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STALWARTNESS CREATIVITY OF ALMIGHTY GOD MAKES THE CHEMICAL WIZARD OF INCREDIBLE CONSTITUENTS

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ABSTRACT

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. In addition to carbon, hydrogen and nitrogen, alkaloids may also contain oxygen, sulfur 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. They can be purified from crude extracts of these organisms by acid-base extraction, or solvent extractions followed by silica-gel column chromatography. Alkaloids have a wide range of pharmacological activities including antimalarial (*e.g.* quinine), antiasthma (*e.g.* ephedrine), anticancer (*e.g.* homoharringtonine), cholinomimetic (*e.g.* galantamine), vasodilatory (*e.g.* vincamine), antiarrhythmic (*e.g.* quinidine), analgesic (*e.g.* morphine), antibacterial (*e.g.* chelerythrine), and antihyperglycemic activities (*e.g.* piperine). Many have found use in traditional or modern medicine, or as starting points for drug discovery. Other alkaloids possess psychotropic (*e.g.* psilocin) and stimulant activities (*e.g.* cocaine, caffeine, nicotine, theobromine), and have been used in entheogenic rituals or as recreational drugs. Alkaloids can be toxic too (*e.g.* atropine, tubocurarine). Although alkaloids act on a diversity of metabolic systems in humans and other animals, they almost uniformly evoke a bitter taste.

KEYWORDS: alkaloids, antimalarial, antiasthma, anticancer, cholinomimetic, vasodilatory, antiarrhythmic, analgesic, antibacterial, antihyperglycemic, psychotropic activities.

INTRODUCTION

The boundary between alkaloids and other nitrogen-containing natural compounds is not clear-cut. Compounds like amino acid peptides, proteins, nucleotides, nucleic acid, amines, and antibiotics are usually not called alkaloids. Natural compounds containing nitrogen in the exocyclic position (mescaline, serotonin, dopamine, etc.) are usually classified as amines rather than as alkaloids. Some authors, however, consider alkaloids a special case of amines.[1]

Naming: The name "alkaloids" (German: *Alkaloide*) was introduced in 1819 by the German chemist Carl Friedrich Wilhelm Meißner, and is derived from late Latin root *alkali* and the suffix -οειδής -('like'). However, the term came into wide use only after the publication of a review article, by Oscar Jacobsen in the chemical dictionary of Albert Ladenburg in the 1880s. There is no unique method for naming alkaloids. Many individual names are formed by adding the suffix "ine" to the species or genus name. For example, atropine is isolated from the plant *Atropa belladonna*; strychnine is obtained from the seed of the Strychnine tree (*Strychnos nux-vomica* L.). Where several alkaloids are extracted from one plant their names are often distinguished by

variations in the suffix: "idine", "anine", "aline", "inine" etc. There are also at least 86 alkaloids whose names contain the root "vin" because they are extracted from *vinca* plants such as *Vinca rosea* (*Catharanthus roseus*); these are called *vinca* alkaloids.[2]


Figure-1: The first individual alkaloid, morphine, was isolated in 1804 from the opium poppy (*Papaver somniferum*).

History: Alkaloid-containing plants have been used by humans since ancient times for therapeutic and recreational purposes. For example, medicinal plants have been known in Mesopotamia from about 2000 BC. 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. A Chinese book on houseplants written in 1st–3rd centuries BC mentioned a medical use of ephedra and opium poppies. Also, coca leaves have been used by South American Indians since ancient times. Extracts from plants containing toxic alkaloids, such as aconitine and tubocurarine, were used since antiquity for poisoning arrows.[3]

Figure-2: Friedrich Sertürner, the German chemist who first isolated morphine from opium.

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", referring to Morpheus, the Greek god of dreams; in German and some other Central-European languages, this is still the name of the drug. The term "morphine", used in English and French, 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).[4]

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). The development of the chemistry of alkaloids was accelerated by the emergence of spectroscopic and chromatographic methods in the 20th century, so that by 2008 more than 12,000 alkaloids had been identified. 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.[5]

Classifications

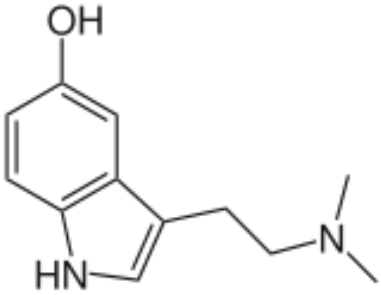


Figure-3: Bufotenin, an alkaloid from some toads, contains an indole core, and is produced in living organisms from the amino acid tryptophan.

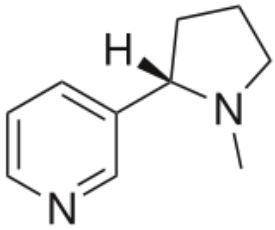


Figure-4: The nicotine molecule contains both pyridine (left) and pyrrolidine rings (right).

Compared with most other classes of natural compounds, alkaloids are characterized by a great structural diversity. There is no uniform classification. Initially, when knowledge of chemical structures was lacking, botanical classification of the source plants was relied on. This classification is now considered obsolete. More recent classifications are based on similarity of the carbon skeleton (*e.g.*, indole-, isoquinoline-, and pyridine-like) or biochemical precursor (ornithine, lysine, tyrosine, tryptophan, etc.). However, they require compromises in borderline cases; for example, nicotine contains a pyridine fragment from nicotinamide and a pyrrolidine part from ornithine and therefore can be assigned to both classes.[6]

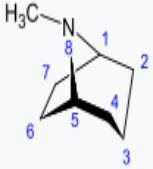
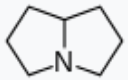
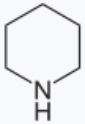
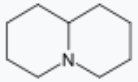
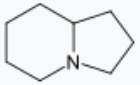
Alkaloids are often divided into the following major groups

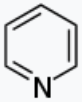
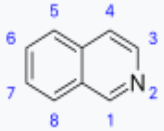
1. "True alkaloids" contain nitrogen in the heterocycle and originate from amino acids. Their characteristic examples are atropine, nicotine, and morphine. This group also includes some alkaloids that besides the nitrogen heterocycle contain terpene (*e.g.*, evonine) or peptide fragments (*e.g.* ergotamine). The piperidine alkaloids coniine and coniceine may be regarded as true alkaloids (rather than pseudoalkaloids: see below) although they do not originate from amino acids.
2. "Protoalkaloids", which contain nitrogen (but not the nitrogen heterocycle) 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. Pseudo alkaloids – 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, galanthamine and homoaporphines do not contain isoquinoline fragment, but are, in general, attributed to isoquinoline alkaloids.[7]

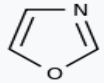
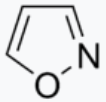
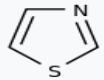
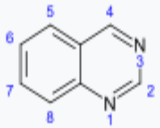
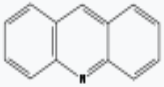
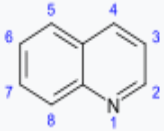
Properties: Most alkaloids contain oxygen in their molecular structure; those compounds are usually colorless crystals at ambient conditions. Oxygen-free alkaloids, such as nicotine or coniine, are typically volatile, colorless, oily liquids. Some alkaloids are colored, like berberine (yellow) and sanguinarine (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 slightly soluble in water (with a solubility of ≥1g/L), whereas others, including morphine and yohimbine are very slightly water-soluble (0.1–1 g/L). Alkaloids and acids form salts of various strengths. These salts are usually freely soluble in water and ethanol and poorly soluble in most organic solvents. Exceptions include scopolamine hydrobromide, which is soluble in organic solvents, and the water-soluble quinine sulfate.[8]

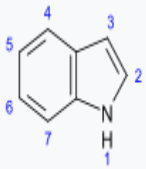
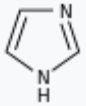
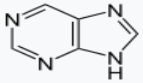
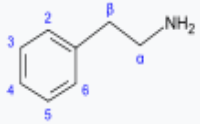
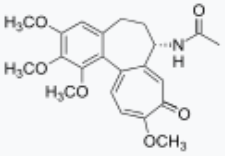
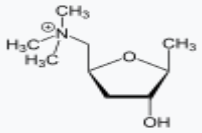
Most alkaloids have a bitter taste or are poisonous when ingested. Alkaloid production in plants appeared to have evolved in response to feeding by herbivorous animals; however, some animals have evolved the ability to detoxify alkaloids. Some alkaloids can produce developmental defects in the offspring 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. These ranged from deformed jaws to cyclopia (see picture). After decades of research, in the 1980s, the compound responsible for these deformities was identified as the alkaloid 11-deoxyjervine, later renamed to cyclopamine.

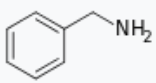
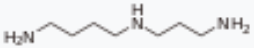
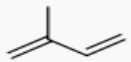
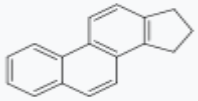
Table 1: Main classes of monomeric alkaloids are listed in the table below.

Class	Major groups	Main synthesis steps	Examples
Alkaloids with nitrogen heterocycles (true alkaloids)			
Pyrrolidine derivatives 		Ornithine or arginine → putrescine → N-methylputrescine → N-methyl-Δ^1-pyrroline	Cuscohygrine, hygrine, hygroline, stachydrine
Tropane derivatives 	Atropine group Substitution in positions 3, 6 or 7	Ornithine or arginine → putrescine → N-methylputrescine → N-methyl-Δ^1-pyrroline	Atropine, scopolamine, hyoscyamine
	Cocaine group Substitution in positions 2 and 3		Cocaine, ecgonine
Pyrrolizidine derivatives 	Non-esters	In plants: ornithine or arginine → putrescine → homospermidine → retronecine	Retronecine, heliotridine, laburnine
	Complex esters of monocarboxylic acids		Indicine, lindelophin, sarracine
	Macrocyclic diesters		Platyphylline, trichodesmine
	1-aminopyrrolizidines (lolines)	In fungi: L-proline + L-homoserine → *N*-(3-amino-3-carboxypropyl)proline → norloline	Loline, *N*-formylloline, *N*-acetylloline
Piperidine derivatives 		Lysine → cadaverine → Δ^1-piperideine	Sedamine, lobeline, anaferine, piperine
		Octanoic acid → coniceine → coniine	Coniine, coniceine
Quinolizidine derivatives 	Lupinine group	Lysine → cadaverine → Δ^1-piperideine	Lupinine, nupharidin
	Cytisine group		Cytisine
	Sparteine group		Sparteine, lupanine, anahygrine
	Matrine group.		Matrine, oxymatrine, allomatridine
	Ormosanine group		Ormosanine, piptantine
Indolizidine derivatives 		Lysine → δ-semialdehyde of α-aminoadipic acid → pipecolic acid → 1 indolizidinone	Swainsonine, castanospermine
Pyridine derivatives	Simple derivatives of pyridine	Nicotinic acid → dihydronicotinic acid → 1,2-dihydropyridine	Trigonelline, ricinine, arecoline

	Polycyclic noncondensing pyridine derivatives		Nicotine, nornicotine, anabasine, anatabine
	Polycyclic condensed pyridine derivatives		Actinidine, gentianine, pediculinine
	Sesquiterpene pyridine derivatives	Nicotinic acid, isoleucine	Evonine, hippocrateine, triptonine
Isoquinoline derivatives and related alkaloids 	Simple derivatives of isoquinoline	Tyrosine or phenylalanine → dopamine or tyramine (for alkaloids Amarillis)	Salsoline, lophocerine
	Derivatives of 1- and 3-isoquinolines		N-methylcoridaldine, noroxyhydrastinine
	Derivatives of 1- and 4-phenyltetrahydroisoquinolines		Cryptostilin
	Derivatives of 5-naftil-isoquinoline		Ancistrocladine
	Derivatives of 1- and 2-benzyl-izoquinolines		Papaverine, laudanosine, sendaverine
	Cularine group		Cularine, yagonine
	Pavines and isopavines		Argemonine, amurensine
	Benzopyrrocolines		Cryptaustoline
	Protoberberines		Berberine, canadine, ophiocarpine, mecambridine, corydaline
	Phthalidisoquinolines		Hydrastine, narcotine (Noscapine)
	Spirobenzylisoquinolines		Fumaricine
	Ipecacuanha alkaloids		Emetine, protoemetine, ipecoside
	Benzophenanthridines		Sanguinarine, oxynitidine, corynoloxine
	Aporphines		Glaucine, coridine, liriodenine
	Proaporphines		Pronuciferine, glaziovine
	Homoaporphines		Kreysiginine, multifloramine
	Homoproaporphines		Bulbocodine
	Morphines		Morphine, codeine, thebaine, sinomenine
	Homomorphines		Kreysiginine, androcymbine
	Tropoloisoquinolines		Imerubrine
	Azofluoranthenes		Rufescine, imeluteine
	Amaryllis alkaloids		Lycorine, ambelline, tazettine, galantamine, montanine
	Erythrina alkaloids		Erysodine, erythroidine

	Phenanthrene derivatives		Atherosperminine
	Protopines		Protopine, oxomuramine, corycavidine
	Aristolactam		Doriflavin
Oxazole derivatives 		Tyrosine → tyramine	Annuloline, halfordinol, texaline, texamine
Isoxazole derivatives 		Ibotenic acid → Muscimol	Ibotenic acid, Muscimol
Thiazole derivatives 		1-Deoxy-D-xylulose 5-phosphate (DOXP), tyrosine, cysteine	Nostocyclamide, thiostreptone
Quinazoline derivatives 	3,4-Dihydro-4-quinazolone derivatives	Anthranilic acid or phenylalanine or ornithine	Febrifugine
	1,4-Dihydro-4-quinazolone derivatives		Glycorine, arborine, glycosminine
	Pyrrolidine and piperidine quinazoline derivatives		Vazicine (peganine)
Acridine derivatives 		Anthranilic acid	Rutacridone, acronicine
Quinoline derivatives 	Simple derivatives of quinoline derivatives of 2–quinolones and 4-quinolone	Anthranilic acid → 3-carboxyquinoline	Cusparine, echinopsine, evocarpine
	Tricyclic terpenoids		Flindersine
	Furanoquinoline derivatives		Dictamnine, fagarine, skimmianine
	Quinines	Tryptophan → tryptamine → strictosidine (with secologanin) → korinanteal → cinhoninon	Quinine, quinidine, cinchonine, cinhonidine
Indole derivatives	*Non-isoprene indole alkaloids*		
	Simple indole derivatives	Tryptophan → tryptamine or 5-Hydroxytryptophan	Serotonin, psilocybin, dimethyltryptamine (DMT), bufotenin
	Simple derivatives of β-		Harman, harmine, harmaline, eleagnine

	carboline		
	Pyrroloindole alkaloids		Physostigmine (eserine), etheramine, physovenine, eptastigmine
	Semiterpenoid indole alkaloids		
	Ergot alkaloids	Tryptophan → chanoclavine → agroclavine → elimoclavine → paspalic acid → lysergic acid	Ergotamine, ergobasine, ergosine
	Monoterpenoid indole alkaloids		
	Corynanthe type alkaloids	Tryptophan → tryptamine → strictosidine (with secologanin)	Ajmalicine, sarpagine, vobasine, ajmaline, yohimbine, reserpine, mitragynine, group strychnine and (Strychnine brucine, aquamicine, vomicine)
	Iboga-type alkaloids		Ibogamine, ibogaine, voacangine
	Aspidosperma-type alkaloids		Vincamine, *vinca* alkaloids, vincotine, aspidospermine
Imidazole derivatives 		Directly from histidine	Histamine, pilocarpine, pilosine, stevensine
Purine derivatives 		Xanthosine (formed in purine biosynthesis) → 7 methylxantosine → 7-methylxanthine → theobromine → caffeine	Caffeine, theobromine, theophylline, saxitoxin
Alkaloids with nitrogen in the side chain (protoalkaloids)			
β-Phenylethylamine derivatives 		Tyrosine or phenylalanine → dioxyphenilalanine → dopamine → adrenaline and mescaline tyrosine → tyramine phenylalanine → 1-phenylpropane-1,2-dione → cathinone → ephedrine and pseudoephedrine	Tyramine, ephedrine, pseudoephedrine, mescaline, cathinone, catecholamines (adrenaline, noradrenaline, dopamine)
Colchicine alkaloids 		Tyrosine or phenylalanine → dopamine → autumnaline → colchicine	Colchicine, colchamine
Muscarine 		Glutamic acid → 3-ketoglutamic acid → muscarine (with pyruvic acid)	Muscarine, allomuscarine, epimuscarine, epiallomuscarine

Benzylamine 		Phenylalanine with valine, leucine or isoleucine	Capsaicin, dihydrocapsaicin, nordihydrocapsaicin, vanillylamine
Polyamines alkaloids			
Putrescine derivatives 		ornithine → putrescine → spermidine → spermine	Paucine
Spermidine derivatives 			Lunarine, codonocarpine
Spermine derivatives 			Verbascenine, aphelandrine
Peptide (cyclopeptide) alkaloids			
Peptide alkaloids with a 13-membered cycle	Nummularine C type	From different amino acids	Nummularine C, Nummularine S
	Ziziphine type		Ziziphine A, sativanine H
Peptide alkaloids with a 14-membered cycle	Frangulanine type		Frangulanine, scutianine J
	Scutianine A type		Scutianine A
	Integerrine type		Integerrine, discarine D
	Amphibine F type		Amphibine F, spinanine A
	Amfibine B type		Amphibine B, lotusine C
Peptide alkaloids with a 15-membered cycle	Mucronine A type		Mucronine A
Pseudoalkaloids (terpenes and steroids)			
Diterpenes 	Lycoctonine type	Mevalonic acid → Isopentenyl pyrophosphate → geranyl pyrophosphate	Aconitine, delphinine
Steroidal alkaloids 		Cholesterol, arginine	Solanidine, cyclopamine, batrachotoxin

Distribution in nature: Alkaloids are generated by various living organisms, especially by higher plants – about 10 to 25% of those contain alkaloids. Therefore, in the past the term "alkaloid" was associated with plants. 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 (for example, black henbane), fruits or seeds (Strychnine tree), root (*Rauvolfia serpentina*) or bark (cinchona). Furthermore, different tissues of the same plants may contain different alkaloids.[9]

Figure-5: Strychnine tree. Its seeds are rich in strychnine and brucine.

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 and a number of insects, markedly ants. Many marine organisms also contain alkaloids. 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.[10]

Extraction: Because of the structural diversity of alkaloids, there is no single method of their extraction from natural raw materials. 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. Plants are thoroughly ground before extraction. Most alkaloids are present in the raw plants in the form of salts of organic acids. The extracted alkaloids may remain salts or change into bases. 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 that 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.[11]

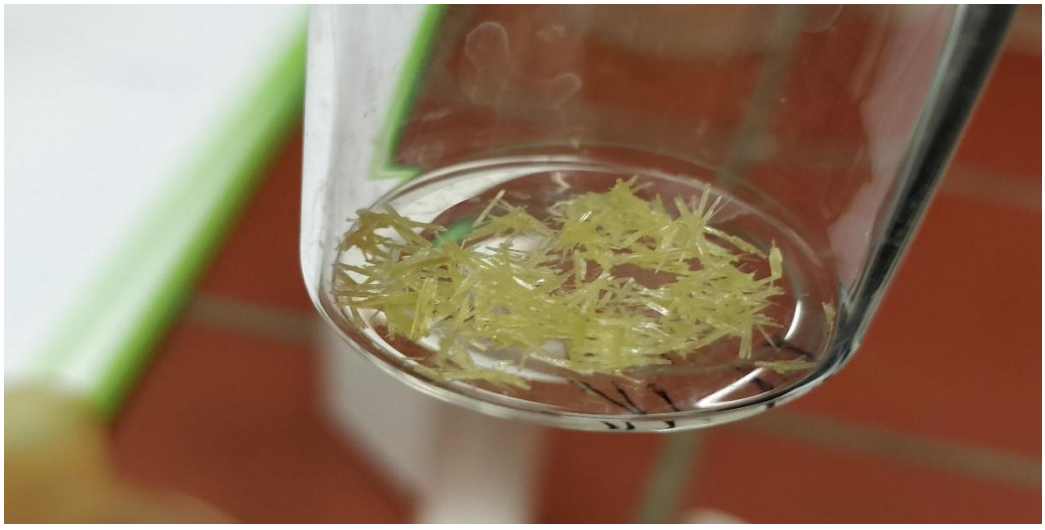


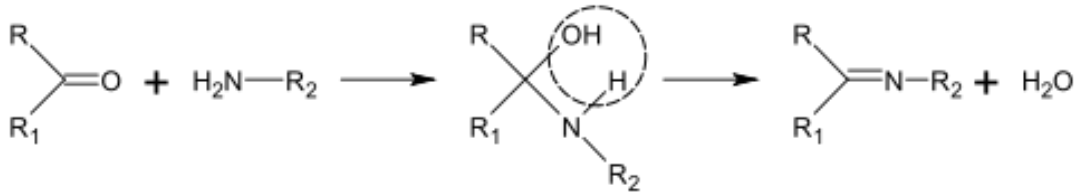
Figure-6: Crystals of piperine extracted from black pepper.

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

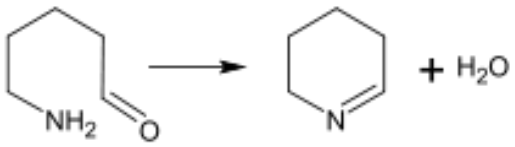
A number of alkaloids are identified from insects, among which the fire ant venom alkaloids known as solenopsins have received greater attention from researchers. These insect alkaloids can be efficiently extracted by solvent immersion of live fire ants or by centrifugation of live ants followed by silica-gel chromatography purification. Tracking and dosing the extracted solenopsin ant alkaloids has been described as possible based on their absorbance peak around 232 nanometers.

Biosynthesis: Biological precursors of most alkaloids are amino acids, such as ornithine, lysine, phenylalanine, tyrosine, tryptophan, histidine, aspartic acid, and anthranilic acid. Nicotinic acid can be synthesized from tryptophan or aspartic acid. Ways of alkaloid biosynthesis are too numerous and cannot be easily classified. However, there are a few typical reactions involved in the biosynthesis of various classes of alkaloids, including synthesis of Schiff bases and Mannich reaction.[12]

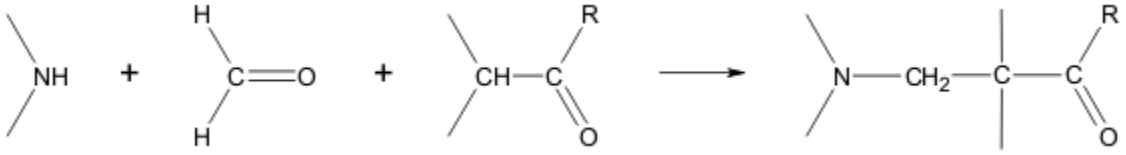
Synthesis of Schiff bases: Schiff bases can be obtained by reacting amines with ketones or aldehydes. These reactions are a common method of producing C=N bonds.



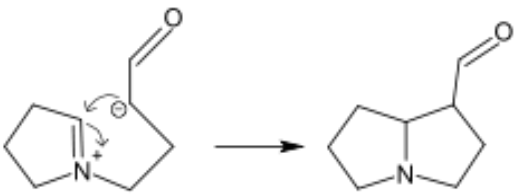
In the biosynthesis of alkaloids, such reactions may take place within a molecule, such as in the synthesis of piperidine:



Mannich reaction: An integral component of the Mannich reaction, in addition to an amine and a carbonyl compound, is a carbanion, which plays the role of the nucleophile in the nucleophilic addition to the ion formed by the reaction of the amine and the carbonyl.[13]



The Mannich reaction can proceed both intermolecularly and intramolecularly.



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:

1. Mannich reaction, resulting in, *e.g.*, voacamine
2. Michael reaction (villalstonine)
3. Condensation of aldehydes with amines (toxiferine)
4. Oxidative addition of phenols (dauricine, tubocurarine)
5. Lactonization (carpaine).

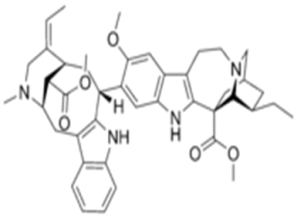


Figure-7: Voacamine

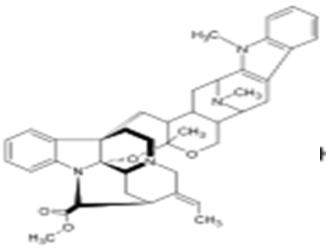


Figure-8: Villalstonine

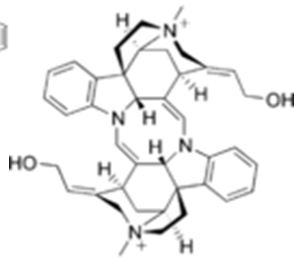


Figure-9: Toxiferine

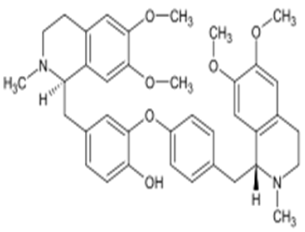


Figure-10: Dauricine

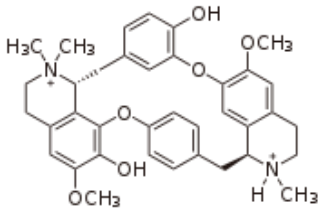


Figure-11: Tubocurarine

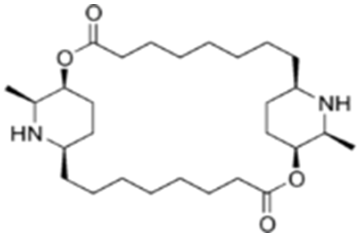


Figure-12: Carpaine

There are also dimeric alkaloids formed from two distinct monomers, such as the *vinca* alkaloids vinblastine and vincristine, which are formed from the coupling of catharanthine and vindoline. The newer semi-synthetic chemotherapeutic agent vinorelbine is used in the treatment of non-small-cell lung cancer. It is another derivative dimer of vindoline and catharanthine and is synthesised from anhydrovinblastine, starting either from leurosine or the monomers themselves.[14]

Biological role: Alkaloids are among the most important and best-known secondary metabolites, i.e. biogenic substances not directly involved in the normal growth, development, or reproduction of the organism. Instead, they generally mediate ecological interactions, which may produce a selective advantage for the organism by increasing its survivability or fecundity. In some cases their function, if any, remains unclear. An early hypothesis, that alkaloids are the final products of nitrogen metabolism in plants, as urea and uric acid are in mammals, was refuted by the finding that their concentration fluctuates rather than steadily increasing. 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, the presence of alkaloids in the plant prevents insects and chordate animals from eating it. However, some animals are adapted to alkaloids and even use them in their own metabolism. Such alkaloid-related substances as serotonin, dopamine and histamine are important neurotransmitters in animals. Alkaloids are also known to regulate plant growth. One example of an organism that uses alkaloids for protection is the *Utetheisa ornatrix*, more commonly known as the ornate moth. Pyrrolizidine alkaloids render these larvae and adult moths unpalatable to many of their natural enemies like coccinelid beetles, green lacewings, insectivorous hemiptera and insectivorous bats.

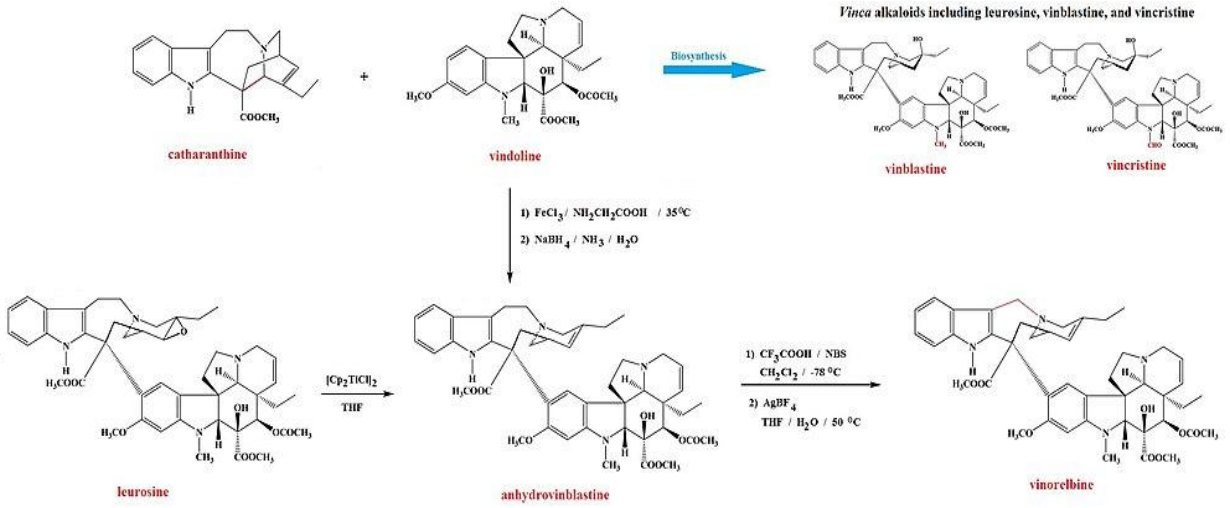


Figure-13: Some Alkaloids.

Another example of alkaloids being utilized occurs in the poison hemlock moth (*Agonopterix alstroemeriana).* This moth feeds on its highly toxic and alkaloid-rich host plant poison hemlock (*Conium maculatum*) during its larval stage. *A. alstroemeriana* may benefit twofold from the toxicity of the naturally-occurring alkaloids, both through the unpalatability of the species to predators and through the ability of *A. alstroemeriana* to recognize *Conium maculatum* as the correct location for oviposition. A fire ant venom alkaloid known as solenopsin has been demonstrated to protect queens of invasive fire ants during the foundation of new nests, thus playing a central role in the spread of this pest ant species around the world.[15]

Applications

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 widely used including the following:

Alkaloid	Action	Alkaloid	Action
Ajmaline	antiarrhythmic	Quinidine	Antiarrhythmic
Emetine	antiprotozoal agent	Quinine	Antipyretic, antimalarial
Ergot alkaloids	Vasoconstriction, hallucinogenic, Uterotonic	Reserpine	antihypertensive
Glaucine	Antitussive	Tubocurarine	Muscle relaxant
Morphine	Analgesic	Vinblastine, vincristine	Antitumor
Nicotine	Stimulant, nicotinic acetylcholine receptor agonist	Vincamine	Vasodilation, antihypertensive
Physostigmine	inhibitor of acetylcholinesterase	Yohimbine	Simulant, 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. For example, naloxone, an opioid receptor antagonist, is a derivative of thebaine that is present in opium.[16]

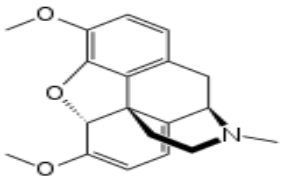


Figure-14: Thebaine

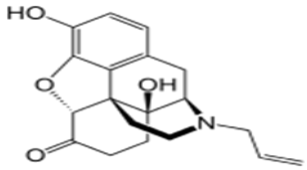


Figure-15: Naloxone.

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.

CONCLUSION

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

Thebaine is used in the synthesis of many painkillers such as oxycodone.

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