LÁRIONAD NÁISIÚNTA CÓIREÁLA DRUGAÍ
NATIONAL DRUG TREATMENT CENTRE
DRUG ANALYSIS LABORATORY

# New Psychoactive Substances Prevalence in Samples Tested in the NDTC laboratory 2010-2015

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**HSE National Drug Treatment Centre Laboratory**

The HSE-NDTC laboratory is the largest specialist provider of drugs of abuse screening for drug treatment services providing a nationwide service to the HSE Addiction Services, hospitals, General Practitioners, voluntary organisations, Department of Education (juvenile detention centres), the Probation Service, the Courts Service, the Medical Council, an Bord Altranais and various occupational health departments.

**Introduction**

In 2013 it was reported that Ireland had the highest use of new synthetic drugs in Europe, with consumption levels three times the EU average, according to the UN Office on Drugs and Crime[1] which that said new psychoactive substances (NPS) were "proliferating at an unprecedented rate" across the world and posed "unforeseen public health" effects.

The Report of the International Narcotics Control Board for 2014 [2], states that in Europe, the availability and abuse of new psychoactive substances remain a major public health challenge, with a record number of such substances being newly identified.

The INCB 2014 Global Synthetic Drugs Assessment[3], notes that the Eurobarometer survey conducted among 12,000 randomly selected youths aged 15-24 across the EU in 2011 recorded the lifetime prevalence of youths that had experimented with "legal substances that imitate the effects of illicit drugs". The highest lifetime prevalence rates were reported by Ireland at 16.3 per cent.

According to 2014 EMCDDA update[4], the data suggests that the growth of the market in new psychoactive substances will continue to pose a range of challenges for public health and drug policy over the next few years. Particular challenges relate to the speed at which new psychoactive substances appear, their open sale and the lack of information on their effects and harms.

Due to clinical demand for testing, since 2008 we have constantly redeveloped our LCMS capability to include several multi-residue testing methods in order to meet the challenge of testing for New Psychoactive Substances. We have reported on this in a number of publications. [6,7,8]

This has involved on-going method development over this time as more drugs were added to the screen. Most recently to unambiguously identify all of the different compounds due to common MRM's and presence of multiple isomers, by separating the screened compounds into 7 groups and optimizing the chromatographic and mass spectrometer parameters utilizing MRM's we can now unambiguously identify over 80 compounds in one run.

**Objective**

The objective of the study is to report on trends in New Psychoactive substances over the period 2010-2015 in samples tested in the NDTC laboratory. "Spice" drugs and related synthetic cannabinoids are not included in the study.

**Materials and Methods**

Analysis was carried our using our in-house screen for multiple compounds with 2 transitions for each separated in a 21 min gradient.
Mobile Phase A: 100:100:800 Buffer: ACN: water
Mobile Phase B: 100:900, buffer: ACN
Buffer: 0.5% formic acid, 25mM ammonium formate

Targeted analysis included the following drugs: 2-methylamphetamine, 4-methylamphetamine, BZP, MDA, N-Methyl-5 APB, Pentedrone, Camfetamine, Ethylone/Butylone, Pentylone, Flurotropacocaine, Benzoylecgonine, methamphetamine, p-methoxyamphetamine, dimethylcathinone, p-methoxymethamphetamine, 3,4 DMMC, MDAT, Methylone, Ketamine, 5-MeO Dalt, Cocaine, 2-Aminoindane, 4-fluoroamphetamine, Bernzocaine, MDAI, p-FPP, 4-EMC, Methedrone, MDEA, 3TFMPP, Desoxypipradol, MDPV, Amphetamine, Pseudoephedrine, Ethcathinone, 3-fluoromethcathinone, MDMA, MPBP, Benzedrone, Dimethocaine, 3-methylamphetamine, 3-methiopropamine, synephrine, Mephedrone, 2-fluoromethcathinone, 4-MEC, MPPP, PVP, 5-IAI, Naphyrone, 4-methylamphetamine, methcathinone, 5-APB, Buphedrone, 4-fluoromethcathinone, N,N-4-trimethylcathinone, mCPP, MBDB, PCat, methoxetamine, MDPBP, 3,4 MD-N-benzylcathinone, BK-2CB, nitracaine, methoxypiperamide, mephtetramine, 25I-NBOMe, alpha-methyltryptamine, 2CB, 25B-NBOMe, 2CE, 2CI, ethylphenidate, 25C-NBOMe.

Compounds were optimised on the mass spectrometer by using the automated compound optimization wizard in Analyst software.

Samples were diluted 1/10 in water (dilute n' shoot) before injecting into the LC/MS for analysis.

**Figure 1: Examples of NPS packaging found in Headshops in Ireland**


**Instrumentation**

**LCMS**

The ABSciex 3200 QTrap method uses Electrospray positive ionisation with multi-reaction monitoring - 2 MRM transitions for each compound tested coupled with Enhanced Product Ion monitoring (EPI) giving full scan data. This is coupled to an Agilent 1100 series HPLC. The column used was an Agilent Poroshell SB 120 C18 coupled with an Agilent Poroshell SB120 UHPLC Guard column.

**Samples**

Urine samples were obtained from participants in a methadone maintenance program screened on a regular basis for drug and alcohol use by immunoassay.
Samples are tested for NPS on request where use of these drugs is suspected. We have also carried out a number of random "sweeps".

**Table 1: Top NPS drugs detected by year**

| | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|---|
| 1 | Mephedrone(13.95%) | MDPBP (12.62%) | 4-methyl ethcathinone (12.24%) | 4-methyl ethcathinone (11.75%) | Pentedrone (9.1%) | PVP (5.84%) |
| 2 | Methylone (5%) | PVP (7.3%) | MDPBP (8.16%) | Mephedrone (4.12%) | PVP (7.9%) | Pentedrone (3.89%) |
| 3 | MDPV (4.22%) | MDAI (2.33%) | PVP (5.1%) | Methylone(3.71%) | 4-methyl ethcathinone (5.91%) | MDPBP (1.17%) |
| 4 | MDPBP (3.85%) | MDPV (2.04%) | N-Ethyl cathinone(3.06%) | PVP (3.71%) | 5-APB (4.04%) | |
| 5 | Butylone/ Ethylone (3.68%) | 3TFMPP (1.67%) | Benzocaine (2.38%) | N-Methyl-5 APB (2.47%) | MDPBP (1.14%) | |
| 6 | BZP (2.63%) | Dimethocaine (1.63%) | Methylone (1.7%) | Benzocaine (2.15%) | Mephedrone (0.91%) | |
| 7 | Buphedrone (2.56%) | Fluorotropacocaine (1.55%) | 3-TFMPP (1.02%) | 4-Fluoromethcathinone (1.95%) | MDPV (0.45%); Methoxetamine (0.45%) | |
| 8 | 4-methyl ethcathinone (1.92%) | 4-methyl ethcathinone (1.48%) | Dimethocaine (0.68%) | Pentedrone (1.33%) | BZP (0.23%); 3,4 DMMC (0.23%) | |
| 9 | 3-TFMPP (1.84%) | Mephedrone (1.48%) | Ketamine (0.34%); BZP (0.34%) | MDPV (1.24%) | Benzocaine (0.23%); mCPP(0.23%) | |
| 10 | N-Ethyl cathinone (1.58%) | N-Ethyl cathinone (1.11%) | | N-Ethyl cathinone (0.82%) | | |

**Results:**

It can be seen from the data in Table 1 that the profile of drugs has changed over time due to the effect of various legislation enacted both here and in Europe. Mephedrone which was the most widely used drug in 2010 (13.95%) had a usage of 0.91% by 2014. Pentedrone was seen at 1.33% in 2013 and was up to 9.1% in 2014. 4-MEC was the NPS of choice in 2012 and 2013 with 12.24 and 11.75% seen respectively.

**Discussion/Conclusion**

Poly drug use is prevalent in the addiction population is seen in many drug related deaths[4]. We have seen that these new psychoactive substances are used within the addiction services cohort.

As evidenced elsewhere in Europe banning specified drugs promoted a game of "Cat and Mouse" whereby as drugs were banned suppliers were racing to produce new drugs to meet demand. A study we conducted in January 2010 of random Methadone maintenance patient urine samples for Methylone, Mephedrone and BZP found that 13.9% were positive for Mephedrone, 3.3% for Methylone, and 0.5% for BZP. In 2011 MDPBP and PVP emerged on the scene as use of banned drugs reduced. 2012 saw the arrival of 4-MEC with a 122% usage rate. 4-MEC was still the most popular in 2013. Pentedrone arrived in 2013, and by 2014 was the most popular at 9.1%, PVP was a close second at 8.1%. So far in 2015 PVP and Pentedrone are the NPS's of choice.

The profile of drugs has changed greatly over the years as various legislative measures were introduced and this is reflected in the drugs detected by us in patient samples[6,7,8].

In terms of the main cathinones seized in 2013 in Europe 3-MMC (341 kg), 4-MEC (201 kg), pentedrone (197 kg) and alpha-PVP (115 kg) accounted for almost 80 % of the total amount seized. Between 2008 and 2013 there has been a **60-fold increase** in the number of seizures of synthetic cathinones.[9]

In Ireland in 2013, the main NPS drugs (excluding synthetic cannabinoids) seized in Ireland were PVP, 4-MEC, Methylone, MDPBP and Fluoroamphetamine.[10] This correlates with our findings. The data demonstrates the on-going challenges in monitoring the use of these dangerous new substances and keeping up with the new drugs as they emerge.

A serious problem for testing laboratories is the long time it takes to get certified reference standards for new drugs which emerge.

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