# Alkaloids part 2

# Plan

- Medicinal plants and crude drugs containing purine alkaloids
- 2. Medicinal plants and crude drugs containing quinoline alkaloids.
- 3. Medicinal plants and crude drugs containing isoquinoline alkaloids
- 4. Medicinal plants and crude drugs containing indole alkaloids
- 5. Medicinal plants and crude drugs containing pseudoalkaloids

# Medicinal plant material containing QUINOLINE ALKALOIDS (Tryptophan derivatives)

**Cinchona bark -** *Cortex Chinae* **Cinchona tree -** *Cinchona succirubra* (*C. ledgeriana, C. calisaya*) **Fam. -** *Rubiaceae* 

Cinchona is indigenous to Colombia, Ecuador, Peru and Bolivia. It is widely cultivated. The drug is derived exclusively from cultivated tree *Act. Comp.* 

5-15 % alkaloids, with quinine, cinchonine the most important quantitatively.

Quinic acid – 5-8%

Cinchotannic acid – 2-4%



quinine (quinidine) cinchonine (cinchonidine) R=H





Quinine occurs as white, odorless, bitter crystals or as a crystalline powder. It is freely soluble in alcohol, ether, and chloroform but slightly soluble in water.

Quinidine is a stereoisomer of quinine. It depresses myocardial excitability, contractility.

# Uses

Cinchona (<u>quinin</u>) is used as bitter tonics for stimulating the appetite and promotion gastric secretion. Cinchona and its alkaloids have been used in the treatment of malaria fever for many years.

<u>Quinidine</u> is used to treat various cardiac arrhythmias, tachycardia and atrial fibrillation.

The patient should be instructed to notify the physician if skin rash, fever, unusual bleeding, ringing in the ears, or visual disturbance occurs.

# Medicinal plant material containing ISOQUINOLINE ALKALOIDS (Tyrosine derivatives)

# **Classification of isoquinoline alkaloids**

Isoquinoline alkaloids	Formula	Medsicinal plant material
Bensilisoquinoline group	CH <sub>3</sub> O CH <sub>3</sub> O C CH <sub>3</sub> O C CH <sub>3</sub> O C C C C C C C C C C C C C C C C C C C	Opium poppy, hydrastis
Phenantrenisoquinoline group R V V N-CH <sub>3</sub> R1	HO HO HO morphine	Opium poppy
Apomorphine group	CH <sub>3</sub> O CH <sub>3</sub> O	Tulip poppy, Boldo

# **Classification of isoquinoline alkaloids**

Isoquinoline alkaloids	Formula	Medsicinal plant
Protopine group	office of the second se	Celandine
Bensphenantredine group	HO HO HO HO HO HO HO HO HO HO HO HO HO H	Celandine Plum poppy
Emetine group	MeO MeO C <sub>2</sub> H <sub>5</sub> CH <sub>2</sub> emetine	Ipecac
Phenantredine group	HO HO N licorine	Ungernia victoris

# **OPIUM**

is the latex, obtained by incision from the unripe capcules (*Capita Papaveris*) of poppy (*Papaver somniferum*) (*Fam. Papaveraceae*) and dried.

Opium is intended only as starting material for the manufacture of galenical preparations. Opium (B.Ph) is required to contain not less than 10% of morphine and not less than 2% of codeine. The tebain content is limited to 3%. *Act. Const.* 

30 alkaloids, which are largely combined with the organic acid meconic acid;

- Sugars;
- Salts;
- Albuminous substances;
- Colouring matters; water;





# Principal alkaloids

Six principal alkaloids are listed opiosite.

The **first group (morphine)** consist of alkaloids which have <u>a phenanthrene nucleus</u>,

**second group (papaverin)** have a <u>benzylisoquinoline structure</u>.

Some of the less important opium alkaloids: protopine and hydrocotarnine are of different structural types.

# **First group (morphine):**

#### morphine, codeine, thebaine.



HO

HC

Morphine



They are the main narcotic constituents. Morphine and its salts are classed as narcotic analgesics; they are strongly hypnotic and narcotic. Their use tends to induce nausea, vomiting, constipation, and habit formation. The usual dose of N-CH<sub>3</sub>morphine sulfate, parenterally, is 10 mg, 6 times a day, as necessary. Morphine is responsible for harmful effects such as lung edema, respiratory difficulties, coma, or cardiac or respiratory collapse, with a normal lethal dose of 120 to 250 mg. Morphine binds to and activates  $\mu$ -opioid receptors in the brain, spinal cord, stomach and intestine. <u>Codeine</u> and its salts are narcotic analgesics and antitussives; they are used as sedatives, especially in allaying coughs. Although its action is similar to that of morphine, codeine is considerably less toxic The usual dose of codeine, codeine phosphate, is: analgesic, 15 to 60 mg every 4 hours as needed; antitussive, 10 to 20 mg every 4 to 6 hours as 11 needed.

# Second group (papaverine)

- Papaverine
- Narceine
- Noscapine



Papaverine

Papaverine hydrochloride is <u>a smooth muscle relaxant</u>. The usual dose, orally, is 150 mg; intramuscularly, 30 mg.

**Meconic acid** constitutes about 5% of opium and can be used as an analytical marker for the presence of opium. Meconic acid gives a red color with ferric chloride.

It is a dicarboxy acid and forms salts with alkaloids. Meconic acid has no physiological activity, and is not used medicinally. It is chemotaxonomic marker for the Papaveraceae.



**Meconic** acid

Tulip poppy herb- Herba Glaucii flaviTulip poppy - Glaucium flavumFam. - Papaveraceae

It is cultivated in Ukraine. Act. Const.

alkaloids: glaucine, protopine, sanguinarine, cheledonine,

- Organic acids:fumaric,
- Mucilaginous,
- flavonoids: rutine





Uses

"Glaucine hydrochlorides", "glauvent", "Broncholytine" antitussives (non-narcotic codeine like)

# **Boldo leaf-** *Folium Boldo* **Boldo -** *Peumus boldus* **Fam. -** *Monimiaceae*

The material of commerce is cultivated in Chile and Peru

#### Act. Const.

Alkaloids – 0,1% (Eur. Ph): boldine, isocordine;

**Volatile oil (2-4%): ascaridole,** monoterpenes.





Cholagogue, hepatoprotective, significant anti-inflamatory, antioxidant. Mild spasmodic discomforts of the gastrointestinal tract; dyspepsia, functional disorders of the hepatobiliary systems. Liver and gall herbal tea formulas; film tablets containing dry extract.<sup>14</sup>

Uses

Plum poppy herb -Herba Macleayae Plum poppy - Macleaya microcarpa Fam. - Papaveraceae

It is originated from Japan and China and cultivated in Ukraine.

#### Act. Const.

alkaloids: sanguinarine, chelerythrine, protopine, berberine





sanguinarine

chelerytrine



# Uses

*"Sanguirytryne"* – antimicrobial, anticholinesterase action; to treat myopathia, paralysis **Celandine Herb** - Herba Chelidonii **Celandine** - Chelidonium majus Fam.- Papaveraceae

Plant is widely distributed in Europe and Central and northern Asia; introdused into North America.

Stems are upright, branchy, naked or pubescent. The leaves are alternate, blue-green the lower ones are petiolate, the top leaves are sessile. The leaves are pinnately-divided with leaflets have a lobed margin. Flowers with four yellow petals and numerous stamens, losing the two sepals on opening. The inflorescence is an umbel. Fruit is narrow, pod-shaped capsule. Entire plant with yellow to orange alkaloid-containing latex.



# • Chem. Const.

# 0.1-1% alkaloids.

- more than 20 alkaloids.
- Chelidonine, sanquinarine, chelerythrine are quantitatively the most important;
- berberine, protopine, stylopine.
- flavonoids,
- saponins,
- ascorbic acid and other plant acids: such as malic and citric acids, carotenoids.



# Uses

- In dysfunctions of the gall bladder, and biliary ducts as a <u>cholagogue</u>, <u>spasmolytic</u>, and weak <u>analgesic</u>; mild sedative, antiinflammatory.
- In folk medicine, the freshly exuded latex is dabbed topically as a <u>treatment for warts</u>. The proven antimitotic effect of chelidonin and skin irritant and <u>cell growth inhibiting</u> properties of both sanguinarin and chelerythrine serve as possible explanation for this traditional use.
   «Ucmin» - cell growth inhibitor

Barbery leaves- Folia Berberidis Barbery root- Radices Berberidis Barbery - Berberis vulgaris Fam. - Berberidaceae

<u>The leaves</u> are obovaite, shortlypetiolate and have a sharply-serrate margin.

<u>The roots are almost cylindrical,</u> yellow, the upper surface is brown- v gray.

# Act. const

alkaloids: berberin,polysacchrides





# Uses

**Tincture and Infuse of leaves – uterotonic action; Berberina bisulfat (from root) holagogue**  **Ungernia leaves-** Folia Ungerniae **Ungernia -** Ungernia victoris **Fam. -** Amaryllidaceae

# *Act. Const.* Alkaloids: galantamin, licorin





galantomin

licorin Uses

galantamin bromhidrat – anticholinesterase action; to treat myopathia, paralysis; **Ipecac - Radices Ipecacuanhae Ipecac - Cepháélis ipecacuánha Fam. - Rubiaceae** 

It is indigenous to Brazil. It is cultivated in Malaysia and India.

Act. const.

Alkaloids 2,5% (emetine, cephaline and psychotrine)



Emetine



Slender rhizomes bear annulated wiry roots.

# Uses

**Decoct and Syrup produce emesis.** Emetine hydrochloride is antiamebic and is used to treat amebic dysentery. It possesses expectorant and emetic properties. 21

# Hydrastis rhizome - *Rhizoma Hydrastidis* Hydrastis or goldenseal- *Hydrastis canadensis* Fam. - *Ranunculaceae*

Goldenseal is plantiful in the forests of the eastern US and Canada

Internally the rhizome and roots show a golden yellow colour.

#### Act. Const.

Alkaloids: hydrastine, berberine,

canadine.



Hidrastine

Uses

The hydrastis alkaloids are used as astringents in inflamation of a mucous membrane. It have been used to control uterine hemorrhage.



22

**Curare or South American arrow poison Crudge dried extract from the bark and steam of** *Strychnos castelnal, S. toxifera, S. crevanxii* Fam. Loganiaceae, *Chondodendron tomentosum* Fam. Menispemaceae

Act. Const.

Alkaloids: (+)-tubocurarine – the most important constituent.



Tubocurarine

The crudge extract exhibits a paralyzing effect on voluntary muscle (curareform effect) by blocking nerve impulses to sceletal muscles in the myoneural junction. It also produces histaminlike effect on blood vessels.

*Tubocurarine chloride* – as skeletal muscle relaxant to secure muscle relaxation in surgical procedures without deep anesthesia, tetanus, shock therapy in neuropsychiatry.



# • histamine

 a compound which is released by cells in response to injury and in allergic and inflammatory reactions, causing contraction of smooth muscle and dilation of capillaries A heterocyclic amine; chem. formula: C5H9N3

# **Peyote, the mexican cactus, mescal buttons – dried tops of** *Lophophora williamsii Fam.- Cactaceae*

It grows in northern Mexico and southwestern United States

Act. const.

Alkaloids: anhalamine, mescalin, mescalin succinamid, peionin





Uses

hallucinogenic activity ; psychotomimetic. It is used in experimental psychiatry

# Medicinal plant material containing INDOLE ALKALOIDS (tryptophan derivatives)



Passionflower herb- Herba Passiflorae Maypop, Purple passionflower, Wild apricot - Passiflora incarnata

Fam. - Passifloraceae

It is a common flower in the southern United States.

**Passionflower**, is a fast growing vine with climbing stems. It has large, intricate flowers with prominent styles and stamens.

The stems can be smooth or pubescent; they are long, possessing many tendrils (spiral). Leaves are alternate and palmately 3-lobed, measuring from 6-15 cm. They have two characteristic glands on the petiole. Flowers have five bluishwhite petals. They exhibit a white and purple *corona*, a structure of fine appendages between the petals and corolla.

USC Herbarium Photo by Linda Lee

The flower normally blooms in July.

# Act. Const.

- Alcaloids: garmine, garmale, garmole 0,01-0,09%
- flavonoids: vitexin, quercetine, hyperoside, apigenine, luteoline, rutine



- Coumarines,
- Pectines

#### Uses

The fresh or dried whole plant has been used as a herbal medicine to treat <u>nervous anxiety and insomnia</u>. A sedative chewing gum has been produced.

"Passit", "Novopassit", "liquid extract "- sedative to treat anxiety and insomnia.

In cooking, the fruit of this variety is sometimes used for jam and jellies

# Rauwolfia root - Radices Rauwolfiae serpentinae Rauwolfia - Rauwolfia serpentina African rauwolfia - Rauwolfia womitoria Fam. - Apocynaceae

Rauwolfia serpentina grows in India, Pakistan, Burma, Thailand, Java. African rauwolfia (R.womitoria) is widely distributed in tropical Africa from the West coast to Mozambique.

Roots usually occur in cylindrical, tortuous pieces about 2-10cm long and 5-22 mm in diameter, rare branched. The outer surface is grayish-yellow or brown, with slight wrinkles, the bark exfoliate readily. The drug breaks readily. The smoothed transverse surface shows a nerrow, yellowish-brown bark and pale yellow wood. Taste bitter.



# Act. Const. alkaloids, 0,7-2,4%.

H<sub>3</sub>CO





- phytosterols,
- fatty acid,
- unsaturated alcohols,
- sugars

# Uses

Rauwolfia preparations and reserpine are used in the management of essential hypertension and in certain neuropsychiatric disordes. Ajmaline, which has pharmacological properties similar to those of quinidine, is marketed for the treatment of cardiac arrhythmias.

Raunatin, rauwasan, reserpin, adelfan, kristepin, antihypertensive, sedative drug; ajmalin, pulsnorma - for the treatment of cardiac arrhythmias. Periwinkle herb- Herba Vincae minoris Periwinkle- Vinca minor Fam. - Apocynaceae

The leaves are green, bright, oppositely arranged, oblong, a petiolate acute base, a pointed apex and an entire margin.

#### Act. Const.

alkaloids: vincamin, isovincamin, vincaminorin,

- flavonoids: robinin,
- leicoantocianidins.





Vincamin

**Devincan**, Vincaton, Vincapan – antihypertensive drugs, improve cerebral circulation and memory.

**Catharanthus herb** - Herba Catharanthi rosei **Madagascar periwinkle** - Catharanthus roseus = Vinca rosea Fam. - Apocynaceae

The plant is probably indigenous to Madagascar, but is now widely distributed throughout warm regions and is much cultivated as an ornamental.

Catharanthus is a perennial evergreen undershrub. Stems are naked or pubescent, nearly cylindrical. The leaves are oppositely arranged, oblong, a petiolate acute base, a rounded apex and an entire margin. In form the flowers resemble those of the common periwinkle and are coloured violet, rose, white



# Act. Const

About 90 alkaloids have now been isolation from Catharanthus. Of particular interest is a group of about 20 dimeric alkaloids which contains those having antineoplastic activity, including vincristine and vinblastine.



**Vinblastine Sulfate** 

**Vincristine Sulfate** 

The plant also contains flavonoids and oxycarbonic acids.

# Uses

The most characteristic effect of these drugs is the arrest of cell division at metaphase, in a manner resembling the effect of colchicines. Both vinblastine and vincristine inhibit the polymerization of tubulin into microtubules.

It has hypotensive, sedative and tranquilising properties.

The alkaloid is being used experimentally for the treatment of a wide variety of neoplasms and is recommended for lymphocytic lymphoma, Kaposi's sarcoma and breast cancer unresponsive to other therapies. Vinblastine is effective as a single agent but is usually administered with other antineoplastic agents in combination therapy for an enhanced therapeutic effect without additive toxicity.

### Nux vomicae consist of the dried ripe seeds of - Semina Strychni (Semen Nux vomicae) Nux vomicae - Strychnos nux vomica Fam.- Loganiaceae

#### Act. Const.

• 0,8-5,3% of the indole alkaloids: strychnine and brucine



 $R_1 = R_2 = H$  - Strychnine  $R_1 = R_2 = OCH_3$  - Brucine

# <image>

# Uses

The alkaloid was formerly used as a circulatory stimulant in such cases as surgical shock. Like other bitters, strychnine improves the appetite and digestion, but it has been considerably misused as a "general tonic".

**Bisonous plant material!** 

# **Ergot** is a dried sclerotium of a fungus- Secale cornutum

*Claviceps purpurea* Fam. - *Clavicepitaceae Ascomycetes* 

•Controlled field cultivation on rye or wheat is the main source of the crude drug.

•The most imported producers are Czech Republic, Hungary, Switzerland.

•The drug consists almost entiry of sclerotia. Each sclerotium is about 1.0-4.0 cm long and 2-7 mm broad; fusiform is shape and usually slightly curved. The outer surface, which is of a dark, violet-black colour, is often longitudinally furrowed and may bear small transverse cracks. Ergot breaks with a short fracture and shows within the thin, dark outer layer a whitish or pinkishwhite central zone of pseudoparenchyma in which darker lines radiating from the centre may be visible. Ergot has a characteristic odour and an unpleasant taste.





# Act. Const

6 pairs of alkaloids predominate in the sclerocium. They are all derivatives of (+)-lysergic acid.

The more physiologically active member of each pair –



lysergic acid

penniclavine

Ergometrine group	<b>Ergometrine</b>
(+ aminoalcogol)	Ergometrinine
Ergotamine group	<b>Ergotamine</b>
(polypeptides)	Ergotaminine
	<b>Ergosine</b> Ergosinine
Ergotoxine group	<b>Ergocristine</b>
(polypeptides)	Ergocristinine
	<b>Ergocriptine</b> Ergocriptinine
	<b>Ergocornine</b> Ergocorninine

In addition to its characteristic alkaloids, ergot contains several pigments, a fixed oil and steroids (ergosterol).

#### • Uses

Ergot preparations were used <u>in labour to assist delivery and</u> <u>to reduce post-partum haemorrhage</u>.

- Ergot produces <u>vasorelaxation</u>, <u>increased cerebral blood</u>
  <u>flow</u>, <u>lowering of systemic blood pressure and bradycardia</u>.
  It also used as <u>sedative agent</u>.
- Ergometrine produces <u>an oxytocic (literally "quick delivery"</u>) effect. It is often known, particularly in the USA, as ergonovine.
- Ergotamine has different action. Ergotamine and the semisynthetic dihydroergotamine salts are employed as <u>specific analgesics for the treatment of migraine.</u>
- <u>Lysergic acid diethylamide (LSD-25)</u>, prepared by partial synthesis from lysergic acid, is a potent specific psychotomimetic
  - *Ergotal, Ergometrine maleat , Ergotamine hydrotartrate -* assist delivery and to reduce post-partum haemorrhage. *Belloid* as sedative. <sup>39</sup>

# Medicinal plant material containing PSEUDOALKALOIDS

Aconite root- radix Aconiti Aconite - Aconitum napellus Fam. - Ranunculaceae

# Act. Const.

terpene ester alkaloids, of which the most important is aconitine.

• other alkaloids such as mesaconitine, hypaconitine, neopelline, napelline and neoline,



Aconitine



Uses

Aconite is a very potent and quick-acting poison which is now rarely used internally, except in homeopathic doses. The drug was formerly used for the preparation of  $a_{41}$  antineuralgic liniment.



# **DELPHINIUM HERB - HERBA DELPHINII Delphinium -** *Delphinium elatum* Fam. Ranunculaceae

Delphinium is a genus of about 300 species of perennial flowering plants, native throughout the Nothern Hemisphere and also on the high mountains of tropical Africa. Many species are cultivated as garden plants.

#### Act. Const.

All parts of the plant contain alkaloid delphinin, licoctonin and its derivatives and are very poisonous, causing vomiting when eaten, and death in larger amounts.

Licoctonin

Pure alkaloids isolated from herbs genus *Delphinium* have curarelike muscle relaxant activity.

Mellictinum







#### **Common yew-***Taxus baccata* **Fam.** *- Taxaceae*

#### Act. Const.

Alcaloids: taxol



Taxol



Uses

#### Paclitaxel, doxitaxel - cytostatic agent.

Nightshade herb- Herba Solani laciniati Nightshade - Solanum laciniatum Fam. - Solanaceae

#### Act. Const.

Alkaloids: solasodine, solanidine.



Solasodine



**Solasodine** – source of steroid hormones progesterone, cortisone;

**Veratrum Rhizome and Roots** - *Rhizomata cum radicibus Veratri* **Hellebore** - *Veratrum lobelianum* **White Hellebore** - *Veratrum album* **Fam.** - *Liliaceae* 

## Act. Const.

steroidal alkaloids : jervine and



Jervine



*Tincture of White Hellebore* is used as insecticides (to treat louse). Veratrum possesses cardiac-depressant and sedative properties. American veratrum is used for the preparation of Veriloid, a mixture of the hypotensive alkaloids

Uses