PRESIDENZA DEL CONSIGLIO DEI MINISTRI
Dipartimento Politiche Antidroga

National Early Warning System

New Drugs 2014

Scientific and technical update on New Psychoactive Substances

Rome, May 14-15 2014

Analytical problems and solutions: the Italian example

Teodora Macchia-ISS

Regione del Veneto - Azienda ULSS 20
Dipartimento delle Dipendenze

Istituto Superiore di Sanità
Dipartimento del Farmaco

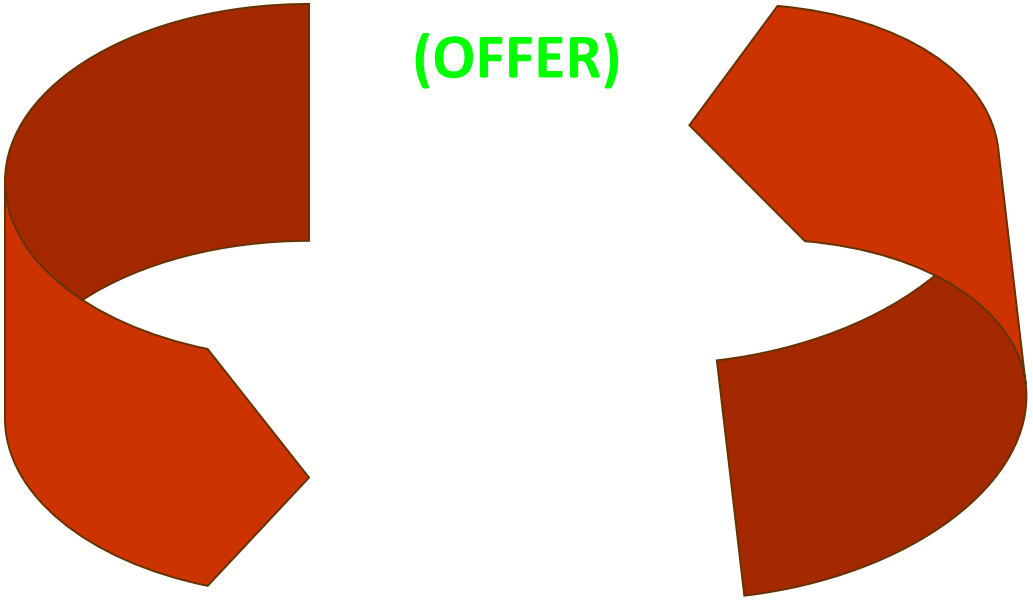
Fondazione "S. Maugeri" IRCCS
Centro Antiveleni Pavia

DPA

NATIONAL EARLY WARNING SYSTEM

AVAILABILITY

(OFFER)



USE

(DEMAND)

™

DPA

NATIONAL EARLY WARNING SYSTEM

- Increasing number of “drugs” (mainly synthetic substances)
- Lack of scientific literature, analytical methods and reference materials
- Screening methods are “unavailable”
- Molecules often very hard to identify in seizures and in biological fluids (shift from old to new drugs)
- Few formal pharmacokinetic and pharmacodynamic studies published in relation to NPS
- Chemical data in relation to NPS is very limited
- Inconsistency : content of products can change over time

TM

DPA

NATIONAL EARLY WARNING SYSTEM

ANALYTICAL

PROBLEMS

™

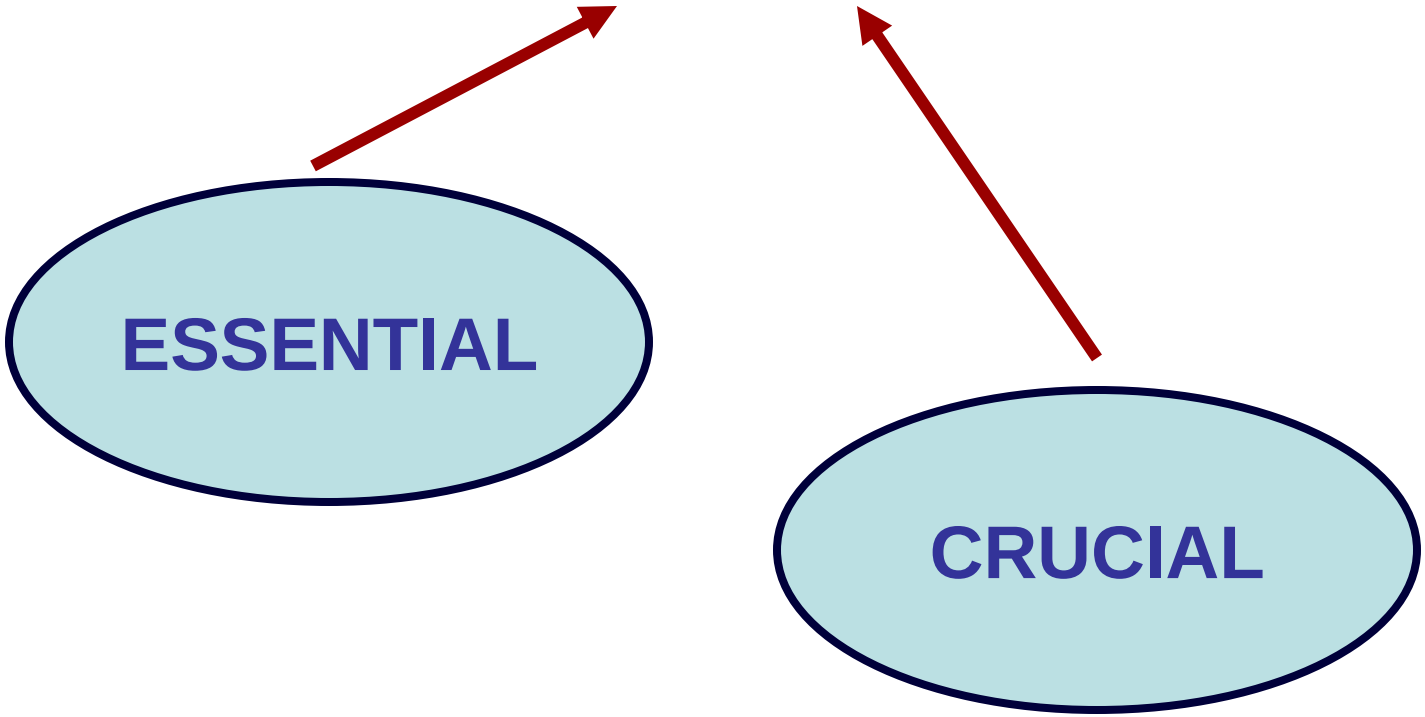
- The current techniques are unlikely to be effective In new drugs sure identification

- On the other hand, irrefutable evidence should be required to subsequent possible actions, measures, control

DPA

NATIONAL EARLY WARNING SYSTEM

ANALYTICAL IDENTIFICATION



™

DPA

NATIONAL EARLY WARNING SYSTEM

To bear laboratories in NPS recognition:

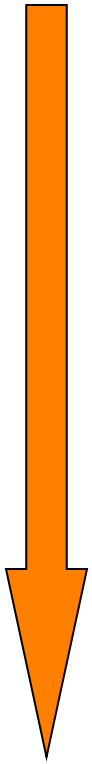
- Standards, reference materials sharing
- Scientific literature finding and sharing
- Timely circulating analytical data on characterized NPS
- Technical dedicated meeting
- New suitable analytical method development and sharing

DPA

NATIONAL EARLY WARNING SYSTEM

Analytical Standards supplied to the collaborative Laboratories ISS-DPA 2010

- JWH-018
- JWH-073
- JWH-200
- JWH-250



CP 47,497
4-FA
Mephedron
MDAI

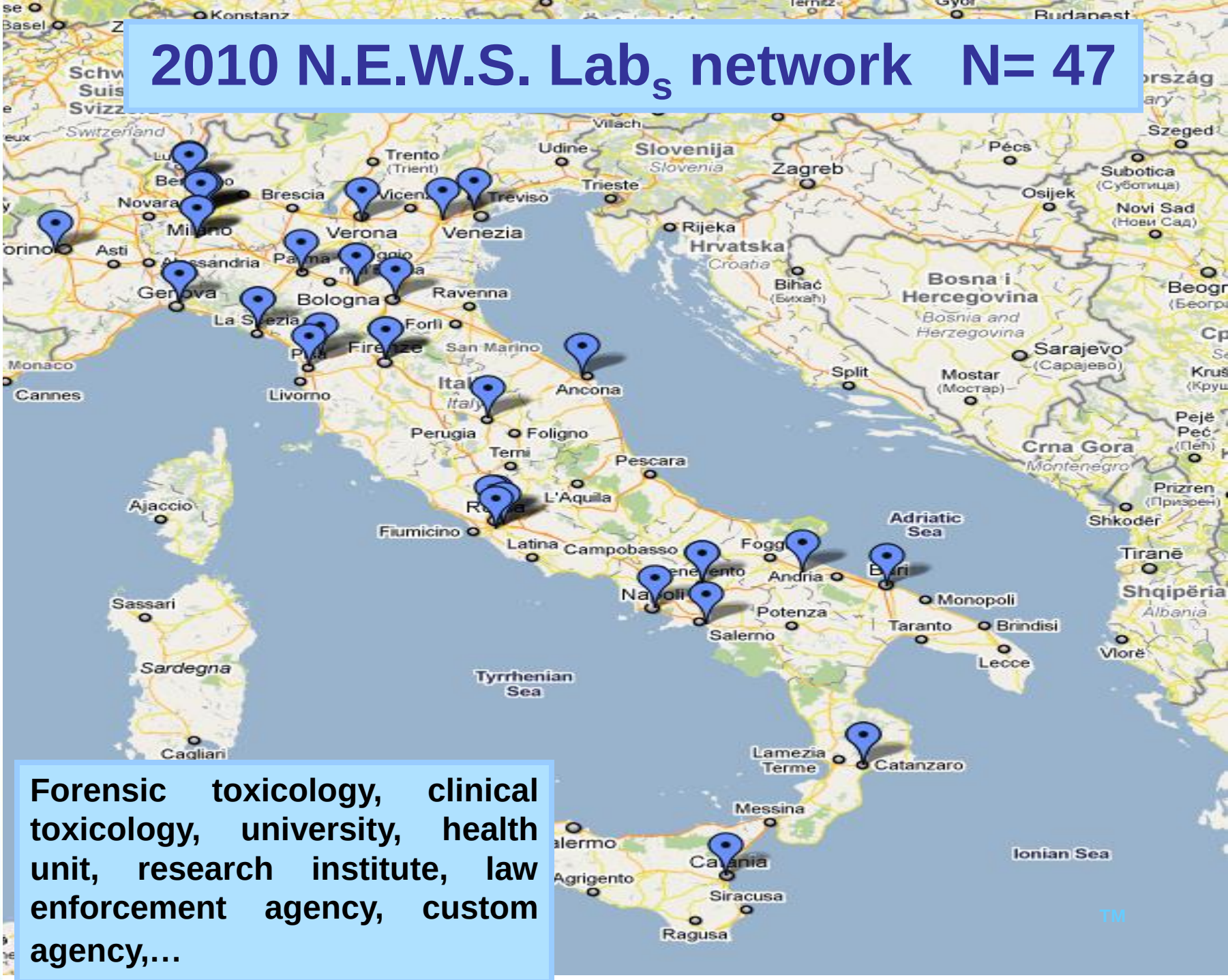
Result: a significant increase in reports (seizures, poisoning, controls) to the System.

™

DPA

NATIONAL EARLY WARNING SYSTEM

2010 N.E.W.S. Lab$_s$ network N= 47



Forensic toxicology, clinical toxicology, university, health unit, research institute, law enforcement agency, custom agency,…

DPA

NATIONAL EARLY WARNING SYSTEM

As result of Generic control, groups of substances have been scheduled

Labs have got to overcome new analytical troubles

More than 100 new molecules to be Identified, in some case quantified

Lack of reference materials

2012-2013: we have supplied collaborative Labs with 37 new synthetic cannabinoids and catinones

TM

37 NEW "DRUGS"

- **Analoghi del 3-(1-naftoil)indolo:**
  JWH-007, JWH-016, JWH-019, JWH-081, JWH-098, JWH-122, JWH-210, JWH-398 e AM-2201;
- **Analoghi del 3-fenilacetilindolo:**
  JWH-203, JWH-251, JWH-302, RCS-8, WIN 48,098;
- **Analoghi del 3-benzoilindolo:**
  AM-694, RCS-4, AM-2233;
- **Naftoilpirroli**
  JWH-147, JWH-307
- **Naftoilnaftaleni**
  CRA-13
- **Cicloesilfenoli**
  CP 47,497 C8-analogo
- **Analoghi del 2-amino-1-fenil-1-propanone:**
  Metcatinone,Metamfepramone, N-Etilcatinone, Metedrone (bk-PMMA) Flefedrone, 3,4-dimetilmetcatinone (3,4-DMMC), 4-metil-N-etilcatinone (4-MEC), Bufedrone, Pentedrone, Metilone (β-keto-MDMA), Etilone (β-keto-MDEA), Butilone (β-keto-MBDB) Pentilone (β-keto-MBDP), Metildiossipirovalerone (MDPV)
- **Naftil analoghi del pirovalerone**
  1-Nafirone, 2-nafirone

8 classes

DPA

NATIONAL EARLY WARNING SYSTEM

TM

DPA

NATIONAL EARLY WARNING SYSTEM

TM

DPA

NATIONAL EARLY WARNING SYSTEM

ISTITUTO SUPERIORE DI SANITA'

Viale Regina Elena 299

00161 Roma

- DIPARTIMENTO DEL FARMACO -

PROGETTO NEWS - ALERT

DPA - I.S.S. - ULSS 20 VR

ELENCO VIALS E SOSTANZE

Posizione Viala	Sostanza	Concentrazione mg/mL	Solvente / Ricostituente	Codice REF	Lotto LOT	Data di Preparazione	Note
1	Methcathinone HCL	0,1	Metanolo	LGCFOR2115.01			ND
2	Dimethylcathinone HCL	0,1	Metanolo	LGCFOR1275.30	151212	15.12.12	
3	Ethcathinone HCL	0,1	Metanolo	CAY-11241	151212	15.12.12	
4	Methedrone HCL	0,1	Metanolo	CAY-10529	151212	15.12.12	
5	4-Fluoromethcathinone HCL	0,1	Metanolo	CAY-10859	151212	15.12.12	
6	3,4-Dimethylmethcathinone HCL	0,1	Metanolo	CAY-9001098	151212	15.12.12	
7	4-Methylethcathinone HCL	0,1	Metanolo	CAY-9001069	151212	15.12.12	
8	Buphedrone Hydrochloride	0,1	Metanolo	CAY-11283	151212	15.12.12	
9	β - Pentedrone	0,1	Metanolo	LGCFOR1275.63	151212	15.12.12	
10	Methylone HCL	0,1	Metanolo	LGCFOR1275.01			ND
11	Ethylone HCL	0,1	Metanolo	LGCFOR1275.02	151212	15.12.12	
12	Butylone HCL	0,1	Metanolo	CAY-10393	151212	15.12.12	
13	Pentylone HCL	0,1	Metanolo	CAY-9000746	151212	15.12.12	
14	1-Naphyrone HCL	0,1	Metanolo	LGCFOR1275.35	151212	15.12.12	
15	Naphyrone HCL	0,1	Metanolo	LGCFOR1275.06			ND
16	JWH-007	0,1	Metanolo	CAY-10266	151212	15.12.12	
17	JWH-016	0,1	Metanolo	CAY-10849	151212	15.12.12	
18	JWH-019	0,1	Acetonitrile	CAY-13633	151212	15.12.12	
19	JWH-081	0,1	Acetonitrile	CAY-10579	151212	15.12.12	
20	JWH-098	0,1	Acetonitrile	CAY-10680	151212	15.12.12	
21	JWH-122	0,1	Acetonitrile	LGCFOR1275.66			ND
22	JWH-147	0,1	Metanolo	CAY-10826	151212	15.12.12	
23	JWH-203	0,1	Acetonitrile	LGCFOR1275.70			ND
24	JWH-210	0,1	Metil Acetato	CAY-10644			ND ?
25	JWH-251	0,1	Metil Acetato	CAY-10578			ND ?
26	JWH-302	0,1	Metanolo	CAY-10722	151212	15.12.12	
27	JWH-307	0,1	Acetonitrile	CAY-10797	151212	15.12.12	
28	JWH-398	0,1	Metanolo	CAY-13636	151212	15.12.12	
29	AM-694	0,1	Acetonitrile	LGCFOR1275.17			ND
30	AM 2201	0,1	Acetonitrile	CAY-10707	151212	15.12.12	
31	RCS-4	0,1	Acetonitrile	CAY-10645	151212	15.12.12	
32	RCS-8	0,1	Metanolo	CAY-10636	151212	15.12.12	
33	CB-13	0,1	Metanolo	CAY-10010398	151212	15.12.12	
34	(±) CP 47,497-C8-homolog	0,1	Metanolo	CAY-13216	151212	15.12.12	
35	Pravadoline (WIN 48,098)	0,1	Acetonitrile	CAY-10006973	151212	15.12.12	
36	AM-2233	0,1	Metanolo	CAY-11008	151212	15.12.12	
37	(MDPV) HCL	0,1	Metanolo	CERM-146			ND

NOTE / LEGENDA

Contenuto di ogni vial: 1 mL

Informazioni riportate su ogni vial: nome sostanza - codice REF - numero di lotto LOT

ND: disponibilità differita, da verificare con la "Data di Preparazione".

GI: già consegnato.

Limitazione della temperatura.

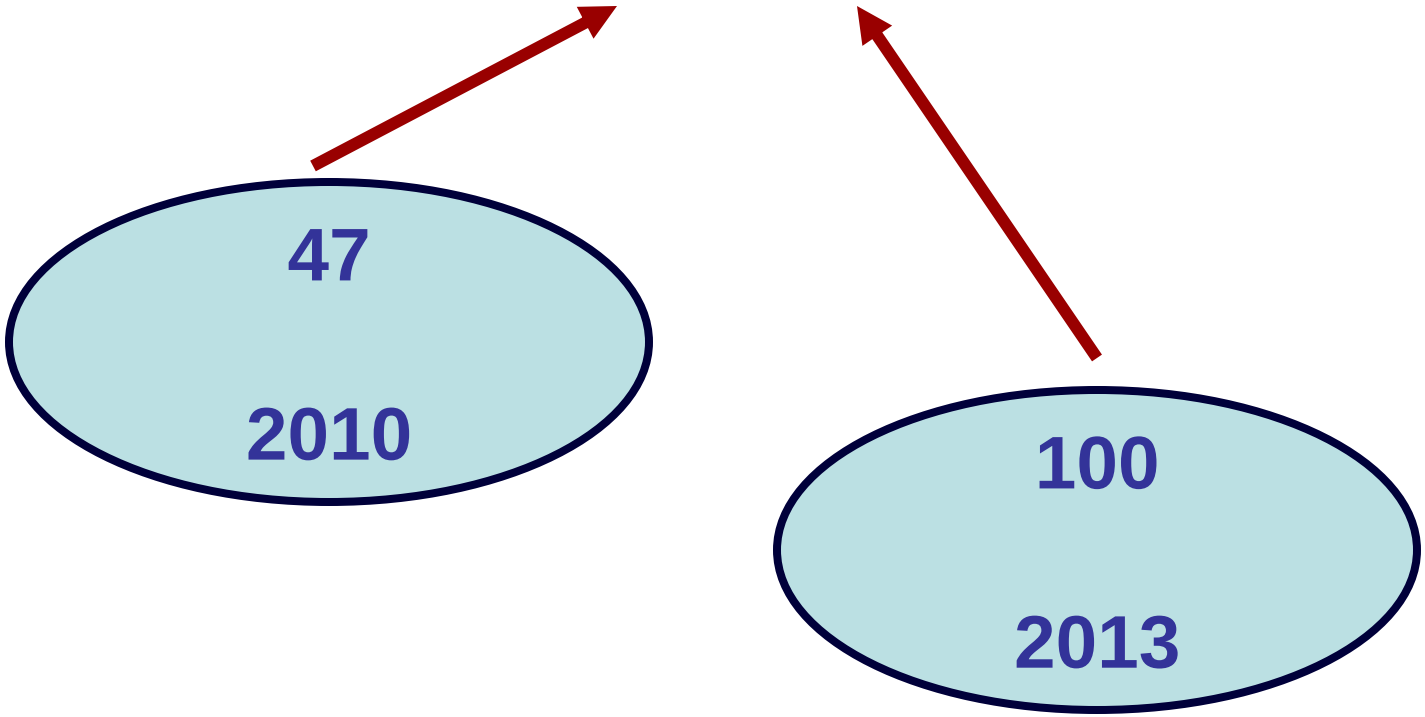
Conservazione al riparo dalla luce

TM

DPA

NATIONAL EARLY WARNING SYSTEM

N.E.W.S. Labs network



TM

DPA

NATIONAL EARLY WARNING SYSTEM

DPA

NATIONAL EARLY WARNING SYSTEM

SYNTHETIC CATHINONES

3-Fluoromethcathinone

(3-FMC)

Butylone

(bk-MBDB)

3,4-dimethyl-methcathinone

(3,4-DMMC)

3,4-Methylenedioxypyrovalerone

(MDPV)

Mephedrone

DPA

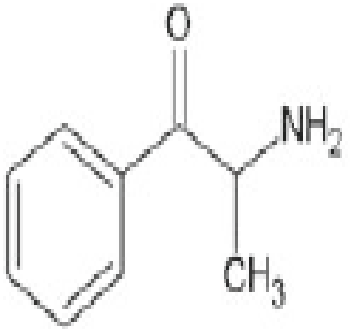
NATIONAL EARLY WARNING SYSTEM

Synthetic cathinones recorded by the NEWS

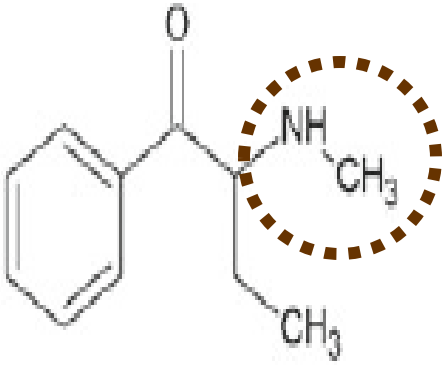
4-MMC	Mefedrone
4-MEC	4-Metiletcatinone
MDPV	3,4-Metilendiossipirovalerone
3-FMC	3-Fluorometcatinone
3-MMC	3-Metilmetcatinone
EC	Etilcatinone
α-PVP	α-Pirrolidinovalerofenone
4-FMC	Flefedrone
O-2482	Nafirone
4-MBC	Benzedrone
3,4-DMMC	3,4-Dimetil-metcatinone
4-BMC	Brefedrone
4-EMC	4-Etilmetcatinone
3-FiMC	3-Fluoro-isometcatinone
4-FC	4-Fluorocatinone
…….	……..
…….	……..

TM

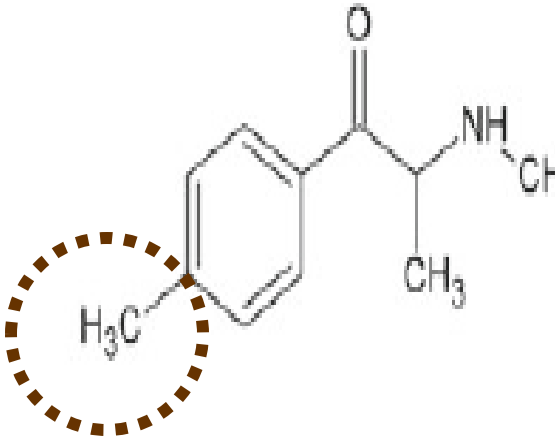
> 40



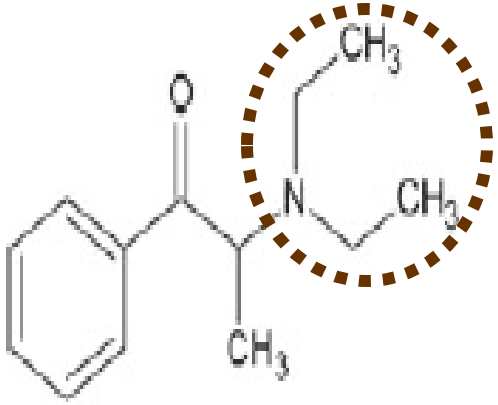
Cathinone



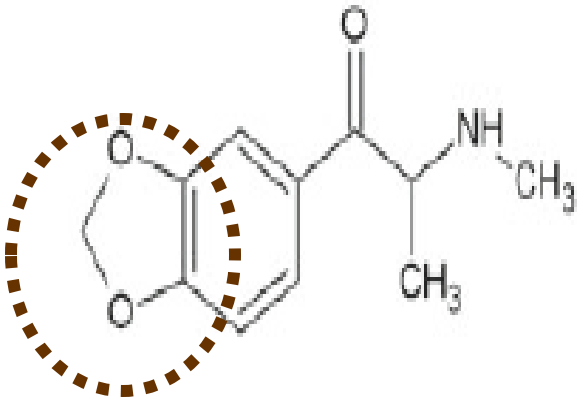
Buphedrone
(Position 3'-substituted)



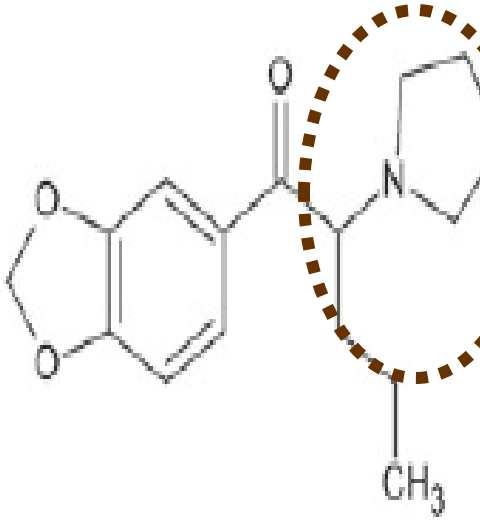
Mephedrone
(Ring-substituted)



Diethylcathinone
(N-alkyl-substituted)



Methylone
(Methylenedioxy-substituted)



MDPV
(Pyrrolidinyl-substituted)

Anal Bioanal Chem (2013) 405:9437–9448
DOI 10.1007/s00216-013-7386-z

RESEARCH PAPER

Simultaneous quantification of 28 synthetic cathinones and metabolites in urine by liquid chromatography-high resolution mass spectrometry

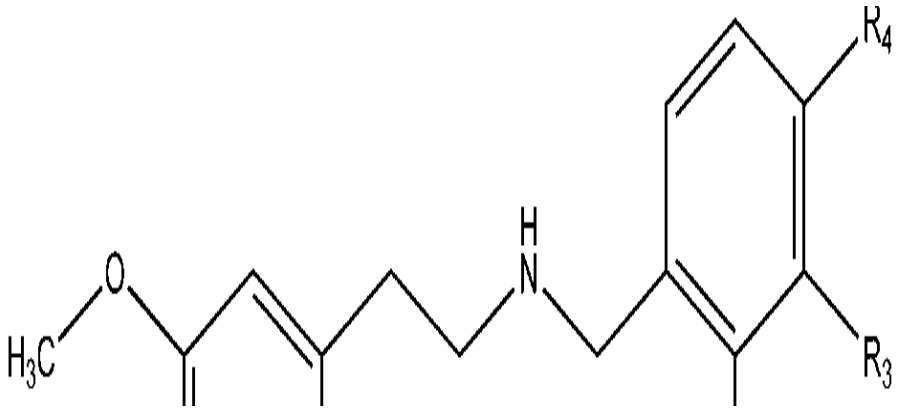
Marta Concheiro · Sebastien Anizan · Kayla Ellefsen · Marilyn A. Huestis

A comprehensive confirmation method for the identification and quantification of synthetic cathinones in urine is needed. We developed a sensitive and specific method for the determination of 28 synthetic cathinones, including four commercially available metabolites in urine by liquid chromatography tandem high resolution mass spectrometry (LC-HRMS).

Characterization of Eleven 2,5-Dimethoxy-*N*-(2-methoxybenzyl)phenethylamine (NBOMe) Derivatives and Differentiation from their 3- and 4-Methoxybenzyl Analogues - Part I

John F. Casale*, Patrick A. Hays
U.S. Department of Justice
Drug Enforcement Administration

ABSTRACT: The characterization of eleven 2,5-dimethoxy-*N*-(2-methoxybenzyl) phenethylamine (NBOMe) derivatives and their 3- and 4-methoxybenzyl analogues via mass spectrometry and infrared spectrometry is presented. Analytical data is presented to differentiate these positional isomers.

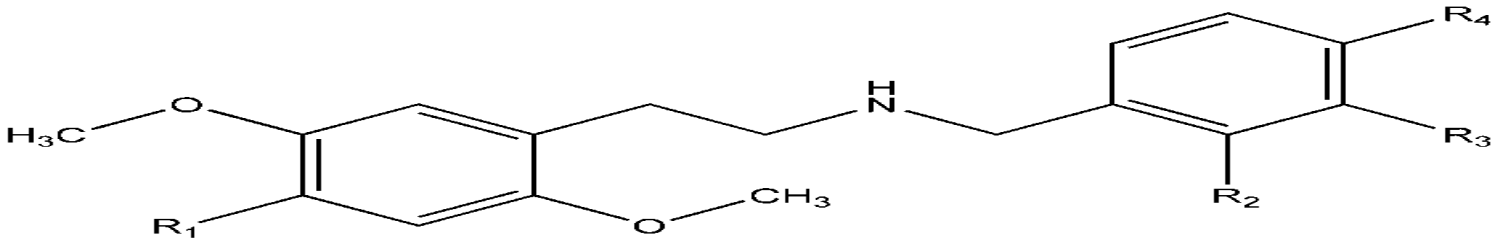


Microgram Journal, Volume 9, Number 2

DPA

NATIONAL EARLY WARNING SYSTEM

2,5-Dimethoxy-*N*-(2-methoxybenzyl)phenethylamine



Compound	R_1	R_2	R_3	R_4
25H-NB2OMe (1)	H	OCH_3	H	H
25H-NB3OMe (2)	H	H	OCH_3	H
25H-NB4OMe (3)	H	H	H	OCH_3
25B-NB2OMe (4)	Br	OCH_3	H	H
25B-NB3OMe (5)	Br	H	OCH_3	H
25B-NB4OMe (6)	Br	H	H	OCH_3
25C-NB2OMe (7)	Cl	OCH_3	H	H
25C-NB3OMe (8)	Cl	H	OCH_3	H
25C-NB4OMe (9)	Cl	H	H	OCH_3
25D-NB2OMe (10)	CH_3	OCH_3	H	H
25D-NB3OMe (11)	CH_3	H	OCH_3	H
25D-NB4OMe (12)	CH_3	H	H	OCH_3
25E-NB2OMe (13)	C_2H_5	OCH_3	H	H
25E-NB3OMe (14)	C_2H_5	H	OCH_3	H
25E-NB4OMe (15)	C_2H_5	H	H	OCH_3
25I-NB2OMe (16)	I	OCH_3	H	H
25I-NB3OMe (17)	I	H	OCH_3	H
25I-NB4OMe (18)	I	H	H	OCH_3
25N-NB2OMe (19)	NO_2	OCH_3	H	H
25N-NB3OMe (20)	NO_2	H	OCH_3	H
25N-NB4OMe (21)	NO_2	H	H	OCH_3
25P-NB2OMe (22)	$CH_2CH_2CH_3$	OCH_3	H	H
25P-NB3OMe (23)	$CH_2CH_2CH_3$	H	OCH_3	H
25P-NB4OMe (24)	$CH_2CH_2CH_3$	H	H	OCH_3
25T2-NB2OMe (25)	CH_3CH_2S	OCH_3	H	H
25T2-NB3OMe (26)	CH_3CH_2S	H	OCH_3	H
25T2-NB4OMe (27)	CH_3CH_2S	H	H	OCH_3
25T4-NB2OMe (28)	$(CH_3)_2CHS$	OCH_3	H	H
25T4-NB3OMe (29)	$(CH_3)_2CHS$	H	OCH_3	H
25T4-NB4OMe (30)	$(CH_3)_2CHS$	H	H	OCH_3
25T7-NB2OMe (31)	$CH_3(CH_2)_2S$	OCH_3	H	H
25T7-NB3OMe (32)	$CH_3(CH_2)_2S$	H	OCH_3	H
25T7-NB4OMe (33)	$CH_3(CH_2)_2S$	H	H	OCH_3

DPA

NATIONAL EARLY WARNING SYSTEM

Fenetylammine N-benzyl substituted

New class of hallucinogen

Esempi:

2,5-Dimethoxy-*N*-(2-methoxybenzyl)phenethylamine (NBOMe)

N-(2-methoxybenzyl)-2,5-dimethoxy-4-**iodo**phenethylamine (**25I-NBOMe**),

N-(2-methoxybenzyl2,5-dimethoxy-4-**chloro**phenethylamine (**25C-NBOMe**),

N-(2-methoxybenzyl)-2,5-**dimethoxy**-4-methylphenethylamine (**25D-NBOMe**).

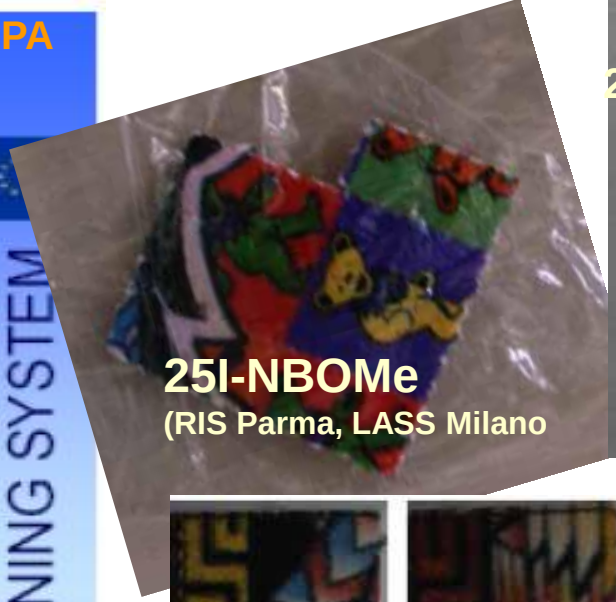
™

- Adam L. Halberstadt , Mark A. Geyer: Effects of the hallucinogen 2,5-dimethoxy-4-iodophenethylamine (2C-I) and superpotent *N*-benzyl derivatives. *Neuropharmacology* **2013** http://dx.doi.org/10.1016/j.neuropharm.2013.08.025

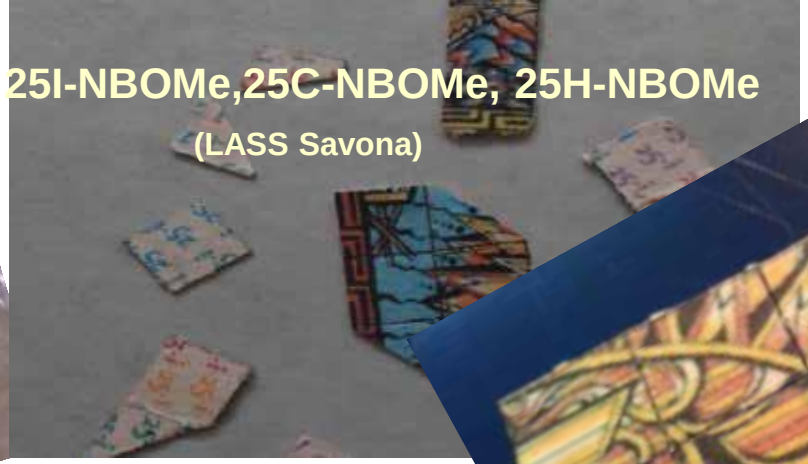
- Simon l. H et al.: Severe clinical toxicity associated with analytically confirmed recreational use of 25I – NBOMe: case series *Clinical Toxicology* (**2013**), DOI: 0.3109/15563650.2013.802795

DPA

NATIONAL EARLY WARNING SYSTEM



25I-NBOMe
(RIS Parma, LASS Milano



25I-NBOMe,25C-NBOMe, 25H-NBOMe
(LASS Savona)

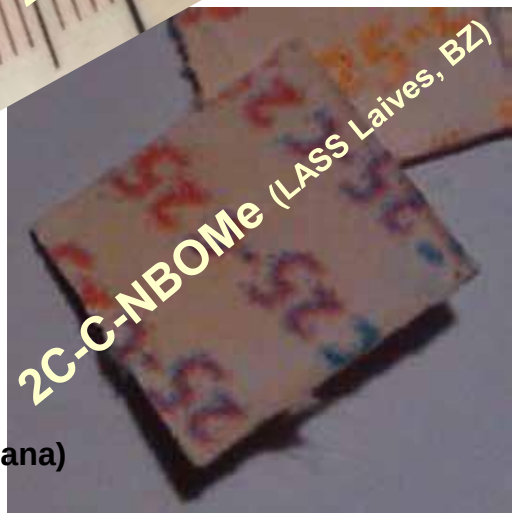
25H-NBOMe, 2C-C-NBOMe,
25I-NBOMe (LASS Verona)

25I-NBOMe e LSD (LASS Alessandria)

25I-NBOMe,LSD (LASS Alessandria)

25H-NBOMe (RIS Parma)

25I-NBOMe (ULSS12 Veneziana)



2C-C-NBOMe (LASS Laives, BZ)

2C-B
(LASS Reggio C.)

TM

Characterization of the Synthetic Cannabinoid XLR11 and Fluoroalkyl Analogs

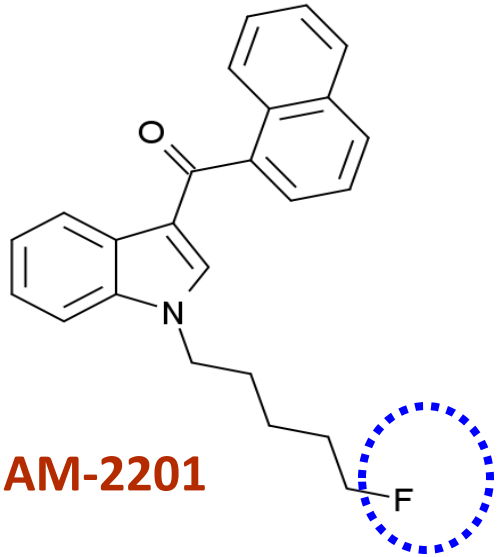
Paul D. Kennedy, Andrei Kornilov (Cayman Chemical Company)
Jason Nawyn (Defense Forensic Science Center, United States Army Criminal Investigation Laboratory (USACIL)

Source: Forensic Drug Review, 14-05-2013

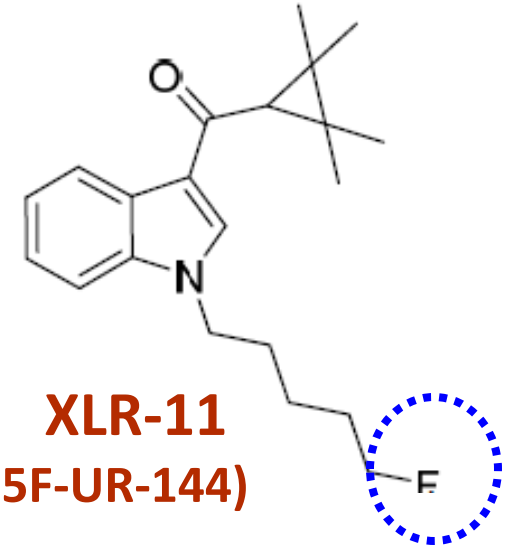
DPA

NATIONAL EARLY WARNING SYSTEM

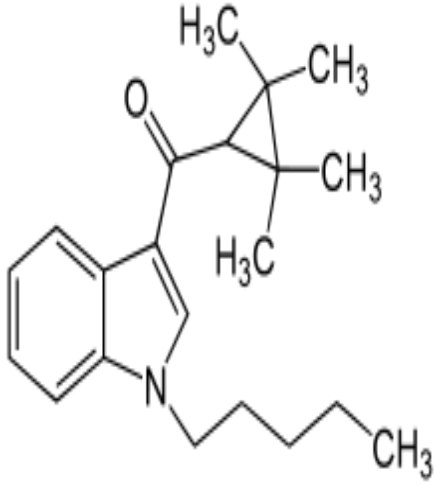
XLR-11 o 5FUR-144 (tetramethyl ciclopropyl ethanoyl indole) is a AM2201 analog and its structure is similar to UR-144 (5Fluorine derivative)



AM-2201



XLR-11
(5F-UR-144)



UR-144

XLR-11 e UR-144 in **sangue e urine**: Randox Laboratories e Tulip Biolabs, Inc.

ELISA immunoassay per UR-144 in **urine** : Tulip Biolabs, Inc.

TM

DPA

NATIONAL EARLY WARNING SYSTEM

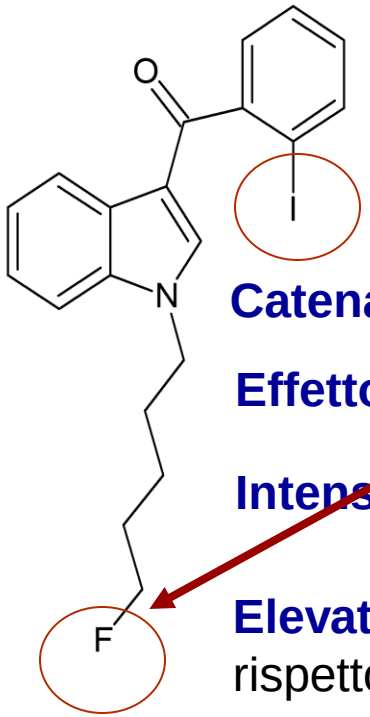
FLUORINE ?

TM

AM-694

1-(5-fluoropentil)-3-(2-iodobenzoil)indolo.

BENZOYLINDOLE



Catena alchilica fluorurata in R1: possibili metaboliti tossici.

Effetto: più duraturo (anche più di 3 ore)

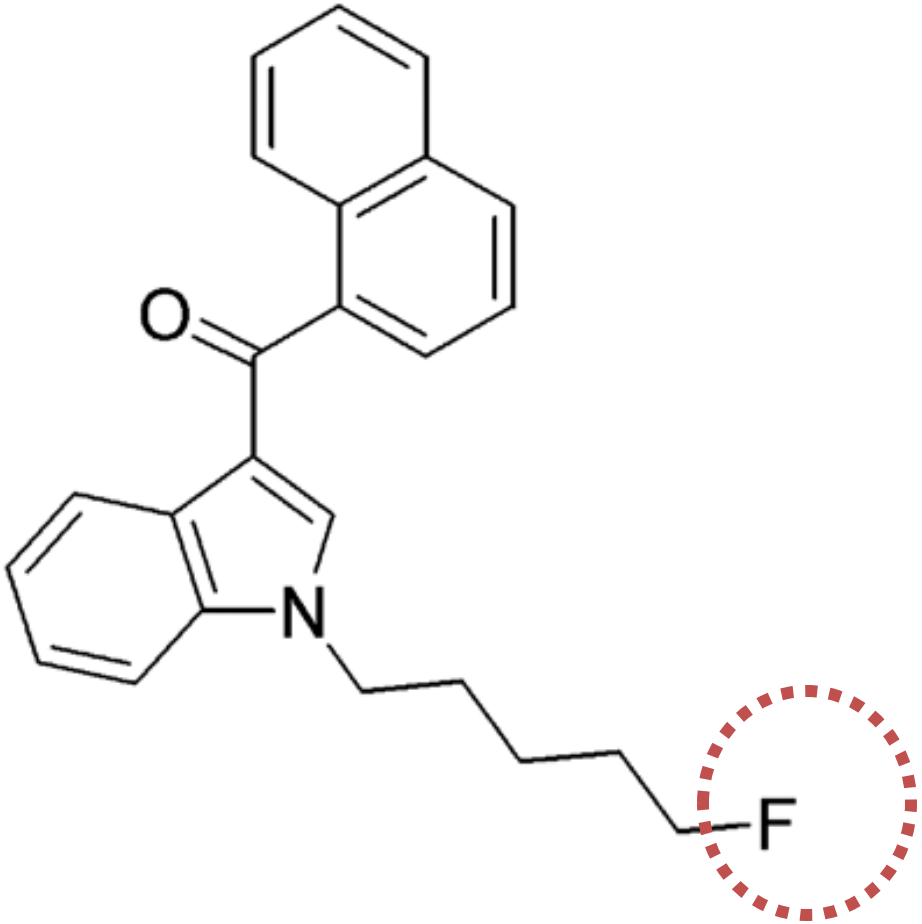
Intensità: costante nel tempo senza forme associate di ansia

Elevata affinità per il recettore **CB_1**, **elevata selettività** rispetto al recettore **CB_2**

n°. Carb. Dispari. CB1,costante di affinità Ki pari a 0.08 nM più di 100 volte superiore a quella del JWH-018 (Ki = 9±5 nM); pari ad 1.44 nM per il CB2

TM

AMMINOALCHILINDOLI

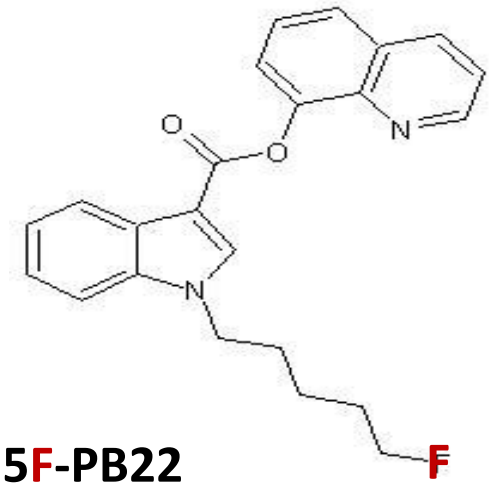


AM-2201

(1-(5-fluoropentyl-1H-indol-3-yl)-(naphthalene-1-yl)methanone)

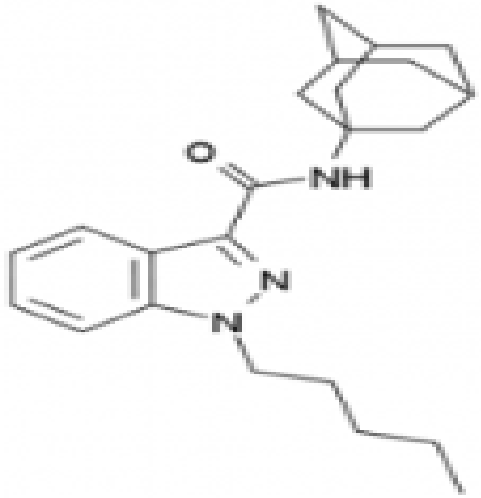
DPA

NATIONAL EARLY WARNING SYSTEM



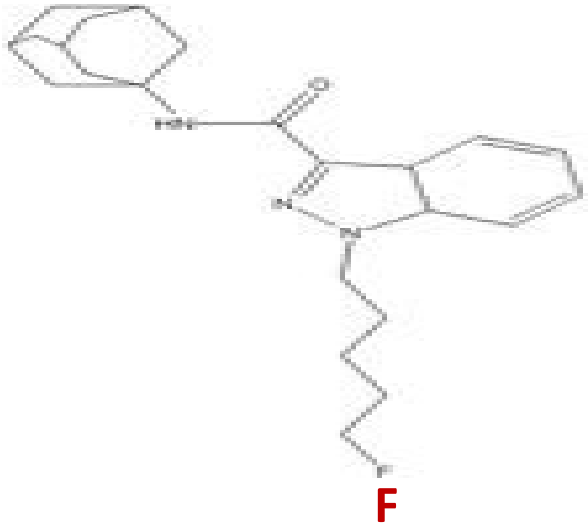
5F-PB22

analogo carbossilato quinolinil derivato della AM-2201



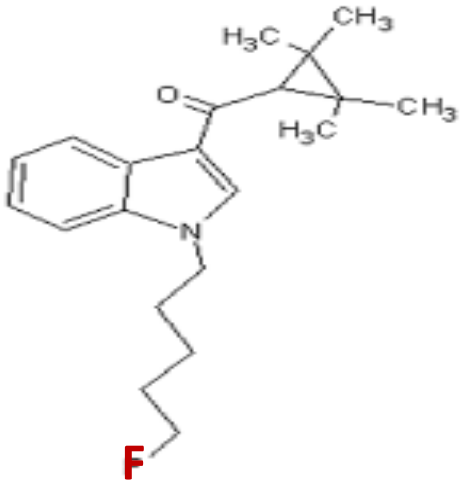
Apinaca, AKB-48

cannabinoide sintetico appartenente alla famiglia degli **indazoli** e possiede un gruppo ammidico legato ad un **sostituente alchilico di tipo adamantile**



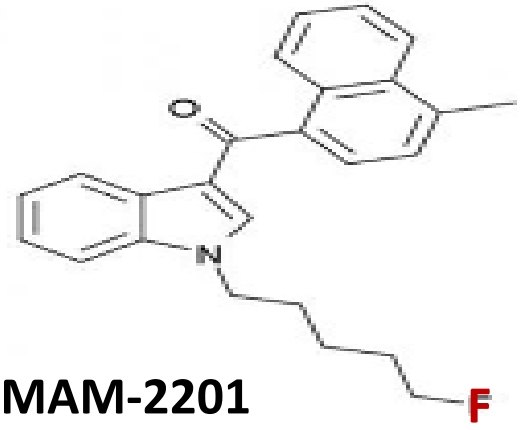
AKB-48F

AKB48 N-(5-fluoropentil) analogo. E' un derivato **indazolico** con sostituzione adamantil carbossamidica.



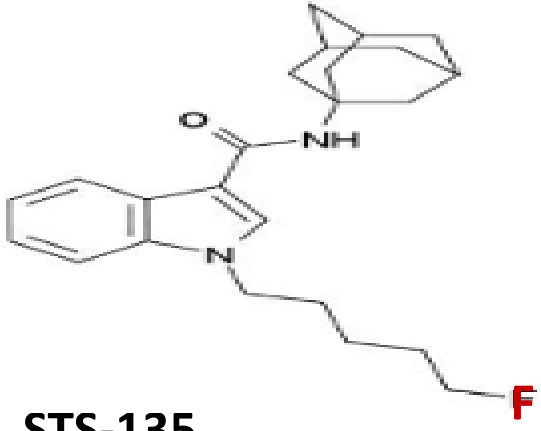
5FUR-144

cannabinoide sintetico, 5-fluoro derivato della UR-144



MAM-2201

Cannab. sint., naftoilindoli. Derivato metilico in posiz 4 del gruppo naftile dell'AM-2201

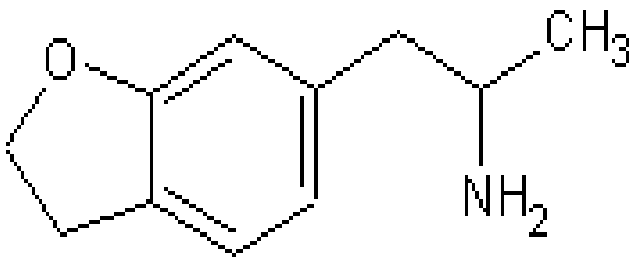


STS-135

cannabinoide sintetico caratterizzato dalla presenza di un gruppo adamantil-carbossammidico

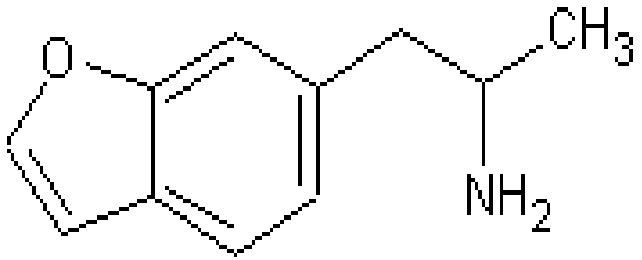
TM

APB Derivatives



6-APDB

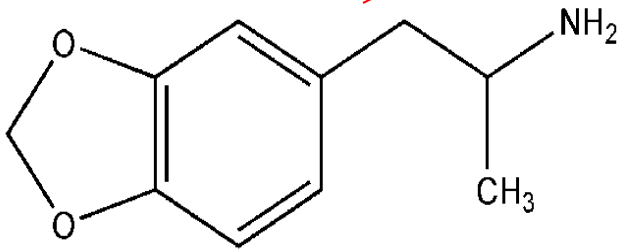
6-(2-aminopropyl)-2,3-dihidrobenzofurane



6-APB

6-(2-aminopropyl)benzofurane

[or 4-desossi-MDA]



MDA

Metylendioxiamfetamine

6-APB acts on the release of:

- **serotonine** (entactogen effect)
- **dopamine** (stimulant effect)
- **norepinephrine** (psychedelic effect)

AFFINITY SEROTONINIC RECEPTORS

5-HT(2A)

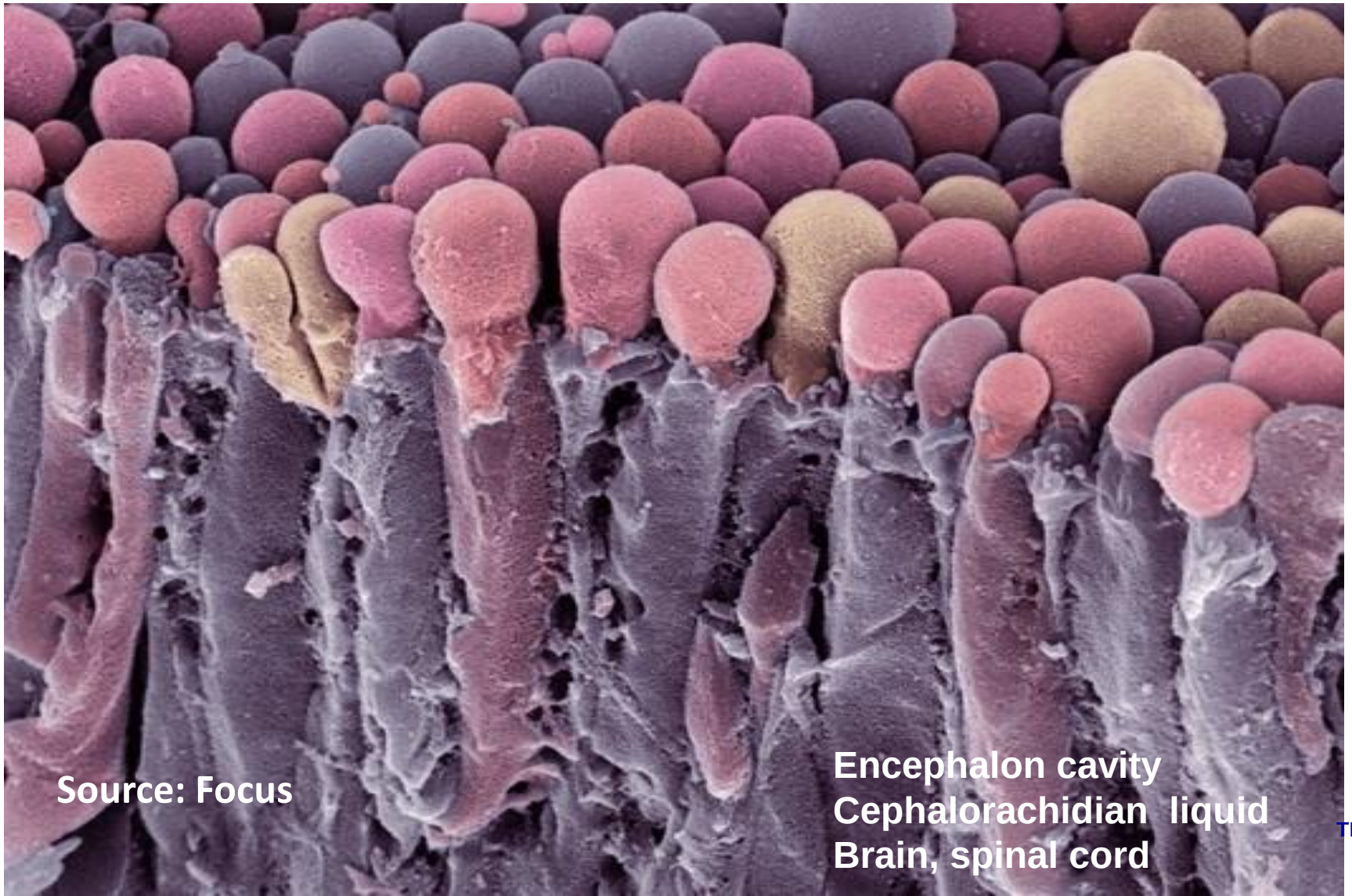
5-HT(2B) ki=3.7 nM

5-HT(2C)

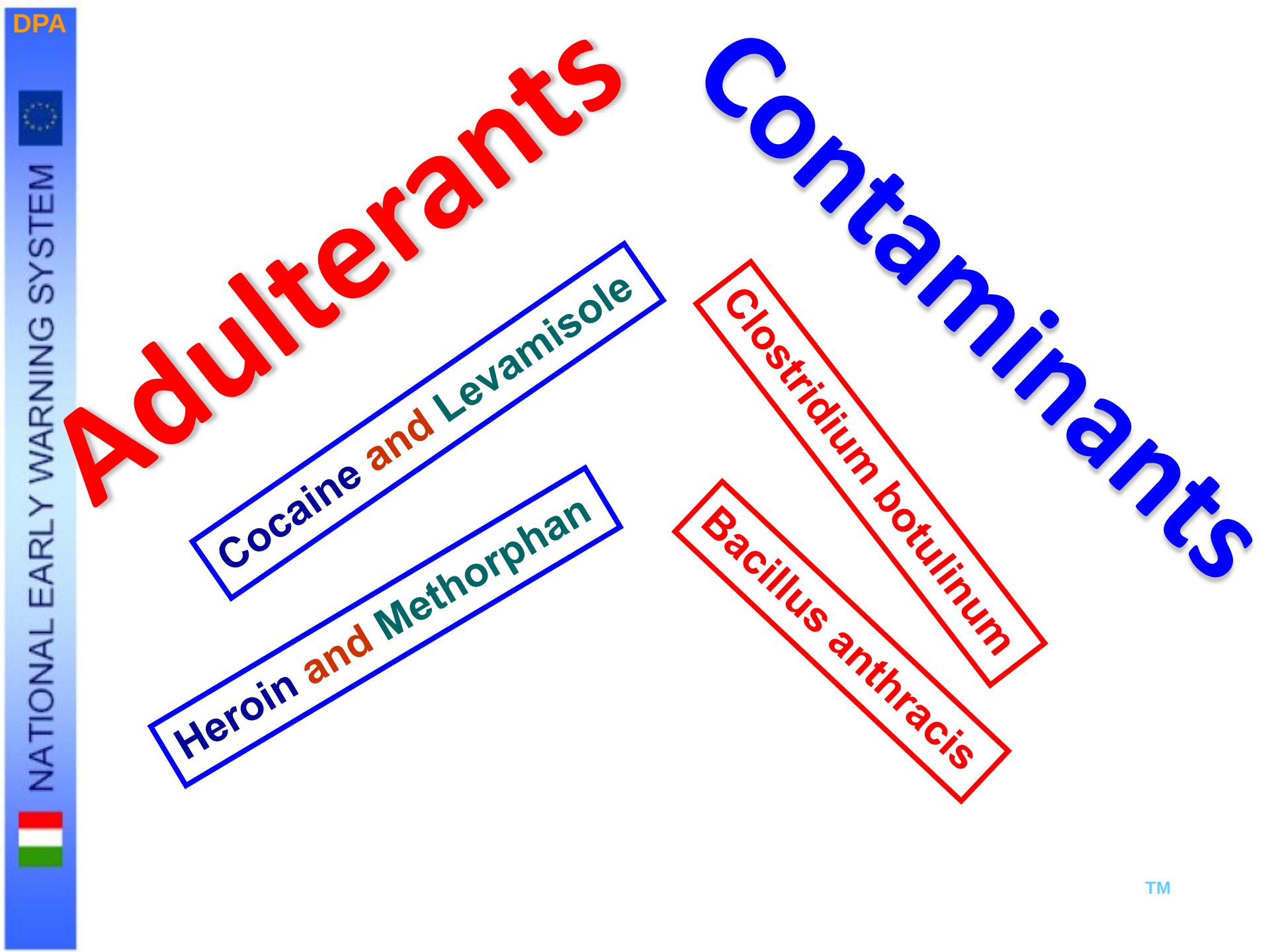
DPA

NATIONAL EARLY WARNING SYSTEM

CHOROID PLEXUS CELLS



™


DPA
NATIONAL EARLY WARNING SYSTEM
Adulterants
Cocaine and Levamisole
Heroin and Methorphan
Contaminants
Clostridium botulinum
Bacillus anthracis
TM

DPA

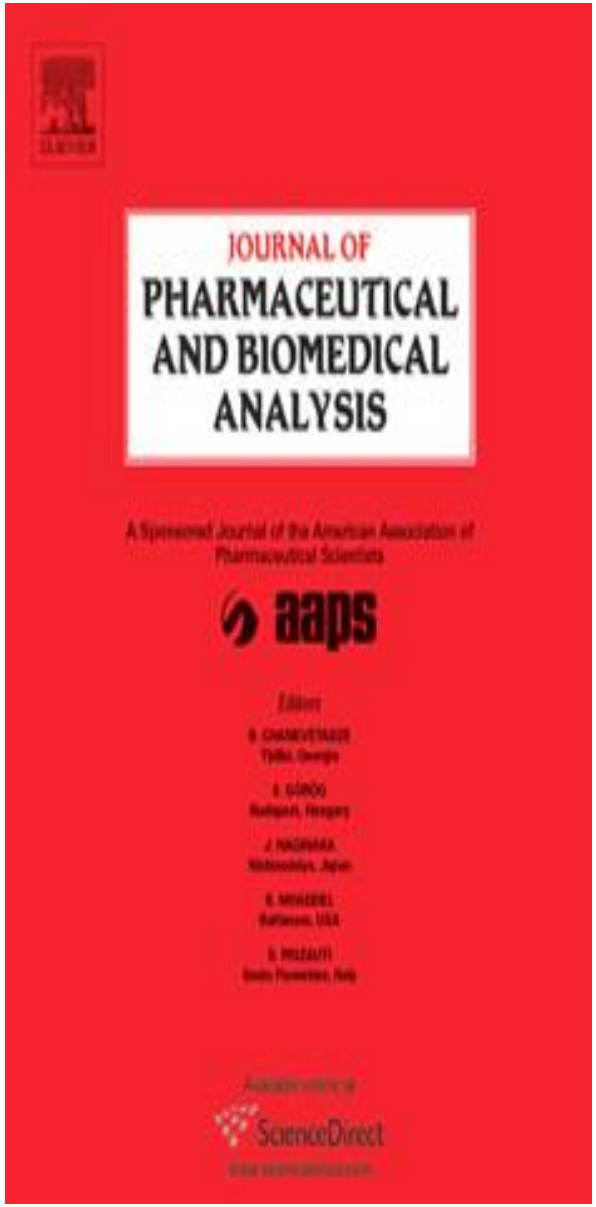
NATIONAL EARLY WARNING SYSTEM

Determination of aminorex in human urine samples by GC-MS after use of levamisole

Elisabetta Bertol, Francesco Mari, Maria Grazia Di Milia, Lucia Politi, Sandra Furlanetto, Steven B. Karch

Abstract

The Drug Enforcement Administration (DEA) reports that as of October 2010, 79% of all cocaine seized in the United States contained levamisole. The equine conversion of levamisole to aminorex has been demonstrated. However, the metabolic fate of levamisole in humans is unknown. Nevertheless, as aminorex is amphetamine-like and hallucinogenic, it may be used as an adulterant to increase the effects of cocaine. We report here the results of in vivo studies demonstrating for the first time that not only equine, but also canine and human metabolism all result in aminorex formation. Levamisole and aminorex were extracted from real urine samples by liquid–liquid extraction and identified and quantified by GC–MS (identification by 3 ions per substance, LLOQ at 0.15 ng/ml for both).



J Pharm Biomed Anal 2011 55(5):1186-1189 doi: 10.1016/j.jpba.2011.03.039. Epub 2011 Apr 6.

For the first time aminorex has been identified as levamisole metabolite in human urine, confirming human in vivo conversion of levamisole to aminorex.

Risk of occurrence of agranulocytosis, but also of a potential epidemic of pulmonary hypertension in chronic cocaine abusers is hypothesized.

DPA

NATIONAL EARLY WARNING SYSTEM

METHORPHAN in heroin

- Increasing number of heroin seizures containing methorphan has been reported to the NEWS

- Deaths and poisoning related to methorphan have been recorded

- Chiral analytical methods to separate methorphan enantiomers in seizures as well as in biological samples are not available enough

DPA

NATIONAL EARLY WARNING SYSTEM

Chiral separation of 12 cathinone analogs by cyclodextrin-assisted capillary electrophoresis with UV and mass spectrometry detection

Gustavo Merola, Hanzhuo Fu, Franco Tagliaro, Teodora Macchia and Bruce R. McCord

DOI: 10.1002/elps.201400077

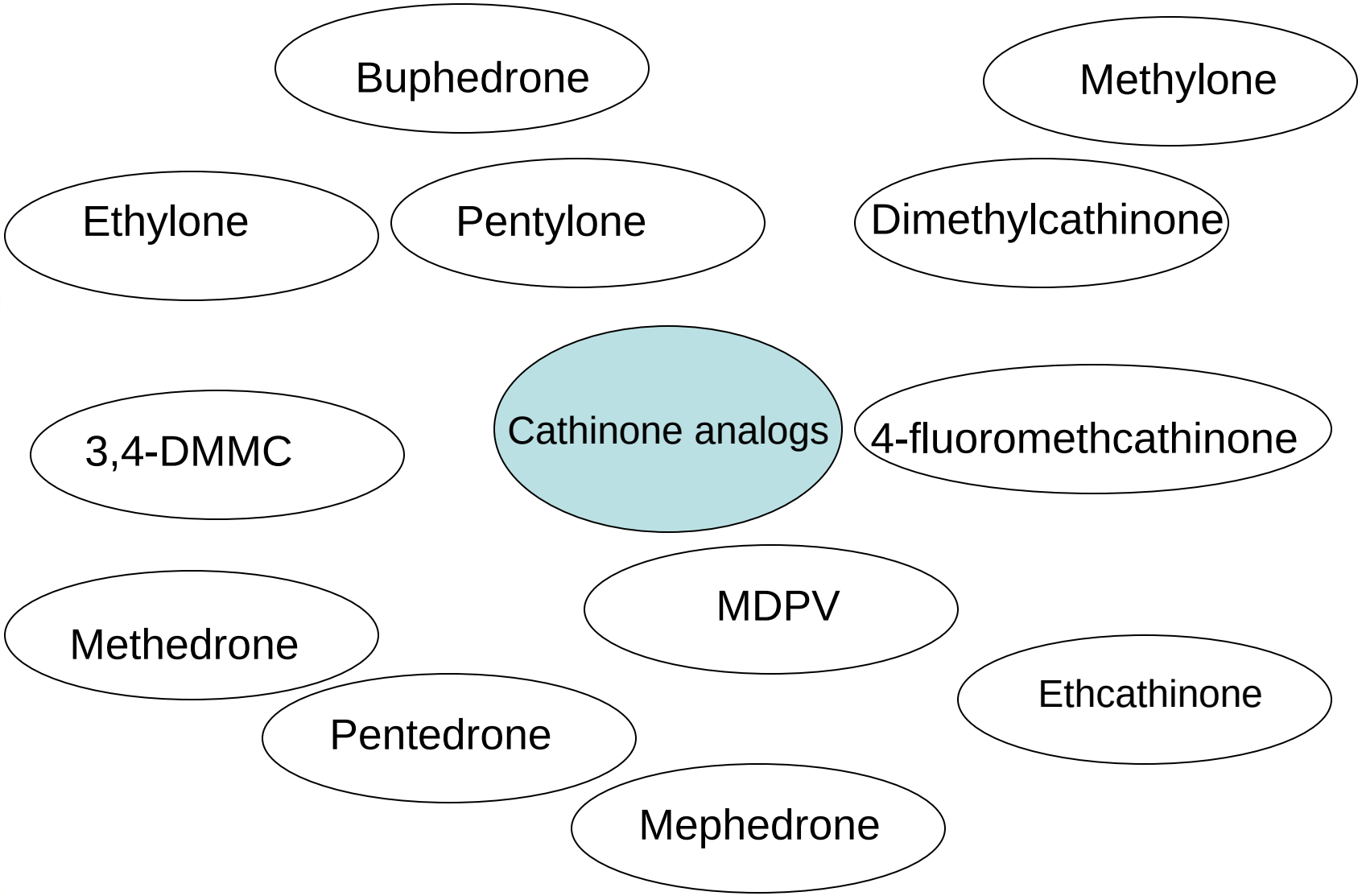
2014

Abstract

In this study, a **rapid chiral separation of 12 cathinones analogs** has been developed and validated using cyclodextrin-assisted capillary electrophoresis (CE) with UV and time of flight mass spectrometric (TOF-MS) detection. Optimum separation was obtained on a 57.5 cm × 50 μm capillary using a buffer system consisting of 10 mM β-cyclodextrin (β-CD) in a 100mM phosphate buffer for CE-UV, and 0.6% (*v*/*v*) highly sulfated-γ-cyclodextrin (HS-γ-CD) in a 50 mM phosphate buffer for CE-MS. In the CE-MS experiment, a partial filling technique was employed to ensure that a minimum amount of cyclodextrin entered the mass spectrometer. All analytes were separated within 18 minutes in the CE-UV separation and identified by TOF-MS. 10 compounds were enantiomerically separated using β-cyclodextrin in the UV mode and an additional 2 more were enantiomerically separated using highly sulfated γ-cyclodextrin in the MS mode. Detection limits down to 1.0 ng/mL were obtained. The method was then applied to examine seized drugs.

DPA

NATIONAL EARLY WARNING SYSTEM



Department of Chemistry-Florida International University, Miami, FL, USA

DPA

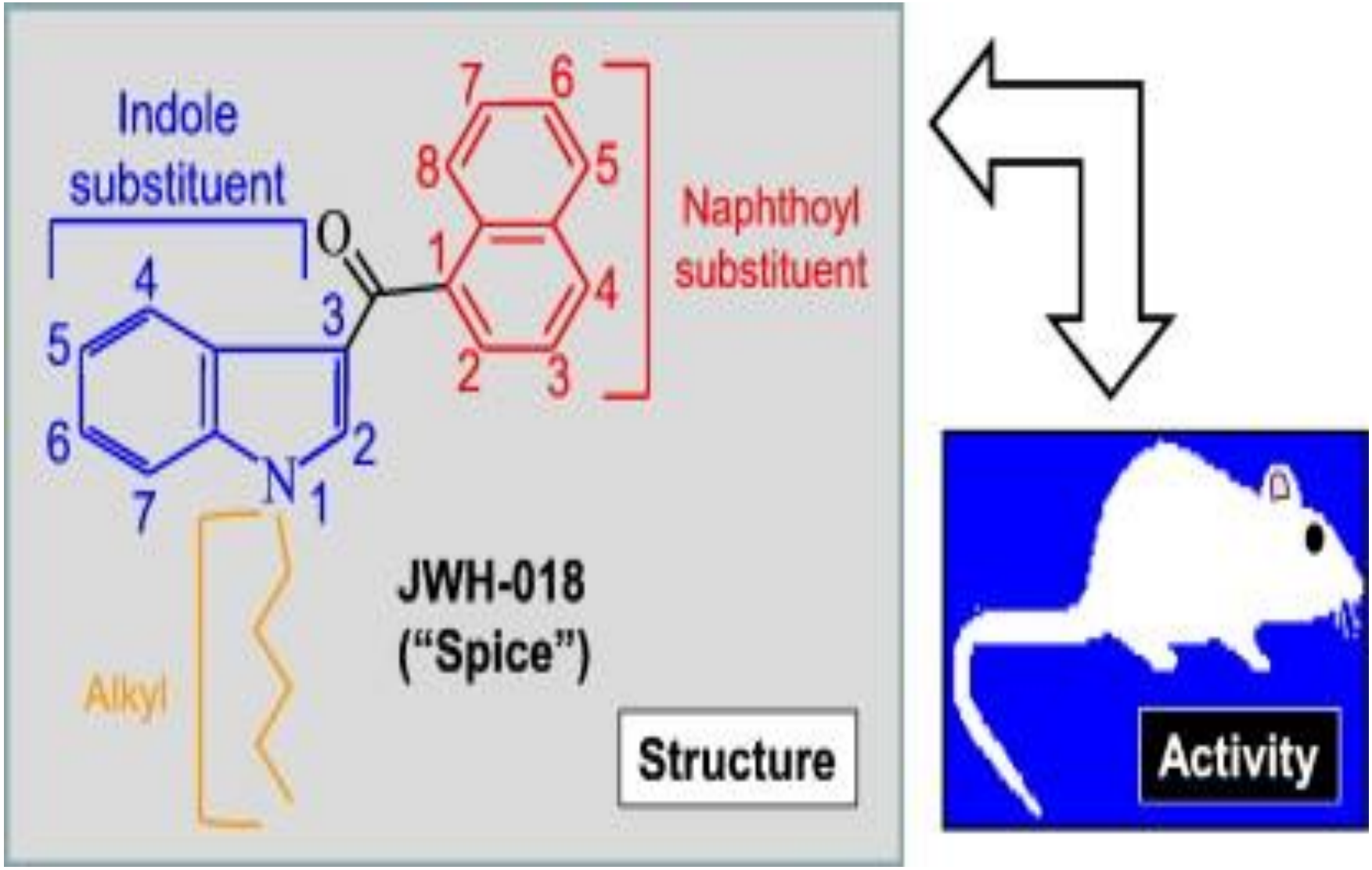
NATIONAL EARLY WARNING SYSTEM

ANALYSIS BUT NOT ONLY .....

DPA

NATIONAL EARLY WARNING SYSTEM

SUPPORT in RESEARCH



Source: Jenny L. Wiley, Julie A. Marusich, John W. Huffman. Moving around the molecule: Relationship between chemical structure and in vivo activity of synthetic cannabinoids. Life Sciences 2014. 97 (1):55-63

Neurotox Res (2013) 24:15–28
DOI 10.1007/s12640-012-9371-2

ORIGINAL ARTICLE

Behavioral Responses to Acute and Sub-chronic Administration of the Synthetic Cannabinoid JWH-018 in Adult Mice Prenatally Exposed to Corticosterone

Simone Macrì · Lara Lanuzza · Gustavo Merola · Chiara Ceci · Stefano Gentili · Antonella Valli · Teodora Macchia · Giovanni Laviola

Received: 21 September 2012 / Revised: 6 December 2012 / Accepted: 21 December 2012 / Published online: 8 January 2013

Abstract Recent data indicate that both availability and consumption of synthetic and natural psychoactive substances, marketed under the name of "legal highs", has increased. Among them, the aminoalkylindole-derivative JWH-018 is widely distributed due to its capability of binding the cannabinoid receptors CB1 and CB2 thereby mimicking the effects of classical drug agonists. To address whether the behavioral effects of the synthetic compound JWH-018 are similar to those induced by classical cannabinoid agonists, we investigated, in outbred CD1 mice, the consequences of its acute and sub-chronic administration (0, 0.03, 0.1, or 0.3 mg/kg, IP) at the level of body temperature, pain perception, general locomotion, and anxiety. In order to address whether the exposure to precocious stressors-modified individual reactivity to this psychoactive substance, we also investigated its effects in adult mice previously exposed to prenatal stress in the form of corticosterone supplementation in the maternal drinking water (33 or 100 mg/L). In the absence of major effects on motor coordination, JWH-018-reduced body temperature, locomotion and pain reactivity, and increased indices of anxiety. Prenatal corticosterone administration-reduced individual sensitivity to the effects of JWH-018 administration in all the aforementioned parameters. This altered response is not due to variations in JWH-018 metabolism. Present data support the hypothesis that precocious stress may affect, in the long-term, the functional status, and reactivity of the endocannabinoid system.

Keywords Emotions · HPA axis · Animal model · Legal highs · Endocannabinoid system

Variabilità individuale in adolescenza e ruolo dello stress prenatale: il caso M.D.M.A.

Teodora Macchia [1] **e Gianni Laviola** [2]
(1)Dipartimento del Farmaco, [2] Dipartimento di Biologia Cellulare e Neuroscienze

from:

***Prenatal stress affects 3,4-methylenedioxymethamphetamine pharmacokinetics and drug-induced motor alterations*.**

S.Morley-Fletcher, M.Puopolo, S.Gentili, G.Gerra, T.Macchia, G.Laviola.

European Journal of Pharmacology 489 (2004) 89-92.

TM

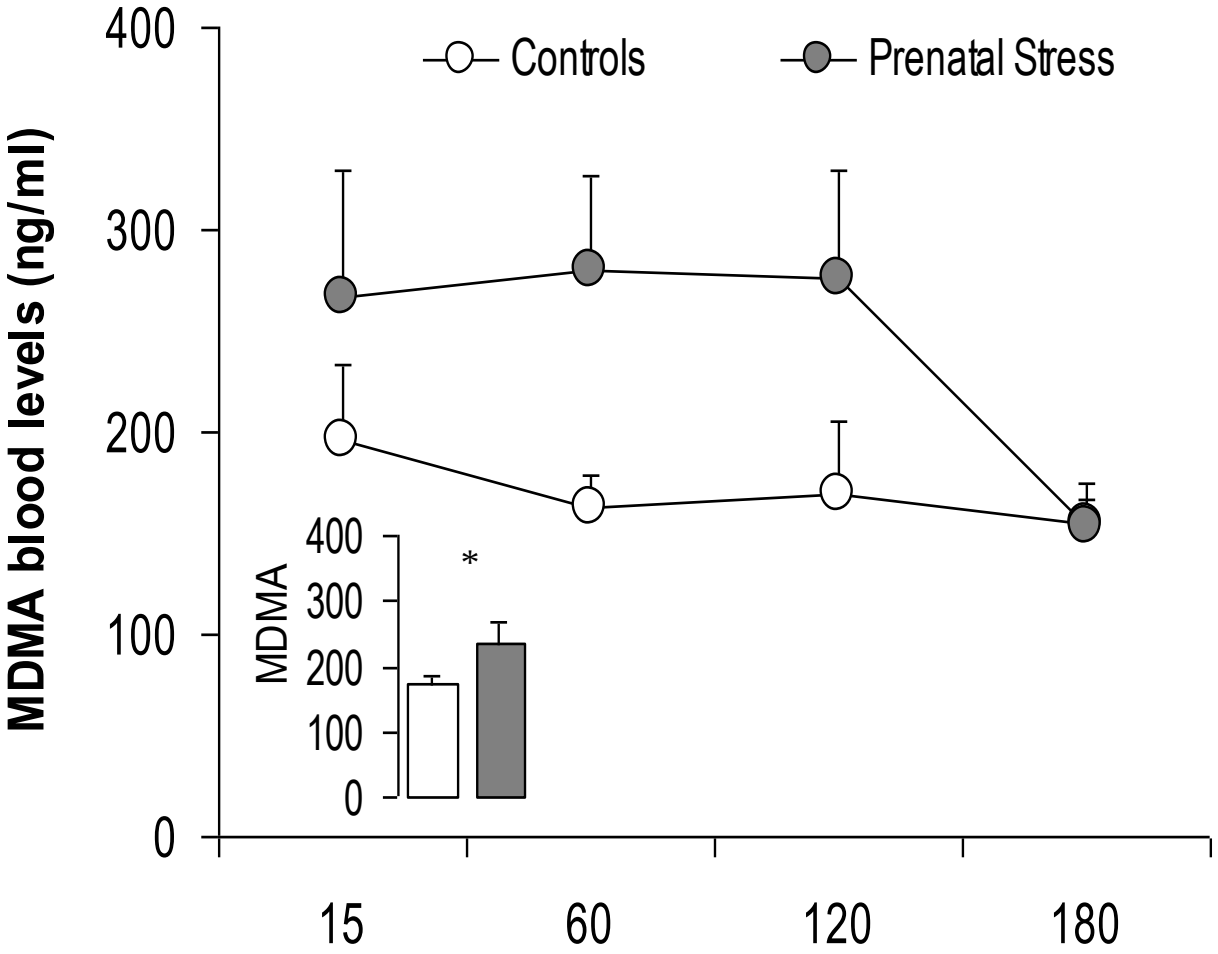


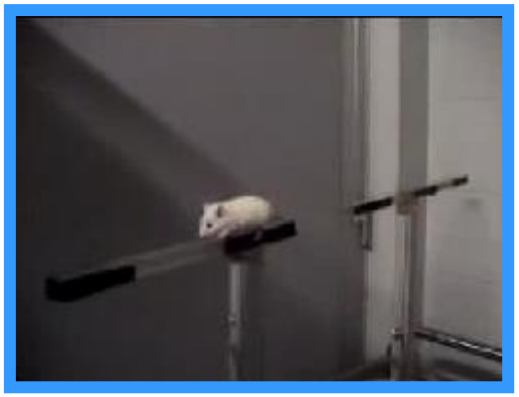
Figura 1. Livelli ematici di MDMA (ng/ml) in **ratti adolescenti, 30 giorni di età**, con stress prenatale e controlli. Ogni punto rappresenta la media ± S.E.M di **sei** animali.

Fonte: S.Morley-Fletcher, M.Puopolo, S.Gentili, G.Gerra, T.Macchia, G.Laviola.
European Journal of Pharmacology 489 (2004) 89-92.

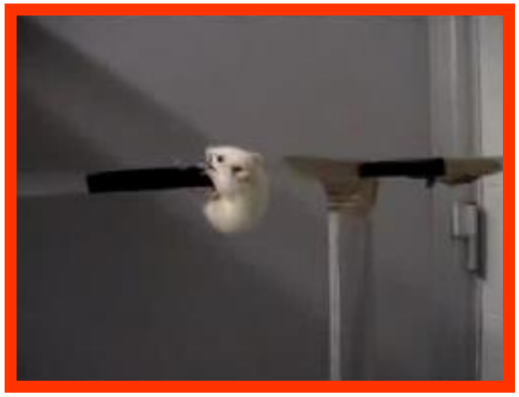
TM

MOTOR PERFORMANCE

controls and ***stressed rats***


C



S

TM

Source: shots from the study published on **European Journal of Pharmacology 489 (2004) 89-92.**

DPA

NATIONAL EARLY WARNING SYSTEM

CONCLUSION

- **Current techniques are unlikely to be effective in new drugs**
- **Comprehensive methods suitable to analyse synthetic cannabinoids and catinones are needed**
- **Diversity of these drugs/drug-like products make development of such methods a challenge**
- **Research, timely data/reference materials/ literature sharing, multiprofessional approach are essential**

The Italian approach to the NPS challenge is jointed and multidisciplinary also in the analytical field

DPA

NATIONAL EARLY WARNING SYSTEM

Thanks for your attention

DPA

NATIONAL EARLY WARNING SYSTEM

LOD

0.25 µg/L

LOQ

0.5-1 µg/L in 0.25 mL di urine

5 µg/L in 1mL di urine (Marinetti, 6 catinoni

Marinetti LJ, Antonides HM (2013) Analysis of synthetic cathinones commonly found in bath salts in human performance and postmortem toxicology: method development, drug distribution and interpretation of results. J Anal Toxicol 37(3):135–146