



STUDENT STUDY PROJECT

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Title of the project: **ALKALOIDS**

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ALKALOIDS

1. Introduction

In nature there are many natural compounds. From among many classes of naturally occurring organic compounds such as carbohydrates, lipids, proteins, amino acids, anthocyanins, flavonoids, and steroids, the one that seems to be quite special is alkaloids. What makes them special? They derived from amino acids and can be synthesized as secondary metabolites by plants and some animals. These compounds play an important role in living organisms. Alkaloids occurred to be extremely important for human beings for ages, besides they are secondary metabolites, what could suggest that they are useless. Alkaloids showed strong biological effects on animal and human organisms in very small doses. Alkaloids are present not only in human daily life in food and drinks but also as stimulant drugs. They showed anti-inflammatory, anticancer, analgesics, local anesthetic and pain relief, neuropharmacologic, antimicrobial, antifungal, and many other activities. Alkaloids are useful as diet ingredients, supplements, and pharmaceuticals, in medicine and in other applications in human life. Alkaloids are also important compounds in organic synthesis for searching new semisynthetic and synthetic compounds with possibly better biological activity than parent compounds.

2. About alkaloids

Alkaloids are a huge group of naturally occurring organic compounds which contain nitrogen atom or atoms (amino or amido in some cases) in their structures. These nitrogen atoms cause alkalinity of these compounds. These nitrogen atoms are usually situated in some ring (cyclic) system. For example, indole alkaloids are those that contain nitrogen atom in indole ring system. Generally based on structures, alkaloids can be divided into classes like indoles, quinolines, isoquinolines, pyrrolidines, pyridines, pyrrolizidines, tropanes, and terpenoids and steroids. Other classification system is connected with a family of plant species that they occur. One of the examples is the opium alkaloids that occur in the opium poppy (*Papaver somniferum*). These two different classification systems cause confusion between their biological distribution and the chemical types of alkaloids, because there is not unmistakable correlation.

Alkaloids (whose name originally comes from “alkali-like”) can react with acids and then form salts, just like inorganic alkalis. These nitrogen atoms can behave like a base in acid-base reactions. In general alkaloids, which are treated as amines, the same as amines in their names, have suffix -ine. Alkaloids in pure form are usually colorless, odorless crystalline solids, but sometimes they can be yellowish liquids. Quite often, they have bitter taste. Now more than 3000 of alkaloids are known in over different 4000 plant species.

These compounds are produced generally by many plant species, mainly by flowering plants and also by some animals. Plants produce and store many organic compounds like amino acids, proteins, carbohydrates, fats, and alkaloids, which are usually treated as secondary metabolites. They are stored in each part of the plant—leaves, stem, root, and fruits of plants—but in different amounts. It was suggested that they are plants’ waste product, but now evidence suggests that they play some important biological function in plants.

Some groups of structurally related alkaloids are present in plants from few to even 30. These alkaloids belong to the same class but have some differences in their structure and one of them usually occurs in majority. Some plant families are very rich in alkaloids. For example, in plants like opium poppy (*Papaver somniferum*) and the ergot fungus (*Claviceps*), there are about 30 different alkaloid types. In plants, their function is still mostly unknown. Alkaloids because of their bitter taste are natural compound to deter herbivorous organisms. In some plants they are used as natural pesticides. It was suggested that alkaloids in plants have a function to protect them from destructive activity of some insect species. Alkaloids are also present in some animal species like frogs (poison dart frogs (*Phyllobates*)), New World beaver (*Castor canadensis*), and lizards, and they are produced by fungi species and ergot.

Besides having the same general name—alkaloids—they have an extreme variety of chemical structures. Some of these compounds seem to have people known for ages because of their wide range of activity on human organisms and also other animals. For thousand years, extracts from plants containing alkaloids had medicinal use as drugs, and they owe their powerful effects thanks to the presence of alkaloids. Morphine was the first alkaloid which was isolated about 1804 from opium poppy in crystalline form. Alkaloids are an interesting group of compounds with a wide range of activities, undesirable and desirable, on animal and human organisms. Alkaloids have diverse physiological effects: antibacterial, antimitotic, anti-inflammatory, analgesic, local anesthetic, hypnotic, psychotropic, and antitumor activity and many others. Nowadays, alkaloids usually from plants rather than from animals are still of great interest to organic chemists, biologists, biochemists, pharmacologists, and pharmacists. Well-known alkaloids include morphine, strychnine, quinine, atropine, caffeine, ephedrine, and nicotine

3. Methods of isolation

Extracts of plants containing alkaloids were known and used because of their diverse activity by people from ages. But ages ago people did not know direct methods to isolate pure compounds from specified plant species. Alkaloids in plants usually exist as aqueous solution in tissues. To isolate them the method called extraction is usually used. For commercially useful alkaloids, special extraction methods were developed. In general mixture containing alkaloid should be dissolved with some solvent with reagents. Extraction method allows recovery of alkaloids from solution. Then, each alkaloid can be separated from mixture and be obtained in pure form. To obtain crystalline form of alkaloids, certain solvents should be used. Another method is chromatography. It uses differences in degrees of adsorption of different alkaloids in some solvent system on solid materials such as silica or alumina.

4. Pharmaceutical and medicinal use of alkaloids

Alkaloids showed quite diverse medicinal properties. Many of them possess local anesthetic properties, but their practical use is limited for clinical purpose. Morphine is one of the most known alkaloids which had been used and still is for medical purposes. This alkaloid is a powerful narcotic which is used for the relief of pain, but its usefulness is limited because of addictive properties.

Structures of alkaloids: (1a) morphine and (1b) atropine.

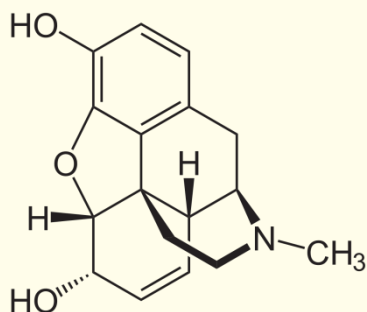


Figure 1a: Morphine

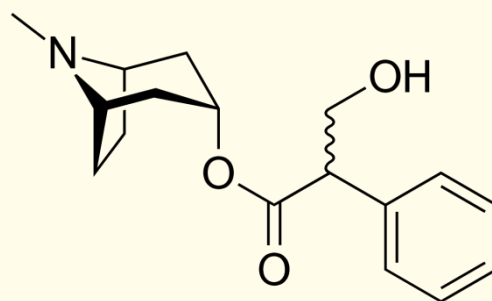


Figure 1b: Atropine

Methyl ether derivative of morphine—codeine—naturally occurring next to morphine in the opium poppy, possesses an excellent analgesic activity and is shown to be relatively nonaddictive. These alkaloids act as respiratory or cardiac stimulants. Next, the alkaloid which is used as medication in many clinical applications is atropine ([Figure 1b](#)). For example, injection with atropine is given to treat bradycardia (low heart rate).

Tubocurarine ([Figure 2](#)) is an alkaloid, is an ingredient of poison curare, and is used in surgery as muscle relaxant. Alkaloids vincristine and vinblastine are used as chemotherapeutic agent in the treatment of many cancer types. Cocaine an alkaloid present in *Erythroxylum coca* is a potent local anesthetic. Ergonovine, an alkaloid from the fungus *Claviceps purpurea*, and the second alkaloid ephedrine isolated from *Ephedra* species both act as blood vessel constrictors. Also ephedrine is used in bronchial asthma and to relieve discomfort of hay fever, sinusitis, and common colds.

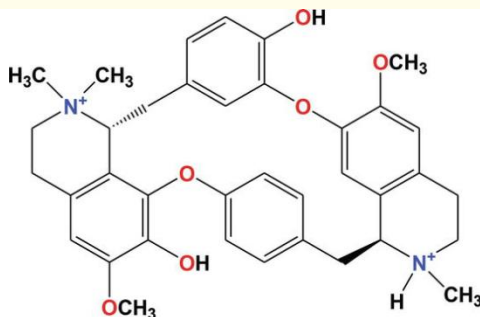


Figure 2: Structure of tubocurarine.

Quinine ([Figure 3](#)) is a powerful antimalarial agent and more often is replaced by synthetic drugs, which are more effective and less toxic. Another alkaloid from *Cinchona* species is quinidine which has medical application as treatment of irregular rhythms of the heartbeat or arrhythmias.

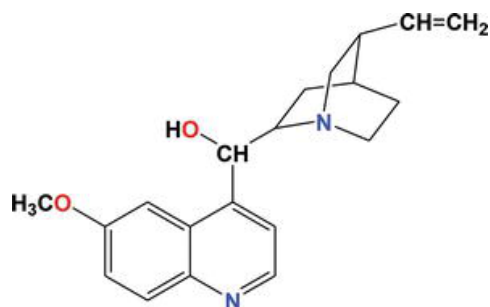


Figure 3: Structure of quinine from Cinchona species.

Colchicine (Figure 4) is another alkaloid, present in plants of Liliaceae family, known for ages to treat acute gout attacks. Another clinically used alkaloid is lobeline isolated from *Lobelia inflata*, which has multiple mechanisms of action.

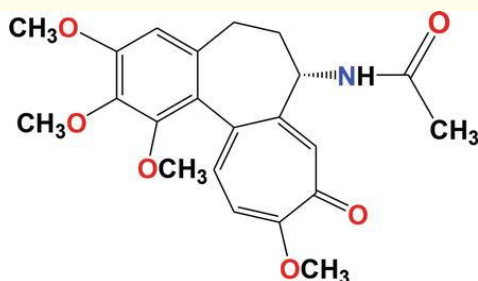


Figure 4: Structure of colchicine.

5. Alkaloids in human food and drinks

Many alkaloids are elements of human diet, both in food and drinks. The plants in the human diet in which alkaloids are present are not only coffee seeds (caffeine, Figure 5), cacao seeds (theobromine and caffeine), and tea leaves (theophylline, caffeine) but also tomatoes (tomatine) and potatoes (solanine). The most common alkaloid is caffeine which has also application as an ingredient of soft drinks like Coca-Cola to improve their taste and in drinks for active people who do sport.



Figure 5: Plant source of caffeine and its structure and powdered caffeine (pure form)

Other known alkaloid with bitter taste used as an ingredient of tonics is quinine ([Figure 3](#)) isolated from *Cinchona* species.

6. Alkaloids as stimulants

Alkaloids stimulate human organisms, for example, central nervous system, or directly work on the human brain. Nicotine ([Figure 6](#)) is an alkaloid obtained from the tobacco plant (*Nicotiana tabacum*) and is a potent stimulant and the main ingredient in tobacco smoked in pipes, cigars, and cigarettes. This alkaloid is highly addictive [1].

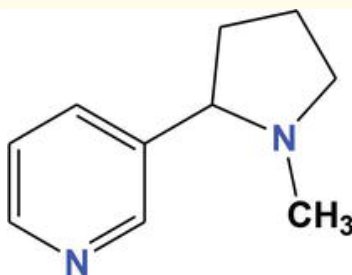


Figure 6: Structure of nicotine.

Cocaine is a narcotic drug, which activity is not suitable for medical purposes. This alkaloid has an opposite effect than morphine. This compound produces in the human body a euphoric hyperarousal state, but high doses of it may lead to fibrillation and death.

7. Dark nature of alkaloids

Some alkaloids are illicit drugs and poisons. Poisonous activities of some alkaloids are known for ages. One of these is strychnine (from *Strychnos* species, [Figure 7](#)). One of the well-known poison curare (obtained from *Chondrodendron tomentosum*) used in the South Africa as narrow poison contains alkaloid tubocurarine.

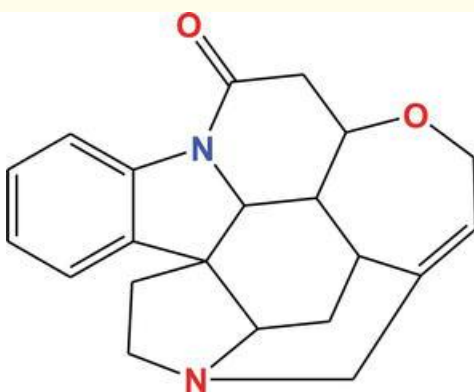


Figure 7: Structure of strychnine.

Coniine is an alkaloid isolated from *Conium maculatum*, which is an active ingredient of poison hemlock. Mescaline isolated from *Anhalonium* species has hallucinogenic activity. Psilocybin is a naturally occurring drug isolated from fungi species *Psilocybe mexicana* and possesses psychedelic activity. During the past decades, many semisynthetic derivatives of naturally occurring alkaloids with various activities have been synthesized. Synthetic derivative of morphine is heroin, and, from lysergic acid naturally present in *C. purpurea*, LSD was produced.

8. Other practical use of alkaloids

Besides activities mentioned above, alkaloids from many different plant species have many other useful applications such as antiparasitic, antiparasmodial, anticorrosive, antioxidative, antibacterial, anti-HIV and insecticidal activities.

9. Conclusion

Alkaloids are very important compounds for human beings. For ages their extracts were used as a cure to rescue people from pain like morphine and some illnesses like quinine in malaria and colchicine in gout. Thanks to alkaloids during ages, people can cure the diseases and improve their life.

Scientists still keep trying to design and synthesize more and more semisynthetic and synthetic alkaloids derived from natural sources of alkaloids. These alkaloids possibly can possess interesting activities for medical, pharmaceutical, synthetic, and many other useful properties.