

**Reggio Calabria, 31 Maggio 2014**

*XVI Congresso Nazionale dei Chimici*

**Chimica, Tossicologia  
ed Antidoping –  
La nuova sfida**

Marco Vincenti, Alberto Salomone,

Enrico Gerace, Denise Caneparo

**Strategie analitiche per la ricerca di  
nuove sostanze psicoattive in  
campioni biologici**





CENTRO REGIONALE  
ANTIDOPING

ALESSANDRO  
BERTINARIA



**È dal cuore sportivo dell'ESPERIENZA OLIMPICA che nasce il CAD, Centro di Eccellenza per la lotta contro l'uso illecito di farmaci e sostanze d'abuso.**



**Individuato dalla Regione Piemonte come Laboratorio di riferimento per la Diagnostica Tossicologica, il CAD si consolida sul territorio torinese nell'ambito della tossicologia ANALITICA, FORENSE, INDUSTRIALE, VETERINARIA E DELLO SPORT, trasformandosi rapidamente in attivo sostenitore della sanità piemontese ed extra-regionale**



**Strumentazione analitica di ultima generazione, innovazione scientifica costante, personale ad elevata specializzazione: queste le basi di un servizio TRASPARENTE, AFFIDABILE, DIVERSIFICATO**

# LA NOSTRA STORIA

2004

Fondazione Consorzio (Regione Piemonte, Università degli Studi di Torino, Istituto di Medicina dello Sport di Torino e Azienda Sanitaria Ospedaliera “San Luigi Gonzaga” di Orbassano)

2006

Partecipazione ai “XX Giochi Olimpici e IX Giochi Paralimpici Invernali” di Torino 2006 come Laboratorio Antidoping

2008

Inizio attività tossicologica

2009

Accreditamento ISO17025 (1° laboratorio in Italia ad aver ottenuto l'accreditamento in campo tossicologico)

2012

Avvio attività Medicina del Lavoro

2014

Avvio attività Biologia Forense

# IL CAD IN NUMERI

- **300.000** DETERMINAZIONI ANALITICHE ANNUE
- **50.000** CAMPIONI ANNUI
- **15.000** PRELIEVI ANNUI
- **42** PUBBLICAZIONI SCIENTIFICHE su riviste internazionali
- **28** DIPENDENTI di cui **10** laureati in Chimica
- **11** METODICHE ACCREDITATE ISO17025  
per un totale di **61** analiti
- **7** PUNTI PRELIEVO CONVENZIONATI tra Piemonte e Liguria



# I NOSTRI CLIENTI

- Aziende e/o Medici Competenti e/o Società di servizi/Laboratori privati nell'ambito di attività di sorveglianza di tipo sanitario e tossicologico ai sensi del D.Lgs. 81/08
- Commissioni Mediche Locali nell'ambito del controllo delle patenti di guida e porto d'armi
- Laboratori pubblici di ASO e ASL e Servizi territoriali di Medicina Legale e per le Tossicodipendenze
- Procure e Tribunali della Repubblica, Ufficiali di Polizia Giudiziaria e Stradale
- Clienti privati

# NUOVE SOSTANZE PSICOATTIVE



1. **Cannabinoidi sintetici**
2. **Catinoni sintetici**
3. **Fenetilammine**
4. **Ketamina e analoghi**
5. **Piperazine**
6. **Triptamine**
7. **Analoghi azepanici**
8. **Fentanili**
9. **Oppioidi**
10. **Analoghi della fenciclidina**



# Ambiti di particolare criticità delle NPS

- *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*

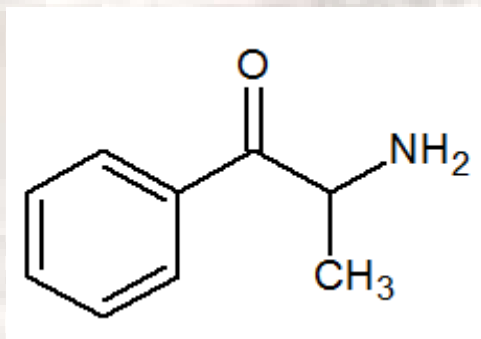
**Quale matrice  
biologica?**

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

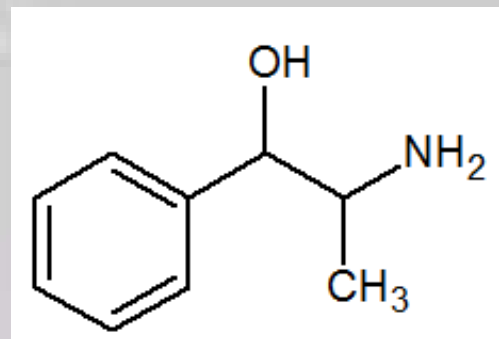


# Catinoni di origine NATURALE

**Catinone**

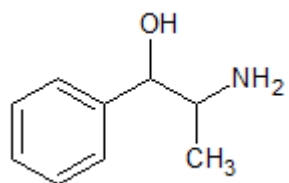


**Catina**

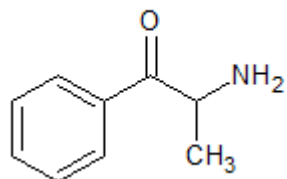


**Capostipite: pianta della Khat (corno d'Africa)**  
**Effetti: eccitante, euforizzante, anoressizzante**



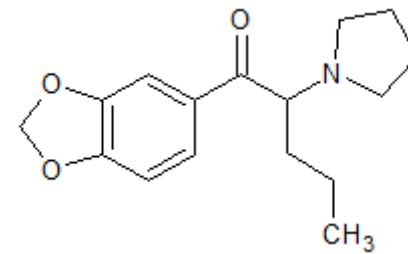
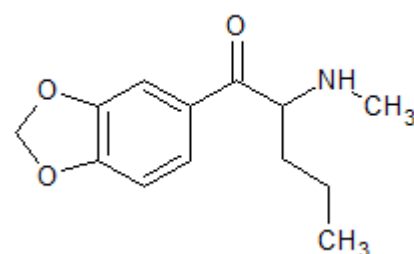
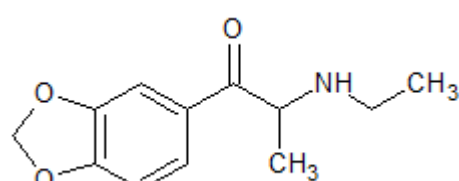
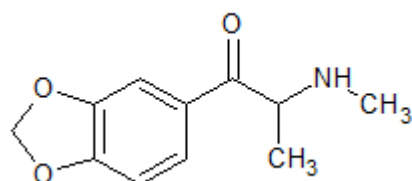
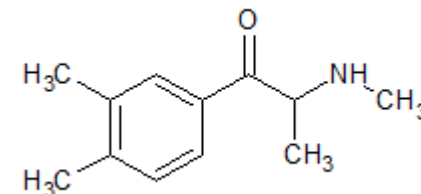
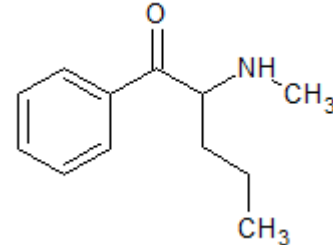
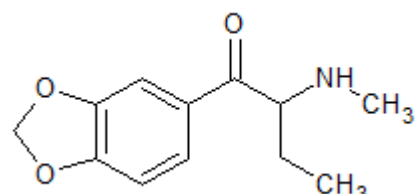
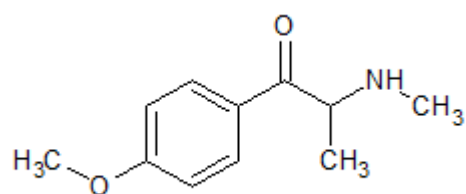
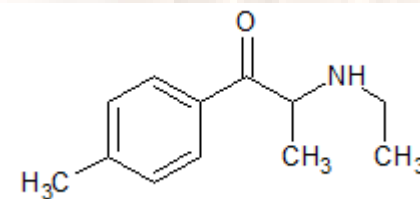
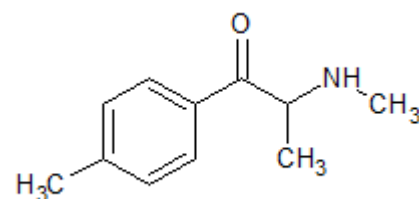
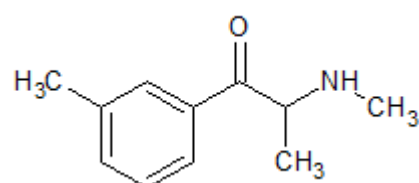
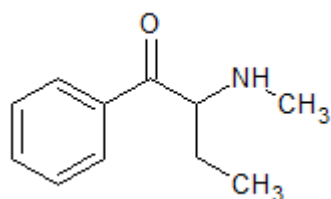
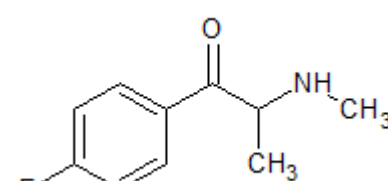
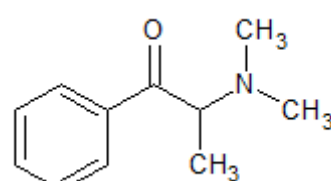
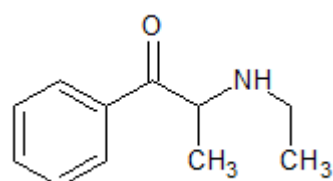
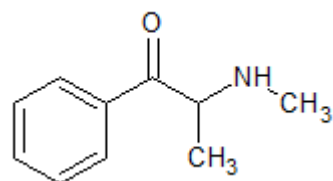


*Catina*



*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?**

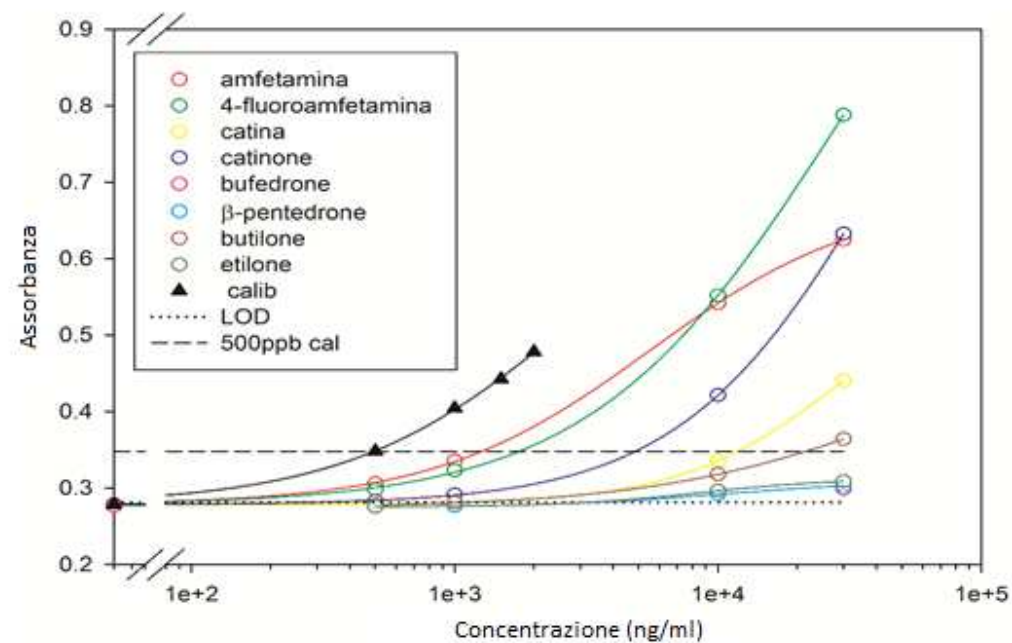
- *Ampio spettro di sostanze e strutture chimiche diverse*
- *Rapida obsolescenza dei kit immunometrici dedicati*
- *Elevati costi di analisi per screening generalizzati*

## **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  |





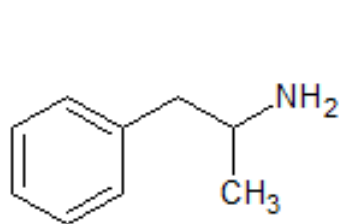
## **Domande:**

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

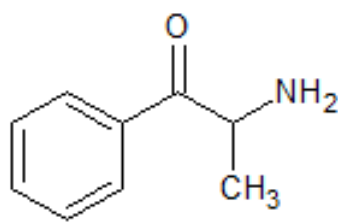
*Le positività agli screening per le amfetamine, che non vengono successivamente confermate in GC-MS o LC-MS, sono davvero “falsi positivi” (da cross-reattività) oppure sono dei “veri positivi” misconosciuti (assunzione di catinoni anziché di amfetamine)?*

## **Occorre verificare!**

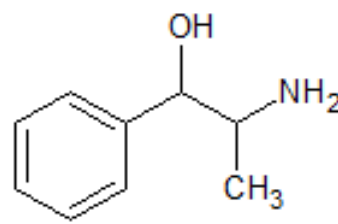
*Sui campioni di urina risultati positivi agli screening per le amfetamine: RICERCA DEI CATINONI*



Amfetamina



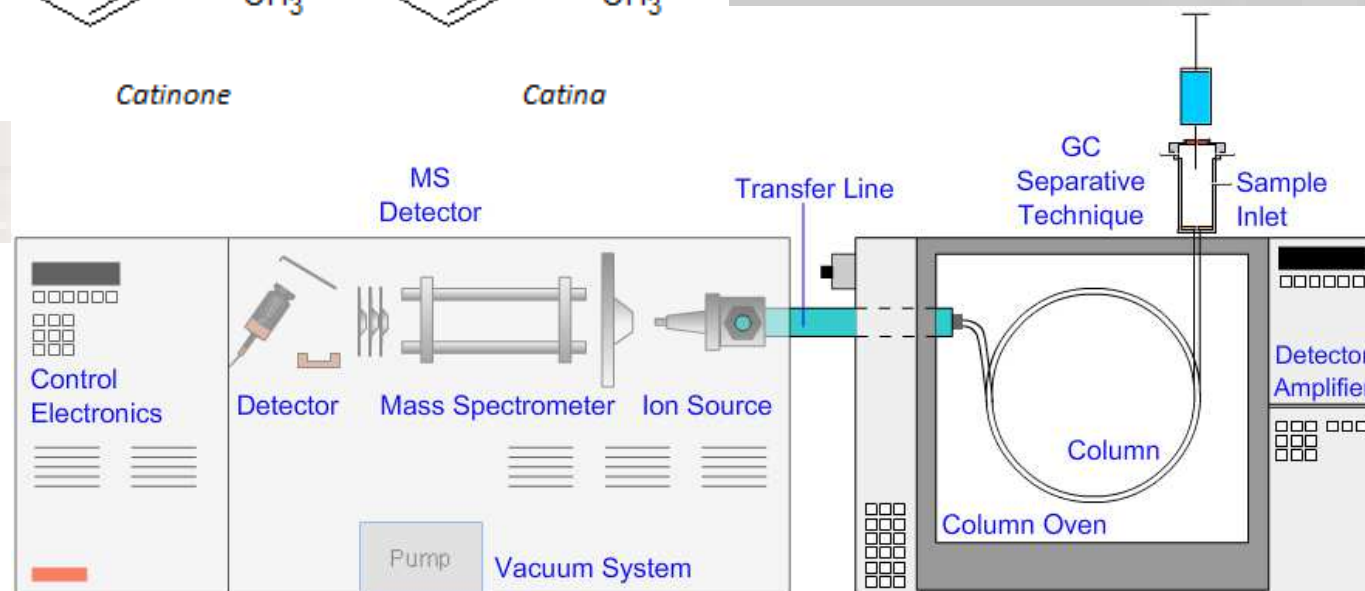
Catinone



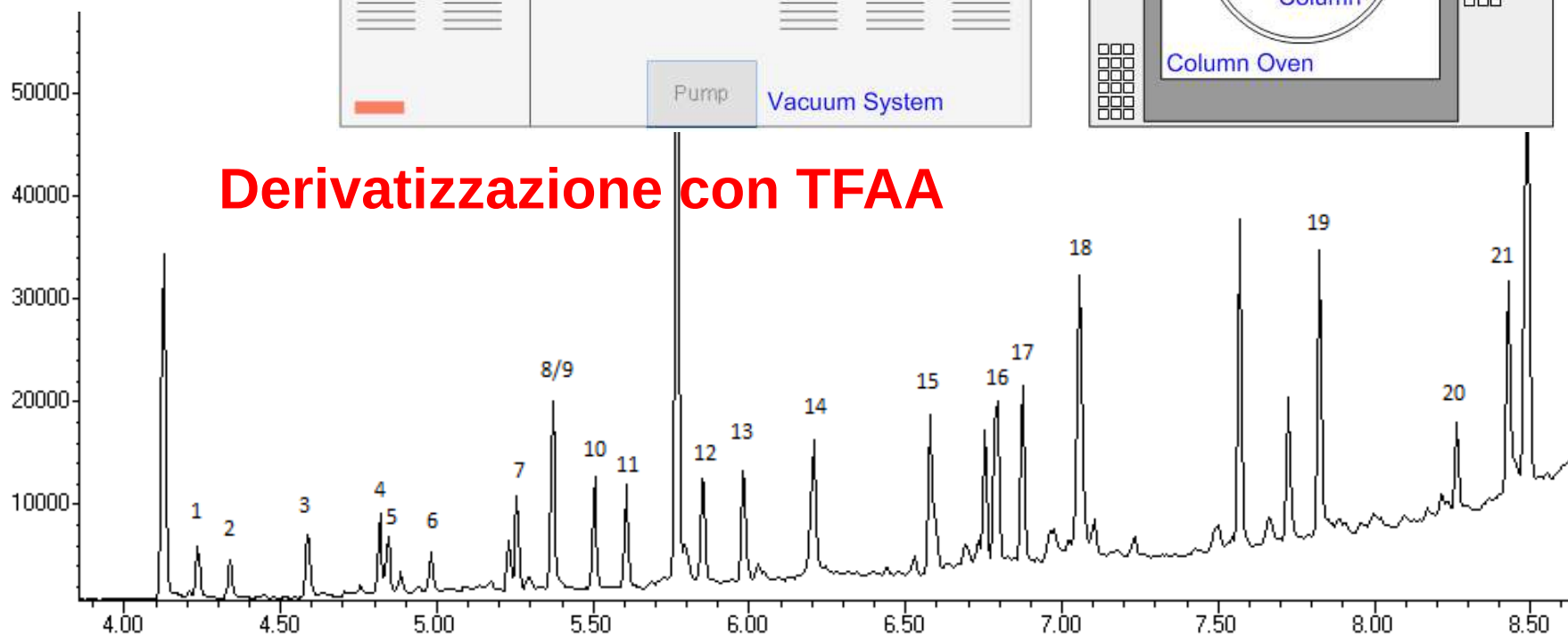
Catina

**Somiglianza  
strutturale**

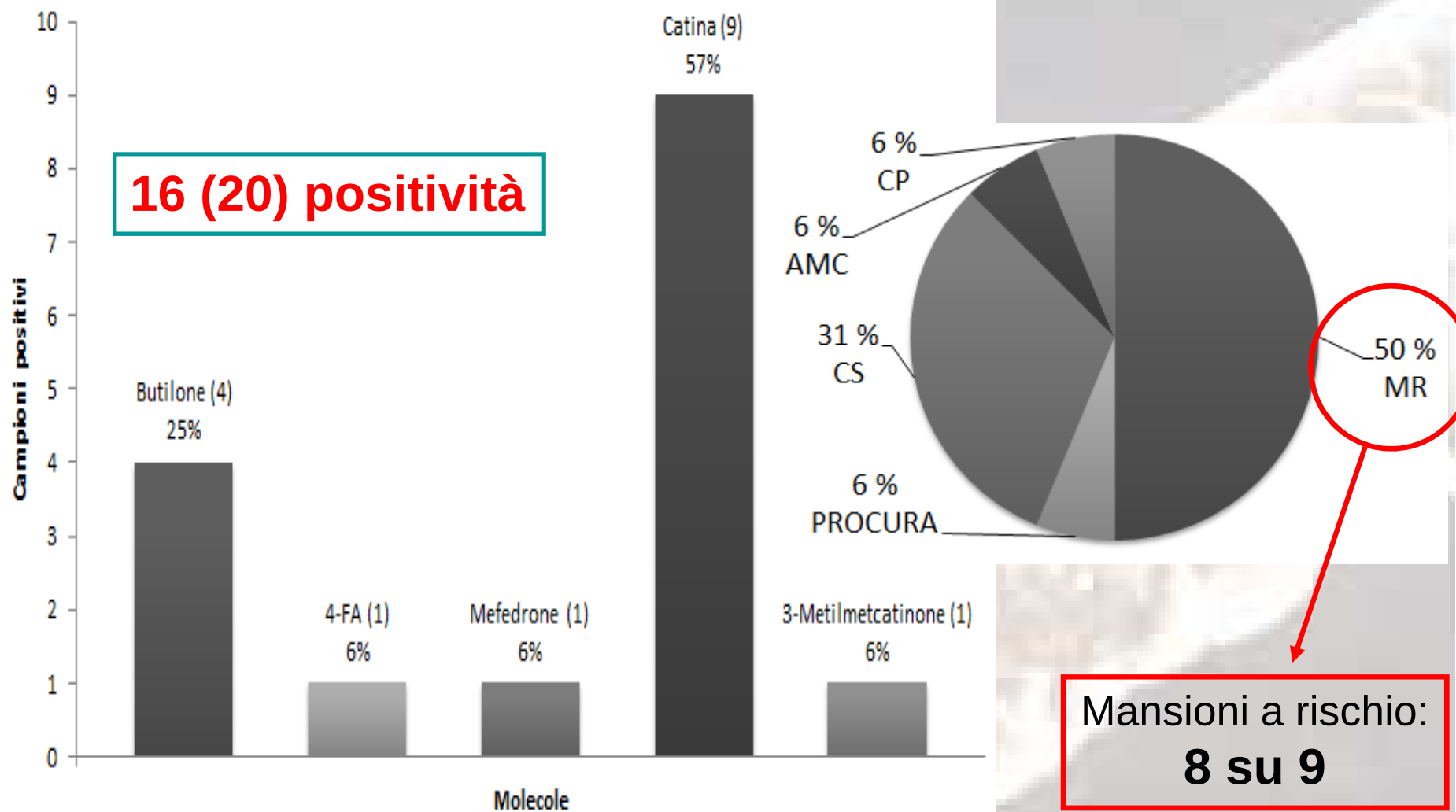
Strumento:  
**GC-MS**



**Derivatizzazione con TFAA**

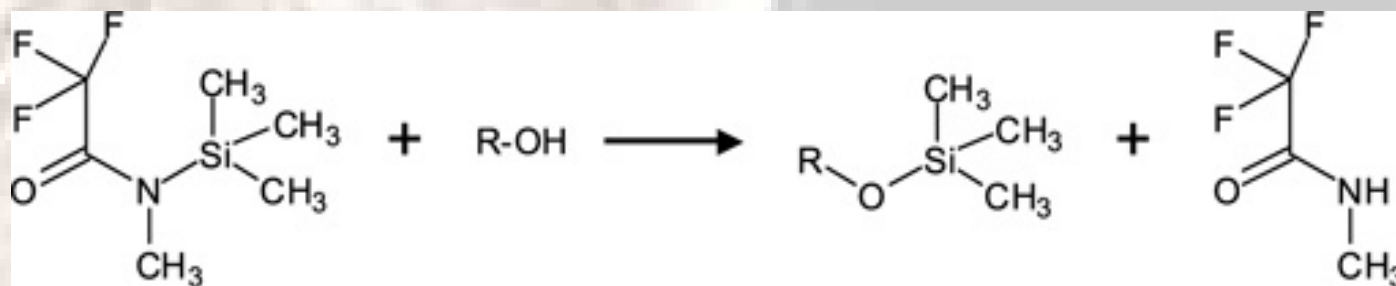


45 soggetti (39 maschi e 6 femmine – età media 27 anni (15÷47))  
18 controlli su strada, 11 commissioni patenti, 9 mansioni a rischio

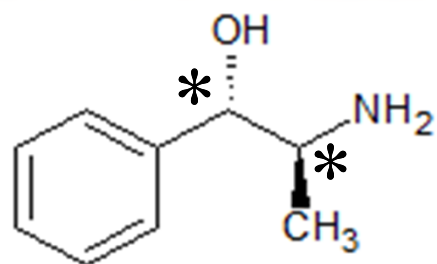


# Analisi di CONFERMA – Metodo MSTFA

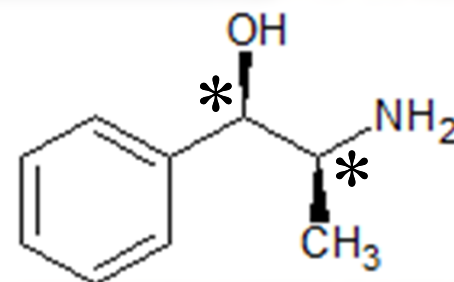
**Derivatizzante: N-metil-N-(trimetilsilil) trifluoroacetamide**



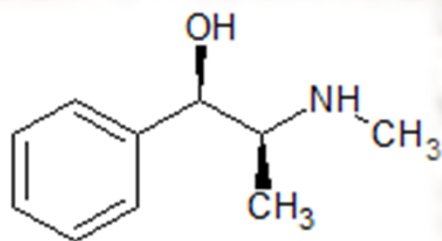
*Analiti:*



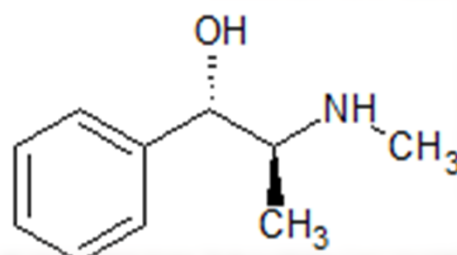
**Nor-pseudoefedrina  
(CATINA)**



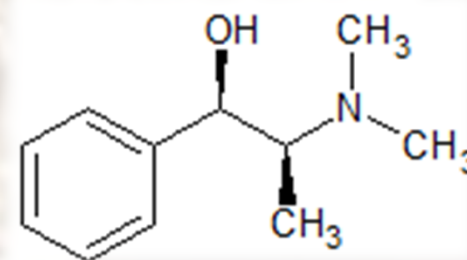
**Nor-efedrina  
(FENILPROPANOLAMMINA)**



**Efedrina**



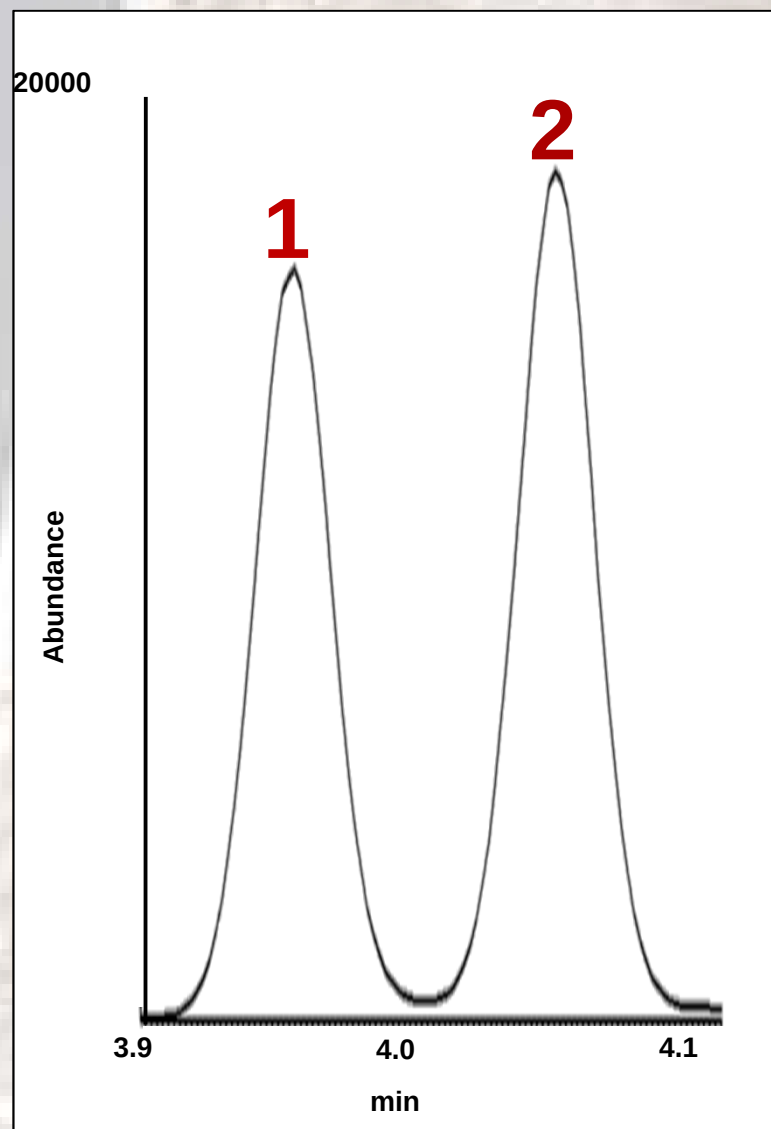
**Pseudoefedrina**



**Metilefedrina**



# Analisi di CONFERMA – Metodo MSTFA



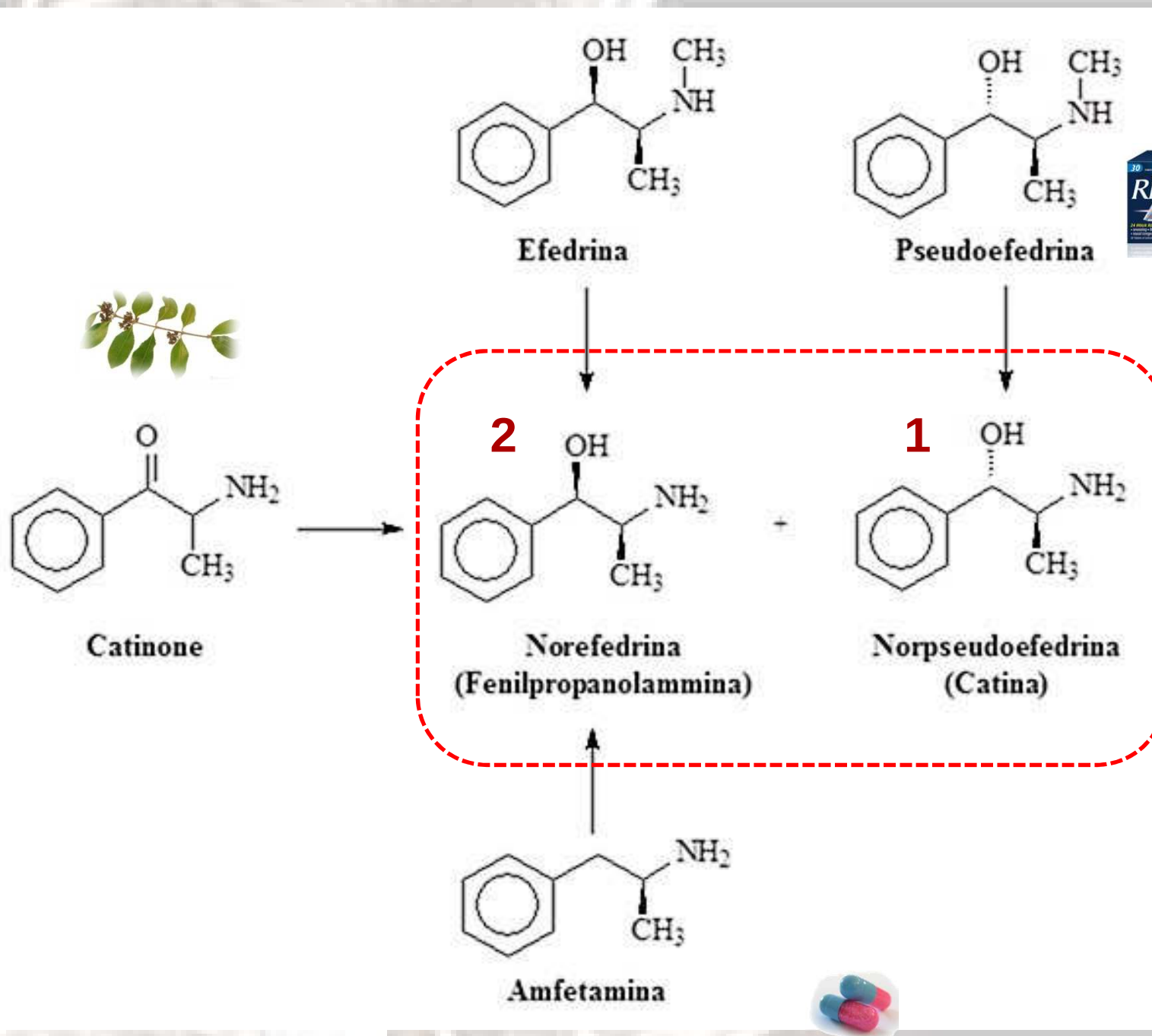
## Fenilpropanolamina

(2)

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

## Catina (1)

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



# CATINONI SINTETICI

## RISULTATI



**45 urine samples  
positive for AMPs**

**19 CONFIRMED**



| Sample | Screening AMPs (ng/mL) | Confirmation result (µg/mL)                              | Other Findings             | Declared Pharmaceuticals |
|--------|------------------------|----------------------------------------------------------|----------------------------|--------------------------|
| 1      | 695                    | Cathine (2.37)                                           | Pseudoephedrine            | Actigrip                 |
| 2      | >2000                  | Phenylpropanolamine (0.08)                               | Amphetamine, THC           | n/a                      |
| 3      | 727                    | Cathine (3.43)                                           | Pseudoephedrine            | Reactine                 |
| 4      | 615                    | Cathine (1.60)                                           | Pseudoephedrine            | Reactine                 |
| 5      | 1248                   | Cathine (5.21)                                           | Pseudoephedrine            | Reactine                 |
| 6      | 828                    | Butylone (1.78)                                          | MDMA, THC                  | n/a                      |
| 7      | >2000                  | Butylone (0.76)                                          | MDMA                       | n/a                      |
| 8      | n/a                    | Butylone (8.39)                                          | MDA, MDMA                  | n/a                      |
| 9      | n/a                    | Butylone (5.51)                                          | MDA, MDMA                  | n/a                      |
| 10     | >2000                  | Phenylpropanolamine (0.20)                               | MDA, MDMA, Opiates, BZE    | n/a                      |
| 11     | >2000                  | Phenylpropanolamine (0.41)<br>4-Fluoroamphetamine (0.85) | Amphetamine, THC           | n/a                      |
| 12     | >2000                  | Phenylpropanolamine (0.11)                               | Amphetamine, Ketamine, BZE | n/a                      |
| 13     | 681                    | Cathine (1.12)                                           | Pseudoephedrine            | n/a                      |
| 14     | 747                    | Mephedrone (80.5)                                        | BZE                        | n/a                      |
| 15     | n/a                    | Cathine (4.96)                                           | Pseudoephedrine            | n/a                      |
| 16     | 507                    | Cathine (0.81)                                           | Pseudoephedrine            | Antihistaminic           |
| 17     | 1561                   | Cathine (3.68)                                           | Pseudoephedrine            | Antihistaminic           |
| 18     | 634                    | Cathine (3.68)                                           | Pseudoephedrine            | Reactine                 |
| 19     | 981                    | 3-Methylmethcathinone (42.7)                             | THC                        | n/a                      |

# CATINONI SINTETICI

## RISULTATI



Butylone → n = 4  
 Mephedrone → n = 1  
 3-MMC → n = 1  
 4-FA → n = 1



| Sample | Screening AMPs (ng/mL) | Confirmation result (µg/mL)                              | Other Findings             | Declared Pharmaceuticals |
|--------|------------------------|----------------------------------------------------------|----------------------------|--------------------------|
| 1      | 695                    | Cathine (2.37)                                           | Pseudoephedrine            | Actigrip                 |
| 2      | >2000                  | Phenylpropanolamine (0.08)                               | Amphetamine, THC           | n/a                      |
| 3      | 727                    | Cathine (3.43)                                           | Pseudoephedrine            | Reactine                 |
| 4      | 615                    | Cathine (1.60)                                           | Pseudoephedrine            | Reactine                 |
| 5      | 1248                   | Cathine (5.21)                                           | Pseudoephedrine            | Reactine                 |
| 6      | 828                    | Butylone (1.78)                                          | MDMA, THC                  | n/a                      |
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| 13     | 681                    | Cathine (1.12)                                           | Pseudoephedrine            | n/a                      |
| 14     | 747                    | Mephedrone (80.5)                                        | BZE                        | n/a                      |
| 15     | n/a                    | Cathine (4.96)                                           | Pseudoephedrine            | n/a                      |
| 16     | 507                    | Cathine (0.81)                                           | Pseudoephedrine            | Antihistaminic           |
| 17     | 1561                   | Cathine (3.68)                                           | Pseudoephedrine            | Antihistaminic           |
| 18     | 634                    | Cathine (3.68)                                           | Pseudoephedrine            | Reactine                 |
| 19     | 981                    | 3-Methylmethcathinone (42.7)                             | THC                        | n/a                      |

# CATINONI SINTETICI

## RISULTATI



Cathine → n = 9  
(ILLICIT)  
Phenylprop. → n = 4  
(LICIT)



| Sample | Screening AMPs (ng/mL) | Confirmation result (µg/mL)                              | Other Findings             | Declared Pharmaceuticals |
|--------|------------------------|----------------------------------------------------------|----------------------------|--------------------------|
| 1      | 695                    | Cathine (2.37)                                           | Pseudoephedrine            | Actigrip                 |
| 2      | >2000                  | Phenylpropanolamine (0.08)                               | Amphetamine, THC           | n/a                      |
| 3      | 727                    | Cathine (3.43)                                           | Pseudoephedrine            | Reactine                 |
| 4      | 615                    | Cathine (1.60)                                           | Pseudoephedrine            | Reactine                 |
| 5      | 1248                   | Cathine (5.21)                                           | Pseudoephedrine            | Reactine                 |
| 6      | 828                    | Butylone (1.78)                                          | MDMA, THC                  | n/a                      |
| 7      | >2000                  | Butylone (0.76)                                          | MDMA                       | n/a                      |
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| 19     | 981                    | 3-Methylmethcathinone (42.7)                             | THC                        | n/a                      |

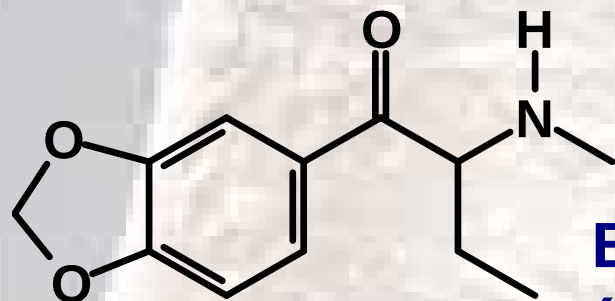


**Screening  
immunom.  
amfetamine**

**Conferme  
GC-MS**

**AMF**

**CAT**

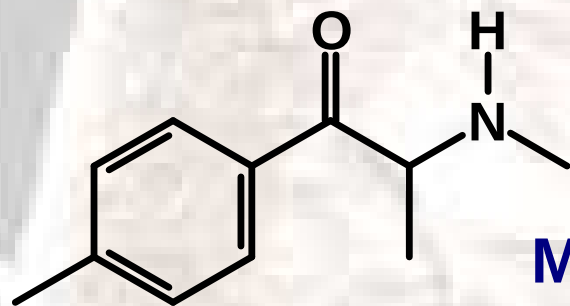


**Butilone  
(4 casi)**

**POS.**

**POS.  
indiretta**

**POS.**

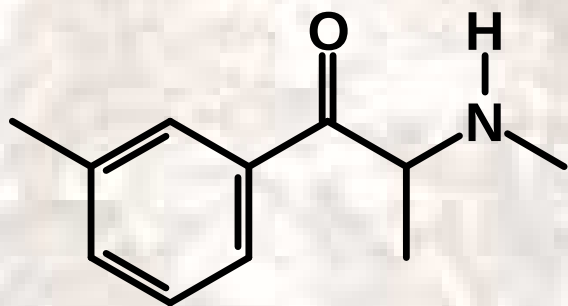


**Mefedrone  
(1 caso)**

**POS.**

**NEG.**

**POS.**

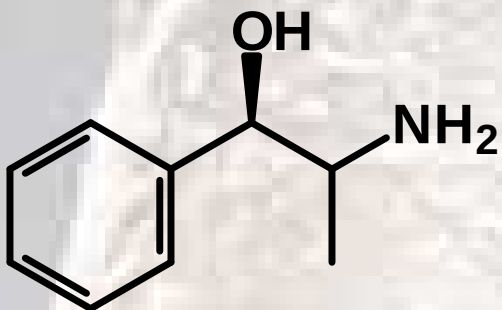


**3-Metilmetcatinone (1 caso)**

**POS.**

**NEG.**

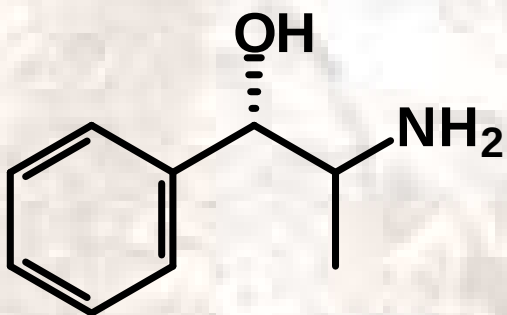
**POS.**



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

da metabolismo  
dell'**amfetamina**

**ILLECITA**

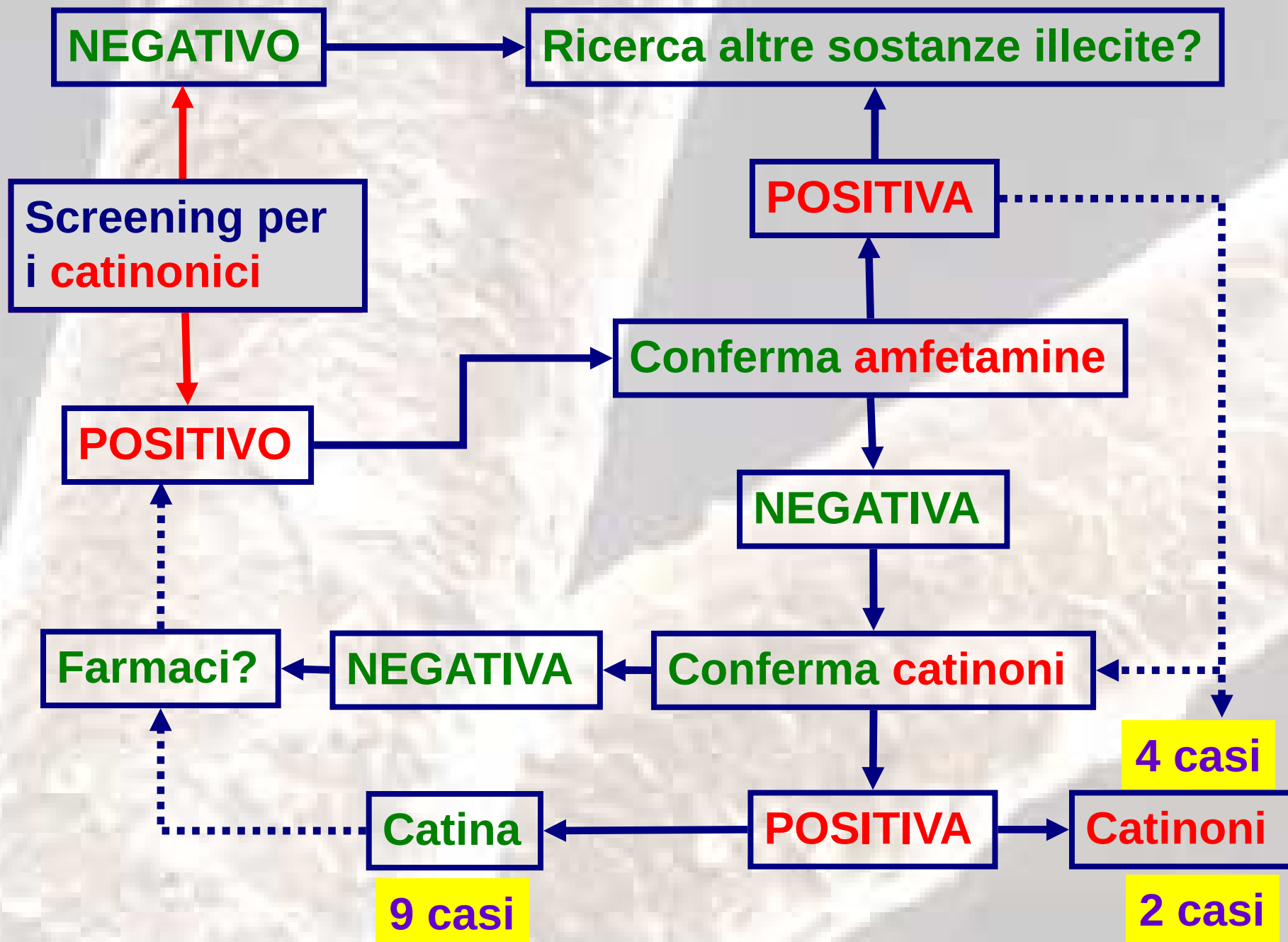


Catina (9 casi)  
(sostanza **illecita**)

**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 catinonici**

- **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 catinonici
- **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

HOME ABOUT CAREERS

About » Office Locations » Phoenix Division » Phoenix Division

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 highs

### NEWS



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

AIRFRANCE

Per scoprire le altre off

Clicca qui



NEWS

SPORT

ENTERTAINMENT

BUSINESS

LIFESTYLE

BREAKING NEWS

LOCAL

VICTORIA

NATIONAL

WORLD

LAW & ORDER

WEIRD

TE

## 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 to almost nothing as i was having to constantly increase my dosage due to the resistance.

14-12-2012, 19:00



EzekielCai  
Silver Member

Thread: Synthetic Cannabinoids UA detection time?

Re: Synthetic Cannabinoids

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

01-23-2013 03:11 PM

Unbalanced  
Opiophorum Member



[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](#)

(despite all of the evidence of ingestion and impairment, admissions, etc).

11-20-2012, 23:02

DaBig  
No Infide



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



< 2



# 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



**DETERMINAZIONE DIRETTA NEI CAPELLI  
DEI CANNABINOIDI ASSUNTI**



A. Salomone et al. Journal of Mass Spectrometry (2012) 47, 604-610

# PRIMO STUDIO

## Research Article

Journal of  
**MASS  
SPECTROMETRY**

Received: 3 January 2012

Revised: 7 March 2012

Accepted: 15 March 2012

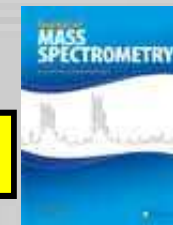
Published online in Wiley Online Library

(wileyonlinelibrary.com) DOI 10.1002/jms.2988

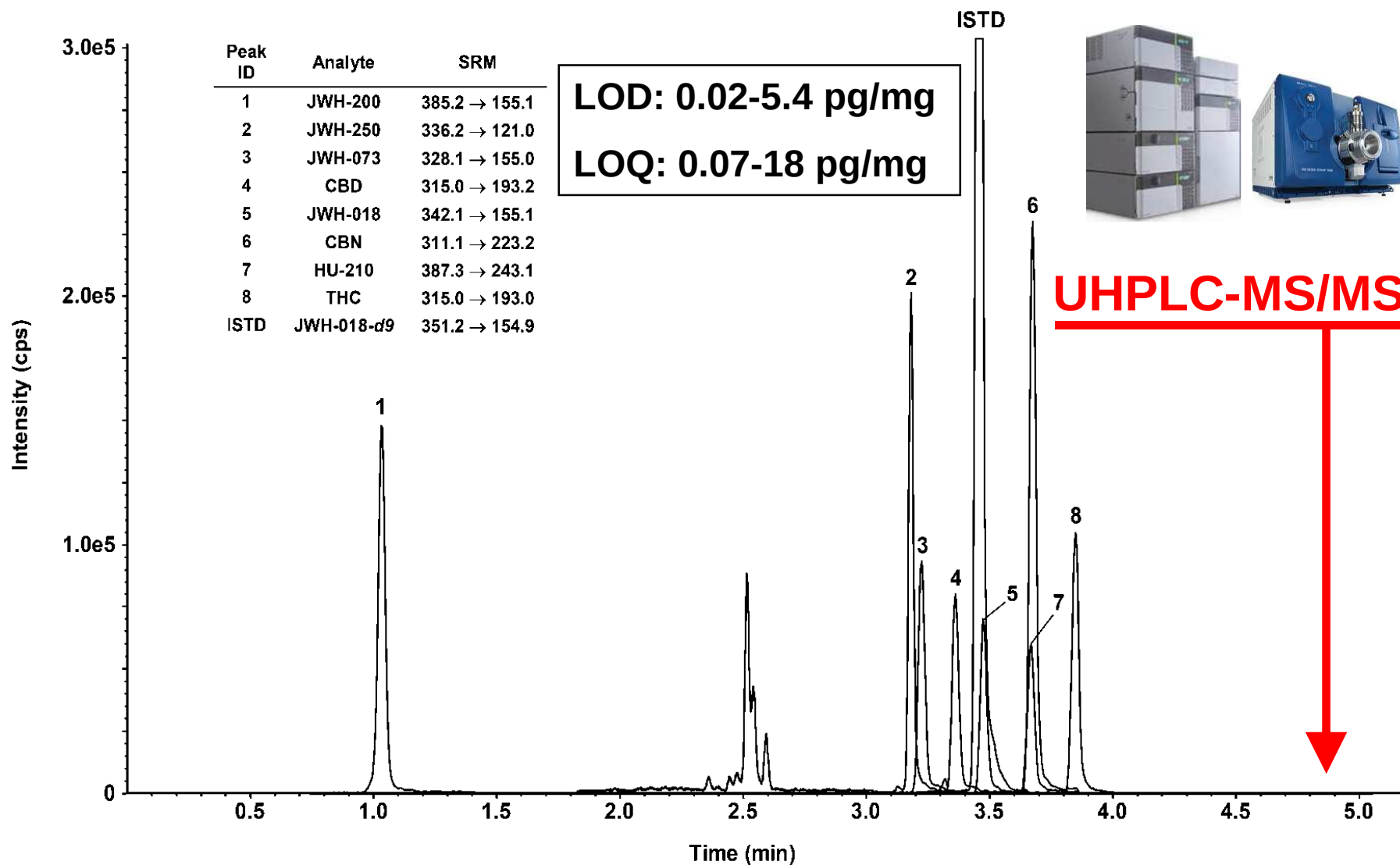
## **Simultaneous analysis of several synthetic cannabinoids, THC, CBD and CBN, in hair by ultra-high performance liquid chromatography tandem mass spectrometry. Method validation and application to real samples**

**A. Salomone,<sup>a\*</sup> E. Gerace,<sup>a</sup> F. D'Urso,<sup>a</sup> D. Di Corcia<sup>a</sup> and M. Vincenti<sup>a,b</sup>**





**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   |

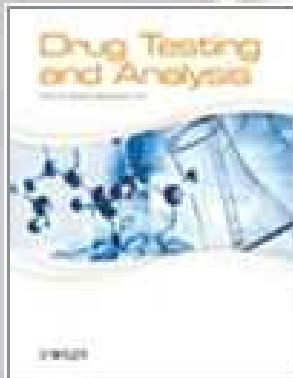
4# Length: 3.5 cm; JWH-250: 208.8 pg/mg

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

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

A. Salomone,<sup>a\*</sup> C. Luciano,<sup>a</sup> D. Di Corcia,<sup>a</sup> E. Gerace<sup>a</sup> and M. Vincenti<sup>a,b</sup>

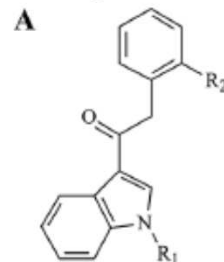


## A. Salomone et al. Drug Testing and Analysis (2014) 6, 126-134

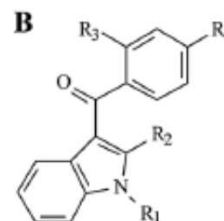


**23 analiti ricercati**  
**Periodo di investigazione**  
**(anno 2011)**

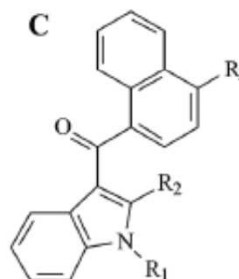
**Confrontare la diffusione dei  
cannabimimetici fra differenti  
popolazioni di consumatori di  
sostanze stupefacenti e alcol**



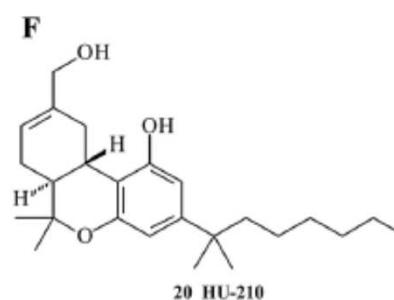
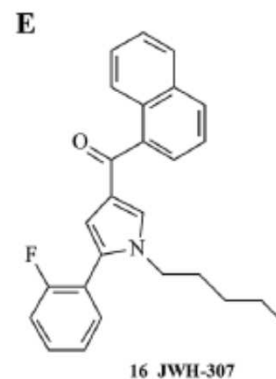
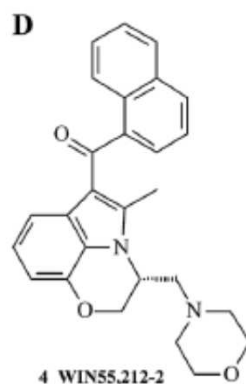
| Compound   | R <sub>1</sub>    | R <sub>2</sub> |
|------------|-------------------|----------------|
| 11 JWH-203 | pentyl            | chloro         |
| 9 JWH-250  | pentyl            | methoxy        |
| 12 JWH-251 | pentyl            | methyl         |
| 17 RCS-8   | 2-cyclohexylethyl | methoxy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



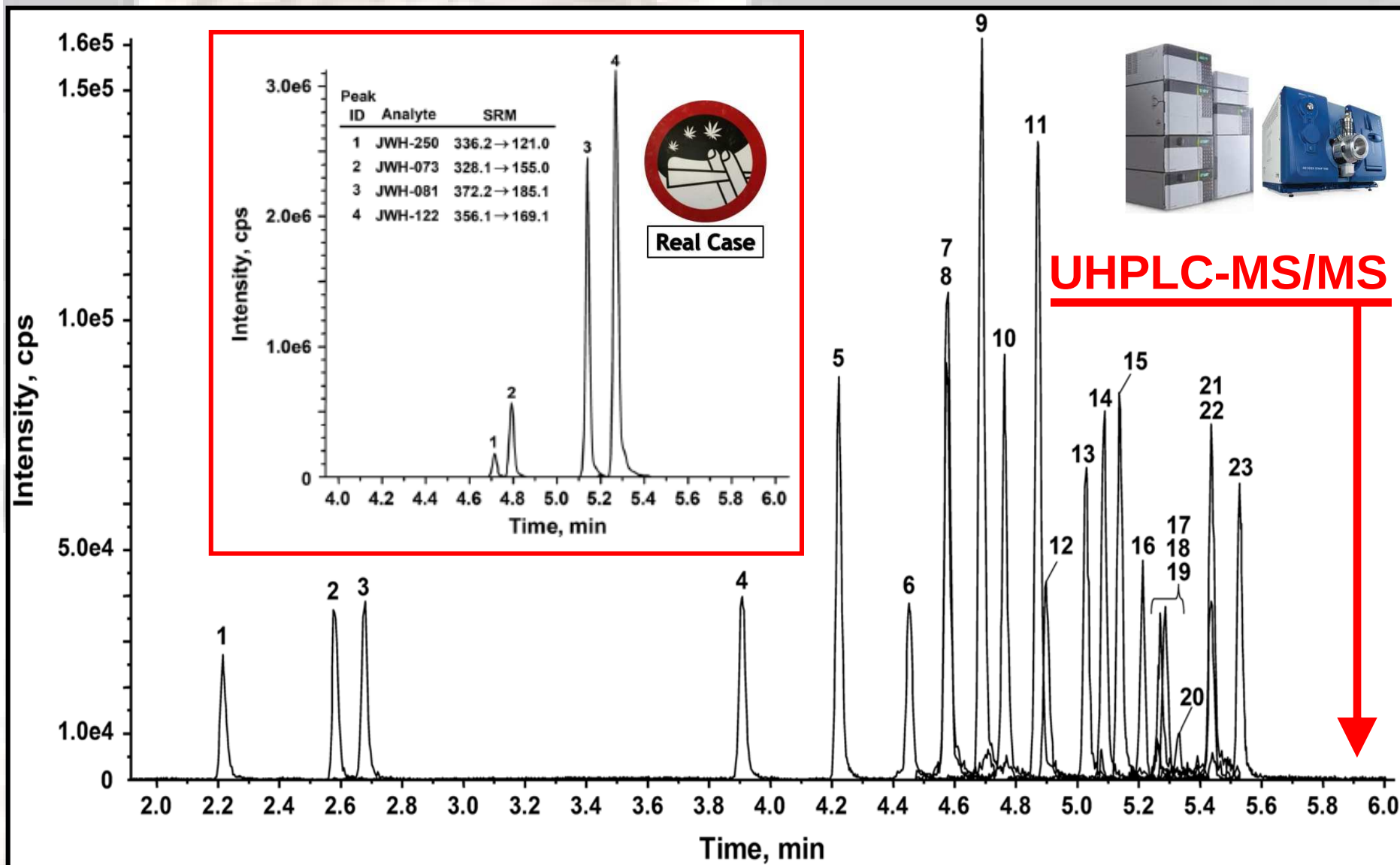
| Compound     | R <sub>1</sub>    | R <sub>2</sub> | R <sub>3</sub> | R <sub>4</sub> |
|--------------|-------------------|----------------|----------------|----------------|
| 5 AM-694     | 5-fluoropentyl    | H              | iodo           | H              |
| 8 RCS-4      | pentyl            |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



| Compound   | R <sub>1</sub>                | R <sub>2</sub> | R <sub>3</sub> |
|------------|-------------------------------|----------------|----------------|
| 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



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

➤ 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 <sup>a</sup>                                                  |
|---------------|-------|-----|--------|--------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|---------|------------------------------------------------------------------------------|
| 1             | A     | 24  | M      | head         | -               | 1.6             | -               | -               | -               | -               | -               | -       | THC: 0.05 ng/mg;<br>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;<br>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;<br>AMP: 3.05 ng/mg;<br>MDMA: 0.56 ng/mg                     |
| 8             | A     | 26  | M      | head         | -               | -               | -               | 8.0             | -               | -               | -               | -       | THC: 4.57 ng/mg;<br>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;<br>BZE: 0.22 ng/mg                                          |
| 14            | B     | 32  | F      | head         | -               | -               | -               | -               | 11.2            | -               | 3.8             | -       | COC: 0.60 ng/mg;<br>BZE: 0.09 ng/mg;<br>MOR: 0.08 ng/mg;<br>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;<br>MDMA: 0.89 ng/mg                        |

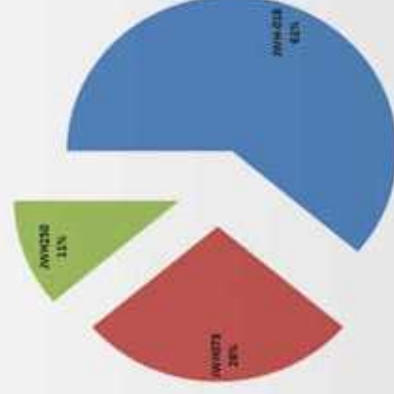
<sup>a</sup>THC:  $\Delta^9$ -tetrahydrocannabinol; MDMA: 3,4-methylenedioxymethamphetamine; AMP: Amphetamine; COC: Cocaine; MOR: Morphine; 6-AM: 6-acetylmorphine.

# DESIGNER DRUGS

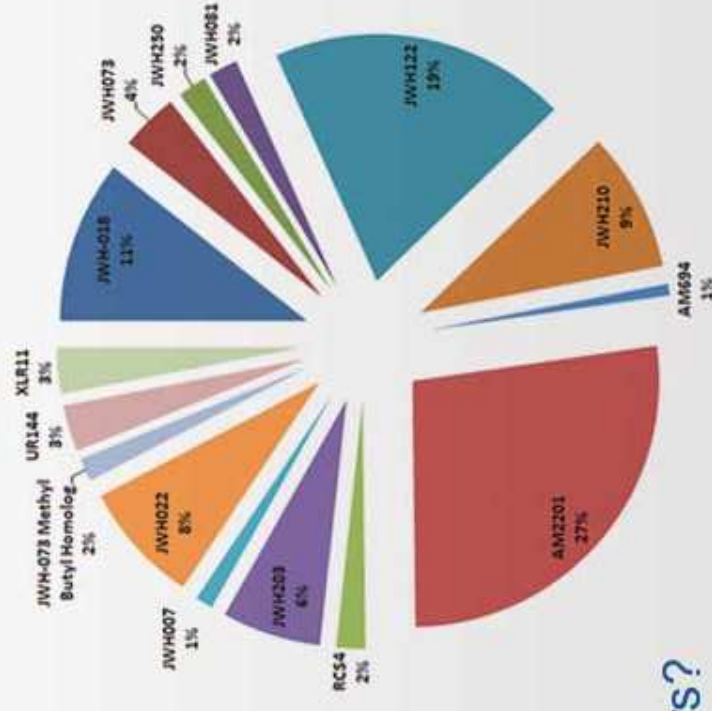
## THE TRENDS REPORT

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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](mailto: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.



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.

Sponsored By:



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



**...E IN ITALIA ?**



## **CANNABINOIDI SINTETICI**

### **ALLERTE 2009-2012**

#### **Analisi dei Capelli 2010-2012**

**JWH-018**

**JWH-073**

**JWH-250**

**JWH-081**

**JWH-122**

**JWH-210**

**JWH-019**

**AM-1220**

Oggetto: Aggiornamento Allerta grado 2 sui **cannabinoidi sintetici** – 3 nuovi casi di intossicazione acuta correlata all'assunzione di cannabinoidi sintetici a Trieste e individuazione, per la prima volta in Italia, dei cannabinoidi sintetici JWH-210 e JWH-019.

Oggetto: Aggiornamento Allerta grado 2 – Individuazione del cannabinoide sintetico **JWH-250** in herbal blend denominato "Forest Green" associato a 3 casi di intossicazione acuta ad Asti

Oggetto: Aggiornamento Allerta grado 2 sui **cannabinoidi sintetici** – "Registrati 4 nuovi casi di intossicazione acuta correlata all'assunzione di cannabinoidi sintetici e individuazione di nuovi prodotti contenenti cannabinoidi sintetici sul territorio italiano"

Oggetto: Informativa "Individuato per la prima volta in Italia il cannabinoide sintetico JWH-200 in una miscela di erbe denominata "Jamaican Spirit" sequestrata in uno smart shop nell'area di Trieste"

Oggetto: Aggiornamento Allerta grado 2 sui **cannabinoidi sintetici** – 3 nuovi casi di intossicazione acuta correlata all'assunzione di cannabinoidi sintetici a Trieste; individuazione di nuove miscele di erbe contenenti cannabinoidi sintetici e di JWH-018 in polvere

# CANNABINOIDI SINTETICI



## Analisi dei Capelli 2010-2012

JWH-018

JWH-073

JWH-250

JWH-081

JWH-122

JWH-210

JWH-019

AM-1220

## INTOSSICAZIONI ACUTE ALLERTE 2009-2012



- nJoy (JWH-018)
- Spice Artic Synergy (JWH-018; JWH-073)
- Bonzai (JWH-018; JWH-081; JWH-122)
- Bonzai Summer Boost (JWH-122)
- Forest Green (JWH-122; JWH-250)
- Jungle Mystic Incense (JWH-122)
- Orange Alesya News (JWH-122)
- Atomic Bomb (JWH-018)
- Non noto (JWH-018; JWH-122)
- JWH-073+JWH-018+JWH-122
- Orange Oxana (Riferito)
- Genie (Non noto)

Fonte: Sistema Nazionale Allerta Precoce



# Studi successivi



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



| 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            |

✓ Studi in condizioni controllate

**INTERPRETAZIONE  
DEI RISULTATI ?**

# CANNABINOIDI SINTETICI

STUDIO n° 3, anno 2014 (in corso)



**Nuovo metodo UHPLC-MS/MS integrato con 10 metaboliti**

**JWH-018**

*JWH 018 4-hydroxypentyl metabolite-D5*

**JWH-073**

*JWH 018 N-(5-hydroxypentyl) metabolite*

**JWH-250**

*JWH 018 N-pentanoic acid metabolite*

**JWH-081**

*JWH 019 5-hydroxyindole metabolite*

**JWH-122**

*JWH 073 N-(4-hydroxybutyl) metabolite*

**JWH-210**

*JWH 073 N-butanoic acid metabolite*

**JWH-019**

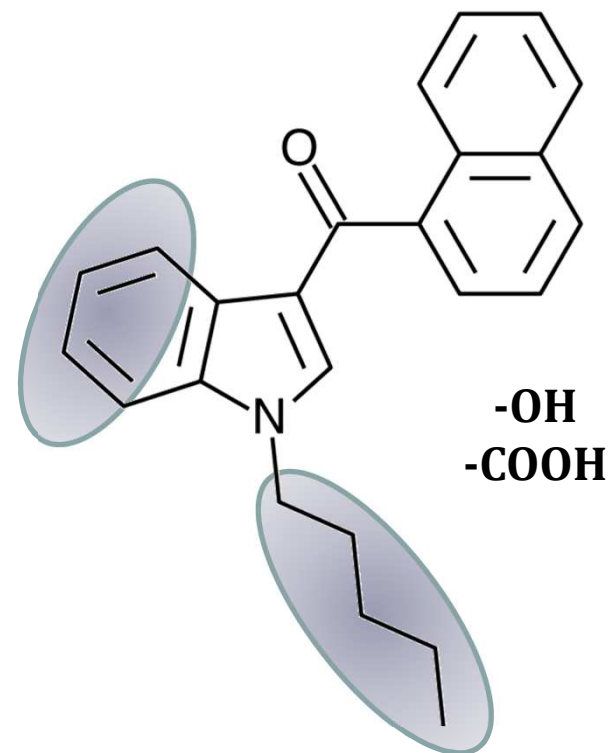
*JWH 081 N-(5-hydroxypentyl) metabolite*

*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**

**STUDIO 2 → 15 capelli positivi → RIVERIFICATI CON IL NUOVO METODO**



# CANNABINOIDI SINTETICI



**STUDIO n° 3, anno 2014 (in corso)**

| Positive case | 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) | METABOLITES (pg/mg) |
|---------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|---------------------|
| 1             | -               | 1.6             | -               | -               | -               | -               | -               | -               | No                  |
| 2             | 17.3            | 7.6             | 83.4            | 12.3            | -               | -               | -               | -               | No                  |
| 3             | -               | 1.9             | 26.9            | -               | -               | -               | -               | -               | No                  |
| 4             | -               | 1.8             | -               | -               | -               | -               | -               | -               | No                  |
| 5             | -               | 5.2             | 5.8             | -               | 11.7            | -               | -               | -               | No                  |
| 6             | 10.4            | 2.0             | 6.0             | -               | 2784            | 2.3             | -               | 1.3             | JWH-122 (2.57)      |
| 7             | -               | 1.8             | -               | -               | -               | -               | -               | -               | No                  |
| 8             | -               | -               | -               | 8.0             | -               | -               | -               | -               | No                  |
| 9             | -               | 50.5            | 6.4             | 194             | 713             | -               | -               | -               | No                  |
| 10            | -               | 1.6             | -               | -               | 756             | -               | -               | -               | JWH-122 (0.23)      |
| 11            | 3.1             | 1.6             | -               | 81.4            | -               | 5.1             | -               | -               | No                  |
| 12            | -               | 9.0             | 4.8             | -               | 40.9            | -               | -               | -               | No                  |
| 13            | -               | -               | -               | -               | 7.4             | -               | -               | -               | No                  |
| 14            | -               | -               | -               | -               | 11.2            | -               | 3.8             | -               | No                  |
| 15            | -               | -               | -               | 47.8            | 15.8            | -               | 4.1             | -               | No                  |



**Nuovo Metodo**



**153 camp. capelli (2012-2013)**

- Consumatori di THC
- Età (18-34 anni)

# CANNABINOIDI SINTETICI

## STUDIO n° 3, Risultati preliminari



| Positive case | 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) |
|---------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|----------------|---------------------|
| 1             | -               | -               | 4.92            | -               | -               | -               | -              | No                  |
| 2             | 2.27            | <LOQ            | -               | -               | -               | -               | -              | No                  |
| 3             | -               | -               | -               | <LOQ            | 2.79            | <LOQ            | -              | No                  |
| 4             | 2.55            | 287             | 32.8            | 22.4            | 61.6            | -               | 0.78           | No                  |
| 5             | 2.15            | 1.89            | < LOQ           | 3.16            | -               | -               | -              | No                  |

**3.3%**  
  
**Positive**

## DIMINUZIONE DELL'INCIDENZA DEI POSITIVI

- Cannabinoidi sintetici **ILLEGALI** (Tab. 1 DPR 309/90, dal 2010)
- Rapido ricambio delle sostanze sul mercato informatico



05/12/2013  
Prot. EWS 278/13

Oggetto: Aggiornamento Allerta grado 3 – “Registrati 2 nuovi casi di intossicazione acuta da cannabinoidi sintetici ed identificati, per la prima volta in Italia, i cannabinoidi sintetici AKB-48F, 5FUR-144, AKB48, 5F-PB22, STS-135 e MAM-2201”

A novembre 2012 la Direzione Centrale Analisi Merceologica e Laboratori Chimici – Ufficio Metodologie e tecnologie chimiche e garanzia della qualità dei laboratori – Agenzia delle Dogane Roma, ha segnalato l'identificazione del cannabinoide sintetico XLR-11 (5-fluoro-UR144).

Fonte: Sistema Nazionale Allerta Precoce

# CONCLUSIONI

- ✓ La diffusione reale delle NSP rimane incerta
- ✓ L'analisi del capello è un utile strumento conoscitivo sul singolo e sulla popolazione
- ✓ E' necessario aggiornare continuamente i metodi analitici per le nuove sostanze
- !! I soggetti sottoposti periodicamente a controllo sono incentivati all'uso delle NSP

- ✓ Discriminazione fra uso cronico e occasionale
- ✓ Valutazione della possibile contaminazione

# CONCLUSIONI ?

