PharmacognosyIII

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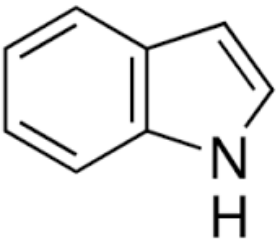
INDOLE ALKALOIDS

A class of alkaloids containing a structural moiety of indole; it is one of the largest classes of alkaloids. Many of them possess significant physiological activity and some of them are used in medicine.

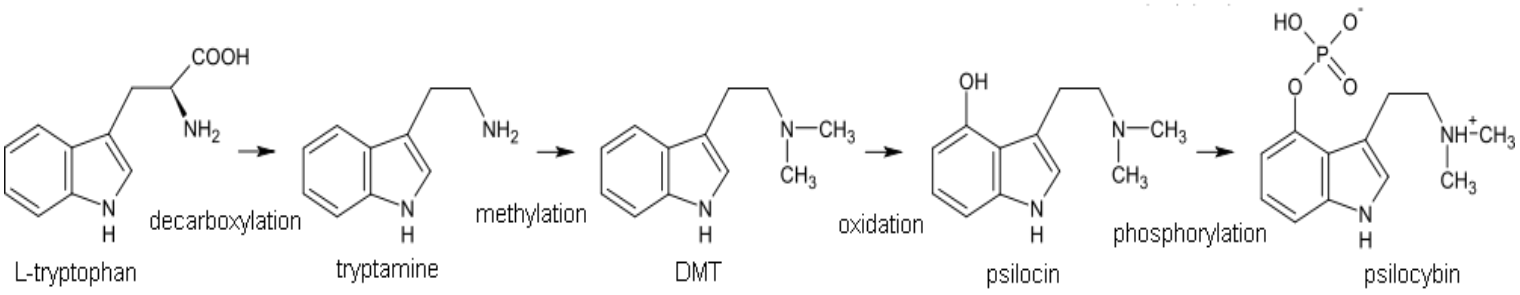


Depending on their biosynthesis, two types of indole alkaloids are distinguished;

1- isoprenoids include isoprene groups and are thus called terpene indole or secologanin tryptamine alkaloids
2- non-isoprenoids indole alkaloids include (Simple derivatives of indole and Simple derivatives of β-carboline)

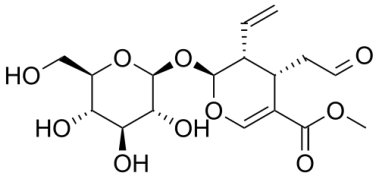
BIOSYNTHESIS

Biogenetic precursor of all indole alkaloids is the amino acid tryptophan. For most of them, the first synthesis step is decarboxylation of tryptophan to form tryptamine. Dimethyltryptamine (DMT) is formed from tryptamine by methylation with the participation of coenzyme of S-adenosyl methionine (SAM).

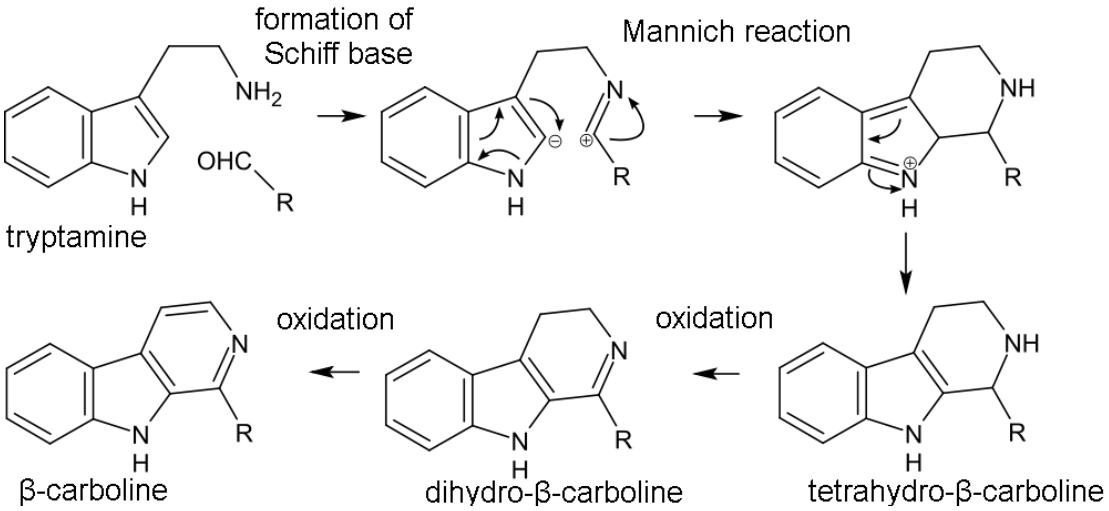


Biosynthesis of β-carboline alkaloids occurs through the formation of Schiff base from tryptamine and aldehyde (or keto acid) and subsequent intramolecular Mannich reaction, where the C(2) carbon atom of indole serves as a nucleophile. Then, the aromaticity is restored via the loss of a proton at the C(2) atom.

In the synthesis of monoterpenoid in indole alkaloids, secologanin plays the role of the aldehyde.

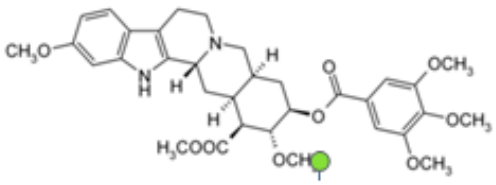


Secologanin



Reserpine

From *Rauavolfia serpentina*, Apocyanaceae. It has been used as a panacea in the Ayurvedic system of medicine.
Reserpine was used as antihypertensive agent, but due to side effects it is now not the drug of choice.

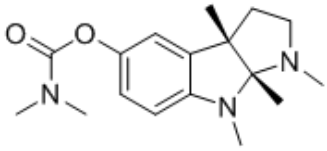


Physostigma, Neostigma and Pyridostigmine

The alkaloids from *Physostigma venenosum*, Fabaceae.

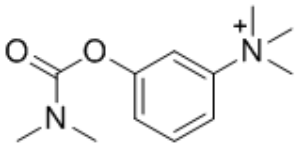
Physostigmine is an inhibitor of acetylcholine esterase resulting in an enhancement of the acetyl choline activity, used in Alzheimer's disease (low acetylcholine).

Physostigmine is used in the eye, increases the cholinergic activity leads to meiosis, contraction of the ciliary muscles & a decreases in the intraocular pressure. It is employed in ophthalmology to treat glaucoma.

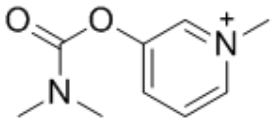


Physostigmine

Neostigmine and pyridostigmine are semisynthtic alkaloids based on physostigmine, which are used to treat mysthenia gravis, a disease characterized by severe muscle weakness.

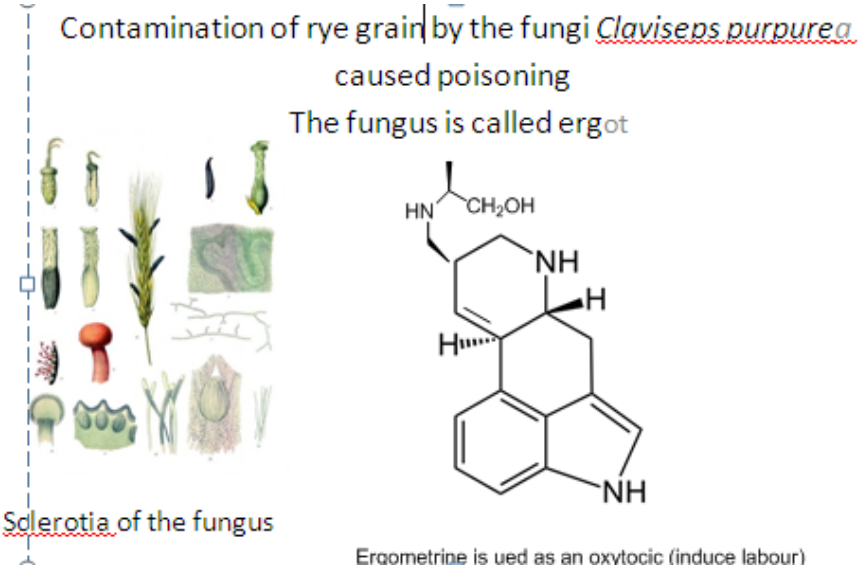


Neostigmine



Pyridostigmine

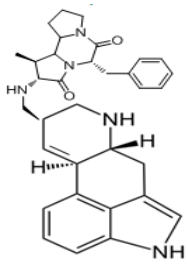
Ergot alkaloids



Ergotamine

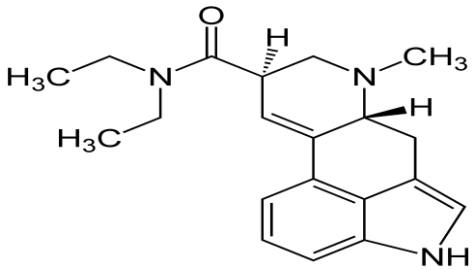
Is used to relief migraine and is still used today, the MOA is probably direct vasoconstriction of the dilated carotid artery bed with a concomitant decrease in the amplitude of pulsations.

Side effects include gangrene.



The ergot alkaloid were used as a template for the semi-synthetic of bromocriptine, pergolide and cabergolide, which have use in neurological disorder such as Parkinson's disease.

Ergot can cause hallucination and the hallucinogenic drug of abuse LSD (lysergic acid diethylamide) is structurally related to them.



LSD

Psilocybin

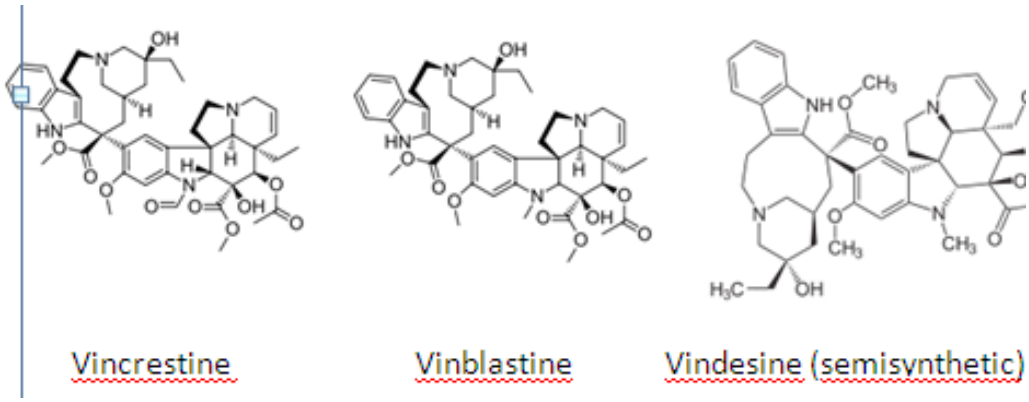
Mushrooms of the genera *Psilocybe, Panaeolus, Conocybe and Stropharia* are known to produce psychoactive substance such as psilocybin, which is salt in the fungi and is converted into psilocin in vivo.

Psilocybin

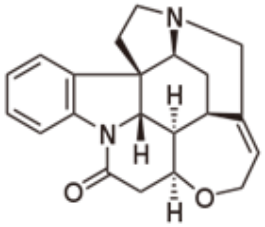
Psilocin

Vinca rosa

Most important group of indole alkaloids from the Madagascar periwinkle Catharanthus roseus, Apocyanaceae. These dimeric indole is difficult to synthesizes and found in low quantities in the plant, so it is very expensive.
Vincristine & Vinblastine bind to tubulin dimers, inhibiting assembly of microtubule structures. Disruption of the microtubules arrests mitosis in metaphase. Therefore, the vinca alkaloids affect all rapidly dividing cell types including cancer cells, but also those of intestinal epithelium and bone marrow
Vinblastine (VBL), sold under the brand name Velban, is used to treat a number of types of cancer. This includes Hodgkin's lymphoma, non-small cell lung cancer, bladder cancer, brain cancer, melanoma, and testicular cancer. It is given by injection into a vein.
Most people experience some side effects. Commonly it causes a change in sensation, constipation, weakness, loss of appetite, and headaches severe side effects include low blood cell counts and shortness of breath.
Vincristine, also marketed under the brand name Oncovin, is a chemotherapy medication used to treat a number of types of cancer. This includes acute lymphocytic leukemia, acute myeloid leukemia, Hodgkin's disease, neuroblastoma, and small cell lung cancer among others. It is given intravenously.
Most people experience some side effects from vincristine treatment. Commonly it causes a change in sensation, hair loss, constipation, difficulty walking, and headaches.



Strychnine and Brucine (dimethoxy strychnine)
are the bitter indole alkaloids from the seeds of Nux vomica.
These alkaloids are CNS stimulant and are highly toxic. Now it is used as rodenticides.



Harmal alkaloids

It is the dried seeds of *Peganum harmala* F: Nitrariaceae.
It contains several alkaloids as harmine, harmane, harmaline, harmalol, others.
Harmine, is a fluorescent harmala alkaloid belonging to the beta-carboline family of compounds.

Peganum harmala has been used to treat pain and to treat skin inflammations, including skin cancers & as an emmenagogue and abortifacient agent. It is also used as an anthelmintic (to expel parasitic worms). Reportedly, the ancient Greeks used the powdered seeds to get rid of tape worms and to treat recurring fevers (possibly malaria).

These alkaloids are psychoactive and used to treat heroin addiction.