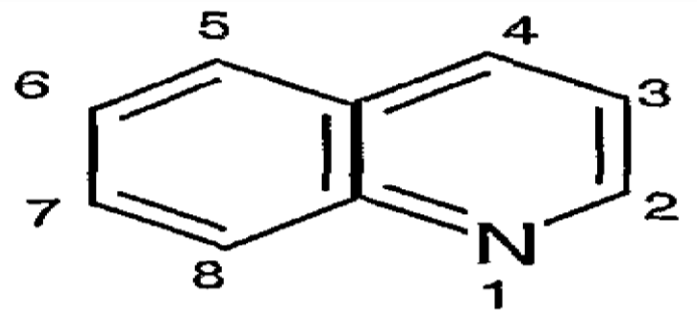
PharmacognosyIII

Lec. 4 **3rd stage 2nd semester** **Year 23-24**

Lecturer: Dr. Jamel Fani

ALKALOIDS

Quinoline alkaloids



Quinoline alkaloids

In general, the alkaloids containing essentially the 'quinoline' nucleus include a series of alkaloids obtained exclusively from cinchona bark, the major members of this particular group are, namely:

- Quinine
- Quinidine
- Cinchonine
- Cinchonidine

More than twenty five alkaloids have been isolated and characterized either from the *Yellow Cinchona* i.e. *Cinchona calisaya* and *Cinchona ledgeriana,* or from the *Red Cinchona* i.e. *Cinchona succirubra* (Family: Rubiaceae).

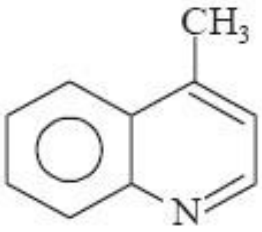
Basic Structures of Cinchona Alkaloids:

Cinchona alkaloids usually possess two rings: quinolone (which consists from benzene ring + pyridine) and bicyclic quinuclidine.

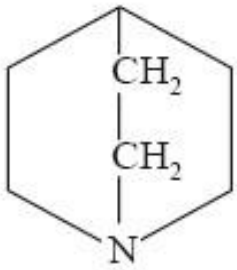
Cinchona possesses the basic skeleton of 9'-rubanol which is derived from the parent compound known as ruban.

Thus, ruban is obtained from the combination of two distinct heterocyclic nuclii, namely:

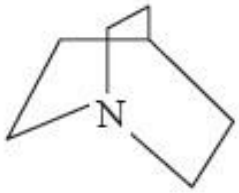
(a) 4-methyl quinoline nucleus, and (b) quinuclidine nucleus.



4-Methyl Quinoline Nucleus

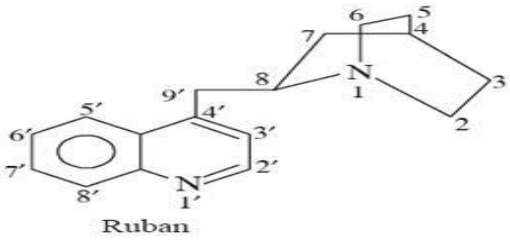


Quinuclidine Nucleus

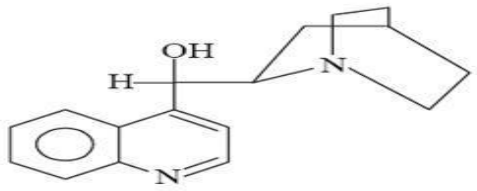


Quinuclidine Nucleus

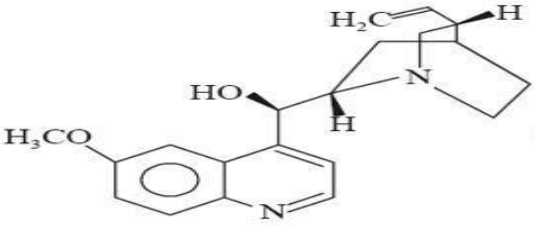
However, this particular nomenclature was suggested by Rabe so as to simplify the naming of such compounds and also to signify its origin from the natural order Rubiaceae.



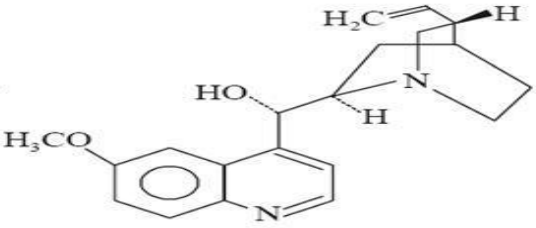
Ruban



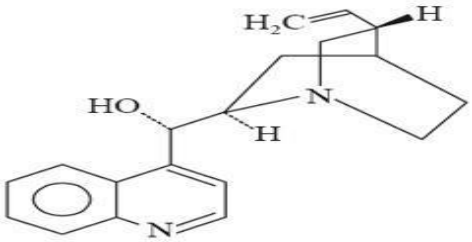
9′-Rubanol



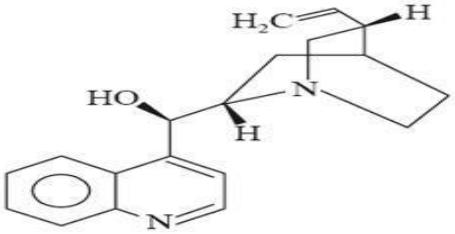
Quinine



Quinidine



Cinchonine



Cinchonidine

Quinine and quinidine are stereoisomers

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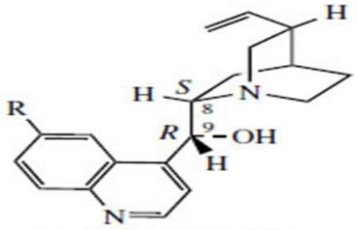
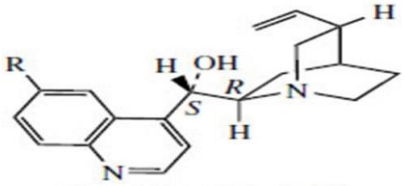
For cinchonine and quinidine C_8= R , C_9 = S

For cinchonidine and quinine C_8 = S , C_9 = R

Stereoisomers are isomeric molecules that have the same molecular formula and sequence of bonded atoms (constitution), but that differ *only* in the three-dimensional orientations of their atoms in space.



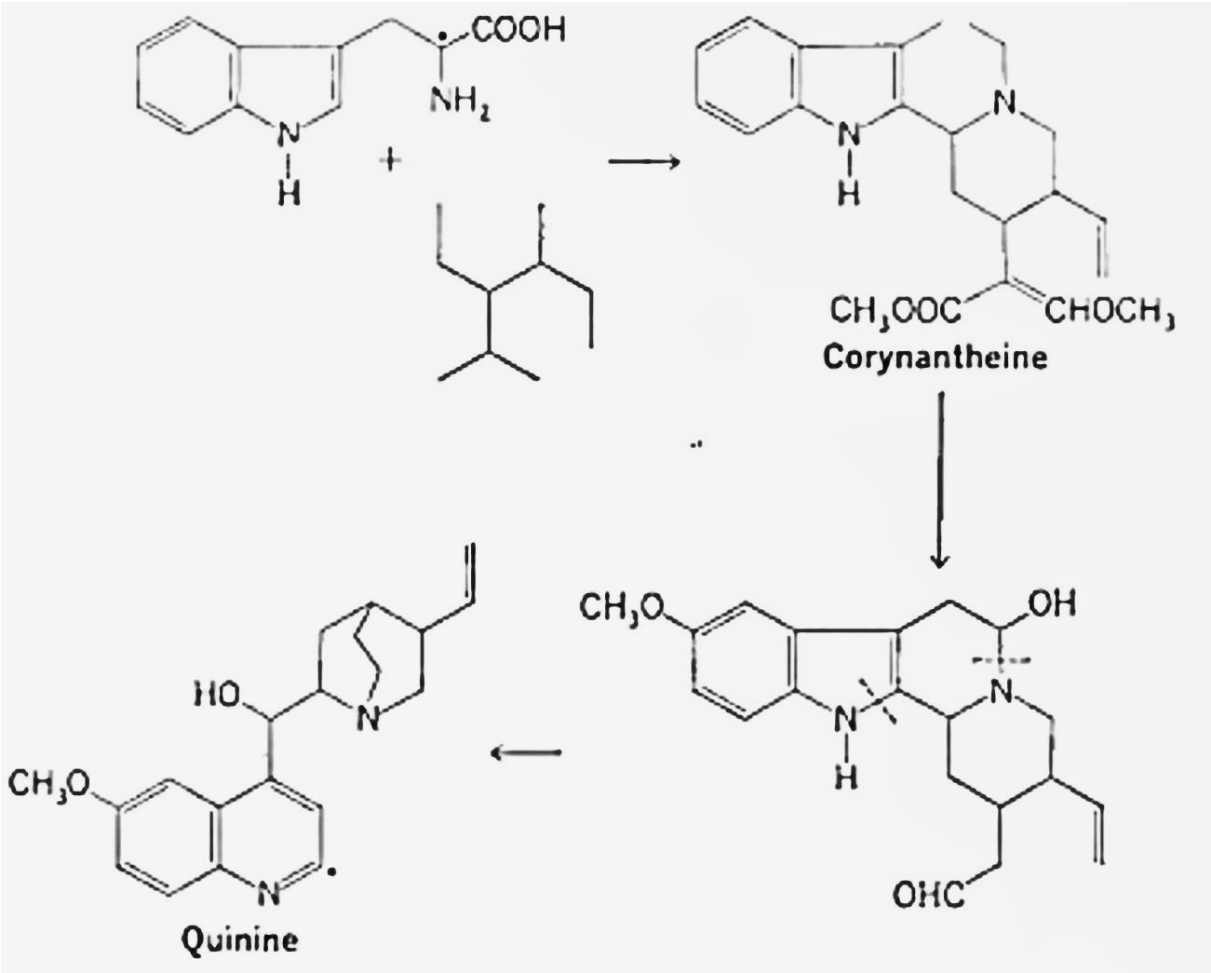
R = OMe, (–)-quinine
R = H, (–)-cinchonidine



R = OMe, (+)-quinidine
R = H, (+)-cinchonine

Biosynthetic pathway:

Studies with labeled geraniol and tryptophan indicate that quinine is metabolically derived from the monoterpenoid-tryptophan pathway.



Identification Tests of Quinine:

Fluorescence Test:

- Quinine gives a distinct and strong blue fluorescence when treated with an oxygenated acid, such as: acetic acid and sulphuric acid.
- This test is very marked and pronounced even to a few mg concentration of quinine.
- Note: The hydrochloride and hydroiodide salts of quinine do not respond to this fluorescence test.

Thalleioquin Test:

- Add to 2-3 ml of a weakly acidic solution of a quinine salt a few drops of bromine-water followed by 0.5 ml of strong ammonia solution, a distinct and characteristic emerald green color is produced.
- The colored product is termed as thalleioquin, the chemical composition of which is yet to be established.
- This test is so sensitive that quinine may be detected to a concentration as low as 0.005%.
- Notes: Quinidine gives also a positive response to this test; but cinchoninine and cinchonidine give a negative test.

Uses:

Cinchona and its alkaloids have been used in the treatment of malaria fever for many years.

Quinine sulfate continues to be used for malaria in many parts of the world (it poison the protozoa), as a tonic, an algesic, in the treatment of cold.

Quinidine is used to treat various cardiac arrhythmias e.g. arterial and ventricular tachycardia, atrial fibrillation and ventricular contraction.

Quinidine is found as salts (sulfate and gluconate).

It depresses myocardial excitability, conduction velocity & contractility.

Totaquine

It is a mixture of total alkaloids, containing not less than 7% and not more than 12% of anhydrous quinine.

It should contain 70-80% of total alkaloids.

It is used as an anti-malarial and for cold but it cannot be used as cardiac depressant. Usual dose 600mg.

Cinchonism or quinism

Treatment with cinchona products result in symptoms of mild cinchonism (which may occur from standard therapeutic doses of quinine).

These symptoms include flushed and sweaty skin, ringing of the ears (tinnitus), blurred vision, impaired hearing, confusion, reversible highfrequency hearing loss, head ache, abdominal pain, rashes, dysphoria, nausea, vomiting and diarrhea. Ringing in the ears is a symptom of toxicity.

When these symptoms are produced as the result of continuous use of cinchona or of quinine, the condition has been called cinchonism.