Alkaloids

The first individual alkaloid, <u>morphine</u>, was isolated in 1804 from <u>poppy</u> (*Papaver somniferum*).



Definition and properties

Alkaloids are a group of naturally occurring <u>chemical compounds</u> (<u>natural products</u>) that contain mostly <u>basic</u> nitrogen atoms. This group also includes some related compounds with neutral and even weakly <u>acidic</u> properties.

Some synthetic compounds of similar structure are also termed alkaloids.

In addition to <u>carbon</u>, <u>hydrogen</u> and <u>nitrogen</u>, alkaloids may also contain <u>oxygen</u>, <u>sulfur</u> and more rarely other elements such as <u>chlorine</u>, <u>bromine</u>, and <u>phosphorus</u>.

Alkaloids are produced by a large variety of organisms including <u>bacteria</u>, <u>fungi</u>, <u>plants</u>, and <u>animals</u>. They can be purified from crude extracts of these organisms by <u>acid-base extraction</u>.

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Many alkaloids are **toxic** to other organisms.

They often have <u>pharmacological</u> effects and are used as <u>medications</u>, as <u>recreational</u> <u>منعش drugs</u>, or in <u>entheogenic مخدر</u> rituals. Examples are the <u>local anesthetic</u> and <u>stimulant cocaine</u>, the psychedelic <u>psilocin</u>, the stimulant منتط <u>caffeine</u>, <u>nicotine</u>, the analgesic منتط <u>morphine</u>, the antibacterial <u>berberine</u>, the anticancer compound <u>vincristine</u>, the anti-hypertension agent <u>reserpine</u>, the <u>anti-cholinergic</u> agent <u>atropine</u>, the vasodilator <u>vincamine</u>, the anti-arrhythmia compound <u>quinidine</u>, the anti-asthma therapeutic <u>ephedrine</u>, and the <u>antimalarial drug quinine</u>.

Although alkaloids act on a diversity of metabolic systems in humans and other animals, they almost uniformly invoke a <u>bitter taste</u>.

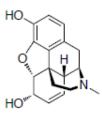
Naming

The concept of "alkaloid".

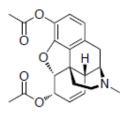
The name "alkaloid was introduced in 1819 by the German chemist <u>Carl Friedrich Wilhelm Meißner</u>, and is derived from late Latin root <u>Latin</u>: alkali.

There is no unique method of naming alkaloids. Many individual names are formed by adding the suffix "ine" to the species or genus name. For example, <u>atropine</u> is isolated from the plant <u>Atropa belladonna</u>, <u>strychnine</u> is obtained from the seed of <u>Strychnine tree</u> (<u>Strychnos nux-vomica L.</u>). If several alkaloids are extracted from one plant then their names often contain suffixes "idine", "anine", "aline", "inine" etc. There are also at least 86 alkaloids containing the root "vin" (extracted from the <u>Vinca plant</u>).

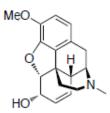
Alkaloids



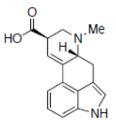
Morphine Papaver somniferum (Plant)



Heroin (diacetyl morphine or diamorphine) a semisynthetic derivative of morphine



Codeine (methylmorphine)

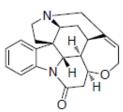


lysergic acid ergot fungi

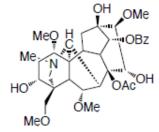
Caffeine Isolated from plants - first 1819 Stimulant Alkaloid



Coniine Neurotoxin from Conium maculatum (Plant)



Strychnine Toxin from *Strychnos nux-vomica* (tree)



Aconitine Toxin from aconite species (plant)

Nicotine Stimulant from the *Nicotiana* (Nightshade) genus (Plants)

Epibatidine Pain killer (200 x more potent than morphine) Epipedobates tricolor (Frog)

Cocaine Erythroxylum coca (Plant) Alkaloid

Nomenclature

Trivial names should end by "ine". These names may refer to:

- The genus of the plant, such as Atropine from Atropa belladona.
- The plant species, such as Cocaine from Erythroxylon coca.
- The common name of the drug, such as Ergotamine from ergot.
- The name of the discoverer, such as Pelletierine that was discovered by Pelletier.
- The physiological action, such as Emetine that acts as emetic, Morphine acts as narcotic.
- A prominent physical character, such as Hygrine that is hygroscopic.

Alkaloids Classifications

Alkaloids are often divided into the following major groups:

1) "True alkaloids", which contain <u>nitrogen</u> in the <u>heterocycle</u> and originate from <u>amino</u> <u>acids</u>. Their characteristic examples are <u>atropine</u>, <u>nicotine</u>, and <u>morphine</u>.

1) "Protoalkaloids", which contain <u>nitrogen</u> and also originate from amino acids. Examples include <u>mescaline</u>, <u>adrenaline</u> and <u>ephedrine</u>.

1) "Pseudalkaloids" – alkaloid-like compounds that do not originate from amino acids. This group includes, <u>terpene</u>-like and <u>steroid</u>-like alkaloids, as well as <u>purine</u>-like alkaloids such as <u>caffeine</u>, <u>theobromine</u>, <u>theacrine</u> and <u>theophylline</u>.

α-Amino Acids used to make Alkaloids

$$H_3N^{\uparrow}$$
 $+NH_3$
 H_3N^{\uparrow}
 $+NH_3$
 $CO_2^ +NH_3$
Ornithine

Chemical properties of alkaloids

- Present in the Plant as- Salt, ester, N-oxide, quaternary compound.)
- Generally very toxic compound.
- Have bitter taste.
- Unstable compound in (Heat, Light, pH changes "some of"

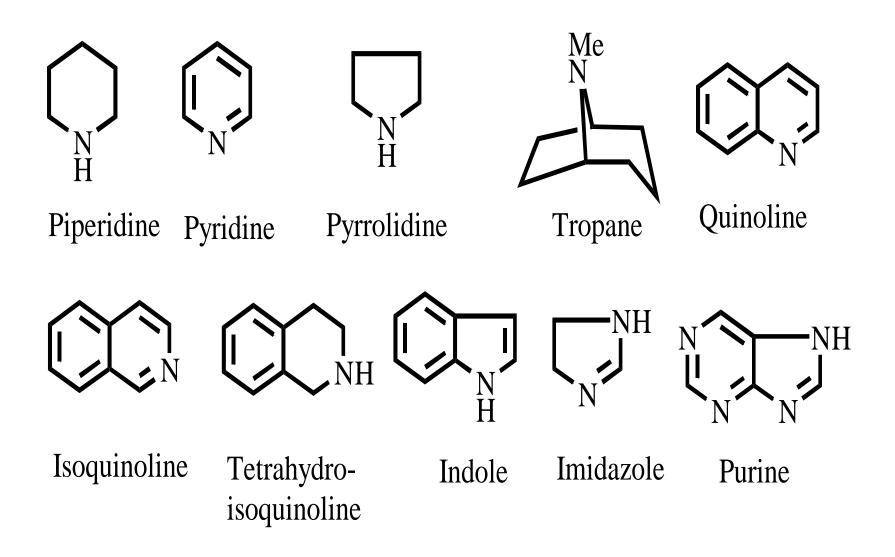
Physicochemical properties

- ❖ Solid crystalline compound (exception are: coniine and Nicotine are liquid (It doesn't have Oxygen in their structure).
- Colorless compound (exception are berberine (yellow), Betaine (red).
- **Sharp melting Point because it's pure compound in crystal form.**
- **❖** Can be either 1º, 2º, 3º or 4⁰ alkaloid:
- **Basicity depends on availability of lone pair of electrons:**
- 1. Electron donating or electron withdrawing neighbors.
- 2. Type of hybridization.
- 3. Aromaticity.

Detection of alkaloid

Wagner's test: (I_2/kI) : Reddish brown precipitate. Mayer's: (HgCl₂ Creamy precipitate with True alkaloid. Hagger's test: (Picric acid) Yellow precipitate with True alkaloid. **Dragendroff:** (Potassium Bismuth Iodide) Reddish Brown precipitate. **Tannic acid solution:** Different alkaloid colored precipitate.

Classifications of Alkaloids according to their chemical structures (groups)

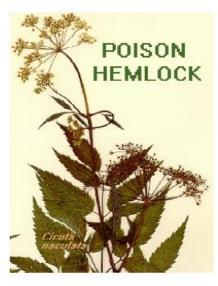


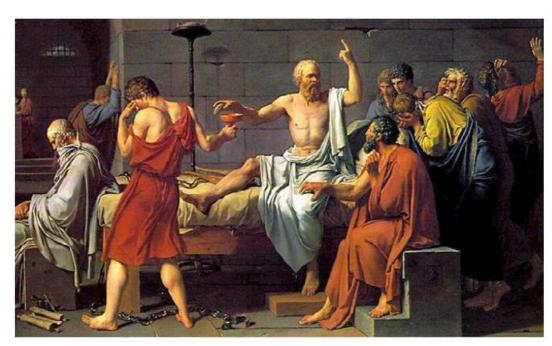
True Alkaloids Piperidine Group

Coniine (Poisons)

Hemlock Alkaloids







Socrates drinking poison hemlock, 399 B.C.

"The Death of Socrates" by Jacques-Louis David (1787)

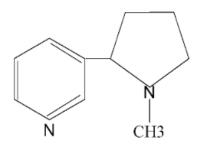
Coniine:

in 399 BC Socrates was sentenced to death for impiety and executed by being forced to drink a potion made from poison hemlock. The toxic component in hemlock is coniine.

Coniine Synthesis

True Alkaloids Pyridine & Pyrrolidine Group Nicotine from Tabacco

Stimulant, Nicotinic acetylcholine Receptor agonist







NICOTINE

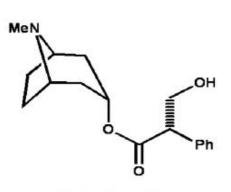
Nicotine Synthesis

True Alkaloids Tropane Group Atropine

Tropane Alkaloids



Atropa belladonna Deadly nightshade



(±)-atropine [(-)-hyoscyamine]

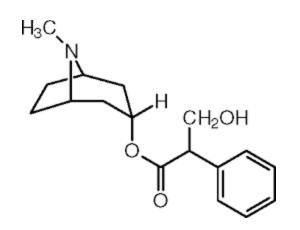


Anticholinergic

Hyoscyamus niger
Henbane

Atropine

Anticholinergic







Atropine Synthesis

Tropane Alkaloids









Erythroxylum coca



Anesthetic agent, at low doses

Cocaine Synthesis

$$\begin{array}{c} O \\ O \\ CH \\ CH \\ CH \\ CH \\ CO_2H \\ CO_$$

Protoalkaloids

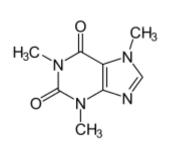
Adrenaline, Hormone

It increases activation of the sympathetic system associated with the energy and excitement of the <u>fight-or-flight response</u>, Increases also blood pressure

Pseudalkaloids

Purine Group Caffeine

Stimulant, Adenosine receptor antagonist

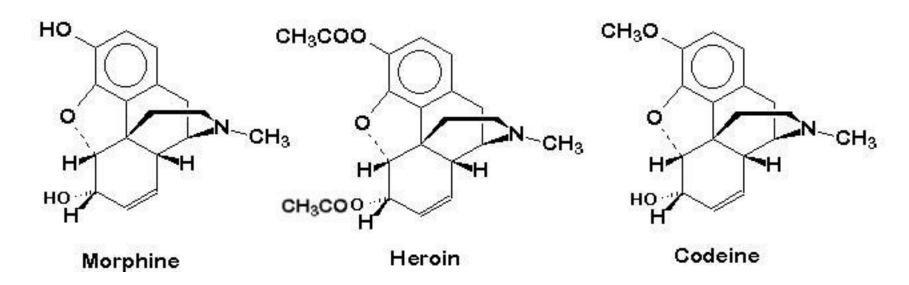








Miscellaneous Group



Narcotic Analgesic

from poppy (Papaver somniferum).





