

Secondary Metabolites (Alkaloids)

Alkaloids are a group of naturally occurring chemical compounds that contain mostly basic nitrogen atoms. This group also includes some related compounds with neutral and even weakly acidic properties. Some synthetic compounds of similar structure are also attributed to alkaloids.

In addition to carbon, hydrogen and nitrogen, alkaloids may also contain oxygen, sulphur and more rarely other elements such as chlorine, bromine, and phosphorus.

Alkaloids are produced by a large variety of organisms, including bacteria, fungi, plants and animals, and are part of the group of natural products (also called secondary metabolites).

Many alkaloids are toxic to other organisms. They often have pharmacological effects and are used as medications, as recreational drugs.

Examples are the local anesthetic and stimulant cocaine, the psychedelic psilocin, the stimulant caffeine, nicotine, the analgesic morphine, the antibacterial berberine, the anticancer compound vincristine, the spasmolysis agent atropine, the anti-arrhythmia compound quinidine, the anti-asthma therapeutic ephedrine, and the antimalarial drug quinine.

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

Alkaloids are often divided into the following major groups:

1. "True alkaloids", which contain nitrogen in the heterocycle and originate from amino acids. Their characteristic examples are atropine, nicotine, and morphine. This group also includes some alkaloids that beside nitrogen heterocycle contain terpene (e.g., evonine) or peptide fragments (e.g. ergotamine).

This group also includes piperidine alkaloids coniine and coniceine although they do not originate from amino acids.

2. "Protoalkaloids", which contain [nitrogen](#) and also originate from amino acids. Examples include [mescaline](#), [adrenaline](#) and [ephedrine](#).
3. Polyamine alkaloids – derivatives of [putrescine](#), [spermidine](#), and [spermine](#).
4. Peptide and cyclopeptide alkaloids.
5. Pseudalkaloids – alkaloid-like compounds that do not originate from amino acids. This group includes, [terpene](#)-like and [steroid](#)-like alkaloids, as well as [purine](#)-like alkaloids such as [caffeine](#), [theobromine](#), [theacrine](#) and [theophylline](#).

Some authors classify as pseudoalkaloids such compounds such as [ephedrine](#) and [cathinone](#). Those originate from the amino acid [phenylalanine](#), but acquire their nitrogen atom not from the amino acid but through [transamination](#).

Some alkaloids do not have the carbon skeleton characteristic of their group. So, [galantamine](#) and homoaporphines do not contain [isoquinoline](#) fragment, but are, in general, attributed to isoquinoline alkaloids.

Properties:

Most alkaloids contain oxygen in their molecular structure; those compounds are usually colourless crystals at ambient conditions. Oxygen-free alkaloids, such as [nicotine](#) or [coniine](#), are typically volatile, colourless, oily liquids. Some alkaloids are coloured, like [berberine](#) (yellow) and [sanguinarine](#) (orange).

Most alkaloids are weak bases, but some, such as [theobromine](#) and [theophylline](#), are [amphoteric](#). Many alkaloids dissolve poorly in water but readily dissolve in [organic solvents](#), such as [diethyl ether](#), [chloroform](#) or [1,2-dichloroethane](#). [Caffeine](#), [cocaine](#), [codeine](#) and [nicotine](#) are water soluble (with a solubility of ≥ 1 g/L), whereas others, including [morphine](#) and [yohimbine](#) are highly water soluble (0.1–1 g/L).

Alkaloids and acids form salts of various strengths. These salts are usually soluble in [water](#) and [alcohol](#) and poorly soluble in most organic solvents. Exceptions include [scopolamine hydrobromide](#), which is soluble in organic solvents, and the water-soluble [quinine sulfate](#).

Most alkaloids have a bitter taste or are poisonous when ingested. Alkaloid production in plants appeared to have evolved in response to feeding by herbivorous animals; however, some animals have evolved the ability to detoxify alkaloids. Some alkaloids can produce developmental defects in the offspring of animals that consume but cannot detoxify the alkaloids.

One example is the alkaloid [cyclopamine](#), produced in the leaves of [corn lily](#). During the 1950s, up to 25% of lambs born by sheep that had grazed on corn lily had serious facial deformations. After decades of research, in the 1980s, the compound responsible for these deformities was identified as the alkaloid 11-deoxyjervine, later renamed to [cyclopamine](#).

In medicine

Medical use of alkaloid-containing plants has a long history and thus when the first alkaloids were isolated in the 19th century, they immediately found application in clinical practice. Many alkaloids are still used in medicine, usually in the form of salts, including the following:-

| Alkaloid | |
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| Ajmaline | antiarrhythmic |
| Atropine , scopolamine , hyoscyamine | anticholinergic |
| Caffeine | Stimulant , Adenosine receptor antagonist |
| Codeine | cough medicine , analgesic |
| Colchicine | remedy for gout |
| Emetine | antiprotozoal agent |
| Ergot alkaloids | sympathomimetic , vasodilator, antihypertensive |
| Morphine | analgesic |

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| <u>Nicotine</u> | <u>Stimulant, Nicotinic acetylcholine receptor agonist</u> |
| <u>Physostigmine</u> | inhibitor of <u>acetylcholinesterase</u> |
| <u>Quinidine</u> | antiarrhythmic |
| <u>Quinine</u> | antipyretics, antimalarial |
| <u>Reserpine</u> | <u>antihypertensive</u> |
| <u>Tubocurarine</u> | Muscle relaxant |
| <u>Vinblastine, vincristine</u> | <u>antitumor</u> |
| <u>Vincamine</u> | <u>vasodilating, antihypertensive</u> |
| <u>Yohimbine</u> | <u>Stimulant, Aphrodisiac</u> |

Many synthetic and semisynthetic drugs are structural modifications of the alkaloids, which were designed to enhance or change the primary effect of the drug and reduce unwanted side-effects. For example, naloxone, an opioid receptor antagonist, is a derivative of thebaine that is present in opium.