

Review on the Role of Traditionally Used Medicinal Plant *Vitex Negundo* and Its Current Pharmacological Aspect

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Abstract

The medicinal shrub *Vitex negundo* Linn. (Nirgundi) is widely utilized in conventional medical systems to treat a variety of ailments such as Ayurveda, Unani, Siddha, and Chinese medicine. The phytochemical profile, historical relevance, and particularly the neuronal pharmacological activities of *Vitex negundo* are critically examined in this paper. Flavonoids, terpenoids, alkaloids, and essential oils are highlighted as its bioactive components, which support its therapeutic properties, including anti-inflammatory, antioxidant, neuroprotective, antipyretic, anxiolytic, and analgesic activities. Significant neuronal benefits are highlighted in the literature study, along with preclinical research showing anxiolytic and antinociceptive effects as well as possible uses in neuroinflammatory and neurodegenerative diseases. More thorough Clinical trials are essential for validating the efficacy, safety, and consistent dosing while clarifying molecular pathways, despite encouraging experimental results. *Vitex negundo* is positioned as a promising candidate for future neurological drug development through the merger of traditional knowledge and modern pharmacological research, but it also emphasizes the necessity of thorough review prior to clinical translation.

Key Words:

Vitex negundo Linn, Traditional medicine (Ayurveda, Unani, Siddha, Chinese), Phytochemistry, Anti-inflammatory, Antifungal activity

History:

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1. INTRODUCTION:

Vitex negundo Linn., Often referred to as Nirgundi or The Verbenaceae family includes the huge, fragrant shrub known as the five-leaved chaste tree. Nearly every aspect of the Plants have significant medicinal properties and are utilized In a number of conventional medical systems, including Ayurveda, Chinese, Siddha, and Unani, for the medical intervention of diverse illnesses¹. "A man cannot pass away from illness in a place where *Vitex negundo* (Nirgundi), *Adhatoda vasica* (Vasaka), and *Acorus calamus* (Vacha) are located—as long as he understands how to use them.. "This is a traditional Indian saying that highlights the immense therapeutic value of these medicinal plants in Ayurveda². *Vitex negundo* Linn. is used in Indian traditional medicine. is regarded as sarvaroganivarani, meaning "a cure for every illness³.

The Mythological Tale of Nirgundi: In India, Nirgundi is regarded as a sacred plant closely connected with mythology. According to traditional belief, it is said to have emerged from the abdomen of Lord Ganesha, one of Hinduism's most venerated deities. This mythological association enhances the sanctity of the plant in Indian culture. In religious practices, the leaves of Nirgundi are offered as a mark of devotion to Lord Shiva and Goddess Parvati (Gouri), signifying its spiritual and ritual importance⁴. Sindhuvaraka is traditionally believed to have come from the temple of Lord Ganesha. The leaves of this plant hold ritual significance, as they are offered to Lord Shiva and Goddess Gouri during the observance of Nitya Somavara Vrata²¹.

As stated by the World Health Organization, nearly 60–65% of the global population relies on herbal and traditional forms of medicine. At present, such remedies are among the most widely used healthcare options worldwide. The shrub *Vitex negundo* Linn. is deciduous and often grows abundantly in landfills and is frequently planted expands, belongs to the Verbenaceae family, which includes about 75 genera and nearly 2,500 species⁵.

Taxonomic / Scientific Classification²³.

Kingdom : Plantae

Order : Lamiales

Division : Tracheobionta

Family : Verbenaceae

Class : Magnoliopsida

Genus : *Vitex*

Species : *Negundo*

Vernacular Names⁷.

English	:	Five leaved chaste tree
Marathi	:	Nirgundi
Sanskrit	:	Nirgundi
Hindi	:	Nirgundi
Gujarati	:	Nagod
Kannada,	:	Nkkilu, Lakkigida.
Punjab	:	Shwari
Assam	:	Aslok
Bengal	:	Nirgundi, Nishinda

2. Geographical Classification

World Distribution: The plant thrives in humid habitats, along mixed open woods, wastelands, and watercourses. Its distribution has been documented in Madagascar, eastern Africa, Sri Lanka, Thailand, Pakistan, Afghanistan, and India⁸. The plant is cultivated commercially in regions of North America, Europe, Asia, and the West Indies, where it serves both as an abundance of timber and food. It is a big, fragrant bush that is spread widely across India up to the level of about 1500 m outside Himalayan area and in a few Himachal Pradesh districts⁹.

Distribution in India

Maharashtra : All districts of Maharashtra.

Karnataka : Ballari district, Kolar district, Chamarajanagar district

Telangana : Khammam district, Mehboobnagar district

Kerala : Every district in Kerala

Andhra Pradesh : Anantapur district, Kadapa district, East Godavari district, Krishna district, Kurnool district, Nellore district, Vizianagaram district, West Godavari district

Tamil Nadu : Dindigul district, Kanchipuram (Changalpattu–CGP) district, Karur district, Krishnagiri district, Salem district, Tiruchirapalli district, Tiruvannamalai district, Villipuram district, Vellore district.

Odisha : Angul district, Balasore district, Bolangir district, Boudh district, Deogarh district, Gajapati district, Kalhandi district Kendrapara district Malkangiri district, Mayurbhanj district, Puri district, Rayagada district, Sambalpur district, Sundergarh district¹².

Habitat and Cultivation Details

Vitex negundo thrives from warm moderate to tropical regions and grows successfully from sea level up to elevations of about 2,000 m. It typically occurs in areas with mean annual rainfall between 600–2,000 mm and can tolerate brief periods of low temperatures down to –10 °C.

It is frequently cultivated as a boundary hedge between agricultural fields and is generally not grazed by cattle. The plant may be easily spread through stem cuttings, and its root suckers can also serve as effective planting material¹⁶.

The species is easily cultivated, favoring light loamy that drains well soils in a warm, bright locations protected from chilly, arid winds. It is also capable of growing in arid, weak soils and accepts both Saline and alkaline conditions¹⁰.

Growth is moderate to fairly fast, and the plant is controllable effectively through coppicing in a rotating fashion period of about two years. It produces root suckers and, when planted along contours at 5-m spacing, yields approximately 0.3 tons of air-dry fuel wood per hectare.

In addition to its practical uses, certain cultivated forms have been chosen for their aesthetic value. The leaves and stems emit a strong aromatic odor, while the flowers possess a distinct musk-like fragrance¹¹.

Morphology

Vitex species usually occur as shrubs or small trees, and only rarely as woody climbers. The stems and branches are bluntly four-angled. The plant is typically a a tiny tree or a thick shrub that grows to a height of approximately ten to twenty feet. Its bark is thin, greyish-brown to greyish-white, with a yellow blaze visible when cut. The young branchlets are either cylindrical or broadly quadrangular, with slight hairiness. The nodes appear ringed, and the internodes range from 3 to 9 cm in length¹³.

Flower-The flowers are bisexual, numerous, and pleasantly fragrant, borne on short stalks measuring about 1–3 mm. The calyx is bell-shaped, five-toothed with acute tips, marked inside with purplish stripes, and hairy on the outside, measuring around 3 × 2 mm. The corolla is funnel-shaped, five-lobed, and two-lipped, usually blue, purple, or lavender. The upper lip is divided into two lobes, light blue in color, ovate in shape with a truncated apex. The lower lip has three lobes; the middle one is obovate, concave, light blue, with a truncated tip about 1 mm long, while the side lobes are dark purple tinged with white, hairy at the base, and sharply pointed, each about 4 × 5 mm. The corolla tube is little at the bottom and gets wider as it moves toward the top, with dense whitish hairs inside the throat and fine hairs outside. There are four stamens, arranged in pairs of unequal length (didynamous), extending beyond the corolla. The filaments are thin, thread-like, 4–5 mm long, while the anthers are oblong, two-celled, and light brown with a whitish tinge¹³.

Fruits- The fruit is a small, rounded drupe, measuring 1–3 mm in diameter. It is partly enclosed (about one-third to three-fourths due of its size An unattractive, cup-like shape persistent calyx in addition to its stalk, which sometimes develops One or two splits that are vertical . At maturity, the fruit turns from pale brown to black . Each fruit consists of two chambers, and each chamber holds two seeds. The surface is smooth, with no marked taste or odor¹⁴.

Roots- The roots are cylindrical, firm, and fibrous, often showing irregular fractures. The outer surface is roughened by longitudinal fissures and small rootlets. In cross-section, the cork appears brownish-gray, , the Center zone shades of gray white, and the xylem a cream-colored. The bark is thin and With ease detachable from the wood. The woody portion is dense and constitutes the major bulk of the root¹⁴.

Leaves- The leaves are palmately compound, borne on petioles measuring about 2.5–3.8 cm in length. They are mostly trifoliate but may occasionally be five-foliate. In trifoliate leaves, the leaflets are lance-shaped to narrowly lance-shaped, with the central leaflet being the largest (5–10 cm long and 1.6–3.2 cm wide) and attached by a petiole of 1–1.3 cm, while the other two are nearly sessile. In the case of five-foliate leaves, the three central leaflets are stalked, whereas the two outer ones are almost sessile. The leaf's topmost layer is smooth and Without hair, while the underside is densely covered with fine hairs.the overall texture of the leaves is leathery¹⁴.



Figure 1. Flower of *Vitex negundo*



Figure 2. Leaves of *Vitex negundo*



Figure 3 Fruits of *vitex negundo*¹⁴.



Figure 4 Bark of *vitex negundo*

3. Traditional medicinal approach of *Vitex negundo* in Ayurveda

The *Vitex negundo* is a well-recognized therapeutic herb widely utilized in traditional healing systems, including Ayurveda, Unani, Siddha, and Chinese medicine¹⁴. Ayurveda, regarded as the

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science of life, emphasizes disease prevention, health promotion, longevity, and treatment of ailments. The documented use of natural products in Ayurveda dates back over 3,000 years. Interestingly, a single plant species is often employed in folk and traditional medicine to treat a wide range of health disorders, A few of which have been scientifically validated. Among such plants, *Vitex negundo* (Nirgundi) has a prominent position in the the Indian medical system. Widely recognized as ‘Sarvaroganivarini,’ (the cure for all diseases), it has long been used in Ayurveda for managing various ailments, supported by pharmacological evidence¹⁷. The Sanskrit term Nirgundi for *Vitex negundo* literally denotes “that which protects the body from diseases.” This medicinal plant is extensively documented in the classical Ayurvedic Samhitas. Ancient Indian texts describe two distinct varieties: the white-flowered form (Shwetapushpi), also referred to as Sindhuvar, and the blue-flowered form (Pushpanilika), which is specifically known in Sanskrit as Nirgundi¹⁸. In the Puranas, *Vitex negundo* is mentioned under four different names. The Matsya Purana refers to it as Nirgundi and Sindhuvara, while the names Nirgundika and Sindhuvaraka occur in the Agni Purana, Matsya Purana, and Brahma Vaivarta Purana (BvP)¹⁹. References to Nirgundi are also found in several post-Vedic texts. These include the Mahabharata (ca. 3000 BCE), Kautilya’s Arthashastra (321–296 BCE), and classical Ayurvedic treatises such as the Kalpasthana, Susruta Samhita (ca. 400 BCE), Astangahridaya (ca. 700 CE), Vaidyamanorama (800–1000 CE), Vrndamadhava (9th century CE), Bangasena, Chakradatta (1055 CE), Rasaratnasamuccaya (ca. 1300 CE), Yogaratnakara (Santarasa, ca. 1400 CE), and Bhavaprakasha (ca. 1550 CE)^{19,10}.

Ayurvedic properties ²².

Hindi/ Sanskrit	English Meaning	Description
Virya	Potency	Considered to have a heating effect
Vipaka	Post digestive effect	Leaves a pungent impact after digestion
Guna	Physical attributes	Possesses lightness and dryness
Rasa	Taste	Primarily bitter and pungent in nature

"*Vitex negundo* negundo has been extensively employed in Ayurvedic formulations and herbal remedies aimed at treating various health disorders.(Ayurvedic formulation containing *vitex negundo*)²⁴.

Nirgundi Thailam – contains *Vitex negundo*; used for Peenisarogum ²⁵.

Vatagajankush Rasa – contains *Terminalia chebula*; indicated in Gridharasi²⁹.

Nirgundi Patra Pinda Sweda – contains *Vitex negundo*; used for Sandhigata vata ²⁶.

Manasamitra Vatakam – contains *Sida acuta*; used for Generalized anxiety disorder ²⁹.

Nirgundi Churna – contains *Vitex negundo*; used in Kidney pain ²⁹.

Vishatinduka Taila – contains *Strychnos nux-vomica*; used for Vatarakta²⁹.

Dashamoola Taila – contains *Aegle marmelos*; used for Kashtrata^{27,28}.

Trivikrama Rasa – contains *Vitex negundo* and Copper; used for Mutrashmari²⁹.

Uses of *vitex negundo* in unani medicinal system- In the Unani system of medicine, *Vitex negundo* (Nishinda) is valued for its diverse therapeutic applications. When administered with milk and dry ginger, it is reported to function as a sexual stimulants The seeds that are pulverized are prescribed in cases of spermatorrhoea, while the plant is also acknowledged for its contraceptive characteristics and its function in managing malarial fever²⁴. The seeds are said to have of *Vitex negundo* anti-inflammatory properties and are traditionally administered with sugarcane vinegar to alleviate swelling³⁰.

Uses of *vitex negundo* in chinese medicinal system- In traditional Chinese medicine, *Vitex negundo* is recognized for its therapeutic applications, particularly in providing symptomatic relief in cases of ocular inflammation and redness, arthritic disorders, and headache management⁸.

4. Phytochemical constituents

The phytoconstituents Secondary metabolites, referred to as phytochemicals, usually exist in complex mixtures that vary based on the organs and developmental phases of the plant. The components of phytochemicals are crucial for authorize research into the plant's true medicinal efficacy³⁹.The extract's Triterpenes, diterpenes, lignan, flavonoids, and volatile oil and flavones were all evaluated in the initial phytochemical investigation. stilbene derivatives, iridoid glycosides, and glycosides³¹.

Leaves

Caroten, vitamin C, friedelin, carotinic, , and other chemical elements are found in *Vitex negundo* Linn leaves α -pinene, β -pinene, linalool, nicotine acetate, benzene epoxide, caryophyllenol, vitexicarpin, viridiflorol, bis (1,1dimethyl) methyl phenol , globulol, spathulenol, β -farnesene, farnesol, Dimethoxy-trans-stilbene 4,4C' 5, 6, 7, 8, 3, 4 Ethoxy, 5-heptamethoxy 5-hydroxy-6,7,8,3'4'-pentamethoxy (5-Odesmethylnobiletin), 5-hydroxy-6,7,8,3',4',5-hexamethoxy (gardeninA), α -copaene, β -caryophyllene, β -elemene, camphene, α -thujene, α -pinene, sebinene, linalool, stearic acid, behenic acid, 5-hydroxy-6,7,8,4'-tetramethoxy (gardeninB), 5-hydroxy-7,3',4',5'-tetramethoxyflavone (corymbosin), terpinen-4-ol, etc. Camphor, camphene, careen, γ -terpinine, 1,8-cineol, or α - Bornyl acetate, nerolidol, β -bisabolol, cedrol, α -guaiene, abieta-7,13-diene, phellendrene, β -phellendrene, α -guaiene, Agnuside, lagundinin, aucubin and nishindaside, viridiflorol,squalene, 2C-p-hydroxybenzoyl mussaenosidic acid, Five-hydroxy-3,7,3C,4' tetramethoxy flavones, Flavanone is composed of 5,3-dihydroxy-7,8,4-trimethoxy The acid p-hydroxybenzoic, 3,4-dihydroxybenzoic acid, isoorientin, luteolin-7-glucoside, 3-tetramethoxyflavone, 3, 6, 7, 4-benzoyloxyhydroxy 5,3,4-teramethoxyflavone, 3,6,7,4-dibenzoyloxy, 5,3,4-tetramethoxyflavone 3,6,7,4-dipanyloxy 5,3-tetramethoxyflavone, 6,7,4-dibutanoyloxy3, 5,3C Tetramethoxyflavone, 3,6,7,4' Dipentyloxy 5,3-Dihexanoyl 3,6,7,4-

tetramethoxyflavone, dimethoxyflavonone, betulinic acid, with ursolic acid 1,4a,5,7a tetrahydro 1 β Dglucosyl (3',4'dihydroxybenzoyloxymethyl), 1-3-rhamnoside, vitegnoside, as well as - trimethoxyflavonone [c] -5-ketocyclopenta luteolin-7-O- β -D-glucosid or pyran-4-carboxylic acid³².

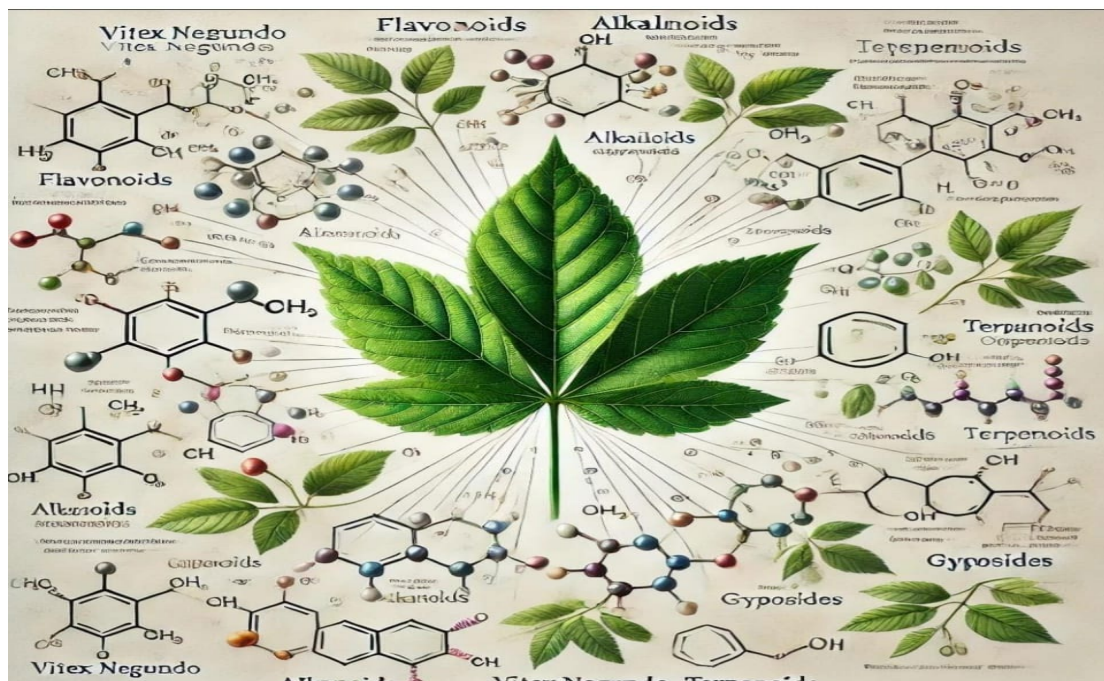
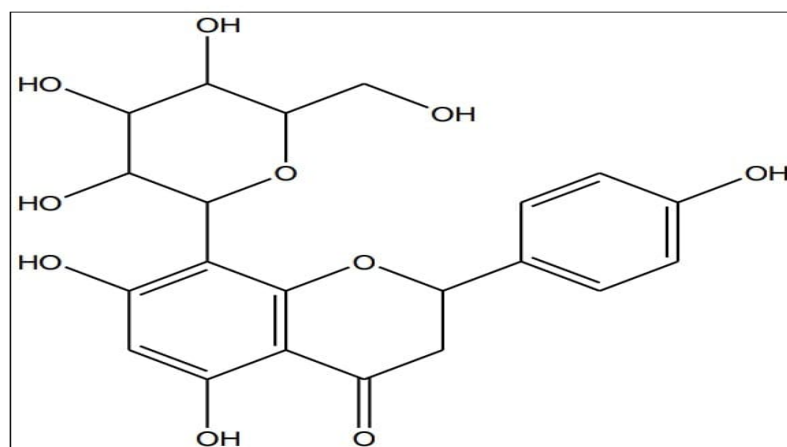


Fig 5. Phytochemical constituents of *vitex negundo* leaves⁴⁴.

Vitex negundo leaves contains phytoconstituents and their derivatives.

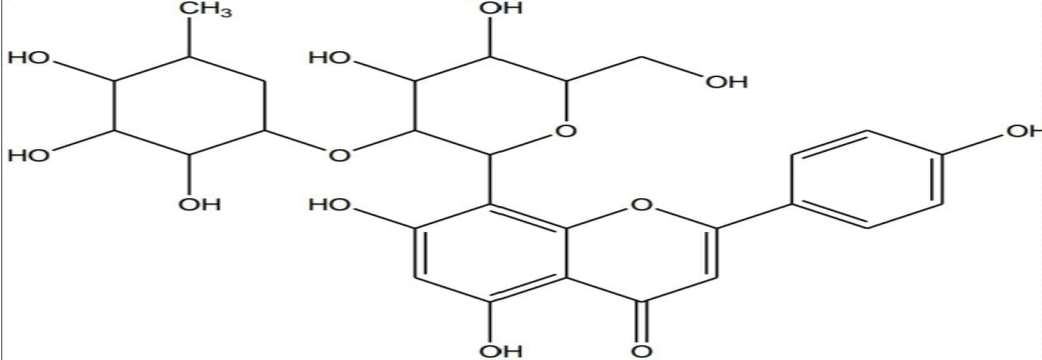
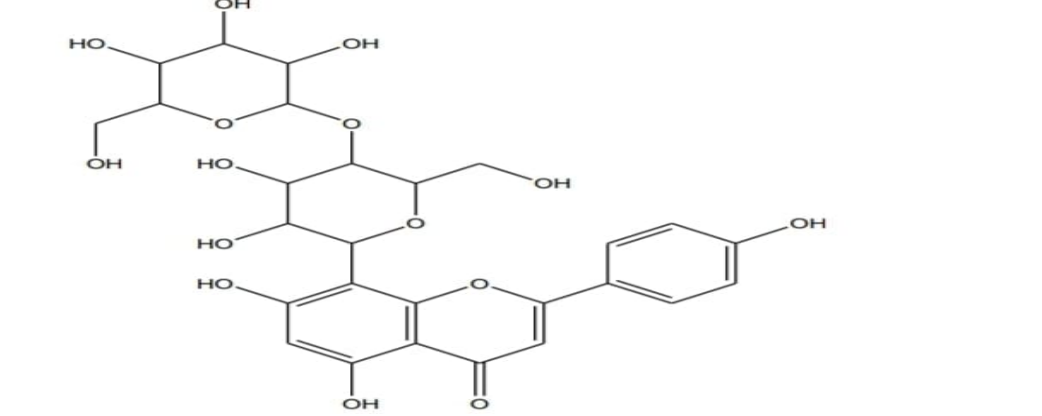
Vitexin

The leaf extract of *Vitex negundo* contains vitexin, which is both naturally occurring and manufactured there. This flavonoid has robust anticancer activity in preclinical cervical, liver, prostate, and breast cancer animals. Vitexin is an appropriate marker for the plant's leaf extract since it can be successfully isolated and identified from *vitex negundo* with low percentage RSDs³³.



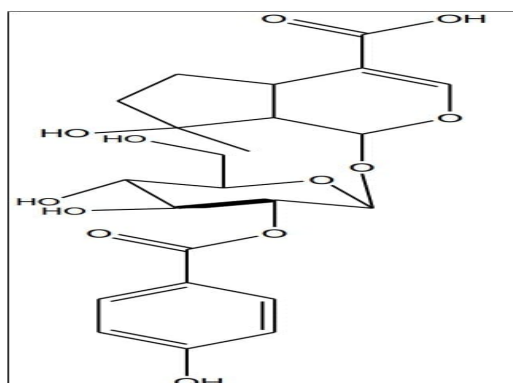
structure of Vitexin

Derivative of vitexin

Name	Structure
Vitexin 2 - o- rhamnosid e	
Vitexin 4 o- rhamnosid e	

Nirgundoside

The active component is nirgundoside, which is present in *Vitex nigrundo* Linn leaves. (Family Verbenaceae) is used in traditional medicine because of its ability to lower inflammation and stop seizures. Iridoids include nirgundoside, also referred to as 2'-hydroxybenzoylmussaenosidic acid. Oglycoside³⁴. Utilizing mass analysis and NMR, various lipid-modified esters of nirgundoside emerged³⁵.

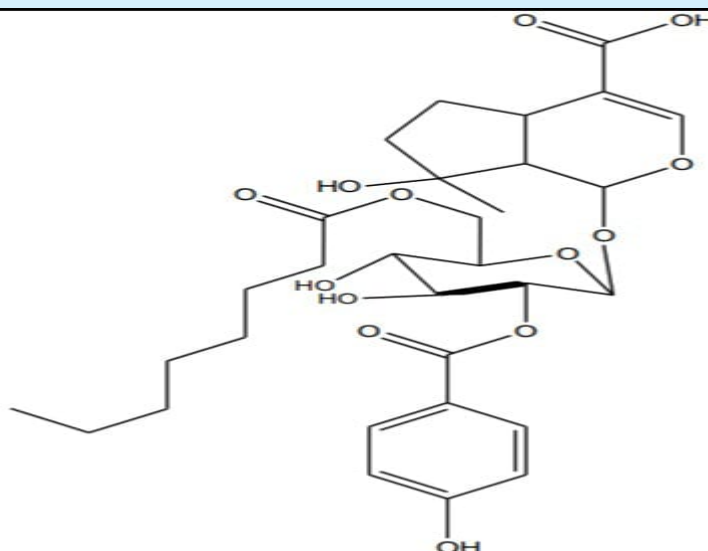


Name of compound

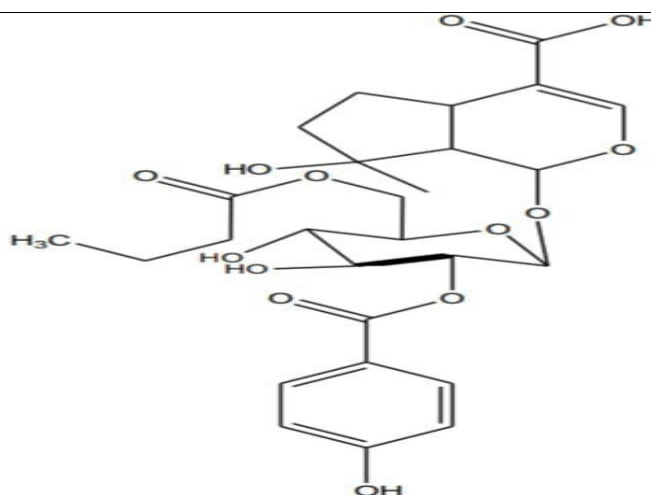
Structure
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Negundoside



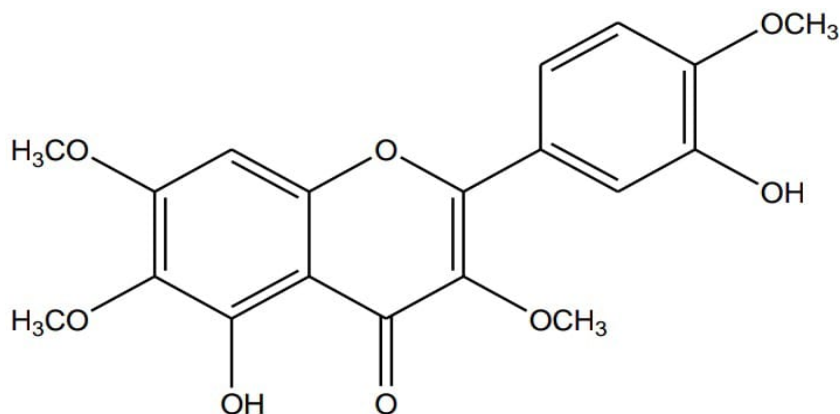
6'-O-Butanoyl Negundoside



Derivatives of Nirgundoside

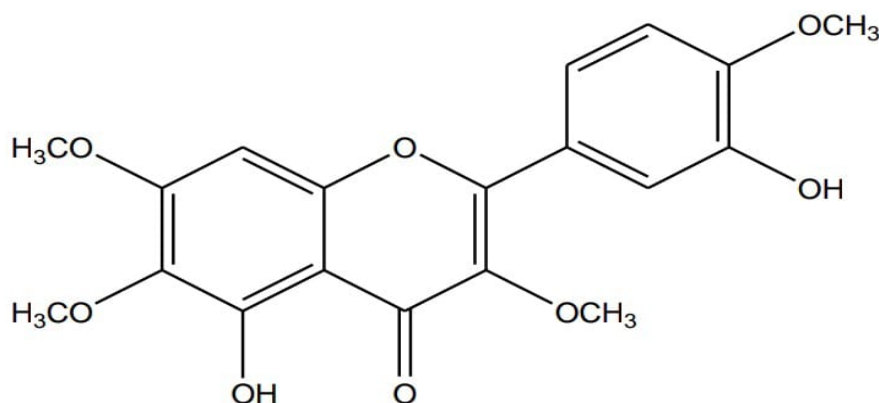
Vitexicarpin

Bioassays were utilized to guide the separation of the extract from *Vitex negundo* leaves that is soluble in chloroform, which produced the discovery of vitexicarpin, a flavone that shown widespread cytotoxicity in a range of human cancerous cell lines. To boost Vitexincarpin's cytotoxic intensity, the compound undertook a number of acylation processes that produced its methylated form (3,5,6,7,3',4' Hexamethoxyflavone), acetylated form (5,3'-Diacetoxy 3,6,7,4'-tetramethoxyflavone), and six additional acylated derivatives³⁶. The compound known as vitexincarpin, which is present The *Vitex negundo* plant's leaves contain used for a number of medicinal purposes, including antibacterial, anticancer, astringent, and combating acne. sedative, cough, vermifuge, antipyretic, insect repellent, anti-inflammatory, and a remedy for catarrhal fever cure, treatment for skin conditions, anti-ulcer actions promoting development of hair, and eczema-relieving³⁷.



Structure of vitexicarpine

Luteolin - The flavonoid found in Nirgundi tree is known luteolin. The rise in demand for luteolin has resulted in Used as nutraceuticals as supplements. Given its anti-inflammatory and antioxidant properties, luteolin contributes to decreased inflammation within a number of vital organs and tissues. Literature claims that luteolin also possesses a range of other uses, encompassing treating fever, diarrhea, wounds, and viruses, as well as operating as a chemical pesticide and repellent³⁸.



. Structure of luteolin

Seeds

3,12-en- 27 oic acid; 2,12-dien-28-oic acid; 2,12-dien-28-oic acid; 2,12-dien-28-oic acid; 2,3-dihydroxyoleana; 2,12-dien-28-oic acid; 2,12-dien-28-oic acid; 2,3-diacetoxy-18-hydroxyoleana; 5,12-dien-28-oic acid The lignan alkaloid vitedoin-A and vitedoin-B of the phenyl naphthalene type, vitedoamine-A; Five additional compounds of lignan Methoxy-phenyl 6-hydroxy-4-(4-hydroxy n-tritriacontane, n-hentriacontane, n-pentatriacontane, n-nonacosane, 5-oxyisophthalic acid, β -sitosterol, p-hydroxybenzoic acid, & 7-methoxy-3,4-dihydro-2 naphthaldehyde³⁹.

Roots

The compounds include vitexin and 2,12-dien-28-oic acid, 2 β ,3 α -diacetoxyoleana, isovitexin, 2 α ,3 α -dihydroxyoleana, and The acid 2 α ,3 β -diacetoxy-18 hydroxyoleana-5,12-dien-28 [10] 3-formyl-4.5-dimethyl-8-oxo-5H-6,7dihydronaphtho; negundin-A; negundin-B; acetyl oleanolic

acid; sitosterol; (+)-diasyringaresinol; (+)-lyoni-resinol; vitrofolal-E and vitrofolal-F; (2, isovitexin)⁴⁰.

Steam and Bark

The bark and stem includes a range of chemicals constituents, includes Vitexin cafeate, 3,6,7,3C,4'-Pentamethoxy-5-Oglucopyranosyl-rhamnoside, Myricetin 4-O-methyl [4C-O-β-D-galactosyl] 3-O- The galactopyranoside -β-D⁴¹. β-amyrrin, epifriedelinol, and oleanolic acid⁴¹. phenyl-cyclopenta Hexadeca methyl, borazine, cyclo-octa siloxane, and siloxane, 2,4,6-nonamethyl, phenyl-cyclopenta siloxane, triphenyl, 3, 5-triophl, Pentamethyl phenyl-disilane, tetracosamethylcyclododeca siloxane, the hexasiloxane 1,1,3,3,5,7,7,9,9,11,11,13,13, 3a,3a'-Dichloro-2α,3α ethano-3β-methyl-cholestan-2a-one, -tetradeca methyl Cyclonona using octadecamethyl siloxanes Cyclo octa siloxane, methyl hexadeca⁴². The flavone 5-hydroxy-3,6,7,3C4'-pentamethoxy 7,8,4-trimethoxy 5-hydroxy-3C dihydroxy flavanone, 12-dien-28-oic acid, 3-hydroxy-olean-5, & 3-acetoxy-olean-12-en-27-oic acid⁴³.

Dried fruits and flowers Germacren-4-ol, (E)-nerolidol, β-selinene, α-cedrene, δ-guaiene, guaia-3,7-dienecaryophyllene epoxide, and ethylhexadecenoate, caryophyllene epoxide, germacrene D, hexadecanoic acid, p-cymene, and valencene⁴⁴.

Fresh leaf, flower, and dried fruit essential oils 4 Guaia-3,7-dienecaryophyllene, Hexadecanoic acid, p-cymene, valencene, epoxide, ethyl-hexadecenoate, α-selinene, germacrene D, β-selinene, α-cedrene, caryophyllene epoxide, (E)-nerolidol, and β-selinene⁴⁵.

5. Medicinal uses

Fruits, roots, bark, and leaves are all very therapeutic. Dasmula arista, a medicine Using for treating fever, flatulence, diarrhea, colitis, and dysentery, and vomiting, has roots as one of its main components and colic⁴⁶.

Fresh leaves

In along with improving the immune system, it is used to treating inflammation, toothaches, eye problems, enlarged spleen, skin ulcers, dengue, rheumatism, dyspepsia, diarrhea, coughs and colds, and asthma. rheumatoid arthritis, bronchitis, and gonorrhoea. have other therapeutic applications as well, such as laxative, tonic, antiseptic, antipyretic, and antihistamine. used as a tonic, vermifuge, sedative, febrifuge, and astringent⁴⁷.

Dry leaves

Dehydrated leaves According it is advisable to tuck leaves under woolen clothes to keep worms and insects away from the fabric. It was used for repelling mosquito and has antiparasitic properties⁴⁷.

Roots and barks:

utilized to treat bodily aches, thirst, and sporadic fever⁴⁶.

Ripe fruits

are cooling, nourishing, and used to relieve dyspepsia and enhance vision⁴⁶.

Young shoots

development anticancer influence on tumor cells in ascites. used for its antibacterial, antipyretic, emmenagogue, lactagogue, vermifuge, and antihistaminic properties. Several species of Vitex, include V. V. rotundifolia, Agnus-castus, and various other species, are significant in the field of pharmacology. used to create fuel, baskets, and an alkali for plant ash dyeing⁴⁷.

Seeds seeds It contains antibacterial, analgesic, antipyretic, and Properties that are anti-inflammatory. It is used to alleviate arthritis, sprains of the muscles, and backaches. Anti-inflammatory, antirheumatism, anticancer, insecticidal, antibacterial, antioxidant, and analgesic effects⁴⁸.

6. Pharmacological Activities**Antimicrobial activity**

34 Indian medicinal plants were investigated for antimicrobial properties by Perumal et al. in 1998, and it was discovered that five various solvent preparations of *vitex negundo* leaves indicated activity utilizing the disc diffusion method at 1000–5000 ppm against everything examined bacteria (*Escherichia coli*, *Klebsiella aerogenes*, *Proteus vulgaris*, and *Pseudomonas aerogenes*)⁴⁹. When checked for the presence of harmful microbes as *S. aureus*, *E. coli*, *K. pneumoniae*, *Bacillus subtilis*, *M. luteus*, and *candida albicans*, the essential oil of *Vitex negundo* Linn leaves exhibited good antibacterial activity when compared to the standard⁵⁰.

Antifungal activity

Inhibition of Fungal Growth Bioactivity prompted the purification of an *Vitex Negundo* linn leaves in an ethanolic extract. produced a novel flavone glycoside and the isolation of five well-known components. proved that at MIC 6.25 µg/ml Compound 5 and Having a novel flavone glycoside high antifungal action against caryptococcus neoformans and Trichophyton mentagrophytes. Aspergillus flavus, Aspergillus niger, Candida albicans, Rhizopus indicus, and Cryptococcus neoformans included among the fungal infections against which the antifungal activity of 100, 200, and 300 µl extracts of ethanol, methanol, and acetone was evaluated. It has been demonstrated through the use of the well diffusion experiment⁵¹.

Antioxidant activity

The activity of antioxidants One serious effect of ionizing radiation on the membranes of cells is oxidative damage. Antioxidants are molecules that may inhibit and stop free radicals and from resulting in damage to cells and difficulties that are connected to health issues like cancer, heart disease, aging, and digestive problems, along with others. Natural antioxidants present in *Vitex negundo* are plentiful in isomeric flavones, iridoid glycosides, and flavonoids, and terpenoids. Thus, a reliable indicator of a plant extract's antioxidant qualities is the amount of total phenol and flavonoid concentration. According to recent research, normal embryonic liver cells' levels of the anti-oxidant enzymes glutathione peroxidase (GPX) and superoxidase dismutase (SOD) were increased by the *Vitex negundo* ethanolic extract (WRL68). Since phenolic compounds like flavanols and flavones are the main contributors of *Vitex negundo's* antioxidant activity, The phytochemical order in which the leaf extract was examined revealed that ethanol was found to be acceptable to ascertain the potential for antioxidants. The DPPH radical scavenging activity, reducing power, ferrous chelating, and antioxidant assays represent some of the other invitro tests that were carried out⁵².

Anti-Inflammatory activity

Reactive oxygen species are linked to a number of Inflammatory conditions. According to Ayurveda, *Vitex negundo* can help with arthritic conditions. The objective of this research was to assess the plant's anti-inflammatory and antioxidant qualities. Total polyphenols were used to standardize the plant's methanol extract. When tested for anti-inflammatory activity using the carrageenan-induced rat paw edema procedure, the standardized extract at a concentration of 100 mg/kg reduced edema in a manner equivalent to that of diclofenac sodium (25 mg/kg). Additionally, when tested for its lipid peroxidation inhibitory effect, the extract significantly decreased the formation of thiobarbituric acid reactive agents and shown strong Activity of the 1,1-diphenyl-2-picrylhydrazyl to scavenge free radicals procedure⁵³.

Antipyretic activity

Activities A disruption in the physiological thermostat cause fever or pyrexia, which raises body temperature and may cause harm to tissues and transplant rejection, inflammation, a malignant tumor, or any other sickness. The body usually keeps a temperature between 36.5 and 37.5°C. According to Ifesinachi, fever comes on by a body temperature that is higher than normal.

Cytokines that promote inflammation include interleukin 1 β , alpha, β , and TNF-alpha are typically produced in greater quantities when tissue is damaged or damaged. These mediators raise prostaglandin E2 (PgE2), which in response triggers the hypothalamus to raise body temperature. As a result, these natural antipyretics are employed to treat high body temperature; nevertheless, excessive usage of synthetic substances has an adverse impact on human health^{54,55}.

Antinociceptive activity:

The antinociceptive activity The ethanolic leaf has been investigated utilizing the acetic acid-induced writhing in mice and the tail flick test in rats. *Vitex-negundo* Linn. extract (p.o.) at 100, 250, and 500 mg/kg. Aspirin (50 mg/kg, p.o.) in the writhing test and meperidine (40 mg/kg, sc) in the tail flick method were utilized as standard controls to compare the effects. The tail flick method's mechanism of central analgesic effect also included an examination of its interaction with naloxone hydrochloride. It demonstrated a significant analgesic effect in both experimental animals in a dose-dependent fashion. It suggested that *Vitex-negundo* Linn. possesses both central and peripheral analgesic effects. neurological systems. Opioid receptors do not appear to be connected to the central analgesic action⁵⁶.

Anxiolytic activity

effect of *Vitex negundo* Linn roots in ethanolic extracts were tested for their anxiolytic activities by EMP, or elevated plus maze, and the Dark and light maze exploration test. Diazepam is an extract from *Vitex negundo* Linn that is utilized as a favorable control was given favorable control given orally to male mice one hour before to the test of behavior. Extract from *Vitex negundo* Linn increased both the number of entries and the proportion of time invested in on EPM's open arms. The time spent in the light-arena increases with Both *Vitex negundo* Linn and diazepam usage rates, showing that the root extract of *Vitex negundo* Linn exhibits significantly strong anxiolytic effects⁵⁷.

Anti-diabetic activity

Apart from its anti-diabetic properties, effects, the extract from the leaves of *Vitex negundo* has an optimistic impact on glycoprotein metabolism. Iridoid glycoside's anti-hyperglycemic action is similar to glibenclamide. When it comes to treating hepatocellular carcinoma, vitexin from *Vitex negundo* fruits displays promise. By stopping the cell cycle at G1/G0, vitexin inhibits the growth of HepG2, Hep3B, and Huh-7 cells as well as the Both independent and dependent on anchorage HepG2 cell growth. In addition, vitexin inhibits the growth of endothelial tubes by lowering VEGF output. In HepG2 cells, treatment with vitexin caused an inhibition of Akt and FOXO3a phosphorylation. In addition, small interfering RNA (siRNA) increased growth inhibition by taking down Akt1, while siRNA reduced the expression of FOXO3a⁵⁸.

Anti cancer activity

Anti-cancer action In recent years, a large number of anti-tumor studies on *Vitex negundo* have become available. A mixture of lignan molecules from *Vitex negundo* seeds called EVn-50 showed a wide antitumor activity through caspase activation and Bcl-2/Bax ratio downregulation in seven models of tumor xenografts, including those for cervical, liver, prostate, and breast tumors. 6- (4-

hydroxy-3-methoxyphenyl) hydroxy-4- A significant lignan in EVn-50, 3-hydroxymethyl-7-methoxy-3,4-dihydro-2-aphthaldehyde, may cause apoptosis in breast, prostate, and ovarian cancer cells by cleaving the protein known as poly ADP ribose polymerase and lowering the Bcl-2/Bax ratio. By blocking mTOR signaling, Additionally, this lignan prevented the choriocarcinoma development in mice with severe combined immunodeficiency syndrome⁵⁹.

Cardioprotective activity

Marathi Prasad et al. proved *Vitex negundo*'s cardioprotective efficacy for the first time. They exhibited observed by controlling the expression of the NF-B and Akt1 signaling cascades, an ethanol extract of *Vitex negundo* can shield rats from ISO-induced MI. They proved the presence of flavonoids that cause this effect, such as 5,7-dihydroxy-6,4'-dimethoxy flavanone⁵⁹.

Antibacterial activity

Gram-positive *Staphylococcus aureus* (MTCC 3160) was the bacteria employed in the antibacterial tests. *Pseudomonas aeruginosa* (MTCC 0741), *Bacillus subtilis* (MTCC 0121), and Gram-positive *Escherichia coli* (MTCC 0051). Every strain utilized in these investigations was acquired from MTCC, IMTECH, Chandigarh, India. Using the diffusion method of agar wells, the antimicrobial capability of each of the three essential oil and subsequent extract samples was assessed. After swabbing nutrient agar plates containing the broth culture of the respective microorganisms (diluted to 0.5 McFarland Standard), the plates were 15 minutes at room temperature to allow for absorption. Guaiene, caryophyllene epoxide, and ethylhexadecenoate are the primary chemical compounds found in leaves that are primarily responsible for the effectiveness of their antimicrobial properties; in flowers, α -selinene and germacren-4-Ol are found⁶⁰.

Neutralization activity of snake venom

In methanol, *Vitex negundo* Linn. root extracts presented in opposition to snake venom activity. Sections obtained from The herb *Vitex negundo* Linn. successfully reduced the deadly effects of the venom of *Naja kaouthia* and *Vipera russellii* in both in vitro and in vivo tests. The venom of *Viperarussellii* has hemorrhagic, coagulant, defibrinogenating, and inflammatory properties that the plant extracts completely prevented. After the plant extract and snake venom mixed together, no discernible bands developed⁴⁴.

Anti-androgenic activity

In both intact adult dogs and castrated prepubertal dogs, the fraction high in flavonoids of *Vitex negundo* seeds displayed impacts on the male reproductive system that are anti-androgenic. Treatment using the The flavonoid-rich fraction disrupted the last stages of spermatogenesis and significantly reduced the testes' and epididymides' contents of RNA, sialic acid, and amino acid, indicating a drop in androgen production this can be undone by taking exogenous testosterone concurrently. [61] additionally, the Flavonoid-rich extract from *Vitex negundo* that has been partially purified seeds disrupts tissue biochemistry, decreases secretory products, causes weight loss in all of the major accessory sex organs, and interferes with male reproductive function. indicators of the function of

accessory sex organs, as well as reduced counts of sperm and slackness in their motility, suggesting that *Vitex negundo* is a possible anti-androgenic substance that may hinder fertility without adversely affecting additional vital organs⁶².

Hepatoprotective activity

Leaf ethanolic extract's ability to prevent hepatotoxicity was examined by giving rats a mixture of three anti-tubercular medications orally for 35 days 7.5 mg/kg of isoniazid, 10 mg/kg of rifampin, and 35 mg/kg of pyrazinamide. Oral dosages of 100, 250, and 500 mg/kg in three grades of *Vitex negundo* leaf ethanolic extract were given for 35 days, 45 minutes before the anti-tubercular challenge. When compared to control, Alkaline, aspartate aminotransferase, alanine aminotransferase, and TB were significantly decreased. phosphate levels, indicating the hepatoprotective efficacy of Leaf ethanolic extract of *Vitex negundo* at 250 and 500 mg/kg dosages. Additional evidence of the hepatoprotective action can be obtained by the histology of the liver section of the rats given 250 and 500 mg/kg of the *Vitex negundo* leaf ethanolic extract⁶³.

Anthelmintic Activity

Ethanolic preparations from *Vitex negundo* were used to test for anthelmintic activity in opposition to *Pheritima*, an Indian earthworm. after death. Tests were performed using different concentrations Both of these extracts, and the results were presented in concepts of the worms' paralysis and death times. Distilled Water served as the control group and piperazine citrate as the reference typical. The plant extracts demonstrated dose-dependent safety⁶³.

Anti-implantation activity

The *Vitex negundo* methanolic extract Linn leaves has anti-implantation activities. The extract has been given to pregnant female mice between Days 1 and 6 of their pregnancy. No When the treated animals were removed via surgery on the fifteenth day of pregnancy., implantation sites were visible. The endometrium of the treated animals indicated biophysical changes. The endometrium of treated rodents showed a change from the control animals' marked rise in superoxide anion radicals. Therefore, physiological alterations brought about by *Vitex negundo* Linn. extract during implantation should be a useful starting point for additional studies on natural contraceptive targets initial implantation⁶⁴.

Mosquito repellent activity

Assessment of *Vitex negundo* L. leaf extracts against *Culex* larvae repellent action on mature vector mosquitoes and tritaeniorhynchus. In the lab, the larvicidal activity of petroleum ether (60–80 degrees C) extracts of *Vitex negundo* leaves against *Culex tritaeniorhynchus* larval stages was assessed. More susceptibility was seen in *C. tritaeniorhynchus* larvae, with respective LC(50) and LC(90) values of 2.4883 and 5.1883 mg/l. The repellent efficacy of two doses, namely 1.5 and 2.0 mg/cm, was tested on Special terricot (68:32) materials, such as collars, headbands, armbands, anklets, and shoulder and pocket strips impregnated with *vitex negundo* leaf extract, are worn by human participants. in a field setting. There were greater effects and 6-hour total protection against mosquito bites at a dosage of 1.5 mg/cm was supplied¹³.

7. Side effects and contraindications

Consuming nirgundi might result in a number of negative impacts and issues.

The ability to control hormone release, especially in women, makes it contraindicated for pregnant women and disrupts oral contraceptives and could make them less effective. If someone has heart illness, nirgundi should be taken under a doctor's care because it affects cardiac function. In addition to causing allergies, changes in menstrual flow may also occur. Additionally, it has been noted that the quantity of milk produced by nursing women varies. Despite differences on the specifics of the change, it is inevitable that it will take place. enhances the release of lethal hormones during pregnancy. decreases oral contraceptives' effectiveness Effect on the workings of the heart It could induce hypersensitivity.

Decreases the amount of milk that new mothers produce Headache, nausea, and stomach problems Rashes.

Symptoms of nausea, headaches, and dry mouth, upset urticaria, tachycardia, and stomach are the typical adverse effects of nirgundi use, albeit in a limited amount of cases.

Serious side effects from nirgundi including dry mouth, affecting the menstrual cycle, and disrupting the hormonal balance in expectant mothers.

A mild upset stomach may occasionally develop after consuming nirgundi powder or juice. When nirgundi oil or paste is utilized, skin irritation may occur⁶⁰.

Less than 2% of the women during monitoring developed mild skin rashes with itching and little gastrointestinal distress. *Vitex negundo* is being taken. During pregnancy, it is not recommended to use it¹⁵.

Contraindication

Given its botanical similarities to the more well researched *V. agnus-castus*, *Vitex negundo* might possess a comparable range of contraindications, such as using progesterone medications and hormone replacement treatments at the same time. *Vitex* encourages the second part of the cycle to produce progesterone. It is also referred to be a contraceptive, and as it may postpone or stop ovulation, it should not be used prior to ovulation. Because it suppresses sexual feelings, the leaf juice is harmful to children. According to human and animal research and experimental data, *Vitex* phytocomponents have hormonal actions and might influence the hormonal pharmaceutical impacts therapy. Based on reports, *Vitex* alters hormonal action, which could change the effects of drugs and possibly the quantities needed for treatment.

fibroids, endometriosis, or uterine or breast cancers, or gland are examples of hormone-dependent disorders that people should not take it, though doing this when pregnant is not advised. Little dosages might make milk production in females, and excessive dosages can reduce it. The prolactin-inhibiting effects of *Vitex* may be partially attributed to its dopaminergic effects, and there is a varying degree of binding between *Vitex*'s diterpene fractions and crude extracts. *Vitex* should only be used by patients with schizophrenia or conditions where dopamine levels are impacted under medical care²¹.

8. Conclusion

A significant medicinal plant with a long tradition of use, *Vitex negundo* has a variety of medicinal properties that support its common application in traditional medical systems. Its abundance of phytochemicals, including flavonoids, terpenoids, alkaloids, and essential oils, is largely responsible for the anti-inflammatory, antioxidant, anti-viral, antibacterial, anticancer, cardioprotective, qualities that have been validated by modern research. The potential of the plant as a source of new medicinal substances is demonstrated by the fusion of traditional knowledge with recent pharmacological research. Comprehensive clinical trials are essential to verify safety, efficacy, and standardized dosage forms, despite encouraging preclinical findings. To fully utilize its medical potential, future study should also concentrate on clarifying exact molecular mechanisms, evaluating synergistic effects with traditional medications, developing modern formulations.

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