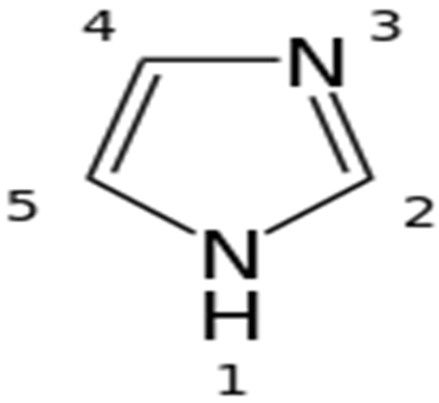
PharmacognosyIII

Lec. 7 **3rd stage 2nd semester** **Year 23-24**

Lecturer: Dr. Jamel Fani

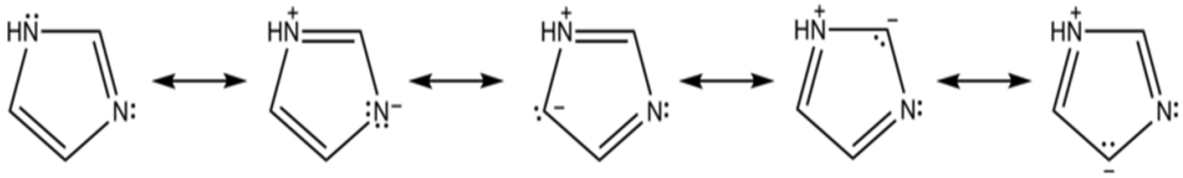
ALKALOIDS

Imidazole alkaloids

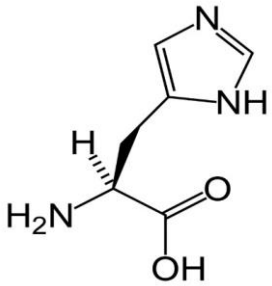


Imidazole alkaloid

Imidazole is a planar 5-membered ring. It exists in two equivalent tautomeric forms because the proton can be located on either of the two nitrogen atoms.



The amino acid L-histidine contains an imidazole ring and is thus the likely precursor of alkaloids containing this ring system.

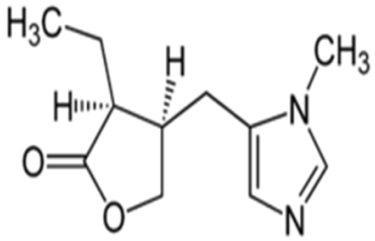


Pilocarpus

Pilocarpus or jaborandi consists of the dried leaflets of *Pilocarpus jaborandi* (Rutaceae). The alkaloid content (0.5–1.0%) consists principally of the imidazole alkaloid pilocarpine. Isomers such as

isopilocarpine are readily formed if base or heat is applied during extraction of the alkaloids. This is a result of enolization in the lactone ring, followed by adoption of the more favorable trans configuration rather than the natural cis. However, the iso alkaloids lack biological activity.

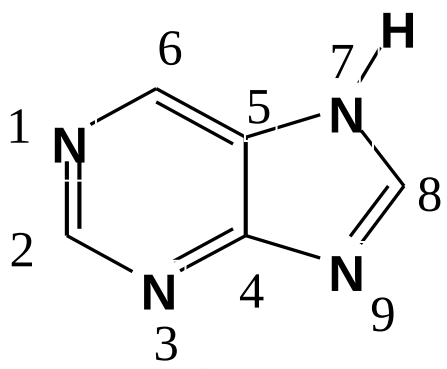
Pilocarpine salts are valuable in ophthalmic practice and are used in eyedrops as miotics and for the treatment of glaucoma. Pilocarpine is a cholinergic agent and stimulates the muscarinic receptors in the eye, causing constriction of the pupil and enhancement of outflow of aqueous humour. Pilocarpine gives relief for both narrow angle and wide angle glaucoma. Pilocarpine is antagonistic to atropine. It has been found that pilocarpine gives relief for dryness of the mouth that results in patients undergoing radiotherapy for mouth and throat cancers. As muscarinic agonists, pilocarpine and analogues are also being investigated for potential treatment of Alzheimer's disease.



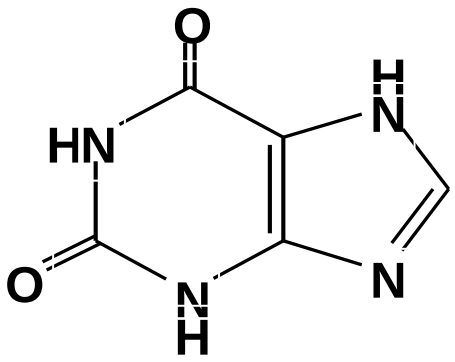
Use of pilocarpine may result in a range of adverse effects, most of them related to its non-selective action as a muscarinic receptor agonist. Pilocarpine has been known to cause excessive sweating, excessive salivation, bronchospasm, increased bronchial mucus secretion, bradycardia, vasodilation, and diarrhea.

Purine (Xanthine) Alkaloids:

- The purines are consisting of **a six-membered pyrimidine** ring fused to **a fivemembered imidazole ring**.
- The pharmaceutically important bases of this group are all methylated derivatives of **2,6 dioxy-purine (Xanthine)**. This group includes mainly **Caffeine**, **theobromine** and **theophylline** alkaloids.
- These alkaloids are weak bases, they give no precipitate with Mayer's reagent.

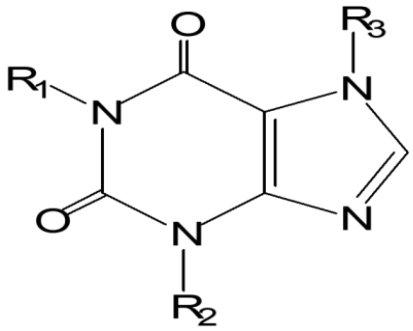


Purine



Xanthine

Caffeine, **Theobromine** and **Theophylline:**



$R_1=R_2=R_3=CH_3$	Caffeine
$R_1=H, R_2=R_3=CH_3$	Theobromine
$R_1=R_2=CH_3, R_3=H$	Theophylline

Caffeine:

- Occurrence:

  Tea leaves (2- 5%), Coffee seeds (1-2 %), Cola leaves (2- 3%), Gurana seeds (2.5- 5 %) and Cacao seeds (0.2- 0.5 %).

- Properties:

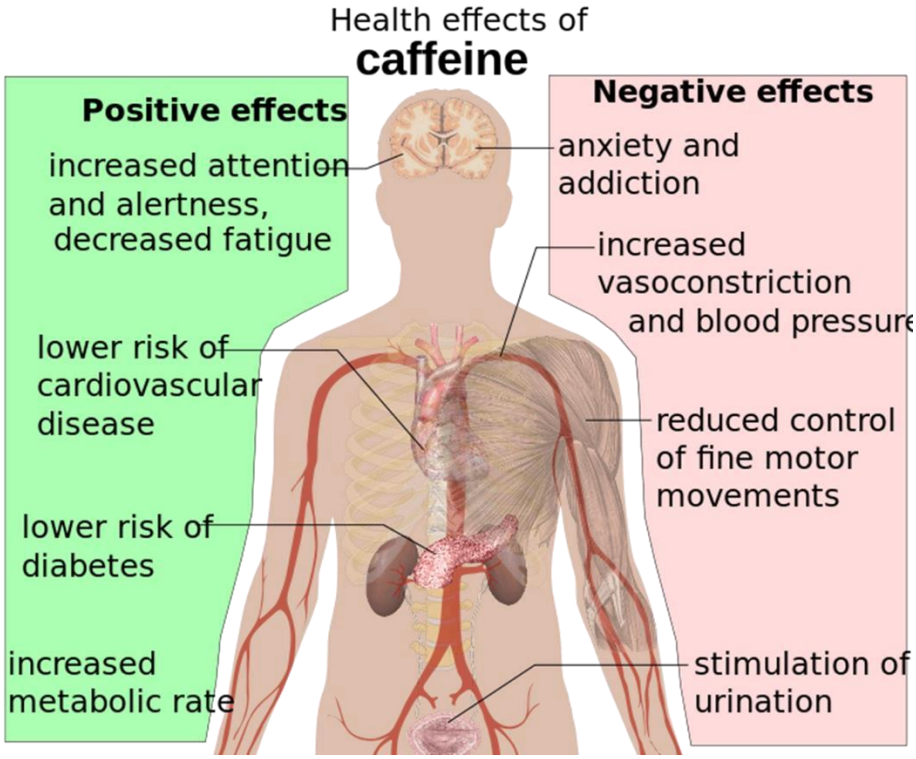
  1- Water soluble. 2- Sublimable.

- Uses:

  Caffeine has a CNS stimulant effect; it is used mainly to relieve headache.

Inside the body caffeine acts through several mechanisms, but its most important effect is to counteract a substance called adenosine that naturally circulates at high levels throughout the body, and especially in the nervous system. In the brain, adenosine plays a generally protective role, part of which is to reduce neural activity levels. Adenosine acts as an inhibitor neurotransmitter that

suppresses activity in the central nervous system. Consumption of caffeine antagonizes adenosine and increases activity in neurotransmission including acetylcholine, epinephrine, dopamine, serotonin, glutamate, norepinephrine, cortisol, and in higher doses, endorphins which explains the analgesic effect to some users. At very high doses (exceeding 500 milligrams) caffeine inhibits GABA neurotransmission. This evidence explains why caffeine causes anxiety, insomnia, rapid heart and respiration rate.



Theobromine:

- Occurrence: Cacao seeds.
- Properties:

1- Sparingly soluble in water. 2- Sublimable. 3- Amphoteric.

In modern medicine, theobromine is used as a vasodilator (a blood vessel widener), a diuretic (urination aid), and heart stimulant.

- Theobromine increases urine production. Because of this diuretic effect, and its ability to dilate blood vessels, theobromine has been used to treat high blood pressure and other circulatory problems including arteriosclerosis, certain vascular diseases, angina pectoris, and hypertension.
- Theophylline
- Occurrence: Traces in Tea leaves and mostly synthetic.

- Properties: Sparingly soluble in water.
- Uses: Theophylline and derivatives are smooth muscle relaxant especially in the upper respiratory tract. They used as bronchodilator. Theophylline also acts as diuretic.

Color tests:

- Murexide test: (caffeine, theobromine and theophylline).

  Crystals of caffeine + drops of concentrated HCl and traces of $KClO_3$ → evaporated on water bath → red color is produced which turns to violet on exposure to ammonia vapor.

- Tannic acid test: (caffeine and theophylline):

  A concentrated solution of the alkaloid + tannic acid → white precipitate is obtained that dissolves in excess of the reagent.

- Ferrous sulfate test: (theobromine):

  To a solution of the alkaloid + drops of concentrated HCl + few drops of Br_2 water + a drop of $FeSO_4$ + few drops of ammonia → Blue color.

Alkaloid biosynthesis in plant

- purine alkaloids