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A snapshot on NPS in Italy: Distribution of drugs in seized materials analysed in an Italian forensic laboratory in the period 2013–2015

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ABSTRACT

The diffusion of New Psychoactive Substances (NPS) in the illicit drug market is a worldwide problem. The aim of the study is to describe the qualitative distribution of drugs of abuse in seized materials confiscated in the Italian territory over the last two years. Between 2013 and 2015 162 seizures of substances purchased through the Internet and confiscated by police authorities were analyzed: 35 seizures (22%) were crystals of 3-methylmethcathinone (3-MMC). Although 3-MMC is subject to the relevant legislation in Italy, it is not controlled in other countries such as the Netherlands, from which the shipments originated. 33 seizures (20%) were crystals of 4-methylethcathinone (4-MEC), 19 seizures (12%) were powders containing methylenedioxypyrovalerone (MDPV). N,N-diallyl-5-methoxytryptamine (5-MeO-DALT) was identified in 5 powders, whereas ethylphenidate in six and pyrrolidinophenones in fourteen seized powders: 6 α-PVP (alpha-pyrrolidinovalerophenone), 6 α-PHP (alpha-pyrrolidinohexiophenone) and 1 α-PVT (alpha-pyrrolidinopentiothiophenone). Other substances identified were cathinones such as pentedrone, methylone, buthylone, ethylone, methedrone, 3-CMC (3-chloromethcathinone), 3,4-dimethylmethcathinone (3,4-DMMC), flephedrone (4-fluoromethcathinone or 4-FMC), 2-FMC and 3-FMC (2- and 3-fluoromethcathinone), MPPP (4-methyl-alpha-pyrrolidinopropiophenone), bk-2C-B (2-amino-1-(4-bromo-2,5-dimethoxyphenyl)ethan-1-one). Other compounds were NM2AI (N-methyl-2-aminoindane), MPA (1-(thiophen-2-yl)-2-methylaminopropane), MTTA (mephtetramine), 4-APB and 6-APB (4- and 6- (2-aminopropyl)benzofuran), 2-fluoromethamphetamine, 1mCPP (1-meta-chlorophenylpiperazine) and diphenidine, detected for the first time in Europe. Only three seizures contained synthetic cannabinoids, consisting of herbal blends soaked in N-(1-adamantyl)-1-pentyl-1H-indazole-3-carboxamide (AKB48), or a mixture of 5-F-AKB48 and BB-22 (1-(cyclohexylmethyl)-8-quinolinyl ester-1H-indole-3-carboxylic acid). In some mixtures of drugs - such as granules - 4-MEC and pentedrone were detected, also with traces of diphenidine on one occasion. In other cases 5-MeO-DALT, ethylphenidate and caffeine were mixed together. In one batch, the mixture was flephedrone and methoxethamine, whereas in another one the sample contained methylone, ethylone, methedrone, 4-fluoroamphetamine, 5-MeO-DALT and 5MeO-MiPT (N-methyl-N-isopropyl-5-methoxytryptamine). In 9 seizures, tablets shipped together with NPS were also found to contain sildenafil. The analyses performed on these seizures showed the presence of a wide number of NPS within the Italian boundaries coming from abroad, therefore this study confirms the threat for the public health, especially when the content of NPS being sold is not reported on the label or misleading.

1. Introduction

The diffusion of NPS in the illicit drug market is a worldwide problem. According to the United Nations Office on Drugs and Crime (UNODC) "2014 Global Synthetic Drugs Assessment", 348 NPS were identified for the first time between 2008 and 2013, 97 of which only in 2013 [1]. The phenomenon is becoming more and more concerning, as in 2014 101 new psychoactive substances were reported for the first time to the EU Early Warning System [2].

Due to the heterogeneous chemical structures of NPS, UNODC classified them in several chemical classes, including synthetic cannabinoids, synthetic cathinones, ketamines and phencyclidine-type substances, phenethylamines, piperazines, benzofurans,

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aminoindanes, tryptamines, plant-based substances and substances not pertaining to any of these. The distribution and the prevalence of these compounds vary across the different geographical areas and, of course, over time [3].

These substances are often designed to be structural analogues of a "traditional" drug or controlled substance, in order to avoid the law and to have a similar psychotropic effect. For instance, methoxetamine is an analogue of ketamine (the 2-chloro group on the phenyl ring is replaced with a 3-methoxy group and the N-methyl group replaced with N-ethyl group instead).

Currently the legislation of NPS varies in each country, even within the European Union. Various decrees were issued in Italy since 2010 to update the list of controlled psychotropic substances: chemical substances are not just cited name by name, but also as groups of structurally related analogues, such as those compounds derived from 3-phenyl acetylindole, the structures analogue to 3-(1-naphtoyl)indole, 3-benzoylindole and the ones derived from 2-amino-1-phenyl-1-propanone [4].

For laboratories involved in drugs analysis, the identification of new substances can be challenging due to the continuous evolving market and, subsequently, the potential lack of reference standard materials and/or analytical data from scientific literature - when their distribution spreads at first. In such circumstances, a special approach involving the combination of several analytical techniques is required for their correct and univocal identification. Besides their identification, another critical issue is that these substances are under control of the law only in some countries, depending on the specific national provisions.

The aim of this study was to describe an observation on the qualitative distribution of drugs in seized materials, showing the results from the analysis of NPS in 162 seizures collected in Italy within the last two years, with an emphasis on whether they should be included or not in the list of substances controlled by the Italian law. For the identification of NPS in unknown seizures an analytical approach, combining different analytical techniques was applied [5,6].

2. Experimental

2.1. Analytical approach

The analytical approach used for identifying unknown NPS along with sample preparation procedures and detailed instrumental conditions are described in detail elsewhere [5,6].

Briefly, all the samples were analysed firstly using GC-MS - in particular cases after specific derivatisation with 2,2,2-trichloroethyl chloroformate [6], then analysed also by LC-HRMS with and without fragmentation to study the accurate mass of the molecule and of its characteristic fragments; moreover, when discrimination between isomers was required, samples were also analysed by NMR.

3. Results

162 samples were analysed between September 2013 and June 2015: in the majority of them (94%), samples contained only one active compound; in the remaining 6% two, three or even seven different substances in the same sample were identified, often containing cathinones.

Fig. 1 shows the pattern of NPS identified sorted by frequency of their presence in the seizures. Chemical structures are shown in Fig. 2, grouped in three main classes: cathinones, synthetic cannabinoids and miscellanea. Fig. 2a shows the substances scheduled as controlled drugs in Italy, while NPS not yet included in the list of the controlled substances are shown in Fig. 2b.

3.1. Cathinones

Cathinones were the most frequently confiscated substances (see Fig. 1). In particular, 3-MMC and 4-MEC were those that recurred more often, followed by MDPV. The identified cathinones had very similar chemical structures: α-PVP and α-PHP differ only for the length of carbon side chain, as well as the 3,4-methylenedioxy cathinones (methylone, butylone and ethylone)

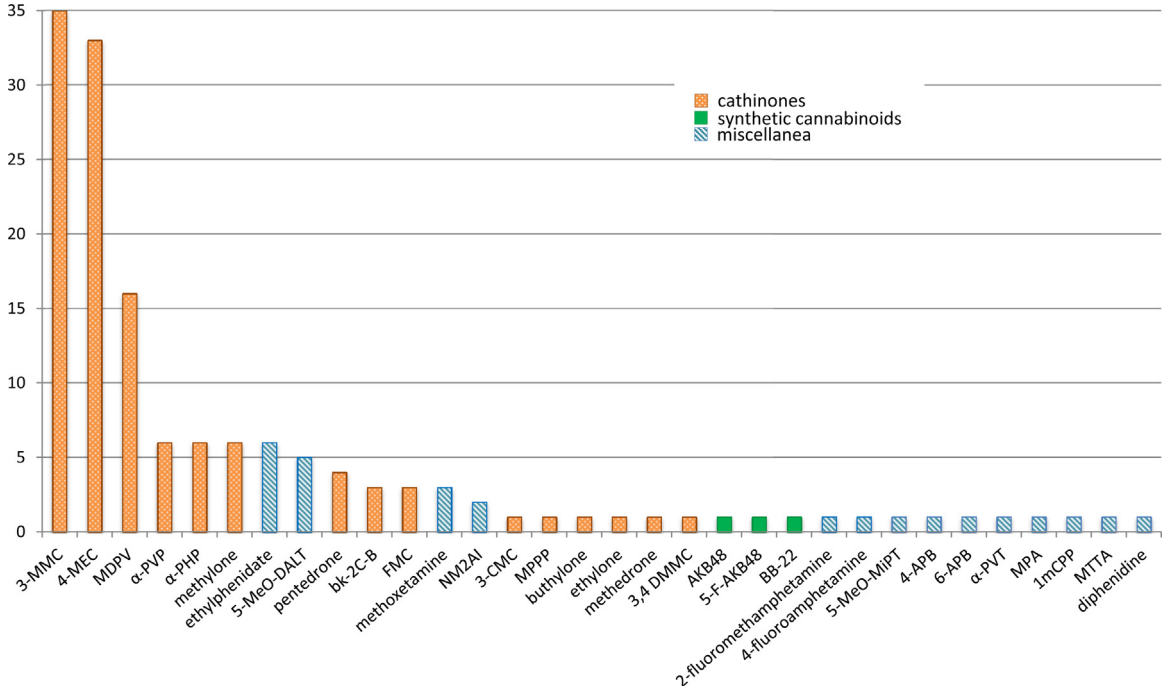

Fig. 1. NPS identified during 2013–2015: in the Y-axis is reported the number of seizures for each substance.