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(Review Article)

## ***Vitex negundo*: Medicinal Values, Biological Activities, Toxicity Studies and Phytopharmacological Actions**

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### **ABSTRACT**

*In recent times, focus on plant research has increased all over the world and a large body of evidence has collected to show immense potential of medicinal plants used in various traditional systems. Over the last few years, researchers have aimed at identifying and validating plant derived substances for the treatment of various diseases. Similarly it has been already proved that various parts of plants such as Leaves, fruits, seeds etc. provide health and nutrition promoting compounds in human diet. The *Vitex negundo* linn is another Indian plant, which have enormous traditional uses against various diseases. The present review aims to compile medicinal values of *Vitex negundo* generated through the research activity using modern scientific approaches and innovative scientific tools.*

**Key Words:** *Vitex negundo*, Pharmacological Activities, Medicinal Values, Nirgundi.

### **INTRODUCTION**

Medicinal plants have been a major source of therapeutic agents since ancient times to cure human disease. The revival of interest in natural drugs started in last decade mainly because of the wide spread belief that green medicine is healthier than synthetic products. Now-a-days, there is manifold increase in medicinal plant based industries due to the increase in the interest of use of medicinal plants throughout the world which are growing at a rate of 7-15% annually. Despite the major advances in the modern medicine, the development of new drugs from natural products is still considered important.<sup>1</sup> Traditional therapeutics based on herbal medicinal principles is time tested and widely accepted across various cultural and socioeconomic strata. However, there is lack of precise guidelines to study the herbal compounds and till date a very meagre portion of this tremendous potential drug-repertoire has been scientifically screened. Hence, there is a real need for scientific evidence based validation of these agents.<sup>2</sup> The evaluation of plant products on the basis of medicinal and therapeutic properties forms a platform for the discovery of newer drug molecules from different plant sources. From the innumerable plants being researched since time immemorial, *Vitex negundo* is important one. This plant of Verbenaceae family is commonly known as Nirgundi (Hindi) and five leaved chaste tree (English). *Vitex negundo* L. (Sambhalu) is an aromatic large shrub or small slender tree of about 3 meter in height with quadrangular branches. It is found in moist area, often on banks of rivers, throughout India, up to an altitude of 1500 meter, also

grown in Mediterranean countries and Central Asia. Various medicinal properties are attributed to it particularly in the treatment of anti-inflammatory, fungal diseases, antioxidant and hepatoprotective disorders.<sup>3,4</sup>

*Vitex negundo*, commonly known as the five-leaved chaste tree (Fig.1, 2 and 3). Herbal remedies are a type of alternative medicine that originates from plants and plant extracts. Used to heal illnesses and disease and to address psychological concerns, herbal remedies have been around for centuries and were the precursor to modern medicine. Herbal remedies are obtained from a wide variety of natural resources including plant leaves, bark, berries, flowers and roots.

Herbal medicine remains a popular alternative throughout China and the Far East and is growing in popularity throughout the United States. Botanicals have been used traditionally by herbalists and indigenous healers worldwide for the prevention and treatment of liver disease. Clinical research in this century has confirmed the efficacy of several plants in the treatment of liver disease. Basic scientific research has uncovered the mechanisms by which some plants afford their therapeutic effects. In recent years many researchers have examined the effects of plants used traditionally by indigenous healers and herbalists to support liver function and treat diseases of the liver. In most cases, research has confirmed traditional experience and wisdom by discovering the mechanisms and modes of action of these plants as well as reaffirming the therapeutic effectiveness of certain plants or plant extracts in clinical studies.

### Taxonomic / Scientific Classification

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

### Vernacular Names

Telugu	: Vaavili
Tamil	: Nirkundi, Vellai-nochi
Hindi	: Shivari, Nirgundi
Malayalam	: Vellanoocchi, 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

### DISTRIBUTION

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

It is common throughout India from coastal belt to subtropical Western Himalayas and Andaman Islands, abundant in drier zones. It is particularly found in Karnataka and Tamilnadu (Wild as well as cultivated).

### MORPHOLOGY

A large shrub or sometimes a small slender tree; bark thin, grey; branchlets quadrangular, whitish with a fine tomentum. Leaves 3-5 foliate; leaflets lanceolate, acute, the terminal leaflet 5-10 by 1.6-3.2 cm. with a petiole 1-1.3 cm. long, the lateral leaflets smaller with a very short petiole, all nearly glabrous above, covered with a fine white tomentum beneath, base acute; common petioles 2.5-3.8 cm long.<sup>3-5</sup> Flowers in pedunculate branched tomentose cymes, opposite along the quadrangular tomentose rachis of a large terminal often compound pyramidal panicle (axillary peduncles in the upper axils sometimes present); bracts 1.5- 2.5 mm long, lanceolatecaduceus. Calyx 3 mm long, white tomentose; teeth triangular, 0.8- 1mm long. Ovary glabrous; style glabrous; stigma forked. Drupe less than 6 mm diameter, black when ripe.<sup>3, 5, 7, 8</sup>

The plant has pungent, bitter, acrid taste; heating, astringent, stomachic, anthelmintic; promotes the growth of hair; useful in disease of the eye, consumption, inflammation, leucoderma, enlargement of the spleen, bronchitis, asthma, biliousness, painful teething of children. The root is an antidote to snake venom. The root is considered tonic, febrifuge and expectorant,<sup>5,6,7</sup> otalgia, arthritis, dyspepsia, colic, rheumatism, leprosy, verminosis, flatulence, dysentery, urinary disorders, wounds, ulcers, bronchitis, cough, malarial fever, haemorrhoids, dysmenorrhoea,

leprosy, skin diseases and general debility. The plant is reported to have expectorant, carminative, digestive, anodyne, antiseptic, alterant, antipyretic, diuretic, emmenagogue, depurative, rejuvenating, ophthalmic, vulnerary and tonic.<sup>7</sup>

The leaves are aromatic, tonic and vermifuge.<sup>5,6</sup> A decoction of Nirgundi leaves is given with the addition of long pepper in catarrhal fever with heaviness of head and dullness of hearing. A pillow stuffed with the leaves of Nirgundi is placed under the head for relief of headache. The juice of the leaves is said to have the property of removing foetid discharges and worms from ulcers.<sup>3,5,6</sup> The flowers are useful in diarrhoea, cholera, fever, haemorrhages, hepatopathy and cardiac disorders. Leaves and bark are useful in scorpion stings, seeds are considered useful in eye diseases in form of *anjan*.<sup>7</sup>

Tincture of root bark in 1 to 2 dr. doses is recommended in cases of irritable bladder and of rheumatism. Powdered root is prescribed for piles as a demulcent for dysentery. Root is used in dyspepsia, colic, rheumatism, worms, boils and leprosy.<sup>3,6</sup>

The leaves are discutient and are useful in dispersing swelling of joints from acute rheumatism and of the testes from suppressed gonorrhoea. The dried fruit acts as a vermifuge.<sup>5,6</sup> Fruit is nervine, cephalic and emmenagogue; dried fruits acts as a vermifuge; flowers are cool and astringent.<sup>6</sup>

### Special Characters

Branchlets have prominent auxiliary spines and leaflets posses numerous minute glad dots. The fragrant white flowers contain many stamens. Fruits resemble wood apple. The tender shoots and leaves are quite brittle.

### Powder Characters

Grey to grayish-brown; thick-walled, angular cells of cork., numerous prismatic crystal of calcium oxalate, crystal fibres, starch grains simple, 5-19  $\mu$  India, mostly round to oval with certric hilum; compound starch grains having 2-3 components, fragments of xylem vessels with bordered pits and thick-walled xylem fibres.

### 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.

**Mode of Propagation:** By seeds and grafts.

### MEDICINAL USES

Roots, Bark, Leaves and fruits are highly medicinal. Roots are one of the ingredients of the drug Dasmula arista; used in colitis, dysentery, diarrhea, flatulence, fever, vomiting and colic.

**Roots and Barks:** Used for relieving intermittent fever, thirst and body pain.

**Leaves:** Used for treating ophthalmia, deafness, indigestion, piles and Jaundice, leaf juices are used in curing catarrh and fever. Tender fruits are bitter astringent, antilaxatives, digestion, promote digestion and strength, as well as overcome diarrhea and dysentery.

**Ripe Fruits:** Nutritious, cooling, used in treating indigestion and to improve vision.

**CHEMICAL CONSTITUENTS**

Leaves contain an alkaloid nishidine, flavonoids like flavones, luteolin-7-glucoside, casticin, iridoid glycoside, an essential oil and other constituents like vitamin-C, carotene, benzoic acid,  $\beta$ -sitosterol and C-glycoside (Hussain et al, 1992).

Seeds contain hydrocarbons,  $\beta$ -sitosterol, benzoic acid and phthalic acid (Hussain et al, 1992), anti inflammatory diterpene, flavonoids, artemisin, tri terpnoids (Chawla et al, 1991, 1992).

Stem bark yields leucoanthrocyanidins (Hussain et al, 1992; chopra et al, 1956).

N.K. Basu *et al.* (1944), G.S. Gupta *et al.* (1973) and V. Joshi *et al.* (1974), reported isolation of n-Tritriacontane, n-hentriacontanol, nhentricontane, n-pentatriacontane, n-nonacosane,  $\beta$ -sitosterol, phydroxybenzoic acid and 5-oxyisophthalic acid; 3, 4- dihydroxybenzoic acid was also isolated from the seeds of *Vitex negundo*.<sup>9,10,11</sup>

U.K. Rao (1977) reported isolation of friedelin, vitamin-C, carotene, casticin, artemetin from leaves.<sup>12</sup>

G.S. Misra & P.M. Subramanian (1980) isolated three new flavones glycosides which were identified as 3,6,7,3',4'-Pentamethoxy-5-Oglucopyranosyl- rhamnoside, vitexin cafeate, 4'-O-methyl myricetin- 3-O-[4''-O- $\beta$ -D-galactosyl]- $\beta$ -D-galactopyranoside.<sup>13</sup>

G. Gu *et al.* (1986) proved the presence of four lipids lionleic acid, oleic acid, stearic acid, palmitic acid in *Vitex negundo*.<sup>14</sup>

S. Li *et al.* (1987), S. Chandra *et al.* (1987), J. Banerji *et al.* (1988), P.T. Kosankar *et al.* (2000) reported from the leaves and twig of *Vitex negundo*, a stilbene derivative, characterised as 4,4'- dimethoxy-trans-stilbene, along with five flavones, 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 (gardenin A), 5-hydroxy-6,7,8,4'-tetramethoxy (gardenin B) and 5-hydroxy-7,3',4',5'-tetramethoxyflavone(corymbosin).<sup>15-18</sup>

Kuo-Chung *et al.* (1989), J. Leopold *et al.* (1998), A.K. Singh *et al.* (2004) and Song-Fa Wang *et al.* (2004) reported isolation of terpinen-4-ol,  $\alpha$ -terpineol, sabenine, globulol, spathulenol,  $\beta$ -farnesene, farnesol, bis (1,1dimethyl) methylphenol,  $\alpha$ -pinene,  $\beta$ - pinene, linalool, terpinyl acetate, caryophyllene epoxide, caryophyllenol along with viridiflorol.<sup>19-22</sup> Pradeep Singh *et al.* (2010) proved the presence of volatile oil which contains ten volatile components like  $\alpha$ -copaene,  $\beta$ -caryophyllene,  $\beta$ -elemene, camphene,  $\alpha$ -thujene,  $\alpha$ -pinene, sebinene, linalool, stearic acid and behenic acid.<sup>23</sup>

L. Sun (1989), J. X. Pan (1989), R Gopal Mallvarapu (1994), V. Singh (1999), R. Dayal (2000), reported isolation of  $\alpha$ -elemene,  $\delta$ - elemene,  $\beta$ -elemene,  $\beta$ -eudesmol, camphor, camphene, careen, 1,8- cineol, 1-oceten-3-ol,  $\gamma$ -terpinine,  $\alpha$ -phellendrene,  $\beta$ -phellendrene,  $\alpha$ - guaiene, abieta-7,13-diene, neral, geranial, bornyl acetate, nerolidol,  $\beta$ -bisabolol, cedrol.<sup>24-28</sup> Vitexicarpin was also isolated from leaves.<sup>22</sup>

S.K. Bhargava (1989) and R.S. Telang *et al.* (1999) isolated two flavones 5,7,3'-trihydroxyflavone, 6,8,4'-trimethoxyflavone.<sup>29,30</sup> A.S. Chawla *et al.* (1991) reported a flavonoid artemetin.<sup>31</sup>

A.S. Chawla *et al.* (1992) and D.S. Hebbalkar *et al.* (1992) reported triterpenoids 3 $\beta$ -acetoxylean-12-en-27-oic acid, 2 $\alpha$ ,3 $\alpha$ - dihydroxyoleana-5,12-dien-28-oic acid, 2 $\beta$ ,3 $\alpha$ - diacetoxyleana-5,12- dien-28-oic acid and 2 $\alpha$ ,3 $\beta$ - diacetoxylean-18-hydroxyoleana-5,12-dien- 28-oic acid.<sup>32,33</sup>

A.S. Chawla *et al.* (1992) and M. Ono *et al.* (2004) isolated a new phenyldihydronaphthalene-type lignan, vitedoin A, a new phenylnaphthalene-type lignan, vitedoamine A and a new trinorlabdane-type diterpene, vitedoin B from the seeds of *Vitex negundo* along with five known lignin derivatives. Their chemical structures were determined mainly on the basis of NMR and MS data.<sup>34,35</sup>

The studies of M. F. Dariyat *et al.* (1994), revealed a four iridoids in the pharmacologically-active fraction of the leaves of *Vitex negundo* L. which were identified as 2'-p-hydroxybenzoyl mussaenosidic acid, agnuside & lagundinin. The data obtained for 2'-phydroxybenzoyl mussaenosidic acid modifies a previous assignment while lagundinin is a newly identified iridoid. Three of the iridoids contain glucosyl and p-hydroxybenzoic acid moieties. In addition to the four iridoids which were reported, two other iridoids were known to occur in the leaves of *Vitex negundo*, aucubin and nishindaside.<sup>36</sup>

J.A. Rideout *et al.* (1999) from the chloroform extract of *Vitex negundo* leaves performed the structure elucidation of vitexilactone and casticin. This is first report on the isolation of vitexilactone from *Vitex negundo*, its structure elucidation by NMR. Casticin was earlier reported as a constituent of *V. negundo*.<sup>37</sup>

V. Krishna *et al.* (2002) isolated  $\beta$ -amyrin, epifriedelinol and oleanolic acid from the heartwood of *Vitex negundo*.<sup>38</sup>

V. Singh *et al.* (2003) isolated the twelve pure compounds, namely 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, agnuside and 2'-phydroxybenzoyl mussaenosidic acid and characterized by spectral data (UV, IR, NMR, & MS) from the different leaf extracts. Squalene is reported for the first time from the *V. negundo* leaves. This is the first report of the isolation of squalene from the leaves.<sup>39</sup>

F. Diaz *et al.* (2003), revealed the known flavones vitexicarpin, methylated, acetylated and six new acylated derivatives, identified as 3'-Benzoyloxy-5-hydroxy-3,6,7,4'-tetramethoxyflavone, 5,3'- Dibenzyloxy-3,6,7,4'-tetramethoxyflavone, 5,3'-Dipropanoyloxy- 3,6,7,4'-tetramethoxyflavone, 5,3'-Dibutanoyloxy-3,6,7,4'-tetramethoxyflavone, 5,3'-Dipent-4-enoyloxy -3,6,7,4'-tetramethoxyflavone, 5,3'-Dihexanoyloxy-3,6,7,4'-tetramethoxyflavone from the chloroform extract of the leaves of *Vitex negundo*.<sup>40</sup>

R. D. Manohar *et al.* (2003) proved the presence of two pentacyclic triterpenoids, betulinic acid (3 $\beta$ -hydroxylup-20-(29)-en-28-oic acid) and ursolic acid (2 $\beta$ -hydroxyurs-12-en-28-oic acid) from *Vitex negundo* leaves along with three other compounds; an aliphatic alcohol n-hentriacontanol, p-hydroxybenzoic acid.<sup>41</sup>

A. Haq *et al.* (2004), R. Dayal *et al.* (2004) from the root of *Vitex negundo* isolated Vitexoside a new flavonoid glycoside and agnuside, R-dalbergiphenol.<sup>42, 43</sup>

A. Malik *et al.* (2006) from the methanolic extracts of the roots isolated eight lignans, identified as negundin A, negundin B, 6- hydroxyl-4-(4-hydroxy-3-methoxy)-3-hydroxymethyl-7-methoxy- 3,4-dihydro-2-naphthaledehyde, vitrofolal E, (+)-lyoniresinol, (+)- lyoniresinol-3 $\alpha$ -O- $\beta$ -D-glucose, (+)-(-)-pinosresinol and (+)- diasyringaresinol.<sup>44</sup>

R. Maurya *et al.* (2007) from the ethanolic extract of the leaves of *Vitex negundo* resulted in the isolation of new

flavones glycoside along with five known compound and characterized as 4',5,7- trihydroxy-3'-O- $\beta$ -D-glucuronic acid-6''-methyl ester, a new naturally occurring compound named vitexoside.<sup>45</sup>

Vanillic acid, p-hydroxybenzoic acid and luteolin were isolated from bark; two new leucoanthocyanidins isolated from stem bark and their structures were determined as 6, 8-di-O-methylleucocyanidin-7 Orhamnoglucoside.

The roots contain a furanoeremophilane. The stem bark contains methyl esters of leucodelphinidin, and leucoanthocyanidins-7-Orhamno- glucoside and the flavonoids, 6-C-glycosyl-5-Orhamnopyranosyl trimethoxy wogonin and acerosin-5-glucoside monoacetate and also contains the flavonones, 6 $\beta$ -glucopyranosyl-7- hydroxy-3',4',5',8-tetramethoxyflavone-5-O- $\alpha$ -Lrhamnopyranoside; 3',7-dihydroxy-4',6,8 trimethoxy flavone-5-O- (6''-O-acetyl- $\beta$ -D-glucopyranoside);3,3',4',6,7-pentamethoxyflavone-5-O-(4''O- $\beta$ -D-glucopyranosyl)- $\alpha$ -Lrhamnopyranoside;4,5,7-trihydroxyflavone-8-(2''-caffeoyl- $\beta$  Dglucopyranoside; and 3,5,5,7-tetrahydroxy-4-methoxyflavone-3-O- (4''-O- $\beta$ -galactopyranosyl) galactopyranoside.

The leaves contain the iridoid glycosides, 2-p-hydroxybenzoyl mussaenosidic acid, 6'- p-hydroxybenzoylmussaenosidic acid, negundoside (C23H28O12), and nishindaside (C15H24O9). They also contain the isomeric flavanones, 5,3-dihydroxy-7,8,4-trimethoxy flavanone and 5,3-dihydroxy-6,7,4-trimethoxy flavanone.

Besides, they contain casticin and the glucosides, leutolin-7-glucoside (C21H20O11) and  $\alpha$ -D-glucoside of a tetrahydroxy monomethoxy flavone (C22H24O12, m.p. 2450). The leaves and twigs contain 5,3'-dihydroxy-6,7,4'-trimethoxy flavone (m.p.135-1360), 3',4',5,5',6,7,8-heptamethoxyflavone, 3-O-desmethyartemetin, 5-Odesmethylnobiletin. The seeds contain 5-oxyisophthalic acid and vitextriterpine (C30H50O8). Several anti-inflammatory substances have also been isolated from the seeds including the diterpene, 5 $\beta$ - hydro-8,11,13-abietatrien-6 $\alpha$ -ol; the triterpene, lanostan-8, 25-dien- 3 $\beta$ -ol; the triterpenoids, 3 $\beta$ -acetoxylean-12-en-27-oic acid, 2 $\alpha$ , 3 $\alpha$ -dihydroxyleana-5,12-dien-28-oic acid, 2 $\beta$ , 3 $\alpha$ -diacetoxyleana- 5,12-dien-28-oic acid and 2 $\alpha$ ,3 $\beta$ -diacetoxyleana-18-hydroxyleana-5,12- dien-28-oic acid (m.p. 205-2060); the Flavonoid, artemetin; and the lignan characterized as 6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)- 3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde (C20H20O6, m.p. 126-127).<sup>46-52</sup>

## PROPERTIES AND ACTION

Rasa : Madhura  
Guna : Laghu  
Virya : Sita  
Vipaka : Madhura  
Karma : Mutrala, Tridosaghna

## Important Formulation

Manasa Mitra Vataka, Amrtarista, Dantyadyarista, Agastya Haritak, Rasayana, Dasamularista, Dasamula Kwatha Churna, Bilvadi Letha. <sup>4</sup>

## Ayurvedic formulations

Vatavyadhi, Sotha, Sula, Agnimandya, Chardi, Mutrakreehra, Amavata.

## PHARMACOLOGICAL ACTIONS

### Analgesic Activity

Ravishankar et al (1985, 1986) found that interperitoneal administration of some leaf and root extracts using different solvents showed analgesic activity.

M.G. Dharmasiri *et al.* (2003) evaluated analgesic activity from the aqueous extract of fresh leaves of *Vitex negundo* in female Wistar rats using hot plate, tail flick and formalin tests. The standard drug used in hot plate and tail flick was aspirin (100 mg/kg).<sup>66</sup>

### Anti-inflammatory Activity and Anti arthritic Activity

The experimental studies using various animal models have demonstrated that different parts of plant especially leaves, fruits, roots and seeds possess anti-inflammatory and anti arthritic activity (Chaturvedi & Singh, 1965; ravishankar et al, 1985, 1986; Chawla et al, 1991, 1992; Tamhankar & Saraf, 1994; Jana et al, 1999).

A.S. Chawla *et al.* (1992) investigated anti-inflammatory activity of chloroform extract of seeds of *Vitex negundo* in Sprague-Dawley male rats in carrageenan induced rat paw edema using Ibuprofen as standard drug.<sup>32</sup> U.K. Rao *et al.* (1977), M.B. Ahmad *et al.* (1989), A.S. Chawla *et al.* (1991), & E. Nylogira *et al.* (2004) reported anti-inflammatory activity of bark, seeds, seed oil and essential oil of *Vitex negundo*.<sup>12, 64, 31, 62</sup> U. Jana *et al.* (1999) reported preliminary anti-inflammatory activity of *Vitex negundo* in albino rats along with *Zingiber officinale* and *Tinospora cordifolia*.<sup>65</sup>

M.G. Dharmasiri *et al.* (2003) investigated anti-inflammatory activity from the aqueous extract of *Vitex negundo* leaves in Wistar rats (male) using carrageenan-induced & formaldehyde-induced rat paw oedema using indomethacin as standard. The early phase of carrageenan-induced rat paw oedema was significantly suppressed in an inversely dose-dependent manner.<sup>66</sup>

R.K. Gupta *et al.* (2006) reported anti-inflammatory activity from the ethanolic extract of *Vitex negundo* leaves in albino rats (of either sex) using carrageenan-induced rat paw oedema and cotton pellet granuloma models using phenylbutazone (10-100 mg) and ibuprofen (10-200 mg) as standards.<sup>67</sup> Pradeep Singh *et al.* (2009) reported anti-inflammatory activity of ethanolic extract of roots.

### Antihyperpigmentation Activity

A. Malik *et al.* (2006) investigated tyrosinase inhibitory potential of lignans isolated from the methanolic extract of *Vitex negundo* roots using SpectraMax 340 microplate reader.<sup>44</sup>

### Immuno-stimulant Activity;

D.D. Singh *et al.* (2005) reported immunostimulatory activity from the extracts of *Vitex negundo* in oxyburst phagocytic assay using human polymorph nuclear cells.<sup>68</sup> J.L. Suri *et al.* reported immunostimulatory potential of two iridoid glucosoides from *Vitex negundo* leaves.<sup>69</sup>

### Hepatoprotective Activity

A. Prabhakar *et al.* investigated hepatoprotective activity of Negundoside & agundoside from *Vitex negundo*. Both compounds were used in combination with one or more pharmaceutical additives which prevent and treat hepatic diseases.<sup>46,47</sup>

### CNS Activity:

M. Gupta *et al.* (1997 & 1999) evaluated CNS activity & anticonvulsant activities of petroleum ether & methanolic extracts of *Vitex negundo* in mice.<sup>74,75</sup>

### Anti-androgenic Activity

S.K. Bhargava (1984, 1986) & R.P. Samy *et al.* (1998) reported antiandrogenic activity of various flavonoids from the seeds of *Vitexnegundo*. The flavonoids which shows estrogenic properties as well as anti-implantation activities are 5, 7, 3'-trihydroxy and 6, 8, 4'-trihydroxy flavones.<sup>76-80</sup>

### Enzyme Inhibition Activity

A.Haq *et al.* (2004) reported anti- lipoxigenase and anti - butyrylcholinesterase potential of two lignans Negundin B and Vitrofolal F.<sup>81</sup>

### Mosquito repellent Activity

P.K. Amancharla *et al.* (1999) tested mosquito repellent activity of aqueous extract of *Vitex negundo* leaves. A new chemical 'rotundial' was tested for the said activity.<sup>82</sup>

### Anticonvulsant Activity

The petroleum and butanol leaf extract have shown protection, whereas, none of root extract has shown protection against maximal electroshock (MES) seizures. Petroleum root extract could only provide protection against Leptazole induced convulsions (Ravihnkar *et al.*, 1985, 1986)<sup>83-88</sup> whereas methanolic leaf extract showed significant protection against Strychnine and Leptazole induced convulsions (Gupta *et al.*, 1999)<sup>75</sup>.

### Antioxidant Activity

G. Zheng *et al.* (1999) & G. Zheng and Z. Luo (1999), M. Onu *et al.* (2004) reported antioxidant potential of Vitodoin A, Vitodoin B and other lignans derivatives from the seeds of *Vitex negundo*.<sup>70, 71, 35</sup> V. Tondon & R.K. Gupta (2005) reported anti-oxidant effect of Vitexin which is a new compound.<sup>72</sup>

O.P. Tiwari & Y.B. Tripathi (2007) evaluated antioxidant property of different fractions of *Vitex negundo* by employing various invitro systems, such as 2, 2'-azino-bis-3-ethyl benzothiazoline-6-sulfuric acid (ABTS), Lipid peroxides (LPO), Superoxide, Hydroxyl radical scavenging and iron chelation. Total antioxidant capacity was determined by the assay based on the performed radical monocation ABTS. LPO was assessed in terms of thiobarbituric acid reactive substances by using egg yolk homogenates as lipid rich media.<sup>73</sup>

### Insecticidal and Pesticidal Activities

The plant products of *V.negundo* are variously reported to possess insecticidal activity against stored product pests, mosquito larvae, house flies and tobacco leaf eating larvae. Leaf oil of the plant is shown to have repellent action against stored product pests (Deshmukh *et al.*, 1982; Prakash & Mathur, 1985; Hebbalkar *et al.*, 1992).

### TOXICITY

Preliminary acute toxicity study of ethanolic leaf extract in albino rats by oral route carried out by Tandon and Gupta (2004) indicated it to be practically nontoxic, as its LD<sub>50</sub> dose recorded was 7.5 g/kg/wt. The stomach showed no histomorphological changes in any of the doses of the

extract studied. However, dose dependent histomorphological changes were observed in the specimens of the heart, liver and lung.<sup>72</sup>

### RECOMMENDED DOSAGE

Almost all its parts like leaves, roots, bark, fruits, flowers and seeds are employed for medicinal purpose and can be used medicinally in the form of powder, decoction, juice, oil, tincture, sugar/water/honey paste, dry extract. Doses recommended, in adults are :juice 10-20ml; decoction, 50-100ml; leaves powder, 1.5-3g; dry leaves extract, 300-600mg (Chaundhary, 1996).

### CONCLUSION

*V. negundo* possesses numerous biological activities proved by many experimental studies. It represents a class of herbal drug with very strong conceptual base for its use. Thus, this plant has great potential to be developed as a drug by pharmaceutical industries, but before it recommending it for clinical use in these conditions, there is a need to conduct clinical trials and prove its clinical utility.

Medicinal plants, which are the backbone of traditional medicine, have in the last few decade been the subject for very intense pharmacological studies; the value of medicinal plants as potential sources of new compounds of therapeutics value and as sources of lead compounds in the drug development. There arises a need therefore to screen medicinal plants for bioactive compounds as a basis for further pharmacological studies. According to the thorough study of the available literature it is quite obvious that the importance of Nirgundi in traditional system of medicine is of utmost significance. Almost all parts of the plant are use in preparing herbal medicines. The plant is known to possess anticancer, antimicrobial, antifeedant, anti-inflammatory, antihyperpigmentation, hepatoprotective, antihistaminic, analgesic and related activities. Scientifically explored exhaustive reports of the plant, their medicinal properties and active chemical constituents have a role in the management of various human ailments. This review attempts to encompass the available literature on *Vitex negundo* with respect to its traditional uses, chemical constituents and summary of its various pharmacological activities.



Fig.1-*Vitex negundo*: Stem with leaves





**Fig.2- *Vitex negundo*:** Flowers with buds.



**Fig.3 - Five-leaved chaste tree**

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