Alkaloids

(Classification & Identification)

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Classification

- **Different systems of classification may be adopted, based on:**
  - **The pharmacological action (biological activity)**
  - **The chemical structure (type of nitrogen, heterocyclic or non-heterocyclic and type of ring structure).**
  - **The biochemical origin (biosynthetic pathway of production in the plant)**
  - **The taxonomical origin (plant families rich in alkaloids).**
- **According to chemical structure, two broad divisions may be recognized:**
  - **Non-heterocyclic or atypical alkaloids that are sometimes called “proto-alkaloids” or biological amines.**
  - **Heterocyclic or typical alkaloids, that are sub-classified into different groups according to their ring structure.**

Pharmacological Classification

Alkaloidals exhibit a wide range of pharmacological activities. They can be used as:

- **Analgesic and narcotics:** e.g. morphine and strychnine
- **CNS stimulants:** e.g. caffeine and strychnine
- **Anticancers:** e.g. vincristine, vinblastine and taxol
- **Mydriatics:** e.g. atropine
- **Myotics:** e.g. eserine and pilocarpine.
- **Anti-asthmatics:** e.g. ephedrine
- **Antitussives:** e.g. codeine.
- **Expectorants:** e.g. lobeline.
- **Anti-hypertensives:** e.g. reserpine
- **Smooth muscle relaxants:** e.g. atropine and papaverine
- **Skeletal muscle relaxants:** e.g. tubocurarine.
- **Anthelmintics:** e.g. pelletierine and arecoline.
- **Antiparasitics:** e.g. quinine and emetine.

Hegnaur's classification

According to Hegnaur's classification, which is based on both, the type of nitrogen and the biochemical origin, three main types of alkaloids have been distinguished:

- **True alkaloids: derived from amino acids and have nitrogen in a heterocyclic ring.**
- **Proto alkaloids: derived from amino acids and do not have nitrogen in a heterocyclic ring.**
- **Pseudo alkaloids: not derived from amino acids but have nitrogen in a heterocyclic ring.**

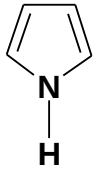
Type of alkaloid	Precursor	Type of nitrogen
True alkaloids	Amino acids	Heterocyclic
Protoalkaloids	Amino acids	Non-heterocyclic
Pseudoalkaloids	Non-amino acids	Heterocyclic

Chemical Classification

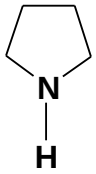
Classification of alkaloids is based on the structure of carbon – nitrogen cycle present in the molecule. Therefore, the Alkaloids can be divided into 14 subgroups according to their ring structure:

1. **Pyrrole and Pyrrolidine derivatives, e.g. Hygrine and Stachydrine.**
2. **Pyrrolizidine derivatives, e.g. Senecio alkaloids.**
3. **Pyridine and Piperidine derivatives, e.g. Trigonelline, Coniine, Arecoline, Lobeline, Pelletierine, Nicotine, Anabasine, Piperine and Ricinine.**
4. **Tropane (Piperidine / N-methylpyrrolidine) derivatives, e.g. Hyoscyamine, Hyoscine, Atropine, Meteloidine, Cocaine and Cinnamyl-cocaine.**
5. **Quinoline derivatives, e.g. Quinine, Quinidine, Cinchonine, Cinchonodine.**
6. **Isoquinoline derivatives, e.g. Papaverine, Narcotine, Hydrastine, Berberine, Emetine, Cephaëline, Tubocurarine, Corydaline.**
7. **Aporphine derivatives, e.g. Boldine.**
8. **Nor-lupinane derivatives, e.g. Sparteine, Cystine, Lupinine, Laburnine.**
9. **Indole derivatives, e.g. Ergometrine, Ergotamine, Physostigmine, Ajmaline, Serpentine, Reserpine, Yohimbine, Aspidospermine, Vincablastine, Strychnine, Bruceine.**
10. **Imidazole derivatives, e.g. Pilocarpine.**
11. **Purine derivatives, e.g. Caffeine, Theobromine.**
12. **Steroidal derivatives (some combined as Glycosides), e.g. Solanine, Veratrum, Funtamine, Conessine.**
13. **Terpenoids derivatives, e.g. Aconitine, Atisine, Lycaconitine.**
14. **Tropolone derivatives, e.g. Colchicines.**

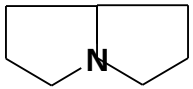
Basic Nucleus of Alkaloids…



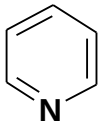
Pyrrole



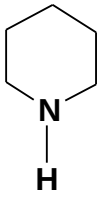
Pyrrolidine



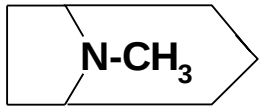
Pyrrolizidine



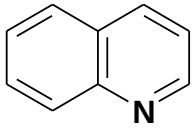
Pyridine



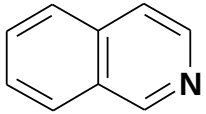
Piperidine



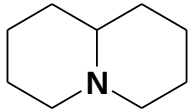
Tropane



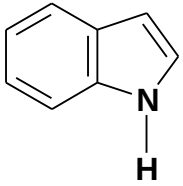
Quinoline



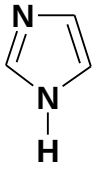
Isoquinoline



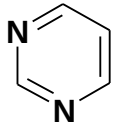
Nor-hipinane



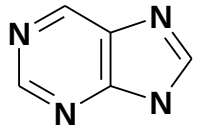
Indole
(Benzopyrrole)



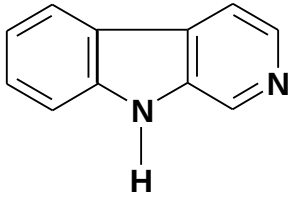
Imidazole



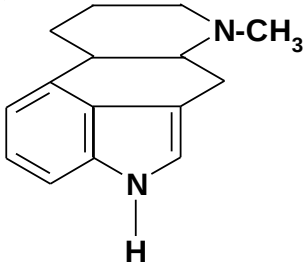
Pyrimidine



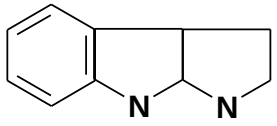
Purine
(Pyrimidine + Imidazole)



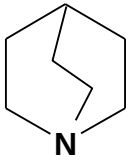
Carboline
(Indole + Pyridine



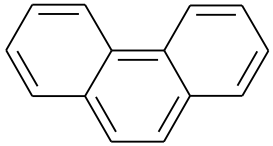
Indole + Hydroquinoline
(in Ergot Alkaloids)



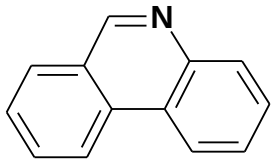
Hydroindole + Pyrrolidine
(in Physostigma Alkaloids)



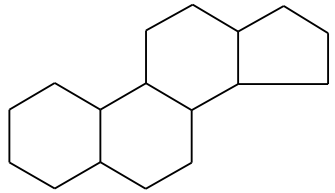
Quinuclidine
(in Cinchona Alkaloids)



Phenanthrene



Phenenthridine



Steroidal

Tests for detection and identification…

Chemical tests commonly performed for detection of alkaloids involve two types of reactions:

- **Precipitation reactions**
- **Color reactions**

Precipitation reactions…

- **Precipitation reactions result amorphous or crystalline precipitates of various colors.**
- **precipitating agent is added to a neutral or slightly acidic aqueous solution of the Alkaloidal salts.**
- **The reagents used contain heavy metals such as Hg, Pt, Bi etc. and form double salts with most alkaloids.**
- **These reactions could be used for extraction and purification.**
- **Care must be taken in the application of these tests as certain alkaloids such as caffeine and some others do not react.**
- **False positive response may be obtained in certain cases as most of the reagents used precipitate proteins, tannins, coumarins and certain flavonoids.**

Color reactions…

- These reactions are usually performed by the addition of color reagents to free bases not to their salts to produce characteristic colored solutions.
- The reagents contain concentrated sulfuric acid and an oxidizing agent.
- They give colors with most alkaloids, or may be specific for one alkaloid or a group of related alkaloids.
- Examples of specific color reactions are:
  - Van-Urk's test for ergot alkaloids:

    A blue color is obtained when treated with p-dimethylaminobenzaldehyde in concentrated sulfuric acid.
  - Vitali's test for solanaceous alkaloids:

    These give a violet color when treated with concentrated nitric acid and alcoholic potassium hydroxide.

Common reagents for Alkaloids

Name of reagent	Composition	Remarks
Alkaloidal precipitants		**Color of precipitate**
1. Mayer's	Potassium mercuric iodide	Creamy white (positive with most alkaloids except caffeine and dilute ephedrine)
2. Wagner's	Iodine in potassium iodide	Reddish brown
3. Hager's	Saturated solution of picric acid	Yellow
4.Dragendorf's	Potassium bismuth iodide	Orange-reddish brown
5. Marme's	Potassium cadmium iodide	Yellow
Color reagents		
1. Froehd's	Ammonium molybdate/sulfuric acid	The colors formed are characteristic. The tests are sensitive to micro amounts and can be used for colorimetric estimations.
2. Mandalin's	Ammonium vanadate/sulfuric acid	
3. Marquis'	Formaldehyde/sulfuric acid	
4. Erdman's	Nitric acid/sulfuric acid	
5. Mecke's	Selenious acid/sulfuric acid	
6. Shaer's	Hydrogen peroxide/sulfuric acid	
7. Rosenthaler's	Potassium arsenate/sulfuric acid	
8. Dragendorf's	Potassium bismuth iodide	