



Phytochemical constituents and pharmacological activities of *Vitex negundo* Linn

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ABSTRACT

Many traditionally used plants hold importance in modern days medical regimen as they have been proved scientifically to possess various activity which are desirable, one of such plant is *Vitex negundo* Linn which is distributed throughout India. It is large aromatic shrub belonging to the family Verbenaceae growing in moist or along the water courses. Phytochemical investigation shows the presence of flavonoids, essential oils, flavonoid glycosides, terpenes, lignans, stilbene derivative and irridoid glycosides and possesses enormous pharmacological activities like anti-inflammatory, antioxidant, analgesic, antipyretic, antibacterial, antitumor, anti-arthritis, anti-amnesic, anxiolytic, larvicidal activity, nephroprotective activity, anti-HIV activity, anti-eosinophilic and anti-snake venom activity. Here in we present a review of all such data related to *Vitex negundo* Linn.

Key words: *Vitex negundo* Linn, Phytochemical constituents, Pharmacological activities, commercial products.

INTRODUCTION

Vitex negundo Linn is a large aromatic shrub (commonly known as Nirgundi, Five leaved chaste tree) belonging to the family Verbenaceae. Almost all the parts of this plant possess great medicinal values and it is employed as a remedy in various traditional systems of medicine like ayurveda, chinese, siddha and unani to treat various diseases. In Indian traditional medicine system *Vitex negundo* Linn is referred as 'sarvaroganivarani' – the remedy for all diseases [1]. A popular local quote of the Bhangalis in the Western Himalayan region of India which translates as – A man cannot die of disease in an area where *Vitex negundo* Linn, *Adhatoda vasica* and *Acorus calamus* are found (provided that he knows how to use them) [2]. Nirgundi in Sanskrit means which protects the body from diseases [3].

*Vitex negundo* Linn**TAXONOMICAL CLASSIFICATION**

Kingdom	- Plantae
Subkingdom	- Tracheobionta
Super division	- Spermatophyte
Division	- Magnoliophyta
Class	- Magnoliopsida
Subclass	- Asteridae
Order	- Lamiales
Family	- Verbenaceae
Genus	- <i>Vitex</i>
Species	- <i>Negundo</i>

VERNACULAR NAMES

Assamese	- Aslok, Pochatia
Bengali	- Beguna, Nishinda,
Hindi	- Nirgundi, Sambhalu,
Kannada	- Karilakki, Lakkagida,
Malyalam	- Karunocci, Noch-chi,
Marathi	- Nirgunda, Nengar,
Oriya	- Thinghawlupa, Niligundi.
Sanskrit	- Nirgundi, Sindhuvara
Tamil	- Nallanocci, Nochi,
Telgu	- Nallavavili, Sindhuvaruma,
Urdu	- Sambhalu, Tukhm sambhalu.

PLANT DESCRIPTION

Vitex negundo Linn is a woody, erect and large aromatic deciduous shrub which grows to small tree of height 2-5 m with quadrangular branches. The leaves are penta foliate and the leaflets are arranged palmately and terminal leaflets are long (4-10 cm) acute with petiolate (1-1.3 long), lanceolate, hairy beneath and both the ends are pointed. The flowers are numerous which are bluish purple in colour and in branched in tomentose cymes and the fruits are round, succulent and black on ripening with four seeds [4,5].

GEOGRAPHICAL DISTRIBUTION

It grows in humid places or along water courses in wastelands and mixed open forests and globally distributed in Afghanistan, Pakistan, India, Srilanka, Thailand, Malaysia, Eastern Africa and Madagascar, America, Europe, China and West Indies [6,7].

PHYTOCHEMICAL CONSTITUENTS

Phytochemical studies on *Vitex negundo* Linn revealed the presence of volatile oil, triterpenes, diterpenes, sesquiterpenes, lignan, flavonoids, flavones, glycosides, iridoid glycosides and stilbene derivative. The detailed of phytochemical constituents is present in each part of the plant is given below:

Leaves

The various chemical constituents present in leaves of *Vitex negundo* Linn leaves are Friedelin, vitamin-C, carotene, casticin, artemetin [8], terpinen-4-ol, α -terpineol, sabinene, globulol, spathulenol, β -farnesene, farnesol, bis (1,1-dimethyl) methylphenol, α -pinene, β -pinene, linalool, terpinyl acetate, caryophyllene epoxide, caryophyllenol, vitexicarpin, viridiflorol [9-12], 4,4''-dimethoxy-trans-stilbene, 5,6,7,8,3'4'5'-heptamethoxy, 5-hydroxy-6,7,8,3'4'-pentamethoxy (5-Odesmethylnobiletin), 5-hydroxy-6,7,8,3'4',5'-hexamethoxy (gardeninA), 5-hydroxy-6,7,8,4'-tetramethoxy (gardeninB), 5-hydroxy-7,3',4',5'-tetramethoxyflavone (corymbosin) [13-16], terpinen-4-ol, α -copaene, β -caryophyllene, β -elemene, camphene, α -thujene, α -pinene, sebinene, linalool, stearic acid and behenic acid [17], α -elemene, δ -elemene, β -elemene, β -eudesmol, camphor, camphene, careen, 1,8-cineol, 1-octen-3-ol, γ -terpinene, α -phellendrene, β -phellendrene, α -guaiane, abieta-7,13-diene, neral, geranial, bornyl acetate, nerolidol, β -bisabolol, cedrol [18-22], 2'-p-hydroxybenzoyl mussaenosidic acid, agnuside, lagundinin, aucubin and nishindaside [23], viridiflorol, squalene, 5-hydroxy-3,6,7,3',4'-pentamethoxy flavone, 5-hydroxy-3,7,3',4'-tetramethoxy flavones, 5,3-dihydroxy-7,8,4-trimethoxy flavanone, p-hydroxybenzoic acid, 3,4-dihydroxybenzoic acid, luteolin-7-glucoside, isoorientin [24], 3'-benzoyloxyhydroxy-3,6,7,4'-tetramethoxyflavone, 5,3'-dibenzoyloxy-3,6,7,4'-tetramethoxyflavone, 5,3'-Dipropoxyloxy-3,6,7,4'-tetramethoxyflavone, 5,3-Dibutanoyloxy-3,6,7,4'-tetramethoxyflavone, 5,3'-Dipentyloxyloxy-3,6,7,4'-tetramethoxyflavone, 5,3-Dihexanoyl 3,6,7,4'-tetramethoxyflavone [25], betulinic acid, ursolic acid [26], dimethoxyflavonone, 5,3'-dihydroxy-7,8,4'-trimethoxyflavonone, 7,8-Dimethylherbacetin-3-rhamnoside, vitegnoside [27], 1,4a,5,7a tetrahydro 1 β Dglucosyl (3',4'-dihydroxybenzoyloxymethyl)-5-ketocyclopenta[c] pyran-4-carboxylic acid, luteolin-7-O- β -D-glucosid [28], 6'-p-hydroxy benzoylmussaenosidic acid [29].

Seeds

The seeds of *Vitex negundo* Linn have chemical constituents such as n-Tritriacontane, n-hentriacontanol, n-hentriacontane, n-pentatriacontane, n-nonacosane, β -sitosterol, hydroxybenzoic acid and 5-oxyisophthalic acid, 3,4-dihydroxybenzoic acid [30-32], artemetin [33], 3 β -acetoxyolean-12-en-27-oic acid, 5 β -hydro-8,11,13-abietatrien-6 α -ol, 2 α ,3 α -dihydroxyoleana-5,12-dien-28-oic acid, 2 β ,3 α -diacetoxyoleana-5,12-dien-28-oic acid and 2 α ,3 β -diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid [34,35], vitedoin A, vitedoamine A, vitedoin B [36,37], 5,7,3'-trihydroxy 6,8,4'-trimethoxy [38], 6-hydroxy-4-(4-hydroxy-3-methoxy-phenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde [39].

Stem and bark

The various chemical constituents present in the stem and bark are 3,6,7,3',4'-Pentamethoxy-5-Oglucopyranosyl-rhamnoside, vitexin cafeate, 4'-O-methyl myricetin-3-O-[4'-O- β -D-galactosyl]- β -D-galactopyranoside [40], β -amyrin, epifriedelinol and oleanolic acid [41], Hepta methyl-phenyl-cyclotetra siloxane, Cyclo heptasiloxane, tetra decamethyl Nona methyl, phenyl-cyclopenta siloxane, Cyclo octa siloxane, hexadeca methyl, Borazine, 2,4,6-triphenyl-1,3,5-tryophl, Nonamethyl, phenyl-cyclopenta siloxane, Tetracosamethylcyclododeca siloxane, penta methyl phenyl-Disilane, Heptasiloxane, 1,1,3,3,5,5,7,7,9,9,11,11,13,13-tetradeca methyl, 3 α ,3 α' -Dichloro-2 α ,3 α -ethano-3 β -methyl-cholestan-2 α -one, Octadecamethyl, cyclonona siloxanes Cyclo octa siloxane, hexadeca methyl [42], p-hydroxy benzoic acid, β -sitosterol [43], 5-hydroxy-3,6,7,3'4'-pentamethoxy flavone, 5-hydroxy-3'dihydroxy-7,8,4'-trimethoxy flavanone, 3 β -acetoxy-olean-12-en-27-oic acid, 3 β -hydroxy-olean-5,12-dien-28-oic acid [44].

Roots

Vitexoside, agnuside, R-dalbergiphenol [45,46], negundin A, negundin B, 6-hydroxy-4-(4-hydroxy-3-methoxy)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde, vitrofolal E, (+)-lyoniresinol, (+)-lyoniresinol-3 α -O- β -d-glucoside, (+)-(-)-pinosresinol, and (+)-diasyringaresinol [47], 2 β ,3 α -diacetoxyoleana-5,12-dien-28-oic acid; 2 α ,3 α -dihydroxyoleana-5,12-dien-28-oic acid, 2 α ,3 β -diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid, vitexin and isovitexin [48], acetyl oleanolic acid, sitosterol, 3-formyl-4,5-dimethyl-8-oxo-5H-6,7-dihydronaphtho (2,3-b) furan (a new furanoeremophilane) [49].

Essential oil of fresh leaves, flowers and dried fruits

The various chemical constituents of essential oil of from leaves, flowers and dried fruits are δ -guaiene, guaia-3,7-dienecaryophyllene epoxide, ethyl-hexadecenoate; α -selinene, germacren-4-ol; caryophyllene epoxide, (E)-nerolidol, β -selinene, α -cedrene, germacrene D, hexadecanoic acid, p-cymene and valencene [50], viridiflorol (19.55%), β -caryophyllene (16.59%), sabinene (12.07%), 4-terpineol (9.65%), γ -terpinene (2.21%), caryophyllene oxide (1.75%), 1-oceten-3-ol (1.59%), and globulol (1.05%) [51].

PHARMACOLOGICAL ACTIVITY**1. Analgesic and anti-inflammatory**

The analgesic activity of *Vitex negundo* Linn leaf extract was carried out using acetic acid writhing test to study the peripheral analgesic effect and central analgesic effect was studied using tail immersion test. The anti-inflammatory activity of *Vitex negundo* Linn leaf extract was studied by using models carrageenin- induced / paw odema for acute inflammations and carrageenin- induced granuloma for sub acute inflammations. Isolated rat uterus was used to study involvement of prostaglandins in the analgesic and anti-inflammatory activity of the leaf extract [52].

2. Anti-inflammatory, anti-oxidant and adjuvant therapy

Anti-inflammatory and anti-oxidant properties of *Vitex negundo* Linn leaves was studied by experimentally induced bowel diseases (IBD). The tissue was assessed biochemically by MPO (myeloperoxidase), catalase (CAT) and superoxide dismutase (SOD) was done in colonic tissue homogenate, in serum (MDA) was estimated. The ethanolic leaf extract showed ($P < 0.05$) reduction in DAI macroscopic and microscopic lesion score as well as significant ($P < 0.05$) improvement in MPO, MDA, CAT, SOD level [53]. Antioxidant properties of polar and n-hexane fractions was evaluated in *in vitro* systems such as 2,2'-Azino-bis-3-ethylbenzothiazoline-6-sulphuric acid (ABTS), lipid peroxide, superoxide or hydroxyl radical scavenging action and iron ion chelation. Based on the assay of performed radical mono cation ABTS total antioxidant potency was determined lipid peroxide was evaluated in lipid rich media of egg yolk homogenates based on the thio barbituric acid reactive substances. Iron ion chelation was determined based on hydroxyl radical induced deoxyribose degradation in the absence of ethylenediamine tetra acetic acid. Polar fractions showed potent antioxidant potential due to trapping of free radicals where as n-hexane fraction had minimum trapping of free radicals [54].

Carrageenin induced hind paw oedema and cotton pellet granuloma test in albino rats were used to study the potential role of *Vitex negundo* Linn leaf extract in sub effective doses as adjuvant with standard anti inflammatory and the study proved that the sub effective doses of *Vitex negundo* Linn potentiated anti inflammatory activity phenylbutazone and ibuprofen and can be used as adjuvant with standard anti inflammatory [55].

3. Antipyretic activity

The yeast induced hyperpyrexia method was used to evaluate the antipyretic activity of methanolic and petroleum ether extract of *Vitex negundo* Linn leaves in groups of male rabbits. Paracetamol was used as the positive standard and 1% CMC was used as control. Compared to petroleum ether extract methanolic extract has excellent antipyretic activity [56].

4. Anti-arthritis activity

Freund's complete adjuvant model (FCA) was used to study the anti-arthritis effect of ethanolic extract of *Vitex negundo* Linn leaf. FCA induced the arthritis and liver function test and radio logical examinations were performed for the analysis anti arthritis activity of leaf extract [57].

5. Antimicrobial

The antimicrobial activity of essential oil of *Vitex negundo* Linn leaves was tested against pathogenic micro organisms such as *S.aureus*, *E.coli*, *K. pneumoniae*, *B.subtilis*, *M.luteus* and *candida albicans* and compared with the standard the essential oil showed good antimicrobial activity [58].

6. Cytotoxic activity

The methanolic, petroleum ether and carbon tetrachloride leaf extract of *Vitex negundo* Linn were screened for antibacterial and cytotoxic activity using disc diffusion method and brine shrimp lethality bioassay respectively. Antibiotic kanamycin and anti tumor agent vincristine sulphate were used as standard and the fractions screened for anti bacterial activity showed prominent zone of inhibition against *Bacillus megatrium*, *Bacillus subtilis*, *Salmonella typhi*, *Vibrio mimicus*, *Aspergillus niger*. When compared to methanolic extract, the petroleum ether and carbon

tetra chloride extract showed significant cytotoxic activity [59]. *In vitro* cytotoxic activity of hydroalcoholic extracts of aerial parts of *Vitex negundo* Linn was studied against DAL(Dalton's ascites lymphoma) and EAC (Ehrlich ascites carcinoma) cell lines. Trypan blue dye exclusion technique on cell counting in vitro was used and hydro alcoholic extracts of *Vitex negundo* Linn showed good *in vitro* cytotoxic activity [60].

7. Anti-eosinophilic activity

Egg albumin induced asthma in guinea pig model was used to study the anti eosinophilic activity of the *Vitex negundo* Linn. The effects of various fractions such as aqueous subfraction, acetone subfraction, chloroform subfraction of the leaves of *Vitex negundo* Linn on the bronchial hyper responsiveness and serum bicarbonate level was evaluated. Aqueous subfraction of the leaves of *Vitex negundo* Linn possessed anti eosinophilic activity [61].

8. Anxiolytic activity

The anxiolytic activity of ethanolic extracts of *Vitex negundo* Linn roots was performed using the elevated plus maze (EMP) and light-dark exploration test in maze. *Vitex negundo* Linn extract are diazepam (used as positive control) was orally administered to male mice one hour before the behavioral evaluation. *Vitex negundo* Linn extract has increase the percentage time spent on and the number of entries to the open arms of EPM. Both the diazepam and *Vitex negundo* Linn treated rates increase the time spent in light-arena reveals that *Vitex negundo* Linn root extract has significantly good anxiolytic activity [62].

9. Antinociceptive activity

The antinociceptive activity of ethanolic *Vitex negundo* Linn leaf extract was performed by tail flick test in rats and writhing test induced by acetic acid in mice. In tail flick test meperidine was used as a standard control, aspirin used as a standard control in writhing test which was compared to the effect of *Vitex negundo* Linn extract. Mechanism of central analgesic action was studied by the interaction of naloxone hydrochloride. *Vitex negundo* Linn extract possesses both central and peripheral analgesic activity [63].

10. Anti amnesic activity

The anti amnesic activity of *Vitex negundo* Linn extract was studied against scopolamine induced amnesia in rats. Based on the stages of memory acquisition, consolidation and retention the scopolamine was given that different stages and anti amnesic activity of *Vitex negundo* Linn was compared with standard donepezil and study proved that the groups treated with *Vitex negundo* Linn extract showed decrease the phenomenon of amnesia through the antioxidant effect thus increases memory [64].

11. Nephroprotective activity

The methanolic extracts of bark was tested for nephroprotective activity against kidney damage which was induced chemically by oral administration of paracetamol in male wistar rats. The kidney damage was studied based on the assessment of biochemical parameters such as serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), alkaline phosphate (ALT), bilirubin, total protein and enzymatic antioxidant SOD, CAT, GSSH, GPx, Px, non enzymatic antioxidants (GSH) and it was concluded that the methanolic extracts of *Vitex negundo* Linn bark shows a significant reduction in biochemical parameters has nephroprotective activity [65].

12. Antiestrogenic activity

The various fractions of *Vitex negundo* Linn leaf extract (n-hexane, chloroform, n-butanol, remnant fraction) was administered to female swiss albino mice to evaluate the anti implantation potential. Mice uterus was used to estimate the lipid peroxidation and assay of superoxide dismutase (SOD) activity. In comparison to control n-hexane fraction treated mice altered the level of superoxide anion radical and superoxide dismutase activity [66].

13. Anti-HIV activity

The anti-HIV activity of ethanolic leaf extract of *Vitex negundo* Linn was studied against HIV-1 reverse transcriptase. Using a non radioactive HIV-RT colorimetric ELISA kit and with recombinant HIV-1 enzyme it was evaluated in vitro. The study concluded that the ethanolic extract exhibits anti HIV activity and the flavonoids as anti-viral agents [67].

14. Larvicidal activity

The larvicidal activity of flavonoid extract of different parts of *Vitex negundo Linn* and *Andrographis paniculata* is performed against the late III or IV instar larvae of *Aedes aegypti* and *Anopheles stephensi* and the two plants showed good larvicidal activity and can be used to synthesis eco- friendly insecticide [68].

15. Anti snake venom activity

Snake venom neutralization by the methanolic roots extracts of *Vitex negundo Linn* and *Emblca officinalis* was performed against the *Vipera russelli* and *Naja kauthia* venom induced lethal activity both in vivo and invitro and since no precipitating bands were found between the plants extract and snake venom which revealed that these plants extracts posses potent anti snake venom activity [69].

COMMERCIAL PRODUCTS

S. No	Manufacture	Name of the product	Uses
1	Himalaya drug co; Bangalore	Antiseptic cream	Wounds, burns, fungal skininfection
		Dental cream	Toothaches Bleeding gums
		Himcolin gel	Erectile dysfunction
		Acne-n-pimple cream	Acne and skin eruptions
		Joint care B cream	Rhuematic disorders
		Muscle and joint rub	Muscle strains , muscoskeletal disorders
		Pilex tablet and cream	Haemorrhoids
		Rumalaya gel and tablets	Inflammatory muscoskeletal disorders
2	Surya Herbal Ltd., Noida, India	V- gel	Vaginitis , cervicitis
		Relief Cream	Joint and Muscle pain, Stiff back
		Rheumanaad Tablet and Cream	Rheumatic Pain, Sprain
3	Ambica Research & Development Pvt. Ltd, New Delhi, India	Ostranil Gel	Osteoarthritis, Lumbago
		Amgesic Arthritis Tablets	Arthritis
4	IndSwift Ltd., Chandigarh, India	Arthrill Capsules and Massage oil	Arthritis, Joint pain, Frozen shoulder, Gout, Cervical spondylitis
5	Hamdard Laboratories, New Delhi, India	Jigreen	Liver ailments
6	Dev's Medical, Kolkata, India	Itone Eye Drops	Eye ailments
7	Trio Health Care Pvt Ltd, Gujarat	Drift ointment	Pain and bleeding in haemorrhoids
8	Charak Pharma Pvt Ltd , Mumbai	Rymanyl capsule	Rheumatid arthritis

CONCLUSION

Medicinal plants have been identified and used throughout human history. Plants synthesize a wide range of phytochemical constituents that are used to perform important biological function. Naturally available these resources provide valuable raw material for future modern scientific research and one must use it wisely. Literature citation revealed that *Vitex negundo Linn* is a popular medicine for human kind. It possess a variety of phytochemical constituents which makes it very effective antimicrobial, cytotoxic, analgesic, anti-inflammatory, anti arthritic, anxiolytic, anti amnesic, antidote for snake venom.

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