



Venom Vanquish: A Comprehensive Review on Ethnobotany and Phytochemistry of Significant Traditional Medicinal Plants

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Abstract

Snakebite is a significant public health concern in many parts of the world, particularly in regions where venomous snakes are prevalent. Snakebites can range from mild to life-threatening, depending on the species of snake, the amount of venom injected, and the location of the bite. Globally, an estimated 5 million people are affected by snake bites each year, according to recent statistics. Since ancient times, traditional medicinal plants have been used to cure a wide range of illnesses, including snake bites. Secondary metabolites contained in plants were efficient in reducing the effects of snake venom. Snake venom is a potent toxin that can cause severe damage to the human body, affecting the nervous system, cardiovascular system, or both. Symptoms can range from mild swelling to life-threatening paralysis, respiratory failure, and hemorrhage. Enzyme activity is inhibited by flavonoids, alkaloids, and tannins, which additionally hinder blood from clotting and lessen inflammation. Treatments for snake bites that are more beneficial and less hazardous could result from the isolation and synthesis of natural drugs. With the use of cutting-edge scientific methods, we can maximize their potential and use their secondary metabolites to develop novel medications and therapies. The study of these plants and their potential uses in contemporary medicine requires more funding and investigation. This will advance our knowledge of these plants and help us create cures for some of the most lethal diseases.

Keywords: Antioxidant Anti-inflammatory, Anti-venomous, Ethnobotany, Phytochemistry, Snake Envenomation, Traditional Medicinal Plants

1. Introduction

Snakebite is a neglected public health issue in many tropical and subtropical countries. Snake bites pose a significant health risk in regions worldwide, especially in remote areas where medical resources are scarce. Exploring the field of ethnobotany, which focuses on the relationship between humans and plants, offers a hopeful path towards the development of innovative treatments for snake bites. Past attempts to control snakebite envenoming have been insufficient, leading to fragmented and inaccurate epidemiological information. A significant number of snakebite victims do not seek medical care at health centres or hospitals and instead rely on traditional remedies. However, the

currently available data indicates that an estimated 4.5 to 5.4 million people suffer from snakebites each year. Out of these cases, approximately 1.8 to 2.7 million individuals experience clinical symptoms, and the complications resulting from snakebites contribute to the deaths of 81,000 to 138,000 people annually reported by the World Health Organization. Due to limited demand, numerous manufacturers have discontinued the production of certain anti-venom products. Consequently, the prices of these products have substantially risen over the past two decades, rendering treatment economically unfeasible for the majority of people requiring it. The escalating costs of anti-venom have also contributed to a decline in demand, exacerbating the situation to the point

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where the availability of anti-venom has significantly decreased or completely vanished in certain regions. Furthermore, the introduction of unsuitable, untested, or counterfeit anti-venom products in certain markets has further eroded trust and confidence in the overall effectiveness of anti-venom therapy. Recent research has provided evidence of the efficacy of various plant-based remedies used in traditional medical systems to address snake bites¹. Medicinal plants have been discovered to be a rich source of secondary metabolites with potential anti-snake venom action². Historically, snake bites have been managed through the utilisation of traditional medicinal practices. Within plants, secondary metabolites are compounds that are not essential for basic plant functions but play a crucial role in the plant's survival and interactions with the surrounding environment. These secondary metabolites present an appealing opportunity for therapeutic advancement, as some have shown promising results in mitigating the detrimental effects of snake venom. The vast diversity of traditional medicinal plants presents an exciting opportunity for scientific investigation. Through rigorous scientific methods, researchers can identify and isolate specific compounds within these plants that hold promise for snake bite treatment. These compounds may exhibit potent anti-venom properties, capable of neutralising the venom's toxic effects or alleviating the symptoms caused by snake bites. By delving deeper into the chemical makeup of these plants, researchers can uncover the mechanisms underlying their healing abilities and optimize their potential for therapeutic use.

2. Snake Bites: A Global Health Concern

Globally, an estimated 5 million people are affected by snake bites each year, according to recent statistics. Shockingly, up to 2.7 million of these cases result in severe injury or even death³. Needless to say, snake bites pose a significant risk to public health, especially in regions such as sub-Saharan Africa and Southeast Asia, where they are a leading cause of both morbidity and mortality⁴.

Snake bites can cause severe physical harm that often leads to several unforeseen economic challenges for the victims. Apart from hefty medical expenses, they may also suffer substantial loss of income due

to the often lengthy treatment required for recovery. Additionally, the adverse impact of snake bites can result in long-term disabilities, further compounding the economic burden on the victim and their family⁵. Rural communities, where healthcare facilities are often sparse, are disproportionately affected since access to anti-venom is limited in such areas. Overall, the economic consequences of snake bites can have significant long-term implications on individuals in several communities and regions globally.

3. Ethnobotanical Studies of Various Traditional Medicinal Plants

Ethnobotany is the study of how different cultures use plants for medicinal, ceremonial, and other purposes. It combines the fields of anthropology, botany, and pharmacology to understand the relationships between people and plants. Traditional medicinal plants are an important part of ethnobotany because they have been used by different cultures for thousands of years to treat various ailments, including snake bites. For example, the Kuna people of Panama use the bark of the *Tabebuia* tree to treat snake bites⁶, while the Quechua people of Peru use the root of the *Chuchuhuasi* tree as an anti-inflammatory⁷.

The plant *Rauvolfia serpentina*, *Andrographis paniculata*, *Tinospora cordifolia*, *Eclipta prostrata*, *Achyranthes aspera*, *Murraya koenigii*, *Aloe vera* plants, *Euphorbia hirta*, *Croton tiglium*, *Vitex negundo*, *Solanum xanthocarpum* and *Azima tetraacantha* were the most commonly listed as being significant for therapeutic purposes, the reason being majority of rural people use medicinal herbs as an alternative to conventional medicine. They heavily rely on the assistance of conventional healers who prescribe these therapeutic herbs for a variety of illnesses. The herbal remedies used to treat snakebites are discussed, as well as how they work. Future research is required to stress the conservation and development of significant medicinal plants in the nation, in addition to screening their biologically active components and pharmacological activities of these plant materials (Table 1).

3.1 *Rauvolfia serpentina*

Plants have historically been used in traditional medicine to heal snakebites. For instance, In India

Table 1. The very significance of choosing the mentioned medicinal plants

S. No	Medicinal Plants	Family	Secondary metabolites	Specific Phytochemicals	Purpose of choice
1.	<i>Rauvolfia serpentina</i> (L.) Benth. ex Kurz	Apocynaceae	Alkaloids	Reserpine, ajmaline, serpentine	Hypotensive and anti-venom properties. Additionally, it has been found to have sedative properties, making it useful in treating anxiety and insomnia ⁸ .
2.	<i>Andrographis paniculata</i> (Burm. f.)	Acanthaceae	Andrographolides	Andrographolide, Neoandrographolide	Effective against snake bites due to their anti-inflammatory ⁹ and anti-snake venom ¹⁰ .
3.	<i>Tinospora cordifolia</i> (Willd.)	Menispermaceae	Alkaloids	Berberine, Palmatine	Reduces the mortality rate in patients who had been bitten by snakes due to their Immunomodulatory and antioxidant properties ¹¹ .
4.	<i>Eclipta prostrata</i> (L.)	Asteraceae	Flavonoids	Wedelolactone, Ecliptofolin	A study conducted on rats showed that treatment with extract of this plant significantly reduced venom's effects (hepatoprotective properties) and increased the rats' survival rate ¹² .
5.	<i>Achyranthes aspera</i> L.	Amaranthaceae	Saponins, Alkaloids	Achyranthine, Achyranthine-B, Oleanolic Acid	Holds the potential to neutralize the harmful substances present in venom, consequently impeding its spread throughout the body ¹³ .
6.	<i>Bergera koenigii</i> L.	Rutaceae	Alkaloids, Carbazole alkaloids	Murrayanine	A case study found a poultice reducing pain and swelling within hours ¹⁴ .
7.	<i>Aloe vera</i> (L.) Burm. f.	Xanthorrhoeaceae	Anthraquinones, Polysaccharides, Flavonoids	Aloin, Emodin, Aloe-emodin, Acemannan	Aloin is an anti-inflammatory that relieves swelling and discomfort ¹⁵ . It also contains antimicrobial qualities that can aid in infection prevention.
8.	<i>Euphorbia hirta</i> L.	Euphorbiaceae	Diterpenoids, Flavonoids	Euphorbin A, Euphorbin B, Kaempferol	It includes ephedrine, a compound that has been revealed to counteract the venom of certain species of snakes ¹⁶ .
9.	<i>Croton tiglium</i> L.	Euphorbiaceae	Diterpenoids	Croton Oil	Mitigate the toxicity of snake venom ¹⁷ .
10.	<i>Vitex negundo</i> L.	Lamiaceae	Flavonoids, Terpenoids, Alkaloids	Agnuside, Vitexin, Negundoside	Anti-inflammatory properties ¹⁸ .
11.	<i>Solanum virginianum</i> L.	Solanaceae	Steroidal glycoalkaloids	Solasonine, Solamargine	Protection against the oxidative damage produced by snake venom ¹⁹ .
12.	<i>Azima tetraacantha</i> Lam.	Salvadoraceae	Triterpenoids, Flavonoids, Alkaloids	Azimine, Azilactone, Lupeol, Quercetin	The plant extracts show potential anti-snake venom action, potentially mitigating cobra venom effects ²⁰ in mice and treating dog's snake bites.

tribal communities like Gonds and Bhils living in the Eastern Ghats, Garhwali, Kumauni, Chhatarpur region of Madhya Pradesh, and Bhojas people dwelling in Chatara block of Uttar Pradesh have all historically used the root of the plant Sarpagandha (*R. serpentina*)

as an antidote for snake venom in India²¹. The plant is administered in the form of a paste, which is applied to the bite site²². Phytochemicals like alkaloids, phenols, tannins, and flavonoids are found in *R. serpentina*²³. New research has indicated that alkaloids present, are

capable of reducing blood pressure and the intensity of snake venom toxicity. Sarpagandha consists of an active ingredient called reserpine, which is thought to block the action of the venom, thus preventing it from entering the bloodstream²⁴. It is also believed to have anti-inflammatory and analgesic properties, and so is used to treat the pain and swelling associated with snakebites²⁵.

3.2 *Andrographis paniculata*

Similarly, chemicals that can suppress the action of snake venom enzymes have been discovered in the leaves of the plant *A. paniculata*²⁶, often known as the "king of bitters," which is frequently used in Ayurvedic medicine. The active ingredients in *A. paniculata* are andrographolides, which are thought to have anti-inflammatory, anti-bacterial, and anti-viral properties²⁷. These properties have led researchers to believe that *A. paniculata* may be effective in treating snake bites. It is available in capsule, tablet, and liquid form. It can also be taken as a tea or powder. A potent target for pharmaceutical regimens, PLA A2 is a tiny enzyme made up of 120–125 amino acid residues when hydrolyses phospholipid with an unsaturated fatty acid at the sn-2 position of the ester link, unsaturated fatty acids and Lysine phospholipid are produced in a calcium-dependent manner²⁸. As a result, the cell membrane's physical properties are altered, impacting cell homeostasis throughout the body, and activating a downstream signal transduction cascade²⁹.

3.3 *Tinospora cordifolia*

In addition to these, *T. cordifolia*, popularly known as Guduchi, a climbing shrub found in India's tropical and subtropical areas, has also been utilized as traditional medicine revered for its potential to heal and protect against snake bites³⁰. The root and stem parts of this plant have the potential to reduce inflammation and improve wound healing through the presence of active compounds, with the most prominent being alkaloids and polyphenols³¹. Alkaloids are compounds that have been found to have anti-venom properties, while polyphenols are compounds that have been found to have anti-inflammatory properties³². This plant is usually taken in the form of a decoction or juice, often also combined with other herbs such as ginger and turmeric. It has also been valued for its immunomodulatory, anti-diabetic, and hepatoprotective properties³³.

3.4 *Eclipta prostrata*

E. prostrata, sometimes referred to as False Daisy or Bhringraj is a tiny, annual plant that may be found all over the world in tropical areas³⁴. *E. prostrata* contains an extensive variety of active compounds, including Ecliptol, a compound with anti-inflammatory and anti-venom properties. It also contains flavonoids, which are known to have anti-bacterial and anti-fungal properties³⁵. Additionally, it contains triterpenoids, which are believed to have anti-viral, anti-bacterial, and anti-inflammatory³⁶ properties, as well as alkaloids, which are known to have anti-parasitic and anti-venom properties³⁷. The plant has been traditionally used to treat snake bites by making a paste of the plant and applying it topically to the affected area. The paste is believed to reduce inflammation and pain, as well as to draw out the venom³⁸. Additionally, it is believed to help reduce swelling, itching, and redness³⁹. It is occasionally combined with other plants including *Piper longum*, *Phyllanthu semblica*, *Terminalia chebula*, *Achyranthes aspera*, *Murraya koenigii*, *Aloe vera*, *Croton tiglium*, *Euphorbia hirta*, *Boerhavia diffusa*, *Ricinus communis*, *Solanum xanthocarpum*, and *Swertia chirata* are a few more plants that have also been used in traditional medicine for treatments for snakebite⁴⁰.

3.5 *Achyranthes aspera*

The prickly chaff flower, also known as *A. aspera*, is an annual plant that grows in tropical and subtropical climates⁴¹. Studies about *A. aspera* plant leaves have shown that they contain several active compounds, including alkaloids, flavonoids, tannins, and saponins⁴². These compounds have been shown to have anti-inflammatory, antispasmodic, and anti-venom properties⁴³. A multitude of forms of *A. aspera* are readily accessible, including capsules, pills, powders, and extracts. Additionally, it may be purchased alongside other herbs and vitamins, such as ginger and turmeric. It's crucial to search for items that are certified organic and free of contamination while buying *A. aspera*⁴⁴. It's also crucial to adhere to the manufacturer's dosage recommendations. In addition, they have been found to inhibit the release of histamine, which is released for active against snake bite⁴⁵.

3.6 *Murraya koenigii*

M. koenigii has therapeutic properties in its leaves, roots, bark, stalks, and flowers⁴⁶. It is believed that the

leaves of this plant contain a compound called koenigin, which can neutralize the venom of poisonous snakes⁴⁷. The leaves are crushed and applied externally to the affected area to reduce the pain and swelling caused by the bite. The leaves of *M. koenigii* are also used to make a decoction, which is taken orally to treat snake bites. This decoction is believed to have anti-inflammatory and antiseptic properties⁴⁸, which can help reduce the pain and swelling caused by the bite. The decoction can also help reduce the risk of infection and speed up the healing process. Along with several other herbs, the entire plant is used to neutralize snake venom⁴⁹.

3.7 *Aloe vera*

Succulent *Aloe vera* plants are indigenous to tropical and subtropical climates. According to Behera *et al.*,⁵⁰ *Aloe vera* is believed to be a powerful natural remedy for a variety of ailments, including snake bites. The plant contains several active compounds⁵¹, such as polysaccharides, glycoproteins, and anthroquinones, which have been found to have anti-inflammatory and antimicrobial properties. Studies indicate that the plant has been found to increase the production of white blood cells, which can help to fight off infection⁵². In addition, *A. vera* has been found to stimulate the production of antibodies, which can help to neutralize the venom and reduce the effects of the bite⁵³.

3.8 *Euphorbia hirta*

An annual herb known as Hairy Spurge, *E. hirta*, is frequently found in tropical and subtropical areas of the world. The leaves of the plant are crushed and applied to the site of the bite, or the juice of the leaves can be extracted and consumed orally⁵⁴. *E. hirta* contains a variety of bioactive compounds such as flavonoids, terpenoids, and alkaloids⁵⁵. These compounds are thought to be responsible for the plant's anti-venom properties. Studies have shown that the plant can neutralize the effects of venom from cobras, kraits, and vipers, as well as other snakes⁵⁶. It is believed that the compounds work by binding to the venom molecules, preventing them from entering the bloodstream and causing tissue damage. In a related research article, it was discovered that ellagic, gallic, and quinic acids extracted from *E. hirta* could suppress the toxicity caused by *Naja naja* venom both *in vivo* and *ex vivo*.

3.9 *Croton tiglium*

In tropical and subtropical areas of the world, there is a shrub called *C. tiglium*, also referred to as *Croton*⁵⁷. The active ingredient in the plant, tigloidine, is believed to be responsible for its protective effects against snake bites. The anti-inflammatory, antioxidant, antidiabetic, wound-healing, and antivenom effects⁵⁸ of this substance are extensively researched. This compound is thought to possess antivenom properties and act as a local anaesthetic. It has been used in traditional medicine for over two thousand years and is still used in many parts of the world today. The Ayurveda recommends using the paste made from croton seeds, which is then combined with a little lime juice and used as a collyrium in certain instances of snakebite⁵⁹.

3.10 *Vitex negundo*

Tall and regal, *V. negundo* stands like a sentinel against the scourge of snake bite. Its potent leaves and bark can be used to create a powerful antidote that can save lives and potentially deadly conditions⁶⁰. The leaves of *V. negundo* contain a variety of compounds that have been found to have antivenom properties⁶¹. These compounds include flavonoids, tannins, essential oils, and alkaloids⁶². The flavonoids are thought to have the strongest antivenom activity, and they are effective against the venom of both cobras and vipers. Tannins, on the other hand, are effective against the venom of kraits and mambas. Essential oils, such as eugenol, are effective against the venom of kraits and mambas, as well as some other species of snakes. Finally, alkaloids, such as vitexin⁶³, are effective against the venom of cobras, vipers, and kraits. In addition to its antivenom properties, *V. negundo* has also been studied for its potential to reduce inflammation and swelling, as well as its ability to reduce pain. Studies have shown that vitexin can help reduce the severity of a snake bite, as well as reduce the risk of complications⁶⁴.

3.11 *Solanum xanthocarpum*

The traditional use of *S. xanthocarpum* as a medicinal plant against snake bites has been passed down through generations, its potency proven by countless successes in the past. The world's tropical and subtropical climates⁶⁵ are home to the shrub known as *S. xanthocarpum*, sometimes referred to as Yellow Berried Nightshade. The medicinal properties of *S. xanthocarpum* can

be attributed to its chemical composition. The plant contains a variety of compounds, including alkaloids, saponins, flavonoids⁶⁶ and tannins. It is renowned for its antivenom, anti-inflammatory, antioxidant, antidiabetic, and wound-healing qualities. The primary active compound in *S. xanthocarpum* is solasodine⁶⁷, which is a steroidal alkaloid. This compound is highly effective in neutralizing the venom of cobras, vipers, and other venomous snakes. Hydroethanolic extracts of the roots of *S. xanthocarpum* have the venom-neutralizing properties of suppressing the venom of poisonous snake *Najanaja*⁶⁸.

3.12 *Azima tetracantha*

A. tetracantha, commonly known as Four-Spined Acacia, is a plant native to Africa and India. It is believed to have many medicinal properties⁶⁹, one of which is its ability to act as an antidote to snake venom. Alkaloids, glycosides, and tannins have been reported to be present in the leaves of *A. tetracantha* in sufficient quantities for neutralizing the venom produced by certain snake species. The poisons found in the venom have been believed to be rendered inactive by the alkaloids in the leaves, while the tannins and glycosides can lessen the venom's effects on swelling and inflammation. Additionally, chemicals in the leaves may lessen the effects of neurotoxins⁷⁰ present in some snake venoms, according to some theories, researchers from India and East Africa discovered that *A. tetracantha* leaves might be utilized to treat poisonous attacks from cobras, kraits, and vipers⁷¹ in their study. The wounded region was then covered with a paste made from crushed leaves and water. It was later determined that the mixture helped to neutralize the poisons in the venom with the help of active ingredients present that work to bind to the venom and prevent it from entering the bloodstream, while its other compounds help to lessen the swelling, by making use of plant's anti-inflammatory and antiseptic properties.

4. Anti-snake Venom Activity of Secondary Metabolites

4.1 *In vitro* Production of Secondary Metabolites

The process of producing secondary metabolites outside of a living organism, also known as *in vitro*

production of secondary metabolites, involves the cultivation of a particular plant or microorganism in a controlled environment⁷². By doing this, researchers aim to replicate the natural production of secondary metabolites that typically occur within the living organism. The production of secondary metabolites *in vitro* has become an increasingly popular technique in the field of pharmaceuticals and has drawn attention for its potential to yield rare and valuable compounds⁷³. This technique has exhibited great potential for manufacturing compounds with the ability to counteract the toxic effects of snake venom.

One instance of an intriguing natural phenomenon is the biosynthesis of resveratrol - a compound known to suppress the activity of some viper venom enzymes⁷⁴. Another fascinating example is the creation of tannins, which are capable of binding to venomous proteins and rendering them harmless⁷⁵.

4.1.1 *The Endangered Medicinal Plants: In vitro Propagation*

Recent investigations on the *in vitro* production of Sarpagandha chemicals and components have yielded encouraging findings. Cell cultures of *R. serpentina*, the plant from which Sarpagandha is derived, were used to efficiently produce ajmalicine, serpentine, and catharanthine⁷⁶. According to one study published in Springer, adding elicitors to cell cultures, such as yeast extract or salicylic acid, significantly enhanced the synthesis of ajmalicine and serpentine⁷⁷. Another work published revealed effective catharanthine synthesis using cell cultures supplemented with plant growth regulators⁷⁸.

Several techniques to synthesize *A. paniculata* chemical substances and components *in vitro* have been established, including Cell suspension culture, Callus culture and Hairy root culture⁷⁹. Several molecular pathways have been identified in the production of *Andrographis paniculata* compounds utilising *in vitro* production methods. The terpenoid biosynthesis pathway, the flavonoid biosynthesis pathway, and the alkaloid biosynthesis pathway are among them. *A. paniculata* contains key bioactive substances like diterpenoids, flavonoids, and Andrographolide⁸⁰. Diterpenoids are produced through the terpenoid biosynthesis pathway, while flavonoids are produced through the flavonoid pathway. Andrographolide,

a key bioactive chemical, is produced through the alkaloid biosynthesis pathway, involving enzymes like geraniol 10-hydroxylase, andrographolide synthase, and cytochrome P450 monooxygenase. Commonly used elicitors include methyl jasmonate, salicylic acid, and chitosan which helps enhance the production of andrographolide, neoandrographolide, and deoxyandrographolide⁸¹.

In the case of *T. cordifolia*, cell cultures and bioreactors can produce chemical compounds in larger quantities and with higher purity than traditional extraction methods⁸². However, other obstacles remain, including improving growing conditions, finding the most effective cell lines, and scaling up the production process. Specific elicitors like methyl jasmonate, salicylic acid and chitosan have been identified to activate the molecular pathways and enhance the production of bioactive compounds like apigenin, luteolin, quercetin gallic acid, caffeic acid, and ellagic acid⁸³.

Several *in vitro* synthesis strategies have been developed, including Cell suspension cultures: In this method, cells are grown in a liquid media and induced to create the desired chemicals. Wedelolactone and ecliptasaponin have both been synthesized using this approach⁸⁴. Hairy root cultures: In this procedure, roots are infected with *Agrobacterium rhizogenes* and driven to produce the desired chemicals. Apigenin emerged using this approach⁸⁵. The treatment with the elicitor methyl jasmonate increased the levels of several bioactive compounds, including wedelolactone and eclipta⁸⁶.

Several notable ways for producing *Croton tiglium* bioactive compounds outside of their native habitat have been established, including cell suspension culture, hairy root culture, and bioreactor culture⁸⁷. Several investigations have demonstrated that these procedures are highly successful at obtaining significantly greater yields of these chemicals than other standard approaches. It includes several chemicals and substances, including phorbol esters, diterpenes, and fatty acids⁸⁸. Common elicitors used include chitosan, salicylic acid, and jasmonic acid.

5. Phytochemical Constituents and its Medicinal Properties

Secondary metabolites are compounds produced by plants that are not directly involved in growth or

reproduction. Instead, they play a variety of roles in the plant's defence against predators and pathogens. Many of these secondary metabolites have medicinal properties and can be used to treat snake bites. For example, alkaloids are a class of secondary metabolites that are often found in traditional medicinal plants used to treat snake bites. These compounds can act as analgesics, anti-inflammatories, and anticoagulants, making them effective at reducing pain and swelling and preventing blood clots from forming. Other secondary metabolites, such as flavonoids and terpenes, also have potential uses in treating snake bites.

Several classes of secondary metabolites have been identified as having anti-snake venom activity, including alkaloids, flavonoids, terpenoids, saponins, steroids, phlotannins, and phenolic compounds.

Sarpagandha contains a variety of secondary metabolites, including alkaloids, glycosides, flavonoids, terpenoids, and saponins. The most abundant and biologically active alkaloids in this plant are known as "reserpine" and "rescinnamine", which have sedative, anti-depressant, and anti-inflammatory properties⁸⁹. Reserpine (Figure 1) is also known to have anti-diabetic and anti-hypertensive effects. Other alkaloids present in Sarpagandha are ajmalicine, serpentinine, and ajmaline. Reserpine has been found to inhibit the activity of certain enzymes in snake venom, thus neutralizing its harmful effects. Ajmalicine (Figure 2) and yohimbine, on the other hand, have been found to work by blocking the effects of venom on the nervous system⁹⁰. Glycosides are sugar-containing compounds that are found in Sarpagandha. The most abundant glycosides are known as "Sarpagine" and "serpentinine", which have anti-inflammatory, anti-diabetic, and anti-hyperglycemia effects. Flavonoids are a group of compounds with antioxidant and anti-inflammatory properties. The flavonoids present in Sarpagandha are luteolin, luteolin-3-O-glucoside, and apigenin. These compounds are effective in neutralizing the effects of venom on the nervous system and other bodily systems. Terpenoids are compounds with a variety of biological activities, such as anti-inflammatory, anti-cancer, and anti-microbial. The terpenoids present in Sarpagandha are β -sitosterol, stigmasterol, and campesterol⁹¹. These compounds are effective in blocking the effects of venom on the nervous system. Saponins are compounds with anti-inflammatory and anti-microbial properties. The

saponins present in sarpagandha are sappanin A and sappanin B⁹². All of these secondary metabolites have been studied extensively for their potential therapeutic benefits.

The aerial sections of the *A. paniculata* have yielded diterpenoids, flavonoids, alkaloids, triterpenoids, and polysaccharides besides other phytochemicals⁹³. Diterpenoids are a class of compounds that contain two terpene groups and are found in many plants. The most common diterpenoids found in *A. paniculata* are andrographolide (Figure 3), neoandrographolide, 14-deoxy-11,12-didehydroandrographolide, 14-deoxyandrographolide, and 14-deoxy-11-hydroxyandrographolide). Flavonoids are polyphenolic compounds found in many plants and are known for their antioxidant properties. The flavonoids isolated from *A. paniculata* include quercetin (Figure 4), kaempferol, apigenin, luteolin (Figure 5), and isoorientin⁹⁴. These compounds have been shown to have antimicrobial, anti-inflammatory, and anticancer properties⁹⁵. Alkaloids are nitrogen-containing compounds that have physiological effects on humans and animals⁹⁶. The alkaloids present in *A. paniculata* include andrographine, andrographolide, andrographidine, andrographinine, and andrographinone. These compounds have been shown to have anti-inflammatory, immunomodulatory, and antioxidant properties. Triterpenoids are a class of compounds that contain three terpene groups. The triterpenoids found in *A. paniculata* include andrographolide, neoandrographolide, 14-deoxy-11,12-didehydroandrographolide, 14-deoxy andrographolide, and 14-deoxy-11 hydroxyandrographolide⁹⁷. These compounds have been shown to have anti-inflammatory, anti-allergic, and anti-tumor properties. Polysaccharides are carbohydrate molecules that are composed of several monosaccharide units. The polysaccharides isolated from *A. paniculata* include arabinogalactan, beta-glucan, and mannan. These compounds have been shown to have antiviral, immunomodulatory, and antioxidant properties⁹⁸.

Several biologically active compounds have been found in the *T. cordifolia*, including alkaloids, flavonoids, terpenoids, saponins, tannins, and phenolic acids, which have been examined for potential medicinal benefits⁹⁹. Researchers have looked at the alkaloids found in *T. cordifolia* to determine how effectively they

could offer protection against the venom of cobras and other snakes. In one study, the alkaloid berberine was found to inhibit the enzyme phospholipase A2, which is responsible for the release of venom from the fangs of snakes. The flavonoids present in the plant have been shown to have antioxidant, anti-inflammatory, and anti-venom properties¹⁰⁰. Several flavonoids, such as quercetin and kaempferol, have been found to inhibit the enzyme hyaluronidase, which is responsible for the spread of venom in the body. The terpenoids present in the plant have been studied for their ability to inhibit the venom of cobras, vipers, and other snakes. The terpenoid picroside-I (Figure 6), was found to inhibit the venom of cobras, while the terpenoid picroside-II (Figure 7), was found to inhibit the venom of vipers¹⁰¹. The saponins present in *T. cordifolia* have been studied for their ability to neutralize the venom of cobras, vipers, and other snakes. The saponintino-sporoside was found to be effective against cobra venom, while the saponin cordifolioside was found to be effective against viper venom. The tannins present in *T. cordifolia* have been studied for their ability to protect against the venom of cobras, vipers, and other snakes. The tannin corilagin was found to be effective against cobra venom, while the tannin tinosporic acid was found to be effective against viper venom. The phenolic acids present in the plant have also been studied for their potential anti-venom properties. The phenolic acid gallic acid was found to be effective against cobra venom, while the phenolic acid caffeic acid was found to be effective against viper venom.

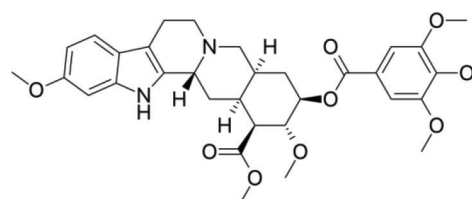


Figure 1. Reserpine.

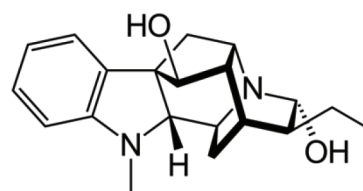


Figure 2. Ajmaline.

Flavonoids, terpenoids, and alkaloids present within *E. prostrata* are incredibly potent, making it a powerful deterrent against even the most venomous of snakes¹⁰². Kaempferol, quercetin, and apigenin are three flavonoids found in *E. prostrata* that are well-known for their anti-inflammatory and antioxidant activities. Particularly kaempferol is renowned for its capacity to inhibit the growth of cancer cells as well as its anti-allergic properties. On the other hand, quercetin is well known for its anti-cancer properties as well as its capacity to decrease inflammation. Finally, apigenin is renowned for its anti-cancer properties as well as its capacity to alleviate inflammation¹⁰³. *E. prostrata* includes a wide range of terpenoids, including ecliptol, myrcene, and eucalyptol. Ecliptol is well known for both its anti-inflammatory and repellent qualities. Myrcene is well-known for its capacity to function as a repellent as well as for its anti-inflammatory and antibacterial properties (Figure 8). Last but not least, eucalyptol is renowned for its anti-inflammatory, anti-bacterial, and repelling properties. In terms of alkaloids, *E. prostrata* contains a variety of compounds, including ecliptine, ecliptol, and ecliptamine. Ecliptine is known for its ability to act as an anti-inflammatory and its anti-cancer activity. Ecliptol is known for its anti-inflammatory and anti-bacterial activity, as well as its ability to act as a repellent¹⁰². Finally, ecliptamine is known for its ability to act as an anti-inflammatory and anti-cancer activity. All of these compounds, when found in combination with *E. prostrata*, can create an incredibly effective defence against snakes. The combination of flavonoids, terpenoids, and alkaloids found in *E. prostrata* has been used for centuries to ward off even the most venomous of snakes, making it a powerful and incredibly effective tool against snakebites¹⁰⁴. This remarkable plant has been used for centuries to protect against snake bites.

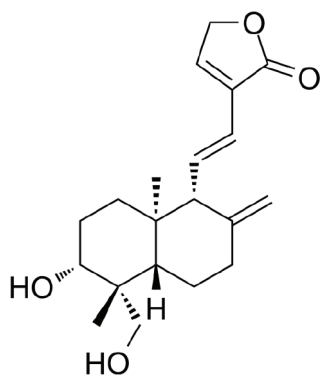


Figure 3. Andrographolide.

Achyranthes aspera has a wide range of complex phytochemicals¹⁰⁵. It includes a diverse spectrum of substances, such as asphenolics, flavonoids, terpenoids, alkaloids¹⁰⁶, lipids, fatty acids, proteins, amino acids, and carbohydrates. The primary constituents of *A. aspera* are carbohydrates, which comprise monosaccharides, disaccharides, oligosaccharides, and polysaccharides. The monosaccharides glucose, fructose, and galactose are all present in *A. aspera*. Sucrose, maltose, and lactose are examples of disaccharides that are made up of two monosaccharides. While polysaccharides are made up of more than 10 monosaccharides, oligosaccharides are made up of three to ten. Starch, cellulose, and pectin are some of the polysaccharides

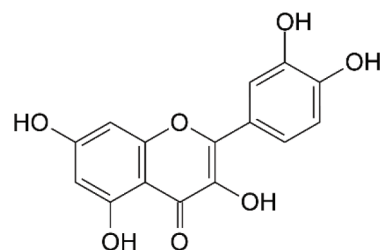


Figure 4. Quercetin.

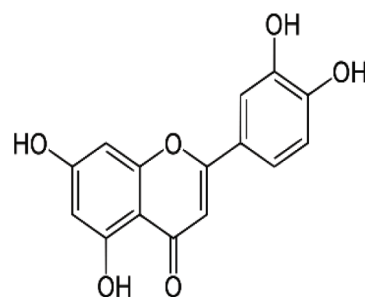


Figure 5. Luteolin.

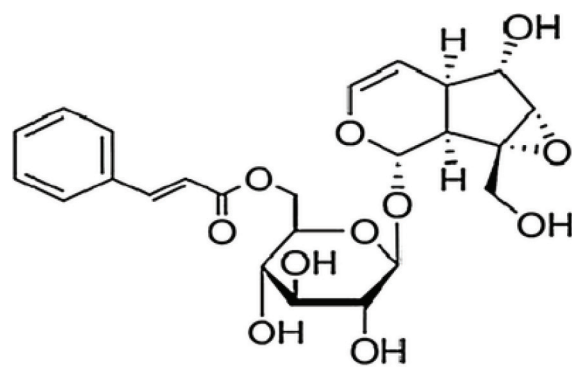


Figure 6. Picoside I.

found. Another important component of *A. aspera* is protein¹⁰⁷, which is made up of amino acids. Alanine, arginine, aspartic acid, cysteine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine are among the amino acids discovered in *A. aspera*¹⁰⁸. Triglycerides, sterols, and phospholipids constitute only some of the fats and oils that are found in *A. aspera* as lipids. The most prevalent type of lipids found are triglycerides, which are made up of three fatty acids and a molecule of glycerol. *A. aspera* contains trace amounts of sterols, a kind of lipid with four fused hydrocarbon rings. Phospholipids are also present in modest amounts in *A. aspera*. They are made up of two fatty acids, a glycerol molecule, and a phosphate group. A range of phenols, flavonoids, terpenoids, and alkaloids are also present in *A. aspera*¹⁰⁹. Studies revealed that it contains phenolics¹¹⁰, or substances with a phenol group, in the form of tannins¹¹¹, flavonoids, and lignans. *A. aspera* contains quercetin, kaempferol, and apigenin (Figure 9), three flavonoids that are substances with a flavonoid group. Studies have suggested that flavonoids may bind to the venom proteins, preventing them from binding to their target cells and thus reducing their toxicity. Limonene (Figure 10), carvone, and menthol are terpenoids, which are substances with a terpene group that are present. Nicotine, strychnine (Figure 11), and quinine are three examples of alkaloids that may be found in this plant. Alkaloids are substances that have an alkaloid group¹¹².

The tree of *M. koenigii* is home to a wide and diverse range of compounds¹¹³, each possessing a distinct set of properties and effects. These compounds include alkaloids, flavonoids, polyphenols, terpenoids, saponins, tannins, and carotenoids¹¹⁴. Carbazole alkaloids are polycyclic aromatic compounds made up of a fused nitrogen heterocyclic ring and a five-membered benzene ring. *M. koenigii* has murrayazoline (Figure 12), murrayanine (Figure 13), murrayanol, and murrayacine as its most prevalent carbazole alkaloids¹¹⁵. On the other hand, flavonoids are polyphenolic substances with a reputation for having anti-inflammatory and antioxidant characteristics¹¹⁶. They are also present in a wide variety of fruits and vegetables. Multiple phenolic groups are found in polyphenols, which are known to have anti-inflammatory, antioxidant, and anti-cancer

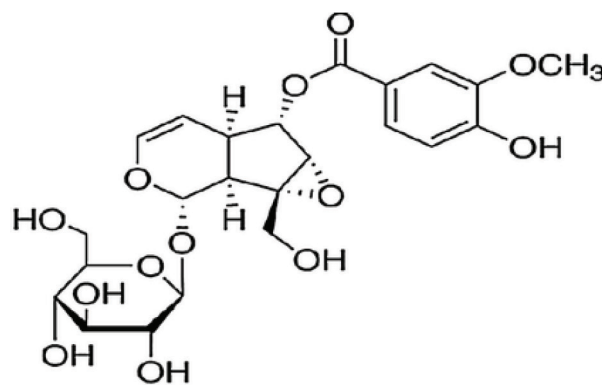


Figure 7. Picroside II.

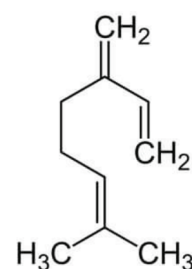


Figure 8. Myrcene.

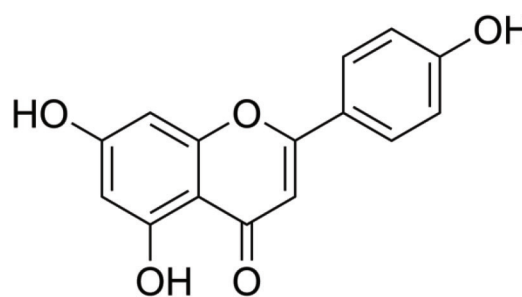


Figure 9. Apigenin.

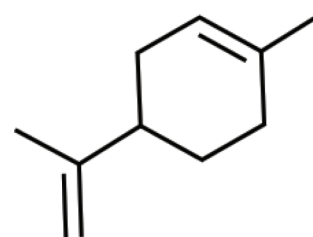


Figure 10. Limonene.

effects¹¹⁷. Terpenoids, which are chemicals formed from isoprene units with five carbons, are well-recognized for having antibacterial and antifungal effects¹¹⁸.

A succulent plant called *A. vera* is well-known for its therapeutic benefits and is frequently utilized

in many different treatments¹¹⁹. Its leaves contain several beneficial secondary metabolites, including chrysophanol, aloin, and aloe-emodin. Aloin has been shown to inhibit the activity of phospholipase A2¹²⁰, an enzyme that is responsible for the toxic effects of snake venom. In addition, aloe emodin has been shown to inhibit the activity of hyaluronidase (Figure 14), an enzyme that is involved in the spread of venom through the body. By inhibiting these enzymes, the bioactive secondary metabolites of *A. vera* can help to reduce the severity of snake bite symptoms. The sap of *A. vera* contains a chemical called aloin¹²¹, which is bitter and yellow-brown. The laxative, anti-inflammatory, and anti-bacterial effects of it are well documented. The *A.vera* sap contains a substance called aloe-emodin (Figure 15)¹²² which has purgative, anti-inflammatory, and antiviral properties. Additionally, it possesses anti-tumor qualities. *A. vera* leaves contain a yellow chemical called chrysophanol (Figure 16), which has anti-inflammatory, antibacterial, and antioxidant activities. The polysaccharides in *A. vera* are composed of sugars, such as glucose and mannose, and are responsible for the plant's anti-inflammatory, antimicrobial, and antiviral effects¹²³.

Secondary metabolites of *E. hirta* have been studied for their potential role against snake bites. The active ingredients in *E. hirta* are mainly terpenoids, flavonoids, and saponins¹²⁴. Terpenoids are a family of chemical molecules that give many plants their distinctive flavour and perfume. They also have a variety of medical uses. In *E. hirta*, the predominant terpenoids are limonene, -caryophyllene (Figure 17), and -humulene (Figure 18). These terpenoids contain anti-inflammatory and antioxidant qualities¹²⁵ that may be useful in the treatment of snake bites¹²⁶. Strong antioxidant qualities have been discovered in limonene, which may help lessen the harm done by snake venom. *E. hirta* contains the flavonoids quercetin, kaempferol (Figure 19), and rutin. These substances have anti-viral, anti-cancer, and anti-inflammatory activities. Particularly, quercetin has been discovered to have potent anti-inflammatory activities and may be helpful in the management of snake bites¹²⁷. Due to their antiviral qualities, kaempferol and rutin may help lower the incidence of subsequent infections following a snake bite. Saponins¹²⁸ present include hederagenin, oleanolic acid, and euphorbin. Hederagenin and oleanolic acid

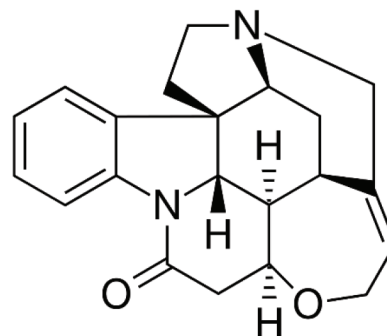


Figure 11. Strychnine.

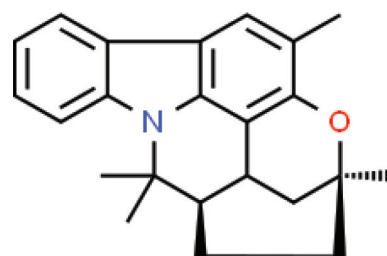


Figure 12. Murrayazoline.

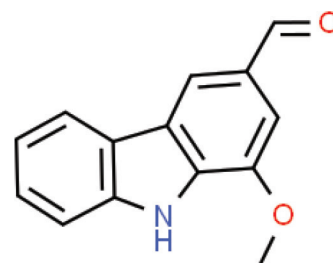


Figure 13. Murrayanine.

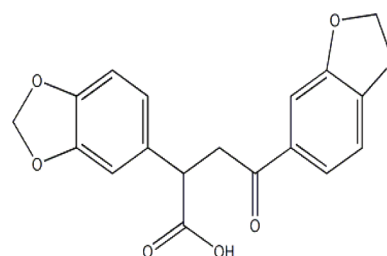


Figure 14. Hyaluronidase.

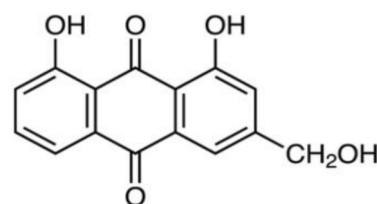


Figure 15. Aloe-emodin.

have both been found to have anti-inflammatory and analgesic properties and could be beneficial in the treatment of snake bites. Euphorbin has been found to have antifungal properties and could help reduce the risk of secondary infections after a snake bite¹²⁹.

Terpenoid chemicals, most of the secondary metabolites discovered in *C. tiglium*¹³⁰, have been investigated for their possible value in treating poisonous snake bites. Crotonic acid, dihydrocrotonic acid, and hydroxy crotonic acid are the three main terpenoids found in *C. tiglium*. Due to their anti-inflammatory and immunomodulatory effects, these substances are thought to have anti-venomic qualities. Other secondary metabolites found in *C. tiglium* include phenolic compounds, alkaloids, and flavonoids in addition to these terpenoid chemicals¹³¹. The anti-inflammatory and antioxidant properties of phenolic substances, including ellagic acid (Figure 20), gallic acid (Figure 21), and cinnamic acid (Figure 22), may assist in mitigating the effects of the venom. Alkaloids have been investigated for their ability to inhibit the activity of venomous enzymes¹³². Examples include crotonine and crotoferine. Finally, flavonoids with anti-inflammatory and anti-allergic properties, including quercetin and kaempferol, may help to lessen the intensity of the symptoms. These secondary metabolites may be useful in treating snake bites in addition to their putative antivenom capabilities. For instance, the ability of certain substances, such as cinnamic acid and crotoferine, to lessen the discomfort brought on by snake bites has been researched. Additionally, some of these substances, such as crotonine and hydroxy crotonic acid, are known to have analgesic and anti-inflammatory properties, which may assist in lessening the pain and swelling brought on by the bite¹³³. Croton oil, which is taken out of the plant's seeds, is one of the most noticeable of these metabolites. Since ancient times, this oil has been used as a traditional treatment for a wide range of illnesses, including snake bites.

V. negundo is a plant that has been traditionally used in many parts of the world to treat snake bites. It contains several phytochemicals that are effective against snake venom¹³⁴. Numerous terpenoids extracted from *V. negundo* have been proven to have anti-venom action in studies¹³⁵. These substances include caryophyllene oxide, linalyl acetate, germacrene D, linalool, and -caryophyllene. The action of snake venom is inhibited

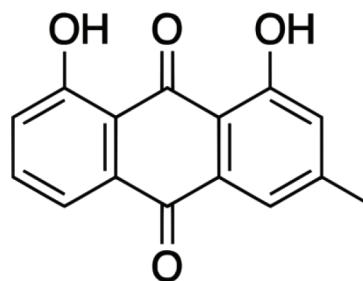


Figure 16. Chrysophanol.

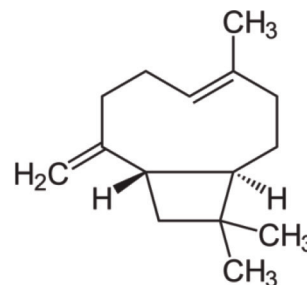


Figure 17. Caryophyllene.

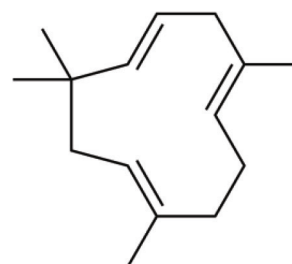


Figure 18. Humulene.

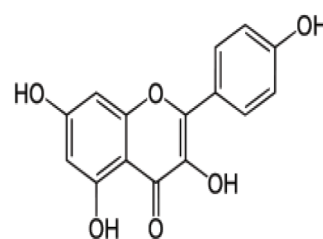


Figure 19. Kaempferol.

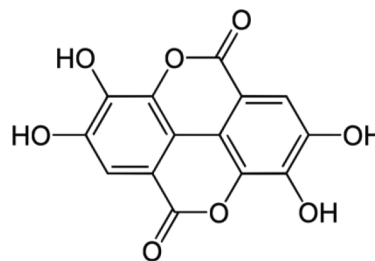


Figure 20. Ellagic acid.

by these substances, making them suitable therapeutic agents for the treatment of snake bites. The alkaloids vitexin (Figure 23), isovitexin (Figure 24), and vitexicarpin have all been isolated from *V. negundo*. These alkaloids have been shown in studies to have anti-snake venom action¹³⁶. *Vitexin* is a possible therapeutic drug for the treatment of snake bites since it has been discovered to specifically block the action of snake venom. Other substances discovered in *V. negundo*, besides its terpenoids and alkaloids, have also been reported to have anti-snake venom action. These include coumarins, phenolic chemicals¹³⁷, and flavonoids. For instance, it has been demonstrated that coumarins like scopoletin and umbelliferone suppress the action of snake venom, making them viable therapeutic agents for the treatment of snake bites. The plant is known to contain a variety of tannins, including gallic acid, ellagic acid, and catechins¹³⁸. These compounds have been shown to possess anti-venom activity *in vitro*, as well as *in vivo*.

S. xanthocarpum is a plant species that is known to possess many phytochemicals with anti-venom properties. These phytochemicals consist of alkaloids, flavonoids, saponins, and tannins. The alkaloids of *S. xanthocarpum* are divided into two groups – the tropane alkaloids and the steroidal alkaloids¹³⁹. The tropane alkaloids are the most abundant and include scopolamine (Figure 25), hyoscyamine (Figure 26), and atropine. These alkaloids act as anticholinergics, meaning they block the action of the neurotransmitter acetylcholine and can have a sedative effect¹⁴⁰. The steroidal alkaloids are less common and include solasodine (Figure 27), solanidine, and solanine. These alkaloids act as anti-inflammatory agents, which can reduce the swelling and discomfort caused by the snakebite¹⁴¹. Flavonoids that have been identified include isorhamnetin, quercetin, kaempferol, and apigenin. Isorhamnetin, the primary flavonoid in *S. xanthocarpum*, has been demonstrated in research to have anti-venom characteristics and to be able to counteract the effects of snake venom. The antibacterial, antifungal, and anti-inflammatory effects of quercetin are well-established¹⁴². Additionally, it can help lessen the pain and swelling brought on by a snake bite, as well as some of the toxins included in snake venom. Another flavonoid, kaempferol, has been discovered and is well-recognized for its capacity to lessen the

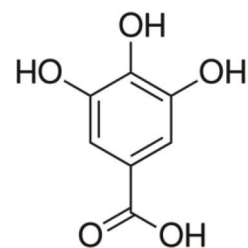


Figure 21. Gallic acid.

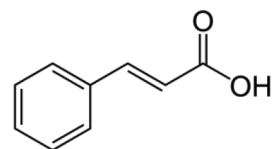


Figure 22. Cinnamic acid.

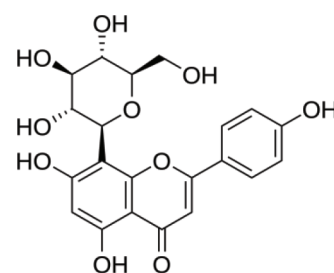


Figure 23. Vitexin.

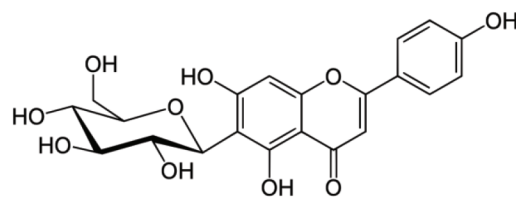


Figure 24. Isovitexin.

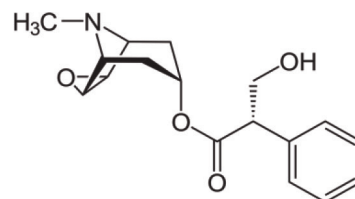


Figure 25. Scopolamine.

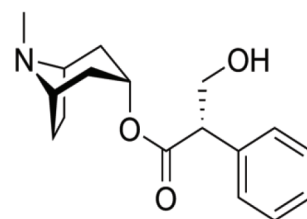


Figure 26. Hyoscyamine.

activity of certain enzymes involved in the formation of snake venom. Apigenin¹⁴³, a substance that is known to have anti-inflammatory, antioxidant, and anti-venom capabilities and is found in *S. xanthocarpum*, helps lessen the discomfort and swelling brought on by snake bites. The saponins found in *S. xanthocarpum* are mainly triterpenoid saponins, which are composed of a sugar molecule and a triterpenoid aglycone¹⁴⁴. Tannins are a class of polyphenolic compounds that are present in many plants. They have been studied for their potential to protect against snake bites.

Flavonoids, alkaloids, and terpenoids are some of the chemical constituents discovered in *A. tetraclantha* to have these qualities. Experts have been looking at the flavonoids in the plant *A. tetraclantha* to see the possibility that they may be used as a treatment for snake bites. The flavonoids luteolin, luteolin-7-diglucuronide (Figure 28), luteolin-7-glucoside, 3-hydroxy-4-methoxybenzoic acid, 4-hydroxybenzoic acid, 4-hydroxy-3-methoxybenzoic acid, and amentoflavone are the most often found compounds in this plant¹⁴⁵. Aconitine (Figure 29), cymarin, cymarin-3-O-beta-D-glucopyranoside, cymarin-1-O-beta-D-glucopyranoside, and cymarin-3-O-beta-D-glucopyranosyl-1-O-beta-D-glucopyranoside are just a few examples of the diverse alkaloid compounds¹⁴⁶ found in *A. tetraclantha*¹⁴⁷. The root of this plant contains an alkaloid substance called aconitine, which is thought to be the plant's most effective anti-venom. It possesses a wide range of pharmacological effects, including those that are anti-inflammatory, analgesic, anti-convulsant, anti-tumour, anti-diabetic, and anti-venom¹⁴⁸. Another alkaloid substance called cymarin, which is present in the root of the plant, is thought to have anti-inflammatory, anti-tumour, and anti-venom properties. The terpenes present in *A. tetraclantha* are primarily monoterpenoids, including limonene, geraniol, linalool, and pinene. Limonene is an acyclic monoterpene that has a strong citrus aroma and is found in the peel of citrus fruits¹⁴⁹. Geraniol is another acyclic monoterpene that has a sweet, rose-like aroma and is found in many essential oils. Numerous flowers contain linalool, a monocyclic monoterpene with a pleasant, flowery scent¹⁵⁰. Conifer tree needles contain the bicyclic monoterpene pinene, which has a powerful pine scent. It also includes sesquiterpenoids like bisabolene, humulene, and caryophyllene in addition to monoterpenoids. Many essential oils¹⁵¹ include caryophyllene, a bicyclic sesquiterpene with a spicy, woody scent. Another bicyclic

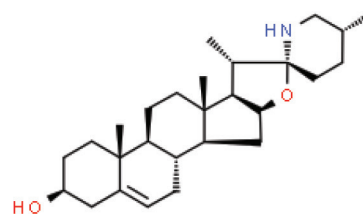


Figure 27. Solasodine.

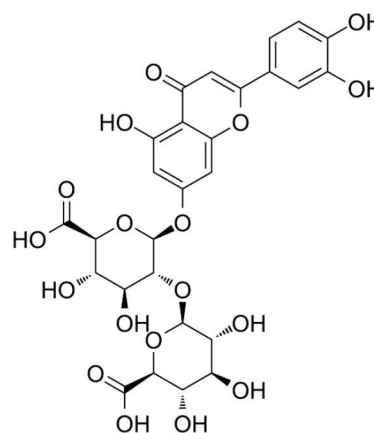


Figure 28. Luteolin-7-diglucuronide.

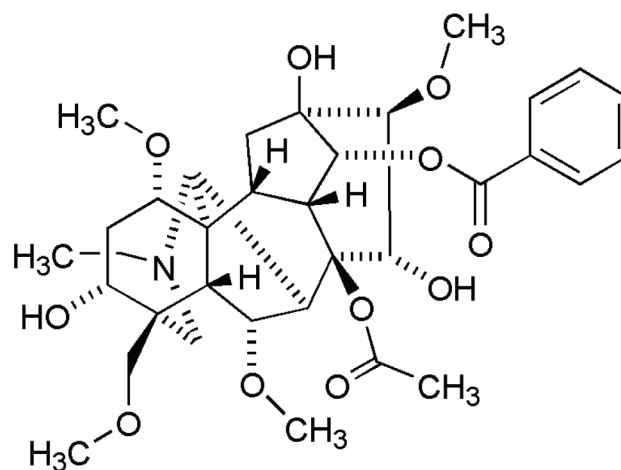


Figure 29. Aconitine.

sesquiterpene with an earthy, woody scent, humulene is present in cannabis and hops. The monocyclic sesquiterpene bisabolene, which is present in chamomile and other flowers, has a pleasant, flowery scent.

6. Future Prospects

Recent studies have provided evidence that the utilization of conventional medicinal plants and their corresponding secondary metabolites is a promising approach to treating

snake bites. The research suggests that these compounds are effective in counteracting venom and can potentially lessen the intensity of the associated symptoms.

From the collection of data, we have delved into a variety of plants that have been conventionally utilized to treat snake bites. Among these, *Sarpagandha* has exhibited encouraging outcomes in clinical trials and has gained widespread employment in modern medical practices. In addition, *A. paniculata*, *T. cordifolia*, *E. prostrata*, *A. aspera* and *M. koenigii* have been identified for their efficacy in treating snake bites although the level of their effectiveness may vary depending on the type of snake. While *Aloe vera*, *E. hirta* and *C. tiglium* have the potential to offer benefits, their usage should be approached with caution due to the potential risks involved. Lastly, *V. negundo*, *S. xanthocarpum*, and *A. tetraacantha* have traditionally been used to treat snake bites, yet additional research is necessary to fully comprehend and establish their effectiveness.

Although plants and compounds can offer a plethora of benefits, it is important to acknowledge their limitations as well. These limitations can arise due to several reasons, including the variation in potency and effectiveness that can occur due to factors such as the specific species of plant used, the preparation method employed, and the dosage consumed. Furthermore, the production and distribution of these treatments are often not standardized or regulated, leading to a lack of consistency and quality control measures.

7. Conclusion

The exploration of ethnobotany and the study of traditional medicinal plants are of great importance in the search for effective treatments for snake bites. By investigating the pharmacological properties of these plants and analyzing their secondary metabolites, researchers have the potential to discover new remedies that are not only safe but also easily accessible to diverse communities worldwide. Although there is still much to learn about these plants and the compounds they contain, recent studies have shown promising results in their efficacy against snake bites. However, further research is necessary to gain a comprehensive understanding of the advantages and challenges associated with the use of traditional medicinal plants and their secondary metabolites.

Pharmacological investigations have revealed various bioactive compounds in traditional medicinal plants that possess anti-venom and anti-inflammatory properties. These compounds can target specific components of snake venom, such as enzymes or toxins, to neutralize their effects or alleviate symptoms. Additionally, some secondary metabolites exhibit anti-inflammatory activity, which can help reduce tissue damage and inflammation caused by snake bites. The exploration of traditional medicinal plants and their secondary metabolites holds promise for the development of effective snake bite treatments. Through the integration of traditional knowledge and scientific research, researchers can identify bioactive compounds with anti-venom and anti-inflammatory properties. However, further research is needed to fully understand the potential benefits and challenges associated with the use of these plants. By conducting rigorous studies, standardizing extracts, and evaluating safety and efficacy, we can unlock the potential of traditional medicine and contribute to the development of improved snake bite treatments.

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