



From a Global Perspective Towards an Integrated Approach for Ophitoxaemia

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Abstract

Ophitoxaemia is the medical term that describes an injury induced by a snake bite which can be fatal in the case of venomous snakes. Bleeding, allergic response, necrosis, and bradycardia are symptoms of venomous bite. Snake venom is from a complex mixture of proteins- enzymes, nonenzymatic polypeptide toxins, and nontoxic proteins. Based on the nature of the toxin and type of snake, the toxins are classified into neuro, cardio, and cytotoxins. This comparative study aims to explore and compare the practice of the traditional *Ayurveda* system and the modern system of medicine for snakebite management. By examining the existing literature and research on both systems, this article will provide insights into their efficacy, safety, and potential for integration.

Keywords: *Ayurveda*, Integration, Limitations, Modern Medicine, Snakebite

1. Introduction

Snakebite is a significant public health issue that affects numerous individuals globally, particularly in regions with a high prevalence of venomous snakes. It poses a considerable burden on healthcare systems and can lead to severe illness and death if not promptly managed. As a result, snakebite management has become a crucial area of study for both traditional and modern medical systems. Snakebite has long been a threat in many areas of the world, particularly in tropical and subtropical climates where venomous snakes are common^{1,2}. It is estimated that snakebites result in tens of thousands of deaths each year, with hundreds of thousands of individuals suffering from long-term disabilities or disfigurement³. The impact is particularly significant in rural and underserved communities where access to healthcare facilities and antivenom therapy may be limited. The traditional *Ayurveda* system, originating

from ancient Indian medicine, has been practised for centuries and encompasses a holistic approach to healthcare. *Ayurvedic* practitioners believe that snakebite is not merely a physical ailment but also affects the mental and spiritual well-being of the individual. *Ayurveda* emphasizes the use of natural remedies, herbal formulations, and specific treatment modalities to manage snakebites. Traditional healers employ various techniques, including venom-neutralizing therapies, to inhibit the effects of snake venom and promote healing⁴.

On the other hand, modern medicine has developed specialized approaches to snakebite management. With advancements in medical science, the modern system of medicine focuses on rapid diagnosis, supportive care, and the administration of antivenom therapy. Highly specific polyvalent antivenoms have been developed to neutralize the venom of various snake species. Modern

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medical professionals employ evidence-based practices, wound management techniques, and monitoring protocols to ensure the best possible outcomes for snakebite victims⁵.

The comparative study between the traditional *Ayurveda* system and modern medicine for snakebite management is significant. It allows for an in-depth exploration and evaluation of the efficacy, safety, and potential integration of these two systems. By examining the existing literature and research on both approaches, healthcare professionals, researchers, and policymakers can gain insights into the strengths and limitations of each system. This comparative analysis aids in identifying potential areas of collaboration and integration, leading to improved snakebite management strategies.

Furthermore, a comparative literature study provides a comprehensive overview of the practices, philosophies, and outcomes associated with snakebite management in different cultural and medical contexts. It enables a broader understanding of diverse therapeutic approaches and helps bridge the gap between traditional and modern medical systems. This knowledge can facilitate informed decision-making in the development of evidence-based protocols, the optimization of healthcare services, and the enhancement of snakebite treatment outcomes.

2. Treatment Strategies

2.1 In *Ayurveda* System of Medicine

Ayurveda, the traditional Indian system of medicine, has a comprehensive approach to the treatment of snakebites. *Ayurvedic* texts provide detailed guidelines and methodologies for managing snakebite cases, focusing on both immediate relief and long-term recovery. The *Ayurvedic* system considers snakebite as a medical emergency and emphasizes the importance of prompt action to minimize the effects of venom on the body. Here are some key aspects of the *Ayurvedic* system of medicine for snakebite:

2.1.1 Identification and Assessment

Ayurvedic practitioners are trained to identify the type of snake and assess the severity of the bite. Different snakes produce different types of venom, which can have varying effects on the body. Proper identification

helps in determining the appropriate treatment strategy⁶.

2.1.2 Immediate First Aid

Ayurveda recommends various immediate first aid measures to be taken at the site of the snakebite. This includes immobilizing the affected limb, keeping the person calm and still, and preventing the venom from spreading further into the body⁶.

2.1.3 Mantra and Chanting

Chanting specific *mantras* is believed to have a therapeutic effect on snakebite. The rhythmic chanting of *mantras* is considered to nullify the effects of the venom and promote healing. It is believed that *mantra* chanting has the power to eliminate poison from the system⁶.

2.1.4 Arishta-Bandhana (Ligation)

Ligation is applied above the bite site using a rope or tourniquet-like bandage. This helps prevent the venom from spreading further into the bloodstream. However, it is important to ensure that the ligation is neither too tight nor too loose to avoid complications⁶.

2.1.5 Utkartana, Nishpidana, and Chushana

Utkartana involves making incisions at the bite site to prevent the further spread of venom. *Nishpidana* is the squeezing of the area around the bite site, while *Chushana* involves sucking out the venomous blood. These measures aim to eliminate the venom from the body⁶.

2.1.6 Agni Karma (Cauterization)

Agni Karma involves the application of heat or cauterization at the site of the snakebite. This technique is believed to destroy the venom present in the skin and muscle layers. Specific types of sticks made from gold or iron are used for this purpose⁶.

2.1.7 Parisheka and Avagaha

Parisheka refers to the application of cold therapies around the bite site. This is done using herbal extracts or cool water to prevent the spread of venom and reduce complications. *Avagaha* involves immersing the affected part in medicated decoctions or lukewarm oil, which helps inactivate venom components⁶.

2.1.8 Raktamokshan and Pratisaran

Raktamokshan involves bloodletting, which is recommended when the body shows symptoms of toxicity. This process aims to eliminate toxic blood from the body. Pratisaran refers to rubbing the area around the bite site with medicated powders or oils to promote bloodletting⁶.

2.1.9 Vamana Karma and Virechana

Vamana Karma is induced vomiting, and Virechana is purgation therapy. These treatments are used in specific cases based on the individual's constitution and the type of snakebite. They aim to eliminate toxins from the body⁶.

2.1.10 Prashamana and Prativisha

Prashamana is the administration of specific herbal preparations to pacify the effects of the venom based on the predominance of doshas (*Vata*, *Pitta*, *Kapha*) in the snakebite. Prativisha refers to the administration of counter poisons to neutralize the effects of the venom⁶.

2.2 Limitations

2.2.1 Lack of Scientific Evidence

The practices mentioned in the text are based on ancient beliefs and traditions, but they may lack scientific evidence to support their effectiveness and safety. Modern medical practices are generally based on rigorous scientific research and clinical trials.

2.2.2 Potential for Complications

Some of the practices described in the text, such as incisions, cauterization, and bloodletting, can carry the risk of complications. Incisions and cauterization may lead to infection, delayed wound healing, and other tissue damage. Bloodletting can result in excessive blood loss and anaemia.

2.2.3 Lack of Standardization

The text mentions different procedures, herbs, and preparations without specifying standardized guidelines for their application. This lack of standardization can lead to inconsistency in practice and potential variations in outcomes.

2.2.4 Contradiction with Modern Medical Practices

Some of the practices described in the text, such as the application of tourniquets or ligatures, incisions, and suction, contradict modern medical recommendations. Contemporary medical guidelines emphasize the importance of immobilization, prompt transport to a medical facility, and the administration of antivenom.

2.3 Modern System of Medicine

In the case of snakebite, the aim should be a rapid and safe transport of the patient to the hospital. Treatment before transfer to the hospital should be only reassurance to the patient and immobilization of the limb. Applying a tight tourniquet or giving a local incision was strictly discouraged.

2.3.1 First-aid Measures

- Ensure airway and breathing. Keep the patient in a warm, well-ventilated room. Keep the patient immobilized. Apply a crepe bandage starting distal to the bite site.
- At least for 2 hours, observe the patient for local swelling and the patient with asymptomatic for more than 2 hours may be discharged and the others must be admitted for observation.
- Local wound care can be given by cleaning the bite site and giving tetanus prophylaxis. General care includes monitoring pulse, blood pressure, respiration, EKGs for arrhythmias, maintaining adequate hydration, and achieving intravenous access.
- If the snakebite becomes infected, antibiotics are administered. Other medications may include benzodiazepines for anxiety and sedation, opioids for pain, fluid replacement, and vasopressor support for shock.
- A tracheostomy may be needed if a laryngeal spasm is present.

2.4 Anti-Snake Venom (ASV) Therapy

ASV is the most effective antidote for snake venom and is required for systemic envenoming treatment. Immunoglobulin [usually a pepsin-refined F(ab)₂ fragment of full Ig G] purified from the plasma of a

horse, mule, or donkey (equine) or sheep (bovine) infected with one or more snake venoms is used as antivenom^{7,8}. The term “specific” antivenom denotes that the antivenom was developed in response to the venom of the snake that bit the patient and that it is thus expected to contain specific antibodies that will neutralize that venom as well as possibly the venoms of closely related species (para specific neutralization). Monovalent (monospecific) antivenom neutralizes only one species of snake’s venom. Polyvalent (polyspecific) antivenom neutralizes the venoms of snake species, which are often the most medically significant in each geographical location⁹⁻¹¹. Antibodies produced against one species’ venom may have cross-neutralizing action against venoms from closely related species. This was referred to as para-specific activity. Only Polyvalent Anti-Snake Venom (PASV) is manufactured in India from horse serum and is created against four of the most significant venomous snakes: *Naja naja* (cobra), *B. caeruleus* (Indian common krait), *Daboia russelii* (Russell’s viper), and *Echis carinatus* (saw-scaled viper).

Haemostatic abnormalities such as spontaneous systemic bleeding and noncoagulable blood in a 20-minute Whole Blood Clotting Test (20 WBCT) are early indicators of systemic envenoming. Ptosis, external ophthalmoplegia, dysphagia, and paralysis are characteristics of neurotoxic symptoms. For cardiovascular disorders including shock and arrhythmia Administration of the antivenom involves systemic and local approaches. This process occurs over 1 hour, allowing for the rapid attainment of effective blood concentration. Alternatively, an intravenous push injection can be employed, administered cautiously at a rate not exceeding 2 ml/min, although this method is more challenging. On the other hand, local antivenom injection at the bite site is not recommended due to its unproven efficacy, extreme pain it causes, and potential for increasing intra-compartmental pressure. For repeat administration, the dosage should be revisited in specific scenarios. These encompass cases where there are persistent or recurring blood coagulability issues (measured by 20WBCT) after 6 hours from the initial dose, instances where patients continue to experience substantial bleeding 1-2 hours after the first ASV dose, and situations where there is a decline in neurotoxic or cardiovascular indicators 1-2 hours following the initial ASV dose.

2.4.1 Limitations

2.4.1.1 Early Anaphylactic Reactions

These occur between 10-180 minutes after commencing the antivenin. “Urticaria, itching, cough, nausea, vomiting, stomach colic, diarrhoea, and tachycardia are some of the clinical symptoms”.

2.4.1.2 Pyrogenic (Endotoxin) Reactions

They arise 1-2 hours after initiating ASV treatment. Fever, rigidity, chills, and low blood pressure are all clinical symptoms.

2.4.1.3 Late (Serum Sickness Type) Reactions

They develop twelve days following ASV medication (mean 7 days). “Fever, nausea, vomiting, arthralgia, arthritis, diarrhoea, itching, recurring urticaria, myalgia, lymphadenopathy, and proteinuria are all clinical symptoms”¹²⁻²⁵.

2.5 Integrated Approach

Despite the limitations in antivenom still, it is the only treatment available for the snakebite. According to WHO, time plays a key role in reducing the mortality rates of the snakebite. To support the antivenom, adjuvant medicine development area includes small molecule development, drug repurposing, isolated phytoconstituents, and herbal extracts after scientific validation can be formulated as drug which has rapid bioavailability and used as an emergency and adjuvant medicine till they reach hospital for the treatment. An overview of the integrated approach is demonstrated in Figure 1.

3. Conclusion

Snakebites remain a major public health concern that needs appropriate management techniques. The classic *Ayurvedic* system and Western medicine both have their approaches to snakebite therapy, each with its advantages and disadvantages. A comparative literature review on a thorough examination of these systems allows for a better knowledge of their efficacy, safety, and prospective integration. According to the review, a few *Ayurvedic* techniques, such as tourniquets or ligatures, incisions, and suction, contradict modern medical standards and may result in difficulties. However, because of the integration of both systems of medicine,

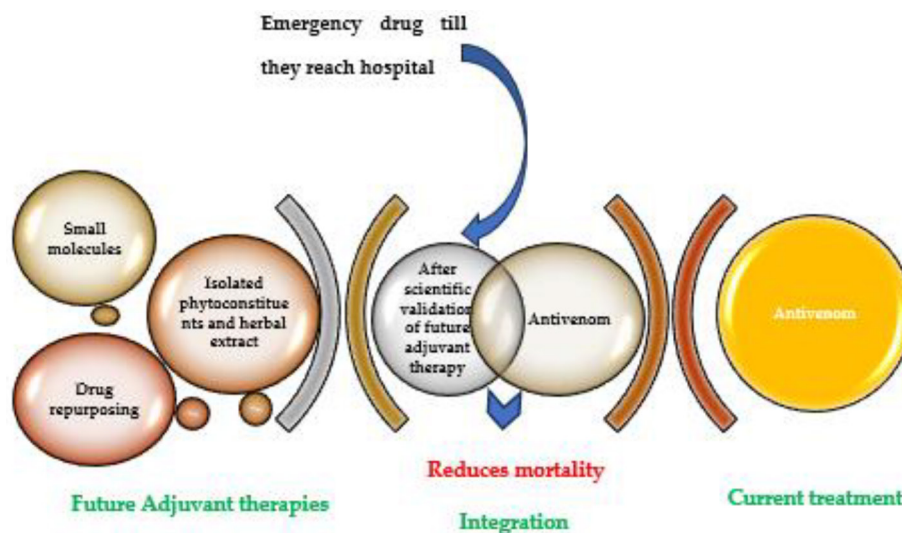


Figure 1. Overview of the integrated approach for ophitoxaemia.

the creation of standardized herbal emergency drugs as supportive treatment and subsequent administration of anti-snake venom will be the association between both systems of medicine, significantly reducing morbidity and fatality rates.

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5. References

1. Kasturiratne A, Wickremasinghe AR, de Silva N, Gunawardena NK, Pathmeswaran A, Premaratna R, *et al.* The global burden of snakebite: A literature analysis and modelling based on regional estimates of envenoming and deaths. *PLoS Med.* 2008; 5(11):e218. <https://doi.org/10.1371/journal.pmed.0050218> PMID:18986210 PMCID: PMC2577696
2. Chippaux JP. Snake-bites: Appraisal of the global situation. *Bull World Health Organ.* 1998; 76:515-24.
3. World Health Organization (WHO). Snakebite envenoming. WHO Press. 2019. Available from: <https://www.who.int/newsroom/fact-sheets/detail/snakebite-envenoming>
4. Jaiswal YS, Williams LL. A glimpse of *Ayurveda* - The forgotten history and principles of Indian traditional medicine. *J Tradit Complement Med.* 2017; 7(1):50-3. <https://doi.org/10.1016/j.jtcme.2016.02.002> PMID:28053888 PMCID: PMC5198827
5. Hamza M, Knudsen C, Gnanathasan CA, Monteiro W, Lewin MR, Laustsen AH, *et al.* Clinical management of snakebite envenoming: Future perspectives. *Toxicol.* 2021; 11:100079. <https://doi.org/10.1016/j.toxcx.2021.100079> PMID:34430847 PMCID: PMC8374517
6. Pandey N, Sharma A, Kadu VA, Shankar G. Critical review to understand the twenty-four *Ayurveda* treatment modalities for the management of snake bite. *J Indian Syst Med.* 2022; 10(1):19-9. https://doi.org/10.4103/JISM.JISM_81_21
7. Gutierrez JM, Leon G, Lomonte B, Angulo Y. Antivenoms for snakebite envenomings. *Inflamm Allergy Drug Targets.* 2011; 10(5):369-80. <https://doi.org/10.2174/187152811797200669> PMID:21745181
8. Gutiérrez JM, Solano G, Pla D, Herrera M, Segura Á, Vargas M, *et al.* Preclinical evaluation of the efficacy of antivenoms for snakebite envenoming: State-of-the-art and challenges ahead. *Toxins.* 2017; 9(5):163. <https://doi.org/10.3390/toxins9050163> PMID:28505100 PMCID: PMC5450711
9. Whalen K. *Pharmacology.* 6th ed. Lippincott Illustrated Reviews; 2015. p. 644-6.
10. Roberts NLS, Johnson EK, Zeng SM, Hamilton EB, Abdoli A, Alahdab F, *et al.* Global mortality of snakebite envenoming between 1990 and 2019. *Nat Commun.* 2022; 13(1):6160. <https://doi.org/10.1038/s41467-022-33627-9>
11. Vanuopadath M, Rajan K, Alangode A, Nair SS, Nair BG. The need for next-generation antivenom for snakebite envenomation in India. *Toxins.* 2023; 15(8):510. <https://doi.org/10.2174/187152811797200669> PMID:21745181
12. Ahmed S, Ahmed M, Nadeem A, Mahajan J, Choudhary A, Pal J. Emergency treatment of a snake bite: Pearls from

- literature. *J Emerg Trauma Shock*. 2008; 1(2):97-105. <https://doi.org/10.4103/0974-2700.43190> PMID:19561988 PMCID: PMC2700615
13. Fry B. Snakebite: When the human touch becomes a bad touch. *Toxins*. 2018; 10(4):170. <https://doi.org/10.3390/toxins10040170>. PMID:29690533 PMCID: PMC5923336
 14. Bénard-Valle M, Neri-Castro EE, Fry BG, Boyer L, Cochran C, Alam M, *et al*. Antivenom research and development. In: Fry BG, editor. *Venomous Reptiles and Their Toxins: Evolution, Pathophysiology and Biodiscovery*. New York: Oxford University Press; 2015. p. 61-72.
 15. Boyer L, Alagón A, Fry BG, Jackson TNW, Sunagar K, Chippaux JP. Signs, symptoms and treatment of envenomation. In: Fry BG, editor. *Venomous Reptiles and Their Toxins: Evolution, Pathophysiology and Biodiscovery*. New York: Oxford University Press; 2015. p. 32-60.
 16. Sutherland SK, Lovering KE. Antivenoms: use and adverse reactions over a 12-month period in Australia and Papua New Guinea. *Med J Aust*. 1979; 2(13):671-4. <https://doi.org/10.5694/j.1326-5377.1979.tb104266.x> PMID:530188
 17. Sutherland SK. Acute untoward reactions to antivenoms. *Med J Aust*. 1977; 2(25):841-2. <https://doi.org/10.5694/j.1326-5377.1977.tb99342.x>
 18. Sutherland SK. Serum reactions. An analysis of commercial antivenoms and the possible role of anticomplementary activity in de-novo reactions to antivenoms and antitoxins. *Med J Aust*. 1977; 1:613-5. <https://doi.org/10.5694/j.1326-5377.1977.tb130959.x> PMID:327229
 19. Malasit P, Warrell DA, Chanthavanich P, Viravan C, Mongkolsapaya J, Singhthong B, *et al*. Prediction, prevention, and mechanism of early (anaphylactic) antivenom reactions in victims of snake bites. *British Medical Journal*. 1986; 292(6512):17-20. <https://doi.org/10.1136/bmj.292.6512.17> PMID:3080048 PMCID: PMC1338972
 20. de Silva HA, Pathmeswaran A, Ranasinha CD, Jayamanne S, Samarakoon SB, Hittharage A, *et al*. Low-dose adrenaline, promethazine, and hydrocortisone in the prevention of acute adverse reactions to antivenom following snakebite: a randomised, double-blind, placebo-controlled trial. *PLoS Med*. 2011; 8(5):e1000435. <https://doi.org/10.1371/journal.pmed.1000435> PMID:21572992 PMCID: PMC3091849
 21. Moran NF, Newman WJ, Theakston RD, Warrell DA, Wilkinson D. High incidence of early anaphylactoid reaction to SAIMR polyvalent snake antivenom. *Trans R Soc Trop Med Hyg*. 1998; 92(1):69-70. [https://doi.org/10.1016/S0035-9203\(98\)90959-2](https://doi.org/10.1016/S0035-9203(98)90959-2) PMID:9692158
 22. Vongphoumy I, Chanthilat P, Vilayvong P, Blessmann J. Prospective, consecutive case series of 158 snakebite patients treated at Savannakhet provincial hospital, Lao People's Democratic Republic with a high incidence of anaphylactic shock to horse derived F(ab')₂ antivenom. *Toxicon*. 2016; 117:13-21. <https://doi.org/10.1016/j.toxicon.2016.03.011> PMID:26995210
 23. León G, Herrera M, Segura Á, Villalta M, Vargas M, Gutiérrez JM. Pathogenic mechanisms underlying adverse reactions induced by intravenous administration of snake antivenoms. *Toxicon*. 2013; 76:63-76. <https://doi.org/10.1016/j.toxicon.2013.09.010> PMID:24055551
 24. Ryan NM, Downes M, Isbister GK. Clinical features of serum sickness after Australian snake antivenom. *Toxicon*. 2015; 108:181-3. <https://doi.org/10.1016/j.toxicon.2015.10.012> PMID:26525657
 25. Tritt A, Gabrielli S, Zahabi S, Clarke AE, Moisan J, Eisman H, *et al*. Short- and long-term management of cases of venom-induced anaphylaxis is suboptimal. *Ann Allergy Asthma Immunol*. 2018; 121(2):229-234.e1. <https://doi.org/10.1016/j.anai.2018.04.006> PMID:29656144