International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Comparative Review of Medicinal Plants with Antivenom Activity Against Vipera russelli: From Traditional Use to Scientific Validation

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ABSTRACT:

The envenomation from a Vipera russelli snakebite poses a significant health concern, especially in rural areas where access to conventional antivenom is limited. This review compiles and analyzes current research on the antivenom properties of various herbal plants that have been historically used against V. russelli venom. Among the plants studied, Calotropis gigantea showed the most powerful and comprehensive venom-neutralizing abilities, successfully obstructing lethality, hemorrhage, necrosis, and edema, often surpassing the efficacy of conventional antivenoms. Vitex negundo and Mimosa pudica exhibited notable enzyme inhibition and anti-inflammatory effects, while Acalypha indica, Hemidesmus indicus, Azadirachta indica, and Emblica officinalis contributed to membrane stabilization, targeted enzyme inhibition, and antioxidant activities. The therapeutic effects are attributed to bioactive plant substances such as flavonoids, tannins, saponins, and alkaloids. These findings emphasize the potential of these plants as cost-effective and easily accessible alternatives or additions to conventional antivenom therapy. Further separation of active compounds and clinical validation are recommended to develop safe and effective plant-based antivenom treatments.

KEY WORDS: Vipera russelli, snakebite toxicity, antivenom therapy, herbal medicines, Calotropis gigantea, Vitex negundo, Mimosa pudica, enzyme suppression, phospholipase A_2, plant compounds, conventional medicine, venom neutralization.

1.INTRODUCTION:

Snakebite envenomation continues to be a major but overlooked global health issue, particularly in rural areas of developing nations where healthcare access is restricted. Every year, about 125,000 deaths globally are caused by venomous snakebites, with India facing an estimated 35,000 to 50,000 of those fatalities. The toxins in the venom mainly lead to serious physiological impacts like inflammation, hemorrhaging, neurotoxicity, and potentially fatal outcomes. Even though the intravenous delivery of animal-derived anti-snake venom (ASV) is the primary and sole specific treatment available, its availability in isolated rural locations is frequently insufficient. Additionally, the use of ASV is linked to negative reactions such as anaphylaxis and serum sickness, arising from the foreign proteins found in the antivenom. These constraints have stimulated the pursuit of alternative, cost-effective, and accessible solutions. Medicinal plants, utilized in traditional medicine for ages, provide a promising source of bioactive compounds like terpenoids, alkaloids, and flavonoids that possess therapeutic potential. These natural substances are not only potent but also tend to result in lower chances of drug resistance in comparison to synthetic medications. Worldwide, approximately 25,000 plant-derived remedies are recorded in traditional medical literature, underscoring their important function in health care. In India, traditional medicinal systems such as Ayurveda, Siddha, and Unani make extensive use of medicinal plants, many of which are documented in ancient texts like the Charaka Samhita, which contains more than 340 plant-based medications.

Herbal medicine, or botanical medicine, is a vital aspect of healthcare globally, with the World Health Organization estimating that nearly 80% of the world's population depends on herbal remedies for basic health care. Plants like Acalypha indica, Hemidesmus indicus, Calotropis gigantea, Emblica officinalis (Amla), Azadirachta indica (Neem), Mimosa pudica, and Vitex negundo are commonly found in tropical and subtropical areas and have been utilized traditionally to address various health issues, including snakebites. Because of the rising global interest in traditional medicine, it is crucial to scientifically verify the pharmacological properties of these medicinal plants, comprehend their mechanisms of action, and tackle their conservation in light of increasing demand. This review seeks to gather and examine existing information on the pharmacognosy, pharmacology, and therapeutic prospects of significant medicinal plants that exhibit venom-neutralizing properties, highlighting their importance as alternative or supplementary therapies for snakebite envenomation and various illnesses.

Comparative Ethnobotanical And Phytopharmacological Profile Of Selected Medicinal Plants In Traditional Medicine:

S.No.	Botanical Name	Family	Common Names	Used Parts	Key Phytochemicals	Main Applications	Distribution / Habitat
1	Acalypha indica	Euphorbiaceae	Indian Nettle, Kuppaimeni	Leaves, Roots	Alkaloids, Flavonoids, Saponins, Phenolics, Steroids	Laxative, Skin ailments, Antihelmintic, Respiratory support	India, SE Asia, Africa; disrupted areas
2	Hemidesmus indicus	Apocynaceae (Periplocaceae)	Anantmool, Indian Sarsaparilla	Roots, Stems, Leaves	MBALD, Coumarins, Flavonoids, Steroids, Tannins	Blood cleanser, Anti-inflammatory, Rejuvenating	India, Sri Lanka, Iran; lowlands, borders
3	Emblica officinalis	Phyllanthaceae	Amla, Indian Gooseberry	Fruits, Seeds	Vitamin C, Emblicanin A/B, Gallic acid, Ellagic acid	Antioxidant, Liver tonic, Hair growth, Rejuvenator	India, SE Asia; mountains, lowlands
4	Azadirachta indica	Meliaceae	Neem, Nimb	Leaves, Bark, Seeds, Oil	Azadirachtin, Nimbin, Nimbolide, Quercetin	Antiseptic, Antifungal, Antimalarial, Pesticide	India, Tropics; arid & moist areas
5	Vitex negundo	Lamiaceae	Nirgundi, Sambhalu	Leaves	Rutin, Flavonoids, Essential oils	Anti-inflammatory, Antivenom, Analgesic	Asia, Africa; water margins, woodlands
6	Mimosa pudica	Fabaceae (Mimosoideae)	Touch-me-not, Lajjalu	Leaves, Roots	Mimosine, Flavonoids, Saponins, Tannins, Glycosides	Sedative, Antivenom, Wound healing, Digestive	Indigenous to Americas; tropics
7	Calotropis gigantea	Apocynaceae	Crown Flower, Ak, Erukku	Roots, Leaves, Latex, Flowers	Calotropin, Calactin, Uscharin, Flavonoids, Cardiac glycosides, Saponins	Anti-inflammatory, Antimicrobial, Pain relief (rheumatism), Snakebite treatment, Respiratory issues	India, SE Asia, Africa; dry sandy soils, roadsides, barren lands

2.MATERIALS AND METHODS:

2.1. Acalypha indica

Figure.1 Acalypha indica

- Objective: Investigated the protective role against hemolysis and lethality induced by V. russelli venom.
- Method of Extraction: Sequential solvent extraction (petroleum ether, benzene, chloroform, acetone).
- In Vitro Test: HRBC membrane stabilization test (2–400 µg/mL).
- In Vivo Assessment: Mice administered venom + extract (250, 500, 750 mg/kg, i.p.).
- Result: The acetone extract demonstrated the highest venom neutralization.

2.2. Mimosa pudica

Figure.2 Mimosa pudica

- Objective: To counteract the lethal, hemorrhagic, and enzymatic impacts of V. russelli venom.
- Extraction: Ethanol and water extracts from the entire plant.
- In Vitro Tests: Inhibition of enzymes (PLA_2, protease, fibrinolytic, coagulant activity).
- In Vivo Assessment: Mortality, swelling, bleeding, and the neutralization of PLA_2-induced hemolysis in mice.
- Effective Dose: 0.13 mg extract neutralized $2\times LD_{50}$ of V. russelli toxin.
- Extra Effects: Reduced swelling (up to 30%) and PLA_2-triggered hemolysis (0.12 mg ED_{50}).

2.3. Vitex negundo

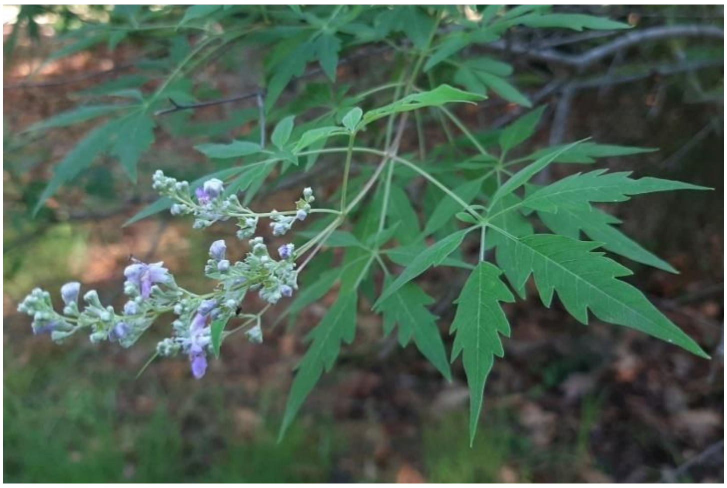

Figure.3 Vitex negundo

• Objective: Assessment of anti-V. russelli venom efficacy both in vitro and in vivo.
• Extraction: Aqueous extracts, ethanol, chloroform from shade-dried leaves.
• Tests Utilized:
Inhibition of edema (in rats).
o Assays for fibrinolytic, PLA_2, hemorrhagic, and coagulant activity.
• In Vivo Experimentation: Mice administered venom with plant extract.
• Dose Effectiveness:
o 0.15–0.17 mg of extract countered $2\times LD_{50}$.

o Inhibition of PLA_2: 0.11–0.13 mg.
o Inhibition of fibrinolysis: 0.13–0.18 mg.
Hemorrhage neutralization is effective across all doses (maximum at 400 mg/kg).

2.4. Calotropis gigantea

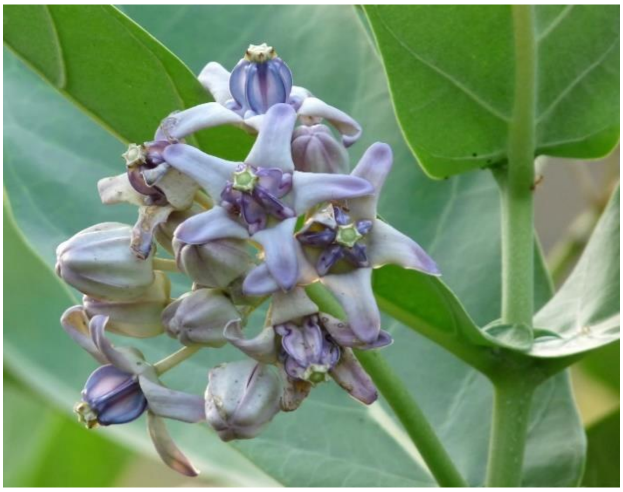

Figure.4 Calotropis gigantea

• Aim: Assessed for the inhibition of enzymes and the neutralization of inflammation caused by V. russelli venom.
• Extraction: Leaves are processed to obtain hydroalcoholic extract; latex is utilized directly.
• Evaluation: Enzyme blocking, swelling decrease, and mortality in mice.
• Application: Investigated both systemic and topical methods.
• Note: While primarily researched for cobra venom, the effects of V. russelli enzymes were also examined.

2.5. Hemidesmus indicus

Figure.5 Hemidesmus indicus

• Aim: Researched the neutralization of systemic effects caused by V. russelli venom.
• Extraction: Root extracts in methanol.
• Bioactive Substances:
o 2-hydroxy-4-methoxy benzoic acid – prevents bleeding and has coagulant properties.
o Lupeol acetate – alleviated edema, PLA_2, hemorrhagic, and cardiotoxic impacts of V. russelli.
• Assessment: Enzyme assays conducted both in vivo (on mice) and in vitro.

2.6. Emblica officinalis

Figure.6 Emblica officinalis

- Aim: Defense against oxidative stress and inflammation induced by V. russelli venom.
- Extraction: Aqueous and hydro-alcoholic extracts of fruit pulp.
- Tests: Evaluated antioxidant and anti-inflammatory effects.
- Application: Investigated for reduction of systemic toxicity due to venom exposure.

2.7. Azadirachta indica

Figure.7 Azadirachta indica

- Aim: Investigated enzyme inhibition and prevention of systemic toxicity caused by V. russelli venom.
- Extraction: Leaf and bark extracts of ethanol and chloroform.
- Tests: Enzyme suppression, inflammation reduction, liver protection response.
- In Vivo Testing: Emphasize minimizing systemic toxicity caused by venom in rodent models.

RESULT AND DISCUSSION:

Plant	Results (Vipera russelli)	Discussion	Mechanism of Action
Acalypha indica	In vitro HRBC membrane stabilization demonstrates dose-dependent suppression of venom-induced hemolysis; in vivo defense in mice with acetone extract	Endorses conventional applications; acetone extract demonstrates optimal venom neutralization, presumably through membrane safeguarding	Stabilizes RBC membranes from venom harm; bioactive tannins, flavonoids, phenolics play a role
Calotropis gigantea	Oral extract enhanced survival (up to 83%) against 2–3 LD_{50} doses of venom; diminished venom-related hemorrhage, necrosis, and edema	More efficient than polyvalent antivenom for bleeding and tissue death; wide-ranging venom counteraction	Alkaloids, flavonoids, tannins, saponins, triterpenoids counteract deadly and tissue-harming elements of venom

Plant	Results (Vipera russelli)	Discussion	Mechanism of Action
Hemidesmus indicus	Methanolic extracts reduced hemorrhage, coagulation, edema, PLA_2 activity; improved antiserum neutralization	Plant compounds enhance venom neutralization and antiserum efficacy; effective systemic protection	2-hydroxy-4-methoxy benzoic acid and lupeol acetate block venom enzymes and associated toxic impacts
Emblica officinalis	Neutralized coagulant, hemorrhagic, defibrinogenating, and inflammatory effects induced by venom; no direct precipitation of venom proteins	Probably counteracts venom through antioxidant and anti-inflammatory mechanisms instead of direct binding to the venom	Disrupts venom enzymatic/toxic functions through antioxidants (flavonoids, tannins, ascorbic acid)
Mimosa pudica	Full neutralization of $2LD_{50}$ venom toxicity; blocked PLA_2, coagulation, fibrinolysis, and swelling development	Neutralization of broad-spectrum venom; likely primary mechanism is enzyme inhibition; effects observed are dose-dependent	Flavonoids, tannins, and alkaloids block PLA_2 and various venom enzymes, lowering toxicity and inflammation
Azadirachta indica	Isolated PLA_2 inhibitor (AIPLAI) demonstrated dose-dependent suppression of venom PLA_2 activity and inhibited hemolysis and inflammation	Promising antivenom candidate targeting enzymes with low toxicity; selective inhibition of PLA_2 crucial for minimizing tissue damage	Binds to or modifies the active site of the PLA_2 enzyme, inhibiting its catalytic function and the resulting toxic effects of venom
Vitex negundo	Total neutralization of $2LD_{50}$ toxicity; marked reduction of edema, bleeding, PLA_2 activity, coagulation, and fibrinolysis	Flavonoids and polyphenols aid in neutralizing venom at multiple targets, similar to polyvalent antivenom	Anti-inflammatory effects and enzyme inhibition from taxaterone and gallic acid derivatives counteract venom toxins

COMPARATIVE CONCLUSION ON ANTIVENOM ACTIVITY AGAINST VIPER RUSSELLI VENOM:

Among the different plant extracts examined for counteracting Vipera russelli venom, Calotropis gigantea exhibited the strongest and most extensive antivenom effects. It greatly enhanced survival rates in animal studies, successfully countered venom-induced lethality, bleeding, tissue damage, and swelling, and demonstrated greater effectiveness than standard polyvalent antivenom in diminishing hemorrhagic and necrotic impacts.

Vitex negundo and Mimosa pudica demonstrated significant antivenom potential, effectively blocking venom-triggered enzymatic activities like phospholipase A_2 (PLA_2), coagulation, and hemorrhage, exhibiting notable protective effects in vivo. These plants offer promising additional treatment options because of their wide-ranging effectiveness.

Acalypha indica and Hemidesmus indicus exhibited notable membrane stabilization and enzyme inhibition, aiding in venom neutralization; however, their overall effectiveness was somewhat lesser than that of C. gigantea and V. negundo.

Azadirachta indica presented a distinct mechanism of action by specifically inhibiting the PLA_2 enzyme, positioning it as a significant option for supplementary therapy aimed at neutralizing enzymatic toxins.

Emblica officinalis showed moderate protective effects primarily through antioxidant and anti-inflammatory mechanisms instead of direct venom neutralization.

In conclusion, Calotropis gigantea emerges as the most promising option for creating plant-derived antivenom for Vipera russelli venom due to its extensive and powerful neutralizing capabilities against various venom-related disorders. Additional phytochemical extraction and clinical research are necessary to fully exploit its therapeutic potential.

From taxaterone, derivatives of gallic acid counteract venom toxins

CONCLUSION:

The thorough assessment of different medicinal plants against Vipera russelli venom shows encouraging natural options and supplements to standard antivenom treatment. Extracts from Calotropis gigantea, Vitex negundo, Mimosa pudica, Acalypha indica, Hemidesmus indicus, Azadirachta indica, and Emblica officinalis showed notable neutralization of venom-induced mortality, bleeding, tissue damage, swelling, and enzymatic functions including phospholipase A_2 and coagulation.

Of these, Calotropis gigantea showed the strongest protective effects against various venom-induced toxicities, demonstrating superior ability to neutralize hemorrhagic and necrotic damage compared to conventional antivenoms. Other plants such as Vitex negundo and Mimosa pudica demonstrated effective enzyme inhibition and anti-inflammatory effects, highlighting their potential for therapy.

Action mechanisms ranged from membrane stabilization and enzyme inhibition (notably PLA_2), to antioxidant and anti-inflammatory effects, as well as disruption of venom-induced coagulation and tissue injury. The existence of bioactive phytochemicals like flavonoids, tannins, saponins, alkaloids, and phenolic compounds supports these antivenom properties.

In general, these plants serve as important resources for creating new, plant-derived antivenom treatments, particularly in areas with limited resources where standard serum therapy is not easily available. Future research ought to concentrate on isolating active substances, clarifying specific mechanisms, and performing clinical trials to convert these discoveries into safe and effective therapies for Vipera russelli envenomation.

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