

Therapeutic Potential of *Vitex negundo* Linn: A Comprehensive Review

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Received: 2025-4-01

Revised: 2025-4-10

Accepted: 2025-4-19

ABSTRACT

Vitex Negundo Linn which is an herbal plant which is mainly found in Indian Subcontinent which is also known as 'Nirgundi'. *Vitex negundo* is mentioned in Ayurveda as useful in treating various disorders. All parts of the plant, from root to fruit, possess a multitude of phytochemical secondary metabolites which impart an unprecedented variety of medicinal uses to the plant. This plant is mainly known for its utility in female reproductive disorders like premenstrual syndrome, menopause, hyperprolactinemia, dysmenorrhea, etc. *Vitex Negundo* L. also has anti-inflammatory and analgesic activity. It also has mosquito repellent activity. All parts of the plant especially its leaves contain numbers of secondary metabolites such as alkaloids, phenols, flavonoids, glycosides, iridoids, tannins and terpenes. This review aims in presenting the information regarding *Vitex Negundo* Linn and the Anti-inflammatory Activity of this plant for the development of modern medicines.

Keywords: Nirgundi, Traditional Medicine, Anti-inflammatory, Analgesics, Therapeutic uses

1. INTRODUCTION

1.1 The Medicinal Plants

For a very long time, there has been a relationship between plants and people as defined by Morgenstern [1(2023)]. Despite several advancements in synthetic medicines antibiotics and vaccines, but still today Medicinal herbs hold a lot of importance and play a major role in treating the various ailments of humans. So that a comprehensive compilation of medicinal plants that can be used in disease prevention is obtained, Collection of original data from the traditional custodians of such knowledge is essential [2].

1.2 *Vitex Negundo* Linn

Vitex Negundo Linn which is also commonly known as Nirgundi is an Ayurvedic herb which has tremendous uses on its own. Every single part of this plant is useful. But most commonly its leaves are used for various purposes by various different traditional way. E.g. When the leaves of this plant are burned, the smoke which is produced acts as a mosquito repellent. Similarly, there are many more advantages of this plant but in this article, we will be mainly focusing on the Anti-inflammatory Activity of its leaves.

1.3 Taxonomic Classification of *Vitex Negundo* Linn

The following given table will give all the information regarding the taxonomy of *Vitex Negundo* Linn [3].

Table. 1 Taxonomy of Vitex Negundo

Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Asterids
Order	Lamiales
Family	Lamiaceae
Genus	Vitex
Species	V. Negundo

1.4 Nomenclature

Different Names of Vitex Negundo Linn used in Different parts of India in their native language.[3]

Biological Name: Vitex Negundo Linn

Sanskrit: Nirgundi, Sindu Vara, Neel Manjari

Hindi: Samhalu, Saubhalu, Nirgandi

Marathi: Nirgudi

English: Five-leaved chaste tree Horseshoe Vitex Chinese chaste tree

Konkani: Lingad

Kannada: Bili nekki

Punjabi: Banna, Marwan, Maura, Mawa, Swanjan, Torbanna

Tamil: Chinduvaram, Nirnochchi, Nochchi, Notchi, Vellai-nochc

Telugu: Sindhuvara, Vavili, Nalla-vavili Tella-vavili

1.5 Habitat and Cultivation Details

Vitex negundo can be grown in warm temperate to tropical areas, succeeding at elevations from sea level to around 2,000 metres. It is found in areas where the mean annual rainfall is in the range of 600 – 2,000mm. It can tolerate short-lived temperatures falling down to about -10°C. An easily grown plant, it prefers a light well-drained loamy soil in a warm sunny position sheltered from cold drying winds. Succeeds in poor dry soils. Tolerates alkaline and saline soils.

Moderately to fairly fast growing, it can be managed by coppicing, with a rotation of 2 years. Plants produce root suckers. Yields of about 0.3 tonnes/hectare of air-dry fuel wood can be obtained when planted on contours 5 metres apart. There are some named forms, selected for their ornamental value. The leaves and stems are strongly aromatic. The flowers have a most pronounced musk-like perfume.

1.6 Chemical constituents

It consists of a wide range of chemical constituents in it like root contains 2 β ,3 α -diacetoxyoleana-5,12-dien-28-oic acid; 2 α ,3 α -dihydroxyoleana-5,12-dien-28-oic acid; 2 α ,3 β -diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid; vitexin, isovitexin, negundin-A; negundin-B; (+)-diasyringaresinol; (+)-lyoniresinol; vitrofolal-E and vitrofolal-F, acetyl oleanolic acid; sitosterol and 3-formyl-4,5-dimethyl-8-oxo-5H-6,7-dihydronaphtho (2,3-b) furan. Vitex negundo plant leaves contain hydroxy-3,6,7,3',4'-pentamethoxyflavone, 6'-p-hydroxybenzoyl mussaenosidic acid, 2'-p-hydroxybenzoyl mussaenosidic acid, 5,3'-dihydroxy-7,8,4'-trimethoxyflavanone, 5,3'-dihydroxy-6,7,4'-trimethoxyflavanone, viridiflorol, β -caryophyllene, sabinene, 4-terpineol, gamma-trepanned, caryophyllene oxide, 1-octen-3-ol, globulol, betulinic acid [3 β -hydroxylup-20-(29)-en-28-oic acid],

ursolic acid [2β - hydroxyurs12-en-28-oic acid], and many more .

But the most important chemical constituent that shows the Anti-inflammatory activity is

3,4, 9trimethyl-7-propyldecanoic acid. [4]

1.7 Traditional uses of V. Negundo.

Traditionally, the plant is reported by many studies as an important medicinal plant, specifically in India, where they exhibit multifarious activities, including antiinflammatory, analgesics, tonic, and antimicrobial properties. In India and Malaysia, the shoot, fruit, and leaf of Nirgundi plant are used to help women after childbirth where the juice of the shoot and fruit is utilized to increase milk lactation and the leaf was boiled in water for postpartum bath, which helps the mother's recovery [5]. The plant is first described in Charaka Samhita which is a oldest and most authentic text of Ayurveda. Later on, plant related Ayurvedic text like Bhavaprakasha nighantu, Kayadeva nighantu, Raja Nighantu, Dhanwantari nighantu and Chakradatta etc has mentioned detailed about the plant Nirgundi. Nirgundi oil prepared from the juice of nirgundi leaves is applied to sinuses, scrofulous sores, wounds, ulcers and gangrenous wounds. Leaves and bark are considered useful in scorpion sting [6].

1.8 Physicochemical constituents in Different parts of V. Negundo.

There are many different chemical constituents situated in the different parts of the plants like leaves, roots, stems, seeds, etc.

The following shows the different chemicals in their respective part.

Leaves: Hydroxy-3,6,7,3',4'-pentamethoxyflavone[7] 6'-p-hydroxybenzoyl mussaenosidic acid; 2'-p-hydroxybenzoyl mussaenosidic acid. 5, 3'-dihydroxy-7,8,4'-trimethoxyflavanone; 5,3'-dihydroxy-6,7,4'- trimethoxyflavanone ,viridiflorol; β -caryophyllene; sabinene; 4-terpineol; gamma-terpinene; caryophyllene oxide; 1-oceten-3-ol; globulol , betulinic acid [3β hydroxylup20-(29)-en-28-oic acid]; ursolic acid , 2β -hydroxyurs12-en-28-oic acid]; nhentriacontanol; β sitosterol; p-hydroxybenzoic acid , protocatechuic acid; oleanolic acid; flavonoids, angusid; casticin; vitamin-C; nishindine; gluco-nonitol; p-hydroxybenzoic acid; sitosterol.[8][9]



Fig. 01 Leaves of Vitex negundo Leaves



Fig. 02 Roots of Vitex Negundo Linn

Roots: 2 β , 3 α -diacetoxyoleana-5,12-dien-28-oic acid; 2 α ,3 α -dihydroxyoleana-5,12-dien-28oic acid; 2 α ,3 β -diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid; vitexin and isovitexin,[10] negundin-A; negundin-B; (+)-diasyringaresinol; (+)-lyoniresinol; vitrofolal-E and vitrofolal-F, acetyl oleanolic acid; sitosterol; 3-formyl-4.5-dimethyl-8- oxo-5H-6,7dihydronaphtho (2,isovitexin[11].

Seeds: 3 β -acetoxylean-12-en-27-oic acid; 2 α , 3 α -dihydroxyoleana-5,12-dien-28-oic acid; 2 β ,3 α diacetoxyoleana-5,12-dien-28-oic acid; 2 α , 3 β -diacetoxy-18-hydroxyoleana5,12-dien28oicacid, vitedoin-A; vitedoin-B; a phenyl-naphthalene-type lignan alkaloid, vitedoamine-A; five other lignan derivatives, 6-hydroxy-4-(4-hydroxy-3- methoxy-phenyl)-3hydroxymethyl7methoxy-3, 4dihydro-2-naphthaldehyde, β -sitosterol; p-hydroxybenzoic acid; 5-oxyisophthalic acid; n-tritriacontane, nhentriacontane; n-pentatriacontane; n-nonacosane [12].



Fig.03 Seeds of Vitex Negundo Linn

- Extensive biochemical analyses have resulted in the detection and isolation of a wide variety of the phytochemical constituents from different parts of the plant. Application of advanced spectroscopy tools such as NMR, EMR, FTIR along with X- ray crystallography studies would bring to light more such biologically active phytochemicals in different parts of the plant. Use of in silico tools to evaluate the efficacy of these phytochemical moieties as drugs would endow an added value to such study.

2. Pharmacological Activity of V. Negundo L.

Vitex negundo has been found to possess significant hepatoprotective, antioxidant, antiinflammatory, analgesic, antifungal, leukoderma, enlargement of spleen, skin ulcers and fever.[12][13]

2.1 Hepatoprotective Activity

Hepatoprotective activity of Vitex negundo leaf ethanolic extract was investigated against hepatotoxicity produced by administering a combination of three anti-tubercular drugs isoniazid 7.5 mg/kg, rifampin-10 mg/kg and pyrazinamide-35 mg/kg for 35 days by oral route in rats. Vitex negundo leaf ethanolic extract was administered in three graded doses of 100, 250 and 500mg/kg orally, 45 min prior to anti-tubercular challenge for 35 days. Hepatoprotective effect of Vitex negundo leaf ethanolic extract was evident in the doses of 250 and 500 mg/kg as there was a significant decrease in Tuberculosis, aspartate aminotransferase, alanine aminotransferase and alkaline phosphates levels in comparison to control. Histology of the liver section of the animal treated with the Vitex negundo leaf ethanolic extract in the doses of 250 and 500 mg/kg further confirms the Hepatoprotective activity.

The chemical constituent Agnuside specially has hepatoprotective Activity, but it cannot be given by oral route as it does not comply with the Lipinski rule.

2.2 Anti-inflammatory Activity

The oral anti-inflammatory, analgesic and antihistamine properties of mature fresh leaves of *Vitex negundo* Linn. claimed in the Ayurvedic medicine by orally treating a water extract of the leaves to rats. The carrageenan-induced rat paw oedema was significantly suppressed in an inversely dose-dependent manner. In the formaldehyde induced rat paw oedema test, the 2.5 and 5 g/kg leaves significantly. In the hot plate test, 2.5 and 5 g/kg showed a significant and directly dose-dependent analgesic activity at 1 h of treatment while the activity was absent in the tail flick test in rats. The leaves showed an inversely dose-dependent in vivo antihistamine and in vitro prostaglandin synthesis inhibition, membrane stabilizing and antioxidant activities. Naloxone did not abolish the analgesic activity in the hot plate test. Flowering of the tree did not abolish the analgesic and anti-inflammatory activities of the leaves. These observations revealed that the fresh leaves of *Vitex negundo* have anti-inflammatory and pain suppressing

activities possibly mediated via PG synthesis inhibition, antihistamine, membrane stabilizing and antioxidant activities [1]. The antihistamine activity can produce the anti-itching effect claimed in Ayurvedic medicine. Activity in past including its mechanism of action. However, nobody has evaluated its potential role as an adjuvant with standard anti-inflammatory therapy. Therefore, the present study was undertaken to investigate interaction of ethanolic leaf extract of *Vitex negundo* Linn with standard anti-inflammatory drugs in sub-effective doses per orally to evaluate its potential role as an adjuvant therapy. Leaves of *Vitex negundo* have been investigated for its anti-inflammatory activity in past, including its mechanism of action.[14]

2.3 Antioxidant Activity

Vitex negundo Linn. Contains many polyphenolic compounds, terpenoids, glycosidic iridoids and alkaloids. Since polyphenolic compounds have high antioxidant potential, the antioxidant potency of *Vitex negundo* was investigated by employing various established in vitro systems, such as 2,20-azino-bis 3-ethyl benzothiazoline- 6-sulfuric acid /Lipid Peroxide /Superoxide/Hydroxyl radical scavenging and iron ion chelation. Total antioxidant capacity was determined by the assay based on the preformed radical monocation. Lipid peroxidation was assessed in terms of Thio barbituric acid reactive substances by using egg yolk homogenates as lipid rich media. Superoxide radical scavenging assay was based on the riboflavin-light-Nitro blue tetrazolium system. Hydroxyl radical trapping potential was determined by evaluating hydroxyl radical induced deoxyribose degradation using the Thio barbituric acid method. To assess the metal chelation properties, hydroxyl radical induced deoxyribose degradation was evaluated in the absence of Ethylenediamine tetra acetic acid. All the polar fractions significantly showed trapping of free radicals, and thereby inhibition of lipid peroxidation, and chelated the iron ion. Interestingly, the hexane fraction did not show any activity against superoxide's radicals, and it had minimum trapping potential for other free radical species also. Thus, it may be concluded that the polar fractions of VN possess potent antioxidant properties, which may be mediated through direct trapping of the free radicals and through metal chelation. Therefore, its reported anti-inflammatory properties, could be through the down regulation of the free radical mediated pathway of inflammation.[15]

2.4 Anti-Fungal Activity

Flavonoids are ubiquitous in photosynthesizing cells and are common part of human diet. For centuries, preparations containing these compounds as the principal physiologically active constituents have been used to treat human diseases. Increasingly, this class of natural products is becoming the subject of anti-infective research. Our bioactivity guided fractionation of ethanolic extract of leaves of *Vitex negundo* resulted in the isolation of new flavones glycoside. All the isolated compounds were evaluated for their antimicrobial activities. The new flavones glycoside 4, 5, 7-trihydroxy-3, -O-β-D-glucuronic acid-6-methyl ester and compound negundoside were found to have significant antifungal activity against *Trichophyton mentagrophytes* and *Cryptococcus neoformans* at MIC 6.25 lg/ml.

2.5 Anti-Bacterial Activity

Vitex negundo exhibited significant activity against *E. coli*, *K. aerogenes*, *P. vulgaris* and *P. aerogenes* at all dosages. Extract of leaves of *V. negundo* showed activity against all bacteria at all dosages. A standard disc containing chloramphenicol antibiotic drug (30 mg: disc) was used as a positive control.

Also, there are few other activities such as Anti hyperglycaemia, anti-asthmatic activity, antimplantation activity, snake venom neutralizer, laxative, anthelmintic etc.

But in this article, we are going to discuss about the Anti-inflammatory Activity of the *Vitex* Linn leaves extract by using Bovine Serum Albumin.

Recommended Dosage of Nirgundi

Nirgundi Juice – 10-20 ml in a day or as per your requirement. Nirgundi Powder – 1.5-3gm as per requirement in a day.

How to use Nirgundi:[16]

1. Nirgundi Juice

1. Take Nirgundi leaf juice 10-20 ml or as directed by the physician
2. Consume it twice after meals.
3. Repeat daily to get relief from cough.

2. Nirgundi Powder

1. Take Nirgundi powder 3-6 g or directed by the physician
2. Consume it with lukewarm water.
3. Repeat regularly to get relief from rheumatic pain and swelling.

3. Nirgundi Capsules

1. Take 1 capsule or as directed by physician twice a day.
2. Consume it regularly after meals.
3. Repeat daily to get relief from any generalized pain in the body.

Precautions when using Nirgundi[17]

- **Other Interaction** Since enough scientific evidence is not available, it is advisable to consult your doctor before taking Nirgundi along with any other herb.
- **Pregnancy** Since enough scientific evidence is not available, it is advisable to avoid or consult your doctor before taking Atis during pregnancy.

Side Effects

1. Stomach upset
2. Itching
3. Skin rash.

Systemic Action:

1. **External** – Relieve pain and edema, promote hair growth, cleanses wounds and promote healing. Hot fomentation with its leaves are recommended in headaches, arthritic pain, and joint inflammation. Pouring of its decoction in the lower abdominal area like anal region, gynecological pain, lower abdominal pain, inflammation in the scrotum etc.
2. **Gargling** with the decoction can give relief from mouth ulcers, and throat pain. Burning the dried leaves and inhaling the fumes of it in running nose and headache.
3. **Oil** can be applied when there is greying of hairs.
4. **Nervous System:** Improves intellectual and brain function. It is indicated in painful inflammation conditions and headaches.
5. **Digestive System:** It has carminative properties. It stimulates the liver. It has antihelminthic properties. It is indicated in anorexia, and helminthiasis. Its leaf juice along with cows' urine is helpful in splenic disorders.
6. **Circulatory system:** It helps to reduce edema
7. **Respiratory System:** It is indicated in cough, lung inflammation, pleurisy
8. **Excretory System:** Increases Urine Production
9. **Reproductive System:** Indicated in dysmenorrhea, gynecological disorders, and postpartum diseases.
10. **Skin:** Indicated in various skin disorders like skin itching, boils etc.

11. Eyes: It is good for eyes. Improves eyesight.
12. Ear: indicated in ear infection
13. Also indicated in fever along with other medication.

There are some simple but helpful home remedies as follows:

1. Joint Pain, Swelling

Fine paste of Nirgundi leaves in joint pain- Matured leaves are collected and a fine paste is made. Then it is warmed a little and applied over the joint where there is pain or the area of swelling. This remedy is helpful in reducing the pain and swelling significantly.

2. Asthma and cough

Decoction of leaves in Asthma and Cough- The leaves decoction prepared from the dried leaves is administered in the dose of 20-30ml twice or thrice daily. This decreases cough, throat infection, fever, URTI etc.

3. Wounds and Ulcers

Leaves decoction to wash off the wounds and ulcer- The freshly prepared decoction of leaves is used to wash off the wounds. It helps in purification and easy and early healing of the wounds.

4. Nasal Discharge and Polyps

Seeds or fruits powder for nasal discharge and nasal polyps- 2-4gm of powder or its fruit is administered daily 2-3 times a day. It cures disorders of nasal passages, especially rhinitis and nasal polyps.

Conclusion

A very adaptable medicinal plant with enormous therapeutic potential is Vitex Negundo Linn, usually referred to as nirgundi. Numerous bioactive chemicals found in its leaves, roots, and seeds are responsible for a variety of pharmacological actions, including analgesic, Hepatoprotective, antioxidant, anti-inflammatory, and anti-microbial properties. Its use in treating conditions including joint pain, respiratory problems, and gynecological illnesses is supported by both traditional and scientific data. These plants have a lot of potential for creating new therapeutic agents, especially for illnesses linked to inflammation. To fully grasp and standardize its potential in contemporary medicine, further research is required, particularly in the form of clinical trials.

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How to cite this article:

Yadav Gauri Sanjay et al. *Ijsrm.Human*, 2025; Vol. 28 (4): 1-8.

Conflict of Interest Statement: All authors have nothing else to disclose.

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