Ornithine derived Alkaloids

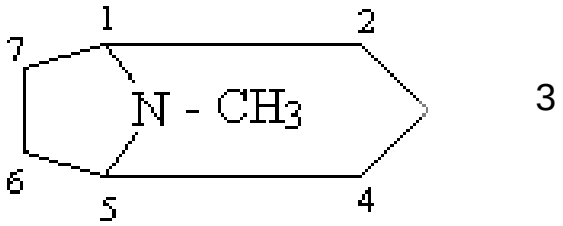
Tropane Alkaloids

(Part IV)

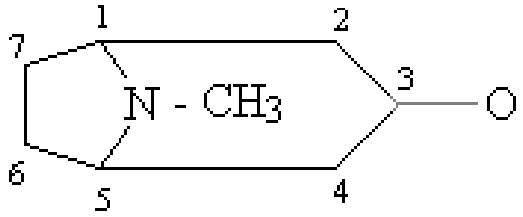
Alkaloids of the Tropane group

There are two important types of tropane alkaloids:

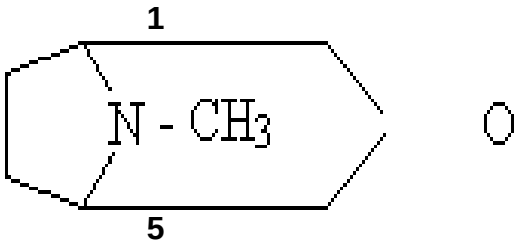
They all possess the tropane nucleus.



Bicyclic system made up of a 5-membered ring (1, N, 5, 6, and 7) and a 6-membered ring (1, 2, 3, 4, 5, N). N is common to both. The nucleus always carries an oxygen in position 3.



The nitrogen is always methylated. The oxygen is substituted with an aromatic acid, therefore , creating an ester.



- **Being esters, they are unstable towards acid and alkali.**

A) SOLANACEOUS ALKALOIDS:

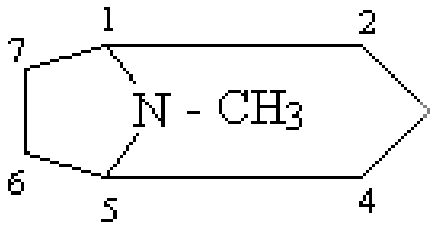
Datura stramonium

Hyoscyamus niger

Atropa belladonna

The 3-hydroxy derivative of tropane is known as TROPINE .

TROPANE



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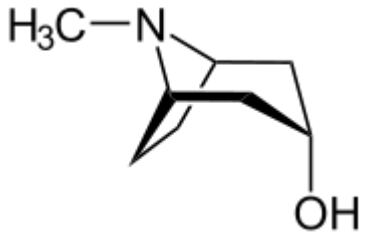
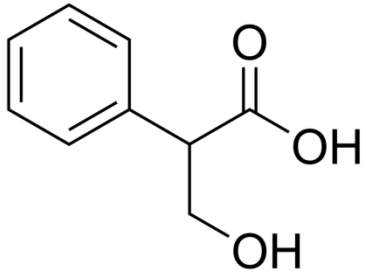
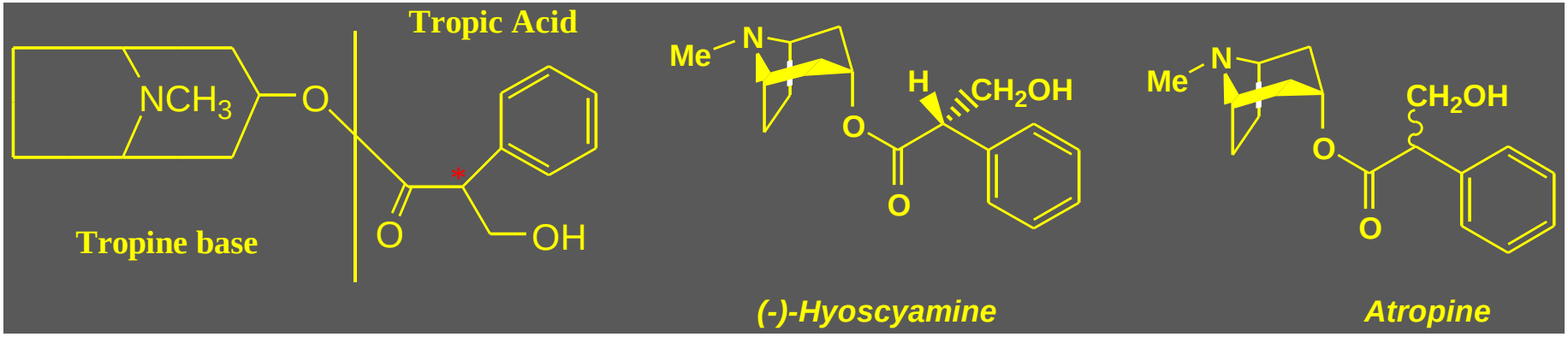


TROPINE

Esterification of tropine with tropic acid yields hyoscyamine (tropine tropate)



TROPIC ACID



Atropine & Hyoscyamine

Hyoscyamine is the major natural alkaloid with negative optical rotation (*l*- form).

During extraction hyoscyamine racemizes to the optically inactive *dl* Atropine.

Both alkaloids composed of tropine base and tropic acid.

Pharmacological actions and uses of Atropine

- Atropine sulfate has an anti-cholinergic effect (parasympatholytic activity).

- It is used in medicine as:

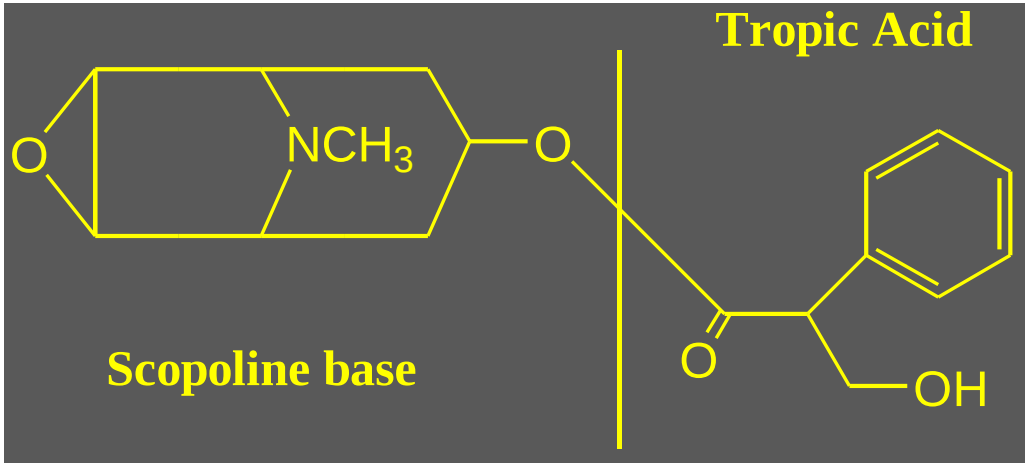
1. A mydriatic (causes dilatation of the eye pupil).
2. An antispasmodic (relaxes the intestinal and bronchial smooth muscles).

3. A pre-anesthetic medication to stop body secretions.
4. A CNS stimulant.
5. An antidote to organophosphorus insecticides.

Hyoscine (Scopolamine)

Hyoscine is an ester of *l*-tropic acid with scopoline base.

Hyoscine is a syrupy liquid.



Effects and uses of Scopolamine (Hyoscine):

- **The action of Scopolamine (Hyoscine) differs from that of Atropine and Hyoscyamine in:**

  → **It has no central nervous system stimulation effect, but in high doses it causes hallucination.**

- **Hyoscine HBr is commonly used in as sedative**
- Has antiemetic effect

N.B. Vitali's test is a special test for solanaceous alkaloids

+ conc HNO_3 & alc. KOH ⟶ **violet colour**

INGREDIENTS:
Active:
Atropine Sulfate 1.0%.
Preservative:
Benzalkonium
Chloride 0.01%.
Vehicle:
Hydroxypropyl
Methylcellulose
(4000 cps) 0.5%.

رقم الصنف

Aut. no. 176

ALCON-COUVREUR
B-2870 Puurs, Belgium

30 Ctd. Tablets

Spasmolgin

ANTISPASMODIC

LOT : 1285
MFG : 3/2005
EXP : 3/2009

Asia pharmaceutical industries

ASIA

Spasmolgin

Composition: Each ctd. tab. contains:
Hyoscine -N-butyl bromide B.P. 10mg

For dosage and indication:
See enclosed instructions.
Attention: Keep in cool and dry place .
Out of reach of children.

6 211160 031870

Buscopan® 10 mg

20 s.c. tablets

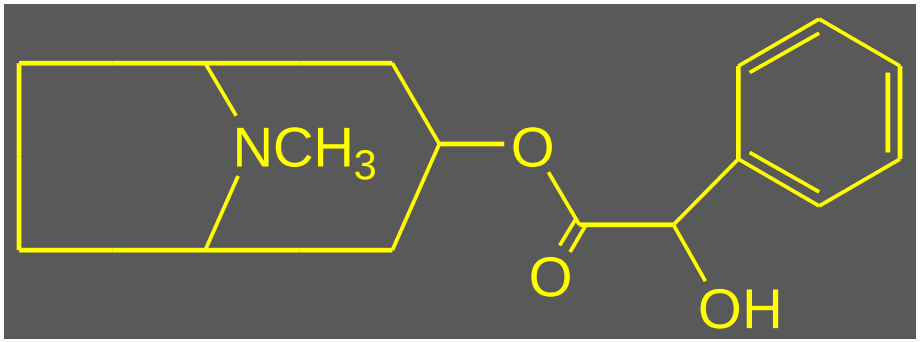
Boehringer Ingelheim

Synthetic and Semisynthetic Derivatives

Homatropine:

Synthetic drug prepared by passing HCl gas in a mixture of tropine base and mandelic acid in the presence of water.

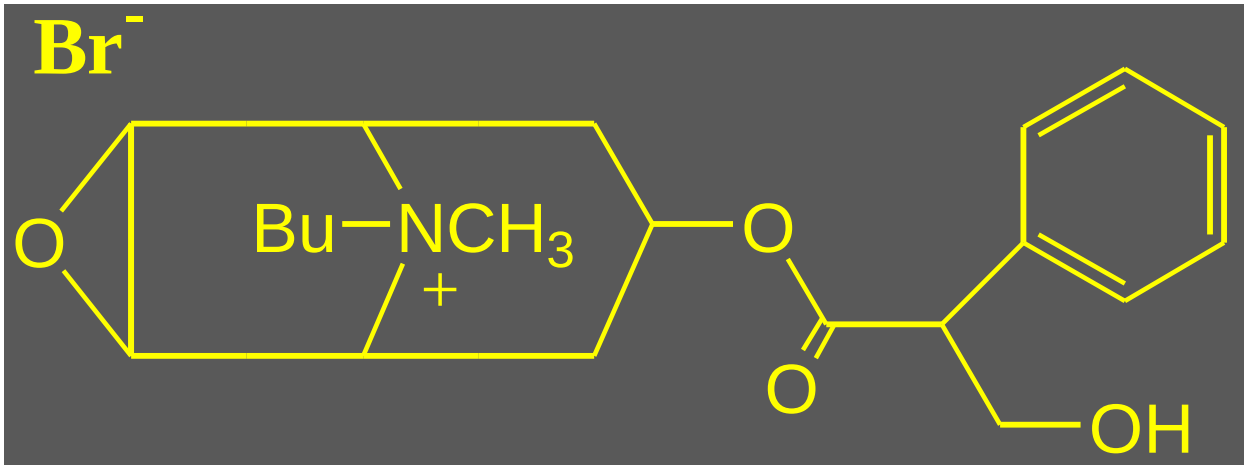
Homatropine is less toxic than Atropine. It is hypnotic in small doses. Homatropine is used as Mydriatic with shorter effect than Atropine.



Hyoscine butyl bromide:

Quaternary Semisynthetic derivative of Hyscine.

It is used as antispasmodic and antiemetic.



B- Erythroxylon (*Coca*) Alkaloids

Occurrence:

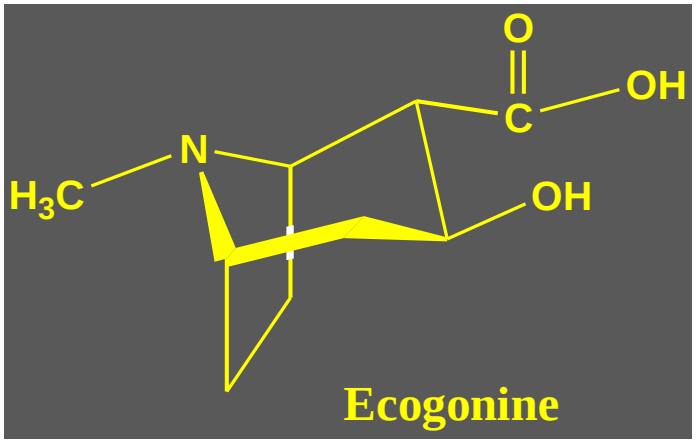
***Coca* leaves contain about 2% total alkaloids.**

Main Alkaloids are:

1- Cocaine.

2- Cinnamylcocaine.

3. α- truxilline.



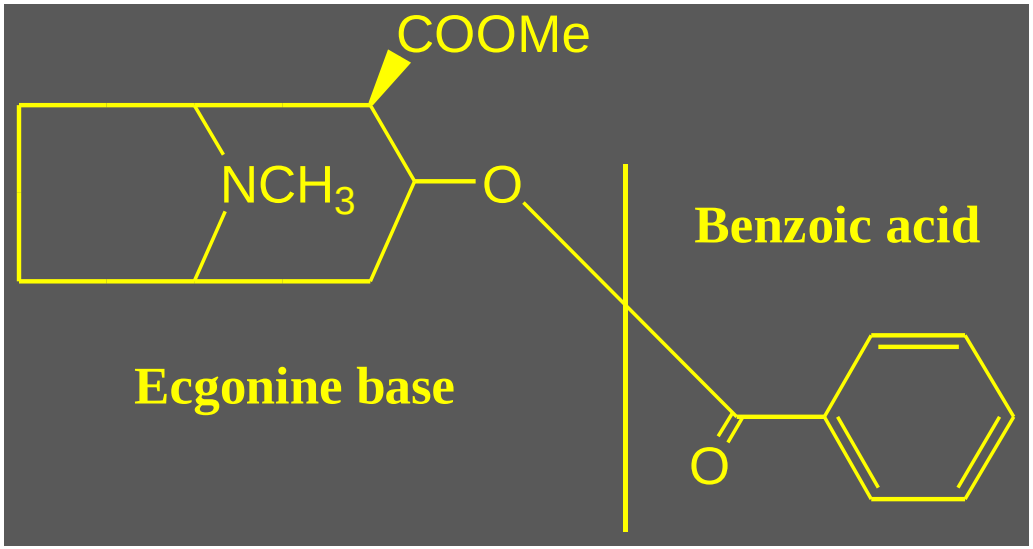
The base for Coca Alakloid is called “Ecogonine”

Cocaine

It is the major Alkaloid in Coca leaves.

Cocaine is diester Alkaloid.

Heating at 160 ^{0}C in conc. HCl leads to hydrolyses of cocaine to MeOH, Benzoic acid and Ecogonine base.



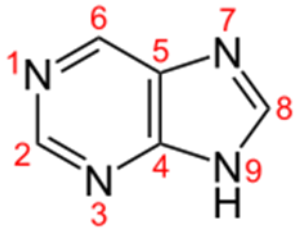
Uses:

Cocaine was used as **local anesthetic.**

Cocaine has a CNS stimulant activity so is one of the widely **abused drugs.**

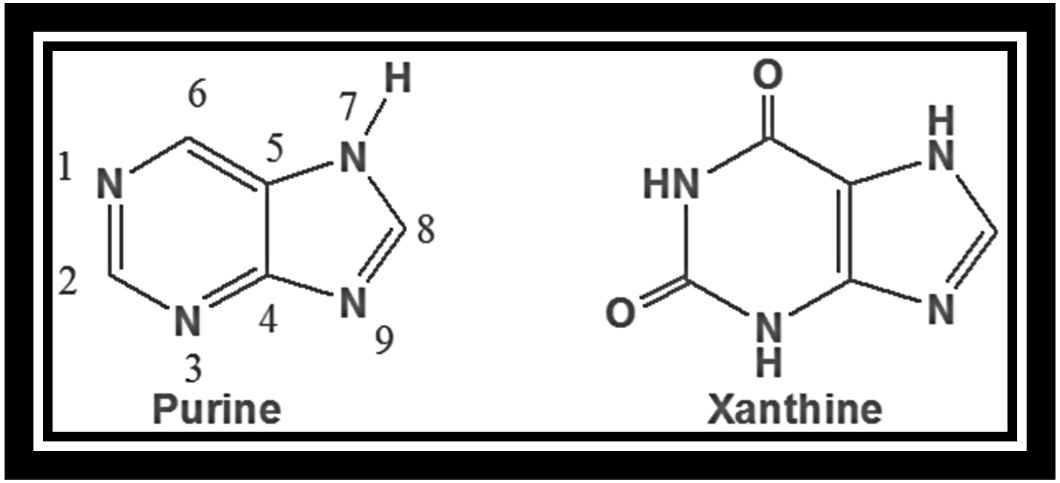
Alkaloids derived from Glycine

Purine Alkaloids

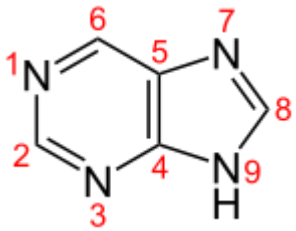


Purine alkaloids

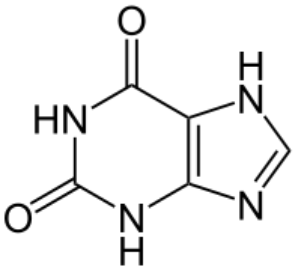
- Purines are derivatives of a heterocyclic nucleus consisting of a six-membered Pyrimidine ring fused to a five-membered Imidazole ring.
- Purines are Psudo alkaloids (Are not derived from amino acids but have nitrogen in a heterocyclic ring)
- The pharmaceutically important bases of this group are all methylated derivatives of 2,6 dioxy-purine (Xanthine).



- These alkaloids are weak bases, they give no precipitate with Mayer's reagent.



Purine alkaloids

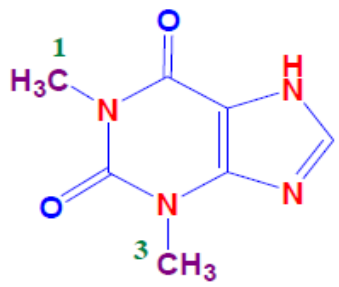


xanthine

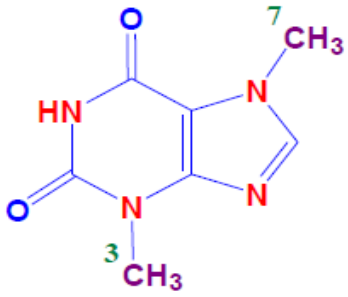
caffeine

theobromine

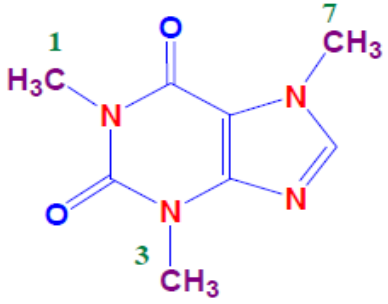
theophyilline



Theophylline
(1,3-dimethylxanthine)



Theobromine
(3,7-dimethylxanthine)



Caffeine
(1,3,7-trimethylxanthine)

- They are all methyl derivatives of xanthine.

Caffeine

- 1,3,7-trimethylxanthine
- Tea leaves (2- 5%), Coffee seeds (1-2 %), Cola leaves (2- 3%), Gurana seeds (2.5- 5 %) and Cacao seeds, (0.2- 0.5 %).
- White powder, bitter taste, very weak base, soluble in hot water, in alcohol and CHCl3, sparingly in ether.
- Sublimable.
- Doesn't precipitate with Mayer's reagent

Theophyline

- 1,3-dimethylxanthine
- Traces in Tea leaves
- White, odorless, bitter crystalline, soluble in H2O, alcohol
- Sparingly soluble in ether and CHCl3

Theobromine

- 3,7-dimethylxanthine (mainly in seeds of *Theobroma cacao*)
- White, odorless, bitter crystalline, sparingly soluble H2O
- Insoluble in ether
- Sublimable

❖ caffeine and theophylline are used in therapeutics

Pharmacology

Caffeine

► stimulation of CNS, effect on the psychic centers

► Causes flow of thought, lessen drowsiness, relieve headaches and gives a sense of comfort and well-being

Theobromine

► Diuretic effect and used in the treatment of various types of edema

Theophylline

► smooth muscle relaxant, myocardial stimulant and diuretic

Identification:

Murexide reaction

Alkaloids + H_2O_2 + HCl gives after evaporation yellow-red color which turns to red-violet upon addition of NH_3.


Bristol-Myers Squibb
100 TABLETS
List 0519-05
Quibron®-T/SR
(Theophylline Anhydrous)
Dividose® Tablets
SUSTAINED RELEASE BRONCHODILATOR
For Oral Use
300 mg

- # 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 wich **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.**

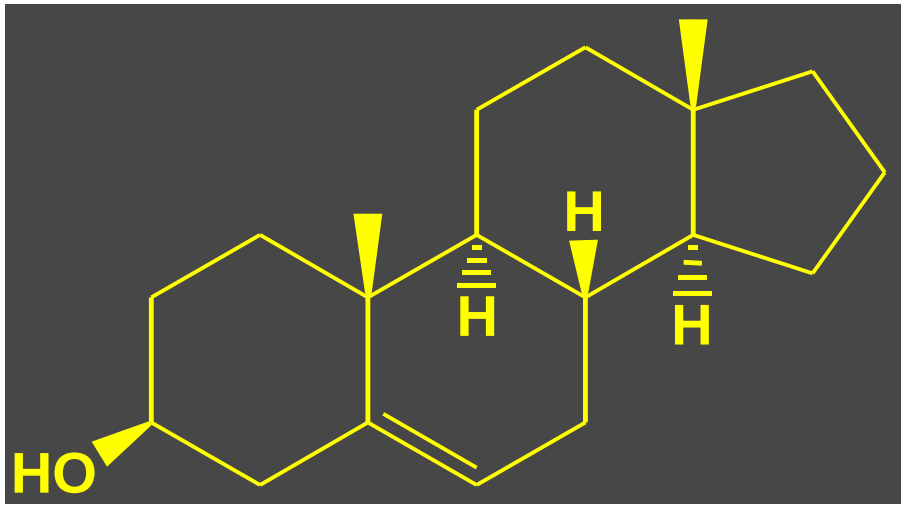
- **Ferrous sulfate test: (theobromine)**:

  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.**

Steroidal Alkaloids

- These contain the **perhydrocyclopentano-phenanthrene skeleton** characteristic of sterols.

- They usually occur in **glycosidal combination** with sugars and thus called **glucoalkaloids** e.g. *Solanum* and *Veratrum* alkaloids.

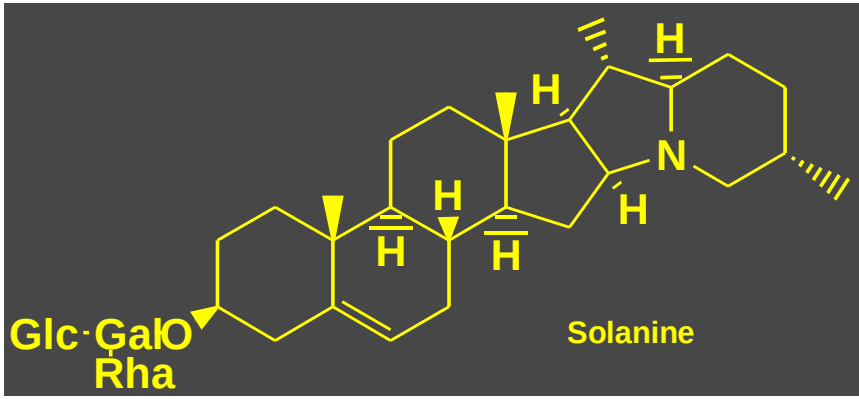


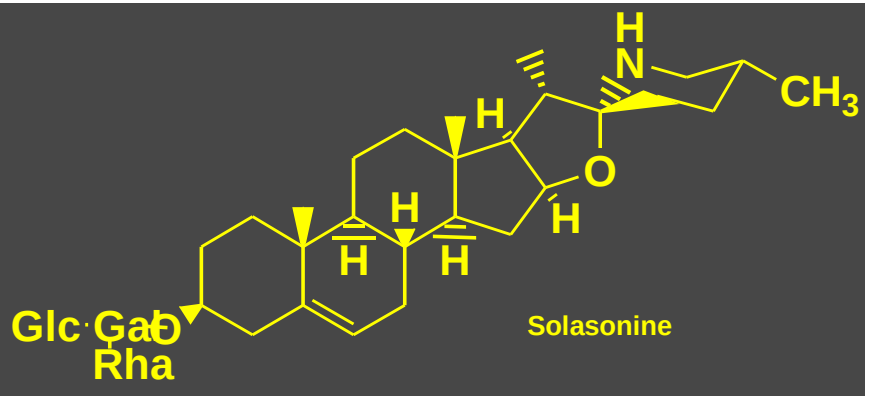
Solanum alkaloids

- **Occurrence:** They occurs in *Solanum spp.*
- **Consitituents:** Solanine, Solasonine.
- **Properties:** They are glucoalklaloids with a sugar parts.
- **Uses:**

  1- The aglycone of both alkaloids are used as a starting material for the synthesis of steroidal drugs.

  2- Solasonine is used as agricultural insecticide.





Diterpene Alkaloids

Taxol

- **Occurrence:** Barks of *Taxus brevifolia* known as Pacific Yew.
- **Yield:** 0.015 %. **The bark** obtained from about **4000 trees** yields about **one kg** of **Taxol.** The amount isolated from three trees is required from treatment of only one cancer patient.

- **Sources:**

  1- Natural. 2- Semisynthesis from Baccatin III.

- **Uses:** Breast, Ovarian, lung and other solid tumors. (Antimitotic agent).