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REVIEW ARTICLE

Herbs as Antidote for Snakebite Treatment in India — Traditional Practices and it's Future Prospects — A Review

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Abstract

Snakebite is a life-threatening neglected tropical infection reporting high mortality across the world including India. Out of the available yearly statistics, this occupational hazard caused 4.5-5.4 million people and nearly 1,38,000 fatalities were reported globally. Several factors such as the low availability of antivenom, inadequate health centers in rural areas, poor transportation facilities affected the higher number of morbidity and mortality cases of snakebite. The prognostic and diagnostic approach towards the snake bite infection is difficult due to its complexity in venom. The conventional therapy is polyvalent antivenom derived from horses or sheep, with its limitations. Traditional physicians use plants and other herbs as their sustainable remedy for snake bite treatment. Nearly, 523 plant species from 122 families reported their neutralizing property against toxic venom. The secondary metabolites extracted from plants are capable of reducing the toxic effects of the venom. Many research works have reported the inhibitory potential of the plant compounds against the snake venom enzymes. Therefore, there is a necessity for increasing therapeutic studies on plant metabolites and the development of an antidote for the better treatment of snakebite. This review article discusses various herbal plants used for snake bites in India.

Keywords: Antidote, Herbs, Herbal Plants, Secondary Metabolite, Snakebite, Snake Venom

1. Introduction

Snakebite envenomation is an occupational health hazard mainly in tropical regions. The specific hardship of envenoming is incredibly hard to gauge because records on snakebite occurrence seem to be infrequent, and current evidence observations are frequently unreliable or not reflective of larger geographical areas. The occurrence of different types of snakes and their highest morbidity due to snake bites is decidedly in south and southeast regions. Several pivotal factors are responsible for the increased rate of mortality in rural areas including inadequate health care, poor transportation facilities, delay in the administration of proper anti-venom, etc.[1] Snakebite is one of the Neglected Tropical Diseases (NTDs) which causes physical complications even after the treatment. The serpent bite envenoming primarily affects the poor which contributes to further poverty. Despite the enormous hardship on survivors, the disease has previously been

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virtually neglected, with few resources dedicated to the advancement of new therapies and diagnostics. There is a need to reduce fatality by implementing first aid treatment. The recent usage of commercially available antivenom in terms of enhancing its efficacy towards venom and reducing side effects caused by bite is the need of the hour. The currently available monovalent antivenoms are employed when threatening snake species are recognized. However, the polyvalent antivenoms are administered in lack of understanding on offending snake species. The potential of polyvalent antivenoms to neutralize a huge spectrum of venoms may come at the expense of lowered efficacy, as when the relative amount of antibodies in a polyvalent antivenom that specifically targets toxins of a particular snake is commonly not as high as that of the percentage of antibodies in a monovalent antivenom designed to target the same venom substances. The current available polyvalent snake anti-venom is required at a bulky dose in some victims[2] and is not much effective for a few snakebites from vipers[3]. Since exploring into substances as envenoming therapies is still in its early stages, a percentage of preclinical studies employing repurposed particles have shown impressive outcomes, such as the broad inhibitory activity of crucial toxin families across several snake species. For example, varespladib, a PLA2 inhibitor that was initially developed to treat coronary heart disease and has previously completed phase III trials shows an antivenom activity to decrease the mortality of mice caused by a viper and elapid from the various geographical area. Batimastat is a matrix metalloproteinase (MMP) inhibitor originally developed as a cancer therapy, also marimastat (developed for cancer) in which both share structural similarity was observed to potently suppress venom activity *in vitro* study of envenoming and to prevent dermonecrosis, deadliness, and hemorrhage induced by snake venom toxins in animal studies[4].

According to the data from WHO (2020), the available information shows that 4.5 to 5.4 million individuals are suffering from snakebite every year. Of these, 1.8 to 2.7 million people experience clinical diseases, and 81,000 to 138000 people lost their lives due to complications. In the newsletter published on 10 July 2020 from WHO, the authors calculated that between 2000 to 2019, India has around 1.2 million victims from snakebite. This shows an average of 58,000 victims suffered every year. Half of the victims are between the age 30 and 69, and more than a quarter of the kids under the age of 15 are affected by snakebites. 70% of the reported deaths between 2001– 2014 are from Andhra Pradesh, Bihar, Uttar Pradesh, Gujarat, Jharkhand, Odisha, Rajasthan, Madhya Pradesh, where people rely on agricultural farmlands for livelihood. The studies show that more risk to snakebites is during the rainy season. The WHO has a goal of decreasing half the number of deaths from snakebites by the year 2030. (WHO).

The variation in the composition of the venom in different snakes causes significant complications when the antivenom is not given accurately[5]. One approach is through a study on potentially active synthetic or natural plant components that inhibits the enzymes present in the venom. The snakebite victims rarely visit rural clinics or hospitals, instead, they depend on traditionally followed medications. In India, there are a variety of plant species used as folk remedies for snakebite treatment. Studies show that there are about 523 medicinal plants from 122 families which has medicinal properties to inhibit the venom from the snake[6]. Nowadays, plants are used for many new drug preparations and formulations for the better treatment of diseases[7.] The medicinal plants have secondary bioactive active compounds that are active against snakebite poison, which can be used as a valuable substitute to the currently available antivenom. In rural and tribal areas, despite the introduction to modern medicines, a large segment of the population depends on folklore methods and plant medications to cure diseases. Thus, the traditional form of medications from plants helps to lead new inventions of drugs or an antidote against snakebite[8]. Plant metabolites have been defined to be used to counteract the efficacy of snake venom. Because it will be designed to optimize infectious disease, prevent pain, help relieve symptoms, enhance energy levels and modify immune response, for improved health and longevity. Snake bite envenomation can be treated with a mono herbal compound or in combination with application areas[9] This review provides a background and summary of a few traditional herbal treatments and management for snake envenomation. The indigenous knowledge from traditional practitioners is broadly examined through various scientific researches in the current scenario. The standard of evidence in reviewed research constrained the scope of this study. Within this regard, an effort is made to assemble available information about certain medicinal plant's novelty for snakebite treatment. Some scientific researches have proven the effectiveness of many of these preparations, and some of those are astonishingly effective for envenomation in different snake species. The applicability of plant metabolic extracts in the published report has demonstrated hope in multiple ways in the management of snakebite envenomation to diminish difficulties and progresses patient's outcomes.

2. Venomous Indian Snakes

The deep forests, the ocean, the grassland, and the desert provide a wide variety of best habitats for snakes in India[10]. Considering their wide range throughout the Indian subcontinent, they are superintended for the cause of medically significant snakebites. There are about 270 species across the nation with different degrees of toxicity. Out of which 60 species of snakes are considered to be poisonous and are responsible for clinically serious envenomation. Serpent species like *Naja naja* (cobra), *Echis carinatus* (saw scaled viper), *Daboia russelii* (russell's viper), and *Bungarus caeruleus* (common krait) are the big four snakes capable of delivering most of snakebite across the nation. The *Naja naja* is the highly poisonous snake and *Bungarus caeruleus* is the lethal and threatening snake causing neuromuscular paralysis[11]. Snakes usually attack people involved in agriculture and construction works. The board grass/foliage covering is suitable for hiding snakes and attacking people when they have been disturbed by unintentional walking on or pricking them, especially vipers. The common krait bites workers and farmers, particularly during the night[12].

Besides the widely distributed "top 4", there are a variety of many other species in localized areas of the country, considered to be likely to cause envenomation. *Naja kaouthia* which is seen on the north-eastern side of India induces more bites than *Naja naja* with equivalently serious effects. The *Bungarus walli*, *Bungarus sindanus*, *Bungarus niger* are seen in the north-east, or west regions and cause fatal poisoning and other consequences. *Ophiophagus hannah* is the most life-threatening snake and is seen very rarely in some parts of India. There are around 15 Pit-vipers (*Crotalinae*) species in India where venoms of neither of these are protected by commonly used polyvalent anti-venom of India. The sea-snakes like *Hydrophiinae*, *Laticaudinae* causes a few bites in the coastal regions of India[13]. A study has mentioned,[14] the lethal dose value of Sri Lankan *Naja Naja* is more toxic compared to the LD_{50} values of *Naja naja* seen in India. They concluded that the lethality of venom between and within species varies due to geographical area, food, age, taxonomic differences, and sex of the snake.

3. Venom – The Mysterious Biological Fluid

Snake venom has a systemic distribution of non-toxic and toxic elements. The venom has protein (enzymes), metal ions, organic molecules (nucleotides), and peptides that are produced by living creatures (animals) to protect themselves from other living species. In serpent species, the venomous gland generates saliva in the form of venom and is transferred through fangs. The snakes like *Naja naja* has fixed front fangs and Vipers with hinged front fangs enabling lengthier fangs as well as causing deep tissue penetration[15]. The main enzymes are phospholipase A2 (PLA2), metalloproteinases, serine proteases, L-amino acid oxidases, 3 finger peptides, c-type lectins, disintegrins, etc. The hemotoxic, cytotoxic, neurotoxic are the main pharmacological effects caused due to snakebite. The enzyme PLA2 is the crucial cause of the neurotoxic and myotoxic effects of snake venom[16]. There are hundreds of toxic compounds present in a single snake species. Despite the ongoing discovery, there are still many serpent species venoms to be uncharacterized. The snake toxins are also used in the field of medicine for treating various pathogenesis[17].

The enzyme PLA_2 is seen more compared to other substances in many of the serpent families. The families like Hydrophidae, Elapidae, Viperidae have more amount of PLA_2 and Colubridae have less amount of PLA_2 content in venom[18]. The physiopathology of crude venom encompasses regional effects such as hemorrhage, extracellular matrix deterioration, muscle degradation, edema, and systemic effects such as cardiotoxicity, deformation in the hematological pathway, neurotoxicity, and myotoxicity. The efficacy, content, velocity of dispersion of target-specific venom toxins from a wound site into circulation are known to affect systemic effects. The venom components engaged in the diffusion are described as "spreading factors," and these comprise hyaluronidase, metalloprotease, and myotoxins[19]. *Bungarus caeruleus* contains β bungarotoxins, which are presynaptic neurotoxins along with PLA2 of venom fractions cause neuromuscular paralysis[20]. With the wide difference in the content of venom in different snake species, the creation of a proper antivenom is difficult at the preclinical stage itself. Studies states that toxic genes present or absent in the genome level determine significant changes in the venom composition of snakes[5].

4. Symptoms and Identification of Bite

The snakebite is a stressful experience, the physiological issues may continue long after the physical recovery. Almost all people are scared of snakes and the unreasonable fear is termed as "ophidiophobia". People worship snakes as representatives of God mainly in the regions of India and Africa. The bite of the snake is unexpected and quick which causes nervousness in the victim[21]. The proteins present in each superfamily contribute remarkable characteristics of structural similarities but differ in their pharmacological effects[22]. Snakebite causes symptoms such as bleeding from the wound, vision problems, heating of the eyes, loss of consciousness, nausea, fatigue, heavy sweating, fang mark in the skin, fever, elevated appetite, lack of muscle strength, vomiting and diarrhea, loss of sensation, rapid heartbeat, tissue death, extreme pain, discoloration of the skin, inflammation at the bite site, dizziness, etc. *Bungarus caeruleus* bite normally does not develop any local effect whereas vipers bite causes inflammation and blood from the wound in the victim[12].

Serpent detection or symptoms identification caused by the bite is crucial for deciding medication sometimes, it is not often feasible. Preferably, the killed snake has been carried along with the victim or local information is necessary for places that have a high rate of snakebite. The snakes like cobras, vipers, krait cause many snakebites across the country. In some places like city areas where polyvalent antivenom is available; detection of snakes has given less importance[12]. Many people believe that all snake species bite causes envenomation. The venomous snake bites are sometimes dry bites that do not provide symptoms in the victim. The non-venomous snakebites are common and do not show symptoms. But most people show anxiety problems if they are bitten by non-venomous snakes[23].

5. Traditional Knowledge on Snakebite Treatment

In India, rural health centers are insufficient, snakebite victims primarily rely on herbal formulations through traditional healers. Traditionally various plant types, the section used, mode of administration rely on its ethnobotanical value including its potency of use against snake venom[24]. The urban and rural citizens have maintained a substantial number of traditional experiences and knowledge of herbal constituents growing in their local areas. The information on indigenous knowledge on herbs is gathered from local communities and herbal physicians[25].

In the medical system of India, traditionally "Vaidya" is regarded as the herbal doctor, who diagnoses diseases and drugs for treatment. Ayurveda practitioners claim that any plant on the planet has important medicinal properties hence, the growing number of citizens in developed and emerging nations are using plants for the better cure of infections. The preparation is generally by using stone blocks or bits of wood to smash plants or portions of them. The juice or paste from leaves, bark, root, seed, stem, and rhizome extracts is administered orally or topically applied on the bite site is intended to neutralize snake envenomation. In the report,[6] states the indigenous plants belong to families of Fabaceae, Acanthaceae, Rubiaceae, Asteraceae, Apocynaceae, Lamiaceae, Caesalpiniaceae, Arecaceae, Curcurbitaceae, Euphorbiaceae, and Zingiberaceae. In recent years, research into the traditional usage of herbal plants has gained significant attention from the scientific community. About 25% of plants are prescribed in drug formulations in pharmaceuticals all over the world[26].

Medicinal herbs are prescribed either individually or in conjunction with anti-ophidian venom compounds or with supporting herbs. An alternative for the currently available conventional anti-venom drug, secondary metabolites is isolated from the plant extracts with properties such as anti-hemorrhage, anti-myotoxic, anti-oxidant, anti-inflammatory, edema, and analgesic. The cultural heritage of herbal plants is on the brink of extinction, it is desperately required to preserve it, particularly through accurate documentation and scientific validation. Traditional herbs are tested to be effective through research, with diminishing adverse issues. However, experimental validation is lacking for most plant phytochemicals for their anti-ophidian property. Among the unexplored indigenous herbs, some are enlisted with traditional therapy information for future research. (Table 1). Therefore, the research of plant antidotes to inhibit snake venom is of great interest to humanity as cheaper and safer technology[27,28].

Table 1. Herbal plants traditionally used for snakebite treatment

Botanical name	Family	Method of application	Mode of administration	References
Aerva lanata	Amaranthaceae	The whole plant extract prepared as juice	Orally	29,30
Ajuga bracteosa	Lamiaceae	The root extracts in the form of a paste	Externally applied	7
Alangium lamarckii	Alangiaceae	The shoot portion is used as a decoction.	Orally	7
Alternanthera sessilis	Amaranthaceae	The paste was made from the leaves and stems of the plant.	Externally applied	26
Amaranthus spinosus	Amaranthaceae	The leaves were made to paste	Externally applied	26
Amaranthus viridis	Amaranthaceae	The paste of stem or leaves	Externally applied	26
Andrographis alata	Acanthaceae	The fresh leaves juice of 50 ml is given for every 2 hours on the bitten day	Orally	31
Andrographis echioides	Acanthaceae	The whole plant paste was mixed with water	Orally	32
Anisomeles indica	Lamiiaceae	The paste is made from leaves.	Externally applied	31
Anisomeles malabarica	Lamiaceae	The leaf juice with water	Orally	24
Ardisia humilis	Myrsinaceae	The plant was crushed and made to paste	Externally applied	33
Arisaema leschenaultii	Araceae	The plant root and fruit/ leaf paste	Externally applied at the bitten area 3 times a day for 8 days	34
Artocarpus heterophyllus	Moraceae	The juice of the plant	Orally 3 times daily	7
Barleria cristata	Acanthaceae	Leaf extract juice and 50 gram of root paste along with honey is used.	Externally applied	8, 35

Barleria prionitis	Acanthaceae	Decoction of the plant	Orally	36
Cassia alata	Caesalpiniaceae	The leaves are made into a paste	Both orally and externally applied	37
Cassia tora	Caesalpiniaceae	The leaf extract and root paste and leaf decoction of 50 ml with cow's milk is given	Externally applied for 30 days and orally given	29,31
Catharanthus roseus	Apocynaceae	The root paste mixed with lime and pepper	Externally applied	34
Clematis triloba	Ranuculaceae	The root was made into a paste	Externally applied	7
Clerodendron inerme	Verbenaceae	Root paste mixed with lime	Externally applied two times daily for a week	34
Cleome viscose	Capparidaceae	The paste of leaf is used	Externally applied	7
Clitoria ternatea	Fabaceae	The root extract with the root of Aristolochia indica and Rauwolfia serpentina	Internally taken	38
Cocculus villiosus	Menispermaceae	The bark root extract of the plant	Both orally and applied externally	7
Costus speciosus	Costaceae	The root and rhizome paste of the plant	Both orally and applied externally	39
Curculigo orchiode	Amaryllidaceae	The root paste of the plant	Externally applied	34
Cyphostemma auriculatum	Vitaceae	The bark was soaked in water	Orally once daily for 7-8 days	40
Daemia extensa	Asclepiaddaceae	The root powder is used	Orally	41
Datura metal	Solanaceae	The root extracts along with garlic	Orally	8
Desmodium gangeticum	Fabaceae	Half cup of root decoction	Orally	8
Drymaria cordata	Caryophyllaceae	The whole plant was crushed and the paste	Externally applied	33
Enicostemma axillare	Gentianaceae	The root extract of the plant	Externally applied	7
Euphorbia hirta	Euphorbiaceae	The plant decoction or latex is used	Orally	6
Ervatamia heyneana	Apocynaceae	The plant root paste was mixed with lemon juice	Externally applied	34
Ficus glomerata	Moraceae	The stem bark pastes of the plant	Externally applied	42
Ficus hirta	Moraceae	The roots were crushed	Externally rubbed at the site	43
Fimbristylis spathacea	Cyperaceae	The plant's fresh root was given	Orally and externally applied	7

Hedychium spicatum	Zingiberaceae	The decoction of roots was used	Orally	24
Helicteres isora	Sterculiaceae	The powder of the bark of the plant	Orally	8
Heliotropium indicum	Boraginaceae	The 50 ml juice of leaves with hot water	Orally	8, 31
Holarrhena pubescens	Apocynaceae	The paste made from the plant was applied to the bitten area twice a day	Externally applied twice a day on the bite site	33
Ipomoea obscura	Convolvulaceae	Leave extract juice was administered	Orally	7
Lantana indica	Verbenaceae	The decoction of leaves is used	Externally applied	6
Leucas cephalotes	Lamiaceae	The decoction of plant was given	Orally two times a day for 6 days	8
Lindenbergia muraria	Scrophulariaceae	The leaf paste of the plant	Externally applied	24
Madhuca indica	Sapotaceae	The plant bark is made of paste	Externally applied	6
Malva sylvestris	Malvaceae	The leaf extract was mixed with lemon juice	Orally	8
Murraya paniculata	Rutaceae	The shady dried leaf or root powder infusion is made	Orally at 1 hour time interval for 2 days	36
Nicotina tabacum	Solanaceae	The plant leaf decoction	Orally for 3 days	6
Ocimum basillicum	Lamiaceae	The plant decoction is used	Orally for a week	29
Optuntia dilleniid	Cactaceae	The paste made from fruit	Externally applied	8
Pavetta indica	Rubiaceae	The paste made from leaves	Externally applied	7
Peucedanum anamallayense	Apiaceae	The paste of the whole plant along with cow's urine	Orally	7
Phyllanthus acidus	Euphorbiaceae	The roots decoction of the plant	Orally	7
Pittosporum tetraspermum	Pittosporaceae	The stem bark pastes along with the cow's urine.	Orally	7
Platanthera susannae	Orchidaceae	The root tuber's paste with lime and salt	Externally applied	34
Plumbago zeylanica	Plumbaginaceae	The paste of the plant is made	Orally	6
Rhinacanthus nasutus	Acanthaceae	The fresh leaves and the leaf paste of the plant	Both orally and externally applied	26

Ruta graveolense	Rutaceae	The paste of the root is used	Internally or externally	44
Semicarpus anacardium	Anacardiaceae	The paste of root was given	Orally for 7 days	7
Sida caprinifolia	Malvaceae	The leaves were made into a paste	Externally or internally used	41
Solanum nigrum	Solanaceae	The dried root paste of the plant	Externally applied	45
Tabernaemontana coronaria	Apocynaceae	The crushed root of the plant with turmeric and salt	Externally applied	34
Tinospora cordifolia	Menispermaceae	The juice of leaf and stem with the paste of garlic.	Externally applied and orally given for 3 to 4 days	6
Tephrosia purpurea	Fabaceae	The plant root decoction with black pepper	Orally for 7 days	6
Thottea siliquosa	Aristolochiaceae	The leaves of the plant	Orally	7
Tiliacora acuminata	Menispermaceae	The paste of leaves of the plant	Externally applied on bite site	42
Tridax procumbens	Asteraceae	The leaves are crushed and made into juice and also the leaf juice is diluted with water	Both orally and externally applied	8
Uracia picta	Fabaceae	The root paste or leaf decoction	Orally two times a day	7
Ventilago maderaspatana	Rhamnaceae	The plant bark infusion	Orally	7
Vitex penduncularis	Verbenaceae	The decoction of the bark of the plant	Orally at a 30 minutes interval	32
Zingiber rubens	Zingiberaceae	The leaves were torn to thin sheets and a rope was tied up with parts of snakebite to prevent the flow of venom in the blood	Externally	46

6. Clinical Manifestation and Management of Snakebite

The popular way of treating snake bite victims is by using a serum made from the snake venom of the bitten snake. Antivenoms are of high price in many regions of the nation and are sometimes available in limited quantity. They are stored as frozen dried ampules than in liquid form, to reduce the risk of reactions. The suggested way of administration of antivenom is intravenous than through the intramuscular route[47]. In India, medication guidelines for antivenom are determined by the amount of specific venom (mg) which can be neutralized by each milliliter (ml) of antivenom. Therefore, studies show that 0.6 mg of *Naja naja,* 0.6 mg of *Daboia russelii*, 0.45 mg of *Bungarus caeruleus*, and 0.45 mg of *Echis carinatus* are to be neutralized for each ml of polyvalent antivenom. [3] Sometimes the snake involved in the bite remains unknown, which creates difficulty in finding the proper dosage of antivenom for the victim where mono-specific antivenoms are readily accessible. Usually, the management techniques to determine snake bite is made easy through clinical and laboratory methodologies[48]. The first dosage of antivenom must not be less than/exceeding 100 ml i.e. 10 vials diluted in 200/250 ml of normal saline. The medication is followed at a time interval of 6 hours if there are no symptoms. Primarily 10-20 ml of dosage must be given slowly to avoid allergic problems. The overall dosage should not exceed 200 ml, i.e. 20 vials for *Bungarus caeruleus*, and 300 ml, i.e. 30 vials for *Daboia russelii* envenomation[12].

The first aid approach varies from place to place because various snakes have different levels of toxicity in venom. Some snakes have minor local effects but cause dangerous regulatory systemic effects and sometimes snake bite area needs pressure immobilization whereas some venom of snakes possesses opposite effects to the victim[12]. The treatment of snake bite victims was commonly using non-oral administration of sheep or horse-derived polyclonal antivenom to neutralize toxins. Even though, the increasing progress of traditional treatment methods; it is necessary to look for other various natural or synthetic compounds that will be providing the same effect of traditionally available antivenom composition[6]. Medicinal plants, herbal remedy prepared using plant extracts contain dozens of active compounds that may be effectively helpful in the design of therapeutic drugs. The recognition and separation of phytochemical components from plant sources were crucial to the framework of drug development.[8]

7. Recent Advancements

The advancement in science and technology that have transpired since the introduction of antiserum-derived antibodies from horses or sheep for counteracting snake venom toxins. Antiserum is the sole effective treatment against snakebite envenomation to date. The irony of snakebite was the limited availability of viable remedies. Timely administration of safe and sufficient antivenoms by a qualified physician should be able to reduce the death rates arising from the poisoning[49]. Many improvements have been made to ensure the safety of antivenom to prevent adverse conditions. The studies include the usage of inhibitors from small molecules, peptide and oligonucleotide-based antibodies, nanotechnological therapeutics, and also novel recombinant polyclonal plant-venom therapy for neutralizing the toxic enzymes present in snake venom. The studies of the small molecular drug, Varespladib at nanomolar and picomolar doses efficiently neutralize the action of enzyme PLA2 in snake venom from different regions. Varespladib at 4 mg/kg showed a rise in survival rate and decreased hemorrhage complications induced by the venom of *Micrurus fulvius, Bungarus multicinctus, Naja atra, Deinagkistrodon acutus,* and *Agkistrodon halys*. Furthermore, a 100% survival rate of treated mice showed when intravenous administration of 8 mg/kg of Varispladib followed by fatal dosage of *Vipera berus* venom injected subcutaneously. The corresponding orally-administrated prodrug, methyl-Varespladib is easily accessible by victims as a first aid, when delay in anti-venom administration. The inhibitors of small molecule also include Marimastat, efficient in neutralizing defibrinogenating activity and Batimastat was better at suppressing haemorrhagic activity. Also, more research in analogs of the linear peptide-based drug becoming as successful as varespladib[50]. The biosynthesis oligoclonal antibody (BOA) contains 20-40 or more toxins inhibiting recombinant human antibodies for a certain amount of venom fractions. The amount and quality of monoclonal antibodies incorporated in the final formulations, BOAs can be tailored to be monovalent or polyvalent against various snake species. A study of [51] designed BOAs made of in vivo mitigating human IgG antibodies against black mamba venom by Phage display technology. Furthermore, synthesizing oligoclonal IgG combinations is cost-effective. The efficacy of BOAs in combination with small molecule inhibitors is evaluated *in vitro* and *in vivo*, neutralizing better than toxins that are inadequately neutralized by BOA or antivenom[52]. Artificial Intelligence (AI) has also become a promising technology for snake identification. AI algorithm identifies snakes using the pictures of the bitten snake, site of snake bite, habitat of a snake. Snake specialists provide the gold standard in the identification of snakes and are essential in the training of the AI algorithm, can be incorporated in healthcare systems in regions with high mortality from snakebite[53].

From the timeline of 1999-2019, research has been conducted for the development of a rapid diagnostic tool for the identification of snake species. Recently, mass spectrometry-based assay and TiO_2-based impedimetric immunosensor techniques are developed for the detection of snake venom fractions. TiO_2-based sensor was capable of characterizing the venom pool of *Bothrops* snake species. TiO2 sol-gel coating on silicon wafer as transducer substrate detects the venom (20 μg/ml) and total duration for impedance result was 41.24 ± 0.05 min. The TiO_2-based biosensor has limitations in detection time, whereas improvement is needed before clinical purposes. Mass spectrometery based analysis is to identify the venom proteomics of the blister fluid from snake bite victims. The approach was unable to identify species-specific variation in venom toxins. The limitation of this technique is due to the absence of particular tissue markers that can unambiguously distinguish various kinds of snake envenomation[54]. In the study of[55] four sets of five swiss mice each group has been tested for detecting the efficacy of mesenchymal stem cells (MSC)-based therapy for snakebite treatment. The group of mice received 50 μg of *Bothrops atrox* venom diluted in 50 μg of Phosphate-Buffered Saline (PBS), 50 μl of MSC secretome is administered intravenously. The results of returning the creatine kinase level showed the secretome from MSC has the potential for reducing muscle damage caused by venom toxins[5.]

The phytochemical constituent flavonoids isolated from plant extracts inhibit the toxicity of snake venom. A recent study has shown the derivatives of flavonoids such as naringenin neutralizes the crude *Naja naja* venom, pinostrobin, and quercetin have neutralization potential against PLA2 of snake venom[56]. An initiative of civil society is the Snakebite Healing and Education Society of India (SHE-India) with an objective of voice for snakebite victims. The nationwide program has members from the national level to the panchayat level, conscientiously working in regions of Rajasthan, Karnataka, Maharashtra, Uttar Pradesh, Jharkhand, Gujarat, West Bengal, and Chhattisgarh. The key activities of the SHE-India are awareness on first aid and prevention of snakebites, improvement of the local healthcare system. SHE-India aims to collaborate with traditional healers in such localities for improving snakebite awareness[57]. Snake bites are frequently treated using medicinal herbs or their derivatives in Indian folklore's ancient medicinal systems. The pharmacological shreds of evidence prove that traditionally used plants for antivenin purposes are currently exploring scientifically in many parts of the world.

8. Herbs as Antidote

Traditional herbs were attributed to their safety, efficacy, cost-effectiveness, and reliance on nearby geographical locations.Various herb and their phytoconstituents were proven to give antivenom action in the Ayurveda[1]. Plants were used in topical or oral application, as a remedy to resist the poisonous effects of snakebite[58]. Plants are the source of natural substances that can be used in drugs and for other specific purposes.The plants have secondary metabolites which include alkaloid, flavonoid, tannins, trace elements, etc. which can be used as an antidote against the venom. The plant molecules were safe for use and their neutralizing potential against venom can help in making new drugs against snakebite[59].Plants produce secondary metabolites having variation in solubility in a solvent system affects the extraction methods of these metabolites. There are many extraction procedures for metabolites that can be classified as conventional (long used) and novel (developed more recently). Conventional methods use organic fluids (hexane, acetone, methanol, ethanol, etc.) or water and are typically carried out at atmospheric pressure, whereas new methods use pressure and/or higher temperature. In this process, the solvents start moving into the stable plant material and dissolve the elements with similar polarities. The high replicability of plant metabolites is attributable to the fact that polar solvents retrieve polar active compounds while non-polar solvents retrieve non-polar active compounds. Solvents such as water, ethanol, chloroform, ethyl acetate, methanol, and others are commonly used in conventional extraction processes, and blends of solvents are used on occasion to improve extraction yield. Traditional solid–liquid extraction methods include Decoction, Infusion, Soxhlet extraction, Maceration, and Hydrodistillation. Several novel extraction methods such as, Microwave assisted extraction (MAE), pressurized liquid extraction (PLE), Ultrasound assisted extraction (UAE), and Supercritical fluid extraction (SFE)[60] has took place. These new techniques can shorten the extraction period, reduce the quantity of solvent used, and increase the extraction efficiency[60].

The *in vitro* and *in vivo* studies are conducted to evaluate the indigenous knowledge of plants to explore their inhibition potential against the venom. However, the efficacy mainly depends on dosage, lethal duration, body mass, the time interval of administration, safety factors of the antivenom drug[61]. The herbal constituents of *Andrographis paniculata, Aristolochia braceteolata, Aristolochia indica, Boerhavia diffusa, Curcuma longa, Dryopteris cochleate, Emblica officinalis, Euphorbia hirta, Leucas aspera, Pergularia daemia, Prosopis aneraria, Rauwolfia serpentina, Tylophora indica, Vitex negundo* are validated scientifically to counteract the *Naja naja* venom. Extracts of medicinal plants such as *Acalpya indica, Achycanthus aspera, Aristolochia braceteolata, Corallocarpus epigaeus, Dichrostaachys cinera, Hemidesmus indicus, Leucas aspera, Momordica charantia, Ophiorrhiza mungos, Strychnos nux-vomica, Tylophora indica, Vitex negundo* neutralizes the venom of *Daboia russellii,* popularly known as Russelli's viper. The Russelli viper were previously nomenclature as *Vipera russellii*, which comes under the Vipera genus. The scientific evidences of plants inhibiting the venom of *Vipera russellii* are *Alstonia scholoris, Aristolochia indica, Boerhaavia diffusa, Calotrpis gigantea, Emblica officinalis, Hemidesmus indicus.* The antivenom neutralizing ability of *Hemidesmus Indicus, Mimosa pudica, Strychnos nux-vomica* are active plants against *Naja Kaouthia* venom. The phenolic acid plant extract of *Martynia annua* has inhibition against 5'nucleotidase of snake venom. The root extracts of *Abrus precatorius* have inhibitory efficiency against the *Bungarus caeruleus* venom. *Azadirachta indica, Crateva magna, Gloriosa superb* has antivenin potential against *Naja nigricollis*. The inhibition activity of aqueous seed extract of *Albizia lebbaeck, Mucuna pruriens* against *Echis carinatus,* and methanolic extracts of *Momoridica charanitia, Solanum xanthocarpum* are active against *Naja naja karachiensis* venom.

Secondary metabolites from plants, as appeared differently from primary metabolites like nucleic acids, amino acids, carbohydrates, fat, and so on, are extremely varied; vast numbers of them have been identified and categorized into various classes. Each plant family, genus, and species give a unique mix of these substances, and they can occasionally be used as taxonomic features to characterize plants. Secondary metabolites do not play a significant role in living cell growth, development, and reproduction, but they often serve as a defense mechanism to preserve a plant from every potential danger in the natural ecosystem, as well as for interspecies defense. Secondary metabolites are frequently produced by altered synthetic pathways derived from primary metabolites, or they share substrates derived from primary metabolites[62].

Many initiatives to plant classification systems have developed over time. Morphological classification, anatomical classification, and chemotaxonomic classification are examples of these. The first two are traditional classifications, while the third is a modern approach to plant classification. The scientific method of chemotaxonomy, also known as chemical taxonomy, is used to classify plants based on their chemical compositions. The core composition of bioactive molecules and their metabolic pathway are frequently unique and confined to taxonomically related species, making categorization beneficial. The four most prominent and frequently used groups of substances for chemotaxonomic categorization are phenolics, alkaloids, terpenoids, and non-protein amino acids[63]. These classes of compounds vary greatly in chemical nature, distribution, and function features. The majorly available secondary metabolites from plants are glycosides, alkaloids, phenolic compounds, flavonoids, terpenoids, tannins, and saponins. Glycosides are substances produced when one or more sugars combine with non-sugar molecules via glycosidic linkage. The glycosides are classified as N-glycoside, O-glycoside, S-glycoside and C-glycoside based on their linkage. O-glycosides, such as rhein, are widely distributed. C-glycosides such as aloin and cascaroside, which have a direct carbon linkage between sugar and non-sugar, are uncommon in surroundings. They can be found in many plants that constitute anthraquinone derivatives. Alkaloids are known for their heterocyclic nitrogen-containing basic compounds. The parent base substance is seen on alkaloid assistances in chemotaxonomic classification. The parent base of indole alkaloids is indole. More than 2,500 indole alkaloids have been separated, primarily from three plant families: Loganiaceae, Apocynaceae, and Rubiaceae[63]. Alkaloids are generated as bioactive molecules by a wide range of organisms, including animals, fungi, and bacteria, but primarily by plants. The majority of them are toxic to animals and can be derived using an acid-base reaction. They have a strong tradition in medicine and have a spectrum of pharmacological effects. Plant phenolic compounds are a massive number of plant secondary components, mostly seen in hydroxylated aromatic rings, produced by teas, fruits, cocoa, vegetables, and other crops that have health advantages. They have anti-inflammatory, anti-carcinogenic, bactericidal, anthlemintic, antioxidant, antimicrobial, antiseptic properties. Flavinoids are water-soluble compounds seen in vacuoles in cells of plants. Flavonoids comprise floral pigmentation, UV filtration, physiological regulator, symbiotic nitrogen fixation, cell cycle inhibitors, and chemical messengers. Tannins are water-soluble phenolic compound that contributes to protein precipitation. They are produced by the shikimic acid pathway and classified into hydrolysable tannins and condensed tannins which are the active constituent in plant-based drugs. Terpenoids are a huge family of phytocompounds with little structural and functional overlap. The mevalonic acid pathway is responsible for the synthesis of terpenoids from acetate and steroids, carotenoids, and gibberelic acid are derivatives of the terpenoid family. Diterpenes are plentiful in the Lamiaceae and have antiviral and antimicrobial activities. The derivatives of nitrogenous terpene have anti-hypersensitive properties which can utilize for drug development. Saponins have several properties including antimicrobial, hemolytic, antioxidant, insecticide, sweetness, solubilization, foaming, bitterness, emulsification, and various other properties. Secondary metabolites prompted the creation of a new field of research known as plant metabolomics, which is dedicated to the identification and detection of the biosynthetic pathways of these compounds, as well as their structural characterization and applications due to its medicinal properties paves a possible growth in novel drug development in future. [62,64]

The anti-ophidian properties of secondary metabolites from the extracts of plants are beneficial in designing an antidote for venom toxins. A summary of active plants for counteracting the snake venom enzymes is enlisted in Table 2. The phytoconstituents D-mannitol, sitosterol derived from Mimosa pudica serve as anti-lethality, anti-proteolytic, anti-myotoxicity, anti-hyalurnidase activities against snake envenomation[65].The active constituenttumerin, rich content of proline in Curcuma longa has a linear mixed-type inhibitory effect on Phosplolipase A2 of *Najanaja*, also a flavonoid compound curcumin effective against PLA2 of *Crotalus atrox*. Di-iso-butyl phthalate isolated from *Emblica officinalis* root extracts inhibits the hemorrhage, myotoxic activity, lethality, free radical generation, coagulant activity, fibrinolysis and defibrinogenation produced by the venom of *Najanaja* and *Viperarussellii*.The 2-hydrozy-4-methoxy-benzoic acid extracted from *Hemidesmus indicus* roots, neutralizes the viper-induced venom lethality, swelling, defibrinogenation and hemorrhagic activities. Also, Lupeol acetate isolated from roots of *Hemidesmus indicus* using methanol as a solvent counteracted the venom-induced edema, SOD activity, hemorrhage, lipid peroxidation, lethality and defibrinogenation. The seed extract of *Strychnosnux-vomica* contains small straight chain compound containing methyl and amie radicals (SNVNF) effective in inhibition of snake venom metalloprotease of *Daboia russellii*[27].The bioactive compounds such as Queercetin-3-O-α-L-rhamnopyranosidequinic acid, quercetin, chlorogenic acid, luteolin, gallic acid, ellagic acid and kaempferol rich in *Euphorbia hirtaneutralizes* PLA2 of Najanaja venom[66,59]. Wedelolactone, compound of *Eclipta albapossess* anti-myotoxic-induced PLA2 activity in *Brothropsjararacussu* and *Crotalus durissustercificus* snake venoms[67,59]. The phytochemical compounds tannins, flavonoids and saponins isolated from methanolic leaf extracts of *Asystasiagangetica* provides 80% efficiency in inhibiting PLA2 of *Naja melanoleuca*. Antraquinones isolated from the roots and leaves of *Cassia occidentalis* provides minimized local effects, neutralize epidermal hyperplasia, restorative angiogenesis caused by *Bootropsmoojeni* species. Enzymes and protein inhibition of Aristolochic acid I, an alkaloid of Aristolochia *species* inhibits the *Najanaja* and *Daboia russelli's*PLA2, hylaronidase, L-aminoacid oxidase, collagenase, protease and peroxidase activities. In addition, leaves extract of *Aristolochia indica* protected mice at high doses of 8 and 16 mg/kg against the lethal effects of *Bothropsatrox* venom[66].

The venom neutralization of *Naja naja* and *Daboia russellii* by *Vitex negundo* extracts of blue and green leaves possess activity against proteolysis, PLA2, procoagulant, fibrinolytic induced by venom. The blue and green leaves exhibit 78% and 76.8%, also 66.4% and 63.4% inhibition against the proteolytic activity of cobra and russellii viper venom. The blue leaves were proven to be more effective in blood coagulation activity, green leaves significantly inhibit the PLA2 activity. The leaves were effective in neutralizing the fibrinolytic activity caused by both venoms. GC-MS analysis predominant peak corresponds secondary metabolite beta phellandrene in blue leaves and taucadinol in green leaves of *Vitex negundo* plant species[68]. The *Andrographis paniculata* is rich in several bioactive compounds includes polyphenols, diterpenoids and flavonoids. Andrographolide, a diterpenoid found in all parts of plants, is obtained as crystalline solids from the extracts of leaves. An indole alkaloid Reserpine, chemical nomenclature as methyl ester 2α, 11-dimethoxy-3-(3, 4, 5-trimethoxybenzoyloxy)-yohimban-1-carboxylic acid is isolated from roots of *Rauwolfia serpentina* plant[10]. *Mucuna pruriens* belongs to Fabaceae is rich in multiform glycoprotein metabolite. The aqueous seed extract (21 mg/kg) neutralizes lactate dehydrogenase, creatinine transaminase and glutamic pyruvic transaminase induced by *Echis carinatus* in rats and possess anticoagulant activity[69]. *Azadirachta indica* PLA2 inhibitor an alkaloid compound derived from *Azadirachta indica*, neutralizes the venom toxins in higher dose of *Naja naja* and *Naja kaouthia* compared to the venom components of *Daboia russellii*[28]. Pharmacological evidence revealed the indigenous knowledge of different plant species belonging to different families is capable of antivenin properties.

Table 2. Scientific validation of traditional plants for snakebite treatment

Botanical name	Family	Method of administration	Plant extract	Snakes	References
Abrus precatorius	Fabaceae	2 or 3 grams of roots or fresh leaves form a paste which is given along with cow's milk or cold water	Root extract	*Bungarus caeruleus*	58
Acalypa indica	Euphorbiaceae	The full plant or leaves made into paste and introduced to the bitten area	Methanolic extract, benzene, acetone, chloroform, petroleum ether extracts	*Daboia russelli*	70
Achyranthes aspera	Amaranthaceae	Root extract mixed with water and given to the victim orally	Aqueous, ethanolic leaves extracts	*Daboia russelli*	71
Albizia lebbeck	Fabaceae	The root extract juice added with 3 or 4 pepper(half) is given orally and a little paste is applied to the bitten area	Methanolic seed extract, Aqueous seed extract	*Echis carinatus*	72,73

Alstonia scholoris	Apocynaceae	The plant bark decoction is given to the victim	Aqueous bark extract, silver nanoparticles from bark extract	*Vipera russellii* venom	74,75
Andrographis paniculata	Acanthaceae	The leaves along with *Andrographis alata* leaves decoction are used externally.	Methanolic extract	*Naja naja* venom acetylcholinesterase and hyaluronidase	76
Aristolochia bracteolata	Aristolochiaceae	The paste of leaves applied externally and also infusion taken orally	aqueous extract	*Daboia russellii*, Naja naja	77
Aristolochia indica	Aristolochiaceae	The fresh roots are ground along *Rauwolfia serpentina* mixed in water taken two times a day for 3 days also root syrup is given orally and root paste is put on to the bitten site.	Water, methanolic, pentane, ethanolic leaf extracts	*Naja naja, Vipera russellii, Bothrops atrox*	66
Asystasia gangetica	Acanthaceae	The leaves are made into a paste and given to the victim	Methanolic leaf extract	PLA2 of *Naja melanoleuca*	66
Azadirachta indica	Meliaceae	The plant extract paste is given orally	Methanolic leaf extract	*Naja nigricollis* venom PLA2	24,28
Boerhaavia diffusa	Nyctaginaceae	Leaf extract juice is applied to the bitten area also the extract is taken orally for 7 days	Ethanolic extract	*Naja naja* PLA2 and *Vipera russellii* sPLA2	78
Calotrpis gigantea	Asclepiadaceae	Root bark paste is made into pills and given orally also leaf extract is applied externally	Methanolic extract	*Vipera russellii* venom	80
Cassia occidentalis	Caesalpiniaceae	The root paste is given orally	Hydroalcoholic leaf extract, ethanolic leaves, and root extracts	*Bothrops moojeni* venom	81,66
Cissampelos pareira	Menispermaceae	The root is made into a paste along with 5 g pepper given once a day for 5 days	Ethanolic extract	*Bothrops diporus* venom	82

Corallocarpus epigaeus	Cucurbitaceae	Root decoction is given internally three to seven times.	Methanolic and aqueous plant extracts	*Daboia russelli*	83
Crateva magna	Capparaceae	The plant is given orally and applied to the bitten area	Ethanolic stem bark plant	*Naja nigricollis*	84
Curuma longa	Zingiberaceae	The paste of the rhizome is applied externally for 3 weeks.	Secondary metabolite from hexane extract	*Naja naja*	58
Dichrostachys cinerea	Araceae	The leaves are made into a paste which is applied locally, the powder of root is also used	Methanolic root extract	*Daboia russellii* venom	85
Dryopteris cochleate	Aspidiaceae	The plant is crushed and the extract is given to the victim two times a day also the roots and leaves are applied to the bitten area	Silver nanoparticle from ethanolic rhizome extract	*Naja naja* venom	86
Eclipta alba	Asteraceae	The whole plant juice is given to the victim for 30 days	Extracts of genetically modified plant and native plant	*Bothrops jararacussu, crotalus durissusterrificus*	67
Emblica officinalis	Euphorbiaceae	The plant leaf and stem infusion are given orally also the root extract with black pepper is given to the victim	Methanolic root extract	*Naja naja, Vipera russelli*	27
Euphorbia hirta	Euphorbiaceae	The plant decoction or latex is administered orally.	Methanolic whole plant extract	*Naja naja*	66
Gloriosa superb	Liliaceae	The paste of plant root or tuber is applied externally for 2-5 days	Tuber's alcoholic extract	*Naja nigricollis*	87
Hemidesmus indicus	Asclepiadaceae	The aqueous extract of the root is made with water and given orally, the root paste is applied 2 or 3 times a day	Methanolic extracts with active compounds isolated	*Daboia russellii, Vipera russellii, Naja kaouthia*	27

Leucas aspera	Lamiaceae	The leaf paste is used internally and externally also the root juice is mixed with goat's milk is given thrice a day for 4 days	Methanolic extract, aqueous extract	*Naja naja, Daboia russelli*	88,77
Martynia annua	Martyniaceae	The decoction of the root is used	Phenolic acid from plant extract	5'nucleotidase of snake venom	89
Mimosa pudica	Mimosaceae	The whole plant extract is filtered and given twice a day for 1 day also leaf paste is applied to the bitten area	Aqueous extract of roots	*Naja kaoathia*	90
Momordica charantia	Cucurbitaceae	The juice of tender root or shoot is applied	Aqueous seed extract, Methanolic plant extract	*Daboia russellii, naja naja karachiensis* (in vitro)	91,92
Moringa oleifera	Moringaceae	The fresh extract of the bark is taken orally also the bark root paste is applied to the bitten area.	Ethanolic extract, ethanolic leaf extract	*Naja haje, Bitis arietens*	93,94
Mucuna pruriens	Fabaceae	The root aqueous extract is given orally two times a day	Aqueous extract of seed	*Echis carinatus*	69
Musa paradisiaca	Musaceae	The extract of the plant is taken orally	Aqueous stem extract	*Brthrops jararacussu*	90
Ophiorrhiza mungos	Rubiaceae	The root juice is given two times a day for 6 days	Aqueous root extract	*Daboia russellii*	95,96
Pergularia daemia	Apocynaceae	The plant leaves decoction is used	Methylene chloride and n-hexane leaf extract	*Naja naja* PLA2 and L-amino acid oxidase	97
Prosopis cineraria	Fabaceae	The bark paste is tied on the bitten area	Aqueous bark extract	*Naja naja*	98
Rauwolfia serpentina	Apocynaceae	The leaf juice is used as an antidote, the roots and leaf buds crushed with milk to make it into a paste used both internally and externally on the affected area	Aqueous root extract	*Naja naja*	10,99

Sida acuta	Malvaceae	The extract of the whole plant is used both internally and externally	Ethanolic plant extract	*Bothrops atrox* venom	100
Solanum xanthocarpum	Solanceae	The fresh leaf extract is used	Methanolic extract	5' nucleotidase of *Naja naja karachiensis*	101
Strychnos nux-vomica	Loganiaceae	The juice of root bark with cow milk is rubbed externally for 3-times a day	Ethanolic extract	*Daboia russellii, Naja kaouthia*	102

The efficacy of plants extracts with suitable solvents rich in secondary metabolites can inhibit the crude venom or purified venom enzymes of snakes. However, inhibition potential of most plants has been tested scientifically against the toxic components of different serpent species.

9. Conclusion

Snakebite is a neglected tropical disease, that causes morbimortality mainly in rural areas. Antivenoms are lifesavers, their limitations have piqued the curiosity of venom toxicologists and medical professionals. The available polyclonal antivenom proceeds to rescue millions of snakebite victims every year, it's indeed clear that better treatment methods were also desperately needed to combat this NTD more efficiently. The envenoming novel drug development is still in its initial phases, it is critical to consider the path followed by drug discovery initiatives for other NTDs to determine appropriate facilitating strategies applicable to snake bite. Studies have been undertaken to target pathogenic and therapeutic elements of venom toxins, as well as their specificity and mechanism of action, for the past several years. It is necessary to establish alternative therapies for the management of local effects at the snakebite area as well as secondary consequences. The herbal plant isolated bioactive compound, as well as their efficacy and potentiality, are being explored as prospective for antivenom therapy. The review focused on indigenous knowledge of medicinal plants across India for snakebite envenomation. In the present study, there were 111 plant species belonging to 51 families used in traditional therapies and pieces of evidence of ethnobotanical research against snake bite. The recent studies of small molecules like Varespladib, nanobodies, biosynthesis oligoclonal antibodies, diagnostic tools for venom identification, mesenchymal stem cell therapy were carried out for the treatment of snakebite. The snake identification using artificial intelligence, the establishment of SHE-India provides one step forward in the management of antivenom. The plant secondary metabolites have the benefit of being readily available in pure form, safe, stable, and are capable of inhibiting the toxicity of venom. The research on drug development using herbal plants was one of the reliable approaches as an antidote for neutralizing the toxic enzymes present in the venom. The indigenous expertise of plant substances has anti-venom properties, gaining more attention for the novel discovery of drugs against snakebite.

It is important to consider the effective strategy for assisting in the scientific breakthrough, advancement, and introduction of effective snakebite drugs that could be used in society quickly after a snakebite takes place and is available at a minimal price to the victim. Significant challenges persist, such as evaluating the number of envenoming drugs that are needed to provide broad-spectrum, defining appropriate dosage of antivenom according to bite, and also overcoming the difficulties associated in using novel therapeutic methodologies in snakebite victims with adherence to new alternative drugs are integrated with the health care system. Even though antivenoms have been already used for a century, many victims still rely on traditional healers which highlights the importance of natural remedies for snake bite envenomation. The exploration of potential bioactive secondary metabolites from plants for snake envenoming and the development of commercially viable anti-ophidian drugs through scientific research studies are essential shortly. Effective research on plant extracts and their medicinally important bioactive compounds will provide the safe alternative therapy as the next generation snake bite medication, thus contributing to reducing the mortality and post complications on victims of snake bite by 2030.

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