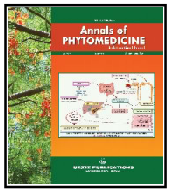
Annals of Phytomedicine 13(1): 407-416, 2024

DOI: http://dx.doi.org/10.54085/ap.2024.13.1.41

Annals of Phytomedicine: An International Journal
http://www.ukaazpublications.com/publications/index.php

Print ISSN : 2278-9839 Online ISSN : 2393-9885



Review Article : Open Access

# A comprehensive review on a potential medicinal plant, *Vitex negundo* L.

**Dhanushkodi Vellaiyan◆, A. Thanga Hemavathy, R. Anitha, S. Sangeetha**, S. Shenbagavalli, Noorjehan A.K.A. Hanif***, K. Yamunarani**, R. Nageswari, S. Rathika and D. Amirtham***

*Anbil Darmalingam Agricultural College and Research Institute, Tiruchirappalli-620027, Tamil Nadu, India*
** Department of Biotechnology, Tamil Nadu Agricultural University, Coimbatore-641003, Tamil Nadu, India*
*** Horticultural College and Research Institute for Women, Tiruchirappalli-620027, Tamil Nadu, India*
**** Agricultural College and Research Institute, Karur-639001, Tamil Nadu, India*

**Article Info**

**Article history**
Received 2 January 2023
Revised 22 Febuary 2024
Accepted 23 Febuary 2024
Published Online 30 June 2024

**Keywords**
Phytochemistry
Medicine
Functions
Applications
*Vitex negundo* L.

**Abstract**

Medicinal plants play the foundation of traditional medicine, and recently, researchers have been the focus of extensive pharmacological research. Various biological activities of *Vitex negundo* L. have been shown in several experimental investigations. The investigations of researchers have highlighted the potential of medicinal plants, therapeutically beneficial chemicals, as well as lead molecules for drug development. Therefore, there is great hope for the pharmaceutical industry to transform this plant into medicine. All parts of plants are used to make herbal remedies. The plant is reported to possess properties that are anti-inflammatory, antihyper pigmentation, hepatoprotective, anticancer, antibacterial, antifeedant, and analgesic. Further, this plant is frequently utilized as a pesticide in fields and storage godown in agriculture. In addition, it is applied to control numerous bacterial and fungal infections in plants. In-depth study is still needed to be applied practically in a variety of fields. However, research trials must be carried out and its therapeutic value established before it is advised for usage in any field.

## 1. Introduction

Since ancient times, natural ingredients have been utilized as traditional medicines due to their wide range of medicinal properties. Conventional plants are abundant in a variety of bioactive substances that boost the immune system and guard against numerous pests and diseases. A considerable number of these substances have completed clinical studies, although a few are still unidentified (Gill and Kumar, 2016). It is crucial to thoroughly assess new bioactive compounds since natural products may originate from either animals or plants; nevertheless, the majority of pharmaceuticals made from natural products are plant-based (Negi and Gill, 2013). The Verbenaceae family tree, *Vitex negundo* L. is well known as the five-leaf chase tree or nirgundi in India. Scientific research has identified more than 270 species of *Vitex*, which may be found in temperate and tropical regions and can range from shrubs to trees (Ganapaty and Vidyadhar, 2005). Traditional medicines from Bangladesh, Indo-China, Indonesia, Nepal, Pakistan, the Philippines, and Sri Lanka all make use of *V. negundo* (Vishwanathan and Basavaraju, 2010; Balraj Singh *et al.,* 2018).

Herbal medicine is becoming more and more well-liked in the US and is still a common substitute in China and the Far East. Herbalists and native healers around the world have long employed botanicals to cure and prevent a wide range of diseases. The processes by which certain plants give their medicinal properties have been revealed by many scientific investigations. An alternative form of treatment made from plants and plant extracts is called herbal medicine. Herbal medicines have been used for millennia to treat illnesses and diseases, as well as psychological issues. They were the forerunners of modern medicine. A wide variety of plant parts, including leaves, stems, berries, bark, blossoms, and roots, may be combined to create herbal remedies (Kambham, 2012). The Philippines, Indonesia, the People's Republic of China, and South Asia are all home to *V. negundo*. There is a practical purpose for every part of the plant, but the most important portion is the extract from the roots and leaves, which is used to create pharmaceuticals. While the entire plant was utilized for medicinal purposes in the past, preparations from the leaves and bark proved to be more potent (Dharmashree *et al.,* 2003).

**Corresponding author: Dr. V. Dhanushkodi**
*Anbil Darmalingam Agricultural College and Research Institute, Tiruchirappalli-620027, Tamil Nadu, India*
**E-mail: dhanushkodi@tnau.ac.in**
**Tel.: +91-9659034441**



## 2. Botanical description

Chinese chaste tree is the common name for *V. negundo*. The genus *Vitex* is home to 250 species, 75 genera, and around 2500 species of dwarf trees and shrubs that thrive in temperate and tropical regions. These plants are members of the Verbenaceae family. Hedgerows of this naturally occurring shrub line roadways, ditches, and public spaces. The dwarf tree or shrub *V. negundo* may reach a maximum height of 8 meters. The bark has a shade of reddish brown. Each of the plant's digitate leaves has five or three lanceolate leaflets. The length of each brochure ranges from 4-10 cm. Every petal's central lower lobe is the longest of all of them. The flower and calyx have dense hairs. The fruit is an egg-shaped to spherical, succulent drupe. When ripe, it turns black or purple (Aamila and Shahina, 2023). Reaching up to 5 meters in height, *V. negundo* is a thin tree with quadrangular branches that typically grows in waste areas. The lanceolate leaves contain 3-5 leaflets that can develop to a length of 4-10 cm. The ventral surface of the leaves is covered in innumerable tiny hairs, while the upper surface is glabrous. Numerous blooms

are generated. The tiny, bluish-purple blooms have a maximum length of 10-20 cm and are grouped in pedunculated tomentose cymes. The fruit is spherical, juicy, and dark in color, when fully ripe and roughly 4 mm across. When the mature seeds are planted in nursery beds, they typically germinate in two to three weeks, grow deep, and robust roots (Azhar-Ul-Haq, 2004).

*V. negundo* is found virtually everywhere in India. Sometimes referred to as Nirgundi in Hindi. Plants are up to 5 meters tall. Plants are densely white and tomentose shrub with many branches that occasionally grow into a short, thin tree. With the terminal leaflets measuring 5 to 10 ×1-3 cm and the smaller lateral leaflets, the leaflets are lanceolate and crenate entirely or intermittently. The leaves are virtually glabrous above and have whitish tomentose underneath. A succulent drupe with a diameter of 5-7 mm and a black color when ripe. The seed has an expanded calyx at the base and is 5-7 mm in diameter. The aromatic blooms are pollinated by insects because they are hermaphrodites, meaning they have both male and female components. A large evergreen shrub with a plethora of branches that may reach heights of 1100-1400 feet. The plant may thrive in low-nutrient soil, but it favors sandy and medium-loamy soils that drain well. September to October is the flowering month. Acidic, neutral, and basic (alkaline) soils are preferred by the plant. It cannot grow in shadow (Kaliyaperumal *et al.,* 2008).


**Figure 1: Different parts of *Vitex negundo* L. used as a phytomedicine.**

## 3. Different parts and their potential values

An astonishing array of health advantages is associated with the potent medicinal herb *V. negundo*. Traditional medicine practitioners in various Asian nations, notably China, have long made use of the plant's whole life cycle, from leaves and blooms to roots and seeds. The traditional medical systems make use of *V. negundo* with the leaves being the most effective part of the plant (Table 1). An effective defense against viral illnesses may lie in herbs that contain bioactive chemicals with immune modulatory properties (Gangwar *et al.,* 2021; Dolly *et al.*, 2022).

**Table 1: Different parts of *V. negundo* and their potential uses**

| S.No. | Parts | Uses | References |
|---|---|---|---|
| 1. | Fresh leaves | It is used to treat dengue, rheumatism, dyspepsia, diarrhea, cold, cough, asthma, and it strengthens the immune system, used for the relief of inflammation, ocular illnesses, toothaches, enlarged spleen, skin ulcers, gonorrhea, rheumatoid arthritis, and bronchitis. Additionally, the leaves have many medicinal uses, including as a laxative, a tonic, an antibiotic, an antipyretic, and an antihistamine. Used as astringent, febrifuge, sedative, tonic, and vermifuge. | Parekh and Chandha, 2006; Jeyaseelan *et al.,* 2010; Horowitz, 1966; Shaukat *et al.,* 2009; Chaturvedi and Singh, 1965 |
| 2. | Dry leaves | When preserving woolen clothing, it is best to insert leaves inside to ward off worms and insects that feed on wool. It has antiparasitic properties and was used to ward off the mosquito. | Hebbalkar *et al.,* 1992; Parveen, 1991 |
| 3. | Young shoots | Anticancer action against ascites tumor cells. Used for vermifuge, lactagogue, emmenagogue, antimicrobial, antipyretic, and antihistaminic properties. Many *Vitex* species, including *V. agnus-castus*, *V. rotundifolia,* and many more species, are important in pharmacology. Used for making baskets, fuel, and an alkali for dyeing with plant ash. | Anonymous, 2001; Chitra *et al.,* 2009; Balraj Singh *et al.,* 2018 |
| 4. | Seeds, and roots | It has anti-inflammatory, analgesic, antipyretic, and antimicrobial properties. It is used to treat backache, muscular sprain, and joint pain. Utilized for analgesic, anti-inflammatory, antirheumatism, antitumor, insecticidal, antimicrobial, and antioxidant purposes. | Gitesh and Bhagyashree, 2024; Shen *et al.,* 2015; Maria Talata *et al.,* 2021; Zhou *et al.,* 2009; Zheng *et al.,* 2014; Kamruzzaman *et al.,* 2013; Kamaraj *et al.,* 2010 |

## 4. Chemical compounds

*V. negundo* contains several chemical compounds that were found during investigations (Table 2). Phytochemical investigations revealed that *V. negundo* contains bioactive flavonoids (Bhargava, 1989), lignans (Zheng *et al.,* 2009), terpenoids (Zheng *et al.,* 2014), and volatile oil. The following substances were listed by Sakshi Yuvraj Bodake (2023) lignan, flavonoids, flavones, glycosides, indoid glycosides, triterpenes, diterpenes, sesquiterpenes, and stilbene derivatives. Dutta *et al.* (1982) discovered two glucosidic iridoids, negundoside, and nishindaside, from the leaves of *V. negundo* viridiflorol, beta-caryophyllene, sabinene, 4-terpineol, gamma terpinene, and several phenols are the primary compounds identified in *V. negundo*. According to Gautam *et al.* (2008), *V. negundo* methanolic extract contains antibacterial flavonoids and related compounds. Negundon A and negundo B, which have tyrosinase inhibitory properties, are present in methanolic preparations of *V. negundo* roots (Malik *et al.,* 2006).

**Table 2: Chemical compounds present in different parts of *V. negundo***

| S.No. | Plant parts | Chemical compounds | References |
|---|---|---|---|
| 1. | Leaves | The identified constituent-p-cymene, cis-ocimene, citronellal, B-curcumene, B caryophyllene, aguaiene, guaia-3,7-diene, 8-guaiene, valencene, caryophyllene epoxide, ethyl 9-hexadecenoate, palmitic acid, (E)-nerolidol, humulene epoxide 1, globulol, humulene epoxide 2, epi-a-cadinol, a-muurolol, a-cadinol and a bisabolol acetate represented about 85.5 % of the total composition of the vital oil of leaf. Discovered thirteen minor chemicals in the essential oil of the leaf, along with the significant components ethyl 9-hexadecenoate, δ-guaiene, caryophyllene epoxide, valencene, α-selinene, and germacren-4-ol. Various substances including volatile oils, lignans, flavonoids, iridoids, terpenes, steroids, and various forms of triterpenes, diterpenes, and sesquiterpenes were isolated. | Gautam, 2008; Khokra *et al.,* 2008 |
| 2. | Flowers | The twelve components found in the essential oil of flowers were as follows: formic acid, n-heptane, p-cymene, β-caryophyllene, trans-a-bergamotene, valencene, a-selinene, β-selinene, germacren-4-ol, caryophyllene epoxide, (E)-nerolidol, whereas P-(1, 1 dimethylethyl). The oil extracted from flowers contained several important components, including toluene (which made up approximately 65% of the oil), sabinene, linalool, terpinen-4-ol, β-caryophyllene, a-guaiene, and globulol (61.8% of the oil), as well as sesquiterpenes, monoterpenes, terpenoids, and sterols. | Khokra *et al.,* 2008 |
| 3. | Fruits | The thirteen constituents namely a copaene, β-caryophyllene, a-cedrene, a-guaiene, guaia-3, 7-diene, a-humulene, aristolene, germacrene D, β-selinene, caryophyllene oxide, n-hexadecanoic acid, palmitolic acid as well as traces of acetyl lactyl glycerate were identified in dried fruit oil crude ethanol extract indicated the presence of alkaloids, glycosides, lignin, the flavonoids and saponins, terpenoids (α-pinene, 1,8-cineole, linalool, caryophyllene oxide, α-guaiene, and germacrene D) and lipids (linolenic acid and palmitic acid) as the major constituents. | Chitra *et al.,* 2009; Pan *et al.,* 1989; Zheng *et al.,* 2014; Cheng-Jian Zheng *et al.,* 2015 |

*V. negundo* contains terpenes (triterpenes, diterpenes, and sesquiterpenes) (Chandramu 2003), lignans, iridoids, volatile oils, and steroids (Chawla *et al.,* 1992). The composition and extraction technique (such as temperature, pH, solvent system, or any other mode of extraction) define the extracts' potential, which in turn affects the extracts' polarity, stability, and efficacy. Within species, there are variations in the chemical makeup that lead to differences in phytochemicals, bioactivity type, and quantity (Gill *et al.,* 2016).

## 5. Application of *V. negundo* in the medical field

Many people have found that using its essential oil helps heal wounds and ulcers. Out of 194 member states, 170 still use traditional herbal remedies that rely on 40,000 to 70,000 plants, according to the World Health Organization. As a result of their biological processes, plants produce secondary metabolites that have various medicinal uses. Although, these phytoconstituents may not be very effective, their pharmaceutical uses lead to improvements in the treatment of chronic disorders (Kaustubh and Nupur, 2022). *V. negundo* plant plays a significant role in phytomedicine because of its diverse phytochemicals. Due to its anti-inflammatory qualities, *V. negundo* is beneficial in the management of inflammatory diseases. The plant has shown antibacterial activity against a range of diseases, such as fungi and bacteria. The plant's ability to heal wounds has long been used. *V. negundo* extracts have the potential to accelerate the healing of cuts and wounds. Preliminary studies indicate that extracts from *V. negundo* may have anticancer qualities. The essential oil of this plant may help heal wounds and ulcers (Khokra *et al.,* 2008).

Shrimp were shown to be cytotoxic by a crude methanolic extract of *V. negundo* (Malik *et al.,* 2006). Mice subjected to hyperuricemia caused by potassium oxonate showed hypouricemic and xanthine oxidase inhibitory effects in response to extracts in water and methanol (Umamaheswari *et al.,* 2007). The researchers Zargar *et al.* (2016) created and used silver nanoparticles, or Ag-NPs, as a means of stabilization and reduction. The MCF-7 human breast cancer cell line was shown to undergo apoptosis when exposed to ethanolic extracts of *V. negundo* leaves (Arulvasu *et al.,* 2010). According to a study by Sathiamoorthy *et al.* (2010), flavone glycosides possess antibacterial and antifungal properties; namely, against Trichophyton mentagrophytes and *Cryptococcus neoformans*. The inhibitory effect against HIV type 1 reverse transcriptase is around 90 % in water and ethanol extracts (Woradulayapinij *et al.,* 2005; Balraj Singh *et al.,* 2018). These extracts may be useful in the treatment of AIDS.

*V. negundo* contains Casticin and chrysoplenol (Gitesh and Bhagyashree, 2024).

India is home to significant medicinal herbs. Although, almost every part of the *V. negundo* plant is used in ayurvedic and unani medicine, the most important components for drug and medication extractions are the leaves and roots (Sandip *et al.,* 2021). The antiacne cream that contained *V. negundo* leaf extract formulations works well for treating skin infections like acne vulgaris (Sakshi, 2023). The leaf' is used as an *in vitro* antioxidant, antibacterial, antihemolytic, and antiproliferative properties. So far, the following characteristics of the plant have been recorded: It has many useful properties, including lowering blood sugar levels, antioxidant, anti-inflammatory, antifungal, antinociceptive, anticonvulsant, antitumor, hepatoprotective, gastroprotective, laxative, antiasthmatic, anxiolytic, anthelmintic, antiarthritic, cardiotonic, and pharmacological interaction with paracetamol. Research on medicinal plants has maintained a steady interest rate since the 1800s. The arrival of Europeans in India sparked a desire to examine traditional activities through scientific prisms (Rekha, 2021; Rahul and Anita, 2023).

The plant contains astringent, cephalic, stomachic, and anthelmintic qualities in addition to a strong, bitter, and caustic taste. As far as medicinal uses, the plant is said to have expectorant, carminative, diuretic, anodyne, antiseptic, antipyretic, emmenagogue, depurative, rejuvenating, ophthalmic, vulnerary, and tonic properties. A wide variety of compounds were discovered, such as stilbene derivatives, flavone glycosides, iridoids, and lignin of a unique phenyl dihydro-naphthalene type. Acne vulgaris is a common skin disorder that results from changes in the skin structures termed pilosebaceous units, which are made up of a hair follicle and the sebaceous gland that is connected to it, as a result of androgen stimulation. Acne cream prepared from *V. negundo* exhibited antimicrobial effectiveness against these bacteria that was comparable to that of the commercial formulation. A variety of phytochemicals, including proteins, carbs, amino acids, saponins, flavonoids, anthraquinones, tannins, and phenolic compounds, were identified in an extract of *V. negundo* leaves using phytochemical screening.

When applied to fabric, ethanol, and water extracts of the leaves of the *V. negundo* is tested for their antibacterial activity against Gram-positive bacteria. Extracts from *V. negundo* leaves exhibit antibacterial activity against sweat of both acidic and alkaline pH values, even after the samples have been repeatedly washed (Sakshi Yuvraj Bodake, 2023). In addition, seeds are also said to possess insecticidal qualities. Its leaf decoction is consumed internally as a febrifuge, vermifuge, expectorant, and diuretic. Traditional Indian medicine has made use of this herb to alleviate rheumatoid arthritis symptoms because of its anti-inflammatory qualities. Flavonoids, lignans, sesquiterpenes, and iridoid glycosides are just a few of the substances that *V. negundo* have produced (Fredyc Diaz *et al.,* 2003).

The leaves of *V. negundo* are used as vermifuge, aromatic, antiparasitic, alterative, and analgesic. The root is used as an expectorant, febrifuge, diuretic, and tonic. Fruit is used as an emmenagogue, cephalic, and nerveine (Kaliyaperumal *et al.,* 2008). India has a lot of *V. negundo* shrubs, which are widely used in folk and traditional medicine. Numerous biological activities, such as those related to mosquito repellent, antiangiogenic, antihepatoprotective, analgesic, inflammatory, antiarthritic, antimicrobial, antihistaminic, CNS depressive, and antifilarial properties, have been reported to be revealed by the leaf extract of *V. negundo*. The plant's numerous phytoconstituents, which include terpenoids, alkaloids, flavonoids, polyphenolic chemicals, and iridoids, among others, may be the cause of these effects. Decoction makes use of many parts of this plant. Leucoderma, sinusitis, gonorrhea, bronchitis, ulcers, and toothaches are just some of the many ailments that may be alleviated by decocting various plant components (Shakshi, 2023).

It is a well-known medicinal herb, and Asian medical systems (Chinese, Malaysian, Indian, Bangladeshi, and Pakistani) have used its parts as a traditional remedy for a range of illnesses. In leaf oil, γ-guaiene, carryophyllene epoxide, and ethyl-hexadecenoate were predominant components; in flower oil, α-selinene, germacren-4-ol, carryophyllene epoxide, and (E)-nerolidol were the main ingredients; and in fruit oil, β-selinene, α-cedrene, germacrene D, and hexadecanoic acid were the main constituents. The only chemical that all three oils had in common was β-caryophyllene. There were α-guaiene and guaia-3,7-diene in the oils of dried fruits and leaves, as well as p-cymene, valencene, caryophyllene epoxide, and (E)-nerolidol in the oils of flowers and leaves. The oil from fruits and leaves was shown to be the most effective against *Spodoptera aureus* and *Escherichia coli*, respectively. The only oil that demonstrated efficacy against *Pseudomonas aeruginosa* (Khokra *et al.,* 2008). The anti-inflammatory and immune-modulatory characteristics of *V. negundo* make it a promising candidate for the treatment of bronchial asthma. Several animal models of asthma have shown that extracts from the leaves of the *V. negundo* plant are effective. It seems to work by stabilizing mast cells, inhibiting acute hypersensitivity responses, and engaging in antieosinophilic activity (Jignesh Patel *et al.,* 2014). This plant plays a significant role in phytomedicine because of its diverse phytochemicals (Table 3). Due to the beneficial effect of *V. negundo*, it is popularly used in the following activities.

## 6. Role of antimicrobial properties of *V. negundo* in disease management

Various sectors made use of essential oils derived from various plant materials, including fresh leaves, flowers, and dried fruits. The medicinal plant *V. negundo* supports a diverse community of endophytic fungi (Banerjee *et al.,* 2006). The stem of *V. negundo* has more endophytic fungus than either the roots or the leaves. The ethanolic *V. negundo* extract had antifungal efficacy against both *Trichophyton mentagrophytes* and *Cryptococcus neoformans*. It was reported that the leaf and twig extracts had antibacterial activity. A new flavone glycoside is one of the additional compounds. The antifungal and antibacterial properties of all six compounds were assessed (Sathiamoorthy *et al.,* 2007). *V. negundo* fruit (seed) extract showed good action against *Fusarium solani* (90 %) nearly as good as the reference medication while *Microsporum canis* (60 %) exhibited only modest activity. Plant extracts may help with the effective use of these natural compounds in the treatment of infectious disorders like bacterial and fungal infections (Shaukat *et al.*, 2009). The antioxidant, antibacterial, antifungal, cytotoxic, and anticancer properties of *V. negundo* extracts have been studied and used in many studies (Chowdhury *et al.,* 2009; Sharma *et al.,* 2011; Tiwari and Tripathi, 2007; Kumar *et al.,* 2010; Chitra *et al.,* 2009; Zhou *et al.,* 2009).

**Table 3: Chemical compounds and their activity of *V. negundo***

| S.No. | Activity | Chemical constituents | References |
|---|---|---|---|
| 1. | Anti-inflammatory activity | The anti-inflammatory impact is regulated by flavonoids and vitamin E *via* modulating the expression of genes that activate macrophages and attract neutrophils. It contains lignin, which has anti-inflammatory effects. | Balraj Singh *et al.,* 2018; Dharmasiri *et al*., 2003; Jana *et al.,* 1999; Nair *et al.,* 1998 |
| 2. | Antioxidant | Iridoid glycosides vitex negheteroins K-L and two coumarin glycosides vitex negheteroins I-J were identified, and all three show promising antioxidant activity. | Balraj Singh *et al.,* 2018 |
| 3. | Antimicrobial | Flavonoids isolated from various portions of the chosen plants (*V. negundo* and *Andrographis paniculata*) were successful in killing *Aedes aegypti* and *Anopheles stephensi* larvae of the late third or early fourth instar. A potential alternative to cholera treatment, the methanolic extract of leaves shows potent vibriocidal action in both laboratory and animal models. A series of pyrazolo (3,4c) pyrazole derivatives were synthesised using the *V. negundo*-$Fe_3O_4$-CuO catalyst. These compounds were subjected to molecular docking, molecular dynamics modeling, and antibacterial and cytotoxic activity screens. | Balraj Singh *et al.,* 2018; Idhayadhulla *et al.,* 2023; Damayanti *et al.,* 1996 |
| 4. | Antidiabetic effect | Insulin signaling directly targets downstream proteins regulated by Akt, such as mTOR. | Balraj Singh *et al.,* 2018 |
| 5. | Apoptosis | Apoptosis, which is essential in cancer signaling, is the culmination of distinct morphology and several metabolic alterations in cell function. *V. negundo*, a pure form of vitexin E. Apoptosis is induced by 6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde. | Balraj Singh *et al.,* 2018 |
| 6. | Anticancer | The anticancer ability of the flavone vitexi carpin was also shown by a chloroform-soluble extract of the leaves of *V. negundo*. | Balraj Singh *et al.,* 2018 |
| 7. | Antivenom | The plant extract inhibited the coagulant, defibrinogenating, inflammatory, and hemorrhage effects caused by *V. russellii* venom. Triterpenoids found in *V. negundo* and *Emblica officinalis* may play a role in the inactivation of venom. The methanolic root extract had a strong ability to neutralize snake venom. | Alam and Gomes, 2003 |
| 8. | Oxidative stress | *V. negundo* leaf hydroethanolic extract fractions protect rats' brains against ethanol-induced oxidative stress. | Balraj Singh *et al*., 2018 |
| 9. | Motility and viability of sperms | In intact adult dogs and castrated pups, a flavonoid-rich fraction (5, 7, 32 -trihydroxy, 6, 8, 42 -tri-methoxy flavones) extracted from seeds inhibits the androgen activity of external testosterone on the male reproductive system. | Balraj Singh *et al.,* 2018 |
| 10. | Menstrual cycle | The dopaminergic actions of *V. negundo*, which are responsible for prolactin inhibition and a role in many disorders, may be further investigated by the scientific community. | Telang *et al.,* 1995 |
| 11. | Pesticide | Enzyme inhibition, antifeeding activity in pest, mosquito repellent activity, and larvicidal activity. | Chandramu *et al.,* 2003; Pushpalatha and Muthukrishnan, 1995; Azhar-Ul-Haq *et al.,* 2006 |

Nirgundi has a wide range of medicinal uses. It has properties that make it effective against both bacteria and fungi. According to Supriya *et al.* (2023), the broadest inhibition zones against *Proteus mirabilis* (21 ± 0.5mm) and *Aspergillus flavus* (18 ± 0.3 mm) were seen in the methanolic extract of *V. negundo*. The anticancer and antibacterial activities of the methanol leaf extract of *V. negundo* were recorded using the potato disc bioassay and the agar disc diffusion technique. The methanol leaf extract showed growth inhibitory efficiency against five different bacteria: *Salmonella typhi*, *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli* (Soriful Islam *et al.,* 2013). This is the first paper that describes how *V. negundo* inhibits *Xanthomonas axonopodis* pv. citri and *Pseudomonas solanacearum* (Jeyaseelan *et al.,* 2010).

## 7. Application of *V. negundo* in pest management

A gas chromatography-mass spectrometer was used to examine the antibacterial activity of three different oils and five separate extracts, as well as fresh leaves, flowers, and dried fruits (Khokra *et al.,* 2008). Because synthetic pesticides are more successful at containing disease-causing organisms, they are now routinely employed worldwide to manage plant illnesses. However, the overuse and haphazard use of these compounds have led to several health and

environmental risks, as well as the development of resistance in certain phytopathogens (Rhouma *et al.,* 2009). Finding safe, efficient, and biodegradable substitute insecticides is therefore desperately needed (Jeyaseelan *et al.,* 2010). *V. negundo* leaves have antibacterial, antifungal, and pesticide qualities. Application of *V. negundo* in pest management is given in Table 4.

**Table 4: Application of *V. negundo* in pest and disease management**

| S.No. | Extracts and products used as a pesticide | Pest and disease controlled | References |
|---|---|---|---|
| 1. | Ethyl acetate, ethanol, methanol, and water-based extracts of *Allium sativum* bulb, flower, and leaf | Antimicrobial activity on *Pseudomonas solanacearum* and *Xanthomonas axonopodis*. | Jeyaseelan *et al.,* 2010 |
| 2. | Methanol extract | The extract is more lethal and effective in destroying *Spodoptera litura*, and it has the lowest LD50 value (423 ppm). Reducing the adult emergence of stored grain pest. | Deepthy *et al.,* 2010; Nithiyagowry and Thulashi, 2023 |
| 3. | Acetone extract | *V. negundo* acetone extract's insecticidal, ovicidal, and growth inhibitory effects on a hazardous lepido pteron pest. Extract against *S. litura and Escherichia vitelli* larvae and egg growth. Reduction in pupal weight of *S. litura*. The extraction of *V. negundo* resulted in the lowest percentage of pupation (3.33 % to 53.33 % of *S. litura* on castor) and the highest (20 to 96.67 %). | Prajapati *et al.,* 2003; Kalavathy *et al*., 1991; Kalavathy *et al.,* 1991; Govindachary *et al.,* 1996; Deepthy *et al.,* 2010 |
| 4. | Alcoholic extracts of leaves | *Spilosoma obliqua* third-instar larvae were killed off at a rate of 74.26 % when exposed to a 2 % concentration of the extract. | Sahayaraj, 1998; Dubey *et al.,* 2004; Kali-yaperumal *et al.*, 2008 |
| 5. | Extracts and essential oils derived | Exhibit antifeedant activities against *S. litura and Culex tritaeniorhynchus*. Insects that attack cumin and tomatoes, as well as the rice tungro virus. | Fagoonee *et al.,* 1983; Sharma *et al.,* 2000; Sundaramari and Ranganathan, 2003 |
| 6. | Viridiflorol, bcaryophyllene, sabinene, 4-terpineol, g-terpinene, caryophyllene oxide, 1-oceton-3-ol, and globulol are some of the primary components found in *V. negundo* extracts | Antifeedants against *Trichoderma castaneum*. | Haridasan *et al.,* 2017 |
| 7. | Burned leaves | It repels mosquitoes from houses. | Venkatachalam and Jebanesan, 2001 |
| 8. | Fresh and dry leaves | Stored grain pests. Bags with rice stored in drum bins protect the grains from insect attack for nine months. | Ahmed and Koppel, 1987; Prakash *et al.,* 1987 |
| 9. | Leaf powder | The most efficient method for decreasing *Calloso-bruchus chinensis* egg production, adult emergence, and seed weight loss. Insects and mosquitoes are scared away by smoke. Repelling bedbugs. | Miah *et al.,* 1993; Guleria and Vasisth, 2009; Prakash, 2004; Pal and Jain, 1998 |
| 10. | Oil and extracts | Various pests, including mosquito larvae, house flies, and tobacco leaf eaters, are found in stored products. Leaf oil can deter pests that can damage stored items. | Prakash and Mathur, 1985; Hebbalkar *et al.,* 1992; Kambham, 2012 |
| 11. | Branches made into brooms for use in paddy fields | Serve as a pesticide for rice fields. | Tarafdar and Raichaudhuri, 1991 |
| 12. | Cow dung, buttermilk, and leaf extract of Adhatoda | Pests that may be found in storage areas include the rice weevil, groundnut cutworm, tomato fruit borer, brinjal leaf beetle, and stem borer. | Narayanasamy, 2006; Ahuja and Ahuja Uma, 2008 |
| 13. | Neem kernel, turmeric rhizome, custard apple leaves, and aloe vera | Effective in combating eriophyid mites, a major coconut pest. | Chellamuthu, 2000 |
| 14. | *V. negundo* herb to prepare earthen pots | To store grains for long periods. | Kulkarni and Kumbojkar 2003; Oudhia, 2010 |
| 15. | Very minimal portions (around 4-10 percent) of *V. negundo* leaves, either by themselves or combined with neem, karanj (*Pongamia pinnata*), or turmeric powder | Storage of rice and black gram. | Ahuja *et al.,* 2010 |

## 8. Conclusion

After reviewing the existing substance, it is evident that *V. negundo* played an important part in the ancient medicinal system. *V. negundo* has a wide range of biological activity. Many experimental studies showed that positive effect in many fields and acts as an herbal medicine for application. Pharmacological studies have focused on medicinal plants, the backbone of traditional medicine, for several years. Research into medicinal plants has focused on their possible production of new therapeutic compounds and lead molecules for drug development. As a result, the pharmaceutical industry has a lot of potential to exploit this plant to produce drugs. The plant's nearly whole life is used to make herbal remedies. Anticancer, antibacterial, antifeedant, anti-inflammatory, antihyperpigmentation, hepato-protective, antihistaminic, analgesic, and related actions are reported to be possessed by the plant. *V. negundo* has insecticides, antifungal, and antibacterial properties in its fresh and dried fruits, as well as in its flowers. Extensive studies conducted by scientists have revealed that the plant antimicrobial and pesticide properties can help control many pests and diseases in the field of agriculture; they help to reduce chemical pesticide accumulation in agricultural produce and save the environment. However, clinical trials must be conducted to establish the plant's therapeutic utility before any recommendations are made on its usage in treating these illnesses. Therefore, to provide a foundation for future pharmacological research, it becomes necessary to screen medicinal plants for bioactive chemicals. This data could pave the way for future studies of newly discovered species in search of interesting chemicals and biological activity; such discoveries might be crucial to the continued existence of human civilizations.

## 9. Challenges and future directions on *V. negundo* in the medical and agricultural fields

- Snake bite is a common problem in many of the places where people are living in rural areas; hence the antivenom properties of *V. negundo* against a variety of snake bites need further investigation.
- *V. negundo* leaves, flowers, and seeds are used as medicinal properties that have to be evaluated and their side effect need to be studied well.
- The anticancer property of *V. negundo* should be studied because it is now an emerging problem in all stage groups of people.
- Before these bioactive chemicals may be used in clinical practice, their active principle, structure-activity connection, and potential synergistic action among them must be thoroughly studied.
- Research into the bioassay and purification procedures required to define the new antibacterial compounds is essential.
- Active drug fractions require isolation, characterization, and pharmacological investigations of active principles.
- More studies are required on flavonoid extract of flower buds of *V. negundo* at a commercial scale.
- Confirmation of the antimicrobial activity needs to be done to produce the product at a commercial scale
- Storage pest is a major problem, particularly in cereals and pulses. Hence, evaluation of *V. negundo i*n different pests needs to be done.
- Actual field trials are to be conducted to prove the efficacy of the extracts at the field level as a pesticide and also to correlate the pharmacological activities with the chemical constituents.
- Mosquitoes and their larval control need to be evaluated, as it is act as vectors for the spreading of many diseases.
- The radical's residual effects on the commodities should be investigated so that they may be critically assessed.
- The impact of the plant materials and their extracts on beneficial and non-target creatures should be studied for toxicity.
- However, further research is needed to explore specific formulations, dosage considerations, and long-term effects.

## Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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**Citation** **Dhanushkodi Vellaiyan, A. Thanga Hemavathy., R. Anitha, S. Sangeetha, S. Shenbagavalli, Noorjehan A.K.A. Hanif, K. Yamunarani, R. Nageswari, S. Rathika and D. Amirtham (2024). A comprehensive review on a potential medicinal plant, *Vitex negundo* L.. Ann. Phytomed., 13(1):407-416. http://dx.doi.org/10.54085/ap.2024.13.1.41.**