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Review Article

A Comprehensive Review Of Phytochemical Profile And Pharmacological Attributes Of *Vitex Nigundo* Linn

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ABSTRACT

Vitex nigundo Linn. is a multipurpose medicinal plant of the family Verbenaceae. It is found in both northern and southern regions of India. Numerous phytochemical elements, including flavonoids, phenols, alkaloids, saponins, terpenoids, tannins, cardiac glycosides, carbohydrates, organic acids, and many other medicinally active compounds, have been identified in the species. This review aims to examine the pharmacological characteristics of *Vitex nigundo* Linn., a plant that has demonstrated properties such as antioxidant, anti- inflammatory, antinociceptive, CNS depressant, anti-fungal, antibacterial, antiallergic, enzyme inhibitory, anticonvulsant, neutralization of snake venom, histomorphology, and cytotoxic effect, hepatoprotective, antihyperglycemic, laxative, and more. Herein, we have compiled a comprehensive review of the phytochemical profile, pharmacological attributes, and therapeutic perspective of this multipurpose plant.

INTRODUCTION

Vitex nigundo Linn., sometimes known as Indian privet, nirgundi, or bana, is a big, aromatic shrub with bluish-purple blossoms extensively found throughout India. The Ayurveda and Unani medical systems have employed it for various therapeutic uses1. The fragrant herb Vitex nigundo Linn. is a member of the Verbenaceae family. It is sometimes referred to as the Five-Leaved Chaste Tree, or nirgundi. Flavonoids, volatile oil, triterpenes, diterpenes, sesquiterpenes, lignan, flavones, glycosides, iridoid glycosides, and stilbene derivatives are among the several chemical components of Vitex nigundo Linn. All portion of the plant has these chemical components2. The extract from Vitex nigundo Linn. exhibits a range of pharmacological properties, including anti-inflammatory, antioxidant, antipyretic, anti- arthritic, analgesic, antibacterial, antitumor, anti-amnesic, anxiolytic, nephroprotective, anti- HIV, antitubercular, and anti-snake venom activities.3

Taxonomical Classification:

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Table 1: Taxonomical classification of *Vitex nirgundo* Linn:

Kingdom	Plantae
Sub-kingdom	Tracheobionta
Super division	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Sub-class	Asteridae
Order	Lamiales
Family	Verbenaceae
Genus	Vitex
species	Negundo

Distribution Profile:

World:

Topical Africa, Asia, and India

India:

Karnataka, Tamil Nādu, Kerala, Andhra Pradesh, Madhya Pradesh and Maharashtra.

PLANT PROFILE

Botanical description:

Vitex nigundo Linn. is a fragrant, woody deciduous shrub that can grow into a small tree. Vitex nigundo Linn. is also known as the five-leaved chaste tree and monk's pepper. Five palm-shaped, pointy leaves make up the plant's most noticeable characteristic. It's a thin, upright tree that grows to be between two and five meters tall, with quadrangular branchlets8. The leaves are made up of five palmately arranged, lanceolate, acute, glabrous, 4-6 cm long, hairy underneath, and pointy at both ends of leaflets. The terminal leaflet has a lengthy petiole, while the lateral leaflets have small ones. There are bluish-purple flowers on up to 30 cm long axial or terminal panicles. The fruit has four spherical seeds and is globose, black, and delicious when ripe9. The branches in the plants that are in the flowering stage or that have leaves that resemble palms are used to heal burns and scars. The seeds are used to treat leprosy, worms, boils, rheumatism, dyspepsia, and colic10.

Figure 1: Plant in flowering stage and plant with leaves showing the palm-like structure of *Vitex nigundo* Linn

CHEMICAL CONSTITUENTS:

The phytochemical components of Vitex nigundo Linn., include flavonoids, phenols, alkaloids, saponins, terpenoids, tannins, cardiac glycosides, carbohydrates, and organic acids. These constituents have been isolated and have demonstrated a range of pharmacological activities, including anti-inflammatory, antinociceptive, antioxidant, antifungal, antibacterial, antiallergic, enzyme inhibitory, anticonvulsant, neutralization of snake venom, histomorphology, and cytotoxic effect, hepatoprotective, anti-hypoglycaemic, laxative7.

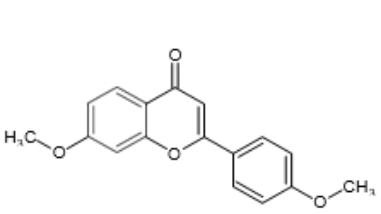
Table 2: Phytochemicals present in different parts of V. negundo Linn.,4

Parts	Phytochemical Constituents
Leaves	- 5-hydroxy-7, 4'-dimethoxy flavone (1) - 5-hydroxy-3,6,7,3',4'-pentamethoxy flavone (2) - 5,7-dihydroxy- 6,4'-dimethoxy flavanone - 7,8-dimethyl herbacetin 3-rhamnoside - 5,3'-dihydroxy-7,8,4'-tri methoxy flavanone - Agnuside (3) - Negundoside (4) - Vitegnoside - Hydroxy-3,6,7,3′,4′-pentamethoxy flavone - 3′-Benzoyloxylhydroxy-3,6,7,4-tetramethoxyflavone 6′-*p*-hydroxy benzoyl mussaenosidic acid; 2′-*p*-hydroxy benzoylmussaenosidic acid - Artemetin (5) - Carotene (6) - Casticin (7) - Friedelin (8) - Stearic acid - Vitamin C - Nishindaside - Aucubin - Luteolin (9) - Terpinen-4-ol - α-Terpinene (10) - *p*-Cymol - α-Terpinolene - Linalool - cis-Sabinene hydrate - Terpenyl-ester - α-Terpineol - -β-Caryophyllene - Neophytadiene Spathulenol
Seeds	5-Oxyisophthalic acid, 3, 4- dihydroxybenzoic acid - 6-hydroxy-4-4-hydroxy-3-methoxyphenyl -3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde - *β*-Sitosterol - *n*-Tritriacontane - *n*-Hentriacontanol

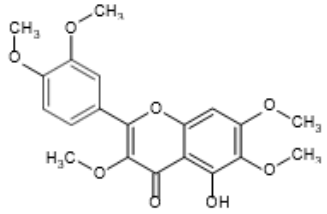
	- *n*-Hentricontane - *n*-Pentatricontane - *n*-Nonacosane *p*-Hydroxybenzoic acid
Roots	- 6-Hydroxy-4-(4-hydroxy-3-methoxy)-3-hydroxymethyl-7-methoxy-3,4- dihydro-2-naphthaledehyde - Agnuside - Negundin A (11) - Negundin B (12) - *R*-dalbergiphenol Vitexoside Vitrofolal E
Bark	- Caryophyllene (E) - Caryophyllene oxide - Virdiflorol - Methyl palmitate - Beyerene isomer - Longifolene - Kolavenol - Mannol - Phytol - Methyl octadecanaote MonooleinLedol
Other parts Flower bonds	- *β*-Caryophyllene - 2,3-dihydrobenzofuran - Flavones 4'-OH,5-OH - 7-di-O'glucoside -Kampferol-3-O-rutinoside5-hydroxy-3,6,7,3',4'-pentamethoxy flavones - Linalool - Naphthalene - Phenol - Phenol,2,3-Bis (1,1- dimethyl) Viridiflorol4-Terpineol
Essential oil of fresh leaves, flowers and dried fruits	-*β*-Caryophyllene -*β*-Selinene -Ethyl-hexadecenoate; -(*E*)-Nerolidol -Guaia-3,7- dienecaryophyllene epoxide -Germacren-4-ol; caryophyllene epoxide -Germacrene D -Globulol -Hexadecanoic acid -*p*-Cymene -Valencene - Sabinene 4-terpineol

Here are some structures for the following compounds:

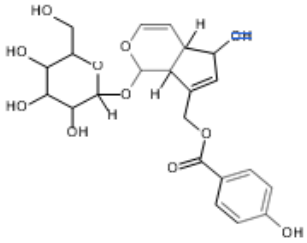
Figure 2: The structures of selected biologically active phytochemicals isolated from different parts of Vitex nigundo Linn



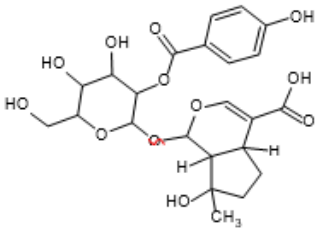
1. 5-hydroxy-7, 4' dimethoxy flavone flavone



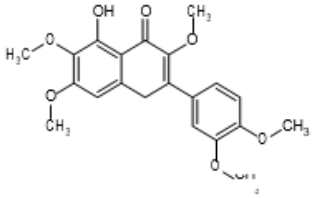
2. 5-Hydroxy-3,6,7,3′,4′-pentamethoxy



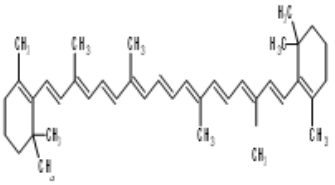
3. Agnuside



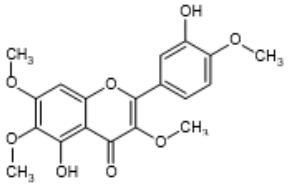
4. Negundoside



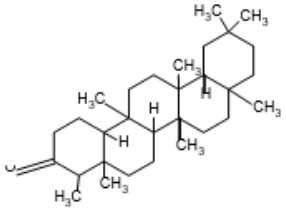
5. Artemetin



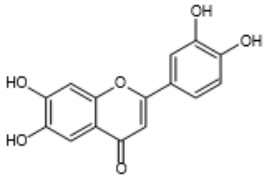
6. Carotene



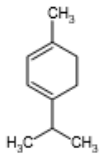
7. Casticin



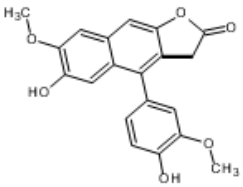
8. Friedelin



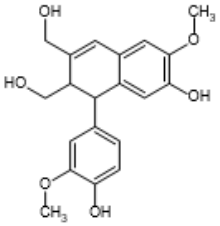
9. Luteolin



10. α-Terpinene



11. Negundin A



12. Negundin B

PHARMACOLOGICAL EFFECTS:

Vitex nigundo Linn contains various therapeutic activities. The activities are displayed in the picture below

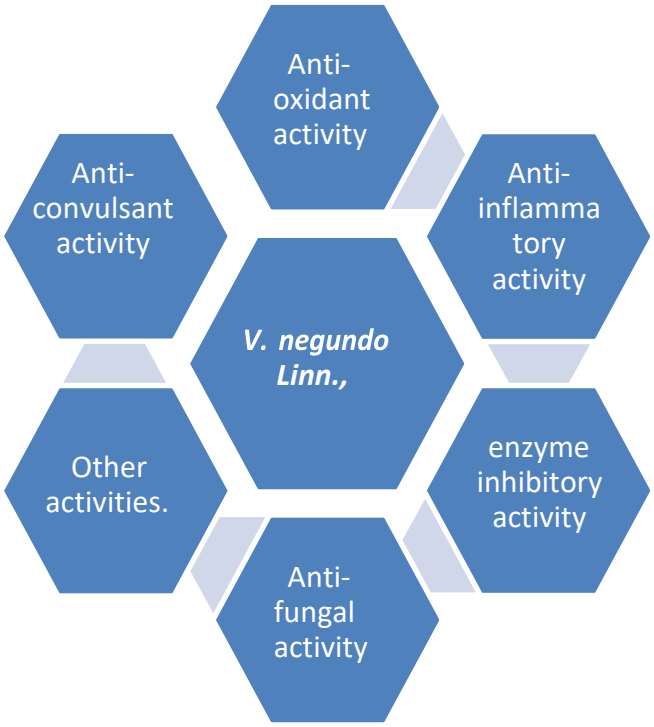


Figure 3: Pharmacological activities of Vitex nigundo Linn7.

Anti-oxidant activity

Anti-oxidant activity:

Leaves and stems of Vitex nigundo were collected from Jakarta, Indonesia (6°15'43.4"S 106°52'39.9" E) and identified at Herbarium Bogoriense, Research Center for Biology, LIPI, Indonesia. Using the maceration procedure at room temperature and 90% ethanol as the solvent, each sample was extracted. The filtrate was filtered using Whatman filter paper after 72 hours, and a rotary evaporator (Buchi R-100) was used to evaporate it at 60°C. Using the GC-MS technique, the antioxidant activity and chemical composition of the leaf and stem extracts were examined. Examples utilized: Trifoliate leaves (TF) weighing 25 gm and penta foliate leaves (PF) weighing 125 gm. A fresh stem weighing 250 gm (S) They used the DPPH assay to measure the antioxidant activity. One milliliter of 0.1 mg DPPH was combined with one ml of sample solutions (at concentrations of 10, 50, 100, 150, and 200 ppm). The mixes were then allowed to settle at room temperature for half an hour. The absorbance of the solutions was measured at 517 nm. They employed ascorbic acid as a positive control and DPPH without sample solution as a negative control11.

Anti-inflammatory activity

First, an anti-inflammatory TPA-induced ear oedema experiment was performed using extracts of Vitex nigundo Linn., dichloromethane, ethanol, and ethyl acetate in water.16 The mechanisms of action and anti-inflammatory and analgesic properties of Vitex doniana Sweet (Verbenaceae) leaf extract were studied. The extract exhibited a dose-dependent increase in reaction latency to thermal pain in mice and a significant ($P<0.05$) inhibition of paw oedema formation in rats produced by agar. The rat stomach mucosa was significantly ($P<0.05$) ulcerated by the extract, and concentration-dependent suppression of hypotonicity-induced red

blood cell hemolysis was also observed. Furthermore, in a concentration-dependent way, the extract strongly ($P<0.05$) reduced the activities of prostaglandin synthase and phospholipase A2.12

Anti-microbial activity

Agar well diffusion bioassay: The agar well diffusion technique was used to assess the essential oil's antibacterial properties. Every bacterial strain was cultured for 24 hours in 0.5 ml of nutrient agar plates, and every fungal strain was cultured in the same way for each sabouraud dextrose agar plate. A sterile cork borer was used to create a well, and 100 µl (0.1 ml) of essential oil solution was added to each well. The sterile molten nutrient agar and sabouraud dextrose agar were seeded at 450C using the 24-hour broth culture of each bacterium and the three-day inoculated fungus culture. Following a 24-hour incubation period at 370C for bacterial plates and a 2-day incubation period at 250C for fungal plates, the diameter of the zones of inhibition was determined. Every well had an equal amount of essential oil, ciprofloxacin to treat germs, and.13

Anti-fungal activity

The substance's antifungal activity was tested using the agar dilution method. The standard treatment consisted of amphotericin B and miconazole, using Sabouraud dextrose agar as the medium. Five different fungus strains were the focus of analytical testing for antifungal activity. Aspergillus flavus, Fusarium solani, Microsporum canis, Candida glabarata, and Candida ablicans. It was a culture of an organism kept alive on Sabouraud Dextrose Agar (SDA). The soup was incubated for a full day at 370C. To make the inoculum, a 24-hour-old culture was diluted in saline. Distilled water was used in the experiment to create a 1:100 dilution. Each of the SDA Petri plates was prepared, and 0.1 ml of diluted culture was added. We let the dish air dry for thirty minutes. In their investigation, a media well was dug, test samples were gathered at a single concentration, and the control was DMSO (Merck) (400 Ug/ml) in well-diluted ethanol with water. In the next well, miconazole and amphotericin B were used as standards. The well's diameter measured 6mm. The plates were incubated for twenty-four hours at 37°C. The zone of fungal growth suppression was measured, and the results were compared with traditional pharmaceuticals. Every experiment was run three times, and the mean linear increase in the zone of inhibition was recorded and calculated using the procedures outlined in (Alves et al., 2000; Janaki et al., 1998).14,15

$$\% \text{ inhibition of fungal growth} = 100 - \frac{\textit{linear growth in test (mm)}}{\textit{linear growth in control (mm)}} \times 100 \text{ test (mm)}$$

Using the agar-well diffusion method, the antifungal activity of the extracted material was evaluated.16 Bioactivity-guided the isolation of an ethanolic extract of the leaves of Vitex nigundo Linn. produced the isolation of a new flavone glycoside along with five well-known compounds. Compound 5 and the new flavone glycoside were found to have significant antifungal activity against cryptococcus neoformans and trichophyton mentagrophytes at MIC 6.25 µg/ml.17 Aspergillus flavus, Aspergillus niger, Candida albicans, Rhizopus indicus, and Cryptococcus neoformans were among the fungal infections against which the antifungal activity of 100, 200, and 300 µl extracts of ethanol, methanol, and acetone was investigated. It was demonstrated with the use of the well diffusion experiment.18

Enzyme inhibitory activity:

The plant can block several different enzymes. Vitex nigundo root extracts demonstrated inhibitory action against butyryl-cholinesterase α- and lipoxygenase enzymes tyrosinase, xanthine-oxidase, and chymotrypsin. The Vitex negund roots' methanolic extract

contains lignins that block tyrosinase. The aqueous extract of the aerial portions of HIV type 1 reverse transcriptase inhibitory activity several studies have also reported on Vitex nigundo Linn.19.

Effect on reproductive potential:

Many different enzymes are inhibited by the plant. Extracted roots from Vitex nigundo Linn., showed inhibiting action towards lipoxygenase and butyryl-cholinesterase α- xanthine-oxidase, tyrosinase, and chymotrypsin. Extract of Vitex negundo roots in methanol has been shown to contain lignins that inhibit tyrosinase. HIV type 1 reverse transcriptase inhibitory action of aqueous extract from aerial portions of additionally, some researchers report on Vitex nigundo Linn20.

Anti-cancer activity:

Research on the histomorphological impact of Vitex nigundo extracts in rats revealed no change in stomach tissue. even by hazardous dosages, however, dose-dependent alterations were noted in the lung, liver, and heart tissues. Using COLO-320 tumor cells, the cytotoxic impact of Vitex nigundo Linn., leaf extracts was investigated and confirmed. According to reports, leaf extracts in chloroform are poisonous to a panel of human cancer cell lines. Conversely, it was stated that the plant extracts weren't cytotoxic to mouse mammary and germinal-lining cells21.

Drug potentiating ability:

It has been observed that administering Vitex nigundo Linn., extracts increases the benefits of popular anti-inflammatory drugs. medications like ibuprofen and phenylbutazone; analgesics like pethidine, morphine, aspirin, and meperidine; sedative-hypnotic medications like diazepam and pentobarbitone, and chlorpromazine; anticonvulsants such valproic acid and diphenylhydantoin22.

Antihepatotoxic activity:

Apart from the previously described functions, preparations of Vitex nigundo Linn., have also been examined for a variety of additional systemic impacts. The hepatoprotective properties of Vitex nigundo's negundoside and agundoside have been investigated action. It has been found that extract from Vitex nigundo Linn., lowers serum levels of aspartate, aminotransferase, bilirubin, and Alanine. Alkaline phosphates, total protein (TP), and aminotransferase levels in liver injury instances. Vitex nigundo Linn., leaf extracts Negundo was discovered to have hepatoprotective action against carbon tetrachloride, d-galactosamine, and other frequently used tubercular medications that cause liver damage23

Anticonvulsant activity:

While butanol leaf extract and petroleum ether have demonstrated protection against electroshock seizures, root extract hasn't had much of an impact. The root's petroleum ether extract might only offer leptazole resistance. It produces convulsions, although methanolic leaf extract demonstrated considerable defense against strychnine and seizures caused by leptazole. The leaf's ethanolic extract exhibits more than only anticonvulsant properties. but can also enhance the effects of many common anticonvulsants, potentially lowering dose-related adverse reactions to a typical anticonvulsant24.

Other activities:

There are reports of the plant's aqueous extract having a laxative effect25. It has also been confirmed that the plant inhibits the production of histamine from mast cells; a leaf extract may have hypoglycemic properties by inhibiting alpha-amylase26. It has also been established that leaf extract possesses CNS depressive properties. It increases the amount of time that mice sleep when given pentobarbitone sodium, diazepam, and chlorpromazine. Vitex nigundo Linn., methanolic root extracts were able to counteract the fatal effects of Vipera russellii and Naja kaouthia venom27.

CONCLUSION

Vitex nigundo Linn., commonly known as Nirgundi or the five-leaved chaste tree, is a multipurpose medicinal plant whose pharmacological qualities have been extensively researched. The review of Vitex nigundo Linn., emphasizes the wide range of medicinal uses for the supplement, such as immunological modulatory, antioxidant, analgesic, and anti-inflammatory properties. As more is discovered about Vitex nigundo Linn., it appears to be a promising plant for human health and may prove to be a useful supplement to both conventional and alternative medicine. Research indicates that the plant Vitex nigundo Linn. has substances that may help lessen pain, combat inflammation, and shield the body from harm. It may be helpful for ailments like skin problems, respiratory issues, and arthritis.

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