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Updated review on venomous snakebites, therapeutic uses and future prospects of Indian traditional medicine

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ABSTRACT: Herbal medicines can make therapeutic drugs and are an essential part of the worldwide healthcare system. Plants have always been an essential part of many indigenous peoples' life. Snakebite is a typical tropical condition that goes unnoticed. Snakebite is still a significant public health issue in many parts of the world, particularly in India, where the disease is particularly prevalent. Morbidity and mortality rates among rural and indigenous populations in the country are among the highest in the world. The problem is made worse by people delaying or refusing to seek medical care because they believe in traditional healers. People worldwide use plants to treat poisonous snakebites as folk medicine. Five hundred twenty-three plant species belonging to the 122 families are recognized as a source of drugs/compounds recognized as a possible cure for snakebite. However, this assessment is limited to a small number of essential plants used in snakebite poisoning in India. The most important groups from which various plants are employed include Acanthaceae, Amaranthaceae, Apocynaceae, Cucurbitaceae, Euphorbiaceae, and Fab Lamiaceae and Moraceae. In this investigation, phytocompounds with anti-venom action were discovered in 29 plants belonging to 22 families used as a traditional medicine to treat poisonous snakebites.

1. INTRODUCTION

Every year, over 50000 people in India are killed by snake bites. Snakes are cold-blooded animals, which means they cannot adjust their internal body temperature. Their body temperature changes due to their surroundings (Simpson & Norris, 2007). Snakes come in over 3000 different species and can be found worldwide. Only 20% of snakes (600 species) are venomous, and only 7% (200 species) can kill humans. There are over 270 snake species in India, with around 60 of them being venomous species, out of which four are the deadliest refereed as big four: Russell's viper (*Daboia russelii*), Common krait (*Bungarus caeruleus*), Indian Cobra (*Naja naja*), Saw-scaled viper (*Echis carinatus*) (Figure 1).

Snake bites can result in modest puncture wounds up to life-threatening conditions. A non-toxic bite from a venomous snake can generate no symptoms, or symptoms of various severities can appear immediately or after a considerable period, up to 36 hours after exposure. The signs and symptoms can be deceiving. A person may show no signs or symptoms

at first but eventually develop respiratory problems and go into shock (Gutiérrez et al., 2017). According to the most afflicted body system, toxic snake venoms might be vasculotoxic, neurotoxic, or myotoxic. The vasculotoxic bite (mainly by snakes of the Viperidae family) causes symptoms ranging from local pain and edema to coagulopathy and cardiac collapse. Ptosis, dysphonia, dysphagia, dysarthria, difficult breathing, and death are symptoms of descending cranial nerve paralysis caused by neurotoxic snakes (such as the cobra). Tissue injury, muscular swelling, discomfort, muscle breakdown, and myoglobinuria result in renal failure in myotoxic snakes (mainly the Hydrophadae) (Domanski et al., 2020).

1.1. Morphological characters of Russell's viper

Russell's viper in India is the leading cause of death. It may be found practically everywhere in India. The body is slender (up to 1.5 meters) the color of the body is light brown. Rings of dark black or brown color can be found all over the body. Venom is a very harmful Hemotoxic (Kotpal, 2010).

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1.2. Morphological characters of Common krait

Its color ranges from blue-black to black. Along the body, there are several white or light-coloured crossbars. The head is slender. The shape of the body is cylindrical and elongated. The upper jaw's third and fourth supra labial is vast and touches the eye, with hexagonal expanded dorsal shields. Venom is very harmful to the nervous system (Kotpal, 2010).

1.3. Morphological characters of Indian Cobra

The color of the body varies from brown to black and is 2 meters long. It dilates the neck and has a black mark on the dorsal side of the skull. The third supra labial shield touches the nose and eye. Venom is poisonous to the nervous system (Kotpal, 2010).

1.4. Morphological characters of Saw scaled viper

It is the most common viper in India after the Russell viper. Color ranges from light to dark, sandy brown to grey, and the smallest of the primary four (0.3 to 0.5 meters). Camouflages are visible in the backdrop, and they have a zigzag darker pattern all over their bodies. Large eyes and a wider head than the neck coils its body into an eight shaped form. Scales are abrasive, and rubbing them produces the sound of a saw cutting wood. Venom is harmful hemotoxic. Hematotoxins are toxins that damage red blood cells, blood clotting, organs, and tissues (Kotpal, 2010).

2. CLINICAL FEATURES OF SNAKEBITE

Despite puncture marks indicating the snake's teeth pierced the skin, a percentage of people bitten by venomous snakes (10% to >60%) will experience negligible or no toxicity-related symptoms (envenoming). The symptoms and signs are exacerbated by fear, medication side effects, and the snake's venom. Even non-envenomed patients may experience flushing, dizziness, and shortness of breath, as well as chest tightness, tremors, perspiration, and acroparaesthesia. Tight straps can cause blocked and ischemic limbs, bite incisions can cause bleeding and sensory loss, and herbal treatments are frequently associated with vomiting. There is swelling, pain, and bruising up the limb, lymphangitis, and sensitive expansion of regional lymph nodes. People bitten by European *Vipera*, *Daboia russelii*, *Bothrops* sp, Australian Elapids, and *Atractaspis engaddensis* may experience early syncope, vomiting, colic, diarrhoea, angioedema, and asthma. The symptoms of severe envenomation include nausea and vomiting (David & Warrell, 1987).

2.1. Laboratory Investigations

There are simple laboratory tests that can detect a snake bite, such as arterial blood gases, electrolytes, complete blood counts, coagulation profiles and creatinine phosphokinase levels, and blood and/or myoglobin in urine (Fuchs et al., 2019). The bite area should be examined for puncture wounds caused by fangs, as well as local symptoms of inflammation, redness, and/or

edoema (Benjamin et al., 2019).

2.2. Snakebites Treatment in Hospital

The species, amount, and type of venom used in most snakebite cases are unknown. In theory, patients should be hospitalised for at least 24 hours. Local edoema usually appears within 15 minutes of a large pit viper envenoming and 2 hours for most other snakes. A krait (*Bungarus*) bite or other elapid or sea snake bite may not cause local envenomation. Fang markings may be difficult to see. Envenoming causes pain and sensitive swelling of lymph nodes draining the bite area. Spontaneous bleeding frequently occurs in the patient's tooth sockets and the nose, eyes, skin, and gastrointestinal system. Coagulable blood indicates venipuncture sites and other lesions. First, neurotoxic envenoming causes ptosis. For example, respiratory muscle power should be reliably measured by vital capacity: trismus, widespread muscle soreness, and brownish-black urine. A 20-minute whole blood clotting test should be performed if procoagulant venom is suspected. Keep track of their vital signs and new symptoms. A parenteral infusion of polyclonal anti-venoms from horses or sheep is commonly used in hospitals to treat snakebites (David & Warrell, 1987; Mehta & Sashindran, 2002).

3. INDIAN TRADITIONAL MEDICINE

Traditional medicine has a long history in India. India's medical literature contains a wealth of knowledge on folklore and traditional characteristics of therapeutically beneficial natural ingredients. Ayurveda, Siddha, and Unani are some of the systems used in Indian traditional medicine (Mukherjee, 2001; Vinothkumar et al., 2019). Despite the overall efficacy of traditional therapy, other venom inhibitors, both synthetic and natural, are needed to supplement or replace the usual anti action. Venom's traditional herbal medicine for snakebite therapy is widely available in rural regions, even if the efficacy of some traditional remedies is questionable in some situations. Snakebites can be treated in various ways, including applying plant leaf juice paste topically, eating leaves and plant components, and drinking herbal syrup. Medicinal herbs are used as antidotes for snakebites in India and other parts of the world. They can be used in conjunction with other anti-snake venoms or botanical allies or on their own. As a result, research into herbal antidotes to snake venom is critical for snakebites treatment (Bhandary et al., 1996; Samy et al., 2008).

3.1. The Theory of Indian Naattu Vaidya

Naattu Vaidyas (plant doctors) and older people with folk knowledge about the benefits of common spices and plants can be found in India. Naattu Vaidyas (plant doctors) and older people with folk knowledge about the benefits of common spices and plants can be found in India. Their native health beliefs, abilities, and cultural traditions are effective in treating a range of illnesses. Some older women with childbirth experience are well-versed in folk cures for common health issues, especially teenage girls, breastfeeding mothers, and pregnant women.

Russell's viper (*Daboia russelii*)**Common krait (*Bungarus caeruleus*)****Indian Cobra (*Naja naja*)****Saw scaled viper (*Echis carinatus*)**

Figure 1. Big Four - Deadliest Indian Snake. Source: Common Indian snakes: a field guide (Whitaker, 2006)

Mother Nature is the one who nurtures us, according to Indian mythology. Hippocrates also stated, "Nature heals, not the doctor." Herbals contain an abundance of medicinal compounds that can be used to treat a variety of ailments and to maintain and improve human health. Every plant, according to Ayurveda, has medicinal powers; all users have to do now is find the right person to demonstrate this. Because several modern drugs have harmful side effects, an increasing number of people in both established and emerging countries are turning to medicinal plants (Patel et al., 2010) .

It is widely assumed that mastering knowledge is the key to any revolution. India is home to nearly 10% of all species on the planet. Indians have employed a wide range of herbs for centuries in ritual and cultural activities. Indians have employed a wide range of herbs for centuries in ritual and cultural activities (Patel et al., 2010) . Consequently, many species are on the verge of extinction due to rapid population increase, disregard for environmental regulations, and global climate change. As a result, the food chain, way of life, cultural and ceremonial practises of thousands of Indians have

all suffered. Many conservation organisations in India are working to stop this decline in biodiversity to preserve it.

3.2. Snakebite Treatment with Indian Medicinal Plants

The current review intends to consolidate knowledge on traditional medicinal herbs used for snakebite management in various locations of India. Future researchers will better understand the various methodologies to treat snakebites due to this research. For snakebite treatment, at least 523 different plant species from 122 different families are effective (Upasani et al., 2017) . However, this assessment is only applicable to a small group of essential plants commonly used in snakebite poisoning in India. The most important groups from which various plants are employed include Acanthaceae, Amaranthaceae, Apocynaceae, Cucurbitaceae, Euphorbiaceae, Fabaceae, Lamiaceae, and Moraceae (Upasani et al., 2017) See (Figure 2) .



Figure 2. The herbal medicines stated below are the most widely used to cure snakebites in India. 1. *Abrus precatorius* Linn, 2. *Achyranthes aspera* Linn, 3. *Acorus calamus* Linn, 4. *Alangium salvifolium* Linn, 5. *Albizia lebbekii* Linn, 6. *Andrographis paniculata*, 7. *Aristolochia indica* Linn, 8. *Bacopa monnieri* Linn, 9. *Boerhaavia diffusa* Linn, 10. *Bombax ceiba* Linn, 11. *Buchanania lanzan* Spr, 12. *Butea monosperma* Lamk, 13. *Calotropis gigantea* Linn, 14. *Cassia fistula* Linn, 15. *Cissampelos pareira* Linn, 16. *Clitoria ternatea* Linn, 17. *Corallocarpus epigaeus*, 18. *Curculigo orchioides* Gaertn, 19. *Gloriosa superba* Linn, 20. *Gymnema sylvestris*, 21. *Hemidesmus indicus* Linn, 22. *Mimosa pudica* Linn, 23. *Moringa oleifera* Lam, 24. *Musa paradisiaca* Linn, 25. *Piper nigrum* Linn, 26. *Rauwolfia serpentina* Linn, 27. *Strychnos nuxvomica* Linn, 28. *Vitex negundo* Linn, 29. *Leucas aspera* Spreng.

3.2.1 *Abrus precatorius* Linn.

Three grams of Leaf or root mixtures, along with seeds, are ground and mixed with water or milk. Leaf or root mixtures and seeds are ground and mixed with water or milk. To treat a toxic bite, use root powder applied topically twice a day for 5–7 days. To consume with lemon juice, combine a pinch of *Abrus precatorius* seed powder with a pinch of *Andrographis paniculata* seed powder (Das & Tag, 2006; B.R. Rao & Sunitha, 2011; Samy et al., 2008; Vijayagiri & Mamidala, 2012; Yabesh et al., 2014).

3.2.2 *Achyranthes aspera* Linn.

Orally, the extract from the whole plant or root is taken. For three weeks, the root paste is also used. Snakebite therapy was also influenced by *Achyranthes bidentata* Blume and *Achyranthes porphyristachya* (B.R. Rao & Sunitha, 2011; Samy et al., 2008).

3.2.3 *Acorus calamus* Linn.

The rhizomes are ground into a paste and mixed with warm water before being applied to the affected area (Samy et al., 2008; Alagesaboopathi., 2013; Sarkhel., 2014).

3.2.4 *Alangium salvifolium* Linn.

Fifteen grams of bark is crushed with 10–12 black peppercorns and 60 g animal fat every two hours to treat snakebite. Internally, a decoction of root bark is taken (Alagesaboopathi, 2013; B.R. Rao & Sunitha, 2011; Samy et al., 2008).

3.2.5 *Albizia lebbek* Linn.

Bark paste is utilised (P.R. Sahu et al., 2015).

3.2.6 *Andrographis paniculata*

To make a decoction, the leaves are combined with those of *Andrographis alata*. Externally, a decoction or extract is used, and there have also been reports that the Khamti tribe of Arunachal Pradesh, India, utilises seed powder orally to cure snake poisoning in the case of *Andrographis paniculata*. Plant paste with mustard oil is used to wounds by the Korku community in central India (Das and Tag (2006); Kadel and Jain (2008); Mohan (2008); Samy et al. (2008); Yabesh et al. (2014).

3.2.7 *Aristolochia indica* Linn.

Fresh roots are mashed in water with *Rouwalfia serpentina* and consumed twice a day (3 days). Snuffing root powder, drinking root juice, and applying root paste locally are all options. The leaves of *Aristolochia bracteolata*, a different species, are mashed into a paste and applied locally, while the infusion is eaten orally (Mohan, 2008; Samy et al., 2008; Vikneshwaran et al., 2008).

3.2.8 *Bacopa monnieri* Linn

On treat, apply a mixture of juice and castor oil to the skin. Orally, a decoction of leaf powder combined with warmed cow's

milk (Alagesaboopathi, 2013; Lal & Singh, 2012).

3.2.9 *Boerhaavia diffusa* Linn.

Hog Weed is another name for it. It is a diuretic, and an expectorant used to treat abdominal pain. The leaves' juice is applied to the skin for seven days and taken orally. Additionally, Linn's *Boerhaavia repens* is beneficial in treating congestive heart failure (Singh & Maheshwari, 1994).

3.2.10 *Bombax ceiba* Linn.

Flowers, fruits, and leaves are mixed and administered to the bitten area (Lal and Singh (2012); P.K. Sahu et al. (2014).

3.2.11 *Buchanania lanzan* Spr.

It has been mentioned in many studies and reviews as being generally applicable, but the preparation technique and parts used are unknown (Jeetendra & Kumar, 2012; P.K. Sahu et al., 2014).

3.2.12 *Butea monosperma* Lamk.

This plant's leaves have traditionally been used to make environmentally-friendly plates for serving food. The leaves of this plant have traditionally been used to make environmentally-friendly plates for serving food. The swelling is treated using a bark based paste. An oral remedy is a lemon juice-one seed paste (Jeetendra & Kumar, 2012; Kumar & Choyal, 2012).

3.2.13 *Calotropis gigantea* Linn.

Dedicated to Hanuman, a deity of mythology, the plant's leaves and blooms are given to him as offerings. Hanuman is renowned for his wisdom, physical strength, loyalty, and politeness, among other qualities. The root or bark is mashed into a paste, formed into pills, and taken orally for relief. The latex from the leaves of this plant is administered to the bitten area. *Calotropis procera* (Ark, Rui) is another species that can help with healing (B.R. Rao & Sunitha, 2011; Samy et al., 2008).

3.2.14 *Cassia fistula* Linn.

Orally, root bark paste and decoction are taken with black pepper. In addition, a stem bark paste is administered to the bitten region. Snakebite treatment also includes *Cassia alata*, *C. obtusifolia*, *C. occidentalis*, *C. sophera*, *C. tora*, and *C. glauca* (Jeetendra & Kumar, 2012; P.K. Rao et al., 2015).

3.2.15 *Cissampelos pareira* Linn

Once a day for five days, use the root paste with long pepper (Basha, 2012; Kumar & Choyal, 2012).

3.2.16 *Clitoria ternatea* Linn .

The root extract is combined with *A. indica* root and *Rauwolfia serpentina* root (Masih et al., 2013; P.K. Sahu et al., 2014).

3.2.17 *Corallocarpus epigaeus*

Three to seven times a day, a decoction produced from roots is taken orally (Basha, 2012; Nagaraju & Rao, 1990).

3.2.18 *Curculigo orchioide Gaertn*

On the afflicted area, the root paste is administered topically (Selvanayagam et al., 1995; Yabesh et al., 2014).

3.2.19 *Gloriosa superba Linn*

To provide relief, the root paste or tuber paste is applied externally to the bitten area for 2–5 days or until relief is obtained (Samy et al., 2008).

3.2.20 *Gymnema sylvestre*

The most often used anti-diabetic medicinal herb to treat antiphidian symptoms. During the first four days, an oral tincture of root or leaf powder is administered. (Samy et al., 2008; Jeetendra & Kumar., 2012; Nagaraju & Rao., 1990).

3.2.21 *Hemidesmus indicus Linn.*

In addition to applying the root paste twice or three times a day, an aqueous extract of the root is taken orally (Mohan, 2008; P.K. Sahu et al., 2014; Samy et al., 2008; Thirumalai et al., 2010).

3.2.22 *Leucas aspera Spreng.*

Both the leaf and the root are advantageous. To treat the bitten area, leaf paste or crushed leaf is applied physically and orally. For four days, the root juice is combined with goat's milk three times a day (Upasani et al., 2017).

3.2.23 *Mimosa pudica Linn*

The plant as a whole has health benefits. During a single day, the whole plant extract is administered twice a day for seven days. Ground leaves are ground into a paste and applied topically to the afflicted area to relieve the pain (Masih et al., 2013; P.K. Sahu et al., 2014; Samy et al., 2008; Thirumalai et al., 2010).

3.2.24 *Moringa oleifera Lam*

Roots and barks are used. It is necessary to take the bark extract orally for three days, while the bark and root tincture must be administered physically (Samy et al., 2008; Rao et al., 2015).

3.2.25 *Musa paradisiaca Linn.*

An oral administration of a plant extract is performed (Samy et al., 2008; Thirumalai et al., 2010).

3.2.26 *Piper nigrum Linn.*

Snakebites are treated with a mixture of seed powder and butter that is taken orally. Orally, a flower paste with ghee is administered for four days (P.K. Rao et al., 2015; Samy et al., 2008).

3.2.27 *Rauwolfia serpentina Linn.*

Rawolf refers to a snake like structure. In India, there are over 86 different species of rauwolfia, but *R. serpentina* is the most widely used and compelling antiophidian plant due to its unique combination of characteristics. The leaves and roots of this plant are used as an antidote. Crushed roots and leaf buds are mixed with milk to make a paste that may be applied both internally and topically to the affected area (Mahishi et al., 2005; Samy et al., 2008).

3.2.28 *Strychnos nuxvomica Linn.*

In order to treat, the root bark juice in cow's milk is massaged onto the skin three to four times a day. The name is a combination of two terms: the root bark juice in cow's milk is used to treat. The powdered seed is also used in some recipes (Samy et al., 2008; Yabesh et al., 2014).

3.2.29 *Vitex negundo Linn.*

The root extract is taken orally, and the bite area is treated with a paste made from the leaves of the plant (Samy et al., 2008; Yabesh et al., 2014).

4. FUTURE DIRECTIONS AND CHALLENGES

The relationship between Indian medicinal herbs and the treatment of snakebite patients is explored in this review study. The Indian medicinal plants, we assumed, would be anti-venomous. Treatment with Indian medicinal plants has limited pharmacology and molecular effects, which is a major feature of this assessment. Snakebite is one of a major public health problem. We may conclude that medicinal plants have a great future. To further understand the processes behind the effects of Indian medicinal herbs in snake bite patients, more pharmacogenomics research and clinical trials are needed.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest associated with this work.

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AUTHOR CONTRIBUTIONS

VG, NA - Research concept and design; VG - Collection and/or assembly of data; VG - Data analysis and interpretation; VG, SD - Writing the article; SD, OG - Final approval of the article.

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