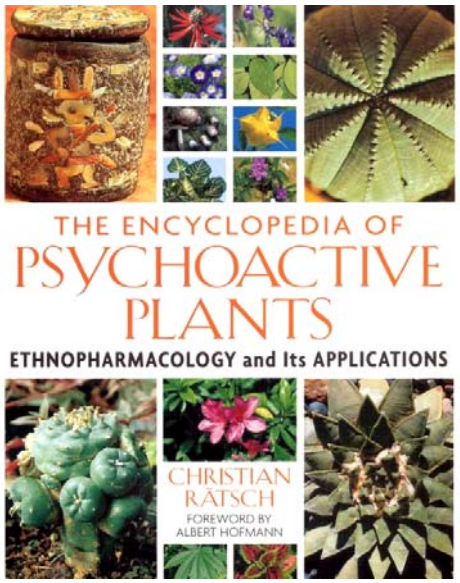
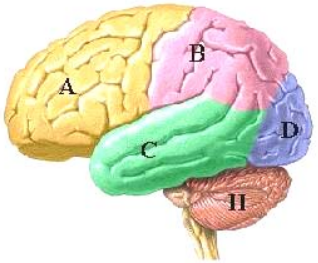




Emerging "herbal drugs" and their ingredients:

Are they all natural?

István Ujváry, PhD

*i*Kem BT

&

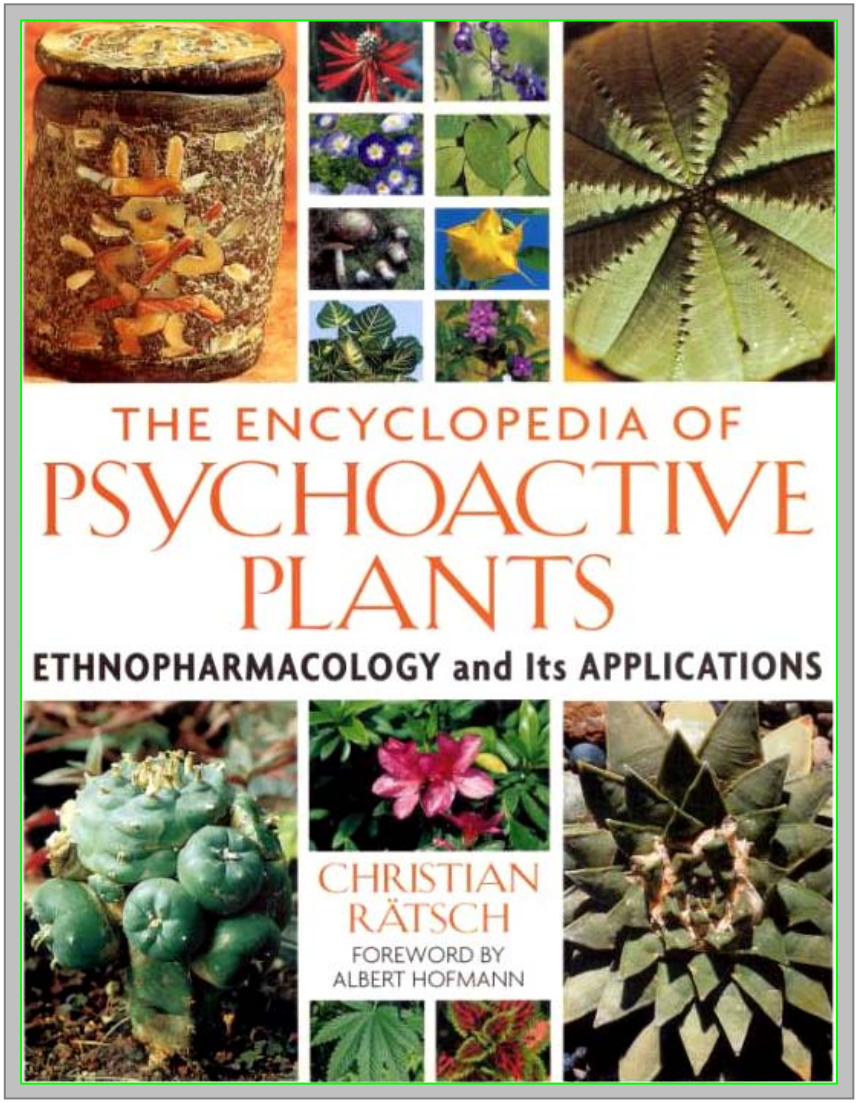
Budapest University of Technology and Economics

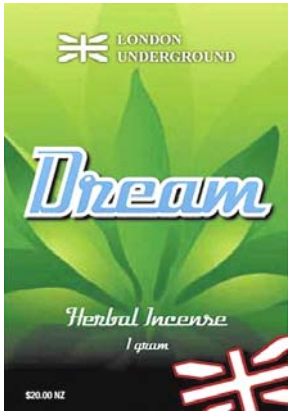
New trends in the area of drug prevention and control. Vilnius, 10 November, 2010

Why do some people use “herbal highs”?

- *legal substitutes of illicit drug*
- *novel type of psychoactivity*
- *new & trendy*
- *perceived to be safe (natural)*
- *other reasons?*

Natural psychoactive drugs *versus* ‘herbal highs’





List of cannabis substitutes according to Rätsch (1998)

The Encyclopedia of Psychoactive Plants ①

Botanical Name	*Popular name*	*Drug*	*Place/Culture*
Alchornea floribunda	niando	root	Africa
Anethum graveolens	dill	herbage	U.S.A.
Argemone mexicana	prickly poppy	leaves	Mexico
Artemisia mexicana	estafiate	herbage	Mexico
Calea zacatechichi	zacatechichi	herbage	Mexico, U.S.A.
● *Canavalia maritima* (*Canavalia obtusifolia*)	frijolillo	leaves	Mexico
Capsicum frutescens	paprika	rotten fruits	U.S.A.
Catharanthus roseus	periwinkle	leaves	Florida
Cecropia mexicana [syn. *Cecropia obtusifolia*]	chancarro	leaves	Mexico (Veracruz)
Cestrum laevigatum (cf. *Cestrum parqui*)	maconha	leaves	Brazil
Cymbopogon densiflorus	lemongrass	flower extract	Tanzania
Daucus carota	carrot	herbage	U.S.A.
Helichrysum spp.	strawflower	herbage	
Helichrysum foetidum	stinking ~	herbage	Zulu/Africa
Helichrysum stenopterum		herbage	Africa
Hieracium pilosella	håret høgeurt, hawkweed	herbage	Denmark
Hydrangea paniculata	hydrangea	leaves	U.S.A.
Hydrangea spp.	hydrangea	flowers, leaves	U.S.A.

- continued -

List of cannabis substitutes according to Rätsch (1998)

The Encyclopedia of Psychoactive Plants ②

Botanical Name	*Popular name*	*Drug*	*Place/Culture*
Lactuca sativa	lettuce	leaves	U.S.A.
Lactuca serriola	wild lettuce	leaves	U.S.A.
Lactuca virosa	wild lettuce (thickened juice)	lactucarium	U.S.A.
● *Leonotis leonurus*	wild dagga	herbage	Hottentots
● *Leonurus sibiricus*	marijuanillo	herbage	Mexico (Chiapas)
Mimosa spp.	dormilona	herbage	San Salvador
Myristica fragrans	nutmeg	seed, aril	U.S.A., Europe
Nepeta cataria	catnip	herbage	cosmopolitan
Nepeta spp.	catnip	herbage	cosmopolitan
Petroselinum crispum	parsley	flowering herbage	U.S.A., Europe
Piper auritum	gold pepper	leaves	Belize
Sceletium tortuosum	kougoed	herbage, roots	South Africa
Sida acuta	malva amarilla, chichibe	herbage	Mexico, Belize
Sida rhombifolia	escobilla	herbage	Mexico
Turnera diffusa	damiana	herbage	cosmopolitan
● *Zornia latifolia*	maconha brava	desiccated leaves	Brazil
● *Zornia diphylla*	maconha brava, yerba de la víbora	leaves	Brazil
unidentified	*Pupusa* / *Chachalana*	herbage	Atacama/Chile
	canna	herbage	South Africa

What is *Spice*?

On product label:

***Spice* is an exotic incense blend that releases a rich aroma when burned.**

Enjoy the enchanting aroma of *Spice*.

Not for human consumption. Keep out of reach of children.

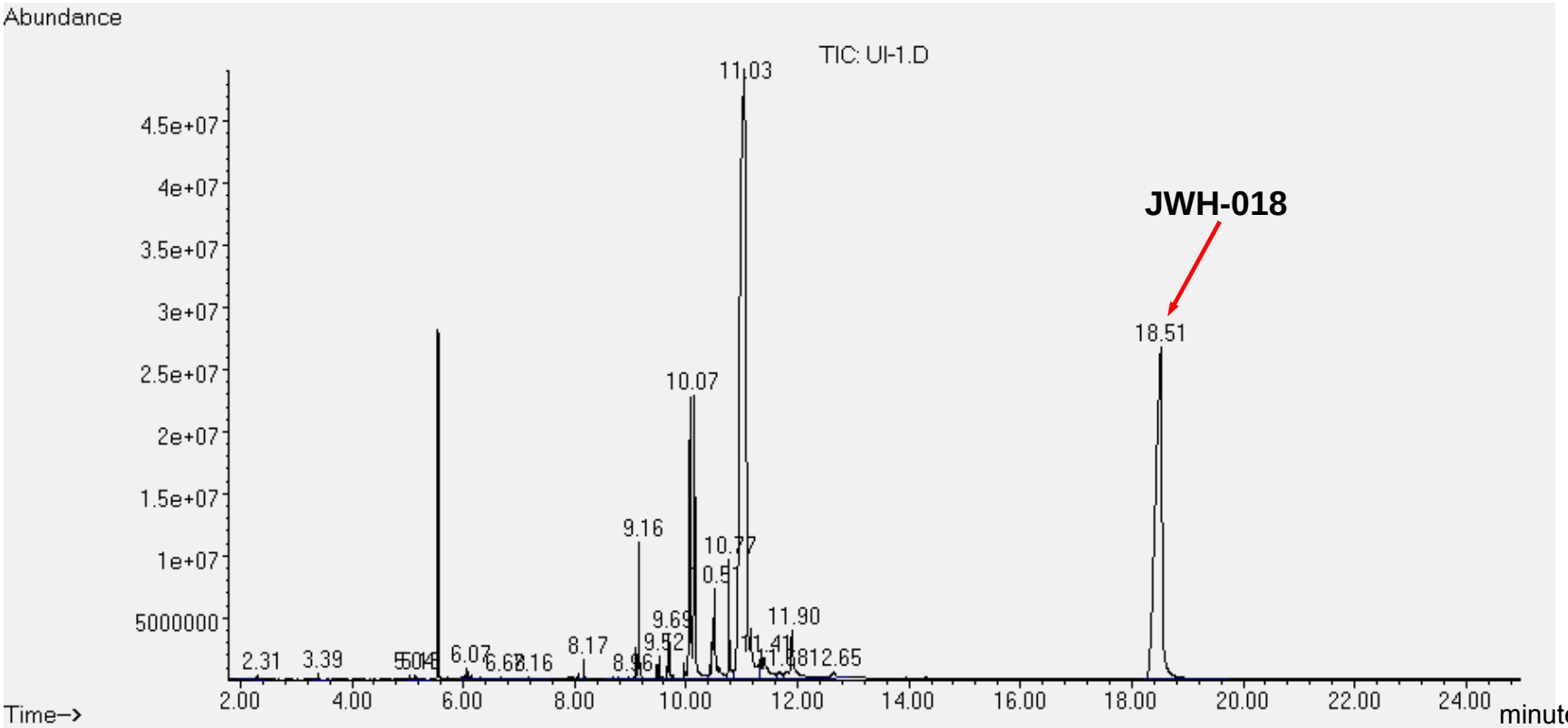
Other "**herbal incense mixtures**":

Gorilla, *Yucatan Fire*, *Smoke*, *Skunk*, *Genie*, *Sence*, *SenCation*, *Galaxy Gold*, *Space Truckin*, *Solar Flare*, *Moon Rocks*, *Blue Lotus*, *Space Rubin*, *Aroma*, *Pep Spice Twisted*, *Scope*, *Magic*, *Forest Humus*, *Smoke XXX*, *etc.*

In the USA: ***K2***

Forensic analysis of *Aroma* herbal mixture sold in Hungary

Gas Chromatography–Mass Spectrometry total ion chromatogram



Institute for Forensic Sciences, Budapest, Hungary (Jan 2009)

Heavy metal & PAH content *Spice Diamond* in Hungary

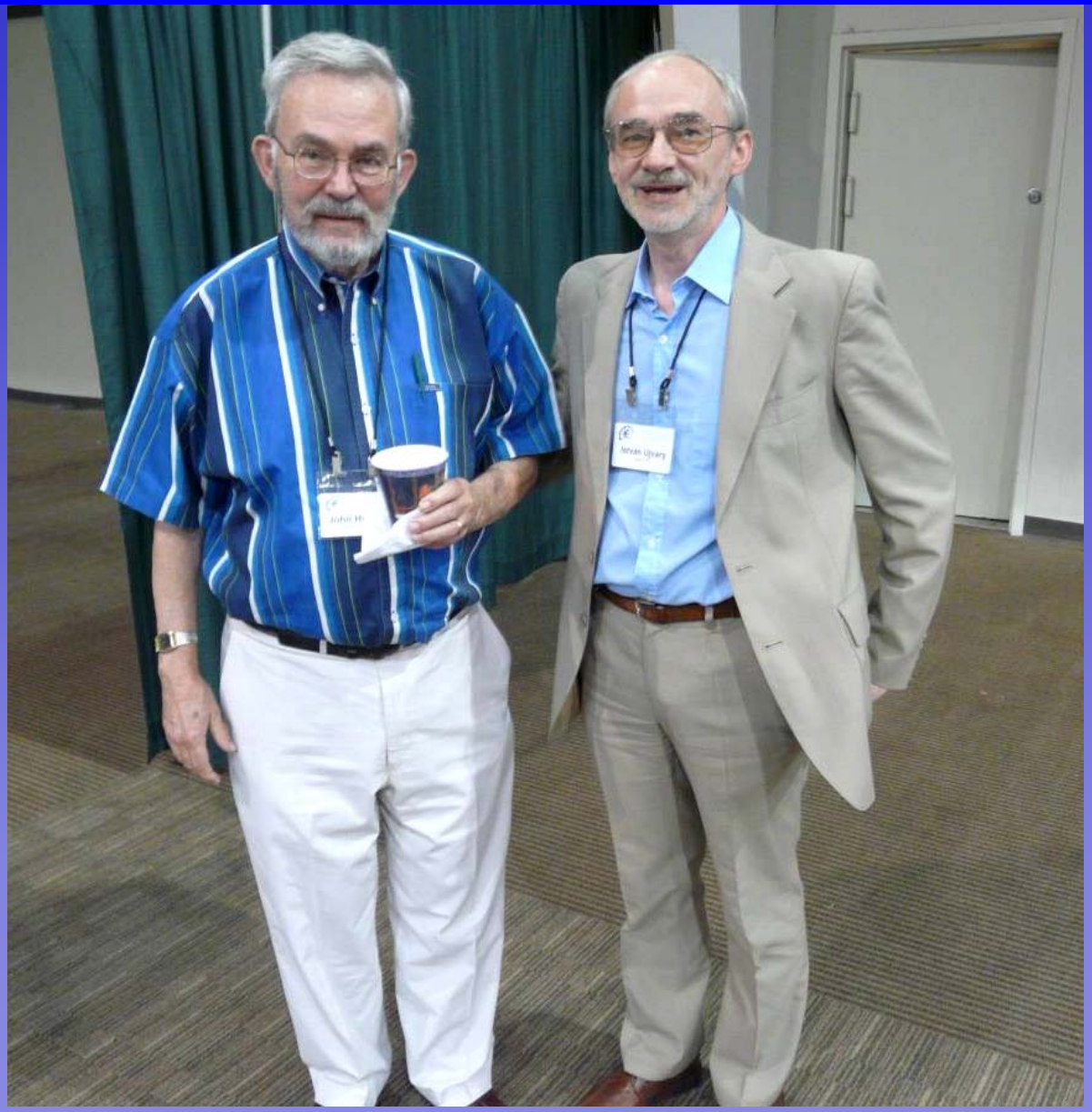
Substance	dried herb, μg/g	smoke, μg/m³
Heavy metals		
Arsenic	<0.08*	<10
Lead	0.80*	<2
Cadmium	0.10*	<2
Chromium	0.90	<6
Polycyclic Aromatic Hydrocarbons		
benzo(b)fluoranthene	-	<0.013*
benzo(k)fluoranthene	-	<0.002*
benzo(a)pyrene	-	<0.002*
benzo(g,h,i)perylene	-	<0.008*
indeno(1,2,3-cd)pyrene	-	<0.056*

*Below the maximum allowed level (*e.g.*, in vegetables or air)

National Public Health and Medical Officer Service, Budapest-Szeged, Hungary (Jan 2009)

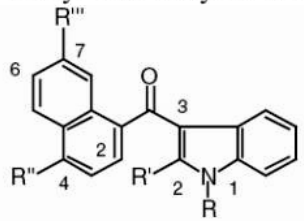
John. W. Huffman

ICRS 19th Annual Symposium Chicago, 2009. július 7-11.



Structure–activity relationships for 1-alkyl-3-(1-naphthoyl)indoles at the cannabinoid CB_1 and CB_2 receptors: steric and electronic effects of naphthoyl substituents. New highly selective CB_2 receptor agonists

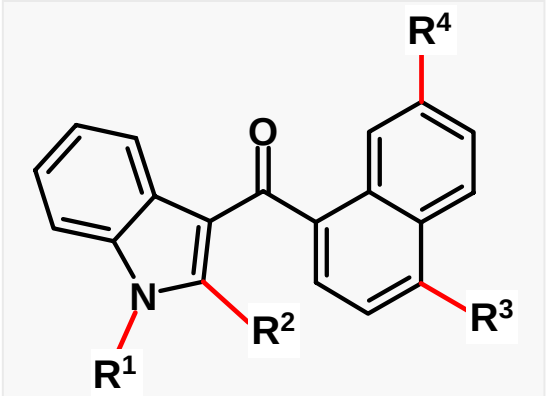
John W. Huffman,[a,*] Gulay Zengin,[a] Ming-Jung Wu,[a] Jianzhong Lu,[a] George Hynd,[a] Kristen Bushell,[a] Alicia L. S. Thompson,[a] Simon Bushell,[a] Cindy Tartal,[b] Dow P. Hurst,[b] Patricia H. Reggio,[b] Dana E. Selley,[c] Michael P. Cassidy,[c] Jenny L. Wiley[c] and Billy R. Martin[c]



Compound	Synthesis	R	R′	R″	R‴	K_i (nM) CB_1	CB_2	Ratio CB_2/CB_1[g]
Δ^9-THC (**1**)						41 ± 2[a]	36 ± 10[b]	1.1
WIN-55,212-2 (**4**)						1.9 ± 0.1[b]	0.28 ± 0.16[b]	6.8
JWH-072[c]		C_3H_7	H	H	H	1050 ± 55[c]	170 ± 54[c]	6.2
JWH-015[c,d] (**6**)		C_3H_7	CH_3	H	H	164 ± 22[c]	13.8 ± 4.6[b]	11.9
JWH-018[c]		C_5H_{11}	H	H	H	9 ± 5[c]	2.9 ± 2.6[c]	3.3
JWH-007[c,d] (**5**)		C_5H_{11}	CH_3	H	H	9.5 ± 4.5[c]	2.9 ± 2.6[c]	3.3
JWH-120 (**41**)	B	C_3H_7	H	CH_3	H	1054 ± 31	6.1 ± 0.7	173
JWH-148	A	C_3H_7	CH_3	CH_3	H	123 ± 8	14 ± 1.0	8.8
JWH-122[e]		C_5H_{11}	H	CH_3	H	0.69 ± 0.5[e]	1.2 ± 1.2	0.6
JWH-149[e]		C_5H_{11}	CH_3	CH_3	H	5.0 ± 2.1[e]	0.73 ± 0.03	6.8
JWH-212	C	C_3H_7	H	C_2H_5	H	33 ± 0.9	10 ± 1.2	3.3
JWH-211	C	C_3H_7	CH_3	C_2H_5	H	70 ± 0.8	12 ± 0.8	5.8
JWH-210	C	C_5H_{11}	H	C_2H_5	H	0.46 ± 0.03	0.69 ± 0.01	0.67
JWH-213	C	C_5H_{11}	CH_3	C_2H_5	H	1.5 ± 0.2	0.42 ± 0.05	3.6
JWH-180	C	C_3H_7	H	C_3H_7	H	26 ± 2	9.6 ± 2.0	2.7
JWH-189	C	C_3H_7	CH_3	C_3H_7	H	52 ± 2	12 ± 0.8	4.3
JWH-182	C	C_5H_{11}	H	C_3H_7	H	0.65 ± 0.03	1.1 ± 0.1	0.6
JWH-181	C	C_5H_{11}	CH_3	C_3H_7	H	1.3 ± 0.1	0.62 ± 0.04	2.1
JWH-239	C	C_3H_7	H	C_4H_9	H	342 ± 20	52 ± 6	6.6
JWH-241	C	C_3H_7	CH_3	C_4H_9	H	147 ± 20	49 ± 7	3.0
JWH-240	C	C_5H_{11}	H	C_4H_9	H	14 ± 1	7.2 ± 1.3	1.9
JWH-242	C	C_5H_{11}	CH_3	C_4H_9	H	42 ± 9	6.5 ± 0.3	6.5
JWH-076	A	C_3H_7	H	H	CH_3	214 ± 11	106 ± 46	2.0
JWH-046[f] (**8**)		C_3H_7	CH_3	H	CH_3	343 ± 38[f]	16 ± 5[f]	21
JWH-048[f] (**9**)		C_5H_{11}	CH_3	H	CH_3	10.7 ± 1.0[f]	0.49 ± 0.1[f]	22
JWH-235	B	C_3H_7	H	H	C_2H_5	338 ± 34	123 ± 34	2.7
JWH-236	B	C_3H_7	CH_3	H	C_2H_5	1351 ± 204	240 ± 63	5.6
JWH-234	B	C_5H_{11}	H	H	C_2H_5	8.4 ± 1.8	3.8 ± 0.6	2.2
JWH-262	B	C_5H_{11}	CH_3	H	C_2H_5	28 ± 3	5.6 ± 0.7	5.0

Indolyl naphthyl ketone cannabinoids – '*Spice*' ingredients

JWH-compounds



chemical & biological similarity:
CB1 receptor agonists

Code	R^1	R^2	R^3	R^4	CB1 affinity constant K_i (nM)
Δ^9-THC	not applicable				**10.2**
JWH-015	C_3H_7	CH_3	H	H	**164**
JWH-018	C_5H_{11}	H	H	H	**9**
JWH-019	C_6H_{13}	H	H	H	**9,8**
JWH-048	C_5H_{11}	CH_3	H	CH_3	**11**
JWH-073	C_4H_9	H	H	H	**8.9**
JWH-081	C_5H_{11}	H	CH_3O	H	**1.2**
JWH-122	C_5H_{11}	H	CH_3	H	**0.69**
JWH-210	C_5H_{11}	H	C_2H_5	H	**0.46**
JWH-398	C_5H_{11}	H	Cl	H	**2.3**

Narcotic drug was cultivated at a Tiszavasvári family house

13 Oct 2010

Hemp was cultivated in the garden of a family house presumably for the production of marijuana. The leaves and buds of the plant were regularly harvested, dried, prepared for sale and also used by the growers themselves. The „quadruped cop" sniffed ca. 800 grams of drug-suspect herbal material hidden in the house.

No controlled drug was found in plants

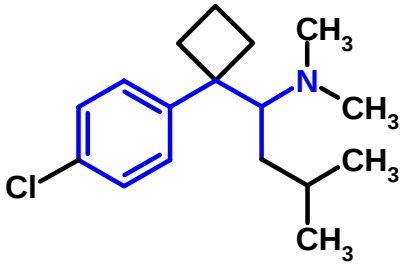
18 Oct 2010

Preliminary chemical analysis did not detect the presence of illegal narcotic substances [THC] in the hemp preparation seized in Tiszavasvári. ***??***

Synthetic weight-loss medicine in herbal drugs

Lida DaiDaihua

bitter orange extract
Tuckahoe (*Fu Ling*)
cassia seed
alflalfa
sweet potato fibre



sibutramine

In January 2010, EMEA recommended supension of sales of **sibutramine** (Reductil®, Lindaxa®, Reduxade®, Meridia®, etc.) due to cardiovascular risk.

Yet, preparations still available on the Internet **:-(**

for example Müller D *et al* (2009) *Dtsch Arztebl Int*, **106**, 218

Newer substances – *HERBALS, PSEUDO-HERBALS*

Opiate substitutes* (due to possible heroin shortage?)

kratom

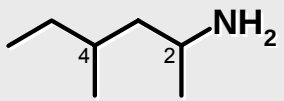
Known traditional plant preparations (mild psychoactivity)

passion flower (*Passiflora incarnata*)

canary grass (*Phalaris* species)

kava (*Piper methysticum*)

wild lettuce, lettuce opium (*Lactuca virosa*)

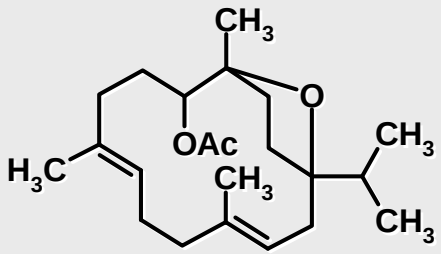


geranamine

(‘dimethylamylamine’**)**

allegedly from geranium oil

stimulant; on the WADA list



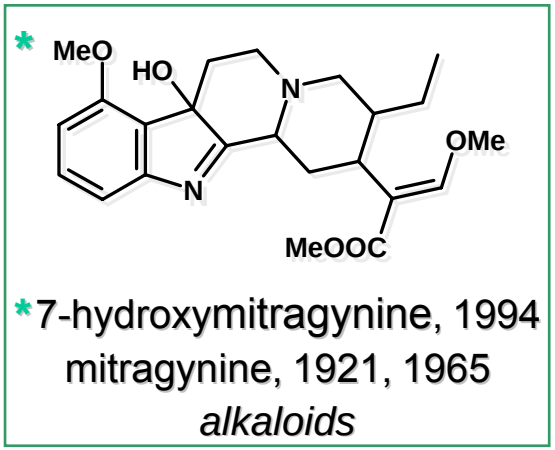
frankincense/olibanum: **incensole acetate**

Boswellia resin; *anxiolytic*, *antidepressant*

Kratom, a Southeast Asian stimulant-narcotic drug

(*Mitragyna speciosa*; krathom, ithang, ketum, biak, puošnioji vožte)

chewing leaves
drinking tea
bitter



*7-hydroxymitragynine, 1994
mitragynine, 1921, 1965
alkaloids

Use: leaves chewed or made into tea (rarely smoked); powdery extract (15x–50x) also available

Effects (dose dependent): 5-15 g leaves: *mild stimulant*

> 15 g leaves: ***sedative*, euphoriant**, antitussive, antidiarrheal, anorectic, analgetic (self-treatment of chronic pain); antimalarial, *etc.*

opium substitute (self-treatment of opioid witdrawal)

Regular use: depression, insomnia, dependence, tolerance; cross-tolerance to morphine

Mode of action: **opioid receptor agonist**; 7-hydroxymitragynine orally more active than morphine
noradrenergic & serotonin systems also affected

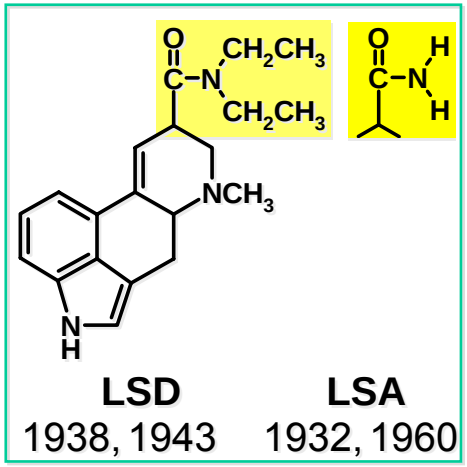
Regulation: Thailand (1943), Myanmar (1993), Malaysia (2003), Australia (2005), Lithuania (2008), Denmark (2009), Latvia (2009), Poland (2009), Romania (2010)

Lysergamide (ergine, LSA, LA-111) **from morning glory seeds**

morning glory or ololiuqui: the 3rd most important ritual hallucinogen of the Aztecs

ergot on rye

Claviceps purpurea



LSD 1938, 1943 **LSA** 1932, 1960

morning glory, badoh negro

Ipomoea violacea (*I. tricolor*)

ololiuqui, ***Rivea corymbosa***

Hawaiian baby woodrose

Argyreia nervosa

Alkaloids (LSA, isoLSA, ergometrine, *etc.*): 0.012% in *Rivea*, 0.06% in *Ipomoea,* 0.3% in *Argyreia* seeds

Dose: 1-2 mg LSA in 3-8 g (100-250) *Ipomoea & Rivea* seeds; 2-3 g (4-6) *Argyreia* seeds; extracts

Effects: LSA ≠ LSD (not hallucinogenic), narcotic-hypnotic (fatigue, apathy, feeling of unreality); alters perception; other alkaloid components are slightly psychostimulatory

Side effects (seeds) **vary**; nausea, vomiting, diarrhea, salivation, dizziness, tachycardia, hypertension, vasoconstriction, numbness of extremities; occasional psychosis

Abuse potential: appears to be low, due to mild effects with dysphoria & unpleasant side effects

Ergot alkaloids in *Ipomoea* & *Argyreia* plants are produced by *Claviceps*-like endophyte fungi not by the plant itself (2006)

Regulation examples (LSA/seeds): USA (LSA, 1966), Australia (LSA), Italy (*An*, *Iv* & *Rc*, 2007), Lithuania (LSA, *An* & *Iv*, 2009), Netherlands (LSA), Poland (*An* & *Rc*, 2009), Russia (*An*, 2009), …

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