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EUROPEAN PROJECT RESPONSE to challenges in forensic drugs analyses

NOVEL NPS - TEST PURCHASES OVER THE INTERNET - WHAT IS IN THE PACKAGE?

Sonja Klemenc, Mojca Janežič, Bojana Koštrun
Ministry of the Interior Police, National Forensic Laboratory (NFL), Ljubljana, Slovenia

1. INTRODUCTION

Over the past few years Europe has seen an unexpected growth in the number, type and availability of new psychoactive substances (NPS). One of the main challenges to respond effectively to new psychoactive substances is the detection of these followed by the correct identification.

One of the aims of the "RESPONSE project" was a systematic (pro-active) tackling and chemical characterizations of the new psychoactive substances (NPS) available over the **Internet** (purchased in the frame of project or by anonymous users). Only the '**surface web'** (accessible via common search engines) was investigated, while "dark web" was not a part of the project interest. The project was mainly focused on powdered forms of compounds (advertised as pure forms) or exceptional on pills and blotters. Herbal or liquid preparation were not in focus of the project.

In recent years around 150 samples have been obtained from different web pages or/and anonymous users who reported internet as the source of samples. The rate of "false advertised" compounds was above our expectations.

Figure 1: web space

Figure 2: Test purchased samples – few examples

Some typical examples of samples packaging are shown on Figure 2. In the frame of RESPONSE project we bought samples from China vendors, European vendor and also from Canada. We noticed several interesting web pages but were not able to receive their offers. Samples from China were labeled only by numbers, no information about the ingredients. Supporting documentation also not informative (samples declared as acrylic paint, vanillin, iron oxide, etc…)..Purchases within EU - the substances are mostly suitable labeled (although often wrong substance is declared). Samples from Canada were packed and labelled with chemical name and structure. The MSDS (even if not perfect) were enclosed into the parcels by the rule. Anyhow, the ingredients often differ from the declared content.

3. RESULTS -SUMMARY

Chemical analyses of test purchases and anonymously collected samples revealed that the rate of the "false advertised" compounds is at approximately 20% - 30% (few examples are shown in Table 3). The worst experience so far was one delivery from Spain, where we received 5 "wrong" compounds out of 6 samples (within a single order). Beside this, we often detected substantial amounts of residual solvents and/ other reactants. Some samples contained mixtures of several active ingredients and/or different isomeric forms of basic compound.

Most common situations, i. e. ordered vs. delivered:

- compounds - from different chemical classes (eg. phenetylamine instead tryptamine)
- positional isomers
- ring, link or chain structure differences (for example indole, indazole for synthetic cannabinoids)
- halogenated instead of no halogenated compound (or other substituent)
- different homologues
- incorrect salt form
- mixtures instead of pure compounds
- reaction intermediate instead of the final product

Table 3: Few examples ordered vs. received

ordered	chemical name/declared at web	class	formula	Mw	received	chemical name	class	formula	Mw
4-Aco DALT	3-{2-[Di(prop-2-en-1-yl)amino]ethyl}-1H-indol-4-yl acetate	tryptamines	C18H22N2O2	298.39	DOIP	1-[2,5-dimethoxy-4-(propan-2-yl)phenyl]propan-2-amine	Phenetylamines	C14H23NO2	237.34
4-Aco DPT	3-[2-(dipropylamino)ethyl] indole	tryptamines	C16H24N2		DOF + DOIP (mixture)	1-(4-fluoro-2,5-dimethoxyphenyl)propan-2-amine + DOIP	Phenethylamines	C11H16FNO2	213.25
AZ-037 (2 different webs)	N-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(5-fluoropentyl)-5-(4-fluorophenyl)-1H-pyrazole-3-carboxamide	cannabinoid	C20H26F2N4O2	392.45	AB-CHFUPYCA	N-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-3-(4-fluorophenyl)-1H-pyrazole-5-carboxamide	cannabinoids	C22H29FN4O2	400.5
2-AiMP	1-(7-Methoxy-benzo[1,3]dioxol-5-yl)-2-methylamino-propan-1-one	cathinones	C12H15NO4	237.255	N-methyl-bk-MMDA-2	1-(6-methoxy-1,3-benzodioxol-5-yl)-2-(methylamino)propan-1-one	cathinones	C12H15NO4	237.255
5-PPDi	1-(2,3-dihydro-1H-inden-5-yl)-2-(pyrrolidin-1-yl)butan-1-one	cathinones	C17H23NO	257.37	5-BPDi	1-(2,3-dihydro-1H-inden-5-yl)-2-(pyrrolidin-1-yl)hexan-1-one	cathinones		
5F-NPB	1-(5-fluoropentyl)-8-quinolinyl ester-1H-indazole-3-carboxylic acid	cannabinoids	C22H20FN3O2	377.4	4F-MHP	methyl 2-(4-fluorophenyl)-2-(2-piperidyl)acetate	Piperidines & pyrrolidines	C14H18FNO2	251.30
FUB-144	[1-(4-Fluorobenzyl)-1H-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone	cannabinoids	C23H24FNO	349.4	5F-AMB	methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3-methylbutanoate	cannabinoids	C19H26FN3O3	363.43
MAB-CHMINACA	N-[1-(aminocarbonyl)-2,2-dimethylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide	cannabinoids	C21H30N4O2	370.49	AMB-CHMICA	methyl 2-{[1-(cyclohexylmethyl)-1H-indol-3-yl]formamido}-3-methylbutanoate	cannabinoids	C22H30N2O3	370.48

2. CHEMICAL CHARACTERIZATIONS

In NFL and FKKT (Faculty of Chemistry and Chemical Technology)samles are characterized by means of methods listed in the Table below.. For test purchased samples we always check if information given at the web page correctly describes the package content.

Table 1: Characterization methods

Method	Results/ information
HPLC-TOF (cheminformatic tools – original software)	**purity by HPLC, exct monoisotopic mass, empirical formula/** Exact mas fit? **NO: the substance is surely not what we ordered;** **YES:** it is likely that substance is what we ordered, but further analyses are required to confirm this (compound can still be something else or different isomere)
GC-MS supported by cheminformatic tools for fragmentation studies	**RT and fragmentation patteren / stuture or parts of structure can be infered** (with different strenght of certainty – dependant on the specifity of MS spectrum; possition of some functional groups is often questionable; some additional information can be obtained by derivatization techniques ; **RT:** for future use in in house library
FTIR FTIR-ATR GC-(MS)- FTIR (solid phase	FTIR-ATR spectra or/and GC-MS-FTIR-(condensed-solid phase) spectra/ funcional groups, salt forms; GC- FTIR solid phase also aplicable for mixtures analyses
Supporting methods	**Ion chromatography (anions), melting point determination, SPME-GC-MS solvents and some presumptive tests, tests of solubility**
NMR (FKKT)	**1H, 13C, 1H–1H gs-COSY, 1H–13C gs-HSQC, 1H–13C gs-HMBC, 1H–15N gs-HMBC, etc./ structure elucidation / verification**

Example:

Two samples were purchased: one as **MAB-CHMINACA** and another one as **MA-CHMINACA**

Table 2: Summary of web vendor data and comments

MAB-CHMINACA	MA-CHMINACA
NAME: N-[1-(aminocarbonyl)-2,2-dimethylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide; **FORMULA:** C21H30N4O2 **Mw:** 370.490 **STUCTURE**: OK	***NAME:*** methyl 2-(1-(cyclohexylmethyl)-1H-indazole-3-carboxamido)-3-methylbutanoate **FORMULA:** C20H28N4O2 analogue ??? **Mw: 395.210 (wrong)** **STUCTURE**: not consistent with the given name
COMMENTS NFL: Name, formula and structure given on the web were consistent. Exact mass theoretical (for the compound above): 370.236876222	**COMMENTS NFL:** 

Chemical characterizations (Figure 3) revealed that both samples contain the compound AMB CHMICA (nevly reported at the time of identification).

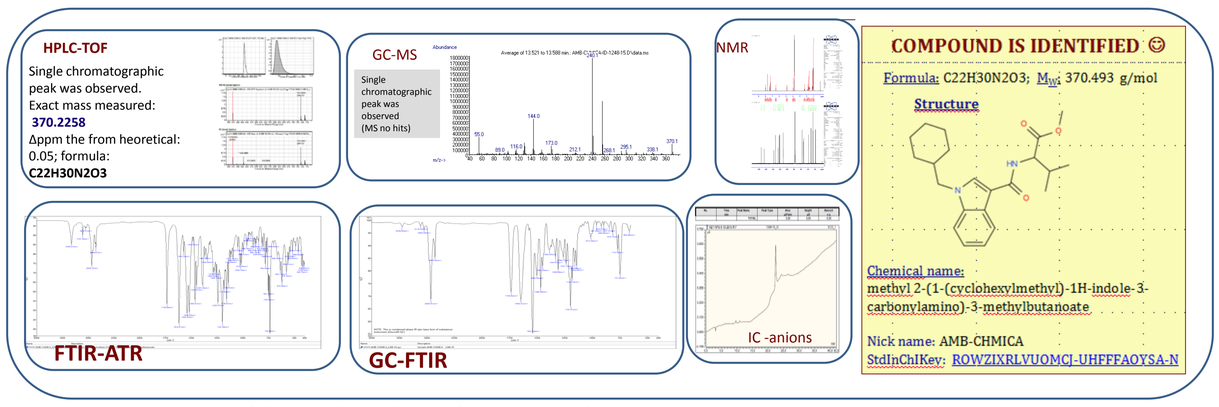

Figure 3: Summary of the results – shown for one sample

4. CONCLUSIONS

The test purchases, show that drugs users can never be sure of what they get when buying from internet vendors. The rate of the "false advertised" compounds is at approximately 20% - 30%. This poses a serious health risks for the population of NPS users. Therefore all activities which can raise the awareness are welcomed and should be enhanced at all levels (national and international EWS stakeholders are the key actors).

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Corresponding author: e-mail: sonja.klemenc@policija.si