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NAMAKKAL

UNIT V

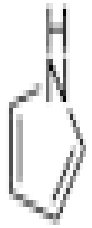
- **Alkaloids, Flavones and Isoflavones (15 Hours)**
- **Synthesis and Structural elucidation of Quinine, Papaverine, Morphine and Reserpine.**
- **Synthesis and structural elucidation of flavones, isoflavones and anthocyanins.**

Alkaloids

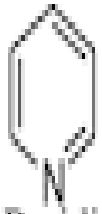
Definition: the term "alkaloid" (alkali-like) is commonly used to designate basic heterocyclic nitrogenous compounds of plant origin that are physiologically active.

Furan

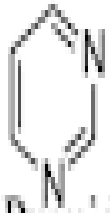
Thiophene



Pyrrole

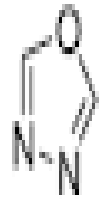


Pyridine



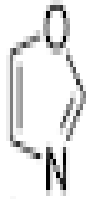
Pyrmidine

Imidazole

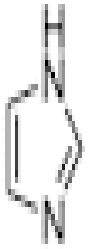


Oxadiazole

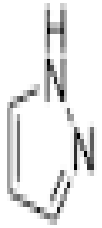
Isoxazole



Oxazole



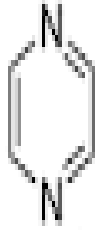
Imidazole



Pyrazole

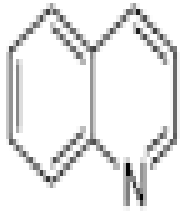
Isothiazole

Thiazole

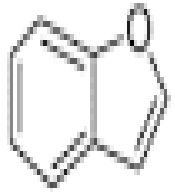


Pyrazine

Isoquinoline



Quinoline



Benzofuran

Benzimidazole

HISTORY

- "Alkaloid" -the Arabic word - "*al-qali*".
- Term alkaloid -coined by messiner -German pharmacist (1819).
- Totally more than 7000 compounds are known in only 5% of the plant species.
- Ninety five percent of plant species are still remain to be examined for alkaloids.

ALKALOIDS

- **Alkaloids** are a class of basic, naturally occurring organic compounds that contain at least one nitrogen atom.
- This group also includes some related compounds with neutral and even weakly acidic properties.
- Some synthetic compounds of similar structure may also be termed **alkaloids**.

ALKALOIDS

- Simply alkaloids are nothing but the basic nitrogenous compound, contains one or more nitrogen in heterocyclic ring system having marked physiological action on human and animals when use in small quantities".

STRUCTURE

Alkaloids- 12000 structures known.

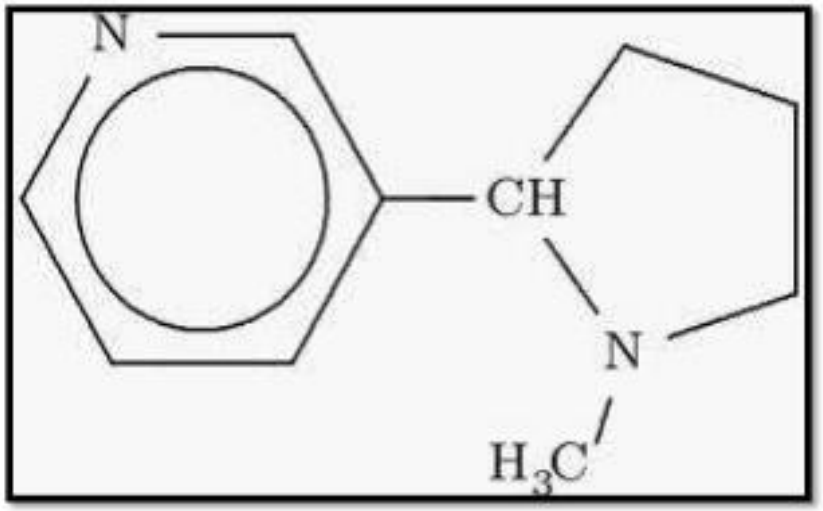
- **Poisons – Conine**
- **Narcotics – Morphine**
- **Stimulants – caffeine**
- **Medicine – Taxol**

GENERAL PROPERTIES OF ALKALOIDS

PHYSICAL PROPERTY

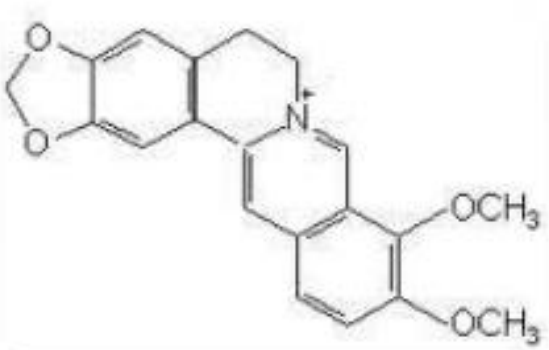
1.Most alkaloids are crystalline solid , but some are liquid

e.g Volatile; --Nicotine , Coniine .Spartine.

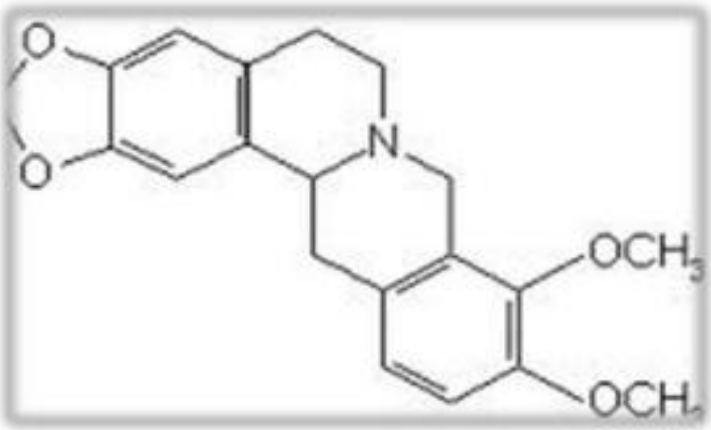


2.Majority of alkaloids are colorless but some are colored, e.g.

Colchicine and berberine(yellow), canadine (orange)



BERBERINE



CANADINE

SOLUBILITY :-difference in solubility used as a base for their isolation and purification from non-alkaloidal bases.

The following can be mentioned :-

a)Both alkaloidal base and there salts are soluble in alcohol.

b).Genarally bases are soluble in organic solvent and alkaloidal salts are soluble in water.

Alkaloid or its Salt				
	Water	Alocohol	Ether	Chloroform
Atropine	460	2	25	1
Atropine sulphate	0.5	5	Insoluble	Insoluble
Morphine	3400	300	5000	1525
Morphine sulphate	15.5	565	Insoluble	Insoluble

CHEMICAL PROPERTIES

- 1.Salt formation :--Due to their basic character alkaloid reacts with acid to form salt
- --strong bases form salt with very weak acid.
- --weak bases forms salt with strong acid
- -- very weak bases form unstable salts.e.g caffeine , Narcotine , piperine.

3)Effect of heat:

Alkaloids are decomposed by heat, except strychnine and caffeine (sublimable).

4). Effect of light and oxygen :

- Decomposed when allowed to stand at a temperature above 70o C .For long time.
- Sensitivity varies in degree with different alkaloids.
- Decomposition occur rapidly and easily when an alkaloid is in solution than when it is in dry form.
- Most tertiary amine alkaloids are easily transformed to the n-oxides.

BASICITY OF ALKALOIDS :--The basicity of alkaloid is due to presence of a lone pair of electron on nitrogen atom.

- --The basicity increased if the adjacent group is electron releasing like alkali .
- -- the basicity decreases if the adjacent group is electron withdrawing like carbonyl and amide group.

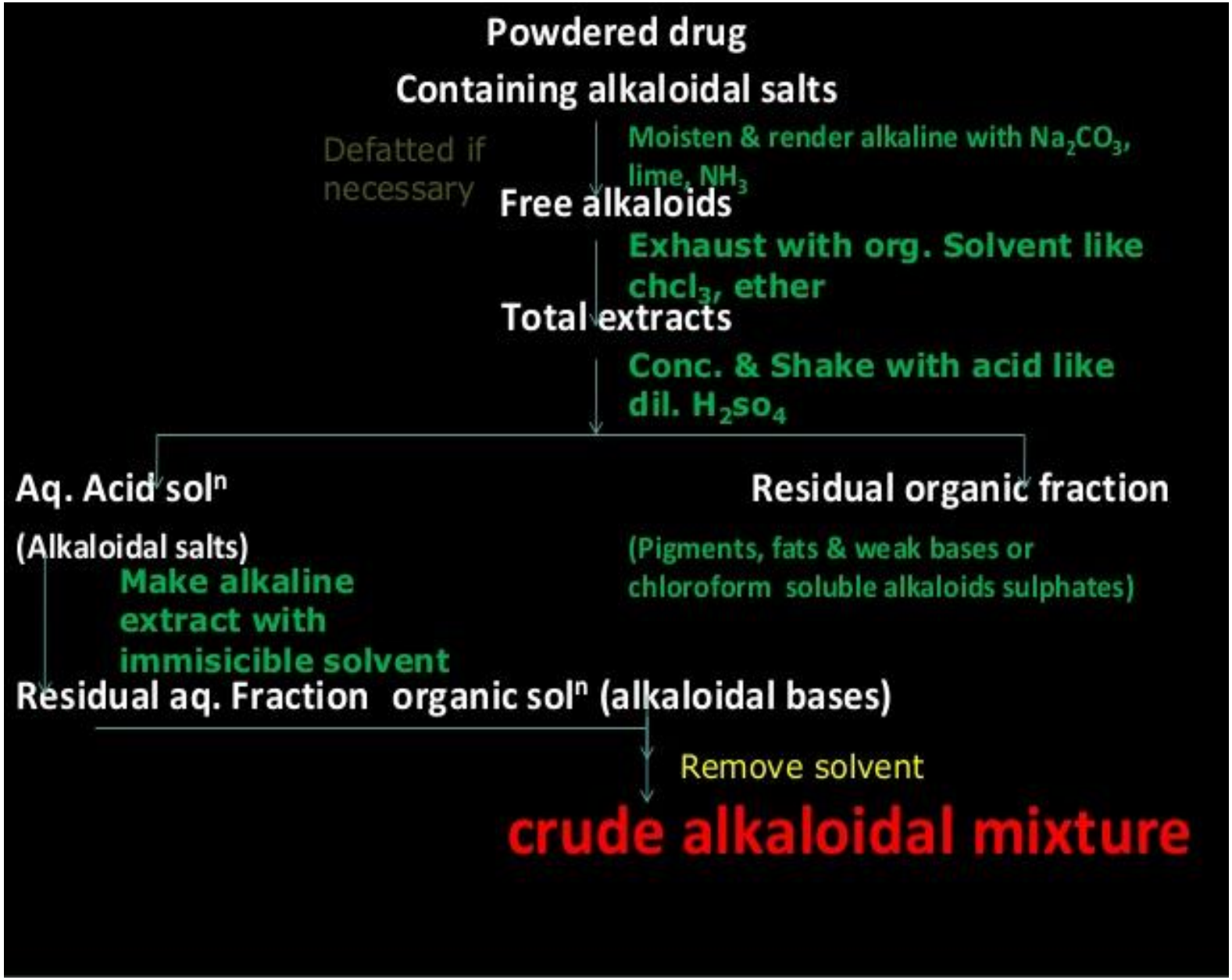
EXTRACTION OF ALKALOIDS

STAS-OTTO METHOD

LOGO

STAS-OTTO METHOD

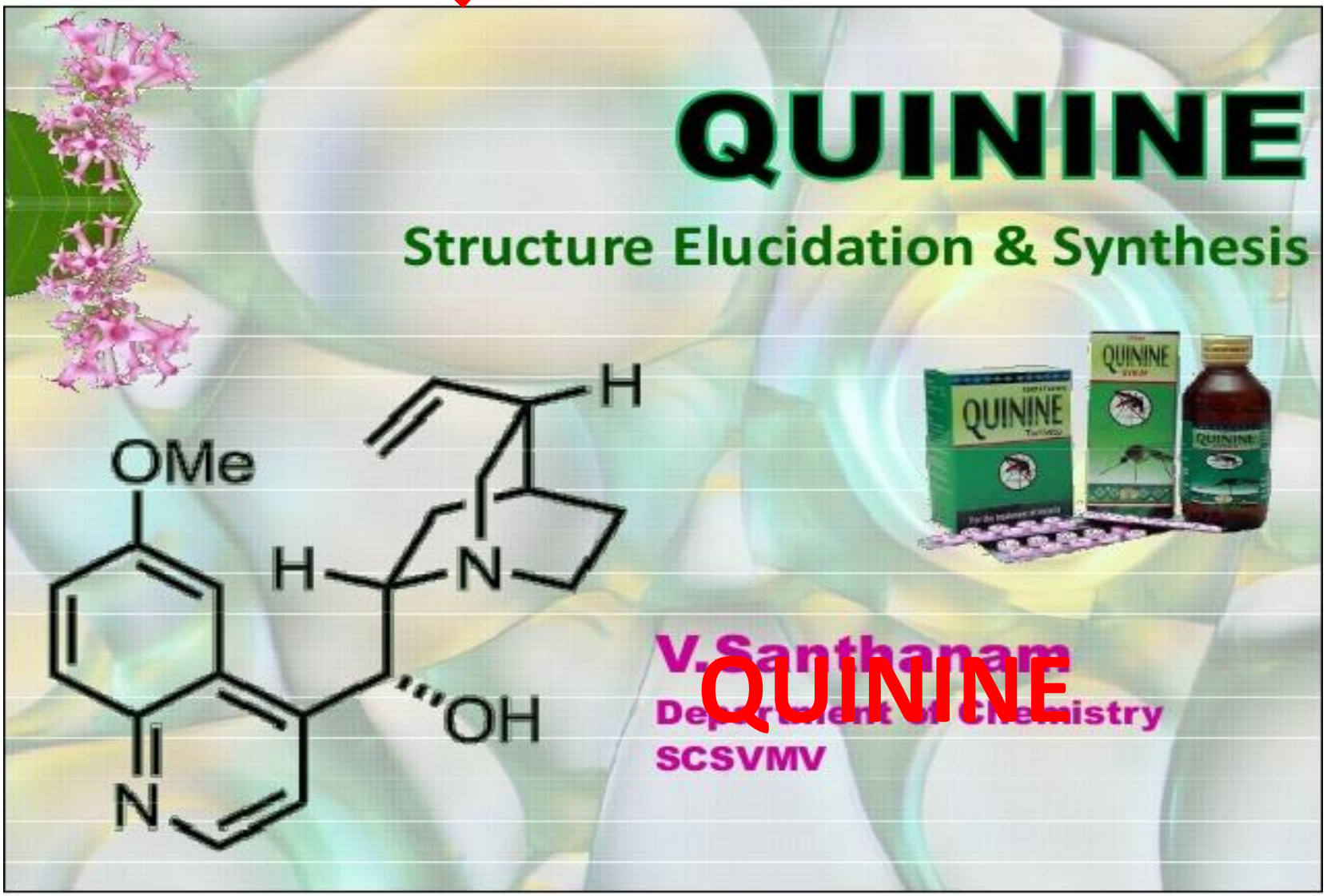
- The technique involve the distribution of alkaloidal bases between acid or aqueous solution and immiscible organic solvent.


Powdered drug
Containing alkaloidal salts
Defatted if necessary
Moisten & render alkaline with Na_2CO_3, lime, NH_3
Free alkaloids
Exhaust with org. Solvent like $chcl_3$, ether
Total extracts
Conc. & Shake with acid like dil. H_2so_4
Aq. Acid sol^n
(Alkaloidal salts)
Residual organic fraction
(Pigments, fats & weak bases or chloroform soluble alkaloids sulphates)
Make alkaline extract with immisicible solvent
Residual aq. Fraction
organic sol^n (alkaloidal bases)
Remove solvent
crude alkaloidal mixture

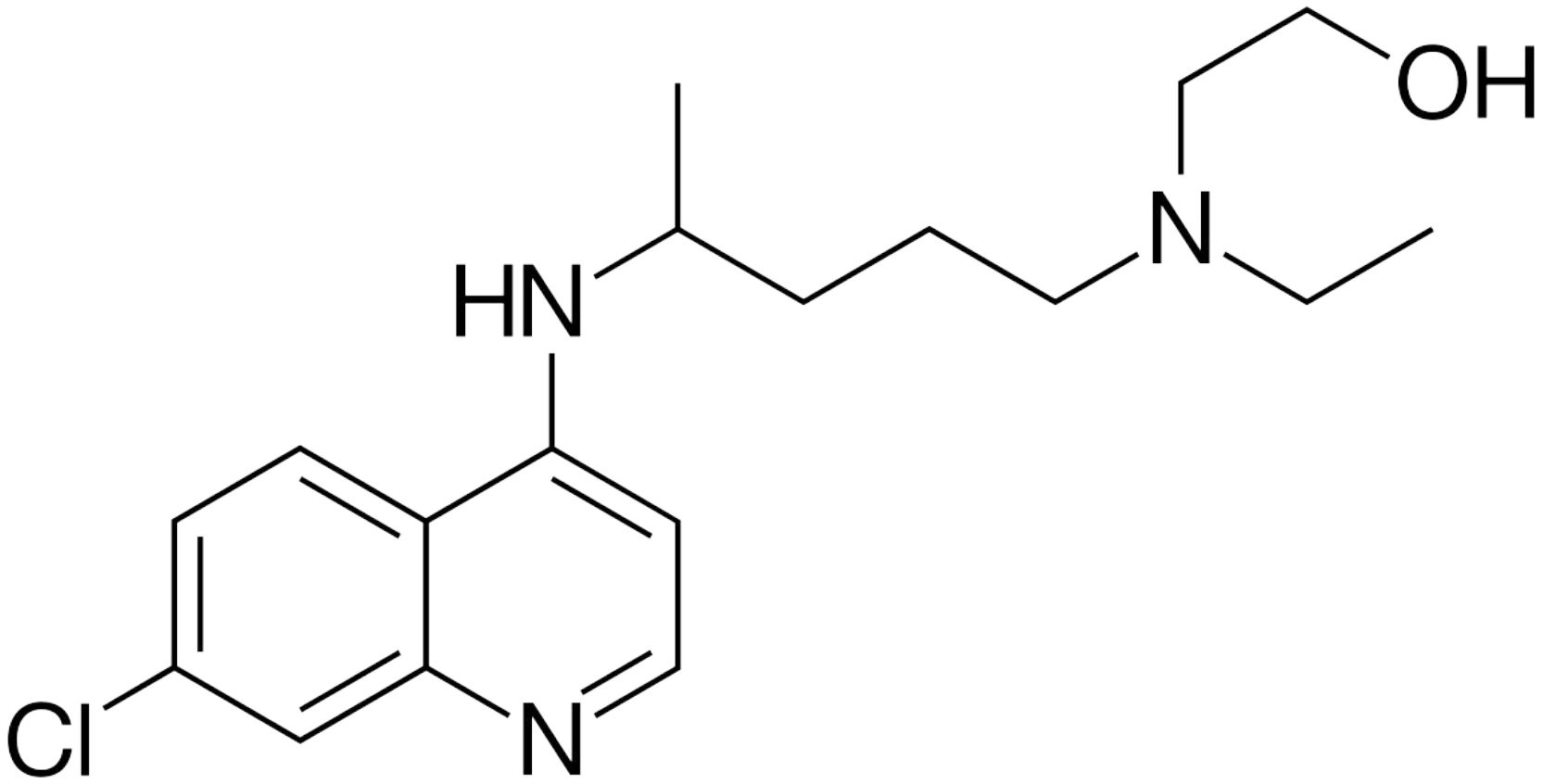
- B).Stage2:-- extract the free alkaloids by hot continous percolation with chloroform or any other organic solvents.
- Concept :-the free alkaloids dissolve together with other substances soluble in solvent.
- C).Stage3:--agitate the chloroform soln. With successive portion of dil.Sulphuric acid separating the aqueous layer before adding the next portion of acid.
- Concept :-the alkaloids are converted into alkaloidal sulphates, which being soluble in water,pass into aqeous layer.

- D)Stage4:--Make the mixed aqueous liquid alkaline with ammonia, collect the precipitate that forms, wash with water and dry.
- Concept :- Ammonia decomposes the alkaloidal sulphates forming ammonium sulphates ,soluble in water ,and the free alkaloid which being practically insoluble in water is precipitated.

QUININ


QUININE
Structure Elucidation & Synthesis
OMe
H
H
N
OH
N
QUININE
QUININE
QUININE
V.Santhanam
Department of Chemistry
SCSVMV

HYDROXYCHLOROQUINE



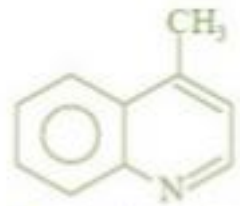
Isolation:-

- **The bark is stripped and dried in the sun.**

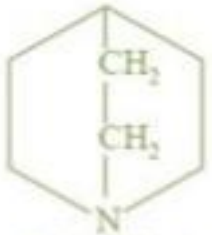
- **This is crushed to a fine powder and then treated with lime and caustic soda solution for several hours and finally extracted with hot petroleum.**

- **The solvent petroleum is drawn off and the petroleum extract is washed with dilute sulphuric acid in a lead lined vessel provided with a powerful stirrer.**

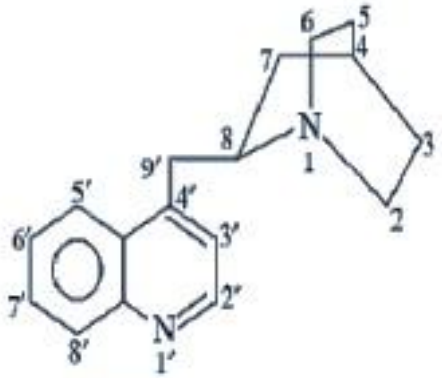
- The acid aqueous layer, while still hot, is neutralised and allowed to stand when the neutral sulphates of the alkaloids (quinine, cinchonine and cinchonidine) crystallise out.
- The mixtures of sulphates of three alkaloids is recrystallised when quinine sulphate, having minimum solubility crystallises out first while the sulphates of cinchonine and cinchonidine remain in the mother liquor.
- The crude quinine sulphate is redissolved in water, decolorised with charcoal and recrystallised until cinchonidine and cinchonine are reduced to the required percentage
- Quinine may be obtained from the sulphate by precipitation with alkali, washing and drying.



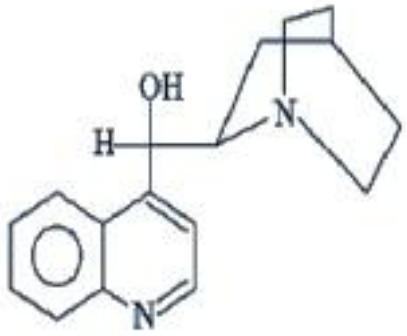
4-Methyl Quinoline Nucleus



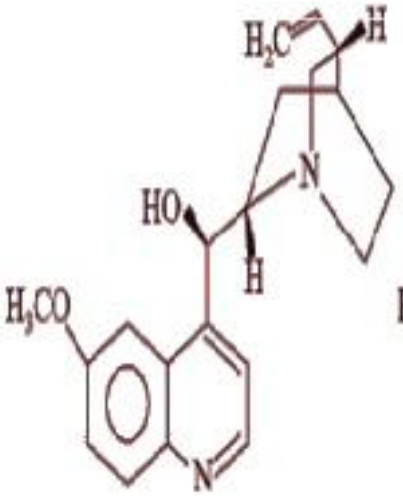
Quinuclidine Nucleus



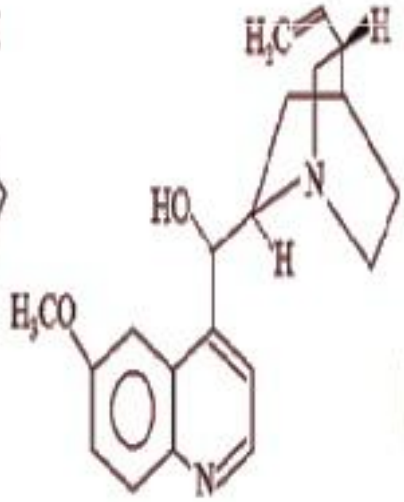
Ruban
[8-9′ Quinuclidyl Methyl Quinoline nucleus]



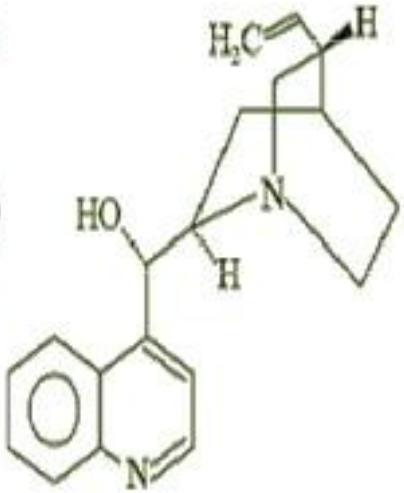
9′-Rubanol



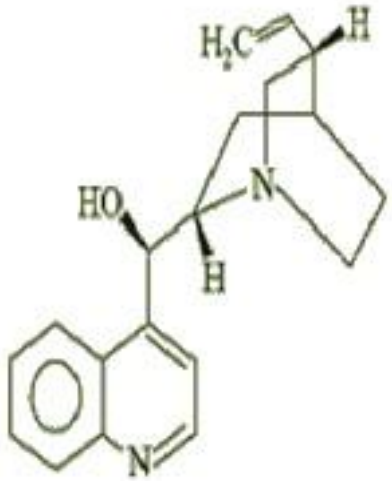
Quinine



Quinidine



Cinchonine



Cinchonidine