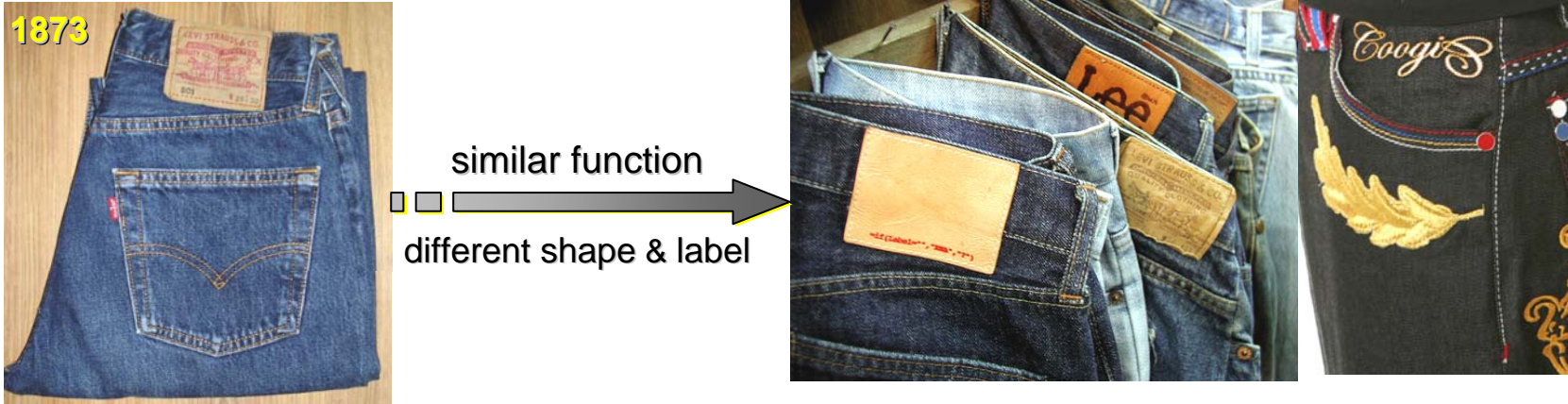


Novel 'designer drugs': Analytical, health and regulatory issues

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New trends in the area of drug prevention and control. Vilnius, 10 November, 2010

Designer jeans – ‘designer drugs’



‘designer drug’ (1985)

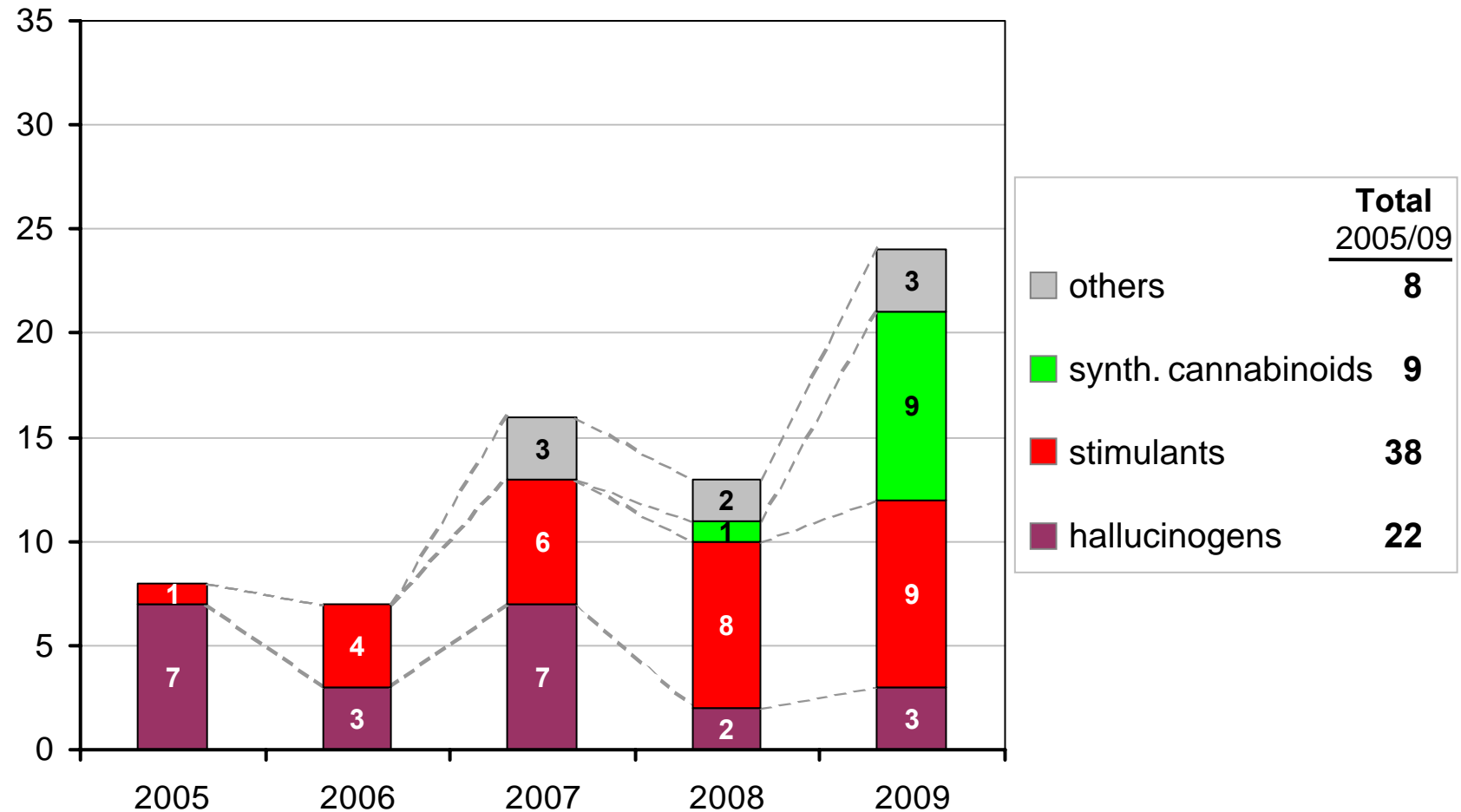
A synthetic analogue of a controlled substance with a slightly altered molecular structure to avoid its classification as an illicit drug.

It has ***similar pharmacological effects*** to the parent controlled substance.

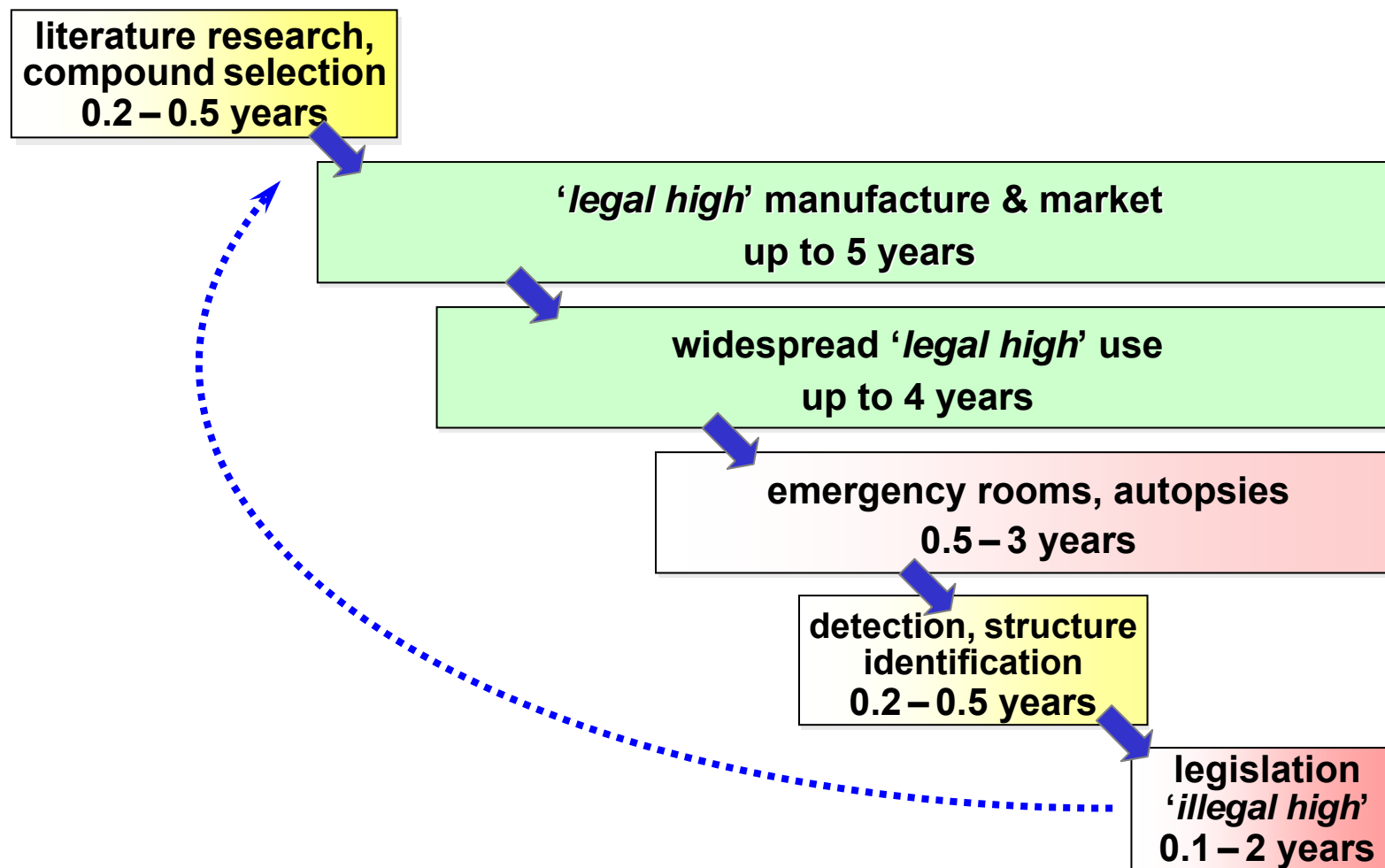
Until regulated, a ‘designer drug’ can be produced, traded, advertised & marketed without restrictions (INTERNET, smart shops) as ***legal high, plant food, ‘research chemical, not for human consumption’, etc.***

The appearance of new psychoactive drugs in the EU by activity type

No. of new drugs



Life span of a 'legal high'

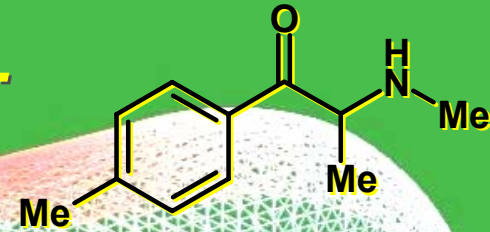


Chemists busy in making 'legal highs' in the lab



Daily Mail Online, 24 April, 2010

Mephedrone in any form...



samples from Hungary

NRG products as 'Legal highs' purchased online in the United Kingdom (April-May 2010)

Label	Cathinone	Other compounds
• NRG-1	mephedrone	
• NRG-1	mephedrone	
• NRG-1	mephedrone (traces)	caffeine
NRG-1	–	caffeine
• NRG-1	mephedrone (traces)	procaine
NRG-1	butylone+MDPV	
• NRG-1	flephedrone	
NRG-1	naphyrone	
• NRG-1	napyhyrone+flephedrone	
• NRG-1	flephedrone+MDPV	
• NRG-2	mephedrone	
• NRG-2	mephedrone	benzocaine
NRG-2	–	inorganic material
NRG-2	–	benzocaine+caffeine
• NRG-2	4-Me-N-Et-cathinone	
NRG-3	??	??

• **Note:**

All sold as '*legal high*'
although mephedrone,
 flefedrone, 4-Me-N-Et-
 cathinone were regulated by
 16 April 2010 in the UK!

Brandt SD *et al* (2010) Analyses of second-generation 'legal highs' in the UK: Initial findings. *Drug Test Anal* (in press)

The case of Ivory Wave 'bath salt' (2006-2010)

also known as Purple Wave, Vanilla Sky or Whack

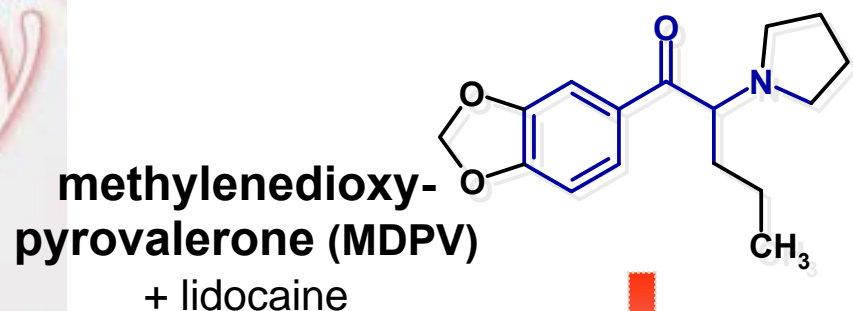


Same brand

Common mode of action
(dopamine & norepinephrine
reuptake inhibition)

Different chemistry

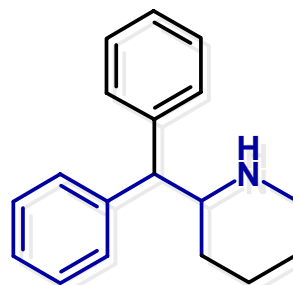
**Unpredictable side
effects**



2006-2010

After regulation in UK & Ireland
(Spring/Summer 2010)

**desoxypipradol
(2-DPMP)**



2010-

Some examples of recently detected new drugs in Hungary (2010)



butylone



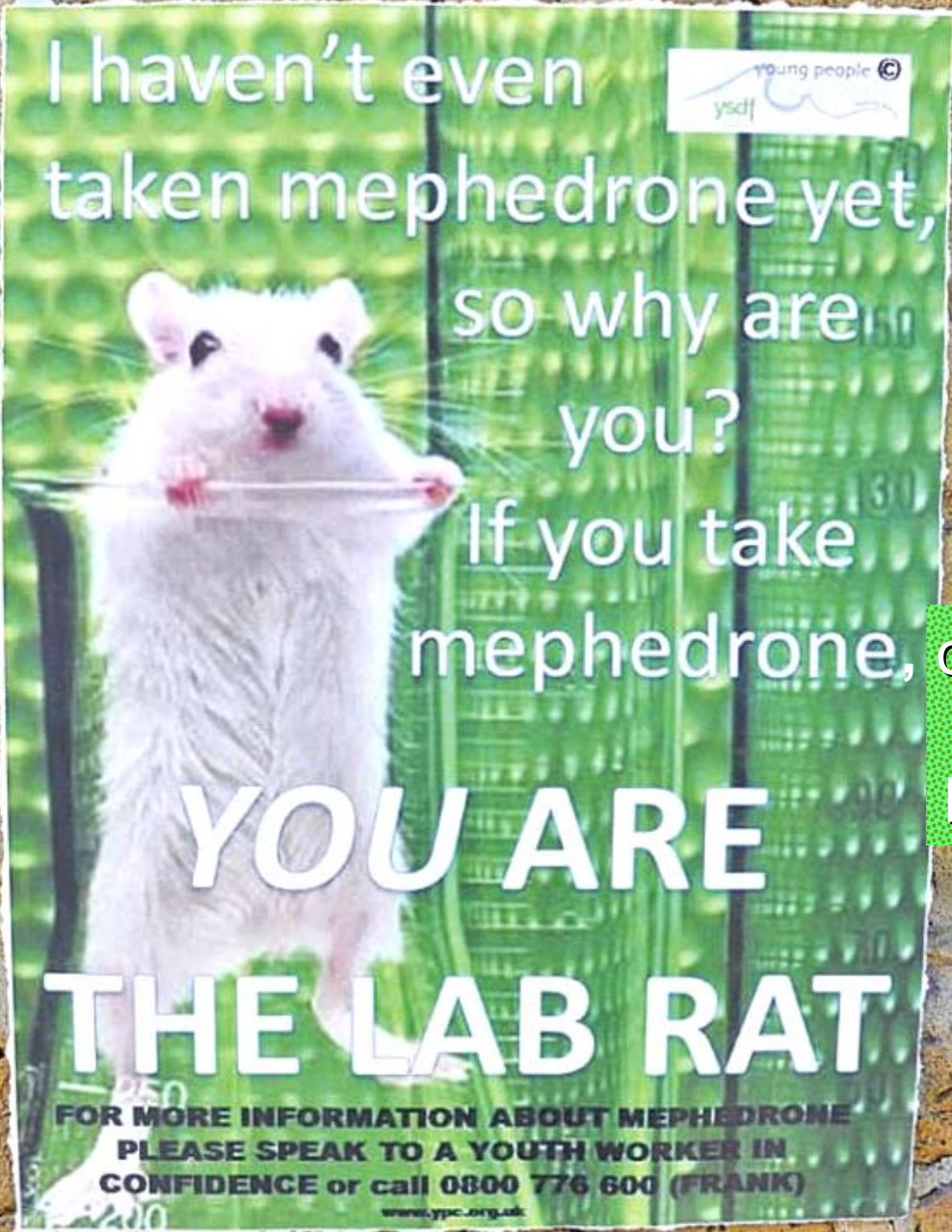
3,4-dimethylmethcathinone



4-fluoroamphetamine



JWH-018 (and JWH-073)



I haven't even
taken mephedrone yet,
so why are
you?
If you take
mephedrone,

**YOU ARE
THE LAB RAT**

FOR MORE INFORMATION ABOUT MEPHEDRONE
PLEASE SPEAK TO A YOUTH WORKER IN
CONFIDENCE or call 0800 776 600 (FRANK)
www.ypc.org.uk

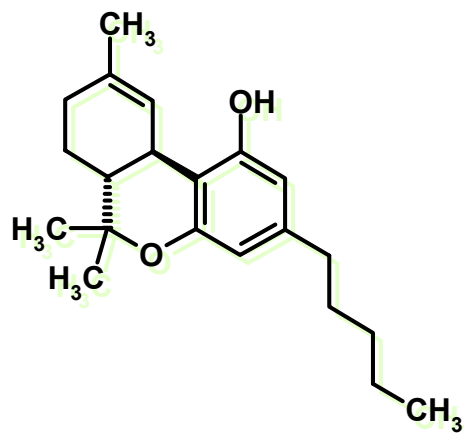
young people ©
ysdf

or MDPV, naphyrone,
MDAI, 4-FMA,
DMMA, JWH-73, *etc.*

Unexpected novel psychoactive drugs

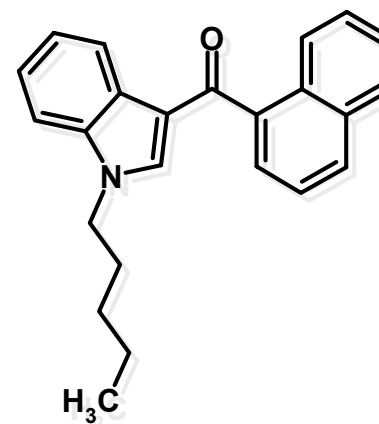
Novel chemistry – old target site

Cannabinoid receptor agonists



THC

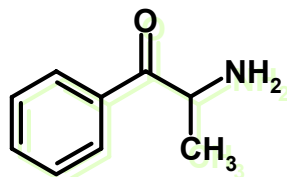
from *Cannabis sativa*



JWH-018

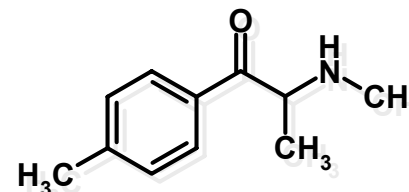
17 such compounds reported

Amphetamine-like psychostimulants



cathinone

from *Catha edulis*



mephedrone

25 analogues reported

How to regulate 'designer drugs'?

§ individual control (universal)

lists specific substances named one by one

§ generic control (UK, Ireland, New Zealand)

defines a family of substances based on substitution patterns in a parent molecule where the type, number and position of substituents may be precisely specified

§ analogue control (USA, Latvia, Norway, New Zealand)

covers a family of substances due to their

- *similar chemical structure*
- *similar pharmacological activity*

§ 'all-encompassing control' (Ireland)

covers essentially all psychoactive substances based on their *activity on the CNS*

Example of individual control

Dėl narkotinių ir psichotropinių medžiagų sąrašų patvirtinimo Žin., 2000, Nr. 4-113

1971 m. psichotropinių medžiagų konvencijos I sąrašas

AL

BDB

Bk-PMMA (Methedrone/Methoxyephedrine, 1-(4-methoxyphenyl)-2-methylaminopropan-1-one)

Brolamfetaminas (Brolamfetamine, DOB)

Catha edulis augalo lapai ir stiebeliai (leaves and straw)

DET

DMA

DMHP

DMT

DOC

DOET

DOI

Eticiklidinas (Eticyclidine, PCE)

Etriptaminas (Etryptamine)

FLEA

3-Fluormetkatinonas (3-fluoromethcathinone)

Gyslotasys vykylis ir jo dalys (Argyreia nervosa plant)

HU-210 (6aR)-trans-3-(1,1-dimethylheptyl)-6a,7,10,10a-tetrahydro-1-hydroxy-6,6-dimethyl-6H-dibenzo[b,d]pyran-9-methanol)

JWH-018 (Naphthalen-1-yl)(1-pentyl-1H-indol-3-yl)methanone arba (Naphthalene-1-yl)(1-butyldol-3-yl)methanone)

Katinonas (Cathinone)

Lizergidas (+)-Lysergide, LSD, LSD-25)

MBDB

MDE

MDMA

Mefedronas (Mephedrone, 4-methylmethcathinone, 1-(4-methylphenyl)-2-methylaminopropan-1-one)

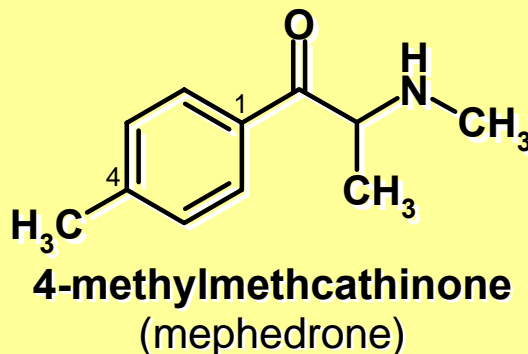
Meskalinas (Mescaline)

4-Metilaminoreksas (4-methylaminorex)

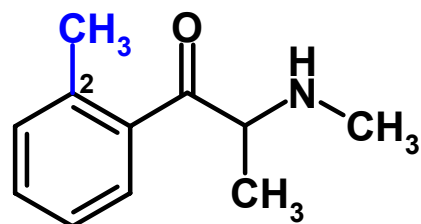
Metkatinonas (Methcathinone)

The problem of methylnmethcathinone isomers & homologues

BUT:

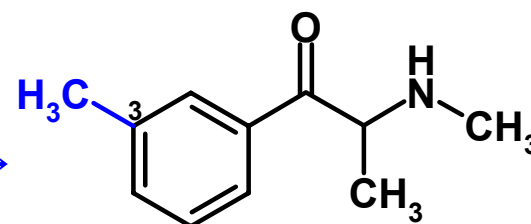


To be regulated in all
EU member states
typically according to
individual listing system



2-methylmethcathinone

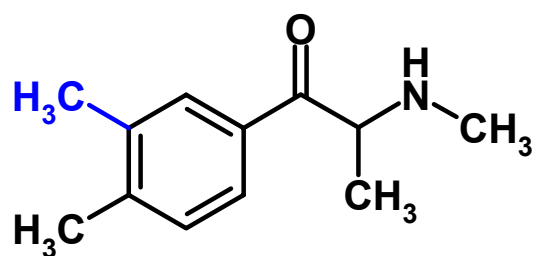
← positional isomers →



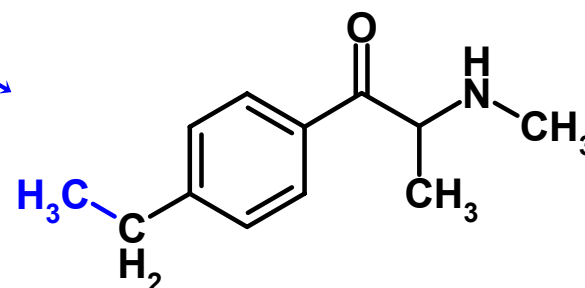
3-methylmethcathinone

?

← homologues →



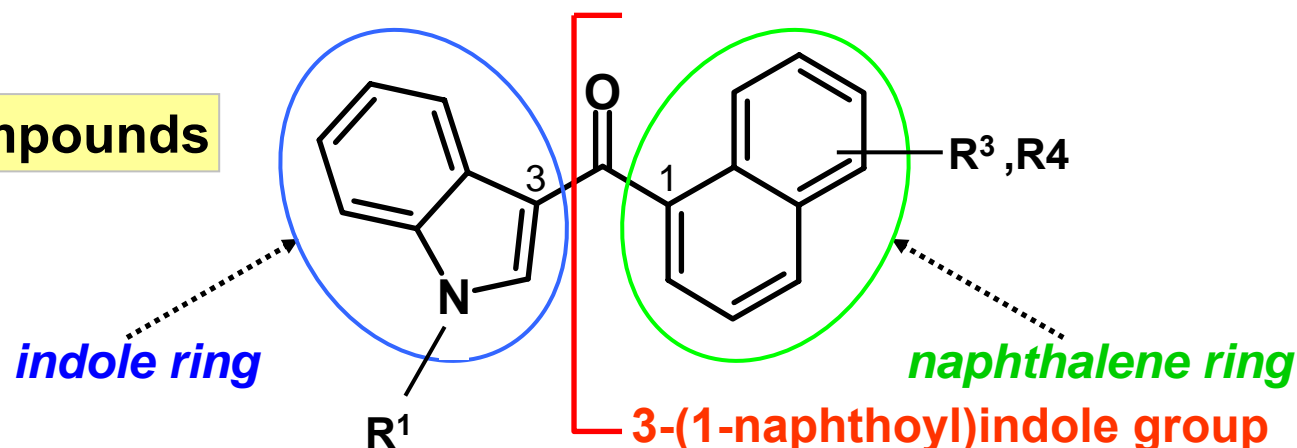
3,4-dimethylmethcathinone



4-ethylmethcathinone

Regulation of indolyl naphthyl ketone cannabinoids according to the generic system in the United Kingdom

JWH compounds



Generic definition:

„Any compound structurally derived from 3-(1-naphthoyl)indole ... by substitution at the nitrogen atom of the indole ring by alkyl, alkenyl, cycloalkyl-methyl, cycloalkylethyl or 2-(4-morpholinyl)ethyl whether or not further substituted in the indole ring to any extent , whether or not substituted in the naphthyl ring to any extent.”

Applicability criteria for generic control

- **the chemical structure of the psychoactive substance is known**
- **there are several compounds already described in the literature**
- **the chemical structures are related and relatively simple**
- **the appearance of further such substances on the drug market is expected**
- **the chemical family can be defined by a simple general chemical formula**

A novel regulation of psychoactive substances – Ireland

Criminal Justice (Psychoactive Substances) Act 2010 (No. 22, 14 July 2010)

Prohibition of sale, etc. of psychoactive substances.

3.— A person who sells / imports / exports a psychoactive substance knowing or being reckless as to whether that substance is being acquired or supplied for human consumption shall be guilty of an offence

Prohibition of sale of certain objects

Prohibition of advertising of psychoactive substances, etc.

“psychoactive substance” means a substance, product, preparation, plant, fungus or natural organism which has, when consumed by a person, the capacity to—

- (a) produce stimulation or depression of the central nervous system of the person, resulting in hallucinations or a significant disturbance in, or significant change to, motor function, thinking, behaviour, perception, awareness or mood, or**
- (b) cause a state of dependence, including physical or psychological addiction;**

Spotting new substances emerging on the horizon

The appearance of new 'legal highs'

- **can be anticipated based on medicinal chemistry literature**, old & new
- **can be noticed on the Internet**
- **can be identified by regular analysis of seized or market samples**
- **can be suspected by getting information from users**
- **can trigger regulation** once composition & risks are clarified
- **cannot** probably **be prevented** but can be discouraged / deterred
- ...
- **will** certainly **cause some surprises & concerns**

DRUG VIGILANCE!

Challenges in detecting new drugs

- **Analytical reference materials and/or spectral data are usually lacking**
- **Forensic/toxicological laboratories routinely use G/MS & IR spectroscopy but for new substances access to NMR spectroscopy is often needed**
- **Examining non-scheduled drugs is not a priority for forensic science organisations in some countries**
- **Detection of new substances in body fluids is especially difficult**
- **The composition of marketed product could change**
- **The Early Warning System is reactive**

Partly based on L. A. King

MESSEGE

Analytical

Synthetic

Forensic

Chemistry: a central science in analysing, solving
and preventing 'drug problems'

A photograph of a person wearing a cowboy hat, a red shirt, a dark jacket, and blue jeans, riding a white horse. The horse is standing on a dirt path in a desert landscape. In the background, there are large, arid hills under a clear blue sky. A yellow speech bubble with the text "Thank you!" is positioned above the rider. A large, flat-topped cactus is visible in the foreground on the right.

Thank you!

Wirikúta, Mexico: home of the peyotl cactus, *Lophophora williamsii*