Centro Regionale Antidoping
Alessandro Bertinaria
LABORATORIO REGIONALE DI TOSSICOLOGIA

EWDTS 2015
LISBOA

Detection of synthetic cannabinoids in hair

Alberto Salomone

Lisbon, 28th May 2015

Rise of NPS ⟶
Arise of critical situations

- Acute intoxication
- Workplace testing
- Driving re-licensing
- Anti-doping analyses
- Roadside controls

DETECTION

- Active use or external contamination
- List of target analytes

INTERPRETATION

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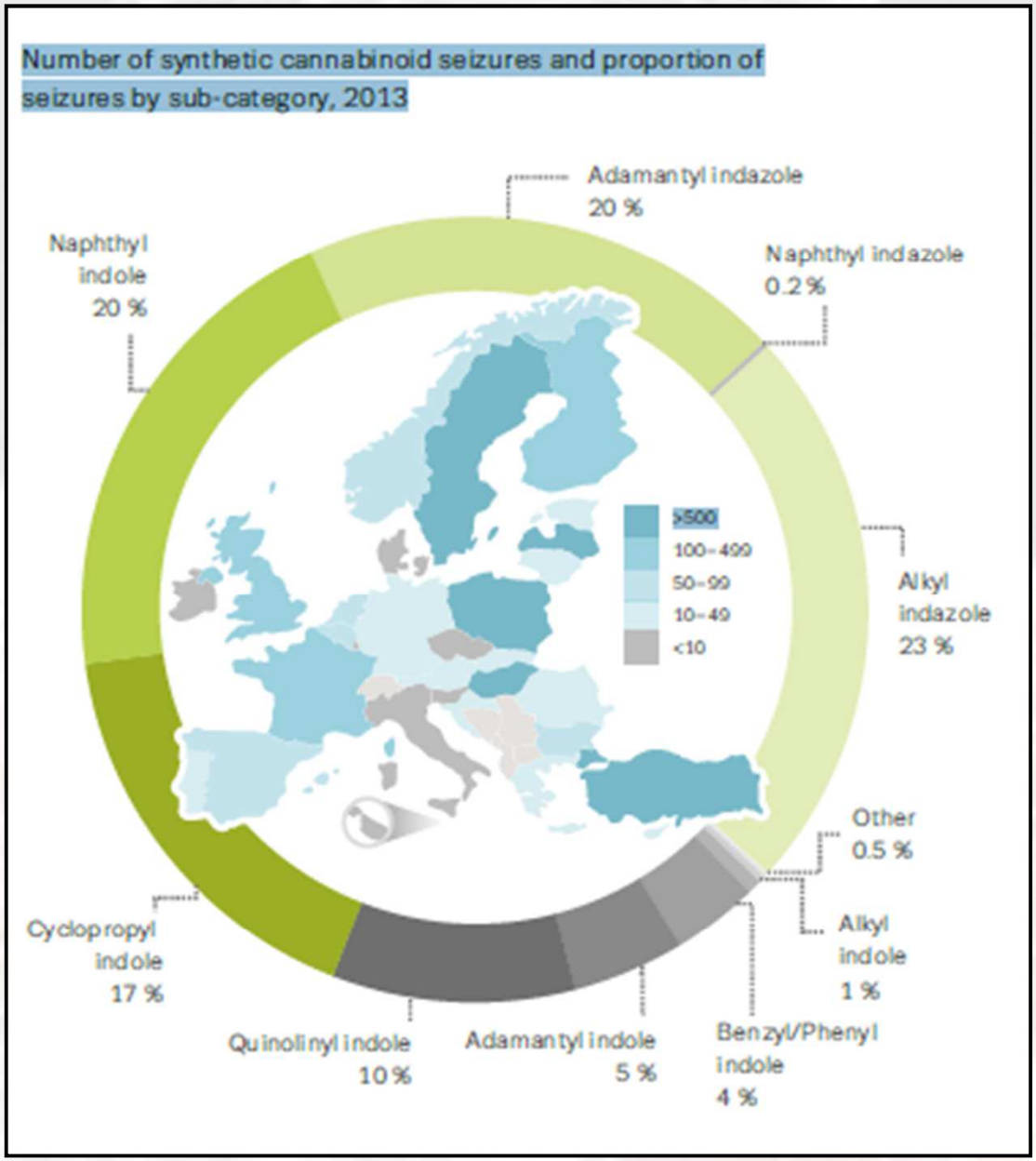
SYNTHETIC CANNABINOIDS

- **Classical cannabinoids**: structurally related to THC (e.g. HU-210)
- **Nonclassical cannabinoids**: cyclohexylphenols or 3-arylcyclohexanols (e.g. CP-47,497)
- **Hybrid cannabinoids**: structural combinations of both classical and nonclassical cannabinoids (e.g. AM-4030)
- **Aminoalkylindoles** (JWH-series, UR-144, XLR-11)
- **Eicosanoids**: endocannabinoids and their synthetic analogues (e.g. AM-356)
- **Others**: Encompassing other structural types (e.g. APINACA)



Update from the EU Early Warning System (March 2015)

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What about real abuse?

- ✓ **The chemical structure is slightly altered to create different drugs with similar properties**

- ✓ **Problems with urine analysis (metabolism, reference standards)**

- ✓ **Very limited data on connection with traffic and occupational accidents**

DETECTION OF PARENT DRUG IN HAIR

- The analytical strategy is facilitated by the wide availability of reference standards
- Most of methods are LC-MS/MS based
- Preliminary information about the current diffusion of NPS and on the characteristics of the users

STUDY 1, year 2012

179 THC Consumers tested for the presence of 5 synthetic cannabinoids

STUDY 2, year 2014

344 among drug and alcohol consumers tested for the presence of 23 synthetic cannabinoids

SYNTHETIC CANNABINOIDS

STUDY 1, year 2012

Research Article

JOURNAL OF MASS SPECTROMETRY

Received: 3 January 2012 Revised: 7 March 2012 Accepted: 15 March 2012 Published online in Wiley Online Library
(wileyonlinelibrary.com) DOI 10.1002/jms.2988

Simultaneous analysis of several synthetic cannabinoids, THC, CBD and CBN, in hair by ultra-high performance liquid chromatography tandem mass spectrometry. Method validation and application to real samples

179 hair samples from frequent cannabis consumers (2010)

14 subjects positive for at least one synthetic cannabinoid (7.82%)

Positive case	Age	Gender	Type of hair	THC (pg/mg)	CBD (pg/mg)	CBN (pg/mg)	JWH-018 (pg/mg)	JWH-073 (pg/mg)	JWH-250 (pg/mg)
1	29	Male	Head	73	42	64	70.5	413.3	–
2	29	Male	Pubic	68	57	67	1.5	–	–
3	18	Male	Head	553	1217	137	38.3	–	–
4	n/a	Male	Head	70	55	36	–	1.3	208.8
5	22	Male	Head	57	<LOQ	39	70.4	37.0	729.4
6	22	Male	Head	57	222	60	–	–	1.5
7	48	Male	Head	54	25	31	44.9	409.3	262.0
8	43	Male	Head	50	24	36	0.8	0.5	–
9	20	Male	Head	69	85	62	–	–	67.4
10	26	Male	Pubic	60	88	60	–	1.7	–
11	32	Male	Head	115	460	51	10.9	66.7	138.6
12	44	Male	Head	59	38	31	0.6	–	–
13	37	Male	Head	417	1862	205	14.8	5.2	2.9
14	20	Male	Head	112	18	47	–	–	26.0
	Age 18-48			50-553 pg/mg			0.6-70.5 pg/mg	0.3-413 pg/mg	1.5-729 pg/mg

SYNTHETIC CANNABINOIDS

STUDY 2, year 2013

Research article

Drug Testing and Analysis

Received: 21 June 2013 Revised: 23 August 2013 Accepted: 29 August 2013 Published online in Wiley Online Library

(www.drugtestinganalysis.com) DOI 10.1002/dta.1556

Hair analysis as a tool to evaluate the prevalence of synthetic cannabinoids in different populations of drug consumers

344 real samples; 15 subjects positive for at least one SC, 12 from THC users

Positive case	Group	Age	Gender	Type of hair	JWH-018 (pg/mg)	JWH-073 (pg/mg)	JWH-250 (pg/mg)	JWH-081 (pg/mg)	JWH-122 (pg/mg)	JWH-210 (pg/mg)	JWH-019 (pg/mg)	AM-1220	Other findings[a]
1	A	24	M	head	-	1.6	-	-	-	-	-	-	THC: 0.05 ng/mg; MDMA: 0.56 ng/mg
2	A	27	F	head	17.3	7.6	83.4	12.3	-	-	-	-	THC: 0.07 ng/mg
3	A	22	M	head	-	1.9	26.9	-	-	-	-	-	THC: 0.05 ng/mg; MDMA: 0.57 ng/mg
4	A	32	F	head	-	1.8	-	-	-	-	-	-	THC: 0.28 ng/mg
5	A	23	M	head	-	5.2	5.8	-	11.7	-	-	-	THC: 0.09 ng/mg
6	A	20	M	head	10.4	2.0	6.0	-	2800	2.3	-	1.3	THC: 0.14 ng/mg
7	A	25	M	head	-	1.8	-	-	-	-	-	-	THC: 0.27 ng/mg; AMP: 3.05 ng/mg; MDMA: 0.56 ng/mg
8	A	26	M	head	-	-	-	8.0	-	-	-	-	THC: 4.57 ng/mg; MDMA: 0.17 ng/mg
9	A	18	M	head	-	50.5	6.4	194	710	-	-	-	THC: 0.09 ng/mg
10	A	23	M	head	-	1.6	-	-	760	-	-	-	THC: 0.11 ng/mg
11	A	21	M	head	3.1	1.6	-	81.4	-	5.1	-	-	THC: 0.24 ng/mg
12	A	23	M	head	-	9.0	4.8	-	40.9	-	-	-	THC: 0.15 ng/mg
13	B	21	M	head	-	-	-	-	7.4	-	-	-	COC: 1.76 ng/mg; BZE: 0.22 ng/mg
14	B	32	F	head	-	-	-	-	11.2	-	3.8	-	COC: 0.60 ng/mg; BZE: 0.09 ng/mg; MOR: 0.08 ng/mg; 6-AM: 0.25 ng/mg
15	B	22	M	head	-	-	-	47.8	15.8	-	4.1	-	COC: 0.61 ng/mg; AMP: 0.53 ng/mg; MDMA: 0.89 ng/mg

Age 18-32

HUMAN PSYCHOPHARMACOLOGY
Hum. Psychopharmacol Clin Exp 2013; **28**: 379–389.
Published online in Wiley Online Library
(wileyonlinelibrary.com) **DOI**: 10.1002/hup.2312

SPECIAL ISSUE ON NOVEL PSYCHOACTIVE SUBSTANCES

"Spiceophrenia": a systematic overview of "Spice"-related psychopathological issues and a case report

Duccio Papanti[1,2]*, Fabrizio Schifano[3], Giulia Botteon[1,2], Francesca Bertossi[4], Jason Mannix[5], Daniela Vidoni[6], Matteo Impagnatiello[2], Elisabetta Pascolo-Fabrici[1,7] and Tommaso Bonavigo[1,4]

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BONZAI (JWH-018, JWH-081, JWH-122)

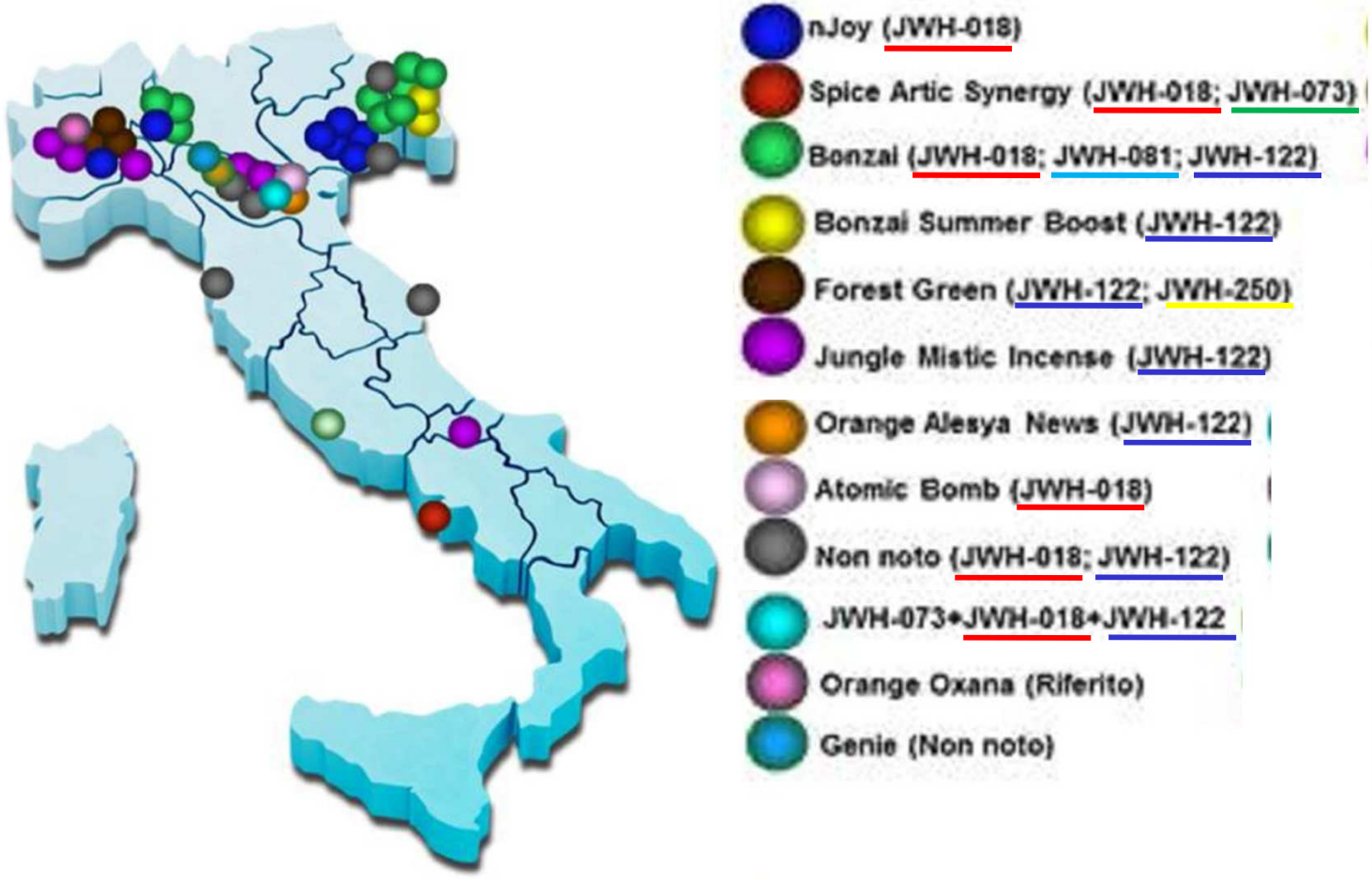
SYNTHETIC CANNABINOIDS

PREVALENCE OF SYNTHETIC CANNABINOIDS

Hair Analysis 2010-2012

- JWH-018
- JWH-073
- JWH-250
- JWH-081
- JWH-122
- JWH-210
- JWH-019
- AM-1220

ACUTE INTOXICATION WARNINGS 2009-2012



Fonte: Sistema Nazionale Allerta Precoce

Ref	Real samples	Number of positive samples	Gender	Age	Range of measurable concentrations
Hutter et al (2012)	Obtained from forensic psychiatry inpatients in 2011. All patients admitted chronic consumptions of SC	8 (7 with polyabuse)	Male (8/8)	20-37	5.1-78 pg/mg (JWH-081) 0.5-24 pg/mg (JWH-250) 0.7-21 pg/mg (JWH-073) 5.1-5.7 pg/mg (JWH-018) 0.5-5.2 pg/mg (JWH-210)
Gottardo et al (2014)	435 hair samples collected in 2010 for driving relicensing	8 (2 with polyabuse)	Not specified	Not specified	16-1280 pg/mg (JWH-081) 125 pg/mg (JWH-122) 12 pg/mg (JWH-250) 17-750 pg/mg (JWH-073) 10-11 pg/mg (JWH-018)
Kim et al. (2013)	18 (individuals suspected of SC use)	18	7 male, 11 female	22-34	<LOQ-1700 pg/mg (JWH-018) 2-55 pg/mg (JWH-073)
Cirimele et al (2014)	232 subjects suspected of narcotic abuse, 131 of them originated from French forensic cases and 101 from foreign legal hair cases	3	Not specified	Not specified	<0.5-1.0 pg/mg (AM-2201) <0.5 pg/mg (JWH-201)

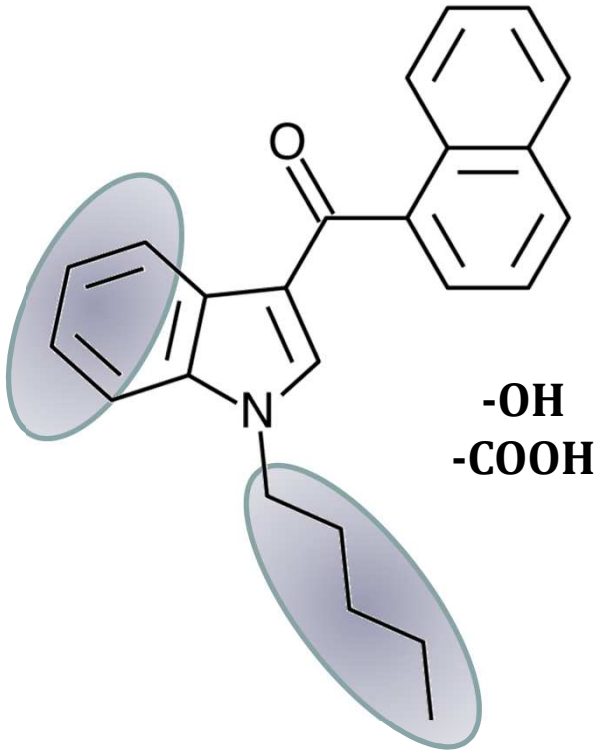
POLYABUSE:

- **active ingredients vary from lot to lot**
- **some blends may contain two or more compounds**

Detection of metabolites and external contamination

New UHPLC-MS/MS method updated with 10 metabolites

JWH-018	*JWH 018 4-hydroxypentyl metabolite-D5*
AM-2201	*JWH 018 N-(5-hydroxypentyl) metabolite*
JWH-073	*JWH 018 N-pentanoic acid metabolite*
JWH-250	*JWH 019 5-hydroxyindole metabolite*
JWH-081	*JWH 073 N-(4-hydroxybutyl) metabolite*
JWH-122	*JWH 073 N-butanoic acid metabolite*
JWH-210	*JWH 081 N-(5-hydroxypentyl) metabolite*
JWH-019	*JWH 122 N-(5-hydroxypentyl) metabolite*
	JWH 210 N-(5-hydroxypentyl) metabolite
	JWH 250 5-hydroxyindole metabolite
	JWH 250 N-(5-hydroxypentyl) metabolite



LOQ: 0.23-0.95 pg/mg

STUDY 2 → 15 positive hair samples → RETESTED WITH THE NEW METHOD

SYNTHETIC CANNABINOIDS

STUDY 3, year 2014 (ongoing)

#	JWH-018 (pg/mg)	JWH-073 (pg/mg)	JWH-250 (pg/mg)	JWH-081 (pg/mg)	JWH-122 (pg/mg)	JWH-210 (pg/mg)	JWH-019 (pg/mg)	AM-1220 (pg/mg)	Met (pg/mg)	Washing solutions
1	-	1.6	-	-	-	-	-	-	No	n/a
2	17.3	7.6	83.4	12.3	-	-	-	-	No	n/a
3	-	1.9	26.9	-	-	-	-	-	No	n/a
4	-	1.8	-	-	-	-	-	-	No	n/a
5	-	5.2	5.8	-	11.7	-	-	-	No	n/a
6	**10.4**	**2.0**	**6.0**	**-**	**2800**	**2.3**	**-**	**1.3**	**2.57**	n/a
7	-	1.8	-	-	-	-	-	-	No	n/a
8	-	-	-	8.0	-	-	-	-	No	n/a
9	-	50.5	6.4	194	713	-	-	-	No	n/a
10	**-**	**1.6**	**-**	**-**	**760**	**-**	**-**	**-**	**0.23**	n/a
11	3.1	1.6	-	81.4	-	5.1	-	-	No	n/a
12	-	9.0	4.8	-	40.9	-	-	-	No	n/a
13	-	-	-	-	7.4	-	-	-	No	n/a
14	-	-	-	-	11.2	-	3.8	-	No	n/a
15	-	-	-	47.8	15.8	-	4.1	-	No	n/a

SYNTHETIC CANNABINOIDS

STUDY 3, year 2014 (ongoing)

THC Cut-off: 50 pg/mg

#	JWH-018 (pg/mg)	JWH-073 (pg/mg)	JWH-250 (pg/mg)	JWH-081 (pg/mg)	JWH-122 (pg/mg)	JWH-210 (pg/mg)	JWH-019 (pg/mg)	AM-1220 (pg/mg)	Met (pg/mg)	Washing solutions
1	-	1.6	-	-	-	-	-	-	No	n/a
2	17.3	7.6	83.4	12.3	-	-	-	-	No	n/a
3	-	1.9	26.9	-	-	-	-	-	No	n/a
4	-	1.8	-	-	-	-	-	-	No	n/a
5	-	5.2	5.8	-	11.7	-	-	-	No	n/a
6	**10.4**	**2.0**	**6.0**	**-**	**2800**	**2.3**	**-**	**1.3**	**2.57**	n/a
7	-	1.8	-	-	-	-	-	-	No	n/a
8	-	-	-	8.0	-	-	-	-	No	n/a
9	-	50.5	6.4	194	713	-	-	-	No	n/a
10	**-**	**1.6**	**-**	**-**	**760**	**-**	**-**	**-**	**<LOQ**	n/a
11	3.1	1.6	-	81.4	-	5.1	-	-	No	n/a
12	-	9.0	4.8	-	40.9	-	-	-	No	n/a
13	-	-	-	-	7.4	-	-	-	No	n/a
14	-	-	-	-	11.2	-	3.8	-	No	n/a
15	-	-	-	47.8	15.8	-	4.1	-	No	n/a

Frequent and active use

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SYNTHETIC CANNABINOIDS

STUDY 3, year 2014 (ongoing)

153 hair samples (2012-2013)

- **THC consumers**
- **Age (18-34 yo)**

#	JWH-018 (pg/mg)	JWH-073 (pg/mg)	JWH-250 (pg/mg)	JWH-081 (pg/mg)	JWH-122 (pg/mg)	JWH-210 (pg/mg)	AM-694 (pg/mg)	METABOLITES (pg/mg)	WASHING SOLUTIONS
1	-	-	4.92	-	-	-	-	No	NEGATIVE
2	2.27	<LOQ	-	-	-	-	-	No	NEGATIVE
3	-		-	<LOQ	2.79	<LOQ	-	No	NEGATIVE
4	2.55	287	32.8	22.4	61.6	-	0.78	No	NEGATIVE
5	2.15	1.89	< LOQ	3.16	-	-	-	No	NEGATIVE

Frequent exposure
Active use?

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SYNTHETIC CANNABINOIDS

STUDY 3, year 2014 (ongoing)

47 hair samples (2014)

- **THC consumers**

#	JWH-018 (pg/mg)	JWH-073 (pg/mg)	JWH-250 (pg/mg)	JWH-081 (pg/mg)	JWH-122 (pg/mg)	AM-2201 (pg/mg)	AM-694 (pg/mg)	METABOLITES	WASHING SOLUTIONS
1	-	-	-	-	1.9	-	-	NEGATIVE	NEGATIVE
2	-	-	-	-	4.9	-	-	NEGATIVE	NEGATIVE
3	9.9	0.9	2.8	-	2.4	715	1.6	018/AM-2201, 073/AM-2201 JWH-122	POSITIVE (AM-2201)

0.5-5.2 pg/mg

#1,2: sporadic exposure or external contamination

#3: active and frequent use of AM-2201

Recent exposure to AM-2201?

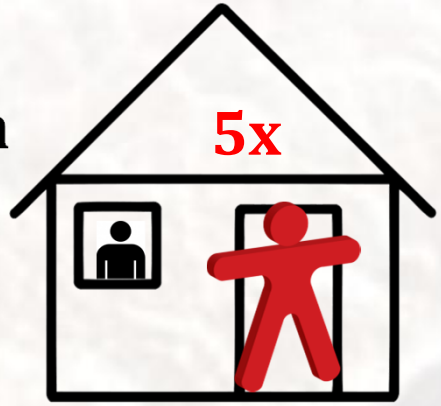
- **Kim et al., 2014: 9 subjects suspected of SCs abuse, 5 male and 4 female, age 21-30 yr**
- **Parent SCs and their monohydroxylated metabolites were identified in the hair samples of all nine cases**

EXTERNAL CONTAMINATION

- **Moosman et al., 2014:**

A: 8 participants involved in the analysis of herbal mixtures;

B: 5 persons living in the same households with participants from group A;



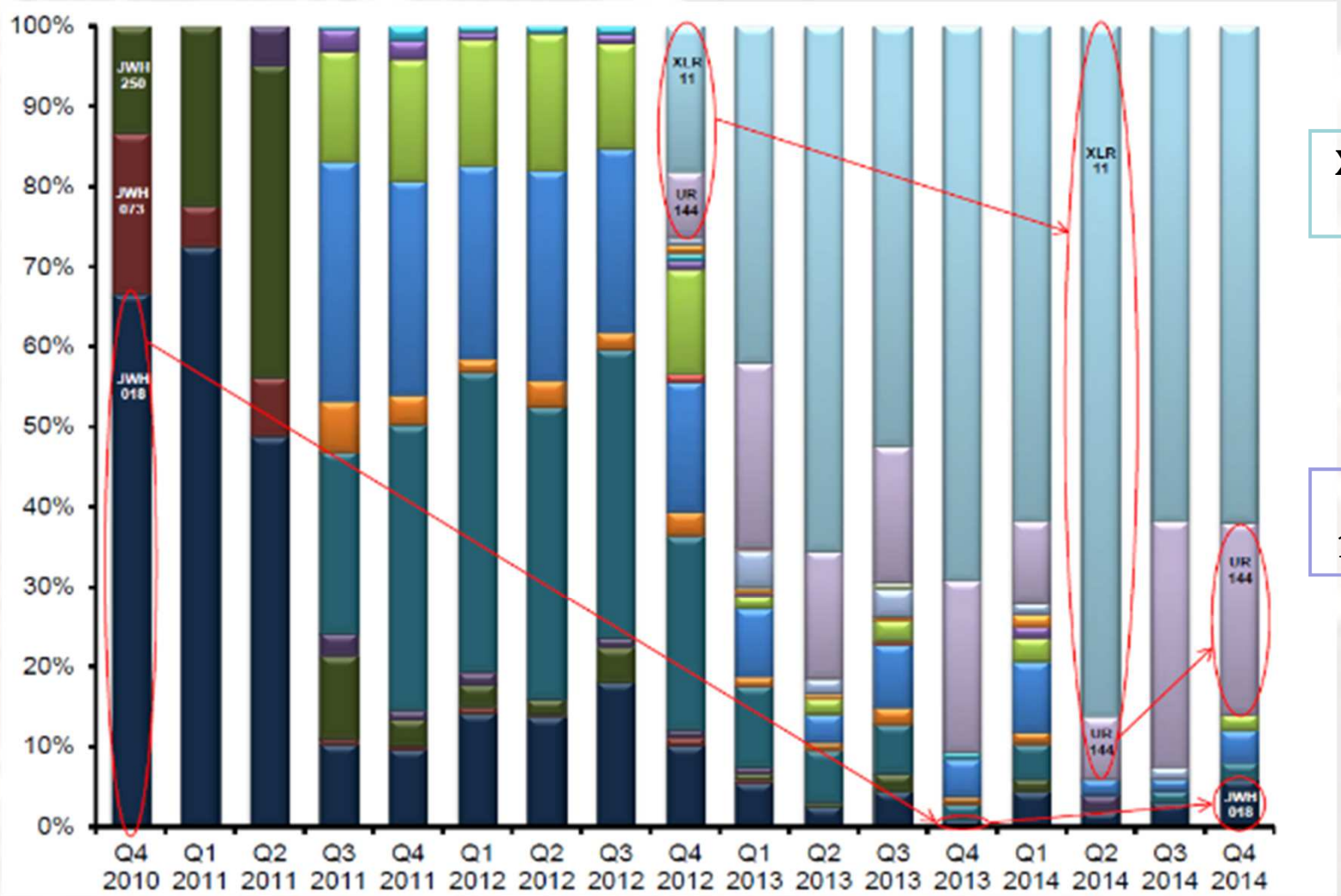
C: 9 participants from laboratory staff not directly in contact with the drug materials

SYNTHETIC CANNABINOIDS

CONCLUSIONS - 1

- Hair analysis is an effective tool to evaluate the prevalence of synthetic cannabinoids in selected populations
- From 2010 to 2014, we observed a decrease in the number of positive samples

Decrease of positive rate: looking at the wrong target?



JWH 018

XLR 11

UR 144

NMS Labs (March 2015)

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SYNTHETIC CANNABINOIDS

CONCLUSIONS - 2

- LOD or cut-offs?
- Metabolites to discriminate between active intake or passive exposure
- Testing is deterrent, update of methods is necessary

Workplace testing/Driving re-licensing

13-12-2012, 22:21

GeographyGeography
Silver Member

Re: Synthetic Cannabinoids and the STANDARD

It's only used to disprove false positives wher
with it would take a long time. They will not 'l

bscribe To Substance Abuse

11-23-2012, 07:00 PM

AndyJ2112
Member

Join Date: Nov 2012
Posts: 1

Synthetic cannabinoid MAM-2112 withdrawal is ******* with me majorly.

So i've been smoking synthetic blends and cannabis for around a year quite infreque
use. A while ago i ordered 2g of the synthetic cannabinoid MAM-2201 online, and sm
to almost nothing as i was having to constantly increase my dosage due to the resis
realized that it was starting to show some negative effects, i spent most of the last
last of the two weeks, i'd rather lay in bed and spark up the white powder....

14-12-2012, 19:00

EzekielCain
Silver Member

Re: Synthetic Cannabinoids and the STANDARD drug test of 2012.

This is true....5 panel won't yield any positive results. My friend has a good job in the healt
be a-ok!

UA detection time?

Opiophorum Member

Hello
Im just interested in how long these synthetic cannabinoids are detectable in ones urine.
But then they prob all have different half lives? (UR-144, 5F-UR-144, AKB-48F, MAM-2201, STS-15

If one is taking UA's which also might get sent for analysis this would be interesting to know how lo
body.

Have a good one,

11-20-2012, 23:02

DaBigBR
No Infidels!

Join Date: Oct 2005
Location: Circling the wagons.
Posts: 15,569

We're seeing this stuff in my area like I'm sure many of you are in yours. The difficulty for our DREs (which now includes yours truly) has been in the testing. We have been sending samples to NMS Labs, but have yet to have a confirmed result, even from admitted "K2" or "spice" users. The trouble is that the compounds on the street change as the laws that aim to restrict them evolve. We're currently seeing a lot of the XLR and UR strain compounds, but NMS does not appear to test for them. The obvious trouble is that unless they happen to have something else on board (which is not uncommon, by any means), we're left with a loser case because we can't establish that it was in their system (despite all of the evidence of ingestion and impairment, admissions, etc).

Anti-doping

Synthetic or not, Kellen Winslow's drug arrest could lead to suspension

New York Jets tight end Kellen Winslow faces suspension in wake of arrest for synthetic week. *(Al Bello / Getty Images)*

By A.J. Perez/NJ.com
Email the author | Follow on Twitter
on January 17, 2014 at 1:38 PM, updated January 17, 2014 at 2:52 PM

Print

New York Jets tight end Kellen Winslow faces suspension for violating the league's drug policy -- even if the NFL doesn't list synthetic marijuana on its banned list.

MORE JETS

Super Bowl 2014: Best story lines for Broncos vs. Seahawks

Sponsored By:

Winslow allegedly told authorities he uses the drug because the league doesn't test for such cannabimimetics, the scientific name for synthetic marijuana.

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Thank you for your attention