Tryptophan Derivatives

INDOL ALKALOIDS

- *Secale Cornutum*
- *Faba calabarica*
- *Semen Strychni*
- *Gelsemium nitidum*
- *Radix Rauwolfiae*
- *Cortex Yohimbae*
- *Aspidiospermae*
- *Herba Catharanthi*
- *Herba Vincae*
- *Cortex Chinconae*

-Harman Alkaloids(*β*-carboline)

- *Semen Pegani*

Radix Rauwolfia

Rauwolfia serpentina (Apocynaceae)

Radix must contain at least 0.15% reserpine-resinnamine group alkaloids.

Rauwolf (German Botanist)16th century

Rauwolfia serpentina; Used against snake bites and psyclological problems in India. Powdered roots, extract and purified alkaloids are used to control hypertension.

Approximately 50 alkaloids are isolated from 25 *Rauwolfia* species.

These alkaloids shows their activity by stimulating the release of serotonin and catecholamines so that sedative and tranquilizer activity occur.

Reserpine; Reserpine absolutely lowers the blood pressure. Decreases pulse number with some euphory. Should be used in schizophrenia.

Reserpine is a drug that is used for the treatment of high blood pressure, usually in combination with a thiazide diuretic or vasodilator. Large clinical trials have shown that combined treatment with reserpine plus a thiazide diuretic reduces mortality of people with hypertension.

Resinnamine; Genetic hypertension (middle level)
Deserpidine; 11-demethoxy reserpine (used like reserpine)
Deserpidine and reserpine are used with diuretics against hypertension.

Reserpine; white/pale yellow, odorless, crystal powder. Sensitive to light (darkens slowly).

Commercial reserpine sources:

R. serpentina (reserpine + resinnamine)

R. micrantha (reserpine + resinnamine)

R. tetraphylla (reserpine + deserpidine)

***R. vomitoria* (reserpine) Mostly used species.**

Reserpine could be used synthetically but not efficient. Preference is natural sources.

The Rauwolfia alkaloids reserpine and deserpidine, two alkaloids from Rauwolfia species, have been widely used for their antihypertensive action. Deserpidine is a compound with limited availability from natural sources, and its synthesis from 1 in six steps (41% overall yield) is reported in literature.

Herba Catharathi

Catharanthus roseus (Apocynaceae)
Native to Madagascar. Ornamental plant.
Flowers in purple, red, white colour.

Traditionally used as hypoglycemic. While hypoglycemic activity was studied, anticancer activity was discovered (Noble, Beer and Cutts – Canadian researchers).

Later, Eli Lilly Company researchers discovered Vinblastine, and Vincristin oncological effects.

Catharanthus roseus (Apocynaceae)
Isolated more than 90 alkaloids. These alkaloids are in bisindole structure.
Catharantine (indole) + vindoline (dihydroindole) stop cell division in metaphase stage like colchicine.

VLB: Hodgkin disease, lymphoma, testicular ca, kaposi sarcoma

VCR: Acut lecemia, Hodgkin disease, Wilm tumor, Ewing sarcoma, estrogenic sarcoma, breast ca, small cell lung ca.

Vindesine: Semisynthetic derivative of vinblastine. Vinblastine derivative with antineoplastic activity against CANCER. Major side effects are myelosuppression and neurotoxicity. Vindesine is used extensively in chemotherapy protocols. Vinkcristin like activity.

Vinorelbine tartarate (Navelbine): Semisynthetic derivative of Vinblastine.

Used for NSCLC, breast ca combined with Cisplatin.

Herba Vincae

- *Vinca minor* (Apocynaceae)
- Grows naturally in Middle and South Europe. Not in Turkey.
- Evergreen plant, with creeping rhizoma.
- Has blur flowers, 0.4-0.9% alkaloids yield.

Significant alkaloid is **vincamine**. Characterized with beta-carboline ring (indole and quinilosidine). Vinkamine is used orally against artherial hypertension. Also boost cognitive function.

Vincamine is sold in Europe as a prescription medicine for the treatment of primary degenerative and vascular dementia.

Cortex Yohimbae

- *Pausinystalia yohimba* (Rubiaceae)
- Stem barks.
- Naturally grows in West Africa.
- Big trees up to 30 m.
- Contains 1-1.5% alkaloid.
- Significant alkaloid is **yohimbine**.

Yohimbine is an indole alkaloid derived from the bark of the Central African yohimbe tree (Pausinystalia yohimbe) that is widely used as therapy for **erectile dysfunction.**

Ajmalicine is the other alkaloid of the plant.

Yohimbine is a vasodilatator. So that it is aphrodisiac.

In ophtalmology used as local anesthetic.

Cortex Yohimbae

- Yohimbine is an indole alkaloid with alpha2-adrenoceptor antagonist activity. It is produced by *Corynanthe johimbe* and *Rauwolfia serpentina*. It has a role as an alpha-adrenergic antagonist, a serotonergic antagonist and a dopamine receptor D2 antagonist. It derives from a yohimbic acid.
- Ajmalicine is a monoterpenoid indole alkaloid with formula C21H24N2O3, isolated from several *Rauwolfia* and *Catharanthus* species. It is a selective alpha1-adrenoceptor antagonist used for the treatment of high blood pressure. It has a role as an antihypertensive agent, an alpha-adrenergic antagonist and a vasodilator agent. It is a monoterpenoid indole alkaloid, a methyl ester and an organic heteropentacyclic compound.

Aspidiospermae species

- *Aspidiospermae* sp. (Apocynaceae)
- South American trees.

- *Aspidiosperma* barks are potential alkaloid sources.

- Yohimbine and aspidospermine are important alkaloids

SEMEN PEGANI,

Peganum harmala (Zygophyllaceae)

dried seeds.

Grows naturally in Mediterranean region, widespread in Central Anatolia.

Also grows in North Africa and Russia.

30 35 cm height.

Globular fruits in 7-9 mm diameter.

Seeds in 3-5 mm size, pyramid shaped, reddish.

Seeds contain 2-3% alkaloids.

Harmine,

Harmane

Harmaline

Harmol are the significant alkaloids.

Harmine, also known as banisterine and as telepathine, a fluorescent harmala alkaloid belonging to the beta-carboline family of compounds. It occurs in a number of different plants, most notably the Middle Eastern plant harmal or Syrian rue (Peganum harmala).

Usage;

Harmine and harmaline anthelminthic.

The fruits of the plant is used as lucky charm in Anatolia.

Plant and harmine alkaloid were investigated for Parkinsons disease.

Antidepressant activity, MAO inhibitor.

CORTEX CINCHONAE

Stem barks of *Cinchona* sp.

Big trees growing naturally in Columbia, Equador, Peru and Bolivia.

C. succirubra varieties and hybrids must not contain less than 6.5% alkaloids.
30-60% of this ratio belongs to quinine type alkaloids.

Stem barks and alkaloids were used traditionally for Malaria. Today synthetic drugs are taking more attention.

Plant is mostly cultivated rather than picking up from nature. Indonesia and India are the important Cinchona producers. It is also cultivated in tansania, Kenya and Bolivia.

C succirubra	*C calisaya*	*C ledgeriana*	*C officinalis*
20-40 mm diameter, 2-6 mm width	12-25 mm diameter 2-5 mm width	12-25 mm diameter 2-5 mm width	12 mm diameter 1 mm width
Significant longitudinal lines, a few red points	**Some longitudinal slits, transverse slits are 6-12 mm away from each other**	**Similar to C. calisaya, transverse slits are much more**	**Transverse slits are more and 6 mm away from each other**
Powder; reddish brown;	Powder, cinnamon colour	Powder, cinnamon colour	Porder; yellowish

The febrifugal properties of bark from trees now known to be in the genus Cinchona were used by many South American cultures prior to European contact, but malaria is an Old World disease that was introduced into the Americas by Europeans only after 1492. The origins and claims to the use of febrifugal barks and powders in Europe, especially those used against malaria, were disputed even in the 17th century. Jesuits played a key role in the transfer of remedies from the New World.

C ledgeriana X C calisaya hybrid contains the more alkaloid.
C ledgeriana X C succirubra grows in a short time and contains much more alkaloid than the wild species.

Anatomically characteristic element is sclerenchyma fibers standing alone. These fibers has thick surface. Some small crystals in the parencyma. Starch is absent.

Thalleioquin test;

sample+sulphuric acid+ Br containing water+ammonia= green colour

Quinine is still known to have a significant role in malaria treatment. Although there is reduced susceptibility to quinine in parts of Southeast Asia and South America, these reductions are not large and quinine is still effective in these areas. It is still the drug of choice for Falciparum Malaria in the first trimester of pregnancy regardless of location. Quinine may also be part of second-line treatment regimens, but it is not standard first-line treatment in endemic areas, because it must be given 3 times daily and is poorly tolerated (bitter taste, nausea, tinnitus, dysphoria, giddiness – a symptom complex termed cinchonism – and hypoglycemia). Poor tolerance reduces adherence to the 1 week regimens needed to achieve high therapy rates where there is resistance. In most cases quinine should be used together with either a tetracycline (e.g., doxycycline or tetracycline) or, in children, clindamycin. These antibiotics are given for 1 week. Oral quinine is also often given to complete a full 7 days of treatment following parenteral treatment for severe malaria. Quinine has been associated with immune thrombocytopenia, and very rarely the hemolytic-uremic syndrome, but serious adverse effects from oral quinine are unusual in uncomplicated malaria, although severe and refractory hypoglycemia may occur in late pregnancy.

Quinidine is a natural cinchona alkaloid which has potent antiarrhythmic activity and has been used for decades in the treatment of atrial and ventricular arrhythmias. Quinidine has been associated with fever, mild jaundice and clinically apparent liver injury in up to 2% of treated patients.