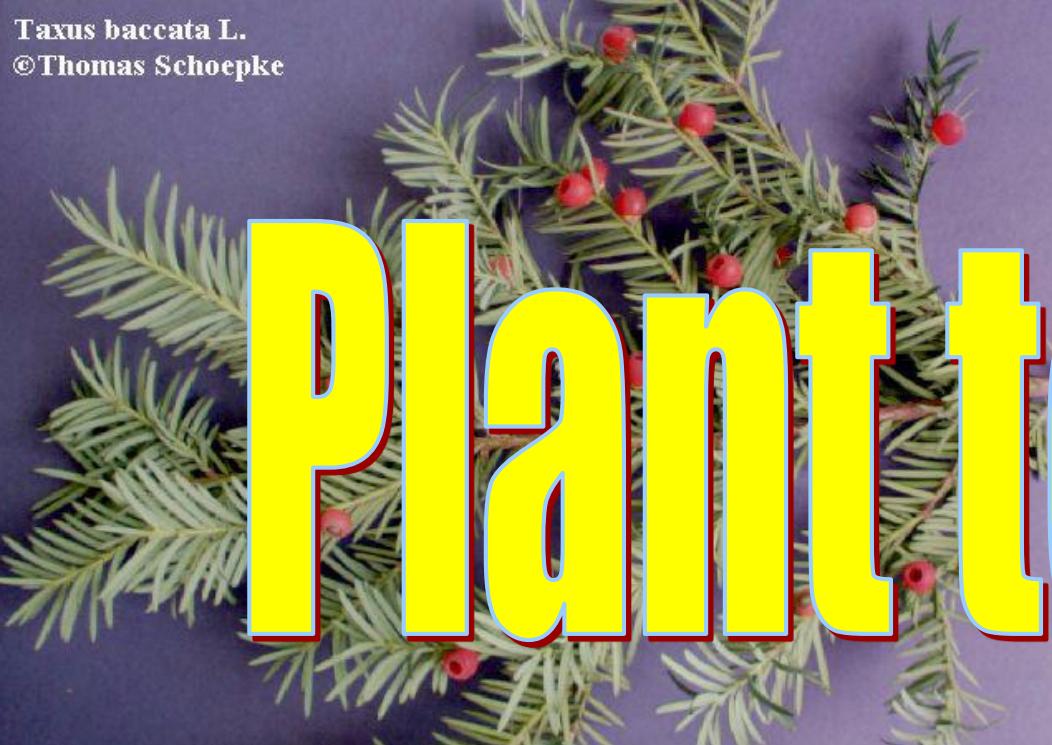


# Plant toxins



# Classification of plant toxins:

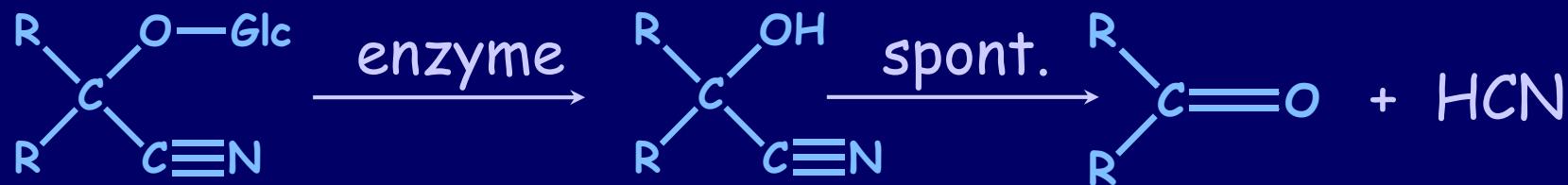
- Nitrogen-containing compounds:
  - Cyanogenic glycosides
  - Alkaloids
- Nitrogen-free compounds
  - Terpenic compounds
  - Photolabile compounds

# Cyanogenic glycosides

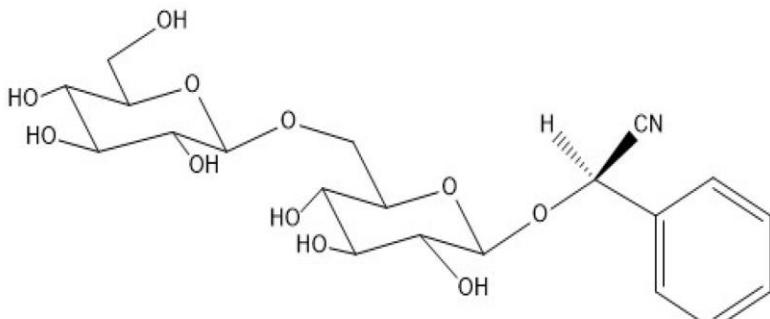
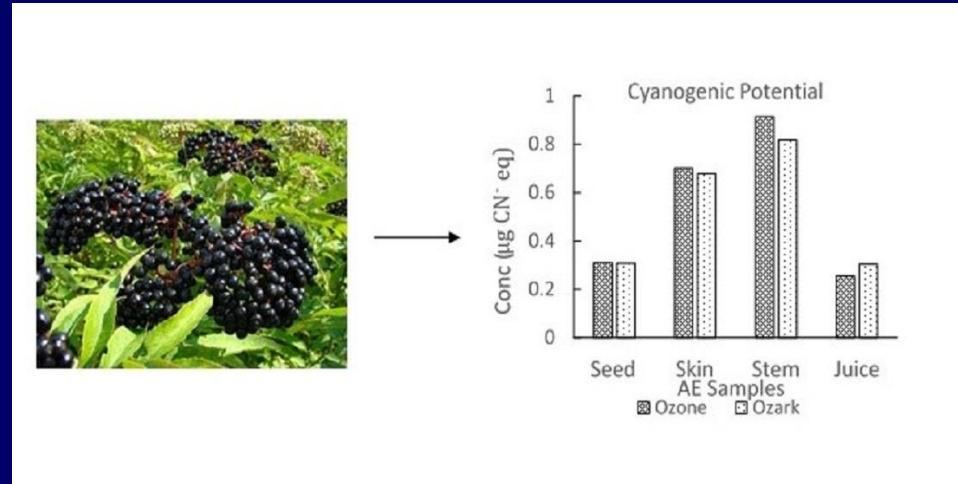


Bitter almonds (Mandloň obecná), clover (jetel), lotus

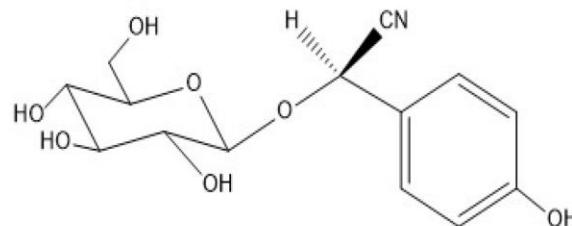
Sheeps, cattle and some snails are immune



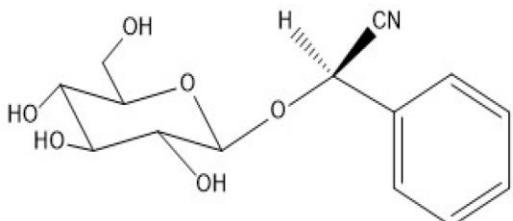
# American Elderberry



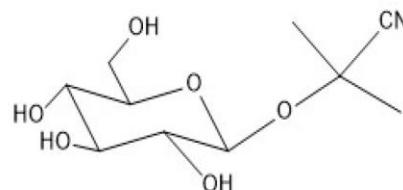
**Amygdalin**



**Dhurrin**

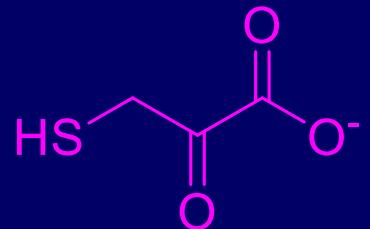


**Prunasin**



**Linamarin**

# Principle of detoxification:



The sulfur originates from mercaptopyruvate from which is released by action of enzyme (3-mercaptopyruvate sururyltransferase)

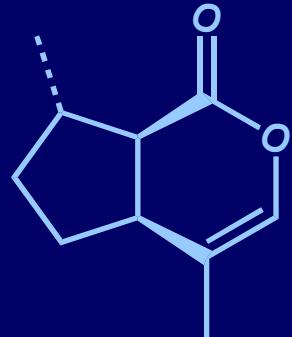
The same mechanism is used for clinical

treatment of cyanide poisoning





*Nepeta Cataria*



Nepetalactone  
Catnip (catmint,  
šanta kočičí)

Repellent and toxic effect  
toward some insect and  
birds

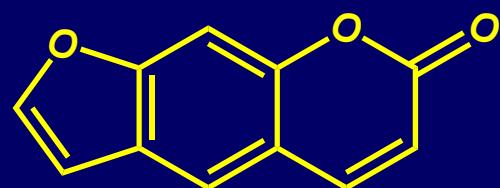
For other sort  
of insect  
attractant



# Fotolabile compounds:



*Petroselinum hortense*



Furocumarins

Also in bergamot  
essential oil, and  
*Heracleum*  
*mantegazzianum*

Psoralen Garden  
parsley (Petržel)



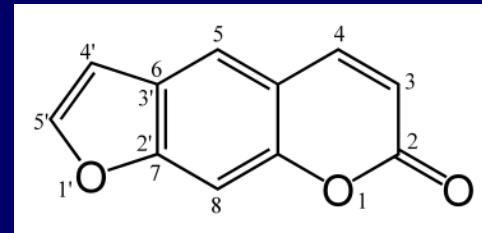
- Decomposed by the action of UV light, exposure results in skin damage by binding of product to pyrimidine bases

# Fotolabile compounds



<http://botanika.wendys.cz>

phototoxic plant. Its sap can cause phytophotodermatitis



furanocoumarin

*Heracleum mantegazzianum* giant hogweed (Bolševník velkolepý)

# Diterpenes:

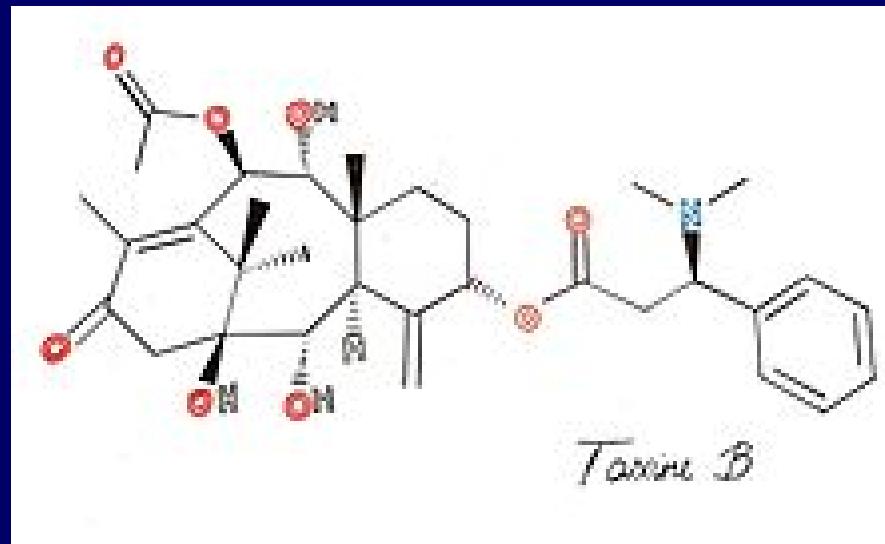
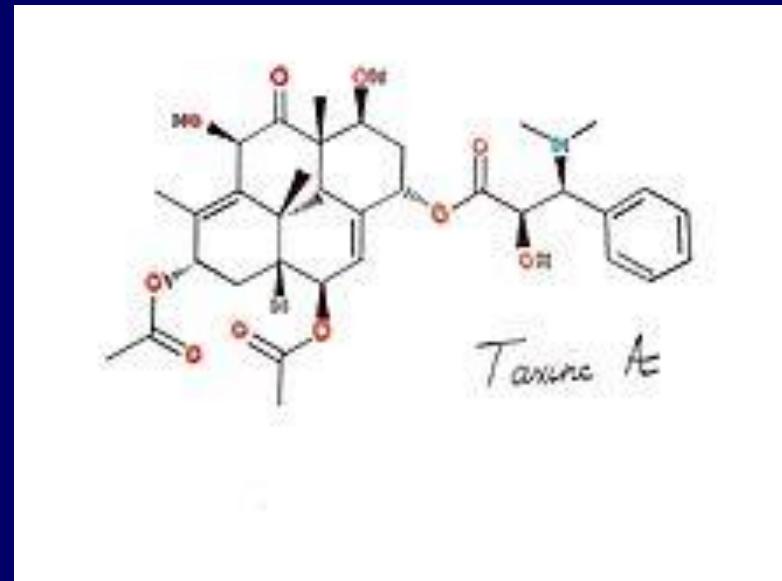
*Taxus baccata* L.  
©Thomas Schoepke



*Taxus Baccata*

Yew tree (Tis červený)

Whole plant toxic except of fruit



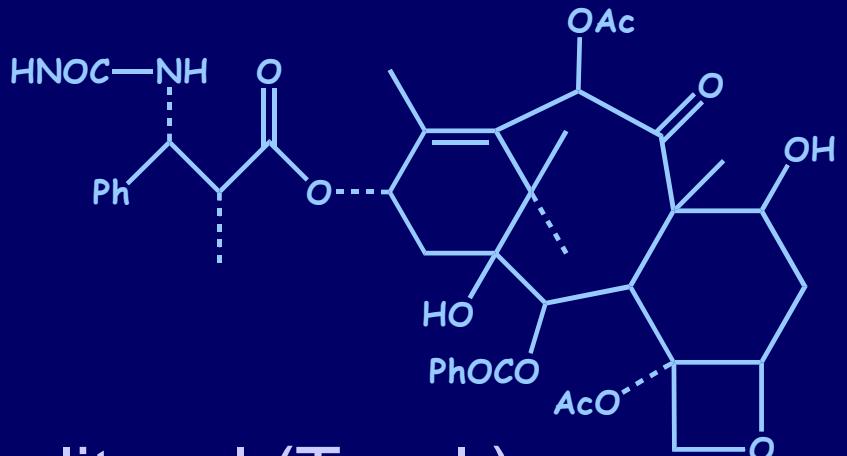
(taxins)

# Diterpenes:



*Taxus Brevifolia*

- used to treat different cancers including ovarian, breast and lungs cancer



Paclitaxel (Taxol®)

Pacific yew

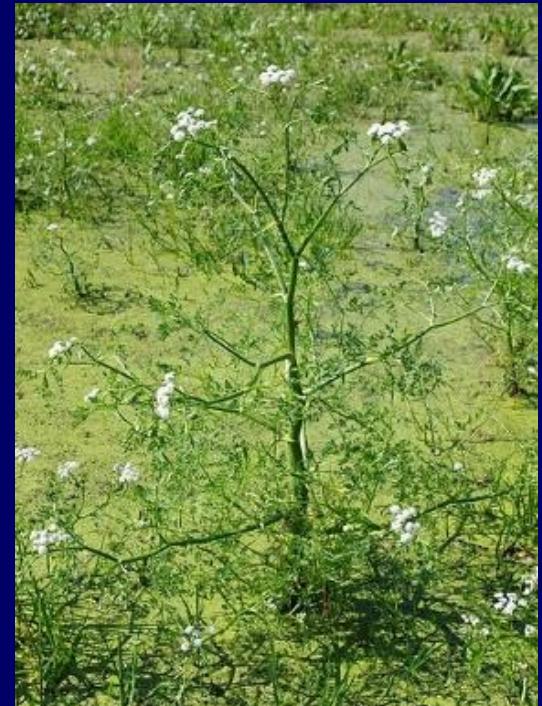


# Water dropwort (water fennel)



Oenanthotoxin (překrvení sliznic, kolikové bolesti)

## *Oenanthe aquatica* (Halucha vodní)



# Urushiol



$R = (CH_2)_{14}CH_3$  or

$R = (CH_2)_7CH=CH(CH_2)_5CH_3$  or

$R = (CH_2)_7CH=CHCH_2CH=CH(CH_2)_2CH_3$  or

$R = (CH_2)_7CH=CHCH_2CH=CHCH=CHCH_3$  or

$R = (CH_2)_7CH=CHCH_2CH=CHCH_2CH=CH_2$  and others

*Toxicodendron radicans*

*Poison Ivy (Jedovatec kořenující)*



# Steroid glycosides



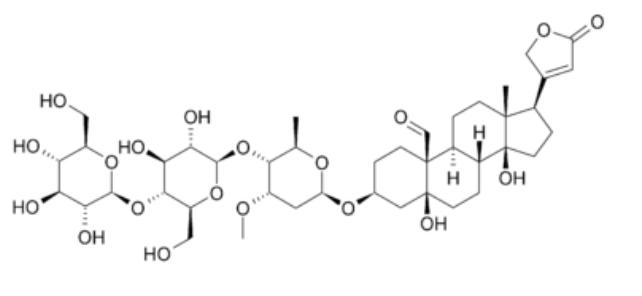
Poison arrow plant

*Acokanthera oblongifolia*



Ouabain

cardiac glycoside that acts by inhibiting the Na<sup>+</sup>/K<sup>+</sup>-ATPase sodium-potassium ion pump  
(but it is not selective)



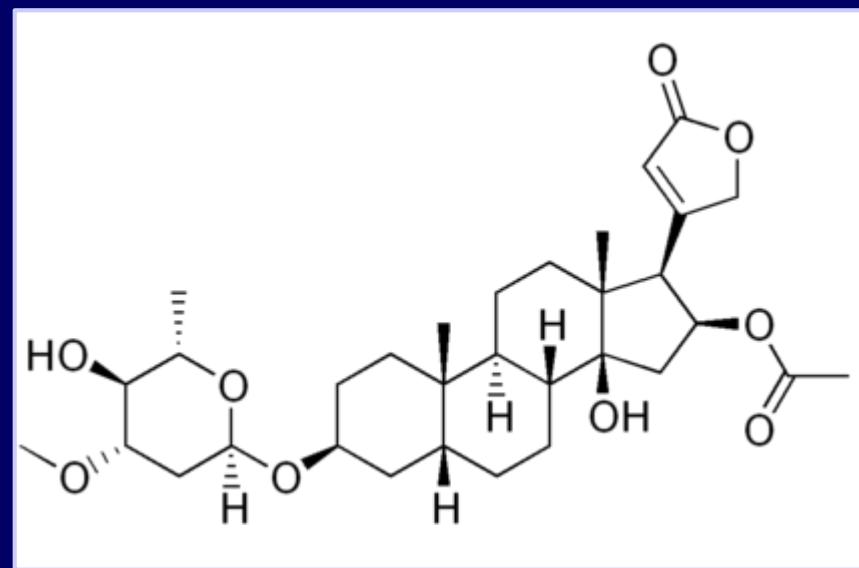
k-strophanthin

# Steroid glycosides



# Nerium oleander

## Oleander



# Oleandrin



# Alkaloids

- Definition: the term “alkaloid” (alkali-like) is commonly used to designate basic heterocyclic nitrogenous compounds of plant origin that are biologically active.

# Classification of alkaloids

- **True (Typical) alkaloids** that are derived from amino acids and have nitrogen in a heterocyclic ring. e.g. Atropine
- **Protoalkaloids** that are derived from amino acids and do not have nitrogen in a heterocyclic ring. e.g. Ephedrine
- **Pseudo alkaloids** that are not derived from amino acids but have nitrogen in a heterocyclic ring. e.g. Caffeine

# Alkaloids

New Definition: Alkaloids are cyclic organic compounds containing nitrogen in a negative state of oxidation with limited distribution among living organisms.

# Alkaloids

## Distribution and occurrence:

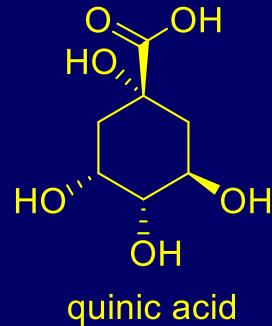
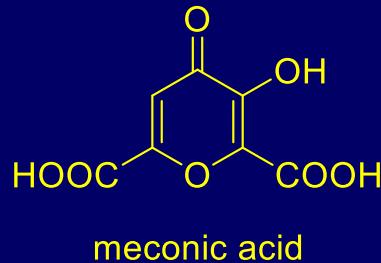
- Rare in lower plants.
- Dicots are more rich in alkaloids than monocots.
- Families rich in Alkaloids: Apocynaceae (Toještovité), Rubiaceae (Mořenovité), Solanaceae (Lilkovité) and Papaveracea (Makovité).
- Families free from Alkaloids: Rosaceae (Růžovité), Labiatae (Hluchavkovité).

# Distribution in Plant:

- All Parts e.g. Datura (Durman).
- Barks e.g. Cinchona (Chinovník)
- Seeds e.g. Nux vomica (Kulčiba)
- Roots e.g. Aconite (Oměj)
- Fruits e.g. Black pepper
- Leaves e.g. Tobacco
- Latex e.g. Opium

# Forms of Alkaloids:

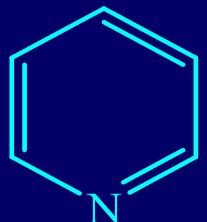
- Free bases
- Salts with Organic acids e.g. **Oxalic, acetic acids**
- Salts with inorganic acids e.g.  $\text{HCl}$ ,  $\text{H}_2\text{SO}_4$ .
- Salts with special acids:
  - e.g. **Meconic acid** in Opium
  - Quinic acid** in *Cinchona*
- Glycosidal form e.g. Solanine in *Solanum*.



# Function in Plants

- They may act as **protective** against insects and herbivores due to their bitterness and toxicity.
- They are, in certain cases, the final **products of detoxification (waste products)**.
- **Source of nitrogen** in case of nitrogen deficiency.
- They, sometimes, act as **growth regulators** in certain metabolic systems.
- They may be utilized as a **source of energy** in case of deficiency in carbon dioxide assimilation.

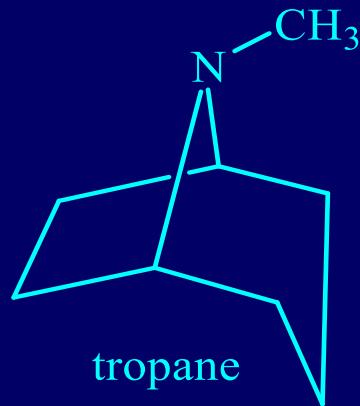
# Classification of alkaloids



pyridine



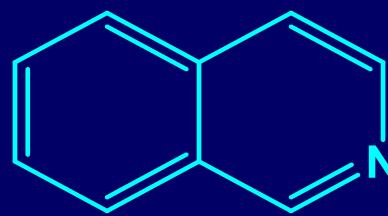
piperidine



tropane



quinoline

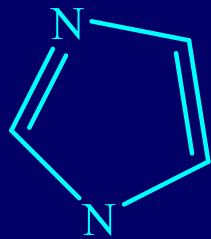


isoquinoline

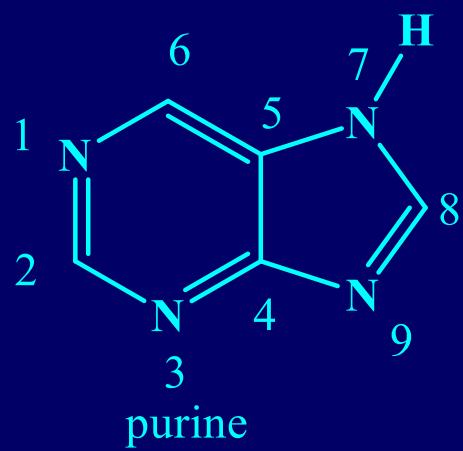
# Classification of alkaloids



indole



imidazole



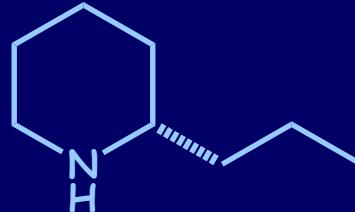
purine



*Connium maculatum*

One of the first alkaloids isolated  
(1827) and first one synthesized in  
the lab (1886, Ladenburg)

less than 0.2g is fatal to humans  
(LD<sub>50</sub> 4 mg/kg - cow, neuromuscular  
receptors-paralysis)



Coniine  
Poison hemlock  
(Bolehlav plamatý)



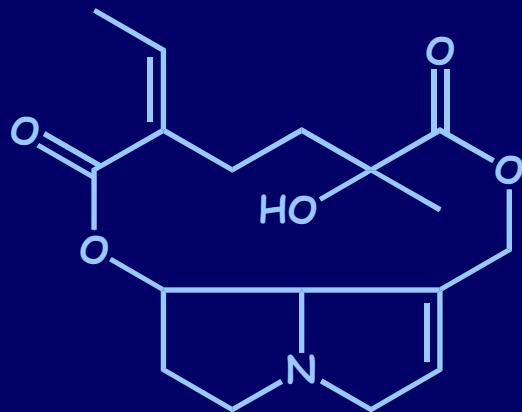
*Sarracenia flava*



# Alkaloids:



*Senecio vulgaris*



Senecionin  
Common groundsel  
(Starček obecný)

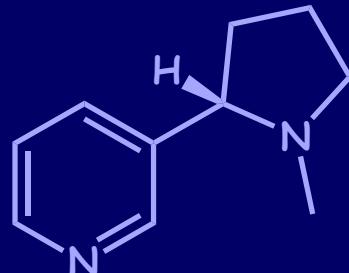
Toxin causes  
liver failure

Secondary  
poisoning from  
cow milk drinking  
were described





*Nicotiana tabacum*

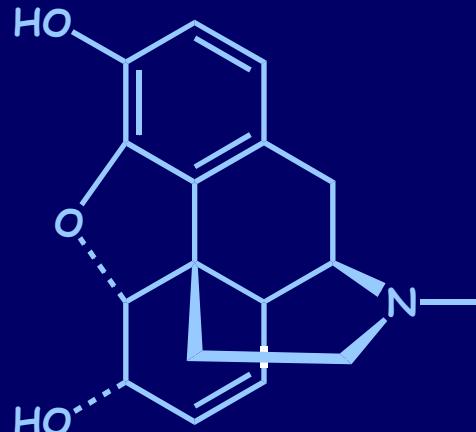


Nicotine  
Virginia tobacco

- Highly toxic - LD<sub>50</sub> about 3 mg/kg (mice)
- Extracts might be used as insecticide
- isolation 1828  
synthesis 1904



*Papaver somniferum*



Morphine  
Opium poppy

- Main component of opium (9 - 14%)
- opium - dried latex from unripe seedpods (contains also codeine a thebaine)
- Isolation 1820
- synthesis 1944

# Strychnine:



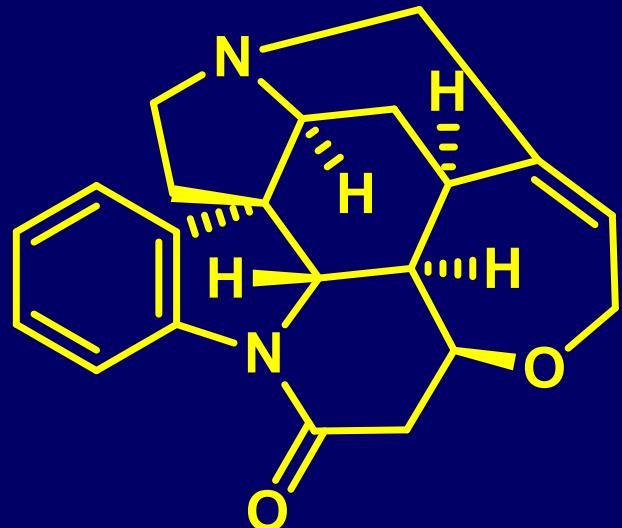
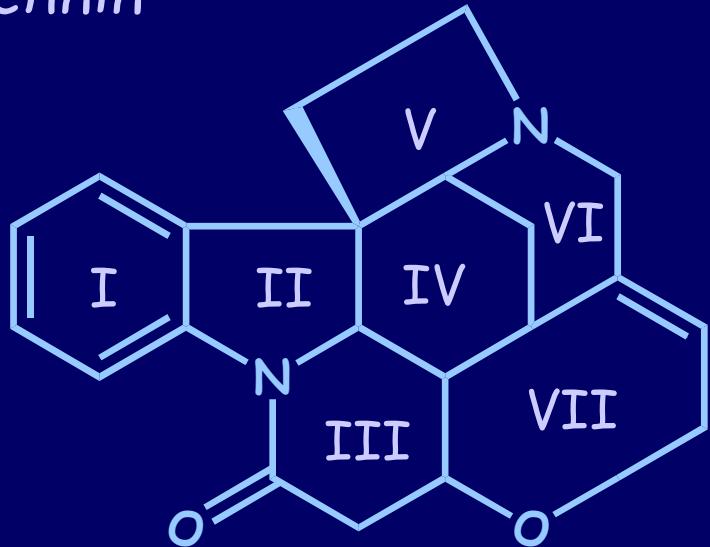
Tree native to east India,  
strychnine tree ,  
*strychnos nux-vomica*  
(Kulčiba dávivá)

Only fruit is toxic

One of the first alkaloids  
isolated - Pierre-Joseph  
Pelletier in 1818

LD50 = 0.16 mg/kg in rats, 1-2  
mg/kg orally in humans,  
glycine receptor inhibitor  
(barbiturates antidotum)

# Strychnin



isolation

1818 (Pelletier)

structure

1946 (Robinson)

synthesis

1954 (Woodward)

stereoselective synthesis

1992 (Overman)



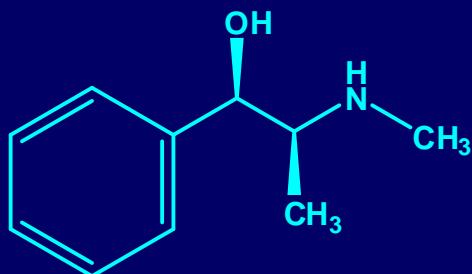
*Colchicum speciosum*  
(Ocún)  
autumn crocus or  
„naked lady“



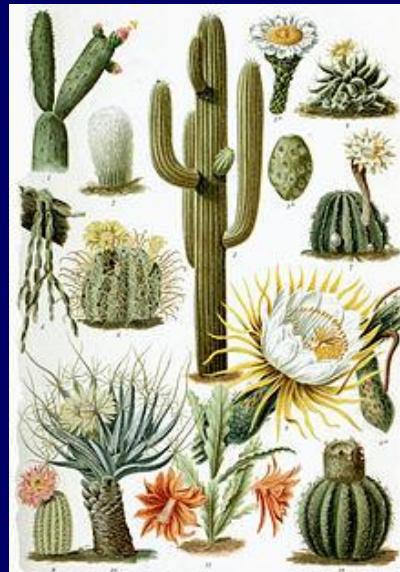
Colchicine  
Treatment of gout

# Classification of alkaloids

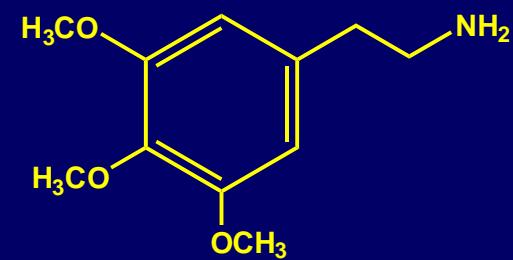
Phenylethylamine a. :



Ephedrine  
*Ephedra fam.*

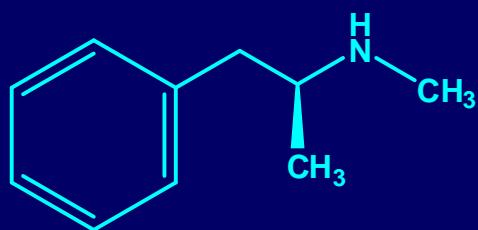


*Lophophora williamsii*

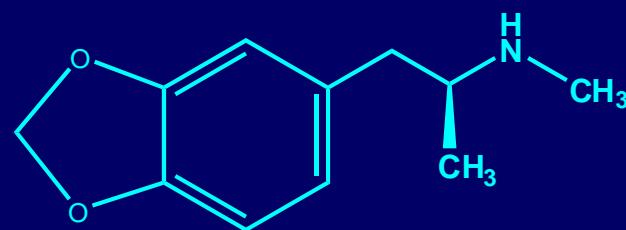


mescaline

# Metamphetamine and MDMA



Pervitin  
(metamphetamine)

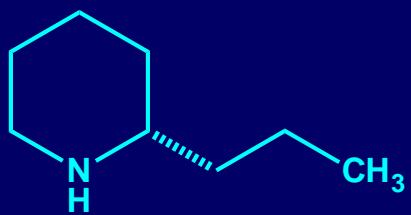


Extasy (MDMA)

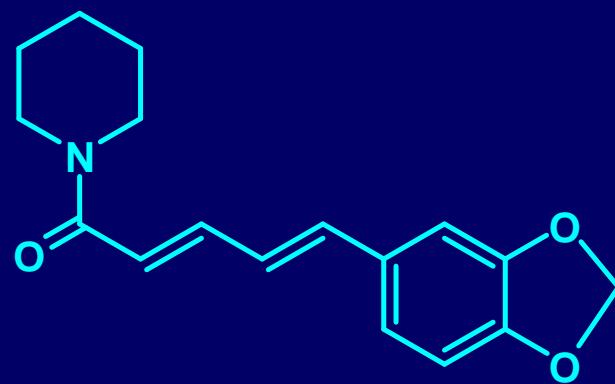
# Purine alkaloids



# Pyridine and piperidine a.



coniine



piperine

# Pyridinové a pyrrolidinové a.



nicotine



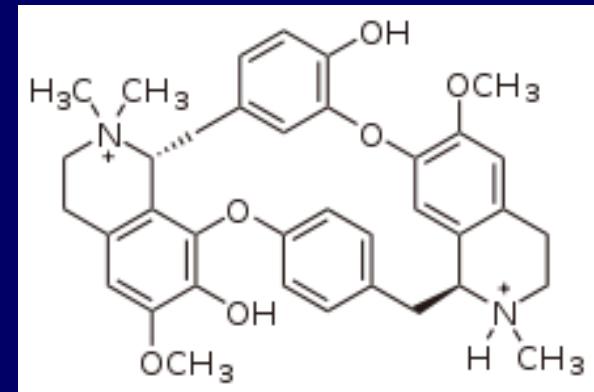
cotinine

# Pyridine and piperidine a.

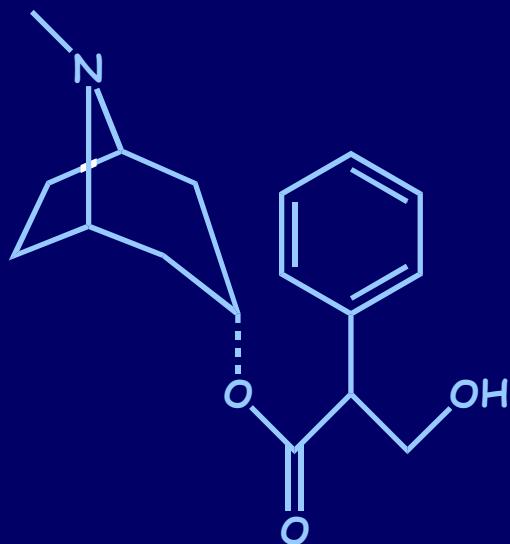
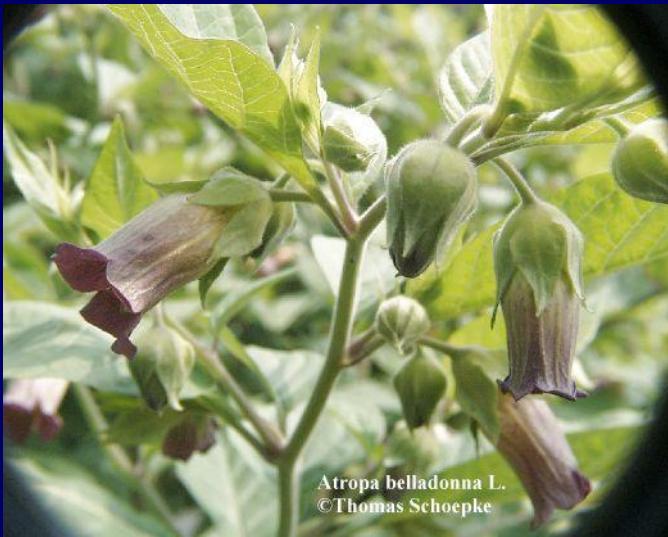


*Strychnos toxifera*

(kulčiba jednodárná)



**Tubocurarine chloride**  
inhibitor of nicotinic  
acetylcholine receptors



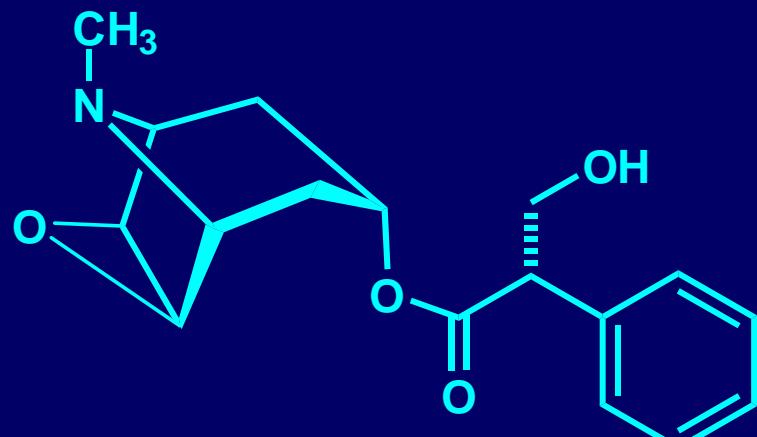
Atropine

Atropa belladonna  
Deadly nightshade

Atropine in the small doses supports CNS, used in ophthalmology as mydriatics

- used also for treatment of Parkinson's disease

# Tropane alkaloids.



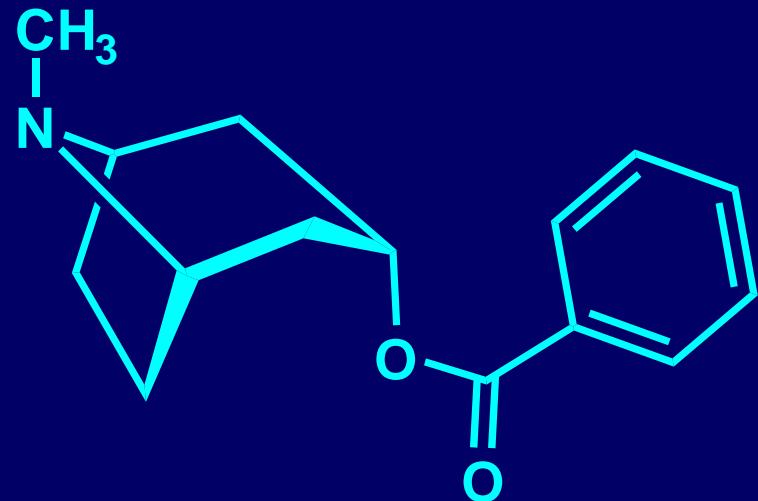
scopolamine

# Cocaine

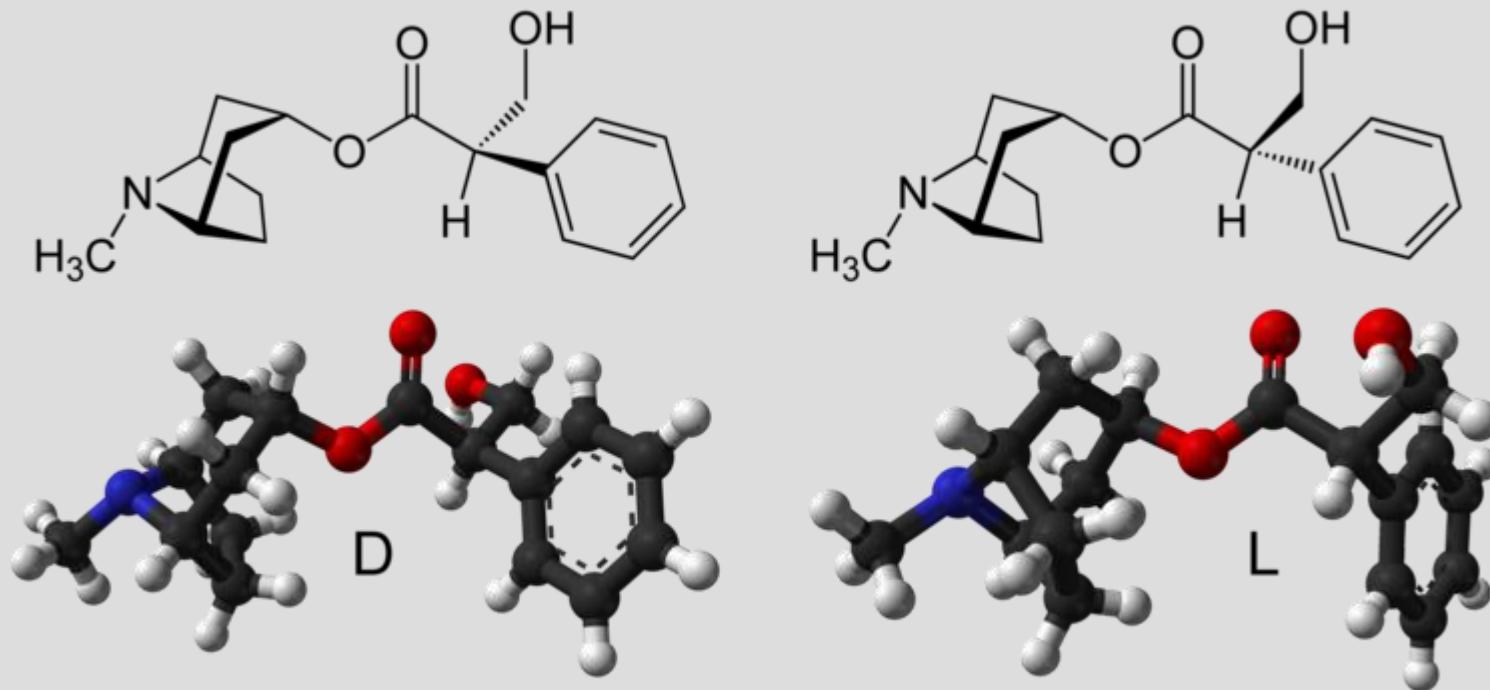


Erythroxylum coca  
(Rudodřev koka)

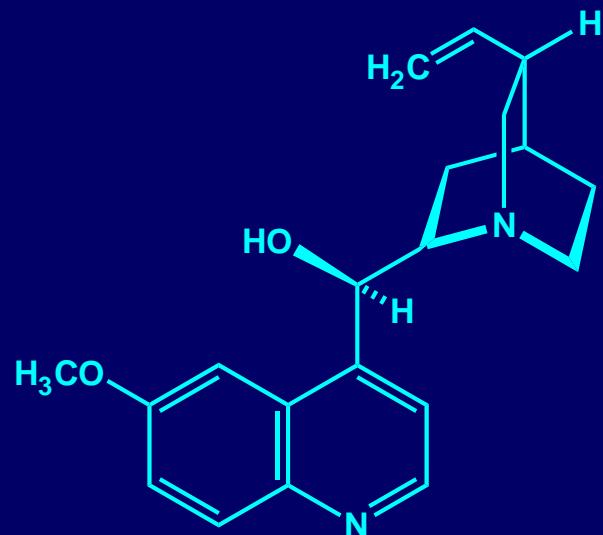
Inhibits reuptake of serotonin, norepinephrine and dopamine.



# Atropine a hyoscyamin



# Quinoline alkaloids

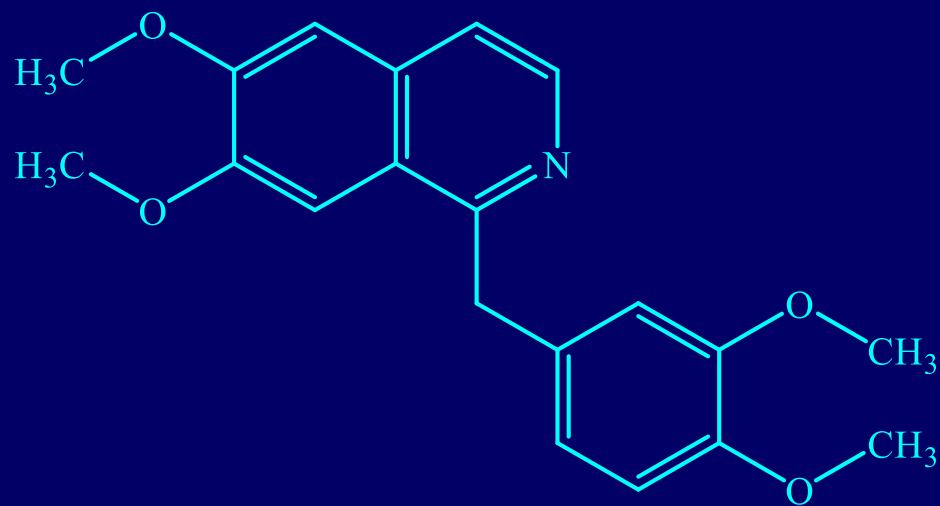


quinine



*Cinchona calisaya*

# Isoquinoline alkaloids



# papaverine

## (Léčba spasmů)

# Indole alkaloids

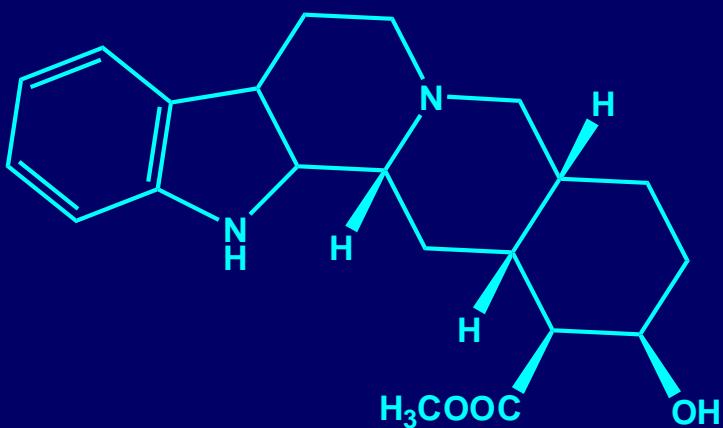


Rauwolfia serpentina  
Indian snakeroot  
(Zmijovice hadová)



Reserpine  
(Léčba hypertenze,  
tranquillizer)

# Indole alkaloids



yohimbine  
*Pausinystalia yohimbe*

# Phenanthrene alkaloids



morphine



heroin ( $R = R' = CH_3CO-$ )  
codeine ( $R = CH_3, R' = H$ )

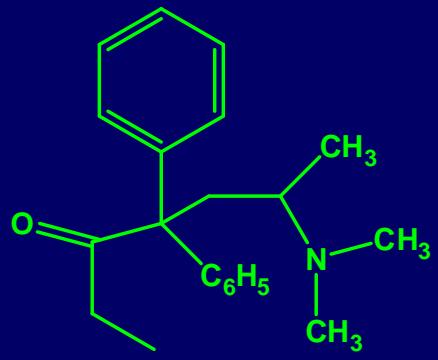
# Morphine rule:

## Structural requirements:

1. Tertiary amine substituted with small alkyl.
2. Quarternary carbon atom.
3. Phenyl group (or its isosteric equivalent) directly attached to quartenary carbon.
4. 2 C spacer between quarternary carbon and tertiary amine



# Morphine rule



# Methadon



# Meperidin



## Buprenorphine (Subutex)