

A Brief Study on Vitex Negundo Linn: Medicinal and Pharmacological Properties

Abdul Quaiyoom¹ , Saumya Tripathi¹ , Shekhar Singh² , Navneet Kumar Verma² 

¹ Assistant Professor, Suyash Institute of Pharmacy, Hakkabad, Gorakhpur, UP, India-273016

² Associate Professor, Suyash Institute of Pharmacy, Hakkabad, Gorakhpur, UP, India-273016

Email: Abdulquaiyoom0786@gmail.com

Corresponding Author: Abdul Quaiyoom

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Abstract-

Vitex Negundo Linn. (Verbenaceae) is a tall, woody, aromatic shrub or occasionally a delicate little tree, ranging from 30-45 cm to as high as 4.5 meters, widely found across numerous regions of India. A simply developed plant, it prefers a light well-drained loamy soil in a warm sunny position sheltered from cold drying winds succeeds in poor dry soils. Plants tolerate temperatures down to about -10°C. Phytochemical studies on Vitex negundo Linn revealed the presence of volatile oil, triterpenes, diterpenes, sesquiterpenes, lignan, flavonoids, flavones, glycosides, iridoid glycosides and stilbene derivative. Most of the plant's components possess medicinal properties and are employed for healing purposes in different traditional medical practices like Ayurveda, Chinese medicine, Siddha, and Unani. The medicinal importance of Vitex negundo described as folklore medicine the scientific community and necessitated experimental evidence for further underline mechanism. The sign from these traditional as well as folk medicine, scientific studies have been designed and conducted in order to pharmacologically validate it uses.

Keywords: *Vitex Negundo, volatile oil, triterpenes, diterpenes, sesquiterpenes, lignan, flavonoids,*

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1. Introduction

Vitex Negundo Linn. (Verbenaceae) [1] is a tall, woody, aromatic shrub or occasionally a delicate little tree, ranging from 30-45 cm to as high as 4.5 meters (**Figure. 1a**), widely found across numerous regions of India [2]. The plant flourishes in humid environments and can be found along waterways in both wastelands and mixed open forests. It has been documented in various locations including Afghanistan, India, Pakistan, Sri Lanka, Thailand, Malaysia, eastern Africa, and Madagascar [3]. The Vitex negundo Linn. (**Figure. 1b**) commonly known as the Five-leaved Chaste tree or Monk's Pepper, is widely used as a medicinal plant across much of India. It is predominantly found in warmer regions, and can grow at elevations up to 1500 meters in the outer Western Himalayas. It shows various pharmacological activities including analgesic, anti-inflammatory, anticonvulsant, antioxidant, insecticidal and pesticidal activities [4]. Most of the plant's components possess medicinal properties and are employed for healing purposes in different traditional medical practices like Ayurveda, Chinese medicine, Siddha, and Unani [5]. 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 [6,7].



2. Taxonomic/Scientific Classification of Vitex Negundo.

The Vitex is derived from the Latin word 'vicio' meaning to tie or bind because of the flexible nature of its stems and twigs [8]. The taxonomy of the plant is as follows;

Table: 1. The Taxonomic Classification of Vitex Negundo.

Kingdom	Plantae-Plants
Sub Kingdom	Tracheobionta - Vascular plants
Super Division	Spermatophyta - Seed plant
Division	Magnoliophyta - Flowering Plant
Class	Magnoliopsida - Dicotyledons
Sub Class	Asteridea
Order	Lamilales
Family	Verbenaceae
Genus	Vitex linn
Species	Vitex negundo Linn. (Chaste tree)

3. Vernacular Names [9].

Table: 2. The Vernacular Names of Vitex Negundo.

Languages	Names
Telugu	Vaavili
Tamil	Nirkundi, Vellai-nochi
Hindi	Shivari, Nirgundi
Malayalam	Vellanocchi, Indranee, Karunacci
Kannada	Nkkilu, Lakkigida, Nekka, Nakkigida
Punjab	Shwari
Assam	Aslok
Bengal	Nirgundi, Nishinda
English	Five leaved chaste tree
Gujarati	Nagod
Marathi	Nirgundi
Punjabi	Sambhalu, Banna
Sanskrit	Nirgundi
Urdu	Sambhalu, Panjangusht
Arabic	Uslaq

4. Botanical Description

Table: 3. Botanical Description of Vitex negundo Linn [10, 11].

Botanical name	Vitex negundo Linn.
Common name	Nirgundi, Nirgundika, Nirgunda, Nilanirgundi, Nirkunnchi, Nallanochi, Nisinda, Nilika, Nilapushpi, Sindhuvara, Sindhuvaram, Sinduya, Sugandhika, Surasa, Suvaha, Sinduka, Sephalika, Shvetasurasa, Svetapuspa, Shephali, Indrasursa, Indranika, Renuka, Vrikshaha.
Flowering season	June to December
Fruiting season	September to February
Habit	Branched Shrub up to 5 meters tall, or small, slender tree.
Duration	Perennial
Plant	It is a branched shrub or tree grown up to 5 meters tall, cylindrical with thin gray bark.
Leaves	Mostly trifoliate, occasionally Pentafoleate, palmate compound petiole up to 2:5:3.8 cm long; in trifoliate the leaflets are lanceolate or narrowly lanceolate, middle leaflet 5 cm to 10 cm long and 1.6:3.2 cm broad with 1 cm to 1.3 cm long petiolule and remaining two sub-sessile; in pentafoleate leaf inner three leaflets have petiolule and remaining two sub-sessile; on top of surface glabrous and tomentose in bottom with leathery texture.
Roots	Cylindrical, hard, longitudinal, narrow, cracks and small rootlets, tough with irregular fractures; the cork region shows grayish brown, middle region greyish-white, and xylem region cream colored.
Flowers	Small, Bluish-purple, cymes peduncled, large forming terminal, often pyramidal panicles.
Fruits	The fruit is light brown to black with rounded drupe, 1 mm to 3 mm in diameter, 1/3rd to 3/4th of its size surrounded by a dull grey cup-like, persistent calyx along with pedicel; calyx cup may show one or two vertical splits; two locules each containing two seeds; smooth texture with uncharacteristic taste and odour.

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 [12, 13].

6. Cultivation and Collection

6.1 Cultivation

It is widely planted as a hedge plant in between the fields and usually not browsed by the cattle. It can be reproduced readily from shoot cuttings. It produces root suckers which may be used as planting material. A simply developed plant, it prefers a light well-drained loamy soil in a warm sunny position sheltered from cold drying winds succeeds in poor dry soils. Plants tolerate temperatures down to about -10°C. The leaves and stems are strongly aromatic. The flowers have a most pronounced musk-like perfume.

6.2 Plant Collection

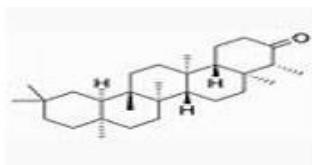
The leaves of *Vitex negundo* Linn. Which predominantly is a habitat in arid places were collected from Uthamaseeli, Near Kallanai Dam, Tiruchirappalli district, Tamil Nadu, India during the month of December-January [14, 15].

7. Phytochemical Constituents

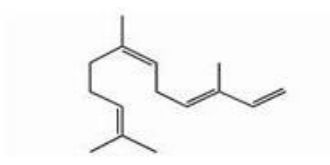
Phytochemical studies on *Vitex negundo* Linn revealed the presence of volatile oil, triterpenes, diterpenes, sesquiterpenes, lignan, flavonoids, flavones, glycosides, iridoid glycosides and stilbene derivative. The detailed of phytochemical constituents is present in each part of the plant is given below [16, 17].

7.1 Leaves

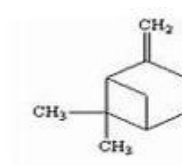
The various chemical constituents present in leaves of *Vitex negundo* Linn leaves are Friedelin, vitamin-C, carotene, casticin, artemetin [18], terpinen-4-ol, α -terpineol, sabinene, globulol, spathulenol, β -farnesene, farnesol, bis (1,1dimethyl) methylphenol, α -pinene, β -pinene, linalool, terpinyl acetate, caryophyllene epoxide, caryophyllenol, vitexicarpin, viridiflorol [19-22], 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) [23-26], terpinen-4-ol, α -copaene, β -caryophyllene, β -elemene, camphene, α -thujene, α -pinene, sabinene, linalool, stearic acid and behenic acid [27], 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, abiet-7,13-diene, neral, geranial, bornyl acetate, nerolidol, β -bisabolol, cedrol [28-32], 2'-p-hydroxybenzoyl musaenosidic acid, agnuside, lagundinin, aucubin and nishindaside [33], 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 [34], 3'-benzoyloxyhydroxy-3,6,7,4- tetramethoxyflavone, 5,3'-dibenzoyloxy-3,6,7,4-teramethoxyflavone, 5,3'-Dipropenyloxy-3,6,7,4'- tetramethoxyflavone, 5,3-Dibutanoyloxy-3,6,7,4- tetramethoxyflavone, 5,3'-Dipentylenoxy-3,6,7,4' tetramethoxyflavone, 5,3-Dihexanoyl 3,6,7,4-tetramethoxyflavone [35], betulinic acid, ursolic acid [36], dimethoxyflavonone, 5,3'-dihydroxy-7,8,4'-trimethoxyflavonone, 7,8-Dimethylherbacetin-3-rhamnoside, vitegnoside [37], 1,4a,5,7a tetrahydro 1 β Dglucosyl (3',4'dihydroxybenzoyloxymethyl)-5-ketocyclopenta[c] pyran-4-carboxylic acid, luteolin-7-O- β -D-glucosid [38], 6'- p-hydroxy benzoylmusaenosidic acid [39].



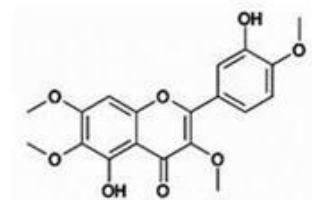
Friedelin



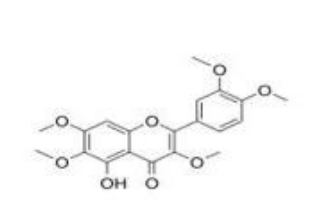
Farnesene



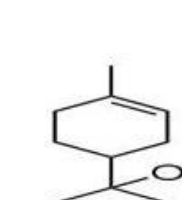
Pinene



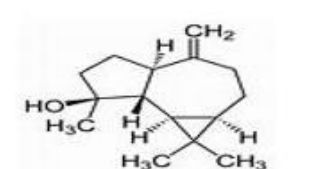
Casticin



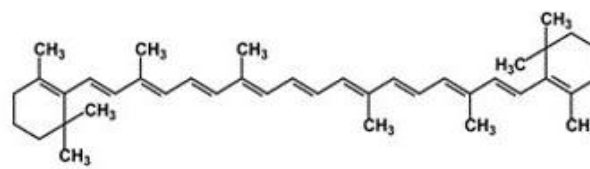
Artemetin



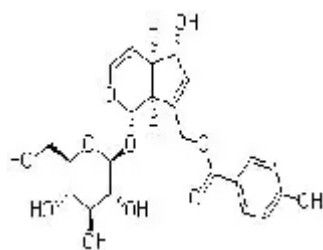
α -terpineol



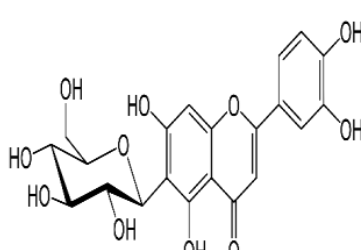
Spathulenol



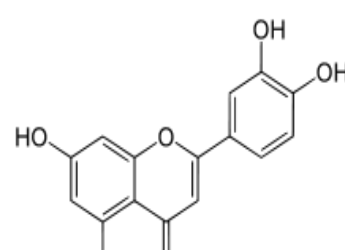
Carotene



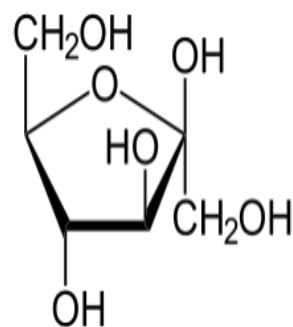
Agnuside



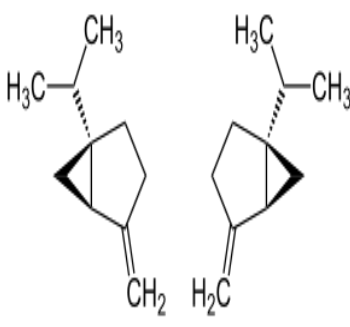
Isoorientin



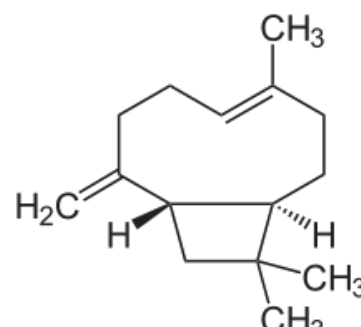
Luteolin



D-Fructofuranose



Sabinene



Caryophyllene

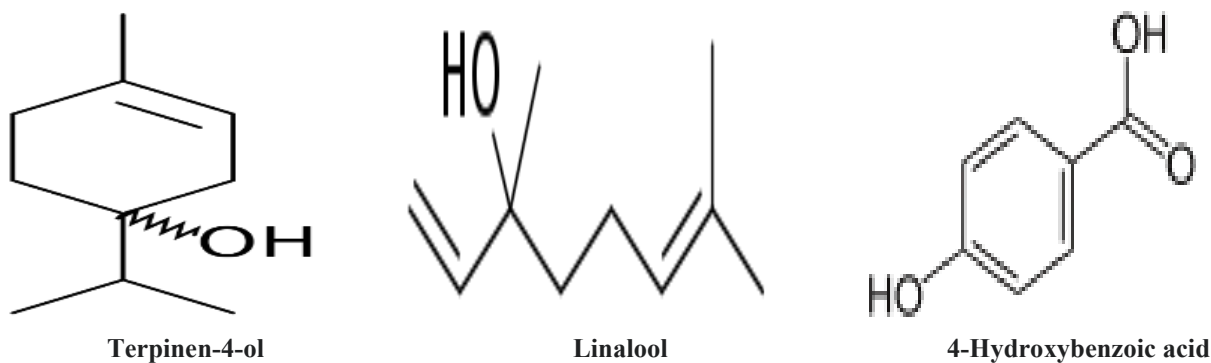


Figure 2: Phytochemical Constituents of Vitex Negundo Leaves

7.2 Stem and Bark

The stem and bark contain a variety of chemical components including Pentamethoxy-5 Oglucopyranosyl rhamnoside, vitexin cafeate, 4'-O-methyl myricetin-3-O-[4'O-β-Dgalactosyl]-β-D-galactopyranoside, β-amyrin, epifriedelinol, oleanolic acid, Hepta methyl-phenylcyclotetra siloxane, Cyclo heptasiloxane, tetra decamethylNona methyl, phenylcyclopenta siloxane, Cyclo octa siloxane, hexadeca methyl, Borazine, 2,4,6-triphenyl-11, 3, 5-tryophl, Nonamethyl, phenyl-cyclopenta siloxane, Tetracosamethylcyclododeca siloxane, penta methyl phenylDisilane, Heptasiloxane, 1,1,3,3,5,5,7,7,9,9,11,11,13,13,- tetradeca methyl, 3a,3a'-Dichloro-2α,3α-ethano-3β-methylcholestan-2a-one, Octadecamethyl, cyclonona siloxanes, Cyclo octa siloxane, hexadeca methyl, p-hydroxy benzoic acid, β-sitosterol, 5-hydroxy-3,6,7,3'4'-pentamethoxy flavone, 5-hydroxy-3'dihydroxy-7,8,4'-trimethoxy flavanone, 3βacetoxy-olean-12-en-27-oic acid, 3β-hydroxy-olean-5, 12-dien-28-oic acid [40].

7.3 Roots

Vitexoside, agnuside, R-dalbergiphenol [41,42], negundin A, negundin B, 6-hydroxy 4-(4-hydroxy-3-methoxy)-3-hydroxymethyl-7-methoxy-3,4-dihydro- 2-naphthaldehyde, vitrofolal E, (+)-lyoniresinol, (+)-lyoniresinol-3α-O-β-d-glucoside, (+)-(-)-pinoresinol, and (+)-diasyringaresinol [43], 2β,3α-diacetoxyoleana-5,12-dien-28-oic acid; 2α,3α-dihydroxyoleana-5,12-dien-28-oic acid, 2α,3β -diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid, vitexin and isovitexin [44], acetyl oleanolic acid, sitosterol, 3-formyl-4.5-dimethyl-8- oxo-5H-6,7-dihydronaphtho (2,3-b) furan (a new furanoeremophilane) [45].

7.4 Seeds

Vitex negundo Linn seeds contain various chemical components such as n-Tritriacontane, n-hentriacontanol, nhentricontane, npentatricontane, n-nonacosane, β-sitosterol, phydroxybenzoic acid, 5-oxyisophthalic acid, 3, 4-dihydroxybenzoic acid, artemetin, 3β-acetoxyolean-12-en-27- oic acid, 5β-hydro8,11,13-abietatrien-6α-ol, 2α,3α-dihydroxyoleana-5,12-dien28-oicacid, 2β,3α-diacetoxyoleana-5,12-dien-28-oicacid, 2α,3β- diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid, vitedoin A, vitedoamine A, vitedoin B, 5,7,3'- trihydroxy 6,8,4'- trimethoxy, and 6-hydroxy-4-(4-hydroxy-3- methoxyphenyl)-3-hydroxymethyl-7-methoxy-3, 4- dihydro-2- naphthaldehyde [46, 47].

7.5 Flowers and Dried Fruits

δ-guaiene; guaia-3,7-dienecaryophyllene epoxide; ethylhexadecenoate; α-selinene; germacren-4-ol; caryophyllene epoxide; (E)-nerolidol; β-selinene; α-cedrene; germacrene D; hexadecanoic acid; p-cymene; and valencene [48].

7.6 Essential oils

The essential oil extracted from Vitex negundo con tains several compounds such as linalool, α-pinene, β-pinene, camphene, limonene, and 1,8-cineole. These compounds exhibit antimicrobial and insec ticidal activities [49].

8. Pharmacological Evidence

The medicinal importance of Vitex negundo described as folklore medicine the scientific community and necessitated experimental evidence for further underline mechanism. The sign from these traditional as well as folk medicine, scientific studies have been designed and conducted in order to pharmacologically validate it uses [50].

8.1. 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, chlorpromazine in mice [51].

8.2. 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 [52,53].

8.3. Antioxidant Activity

Antioxidants are substances which have a very significant role in the human body's defence system. It inhibits or delays the process of oxidation even at a very low concentration [54]. The antioxidant elements of the plants act as radical scavengers against free radicals and inhibit them from causing problems related to human health like cancer, heart disease, aging, etc. [55]. *V. negundo* comprises poly phenolic compounds, these compounds have high antioxidant potential that results in the antioxidant activity of the plant [56]. The methanolic leaf extract of *V. negundo* was evaluated for its antioxidant activity by 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay, lipid peroxidation inhibitory assay [57], nitric oxide radical scavenging assay, hydrogen peroxide scavenging assay and superoxide scavenging assay [58]. The ethanolic leaf extract reports antioxidant activity, in which DPPH assay, hydrogen peroxide scavenging assay, total antioxidant capacity assay [59], β -carotene linoleic acid assay [60] and phosphomolybdenum assay [61] were carried out. The antioxidant activity of hexane extract and essential oil of the leaves of *V. negundo* was evaluated via DPPH assay, ferric ion reducing antioxidant power (FRAP) assay and β -carotene linoleic acid assay [62]. The antioxidant activity of the essential oil was examined through 2, 2'-azino-bis (3-ethylbenzthiazoline-6-sulphonic acid) (ABTS) radical scavenging assay [63]. The acetone and aqueous leaf extract of *V. negundo* exhibited antioxidant activity by DPPH radical scavenging assay [64]. The antioxidant activity of chloroform extract of the leaves of *V. negundo* was determined by phosphomolybdenum method and nitric oxide scavenging assay [65]. The ether extract of the leaves showed good antioxidant activity in DPPH assay [66]. The leaf extract of *V. negundo* helped in lowering the levels of superoxide dismutase, glutathione peroxidase, and catalase in Freund's adjuvant induced arthritic in a rat model [19]. The antioxidant activity of *V. negundo* was studied in rats using an oxidative stress model induced by ethanol [55]. The seed extract of *V. negundo* showed antioxidant activity, which was evaluated using in vitro lipid peroxidation assay in rat liver homogenate [68].

8.4. Anxiolytic Activity

Anxiety is an emotion that actually occurs in response to perceived fear and apprehension. It can be seen in many individuals, and it could be transient or episodic [69]. About one-eighth of the world's population is affected by anxiety. In recent years, it has been discovered that the secondary metabolites produced by some of the plants can directly or indirectly act as an anxiolytic drug [70]. The ethanolic extract of the leaves of *V. negundo* showed anxiolytic activity in Swiss albino mice using an elevated plus maze test [69]. The ethanolic root extract has reported anxiolytic activity in Swiss albino mice [male] using light-dark exploration and elevated plus maze test [71]. The anxiolytic action of the stem of *V. negundo* was studied using an elevated plus maze test in laca mice, and it was found that the aqueous extract of the stem showed moderate anxiolytic activity [72].

8.5. Anticancer Activity

Cancer is a multifactorial disease with uncontrolled cell growth and proliferation targeting immune system [73]. Dynamic nature and gene network indulged in cancer renders the researchers with the challenging task of designing therapeutic drugs [74]. Screening of several phytochemicals led to the isolation of flavonoids, schrysoplenetin and chrysosplenol D exhibiting effect against human pancreatic cancer (PANC-1). Furthermore, Chrysoplenetin proved effective against 25 cancer cell lines of lung, breast, colon, melanoma, ovarian, prostate and stomach at the submicro molar range [75]. The chloroform-soluble extract of the leaves of *V. negundo* isolated the flavone vitexicarpin also exhibits anticancer property [76]. 5,3'-Dihydroxy-6,7,4' trimethoxyflavanone (DHTMF), constituents of *V. rotundi folia* suppressed growth and induced apoptosis by decreasing expression of Bcl-2 and increasing Bax level and cleaved caspase-3 in lung carcinoma cells, in a dose-dependent manner. DHTMF treatment reduced the phosphorylation of Akt and mammalian target of rapamycin (mTOR), vascular endothelial growth factor (VEGF), hypoxia-inducible fac tor (HIF-1 α) which are key proteins in angiogenesis. Along with this, DHTMF reduced CD34 expression, tube formation and migration in human umbilical vein endothelial cells (HUVECs). This study highlights the role of DHTMF in inhibition of angiogenesis as apoptosis via the Akt/mTOR pathway [77]. Similarly, vitexin compound 2 (VB2) inhibits proliferation and apoptosis in human choriocarcinoma JEG-3 cell lines by inhibiting the expression of mTOR and 4E-BP1 [78]. Even-50 also inhibits cell growth and induce apoptosis in MCF-7 and MCF-7/TAM-R cells by down-regulating ERK1/2 phosphorylation in MAPK signal pathway and Akt signal pathway [79]. Casticin targets and suppresses NF- κ B and MAPK signaling in lipopolysaccharide-stimulated mouse macrophages by inhibiting COX-2 and

iNOS expression. Casticin from fruits of *V. rotundifolia* inhibits the nitric oxide and PGE₂, decreased the level of interleukin, IL-6, and tumor necrosis factor α (TNF- α) and thus, induces apoptosis. Along with this, casticin suppresses the expression of iNOS and COX-2 and increased HO-1 and Nrf2 production. Furthermore, casticin significantly inhibited NF- κ B subunit p65 proteins in the nucleus and decreased Akt and MAPK activation [80].

8.6. Hepatoprotective Activity

Negundoside and Agundoside from *Vitex negundo* have been studied for their hepatoprotective activity. Extract of *Vitex negundo* is reported to decrease Serum Bilirubin, Aspartate, Aminotransferase, Alanine Aminotransferase, Alkaline Phosphates and Total Protein (TP) levels in case of liver damage. Leaf extracts of *Vitex negundo* were found to possess hepatoprotective activity liver damage induced by D-galactosamine [81], 1987), commonly used tubercular drugs and carbon tetrachloride [82].

8.7. Laxative Activity:

The aqueous leaves extract of the *V. negundo* at the dose of 100 mg/kg and 200 mg/kg were reported as good laxative properties in albino rats [83].

8.8. Anti-Diabetic Effect

The leaves extract of *V. negundo* has a productive effect on glycoprotein metabolism in addition to its antidiabetic effect. The anti-hyperglycemic effect of iridoid glucoside is comparable with glibenclamide [84]. Vitexin from the seed of *V. negundo* is promising in combating hepatocellular carcinoma. Vitexin suppresses the proliferation of HepG2, Hep3B, Huh-7 cells and inhibits the anchorage-dependent and independent HepG2 cell growth by arresting cell cycle at G1/G0. Vitexin also reduces the secretion of VEGF which results in the inhibition of endothelial tube formation. Phosphorylation of Akt and FOXO3a were downregulated by treatment of vitexin in the HepG2 cells. Furthermore, knock down of Akt1 by small interfering RNA (siRNA) enhanced growth inhibition, whereas silencing FOXO3a by siRNA decreases the level of expression. Akt controls the downstream proteins such as mTOR which are a direct target of insulin signaling, thus forming the link between cancer and diabetes [85].

8.9. Analgesic Activity

Pain is a warning signal, which is defined as an unpleasant sensory and emotional occurrence related to the actual tissue or organ damage that causes discomfort [86]. For alleviating integumental and visceral pain, the plant *V. negundo* may be applicable [87]. The methanol and petroleum ether leaf extracts of *V. negundo* showed peripheral analgesic properties in a dose-dependent manner in young Swiss albino mice of either sex by inhibiting writhing caused by acetic acid [88]. The methanolic extract showed a higher analgesic effect than petroleum ether extract. The hydroalcoholic extract of *V. negundo* leaves also exhibited central analgesic activity in mice in the tail immersion test [89]. The aqueous extract of the mature fresh leaves of *V. negundo* suppressed the pain and showed analgesic activity in Wistar rats (female) using tail flick, hot plate and formalin tests [90]. The analgesic activity of *V. negundo* is because of the inhibition of prostaglandin synthesis [87] and suppression of oxidative stress [91]. The methanolic root extract also exhibited analgesic activity in albino rats of either sex using Eddy's hot plate and radiant heat tail-flick method [92]. The ethanolic extract of *V. negundo* flowers also showed analgesic activity in Swiss albino mice using the tail flick test and writhing test [93].

8.10. Anthelmintic Activity

The ethanolic extract of *Vn* was validated for anthelmintic activity against Indian earthworm *Pheritima posthuma* by Trapti et al. [94].

8.11. Anti-Larval Activity

The works of Nathan et al. suggested that the *Vn* is an effective bio-control agent against the Rice leaf-folder, *Cnaphalocrocis medinalis* [95].

8.12. Wormicidal Activity:

Ethanolic extracts of *Moringa oleifera* and *Vitex negundo* were taken for anthelmintic activity against Indian earthworm *Pheritima posthuma*. Dose dependent activity was observed in both plant extracts but *Moringa oleifera* shows more activity as compared to *Vitex negundo* [96].

8.13. Anti-Snake Venom Activity

Durairaj B et al., 2014 observed the anti-snake venom activity of hydroethanolic extracts of *Vitex negundo* leaves. The study showed that blue leaf extract of *Vitex negundo* has more potent antioxidant and anti-snake venom neutralizing effect [97]. Alam MI et al., 2003 investigated the anti-snake venom activity of root extract of *Vitex negundo*. This plant extract significantly antagonized the viperid *Vipera russellii* and *Naja kaouthia* venom. The observed confirmed that the plant extracts possess potent snake venom neutralizing capacity and need further investigation [98].

8.14. Antieosinophilic Activity

Atel JI et al., 2013 studies the antieosinophilic activity of petroleum ether leaves extract of *Vitex negundo* in guinea pig by using egg-albumin induced antieosinophilic activity. This study showed that petroleum ether extract of *Vitex negundo* reduce bronchial hyper responsiveness, asthma and various inflammation, immunology, allergy diseases [99].

8.15. Anti-Androgenic Activity

S.K. Bhargava (1984, 1986) & R.P. Samy et al. (1998) reported antiandrogenic activity of various flavonoids from the seeds of *Vitex negundo*. The flavonoids which shows estrogenic properties as well as anti-implantation activities are 5, 7, 3'-trihydroxy and 6, 8, 4'-trihydroxy flavones [100-104].

8.16. Effect on Reproductive Potential

Contrasting results have been obtained from researches on the reproductive potential of Vn. The inhibitory effect of Vn. extract on reproduction and spermatogenesis in male rats [105] was proved in certain studies. Whereas, Hu et al. [106] revealed that the same extract acted as an aphrodisiac [107] having estrogen-like activity and proposed its use in hormone replacement therapy. Kakadia et al. studied the potential of Vn. seeds to treat polycystic ovarian syndrome [108].

8.17. Enzyme-Inhibitory Activity

Various enzymes like butyryl-cholinesterase [109], lipoxygenase, α chymotrypsin [110], xanthine oxidase [111] and tyrosinase [109] were shown to be inhibited by Vn. root extracts. Woradulayapinij et al. reported the inhibitory action of aqueous Vn. extract against HIV-1 reverse transcriptase [112].

8.18. 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 [113].

8.19. Antihyperpigmentation Activity

A. Malik et al. (2006) investigated tyrosinase inhibitory potential of lignans isolated from the methanolic extract of *Vitex negundo* roots using Spectra Max 340 microplate reader [114].

8.20. Folk Medicine

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 uses of *Vitex negundo* Linn. in folk medicine in India given in table [115, 116].

9. Marketed Products





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