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Review article

Alkaloids: structures, sources, and therapeutic potential

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ABSTRACT

Alkaloids are a broad class of naturally occurring substances that are present in microbes, plants, and mammals. They are distinguished by their strong biological effects and essential nitrogen-containing structure. They can be categorized according to their pharmacological activity, chemical structure, or biosynthetic mechanism. The opium poppy's morphine, an alkaloid that relieves pain, atropine, which treats bradycardia and organophosphate poisoning, vinblastine, a chemotherapeutic drug for cancer, quinine, an antimalarial from the Cinchona tree, and cocaine, a stimulant and local anesthetic, are a few examples. Tests such as the Dragendorff, Mayer, and Wagner tests can be used to identify alkaloids. Alkaloids are a crucial topic for pharmacological research and development because of their special qualities and therapeutic uses, which could lead to the creation of cures for a number of illnesses.

Keywords: Alkaloids, Secondary metabolites, Cancer.

INTRODUCTION

W. Meissner initially defined alkaloids in 1818, and it was applied to any organic substances originating from plants that have a basic character. Later research revealed that the nitrogen atom is part of the structure of alkaloids in a heterocyclic ring system. With the help of several scientific findings, the properties that characterize this class of secondary metabolites evolved, leading to the introduction of numerous chemical structures into this class of molecules. The kingdom of plants, people, marine life, fungi, and other microorganisms have all been shown to contain alkaloids [1].

The possibility of therapeutic substances in natural products and their derivatives has long been recognized. Plants have been a major source of inspiration for new medicinal compounds, as drugs developed from them have greatly enhanced human health and well-being. For many years, it has been known that natural products and their derivatives may contain medicinal ingredients. Since plant-derived medications have significantly improved human health and well-being, plants have served as a primary source of inspiration for new therapeutic molecules. The main benefits of using medications derived from plants are that they are more cost-effective, provide significant therapeutic benefits, and are generally safer than synthetic counterparts [2].

Both primary and secondary metabolism in plants produce a wide variety of metabolic products. Every living cell produces primary metabolites through essential metabolic processes. On the other hand, only significant tissues that are essential to particular functions contain specialized metabolites, which are produced from the main metabolism. Nitrogen is a defining ingredient in the chemical structures of alkaloids, which are naturally occurring specialized metabolites. The unique arrangement of atoms in alkaloids' chemical structures is thought to be the source of their biological potency [3].

Alkaloids: Substances that contain nitrogen and frequently have strong biological effects (such as vinblastine, morphine, and caffeine).

Flavonoids: Phenolic substances that have antibacterial, anti-inflammatory, and antioxidant qualities (such as anthocyanins, kaempferol, and quercetin).

Terpenoids, also known as isoprenoids, are chemicals with a variety of structures and functions that are derived from isoprene units. Examples of these include ginsenosides, beta-carotene, and limonene.

Phenolic acids: basic phenolic chemicals, such as gallic acid and caffeic acid, that have antibacterial and antioxidant qualities.

Glycosides: Substances that have a sugar moiety joined to a non-carbohydrate aglycone (such as cardiac glycosides and anthraquinone glycosides).

Saponins: Glycosides having surfactant qualities, such as ginseng saponins, are frequently utilized as natural detergents.

Tannins: Polyphenolic substances (such as catechins and theaflavins) that can bind proteins and other molecules [4].

Some compounds may fall under more than one category, and these classes are not all-inclusive. The potential therapeutic uses of medicinal plant metabolites have been thoroughly investigated.

Alkaloid

Definition: Basic substances that include nitrogen and have high physiological activity

Figure 1: Structure of Alkaloid

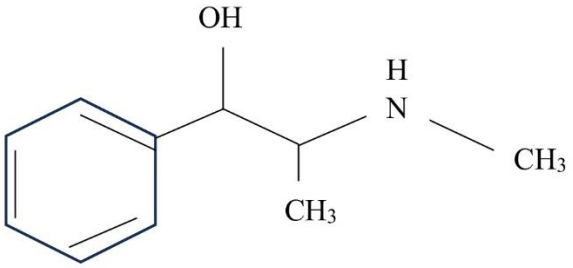
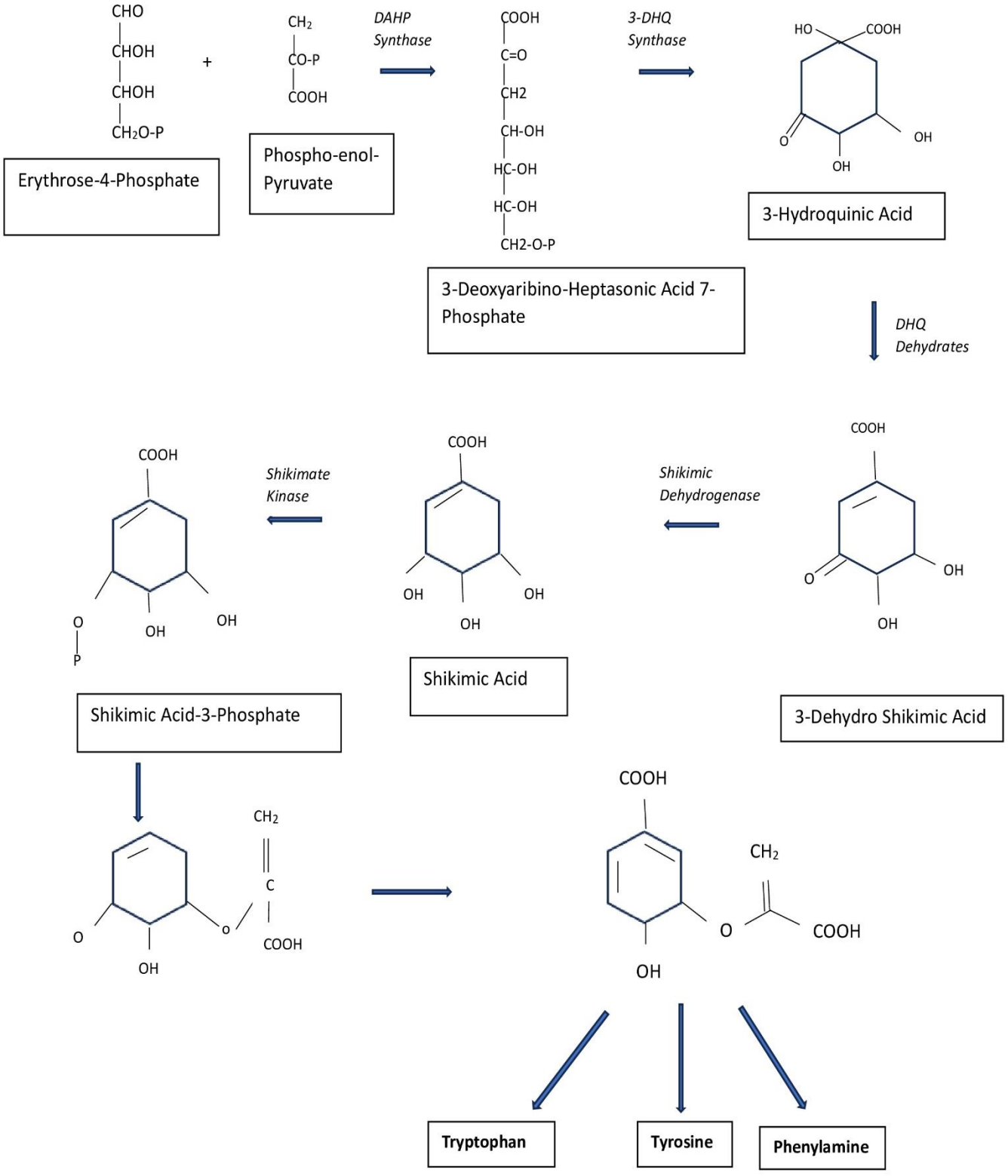


Figure 2: Shikimic acid pathway



Classification of alkaloid

There are other ways to categorize alkaloids, but this is a popular method.

According to the chemical structure

True alkaloids, such as nicotine, morphine, and quinine, have a heterocyclic ring with nitrogen.

Nitrogen is present in protoal kaloids, such as ephedrine and cathinone, but not in a heterocyclic ring.

Pseudoalkaloids: Nitrogen-containing terpenoid or steroidal chemicals (e.g., veratramine, solanidine)

Based on biosynthetic pathway

Originating from amino acids: Tyrosine, tryptophan, or lysine are among the amino acids that are used to biosynthesize a variety of alkaloids (for example, morphine from tyrosine and vinblastine from tryptophan).

Derived from different pathways: Terpenoids and polyketides are two examples of precursors that are used in the biosynthesis of certain alkaloids.

Based on pharmacological activity

Stimulants: nicotine and caffeine

Painkillers: codeine and morphine

Quinine and quinidine are antimalarials.

Vinblastine and vincristine are anticancer agents

Metabolic pathway

Shikimic acid pathway

Acetate malonate pathway

Amino acid pathway

Shikimic acid pathway

The aromatic amino acid biosynthesis route produces the hydroaromatic metabolite shikimic acid (SA). The shikimate route begins with the coupling of the pentose phosphate pathway with glycolysis to create 3-deoxy-D-arabinoheptulosonate-7-phosphate (DAHP), which is catalyzed by DAHP synthase isoenzymes (aroF, aroG, and aroH). To create shikimate, the resultant DAHP is further catalyzed by three enzymatic steps. The shikimate kinase then converts shikimate to shikimate-3-phosphate. Additionally, chorismic acid channels shikimate-3-phosphate to produce the aromatic amino acids phenylalanine, tyrosine, tryptophan, and other aromatic compounds [5, 6].

Shikimate pathway explanation

Phosphoenolpyruvate (PEP) and erythrose 4-phosphate condense to create 3-deoxy-D-arabino-heptulosonate 7-phosphate (DAHP), which is the first step in the route.

Cyclization: After a phosphate group is removed, DAHP is cyclized to produce 3-dehydroquinate (DHQ).

Dehydration: A dehydration process transforms DHQ into 3-dehydroshikimate (DHS), creating a double bond.

Reduction: Shikimate is the new DHS.

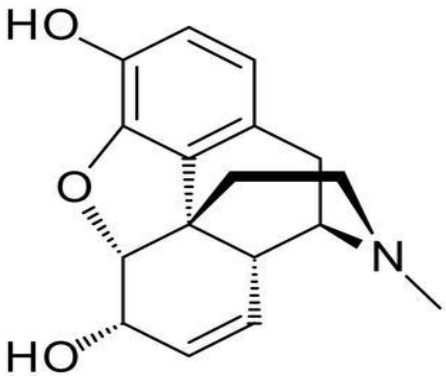
Phosphorylation: Shikimate is converted to shikimate 3-phosphate via phosphorylation.

Enolpyruvyl transfer: PEP forms 5-enolpyruvylshikimate 3-phosphate (EPSP) by giving shikimate 3-phosphate an enolpyruvyl group.

Chorismate formation: After a phosphate group is eliminated, EPSP is changed into chorismate. Chorismic Acid act as branching point they form secondary metabolite as tyrosine, tryptophan, phenylamine.

Morphine
Structure

Figure 3: Morphine



Introduction of morphine

An opiate alkaloid that occurs naturally, morphine is mostly derived from the dried latex of the opium poppy (Papaver somniferum). In clinical medicine, it is regarded as the gold standard for pain management and is among the strongest analgesics available.

Class of chemical: Isoquinoline alkaloid (derivative of phenanthrene)

Chemical formula: $C_{17}H_{19}NO_3$

Source: 8–17% of the weight of opium poppy latex is morphine. Nature: White, crystalline powder with a bitter flavour that dissolves readily in alcohol and only minimally in water. History & Discovery: German chemist Friedrich Sertürner isolated it for the first time in 1804. Because of its calming properties, it was named "morphine" after the Greek deity of dreams, Morpheus. became extensively utilised following the mid-19th century development of the hypodermic syringe [7].

Uses

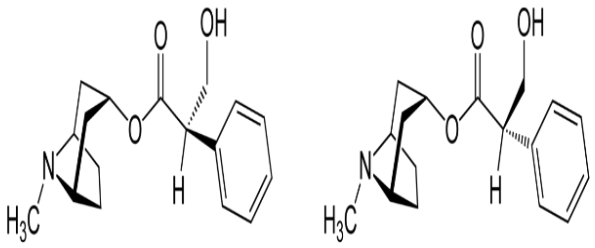
It is employed as a local anaesthetic.

It is used as an analgesic (Painkiller)

In the treatment of nerve gas poisoning

Atropine
Structure

Figure 4: Atropine



Definition

Atropine is a naturally occurring tropane alkaloid that is mostly derived from plants of the Solanaceae (nightshade) family, including Hyoscyamus niger (henbane), Datura stramonium (jimsonweed), and Atropa belladonna (deadly nightshade).

Chemical characteristics

Tropane Alkaloid $C_{17}H_{23}NO_3$

A racemic combination of D- and L-hyoscyamine, of which only the L-isomer exhibits pharmacological activity.

Physical characteristics: odourless, white, crystalline powder

Alcohol- and water-soluble; a bitter flavour.

Sources: Atropa Belladonna

Medical uses

Eye dilation: In order to dilate pupils for eye tests or procedures, atropine is utilized.

Treatment for bradycardia: When cardiac beats are unusually sluggish, atropine can raise heart rate.

Treatment of organophosphate poisoning: Atropine is used as a counteragent for poisoning brought on by nerve agents or pesticides.

Additional possible applications

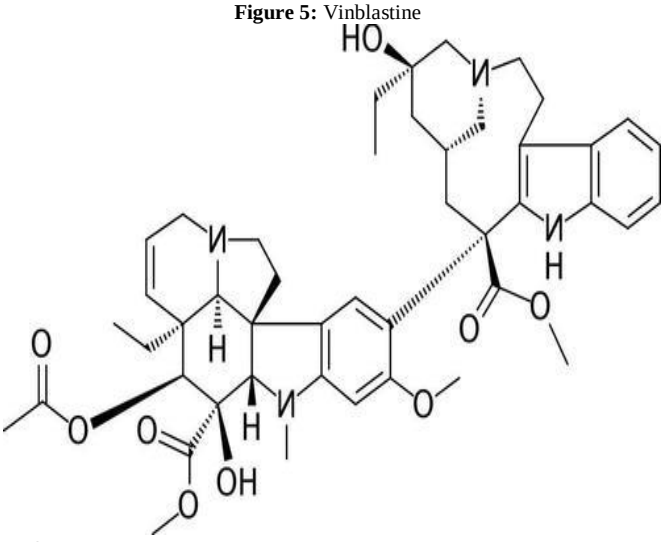
Digestive disorders: Peptic ulcers and irritable bowel syndrome (IBS) can be treated with atropine.

Motion sickness: Although it's not the most popular remedy, atropine has been used to prevent motion sickness [8].

Vinblastine

Structure

Figure 5: Vinblastine



Definition

A vinca alkaloid called vinblastine is extracted from the plant Catharanthus roseus, sometimes known as Madagascar periwinkle. It is a cytotoxic chemotherapy drug used to treat cancer.

Chemical nature: alkaloid of dimeric indole–indoline

Molecular formula: $C_{46}H_{58}N_4O_9$

Sources: Originated from the plant's combination of vindoline and catharanthine.

Physical Characteristics: White to off-white crystalline powder in appearance

Molecular formula: $C_{46}H_{58}N_4O9$

Taste: Tasteless, odourless

Melting point: at 2150–2180C

Soluble in methanol, ethanol

Applications in medicine

Hodgkin's and non-Hodgkin's disease treatment

Lymphoma

Cancer of the ovaries

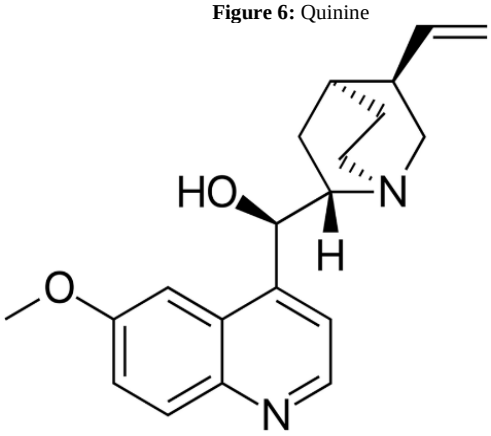
Cancer of the breast

Sarcoma Kaposi

Quinine

Structure

Figure 6: Quinine



Definition

An alkaloid that occurs naturally, quinine has antipyretic, analgesic, and antimalarial effects. It is extracted from the Cinchona tree's bark.

Source: Cinchona ledgeriana, Cinchona officinalis, and related species' bark is a member of the Cinchona alkaloids group, which also contains quinidine and cinchonidine.

Nature of chemicals

Class: Alkaloid quinoline

Formula for molecules: $C_{20}H_{24}N_2O_2$

Mass of a molecule: 324.43 g/mol

Optical isomer: Levo-rotatory form is pharmacologically active.

Physical Properties:

Appearance: crystalline white powder

Taste: intensely bitter. Solubility: water-soluble to a slight extent; soluble in alcohol and chloroform

Melting Point:177 is the melting point.

Stability: Decomposes with intense heat and light, but remains stable when dry.

Uses of medicine

Malaria treatment, particularly for Plasmodium falciparum, which is resistant to chloroquine

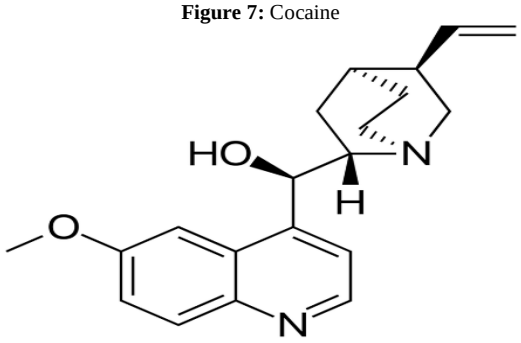
Clindamycin treatment for babesiosis; limited use because of negative effects; leg cramps at night.

Antimalarial: Used to treat malaria, particularly infections caused by Plasmodium falciparum that are resistant to chloroquine.

Analgesic and antipyretic: lowers fever and eases minor discomfort; used historically before the invention of modern medications [9].

Cocaine
Structure

Figure 7: Cocaine



Overview: The coca leaves are used to extract the cocaine alkaloid. The leaves of the coca plant (Erythroxylum coca and Erythroxylum novogranatense) are the natural source of cocaine, a tropane alkaloid. It stimulates the central nervous system and has strong local anaesthetic effects.

Nature of chemicals

Tropane alkaloid class

Formula for molecules: $C_{17}H_{21}NO_4$

Exists mainly as the levorotatory form in nature Often used as cocaine hydrochloride in medicine

Source plant: Colombian Erythroxylum coca

Physical characteristics

Appears as a pure form, colourless to white crystalline powder

Molecular formula: $C_{17}H_{21}NO$

Molecular mass: 303.35 g/mol

Flavour: Bitter

Odour: No smell

Melting point (free base form): 98–99 °C

Boiling point: 187 °C

Solubility: Cocaine hydrochloride is easily soluble in water and soluble in ether, alcohol, and chloroform.

Optical activity: isomer of levorotation [10].

Uses

Local anaesthesia: Because it combines anaesthetic and vasoconstrictor properties, it is used in some ENT surgeries, such as nasal, lacrimal duct, and laryngeal procedures.

Topical anaesthesia: Used on mucous membranes to numb the region and stop bleeding when doing minor surgery. Stimulants in beverages and tonics.

Identification test for alkaloid

Dragendorff's test: orange or reddish-brown precipitate in potassium bismuth iodide solution. Principle: Alkaloids and bismuth iodide combine to form an insoluble compound.

Mayer's test: Cream or pale-yellow precipitate in a potassium mercuric iodide solution. Insoluble mercury-iodide complexes are formed by alkaloids.

Wagner's test: Iodine in a solution of potassium iodide. A reddish-brown substance. Alkaloids create an iodine compound that is insoluble.

The saturated picric acid solution in Hager's test: yellow precipitation. Alkaloids form insoluble picrate salt.

Tannic acid test: 10% tannic acid solution: buff-coloured precipitate. Alkaloids form insoluble tannate salt.

The test for picrolonic acid and its solution: yellow precipitation. Alkaloid–picrolonate complex formation.

Iodine in potassium iodide: Mayer's test: yellow precipitation. Like Mayer's principle,

Test for phosphotungstic acid: Phosphotungstic acid sample: yellow or white precipitation. Alkaloids create phosphotungstate, which is insoluble [11].

CONCLUSION

A broad class of naturally occurring substances with considerable medicinal promise are alkaloids. These nitrogen-containing compounds, which come from microbes, plants, and animals, have strong biological effects. The definition and classification of alkaloids have changed over time, with a history that dates back to 1818. Many alkaloids have been transformed into contemporary medications, and they have been utilized in traditional medicine for ages. Morphine, atropine, vinblastine, quinine, and cocaine are examples of alkaloids; each has special qualities and uses in medicine. Numerous assays, such as the Dragendorff, Mayer, and Wagner tests, can be used to identify alkaloids. Alkaloids are still a key topic for pharmacological study and development because of their intricate structures and biological activities, which may help treat a range of illnesses. Human health and well-being have greatly benefited from the study of alkaloids, and more research is anticipated to find novel medicinal uses for these substances.

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