ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

REVIEW ARTICLE

A REVIEW OF ETHNOMEDICINAL PLANT-*Vitex negundo* Linn

*** Fauziya Basri, H.P. Sharma, Sazya Firdaus, Paras Jain and Alok Ranjan**
Laboratrory of Plant Physilogy and Biotechnology
University Department of Botany, Ranchi University, Ranchi-834008, India

Manuscript Info

Manuscript History:

Received: 12 January 2014
Final Accepted: 23 February 2014
Published Online: March 2014

Key words:
Vitex negundo, traditional medicine, pharmacology, phytochemicals, anticancer.

Corresponding Author

Fauziya Basri
fauziyabasri@gmail.com

Abstract

Vitex negundo belongs to family Verbenaceae and grows as small tree with thin grey bark. The plant is widely distributed and also has pharmacological actions against wide spectrum of diseases in traditional system of medicines. All parts of the plant especially its leaves contain numbers of secondary metabolites such as alkaloids, phenols, flavonoids, glycosidic irridoids, tannins and terpenes. Because of the richness in phytochemicals, the plant is attributed to possess a number of therapeutic uses; antimicrobial, anti-inflammatory, astringent, bronchodilator, CNS-depressant, detoxicant, diuretic, emmenagogue, anticancer and hepatoprotective etc. It is also used as repellent, insecticide and larvicidal. Leaf extract is employed as nervine tonic, tranquilizer and vermifuge. This review aims at presenting a comprehensive information on phytochemical constituents and therapeutic uses which can be helpful in development of modern medicine.

Introduction

Majority of population across the globe depends on traditional remedies against a large repertoire of diseases. Traditional medicine is not known to cause any notable derogatory effects and are readily available at affordable prices (Kirtikar *et. al.*,1984). Majority of the traditional medicines used in healthcare are obtained from plants. *Vitex negundo* Linn. (Verbenaceae), locally known as 'Nirgundi/ Sindhvar' is an important medicinal plant and is used for treatment of a wide spectrum of health disorders in traditional and folk medicine; some of which have been experimentally validated. It is widely planted as a hedge plant along the roads. Traditionally it is reported to have multifarious activities such as analgesic, anti-inflammatory, antioxidant, insecticidal, antimicrobial, anticancer, galactogogue, tonic, febrifuge, expectorant and diuretic properties.

Classification

Kingdom - Plantae
Order - Lamilales
Family - Verbenaceae
Genus - *Vitex*
Species - *Vitex negundo* L.

Fig.1: Plant of *Vitex negundo*; A- plant with leaves showing palm like structure, B- plant in flowering stage

Botanical description

Vitex negundo is a woody, aromatic deciduous shrub growing to a small tree. *Vitex negundo* is also known as the five-leafed chaste tree or monk's pepper. Its most striking feature centers on a cluster of five pointed leaves resembling a palm (fig. 1A). It is an erect, 2-5 m in height, slender tree with quadrangular branchlets. The leaves have five leaflets palmately arranged, which are lanceolate, acute, glabarous, 4-10 cm long, hairy beneath and pointed at both ends**.**The terminal leaflet has a long petiole whereas, the lateral ones have short petiole. Flowers are bluish purple in colour borne on axillary or terminal panicle upto 30 cm long (fig 2A). The fruit is succulent globose, and black when ripe with four seeds, rounded and about 4 mm in diameter (Meena *et. al.*, 2011).

Habitat

It thrives in humid places or along water courses in wastelands and mixed open forests and has been reported to occur in India, Pakistan, Afghanistan, Sri Lanka, Thailand, Malaysia, eastern Africa and Madagascar. It is grown commercially as a crop in parts of Asia, Europe, North America and West Indies. It is used as a food crop and also as a source of timber. A large aromatic shrub, the plant is distributed throughout the greater part of India up to an altitude of 1500 m in the outer Himalayas (Khare, 2004**)**.

Traditional medicinal uses

Use of *Vitex negundo* has been reported in Charaka Samhita, the most ancient and authorative text book of Ayurveda, Unani and in Chinese traditional medicine systems. Different parts of the plant have varied uses: **Leaf**- anti-inflammatory, analgesic, removes foetid discharges and worms from ulcers, analgesic, antihistaminic property, snake venom neutralizing capacity, hepatoprotective and CNS depressant activities (Muthuswamy *et. al.*, 2012); **Flowers**- astringent, febrifuge, anti diarrhoeic; prescribed in liver complaint; **Oi**l- applied to sinus, scrofulous sores; **Fruits** -nervine stimulant, emmenagogue and vermifuge; **Seed**- antitoxin; **Root**- tonic, febrifuge, expectorant and diuretic; **whole plant**- galactagogue, emenagogue, antigastalgic, antiflatulant, antiparasitic and analgesic.(Arora *et. al.*, 2011)

Vitex negundo is a component of a number of commercially available herbal formulations and has also shown potential as an effective bio-control agent. Various therapeutic uses have been enlisted in Table 1 that emphasizes on its multiple uses across various countries.

Table 1 – Uses of V. negundo in folk medicine

Used in	Plant part used	Country	References
Gastrointestinal disorders Diarrhoea	Flowers	India, Pakistan	Shaukat *et. al.*,2009 Warrier *et. al.*, 2002
Dysentary	Powdered roots Tincture from roots and bark		
Flatulence/ Irritable bladder	Whole plant as antiflatulent Tincture from roots and bark		
Dyspepsia	Powdered roots		
Cholera	Flowers		
Colic	Powdered roots		
Headache	Crushed leaf poultice Leaf is smoked Pillow stuffed with leaves	Bangladesh India Malaysia	Khan *et. al.*,2006 Avadhoot *et. al.*,1991 Ong.,2008
Eye disease/ Cataract/ Watery eyes	Fruits Pillow stuffed with leaves Leaf decoction improves eye sight	Sri Lanka, India	Kirtikar *et. al.*, 1984 Jain *et. al.*, 1984
Respiratory disorders Cough	Used as expectorant Root decoction Leaf juice	China, India	Au *et. al.*, 2008 Muthu *et. al.*,2006 Rajadurai *et. al.*, 2009
Common cold, Flu, Sore Throat	Leaf juice	China	Au *et. al.*, 2008
Whooping cough	Leaf	Nepal	Joshi *et. al.*, 2000
Bronchitis	Root decoction	India	Ivan, A.R. ,2005
Asthma	Root decoction	India	Basavaraju *et. al.*, 2009
Sinusitis	Essential oils from leaf, crushed leaf poultice	Nepal	Joshi *et. al.*, 2000

Gynaecological disorders Dysmenorrhoea Gonorrhoea Dysfunctional uterine	Leaf and shoot juice, whole plant	Malaysia	Tandon *et. al.*, 2008 Tasduq *et. al.*, 2008
Galactogogue	Shoot juice, fruits	Malaysia, India	
Post partum bath and recovery	Leaf boiled in water	Malaysia India	
Skin diseases Eczema, Carbuncles, Abscesses Leprosy	Powdered roots Essential oils from leaves	India	Saikia *et. al.*, 2006
Burns	Stem decoction	India	Ladda *et. al.*, 2012
Rheumatism	Powdered root, Tincture from root and bark, fresh leaf juice	Sri lanka	Kirtikar *et. al.*, 1984
Cancer	Stem bearing flowers, Leaves	Philippines, India	Graham *et. al.*,2000 Basavaraju *et. al.*, 2009
Gout	Fresh leaf juice	China	Woradulayapinij *et. al.*, 2005
Jaundice/ liver disorders	Flowers	India	Pattanaik *et. al.*, 2008
Malaria	Roots, Whole plant	Bangladesh	Khan *et. al.*,2006
Catarrhal fever	Leaf decoction with long pepper	Bangladesh	Khan *et. al.*,2006 Ladda *et. al.*, 2012
Wounds and ulcers	Used as febrifuge leaf decoction, roots		Kirtikar *et. al.*, 1984
Dentistry	Used as tooth brush, Leaf decoction	India, Sri lanka, Pakistan	Hamayun., 2005 Jabeen *et. al.*, 2009
As Diuretic	Roots, Leaf juice	India	Arora *et. al.*, 2011
As Astringent	Flowers, Leaves		Arora *et. al.*, 2011
As Tonic	Roots, leaves,flowers	India	Arora *et. al.*, 2011
Anti allergic	Leaves	Pakistan	Zabihullah *et. al.*,2006

Backache, Chest pain, Bodyache	Used as analgesic gaqueous extract of leaves and fruits	India,China, Pakistan	Hamayun., 2005
Swellings	Aqueous extract of leaves, Plaster of crushed leaves Oral administration of seeds with sugar cane vinegar	India	Chawla *et. al.*, 1992
Antitoxin	Aqueous extract prevents spreading of toxin Leaf and bark used agains Scorpion sting Roots as antidote for snake venom	India	Samy *et. al.*, 2008
Antifeedant, Fumigant, Insecticide	Dried leaves and Leaf extract Fresh leaves burnt with grass acts as mosquitoe repellent	India	Ladda *et. al.*, 2012 Pushpalatha *et. al.*,1995

Phytochemistry

The plant is rich in large number of secondary metabolites. The presence of some of these phytochemicals in different extracts have been shown in table 2 and structure of some specific ones have been depicted in figure 2.

Table 2: Preliminary Phytochemical analysis of various extracts of *V. negundo* (Sahayaraj *et. al.*, 2008)

Secondary metabolite	**Choloroform extract**	**Benzene extract**	**Water extract**
Steroids	+	+	-
Triterpenoids	+	+	-
Carbohydrates	+	+	+
Alkaloids	-	-	+
Phenolic compounds	+	-	+
Saponins	+	+	+
Xantho proteins	-	-	+
Tannins	+	-	+
Flavonoids	+	+	+

+ indicates present and – indicates absence

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

Seeds - 3β -acetoxyolean-12-en-27-oic acid; 2α, 3α-dihydroxyoleana-5,12-dien-28-oic acid; 2β,3α diacetoxyoleana-5,12-dien-28-oic acid; 2α, 3β-diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid; vitedoin-A; vitedoin-B; a phenylnaphthalene-type lignan alkaloid, vitedoamine-A; β-sitosterol; p-hydroxybenzoic acid; 5-oxyisophthalic acid; n-tritriacontane, n-hentriacontane; n-pentatriacontane; n-nonacosane ; 6-hydroxy-4-(4-hydroxy-3- methoxy-phenyl)-3-hydroxymethyl-7-methoxy-3, 4-dihydro-2-naphthaldehyde

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

Roots - 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 , negundin-A; negundin-B; (+)-diasyringaresinol; (+)-lyoniresinol; vitrofolal-E and vitrofolal-F ,acetyl oleanolic acid; sitosterol.

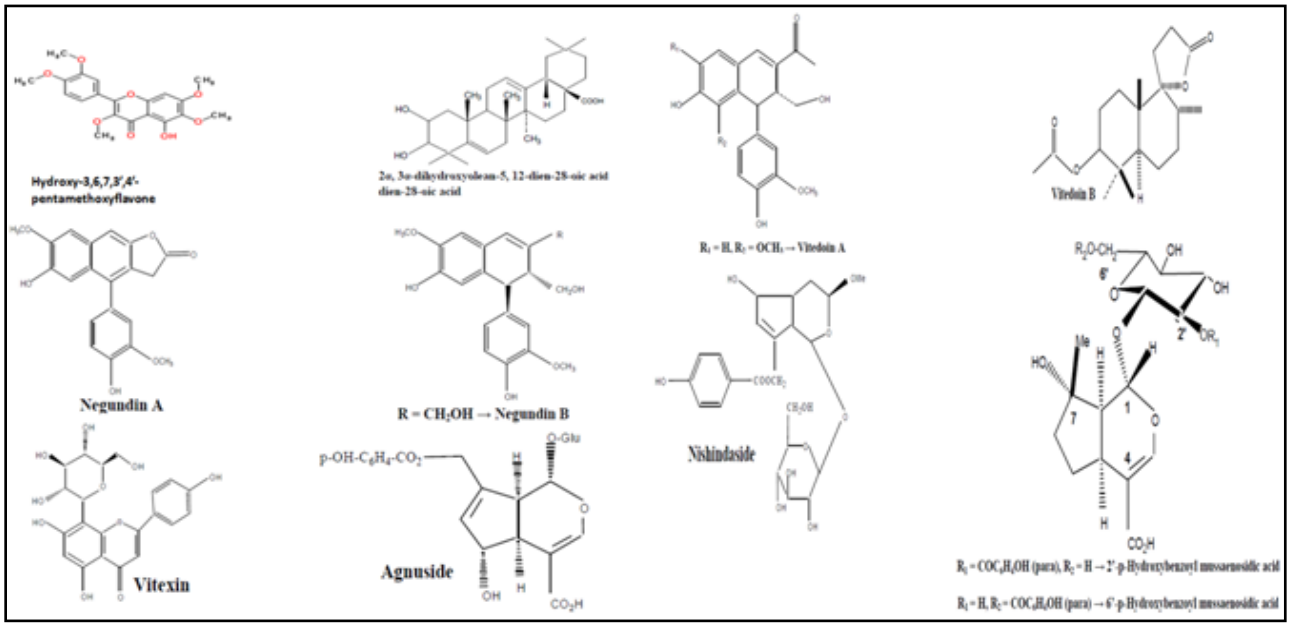

Fig. 2: Structure of some important bioactive compounds from *Vitex negundo*

Pharmacological Evidence

It has been estimated that 14-28% of higher plant species are used medicinally and that 74% of pharmacologically active plant derived components were discovered after follow up on ethno medicinal use of the plants (Das *et. al.*, 2010). In recent years, secondary plant metabolites (phytochemical) have been extensively investigated as a source of medicinal agents.

All parts of *Vitex negundo*, from root to fruits, possess a multitude of phytochemicals as secondary metabolites which impart a variety of medicinal uses to the plant. Demands of the scientific community have necessitated experimental evidence to further underline the medicinal importance of *Vitex negundo*. Taking cue from these traditional and folk systems of medicine, scientific studies have been designed and conducted in order to validate pharmacological claims.

Antimicrobial activity

The antimicrobial activity of the plant extract is strengthened in the presence of antioxidant compounds (Ricardo *et. al.*,2011).It has been suggested that the antimicrobial activity of the plant is mainly due to the presence of essential oils, flavonoids, terpenoids, alkaloids, tanins, saponins and other natural polyphenolic compounds or free hydroxyl groups in plant extracts (Ramkumar *et. al.* 2004; Soetan, 2006). Presence of flavonoids, terpenoids and tannins in *Vitex negundo* have been detected in various studies (Panda *et. al.*,2009).

Beside its antimicrobial property it is also reported for its larvicidal, repellent and pesticidal activities. Importantly it is considered to be good pesticide as it is required in very small amounts and safe specifically to mammals. Recently attention and interest have followed on bioinsecticides and biopesticide for Integrated Pest Management (IPM) strategies (Rosell et al., 2008). An aqueous extract of its leaves was found to have toxic effects on lepidoterans such as on ground nut pests *Spodoptera litura* and *Helicoverpa armigera*. The extracts at higher doses act as antifeedant, while the lower dilution of the same plant is oral toxicant (Sahayaraj., 2011). Its activity against various pest and microbes have been summarized in Table 2.

Table 3: Effect of *Vitex negundo* Linn. on Different Pathogens and Pests (Viswanathan *et. al.*, 2010)

Sl. No.	ACTIVITY	ACTION AGAINST	References
1.	Anti-bacterial	*Escherichia coli, Klebsiella aerogenes, Proteus vulgaris and Pseudomonas aerogenes* (Bacteria)	Samy *et. al.*, 1998
2.	Anti- feedant	*Spodoptera litura* (Asian army-worm), *Achoea janata* (Castor semi-looper)	Sahayaraj., 2008
3.	Anti-filarial	*Brugia malayi* (Microfilarial parasite)	Sahare., 2008
4.	Anti-fungal	*Alternaria alternata, Curvularia lunata Trichophyton entagrophytes, Cryptococcus neoformans, Aspergillus niger, Candida albicans*	Guleria *et. al.*, 2006 Sathiamoorthy *et. al.*,2007 Aswar *et. al.*,2009
6.	Insecticidal	*Callosobruchus maculatus* (Pulse beetle) *Phthorimaea operculella* (Potato-tuber moth) *Sitotroga cerealella* (Angoumois grain moth) *Aphis citricola* (Spirea aphid*), Aphis gossypii* (Melon or Cotton aphid), *Myzus persicae* (Green peach aphid)	Paneru *et. al.*,2001 Das., 1995 Rajendran *et. al.*, 2008 En-shun *et. al.*, 2009
7.	Larvicidal	*Anopheles subpictus, Culex tritaeniorhynchus* (Mosquitoes) *Culex quinquefasciatus* (Mosquito) *Anopheles stephensi* (Mosquito) *Plutella xylostella* (Diamond-back moth) *Cnaphalocrocis medinalis* (Rice leaf-folder) ,*Plasmodium falciparum*	Kamaraj *et. al.*, 2008 Karmegam *et. al.*,1997 Kannathasan *et. al.*, ,2007 Rahuman et al., 2009 Nathan *et. al.*, 2006
8.	Mosquito repellent	*Culex tritaeniorhynchus, Aedes aegypti* (Mosquito)	Karunamoorthi, K.,2008 Hebbalkar *et. al.*,1992

Anti-inflammatory and Analgesic activity

Anti-inflammatory refers to the property of a substance or treatment that reduces inflammation. Anti-inflammatory drugs make about half of analgesics, alleviate pain by reducing inflammation as opposed to opioids, which affect the central nervous system. The anti-inflammatory property of *Vitex negundo* has been validated by clinical trials on rat. It has been confirmed that leaf extract prevents carrageenan-induced rat paw edema and formaldehyde-induced rat paw edema (Jana *et. al.*, 1999). Anti-inflammatory properties of *Vitex negundo* extracts in acute and sub-acute inflammation is also reported. The anti inflammatory activity of the plant have been extensively studied by several workers (Sharma et.al.,1980; Telang *et. al.*,1999). This activity has been attributed to prostaglandin synthesis inhibition, antihistamine and antioxidant activities of the plant (Dharmasiri *et. al.*,2003).The anti-inflammatory properties of the plant have been extensively investigated, while studies relating to its psychopharmacological and especially dopaminergic properties of this plant needs to be done.

Anti-oxidant activity

Anti-oxidants are substances capable for neutralizing free radicals and prevent them from causing cell damage and health related problems such as cancer, aging, heart diseases and gastric problems etc (Sen *et. al.*, 2010) .

Vitex negundo is a source of natural antioxidants (Rabeta *et. al.*, 2013). Vitedoin A, one of the phytochemical present in the plant acts as a strong antioxidant (Ono *et. al.*, 2004). Its antioxidant activity is reported to be even more than that of vitamin E and L-cysteine .

The anti-oxidant potential of leaf extracts of *Vitex negundo* has also been validated by various methods. The extracts were useful in decreasing levels of superoxide dismutase, catalase and glutathione peroxidase in Freund's adjuvant induced arthritic-rat (Devi *et. al.*, 2007). The extracts also possess the ability to combat oxidative stress by reducing lipid peroxidation owing to the presence of flavanones, vitamin C and carotene (Vishal *et. al.*, 2005).

Antioxidant effects of plant extracts are mainly due to the presence of phenolic compounds such as flavonoids, phenolic acids, tannins and phenolic diterpenes (Preethi *et. al.*, 2010).They are safe to be consumed by human and animal (Chew *et. al.*, 2009). Flavonoids in particular have been shown to have potent antioxidant and have free radical scavengering activity (Narayana *et. al.*, 2001).

This plant also contains a number of polyphenolic compounds, terpenoids, glycosidic irridoids and alkaloids. A study done by Tiwari and Tripathi (2006) has shown that all fraction of *Vitex negundo* have potent scavenging activity for ABTS radical cation in a dose dependent manner (Tiwari *et. al.*, 2006). *Vitex negundo* extracts also exhibits scavenging activity towards DPPH radicals. The property may be attributed to the existence of polyphenols and flavonols in *Vitex negundo* (Rabeta *et. al.*, 2013).

Enzyme-inhibitory activity

The plant possess inhibitory action against a number of enzymes. Root extracts of *Vitex negundo* showed inhibitory activity against enzymes such as lipoxygenase and butyryl-cholinesterase (Azhar-Ul-Haq *et. al.*, 2004); α-chymotrypsin (Lodhi *et. al.*, 2008); xanthine-oxidase (Umamaheswari et, al., 2007) and tyrosinase (Azhar-Ul-Haq *et. al.*, 2004). Tyrosinase inhibitory lignins have been found in the methanolic extract of the roots of *Vitex negundo* (Mary *et. al.*, 2006).The HIV type 1 reverse transcriptase inhibitory activity of the water extract of the aerial parts of *Vitex negundo* is also reported by some researchers (Tandon *et. al.*, 2005) .

Effect on reproductive potential

The flavonoid rich fraction of seeds of *Vitex negundo* caused disruption of the later stages of spermatogenesis in dogs (Bhargava, 1989) and interfered with male reproductive function in rats (Das *et. al.*, 2004). As such the plant is said to have anti androgenic properties. It must however be noted that these findings are in sharp contrast with the traditional use of *Vitex negundo* as aphrodisiac (Khare, 2004). Ethanolic extracts of *Vitex negundo* showed estrogen-like activity so it can be used in hormone replacement therapy (Hu *et. al.*, 2007).

Anti cancer activity

Studies on histomorphological effect of *Vitex negundo* extracts in rats showed that stomach tissue remain unaffected even by toxic doses (Tandon *et. al.*, 2004), while dose-dependent changes were observed in the heart, liver and lung tissues. Cytotoxic effect of leaf extracts of *Vitex negundo* was tested and affirmed using COLO-320 tumour cells (Smit *et. al.*, 1995). It has been reported by Diaz *et. al.* (2003) that the chloroform extracts of leaves is toxic to human cancer cell line panel. On the contrary Yunos *et . al. (*2005) reported that the plant extracts were non-cytotoxic on mammary and genito-urinary cells of mice.

Drug potentiating ability

Administration of *Vitex negundo* extracts is reported to enhance the effect of commonly used anti-inflammatory drugs, such as ibuprofen and phenylbutazone (Tandon *et. al.*, 2006); analgesics such as meperidine, aspirin (Gupta *et. al.*, 2005); morphine and pethidine; sedative-hypnotic drugs, like pentobarbitone, diazepam (Gupta *et. al.*, 1997) and chlorpromazine (Gupta *et. al.*, 1999); anti-convulsive agents, such as diphenylhydantoin and valporic acid (Tandon *et. al.*, 2005).

Anticonvulsant activity

The petroleum ether and butanol leaf extract have shown protection against electro shock seizures, whereas root extract has shown little effect. Petroleum ether extract of root could only provide protection against leptazole induced convultions, whereas methanolic leaf extract showed significant protection against both strychnine and leptazole induced convultions (Tandon *et. al.*, 2005). Ethanolic extract of leaf shows not only anticonvulsant activity but also can potentiate the effects of 10 standard anticonvulsants, which may help to reduce dose and dose related side effects of standard anticonvulsants (Mahalakshmi *et. al.*,2010).

Hepatoprotective activity

In addition to the above mentioned activities *Vitex negundo* extracts have also been tested for a range of other systemic effects. Negundoside and Agundoside from *Vitex negundo* have been studied for their hepatoprotective activity. Extract of *Vitex negundo* is reported to decreases 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 against liver damage induced by d-galactosamine(Yang *et. al.*, 1987), commonly used tubercular drugs and carbon tetrachloride (Tandon *et. al.*,2008) .

Other activities

The aqueous extract of the plant is reported for its laxative effect (Tasduq *et. al.*, 2008). Anti-histaminic activity of the plant against histamine release from mast cells has also been validated : the leaf extract have potential hypoglycemic activity mediated by inhibition of alpha-amylase (Devani *et. al.*, 2013). The CNS depressant activity of leaf extract has also been confirmed (Gupta *et. al.*,1997). It potentiate the sleeping time induced by pentobarbitone sodium, diazepam and chlorpromazine in mice. Methanolic root extracts of *Vitex negundo* showed antagonization of the lethal activity induced by venom of *Vipera russellii* and *Naja kaouthia* (Alam *et. al.*, 2003).

Conclusion

Vitex negundo is one of the very important plants which have wide applications in traditional systems of medicines. All parts of the plant, from root to fruits, possess a multitude of phytochemicals as secondary metabolites; nishindaside, mussaenosidic acids, vitedoin, negundin and vitexin are some important bioactive agents which impart a variety of medicinal uses to the plant. It is highly hepatoprotective, anticonvulsant and also anticancer.

Besides its therapeutic properties it is also reported to have larvicidal, repellent and pesticidal activities. However, different phytochemicals from the plant has been isolated and studied for their pharmacological activities but still trials are required at pre-clinical and clinical levels before drug designing.

References

1. **Alam, M.I. and Gomes, A. (2003)**: Snake venom neutralization by Indian medicinal plants (*Vitex negundo* and *Emblica officinalis*) root extracts. Journal of Ethnopharmacology. 86: 75-80.
2. **Arora, V., Lohar, V., Singhal, S.and Bhandari, A. (2011)**: *Vitex negundo* - A Chinese Chaste Tree. International Journal of Pharmaceutical Innovations., 1(5): 9- 20.
3. **Aswar, P.B., Khadabadi, S.S., Kuchekar, B.S., Rajurkar, R.M., Saboo, S.S. and Javarkar, R.D. (2009)**: In vitro evaluation of anti-bacterial and anti-fungal activity of *Vitex negundo* (Verbenaceae). Ethnobotanical Leaflets. 13: 962-967.
4. **Au, D.T., Wu, J., Jiang, Z., Chen, H., Lu, G. and Zhao, Z. (2008)**:Ethnobotanical study of medicinal plants used by Hakka in Guangdong, China. Journal of Ethnopharmacology. 117 : 41-50.
5. **Avadhoot, Y. and Rana, A.C. (1991)**: Hepatoprotective effect of *Vitex negundo* against carbon tetrachloride induced liver damage. Arch. Pharm. Res. 14(1): 96-98.

6. **Azhar-Ul-Haq, Malik, A., Anis, I., Khan, S.B., Ahmed, E., Ahmed, Z., Nawaz, S.A. and Choudhary, M.I. (2004)**: Enzyme inhibiting lignans from *Vitex negundo*. Chemical and Pharmaceutical Bulletin. 52: 1269-1272.
7. **Basavaraju, R., Vennel Raj, J. and Bhiravamurthy, P.V. (2009)**: Medicinal plant resources of Puttaparthi mandal- Taxonomic overview and need for conservation. Ethnobotanical Leaflets. 13:1382-1400.
8. **Bhargava, S. (1989)**: Antiandrogenic effects of a flavonoid-rich fraction of *Vitex negundo* seeds: A histological and biochemical study in dogs. Journal of Ethnopharmacology. 27:327-339.
9. **Chawla, A.S., Sharma, A.K. and Handa, S.S. (1992)**: Chemical investigation and inflammatory activity of *Vitex negundo* seeds. Jour. Nat. Prod.55 (2): 163-167 .
10. **Chew, Y.L., Goh, J.K. and Lim, Y.Y.(2009)**: Assessment of *in vitro* antioxidant capacity and polyphenolic composition of selected medicinal herbs from Leguminosae family in Peninsular Malaysia. Food Chemistry. 116: 13-18.
11. **Das, G.P. (1995)**: Plants used in controlling the potato tuber moth, *Phthorimaea operculella* (Zeller). Crop Protection. 14: 631-636.
12. **Das, S., Parveen, S., Kundra, C.P. and Pereira, B.M. (2004)**: Reproduction in male rats is vulnerable to treatment with the flavonoid-rich seed extracts of *Vitex negundo*. Phytother Res.18(1): 8-13.
13. **Das, K., Tiwari, R.K.S. and Shrivastava, D.K.(2010)**: Techniques for evaluation of medicinal plant products as antimicrobial agent. Current methods and future trends. J Med Plant Res. 4(2):104-111.
14. **Devani, U., Pandita, N., and Kachwala, Y.(2013)**: Evaluation of inhibitory activity of *Vitex negundo* and *Terminalia chebula* by alpha amylase inhibiton assay in management of diabetes. Asian Journal of Plant Science and Research.3(2):6-14.
15. **Devi, P.R., Kumari, S.K. and Kokilavani, C. (2007)**: Effect of *Vitex negundo* leaf extract on the free radicals scavengers in complete Freund's adjuvant induced arthritic rats. Indian Journal of Clinical Biochemistry. 22:143-147.
16. **Dharmasiri, M.G., Jayakody, J.R.A.C., Galhena, G., Liyanage, S.S.P. and Ratnasooriya, W.D. (2003)**: Anti-inflammatory and analgesic activities of mature fresh leaves of *Vitex negundo*. Journal of Ethnopharmacology. 87: 199-206.
17. **Diaz, F., Chavez, D., Lee, D., Mi, Q., Chai, H.B., Tan, G.T., Kardono, L.B.S., Riswan, S., Fairchild, C.R. and Wild, R. (2003)**: Cytotoxic flavone analogues of vitexicarpin, a constituent of the leaves of *Vitex negundo*. Journal of Natural Products. 66:865-867.
18. **En-shun, J., Ming, X., Yu-qing, L. and Yu-feng, W. (2009)**: Toxicity of *Vitex negundo* extract to aphids and its co-toxicity with imidacloprid. Chinese Journal of Applied Ecology. 20: 686-690.
19. **Graham, J.G., Quinn, M.L., Fabricant, D.S. and Farnsworth, N.R. (2000)**: Plants used against cancer–an extension of the work of Jonathan Hartwell. Journal of Ethnopharmacology. 73 :347-377.
20. **Guleria, S. and Kumar, A. (2006)**: Antifungal activity of some Himalayan medicinal plants using direct bioautography. Journal of Cell and Molecular Biology. 5: 95-98.
21. **Gupta, M., Mazumder, U.K., Bhawal, S.R. and Swamy, S.M.K. (1997)**: CNS activity of petroleum ether extract of *Vitex negundo* Linn in mice. Indian Journal of Pharmaceutical Sciences. 59: 240-245.
22. **Gupta, M., Mazumder, U.K. and Bhawal, S.R. (1999)**: CNS activity of *Vitex negundo* Linn. in mice. Indian Journal of Experimental Biology. 37: 143-146.
23. **Gupta, R.K. and Tandon, V.R. (2005)**: An experimental evaluation of anticonvulsant activity of *Vitex negundo*. Indian Journal of Physiology and Pharmacology. 49: 163-172.
24. **Hamayun, M. (2005)**: Ethnobotanical studies of some useful shrubs and trees of district Buner, NWFP, Pakistan. Ethnobotanical Leaflets. 9.
25. **Hebbalkar, D.S., Hebbalkar, G.D., Sharma, R.N., Joshi, V.S. and Bhat, V.S. (1992)**: Mosquito repellant activity of oils from *Vitex negundo* Linn. leaves. Indian Journal of Medical Research. 95: 200-203.
26. **Hu, Y., Zhang, Q., Hou, T., Xin, H., Zheng, H., Rahman, K. and Qin, L. (2007)**: Estrogen-like activities in *Vitex* species from China determined by a cell based proliferation assay. Pharmazie. 62: 872-875.
27. **Ivan, A.R. (2005)**: Medicinal plants of the world: chemical constituents, traditional and modern medicinal uses .New Jersey: Humana press.510.
28. **Jabeen, A., Khan, M., Ahmad, M., Zafar, M. and Ahmad, F. (2009)**: Indigenous uses of economically important flora of Margallah Hills National Park, Islamabad, Pakistan. African Journal of Biotechnology. 8: 763-784.

29. **Jain, S.P. and Puri, H.S. (1984)**: Ethnomedicinal plants of Jaunsar-Bawar hills, Uttar Pradesh, India. Journal of Ethnopharmacology., 12: 213-222.
30. **Jana, U. And Chattopadhyay, R.N. (1999)**: Preliminary studies on anti-inflammatory activity of *Zingiber officinale Rosc*, *Vitex negundo* Linn and *Tinospora cordifolia* (wild) Miers in albino rats. Indian J Pharmacol. 31: 232-233.
31. **Joshi, A.R. and Joshi, K. (2000)**: Indigenous knowledge and uses of medicinal plants by local communities of the Kali Gandaki watershed area, Nepal. Journal of Ethnopharmacology. 73:175-183.
32. **Kamaraj, C., Rahuman, A. and Bagavan, A. (2008)**: Antifeedant and larvicidal effects of plant extracts against *Spodoptera litura* (F.), *Aedes aegypti* L. and *Culex quinquefasciatus* Say', Parasitology Research. 103: 325-331.
33. **Kannathasan, K., Senthilkumar, A., Chandrasekaran, M. and Venkatesalu, V. (2007)**: Differential larvicidal efficacy of four species of *Vitex* against *Culex quinquefasciatus* larvae. Parasitology Research. 101: 1721-1723.
34. **Karmegam, N., Sakthivadivel, M., Anuradha, V. and Daniel, T. (1997)**: Indigenous plant extracts as larvicidal agents against *Culex quinquefasciatus* Say. Bioresource Technology. 59: 137-140.
35. **Karunamoorthi, K., Ramanujam, S. and Rathinasamy, R. (2008)**: Evaluation of leaf extracts of *Vitex negundo* L. (Family: Verbenaceae) against larvae of *Culex tritaeniorhynchus* and repellent activity on adult vector mosquitoes. Parasitology Research. 103: 545-550.
36. **Khan, N. and Rashid, A. (2006)**: A study on the indigenous medicinal plants and healing practices in Chittagong Hill tracts (Bangladesh). African Journal of Traditional, Complementary and Alternative Medicines., 3: 37-47.
37. **Khare CP. (2004)**: Encyclopedia of India Medicinal plants. Spinger Verlange, Berline, Heidelberge, New York.,474-476.
38. **Kirtikar, K.R. and Basu, B.D. (1984)**: Indian Medicinal Plants.Bishen Singh Mahendra Pal Singh, Dehradun,1984.
39. **Ladda, P.L. and Magdum, C.S. (2012)**: *Vitex negundo* Linn.- Ethnobotany, Phytochemistry and Pharmacology- A Review. Int.Journal in Advances inPhysics, Biology and Chemistry. Vol. 1(1): 111-120.
40. **Lodhi, A., Choudhary, I., Malik, A. and Ahmad, S. (2008)**: A Chymotrypsin inhibition studies on the lignans from *Vitex negundo* Linn. Journal of Enzyme Inhibition and Medicinal Chemistry. 23: 400-405.
41. **Mahalakshmi, R., Rajesh, P., Ramesh, N., Balsubramanian, V. and Kanan, V.R. (2010)**: Hepatoprotective activity on *Vitex negundo* Linn. (verbanaceae) by using wistar albino rats in ibuprofen induced model. International journal of pharmacology. 1-6.
42. **Mary, R.A. and Villasenor M. (2006)**: Comparative anti - hyperglycemic potentials of medicinal plants. Journal of Ethnopharmacology. 104(1-2): 129-131.
43. **Meena, A. K., Niranjan, U.S., Rao, M.M. , Padhi, M.M. and Ramesh Babu. (2011)**: A review of the important chemical constituents and medicinal uses of *Vitex* genus. Asian Journal of Traditional Medicines.6 (2.)
44. **Muthu, C., Ayyanar, M., Raja, N. and Ignacimuthu, S. (2006):** Medicinal plants used by traditional healers in Kancheepuram District of Tamil Nadu, India. Journal of Ethnobiology and Ethnomedicine. 2: 43-52.
45. **Muthuswamy, U., Kuppusamy, A., Nandagopi, U., Thirumalaisamy, S. and Varadharajan S. (2012)**: Protective effect of the leaves of *Vitex negundo* against ethanol-induced cerebral oxidative stress in rats. Tanzania J Health Res., 14(1): 1-1.
46. **Narayana, K.R., Reddy, M.S., Chaluvadi, M.R. and Krishna, D.R. (2001)**: Bioflavonoids, classification, pharmacological, biochemical effects and therapeutic potential. Indian J Pharmacol.33: 2-16.
47. **Nathan, S.S., Kalaivani, K. and Murugan, K. (2006)**: Behavioural responses and changes in biology of rice leaf folder following treatment with a combination of bacterial toxins and botanical insecticides. Chemosphere. 64: 1650-1658.
48. **Ong,H.C.(2008)**: Tumbuhan liar-khasiat ubtan and kegunaan lain. Kuala Lumpur: Utusan publication& distributors Sdn Bhd.121.
49. **Ono, M., Nishida, Y., Masuoka, C., Li, J., Okawa, M., Ikeda, T. and Nohara, T. (2004)**: Lignan derivatives and a norditerpene from the seeds of *Vitex negundo*. Journal of Natural Products. 67: 2073-2075.
50. **Panda, S.K., Thatoi, H.N. and Dutta S.K.(2009)**: Antibacterial activity and phytochemical screening of leaf and bark extracts of *Vitex negundo* L. from similipal biosphere reserve, Orissa. J Med Plant Res.3(4): 294-300.

51. **Paneru, R.B. and Shivakoti, G.P. (2001)**: Use of botanicals for the management of pulse beetle (*Callosobruchus maculatus* F.) in lentil. Nepal Agriculture Research Journal. 4-5: 27-30.
52. **Pattanaik, C., Reddy, S.C. and Murthy, M.S.R. (2008)**: An ethnobotanical survey of medicinal plants used by the Didayi tribe of Malkangiri district of Orissa, India.Fitoterapia. 79: 67-71.
53. **Preethi, R., Devanathan, V.V. and Loganathan M. (2010)**: Antimicrobial and antioxidant efficacy of some medicinal plants against food borne pathogens. Advan. Biol Res. 4 (2): 122-125.
54. **Pushpalatha, E. and Muthukrishnan, J.(1995)**: Larvicidal activity of a new plant extracts against *Culex quinquefasciatus* and *Anopheles stephensi*. Indian J. Malariol.32 (1): 14-23.
55. **Rabeta, M. S. and An Nabil, Z. (2013)**: Total phenolic compounds and scavenging activity in *Clitoria ternatea* and *Vitex negundo* Linn. International Food Research Journal. 20(1): 495-500 .
56. **Rahuman, A., Bagavan, A., Kamaraj, C., Vadivelu, M., Zahir, A., Elango, G. and Pandiyan, G. (2009)**: Evaluation of indigenous plant extracts against larvae of *Culex quinquefasciatus* Say (Diptera: Culicidae). Parasitology Research. 104: 637-643.
57. **Rajadurai, M., Vidhya, V., Ramya, M. and Bhaskar, A. (2009)**: Ethno-medicinal plants used by the traditional healers of Pachamalai hills, Tamilnadu, India. Ethnomedicine. 3: 39-41
58. **Rajendran, S. and Sriranjini, V. (2008)**: Plant products as fumigants for stored-product insect control. Journal of Stored Products Research. 44: 126-135.
59. **Ramkumar, K.M., Rajaguru, P. and Ananthan, R.(2004)**: Antimicrobial properties and phytochemical constituents of an antidiabetic plant *Gymnema montanum*. Advan. Biol Res. 1 (1-2): 67-71.
60. **Ricardo SA, Luis AP, Joel LA, Blanca AAG, Noemi WT. (2011)**: Antimicrobial and antioxidant activities of plants from Northeast of Mexico. Evid. Based Complement. Alternat. Med. Article ID 536139: 6 pages.
61. **Rosell, G., Quero, C., Coll, J. and Guerrero, A. (2008)**: Biorational insecticides in pest management. J. Pesticide Sci. 33(2): 103–121.
62. **Sahare, K.N., Anandhraman, V., Meshram, V.G., Meshram, S.U., Reddy, M.V., Tumane, P.M. and Goswami, K. (2008):** Anti-microfilarial activity of methanoloic extract of *Vitex negundo* and *Aegle marmelos* and their phytochemical analysis. Indian Journal of Experimental Biology. 46: 128-131.
63. **Sahayaraj, K and Ravi, C. (2008):** Preliminary phytochemistry of *Ipomea carnea* Jacq and *Vitex negundo* leaves. Int. J. chemical society. 6(1): 1-6.
64. **Sahayaraj, K. (2011):** Aqueous and water extracts of chosen botanicals on *Helicoverpa armigera, Hubner* and *Spodoptera litura* Fab. Journal of Agricultural Technology. 7(2): 339-347.
65. **Saikia, A., Ryakala, V., Sharma, P., Goswami, P. and Bora, U. (2006)**: Ethnobotany of medicinal plants used by Assamese people for various skin ailments and cosmetics. Journal of Ethnopharmacology.106 : 149-157.
66. **Samy, R.P., Ignacimuthu, S. and Sen, A. (1998)**: Screening of 34 Indian medicinal plants for antibacterial properties. Journal of Ethnopharmacology. 62: 173-182.
67. **Samy, R.P., Thwin, M.M., Gopalakrishnakone, P. and Ignacimuthu, S. (2008)**: Ethnobotanical survey of folk plants for the treatment of snakebites in Southern part of Tamil nadu, India. Journal of Ethnopharmacology. 115: 302-312.
68. **Sathiamoorthy, B., Gupta, P., Kumar, M., Chaturvedi, A.K., Shukla, P.K. and Maurya, R. (2007)**: New antifungal glycoside from *Vitex negundo*. Bioorganic and Medical Chemistry Letters. 17: 239-242.
69. **Sen, S., Chakraborty, R., Sridhar, C. , Reddy, Y. S. R. And De, B.(2010)**: Free Radicals, Antioxidants, Diseases And Phytomedicines: Current Status And Future Prospect. International Journal of Pharmaceutical Sciences Review and Research.3(1): 91-100.
70. **Sharma, A.K. and Singh, R.H. (1980)**: Screening of anti-inflammatory activity of certain indigenous drugs on carrageenin induced hind paw oedema in rats. Bull Med ethnobot Res. 1: 262-271.
71. **Shaukat, M., Huma, S. , Umbreen, F., Arfa, K. and Ghazala. H.R. (2009)**: Antifungal activities of *Vitex negundo* L. Pak.J.Bot., 41(4): 1941-1943.
72. **Smit, H.F., Woerdenbag, H.J., Singh, R.H., Meulenbeld, G.J., Labadie, R.P. and Zwaving, J.H. (1995)**: Ayurvedic herbal drugs with possible cytostatic activity. Journal of Ethnopharmacology. 47: 75-84.
73. **Soetan, K.O., Oyekunle, M.A., Aiyelaagbe, O.O. and Fafunso, M.A. (2006)**: Evaluation of the antimicrobial activity of saponins extract of *Sorghum Bicolor* L. Moench. African J Biotechnol. 5 (23): 2405-2407.
74. **Tandon, V. and Gupta, R.K. (2004)**: Histomorphological changes induced by *Vitex negundo* in albino rats. Indian journal of pharmacology. 36: 176-177.

75. **Tandon, V.R. and Gupta, R.K. (2005)**: An experimental evaluation of anticonvulsant activity of *Vitex-negundo*. Indian Journal of Physiology and Pharmacology. 49:199-205.
76. **Tandon, V.R. and Gupta, R.K. (2006)**: Anti-inflammatory Activity and Mechanism of Action of *Vitex negundo* Linn. International Journal of Pharmacology. **2**: 303-308.
77. **Tandon, V.R., Khajuria, V., Kapoor, B., Kaur, D. And Gupta, S. (2008)**: Hepatoprotective activity of *Vitex negundo* leaf extract against antitubercular drugs induced hepatotoxicity. Fitoterapia.29(7-8): 533-538
78. **Tasduq, S.A., Kaiser, P.J., Gupta, B.D., Gupta, V.K. and Johri, R.K. (2008)**: Negundoside, an irridiod glycoside from leaves of *Vitex negundo*, protects human liver cells against calcium-mediated toxicity induced by carbon tetrachloride', World Journal of Gastroenterology. 14: 3693-3709.
79. **Telang, R.S., Chatterjee, S. and Varshneya, C. (1999)**: Studies on analgesic and anti-inflammatory activities of *Vitex negundo* Linn. Indian journal of pharmacology. 31: 363-366.
80. **Tiwari, O.P. and Tripathi, Y.B. (2006)**: Antioxidant properties of different fractions of *Vitex negundo* Linn. Food Chemistry. 100: 1170-1176.
81. **Umamaheswari, M., AsokKumar, K., Somasundaram, A., Sivashanmugam, T., Subhadradevi, V. and Ravi, T.K. (2007)**: Xanthine oxidase inhibitory activity of some Indian medical plants. Journal of Ethnopharmacology. 109: 547-551.
82. **Vishal, T. and Gupta, R.K. (2005)**: Effect of *Vitex negundo* on oxidative stress. Indian journal of pharmacology. 37.
83. **Vishwanathan, A.S. and R. Basavaraju (2010)**: A Review on *Vitex negundo* L. – A Medicinally Important. Plant.EJBS .3 (1): 30-42.
84. **Warrier, P.K. and Nambiar, V.P.K. (2002)**: Indian Medicinal plants: A compendium of 500 species. Chennai: Orient Longman Private limited. Vol 5: 387.
85. **Woradulayapinij, W., Soonthornchareonnon, N. and Wiwat, C. (2005)**: In vitro HIV type 1 reverse transcriptase inhibitory activities of Thai medicinal plants and *Canna indica* L. rhizomes. Journal of ethnopharmacology .101(1-3): 84-89.
86. **Yang, L., Yen, K., Kiso, Y. and Hikino, H. (1987)**: Antihepatotoxic actions of formosan plant drugs. Journal of Ethnopharmacology. 19: 103-110.
87. **Yunos, N.M., Mat Ali, R., Kean, O.B. and Abas, R. (2005)**: Cytotoxicity Evaluations on *Vitex negundo* Anti-inflammatory Extracts. Malaysian Journal of Science. 24: 213-217.
88. **Zabihullah, Q., Rashid, A. and Akhtar, N. (2006)**: Ethnobotanical survey of Kot Manzary Baba valley, Malakand Agency, Pakistan. Pakistan Journal of Plant Sciences. 12:115-121**.**