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**NIRGUNDI HERB USED IN ANCIENT INDIAN MEDICINE -
PHYTOCHEMICAL AND PHARMACOLOGICAL REVIEW**

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NIRGUNDI HERB USED IN ANCIENT INDIAN MEDICINE - PHYTOCHEMICAL AND PHARMACOLOGICAL REVIEW

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ABSTRACT:

Vitex negundo is a succulent plant of family *Verbenaceae* commonly found in tropical and subtropical xeric wood. It is a large, aromatic **shurb** with quadrangular densely whitish tomentose branchlets, up to 4-5m in height or sometimes a small slender tree, found throughout the greater part of India widely used as an analgesic medicine. The plant is prescribed in the ancient *Ayurvedic* literature as a general tonic and analgesic, with specific *vatahara* properties. The plant is believed to be useful in *Krim* (worm infestation), *kushta* (skin Diseases), *Aruchi* (Anorexia), *Kaphajvrana*, *pliha* (Spleen Diseases), *gulma* (Abdominal Lumps), *shopha* (Oedema), *pradar* (Lucoria), *Adhman* (Abdominal distension), *Nadivra* (Sinus Tract) *Dushtavrama* (Infected Ulcer). *Pama*, *Apachi*, *Sphota* (Dermal Pathologies). All types of ulcers. *Katigatavata* (Lumbar Spondylitis), *kasa* (Cough), *Apasmar* (Epilepsy), *Snayuk Grudhrasi*, *sandivata*, *Vataroga* (Orthopedic Deformities) apply as externally or orally as required. Efforts have been made by researchers to verify the efficacy of the plant through scientific biological screening. The scrutiny of literature revealed some notable pharmacological activities of the plant such as Antibacterial, Anti-inflammatory, Analgesic agent Increases granulation tissue formation, *Vrana Shodhan*, *Vrana Ropana*. Presented in this review such that the potential use of the plant either in pharmaceuticals or as agriculture resource can be evaluated. The present review is an attempt to highlight phytochemicals, various traditional uses as well as pharmacological reports on *Vitex negundo*. Linn

Key Words: *Samhalu*, three chest leaves, *Nirgundi*, *Ayurved*, *Vitex negundo*.

INTRODUCTION

A large, aromatic shrub with quadrangular densely whitish tomentose branchlets, up to 4-5m in height or sometimes a small slender tree, found throughout the greater part of India. Ascending to an altitude of 1500m. In the outer Himalayas. Bark thin, gray, leaves 3-5 foliolate leaflet's - lanceolate, entire or rarely crenate terminal leaflet's 5-10cm X 1.6 - 3.2cm lateral leaflets smaller, all nearly glabrous above white tomentose beneath. Flowers bluish purple small in peduncled cymes, forming large, terminal, often compound pyramidal panicles; fruits globose, black when ripe, 5-6mm diam. Invested at the base with enlarged calyx. The roots in the Commercial drug as big cylindrical, somewhat tortuous pieces with very few attached rootlets. Some of the pieces measure 0.25 to 5.0 cm. in diameter, the outer bark is grayish brown of exhibits longitudinal cracks. The wood is pale yellow. The root is hard & tough and break with an irregular fracture. The drug has no pleasant taste or odour. The rate of growth of the shrub is moderate, with seven rings per 2.5 cm. of radius, given a mean annual girth increment of 2.3 cm. useful Parts are Roots, fruit, flower, leaves, bark.^[1] The present review will possibly help to bridge between traditional claims and modern therapy on *vitex negundo* L. and also pinpoints unexplored

potential of it. The plant finds mention in the verses of the Charaka Samhita which is unarguably the most ancient and authoritative textbook of Indian Ayurveda. *Vitex negundo* Linn. has been designated as an anthelmintic and is prescribed as a vermifuge in the exposition on the Charaka Samhita. Other Ayurvedic uses of *Vitex negundo* Linn. are people sleep on pillows stuffed with *Vitex negundo* Linn. leaves to dispel catarrh and headache and smoke the leaves for relief. Crushed leaf poultice is applied to cure headaches, neck gland sores, tubercular neck swellings and sinusitis. Essential oil of the leaves is also effective in treatment of venereal diseases and other syphilitic skin disorders. A leaf decoction with *Piper nigrum* is used in catarrhal fever with heaviness of head and dull hearing. A tincture of the root-bark provides relief from irritability of bladder, rheumatism and in dysmenorrhea. Formulations described in Anubhoga Vaidya Bhaga, a compendium of formulations in cosmetology, in outlining the use of *Vitex negundo* Linn. leaves along with those of *Azadirachta indica*, *Eclipta alba*, *Sphaeranthus indicus* and *Carum copticum* in a notable rejuvenation treatment known as *Kayakalpa*.^[2,3]

Materials and Methods**Classification of the plant:****Latin Name :** Vitex negundo. Linn.**Gana :** Vishaghna, Krimighna (Charak), Surasadi Gana (Su.)**Taxonomic Classification** [4]

Kingdom - Plantae ;Subkingdom - Tracheobionta ;Super Division - Spermatophyta ;Division - Magnoliophyta ;Class - Magnoliopsida ;Sub Class - Asteridae ;Order - Lamiales ;Family - Verbenaceae;Genus - Vitex ;Species - negundo ;

Vernacular names:- Assam - Aslok ;Bengal - Nirgundi, Nishinda ;English - Five leaved chaste tree ;Gujarati - Nagod ;Hindi - Nirgundi ;Kannad - Lakkigida, Nekka, Nakkilu, Nakkigida ;Malayalam - Indranee, Karunacci ;Marathi - Nirgundi ;Punjabi - Sambhalu, Banna; Telgu- Tellavavili; Sanskrit - Nirgundi

Habitat: The plant is found throughout India, Ceylon- Afghanistan, tropical Africa, Madagascar, China .The plant occurs in Bengal, Southern India and Burma also.[5,6] It is common in waste places around villages, river banks, moist localities and in the deciduous forests. [7]

Types : (A) Nilapushpi (B) Shwetpushpi [6]

Ayurvedic properties :-Rasa Katu (pungent), Tikta (bitter) Guna Laghu (Ruksha), Ruksha (dry) Virya Ushna (hot) Vipaka Katu (pungent) ; Doshakarma Kapha-Vata Shamaka [2]

Phytochemistry:

Phytochemical constituents of different plant parts of Vitex negundo:-

Leaves:- 6'-p-hydroxybenzoyl mussaenosidic acid; 2'-p-hydroxybenzoyl mussaenosidic acid viridiflorol; β -caryophyllene; sabinene; 4-terpineol; gamma-terpinene; caryophyllene oxide; 1-oceten-3-ol; globulol; 5,3'-dihydroxy-7,8,4'-trimethoxyflavanone; 5,3'-dihydroxy-6,7,4'-trimethoxyflavanone; 5-hydroxy -3,6,7,3',4'-pentamethoxy flavones; 5,7 dihydroxy-6,4' dimethoxy flavanone; 5hydroxy-7,4' dimethoxy flavones; 5,3'-dihydroxy-7,8,4'-trimethoxy flavanone; betulinic acid [β -hydroxylup-20-(29)-en-28-oic acid]; ursolic acid [2β -hydroxyurs-12-en-28-oic acid]; n-hentriacontanol; β -sitosterol; p-hydroxybenzoic acid; protocatechuic acid; oleanolic acid; flavonoids angusid; casticin; vitamin-C; nishindine; gluco-nonotol.

Seeds:-3 β -acetoxylean-12-en-27-oic acid; 2 α , 3 α -dihydroxyleana-5,12-dien-28-oic acid; 2 β ,3 α -diacetoxyleana-5,12-dien-28-oic acid; 2 α , 3 β -diacetoxylean-18-hydroxyleana-5,12-dien-28-oic

acid; vitedoin-A; vitedoin-B; a phenylnaphthalene-type lignan alkaloid, vitedoamine-A; five other lignan derivatives, 6-hydroxy-4-(4-hydroxy-3-methoxy-phenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde, β -sitosterol; p-hydroxybenzoic acid; 5-oxyisophthalic acid; n-tritriacontane, n-hentriacontane; n-pentatriacontane; n-nonacosane.

Roots: 2 β ,3 α -diacetoxyleana-5,12-dien-28-oic acid; 2 α ,3 α -dihydroxyleana-5,12-dien-28-oic acid; 2 α ,3 β -diacetoxylean-18-hydroxyleana-5,12-dien-28-oic acid; vitexin; isovitexin, negundin-A; negundin-B; (+)-diasyringaresinol; (+)-lyoniresinol; vitrofolal-E; vitrofolal-F, acetyl oleanolic acid; sitosterol; 3-formyl-4,5-dimethyl-8-oxo-5H-6,7-dihydronaphtho (2,3-b)furan.

Essential oil of fresh leaves, flowers and dried fruits :- 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. 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%). Viridifloro

Strength as per ayurvedic pharmacopoeia of india: [6]

Total ash 6.055 % ;Carbohydrate 7.5-10.57 %;Acid insoluble ash 0.920 % ;Crude fiber 25.50-30.50 %Water soluble ash 1.460 % ;Fat 5.00-9.00 %Pet. Ether extractive 0.912 % ;Alkaloids 0.5 %Benzene extractive 0.535 % ;Bitter 5 %Chloroform extractive 0.433 %; Proteins 12.22-15.23 %Alcohol extractive 24.330 % ;Moisture 15.00-18.70 %Water-soluble extractive Not less than 20 % ;Foreign Matter 1.9-2.0 %.

Traditional uses:-[41] Traditional medicine mainly comprises of Indian Ayurveda (i.e. various *nighantus* and *samhita*), Arabic Unani medicine and traditional Chinese medicine used this drug as *krimighna* (Antihelmintic), *shothahara* (Anti-inflammatory) and *shulhara* (Analgesic) agent [41, 42]. In Asia and Latin America, populations continue to use traditional medicine as a result of historical circumstances and cultural beliefs. Traditional medicine accounts for around 40% of all health care delivered in China. Up to 80 % of the population in Africa uses traditional medicine to help meet their health care needs. Folklore systems of medicine continue to serve a large segment of population, especially those in rural and tribal areas, regardless of the advent of

modern medicine. The entries regarding the multifarious applications of *Vitex negundo* Linn. in folk medicine have been grouped regionally to emphasize the ethanobotanical diversity and ubiquity of the plant; and the details have been laid out in table 1 [10, 12]

Table No 1 showing ethanobotanical diversity of nirgundi

| Sr no | Country | Region | Local name | Used in treatment of |
|-------|--------------|------------|----------------|--|
| 1 | Bangladesh | Chittagong | ... | Weakness, Headache, Vomiting, Malaria, Black fever |
| 2 | China | Guangdong | Bugingiab | Common cold, Flu and Cough |
| 3 | Nepal | Kali | Gandaki Simali | Sinusiti, Whooping cough |
| 4 | Pakistan | Buner | Marvandaey | Chest-pain, Backache, Used as toothbrush |
| 5 | Philippines- | - | - | Cancer |
| 6 | Sri Lanka | - | Nilnikka | Eye disease, Toothache, Rheumatism |

Pharmacological uses

Demands of the scientific community have necessitated experimental evidence to further underline the medicinal importance of *Vitex negundo* Linn. described above. Taking cue from these traditional and folk systems of medicine, scientific studies have been designed and conducted in order to pharmacologically validate these claims. The decoction of leaves is used for treatment of inflammation, eye-disease, toothache, leucoderma, enlargement of the spleen, ulcers, cancers, catarrhal fever, rheumatoid arthritis, gonorrhea, sinuses, scrofulous sores, bronchitis and as tonics. As vermifuge, lactagogue, antibacterial, antipyretic, antihistaminic, analgesic, insecticidal, ovicidal, growth inhibition and morphogenetic agents. antigenotoxic, antihistamine, CNS depressant activity and anti-fertility effects were reported from the leaves of *Vitex negundo* Linn [16].

1] Anti-inflammatory activity: The sub-effective dose of *Vitex negundo* Linn. potentiated anti-inflammatory activity of phenylbutazone and ibuprofen significantly in carrageenin induced hind paw oedema and cotton pellet granuloma models. The potentiation of anti-inflammatory activities phenylbutazone and ibuprofen by *Vitex negundo* Linn. indicates that it may be useful as an adjuvant therapy along with standard anti-inflammatory drugs. Yunos et al. and Jana et al. established anti-inflammatory properties of *Vitex negundo* Linn. extracts in acute and sub-acute

inflammation which are attributed to prostaglandin synthesis inhibition. [3,24.]

2] Anti-nociceptive activity: Tail flick test in rats and acetic acid induced writhing in mice were employed to study the antinociceptive activity of ethanolic leaf extract of *Vitex-negundo* Linn. (100, 250 and 500 mg/kg, p.o). The effect was compared with meperidine (40 mg/kg, sc) in tail flick method and aspirin (50 mg/kg, p.o) in writhing test as a standard control respectively. An interaction with naloxone hydrochloride was also studied in tail flick method for its mechanism of central analgesic action. It showed significant analgesic activity in dose dependant manner in both the experimental models. It suggested that *Vitex-negundo* Linn. possesses both central and peripheral analgesic activity. The central analgesic action does not seem to be mediated through opioid receptors. It may prove to be a useful adjuvant therapy along with standard analgesic drug [25].

3] CNS depressant activity: A methanolic extract of the leaves of *Vitex negundo* Linn. was found to significantly potentiate the sleeping time induced by pentobarbitone sodium, diazepam and chlorpromazine in mice. fractionation of ethanolic extract of leaves of *Vitex negundo* Linn. resulted in the isolation of new flavone glycoside along with five known compounds. All the isolated compounds were evaluated for their antimicrobial activities. The new flavone glycoside and compound 5 were found to have significant antifungal activity against *Trichophyton mentagrophytes* and *Cryptococcus neoformans*. [8]

4] Antifungal activity: Bioactivity guided fractionation of ethanolic extract of leaves of *Vitex negundo* Linn. resulted in the isolation of new flavone glycoside along with five known compounds. All the isolated compounds were evaluated for their antimicrobial activities. The new flavone glycoside and compound 5 were found to have significant antifungal activity against *Trichophyton mentagrophytes* and *Cryptococcus neoformans* at MIC 6.25 g/ml [26].

5] Antioxidant Activity: The antioxidant potency of *Vitex negundo* Linn. was investigated by all the fractions of *Vitex negundo* Linn. exhibited a potent scavenging activity for (2, 2'-azino-bis 3-ethyl benzothiazoline-6-sulfuric acid) ABTS radical cations in a concentration dependent manner, showing a direct role in trapping free radicals. The polar fractions of *Vitex negundo* Linn. possess potent antioxidant properties. Tandon and Gupta have also reported similar antioxidant properties of *Vitex negundo* Linn. in rats, by using ethanol

induced oxidative stress model [27,28]. The extracts also possess the ability to combat oxidative stress by reducing lipid peroxidation owing to the presence of flavones, vitamin C and carotene. Rooban et al. evaluated the antioxidant and therapeutic potential of *Vitex negundo* Linn. flavonoids in modulating solenoid-induced cataract and found it to be effective [3,29].

6] Enzyme-inhibitory activity: Root extracts of *Vitex negundo* Linn. showed inhibitory activity against enzymes such as lipooxygenase and butyrylcholinesterase, α -chymotrypsin, xanthine-oxidase and tyrosinase. Also reported the HIV type 1 reverse transcriptase inhibitory activity of the water extract of the aerial parts of *Vitex negundo* Linn. [30].

7] Anticonvulsant activity: Maximal electroshock seizures (MES) in albino rats and pentylenetetrazole (PTZ) induced seizures in albino mice were used to study anticonvulsant activity of *Vitex negundo* Linn. leaf extract. The test drug dose (1000 mg/kg, p.o) showed 50% protection in clonic seizures and 24-hour mortality against PTZ induced seizures. It also decreased number and duration of convulsions significantly. *Vitex negundo* Linn. Potentiated anticonvulsant activity of valproic acid. The anticonvulsant activity of *Vitex negundo* Linn. Has not been found equi-effective with standard drugs. Moreover, the potentiation of diphenylhydantoin and valproic acid by *Vitex negundo* Linn. indicates that it may be useful as an adjuvant therapy along with standard anticonvulsants and can possibly lower the requirement of diphenylhydantoin and Valproic Acid. [3,31].

8] Antibacterial studies: Essential oils and successive ethyl acetate and ethanol extracts of *Vitex negundo* Linn. showed antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa* bacterial strains. Main constituents identified in leaves oil were dguaiene, carryophyllene epoxide and ethylhexadecenoate; In flowers oil α -selinene, germacren-4-ol, carryophyllene epoxide and (E)-nerolidol while fruit oil showed β -selinene, α -cedrene, germacrene D and hexadecanoic acid as the main constituents which help for antibacterial activity. [40]

9] Antiallergic Activity: Ethanolic extract of *Vitex negundo* Linn. showed antiallergic activity against immunologically induced degranulation of mast cells. It also inhibited edema during active paw anaphylaxis in mice. The extract significantly inhibited both the initial and later sustained

phases of tracheal contractions. The initial phase was primarily due to histamine and the latter phase was due to release of lipid mediators from arachidonic acid. Inhibition of the latter phase may be secondary to inhibition of arachidonic acid by the ethanolic extract. [40]

10] Snake venom neutralization activity: The methanolic root extracts of *Vitex negundo* Linn. And *Emblica officinalis* showed antisnake venom activity. The plant *Vitex negundo* Linn. extracts significantly antagonized the *Vipera russellii* and *Naja kaouthia* venom induced lethal activity both in in vitro and in vivo studies. *Vipera russellii* venom-induced haemorrhage, coagulant, defibrinogenating and inflammatory activity were significantly neutralized by both plant extracts. No precipitating bands were observed between the plant extract and snake venom [8,31,32].

11] Effect on reproductive potential: The flavonoid rich fractions of seeds of *Vitex negundo* Linn. Caused disruption of the latter stages of spermatogenesis in dogs and interfered with male reproductive function in rats. It must however be noted that these findings are in sharp contrast with the traditional use of *Vitex negundo* Linn. as aphrodisiac. Hu et al. determined that ethanolic extracts of *Vitex negundo* Linn. Showed estrogen-like activity and propounded its use in hormone replacement therapy [8,33].

12] Histomorphological and cytotoxic effects: Tandon and Gupta studied the histomorphological effect of *Vitex negundo* Linn. extracts in rats and found the stomach tissue to be unaffected even by toxic doses; while dose-dependent changes were observed in the heart, liver and lung tissues. Cytotoxic effect of leaf extracts of *Vitex negundo* Linn. was tested and affirmed using COLO-320 tumour cells. On one hand, Diaz et al. found the chloroform extracts of *Vitex negundo* leaves to be toxic to a human cancer cell line panel. Yunos et al. reported that *Vitex negundo* Linn. extracts were noncytotoxic on mammary and genito-urinary cells of mice. [34]

13] Hepatoprotective activity: The ethanolic extract of *Vitex negundo* Linn. at 250 and 500 mg/kg doses significantly decrease Serum Bilirubin, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphates (ALP) and Total Protein (TP) levels against hepatotoxicity (HT) produced by administering a combination of three antitubercular drugs isoniazide (7.5 mg/kg), rifampin (10 mg/kg) and pyrazinamide (35 mg/kg). Alcoholic extract of the seeds of *Vitex*

negundo Linn. showed the hepatoprotective action against carbon tetrachloride induced liver damage. The extract was found to be effective in preventing liver damage which was evident by morphological, biochemical and functional parameters³. Nirgundi exerts a protective effect on CYP2E1- dependent CCl₄ toxicity via inhibition of lipid peroxidation, followed by an improved intracellular calcium homeostasis and inhibition of Ca²⁺ dependent proteases^[35,36].

14] Hypoglycemic activity: Villasenor and Lamadrid have provided an account of the antihyperglycemic activity of *Vitex negundo* Linn. Leaf extracts^[37,38].

15] Laxative activity: The aqueous extract of the *Vitex negundo* Linn. leaves at doses 100 and 200 mg/kg was investigated for laxative activity according to Cappaso *et al.* in albino rats were compared with standard drug agar-agar (300 mg/kg, p.o.) in normal saline.

16] Immuno-modulatory activity: Immuno-modulatory effect of *Vitex negundo* Linn. extracts has been reported by Ravishankar and Shukla. The decoction of leaves is considered as tonic, vermifuge and is given along with long pepper in catarrhal fever^[39].

17] Drug potentiating ability: Administration of *Vitex negundo* Linn. extracts potentiated the effect of commonly used anti-inflammatory drugs such as ibuprofen and phenylbutazone analgesics such as meperidine, aspirin, morphine and pethidine; sedative-hypnotic drugs like pentobarbitone, diazepam and chlorpromazine; anti convulsive agents such diphenylhydantoin and valproic acid^[28].

18] Antimicrobial activity: Antimicrobial activity of Nirgundisiddha taila was tested upon three organisms i.e. *E. coli*, streptococcus Aureus & *Pseudomonas Aeruginosa*. This Drug has Antimicrobial activity against *E. coli* culture but not effective against cultures of *S. Aureus* and *Pseudomonas* in the above test using culture medium as sterile soyabean casein Digest medium.

Toxicology :- Drug has been used since ancient time so the proper administration of this herb in appropriate doses not cause harm.^[41]

Doses in adults :- Juice-15-20 ml ; Decoction 50-10ml ; Leaves powder 1.5 to 3 gm, Dry leaves extract :-300-600mg.^[6,42]

CONCLUSION

In recent year, ethnobotanical and traditional uses of naturally compound, especially plant origin receive much attention as they were well tested for their efficacy generally believed to be safer for human use. They obviously deserve scrutiny on modern scientific lines such as phytochemical investigation, biological evaluation on experimental animal models, toxicity studies, investigation of molecular mechanism of action of isolated phytoprinciples and their clinical trials. Thorough screening of the literature available on *Vitex negundo* Linn. depicted the fact that it is a popular remedy.

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