



# Research chemical drugs: the state of the art

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# Research Chemicals



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## Liquid chromatography–atmospheric pressure ionization electrospray mass spectrometry determination of “hallucinogenic designer drugs” in urine of consumers

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Roberta Pacifici<sup>a</sup>, Piergiorgio Zuccaro<sup>a</sup>, Magi Farré<sup>b,c</sup>, Rafael de la Torre<sup>b,d</sup>

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### Abstract

A procedure based on liquid chromatography–mass spectrometry (LC–MS) is described for determination of 3,4-methylenedioxy-methamphetamine (MDMA), 2,5-dimethoxy-4-methyl-phenethylamine (2C-D), 4-bromo-2,5-dimethoxy- $\beta$ -phenethylamine (2C-B), 1-(8-bromo-2,3,6,7-tetrahydrobenzo[1,2-b:4,5-b'] difuran-4-yl)-2-aminoethane (2C-B-Fly), 4-ethylthio-2,5-dimethoxy- $\beta$ -phenethylamine (2C-T-2), 4-iodo-2,5-dimethoxy- $\beta$ -phenethylamine (2C-I), and 4-ethyl-2,5-dimethoxy- $\beta$ -phenethylamine (2C-E), 1-(*m*-chlorophenyl)piperazine (*m*-CPP), 4-hydroxy-*N,N*-diisopropyltryptamine (4-OH-DIPT) and 4-acetoxy-*N,N*-diisopropyltryptamine (4-acetoxy-DIPT) in urine of consumers using 3,4-methylenedioxypropylamphetamine (MDPA) as internal standard.

# Research Chemicals

- Research Chemical vs. Designer drugs
  - Different mean by different people
  - Some times used as interchangeable terms

# Research Chemicals



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## “Research Chemicals”: Tryptamine and Phenethylamine Use Among High-Risk Youth

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<sup>2</sup>*Community, Health Outcomes, Intervention and Research Program, The Saban Research Institute, Childrens Hospital Los Angeles, Los Angeles, California, USA*

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### Abstract

Tryptamines and phenethylamines are two broad categories of psychoactive substances with a long history of licit and illicit use. Profiles of users of recently emerging tryptamines and phenethylamines are nonexistent, however, since surveillance studies do not query the use of these substances. This manuscript describes the types, modes of administration, onset of use, and context of use of a variety of lesser known tryptamines and phenethylamines among a sample of high-risk youth. Findings are

# Definition

- **Designer drugs**
  - Substances intended for recreational use which are chemical congeners of illicit drugs or derivatives of approved drugs that are synthesized by “**street chemists**” with the purpose of circumventing the law
- **Research Chemicals (RC)**
  - Substances intended for recreational use which are chemical congeners of illicit drugs or derivatives of approved drugs that are synthesized by “**fine chemistry companies**” that are sold for research or analytical purposes. Purpose is circumventing the law

# Designer drugs. Classification

- Phenylethylamines (amphetamine – mescaline derivatives): entactogen and hallucinogenic amphetamines: MDMA, 2-CE
- Tryptamines: 5-MeO-tryptamine
- Ephedrines: methcathinone or ephedrone, methylnmethcathinone or mephedrone
- Piperazines: 1-benzylpiperazine or BZP
- Pyrrolidinophenones: MPPP
- Opioids: fentanyl (alfa-methyl-fentanyl) and meperidine derivatives (MPTP)
- Arylhexilamines: phencyclidine derivatives (PCE, TCP)
- Cannabinoids: spice drugs (JWH-018)
- Methaqualone: mecloqualone
- Others (GHB)

# Designer drugs: Spice drugs

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## Spice (drug)

From Wikipedia, the free encyclopedia

**Spice** is a brand name for a mixture of [herbs](#) that has been sold in [smartshops](#) in Europe, Canada and other parts of the world since around 2002, purportedly as an [incense](#), as well as over the Internet as an "herbal smoking blend". Even though the manufacturer officially warns against human ingestion of Spice, it is usually smoked for its [cannabis](#)-like effects which are believed to be caused by a mixture of synthetic [cannabinoid](#) drugs. Several different "flavours" of Spice have been marketed which have been shown to contain different proportions of the synthetic cannabinoid active ingredients, and reportedly produce subtly different effects. A large number of competing products made by other manufacturers have also subsequently appeared around the world.



A bag of Spice

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    - 2.3 [France](#)
    - 2.4 [Poland](#)
    - 2.5 [World](#)
- Camphora mangina*, *Nymphaea odorata*, *Scutellaria nana*, *T. scutellaria*, *Leonurus sibiricus*, *Leonurus japonicus*, *Leonurus japonicus*, *Leonurus japonicus*. However when the product was analysed by laboratories in Germany and elsewhere, it was found that many characteristic "fingerprint" molecules expected to be present from the claimed plant ingredients could not be located, and also large amounts of synthetic [tocopherol](#) present. This suggested that the actual ingredients might not be the same as what was on the packet, and a German government risk assessment of the product conducted in November 2008 concluded that it was unclear whether the plant ingredients were, where the synthetic tocopherol had come from, and whether the subjective cannabis-like effects were produced by any of the claimed plant ingredients or instead might possibly be caused by a synthetic cannabinoid drug.<sup>[1]</sup>

### Synthetic cannabinoid ingredients

On December 15th 2008, it was announced by German pharmaceutical company THCPHarm, that [JWH-018](#) had been found as an active component in at least three versions of the supposedly "herbal" smoking blend, cannabis substitute drug Spice, which had been sold in a number of countries around the world since 2002 as an "incense" or legal substitute for marijuana.<sup>[2][3][4][5]</sup>

On January 19th 2009, it was announced by the [University of Freiburg](#) in Germany that the other main active substance in Spice was an undisclosed [analogue](#) of the synthetic cannabinoid [CP 47,497](#).<sup>[6]</sup> On the 22nd January 2009, CP 47,497 along with its dimethylheptyl and dimethylnonyl [homologues](#), were added to the German controlled drug schedules ("Betäubungsmittelgesetz") and their analogues had apparently been used in the various different varieties of Spice.

Another potent synthetic cannabinoid, [HU-210](#), has been reported to have been found in Spice seized by the [US Customs & Border Protection](#)<sup>[9]</sup> but no independent confirmation of this result has yet been made.

### Legal status

# Designer drugs: Spice drugs



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## JWH-018

From Wikipedia, the free encyclopedia

**JWH-018 (1-pentyl-3-(1-naphthoyl)indole)** is an [analgesic](#) drug from the aminoalkylindole family, which acts as a [cannabinoid](#) agonist at both the CB<sub>1</sub> and CB<sub>2</sub> receptors, with some selectivity for CB<sub>2</sub>.<sup>[1][2][3]</sup> It produces effects in animals very similar to those of THC itself, but with a shorter duration of action.<sup>[*citation needed*]</sup>

On December 15th 2008, it was announced by German pharmaceutical company **THC Pharm**, that JWH-018 was found as one of the active components in at least three versions of the herbal blend **Spice**, which has been sold as an incense, in a number of countries around the world since 2002.<sup>[4][5][6]</sup>

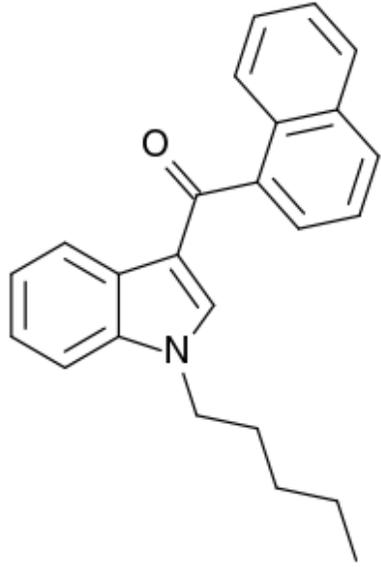
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**Austria** [\[edit\]](#)

The Austrian Ministry of Health announced on 18th December 2008 that Spice would be



JWH-018

Systematic (IUPAC) name	Naphthalen-1-yl-(1-pentylindol-3-yl)methanone
Identifiers	
CAS number	209414-07-3

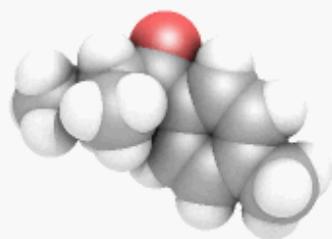
# Research Chemicals. Classification

- Phenylethylamines (amphetamine – mescaline derivatives): entactogen and hallucinogenic  
amphetamines: MDMA
- Ephedrines: methcathinone or ephedrone,  
methyImethcathinone or mephedrone
- Tryptamines: 5-MeO-tryptamine

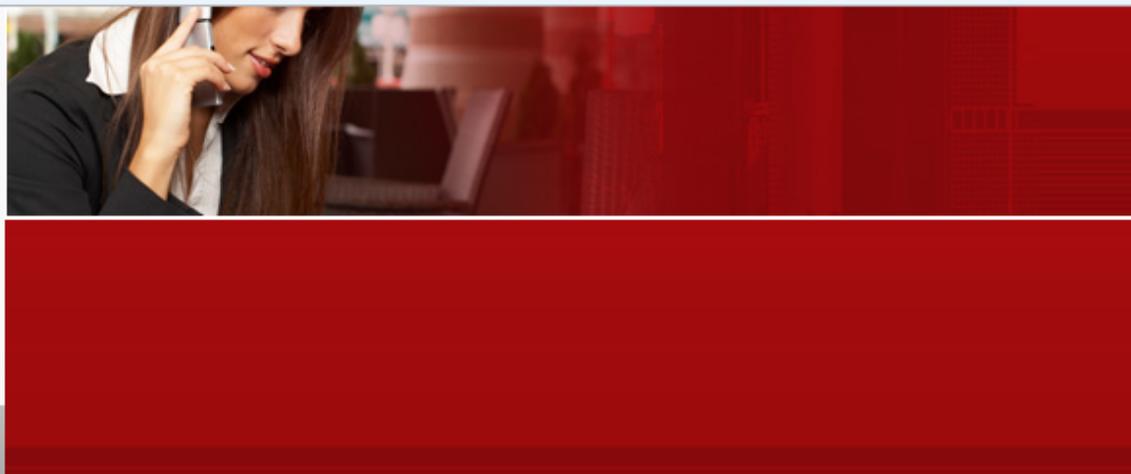
# Distribution

- **Designer drugs**
  - Illegal market
  - Massive production and low quality
  - Local or wide distribution by drug dealers
  - Prize depends of disponibility
  - Millions of recreational users
- **Research Chemicals**
  - Legal or pseudo legal market
  - Limited production and high quality product
  - Disclaimer advice
  - Wide distribution trough internet sites
  - Powder capsulated by users
  - Prize high (depends of purity)
  - Selected population. Closed forums (in Spain)

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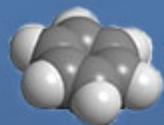
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<b>TRC03 - 4Acetoxy-DIPT</b> N,N-Diisopropyl-4-Acetoxytryptamine hydrochloride CAS ??? 99.0%	500MG 1GM 5GM	\$ 175.00 \$ 300.00 \$ 1400.00	<a href="#">ADD</a> <a href="#">ADD</a> <a href="#">ADD</a>
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## Methylenedioxypropylamphetamine

From Wikipedia, the free encyclopedia

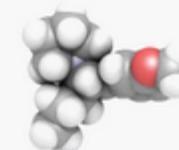
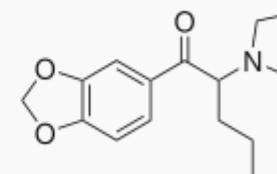
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**Methylenedioxypropylamphetamine** (**MDPV**, **MDPK**<sup>[*citation needed*]</sup>, "**Sonic**"<sup>[*citation needed*]</sup>, "**Magic**"<sup>[*citation needed*]</sup>, "**Monkey Dust**"<sup>[*citation needed*]</sup>, etc) is a [psychoactive drug](#) with [stimulant](#) and [aphrodisiac](#) properties via acting as a [norepinephrine-dopamine reuptake inhibitor](#) (NDRI), reportedly with four times the [potency](#) of [methylphenidate](#) (Ritalin, Focalin, Concerta).<sup>[1]</sup> MDPV has no history of FDA approved [medical use](#) but has been sold since around 2007.<sup>[2]</sup>

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### Appearance



Methylenedioxypropylamphetamine

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    - e.g. **alfa-methyl-fentanyl**
  - New chemicals with scarce data in animal or in humans (not controlled)
    - e.g. **phenylethylamines and PHIKAL**
  - Defective synthesis (impurities or contamination) and/or wrong synthesis
    - e.g. **MPPP and MPTP-induced parkinsonism**
  - Fake
- Research Chemicals
  - Fake internet sites

# Designer drugs

*Movement Disorders*  
Vol. 23, No. 15, 2008, pp. 2224–2231  
© 2008 Movement Disorder Society

## Parkinsonism and Dystonia Caused by the Illicit Use of Ephedrone—A Longitudinal Study

Marianna Selikhova, MD, PhD,<sup>1,2</sup> Ljuda Fedoryshyn, MD, PhD,<sup>3</sup> Yuri Matviyenko, MD, PhD,<sup>4</sup> Irena Komatska, MD,<sup>5</sup> Marianna Kyrylychuk, MD,<sup>3</sup> Leszek Krolicki, MD, PhD,<sup>6</sup> Andrzej Friedman, MD, FRCP,<sup>7</sup> Andrew Taylor, MD, PhD,<sup>8</sup> H. Rolf Jäger, MD, PhD,<sup>9</sup> Andrew Lees, MD, FRCP,<sup>1\*</sup> and Yanush Sanotsky, MD, PhD<sup>2</sup>

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<sup>3</sup>Department of Neurology, Lviv Regional Clinical Hospital, Lviv, Ukraine

<sup>4</sup>Department of Neurology, Danylo Halysky Lviv National Medical University, Lviv, Ukraine

<sup>5</sup>Department of MRI, Central Hospital of the Lviv Regional Railway, Lviv, Ukraine

<sup>6</sup>Department of Nuclear Medicine, Medical University of Warsaw, Warsaw, Poland

<sup>7</sup>Department of Neurology, Medical University of Warsaw, Warsaw, Poland

<sup>8</sup>Centre for Clinical Science and Measurement, University of Surrey, Guildford, Surrey, United Kingdom

<sup>9</sup>Department of Neuroimaging, Institute of Neurology, UCL, United Kingdom

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## A Parkinsonian Syndrome in Methcathinone Users and the Role of Manganese

Ainārs Stepens, M.D., Ināra Logina, Ph.D., Viesturs Liguts, Ph.D., Pauls Aldiņš, M.D., Ilze Ekšteina, M.D., Ardis Platkājis, Ph.D., Inese Mārtiņšone, M.Sci., Elmārs Tērauds, M.D., Baiba Rozentāle, Ph.D., and Michael Donaghy, F.R.C.P.

ABSTRACT

### BACKGROUND

A distinctive extrapyramidal syndrome has been observed in intravenous methcathinone (ephedrone) users in Eastern Europe and Russia.

### METHODS

We studied 23 adults in Latvia who had extrapyramidal symptoms and who had injected methcathinone for a mean ( $\pm$ SD) of 6.7 $\pm$ 5.1 years. The methcathinone was manufactured under home conditions by potassium permanganate oxidation of ephedrine or pseudoephedrine. All patients were positive for hepatitis C virus, and 20 were also positive for the human immunodeficiency virus (HIV).

### RESULTS

The patients reported that the onset of their first neurologic symptoms (gait disturbance in 20 and hypophonia in 3) occurred after a mean of 5.8 $\pm$ 4.5 years of methcathinone use. At the time of neurologic evaluation, all 23 patients had gait disturbance and difficulty walking backward; 11 patients were falling daily, and 1 of these patients used a wheelchair. Twenty-one patients had hypophonic speech in

From the Department of Neurology (A.S., I.L.), the Department of Anesthesiology and Intensive Care (V.L.), the Department of Classical Infectology, Tuberculosis, and AIDS (P.A., I.E., B.R.), the Department of Radiology (A.P.), the Institute of Occupational and Environmental Health (I.M.), and the Department of Psychiatry and Addiction (E.T.), Riga Stradins University, Riga, Latvia; and the Department of Clinical Neurology, University of Oxford, Oxford, United Kingdom (M.D.). Address reprint requests to Dr. Donaghy at the Department of Clinical Neurology, University of Oxford, Level 3, West Wing, John Radcliffe Hospital, Headington, Oxford OX3 9DU, United Kingdom, or at joanna.wilkinson@cneuro.ox.ac.uk.

N Engl J Med 2008;358:1009-17.

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# Research Chemicals

- Summary
  - Relatively new phenomena
  - Epidemiology ?????
  - Users with some degree of expertise looking for new experiences
  - Subgroups of users connected to harm reduction organizations
  - Internet-based
  - Future ?????



**Grazie**  
**Thank you for your attention**

**Magí Farré and Marta Torrens**

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