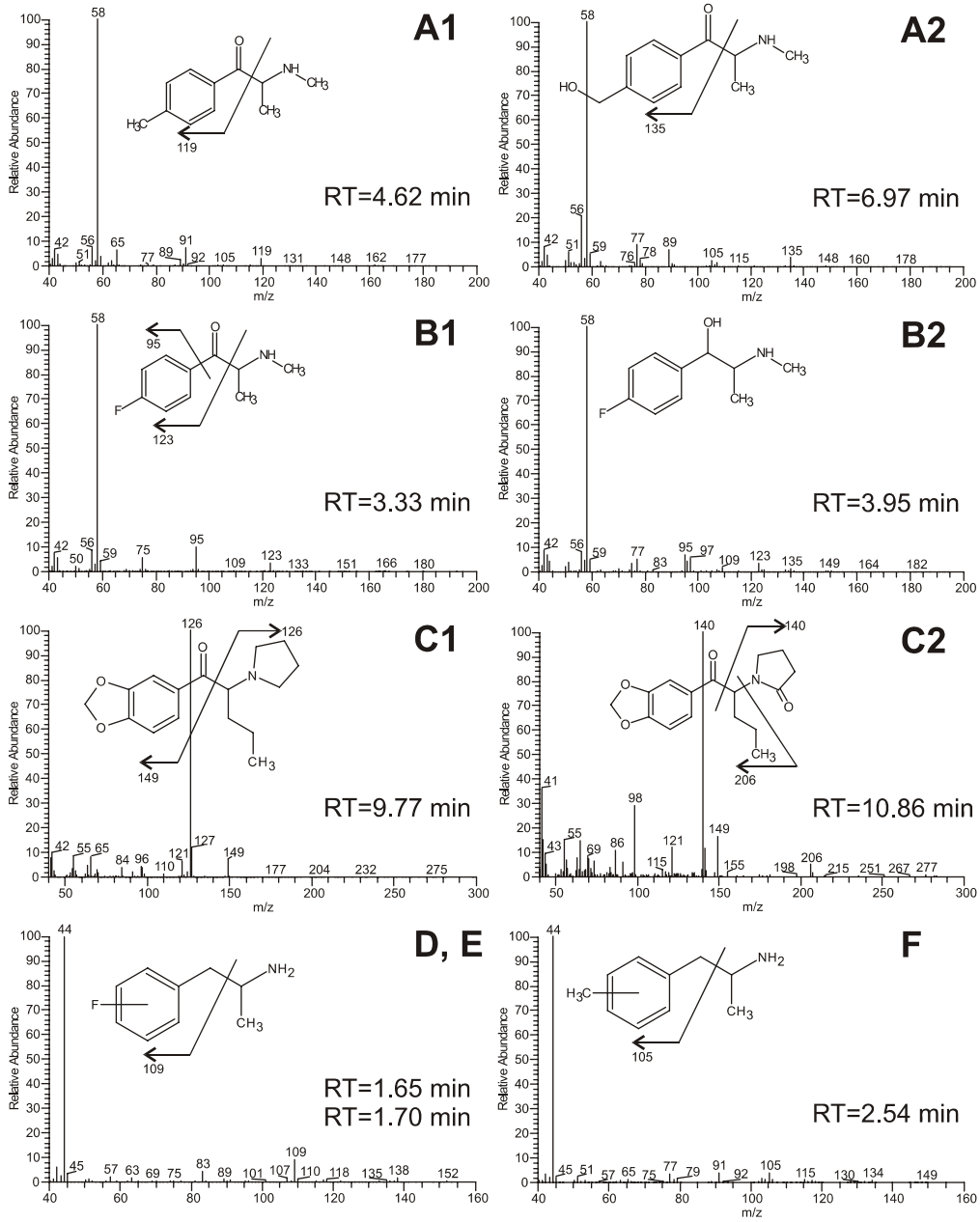


**Fig. 1**. EI mass spectra of mephedrone (A1, MW=177), hydroxymephedrone (A2, MW=193), flephedrone (B1, MW=181), dihydroflephedrone (B2, MW=183), methylenedioxypyrovalerone (C1, MW=275), oxo-metabolite (C2, MW=289), fluoroamphetamine (D, E: two isomers with identical mass spectra, MW=153) and methylamphetamine (F, MW=149; ortetamine elutes at 2.59 min under these conditions). ISTD (diphenylamine) retention time: 6.0 min.

*Conclusion*

The GC-MS screening of volatile compounds might be adapted to include these novel stimulants in urine, as they are structurally related to ephedrine- and amphetamine-like substances and will be extracted under the same conditions. As category S6 of the Prohibited List is open for "*other substances with a similar chemical structure or similar biological effects*", these designer stimulants are to be considered as related compounds, administration of which may (or shall?) result in an adverse analytical finding. Therefore, antidoping laboratories are advised to update their screening procedures whenever possible.

*References*

1. Perrenoud L, Saugy M, Saudan C. (2009) Detection in urine of 4-methyl-2-hexaneamine, a doping agent. J Chromatogr B Analyt Technol Biomed Life Sci 877(29), 3767-3770.

2. Camilleri A, Johnston MR, Brennan M, Davis S, Caldicott DG. (2010) Chemical analysis of four capsules containing the controlled substance analogues 4-methylmethcathinone, 2-fluoromethamphetamine, alpha-phthalimidopropiophenone and N-ethylcathinone. Forensic Sci Int. 197(1-3), 59-66.

3. Westphal F, Junge T, Rösner P, Sönnichsen F, Schuster F. (2009) Mass and NMR spectroscopic characterization of 3,4-methylenedioxypyrovalerone: a designer drug with alpha-pyrrolidinophenone structure. Forensic Sci Int. 190(1-3), 1-8.

4. Archer RP. (2009) Fluoromethcathinone, a new substance of abuse. Forensic Sci Int. 185(1-3), 10-20.

5. Meyer MR, Wilhelm J, Peters FT, Maurer HH. (2010) Beta-keto amphetamines: studies on the metabolism of the designer drug mephedrone and toxicological detection of mephedrone, butylone, and methylone in urine using gas chromatography-mass spectrometry. Anal Bioanal Chem. 397(3), 1225-1233.

6. Brandt SD, Sumnall HR, Measham F, Cole J. (2010) Analyses of second-generation 'legal highs' in the UK: Initial findings. Drug Test Anal. (Epub ahead of print).