

Snakebite Envenoming: From Ayurvedic Vishachikitsa to Modern Antivenom Therapy—A Critical and Integrative Review

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Abstract

Background: Snakebite envenoming is a major neglected tropical disease and an important cause of preventable mortality and long-term disability, particularly in rural and agricultural communities. The World Health Organization estimates that approximately 4.5–5.4 million people are bitten by snakes annually, with 1.8–2.7 million developing clinical envenoming and tens of thousands dying from its complications. India carries a particularly substantial burden, with the Indian “Big Four”—*Naja naja*, *Bungarus caeruleus*, *Daboia russelii* and *Echis carinatus*—responsible for a large proportion of clinically important envenomations.

Objective: To critically review the classical Ayurvedic framework of Sarpa Visha and compare its diagnostic and therapeutic principles with contemporary understanding of snakebite envenoming, including modern antivenom therapy, supportive management, limitations of existing antivenoms and emerging therapeutic approaches.

Methods: A structured literature search will be conducted using PubMed/MEDLINE, Scopus, Web of Science, Google Scholar and selected authoritative databases. Classical Ayurvedic texts, including Charaka Samhita, Sushruta Samhita, Ashtanga Hridaya and Ashtanga Sangraha, together with relevant literature on Agadatantra and regional traditions of Visha Chikitsa, will be reviewed. Contemporary evidence concerning snake venom composition, clinical syndromes, antivenom efficacy, adverse reactions, venom geographic variation, supportive management and novel therapeutics will also be synthesized.

Results: The review will synthesize Ayurvedic descriptions of Sarpa Visha, including classification of snakes, clinical progression and stage-based management, alongside modern syndromic classification of neurotoxic, haemotoxic, cytotoxic and mixed envenoming. Current evidence indicates that antivenom remains the principal specific therapy capable of preventing or reversing most systemic effects of snake envenoming when appropriately administered. However, geographical venom variation, incomplete toxin coverage, delayed presentation, inadequate availability and limitations of existing polyvalent antivenoms remain important challenges, particularly in India and South Asia.

Conclusion: Agadatantra represents an important historical knowledge system concerning snake envenomation, while modern toxicology provides validated approaches to diagnosis, resuscitation, antivenom therapy and supportive care. A scientifically responsible integrative approach should preserve classical knowledge while subjecting potentially useful Agada formulations and therapeutic concepts to contemporary experimental and clinical validation.

Keywords: Snakebite envenoming; Sarpa Visha; Vishachikitsa; Agadatantra; antivenom; snake venom; Ayurveda; Agada; toxicology; integrative medicine.

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Introduction

Snakebite envenoming is a medically important toxicological emergency with potentially fatal neurological, haemorrhagic, renal, cardiovascular and local tissue complications. Its burden is concentrated in tropical and subtropical regions, especially among rural communities with limited access to timely healthcare. ^[1,2] WHO identifies high-quality antivenom as the most effective treatment for preventing or reversing most systemic effects of snake envenoming, while emphasizing rapid immobilization, transport and appropriate supportive care. ^[1,2]

In India, clinically important envenoming has historically been associated with the Big Four: *Naja*

naja, *Bungarus caeruleus*, *Daboia russelii* and *Echis carinatus*. However, contemporary venom research demonstrates substantial interspecific, intraspecific and geographic variation, and medically important species outside the Big Four can also cause severe disease. ^[3–7] These findings have implications for antivenom design, clinical recognition and regional public-health planning.

Ayurveda describes Sarpa Visha within Agadatantra, with detailed traditional descriptions of venomous snakes, clinical manifestations, progression and treatment. ^[8–11] The present review therefore examines the classical Ayurvedic framework alongside contemporary toxicology, with particular

attention to areas of possible convergence, limitations of comparison and opportunities for evidence-based research

2. Objectives

* To review the classical Ayurvedic description and classification of Sarpa Visha.

* To summarize the clinical manifestations and progression of snake envenomation described in Ayurvedic literature.

* To review contemporary understanding of snake venom, clinical syndromes and modern management.

* To critically examine Ayurvedic Agada formulations and other Vishachikitsa practices in light of available pharmacological and clinical evidence.

* To identify evidence gaps and future research priorities for integrative snakebite research.

3. Ayurvedic Perspective of Sarpa Visha

3.1 Sarpa Visha and Agadatantra

Agadatantra is the Ayurvedic discipline concerned with poisons, toxic substances, their manifestations, diagnosis, management and medico-toxicological principles. Sarpa Visha occupies an important position within this discipline. Classical texts describe snake classification, venom characteristics, routes and patterns of spread, clinical progression and treatment principles.

3.2 Classification of Snakes

Classical Ayurvedic texts describe categories of venomous snakes, traditionally including Darvikara, Mandali and Rajimanta groups. These descriptions include morphological and clinical characteristics. [9,10.] Modern interpretation should be cautious because classical taxonomic categories do not necessarily correspond exactly to contemporary zoological species or venom phenotypes.

Table 1. Ayurvedic Classification of Venomous Snakes and Corresponding Classical Clinical Features

Ayurvedic group	Classical description / features	Potential modern clinical relevance	Evidence limitation
Darvikara	Classical group of venomous snakes described with characteristic morphology and clinical features.	May be discussed alongside predominantly neurotoxic presentations in a cautious clinical comparison.	Not a direct zoological or venom-phenotype equivalent; species-level validation is required.

Mandali	Classical group associated with characteristic morphology and manifestations of visha.	May be discussed alongside haemotoxic/pr ocoagulant presentations.	Not a direct taxonomic equivalent; correlation requires species- and syndrome-level validation.
Rajimanta	Classical category of venomous snakes described in Ayurvedic literature.	Historical classification relevant to Sarpa Visha documentation.	Modern correspondence cannot be assumed without contemporary validation.

3.3 Visha Vega and Clinical Progression

The concept of Visha Vega describes progressive manifestations following exposure to poison. [9,10.] Some elements can be discussed alongside modern observations of evolving envenomation; however, direct equivalence should not be assumed without clinical evidence.

Table 2. Comparison of Sarpa Visha Manifestations with Modern Envenoming Syndromes

Ayurvedic concept / manifestation	Modern clinical framework	Possible relevance	Evidence limitation
Sarpa Visha	Snake envenoming	Historical toxicological framework for describing snake envenomation.	Terminology and mechanisms are not identical.
Visha Vega / progressive manifestations	Clinical progression of envenoming	May provide a historical model for progression after exposure.	Direct correlation remains uncertain without

			clinical evidence.
Neurotoxic manifestations	Neurotoxicity / neuroparalysis	Potential clinical comparison where compatible manifestations occur.	Requires species- and syndrome-level validation.
Haemotoxic manifestations	Coagulopathy / haemorrhage / procoagulant effects	Potential clinical comparison.	Classical descriptions should not be treated as modern mechanistic diagnoses.
Local tissue injury	Cytotoxic/ local tissue injury	Possible area of clinical comparison.	Direct equivalence requires evidence.

3.4 Vishachikitsa

Classical management includes measures intended to limit venom spread, remove or neutralize poison, support the affected individual and administer Vishaghna or Agada preparations^[8,11]. The historical importance of these measures is considerable, but their contemporary therapeutic value requires pharmacological, toxicological and clinical validation.

4. Modern Understanding of Snake Envenoming

4.1 Venom Composition

Snake venoms are complex mixtures of proteins, peptides, enzymes and other bioactive molecules. Their composition varies among species, geographic populations and individual snakes. Clinically important effects may include neurotoxicity, coagulopathy, haemorrhage, cytotoxicity, myotoxicity and cardiovascular effects.

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5.2 Clinical Syndromes

Clinically, snake envenoming may present predominantly with neurotoxicity, haemotoxic or

procoagulant effects, local cytotoxic injury, myotoxicity, or combinations of these manifestations. Recognition of the syndrome is essential for appropriate monitoring and treatment.

5.3 Antivenom Therapy

Antivenom is the principal specific therapy for systemic snake envenoming. It consists of immunoglobulins or immunoglobulin fragments capable of binding venom components and reducing their biological effects. Its effectiveness depends on appropriate product selection, timely administration and adequate neutralization of the clinically relevant venom components.

Table 3. Modern Antivenom Therapy

Aspect	Key points
Mechanism	Antivenom contains immunoglobulins or immunoglobulin fragments that bind venom components and reduce their biological effects.
Indications	Principal specific therapy for systemic snake envenoming when clinically indicated.
Effectiveness	Depends on appropriate product selection, timely administration and adequate neutralization of clinically relevant venom components.
Limitations	Geographic venom variation, incomplete toxin coverage, delayed presentation, availability, cost and adverse reactions.
Indian/South Asian challenge	Variation in venom composition and contribution of species outside traditional priority groups complicate antivenom development and deployment.
Emerging alternatives	Novel small-molecule inhibitors and engineered antibody-based approaches are emerging areas of therapeutic development.

5.4 Limitations of Current Antivenoms

Important limitations include geographic venom variation, incomplete neutralization of some toxin components, delays in treatment, product

availability, cost and adverse reactions. In India and South Asia, variation in venom composition and the contribution of species outside traditional priority groups present important challenges for antivenom development and deployment.

6. Ayurvedic Agada Formulations: Evidence and Research Potential

Numerous Agada formulations are described in classical literature for Vishachikitsa. Examples discussed in the literature include Mahaagada, Sanjivana Agada, Drakshadi Agada, Lodhraseetadi Agada and other formulations described for snakebite or broader toxicological indications.

Table 4. Major Ayurvedic Agada Formulations Described for Snake Envenomation

Formulation	Classical indication / context	Dosage or form	Available evidence / research status
Mahaagada	Described in classical Vishachikitsa literature for toxicological indications including snake envenomation.	Orally – 1,2 grams Anupana – Madhu Used as Nasya, Anjana, Abhayaanga	Primarily classical textual evidence; requires standardized pharmacological and clinical evaluation.
Sanjivana Agada	Classical Agada formulation described in Vishachikitsa.	4 vati	Requires distinction between textual evidence and experimental/clinical evidence.
Drakshadi Agada	Described for snakebite or broader toxicological indications in the literature.	Orally – 1,2 grams	Evidence should be categorized as classical, pharmacognostic, in-vitro, animal or clinical.
Lodhraseetadi Agada	Described in classical literature for Vishachikitsa	Orally – 1,2	Contemporary efficacy should not be inferred from

	indications.	grams	traditional use alone.
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A publication-quality review should distinguish clearly between classical textual evidence, pharmacognostic evidence, in-vitro studies, animal studies, observational clinical reports and controlled clinical trials. Traditional use alone should not be presented as proof of efficacy.

Potential research pathways include standardization of formulations, chemical fingerprinting, venom-enzyme inhibition studies, neutralization assays, animal models, pharmacokinetic studies, safety evaluation and carefully designed clinical trials.

Table 5. Evidence Framework for Ayurvedic Agada Research

Evidence level	What should be assessed	Interpretation
Classical textual evidence	Source text, edition, formulation composition, indication and dosage/form.	Documents historical use; does not establish modern efficacy.
Pharmacognostic evidence	Authentication, standardization and quality control of ingredients/formulations.	Supports reproducibility and identity.
In-vitro evidence	Venom-enzyme inhibition and venom-neutralization assays.	Generates mechanistic hypotheses; does not by itself establish clinical benefit.
Animal evidence	Appropriate validated venom models, safety and neutralization outcomes.	Provides preclinical evidence; translation to humans remains uncertain.
Clinical evidence	Observational studies and controlled clinical trials with standardized outcomes.	Required for reliable assessment of clinical efficacy and safety.

7.1 Integrative Comparison

Ayurvedic concept	Modern framework	Potential relevance	Evidence limitation
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Sarpa Visha	Snake envenoming	Historical toxicological framework	Terminology is not identical
Darvik ara	Predominantly neurotoxic syndromes	Possible clinical comparison	Requires species- and syndrome-level validation
Mandal	Predominantly haemotoxic/procoagulant syndromes	Possible clinical comparison	Not a direct taxonomic equivalent
Visha Vega	Clinical progression	May provide a historical model of progression	Direct correlation is uncertain
Agada	Potential pharmacological/antitoxic therapy	Source of testable therapeutic hypotheses	Insufficient high-quality clinical evidence
Vishaghna drugs	Potential antitoxic/pharmacological activity	Candidates for mechanistic research	Requires standardized experimental validation

8. Research Gaps

- Limited high-quality clinical evidence for most Ayurvedic Agada formulations used in snakebite.
- Insufficient standardization and chemical characterization of multi-ingredient formulations.
- Need for species- and venom-specific pharmacological testing.
- Limited translation from in-vitro findings to validated in-vivo and clinical outcomes.

- Need for region-specific research because venom composition and antivenom performance vary geographically.
- Need for rigorous safety assessment and standardized reporting of adverse events.
- Need for multidisciplinary collaboration among Ayurvedic toxicologists, modern toxicologists, pharmacologists, herpetologists and clinicians.

Table 6. Research Gaps and Future Priorities

Research gap	Priority action
Limited high-quality clinical evidence	Conduct ethically designed, adequately reported clinical studies where justified.
Poor standardization and chemical characterization	Standardize multi-ingredient formulations and perform chemical fingerprinting.
Insufficient species-/venom-specific testing	Evaluate candidate formulations against relevant regional venoms and toxins.
Limited translation from in-vitro to clinical outcomes	Use validated in-vivo models followed by appropriately designed clinical research.
Geographic variation in venom and antivenom performance	Prioritize region-specific venom characterization and therapeutic evaluation.
Safety and adverse-event reporting gaps	Implement standardized safety assessment and adverse-event reporting.
Need for multidisciplinary collaboration	Integrate Ayurvedic toxicologists, modern toxicologists, pharmacologists, herpetologists and clinicians.

9. Future Directions

Future research should prioritize rigorous characterization of candidate Agada formulations, standardized venom-neutralization assays, mechanistic studies against relevant venom toxins, appropriate animal models and ethically designed clinical trials. Integrative research should focus on questions that can be empirically tested rather than attempting to establish equivalence between

classical terminology and modern toxicological mechanisms.

Modern therapeutic development is also moving toward novel small-molecule inhibitors and engineered antibody-based approaches. These developments provide an opportunity to investigate whether selected Ayurvedic pharmacological leads can contribute to future venom-targeted therapeutic discovery, provided that safety and efficacy are established through contemporary research methods.

10. Conclusion

Snakebite envenoming remains a major toxicological and public-health challenge. Agadatantra contains a substantial historical body of knowledge concerning Sarpa Visha, including classification, clinical manifestations, progression and therapeutic concepts. Modern toxicology provides validated approaches to emergency care, antivenom therapy and supportive management. A scientifically responsible integrative approach should preserve and critically examine classical knowledge while requiring contemporary experimental and clinical validation before therapeutic claims are made. The most promising future lies in evidence-driven collaboration between traditional knowledge systems and modern venom research.

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