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ETHNOPHARMACOLOGICAL DIVERSITY OF NAGALAND'S MEDICINAL PLANTS: BRIDGING TRADITIONAL WISDOM WITH MODERN SCIENCE

Suman Saha[1]*, Nandini Goswami[2], Pragya Baghel[3]

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ABSTRACT
Nagaland, a biodiversity hotspot, harbors diverse indigenous tribes with a rich legacy of traditional medicine. This study explores the ethnomedicinal knowledge of the Naga people and its scientific basis. We reviewed plants used in traditional practices, including *Centella asiatica*, *Acorus calamus*, *Juglans regia*, *Eupatorium adenoporum*, and *Mimosa pudica*. Scientific literature supports the therapeutic potential of these plants, aligning with their traditional uses. *Centella asiatica* exhibits wound-healing and anti-inflammatory properties. Acorus calamus possesses antimicrobial and anti-inflammatory effects. Juglans regia displays antioxidant and sedative activities. Eupatorium adenoporum's flavonoids inhibit acetylcholinesterase, suggesting benefits for neurological disorders. Mimosa pudica shows promise for its antiepileptic and anti-inflammatory properties. The documented knowledge can bridge the gap between traditional medicine and modern healthcare. Collaborative efforts are crucial to preserve this ethnomedicinal wisdom and explore its potential for novel therapeutic discoveries.

INTRODUCTION

Nagaland, a compact state in northeast India, lies within the Indo-Burma biodiversity hotspot. Its terrain spans diverse climates, ranging from warm and subtropical plains to moderate sub-montane slopes and cool, temperate high hills. This geographical variety supports a rich array of flora and fauna. The Naga tribe, comprising numerous indigenous groups such as Angami, Ao, Chakhesang, Chang, and others, call this region home. Agriculture stands as their primary occupation, deeply intertwined with their cultural identity. Across centuries, the Naga tribe has relied on traditional knowledge of medicinal plants, passed down orally or through traditional medicine practitioners, to address various ailments. However, the lack of written documentation puts this valuable ethnomedicinal wisdom in jeopardy of being lost.

The risk of losing ethnomedicinal knowledge due to the absence of documented records emphasizes the urgency of collaborating with indigenous communities to compile and preserve this invaluable heritage. Scientific research merging traditional

[1]*Nurul Islam College of Pharmacy, Khagenhat, Falakata, Alipurduar, West Bengal, India, 736121*
[2]*KLE College of Pharmacy, Bengaluru, Karnataka, India, 560010*
[3]*Himalayan Institute of Pharmacy, Department of Pharmaceutics, Majhitar, Rangpo, East Sikkim, 737136*

For Correspondence:** **sumansaha82@gmail.com

wisdom with contemporary methodologies can bridge the gap between ancient practices and modern healthcare, potentially benefiting both the Nagaland region and global medicinal advancements [1]. Nagaland, situated in Northeastern India, spans 16,579 square kilometers between latitudes 25º06' – 27º04' N and longitudes 93º20'–95 º 15' E. It shares borders with Arunachal Pradesh to the north, Assam to the west, Manipur to the south, and Myanmar to the east. The altitude ranges from 194 meters to 3048 meters, with Saramati, in Kiphire district along the Myanmar border, marking its highest peak. Renowned for its rich biodiversity, Nagaland is a true epicenter of diverse ecosystems.

This region has 17 distinct indigenous tribes, including significant groups like the Angami, Ao, Lotha, Sumi, Sangtam, Chang, Khiamniungan, and Konyak, alongside several sub-tribes. Each tribe boasts a unique cultural heritage intricately woven into their daily lives. Passed down through generations via oral traditions, these customs and practices reflect the communities' deep connections with their ancestors and the land they inhabit [2].

MATERIALS AND METHODS

This scientific investigation used a carefully designed methodology to collect data. This involved search engines and scientific databases like Google Scholar and PubMed, online libraries, and relevant websites. Various keywords like Traditional medicine, ethnomedicinal knowledge, pharmacological properties, bioactive compounds, indigenous communities, and medicinal plants were used to collect literature. Scholarly articles, peer-reviewed publications, and credible literature relevant to the research were included for further study. Amongst the collected literature, only abstracts, manuscripts written in languages other than English, and manuscripts with irrelevant context were excluded from the study.

Some traditional plants used by the people of Nagaland

Centella asiatica (L.), a creeping herb thriving in tropical and subtropical regions worldwide, belongs to the Apiaceae family. Traditionally used for centuries, it boasts a unique chemical profile. The aerial parts are rich in triterpene glycosides, particularly asiaticoside (reported to be around 30-60% of dry weight [3]), madecassic acid, and asiatic acid, alongside other bioactive compounds like polyacetylenes and volatile oils [3, 4]. These have been linked to a range of pharmacological activities: asiaticoside, for instance, has shown promise in accelerating wound closure by promoting collagen synthesis at concentrations as low as 10 µg/ml in vitro studies [4]. Additionally, triterpenes like asiaticoside exhibit anti-inflammatory effects by inhibiting pro-inflammatory mediators, with studies suggesting potential for topical applications at concentrations of 1% [5]. Animal models have shown extracts of *Centella asiatica* to improve cognitive function and memory, highlighting its potential neuroprotective properties [6]. Interestingly, research suggests these triterpenes may be responsible for the plant's regenerative properties, with studies indicating an increase in skin cell proliferation by up to 20% [7]. The plant's traditional use across various cultures aligns with this emerging scientific evidence, underlining its potential as a source of novel therapeutic agents and the importance of exploring traditional knowledge systems for drug discovery [8-10].

***Acorus calamus* Linn.**

Acorus calamus L., commonly known as the sweet flag, is an aromatic perennial herb from the Araceae family. Its rhizomes, containing a unique blend of bioactive compounds, have been used in traditional medicine for centuries. The rhizomes are rich in sesquiterpeneoids like 6β,7β(H)-cadinane-1α,4α,10α-triol and 1β,7α(H)-cadinane-4α,6α,10α-triol, alongside other compounds such as L-malic acid and ent-4β,10α-dihydroxyaromadendrane [11]. The essential oil boasts β-asarone (reported to be around 3-4% of the oil [12]), calarene, and euasarone, which contribute to various pharmacological activities [12].

Studies have shown *Acorus calamus* extracts exhibit significant anti-inflammatory properties at concentrations as low as 50 µg/ml, potentially due to the inhibition of pro-inflammatory mediators [13]. Further, the antioxidant capacity of the plant has been measured using DPPH free radical scavenging assay, with IC50 values ranging from 15-20 µg/ml, highlighting its potential for oxidative stress management [14]. In some studies, *Acorus calamus* extracts have demonstrated antimicrobial activity against various bacterial and fungal strains, with MIC values ranging from 0.125 to 1 mg/ml [15]. The diverse chemical composition and demonstrated biological activities of *Acorus calamus*, including its thrombolytic (clot-dissolving) and anthelmintic (worm-expelling) properties, warrant further investigation [15,16]. The traditional use of Acorus calamus

across cultures aligns with this emerging scientific evidence, making it a promising candidate for novel drug discovery.

***Juglans regia* L.**

The common walnut tree, *Juglans regia L.* (Juglandaceae family), is a treasure trove of bioactive compounds, particularly in its leaves. These leaves are rich in flavonoid glycosides, including kaempferol-3-O-rutinoside (estimated at 2-3% of dry leaf weight [1]) and quercetin derivatives like quercetin-3-O-galactoside [17]. These flavonoids are the key players behind *Juglans regia* impressive antioxidant properties. Studies have shown that Juglans regia extracts can effectively reduce reactive oxygen species (ROS) levels in immune cells (RAW 264.7 macrophages) by up to 70% at concentrations of 10 μg/ml [18]. Furthermore, IC50 values less than 10 μg/ml show their radical scavenging activity, highlighting their exceptional potential for oxidative stress management [18]. But *Juglans regia*'s benefits extend beyond antioxidant activity.

Extracts from the bark exhibit significant antimicrobial activity against a broad spectrum of microbes, including Staphylococcus aureus, a common cause of skin infections, and Candida albicans, a fungal pathogen associated with candidiasis [19]. In these studies, the bark extracts demonstrated minimum inhibitory concentrations (MICs) against these pathogens, ranging from 0.5 to 1 mg/ml [20]. Additionally, Juglans regia bark extracts have been shown to elevate saliva pH, potentially offering a natural approach to reducing plaque formation by creating an environment less hospitable to cavity-causing bacteria [20]. Perhaps most surprisingly, Juglans regia extracts and the isolated compound juglone have demonstrated sedative properties at specific doses. Research has shown that a 6.5 mg/kg dose of the walnut extract and a remarkably low 0.125 mg/kg dose of juglone induced significant sedation in animal models, as measured by actimeter and sleep potentiation tests [19]. These effects were comparable to those observed with commonly used medications like diazepam at a dose of 2 mg/kg [19].

Juglans regia's diverse chemical makeup and demonstrated pharmacological activities solidify its position as a fascinating subject for further scientific exploration. The abundance of flavonoids with their potent antioxidant effects positions *Juglans regia* as a potential natural source of antioxidants. Bark extracts show promise as broad-spectrum antimicrobial agents and potentially as natural aids for oral health. The observed sedative properties of juglone, particularly at such low doses, warrant further investigation to explore its potential as a natural sedative alternative. Future research focused on elucidating the mechanisms of action of these bioactive compounds and establishing their safety profiles is crucial to unlocking their full therapeutic potential in various health domains.

Eupatorium adenoporum

This noxious and invasive weed from the Asteraceae family is widely distributed in regions spanning Mexico, India, New Zealand, Australia, and China. Essential oils derived from the plant's inflorescences contain sesquiterpenes, while the roots contain a combination of sesquiterpenes and monoterpenes. Studies have demonstrated that these essential oils exhibit significant antioxidant, phytotoxic, and antimicrobial activities [20].

The plant has yielded fifteen isolated flavonoid compounds, including 7-O-(6-O-caffeoyl-β-D-glucopyranoside, quercetagetin-7-O-(6-O-p-coumaroyl-β-glucopyranoside, chrysoplenetin, 4'-methyl quercetagetin 7-O-(6''-O-E-caffeoyl glucopyranoside, 5,4'-Dihydroxytlavone, kaempferol-3-O-β-D-glucopyranoside, kaempferol, 3-hydroxy-phloridzin, quercetin-3-O-β-D-glucopyranoside, naringenin, chrysoeriol, artemetin, methylenebisphloridzin, fortunellin, and rutin. Among these, 7-O-(6-O-caffeoyl-β-D-glucopyranoside), 4'-methyl quercetagetin 7-O-(6''-O-E-caffeoyl glucopyranoside), and quercetagetin-7-O-(6-O-p-coumaroyl-β-glucopyranoside) have been identified as the most potent compounds inhibiting the acetylcholinesterase enzyme in Caenorhabditis elegans and Spodoptera litura, with IC50 values ranging from 12.08 to 89.06 micrograms per milliliter. Scientifically, *Eupatorium adenoporum* raises concerns due to its invasive nature and potential ecological impact.

However, its chemical composition, particularly the flavonoid compounds isolated from it, presents opportunities for pharmacological research. The discovery of flavonoids with acetylcholinesterase inhibitory activity from this weed highlights the potential for novel bioactive compounds with possible therapeutic implications, especially in neurological disorders. Further investigation into these compounds' mechanisms of action and safety profiles is essential for evaluating their pharmaceutical potential [21-23].

Traditional medicinal plants are used for various ailments [33]

SNo.	Plants	Family	Parts used	Traditional uses
1.	*Allium Chinese* G.Don	Amaryllidaceae	Whole plant	Fever, stomach-ache, sore throat, cough, diarrhea, dysentery, chest pain, and early stages of cancer
2.	*Begonia palmata* D. Don	Begoniaceae	Leaves, roots	Antipyretic, astringent, haematemesis
3.	*Centella asiatica* (L.) Urb.	Apiaceae	Whole plant	Blood pressure, neurological diseases, rheumatism, gastritis, syphilis, skin disorder, etc.
4.	*Clematis napaulensis* DC	Ranunculaceae	Leaves, stems, roots	Skin diseases and rheumatism
5.	*Clerodendrum colebrookianum* Walp	Verbenaceae	Leaves	Antiseptic, tonicbronchitis, malaria, hypertension.
6.	*Elaeocarpus floribundus* Blume.	Elaeocarpaceae	Fruit	Blood pressure, nausea, tonic
7.	*Elsholtzia blanda* Benth.	Lamiaceae	Leaf	Kidney and bladder disorders, diabetes, hypertension,
8.	*Equisetum ramosissimum* Desf	Equisetaceae	Whole plant	Urinary tract infections and kidney diseases
9.	*Gynura nepalensis DC*	Asteraceae	Leaves, tender stem	Cuts and wounds, gastritis
10.	*Habenaria dentata (Sw.) Schltr*	Orchidaceae	Rhizhome	Kidney failure, impotency, tonic
11.	*Lobelia nummularia Lam*	Campanulaceae	Whole plant	Cuts and wounds, gall bladder disorder, kidney stone, urinary tract infection
12.	*Molineria capitulate (Lour)*	Hypoxidaceae	Rhizome	Jaundice, haemostatic, diarrhoea. dysentery, eye and ear drop, constipation
13.	*Plantago asiatica subsp. erosa (Wall)*	Plantaginaceae	Whole plant	Dysentery, burns and cuts, astringent, cooling, febrifuge, diuretic and tonic, toothache, piles
14.	*Polygonum mole D. Don*	Polygonaceae	Leaves and stems	Blood purification.
15.	*Pouzolzia viminea Wedd*	Urtiteceae	leaves and roots	Skin infection and wound healing
16.	*Rubia sikkimensis Kurz*	Rubiaceae	Whole plant, stem, and root	Urinary tract infections, an antidote for snake bite
17.	*Tainia viridifusca (Hook.) Benth. & Hook.*	Orchidaceae	Rhizome	Skin disease and cracked heels
18.	*Taxus wallichian Zuccarini*	Taxaceae	Leaves, bark	Bronchitis, epilepsy, giddiness; antiseptic, aphrodisiac, sedative, anticancer, etc.
19.	*Thalictrum foliolosum A.P. de candolle*	Ranunculaceae	Roots	Fever, malaria, typhoid
20.	*Zanthoxylum armatum DC*	Rutaceae	Leaves and seeds	Fever, headache, indigestion, respiratory problem, joint pain, skin allergy

Mimosa pudica

Mimosa pudica, commonly known as touch-me-not or sensitive plant, belongs to the Fabaceae family. The oil extract from this plant comprises various chemical components, including N-dl-Alanylglycine, dl-Alanin ethyl ester, dl-Alanyl-dl-Valine, 1-Alanine ethyl amide, d-Alanin, 9,12-Octadecadienoic acid (Z, Z), methyl ester, 1-Octanamine, N-methyl, 11,13-Eicosadienoic acid, methyl ester, 1-Butanamine, N-methyl, Meglumine, 2-methylamino-N-phenyl-acetamide, 2,5-Dimethoxy-4-(methylsulphonyl), 1,3-Dioxolane-4-methanol, and 9,12-Octadecadien-1-ol (Z, Z) [24]. Additionally, the plant's whole parts yielded two new compounds of C-glycosylflavones:

6,7,30,40-tetrahydroxyl-8-C-[a-L-rhamnopyranosyl-(1 → 2)]-b-D-glucopyranosyl flavone and 5,7,30,40-tetrahydroxy-8-C[b-D-apiose-(1 → 4)]-b-D-glycopyranosyl flavones [25]. Studies have shown that the leaf extract of *Mimosa pudica* has potential antiepileptic effects, inhibiting strychnine (STR) and pentylenetetrazolo (PTZ)-induced seizures in mice with ED50 values of 950 mg/kg and 1200 mg/kg i.p., respectively [26]. Additionally, the extract antagonizes NMDA-induced Turning behavior in mice, though it shows no effect in PIC-induced seizures in mice [27]. Pharmacologically, *Mimosa pudica* exhibits diverse activities, including antioxidant, antibacterial, anti-gout, anti-inflammatory, antidiabetic, and diuretic properties [28]. Futher, *Mimosa pudica* presents a rich array of phytochemicals with potential therapeutic applications. Its various pharmacological activities align with traditional uses and underscore its potential in medicine [29]. The plant's ability to inhibit seizures and its diverse range of effects suggest its promising role in neurological and metabolic disorders. Further research into the mechanisms behind these actions and the safety profiles of its compounds is vital for exploring their potential in pharmaceutical and therapeutic applications [30-32].

DISCUSSION

This study highlights the potential of various plants documented in their ethnomedicinal knowledge for addressing a range of ailments. The documented uses of *Centella asiatica* for wound healing and cognitive function align with emerging scientific evidence on its ability to promote collagen synthesis at concentrations as low as 10 μg/ml in vitro studies [33]. Additionally, animal models have shown extracts of *Centella asiatica* to improve cognitive function and memory, supporting its potential neuroprotective properties [34]. Similarly, *Acorus calamus's* traditional use for inflammation and microbial infections finds support in research demonstrating its anti-inflammatory effects by inhibiting pro-inflammatory mediators, with studies suggesting potential for topical applications at concentrations of 1% [35]. Furthermore, *Acorus calamus* extracts have demonstrated antimicrobial activity against various bacterial and fungal strains, with MIC values ranging from 0.125 to 1 mg/ml in some studies [36]. Juglans regia's established role as an antioxidant and potential sedative in Naga medicine aligns with scientific studies on its flavonoid content (e.g., kaempferol-3-O-rutinoside at 2-3% of dry leaf weight) [37] and observed sedative effects at remarkably low doses (Juglone at 0.125 mg/kg) in animal models [37]. However, some plants like *Eupatorium adenoporum*, while traditionally considered a weed, present a fascinating opportunity. The discovery of acetylcholinesterase inhibitory activity in its flavonoid compounds opens doors for exploring its potential in neurological disorders like Alzheimers. This highlights the importance of investigating even non-traditionally used plants for their potential therapeutic value, mirroring similar discoveries made with *Catharanthus roseus* (commonly known as the Madagascar Periwinkle), a flowering plant traditionally used for diabetes but later found to contain vincristine and vinblastine, effective cancer treatments [35]. A crucial caveat to this discussion is the limitations associated with some of the presented evidence. While many studies support the traditional uses, some rely on in vitro or animal model data. Further research must translate these findings into safe and effective human clinical applications. Rigorous clinical trials are essential to determine optimal dosages and potential side effects and identify any interactions with existing medications. One of the most significant strengths of this exploration lies in its emphasis on collaboration. Partnering with the Naga communities is vital for respectful knowledge exchange, ensuring fair benefit-sharing, and promoting the sustainable use of their natural resources. Several kinds of literature discuss other medicinal plants in India with various therapeutic activities [38 – 42]. This collaborative approach can empower these communities while fostering scientific advancements, as exemplified by the successful collaboration between the Yanomami tribe and researchers that led to the discovery of Spirantherin-A, a promising antimalarial compound derived from a rainforest plant [37].

CONCLUSION

This study on ethnomedicinal practices of the Naga tribe in Nagaland reflects the critical need for collaborative research efforts. The rich tradition of using medicinal plants passed down through generations offers a treasure trove of potential therapeutic agents. The scientific exploration of plants like *Centella asiatica, Acorus calamus, Juglans regia, Eupatorium adenovirus, Mimosa pudica* has provided compelling evidence for their potential applications in wound healing, cognitive function, inflammation, infection control, sedation, epilepsy, and potentially even neurological disorders. However, further research is vital to unlock the full potential of this ethnomedicinal wisdom. Future studies should focus on elucidating the specific mechanisms by which these plants exert

their effects, alongside rigorous assessments of their safety profiles. By bridging the gap between traditional knowledge and modern scientific methodologies, this collaborative approach can lead to the development of novel therapeutic strategies and contribute significantly to advancements in global healthcare. This treasured heritage of the Naga people has the potential to not only benefit their own communities but also offer solutions for a wider range of health challenges on a global scale.

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Nil

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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