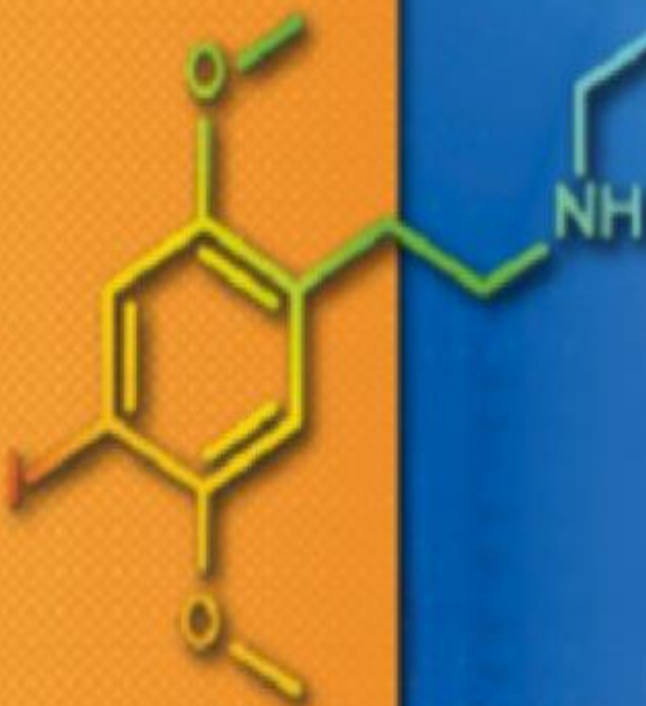


Orbassano (TO)
22 Gennaio 2014



Centro Regionale
Antidoping
Alessandro Bertinaria

LABORATORIO REGIONALE DI TOSSICOLOGIA



Strategie analitiche per la ricerca di
Nuove Sostanze Psicoattive
in campioni biologici

Marco Vincenti

New Drugs

Nuove Sostanze Psicoattive



U.S. DEPARTMENT OF DEFENSE

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> Contracts

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DOD Adds Synthetic Marijuana to Random Drug Testing

By Army Sgt. 1st Class Tyrone C. Marshall Jr.
American Forces Press Service

WASHINGTON, Dec. 13, 2013 – The Defense Department has expanded its zero tolerance for the use of illicit drugs to include synthetic marijuana, also known as “spice,” the director of DOD’s drug testing and program policy said here today.



PRESIDENZA DEL CONSIGLIO DEI MINISTRI

Dipartimento Politiche Antidroga



Ambiti di particolare criticità

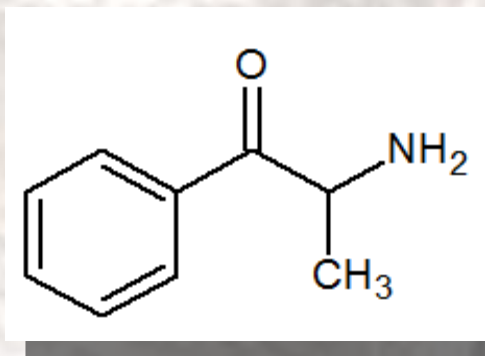
- *Intossicazioni acute*
- *Incidentalità stradale e controlli su strada*
- *Mansioni lavorative che comportano rischi per terzi*
- *Reintegro della patente di guida - porto d'armi*
- *Doping sportivo*

**Quale matrice
biologica?**

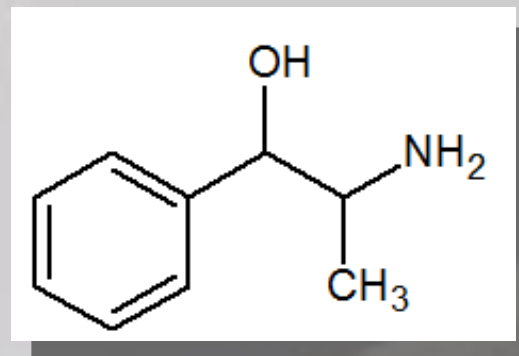
- *Urina*
- *Sangue*
- *Capelli*
- *Fluido orale*

Catinoni di origine NATURALE

Catinone

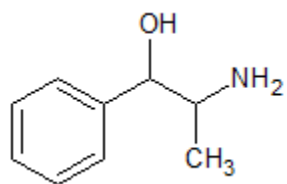


Catina

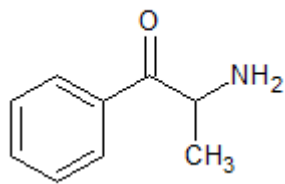


Capostipite: pianta della Khat (corno d'Africa)
Effetti: eccitante, euforizzante, anoressizzante



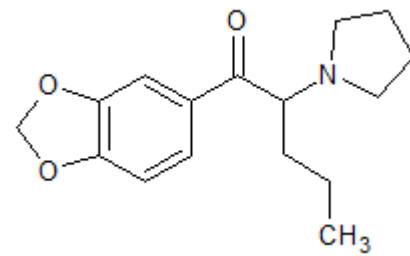
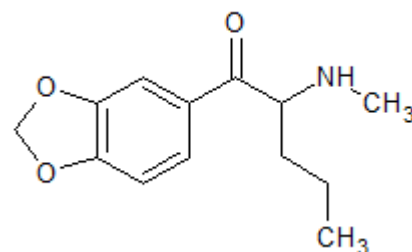
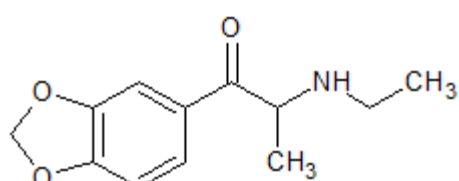
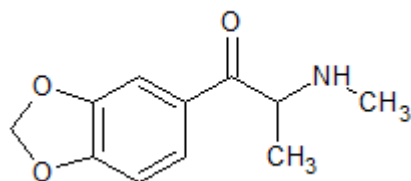
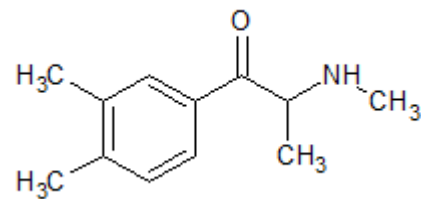
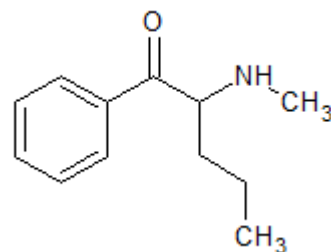
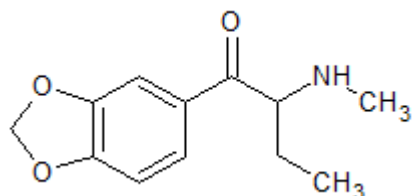
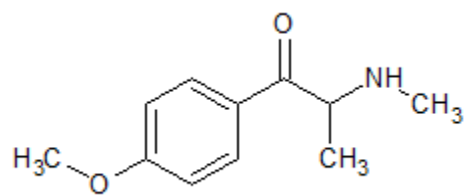
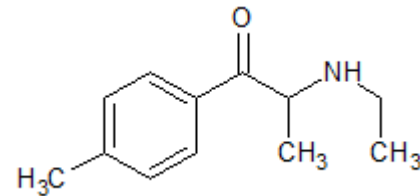
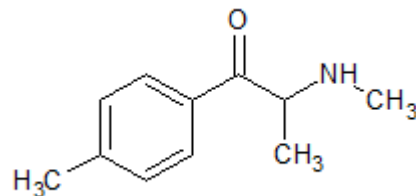
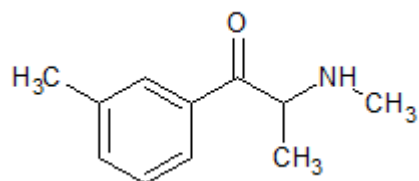
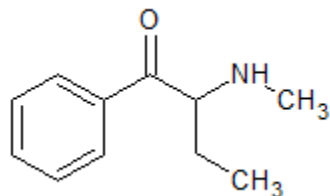
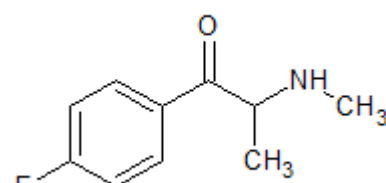
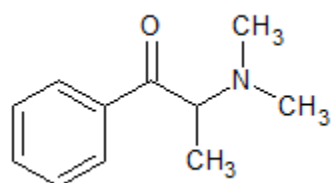
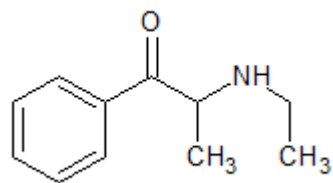
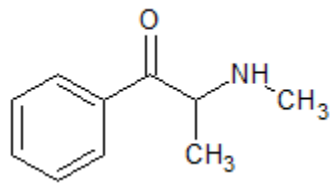


Catina



Catinone

Catinoni sintetici



Caratteristiche dei cationi

- *Struttura chimica di tipo amfetaminico (idrofilica)*
- *Elevata escrezione della sostanza assunta*
- *Possibilità di ricerca sulla matrice urinaria*

Metodi immunometrici dedicati?

- *Ampio spettro di sostanze e strutture chimiche diverse*
- *Rapida obsolescenza dei kit immunometrici dedicati*
- *Elevati costi di analisi per screening generalizzati*

Quale risposta ai kit per amfetamine?

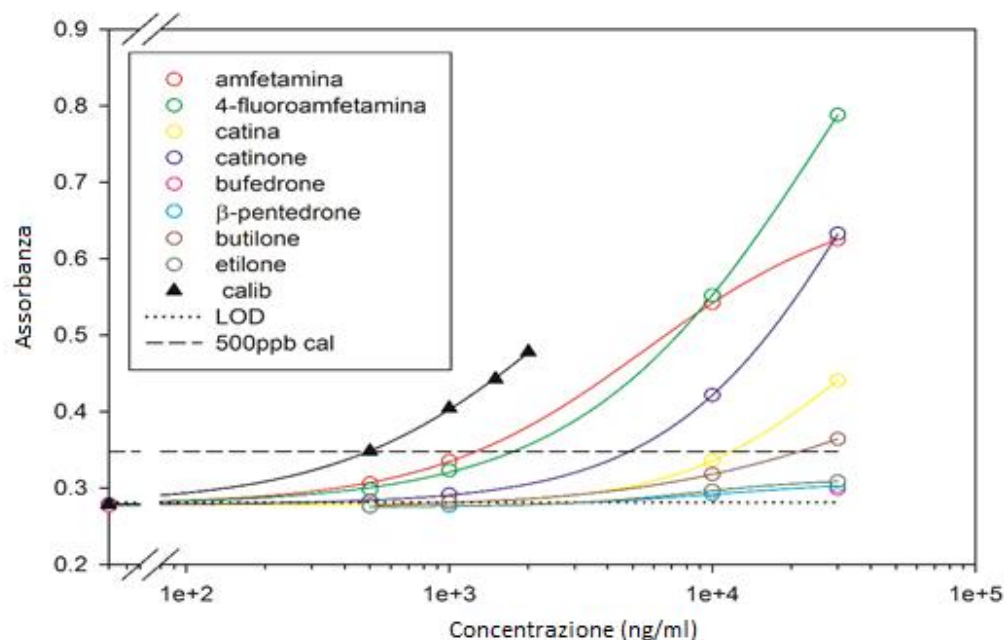
Analisi di SCREENING: metodi EMIT

AmpSQ

	LOD	
	Concentrazione stimata	CR%
Amfetamina	63	28.6
4-Fluoroamfetamina	67	26.9
Catina	1055	1.7
Catinone	285	6.3
Bufedrone	7705	0.2
β -Pentedrone	7992	0.2
Butilone	1348	1.3
Etilone	6973	0.3
Pentilone	586	3.1

EcstSQ

	LOD	
	Concentrazione stimata	CR%
MDMA	205	28.8
4-Fluoroamfetamina	1090	5.4
Metedrone	2250	2.6
Butilone	684	8.6
Etilone	2484	2.4
Pentilone	7818	0.8



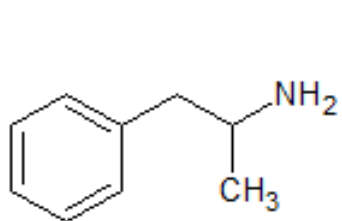
Domande:

Le positività riscontrate negli screening per le amfetamine, usando metodi immunochimici, derivano dall'assunzione di amfetamine, di cationi, o di entrambi?

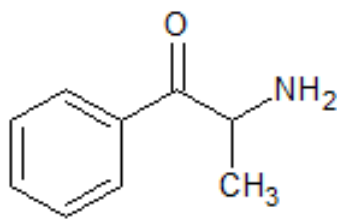
Le positività agli screening per le amfetamine, che non vengono successivamente confermate in GC-MS o LC-MS, sono davvero “falsi positivi” (da cross-reattività) oppure sono dei “veri positivi” misconosciuti (assunzione di cationi anziché di amfetamine)?

Occorre verificare!

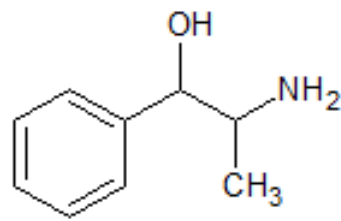
45 campioni di urine risultate positive agli screening per le amfetamine: RICERCA DEI CATINONI



Amfetamina



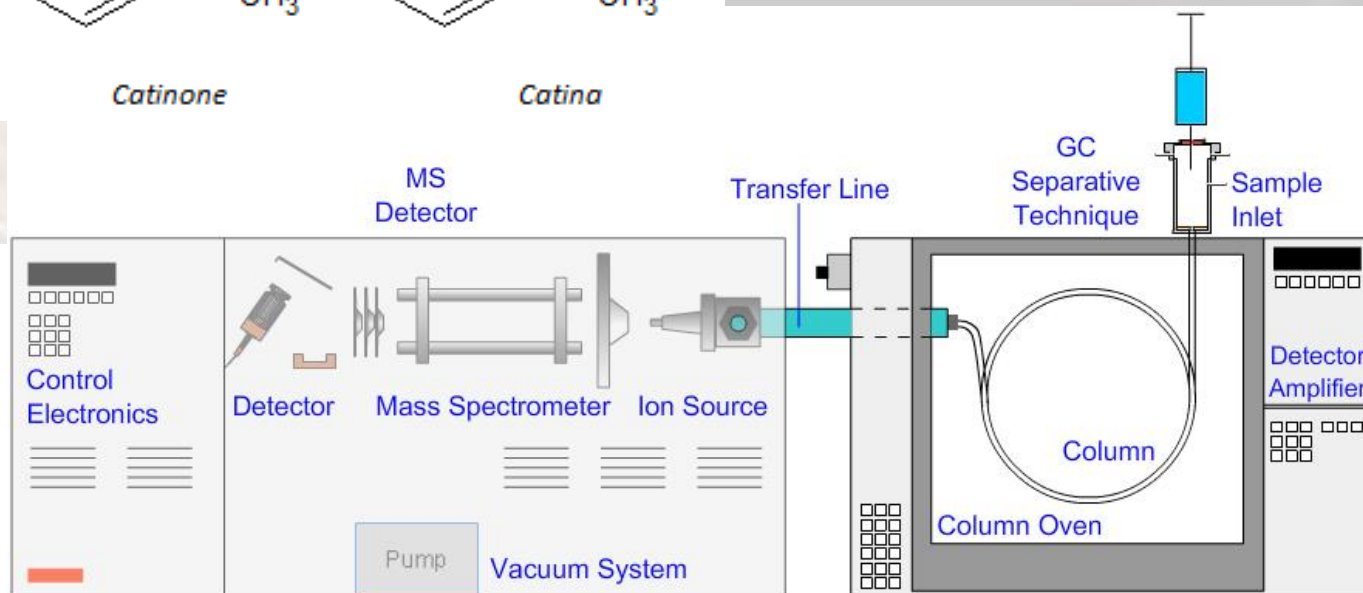
Catinone



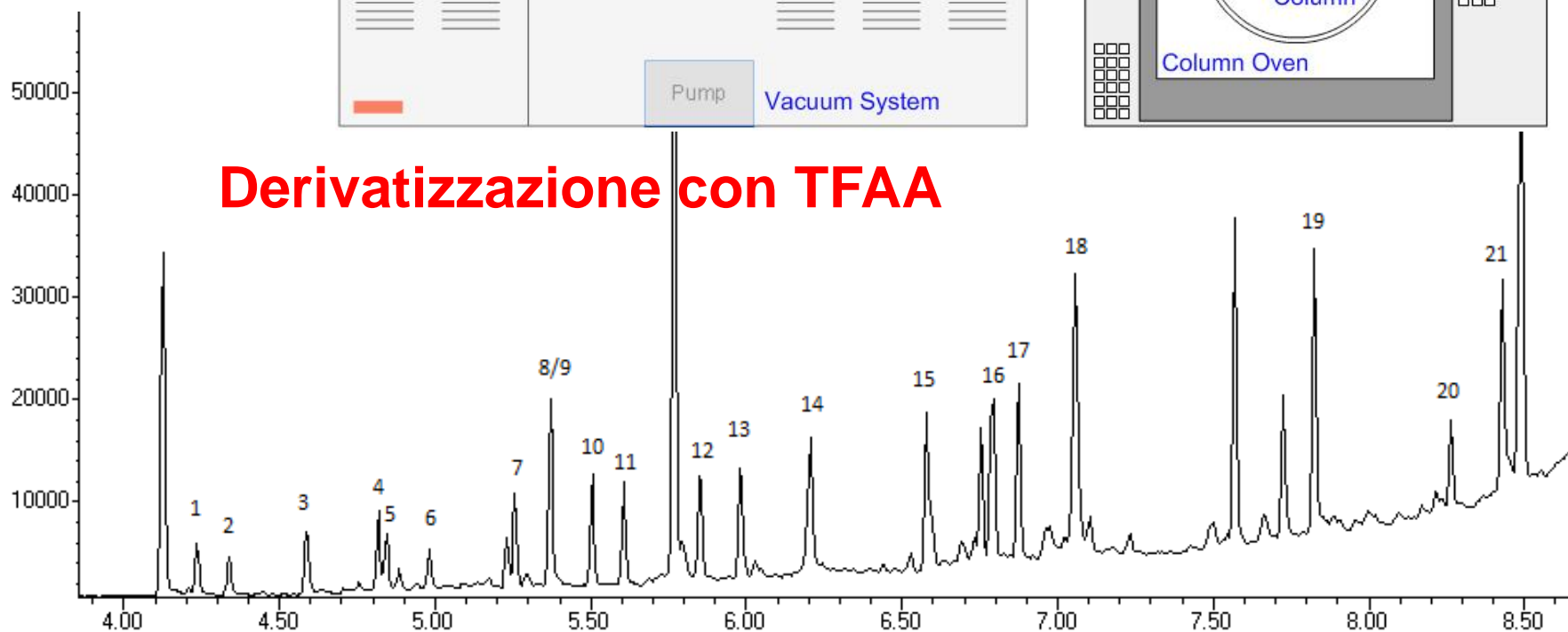
Catina

**Somiglianza
strutturale**

**Strumento:
GC-MS**

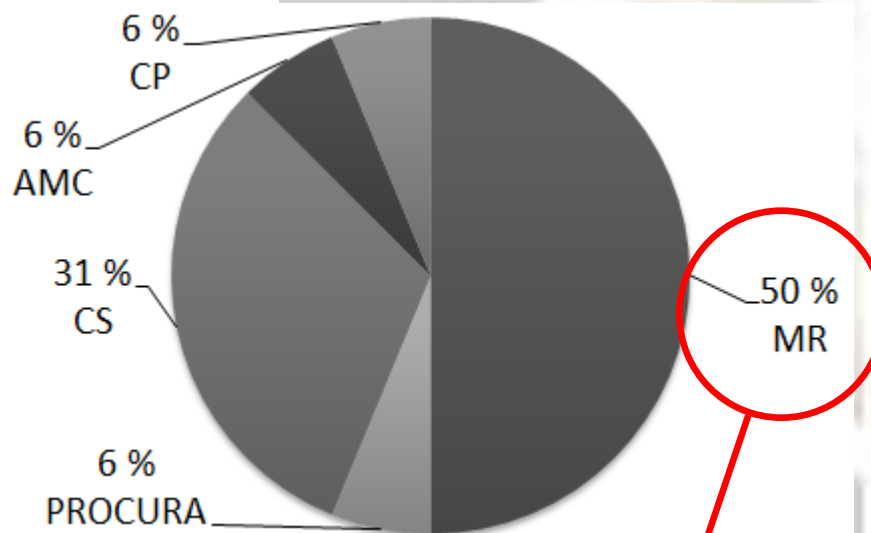
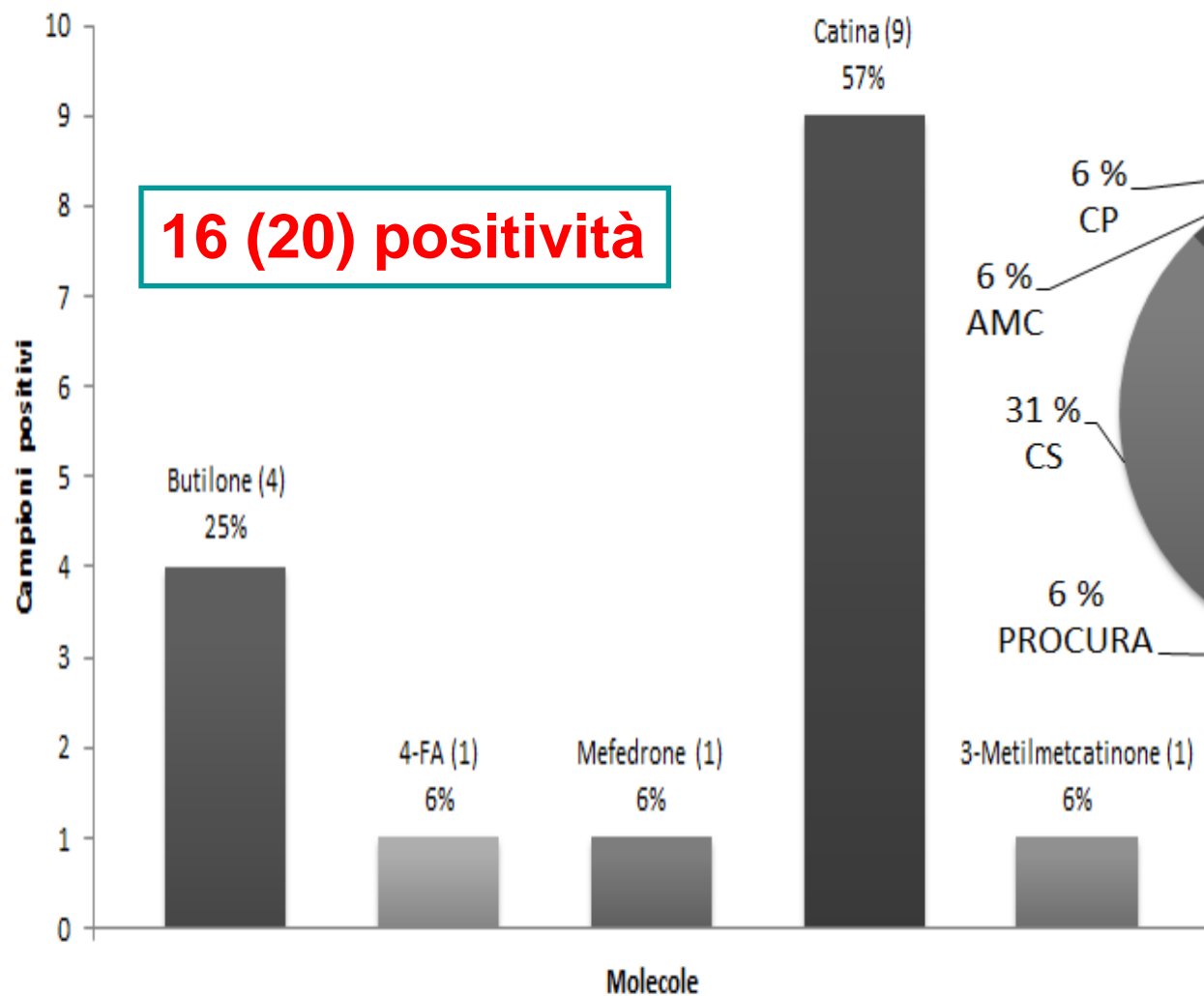


Derivatizzazione con TFAA



45 soggetti (39 maschi e 6 femmine – età media 27 anni (15÷47))
18 controlli su strada, 11 commissioni patenti, 9 mansioni a rischio

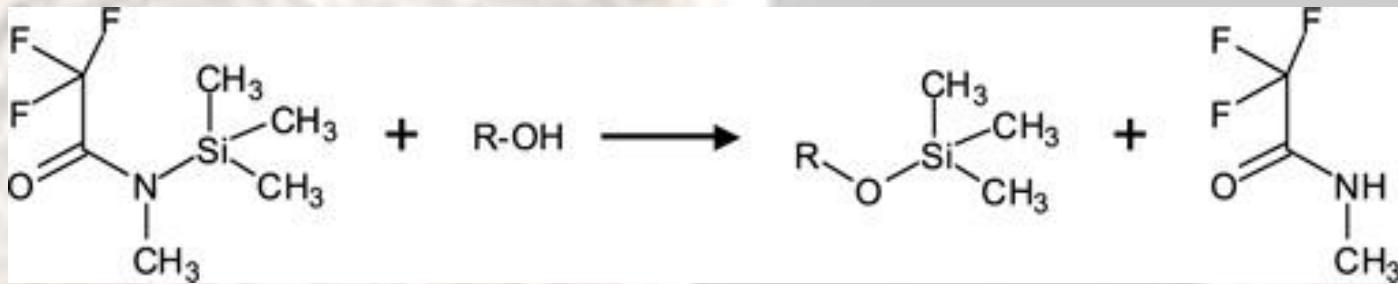
16 (20) positività



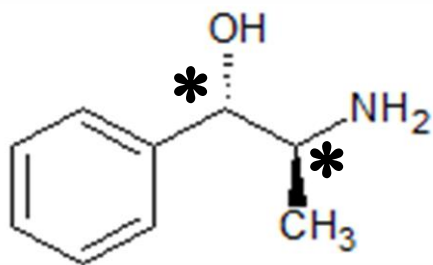
Mansioni a rischio:
8 su 9

Analisi di CONFERMA – Metodo MSTFA

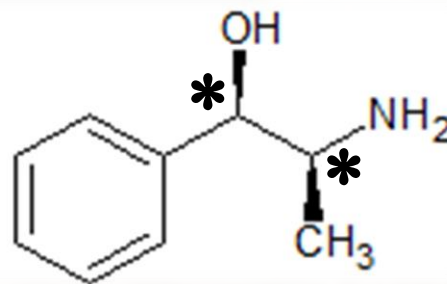
Derivatizzante: N-metil-N-(trimetilsilil) trifluoroacetamide



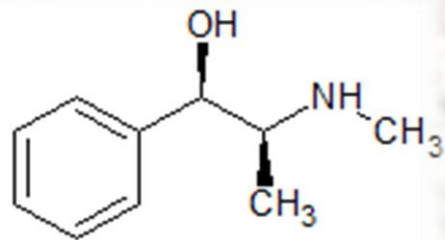
Analiti:



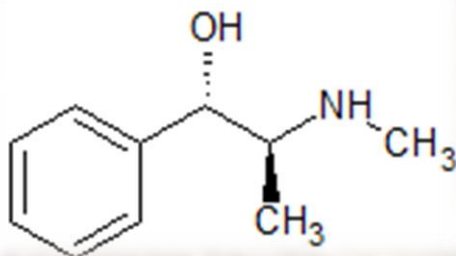
Nor-pseudoefedrina
(CATINA)



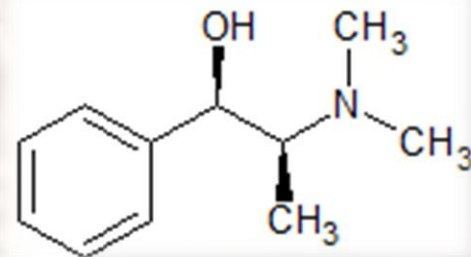
Nor-efedrina
(FENILPROPANOLAMMINA)



Efedrina



Pseudoefedrina

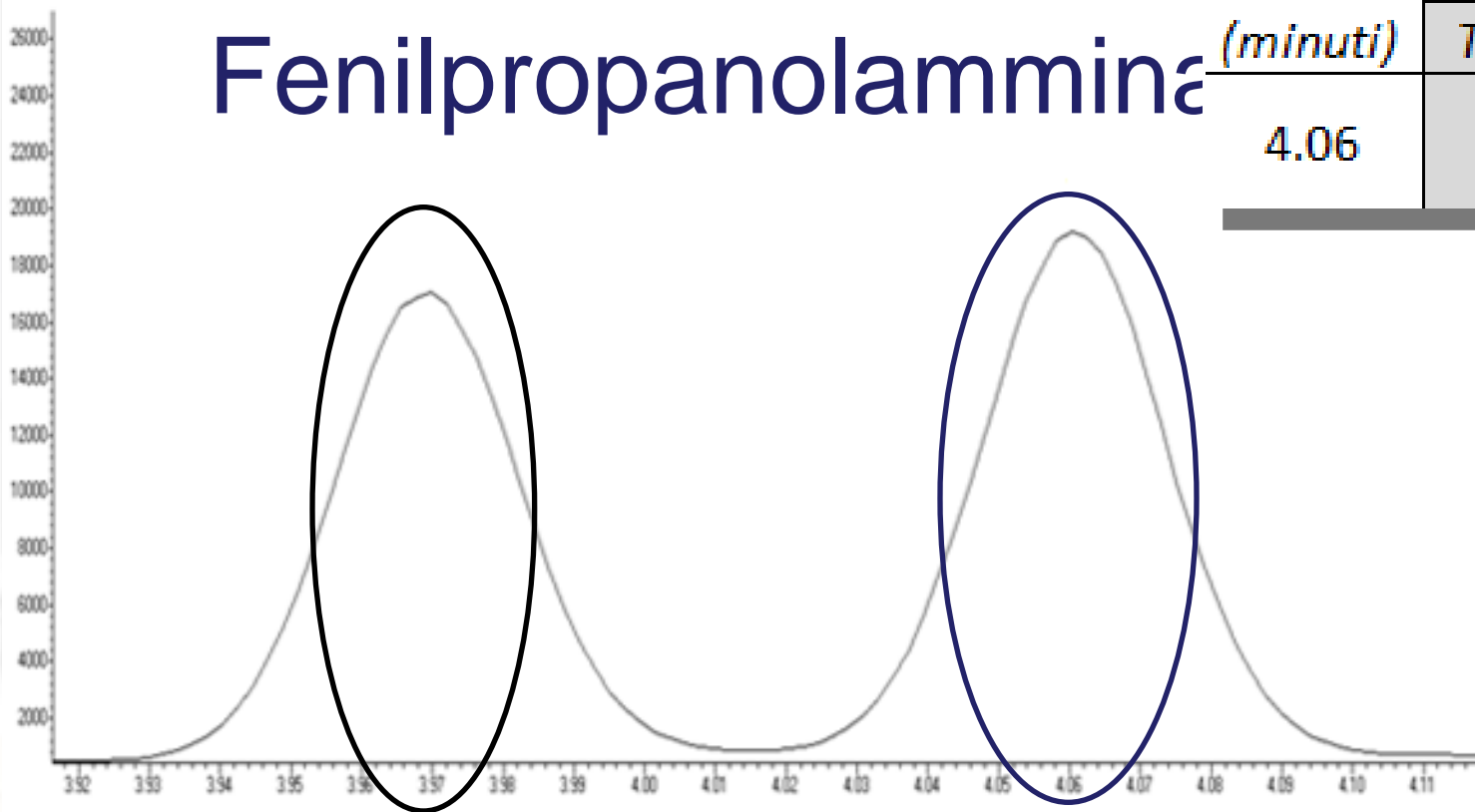


Metilefedrina

Analisi di CONFERMA – Metodo MSTFA

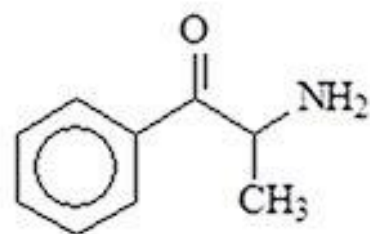
Fenilpropanolammina

<i>RT</i> <i>(minuti)</i>	<i>Ioni (m/z)</i>	
	<i>Target</i>	<i>Altri</i>
4.06	116	147, 280, 117

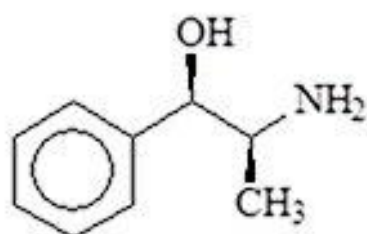


Catina

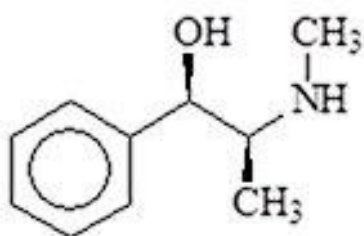
<i>RT</i> <i>(minuti)</i>	<i>Ioni (m/z)</i>	
	<i>Target</i>	<i>Altri</i>
3.97	116	147, 280, 117



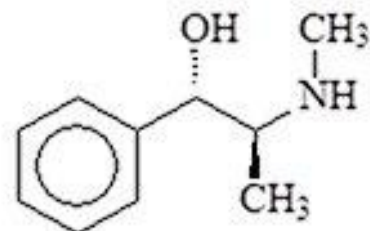
Catinone



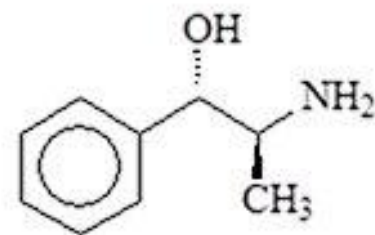
**Norefedrina
(Fenilpropanolammina)**



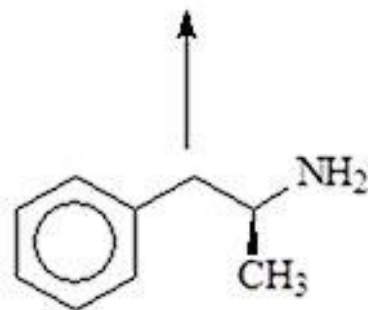
Efedrina



Pseudoefedrina



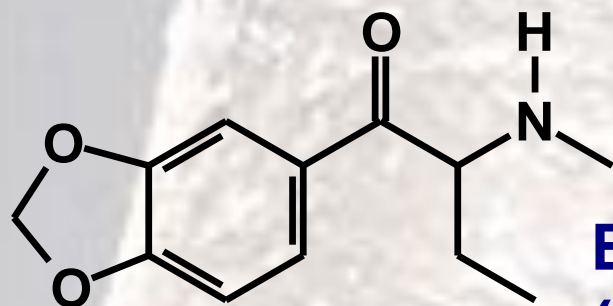
**Norpseudoefedrina
(Catina)**



Amfetamina



Campione	Screening per amfetamine (ng/mL)	Risultato conferma	Concentrazione (µg/mL)	Altre positività	Farmaci assunti contenenti Pseudoefedrina
1	695	Catina →	2,37	Pseudoefedrina	Actigrip
2	>2000	Fenilpropanolamina →	0,08	Amfetamina e THC	Dato non disponibile
3	727	Catina →	3,43	Pseudoefedrina	Reactine
4	615	Catina →	1,60	Pseudoefedrina	Reactine
5	1248	Catina →	5,21	Pseudoefedrina	Reactine
6	828†	Butilone	1,78	MDMA e THC	Dato non disponibile
7	>2000	Butilone	0,76	MDMA	Dato non disponibile
8	Non disponibile	Butilone	8,39	MDA e MDMA	Dato non disponibile
9	Non disponibile	Butilone	5,51	MDA e MDMA	Dato non disponibile
10	>2000	Fenilpropanolamina →	0,20	MDA, MDMA, Oppiacei e Cocaina	Dato non disponibile
11	>2000	Fenilpropanolamina 4-Fluoroamfetamina →	0,41 0,85	Amfetamina e THC	Dato non disponibile
12	>2000	Fenilpropanolamina →	0,11	Amfetamina, Ketamina e Cocaina	Dato non disponibile
13	681	Catina →	1,12	Pseudoefedrina	Dato non disponibile
14	747	Mefedrone	80,5	/	Dato non disponibile
15	Non disponibile	Catina →	4,06	Pseudoefedrina	Dato non disponibile
16	507	Catina →	0,81	Pseudoefedrina	Antistaminico (non precisato)
17	1561	Catina →	3,68	Pseudoefedrina	Antistaminico (non precisato)
18	634	Catina →	3,66	Pseudoefedrina	Reactine
19	981	3-Metilmetcatinone	42,7	THC	Dato non disponibile



**Butilone
(4 casi)**

**Screening
immunom.
amfetamine**

POS.

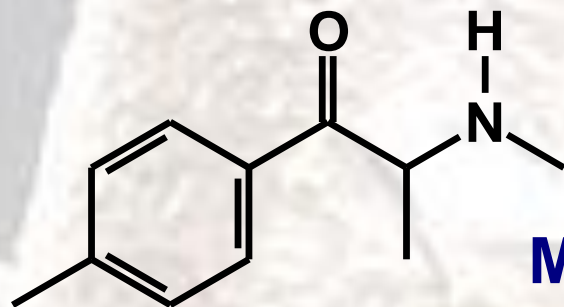
**Conferme
GC-MS**

AMF

CAT

**POS.
indiretta**

POS.

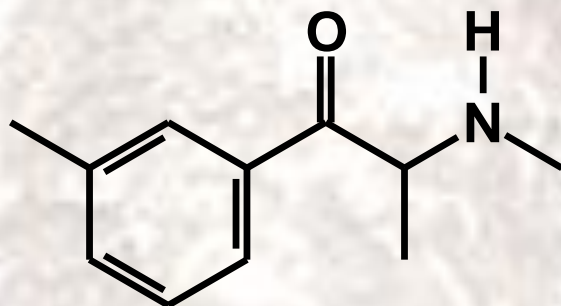


**Mefedrone
(1 caso)**

POS.

NEG.

POS.

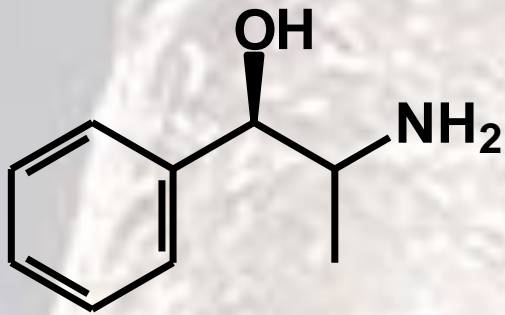


3-Metilmetcatinone (1 caso)

POS.

NEG.

POS.

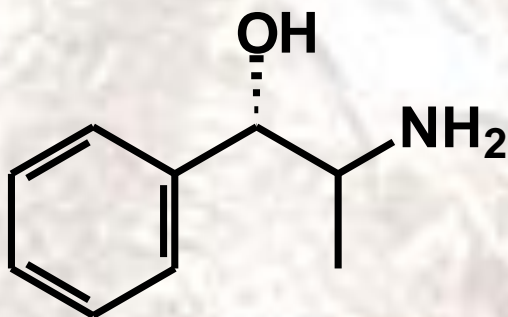


Fenilpropanolamina (4 casi)
(sostanza **non illecita**)



da metabolismo
dell'**amfetamina**

ILLECITA



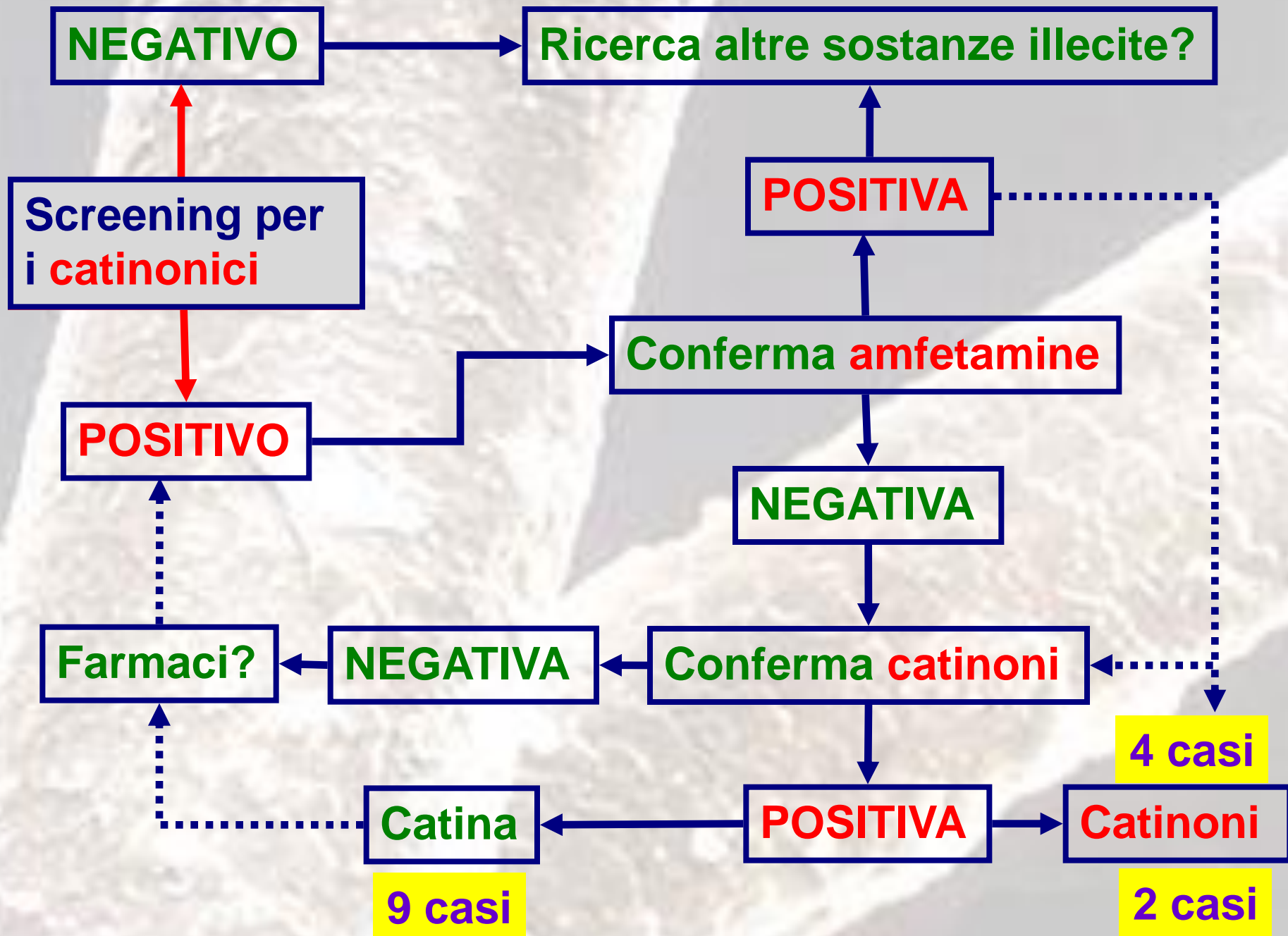
Catina (9 casi)
(sostanza **illecita**)



LECITA

da metabolismo
pseudoefedrina
(antistaminici)

da metabolismo:
-catinone



11 campioni su 19 sono risultati:
Negativi alla conferma per le amfetamine
Positivi alla conferma per i cationici

- **Opportunità:** riscontri di positività alle analisi di screening per le amfetamine con metodi EMIT
- **Rischio:** che le positività (**vere**) non vengano confermate se non si dispone di un metodo in GC-MS per la conferma dei cationici
- **Rischio:** che false positività non vengano riconosciute come tali, se non è chiaro il quadro anamnestico e lo spettro dei farmaci assunti

CANNABINOIDI SINTETICI: **AZIONI LEGALI**

DEA UNITED STATES
Drug Enforcement Administration

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PHOENIX NEWS

November 6, 2012
Contact: Public Information Officer
Number: 602 664-5725

DEA NEWS: Valley-wide Synthetic Drug Takedown
Investigation targeted the production and distribution of synthetic drugs



Various brands of Spice seized at a retail outlet in North Scottsdale.

Multiple Spice vials at the manufacturing warehouse, packaged and sorted for distribution to retail outlets.

News | Government

House Approves Ban on Synthetic Pot

The bill was introduced by Rep. Joseph McNamara of Cranston.

European Commission takes decisive action against legal highs

NEWS

Melbourne 9°C - 18°C . Possible late shower.

AIRFRANCE
Per scoprire le altre offerte
Clicca qui

NEWS SPORT ENTERTAINMENT BUSINESS LIFESTYLE

BREAKING NEWS LOCAL VICTORIA NATIONAL WORLD LAW & ORDER WEIRD

Kilos of drug Venom seized in Perth's southern suburbs

Topics: stock, synthetic cannabis, yepoon


Two kilograms of suspected synthetic drugs seized in region

Chris Schwarten | 29th Nov 2012 5:00 AM | Updated: 1:23 PM

Comments (53) »

Social Network

13-12-2012, 22:21



GeographyGeography
Silver Member

ic cannabis

Like Edit

Subscribe To Substance Abuse

11-23-2012, 07:00 PM


AndyJ2112
Member

Join Date: Nov 2012

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

So i've been smoking synthetic blends and cannabis for around a year quite infrequently. A while ago i ordered 2g of the synthetic cannabinoid MAM-2201 online, and soon after it went to almost nothing as i was having to constantly increase my dosage due to the resistance. I'm not sure if this is just me or if it's a common side effect of synthetic cannabinoids. I'm looking for someone who has experienced this or knows how to deal with it.

14-12-2012, 19:00



EzekielCali
Silver Member


Re: Synthetic Cannabinoids

This is true....5 panel won't be a-ok!

Thread: Synthetic Cannabinoids UA detection time?


01-23-2013 03:11 PM

Unbalanced
Opiophorum Member



Erowid Experience Vaults

Index Full List Search Submit Settings About Main Vaults



Erowid is a one-of-a-kind resource
We are an educational non-profit dedicated to providing a balanced examination of psychoactive drugs and drug use--to reduce harms, improve benefits, and support appropriate policies. The site is made possible by \$5, \$10, and \$50 donations from visitors. Please pitch in!

Cannabinoid Droid
JWH-210
by [Psyonic One](#)

Index Full List Search Submit Settings About Main Vaults

2013 is a year of change for drug policy, for novel psychoactive substances, and for Erowid Center
Though the last 10 years have seen a resurgence of support for psychedelic research and cannabis legalization, there is still a surprising lack of backing for direct education about the responsible use of psychoactive drugs. Please donate!

A Pleasant Surprise
JWH-018
by [DarkTryptamine](#)

11-20-2012, 23:02



DaBic
No Infidels

Join Date: Location: Posts: 15

Effetti avversi & Intossicazioni acute



SAMHSA News Release

Date: 12/4/2012 9:00 AM
Media Contact: SAMHSA Press Office
Telephone: 240-276-2130

First-of-its-kind report finds that street forms of “synthetic marijuana” products linked to thousands of hospital emergency departments visits each year

Young people, particularly males, most often involved

3 deaths may be tied to synthetic marijuana in Colorado

By **Jacque Wilson**, CNN

September 7, 2013 -- Updated 1550 GMT (2350 HKT)

Smoking synthetic marijuana may damage kidneys

Cathy Payne, USA TODAY 7:11 p.m. EST February 14, 2013

Synthetic Marijuana Use During Pregnancy Can Cause Symptoms of Preeclampsia and Eclampsia

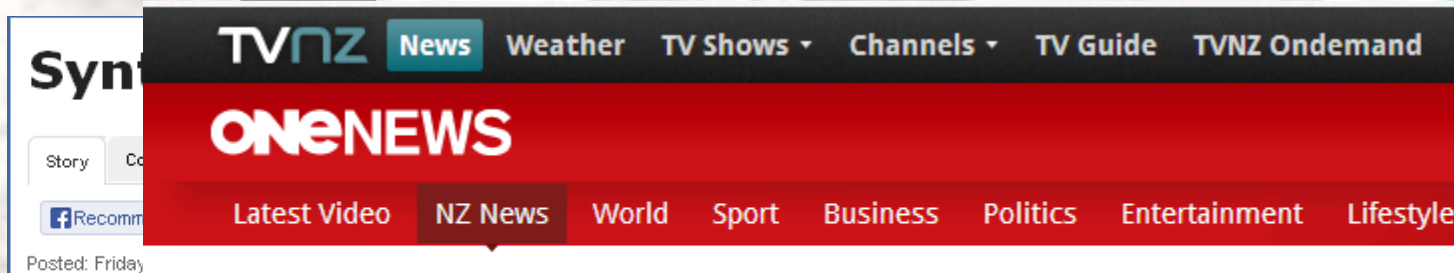
FILED UNDER HEALTH & WELLNESS, SUBSTANCE ABUSE BY LENA BUTLER



QUAL E' LA REALE INCIDENZA D'ABUSO?



- ✓ L'analisi dell'urina è problematica
(rapido metabolismo, assenza di standard)
- ✓ Mancanza di dati affidabili sull'incidenza dei cannabinoidi
quale causa di incidenti stradali e lavorativi



More employers testing for synthetic cannabis use

Published: 9:02AM Wednesday June 05, 2013 Source: ONE News



**DETERMINAZIONE DIRETTA NEI CAPELLI
DEI CANNABINOIDI ASSUNTI**



PRIMO STUDIO

Research Article

Journal of
**MASS
SPECTROMETRY**

Received: 3 January 2012

Revised: 7 March 2012

Accepted: 15 March 2012

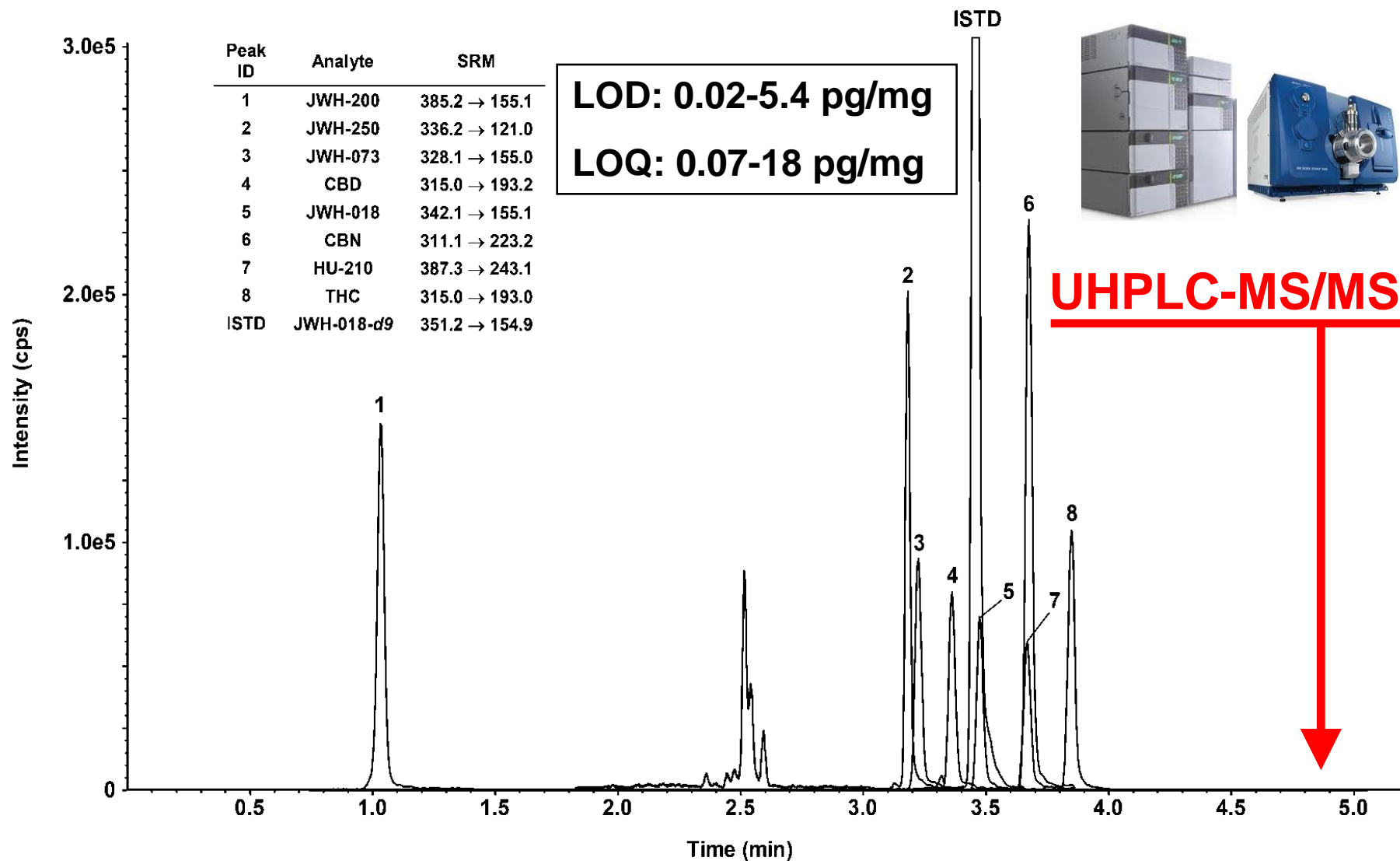
Published online in Wiley Online Library

(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

A. Salomone,^{a*} E. Gerace,^a F. D'Urso,^a D. Di Corcia^a and M. Vincenti^{a,b}

Determinazione di 5 cannabinoidi sintetici, THC, CBD e CBN nei capelli





179 campioni di capelli da consumatori abituali di cannabis (2010)

14 soggetti positivi ad almeno un cannabinoide sintetico (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

4# Length: 3.5 cm; JWH-250: 208.8 pg/mg
 6# Length: 3.0 cm; JWH-250: 1.5 pg/mg



Consumo cronico
 Uso occasionale
 Contaminazione esterna



A. Salomone et al. Drug Testing and Analysis (2014) 6, 126-134

SECONDO STUDIO

23 CANNABINOIDI SINTETICI

Research article

Drug Testing
and Analysis

Received: 21 June 2013

Revised: 23 August 2013

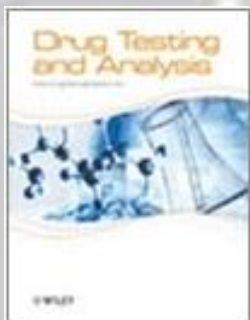
Accepted: 29 August 2013

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

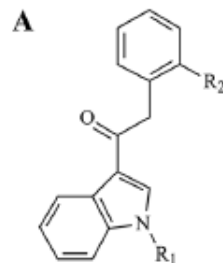
Hair analysis as a tool to evaluate the prevalence of synthetic cannabinoids in different populations of drug consumers

A. Salomone,^{a*} C. Luciano,^a D. Di Corcia,^a E. Gerace^a and M. Vincenti^{a,b}

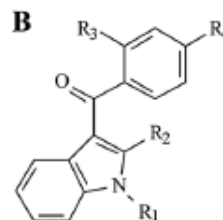


23 analiti ricercati
Periodo di investigazione
(anno 2011)

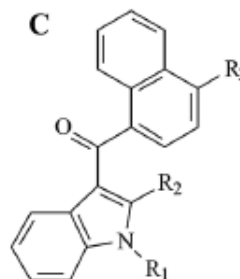
**Confrontare la diffusione dei
cannabimimetici fra differenti
popolazioni di consumatori di
sostanze stupefacenti e alcol**



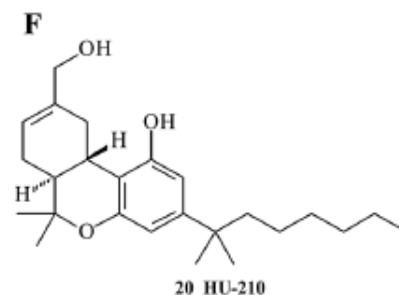
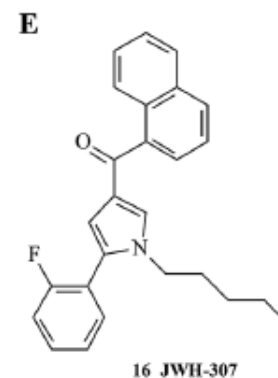
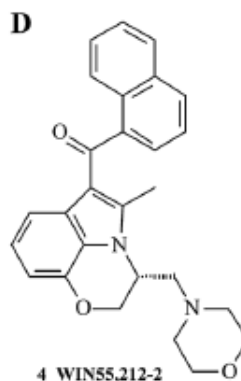
Compound	R ₁	R ₂
11 JWH-203	pentyl	chloro
9 JWH-250	pentyl	methoxy
12 JWH-251	pentyl	methyl
17 RCS-8	2-cyclohexylethyl	methoxy



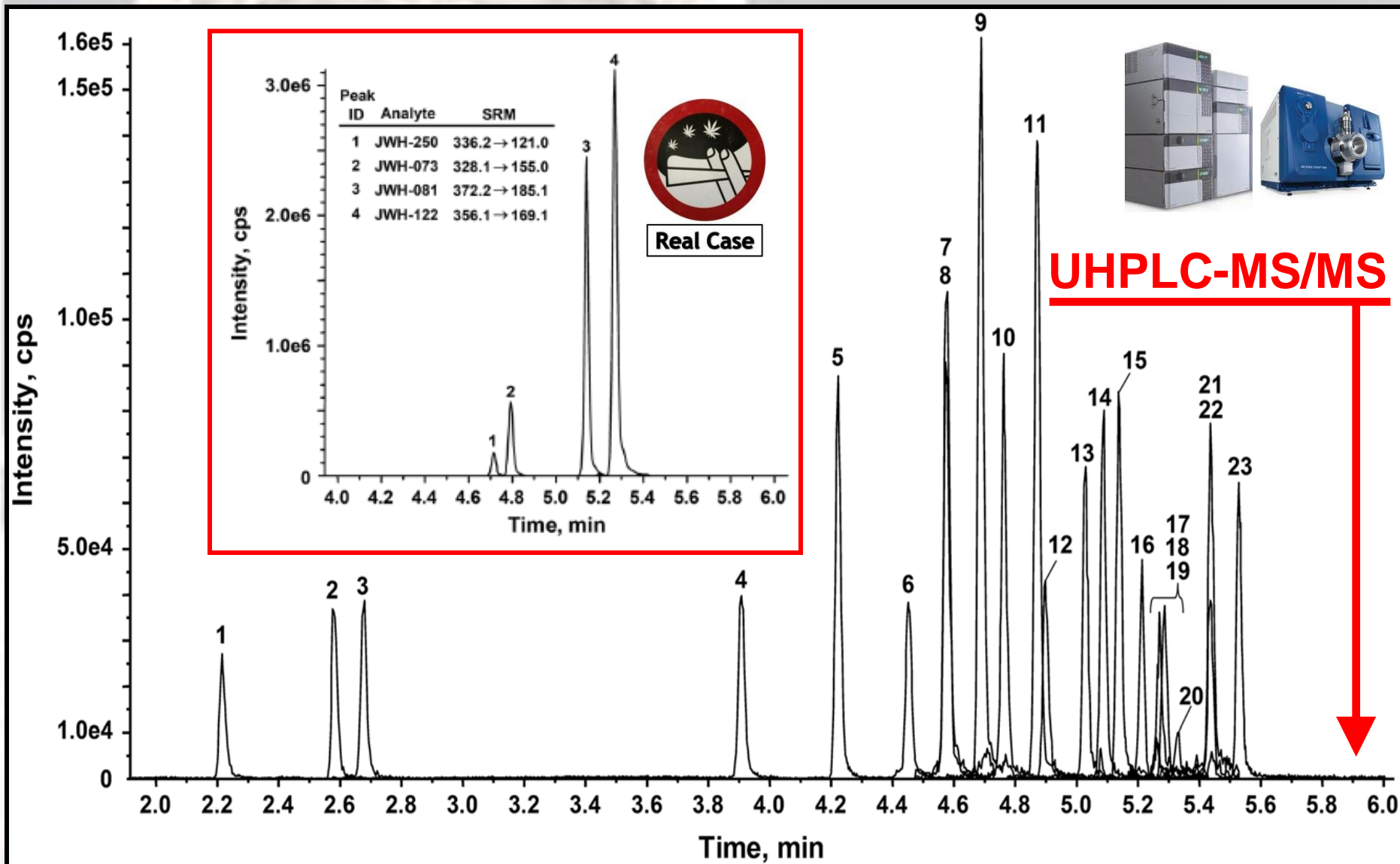
Compound	R ₁	R ₂	R ₃	R ₄
5 AM-694	5-fluoropentyl	H	iodo	H
8 RCS-4	pentyl	H	H	methoxy
1 WIN 48,098	4-ethylmorpholino	methyl	H	methoxy



Compound	R ₁	R ₂	R ₃
2 AM-1220	1-methylpiperidin-2-yl-methyl	H	H
6 AM-2201	5-fluoropentyl	H	H
15 JWH-007	pentyl	methyl	H
7 JWH-015	propyl	methyl	H
13 JWH-018	pentyl	H	H
19 JWH-019	hexyl	H	H
23 JWH-020	heptyl	H	H
10 JWH-073	butyl	H	H
14 JWH-081	pentyl	H	methoxy
18 JWH-122	pentyl	H	methyl
3 JWH-200	2-morpholin-4-yl-ethyl	H	H
21 JWH-210	pentyl	H	ethyl
22 JWH-398	pentyl	H	chloro



Determinazione di 23 cannabinoidi sintetici in campioni di capelli



➤ 344 campioni di capelli

- 264 già positivi a sost. stupefacenti
- 80 già positivi ad alcol (EtG > 30)

Table 3. Synoptic summary of real samples positive to synthetic cannabinoids

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

^aTHC: Δ^9 -tetrahydrocannabinol; MDMA: 3,4-methylenedioxymethamphetamine; AMP: Amphetamine; COC: Cocaine; MOR: Morphine; 6-AM: 6-acetylmorphine.

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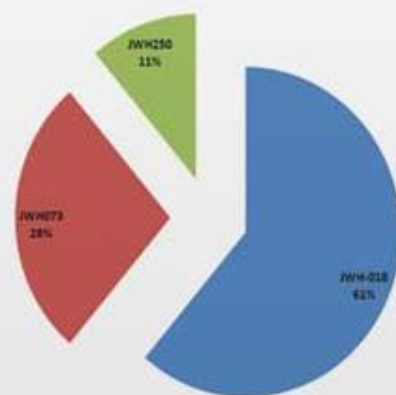
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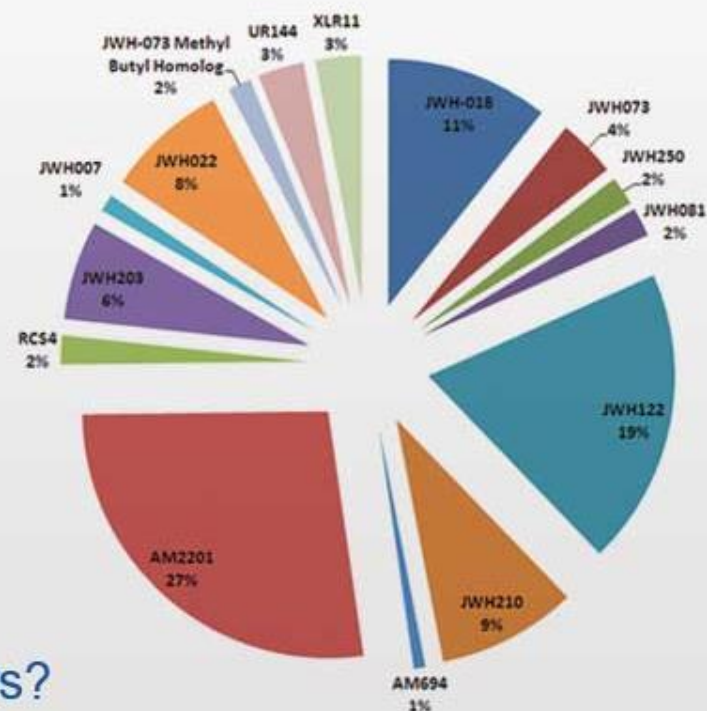
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DEA Designer Drug Takedown Acetyl Fentanyl Testing at NMS



2010 to 2012



 are you ready for the next 2 years?

25 September 2013, 2.14pm BST

Fast market for legal highs poses challenge for scientists



First you've got to work out what's in it. Ohio Sea Grant and Stone Lab

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 weed. (Al Bello / Getty Images)



By [A.J. Perez/NJ.com](#)

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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.



Winslow appears to be correct: The NFL doesn't yet test for synthetic weed and the typical urine test for marijuana won't detect it.

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



Don't Miss: [Jets photos!](#)



Studi successivi



Cut-off per THC internazionalmente accettato: 50 pg/mg



✓ Dati di letteratura scarsi per i cannabinoidi sintetici

Cut-off ?

✓ Ulteriori studi necessari

Assunzione cronica

Uso occasionale

Contaminazione esterna



✓ Determinazione di metaboliti (+ rapporto *parente/metabolita*)
o marcatori alternativi

✓ Studi in condizioni controllate

GRAZIE !

