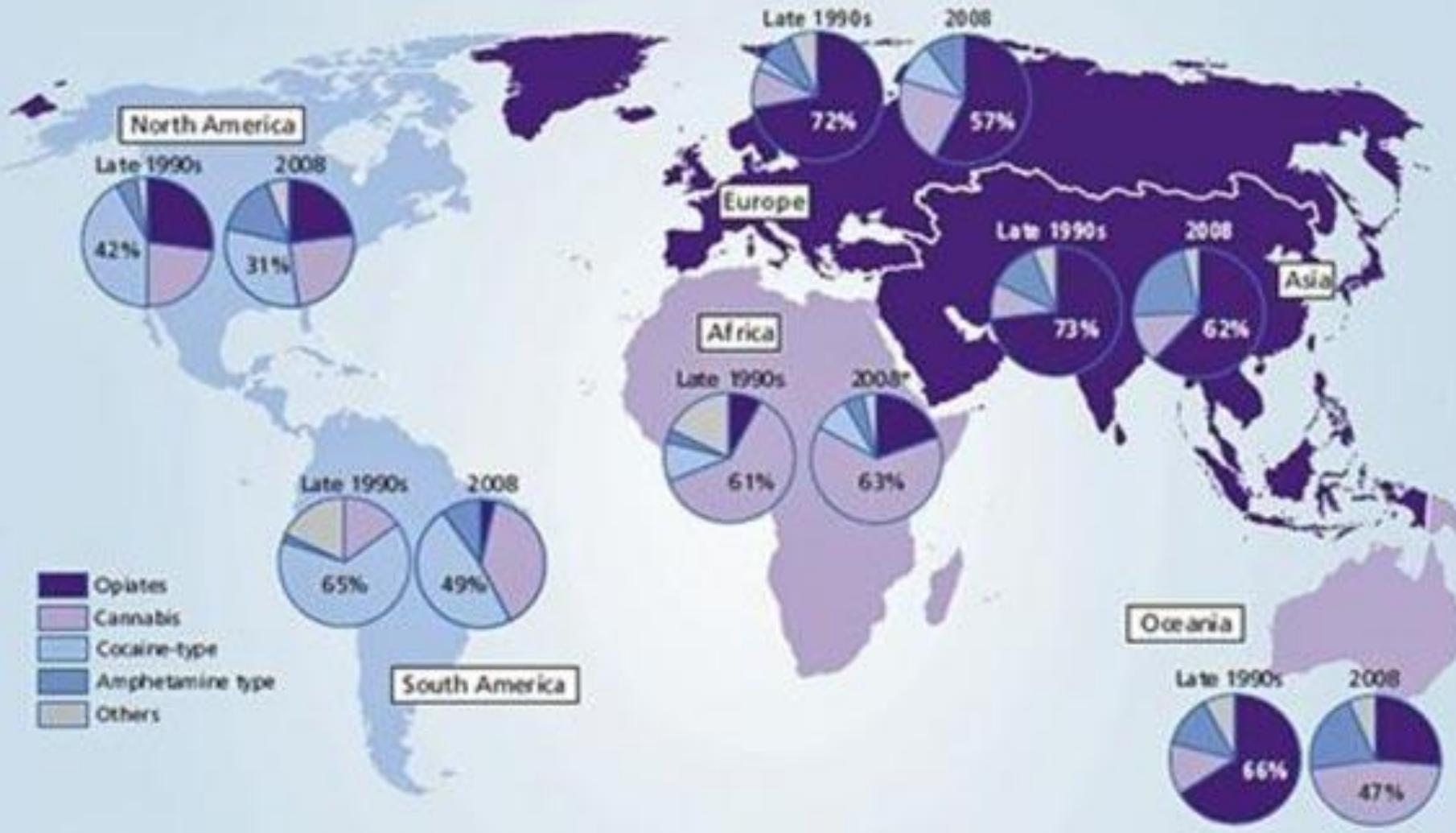
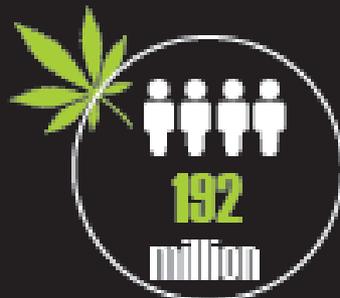


Trends in use of narcotic compounds



Trends in use of narcotic compounds

Number of past-year users in 2016



cannabis



opioids



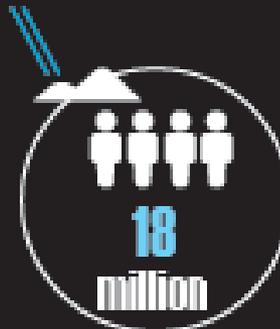
**amphetamines and
prescription stimulants**



"ecstasy"



opiates



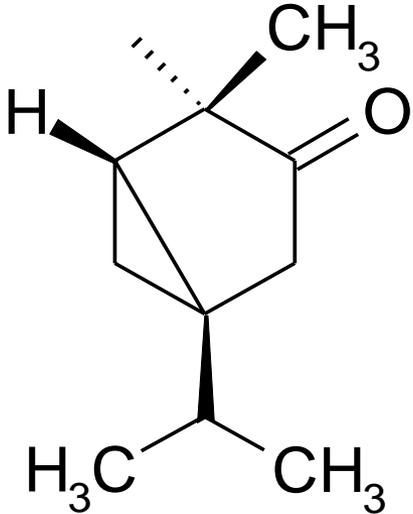
cocaine

Estimates of money volumes in the "retail" market of Europe

- Year 2013
 - In total 24.3 miliard Euro (21-31)
 - Cannabis 38 % (9.8 miliard)
 - Heroin 28 % (6.8 miliard)
 - Cocain 24 % (5.7 miliard)
 - Amphetamines 8 %
 - MDMA 3 %
- „Catching“
 - Cannabis, cocain, MDMA

- Thujon

- Natural mixture of isomers α, β (33% α , 67% β)
- *Artemisia absinthium*,
Artemisia vulgaris
Salvia officinalis,
Salvia sclarea
- *Tanacetum vulgare*
- *Thuja occidentalis*
- Folk medicine:
 - Abortive, emenagogue, digestive, carminative, antiphlogistic, anthelmintic



- Analgesic, analeptic, antidepressive
- Toxicity:
 - CNS effect
 - Tonic-clonic convulsions, cumulative effect
 - Absinthism
 - » hyperexcitability, hallucinations
 - Nephrotoxicity (degenerative changes)
 - Hepatotoxicity
 - Dependent on dosage and sensitivity
- Mechanism of effect:
 - Blocker of GABA_A chloride channel (similar to picrotoxine)
 - α -thujon 2.3 times more effective than β -thujon
 - Low affinity to cannabinoid receptor
 - Metabolism:
 - Reduction of keton to hydroxyl, excretion via urine
 - 7-OH-thujon, dehydrothujon – also active
- Absinthism
- Oscar Wilde:
 - „After the first glass [of absinthe] you see things as you wish they were. After the second, you see things as they are not. Finally, you see things as they really are, and that is the most horrible thing in the world.“

French method
Bohemian method

Blanche
Verte
Absenta
Hausgemacht
Bohemian-style



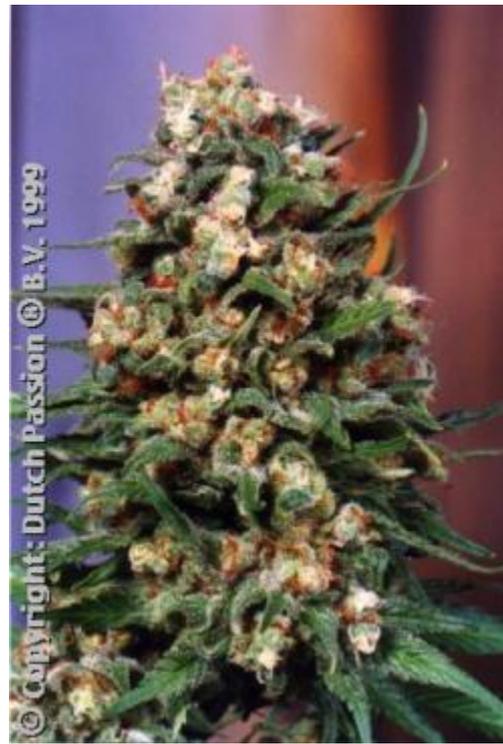
Cannabis spp.

- *Cannabis indica* Lam., *C. sativa* L., *C. ruderalis* Janisch.
- **Shen-nung** (2737-2697 B.C.)
 - malaria, constipation, rheumatism, Gynecologic problems
- **Vine with hemp resin**
 - Surgical anaesthetic
- **European folk medicine**
 - asthma, cough therapy
 - epilepsy, sleep disorders, convulsions
 - pain, rheumatism
 - Externally
 - Skin inflammations and infections
- **Today's application**
 - glaucoma
 - Lowering of intraocular pressure
 - nausea, vomiting, anorexia
 - cancer (*in vitro* and *in vivo* start of apoptosis – malignant glioma, breast cancer)
 - Parkinson disease, sclerosis multiplex
 - Immunomodulation – Crohn disease
 - Antibiotic and antiviral effect

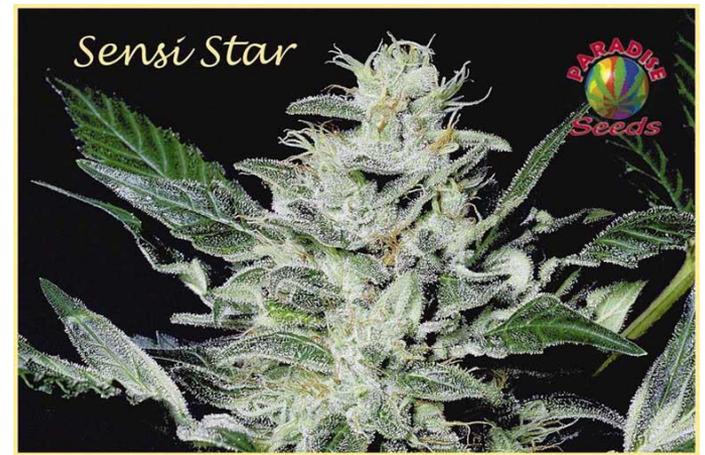




AK-47



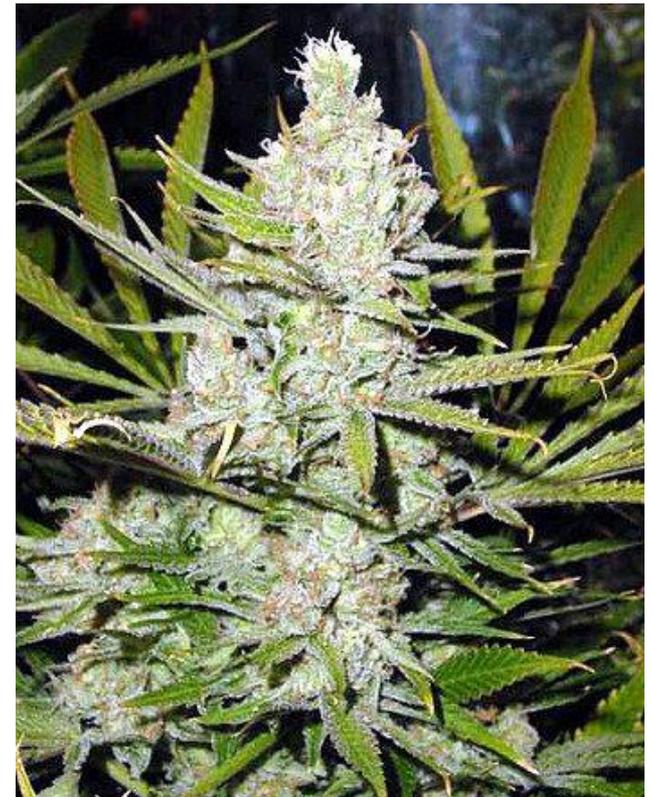
Skunk n.1



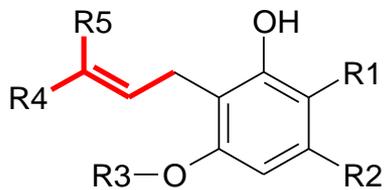
Sensi Star



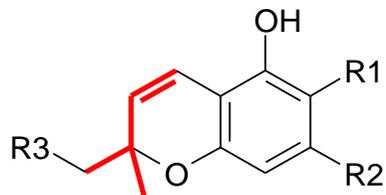
Jack Herer



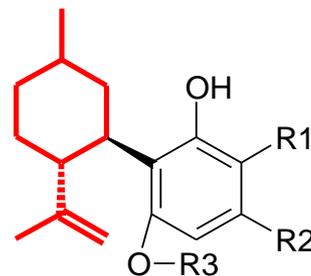
Nothern Lights



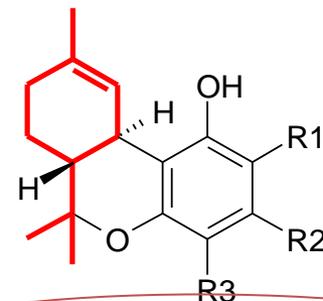
CBG-type cannabinoids



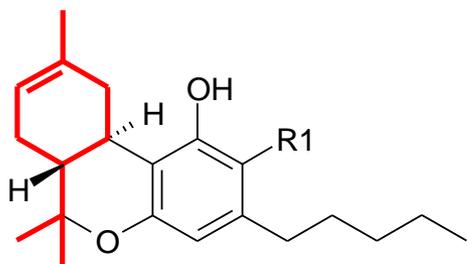
CBC-type cannabinoids



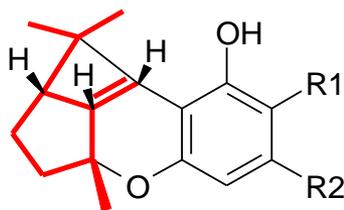
CBD-type cannabinoids



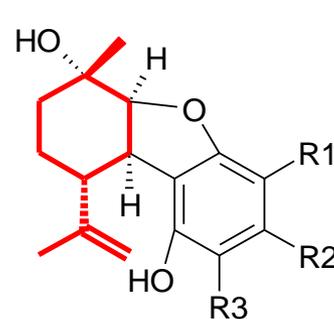
δ^9 -trans-THC-type cannabinoids



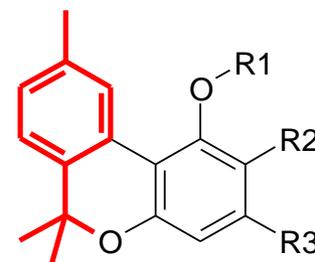
δ^8 -trans-THC-type cannabinoids



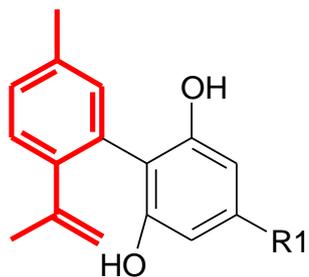
CBL-type cannabinoids



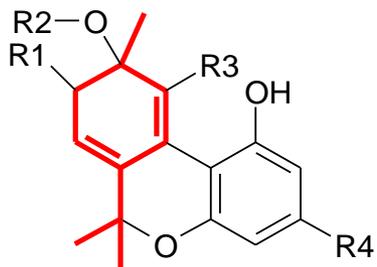
CBE-type cannabinoids



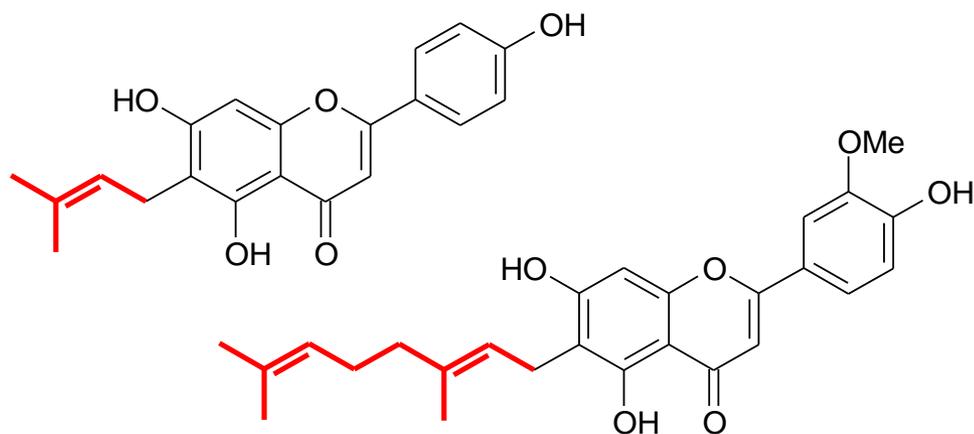
CBN-type cannabinoids



CBND-type cannabinoids

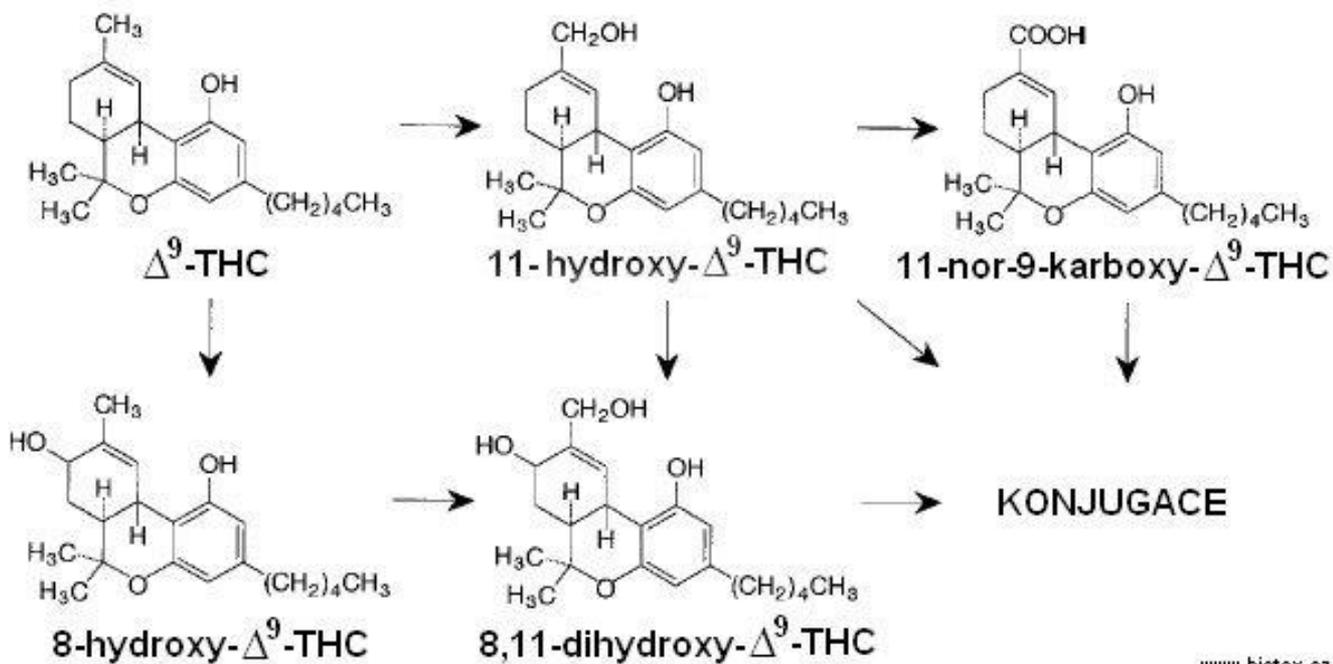


CBT-type cannabinoids

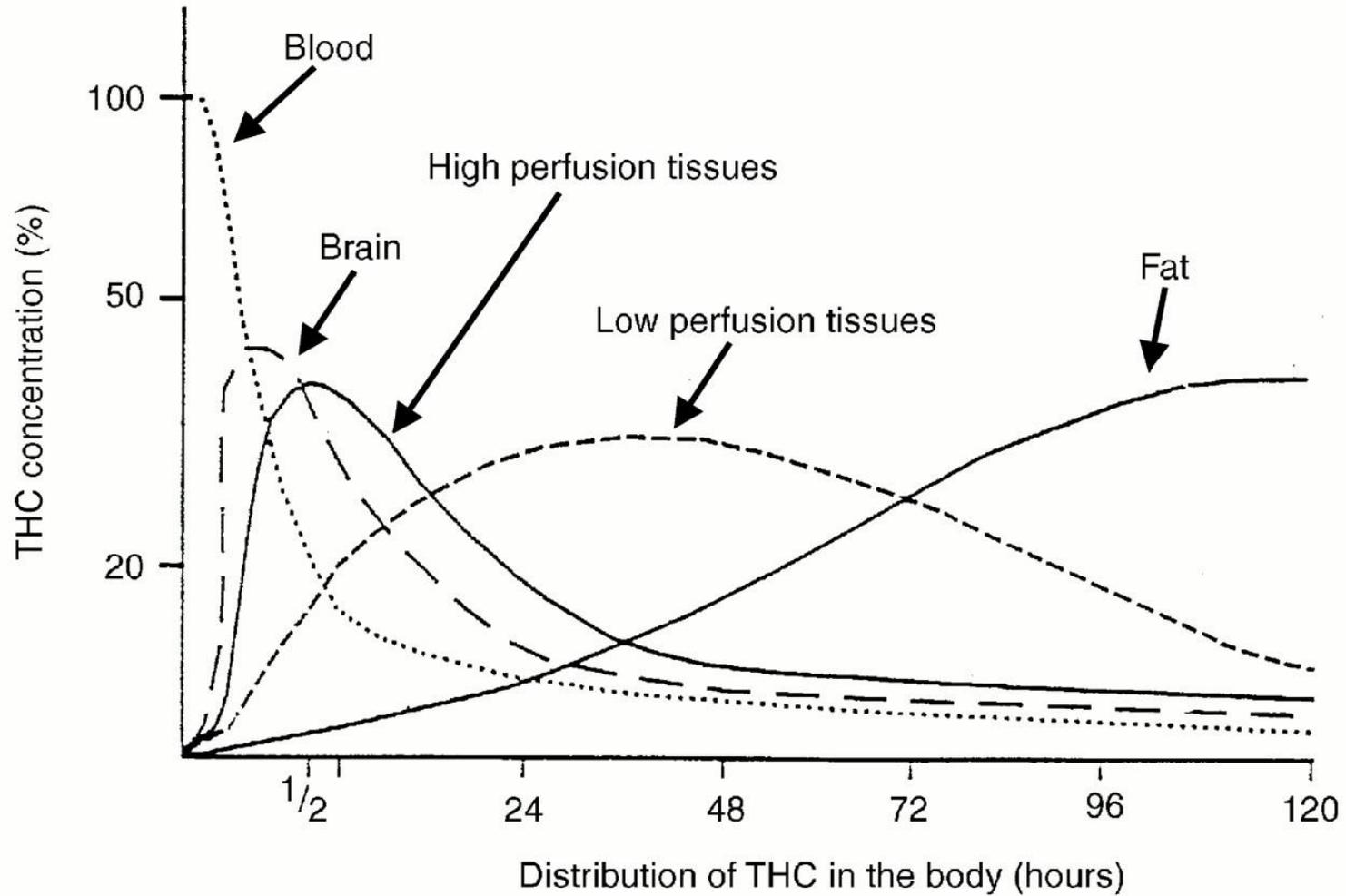


- **Cannabis as drug – THC content**
 - **Marihuana** (female inflorescence) cca 1% THC
 - **Hašhish** (resin obtained by chipping or munching of female inflorescence) cca 5 %
 - **Hashish oil** (extract) 20% THC
- **Main contain THC** (levorotary form), CBD (canabidiol) – sedative and antibiotic effect, canabinol (CBN) – high amount of CBN - effect similar to THC, but with feeling of fatigue and drowsiness
- **THC is oxidized by air oxygen** (higher temperature increases effect) to non-active compounds
 - Should be stored in cold and hermetically closed wessels
- **THC soluble in fat and alcohol** (lipophilic), non well in water

- **Biotransformation**
 - Cumulation in organism
 - Half-time 27 days



Distribution of THC in the body.



C. HEATHER ASHTON BJP 2001;178:101-106

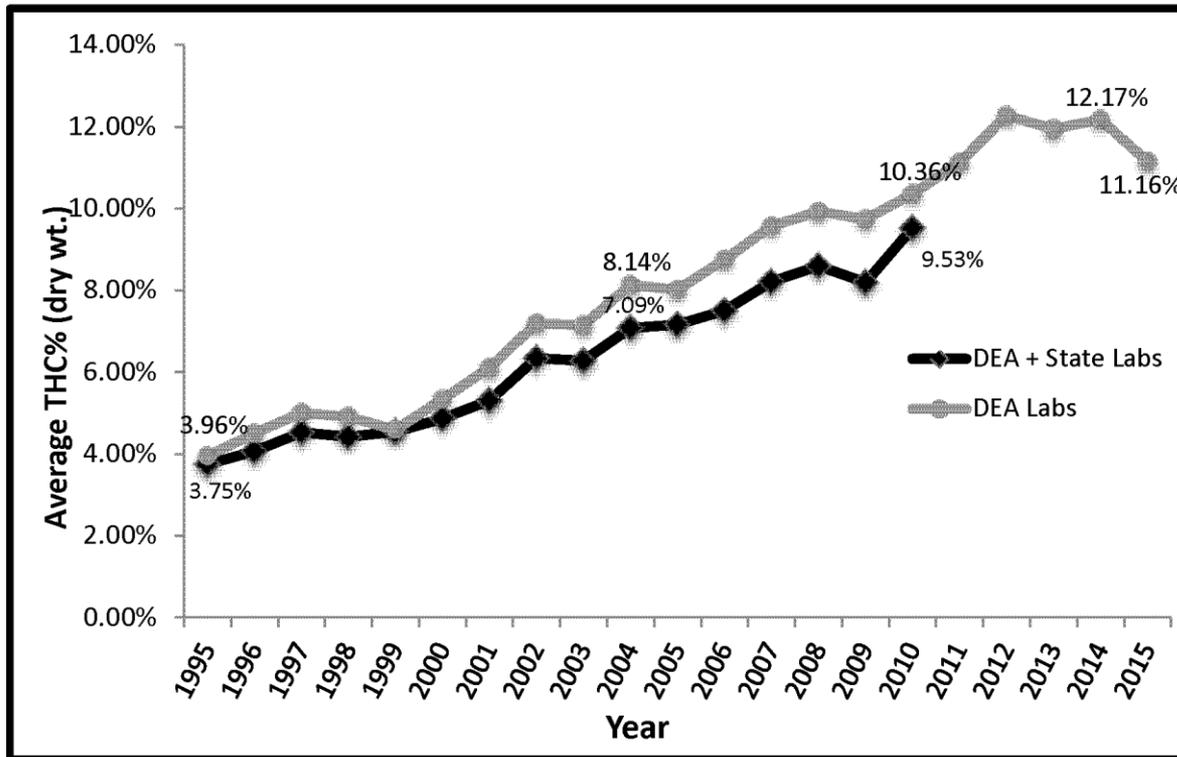
THE BRITISH JOURNAL
OF PSYCHIATRY

- Cannabis as a drug
 - Way of application
 - Inhalation, smoking
 - Peroraly



Figure 1. Average Percentage of Δ^9 -THC in Samples of Seized Marijuana (1995 – 2015)*

(Source: The University of Mississippi Potency Monitoring Program, Quarterly Report # 131)



*PMP discontinued analysis of state samples after 2010.

**Data for 2015 are incomplete. Figure 1 contains percentage of Δ^9 -THC data through Dec. 22. Due to lack of funding, 4,177 samples haven't yet been analyzed.

- **Cannabis as drug – effects**

- **Psyche** – effect on CNS

- Canabinoid receptors
 - THC
 - Endogenous cannabinoids

- **Lungs** – smoking

- Similar to tobacco
- Little bit different style of smoking
- 1 joint – 9 cigarettes

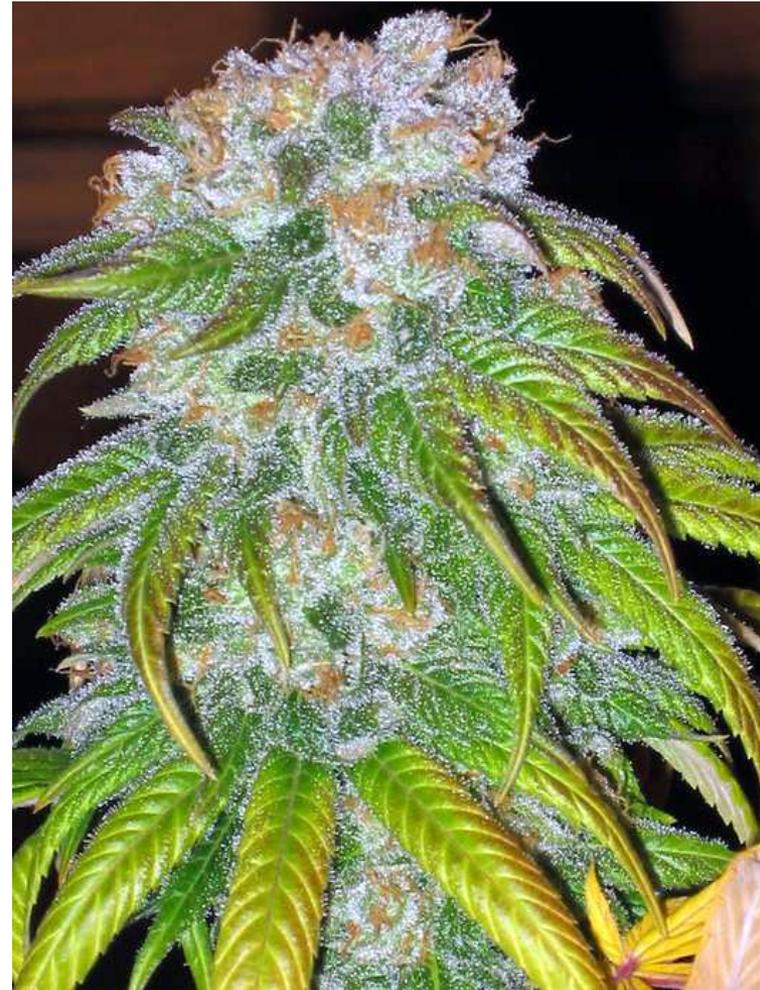
- **Fertility**

- Effect on spermias

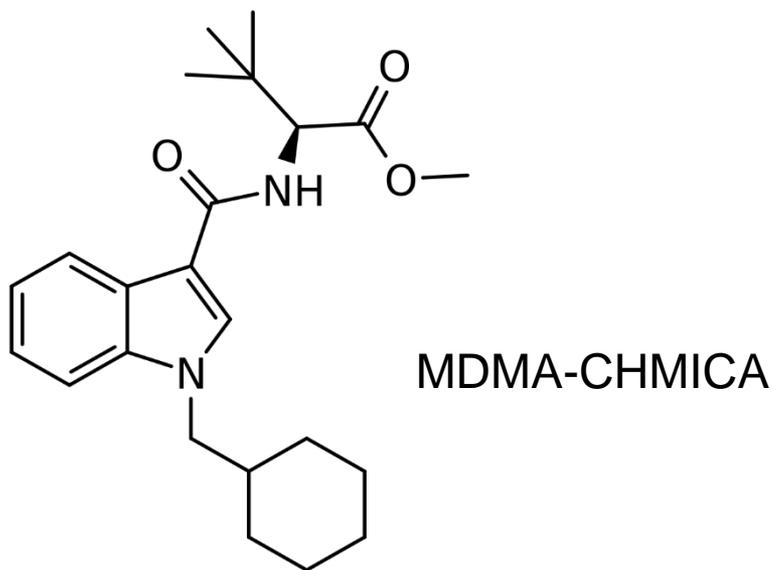
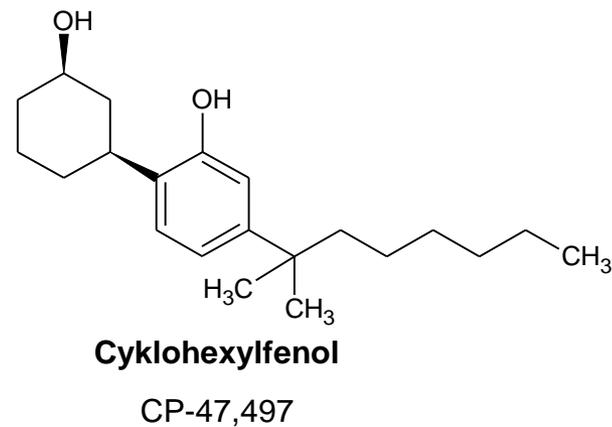
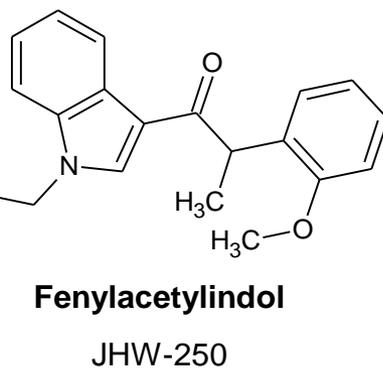
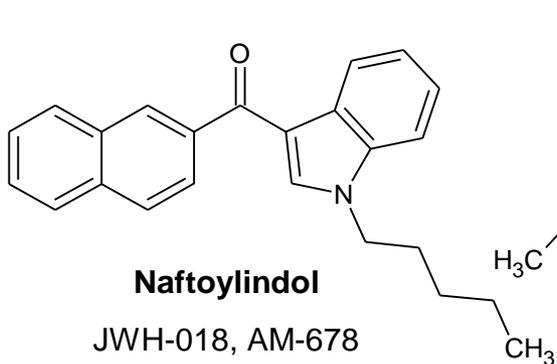
- **Effect on foetus**

- Slower development of children

- **Risk of higher occurence of schizophrenia?**

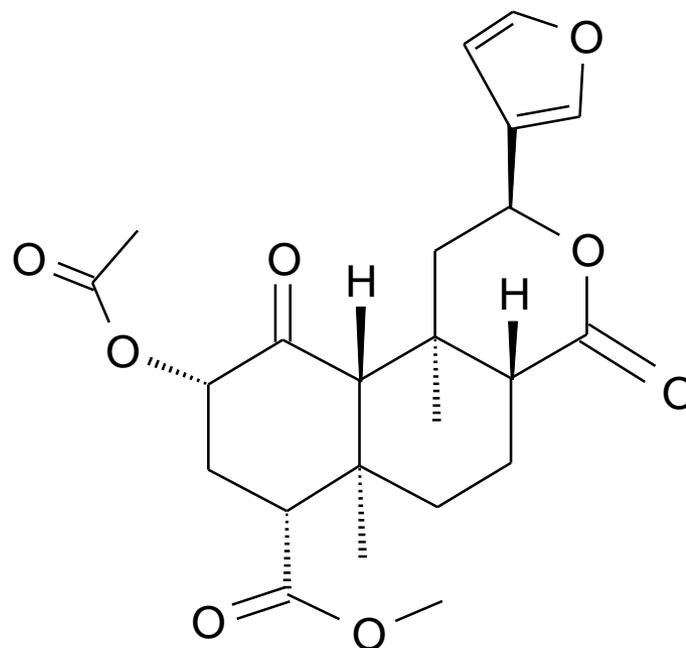


Syntethic cannabinoids



– Salvinorin A

- Diterpen of clerodadiene type
- *Salvia divinorum* Lamiaceae
- Hallucinogenic
- Shamanic plant, *Hierba de la Pastora*



– ***Salvia divinorum***

- 100 grams of drug
 - Chewing
 - Maceration
- Smoking of dry leaves and extracts
- **Effect**
 - Euphoric states
 - Colored visions and hallucinations
 - Rush

– **Salvinorin A**

- Selective inhibitor kappa-opioid receptors
- Agonist of D2 receptors
- Do not affect 5-HT_{2A} receptor

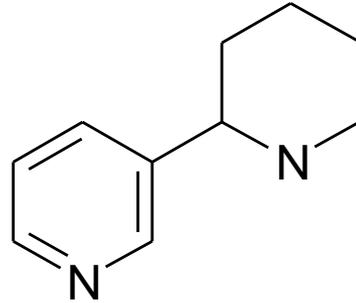




"Salvia Dainorum" by Luke Brown. www.spectraleyes.com

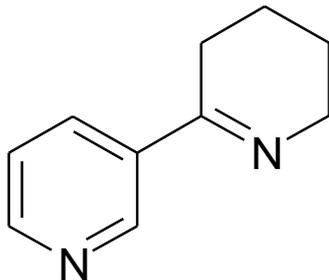
- Anabasine

- *Nicotiana* spp.
Solanaceae
- *Anabasis aphylla*
Chenopodiaceae
- Similar to nicotine
- Highly toxic
- Often intoxications
- Teratogen
 - Poultry, cattle, pigs
 - So called arthrogryposes



- Anabaseine

- *Aphaenogaster rudis*

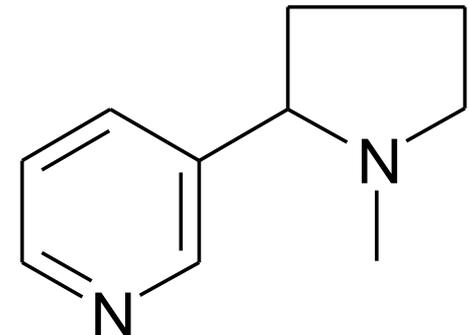


- **Nicotine**

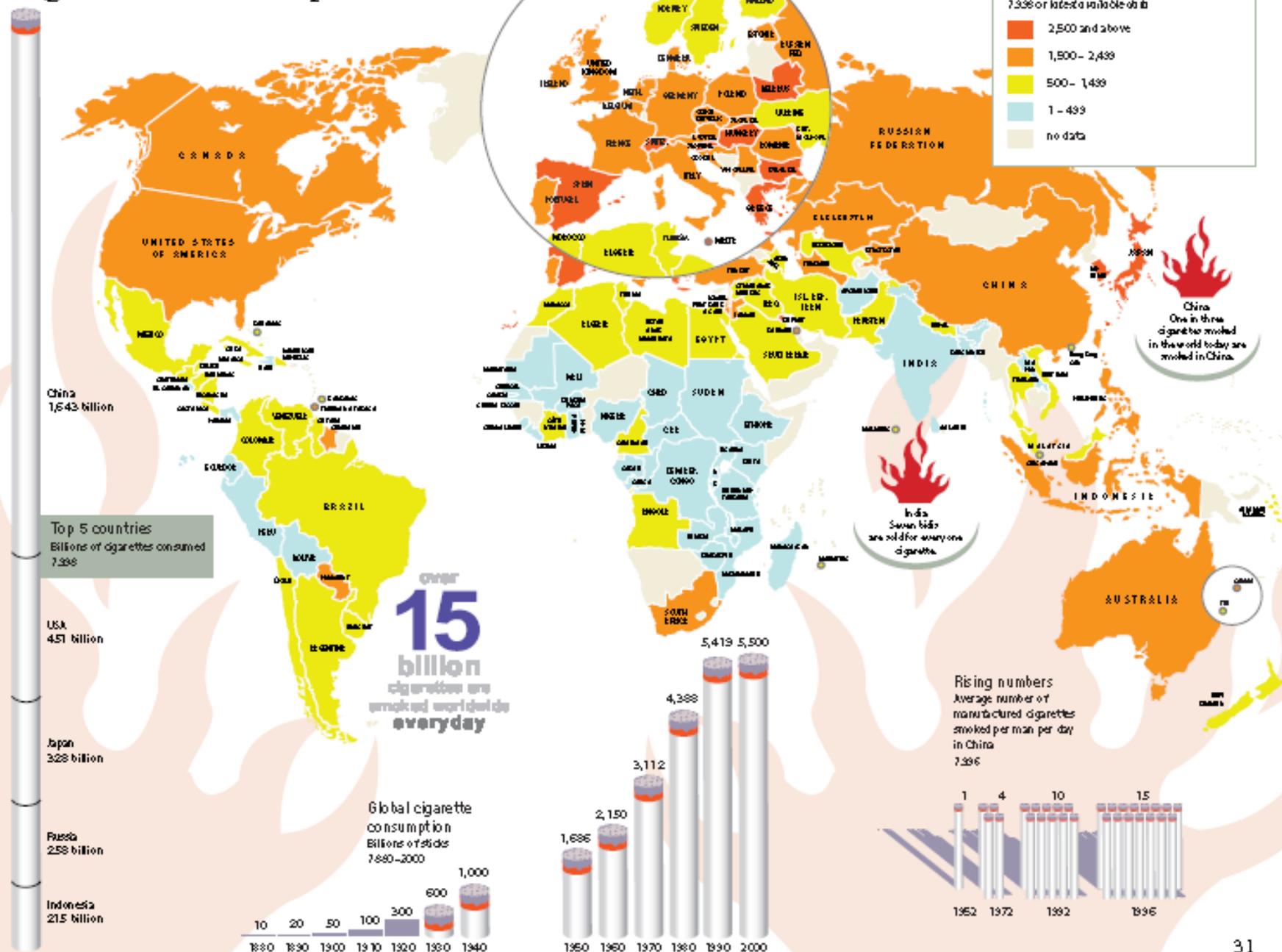
- *Nicotiana* spp. Solanaceae
- Highly toxic
- Common intoxication
- N-receptors – parasympatomimetic

Acute intoxication

- Smoking: headache, pallenes, cold sweat, tremor, vertigo, nauzea and vomiting
- Perorally: higher doses produce starting nausea with deep breathing, vomiting, furthermore tremor, convulsions, death caused by paralysis of respiratory muscles. Dose of 40-60 mg of nicotine is deadly up to 10 minutes

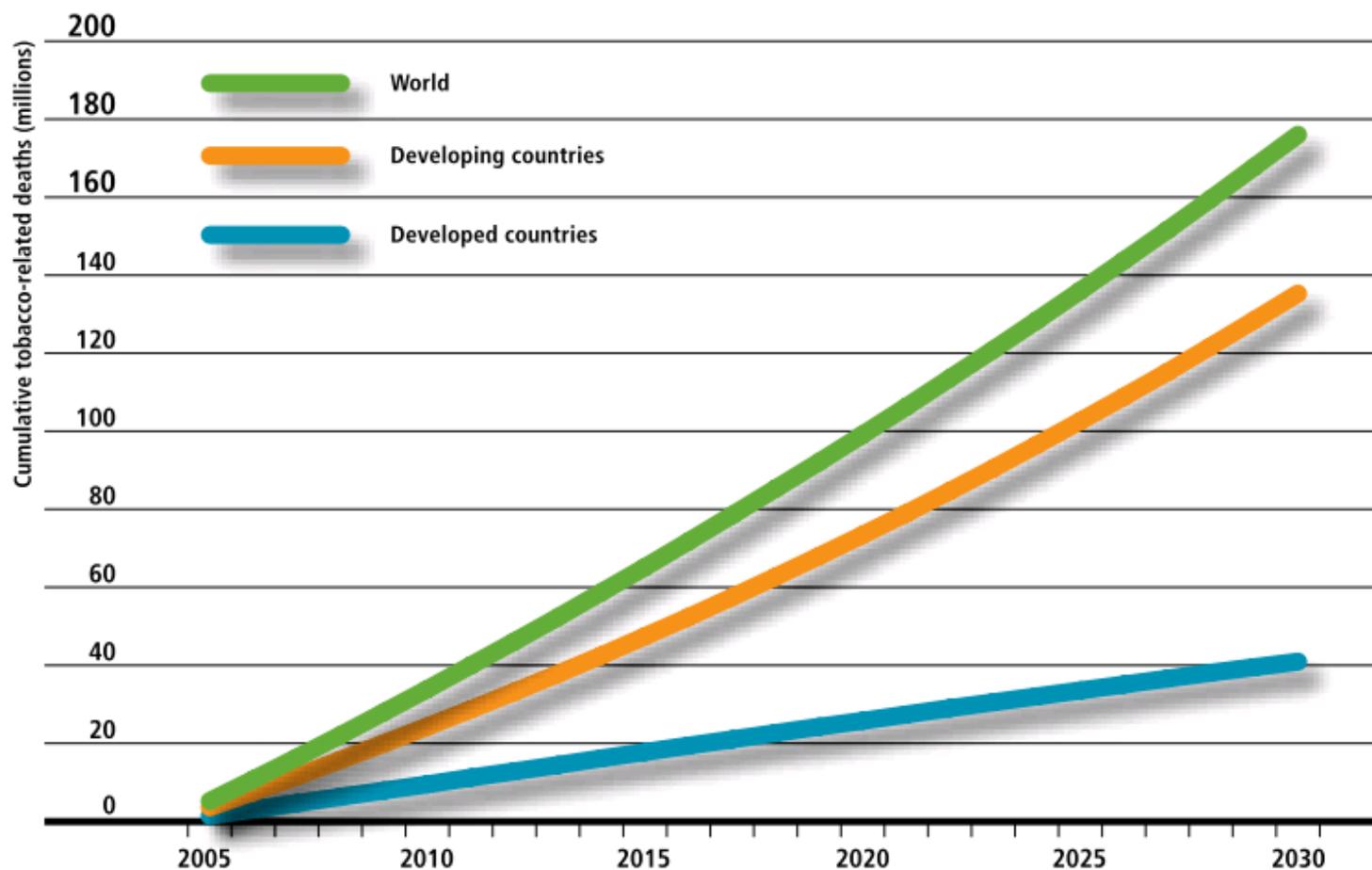


Cigarette Consumption



TOBACCO WILL KILL OVER 175 MILLION PEOPLE WORLDWIDE BETWEEN NOW AND THE YEAR 2030

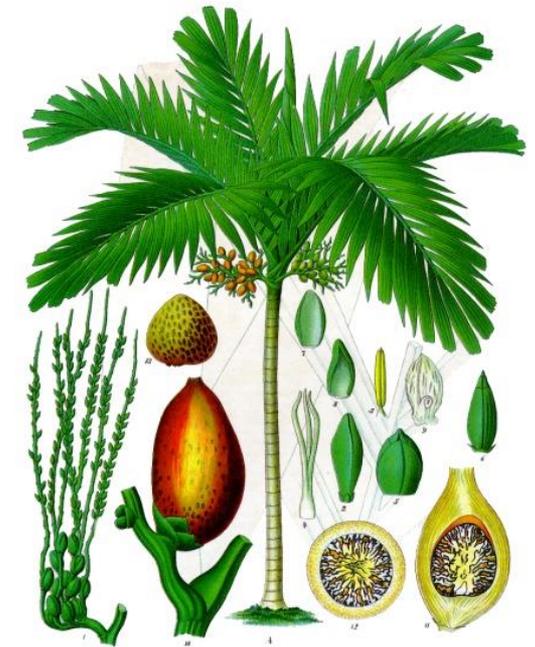
Cumulative tobacco-related deaths, 2005–2030



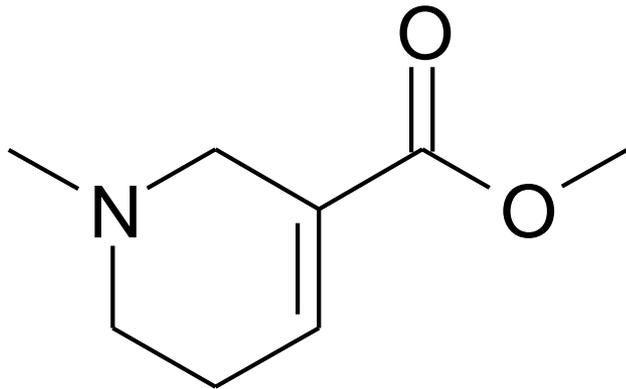
Source: Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Medicine*, 2006, 3(11):e442.

- Arecoline

- *Areca catechu* betel Arecaceae
- Muscarine effect
- Higher doses can affect also nicotinic receptors
- Salivation, perspiration, miosis



Areca catechu L.
Image processed by Thomas Schoepke
www.plant-pictures.de



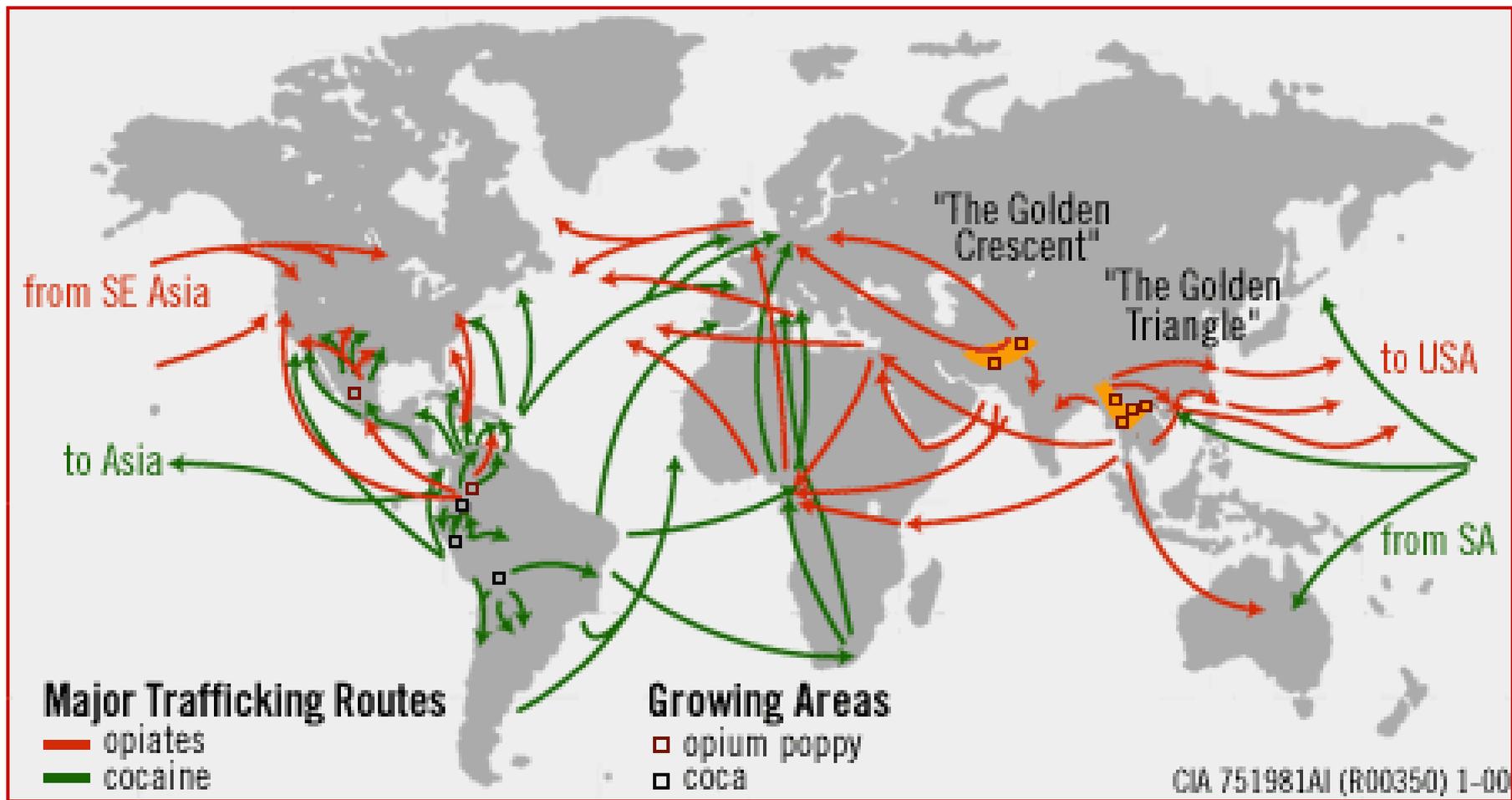
- **Cocaine**

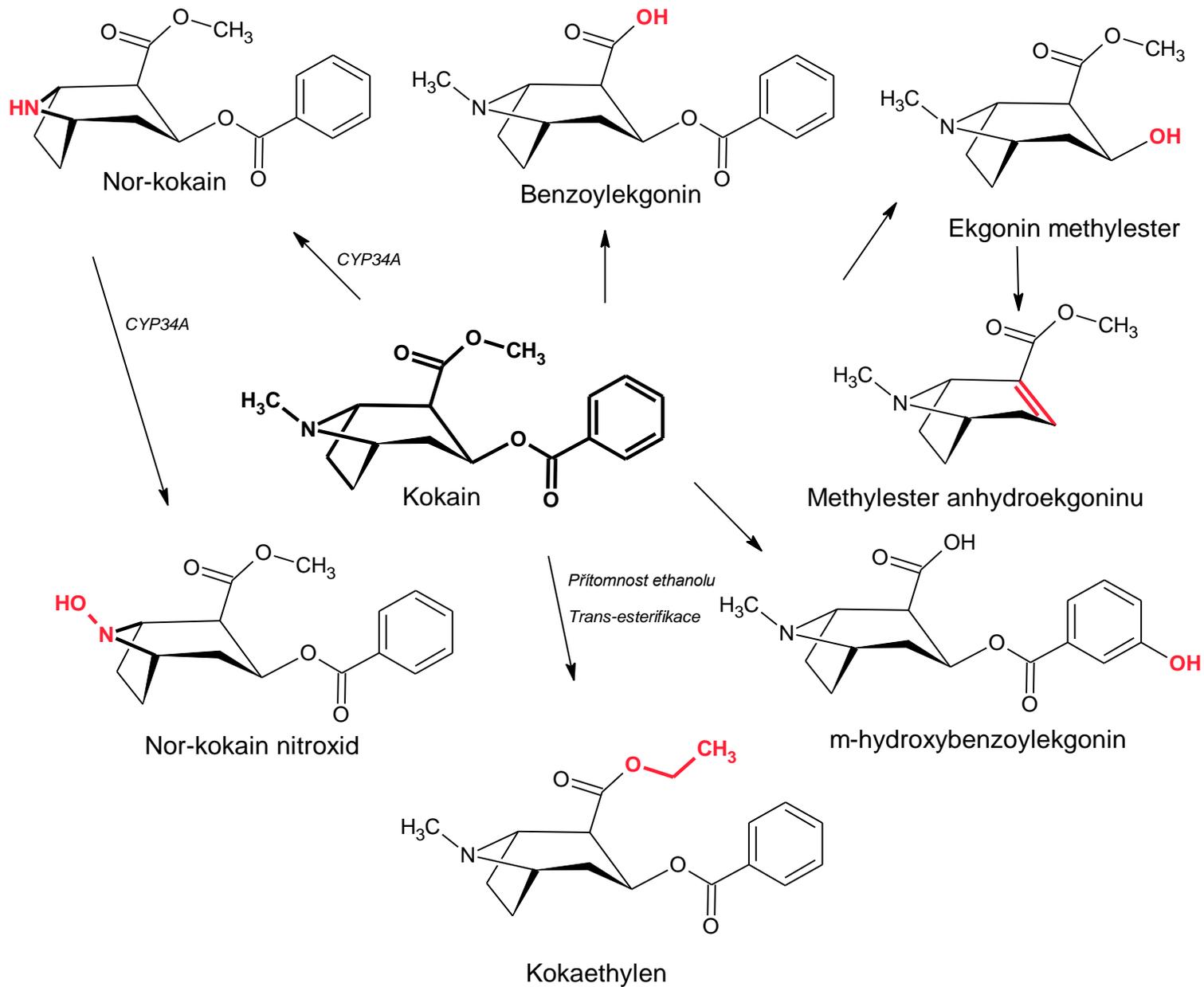
- *Erythroxylon cocca*,
Erythroxylaceae

- History

- Indians for tribe of Chibcha
- Inkas
- Spanish
- Coca-cola till 1904
- 1860 Albert Niemann – pure cocaine
- Sigmund Freund, Carl Coller







–Metabolism

– Formation of ethylderivate during ethanol intoxication

– Mechanismus účinku

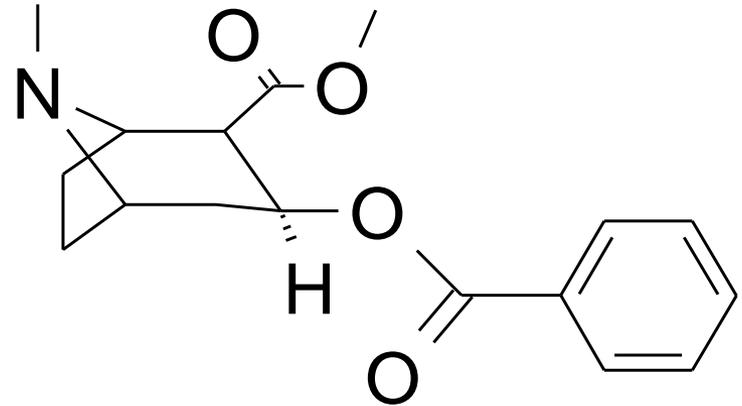
- Indirect sympatomimetic (inhibitor reuptake of noradrenaline)
- Block of ion channels of neurons (disorder of signal transmission)
- Adrenergic stimulation

– Peripheral effects

- Vasoconstriction, hypertermia, mydriasis
- Low doses - ↓ of heart rate
- High doses - ↑ of heart rate, cardiac arrest

– Central stimulation

- Euphoria, exhaustion of neurotransmitteres (NA), short depressive effect
- Rise of psychic dependence
 - Does not trigger physical dependence
- Intellectual stimulation, hyperactivity, hyperlucidity
- Self-delusion, paranoid psychosis



- Cocaine

- Complication during usage

- Cardiovascular arrest

- Way of administration

- As chlorid or base

- Chlorid

- Snuffling, i.v.

- Base

- Smiking (crack),
inhalation

- Mixture with heroine

- snowball

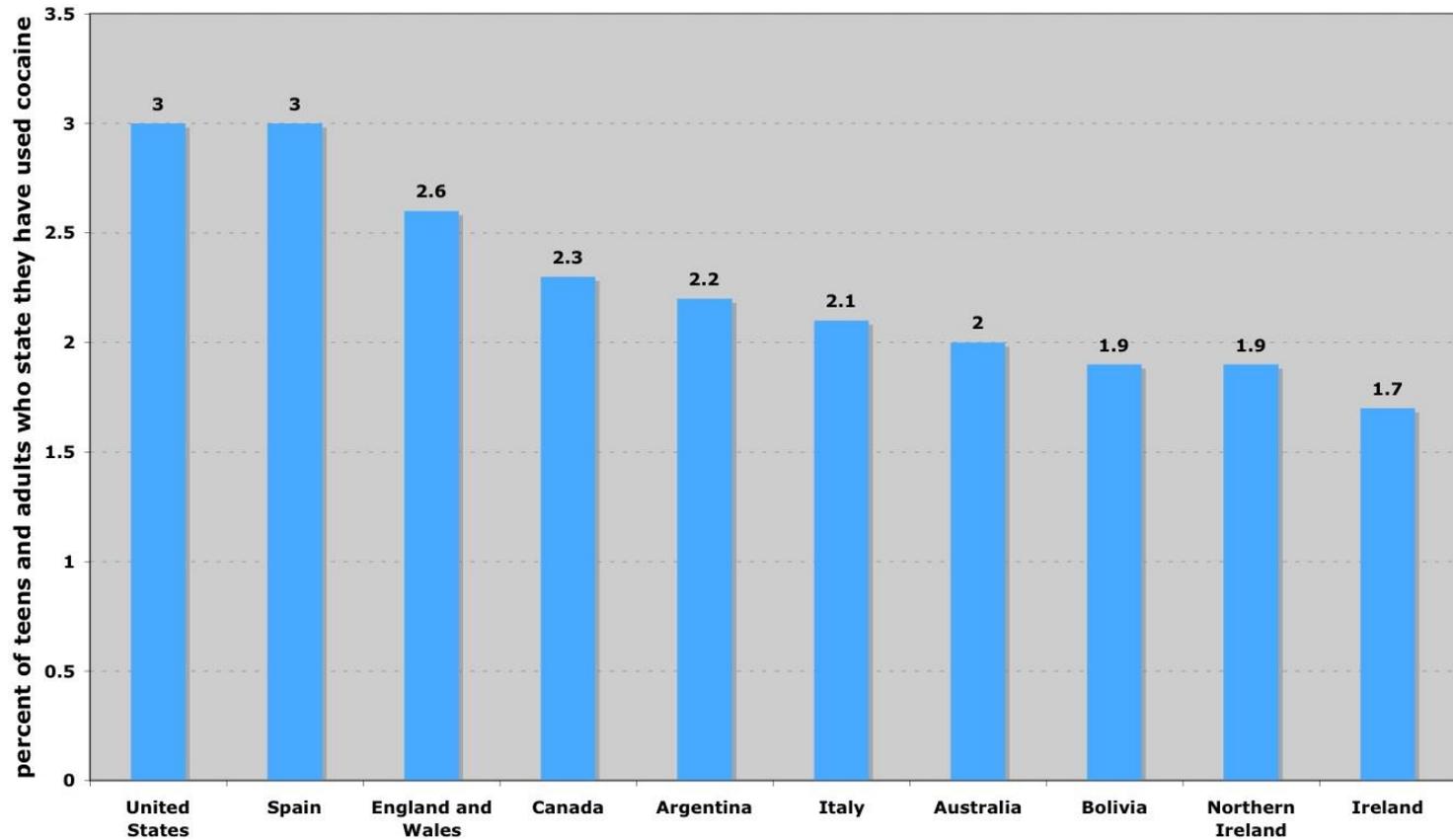
- Mixture with alcohol

- Cardiotoxic

- Highly euphorizing



Top Ten Cocaine Using Countries
©2009 "Ranking America" (<http://rankingamerica.wordpress.com>)



Data from the United Nations Office on Drugs and Crime
<http://www.unodc.org/unodc/en/illicit-drugs/index.html>

Global coca bush cultivation and cocaine manufacture, 2006–2016

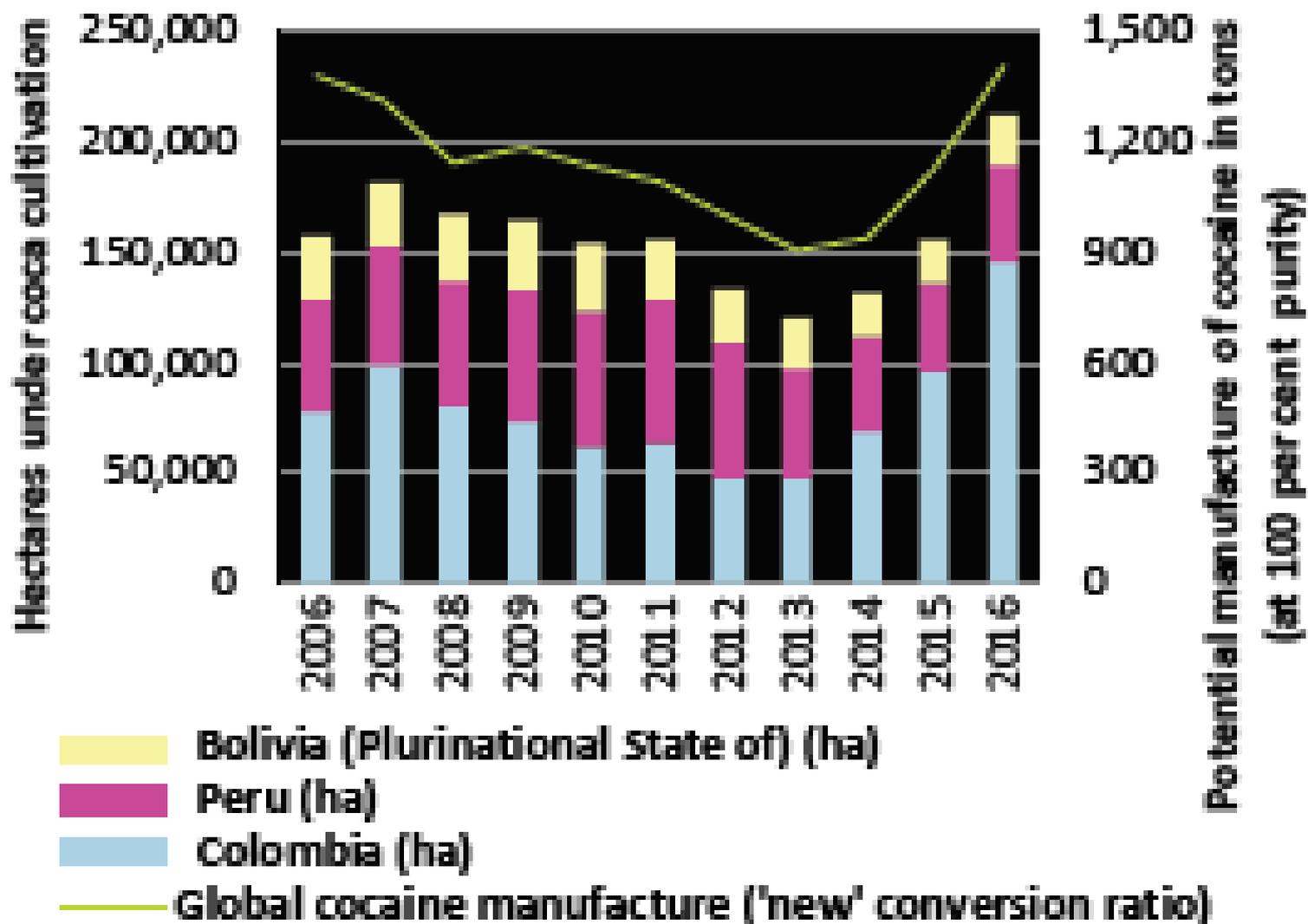
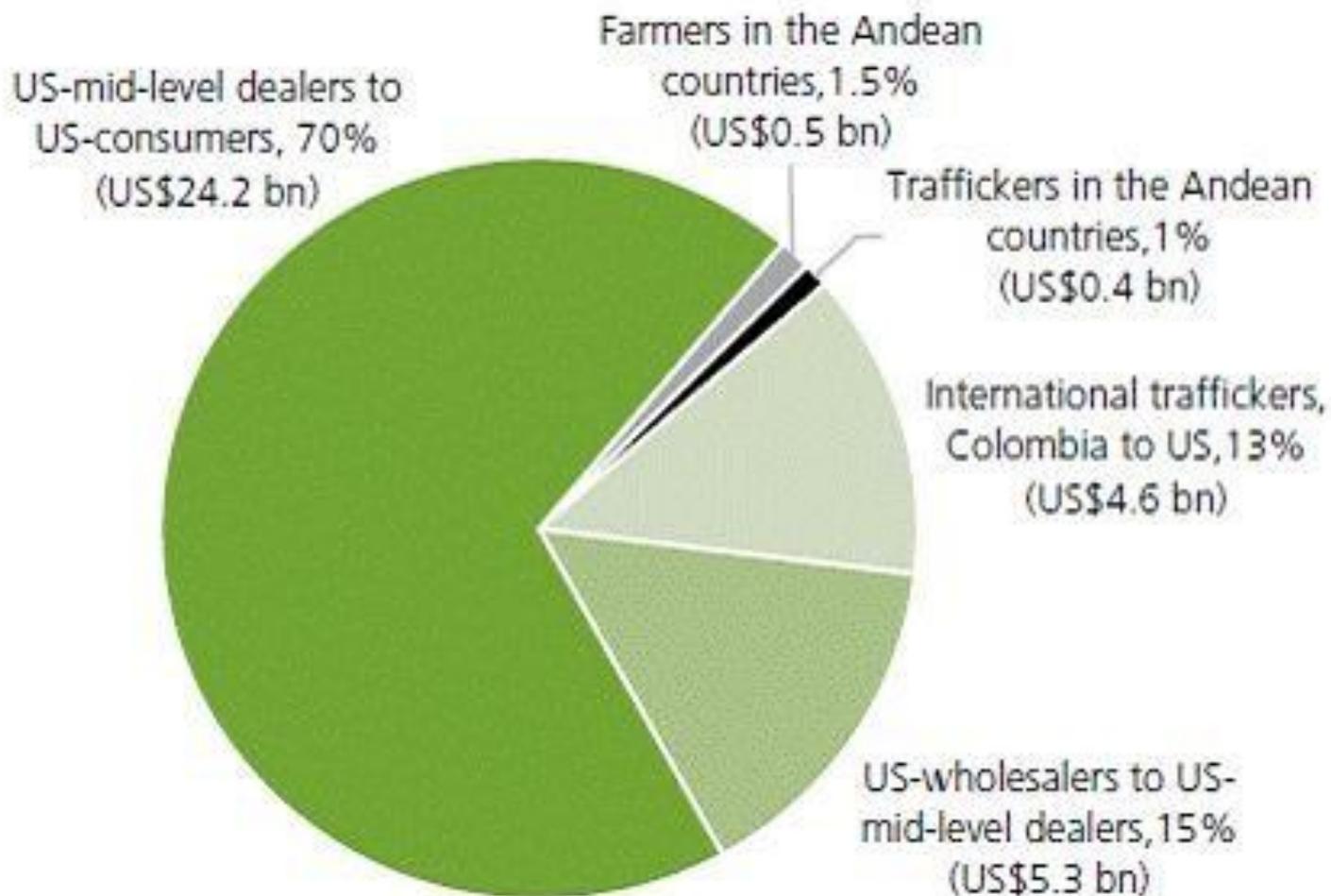


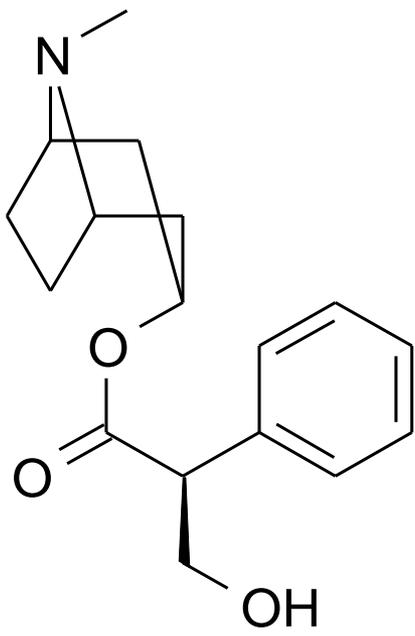
FIG. 87:

**DISTRIBUTION OF GROSS PROFITS (IN %)
OF THE US\$ 35 BILLION US COCAINE
MARKET, 2008**



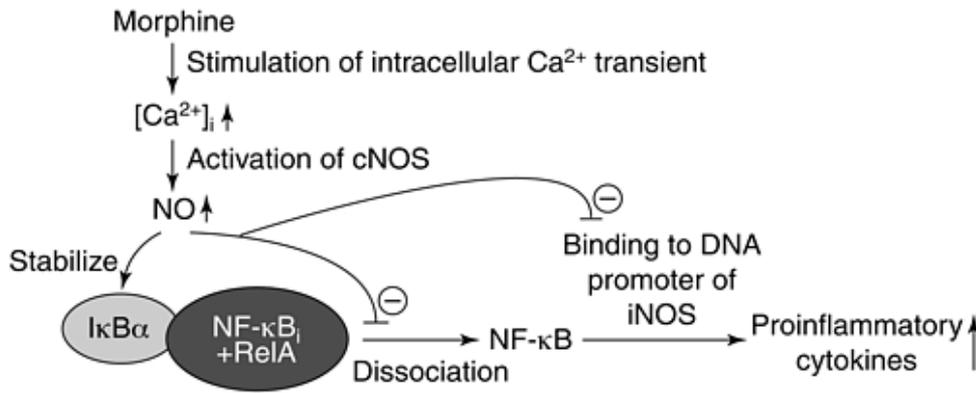
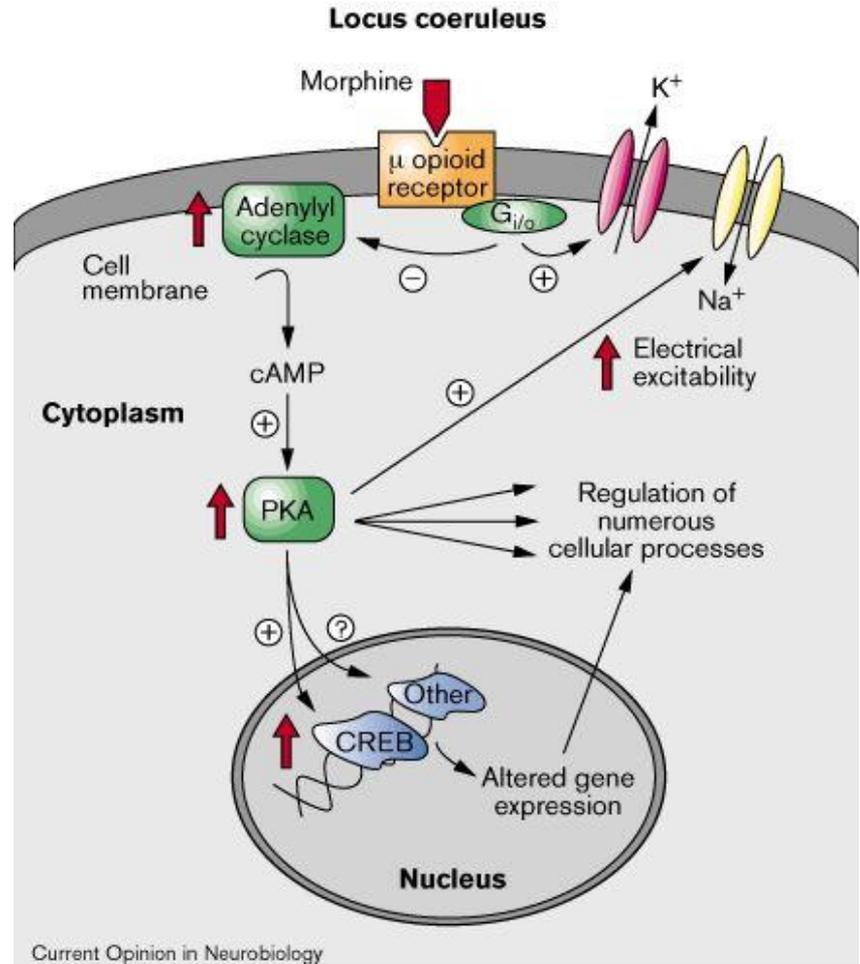
Source: Original calculations

- Tropane alkaloids
 - Azabicyclo[3,2,1]octan
 - Apoatropin, atropin, hyoscyamin, scopolamin
 - Solanaceae
 - Parasympatolytics
 - Competitive antagonists of acetylcholinergic receptors
 - Muscarine type
 - Intoxication
 - Red pigmentation of face, dry mucose, thirst
 - Tachycardia, mydriasis
 - Hypertermia, central excitation, hallucination
 - Coma, respiratory failure

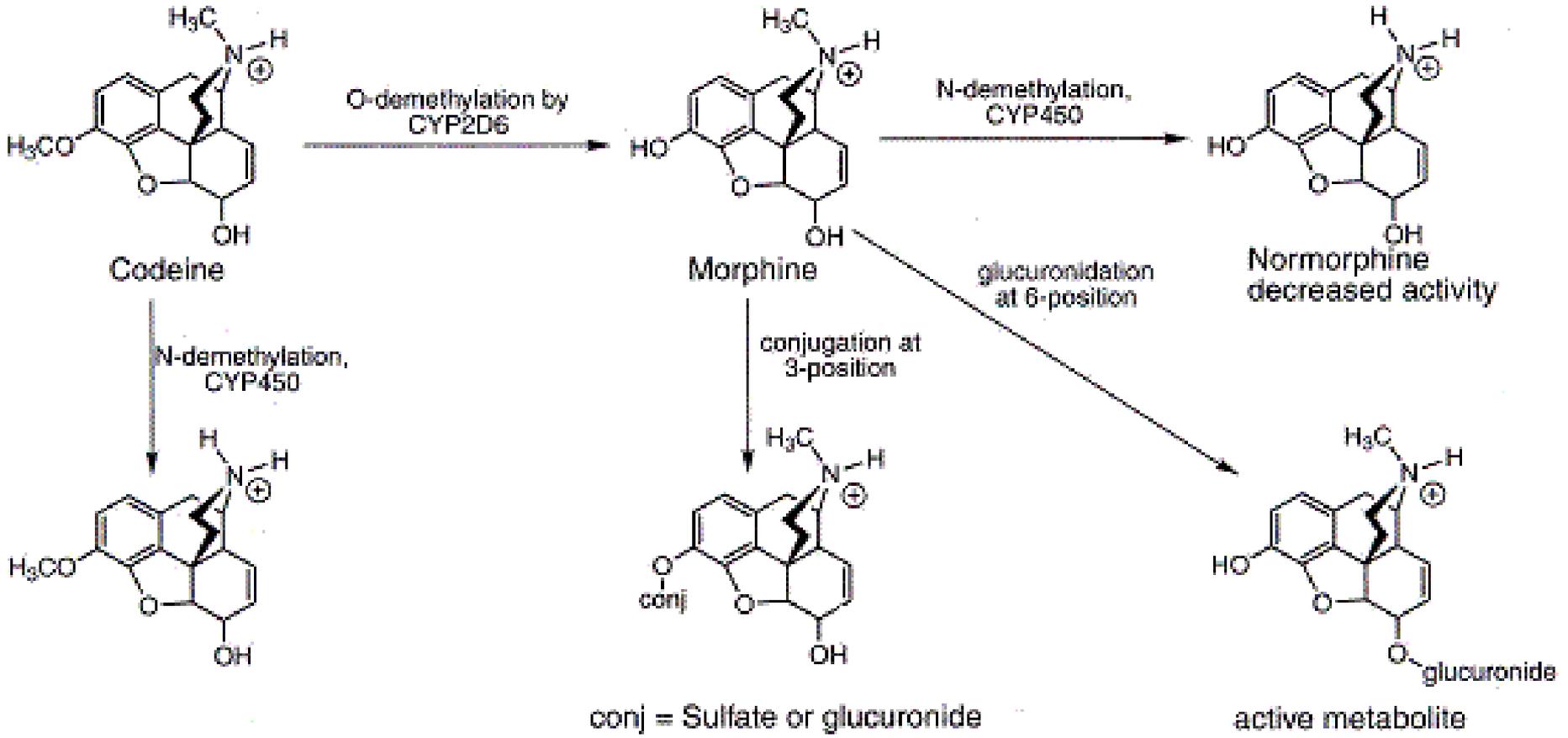


Morphine, codeine, heroine

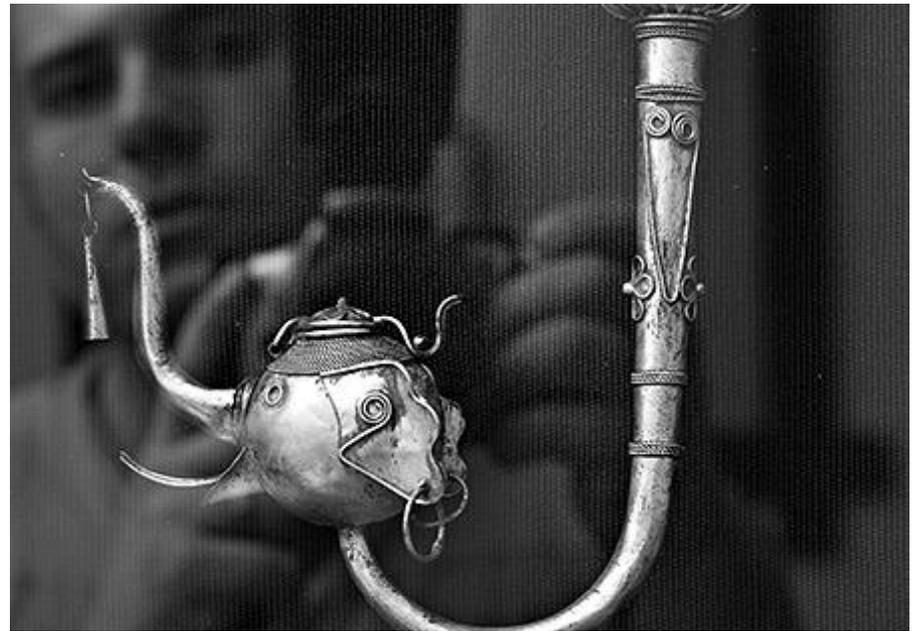
- Morphinan alkaloids
- Effective levorotary form
- Morphinan type of alkaloids
 - Typical for *Papaver* spp. Papaveraceae
 - Morphine
 - P. somniferum*, *P. setigerum* Papaveraceae
- Stereospecific, reversible linkage to opioid receptors
 - At different levels of CNS
- Agonist at presynaptic receptors of myelinated fibers of small diameter
 - Nociception, inhibition of substance P release
 - Uprise of physical dependance
 - Inhibition of enkephaline production and simultaneous occupation of receptors
 - Insufficiency of natural ligands and morphinans
 - » Withdrawal syndrome
- Effect on respiration
 - Depression of respiratory centre
 - Decrease of sensitivity to hypoxia and pCO₂
 - Dependent on dose
 - Tempo of onset dependent on way of administration
- Miosis of central origin
- Depression of centre for cough
- Complex effect on centre for vomiting
 - Nausea and vomiting
- Influence on hypophysis
 - ↓secretion of FSH, LH, ACTH
- Influence on hypothalamus
 - ↑secretion of ADH
- Influence on fibers of smooth muscles
 - Constipation and urinary retention



- Metabolism of morphine



- Symptoms of withdrawal
 - Chronic users
 - Nasal bleeding, perspiration, lachrymation, anxiety
 - Mydriasis, myalgia and pain of joints
 - Insomnia, tachycardia, arrhythmias, polypnoe, dispnoe
 - Nausea, diarrhea
- Acute intoxication
 - Usually overdose from different reasons
 - High dosage
 - Immediate depression of CNS
 - Lower dosage
 - Initial short stimulation
 - Successive malaise, fatigue, somnolence
 - Heart rate decreases and tends to fade
 - Respiration slow and shallow
 - Loss of consciousness
 - Relaxation of muscles, extinction of reflexes
 - Cold, pale, wet skin
 - If the dose high enough
 - Coma, relaxation of muscles
 - Circulatory failure, cyanosis
 - Death caused by CNS depression
 - Respiratory arrest

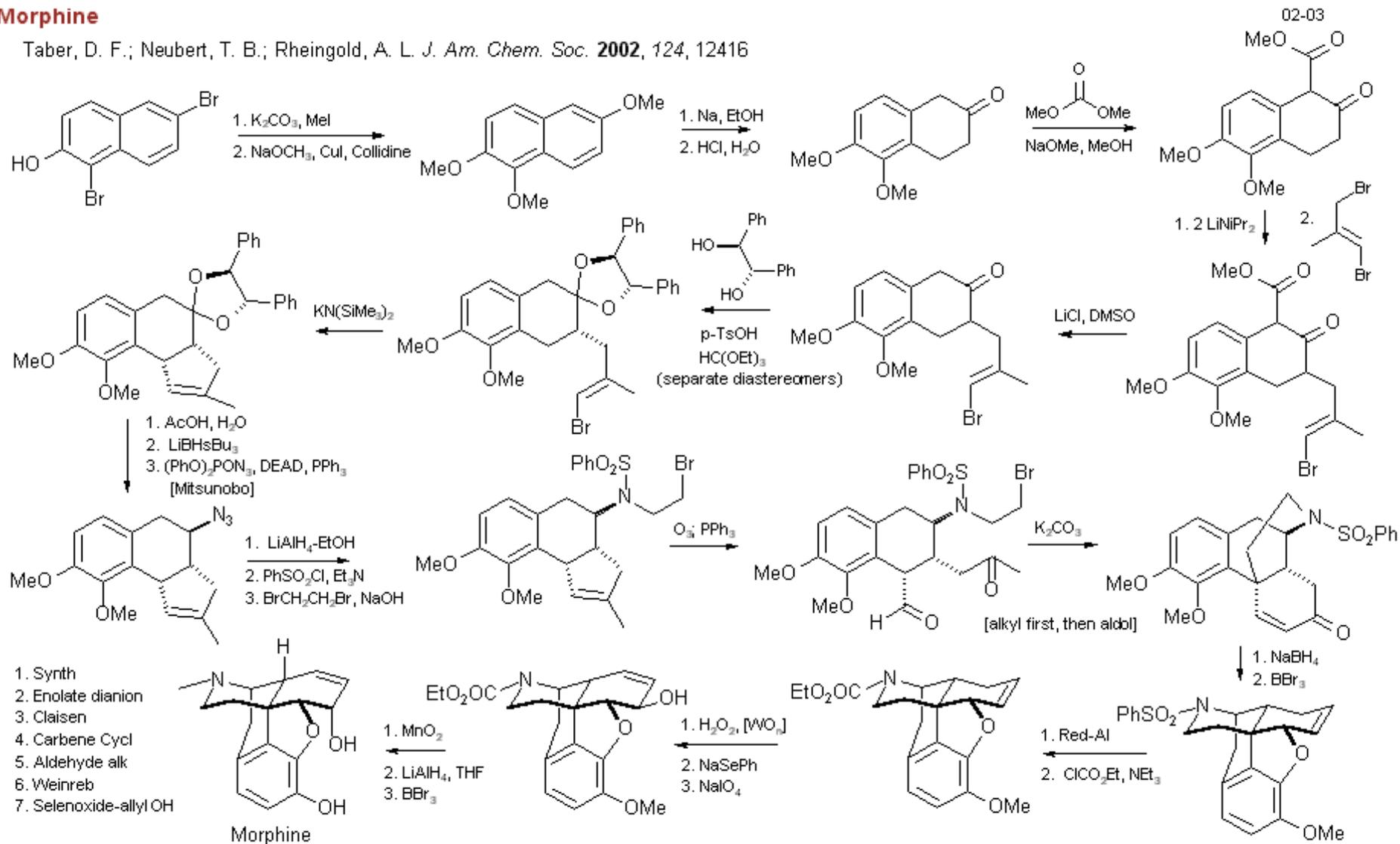


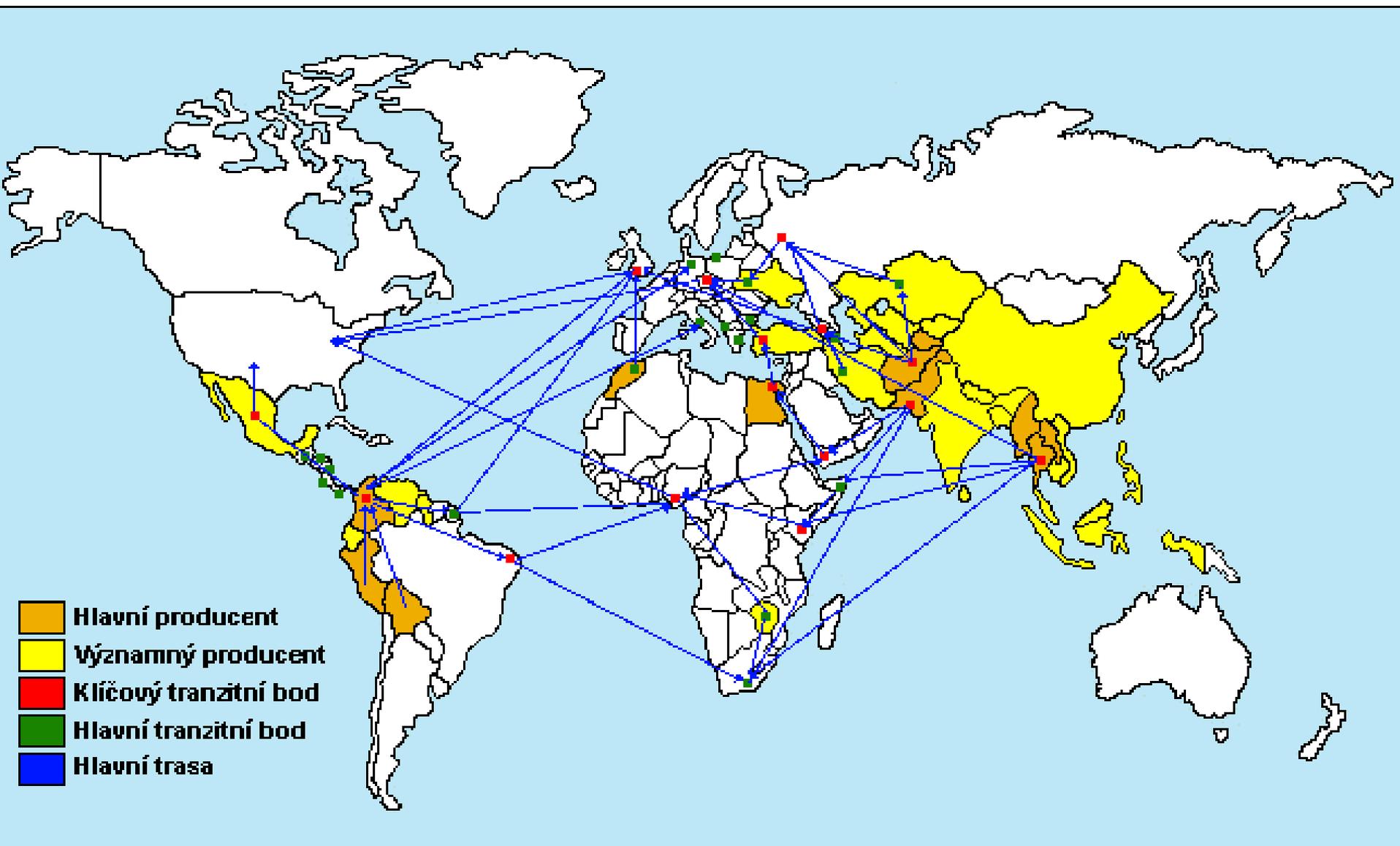
- Chronic intoxication
 - Morphinism
 - Short time of uprise
 - Strong analgetic
 - Experiments with drug
 - Tolerance to dosage
 - Combination of health problems
 - Social excommunication
 - » Psychical and physical dilapidation
 - Criminality
 - Prognosis adverse
 - » Accompanying diseases
 - » Suicidal tendencies



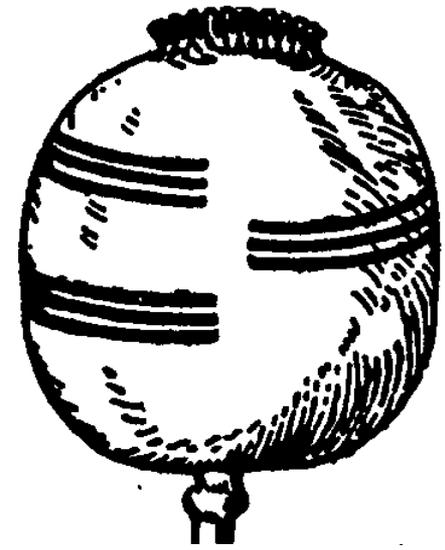
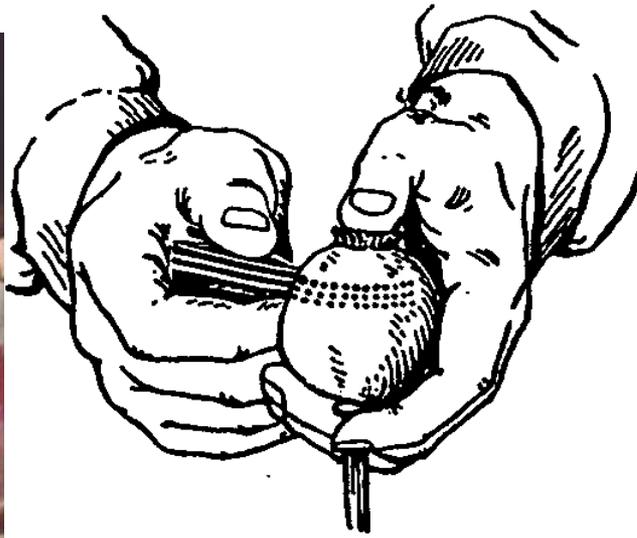
Morphine

Taber, D. F.; Neubert, T. B.; Rheingold, A. L. *J. Am. Chem. Soc.* **2002**, *124*, 12416

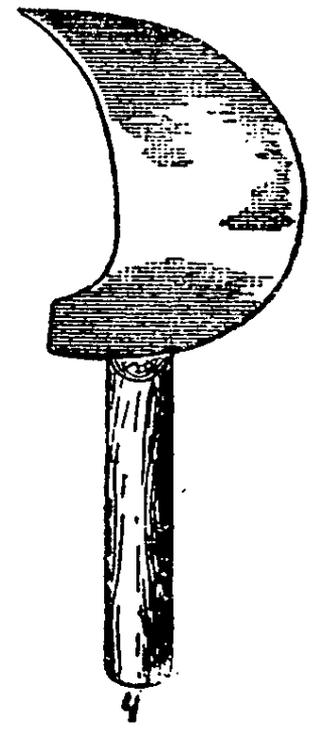
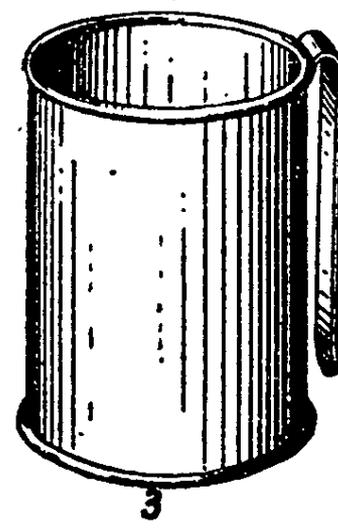
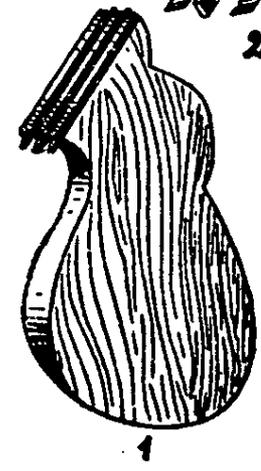
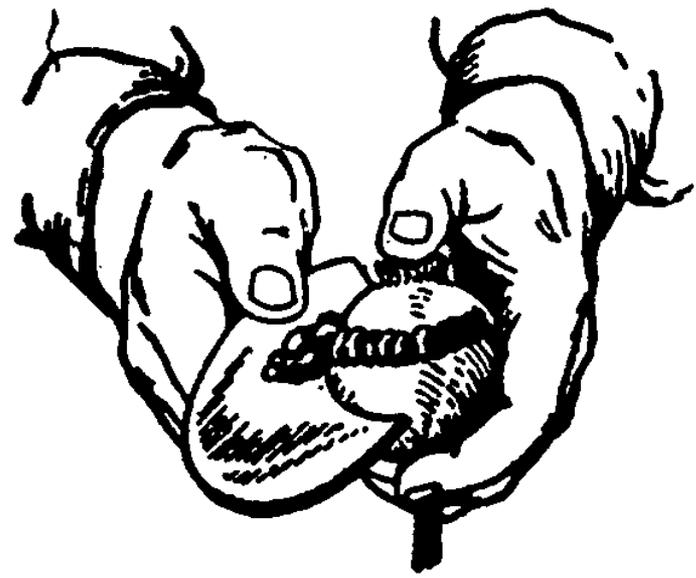
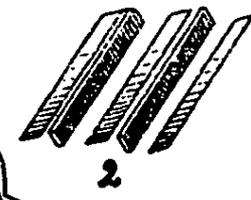


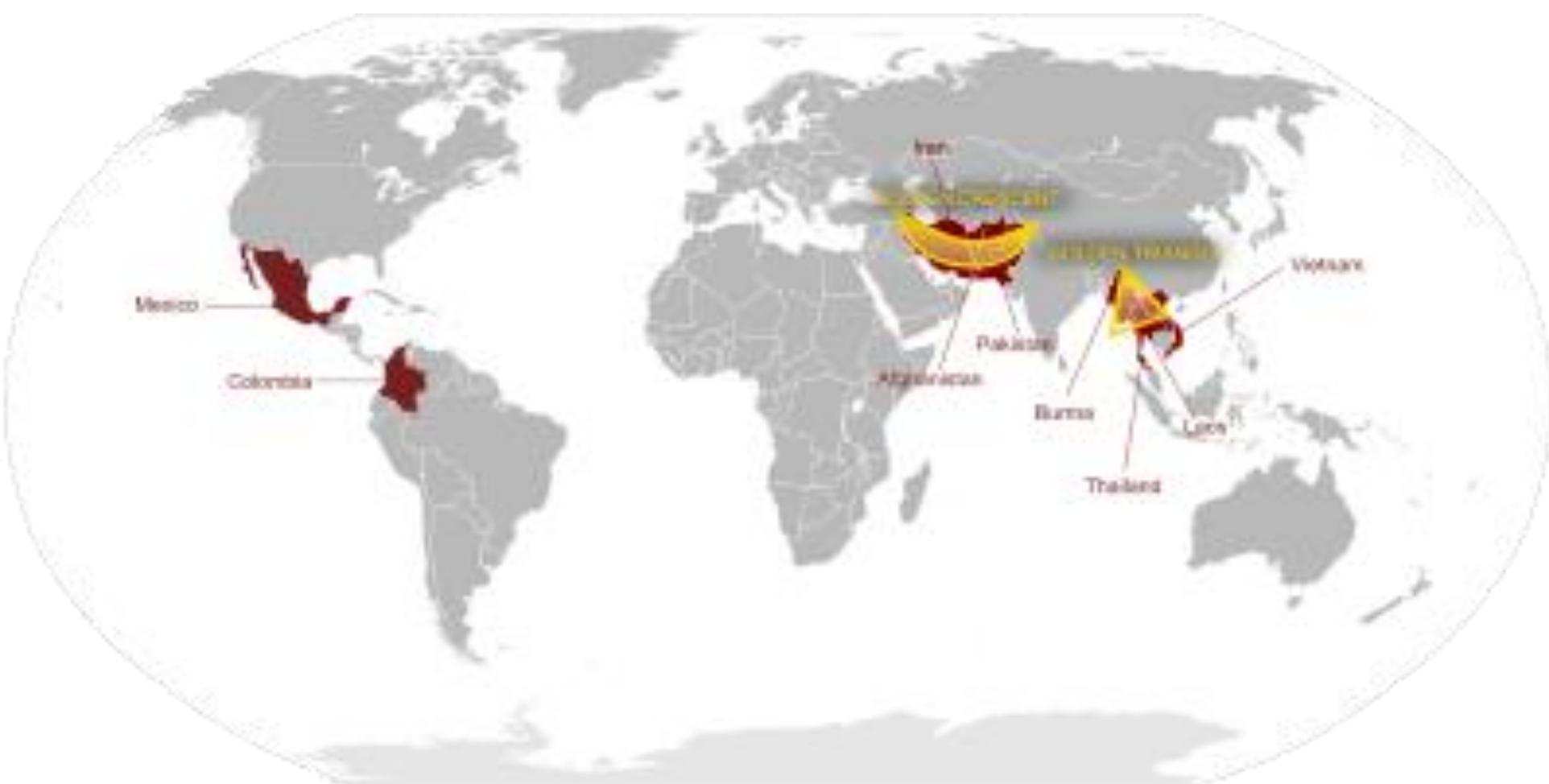


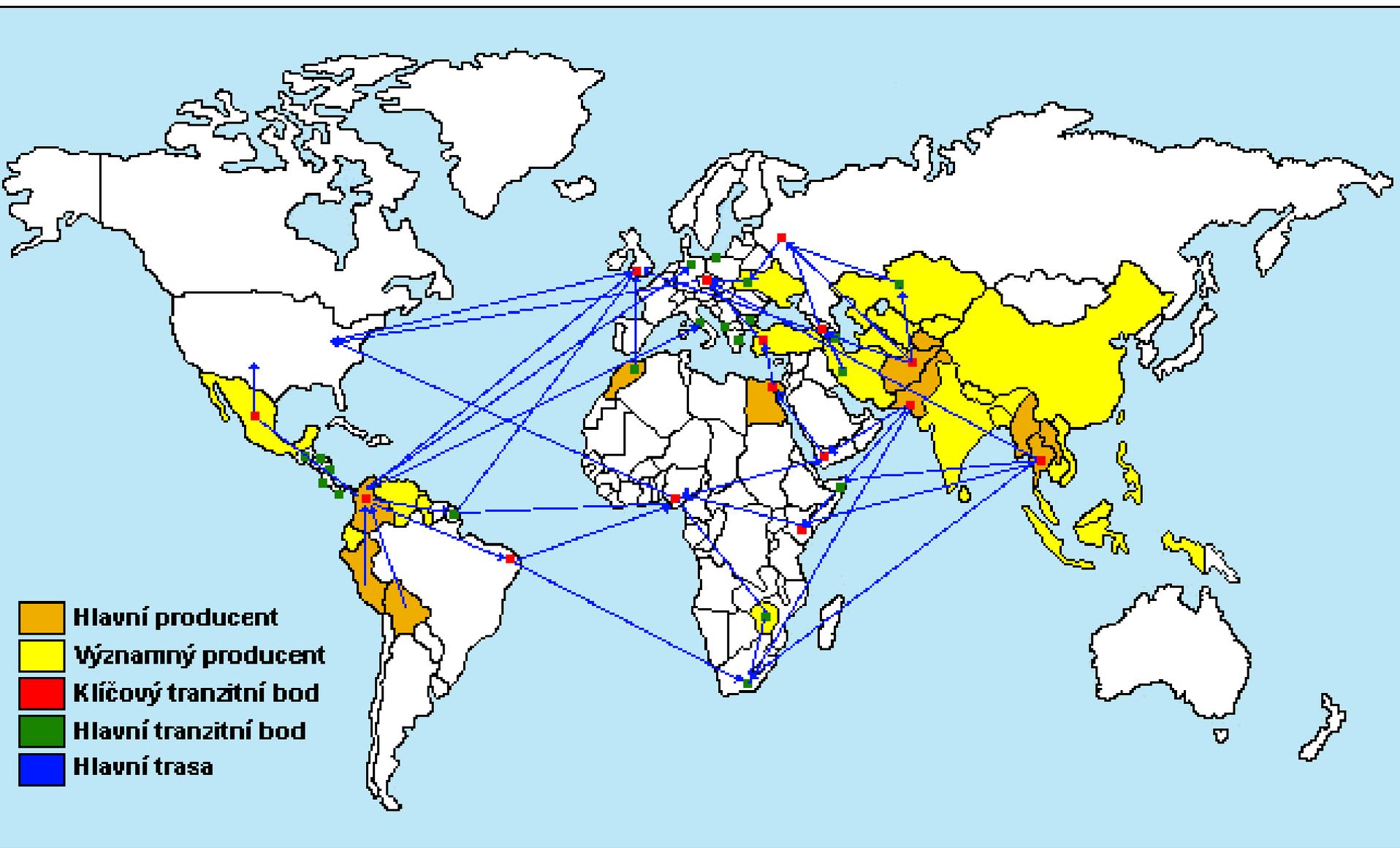
<http://www.mujiweb.cz/www/jpdepot/danger/Drugs.htm>



www.rawa.oi

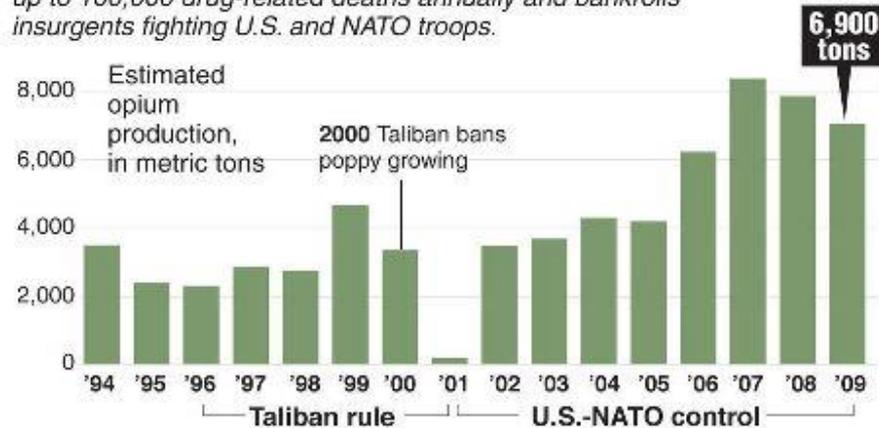






Afghanistan's deadly crop

Afghanistan produces 90 percent of the world's opium*. The drug causes up to 100,000 drug-related deaths annually and bankrolls insurgents fighting U.S. and NATO troops.



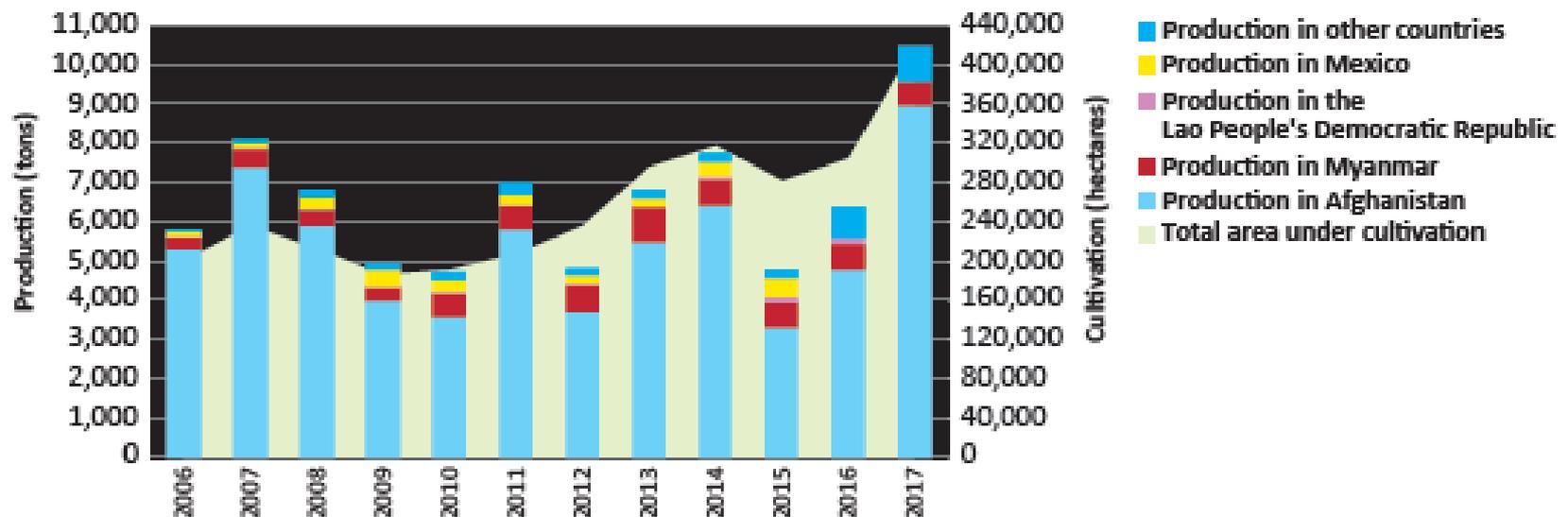
Source: U.N. Office on Drugs and Crime

Graphic: Judy Treible

*Heroin is made from opium

© 2009 MCT

Opium poppy cultivation and production of opium, 2006-2017^a

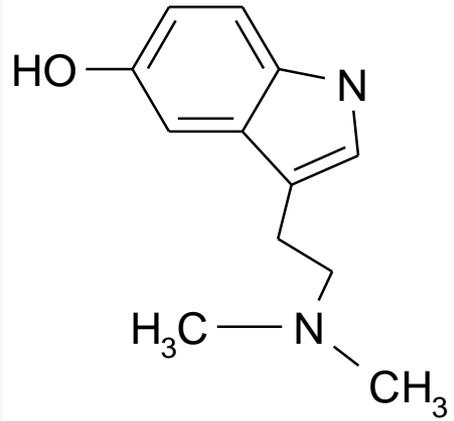


• Tryptamines



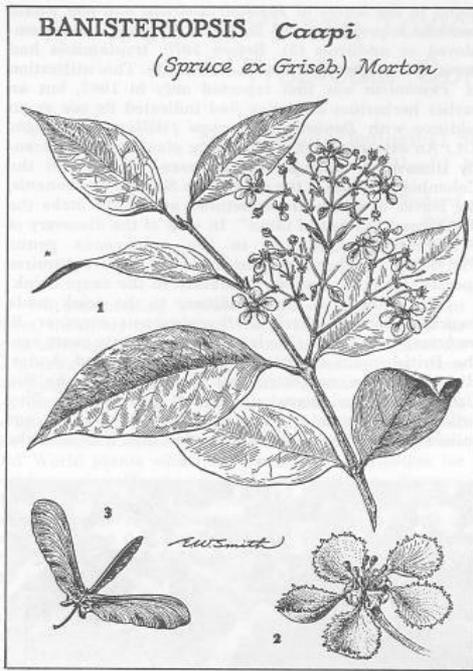
– Bufotenine

- In water poorly soluble compounds
- *Piptadenia peregrina* Mimosaceae
 - Cojoba Tree
- *Arundo donax* Poaceae
- Several fungi and frogs
- Intoxication
 - Hallucinogenic effect, influence on psychic
 - » Similar to LSD and mescaline
 - Frame of mind: anxiety, perception disorders
 - Mydriasis, hypertension
 - High dosage
 - » Respiratory paralysis
 - » Motoric paralysis



– N,N-dimethyltryptamine (DMT)

- *Prestonia amazonica* Apocynaceae
- *Piptadenia peregrina* Mimosaceae
- Shortly effective hallucinogenic compound
 - 0,7-1mg/kg
- Model psychosis
 - Vegetative symptomatology
 - Emotional and perception disorders
 - Illusions and visions
 - Space-time distortions





Tukanoan Indian with stems of three "kinds" of caapi preparatory to making hallucinogenic drinks from the bark, Rio Vaupes, Colombia. (Photograph by G. Reichel-Dolmatoff)

VIROLA

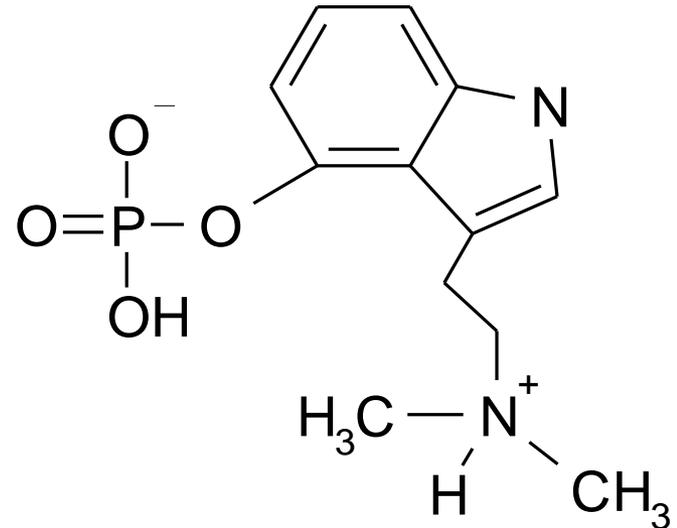
theiodora

(Spr. ex Bth.)

Warburg



- **Psilocyne, psilocybine**
 - *Psilocibe, Conocybe, Stropharia*



- ***Psilocybe***
 - 0,2 % to 0,6 % of psilocybine
 - 10 mg p.o. dose
 - Chewing – better absorption from oral cavity
 - 8 hours for excretion cca 80 %, 5-6 hours of effect

- **Starting symptoms**

- Headache, anxiety and weariness, unwitting yawning (often without drowsiness), extraordinary convulsions, balance disorders, tremor and sweating.

- **Psychic symptoms**

- Deformation of reality perception, warm colored visions, caleidoscopic effect
- Changes of mood, euphoria, happiness, extraordinary depression and irritation
- Psychoses connected with depersonalisation, disorders of time perception, direction and distance, false imaginations

- **Acute toxicity**

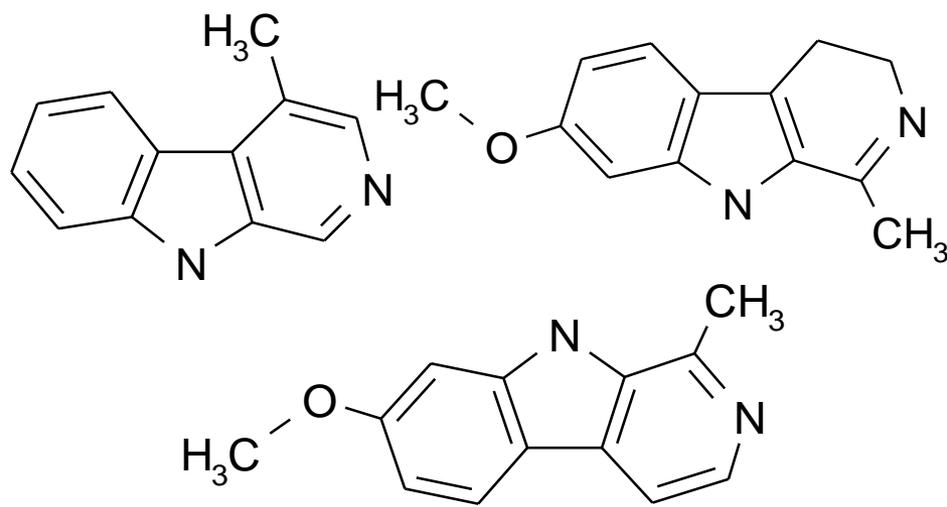
- Relatively low (deadly dosage of psilocybine for human is approx. 17 gramů)
- Risk of hasty decisions
- Latent psychic diseases (for example schizophrenia)





- β -carboline indol alkaloids

- Harmane, harmaline, harmine
- *Peganum harmala*, *Zygophyllum fabago*, *Tribulus terrestris*
Zygophyllaceae
- *Passiflora incarnata* Passifloraceae
- Inhibitory MAO
 - Elevated levels of neuromediators
 - » Serotonine, noradrenaline
 - Especially in brain
 - » Central effect
 - Early symptoms of intoxication
 - » Nausea, vomiting, pale skin
 - » Signs of aggression
 - Further progression
 - » Half-sleep with dreaming
 - » Hallucinations



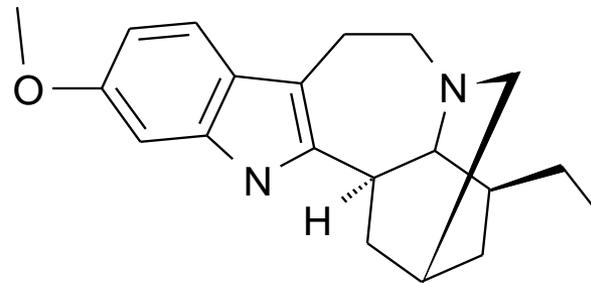
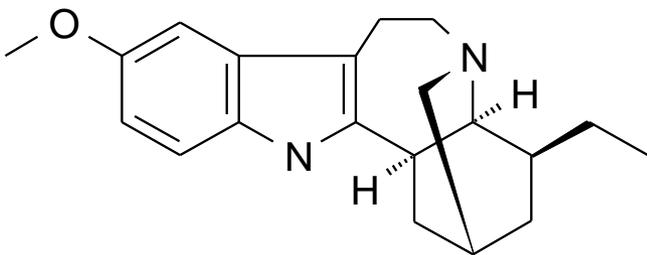


Peganum harmala



– Ibogaine, tabernathine

- Tabernanthe iboga, Voacanga spp. Apocynaceae
- Activity in CNS
 - Inhibitor of neuronal nicotine receptors
 - Lower dosage
 - » Central stimulation
 - » Tremor, bristlin hair
 - » Salivation, mydriasis
 - » Anxiety, aggression
 - High doses
 - » Hallucination - serotonin effect
 - » Deep depression and anxiety
- Cardiovascular system
 - Negative inotropic and chronotropic effect





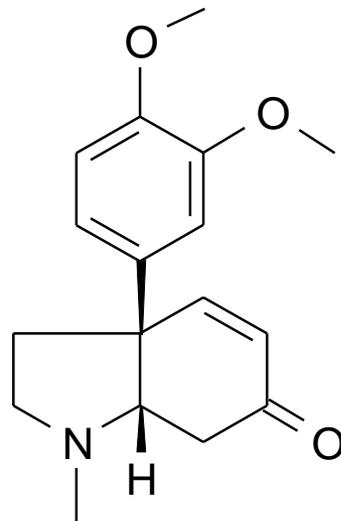


- Other indol alkaloids
 - **Mezembrenone, mezembrine, mezembrinol**

- phenyloxyindols
- *Sceletium* alkaloids
- Aizoaceae
- Narcotic, coca-like effect
- Addictive drug
 - channa



Kosmatec



- **Amines**

- **Ephedrine**

- Aromatic amine
- *Ephedra* spp. Ephedraceae
- Sympathomimetic activity
 - Increase of blood pressure and peripheral vasoconstriction
 - Penetration to CNS
- Acute intoxication
 - Sweating, headache, anxiety
 - Muscular weakness and tremor
 - Mydriasis
 - Palpitation
 - Insomnia



- **Galegine**

- *Galega officinalis* Fabaceae
- Derivative of guanidine
- Damage of mitochondrial function
- Convulsions, breath difficulties, pulmonary edema



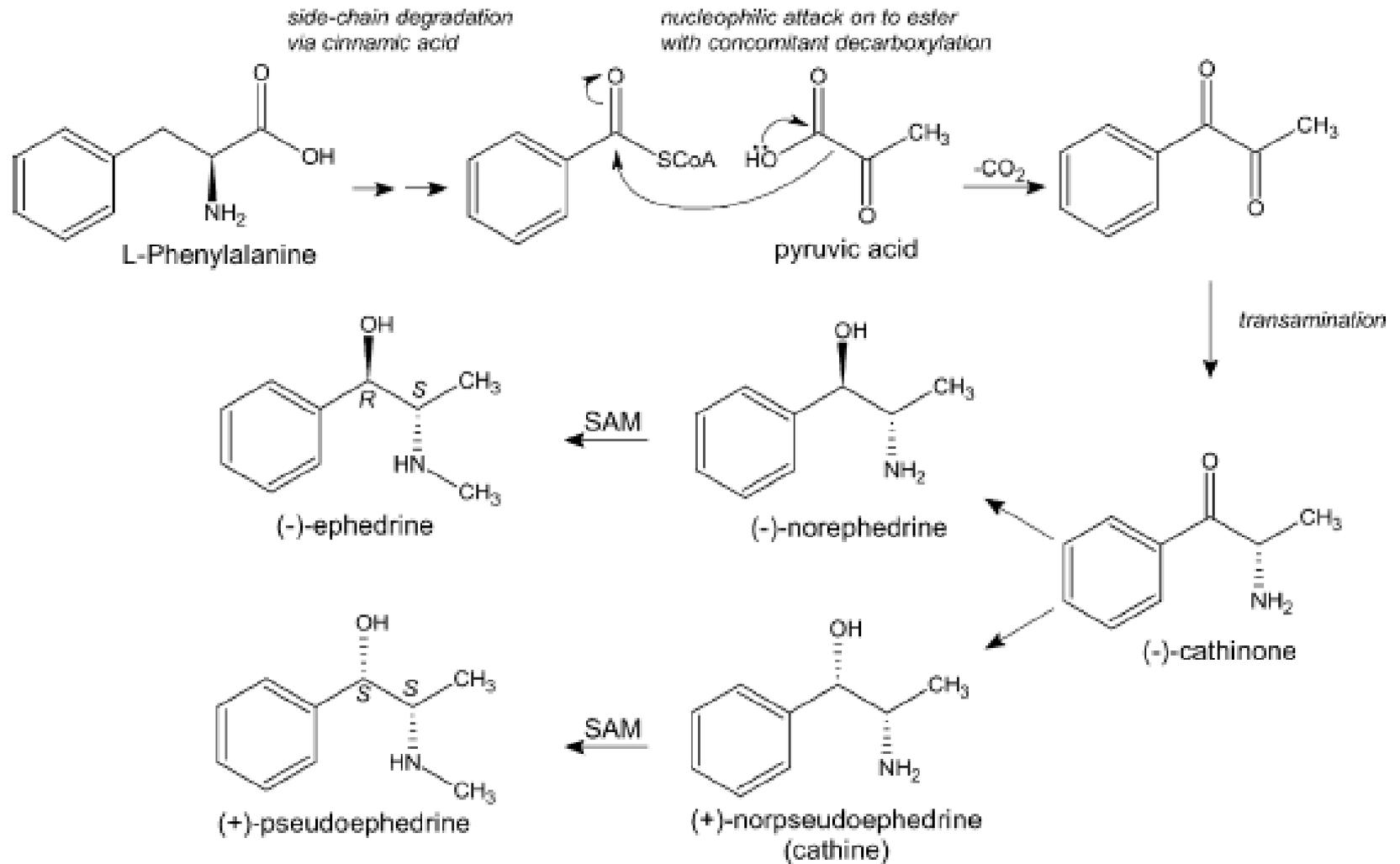


Fig. 1. Synthesis of ephedrine and related alkaloids.

– Khatamines

- Arylalkylamines
- *Catha edulis*, *Maytenus crucorii*
Celestraceae
- *Ephedra* spp. Ephedraceae
- **Khatine and khatinone** the most important
- **Khatinone**
 - Similar properties to amphetamine
 - During drying converts to norpseudoephedrine and norephedrine
- Drug is used via chewing
 - North-East Africa
 - Fast decomposition prevents large transportation and business
 - Suppression of sleep, stimulation, against fatigue
- Intoxication
 - Anorexia, hyperthermia, stimulation of respiratory centre
 - Mydriasis, arrhythmia, hypertension
 - Psychic symptoms
 - » Anxiety, panic attack, aggressivity

