COMPOUNDS AFFECTING AUTONOMOUS (VEGETATIVE) NERVOUS SYSTEM

Chemical transmission between neurons is mediated using transmitters (neurotransmitters).

Transmitters are deliberated from neuronal terminations into space of synapsys, they cross synapses and activate or inhibit postsynaptic cells by binding to specialized molecules of receptors.

Autonomous neural system is into some rate independent and its activity is not under control of will.

It affects processes: heart activity, tonus and motility of smooth muscles, digestion, glandular secretion, eye control…

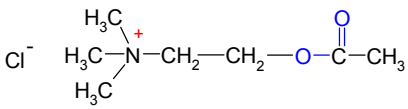
ANS – part of neurohumoral regulatory system, which in coordination with CNS adapts reactions of organism to changes of inner and outer environment

PERIPHERAL PART OF AUTONOMOUS NEURAL SYSTEM - NERVES SYMPATIC AND PARASYMPATIC

PARASYMPATICUS

- participates on anabolic processes
- Increases secretion of digestive tract and its motility
- increases stock of storage compounds (glycogene)
- tranquilize heart action
- Increases the blood supplies of organs

Mediator is acetylcholine

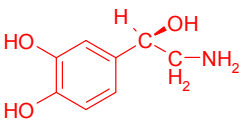


SYMPATICUS

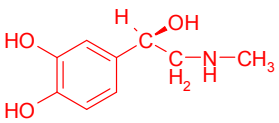
- Mobilizes to sharp deffensive and adaptation reactions
- accelerates heart action
- increases blood pressure
- Trgggers utilization of storage compounds

Mediator is noradrenaline

Component of system is adrenal gland → adrenalin



noradrenaline



adrenaline

DIVISION OF COMPOUNDS AFFECTING AUTONOMOUS NEURAL SYSTEM

SYMPATOTROPIC COMPOUNDS

- sympatomimetics
  (adrenomimetics, adrenergic compounds)
  working as sympaticus irritation
- sympatolytics
  (adrenolytics, adrenergic blockers, antiadrenergic compounds)
  block effects of sympaticus stimulation, sometimes block effects of sympatomimetics

PARASYMPATOTROPIC COMPOUNDS

- parasympatomimetics
  acting as parasympaticus irritation
- parasympatolytics
  block parasympaticus stimulation and block effects of parasympatomimetics

DIRECT SYMPATOMIMETICS

NOREPINEPHRINE = NORADRENALINE (ČL 2005)

Natural mediator

Usage:

- Peripheral analeptic for treatment of collapses
- During intoxication by hypnotics or narcotics

EPINEPHRINE = ADRENALINE (ČL 2005)

Hormone of medulla of adrenal gland

Usage:

- Peripheral analeptic for treatment of collapses
- During intoxication by hypnotics or narcotics
- Vasoconstringent admixture to local anesthetics solutions
- Bronchodilator
- Antiallergic

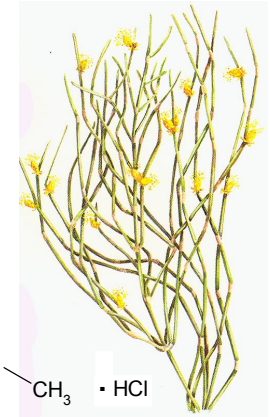
INDIRECT SYMPATOMIMETICS INCREASE IN PLCE OF EFFECT
LEVEL OF NEUROMEDIATOR

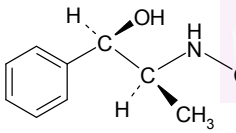
EPHEDRINUM – EPHEDRINE (ČL 2005)

Ephedrini hydrochloridum – Ephedrine HCl

Source: *Ephedrae herba* – mahuang herb
Ephedra sinica - Joint-pine, Jointfir, Mormon-tea, mahuang; *E. distachya* – (Ephedraceae). Broom-like gymnosperm shrubs with coupled scale-like leaves

Drug: in autumn harvested dried branches, brown-green colour. Producers: China, India, Pakistan, Spain)
CC: 0,5-1,5 % of alkaloids (cca 75 % of ephedrine), tannins, saponins
Usage: antiasthmatic, analeptic, peripheral vasoconstringent, central stimulant
Ephedrinism





(1R,2S)

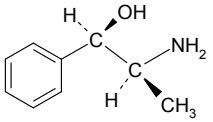
INDIRECT SYMPATOMIMETICS
KHAT

Source: *Catha edulis* – khat (Celastraceae). Evergreen shrub native to Yemen, Ethiopia and Solmalia. Natives chew fresh leaves - khat.

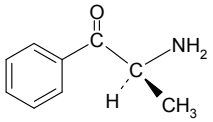
Drug: dried leathery leaves

CC: norpseudoephedrine = cathine, cathinone, flavonoids

Effects: euphoria, after repeated use starts addiction
loss of appetite
cathine – lead compound for synthetic anobesics



cathine



cathinone

SYMPATOLYTICS – ADRENOLYTICS

SYMPATOLYTICS BLOCKS ADRENERGIC REACTIONS.

AS DIRECT SYMPATOLYTICS, BLOCKING
α1 ADRENERGIC RECEPTORS ACT
NATIVE AND DH-DERIVATIVES OF ERGOT ALKALOIDS

SECALE CORNUTUM – ERGOT

Source: *Claviceps purpurea* – ergot (Clavicipitaceae) – fungus parasiting on the rye and some other plants of Poaceae family

Fungal attack changes the *ovaria* of plants to thought, dark-purple *sclerotia*.

Ergot is used as a therapeutical agent from medieval ages.

- 1808 Stearns in USA – effect of ergot on the management of labor
- 1875 Tanret in France – first crystalline product from ergot
- From 1917 Stoll and Hoffmann in Sandoz Co. – obtained pure alkaloids and enabled their application in therapy.
- From 1954 M. Semonský in VÚFB – antimigraenics, venopharmacs
- Today known more than 50 native alkaloids
- Numerous derivatives and semi-synthetic derivatives
- Research continues

SECALE CORNUTUM – ERGOT

SECALE CORNUTUM – ERGOT

Increased consumption of ergot alkaloid is solved:

- by increasing of sown area
- by artificial infection of rye (preparation of material with *conidias* of required type – ergotamine, ergotoxine or ergocristine), 6-8 weeks after infection *sclerotia* are harvested
- by using *in vitro* saprophytic culture

Paspalum dilatatum (strain *Claviceps paspali*) produce during submersal cultivation up to 10 % of free lysergic acid, which can be used for preparation of semisynthetic analogues

In present time submersal cultivation and production of ergotoxine type

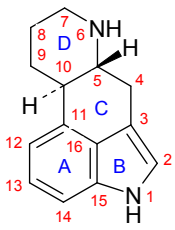
SECALE CORNUTUM – ERGOT

CONTENT COMPOUNDS

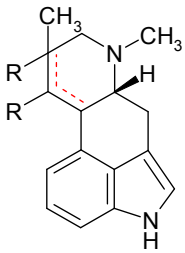
- **Hemiterpenic indol alkaloids**
  - clavines – derivatives of 6,8-dimethylergoline
  - amides
  - peptides of lysergic acid

- Further compounds
  - building material of cell walls
  - fatty oil up to 35 %
  - ergosterol
  - tyramin, histamin
  - pigment (clavorubine, ergoflavine, secalonic acid)

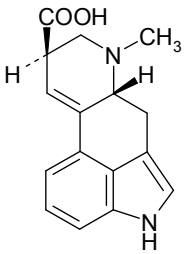
SECALE CORNUTUM – ERGOT



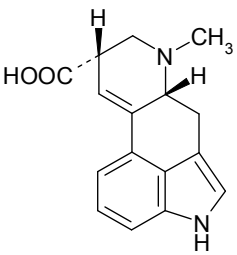
ergoline



clavine
R = H, OH

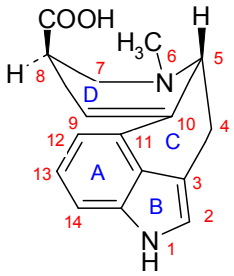


lysergic acid
(5R, 8R)



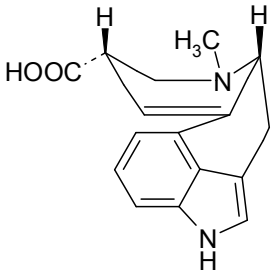
isolysergic acid
(5R, 8S)

LYSERGIC AND ISOLYSERGIC ACID IN SPACE



(5R,8R) lysergic acid

active alkaloids, suffix - ine
for example: ergometrine



(5R,8S) isolysergic acid

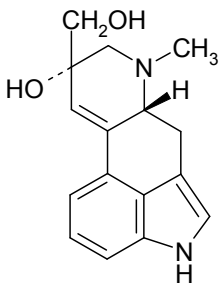
non-active alkaloids, suffix - inine
for example: ergometrinine

SECALE CORNUTUM – ERGOT

CLAVINE ALKALOIDS

Clavine alkaloids number ≥ 20

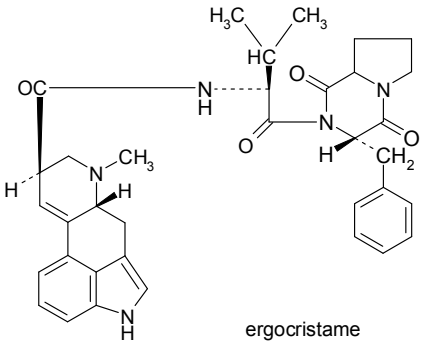
- carboxylic group at C_8 reduced to primary alcoholic group or to methyl group
- not used in therapy
- subject of studies



peniclavine

SECALE CORNUTUM – *ERGOT*

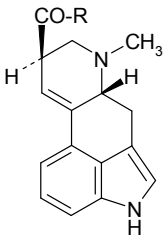
LACTAM PEPTIDE ALKALOIDS



ergocristame

SECALE CORNUTUM – ERGOT

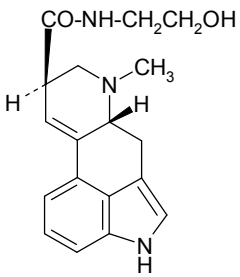
SIMPLE AMIDES



Ergine R = NH_2

Ergometrine R = CH_3-CH$(NH)_2$-CH_2OH

uterotonic

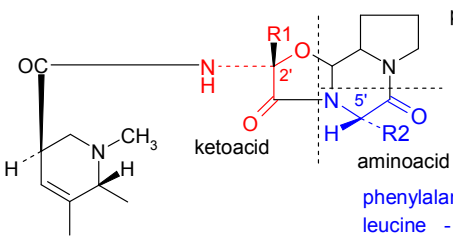


α-hydroxyethylamide of lysergic acid

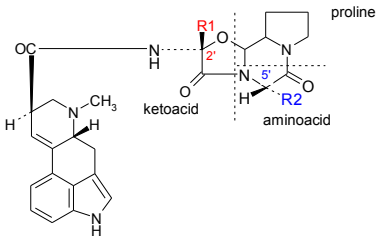
Paspalum dilatatum, submersal cultures

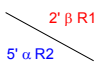
ERGOT ALKALOIDS PEPTIDIC
ERGOTAMINE AND ERGOTOXINE GROUP

α-hydroxyvaline -CH_3
α-amino-N-butyrate - C_2H_5
α-hydroxyvaline -$CH(CH_3)_2$



phenylalanine - CH_2-C_6H_5
leucine - $CH_2CH(CH_3)_2$
isoleucine - $CH(CH_3)C_2H_5$
valine - $CH(CH_3)_2$



2' β R1 / 5' α R2	ergotamine group	ergostine group	ergotoxine group
	CH_3	$C(H_2)-CH_3$	$CH(CH_3)_2$
	ergotamine	ergostine	ergocristine
	ergovaline	ergonin	ergocornine
	ergosine	ergoptin	ergocryptine
	β-ergosin	β-ergoptin	β-ergocryptine

ERGOT ALKALOIDS – USAGE

ISOLATED ALKALOIDS AND THEIR DERIVATIVES

block α_1-adrenergic receptors

Ergometrini maleas – Ergometrine-maleinate (ČL 2005)

- Uterotonic

Ergotamini tartras – Ergotamine-tartrate (ČL 2005)

- Uterotonic
- Component of antimigrainics and sedatives

Methylergometrinium tartaricum – Methylergometrine-tartrate

- Uterotonic

Dihydroergocristini mesilas – Dihydroergocristine-mesylate (ČL 2005)

- Alpha-sympatolytic – for therapy of peripheral blood supply, vasodilatant.
- Component of antihypertensives

Dihydroergotamini mesilas – Dihydroergotamine-mesylate (ČL 2005)

- Alpha-sympatolytic- for disorders of peripheral blood supply
- Antimigrainic

α_2-RECEPTOR BLOCKER - YOHIMBINE

Source: *Pausinystalia yohimbe* – yohimbe (Rubiaceae). Up to 30 m tall tree from Cameroon and Congo

Drug: dried bark of stems and branches

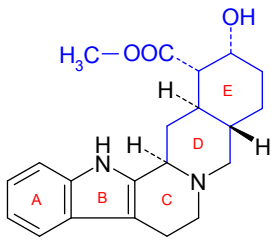
CC: alkaloid 1-1,5 %, main is yohimbine (trans anelation of rings C/D and D/E)
tannins

Bark is used for alkaloids isolation

Effect: yohimbine dilates peripheral blood vessels and lowers blood pressure

Usage:

- rarely as antihypertensive
- adjuvant during *impotentia coeundi* of neurastenic origin
- aphrodisiac



PARASYMPATOMIMETICS

DIRECT PARASYMPATOMIMETICS

- Pilocarpine
- Arecoline
- Muscarine
- Nicotine in small doses

INDIRECT PARASYMPATOMIMETICS
(reversible inhibitors of acetylcholin-esterase)

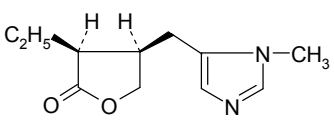
- Physostigmine
- Galanthamine

PILOCARPINI NITRAS – PILOCARPINE-NITRATE (ČL 2005)
PILOCARPINI HYDROCHLORIDUM – PILOCARPINE-HYDROCHLORIDE (ČL2005)

Source: *Pilocarpus jaborandi* – jabornadi, *P. racemosus, P. microphyllus* (Rutaceae); shrubs and small trees from South America (Brazil, Paraguay)

Drug: dried, leathery, ellipsoid leaves. Bright points show through – glandules with essential oil. Storage rapidly decreases the alkaloid content

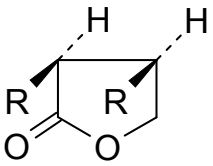
CC: 0,5-5 % alkaloids – substituted imidazols. Prevalent pilocarpine. Stable at pH 3-5.



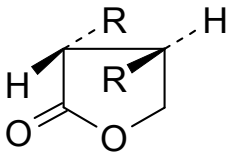
Effect: Increases secretion of salivary and perspiratory glands, induces miose and lowers intraocular pressure

Usage: glaucoma, hydragogum for acute hydrops of labyrinth, rarely diaphoretic

ISOMERISM OF PILOCARPINE AT BUTYROLACTONE RING



cis = normal form
stable at pH 3 - 5



trans = iso-compounds
not effective

PHYSOSTIGMINI SALICYLAS – PHYSOSTIGMINE-SALICYLATE (ČL2005)
PHYSOSTIGMINI SULFAS – PHYSOSTIGMINE-SULPHATE (ČL 2005)

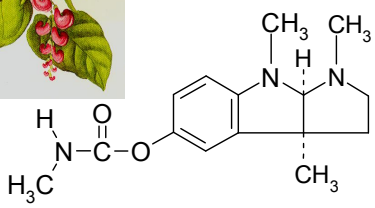
Source: *Physostigma venenosum* – calabar bean (Fabaceae); climbing wine from tropic West Africa. Fruit is a pod containing seeds

Drug: kidney-shaped, pale, dark-brown seeds (resembling beans). Used for physostigmine isolation.

CC: 0,1-0,2 % alkaloids, main is physostigmine (syn. eserine). Further fatty oil. At pH ≥ 5 hydrolysis producing ineffective compounds

Effect: reversible inhibitor of acetylcholinesterase

Usage: miotic during glaucoma, less at atonia of internal organs and for treatment of neurologic disorders



GALANTHAMINUM – GALANTHAMINE

Source: *Galanthus nivalis* – snowdrop (Amaryllidaceae). Perennial plant of humid mountain meadows and deciduous woods

Drug: up to 3 cm big bulbs, processed fresh for alkaloid isolation

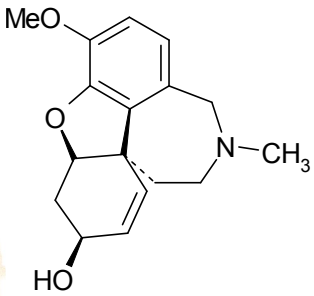
CC: norballadine alkaloids, their content and spectrum is variable; mucilage, starch, organic acids

Effect: reversible inhibitor of acetylcholinesterase

Usage:

- ophthalmology at glaucoma
- post-surgical paresis
- paralysis of guts and bladder
- Damage of central motoric neurons
- status after poliomyelitis
- neurodenerative diseases

Alternative sources: *Galanthus woronovii* (Caucasus)
Ungernia victoria (South America)



MUSCARINE

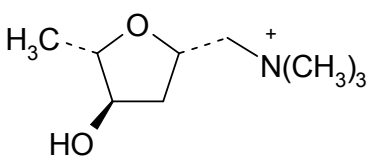
Source: *Amanita muscaria* – fly agarics (Agaricaceae)

Effect: Affects exclusively at receptors of peripheral effectoric cells of parasympaticus (therefore assignation of these receptors – muscarine type, M-receptors)

Toxicological importance, causes:

- miose
- diarrhea, convulsions
- bronchoconstriction
- Decrease of blood pressure leading to collapse
- Increase of glandular secretion

Usage: experimentally



ARECOLINUM – ARECOLINE

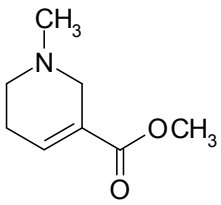
Source: *Areca catechu* – areca nut palm, Betel, (Palmae); slim stem terminated by bunch of fan-shaped leaves; India, southeast Asia; cultivated in India, Bangladesh, Indonesia, east Africa - Tanzania

Drug: Arecae semen – areca nut, seed Ø 2 cm embedded in fibrous drupe

CC: 0,2-0,5 % of alkaloids, main is arecoline; 50-60 % of sugars; 15 % fats; tannins; flavans

Effect: arecoline targets M-receptors. Causes
- miose
- stimulation of peristaltic
- Increases salivation

Usage:
- Diaphoretic
- Veterinary anthelmintic, taenicide
- For chewing ≥ 200 millions of people for psychoactive effect
- Tested for treatment of neurodegenerative diseases



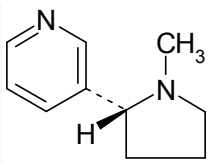
NICOTINE

Source: *Nicotiana tabacum, N. rustica* – tobacco (Solanaceae); cultivated for production of leaves to smoke, chew and snuff.

CC: 2-10-15 % of alkaloids, main is (S)-(–)-nicotine = volatile liquid base; anabasine, nornicotine and others, 40 % of saccharides (starch, pectin, cellulose, sugars), 15-20 % organic acid

Effect:
- at low doses stimulates, at high doses blocks ganglia (nicotine cholinergic receptor)
- stimulates CNS - addiction
- Increases motility and secretion of GIT

Toxicological importance
Insecticide



PARASYMPATOLYTICS AND SPASMOLYTICS

PARASYMPATOLYTICS – compounds blocking muscarinic effects of acetylcholine and cholinomimetics.

Induce:

- spasmolysis
- mydriasis, accomodation paralysis
- Decrease of secretion of glands - salivary, perspiratory, bronchial, gastric
- tachycardia (above 90 strokes / min)

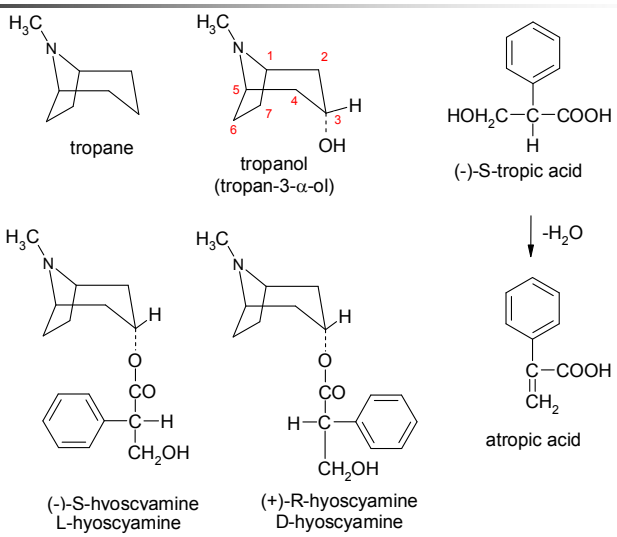
SPASMOLYSIS – release of pathologically increased contractibility of smooth muscles and peristaltic

- GIT
- urinary tract
- biliar ways

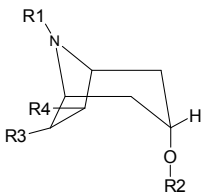
SPASMOLYTICS

NEUROTROPIC	MUSKULOTROPIC, myotropic, papaverine type
anticholinergic, atropine type	
Affect parasympatic inervation of smooth muscle	Release convulsions by direct affecting of cells of smooth muscles
Atropine, scopolamine	Papaverine, khelline

TROPANE ALKALOIDS – NEUROTROPIC SPASMOLYTICS

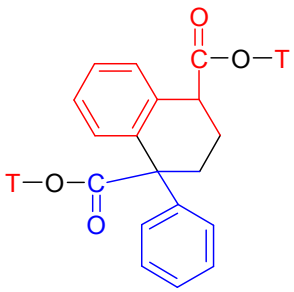


TROPANE ALKALOIDS – NEUROTROPIC SPASMOLYTICS



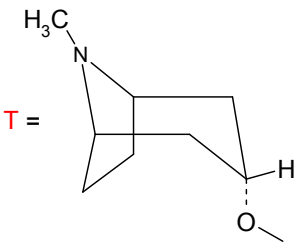
	R1	R2	R3	R4
tropanol	CH3	H	H	H
hyoscyamine	**CH_3**	**tropoyl**	**H**	**H**
norhyoscyamine	H	tropoyl	H	H
apoatropine	CH_3	atropoyl	H	H
valeroidine	CH_3	isobutyryl	OH	H
meteloidine	CH_3	tigloyl	OH	OH
scopine	CH_3	H	—O—	
scopolamine	**CH_3**	**tropoyl**	—O—	
norscopolamine	H	tropoyl	—O—	
aposcopolamine	CH_3	atropoyl	—O—	

TROPANE ALKALOIDS – NEUROTROPIC SPASMOLYTICS



belladonine

T =



tropyl-

BELLADONNAE FOLIUM – DEADLY NIGHTSHADE LEAVES (ČL 2005)

Source: *Atropa belladonna* – deadly nightshade (Solanaceae). Perennial 1,5 tall herb, Europe, for pharmaceutical purposes is cultivated

Drug: dried leaf sometimes with flowering or fruit bearing tips, harvested VI-VIII

CC:

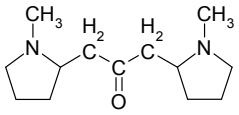
- 0,2-1 % tropane alkaloids, (-) S-hyoscyamine, racemizing to atropine; scopolamine (hyoscine); during drying is formed apoatropine and via further dimeriztion belladonine
- coumarins scopoline and scopoletine
- flavonoids, tannins
- Sand of CaOx

Usage: for isolation of alkaloids and preparation of chosen galenic

BELLADONNAE RADIX – DEADLY NIGHTSHADE ROOT

Source: as *Folium belladonnae*

Drug: dried, cylindric, cut roots. Externally grey-brown, inside grey-white, when broken produce dust - starch.
Cultivated, harvest of plant 3-4 years old

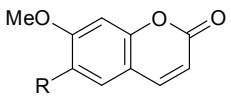


cuscohygrine

CC:

- 0,4-0,8 % tropane alkaloids, (-) S-hyoscyamine, atropine; scopolamine; apoatropine, belladonine, hygrines
- coumarins scopoline and scopoletine
- starch
- sand of CaOx

Usage: for isolation of alkaloids and for preparation of galenic



scopoletine R=OH
scopoline R=O-Glc

STRAMONII FOLIUM – THORN APPLE LEAVES (ČL 2005)

Source: *Datura stramonium* – thorn apple (Solanaceae); one-year herb, weed. For pharmaceutical purposes is cultivated. Spectacular with flowers and big fruits

Drug: dried, thin, fragile leaves, harvest V-IX;

CC: 0,1-0,6 % of tropane alkaloids, (-)-S-hyoscyamine, scopolamine; less apoatropine, belladonine

- coumarins scopoline and scopoletine
- flavonoids, tannins
- aggregates CaOx

Usage: for isolation of alkaloids and for preparation of galenics

HYOSCYAMI FOLIUM – HENBANE LEAVES

Zdroj: *Hyoscyamus niger* – henbane (Solanaceae); biennial herb from rubbles; cultivated one-year form

Drug: dried pale gray-green, from both side trichomous toothed leaves, VI-VIII.

CC:

- 0,03 – 0,15 % tropane alkaloids hyoscyamine, scopolamine
- flavonoids, tannins, coumarins
- crystalls of calcium oxalate

Usage: material for alkaloid isolation

More benefits from in Egypt cultivated *Hyoscyamus muticus*, contaning up to 1,5 % of alkaloids

FURTHER SOURCES OF TROPANE ALKALOIDS

Hyoscyamus muticus (Egypt), Herb contains 0,6-1,5 % of alkaloids

Scopolia carniolica (Balcan peninsula, Rusia), root contains 0,4-1 % of alkaloids

Duboisia myoporoides (Australia), Folium containns up to 4 % of alkaloids
Leichardtii

Datura arborea (South America), Folium contains up to 0,4 % of alkaloids

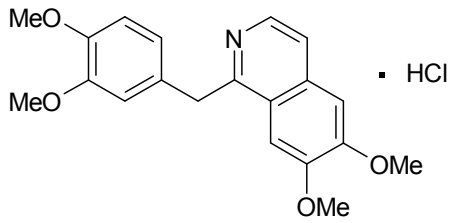
Datura metel (Africa, trop. Asia), Folium contains cca 0,55 % of alkaloids

Occurrence in plants of Convolvulaceae, in some fungi *(Sclerotinia, Corticium)*

MUSCULOTROPIC SPASMOLYTICS

Papaverini hydrochloridum – Papaverine hydrochloride (ČL 2005)
Source: Opium (0,5-1,3 %); poppy straw
Usage: spasmolytic effects is observed at smooth muscles of:

- GIT
- Cardiovascular system
- Respiratory tract
- Urinary tract



MUSCULOTROPIC SPASMOLYTICS
VISNAGAE FRUCTUS – KHELLA FRUIT

Source: *Ammi visnaga* – bisnaga,
toothpickweed, khella (Apiaceae);
one-year, 80 cm tall herb;
Mediterranian.
Producers: Egypt, Maroc, south of USA

Drug: dried ellipsoid doubled-achenes 2 mm long

Contain compounds:

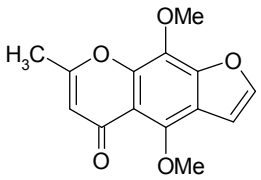
- Furanochromones (1,5-3 %)
- Pyranocoumarins (0,2-0,6 %)

MUSCULOTROPIC SPASMOLYTICS
VISNAGAE FRUCTUS – KHELLA FRUIT

Khellin –furanochromone derivatives

Usage:

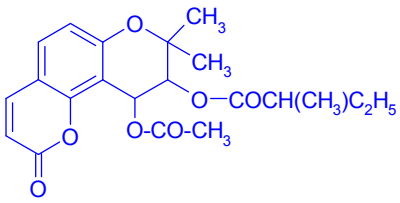
- spastic bronchitis
- asthma bronchiale
- angina pectoris
- Intestinal, biliar and kidney colic



Visnadine – pyranocoumarine derivatives

Usage:

Coronary vazodilatant (increases flow through coronary blood vessels)



CHELIDONII HERBA – TETTERWORT HERB (ČL 2005)

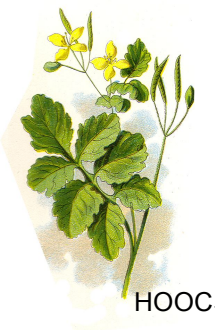
Source: *Chelidonium majus* – greater celandine, tetterwort (Papaveraceae);

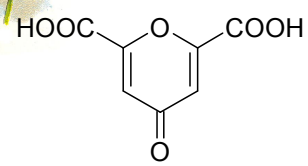
Perennial herb of Europe and Asia.

Lactifers – orange colored latex containing alkaloids and proteolytic enzymes (etches eye cornea)

Drug: dried whole or cut flowering herba

CC: at least 0,6 % of alkaloids expressed as chelidonine; alkaloids bonded on chelidonic acid; contain of alkaloids in % roots 0,1-1,4; herb 0,01-0,5; fruits 0,6-1,5; seeds 0

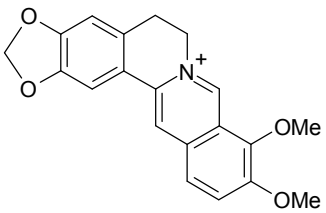




kyselina chelidonová

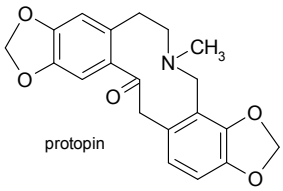
CHELIDONII HERBA – TETTERWORT HERB (ČL 2005)
ALKALOIDS

1) Berberinový typ

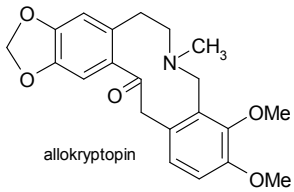


berberin - choleretikum

2) Protopinový typ



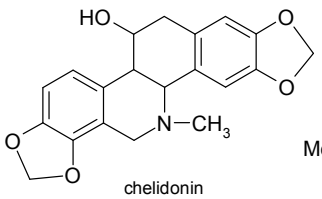
protopin



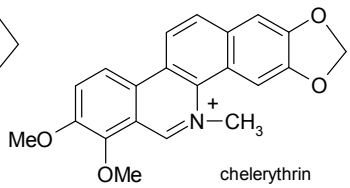
allokryptopin

CHELIDONII HERBA – TETTERWORT HERB (ČL 2005)
ALKALOIDS

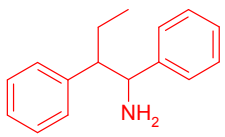
3) Benzofenanthridinový typ



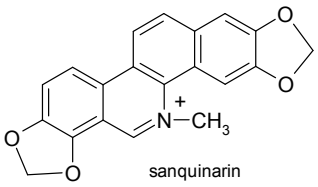
chelidonin



chelerythrin



stilbylethylamin



sanquinarin

CHELIDONII HERBA – TETTERWORT HERB (ČL 2005)

Effect:

- weak central sedative
- spasmolytic
- choleretic
- cytotoxic
- antibacterial (G+)
- high toxicity of alkaloids, proteolytic enzymes

Usage:

- spasmolytic
- choleretic
- inoperable gut polyposes

National pharmacopoeias list CHELIDONII HERBA RECENS

RUTAE HERBA – COMMON RUE AERIAL PART

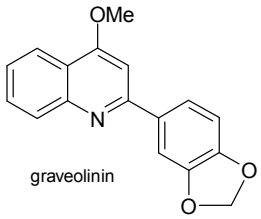
Source: *Ruta graveolens* – common rue (Rutaceae); evergreen shrub of Mediterranean; cultivated; on the leaves trichomes containing dermatotropic essential oil

Druga: dried aerial part harvested before flowering V, VI

CC: 0,05-0,15 % of alkaloids, 0,05-0,7 % of essential oil (pinene, limonene, cineol); furanocoumarins; rutosid – first time discovered in this plant

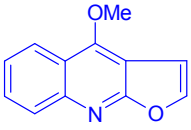
RUTAE HERBA – COMMON RUE AERIAL PART
ALKALOIDS

1) Chinolinový typ

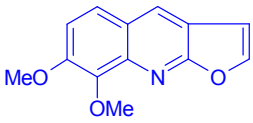


graveolinin

2) Furochinolinový typ

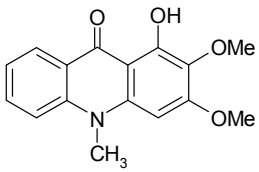


diktamnin

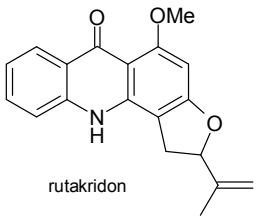


skimmianin

3) Akridinový typ

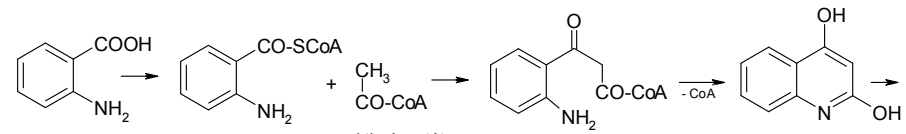


arborinin

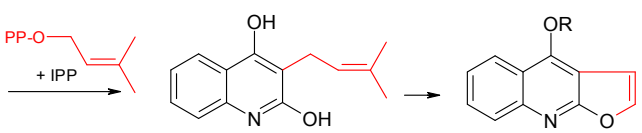


rutakridon

RUTAE HERBA – COMMON RUE AERIAL PART
BIOSYNTHESIS OF ALKALOIDS

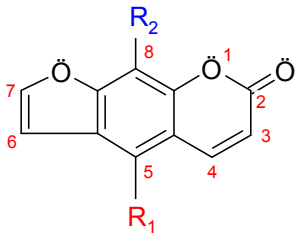


kys. anthranilová — aktivace — aktivní acetát — ketokyselina — 2,4-dihydroxychinolin



3-dimethylallyl-2,4-dihydroxychinolin — furanochinolin

RUTAE HERBA – COMMON RUE AERIAL PART
PHOTOSENSIBILISING FURANOCOUMARINS



	R_1	R_2
psoralen	H	H
xanthotoxin	H	OCH_3
imperatorin	H	$O\text{-}CH_2\text{-}CH(CH_3)_2$
bergapten	OCH_3	H
isopimpinellin	OCH_3	OCH_3

RUTAE HERBA – COMMON RUE AERIAL PART

Effect:

- spasmolytic
- choleretic
- weakly uteroconstrict (alkaloids and furanocoumarins)
- during p.o. application increases uptake of blood into GIT (spices of Mediterranean)
- Congestion of small pelvis – contraindication in pregnancy

Usage:

- folk medicine - spasmolytic; choleretic
- furanocoumarins – vitiligo, pigmentation disorders

DRUGS AFFECTING PERIPHERAL NEURAL SYSTEM

LOCAL ANAESTHETICS

induce local anesthesia as a result of reversible blockade of excitement transmission in sensitive neuron

- cocaine
- menthol
- eugenol

PERIPHERAL MYORELAXANTS

specifically brake neuromuscular transfer of irritation; lower tonus of skeletal muscles and induce its full slump and inability of contraction

- curare (Menispermaceae)
- curare (Loganiaceae)

COCAINI HYDROCHLORIDUM – COCAINE HYDROCHLORIDE (ČL 2005)

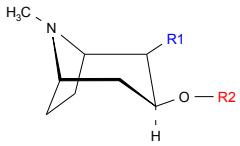
Source: *Erythroxylum coca* – coca (Erythroxylaceae); evergreen shrub (up to 5 m); widely do not grows;
It is cultivated as low shrub at 600-1000 m above sea level, constant temperature and humidity (Bolivia, Peru, Columbia, Java)

Drug: dried leaves

- Huanuco - from Bolivia – big, dark green leathery leaves
- Truxillo - from Peru and Columbia – thin, smaller, bright green leaves

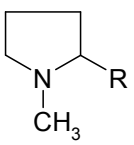
CC: 0,7-2,5 % of alkaloids derived from pseudotropine, ekgonine, hygrine;
tannins, essential oil

ALKALOIDS PRESENT IN LEAVES OF *ERYTHROXYLUM COCA*

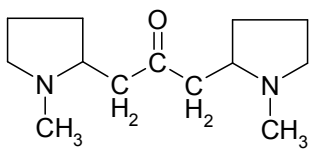


	R1	R2
kokain	**$COOCH_3$**	**$OC\text{-}C_6H_5$**
ekgonin	COOH	H
benzoylekgonin	COOH	$OC\text{-}C_6H_5$
cinnamoylkokain	$COOCH_3$	$OC\text{-}CH{=}CH\text{-}C_6H_5$
methylekgonin	$COOCH_3$	H
tropakokain	H	$OC\text{-}C_6H_5$
α-truxillin	$COOCH_3$	$C_6H_5 - \underset{H}{\overset{H}{C}} - \underset{H}{\overset{H}{C}} - COOH$ $— CO - \underset{H}{\overset{H}{C}} - \underset{H}{\overset{H}{C}} - C_6H_5$
β-truxillin	$COOCH_3$	$C_6H_5 - \underset{H}{\overset{H}{C}} - \underset{H}{\overset{H}{C}} - COOH$ $C_6H_5 - \underset{H}{\overset{H}{C}} - \underset{H}{\overset{H}{C}} - CO -$

ALKALOIDS PRESENT IN LEAVES OF *ERYTHROXYLUM COCA*

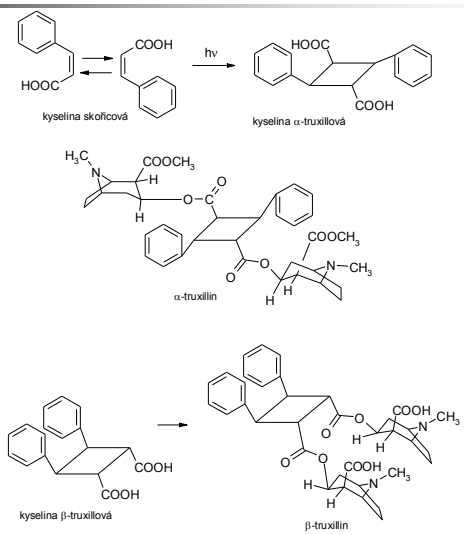


hygrin, $R=CH_2COCH_3$
hygrolin, $R=CH_2CH(OH)CH_3$



kuskohygrin

ALKALOIDS PRESENT IN LEAVES OF *ERYTHROXYLUM COCA*



COCAINE

- COCAE FOLIUM – probably oldest drug used for euphorising effect (2500 BC in graves of „*Huaca Prieto*" – Inkas leaders
- Spanish conquistadors imported drug into Europe in 18th century, boom in 19th century, for example Vinum Marianum (Angelo Mariani)
- 1859 isolation of cocaine (Niemann), 1884 described local anesthetic and vasoconstrict, used without knowledge of chemical structure
- 1888-1900 Willstätter elucidated structure
- 1905 willful change of structure → procaine
- 1955 Hardegger and Ott – absolute configuration
- Misused for euphorizing effect (lowering of noradrenaline, serotonin and dopamin reuptake), increases muscular output, takes away feelings of hunger
- Decompose in GIT, therefore i.v. application or snuffing, triggers strong physical dependence
- According to literature 650 tons of cocaine per year, 2 % for medicinal purposes

Usage: surface anesthesia in ophtalmology and ORL, stomatology

MENTHOLUM RACEMICUM – RACEMIC MENTHOL (ČL 2005)

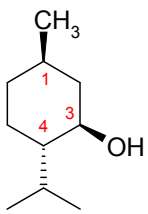
Menthol induces on the skin feelings of cold via specific stimulation of neural terminations for cold perception.

Decreases mucosal secretion:

- weak anesthetic
- antipruriginose

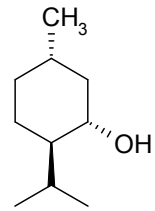
Menthae piperitae folium (ČL 2002)

Menthae piperitae etheroleum (ČL 2002)



(1R,3R,4S)-3-p-menthanol

přírodní



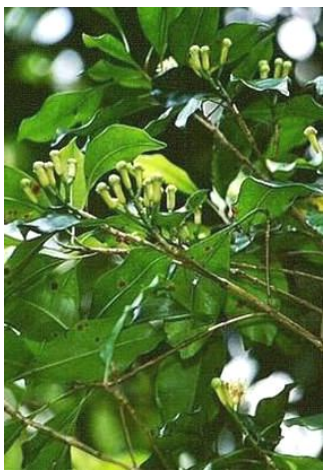
(1S,3S,4R)-

CARYOPHYLLI FLOS – clove flower (ČL 2005)
CARYOPHYLLI ETHEROLEUM – clove essential oil (ČL 2005)
EUGENOL

Source: *Syzygium aromaticum* – clove (Myrtaceae); tree cultivated in tropics

Drug: whole flower buds dried untill obtain red-brown pigmentation. Contain at least 150 ml of essential oil / 1 kg of drug. Obtained by distillation with water steam.

CC: essential oil containing 70-85 % of eugenol, 10 % of β-caryophylene, aliphatic and aromatic terpenoids



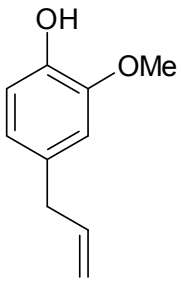
CARYOPHYLLI FLOS – clove flower (ČL 2005)
CARYOPHYLLI ETHEROLEUM – clove essential oil (ČL 2005)
EUGENOL

Usage:

- topic preparation for treatment of small wounds
- infection of oral cavity (oral hygiene)
- spices
- Indonesia – cigarettes „KRETEK"
- cosmetics – Old Spice

EUGENOL
CARYOPHILLI ETHEROLEUM
In stomatology:

- local anesthetics
- desinficiens



eugenol
4-allyl-2-methoxyfenol

NATURAL COMPOUNDS USED IN OPHTALMOLOGY

MIOTICS – narrowing pupil, lowering intraoccular pressure, increasing curvature of lens, induce loss of accomadation

Usage: glaucoma

- *Pilocarpinum chloridum*
- *Physostigminum salicylatum*
- *Galanthaminum bromatum*

MYDRIATICS – expanding pupil, increasing intraoccular pressure, induce disorder of accomodation

Usage: physical examination of eye background, after post-surgical adhesions

- *Atropinium sulfuricum*
- *Homatropinium bromatum*

LOCAL ANESTHETIC

- *Cocainum hydrochloridum*

Also mydriatic and vasoconstringent

PERIPHERAL MYORELAXANTS
CURARE

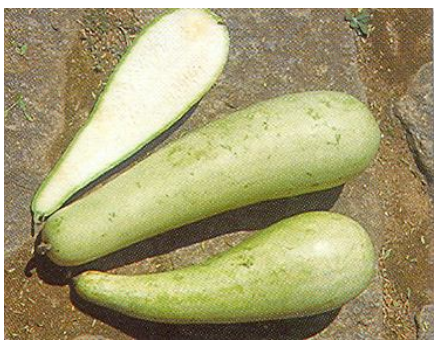
Curare – indian arrow poison with myorelaxant effect. Toxic only when applied parenterally. *Per os* not-effective.

- used by Indians in firth of Amazon and Orinoco to hunt wild animals
- Thickened water extract from parts of *Chondrodendron, Telito- xicum, Anomospermum* and *Strychnos* species.
- Previously classified according to package (charakteristic for certain areas): tubo curare – in bambus tubes, pot curare – in earthen pots, calebas curare – in fruits of bottle trees

In present time: division of curare according to botanic origin and chemical constitution

Calebas curare in emptied fruits
Lagenaria vulgaris, *L. siceraria* and *Crescentia cujete*

Lagenaria vulgaris



Lagenaria siceraria

MENISPERMACEAE CURARE

Source: *Chondrodendron tomentosum* (Menispermaceae). Climbing tropical wine of Amazonian, Peruan, Columbian rainforests

Drug: into solid consistence thickened water extract from do pevné konzistence zahuštěný vodní extrakt kořenů, kůry a listů

OL: směs alkaloidů s převahou tubokurarinu. Získá se isolací z vodného roztoku jako pikrát, pro aplikaci se užívá chlorid.

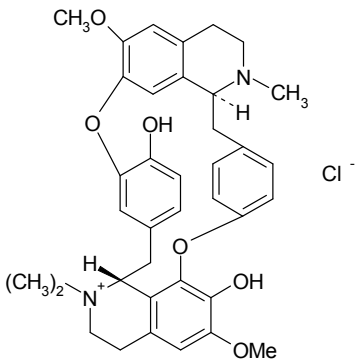
Další zdroje: rostliny rodu *Anomospermum, Telitoxicum*

TUBOCURARINII CHLORIDUM – TUBOKURARINIUM-CHLORID (ČL 2005)

Použití:

- Svalové relaxans v hrudní a břišní chirurgii při celkové anesthesi
- K uvolnění spasticity svalů
- K uvolnění tetanických křečí
- Diagnostikum *myasthenia gravis*

TUBARINE inj.



LOGANIACEAE KURARE

Zdroj: *Strychnos toxifera, S. castelnaei, S. crevauxii* – Kulčiba jedovatá (Loganiaceae); stromy Amazonie, Peru, Kolumbie

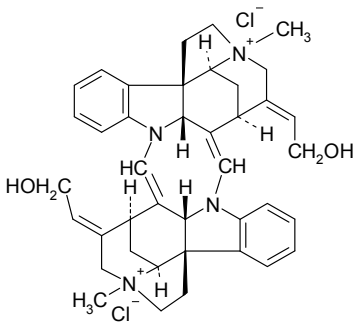
Droga: do pevné konzistence zahuštěný vodní extrakt kůry a listů

OL: deriváty bisindolových alkaloidů typu strychninu: C-toxiferin, C-kurarin

C-TOXIFERIN
ALCURONII CHLORIDUM – ALKURONIUMCHLORID (ČL 2005)

Použití:

- pro přípravu polosyntetického ALKURONIUMCHLORIDU (methyly kvarternizující dusíky jsou nahrazeny allylem)
- Svalové relaxans v hrudní a břišní chirurgii při celkové anesthesi
- K uvolnění spasticity svalů
- K uvolnění tetanických křečí



ALLOFERIN inj.