Presence and composition of cathinone derivatives in drug samples taken from a Drug Test Service in Spain (2010–2012)

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Objective  The aim of this study was to describe the presence and composition of cathinone derivatives (CDs) in drug samples analyzed at a Drug Testing Service.

Material and methods  Data provided by the Drug Testing Service at Energy Control (a Spanish organization working in risk reduction among recreational drug users) were obtained from samples delivered as, or containing CDs, between January 2010 and June 2012. Specimens were identified by combining thin layer chromatography and gas chromatography associated with mass spectrometry.

Results  Two hundred and thirty-seven (3.8%) of the 6199 samples were delivered as, or contained CDs. 22 different CDs were detected, alone or in different combinations. Methylone (24.9%), mephedrone (24.5%), 4-methylethcathinone (9.28%), and methylenedioxypyrovalerone (6.8%) were the most common CDs. These substances were also found in 80 (1.3%) of 6042 samples delivered allegedly containing drugs different from CDs (such as 3,4-methylenedioxy-N-methylamphetamine (MDMA), amphetamines, ketamine...).

Conclusions  Cathinone derivatives were markedly present in the Spanish drug market during the studied period. There is no evidence to conclude that use of CDs will become widespread or relevant for public health, but the phenomenon must be followed, as the potential risks of these new drugs of abuse are substantial. Copyright © 2013 John Wiley & Sons, Ltd.

KEY WORDS—cathinones; mephedrone; cathinone derivatives; legal highs

INTRODUCTION

An increasing number of synthetic cathinones have appeared in the European drug scene during the last 5 years. Synthetic cathinones are derivatives of cathinone, a naturally occurring beta-ketone amphetamine analog, which possess amphetamine-like properties and the ability to modulate monoamine neurotransmission causing distinct psychoactive effects (Prosser and Nelson, 2012). There is growing evidence that these substances are becoming popular among recreational drug users in Europe (EMCDDA, 2011a).

In this context, Legal Highs have received special attention during the past years. Legal Highs are defined as a range of chemical and herbal preparations marketed as legal alternatives to popular but illicit recreational drugs (Ayres and Bond, 2012). They are generally sold online as bath salts, bong cleaners, incenses, or fertilizers. The composition of the substances is never written on the labels, and neither is there any dosage information, precautions, or contraindications. They usually include the warning “not for human consumption” in order to avoid health and safety controls. But contradicting this statement, they also include the message “only for people over 18” and some of them include the warning “keep away from the reach of children”. A wide range of psychoactive substances (including synthetic cannabinoids, dissociatives as methoxetamine, or natural psychedelics) have been detected as components of Legal highs, but a significant proportion of them are based on synthetic cathinones (Davies et al., 2010; Ayres and Bond, 2012; Zuba and Byrska, 2012). Very few data are available concerning this recent phenomenon and most of them come from toxicological studies (Coppola and Mondola, 2012; Meyer et al., 2012), forensic studies (Sorensen, 2011; Rust et al., 2012), or police seizures (EMCDDA, 2011b; Sacco, 2011), but there is not much data available obtained from drug users (Dargan et al., 2010).
Energy Control is a Spanish non-governmental organization, which works in the field of risk and harm reduction among recreational drug users. One of its programs is the Drug Testing Service (DTS), which allows users to submit samples of their drugs to a central facility to have their content tested, as well as to obtain information and receive advice on risk reduction. Typical users of this service are non-problematic young people that use drugs in recreational settings (clubs, parties, raves). We performed a search in our database to describe the presence and composition of cathinone derivatives (CDs) in drug samples obtained between January 2010 and June 2012.

MATERIAL AND METHODS

The identification of the specimens was performed through a combination of different validated analysis techniques. In order to detect the substances and check for potentially toxic adulterants, two different chromatographic techniques were used: thin layer chromatography (TLC) at Energy Control’s headquarters and gas chromatography associated to mass spectrometry at the Municipal Institute for Medical Research in Barcelona (IMIM – Hospital del Mar). For the TLC technique, TLC Silica gel 60 F254 (Ref: 1.05554.0001, from Merck) as a stationary phase was used. The TLC plate was developed with three different solvent systems: methanol/25% ammonia solution (100:2.5), 100% methanol (1 mg/mL), and 100% acetone (1 mg/mL). After development, the analytes were identified by comparing their position (retention factor) with those of the drug standards; and their color in the Marquis and the p-DMAB colorimetric test with a reference standard. The reference standards were supplied by IMIM.

To confirm TLC results, samples were analyzed using the gas chromatography associated to mass spectrometry technique, performed in an Agilent 5890 series II gas Chromatograph coupled to a 5971A quadrupole mass spectrometer detector (Agilent; Hewlett-Packard Company, Wilmington, Delaware, USA). The gas chromatograph was fitted with 6890 auto sampler injector. Samples were injected in split mode into a 12 m × 0.2 mm i.d., 0.33 μm film thickness 5% phenylmethylsilicone column (ULTRA-2, Agilent Technologies). The oven temperature was initially maintained at 90 °C for 2 min and programmed to reach 300 °C at 20 °C per min. It was finally maintained at 300 °C for 4 min, the total run time was 14.5 min. Insert liners packed with silanized glasswool were used. The injector and the interface were operated at 280 °C. Helium was used as carrier gas at a flow rate of 0.48 mL/min. The mass spectrometer was operated in electron impact ionization mode at 70 eV. Qualifying ions selected for analytes under investigation were: m/z 215, 230, and 259.

In order to confirm the mass spectra, the 2007 Wiley–VCH Verlag GmbH & Co. KgAa, Weinheim (Germany) and the Searchable Mass Spectral Library Version 1.6 (http://www.swgdrug.org/ms.htm) reference library were used.

RESULTS

In 2.5-year period, during which the study was conducted, 237 of the 6199 samples analyzed in the DTS (3.8%) were delivered as or contained CDs. Users were mainly male (89.9%), with a mean age of 30.56 years (SD: 6.89; range: 18–50 years). A total of 203 (85.8%) of the received samples came from 13 of the 17 regions of Spain, mainly from major cities (19.8% from Barcelona, 16.9% from Madrid, and 6.3% from Valencia) and 34 (14.2%) through the Internet.

Table 1 shows a summary of the analyses performed during this period.

Cathinone derivatives were detected in 228 (96.2%) of the samples. A total of 128 samples (57.8%) contained one single unadulterated psychoactive compound, 18 (7.6%) samples contained two or more different CDs, and 9 (3.8%) did not contain CDs at all. By-products of the synthesis were detected in 33 (13.9%) samples. Several adulterants were also found: caffeine in 31 samples (13.1%) and local anesthetics (lidocaine, tetra-caine . . .) in 14 samples (5.9%). Of the 228 confirmed CD samples, 204 (89.5%) were in powder, crystal or granulate form, 10 (4.4%) were pills or encapsulated, and the remainder in other forms (e.g., liquid). Methy-lone (59 samples; 24.9%) and mephedrone (58 samples; 24.5%) were the most frequently detected CDs, followed by 4-methylathcathinone (22 samples; 9.28%) and methylene-dioxypyrovalerone (16 samples; 6.8%)21.

Among the 237 samples sent to the DTS that contained CDs, 157 samples (66.2%) were marked as CDs, 27 (11.4%) supposedly contained MDMA/3,4-methy-lenedioxyamphetamine (MDA), 25 (10.4%) as Legal Highs, 7 (3%) as unknown substances and the remaining 21 (9%) as other illegal drugs (e.g., amphetamine, ketamine . . .) Out of the samples received as CDs, 129 (82.7%) contained the expected drug. We also found CDs in 80 (1.3%) of 6042 samples that had been delivered allegedly containing other drugs different from CDs, mostly in samples submitted to analysis as MDMA (27 samples). Twenty-five (50%) of the 50 total Legal Highs analyzed in the study period contained some type of CD and 8 (16%) of the samples contained more than one CDs.
DISCUSSION

The aim of this study is to contribute to the evaluation and investigation of this new phenomenon. Our data support the idea of a tendency, in the Spanish recreational drug market, towards a diversification and an increase in the availability of cathinones. Although we have received samples from all over the country, our data are limited and may not be representative of the whole market, making it difficult to extrapolate and monitor tendencies. Even so, there is not enough evidence to conclude that the consumption of CDs will become widespread or relevant for public health.

Methylone, methylenedioxypyrovalerone, and 4-methylethcathinone seemed to become more popular in the last 2 years, but the detection of mephedrone in samples is falling. This shows us that these trends are driven by a wide range of factors, which are very difficult to predict (UNDOC, 2012).

Fiscalization of mephedrone in 2010 could be linked to the tendency towards a decrease in its use reflected in our study (EMCDDA, 2011a). But the ban of mephedrone could also explain or contribute to the rise of other CDs (footnote 2 in Table 1). These substances are probably used by producers to avoid legal restrictions, although their potential risks could be even higher than those of mephedrone, as most of them have never been tested in humans or animals. Considering the long time necessary to illegalize a substance and the facility to synthesize and market new ones, this effect should be taken into account.

The detection of substances commonly used as adulterants for other recreational drugs (caffeine, lidocaine) can be explained by a possible intent to mimic the effects of illegal drugs (amphetamine, cocaine, etc.); it also may be interpreted as an indicator of their inclusion in the illegal drug markets, as these adulterants would have been added by successive intermediaries. We have also detected that samples containing CDs have been sold as MDMA or other illegal drugs. This fact should also be taken into consideration from a public health perspective.

The increasing presence of samples with multiple substances and combinations of various CDs and the detection of various psychoactive substances in the same sample are factors that probably increase health risks (Marusich et al., 2012; Simmler et al., 2013; Wood et al., 2012). Our results from the Legal High samples, the composition and associated risks of which are impossible to anticipate, are consistent with other international studies (Ayres and Bond, 2012; Zuba and Byrsk, 2012), which strongly recommend further investigations. For these reasons, we conclude that even without evidence of a growing public health problem, it seems advisable to monitor this trend and look for new information sources.

CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

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REFERENCES


