Plant Science Review

PLANT SCIENCE REVIEW

Review Article

Journal homepage: https://psr.crcjournals.org/

ISSN No: 3041-7279

A comprehensive review of an Unani potent drug *Bukan Booti (Lippia Nodiflora)*: An evidence-based approach

Heena Khan[1], Zarin Fatima*[1], Nazia Sadaf[2], Afreen Ahmed[3] and Sadaf Nawaz[4]

[1]*Department of Ilmul Saidla, Ajmal Khan Tibbiya College, Aligarh Muslim University, Aligarh, Uttar Pradesh 202002-India*
[2]*Department of Tahaffuzi wa Samaji Tib, Tibbiya College, Aligarh Muslim University, Aligarh, Uttar Pradesh 202002-India*
[3]*Department of Tashreeh wa Manafeul Aza, Tibbiya College, Aligarh Muslim University, Aligarh, Uttar Pradesh 202002-India*
[4]*Department of Ilaj bit Tadbeer, Tibbiya College, Aligarh Muslim University, Aligarh, Uttar Pradesh 202002-India*

Received 24 February 2025 | Revised 21 March 2025 | Accepted 22 April 2025 | Available Online 19 May 2025

*Corresponding Author: **Zarin Fatima** | Email Address: **gn9674@myamu.ac.in**

Citation: Heena Khan, Zarin Fatima, Nazia Sadaf , Afreen Ahmed and Sadaf Nawaz (2025). A comprehensive review of an Unani potent drug *Bukan Booti (Lippia Nodiflora)*: An evidence-based approach. ***Plant Science Review***.
DOI: https://doi.org/10.51470/PSR.2025.06.01.36

Abstract

Lippia nodiflora (Linn.) Greene, commonly known as frog fruit or Bukan Booti in Unani medicine, is a creeping perennial herb from the Verbenaceae family. This comprehensive review examines the botanical, phytochemical, and pharmacological aspects of this medicinally important plant. Native to tropical and subtropical regions, L. nodiflora is widely distributed across India, particularly in wet habitats along riverbanks and irrigation channels. The plant demonstrates remarkable ecological adaptability, thriving in flood-prone areas while maintaining drought tolerance. Traditional medicine systems, particularly Unani and Ayurveda, have utilized L. nodiflora for treating various ailments, including fever, respiratory disorders, urinary problems, and inflammatory conditions. The plant's therapeutic properties are attributed to its rich phytochemical profile, containing flavonoids (hispidulin, nepetin, luteolin derivatives), phytosterols (β-sitosterol, stigmasterol), and various bioactive compounds. Modern pharmacological studies have validated many traditional uses, demonstrating significant antimicrobial, antidiabetic, antihypertensive, antioxidant, hepatoprotective, and anticancer activities. Recent research has also explored its potential in nanotechnology applications for the biosynthesis of zinc oxide and silver nanoparticles. This review highlights L. nodiflora's promising therapeutic potential and its role as a bridge between traditional knowledge and contemporary drug discovery.

Keywords: *zinc oxide, silver nanoparticles, bioactive compounds, antimicrobial, antidiabetic, antihypertensive, antioxidant, hepatoprotective.*

Introduction

The Lippia nodiflora, belonging to the family Verbenaceae, is a widely distributed creeping herb native to tropical and subtropical climates. Globally recognized for its ecological adaptability and medicinal significance, it thrives particularly in moist, grassy habitats, often seen near riverbanks, canal edges, and flooded plains. In India, five species of Lippia have been reported, of which L. nodiflora (synonym *Phyla nodiflora*) holds prominent therapeutic value. This herb features sprawling stems that root at nodes and display profuse branching, enabling its extensive coverage in favorable environments. The plant's distribution spans the Upper Gangetic plains, the Mediterranean region, Sri Lanka, and Indian states like Kerala, Maharashtra, Karnataka, Uttar Pradesh, Tamil Nadu, and Rajasthan [1]. Commonly called frog fruit in English and *Jalapippali* in regional languages, it holds an established position in Indian traditional medicine.

India's vast biodiversity supports the preservation and practice of herbal traditions such as Unani, Ayurveda, and Siddha. In many rural and tribal communities, where access to allopathic medicine is limited, traditional herbs like L. *nodiflora* are still relied upon for their therapeutic value. Over centuries, communities have identified the medicinal properties of L. *nodiflora* through empirical knowledge and sustained application. The herb is utilized to treat fever, respiratory ailments, wounds, and kidney disorders among other conditions [2]. As global interest in traditional medicine rises, scientific validation of such medicinal plants is becoming increasingly important. Around 70–80% of the global population continues to depend on herbal medicine for primary healthcare. Within this context, L. *nodiflora* emerges as a promising candidate for the development of standardized herbal formulations, linking traditional practices with modern scientific innovation [3].

Taxonomic Classification [1][2]
Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Lamialas
Family: Verbenaceae
Genus: *Phyla*
Species: *nodiflora*

Synonyms: *Lippia reptans*, *Lippia incisa*, *Phyla nodiflora*, *Lippia reptans* Kunth, *Phyla incisa* Small)
Common names: Frog-fruit, Matchweed, Creeping Lip, Wedge-leaf, Turkey-tangle, Capeweed, Matgrass [2][3][4].

Vernacular Names: [5]
Hindi: Bakkan
Bengali: Bhui-okra
Marathi: Ratoliya
Gujrati: Ratveliyo, ratoliya
Telugu: Bokenaku, bokkena
Tamil: Poduthalai
Kannad: Nela-hippali
Malyalam: Kattu-thippali
Oriya: Bukkan
Punjab: Bhuiokra, mokna, bukan

Geographic Distribution
Lippia nodiflora is found across tropical and subtropical regions, including India, Sri Lanka, Ceylon, Baluchistan, South and Central America, and parts of Tropical Africa. It is native to California. In India, it is especially common in Andhra Pradesh, Karnataka, Kerala, Maharashtra, Rajasthan, Tamil Nadu, Uttar Pradesh, and West Bengal. It thrives in wet environments such as rice fields, irrigation bunds, canal edges, and roadsides throughout tropical regions [1][3][6].

Habitat and Ecology
Lippia nodiflora is well adapted to environments with fluctuating moisture levels. It flourishes in areas that experience seasonal flooding or are near springs and rivers, especially where soils are rich in clay or clay-loam and capable of retaining moisture. It is commonly observed in floodplains, wetlands, and agricultural bunds. While it thrives in waterlogged conditions for short durations, prolonged submersion in turbid water for over a month can cause plant death. Interestingly, this species demonstrates notable drought tolerance. During dry spells, the plant may enter a dormant state and quickly resume growth when moisture is available again. Its ability to grow on elevated ridges or sandy loam near wet zones showcases its broad soil adaptability. L. nodiflora also displays resilience to frost, with regrowth from nodes occurring once temperatures rise. Unlike many invasive plants, it does not require disturbance or grazing for colonization. It is capable of spreading in undisturbed areas including protected reserves and light forests. The plant's rapid propagation via rooting nodes and extensive coverage makes it a successful colonizer in both disturbed and undisturbed ecosystems [3].

Morphological characteristics
It is a low-growing, much-branched herb that spreads horizontally along moist areas like irrigation channels and riverbanks, often found up to 900 meters elevation in hilly regions [5].

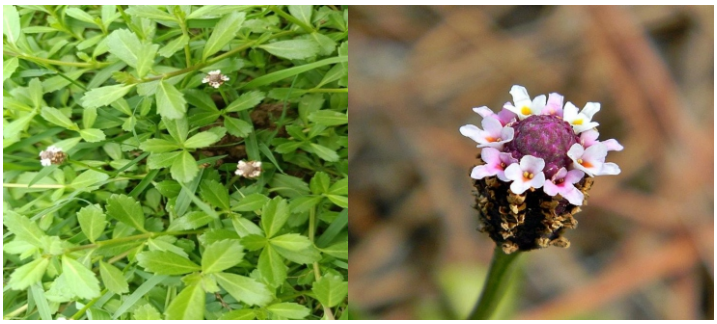

Fig. 1: Lippia nodiflora and flower

Macroscopic characters
The young stems are green to purplish, slender (2–3 mm thick), and range in length from 30 to 95 cm. As they mature, the stems become woody and grayish. Roots emerge from the leaf axils at stem nodes, and the plant develops a deep taproot (50–60 cm, occasionally deeper), accompanied by an extensive fibrous root system.
Leaves are arranged oppositely at the nodes, oblong to rounded, and measure 10–20 mm in length and 3–7 mm in width. The leaf margins are either entire or slightly serrated near the tip, tapering to a short petiole (2–5 mm). A fine layer of hair, giving the leaves a gray-green hue (canescence), is commonly observed. Inflorescences are small, dense, cylindrical spikes (10 mm diameter), emerging from axils on long stalks (15–45 mm). Each flower has a tubular corolla with a bilabiate structure: the lower lip is two-lobed and yellow at the base, while the upper lip is three-lobed. Flowers range from white to purple in color. The fruit is a schizocarp about 1–1.5 mm in diameter, releasing two flattened, brown seeds upon maturity [3].

Microscopic Characters
The stem surface bears multicellular rhomboidal Malpighian hairs and wax deposits with elongated ridges and bulbous ends. Sessile glands and rosy crystalline deposits are also visible. Transverse section reveals a bilobed structure with deep grooves. The epidermis consists of one layer of subspherical cells. The cortex has 7–8 layers of parenchymatous cells, some containing inclusions. A defined cambial ring separates the outer phloem and inner xylem. The central medulla is made up of parenchyma, with some cells storing phenolic content. Root sections display a rough surface and sparse root hairs. The epidermis has discontinuous, radially elongated cells with wavy walls. A distinct cambium is visible between the phloem and xylem. The medullary region shows a stellate (star-shaped) arrangement.

Leaf microscopy shows a higher density of trichomes and sessile glands on the lower surface compared to the upper. Stomata are more frequent on the upper surface (320/mm², stomatal index 30) than the lower (200/mm², index 22). Stomata are of diacytic and anisocytic types. A central vascular bundle is present in the midrib, enclosed in a bundle sheath. The transverse section of the lamina reveals a distinct upper epidermis, 1–2 layers of palisade cells, 4–6 layers of spongy mesophyll, and a lower epidermis. Floral structures include a wax-covered calyx with undulated patterns and rudimentary unicellular hairs. The corolla has striated, rosy petaloid wax without hairs. The stigma is peg-shaped, and the style is short and slightly rough in texture.
Seeds are heart-shaped with a convex dorsal and rimmed ventral surface. Epidermal cells on the dorsal side appear undulated and free from deposits, while the ventral surface shows smooth cells with variable deposits [7].

Description of *Lippia nodiflora* in Unani Literature
In Unani literature, it is commonly known as *Bukan Booti,* but in some parts called *Bukam Booti,* also known as *Aspa Booti*. It is an herb that grows in India and commonly spreads along the ground, especially near riverbanks and canal edges. The branches are thin, and the leaves are small, long, pointed, and somewhat broad, often with slight serrations along the edges. The tips of the leaves may appear slightly rounded, while the base where the leaf connects to the branch is narrow. A small, round flower appears at each node of the branch. The plant emits a smell similar to that of fish [8][9].

Temperament (*Mizaj*):
Cold and dry **[9]**
According to the Vaidyas (Ayurvedic practitioners), it is cold in nature. However, the author of *Makhzan al-Adwiya* describes it as hot and dry [8].

Harmful Effect (*Muzir*):
It may be harmful for individuals with a hot temperament (*Garm Mizaj*) [9].

Correctives (*Musleh*):
Black pepper and honey [9]

Dosage:
One tola (approximately 11.66 grams) [9]

Actions (*Afa'al*):
According to Unani physicians, it removes morbid and toxic matters which are produced due to the excess of yellow bile and phlegm. It has *mubarrid* (febrifuge), *musaffi khoon* (blood purifier), *mudir* (diuretic), *mufattit-e-hasat* (lithotryptic), *munaffis balgham* (expectorant), *dafe zeequn nafas* (antiasthamatic), *dafe jaraseem* (antimicrobial), *musakkin-e-alam* (analgesic), Sedative properties. On the basis of these properties, it is commonly used in fever, epistaxis, boils, swellings, cough, haemorrhoids, palpitation, loss of consciousness, retention of urine, and renal calculus [8][9].

Formation of zinc nanoparticles using Bukan Booti
It is also used in the preparation of calx (*shagufta*) of Zinc. The herb's leaves are ground and sprinkled on molten zinc to produce a fine white calx [8].

Therapeutic uses
Fever:
Decoction of the leaves is used to manage low-grade fevers and fevers linked to excess phlegm.

Renal disorders:
Its diuretic action benefits those with urinary retention, burning micturition, and kidney stones.

Epistaxis (*Ruaaf*)
Ground with black pepper, it is applied for nosebleeds

Cough
It is useful for *sual* (cough) which occurs due to *burudat* (cold)

Boil, swellings, cuts, and wounds:
Applying its paste on boils causes them to ripen and burst**.** [8]
Nutool (irrigation) with the decoction of leaves on *awram* (inflammations) gives a beneficial effect [10]. A poultice of the plant is applied on swollen cervical glands, for erysipelas and chronic indolent ulcers [11]. Being sedative and blood-purifying, it is also used in blood impurity disorders.

Hemorrhoids
To treat piles, fill a used clay pot with its leaves, add water, and bury it in a compost heap. After fifteen days, remove it and drink one cup daily from it. Avoid sour and flatulent foods during this treatment. Piles will be completely cured [8].

Palpitation
It is also beneficial in palpitation (*Khafqaan Haar*) caused by excessive bile [8][9].

Alopecia areata
Juice of the leaves is used in hair oils for treating patchy hair loss. [11]
Phyla nodiflora contains a bioactive compound, 1'-Hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one, which demonstrates promising therapeutic potential for treating androgen-related hair loss. Computational docking studies reveal that this phytochemical exhibit strong binding affinity to the androgen receptor, suggesting its ability to interfere with normal receptor function. Since dihydrotestosterone and other androgens activate the androgen receptor, leading to hair follicle miniaturization and subsequent hair loss, this compound's inhibitory interaction may prevent such activation. By blocking the receptor's active site, the phytochemical could potentially reduce the downstream signaling cascades responsible for follicular damage and hair thinning. These findings indicate that *P. nodiflora* derived compounds may serve as natural alternatives for developing

anti-alopecia treatments, offering a plant-based approach to managing androgen-induced hair loss through receptor-mediated mechanisms [19].

Phytochemical Constituent

Lippia nodiflora contains a diverse array of phytochemicals, which are distributed across various parts of the plant such as flowers, leaves, and the whole plant. These compounds are primarily responsible for the plant's pharmacological activities.

Compound	Plant Part	Reference
6-Hydroxyluteolin-7-O-aposide	Flowers	[6]
Luteolin-7-O-glucoside	Flowers	[6]
6-Hydroxyluteolin	Flowers, Leaves	[6]
Nepetin	Flowers, Leaves	[6]
Betalifolin	Flowers	[6]
Nodiflorin A & B	Leaves, Whole Plant	[5][6]
Nodifloridin A & B	Leaves, Whole Plant	[5][6]
Lippiflorin A	Leaves	[6]
Lippiflorin B	Leaves	[6]
Nodifloretin	Leaves	[6]
β-Sitosterol (glucoside)	Leaves	[6]
γ-sitosterol (glucoside)	Leaves	[18]
Stigmasterol (glucoside)	Leaves	[5]
Fructose, Glucose, Lactose, Maltose, Xylose	Whole Plant	[5]
Essential oil, Resin	Whole Plant	[5]
Potassium nitrate	Whole Plant	[5]
Non-glucosidic bitter substance	Whole Plant	[5]

These bioactive compounds, especially flavonoids and phytosterols, play a vital role in the therapeutic properties of L. *nodiflora*. Their presence justifies the traditional use of the plant in managing inflammation, microbial infections, metabolic disorders, and oxidative stress-related conditions.

Pharmacological actions

Numerous scientific investigations have validated the traditional uses of *Lippia nodiflora*, highlighting its multifaceted pharmacological potential.

1.Antibacterial activity

Lippia nodiflora exhibits broad-spectrum antimicrobial activity against gram-positive bacteria, gram-negative bacteria, and fungi. The antimicrobial properties are attributed to bioactive compounds including flavonoids, terpenoids, phenolic acids, and alkaloids present in the plant. Various extraction methods demonstrate different efficacy levels. Methanolic and ethanol extracts show strong inhibitory effects with zones ranging from 3-12 mm, while petroleum ether fractions produce 6-10 mm zones. Aqueous extracts are effective against most pathogens but ineffective against *Staphylococcus aureus* and *Micrococcus luteus*. *S. aureus* exhibits the highest susceptibility, followed by *Escherichia coli*, *Bacillus subtilis*, and *Klebsiella pneumoniae*. The effectiveness against *S. aureus* and *B. subtilis* is particularly valuable since these pathogens cause serious complications in liver-compromised patients. These findings validate the traditional use of *L. nodiflora* for treating infections and highlight its potential for developing natural antimicrobial agents [12][13][14][15][16].

Antidiabetic and Hypolipidemic Effect

Multiple research investigations have established the antidiabetic properties of *Lippia nodiflora* through various mechanisms. Plant extracts prepared using methanol as a solvent exhibited notable glucose-lowering and lipid-regulating activities when tested in experimentally induced diabetic animal models using streptozotocin. Among the bioactive constituents identified, γ-sitosterol emerged as a particularly effective compound, demonstrating its ability to control elevated blood sugar levels by stimulating insulin release and blocking hepatic glucose production pathways. Computational molecular docking studies further revealed that n-hexadecanoic acid, another significant phytochemical present in the plant, shows strong binding interactions with Protein Tyrosine Phosphatase 1B, an enzyme that negatively modulates insulin signaling cascades. Given that this enzyme represents an important drug target for managing type 2 diabetes, these collective findings highlight the potential of L. *nodiflora* as a valuable botanical resource for developing natural therapeutic interventions against diabetes through multiple complementary pathways involving glucose metabolism regulation and insulin sensitivity enhancement [17][18][19].

Antihypertensive effect

L. *nodiflora* has shown antihypertensive activity in DOCA-salt-induced hypertensive rats. Its extract significantly reduced systolic and diastolic blood pressure, likely due to its angiotensin-converting enzyme (ACE) inhibitory action and diuretic effect. This supports its traditional use in cardiovascular disorders [20].

Antioxidant and Free Radical Scavenging Effects

The methanolic extract of L. *nodiflora* exhibits strong in vitro antioxidant activity through multiple mechanisms, including free radical scavenging, hydrogen donation, and lipid peroxidation inhibition. Key antioxidants like β-sitosterol and polyphenols are responsible for these protective effects [21][22].

Anticancer effect

Lippia nodiflora demonstrates significant anticancer potential through multiple mechanisms across different cancer types. Leaf extracts exhibit cytotoxic effects against lung and prostate cancer cells, inducing apoptosis at concentrations as low as 20 µg/mL within 24 hours. The anticancer activity is strongly linked to reactive oxygen species-mediated apoptotic cell death, correlating with the plant's antioxidant properties. Morphological changes characteristic of programmed cell death has been observed in treated cancer cells, confirming the pro-apoptotic effects. Additionally, computational studies reveal that stigmasterol, a phytosterol constituent of the plant, shows strong binding affinity toward Cyclin A, a cell cycle regulator frequently

overexpressed in malignant cells. This interaction suggests a potential mechanism for inhibiting tumor cell proliferation by disrupting cell cycle pathways. While the specific bioactive compounds responsible for these effects require further characterization, these findings collectively highlight the therapeutic promise of *L. nodiflora* as a natural source for developing novel anticancer agents targeting multiple cancer types through diverse molecular pathways [19][23][24][25].

Hepatoprotective effect

Pre-treatment with L. *nodiflora* extract has been found to suppress inflammatory markers such as IL-1β, TNF-α, and NF-κB in liver cell models exposed to lipopolysaccharides. This indicates its use in managing inflammation-related liver disorders [13].

Gastroprotective effect

Experimental evidence suggests that different fractions of L. *nodiflora* extracts help reduce gastric ulcer index in ethanol-induced models, likely due to its antioxidant and anti-inflammatory constituents [26].

Antihyperuricemic agents

L. *nodiflora* extracts have shown uric acid-lowering effects by inhibiting xanthine oxidase enzymes and promoting uric acid excretion. This supports its use in conditions like gout and hyperuricemia [27].

Neuropharmacological activity

Phytochemical analysis of *Lippia nodiflora* extracts has identified a diverse array of bioactive compounds with potential neurological applications. The plant contains various flavonoids, including flavanones and flavones, which are predominantly concentrated in chloroform and ethanolic preparations. A comprehensive range of bioactive constituents has been documented, including aglycones such as hispidulin, jaceosidin, nepetin, hydroxyluteolin, and nodiflorin mono- and disulfates, alongside glycosides like lippiflorin A and B, nodifloretin A and B, nodiflorin A and B, and nodifloridin A and B. Many of these phytoconstituents are recognized for their central nervous system activity, suggesting that *L. nodiflora* may exhibit CNS depressant properties and hold therapeutic potential for neuropharmacological applications. The presence of these specialized metabolites supports the plant's traditional use in nervous system-related disorders and warrants further investigation into its neurological therapeutic mechanisms [28].

Synthesis of Nanoparticles

Lippia nodiflora has been explored for its role in green nanotechnology, especially in the biosynthesis of zinc oxide (ZnO) and silver nanoparticles (AgNPs). These processes utilize plant extracts as natural reducing and capping agents, eliminating the need for harmful chemicals. In one study, aqueous flower extracts of L. *nodiflora* facilitated the rapid synthesis of ZnO nanoparticles within the size range of 9–10 nm. The biosynthesized ZnO NPs showed promising applications in biomedical and environmental fields due to their high surface reactivity and biocompatibility [29]. Similarly, AgNPs synthesized using the aqueous extract of aerial parts of the plant were characterized using various analytical techniques including UV-Vis spectroscopy, FTIR, XRD, SEM, EDX, and TEM. These silver nanoparticles exhibited well-defined crystalline structure and a uniform size distribution between 30–60 nm. They also demonstrated significant antibacterial and antioxidant properties, validating the plant's utility in sustainable nanoparticle production [30]. The ability of L. *nodiflora* to function as both a reducing and stabilizing agent in nanoparticle synthesis underscores its relevance in green chemistry and expands its potential beyond traditional therapeutic uses.

Future Perspectives

Future studies on *Bukan Booti* should focus on testing the plant in human patients to prove its traditional uses in Unani medicine. Scientists need to find new active compounds in the plant and understand how they work in the body. It is important to check if the plant is safe for long-term use and create standard medicines with proper quality control. Using modern technology like nanoparticles to deliver the medicine better and working together with traditional Unani doctors and modern researchers will help make this valuable plant more useful for treating diseases.

Conclusion

Lippia nodiflora is a versatile medicinal herb valued in traditional systems like Unani and Ayurveda. Its broad pharmacological properties—such as antimicrobial, antioxidant, and antidiabetic effects—are supported by both classical texts and modern research. The plant's rich phytochemical content and role in green nanotechnology further enhance its therapeutic relevance. With continued scientific validation, L. *nodiflora* may play a significant role in future herbal and pharmaceutical developments.

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