EXPLORING THE AYURVEDIC KNOWLEDGE ON ENVENOMATION: A REVIEW ON ETHNO PHARMACOLOGICAL APPROACH

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ABSTRACT

Envenomation is one of the significant public health issues in several tropical and subtropical countries due to high morbimortality. In developing countries like India their management is basically inadequate due to poor transportation and subsequent delay in antivenom administration. So improvement in the therapeutic approaches to envenomation is necessary and therefore the medicinal plants, available locally, which have been used since ages to treat a great variety of diseases including Envenomation, needs attention. Ayurveda, a well-established medical paradigm from ancient India dealt comprehensively on management of acute envenomation and treatment of its complications with the usage of abundant medicinal plants. The present study was designed to bring together information on medicinal plants with antivenin properties and actions. Data has been collected with prominence on the plants, family, parts used, indications, mode of use etc. from Ayurveda literatures in an ethnobotanical perspective. In recent years, many studies have been published on pharmacological confirmation of antivenin potential of these plants against a broad range of envenomation, including enzyme inhibiting activity, anti-hemolytic activity, anti-proteolytic activity, anti-cytotoxicity and anti-myotoxicity. However, several plants claimed to be Vishahara (anti-poisonous) in Ayurveda need to be explored scientifically for their antivenin potential.

Keywords: Envenomation, Ayurveda, Vishahara, Anti-Venom

INTRODUCTION

The introduction of venom into a body by means of the bite or sting of a venomous animal is envenomation.1 Envenomation is considered as a significant public health problem especially in rural populations across the globe.2 Numerous species of spiders, scorpions, insects, centipede, mollusks, jelly fish, sea anemones, fishes, snakes, lizards, frogs, moles, platypus, shrews are animals capable of producing venom.3 WHO enlists snake bite, cat bite, dog bite and monkey bites under animal bites. Amongst venomous animals, snake bite is considered to be the cause for the utmost burden of human suffering. Current estimates indicate that snake envenoming affects 2.4 million people and result in 94,000–1,25,000 deaths every year, with an additional 4,00,000 amputations and other severe health consequences, such as infection, tetanus, scarring, contractures and psychological sequelae.4 Scorpion stings is another common yet neglected health issue especially found lethal in young children.5 Bite by rabid mammals (99% dog-mediated) is estimated to cause 59,000 human deaths annually in over 150 countries, with 95% of cases occurring in Africa and Asia.6 The burden of venomous bites and stings causing mortality and morbidity continues to be a serious concern for the people and the health-care providers in developing countries despite the successful outcomes with anti-venom therapy. Most Envenomation happens in the world’s most remote and poorly developed tropical communities where majority of victims do not seek hospital treatment but prefer indigenous snake bite remedies.7 The lack of medical facility in the vicinity in the rural area is considered as one of the major reasons for seeking traditional healers. Measures adopted by traditional healers are blamed as the reason for poor outcomes in cases of envenomation. Few beliefs regarding snake bite and health seeking behavior studies conducted in Sri Lanka found that people firmly believed in Ayurvedic treatment for snake bite.8 Both traditional and conventional systems of medicine have limitations for management of envenomation from lack of resources and awareness. Evidence based, scientifically sound, integrative or multidisciplinary approach of native medical systems and conventional medical systems is the need of the hour for strengthening the health care in envenomation. The broad aim of this article is to provide a general outline on descriptions of poisons and their management from an Ayurvedic perspective. This article reviews the ethnobotanical aspect and pharmacological researches on anti-poisonous herbs delineated in Ayurveda.

Ayurveda understanding and approach to Envenomation

Ayurveda is considered as the earliest medical system with a specialized discipline of toxicology (Agada Tantra) in a codified form with texts and scriptures. Acharya Sushruta, the father of surgery in his treatise, Sushruta Samhita dealt extensively on toxicology in one of the six cantos i.e. Kalpa sthana. Consciousness of the security of the king and the methods employed for his protection from accidental and homicidal poisoning are important applied aspects of the subject of toxicology during ancient times. Various observations that one comes across in the treatise seems relevant even at present. Acharya Agnivesha, in his treatise Charaka Samhita observes that “Even an acute poison can become an excellent drug if properly administered and similarly a drug if not properly administered becomes an acute poison”.9 William Withering (1789) makes a
similar observation that poison in small doses are the best medicines and useful medicines in too large doses are poisons.10 Ayurveda understands Visha (poison/toxin) as Akritrima (natural) and Kritrima (artificial). Akritrima is further categorized as Silavara (animinate) and Jangama (animate). Kritrima Visha is developed by combination of two poisonous materials and combination of non-poisonous materials is Gara (concocted poison). Incompatible food (Virudhaahara) is also considered similar to Gara.11 Inanimate poisons include poisons of plant origin, toxic minerals, metals and metal ores in their natural form. Animate poisons include venoms of poisonous varieties of snakes, scorpions, spiders, rabid animals, insects, worms, fishes, frogs etc. Visha of mild potency, continuing to exist in the body for many years which is of animinate or inanimate origin and constantly polluting the bodily tissues thereby leading to chronic ailments is termed as Dushi Visha.12 The principles of management of Dushi Visha described in Ayurveda could be utilized for the management of long-term specific and nonspecific complications following envenomation.

Visha is attributed with ten qualities as per Ayurveda such as Laghu (lightness), Ruksa (unctuousness), Ashu (quickness), Vishada (non-sliminess/clear), Vyavayi (spreading without digestion/ pervades all body before getting digested) Tikshna (sharppness), Vikasi (relaxant), Sukshma (minuteness), Ushna (hotness) and Anirudhaya rasa (indistinct taste). All these properties of poison by virtue of its quickness vitiate the Tridoshas thus hindering them to perform normal functions attributed to them. Biotransformation, a function of the Tridoshas is adversely affected precipitating retention of toxins in the body and blocking their elimination.13 Ayurvedic texts quote that Ojas, the prime substance imparting immunity to the body is vitiated by Visha (toxic substance or poison). Visha, by virtue of its ten properties deactivate the ten opposite qualities of Ojas leading to impaired immunity and death. The signs and symptoms and principles of treatment of animate and inanimate poisons in general are based on Tridoshas and also on the Visha vega (toxic manifestation within a bodily tissue).14 Twenty-four methods of therapy are described by Acharya Charaka in his treatise, Charaka Samhita for the management of Visha. Treatment starts from ligation (Arishta bandhana) above the affected part and ends in revival of the apparently dead (Mrutsanjivana). Administration of specific antidotes for combating envenomation is part of these twenty-four methods of therapy.14

Ayurvedic medicinal plants for different Envenomation: Ethno pharmacological perspective

All the three major treatises of Ayurveda have chapters dedicated for Envenomation. Several hundreds of drugs of plant, mineral and animal origin are utilized for the management of envenomation under the term Vishahara in Ayurveda treatises. In the current review we have presented more than hundred plant drugs being recorded in Ashtanga Hridaya (Table 1) for the management of a variety of envenomations.15 Interestingly more herbs are recorded for the management of spider venom followed by snake bite, rat bite, scorpion sting respectively which is depicted as a figure (Figure 1). The identity of the plant source has been confirmed from Encyclopedia on Indian Medicinal plants in FRLHT’s ENVIS Resource Partner on Medicinal Plants.16 Medicinal plants belonging to 61 families have been identified used in treating envenomation. Many plants belonging to Fabaceae (14), Curcurbitaceae (6), Verbenaceae (5) and Zingiberaceae (4) were found used to treat different kinds of bite (Figure 2). Fabaceae was cited as the botanical family consisting of the greatest number of plants reputed against snake bite.17 The plant part designated in the classical text has been reported here for researchers to utilize the information for new drug development. In case the specific part is not mentioned then the useful part indicated in the Ayurveda pharmacopeia18 is reported here. Acharyas have preferred using sustainable plant parts like leaves, stem bark, fruits and flowers wherever possible, even though use of roots are also common. Ayurvedic texts specify that wherever the useful part is not specified in a given context, then root is to be procured.19 These medicinal plants are intended for use either internal or external or both in different dosage forms such as juice, aqueous decoctions, medicated jams, powders, fermented drinks, pastes etc.

Scientifically validated Visha hara herbs with anti-venom activity

Several plant species have been studied for pharmacological evidence against snake venoms including inhibitory potential against hyaluronidase, phospholipase, proteolytic, hemorrhagic, myotoxic and edematogenic activities. However, research into Ayurvedic anti-venom herbs is still in a very premature stage. Very few (approximately 22%) of the species used in Ayurvedic medicine against various Envenomation were studied in preclinical assays with different snake venoms as shown tabulated (Table 2) along with details of the extract and the research model. Some medicinal plants used repeatedly in the management have not been explored such as Valeriana wallchii DC, Saussurea lappa (Decne.) Sch. Bip, Coscinium fenestratum (Goeth.) Celebr., Glycyrrhiza glabra L., Acorus calamus L. Messa ferre L. etc.

CONCLUSION

Medicinal plants Albizia lebbeck (L.) Benth., Valeriana wallchii DC., Saussurea lappa (Decne.) Sch. Bip., Curcuma longa L., Piper longum L., Coscinium fenestratum (Goeth.) Celebr. Glycyrrhiza glabra L., Zingiber officinale Rosc., Acorus calamus L., Vitex negundo L., Aegle marmelos (L.) Corrêa, Clitoria ternatea L., Amaranthus spinosus L. occupy prime place in the management of envenomation in Ayurveda. These drugs are administered in different dosage forms, through enteral and parenteral routes to treat Cobra, Viper, Krait envenomation, spider and scorpion venom, rat bite and rabid dog bite. Most of these medicinal plants are scantily studied for their role in envenomation and hence researchers can thoroughly screen these herbs for anti-venom new drug development.

Table 1: Ethno-botanical information on Ayurvedic drugs used in the management of Envenomation
| Plant name                                   | Family               | Habit             | Plant part used | Ailment treated                                                                 | Other details                  |
|----------------------------------------------|----------------------|-------------------|-----------------|---------------------------------------------------------------------------------|--------------------------------|
| Achyranthes aspera L.                        | Amaranthaceae        | Herb              | Whole plant     | Snake bite – viper and krait, spider venom                                        | Internal                       |
| Aconitum heterophyllum Wall. ex Royle        | Ranunculaceae        | Herb              | Tuber           | Snake bite – viper and krait, insect bite                                         | Internal and External          |
| Acorus calamus L.                            | Acoraceae            | Herb              | Rhizome         | Viper bite, insect bite, spider venom, rat bite                                   | Internal and External          |
| Adhatoda vasica Nees                        | Acanthaceae          | Shrub             | Root, Leaves    | Snake bite, spider venom, scorpion sting, rat bite                                | Internal                       |
| Aegle marmelos (L.) Corrêa                  | Rutaceae             | Tree              | Root            | Snake bite – viper, cobra and krait, spider venom, rat bite                       | Internal and External          |
| Alangium salvifolium (L.f.) Wangerin        | Cornaceae            | Small tree        | Bark            | Spider venom, rat bite                                                           | Internal for Emesis, external  |
| Albizia lebbeck(L.) Benth                   | Fabaceae             | Tree              | Stem, bark, flowers, fruit, root | Snake bite – viper and krait, spider venom                                      | Internal and External          |
| Albizia procera (Roxb.) Benth.              | Fabaceae             | Tree              | Stem bark, seeds | Snake bite – viper, cobra and krait, rat bite                                    | Internal and External          |
| Amaranthus spinosus L.                      | Amaranthaceae        | Herb              | Root, whole plant| Snake bite – viper, cobra and krait, rat bite                                    | Internal and External          |
| Aquilaria agallocha Roxb.                   | Thymelaeaceae        | Evergreen tree    | Heartwood       | Spider venom                                                                   | External                       |
| Aristolochia indica L.                      | Aristolochiaceae     | Perennial climber | Root            | Snake bite – viper, cobra and krait                                              | Internal and External          |
| Azadirachta indica A. Juss.                 | Meliaceae            | Tree              | Bark, leaves    | Spider venom                                                                   | Internal and external          |
| Baliospernum montanum (Wild.) Müll. Arg.    | Euphorbiaceae        | Under shrub       | Root, seed, leaf | Spider venom                                                                   | External                       |
| Bambusa arundinacea Wild.                   | Poaceae              | Herb              | Seeds, tender stem | Viper bite, spider venom                                                         | Internal and external          |
| Boerhaavia diffusa Linn.                    | Nyctaginaceae        | Herb              | Whole plant, root | Rat bite                                                                        | Internal                       |
| Boswellia serrata Roxb.                     | Burseraceae          | Tree              | Resin           | Snake bite – viper, cobra and krait                                              | Internal                       |
| Caesalpinia sappan L.                       | Fabaceae             | Tree              | Heartwood       | Insect bite, spider venom                                                        | Internal and External          |
| Callicarpa macrophylla Vahl                 | Verbenaceae          | Evergreen shrub   | Fruit           | Spider venom                                                                   | External                       |
| Calophyllum inophyllum L.                    | Calophyliaceae       | Evergreen tree    |                 |                                                                                  |                                |
| Calotropis gigantea (L.) Dryand.             | Apocynaceae          | Shrub             | Root, flower latex | Snake bite, scorpion sting, rhabid animal bite                                   | Internal and External          |
| Catunaregam spinosa (Thumb.) Tiran.         | Rubiaceae            | Small tree        | Fruit           | Spider venom, rat bite                                                           | Internal and External          |
| Cedrus deodora (Roxb.) G. Don               | Pinaceae             | Tree              | Heartwood       | Snake bite, scorpion sting, spider venom, rat bite                                | Internal and External          |
| Cinnamomum tamala (Buch.-Ham.) T. Nees and Eberm. | Lauraceae          | Tree              | Bark, leaves    | Spider venom                                                                   | Internal and External          |
| Cinnamomum zeylanicum Nees                  | Lauraceae            | Small evergreen tree | Bark           | Spider venom                                                                   | Internal                       |
| Cirrhzus colocynthis (L.) Schrad.            | Cucurbitaceae        | Creeper           | Fruit           | Snake bite – viper, cobra and krait                                              | Internal                       |
| Clerodendrum phlomidis L.f.                 | Verbenaceae          | Shrub             | Root            | Spider venom                                                                   | Internal                       |
| Clerodendrum serratum (L.) Moon             | Verbenaceae          | Shrub             | Root            | Spider venom                                                                   | Internal                       |
| Clitoria ternatea L.                        | Fabaceae             | Perennial climber | Root            | Snake bite – viper, cobra and krait, rat bite                                    | Internal                       |
| Coixlacryma-jobi L.                         | Poaceae              | Annual herb       | Root            | Viper bite                                                                      | Internal                       |
| Coleus vettiveroides Jacob                  | Lamiaceae            | Perennial herb    | Whole plant     | Spider venom                                                                   | External                       |
| Cordia myxa L.                              | Boraginaceae         | Small tree        | Fruit           | Snake bite – viper, cobra and krait, spider venom                                | Internal                       |
| Coscinium fenestratum (Goetgh.) Colebr.     | Menispermaceae       | Climbing shrub    | Wood            | Snake bite – viper, cobra and krait, spider venom, scorpion sting, insect bite, rat bite | Internal and External          |
| Crotonaescu nurvala Buch.-Hum.              | Capparaceae          | Tree              | Bark            | Spider venom                                                                   | Internal                       |
| Crocus sativus L.                           | Iridaceae            | Herb              | Stigma          | Spider venom, rat bite                                                          | External                       |
| Curcuma longa L.                            | Zingiberaceae        | Herb              | Rhizome         | Snake bite – viper, cobra and krait, spider venom, scorpion sting, insect bite, rat bite | Internal and External          |
| Plant Name                        | Family                 | Habitat          | Part Used                                      | Medicinal Use                                      | Mode of Use              |
|----------------------------------|------------------------|-------------------|-----------------------------------------------|---------------------------------------------------|--------------------------|
| Cyclea peltata (Lam.) Hook. f. and Thomson | Menispermaceae         | Twining shrub     | Whole plant                                   | Snake bite, insect bite and spider venom           | Internal and External    |
| Cyperus esculentus L.            | Cyperaceae             | Perennial herb    | Whole plant                                   | Spider venom                                      | Internal                 |
| Cyperus rotundus L.              | Cyperaceae             | Perennial herb    | Whole plant                                   | Spider venom                                      | Internal                 |
| Datura metel L.                  | Solanaceae             | Perennial herb    | Leaves, root                                  | Snake bite, rabid animal bite                      | Internal and External    |
| Desmodium triflorum (L.) DC.     | Fabaceae               | Herb              | Whole plant                                   | Rabid animal bite                                 | External                 |
| Dipteroecarpus alatus Roxb. ex G. Don | Dipteroecarpaceae     | Tree              | Wood                                          | Rabid animal bite                                 | External                 |
| Elettaria cardamomum (L.) Maton  | Zingiberaceae          | Herb              | Fruit                                         | Snake bite, Insect bite and spider venom           | Internal and External    |
| Emblica officinalis Gaertn.      | Phyllanthaceae         | Tree              | Fruit                                         | Snake bite, scorpion sting, spider venom, rat bite | Internal and External    |
| Euphorbia hirta L.               | Euphorbiaceae          | Herb              | Whole plant                                   | Spider venom                                      | External                 |
| Feronia limonia (Linn.) Swingle  | Rutaceae               | Large tree        | Fruit pulp, fruit, root, leaves, flower, bark | Snake bite-krait, cobra, viper venom, rat bite     | Internal                 |
| Ficus benghalensis L.            | Moraceae               | Large tree        | Tree bark                                     | Snake bite-krait, cobra, viper venom, insect bite | Internal                 |
| Ficus glomerata Roxb.            | Moraceae               | Large tree        | Tree bark                                     | Snake bite-krait, cobra, viper venom, insect bite | Internal                 |
| Ficus lacor Buch-Ham             | Moraceae               | Large tree        | Tree bark                                     | Snake bite - krait, cobra, viper venom, insect bite | Internal                 |
| Ficus religiosa L.               | Moraceae               | Large tree        | Tree bark                                     | Snake bite - krait, cobra, viper venom, insect bite | Internal                 |
| Flacourtia jaungomas (Lour.) Raeusch. | Salicaceae             | Tree              | Bark, fruit                                   | Spider venom                                      | External                 |
| Gloriosa superba L.              | Liliaceae              | Herb              | Root                                          | Spider venom                                      | Internal and External    |
| Glycyrrhiza glabra L.            | Fabaceae               | Perennial herb    | Root                                          | Spider venom                                      | Internal and External    |
| Gmelina arborea Roxb.            | Verbenaceae            | Deciduous tree    | Root, fruit                                   | Snake bite – krait, viper, cobra                  | Internal and External    |
| Hemidesmus indicus (L.) R. Br. ex Schult. | Asclepiadaceae        | Training vine     | Root                                          | Rat bite, spider venom                            | External                 |
| Indigofera tinctoria L.          | Fabaceae               | Shrub             | Root                                          | Rat bite, spider venom                            | External                 |
| Lageronia siceraria (Molina) Standl. | Cucurbitaceae         | Annual vine       | Fruit                                         | Rat bite                                          | Internal                 |
| Luffa acutangula (L.) Roxb.      | Cucurbitaceae          | Annual vine       | Fruit                                         | Spider venom                                      | External                 |
| Luffa cylindrica (L.) M. Roem.    | Cucurbitaceae          | Annual vine       | Fruit                                         | Spider venom                                      | External                 |
| Luffa echinata Roxb.             | Cucurbitaceae          | Annual vine       | Fruit                                         | Rat bite                                          | Internal                 |
| Malaxis acuminata D. Don         | Orchidaceae            | Terrestrial orchid | Rhizome                                       | snake bite – krait, viper, cobra                  | Internal                 |
| Mesua ferrea L.                  | Clusiaceae             | Evergreen tree    | Dry flower, stem                              | All types of Envenomation, Viper bite and spider venom, insect bite | Internal and External    |
| Microstylis wallichii Lindl.     | Orchidaceae            | Terrestrial orchid | Rhizome                                       | snake bite – krait, viper, cobra                  | Internal                 |
| Moringa oleifera Lam.            | Moringaceae            | Tree              | Bark, fruit                                   | Rat bite                                          | Internal                 |
| Narcondostachys jatamansi (D. Don) DC | Caprifoliaceae        | Perennial herb    | Root                                          | Snake bite                                        | Internal and External    |
| Nerium oleander L.               | Apocynaceae            | Shrub             | Root, flower                                  | Snake bite – krait, cobra, viper                  | Internal and External    |
| Nymphaea alba L.                 | Nymphaeace             | Aquatic herb      | Flower                                        | Snake bite - krait                                | Internal                 |
| Ocimum sanctum L.                | Lamiaceae              | Herb              | Whole plant                                   | All types of Envenomation, Snake bite – krait, cobra and krait, spider venom, scorpion sting, insect bite, rat bite | Internal and External    |
| Ocimum tenuiflorum L.            | Lamiaceae              | Herb              | Whole plant                                   | All types of Envenomation, Snake bite – krait, cobra and krait, spider venom, scorpion sting, insect bite, rat bite | Internal and External    |
| Onosma bracteata Wall.           | Boraginaceae           | Perennial herb    | Whole plant                                   | Rabid animal bite                                 | External                 |
| Operculina turpethum (L.) Silva Manso | Convolvulaceae       | Herb              | Root                                          | Insect bite, spider venom, rat bite                | Internal                 |
| Pergularia daemia (Forssk.) Chiov. | Asclepiadaceae        | Perennial herb    | Whole plant                                   | Spider venom                                      | External                 |
| Plant name | Plant part and Extract used | Model studied                                                                 | Reference |
|------------|-----------------------------|-------------------------------------------------------------------------------|-----------|
| Abutilon indicum (L.) Sweet | Hexane and methanolic leaf extract | Enzyme inhibiting activity on Echis carinatus s (Saw scaled viper) | 20        |
| Achyranthes aspera L. Corêa | Aqueous and ethanolic extract of the leaves | Inhibition of phospholipase activity, Inhibition of Procoagulant activity, Inhibition of Hemolytic activity | 21        |
| Acorus calamus L. | Root extract using distilled water | Neutralization of lethality, edema-forming activity, hemorrhagic activity, phospholipase activity (PLA2) and pro-coagulant activity caused by Echis carinatus venom | 22, 23    |

Table 2: Anti-venom activity and their model reported
| Species                              | Extracts/Preparations                                                                 | Activities                                                                 | References |
|-------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------|------------|
| Aegle marmelos (L.) Corrêa          | Methanolic extract of Leaf, stem and root bark                                        | Inhibition of effect of the enzymatic components present in the venom of the Viperidae family | 24         |
| Albizia lebbeck (L.) Benth          | Seed methanolic extract - hot extracts by the Soxhlet method using different solvents (1:25 w/v) with increasing polarity (n-hexane, chloroform, ethyl acetate, methanol and water) | Neutralization potential against the toxic enzymes of ECV (proteases and hyaluronidases), prevented the characteristic ECV induced hemorrhage and myotoxicity | 25         |
| Andrographis paniculata (Burman f.) | Dried Ariel part (after 90 – 120 days of sowing) Alcoholic extract Dried Ariel part - Ethanolic extract | Anti-cobra venom activity Anti-scorpion venom activity                           | 26         |
| Aristolochia indica L.              | Aristolochic acid and its derivatives from the aqueous root extract                   | In vitro Assay for L-amino acid oxidase (LAAO) – Russel viper venom In vivo    | 27         |
| Azadirachta indica A. Juss.         | Methanolic leaf extract                                                              | In vitro- PLA2 Inhibitor activity – inhibits the cobra and Russell's viper venoms | 28         |
| Caesalpinia cristia L.              | Seeds and leaves                                                                     | Anti-Contractile skeletal muscle against Bites arietans                        | 29         |
| Calotropis gigantea (L.)            | Methanolic extract of plant                                                           | Neutralization of Haemorrhagic Activity, Neutralization of Necrotizing Activity, Neutralization of Edema forming activity | 30         |
| Cinnamomum tamala (Buch.-Ham.) T. Nees and Eberm | Aqueous and alcoholic extracts of dried bark                                         | In vivo and In vitro models were used to determine the anti-venom capacity of the plant extract by using two dose levels and it showed a significant neutralization of lethality, PLA2 activity and bleeding time. | 31         |
| Coix lacryma-jobi L.                | Ethanolic root extract                                                               | Neutralization of venom-induced HRBC lysis, inhibition of PLAr2, nucleotidase (DNase), fibrinogenolytic enzyme activity | 32         |
| Curcuma longa L.                    | Rhizome extract                                                                       | Enzyme inhibition activity, anti cytotoxicity and anti myotoxicity against Naja venom Anti hemorrhagic activity against Both Rop jararaca venom and anti lethal activity against Crotalus durissus terrificus venom | 33 34      |
| Cyclea peltata (Lam.) Hook. f. & Thomson | Aqueous extract of Cyclea peltata root                                               | Ex vivo neutralization tests such as acetylcholinesterase, protease, direct hemolysis assay, phospholipase activity and procoagulant activity | 35         |
| Emblica officinalis Gaertn.         | Methanolic root extract                                                              | In vitro and in vivo- V. russelli and N. kaouthia induced hemorrhage, coagulant, defibrinogenating and inflammatory activity | 36         |
| Euphorbia hirta L.                  | Whole plant methanolic extract                                                       | Protease, PLA2, hyalurondase and hemolytic inhibitory activity of Naja ora venom induced toxicity | 37 38      |
| Gloriosa superba L.                 | Root ethanolic extract                                                                | In vitro and in vivo neutralizing effect against the venom of Naja nigrig collis | 39         |
| Hemidesmus indicus (L.) R. Br. ex Schult. | Methanolic extract of root                                                          | In vitro and In vivo studies- viper venom-induced lethal, hemorrhagic, coagulant and anticoagulant activity | 40 41      |
| Indigofera tinctoria L.             | Ariel parts methanolic extract                                                       | In vitro and in vivo neutralizing effect against the venom of Naja nigrig collis | 42         |
| Piper longum L.                     | Ethanolic extract of fruits                                                           | Inhibited venom induced lethality, hemorrhage, necrosis, defibrinogenation and inflammatory paw edema, reduced venom induced mast cell degranulation | 43         |
| Symplocos racemosa Roxb.            | Methanolic extract of stem bark                                                       | Enzyme inhibition activity against phosphodiesterase l | 44         |
| Vitex negundo L.                    | Methanolic root extract                                                              | Anti-lethal activity, anti hemorrhagic activity, coagulant, defibrinogenating, fibrinolytic activity | 45         |
| Vitis vinifera L.                   | Methanolic seed extract                                                              | Dabeus/Piper russelli induced proteolytic and hyaluronidase activities, pro-coagulant activity | 46         |
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