

Alkaloid

Alkaloids are a group of naturally occurring chemical compounds which mostly contain basic nitrogen atoms. This group also includes some related compounds with neutral^[2] and even weakly acidic properties.^[3] Also some synthetic compounds of similar structure are attributed to alkaloids.^[4] Beside carbon, hydrogen and nitrogen, molecules of alkaloids may contain sulfur and rarely chlorine, bromine or phosphorus.^[5]

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 can be purified from crude extracts by acid-base extraction. Many alkaloids are toxic to other organisms. They often have pharmacological effects and are used as medications, as recreational drugs, or in entheogenic rituals. Examples are the local anesthetic and stimulant cocaine, the stimulant caffeine, nicotine, the analgesic morphine, or 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.^[6]

The boundary between alkaloids and other nitrogen-containing natural compounds is not clear-cut.^[7] Compounds like amino acid peptides, proteins, nucleotides, nucleic acid, amines and antibiotics are usually not called alkaloids.^[2] Natural compounds containing nitrogen in the exocyclic position (mescaline, serotonin, dopamine, etc.) are usually attributed to amines rather than alkaloids.^[8] Some authors, however, consider alkaloids a special case of amines.^{[9] [10] [11]}



The first individual alkaloid, morphine, was isolated in 1804 from poppy (*Papaver somniferum*).^[1]

Naming

The name "alkaloids" (German: *Alkaloide*) was introduced in 1819 by the German chemist Carl F.W. Meissner,^[12] and is derived from late Latin root *Latin: alkali* (which, in turn, comes from the Arabic *al qualja* - "ashes of plants") and the suffix *Greek: εἶδος* - "like".^[13] However, the term came into wide use only after the publication of a review article by O. Jacobsen in the chemical dictionary of Albert Ladenburg in the 1880s.^[14]

There is no unique method of naming alkaloids.^[15] Many individual names are formed by adding the suffix "-ine" to the species or generic alkaloids. For example, atropine is isolated from the plant *Atropa belladonna*, strychnine is obtained from the seed of Strychnine tree.^[5] 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 *Vinca* plant)^[16].

History

Alkaloid-containing plants were used by humans since ancient times for therapeutic and recreational purposes. For example, medicinal plants have been known in the Mesopotamia at least around 2000 BC.^[17] The *Odyssey* of Homer referred to a gift given to Helen by the Egyptian queen, a drug bringing oblivion. It is believed that the gift was an opium-containing drug.^[18] A Chinese book on houseplants written in I-III centuries BC mentioned a medical use of Ephedra and opium poppies.^[19] Also, coca leaves were used by South American Indians since ancient times.^[20]

Extracts from plants containing toxic alkaloids, such as aconitine and tubocurarine, were used since antiquity for poisoning arrows.^[17]

Studies of alkaloids began in the 19th century. In 1804, the German chemist Friedrich Sertürner isolated from opium a "soporific principle" (Latin: *principium somniferum*), which he called "morphium" in honor of Morpheus, the Greek god of dreams (the modern name "morphine" was given by the French physicist Joseph Louis Gay-Lussac). A significant contribution to the chemistry of alkaloids in the early years of its development was made by the French researchers Pierre Joseph Pelletier and Joseph Bienaimé Caventou who discovered quinine (1820) and strychnine (1818). Several other alkaloids were discovered around that time, including xanthine (1817), atropine (1819), caffeine (1820), coniine (1827), nicotine (1828), colchicine (1833), sparteine (1851) and cocaine (1860).^[21]



Friedrich Sertürner, the German chemist who first isolated morphine from opium.

II. Ueber ein neues Pflanzenalkali (Alkaloid).

Vom
Dr. W. Meissner.

Die Reihe leicht zersetzbarer Pflanzenalkalien, zu welcher das Morphem uns den Weg gebahnt hat, scheint sich mit jedem behutsamen Schritt der Pflanzenanalyse zu vermehren, wie dies noch neuerlich die Auffindung des Strychnin in der faba St. Ignatii und nux vomica durch Pelletier und Caventou bestätigt. Zu den schon bekannten kann ich nun noch ein neues hinzufügen, welches ich zu Anfang dieses Jahres in dem Sabadillsamen fand, und nicht ohne Schwierigkeiten für einen eigenthümlichen alkalischen Pflanzenkörper erkannte.

Man erhält ihn, indem man den Saamen mit mä-
ßig starken Alkohol ausziehet, diesen bei gelinder
Wärme verdampft, oder aus einer Retorte überdestil-
lirt, den harzigen Rückstand mit Wasser behandelt,
die braune Auflösung filtrirt, und solange mit kohlen-
stoffsäuerlichem Kali versetzt, als noch die geringste
Trübung entsteht, den Niederschlag so oft mit Was-
ser auswäscht, bis dieses ungefärbt abläuft, und in
gelinder Wärme trocknet.

Der auf diese Art erhaltene Stoff besitzt eine et-
was schmutzig weiße Farbe; keinen bemerklichen Ge-
ruch, einen sehr brennenden Geschmack, wobei man
noch eine sehr unangenehm kratzende Empfindung im
Schlund bemerkt, die auch entsteht, wenn man kaum

The article which introduced the concept
of "alkaloid".

The first complete synthesis of an alkaloid was achieved in 1886 by the German chemist Albert Ladenburg. He produced coniine by reacting 2-methylpyridine with acetaldehyde and reducing the resulting 2-propenyl pyridine with sodium.^{[22] [23]} The development of chemistry of alkaloids was accelerated by the emergence of spectroscopical

and chromatographical methods in the 20th century and by 2008 more than 12,000 alkaloids were identified.^[24]

Classification

Compared with most other classes of natural compounds, alkaloids are characterized by a great structural diversity and there is no uniform classification of alkaloids.^[25] Historically, first classification methods combined alkaloids by the common natural source, e.g., a certain type of plants. This classification was justified by the lack of knowledge about the chemical structure of alkaloids and is now considered obsolete.^{[5] [26]}

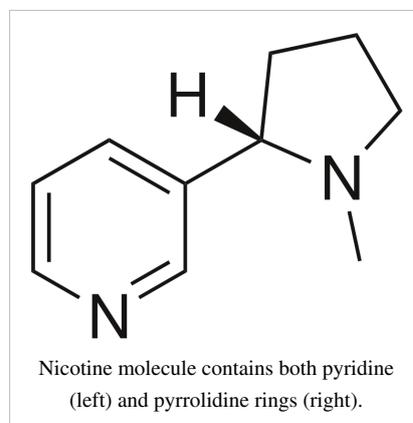
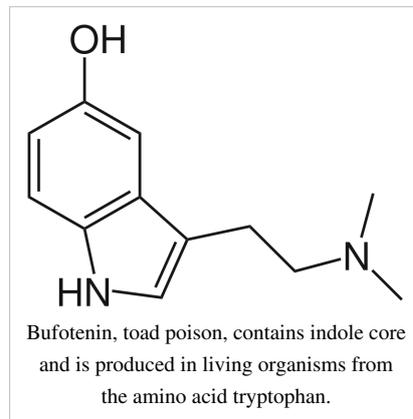
More recent classifications are based on similarity of the carbon skeleton (e.g., indole, isoquinoline and pyridine-like) or biogenetic precursor (ornithine, lysine, tyrosine, tryptophan, etc.).^[5] However, they require compromises in borderline cases;^[25] for example, nicotine contains a pyridine fragment from nicotinamide and pyrrolidine part from ornithine^[27] and therefore can be assigned to both classes.^[28]

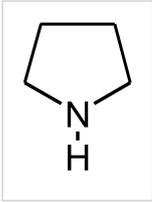
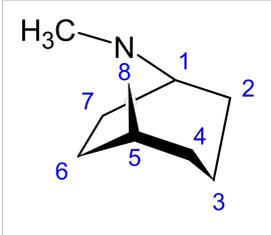
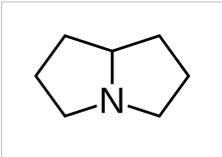
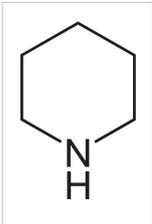
Alkaloids are often divided into the following major groups:^[29]

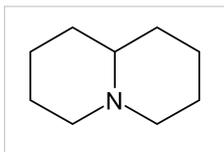
1. "True alkaloids", which contain nitrogen in the heterocycle and originate from amino acids.^[30] Their characteristic examples are atropine, nicotine and morphine. This group also includes some alkaloids which beside nitrogen heterocycle contain terpene (e.g. evonine^[31]) or peptide fragments (e.g. ergotamine^[32]). This group also includes piperidine alkaloids coniine and coniceine^[33] although they do not originate from amino acids.^[34]
2. "Protoalkaloids", which contain nitrogen and also originate from amino acids.^[30] Examples include mescaline, adrenaline and ephedrine.
3. Polyamine alkaloids – derivatives of putrescine, spermidine and spermine.
4. Peptide and cyclopeptide alkaloids.^[35]
5. Pseudalkaloids – alkaloid-like compounds which do not originate from amino acids.^[36] This group includes, terpene-like and steroid-like alkaloids,^[37] as well as purine-like alkaloids such as caffeine, theobromine and theophylline.^[38] 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.^{[39] [38]}

Some alkaloids do not have the carbon skeleton characteristic of their group. So, galantamine and homoaporphines do not contain isoquinoline fragment, but are generally attributed to isoquinoline alkaloids.^[40]

Main classes of monomeric alkaloids are listed in the table below:



Class	Major groups	Main synthesis steps	Examples
<i>Alkaloids with nitrogen heterocycles (true alkaloids)</i>			
Pyrrolidine derivatives ^[41] 		Ornithine or arginine → putrescine → N-methylputrescine → N-methyl- Δ^1 -pyrroline ^[42]	Hygrine, hygroline, stachydrine ^{[43] [41]}
Tropane derivatives ^[44] 	Atropine group Substitution in positions 3, 6 or 7	Ornithine or arginine → putrescine → N-methylputrescine → N-methyl- Δ^1 -pyrroline ^[\]	Atropine, scopolamine, hyoscyamine ^{[44] [41]} ^[45]
Cocaine group Substitution in positions 2 and 3	Cocaine, ecgonine ^{[44] [46]}		
Pyrrolizidine derivatives ^[47] 	Non-esters	In plants: ornithine or arginine → putrescine → homospermidine → retronecine ^[42]	Retronecine, heliotridine, laburnine ^{[47] [48]}
Complex esters of monocarboxylic acids	Indicine, lindelophin, sarracine ^[47]		
Macrocyclic diesters	Platyphylline, trichodesmine ^[47]		
1-aminopyrrolizidines (lolines)	In fungi: L-proline + L-homoserine → N-(3-amino-3-carboxypropyl)proline → norloline ^{[49] [50]}	Loline, N-formylloline, N-acetylloline ^[51]	
Piperidine derivatives ^[52] 		Lysine → cadaverine → Δ^1 -piperideine ^[53]	Sedamine, lobeline, anaferine, piperine ^[54] ^[33]
	Octanoic acid → coniceine → coniine ^[34]	Coniine, coniceine ^[34]	

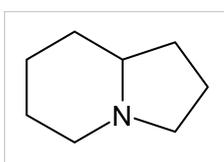
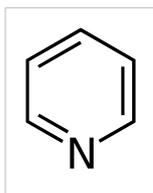
Quinolizidine derivatives^{[55] [56]}

Cytisine group

Sparteine group

Matrine group

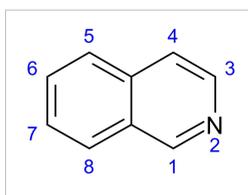
Ormosanine group

Indolizidine derivatives^[61]Pyridine derivatives^{[64] [65]}

Polycyclic noncondensing pyridine derivatives

Polycyclic condensed pyridine derivatives

Sesquiterpene pyridine derivatives

Isoquinoline derivatives and related alkaloids^[69]Derivatives of 1- and 3-isoquinolines^[73]Derivatives of 1- and 4-phenyltetrahydroisoquinolines^[70]Derivatives of 5-naftil-isoquinoline^[75]

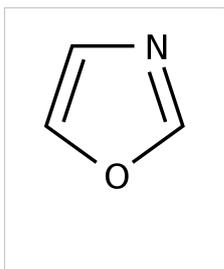
Lupinine group

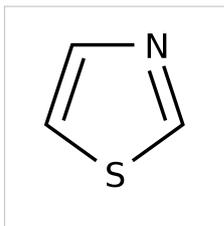
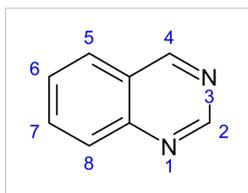
Cytisine^[55]Sparteine, lupanine, anahygrine^[55]Matrine, oxymatrine, allomatridine^[55]
[58] [59]Ormosanine, piptantine^{[55] [60]}

Simple derivatives of pyridine

Nicotine, nornicotine, anabasine,
anatabine^{[64] [67]}Actinidine, gentianine, pediculinine
[68]Nicotinic acid, isoleucine^[11]Simple derivatives of isoquinoline^[70]N-methylcoridaldine,
noroxyhydrastinine^[73]Cryptostilin^{[70] [74]}Ancistrocladine^[75]Lysine → cadaverine →
 Δ^1 -piperidine^[57]Lysine → δ -semialdehyde of
 α -amino adipic acid → pipercolic
acid → 1 indolizidinone^[62]Nicotinic acid →
digidronikotinovaya acid →
1,2-dihydropyridine^[66]Evonine, hippocrateine, triptonine
[65] [66]Tyrosine or phenylalanine →
dopamine or tyramine (for
alkaloids Amarillis)^{[71] [72]}Lupinine, nupharidin^[55]Swainsonine,
castanospermine^[63]Trigonelline, ricinine,
arecoline^{[64] [67]}Salsoline, lophocerine
[69] [70]

Derivatives of 1- and 2-benzyl-isoquinolines [76]	Papaverine, laudanosine, sendaverine		
Cularine group [77]	Cularine, yagonine [77]		
Pavines and isopavines [78]	Argemonine, amurensin [78]		
Benzopyrrocolines [79]	Cryptaustoline [70]		
Protoberberines [70]	Berberine, canadine, ophiocarpine, mecambidine, corydaline [80]		
Phtalidisoquinolines [70]	Hydrastine, narcotine (Noscapine) [81]		
Spirobenzylisoquinolines [70]	Fumaricine [78]		
Ipecacuanha alkaloids [82]	Emetine, protoemetine, ipecoside [82]		
Benzophenanthridines [70]	Sanguinarine, oxynitidine, corynoloxine [83]		
Aporphines [70]	Glaucine, coridine, liriodenine [84]		
Proaporphines [70]	Pronuciferine, glaziovine [70] [79]		
Homoaporphines [85]	Kreysiginine, multifloramine [85]		
Homoproaporphines [85]	Bulbocodine [77]		
Morphines [86]	Morphine, codeine, thebaine, sinomenine [87]		
Homomorphines [88]	Kreysiginine, androcymbine [86]		
Tropoloisoquinolines [70]	Imerubrine [70]		
Azofluoranthenes [70]	Rufescine, imeluteine [89]		
Amaryllis alkaloids [90]	Lycorine, ambelline, tazettine, galantamine, montanine [91]		
Erythrite alkaloids [74]	Erysodine, erythroidine [74]		
Phenanthrene derivatives [70]	Atherosperminine [70] [80]		
Protopins [70]	Protopine, oxomuramine, corycavidine [83]		
Aristolactam [70]	Doriflavin [70]		
Oxazole derivatives [92]	Tyrosine → tyramine [93]	Annuloline, halfordinol, texaline, texamine [94]	

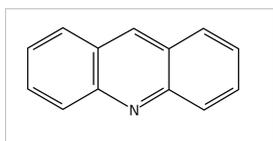
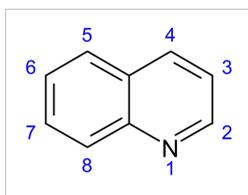


Thiazole derivatives^[95]1-Deoxy-D-xylulose 5-phosphate (DOXP), tyrosine, cysteine^[96] Nostocyclamide, thiostrepton^[95] [97]Quinazoline derivatives^[98]3,4-Dihydro-4-quinazolone derivatives Anthranilic acid or phenylalanine Febrifugine^[100]
or ornithine^[99]

1,4-Dihydro-4-quinazolone derivatives

Glycorine, arborine, glycosminine^[100]

Pyrrolidine and piperidine quinazoline derivatives

Vazicine (peganine)^[92]Acridine derivatives^[92]Anthranilic acid^[101] Rutacridone, acronicine^[102] [103]Quinoline derivatives^[104] [105]

Simple derivatives of quinoline derivatives of 2 - quinolones and 4-quinolone

Anthranilic acid → 3-carboxyquinoline^[106] Cusparine, echinopsine, evocarpine^[107] [105] [108]

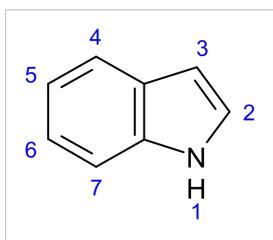
Tricyclic terpenoids

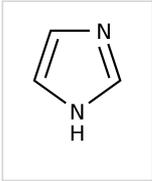
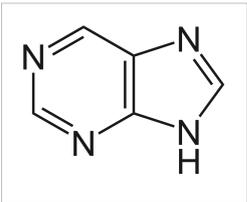
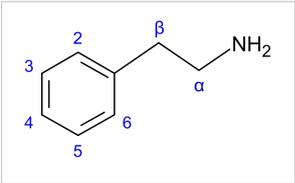
Flindersine^[109] [105]

Furanoquinoline derivatives

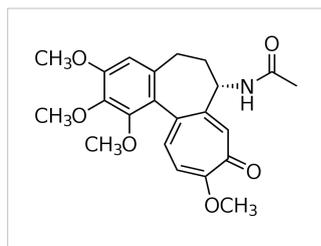
Dictamnine, fagarine, skimmianine^[105] [110] [111]

Quinines

Tryptophan → tryptamine → strictosidine (with secologanin) → korinanteal → cinchonin^[72] []Quinine quinidine cinchonine, cinchonidine^[109]Indole derivatives^[87]*Non-isoprene indole alkaloids*

Simple indole derivatives ^[112]	Tryptophan → tryptamine or 5-hydroxytryptofan ^[113]	Serotonin, psilocybin, dimethyltryptamine (DMT), bufotenin ^{[114] [115]}
Simple derivatives of β -carboline ^[116]	Harman, harmine, harmaline, eleagnine ^[112]	
Pyrroloindole alkaloids ^[117]	Physostigmine (eserine), etheramine, physovenine, eptastigmine ^[117]	
<i>Semiterpenoid indole alkaloids</i>		
Ergot alkaloids ^[87]	Tryptophan → chanoclavine → agroclavine → elimoclavine → paspalic acid → lysergic acid ^[117]	Ergotamine, ergobasine, ergosine ^[118]
<i>Monoterpenoid indole alkaloids</i>		
<i>Corynanthe</i> type alkaloids ^[113]	Tryptophan → tryptamine → strictosidine (with secologanin) ^[113]	Ajmalicine, sarpagine, vobasine, ajmaline, yohimbine, reserpine, mitragynine ^{[119] [120]} , group strychnine and (Strychnine brucine, aquamicine, vomicine ^[121])
Iboga-type alkaloids ^[113]	Ibogamine, ibogaine, voacangine ^[113]	
Aspidosperma-type alkaloids ^[113]	Vincamine, vincotine, aspidospermine ^{[122] [123]}	
Imidazole derivatives ^[92]		Directly from histidine ^[124]
		Histamine, pilocarpine, pilosine, stevensine ^{[92] [124]}
Purine derivatives ^[125]		Xantosine (formed in purine biosynthesis) → 7-methylxanthosine → 7-methylxanthine → theobromine → caffeine ^[72]
		Caffeine theobromine theophylline saxitoxin ^{[126] [127]}
Alkaloids with nitrogen in the side chain (protoalkaloids)		
β -Phenylethylamine derivatives ^[79]		Tyramine, ephedrine, pseudoephedrine, mescaline, cathinone, catecholamines (adrenaline, noradrenaline, dopamine) ^{[11] [129]}
		Tyrosine or phenylalanine → dioxypheylalanine → dopamine → adrenaline and mescaline tyrosine → tyramine phenylalanine → 1-phenylpropane-1,2-dione → cathinone → ephedrine and pseudoephedrine ^{[11] [39] [128]}

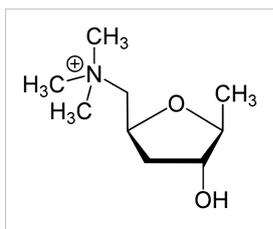
Colchicine alkaloids [130]



Tyrosine or phenylalanine →
dopamine → autumnaline →
colchicine [131]

Colchicine,
colchamine [130]

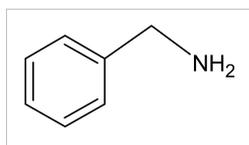
Muscarine [132]



Glutamic acid → 3-ketoglutamic
acid → muscarine (with pyruvic
acid) [133]

Muscarine, allomuscarine,
epimuscarine,
epiallomuscarine [132]

Benzylamine [134]

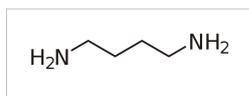


Phenylalanine with valine, leucine
or isoleucine [135]

Capsaicin,
dihydrocapsaicin,
nordihydrocapsaicin [134]
[136]

Polyamines alkaloids

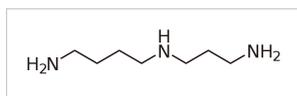
Putrescine derivatives [137]



ornithine → putrescine →
spermidine → spermine [138]

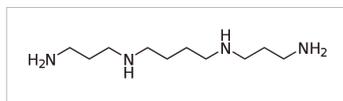
Paucine [137]

Spermidine derivatives [137]



Lunarine, codonocarpine [137]

Spermine derivatives [137]



Verbascenine, aphelandrine [137]

Peptide (cyclopeptide) alkaloids

Peptide alkaloids with a 13-membered
cycle [139] [35]

Numularine C type

From different amino acids [35]

Numularine C,
numularine S [35]

Ziziphin type

Ziziphin A, sativanine H [35]

Peptide alkaloids with a 14-membered
cycle [139] [35]

Frangulanine type

Frangulanine, scutianine J [139]

Scutianine A type

Scutianine A [35]

Integerrine type

Integerrine, discarine D [139]

Amphibine F type

Amphibine F, spinanine A [35]

Amfibine B type

Amphibine B, lotusine C [35]

Peptide alkaloids with a 15-membered cycle [139]

Mucronine A type

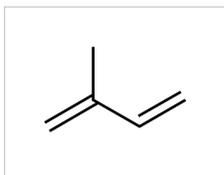
Mucronine A [139] [32]

Pseudoalkaloids (terpenes and steroids)

Diterpenes [32]

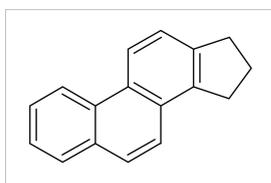
Licoctonine type

Mevalonic acid →
 izopentenilpyrophosphate →
 geranyl pyrophosphate [140]
 [141]

Aconitine, delphinine [32]
[142]

Steroids [143]

Cholesterol, arginine [144]

Solasodine, solanidine,
veralkamine [145]

Properties

Most alkaloids contain oxygen; those compounds are usually colorless crystals at ambient conditions. Oxygen-free alkaloids, such as nicotine^[146] or coniine^[22], are typically volatile, colorless, oily liquids.^[147] Some alkaloids are colored, like berberine (yellow) and sanguinarine (orange).^[147]

Most alkaloid are weak bases, but some are amphoteric, for example theobromine and theophylline.^[148] Most alkaloids are poorly soluble in water but readily dissolve in organic solvents, such as diethyl ether, chloroform and 1,2-dichloroethane. However, caffeine dissolves well in boiling water.^[148] With acids, alkaloids form salts of various strengths. Those 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 water-soluble quinine sulfate.^[147]

Most alkaloids have a bitter flavor. It is believed that plants evolved the ability to produce these bitter substances, many of which are poisonous, in order to protect themselves from animals; however, animals in turn evolved the ability to detoxify alkaloids.^[149] Some

alkaloids can produce developmental defects in the offspring of animals that consume them but cannot detoxify them. A characteristic example is the alkaloid cyclopamine, which is present in the leaves of corn lily. During the 1950s, up to 25% lambs born by sheep that had grazed on corn lily suffered serious facial defects. Those defects ranged from deformed jaws to cyclopia (see picture). After decades of research, in 1980s, the substance that was responsible for the deformities was identified as the alkaloid 11-deoxyjervine, which was renamed cyclopamine.^[150]



Head of a lamb born by a sheep which ate leaves of the corn lily plant. The cyclopia in the calf is induced by the alkaloid cyclopamine present in the plant.

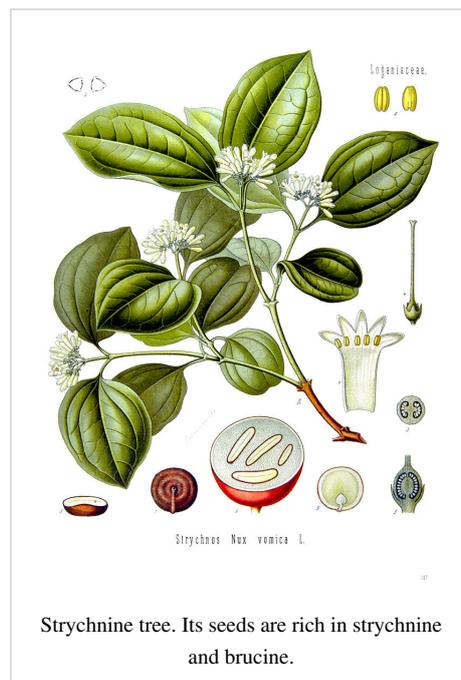
Distribution in nature

Alkaloids are generated by various living organisms, especially by higher plants – about 10 to 25% of those contain alkaloids.^[151] ^[152]

Therefore, in the past the term "alkaloid" was associated with plants.^[153]

The alkaloids content in plants is usually within a few percent and is inhomogeneous over the plant tissues. Depending on the type of plants, the maximum concentration is observed in the leaves (black henbane), fruits or seeds (Strychnine tree), root (Rauwolfia serpentina) or bark (cinchona).^[154] Furthermore, different tissues of the same plants may contain different alkaloids.^[155]

Beside plants, alkaloids are found in certain types of fungi, such as psilocybin in the fungus of the genus *Psilocybe*, and in animals, such as bufotenin in the skin of some toads.^[15] Many marine organisms also contain alkaloids.^[156] Some amines, such as adrenaline and serotonin, which play an important role in higher animals, are similar to alkaloids in their structure and biosynthesis and are sometimes called alkaloids.^[157]



Strychnine tree. Its seeds are rich in strychnine and brucine.

Extraction

Because of the structural diversity of alkaloids, there is no single method of their extraction from natural raw materials.^[158] Most methods exploit the property of most alkaloids to be soluble in organic solvents but not in water, and the opposite tendency of their salts.

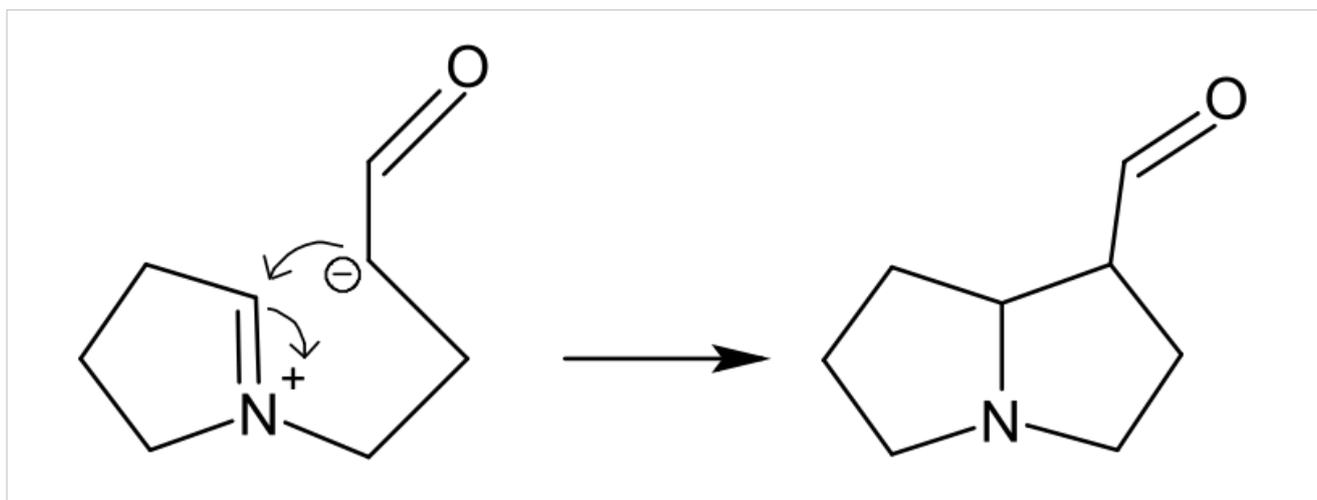
Most plants contain several alkaloids. Their mixture is extracted first and then individual alkaloids are separated.^[159] Plants are thoroughly ground before extraction.^[158] ^[160] Most alkaloids are present in the raw plants in the form of salts of organic acids.^[158] The extracted alkaloids may remain salts or change into bases.^[159] Base extraction is achieved by processing the raw material with alkaline solutions and extracting the alkaloid bases with organic solvents, such as 1,2-dichloroethane, chloroform, diethyl ether or benzene. Then, the impurities are dissolved by weak acids; this converts alkaloid bases into salts which are washed away with water. If necessary, an aqueous solution of alkaloid salts is again made alkaline and treated with an organic solvent. The process is repeated until the desired purity is achieved.

In the acidic extraction, the raw plant material is processed by a weak acidic solution (e.g., acetic acid in water, ethanol or methanol). A base is then added to convert alkaloids to basic forms which are extracted with organic solvent (if the extraction was performed with alcohol, it is removed first, and the remainder is dissolved in water). The solution is purified as described above.^[158] ^[161]

Alkaloids are separated from their mixture using their different solubility in certain solvents and different reactivity with certain reagents or by distillation.^[162]



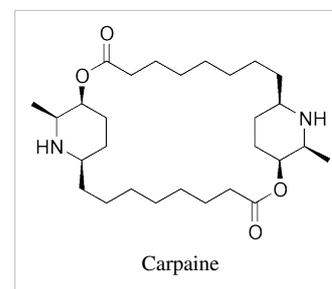
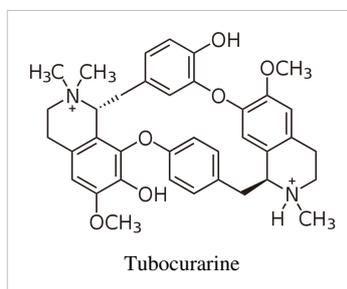
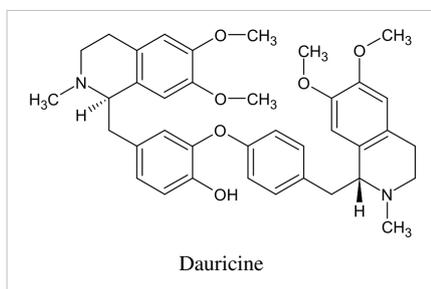
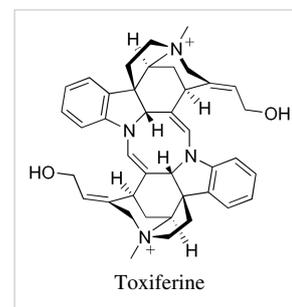
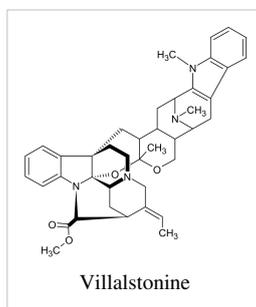
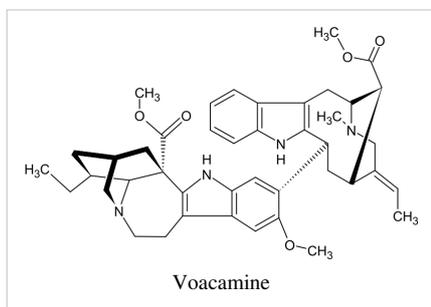
Crystals of piperine extracted from black pepper.



Dimer alkaloids

In addition to the described above monomeric alkaloids, there are also dimeric, and even trimeric and tetrameric alkaloids formed upon condensation of two, three and four monomeric alkaloids. Dimeric alkaloids are usually formed from monomers of the same type through the following mechanisms:^[168]

- Mannich reaction, resulting in, e.g., voacamine
- Michael reaction (villalstonine).
- Condensation of aldehydes with amines (toxiferine).
- Oxidative addition of phenols (dauricine, tubocurarine).
- Lactonization (carpaine).



The biological role

The role of alkaloids for living organisms which produce them is still unclear.^[169] Initially it was assumed that the alkaloids are the final products of nitrogen metabolism in plants, and urea in mammals. Later it was shown that alkaloid concentrations varies over time and this hypothesis was refuted.^[7]

Most of the known functions of alkaloids are related to protection. For example, aporphine alkaloid liriodenine produced by the tulip tree protects it from parasitic mushrooms. In addition, presence of alkaloids in the plant prevents insects and chordate animals from eating it. However, some animals adapted to alkaloids and even use them in their own metabolism.^[170] Besides, such alkaloid-related substances as serotonin, dopamine and histamine are important neurotransmitters in animals. Alkaloids are also known to regulate plant growth.^[171]

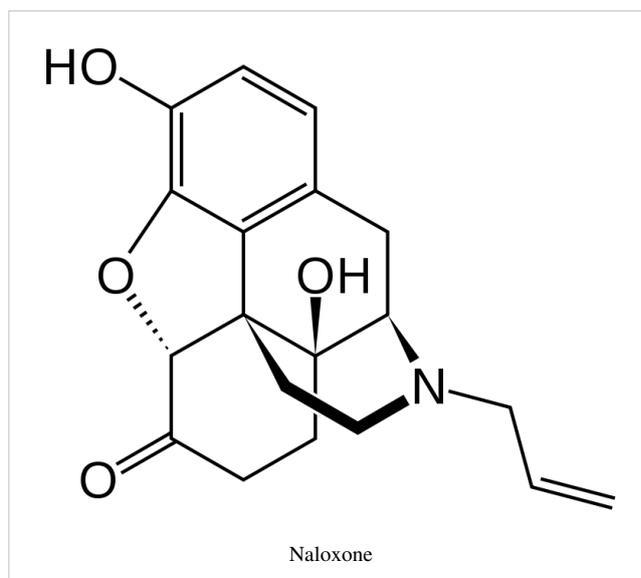
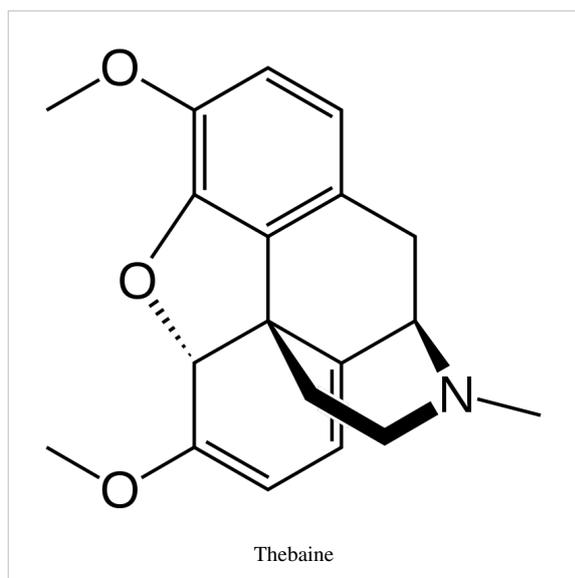
Applications

In medicine

Medical use of alkaloid plants has a long history, and thus when the first alkaloids were synthesized in the 19th century, they immediately found application in clinical practice.^[172] Many alkaloids are still used in medicine, usually in the form of salts, including the following:^[7] ^[173] :

Alkaloid	Action
Ajmaline	antiarrhythmic
Atropine, scopolamine, hyoscyamine	anticholinergic
Vinblastine, vincristine	antitumor
Vincamine	vasodilating, antihypertensive
Codeine	cough medicine
Cocaine	anesthetic
Colchicine	remedy for gout
Morphine	analgesic
Reserpine	antihypertensive
Tubocurarine	Muscle relaxant
Physostigmine	inhibitor of acetylcholinesterase
Quinidine	antiarrhythmic
Quinine	antipyretics, antimalarial
Emetine	antiprotozoal agent
Ergot alkaloids	sympathomimetic, vasodilator, antihypertensive

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.^[174] For example, naloxone, an opioid receptor antagonist, is a derivative of thebaine which is present in opium.^[175]



In agriculture

Prior to the development of a wide range of relatively low-toxic synthetic pesticides, some alkaloids, such as salts of nicotine and anabasine, were used as insecticides. Their use was limited by their high toxicity to humans.^[176]

Use as psychoactive drugs

Preparations of plants containing alkaloids and their extracts, and later pure alkaloids have long been used as psychoactive substances. Cocaine and cathinone are stimulants of the central nervous system.^{[177] [178]} Mescaline and many of indole alkaloids (such as psilocybin, dimethyltryptamine and ibogaine) have hallucinogenic effect.^[179] Morphine and codeine are strong narcotic pain killers.^[181]

There are alkaloids that do not have strong psychoactive effect themselves, but are precursors for semi-synthetic psychoactive drugs. For example, ephedrine and pseudoephedrine are used to produce methcathinone (ephedrine) and methamphetamine.^[182]

See also

- Amine
- Base (chemistry)
- Natural products
- Secondary metabolite

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