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A review on therapeutic potential of Eaegantha Thailam - Traditional siddha polyherbal formulation for treating arthropod envenomation

B Abarna[1*], M Raghavi[1], R Karpagambal[1], R Sathish Adithya[2]
[1] Department of Nanju Maruthuvam (Siddha Toxicology), National Institute of Siddha (Affiliated to TN. Dr. MGR Medical University), Tambaram Sanatorium, Tamil Nadu, India
[2] Associate Professor, Department of Nanju Maruthuvam (Siddha Toxicology), National Institute of Siddha (Affiliated to TN. Dr. MGR Medical University), Tambaram Sanatorium, Tamil Nadu, India

Abstract
Eaegantha Thailam, a traditional Siddha medicinal formulation, has been indicated to treat arthropod bites and stings. This study aimed to investigate the pharmacological properties of its ingredients, exploring their potential in alleviating arthropod bite and stings. Siddha medicine Eaegantha thailam utilizes bitter taste to counteract toxins and venoms, promoting digestion, detoxification, and nervous system calmness. Herbs used in this formulation exhibit anti-inflammatory, antioxidant, antimicrobial, and antivenom properties, mitigating venom-induced symptoms. Phytochemical constituents such as strychnine, nimbin, and bhilawanol promote wound healing, immune response, and detoxification. Anupanam, a pharmacological concept, enhances drug delivery and bioavailability through strategic combinations, optimizing treatment efficacy and enabling personalized medicine. By restoring balance of three humors (Vata, Pitta, Kapha) in the body, Siddha medicine offers a holistic approach in treating venomous bites and inflammatory conditions, providing a complementary solution to modern medicine and promoting natural healing and well-being.

Keywords: Arthropod bite, Siddha medicine, Eaegantha thailam, taste philosophy, Kuzhi thailam, distillate

Introduction

The term "bug bite" encompasses bites and stings from arthropods, a frequent event that may lead to serious health consequences. As the largest animal kingdom division, arthropods, including insects and arachnids, can inflict bites and stings that lead to localized reactions like redness, swelling, and hives, as well as systemic reactions like anaphylaxis, organ failure, and even death. Insect bites and stings are classified into two distinct categories: venomous (e.g., from certain spiders, scorpions, and insects) and non-venomous (e.g., from mosquitoes, flies, and fleas) [1]. A sting is a defensive response by a venomous insect, characterized by the injection of biologically active venom through a modified ovipositor or stinger, resulting in pain, inflammation, and potential systemic effects [2]. Non-venomous insect bites typically cause localized pruritus, whereas venomous spider bites (e.g., Lactrodectus, Loxosceles) can result in severe systemic neurotoxicity or localized cytotoxicity, respectively. Notably, most household spiders are non-venomous.

The saliva from these bites can trigger allergic responses, and the mechanical injury can introduce bacteria, leading to infection. Moreover, arthropods can transmit diseases like bacteria, viruses, and protozoa, making them a significant public health concern. The impact of arthropod bites extends beyond individual health, as they play a significant role in vector borne infection. [1]

Siddha medicine, an ancient Indian system of medicine, harmoniously blends philosophy and science, embracing a holistic approach to wellness, synchronizing mind, body, and spirit for optimal health and balance. The Siddha formulations are classified as 32 types of internal and 32 types of external medicines. Medicated oil (Thailam) is one among them and is used both internally and externally. Thailam is a medicated oil preparation and is prepared by boiling the decoction, juice, milk and pastes of herbal drugs with or without oils as mentioned for a specific period and filtered. It retains its medicinal value for one year [3, 4]**.** The derivatives of ennei (nei) are classified as 12 types, *viz*, Kothi nei (oil obtained by boiling process), Urukku nei (oil obtained by process of melting), Puda nei (oil obtained from incineration in pit), Theeneer nei (oil obtained by distillation), Suriya puda nei (oil obtained by sun exposure), Mann nei (oil oozing from earth), Mara nei (oil obtained from trees), Silai nei (oil obtained from mountains), Neer nei (solvent extraction soaking method), Aavi nei (oil obtained by condensation), Sudar nei (oil obtained by flaming process), Iyandhira nei (oil obtained by mechanical pressing) [3, 4]. These are further categorized to 5 types *viz*, Mudi nei – hair oil, Kudi nei – Taken orally, Pidi nei – Massage oil, Tholai nei – applied in 9 holes of the body, Silai nei – applied to ulcers. Eaegantha thailam is one such formulation of Kudi nei that comes under the category of Puda nei [3]. Eaegantha Thailam, a traditional polyherbal formulation, has been documented in literary sources for its effectiveness as antivenom especially beetle and ticks bite (*Vandu kadi*) [5,6]. The formulation consists of 8 herbal ingredients *viz*, *Alangium salvifolium* Linn, *Calophyllum inoplyllum* Linn, *Strychnos nux-vomica* Linn, *Semecarpus anacardium* Linn, *Croton tiglium* Linn, *Luffa cylindrical* Linn, *Cadaba trifoliata* Roxb, *Azardirachta indica* A. Juss [5]. Each ingredient in this formulation likely contributes specific pharmacological property for counteracting toxins and providing relief from toxic bites. The term destructive distillation generally refers to the processing of organic material without air or in the presence of a minimal amount of oxygen and other reagents, catalysts, or solvents, such as steam or phenols by heating it to a high temperature. It works on the principle of pyrolysis and large molecules are “cracked” during the process. The destructive distillation

process might enhance the ingredients by increasing the bio availability of active components [7]. The controlled heat and anaerobic conditions of this process might help in extracting the oil and active principles of these seeds leading to a formulation that is rich in therapeutic agents capable of envenomation. Thus, this study aims to review of therapeutic potential of ingredients of Eaegantha thailam and its adjuvant.

Pathophisiology of arthropod venom

Arthropod venoms exhibit diverse compositions and mechanisms, reflecting their unique evolutionary pressures and adaptations. Insect venom is greatly composed of proteins, peptides, enzymes and other small molecules. Bee venom, for instance, primarily consists of melittin (50-55%), a potent peptide disrupting cell membranes and inhibiting cellular respiration. This effect is amplified by phospholipase A, hyaluronidase, histamine, and MCD (Mast Cell Degranulation) peptide, which contribute to cell destruction, inflammation, and allergic responses [8]. Similarly, wasp and hornet venoms share similarities with bee venom but uniquely contain acetylcholine, a neurotransmitter facilitating pain transmission, and wasp/hornet kinin, which enhances their toxic effects [9].

Other arthropod venoms possess distinct components, such as the black widow spider's alpha-latrotoxin, a potent neurotoxin inducing excessive neurotransmitter release [10]. Fire ant venom is predominantly composed of Piperidine alkaloids, inducing cellular toxicity and a characteristic burning sensation [11]. Ants, like harvester ants, possess formic acid-based venom with varied protein content and allergic potential. Bark scorpion venom contains a complex mixture of serotonin, enzymes, and bioactive compounds, causing neurotoxicity by disrupting normal neuronal function and leading to neuromuscular and autonomic hyperactivity. In contrast, brown recluse spider venom induces tissue destruction and cell death through Sphingomyelinase D and a levaterenol-like substance, causing blood vessel constriction. Bullet ants (*Paraponera clavata*) produce a toxin called poneratoxin a neuro peptide affects the voltage-dependent sodium channels and blocks the synaptic transmission. Understanding the unique composition and mechanisms of each venom informs treatment and management strategies for stings and bites, highlighting the importance of continued research into these complex biological systems [12].

Table 1: Representing the lethal dose of common arthropod venom

S. No	Arthropod	LD_{50} For Rodents
1	Honey Bee (Apis mellifera)	2.8 [13]
2	Wasp (Apocrita)	2.5(Purified toxin) [14]
3	Yellow jacket (Vespula spp.)	3.5 [13]
4	Giant Hornet (Vespa mandarinia)	4.6 [13]
5	Harvester Ant (Pogonomyrmex barbatus)	0.12 [13]
6	Yellow Fat-tailed Scorpion (Androctonus australis)	0.32 [15]
7	Asian Giant Hornet (Vespa simillima)	4.1-5.7 [16]
8	Black Widow (Latrodectus mactans)	0.90 [14]
9	Death stalker Scorpion (Leiurus quinquestriatus)	0.25 [14]
10	Bark Scorpion (Centruroides exilicauda)	1.12-1.46 [14]
11	Asian Giant Centipede (Scolopendra subspinipes)	60 (IV 2.35) [14]

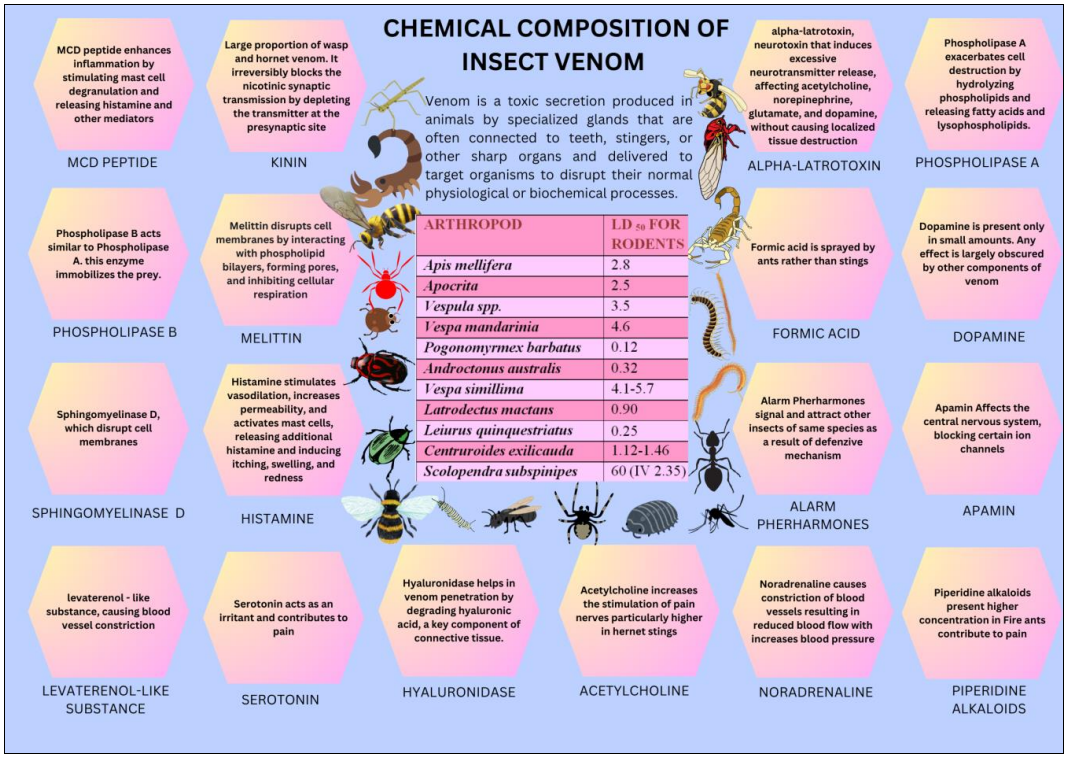

Fig 1: Chemical composition of arthropod venom

The Siddha system of medicine utilizes various formulations for the treatment of bites and stings. One such formulation is Eaegantha thailam.

Method of preparation

Ingredients

1. *Alangium salvifolium* Linn
2. *Calophyllum inoplyllum* Linn
3. *Strychnos nux-vomica* Linn
4. *Semecarpus anacardium* Linn
5. *Croton tiglium* Linn
6. *Luffa cylindrical* Linn
7. *Cadaba trifoliata* Roxb
8. *Azardirachta indica* A. Juss

The ingredients 1-8 are coarsely grinded and transferred to an earthen pot with several small holes at the base was prepared, and thin wires were bent and arranged so that they converged through these holes, positioned a few inches above the bottom of the pot. The mouth of the pot was securely sealed with an earthen plate, which was fixed in place using a mud-clay-coated cloth. The oil was extracted through the destructive distillation with controlled heat management, and it was collected in a vessel placed at the centre of a pit beneath the pot. To heat the pot, cow dung cakes were arranged around and on top then ignited. Once the distillation process was complete, the pot was allowed to cool, after which the upper part was removed, and the oil was carefully collected from the vessel at the bottom [5, 7]. Similarly, oil is extracted from dried donkey dung cakes and mixed in equal ratio with above extracted oil [5].

Adjuvant: *Anthocephalus cadamba* Roxb seed and sulphur each 35g should be taken purified and powdered [5].

Dose: 1kaasu edai (10g) both Adjuvant and oil – BDS [4,5]

Indications: [5]

Table 2: Indications of Eaegantha Thailam

S. No	Dosage	Indication
1.	10g oil with 10g chooranam, 7 Days, BD	Tick Bite
2.	10g oil with 10g chooranam, 10 Days, BD	Leech Bite
3.	10g oil with 10g chooranam, 15Days, BD	All kind of Poisonous bites
4.	10g oil with 10g chooranam, 1 month, BD	Red Leech Bite
5.	10g oil with 10g chooranam, 1 mandalam (48 Days), BD	Acts as a Tonic
6.	10g oil with 10g chooranam, 2 Mandalam (96 Days), BD	Medicine won't let poison into the body

Literature review

Table 3: Drug profile of Eaegantha Thailam

S. No	Ingredient	Botanical Name	Family	Taste	Potency	Division
1	Azhinjil Seed	*Alangium salvifolium* Linn	Alangiaceae	Bitter	Hot	Pungent [17]
2	Punnai Seed	*Calophyllum inoplyllum* Linn	Clusiaceae	Bitter	Hot	Pungent [17]
3	Etti Seed	*Strychnos nux-vomica* Linn	Loganiaceae	Bitter	Hot	Pungent [17]
4	Semecarpus seed	*Semecarpus anacardium* Linn	Anacardiaceae	Bitter	Hot	Pungent [17]
5	Croton Seed	*Croton tiglium* Linn	Euphorbiaceae	Bitter	Hot	Pungent [17]
6	Peipeerku seed	*Luffa cylindrical* Linn	Cucrbitaceaea	Bitter	Hot	Pungent [17]
7	*Vi*zhuthi seed	*Cadaba trifoliata* Roxb	Capparidaceae	Bitter	Hot	Pungent [8]
8	Vembu seed	*Azardirachta indica* A. Juss	Meliaceae	Bitter	Hot	Pungent [17]
1	Donkey dung	*Equus asinus asinus*	NA	NA	NA	NA
Adjuvant						
1	Kadapankottai	*Anthocephalus cadamba*	Rubiaceae	Astringent, Bitter	Hot	Pungent [17]
2	Ganthagam	Sulphur [S]	NA	Bitter Astringent	Hot	Pungent [3]

Table 4: Summary of research on ingredients of Eaegantha Thailam

S. No	Ingredient	Phytochemical Composition	Activity
1.	*Alangium salvifolium* Linn	Alamanine, alangimaridine, emetine, cephaeline, psychotrine, alangimarine [18]	Anti-inflammatory activity, Diuretic, Antimicrobial activity [19] Antioxidant activity [20]
2.	*Calophyllum inoplyllum* Linn	Calophyllolide, Xanthone, epicatechin, calophynic acid, calophyllic acid, caloxanthone b, macluraxanthone, betasitosterol, linoleic acid, cinnamic acid, inophyllum e, arachidic acid, ponnalide [21]	Antioxidant activity [23]
		Callophyllum Seed oil	Anti-inflammatory activity [22] Antioxidant activity [23]
		Calophyllolide	anti-inflammatory activity, anti-coagulant activity, anti-microbial activity, wound healing activity [24]
3.	*Strychnos nux-vomica* Linn	strychnine and brucine other constituents include minor alkaloids, glycoside, chlorogenic acid mannosan, and galactan, strynuxlines A and B, and iridoid glucoside [25]	Anti-ophidian activity – *in vitro* and *In vivo* [26] Antioxidant and anti-inflammatory activity [27]

			Anti-histamine activity, antioxidant activity [28]
4.	*Semecarpus anacardium* Linn	Bhilawanol,Anacardoside, anacardiac acid, aromatic amines, biflavantetrahydrorobusta-flavone-and tetrahydro amentoflavone, bi flavonides A, B and C, [29]	Antioxidant Anti-inflammatory immunomodulatory Antimicrobial [30] Antivenom [26]
5.	*Croton tiglium* Linn	Phorbol esters, Phorbol-pentaacetate, γ-Himachalene, 5-hydroxy-2-pyridinemethanol, 4(1H)-quinolinone [30]	Antioxidant Anti-inflammatory activity Immunomodulatory activity haemagglutinating activity [31]
6.	*Cadaba trifoliata* Roxb	Stearic acid, oleic acid acid, arachidic acid, hyoscine, palmitoic acid, oleic acid [32]	Anti-inflammatory Antioxidant [33]
7.	*Azardirachta indica* A. Juss	Azardirol, gedunin, nimbinene, triterpenoids, Azardirone, nimbidiol, myristic acid, nimbin, Azardirachtin, nimbanal [34]	Antioxidant Anti-inflammatory [34] Antivenom [26]
		Nimbin, Gedunin	Immunomodulatory [34]
		Nimbin	Antihistamine activity [34]
		Azadirachtin, Mahmoodin, Gedunin, Nimbolide	Antimicrobial [34]
		Nimbidin, Sodium nimbidate	Anti-inflammatory [34]
8.	*Luffa cylindrical Linn*	Cucurbitacin B, cucurbitacin E, Luffin a, b, Luffins P1, Bryonolic acid, Phenanthrene, Myrstic acid, Isomultiflorenol, Lauric acid, α-spinasterol, (-)-Butyrospermol [35]	Anti-inflammatory [36], Antimicrobial [36,37], immunomodulatory [38] Antioxidant [35] Antivenom activity [26]
		Bryonolic acid	Inhibits passive cutaneous anaphylaxis and delayed hypersensitivity [36]
		Phenanthrene	antiplatelet aggregation [36]
9.	Donkey dung	hexane, acetic acid, aconitane, beta carotene, dimethyl amine [39]	Antibacterial activity [39] Wound healing activity [39]
10.	*Anthocephalus cadamba* Roxb	Naringenin-5-O-α-L-rhamnopyranoside, 4′-O-methylliquiritigenin-7-O-α-L-rhamnopyranoside, naringenin 4′-methylether 7-xyloside, *β*-sitosterol-3-O-D-galactopyranoside cadambagenic acid, cadamine, quinovic acid, *β*-sitosterol, cadambine [40]	Antimicrobial, wound healing, antioxidant activities [41] Anti-ophidian [40] Antioxidant activity [40]
11.	Sulphur	Thiobenzoic acid S-benzyl esters and thioesters, derived from 2-sulfenyl ethylacetate [42]	Antiophidian activity [42], Anti-inflammatory activity [43], Anti-Microbial activity [44]

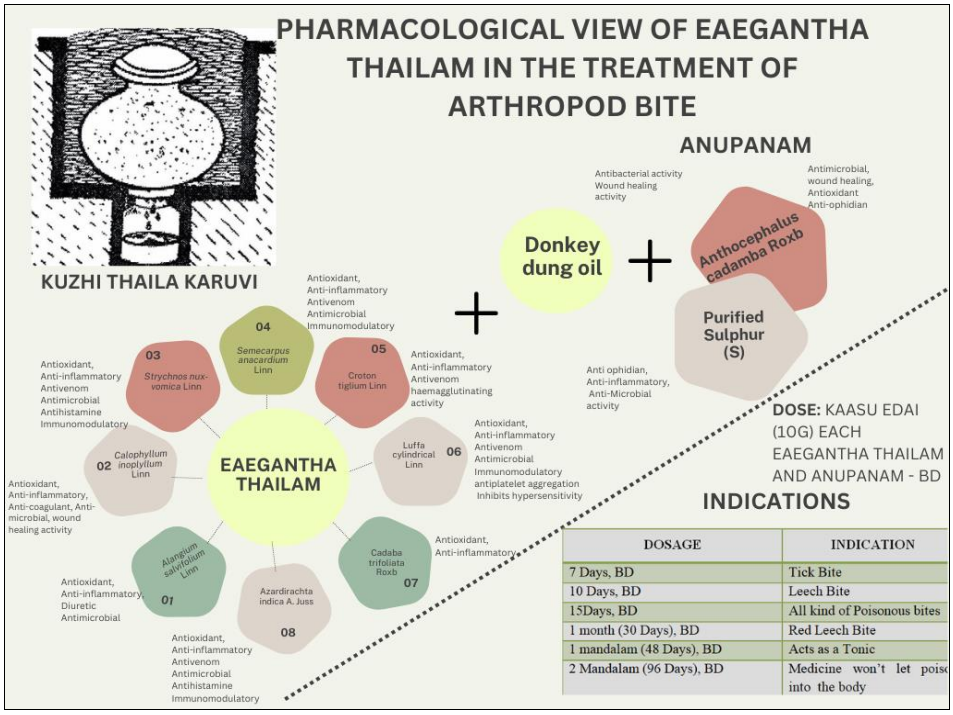

Fig 2: Pharmacological view of eaegantha thailam in the treatment of arthropod bite

Discussion

Venom is a toxic secretion produced in animals by specialized glands that are often connected to teeth, stingers, or other sharp organs and delivered to target organisms to disrupt their normal physiological or biochemical processes. The insects utilize highly toxic venom for predation, defense, and competitor deterrence are believed to possess evolutionary advantages. A sting is a highly specialized tool whose function is the delivery of venom [45].

In Siddha medicine, the taste of a substance plays a significant role in its therapeutic action. Among the six tastes (sweet, sour, salty, bitter, pungent, and astringent), bitter taste is particularly valued for its ability to neutralize toxins and venoms. The philosophical basis of this idea is rooted in the principle that the bitter taste helps counteract poisons by pacifying aggravated doshas and enhancing digestion [47]. It is believed to stimulate appetite, promote the digestion of undigested food, and facilitate detoxification by activating the liver and expelling waste.

Moreover, bitter substances are often considered to possess nervine tonic properties, which means they help strengthen and calm the nervous system [47]. These properties make them especially useful in treating conditions related to nervous system dysfunction, including those caused by venomous bites. The faster digestion of bitter substances compared to other tastes further supports their role in treating acute and severe conditions like poisoning or inflammation.

According to the Thiridhodam philosophy, health is maintained through the balance of three humors or dosham: Vata, Pitta, and Kapha. Venomous bites and stings disturb this balance, particularly affecting a subtype called Vathapitham (a combination of Vata and Pitta doshas). When Vathapitham is disrupted, it leads to a chain of pathological changes, causing symptoms like inflammation, pain, fever, and tissue damage [48]. Restoring the doshic balance is the primary aim of therapeutic interventions in such cases. Bitter-tasting remedies, especially in the form of polyherbal formulations or thailam (medicated oils), help detoxify the body, soothe inflammation, and alleviate pain, thus addressing the root cause of the disease. These formulations act not only on a symptomatic level but also target the systemic imbalance caused by venomous toxins [49].

In Siddha Science, Anupanam and dosage plays a vital role in treating diseases. Anupanam, a concept integral to pharmacology, encompasses adjuvants, vehicles, and carriers that optimize drug delivery. These auxiliary substances enhance absorption, interaction, and bioavailability, thereby augmenting therapeutic efficacy [49]. The distinctive application of Anupanam lies in its synergistic potential, where its strategic combination with tailored formulations – whether singular or compound – amplifies the therapeutic efficacy of the medication [50]. Anupanam adapts drugs for various diseases through strategic combinations, addressing availability constraints by enhancing bioavailability, targeting subtler tissues, and optimizing treatment efficacy, thereby enabling personalized medicine, improving patient outcomes, and increasing treatment possibilities, with key applications including disease-specific formulations, targeted drug delivery, and substitute therapies [49]. For Eaegantha thailam, the drug is advised to be taken along with a specific chooranam- combination of purified sulphur and *Anthocephalus cadamba* Roxb Seed. These combinations have an astringent and bitter taste. Bitter taste is fastly counteracting the venom thus providing an antivenom property and astringent taste purifies the blood that is removes the toxins mixed in blood. Thus, the formulation Eaegantha thailam when taken along with the Anupanam above mentioned chooranam.

From Table – 4, Medicinal plants such as *Alangium salvifolium*, *Calophyllum inophyllum*, *Strychnos nux-vomica*, and *Azadirachta indica* possess a rich array of phytochemicals, exhibiting anti-inflammatory, antioxidant, antimicrobial, and antivenom properties. These therapeutic compounds play a vital role in mitigating venomous bite symptoms by reducing inflammation, tissue damage, and oxidative stress, while promoting wound healing and combating infections. *Strychnos nux-vomica* and *Azardirachta indica* exhibit antihistamine activity, countering the toxic effects of histamine, a key mediator in allergic responses and venom component. Their bioactive compounds, strychnine and nimbin, mitigate histamine-induced symptoms like increased vascular permeability, smooth muscle contraction, and gastrointestinal disturbances. This antihistamine property offers therapeutic benefits in managing allergic reactions, anaphylaxis, venomous bites, and inflammatory disorders, positioning them as natural complements to conventional treatments. Key bioactive constituents, including xanthones and alkaloids, demonstrate potent anti-inflammatory and anti-ophidian activities, countering venom-induced toxicity. Specifically, Xanthones from *Calophyllum inophyllum* and alkaloids from *Strychnos nux-vomica* exhibit robust anti-inflammatory effects, whereas Azadirachtin and nimbin, from Azadirachta indica, exhibit immunomodulatory effects, regulating cytokine production, T-cell/B-cell responses, and phagocytic activity. They boost immune defense, mitigate autoimmune diseases, enhance wound healing, and reduce inflammation, showing promise in treating immunological disorders, inflammatory diseases, infections, and cancer. Bhilawanol, exhibits potent antioxidant and anti-inflammatory properties, synergistically mitigating venom-induced disruptions in physiological pathways. It neutralizes free radicals, inhibits inflammatory mediators, protects cellular membranes, and promotes wound healing. Bhilawanol reduces inflammation, boosts immunity, and treats venomous bites. By targeting toxins like poneratoxin, melittin and phospholipase A, these phytochemicals offer a complementary approach to conventional therapies, holding promise for developing effective phytochemical-based treatments for venomous bites, and potentially improving patient outcomes.

Conclusion

The findings of this study support the value of traditional knowledge and offer a starting point for innovative drug development. By integrating traditional Siddha principles with modern scientific research, healthcare professionals can develop effective, phytochemical-based treatments for arthropod bites, offering a promising alternative to conventional therapies.

References

1. Singh S, Mann BK. Insect bite reactions. Indian J Dermatol Venereol Leprol,2013:79(2):151-164. doi: 10.4103/0378-6323.107629. PMID: 23442453.

2. Rook A, Wilkinson DS, Ebling FJB, Champion RH, Burton JL, editors. Textbook of dermatology. 4th ed. Oxford: Blackwell Scientific Publications.
3. Thiyagarajan R. Gunapadam Thaathu Jeeva Vaguppu. 4th ed. Chennai: Department of Indian Medicine and Homeopathy, 2004.
4. World Health Organization. WHO International Standard Terminologies on Siddha Medicine. Geneva: World Health Organization, 2022, 248. License: CC BY-NC-SA 3.0 IGO.
5. Murugesa Mudhaliyaar K S. Nanju Murivu Nool. Indian Medicine and Homeopathy Department, 2006, 120.
6. Sambasivam Pillai TV. Tamil Dictionary. Vol,1-5. 4th ed. Chennai: Tamil Nadu Siddha Medical Council, 1992.
7. Sahayam S, Savariraj R, Chellappan D, Sriram S, Perumal R, Brindha P. Acute toxicity profiles of Siddha medicine Sivanarvembu kuzhi thailam on rats. Biomed Pharmacol J,2020:13:1137-1143. doi: 10.13005/bpj/1981.
8. Ali M. Studies on bee venom and its medical uses. Int J Advancements Res Technol,2012:1:69-83. Available from: https://www.researchgate.net/publication/258650193_Studies_on_Bee_Venom_and_Its_Medical_Uses.
9. Luo L, Kamau PM, Lai R. Bioactive peptides and proteins from wasp venoms. Biomolecules,2022:12(4):527. doi: 10.3390/biom12040527. PMID: 35454116.
10. Williams M, Sehgal N, Nappe TM. Black widow spider toxicity. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2024. [Updated 2023 Aug 7: accessed 2024 Oct 17]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499987/.
11. Xu G, Chen L. Biological activities and ecological significance of fire ant venom alkaloids. Toxins,2023:15(7):439. doi: 10.3390/toxins1507043.
12. Szolajska E, Poznanski J, Ferber ML, *et al*. Poneratoxin, a neurotoxin from ant venom: structure and expression in insect cells and construction of a bio-insecticide. Eur J Biochem,2004:271(11):2127-2136. doi: 10.1111/j.1432-1033.2004.04128.x.
13. Brunning A. The chemical compositions of insect venoms. Compound Chemicals Blog [Internet], 2014. Available from: https://compoundchem.com.
14. Table. Available from: https://members.tripod.com/~c_kianwee/rpotent.htm.
15. Coelho P, Sousa P, Harris DJ, van der Meijden A. Deep intraspecific divergences in the medically relevant fat-tailed scorpions (Androctonus, Scorpiones). Acta Trop,2014:134:43-51. doi: 10.1016/j.actatropica.2014.02.002.
16. Nadolski J. Effects of the European hornet (Vespa crabro Linnaeus 1761) crude venom on its own species. J Venom Anim Toxins Incl Trop Dis,2013:19(1):4. doi: 10.1186/1678-9199-19-4. PMID: 24499044: PMCID: PMC3707105.
17. Murugesa Mudhaliyaar K S. Gunapadam part 1 Mooligai vagupppu. Indian Medicine and Homeopathy Department, 2013:270:715.
18. Ghosh S, Sarkar T, Chakraborty R. Ankol plant (Alangium salvifolium) - The treasure trove of bioactives and medicinal potential. Food Biosci,2023:51:102230. doi: 10.1016/j.fbio.2022.102230.
19. Sharma AK, Agarwal V, Kumar R, Balasubramaniam A, Mishra A, Gupta R. Pharmacological studies on seeds of Alangium salvifolium Linn. Acta Pol Pharm,2011:68(6):897-904. PMID: 22125955.
20. Tiwari R, Sharma T. Ethnopharmacology, antioxidant activities, and phytochemical screening of bioactive extracts from the seeds of Alangium salvifolium, a medicinal plant. Defence Life Sci J,2023:8:203-208. doi: 10.14429/dlsj.8.18532.
21. Ferdosh S. The extraction of bioactive agents from Calophyllum inophyllum L., and their pharmacological properties. Scientia Pharmaceutica,2024:92(1):6. doi: 10.3390/scipharm92010006.
22. Nalimanana NR, Tombozara N, Razafindrakoto ZR, Andrianjara C, Ramanitrahasimbola D. Anti-inflammatory and analgesic properties, and toxicity of the seed's ethanol extract of Calophyllum inophyllum L. from the eastern region of Madagascar. S Afr J Bot,2022:150:466-472. doi: 10.1016/j.sajb.2022.08.020.
23. Gupta S, Gupta P. The genus Calophyllum: review of ethnomedicinal uses, phytochemistry and pharmacology. In: Bioactive Natural Products in Drug Discovery, 2020, 215-242. doi: 10.1007/978-981-15-1394-7_5. PMCID: PMC7191991.
24. Nguyen VL, Truong CT, Nguyen BCQ, Vo TV, Dao TT, Nguyen VD, *et al*. Anti-inflammatory and wound healing activities of calophyllolide isolated from Calophyllum inophyllum Linn. PLoS One, 2017, 12(10). doi: 10.1371/journal.pone.0185674. PMID: 29020015: PMCID: PMC5636079.
25. Akbar S. Strychnos nux-vomica L. (Loganiaceae). In: Handbook of 200 Medicinal Plants. Cham: Springer, 2020. doi: 10.1007/978-3-030-16807-0_175.
26. Lakhmale S, Acharya R, Yewatkar N. Ethnomedicinal claims on antivenom activity of certain fruit and seed drugs - a review. Ayurpharm Int J Ayur Alli Sci,2012:1:21-29. Available from: https://www.researchgate.net/publication/272498021_Ethnomedicinal_claims_on_antivenom_activity_of_certain_fruit_and_seed_drugs-a-review
27. Chaurasia S. Anti-inflammatory and antioxidant activity of Strychnos nux-vomica Linn. Am Eurasian J Sustain Agric,2009:3:244-252. Available from: https://www.researchgate.net/publication/273030625_Anti-inflammatory_and_Antioxidant_Activity_of_Strychnos_nux_vomica_Linn
28. Singh S, Chakraborthy G. Evaluation of anti-asthmatic and antioxidant potentials of seed extract of Strychnos nux vomica L. Res J Pharm Tech,2020:13:114. Available from: https://doi.org/10.5958/0974-360X.2020.00023.2
29. Waghmare AR, Waghaye R. A critical review on Bhallataka (Semecarpus anacardium Linn). Int Ayur Med J, 2016. Available from: http://www.iamj.in/posts/images/upload/3361_3370.pdf
30. Singh D, Aggarwal A, Mathias A, Naik S. Immunomodulatory activity of Semecarpus anacardium extract in mononuclear cells of normal individuals and rheumatoid arthritis patients. J

Ethnopharmacol,2006:108(3):398-406. doi:10.1016/j.jep.2006.05.028
31. Dey T, Saha S, Ghsoh P, Adhikari S. A comprehensive review on medicinally important plant, Croton tiglium L. Available from: https://www.researchgate.net/publication/326404907_A_Comprehensive_Review_on_Medicinally_Important_Plant_Croton_Tiglium_L
32. Gupta AK. Reviews on Indian medicinal plants. New Delhi: Indian Council for Medical Research, 2004.
33. Manokari M, Faisal M, Alatar AA, *et al*. *In vitro* regeneration and structural and physiological modifications in the foliages of Cadaba trifoliata (Roxb.) Wight & Arn.: An endemic tree of the family Capparaceae. Russ J Plant Physiol,2024:71(1):122. doi:10.1134/S1021443724606293
34. Uzzaman S. Pharmacological activities of neem (Azadirachta indica): A review. Int J Pharmacogn Life Sci, 2019, 1. doi:10.33545/27072827.2020.v1.i1a.8
35. Akinyinka AK, Eleyowo OE, Oladipo OM. A review on the ethnobotanical uses, phytochemistry and pharmacological effect of Luffa cylindrica. In: Natural Drugs from Plants. IntechOpen, 2022. doi:10.5772/intechopen.98405
36. Muthumani P, Meera R, Mary S, *et al*. Phytochemical screening and anti-inflammatory, bronchodilator and antimicrobial activities of the seeds of Luffa cylindrica. Res J Pharm Biol Chem Sci,2010:1(1):11-22.
37. Oyetayo O, Ajewole V. Phytochemical profile and antibacterial properties of the seed and leaf of the luffa plant (Luffa cylindrica). J Pharmacol Toxicol,2007:2(6):586-589. doi:10.3923/jpt.2007.586.589
38. Azeez M, Bello O, Adedeji A. Traditional and medicinal uses of Luffa cylindrica: A review. J Med Plants Stud,2013:1(5):102-111. doi:10.9790/2172-01510211
39. Shafiee HA, Moravej-Salehi E. Anbarnesa: The past tradition, the future medicine. Iran Red Crescent Med J, 2015, 17(12). doi:10.5812/ircmj.29536
40. Dwevedi A, Sharma K, Sharma YK. Cadamba: A miraculous tree having enormous pharmacological implications. Pharmacogn Rev,2015:9(18):107-113. doi:10.4103/0973-7847.162110
41. Umachigi SP, Kumar GS, Jayaveera K, *et al*. Antimicrobial, wound healing and antioxidant activities of Anthocephalus cadamba. Afr J Tradit Complement Altern Med,2007:4(4):481-487.
42. Henao Castañeda IC, Pereañez JA, Jios JL. Substituted thiobenzoic acid S-benzyl esters as potential inhibitors of a snake venom phospholipase A2: synthesis, spectroscopic and computational studies. J Mol Struct,2012:1028:7-12. doi:10.1016/j.molstruc.2012.06.031
43. Zhao C, Rakesh KP, Ravidar L, Fang WY, Qin HL. Pharmaceutical and medicinal significance of sulfur (SVI)-Containing motifs for drug discovery: A critical review. Eur J Med Chem,2019:162:679-734. doi:10.1016/j.ejmech.2018.11.017
44. Shanmugapriya P, Christian GJ, Vajrai R, *et al*. Antimicrobial efficacy of Gandhagam (raw sulphur), purified Gandhagam and Gandhaga Mezhugu - a traditional Siddha formulation. J Pure Appl Microbiol,2013:7:1-4.
45. Fry BG, Casewell NR, Wuster W, *et al*. The structural and functional diversification of the Toxicofera reptile venom system. Toxicon,2012:60:434-448. doi:10.1016/j.toxicon.2012.02.013
46. Uthamarayan KS. Siddha Marthuvanga Surukkam. 3rd ed. Chennai: Indian Medicine and Homeopathy Department, 2016:36:41.
47. Venugopal PM. Udal Thathuvam. Chennai: Indian Medicine and Homeopathy Department, 2013, 377.
48. Mahadevan L. Thiridhosa Meiporul Nyana thathuva vilakkam,1st ed. Chennai: Saradha Mahadeva Iyer Educational Trust and Charitable Trust, 2018:291:938.
49. Pandey N, Tripathi AK. Therapeutic potential of Anupaan: Drug delivery vehicle in Ayurveda. Int J Health Sci Res, 2022, 12(11). doi:10.52403/ijhsr.20221105
50. Mallika, Ponraj K. A study on Anupanam and brief discussion on its various types. Int Ayur Med J, 2017. Available from: http://www.iamj.in/posts/images/upload/1092_1104