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Review Article……!!!

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VITEX NEGUNDO LINN. LEAVES EXTRACT: PHARMACOGNOSTIC INSIGHTS, PHYTOCHEMISTRY, PHARMACOLOGICAL POTENTIAL, AND APPLICATIONS IN NOVEL DRUG DELIVERY SYSTEMS

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Keywords:

Vitex negundo; Nirgundi; phytochemistry; pharmacognosy; pharmacological activities; novel drug delivery systems

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ABSTRACT

Vitex negundo Linn., commonly known as Nirgundi or Chinese chaste tree, is a medicinal plant widely recognized in Ayurveda, Unani, and other traditional systems of medicine for its diverse therapeutic properties. Among its various parts, the leaves are particularly rich in bioactive constituents, including flavonoids, iridoid glycosides, terpenoids, phenolic acids, alkaloids, and essential oils, which contribute to a broad spectrum of pharmacological activities. This review consolidates current knowledge on the pharmacognosy, macroscopic and microscopic features, phytochemistry, and pharmacological actions of *V. negundo* leaves, highlighting activities such as anti-inflammatory, antimicrobial, antioxidant, anticancer, antiasthmatic, and wound healing effects. Special emphasis is placed on the integration of leaf extracts into novel formulation strategies, including nanoparticles, phytosomes, gels, and transdermal patches, aimed at enhancing bioavailability, therapeutic efficacy, and patient compliance. Safety and toxicological data suggest a wide margin of safety at traditional doses, although large-scale clinical trials and standardized extraction protocols are still needed. Future prospects lie in advanced formulation development, green nanotechnology applications, and evidence-based validation through rigorous clinical research.

1. Introduction

Vitex negundo Linn., commonly known as Nirgundi in Sanskrit and Hindi, and Chinese chaste tree in English, is a large aromatic shrub belonging to the family *Lamiaceae*. It is widely distributed in tropical and subtropical regions of Asia, including India, China, and the Philippines. The plant is recognized for its distinctive palmate leaves, aromatic odor, and clusters of small purple to blue flowers[1]. Various parts of the plant leaves, roots, seeds, and flowers—are used for medicinal purposes, but the leaves are considered the most pharmacologically active and are extensively studied for their therapeutic potential[2].

Importance in Ayurveda, Unani, and Traditional Medicine

In Ayurveda, *Vitex negundo* is classified under Vedanasthapana (analgesic) and Shothahara (anti-inflammatory) categories and is prescribed for the management of rheumatic pain, inflammation, fever, cough, and skin disorders. Unani medicine also recognizes *Nirgundi* for its Muqawwi-i-Aasab (nervine tonic), Daf-e-Waja (pain-relieving), and Muhallil-e-Waram (anti-inflammatory) properties. Traditional healers in Southeast Asia use the leaves for treating asthma, headaches, wounds, and as a mosquito repellent. Its long history of ethnomedicinal application forms a strong basis for modern pharmacological investigations[3].

Among all plant parts, the leaves of *Vitex negundo* are particularly rich in bioactive compounds, including flavonoids, iridoid glycosides, terpenoids, and essential oils, which are linked to its diverse pharmacological activities. Extracts from the leaves have demonstrated anti-inflammatory, antimicrobial, antioxidant, anticancer, and wound-healing properties in preclinical studies. Additionally, the leaves are more easily available, renewable, and sustainable for large-scale extraction compared to roots or seeds, making them an ideal focus for both research and formulation development[4].

The aim of this review is to comprehensively summarize the pharmacognostics characteristics, phytochemistry, and pharmacological activities of *Vitex negundo* Linn. leaves, with a special emphasis on their incorporation into novel drug delivery systems. The scope includes traditional knowledge, microscopic and macroscopic evaluation, bioactive compounds, experimental pharmacological data, and recent advancements in formulation approaches such as nanoparticles, gels, phytosomes, and transdermal systems. This integrative approach aims to bridge traditional uses with modern pharmaceutical applications, highlighting research gaps and future prospects.

Pharmacognostic Description

2.1 Taxonomical Classification

- Kingdom: Plantae
- Division: Magnoliophyta
- Class: Magnoliopsida
- Order: Lamiales
- Family: Lamiaceae

- Genus: *Vitex*
- Species: *negundo* Linn.

2.2 Geographical Distribution

Vitex negundo Linn. is native to the tropical and subtropical regions of Asia and Africa, and has now become naturalized in several parts of the world due to its adaptability and medicinal importance. In India, it is commonly found along riverbanks, roadsides, open fields, and wastelands, thriving in both plains and lower Himalayan regions up to an altitude of 1500 meters. It is extensively distributed across China, particularly in the southern provinces, as well as in Sri Lanka, Bangladesh, Pakistan, Myanmar, Thailand, Malaysia, and Vietnam[5]. In the Philippines, locally known as *Lagundi*, it is cultivated on a large scale as part of the government's herbal medicine program. The plant also grows in tropical Africa and has been introduced to Hawaii and parts of Central America.Its ability to tolerate poor soils, drought conditions, and seasonal flooding has contributed to its wide geographical range. The presence of *V. negundo* in diverse climatic zones underlines its ecological resilience and potential for large-scale cultivation for pharmaceutical use[6].

2.3 Macroscopy (Leaf Morphology)

The leaves of *Vitex negundo* are compound, palmate, typically composed of 3 to 5 lanceolate to ovate leaflets arranged in an opposite phyllotaxy.

- **Shape:** Individual leaflets are lanceolate (narrow, tapering to the tip) or ovate (egg-shaped), with acuminate apices and entire to slightly serrated margins. The central leaflet is usually the largest, with lateral leaflets progressively smaller.
- **Size:** Leaflets range from 4–10 cm in length and 1–3 cm in width, with the central leaflet reaching up to 12 cm in favorable conditions.
- **Surface & Texture:** The upper surface is smooth or slightly pubescent (hairy), while the lower surface is more densely covered with fine, whitish hairs.
- **Color:** Dark green on the upper surface, paler or grayish-green beneath due to the presence of fine hairs.
- **Odor:** Strong aromatic fragrance due to volatile oils, detectable even in dried leaves.
- **Taste:** Slightly bitter, attributed to the presence of flavonoids and terpenoids.
- **Petiole:** Long, slender petioles ranging from 2–6 cm, supporting the compound structure[7-8].

Figure 1. *Vitex negundo* plant.

2.4 Microscopy

2.4 Microscopy (Leaf Anatomy)

Microscopic examination of ***Vitex negundo*** Linn. leaves reveals several distinct anatomical featuresthat serve as diagnostic markers for authentication and quality control of crude drug material:

- **Presence of Glandular Trichomes:** The leaf surface, particularly on the lower epidermis, bears abundant uniseriate glandular trichomes. These trichomes secrete volatile essential oils rich in terpenoids, contributing to the plant's characteristic aromatic odor and defensive properties against herbivores and pathogens.
- **Epidermis with Stomata (Anomocytic Type):** The epidermal layer is composed of polygonal cells with a thin cuticle. Stomata are predominantly anomocytic (surrounded by a varying number of epidermal cells without distinct subsidiary cells), distributed more abundantly on the abaxial (lower) surface than on the adaxial (upper) surface.
- **Palisade Cells Rich in Chloroplasts:** The mesophyll is differentiated into a single layer of elongated palisade cells, densely packed with chloroplasts, optimizing photosynthetic activity.
- **Xylem Vessels with Lignified Walls:** The vascular bundles are bicollateral and surrounded by bundle sheath cells. The xylem vessels possess thick, lignified walls, providing mechanical strength and efficient water conduction.
- **Calcium Oxalate Crystals in Mesophyll:** Prismatic and cluster forms of calcium oxalate crystals are observed within the mesophyll tissue. These crystals are considered a protective feature, deterring herbivory[9-11].

Diagnostic Value:

The combination of glandular trichomes**,** anomocytic stomata**,** chloroplast-rich palisade cells**,** lignified xylem vessels**,** andcalcium oxalate crystalsserves as a reliable set of microscopic markers for identifying and standardizing***V. negundo*** leaves in raw drug form or powdered samples[12].

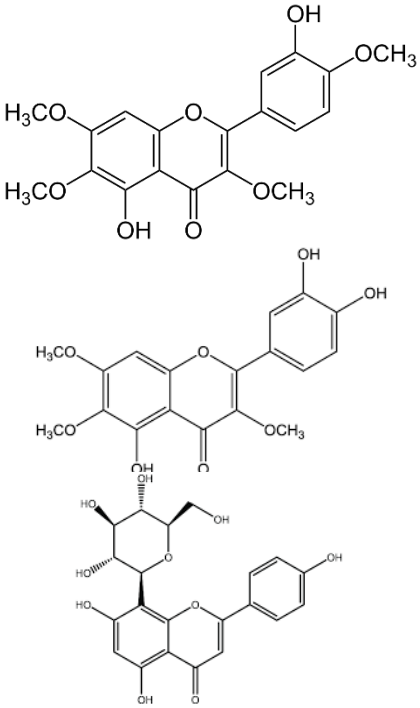
3. Phytochemistry of *Vitex negundo* Leaves

The leaves of *Vitex negundo* Linn. are a rich source of structurally diverse secondary metabolites that contribute to its pharmacological activities[12-14].

3.1 Flavonoids

Flavonoids are the most extensively studied constituents in *V. negundo* leaves, known for their antioxidant, anti-inflammatory, and anticancer activities.

- **Casticin** – A polymethoxylated flavone with anti-inflammatory, anticancer, and neuroprotective effects, acting via inhibition of NF-κB and COX-2 pathways.
- **Chrysoplenol-D** – Exhibits bronchodilatory and antiasthmatic properties, attributed to mast cell stabilization and smooth muscle relaxation.
- **Vitexin and Isovitexin** – C-glycosylated flavones with strong antioxidant, anti-diabetic, and cardioprotective activities.

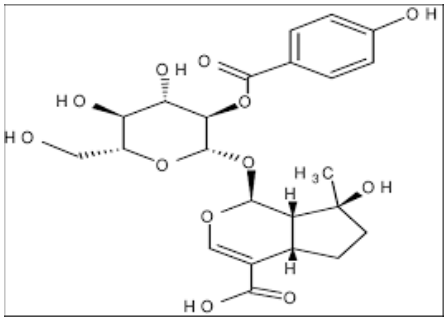


Casticin Chrysoplenol-D Vitexin

3.2 Iridoid Glycosides

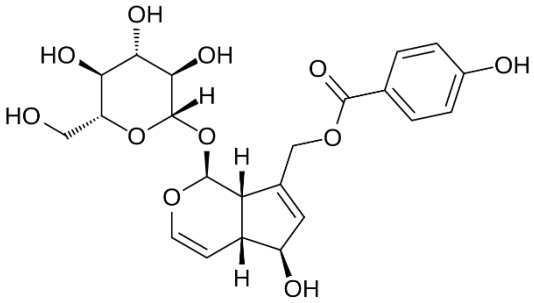
Iridoid glycosides are monoterpenoids with pronounced anti-inflammatory and hepatoprotective effects.

- **Negundoside** – Unique to *V. negundo*, it has shown potent free radical scavenging activity and inhibition of lipid peroxidation.



Negundoside

- **Agnuside** – Demonstrates antimicrobial and hepatoprotective properties, along with potential modulation of inflammatory mediators.



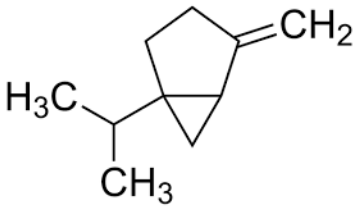
Agnuside

3.3 Terpenoids

Terpenoids contribute to the plant's aroma and bioactivity.

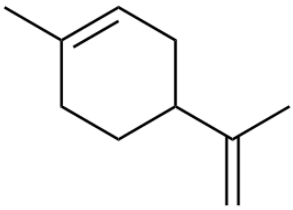
- **α-Pinene** – Possesses antimicrobial and anti-inflammatory activity, often found in essential oils.

- **Sabinene** – Known for antioxidant and antifungal effects.



Sabinene

- **Limonene** – Exhibits gastroprotective, antioxidant, and mood-enhancing properties.



Limonene

3.4 Phenolic Acids

Phenolic acids act as powerful antioxidants and enzyme modulators.

- **p-Hydroxybenzoic Acid** – Antioxidant and antimicrobial agent.
- **Ferulic Acid** – Anti-inflammatory and photoprotective compound, known to stabilize collagen in connective tissue.

3.5 Alkaloids &Lignans

Although less abundant than flavonoids, these compounds exhibit potent bioactivities.

- **Nisheline** – An alkaloid reported to have antimicrobial activity.
- **Vitedoin-A** – A lignan with cytotoxic and anti-proliferative effects on cancer cell lines.

3.6 Essential Oils

The essential oil fraction of *V. negundo* leaves is rich in monoterpenes and sesquiterpenes responsible for the plant's distinctive aroma and insect-repellent properties.

- **Caryophyllene** – Anti-inflammatory sesquiterpene that modulates CB2 cannabinoid receptors.
- **Cineole (Eucalyptol)** – Expectorant, bronchodilator, and antimicrobial agent.
- **Eugenol** – Analgesic and antiseptic compound with widespread use in dental preparations.

Pharmacological Relevance:

The synergy between these phytochemicals underlies the broad spectrum of pharmacological activities attributed to *Vitex negundo* leaves, including anti-inflammatory, antimicrobial, antioxidant, anticancer, antiasthmatic, and wound-healing effects. This chemical diversity also makes the plant extract a promising candidate for novel formulation development aimed at enhancing bioavailability and targeted delivery.

4. Pharmacological Activities

4. Pharmacological Activities of *Vitex negundo* **Linn. Leaves**

4.1 Anti-inflammatory & Analgesic Activity

The leaf extract of ***Vitex negundo*** exhibits strong anti-inflammatory and analgesic effects by inhibiting cyclooxygenase-2 (COX-2), tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6) pathways, thereby reducing prostaglandin synthesis and inflammatory signaling. These effects, attributed mainly to casticin and

negundoside, have been validated in vivo using carrageenan-induced rat paw edema models and confirmed through analgesic assays such as tail-flick and hot-plate tests[15-16].

4.2 Antimicrobial Activity

Vitex negundo leaves demonstrate broad-spectrum antimicrobial potential, effectively inhibiting bacterial strains such as ***Staphylococcus aureus***, ***Escherichia coli***, and fungal pathogens like ***Candida albicans***. The essential oil, rich in cineole, eugenol, and caryophyllene, exhibits both bactericidal and fungicidal activity, primarily through disruption of microbial membranes and enzyme inactivation[17-18].

4.3 Antioxidant Activity

The methanolic and ethanolic extracts of the leaves show significant antioxidant potential in DPPH, ABTS, and FRAP assays due to the presence of phenolic acids and flavonoids, which scavenge free radicals, chelate metal ions, and inhibit oxidative stress–induced damage[19-20].

4.4 Anticancer Activity

Phytoconstituents such as casticin and vitedoin-A from the leaves possess cytotoxic effects against breast (MCF-7) and cervical (HeLa) cancer cell lines by inducing apoptosis, causing cell cycle arrest, and modulating tumor suppressor and apoptotic pathways, with minimal toxicity to normal cells in vitro[21].

4.5 Antiasthmatic& Anti-allergic Activity

The leaf extract has shown significant antiasthmatic and anti-allergic effects by reducing eosinophil infiltration, stabilizing mast cells, and preventing histamine release, thereby alleviating airway inflammation and bronchoconstriction in experimental models[22].

4.6 Wound-Healing Activity

Topical formulations containing ***Vitex negundo*** leaf extract accelerate wound healing by enhancing collagen synthesis, promoting epithelialization, and preventing microbial infections, leading to faster wound contraction and improved tissue repair in animal models[23].

5. Novel Formulations Containing *Vitex negundo* **Linn. Leaves Extract**

5.1 Nanoparticles &Nanogels

Silver nanoparticles synthesized using ***Vitex negundo*** leaf extract act as potent antimicrobial agents for coatings, wound dressings, and biomedical surfaces, offering enhanced stability and bioactivity due to the plant's phytochemicals acting as both reducing and capping agents[24-26].

5.2 Herbal Topical Gels

Hydroalcoholic extracts of ***Vitex negundo*** leaves have been incorporated into carbopol- or guar gum–based gels that exhibit strong anti-inflammatory activity, making them effective for arthritis pain relief and localized swelling reduction[27-28].

5.3 Polyherbal Creams & Ointments

Polyherbal topical preparations containing ***Vitex negundo*** leaf extract, often combined with other medicinal plants, are formulated for wound healing and treatment of skin infections,

benefiting from synergistic antimicrobial and anti-inflammatory effects[29].

5.4 Phytosomes

Flavonoid-rich extracts of ***Vitex negundo*** are encapsulated in phospholipid-based phytosomes to improve solubility, permeability, and oral bioavailability, thereby enhancing systemic therapeutic outcomes compared to crude extracts[30].

5.5 Transdermal Patches

Transdermal drug delivery systems incorporating ***Vitex negundo*** extract provide controlled and sustained release of active compounds, ensuring prolonged analgesic and anti-inflammatory action with improved patient compliance[31].

6. Safety, Toxicology, and Regulatory Aspects

Vitex negundo Linn. leaves are generally recognized as safe when consumed in traditional therapeutic doses, as evidenced by centuries of use in Ayurveda, Unani, and folk medicine without widespread reports of toxicity. Preclinical toxicity studies in rodents, involving acute and sub-chronic administration of leaf extracts at doses several times higher than traditional usage levels, have shown no significant adverse effects on body weight, hematological parameters, liver function, or kidney function. Histopathological examinations of major organs have also indicated no observable tissue damage.

However, like many medicinal plants, the phytochemical profile and safety margin can vary depending on factors such as geographical origin, harvesting season, extraction method, and dosage form. While animal studies provide encouraging safety data, human clinical safetyevaluations remain limited**.** Occasional reports of mild gastrointestinal discomfort or allergic skin reactions exist, but these are rare and often linked to improper dosing or crude preparations.

From a regulatory perspective, ***Vitex negundo*** leaf preparations are included in several pharmacopeias and official herbal monographs, such as the ***Ayurvedic Pharmacopoeia of India*** and the ***Philippine Department of Health's Herbal Medicine List*** (as ***Lagundi***). However, for use in modern pharmaceutical formulations, especially novel drug delivery systems, standardized extracts with defined active marker compounds are essential to ensure batch-to-batch consistency, efficacy, and safety.

Given its pharmacological potential, the next step in its integration into evidence-based medicine is rigorous standardization, advanced toxicological profiling, and well-designed clinical trials to establish optimal dosing, long-term safety, and potential herb–drug interactions.[32]

7. Conclusion

Vitex negundo Linn. leaves extract exhibits a broad pharmacological spectrum, encompassing anti-inflammatory, antimicrobial, antioxidant, anticancer, antiasthmatic, and wound-healing activities, supported by both traditional medicinal knowledge and modern experimental studies. Its rich phytochemical profile,

comprising flavonoids, iridoid glycosides, terpenoids, phenolic acids, alkaloids, and essential oils, underpins its diverse therapeutic potential.

Incorporating ***V. negundo*** leaf extract into novel drug delivery systems, such as nanoparticles, phytosomes, gels, and transdermal patches, holds promise for enhancing therapeutic efficacy, stability, and patient compliance. By bridging traditional ethnopharmacological wisdom with cutting-edge pharmaceutical technology, ***V. negundo*** can be developed into standardized, safe, and effective herbal medicines for global healthcare.

However, to realize this potential, it is imperative to conduct rigorous clinical trials**,** adoptstandardized extraction and quality control measures**,** and explore innovative formulation strategies. Such integrative research will pave the way for transforming ***V. negundo*** from a traditional remedy into a scientifically validated and globally accepted therapeutic agent.

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