Phytopharmacological Review of *Vitex Negundo* (Sambhalu)

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Summary

The diverse culture of our country is a rich source of traditional medicines, many of which are of plant origin. Scientific data on such plant derivatives could be of clinical use. *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 meters. The paper highlights on the pharmacological actions, traditional uses and phytochemistry of the plant. The plant has pungent, bitter, acrid taste; heating, astringent, cephalic, stomachic, anthelmintic properties. The plant is reported to have expectorant, carminative, digestive, anodyne, antiseptic, alterant, antipyretic, diuretic and emmenagogue, depurative, rejuvenating, ophthalmic, vulnerary and tonic properties. Flavone glycosides, stilbene derivative, new phenyldihydronaphthalene-type lignin, iridoids, flavonoids and many more categories were isolated. In the present review the therapeutic value of the plant and medicinal properties of its various parts have been discussed to provide collective information on this multipurpose commercial fruit crop.

Keywords *Vitex negundo,* Nirgundi, pharmacological activities, phytochemistry, stilbene derivatives, traditional uses.

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.[1]

Traditional therapeutics based on herbal medicinal principles is time tested and widely accepted across various cultural and socio-economic 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.[2]

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.[3, 4]

Taxonomic Classification

Kingdom	-	Plantae
Subkingdom	-	Tracheobionta
Super Division	-	Spermatophyta

Division	-	Magnoliophyta
Class	-	Magnoliopsida
Sub Class	-	Asteridae
Order	-	Lamiales
Family	-	Verbenaceae
Genus	-	*Vitex*
Species	-	*negundo*

Vernacular names

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

Geographical Source

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

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 lancoelate, 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 glaborous above, covered with a fine white tomentum beneath, base acute; common petioles 2.5-3.8 cm long.[3,4,5] 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, lancoelate

caduceus. Calyx 3 mm long, white tomentose; teeth triangular, 0.8-1mm long. Ovary glaborous; style glaborous; stigma forked. Drupe less than 6 mm diameter, black when ripe.[3,5,7,8]

Ethanobotanical Claims

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,[5,6,7] 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.[7]

The leaves are aromatic, tonic and vermifuge.[5,6] 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.[3,5,6] 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*.[7]

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.[3,6]

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.[5,6] Fruit is nervine, cephalic and emmenagogue; dried fruits acts as a vermifuge; flowers are cool and astringent.[6]

Ayurvedic Formulations

Vatagajankusa Rasa, Mahavata Vidhvansana Rasa, Ykrtptihara Lauha, Dasamula Taila, Trivikrama Rasa, Nirgundi Taila, Visa Tinduka Taila.[4]

Phytochemical Profile

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, n-hentricontane, n-pentatricontane, n-nonacosane, β-sitosterol, p-hydroxybenzoic acid and 5-oxyisophthalic acid; 3, 4-dihydroxybenzoic acid was also isolated from the seeds of *Vitex negundo*.[9,10,11]

U.K. Rao **(1977)** reported isolation of friedelin, vitamin-C, carotene, casticin, artemetin from leaves.[12]

G.S. Misra & P.M. Subramanian **(1980)** isolated three new flavone glycosides which were identified as 3,6,7,3',4'-Pentamethoxy-5-O-glucopyranosyl-rhamnoside, vitexin cafeate, 4'-O-methyl myricetin-3-O-[4''-O-β-D-galactosyl]-β-D-galactopyranoside.[13]

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

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-O-desmethylnobiletin), 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).[15,16,17,18] 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, α-terpineol, sabenine, globulol, spathulenol, β-farnesene, farnesol, bis (1,1dimethyl) methylphenol, α-pinene, β-pinene, linalool, terpinyl acetate, caryophyllene epoxide, caryophyllenol along with viridiflorol.[19,20,21,22] Pradeep Singh *et al.* **(2010**) proved the presence of volatile oil which contains ten volatile components like α-copaene, β-caryophyllene, β-elemene, camphene, α-thujene, α-pinene, sebinene, linalool, stearic acid and behenic acid.[23]

L. Sun **(1989)**, J. X. Pan **(1989)**, R Gopal Mallvarapu **(1994)**, V. Singh **(1999)**, R. Dayal **(2000)**, reported isolation of α-elemene, δ-elemene, β-elemene, β-eudesmol, camphor, camphene, careen, 1,8-cineol, 1-oceten-3-ol, γ-terpinine, α-phellendrene, β-phellendrene, α-guaiene, abieta-7,13-diene, neral, geranial, bornyl acetate, nerolidol, β-bisabolol, cedrol.[24, 25, 26, 27, 28] Vitexicarpin was also isolated from leaves.[22]

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

A.S. Chawla *et al.* **(1992)** and D.S. Hebbalkar *et al.* **(1992)** reported triterpenoids 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 and 2α,3β-diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid.[32, 33]

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.[34, 35]

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'-p-hydroxybenzoyl 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. [36]

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*.[37]

V. Krishna *et al.* **(2002)** isolated β-amyrin, epifriedelinol and oleanolic acid from the heartwood of *Vitex negundo*.[38]

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'-p-hydroxybenzoyl 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.[39]

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'-Dibenzoyloxy-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*.[40]

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

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.[42, 43]

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-3α-O-β-D-glucose, (+)-(-)-pinoresinol and (+)-diasyringaresinol.[44]

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-β-D-glucuronic acid-6''-methyl ester, a new naturally occurring compound named vitexoside.[45]

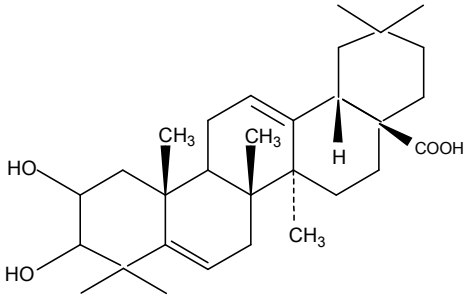
Vanillic acid, p-hydroxybenzoic acid and luteolin were isolated from bark; two new leucoanthocyanidins isolated from stem bark and their

structures were determined as 6, 8-di-O-methylleucocyanidin-7-O-rhamnoglucoside.

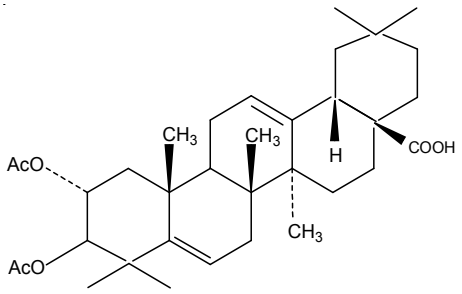
The roots contain a furanoeremophilane. The stem bark contains methyl esters of leucodelphinidin, and leucoanthocyanidins-7-O-rhamno-glucoside and the flavonoids, 6-C-glycosyl-5-O-rhamnopyranosyl trimethoxy wogonin and acerosin-5-glucoside monoacetate and also contains the flavonones, 6β-glucopyranosyl-7-hydroxy-3',4',5',8-tetramethoxyflavone-5-O-α-L-rhamnopyranoside;3',7-dihydroxy-4',6,8 trimethoxy flavone-5-O-(6"-O-acetyl-β-D-glucopyranoside);3,3',4',6,7-pentamethoxyflavone-5-O-(4"O-β-D-glucopyranosyl)-α-L-rhamnopyranoside; 4,5,7-trihydroxyflavone-8-(2"-caffeoyl-β- D-glucopyranoside; and 3,5,5,7-tetrahydroxy-4-methoxyflavone-3-O-(4"-O-β-galactopyranosyl) galactopyranoside.

The leaves contain the iridoid glycosides, 2-p-hydroxybenzoyl mussaenosidic acid, 6'- p-hydroxybenzoylmussaenosidic acid, negundoside ($C_{23}H_{28}O_{12}$), and nishindaside ($C_{15}H_{24}O_9$). They also contain the isomeric flavanones, 5,3-dihydroxy-7,8,4-trimethoxy flavanone and 5,3-dihydroxy-6,7,4-trimethoxy flavanone.

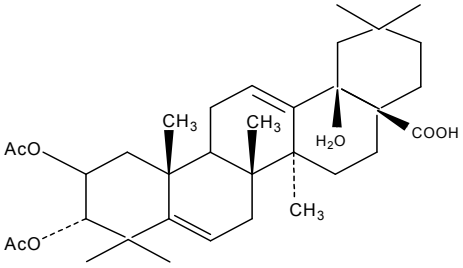
Besides, they contain casticin and the glucosides, leutolin-7-glucoside ($C_{21}H_{20}O_{11}$) and α-D-glucoside of a tetrahydroxy monomethoxy flavone ($C_{22}H_{24}O_{12,}$ m.p. 245^0). The leaves and twigs contain 5,3'-dihydroxy-6,7,4'-trimethoxy flavone (m.p.135-136^0), 3',4',5,5',6,7,8-heptamethoxyflavone, 3-O-desmethylartemetin, 5-O-desmethylnobiletin. The seeds contain 5-oxyisophthalic acid and vitextriterpine ($C_{30}H_{50}O_8$). Several anti-inflammatory substances have also been isolated from the seeds including the diterpene, 5β-hydro-8,11,13-abietatrien-6α-ol; the triterpene, lanostan-8, 25-dien-3β-ol; the triterpenoids, 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 and 2α,3β-diacetoxy-18-hydroxyoleana-5,12-dien-28-oicacid (m.p. 205-206^0); the Flavonoid, artemetin; and the lignan characterized as 6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde ($C_{20}H_{20}O_{6,}$ m.p. 126-127^0).[46, 47, 48, 49, 50, 51, 52]



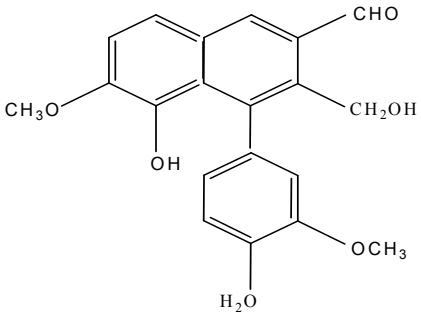
2α, 3α-dihydroxyolean-5, 12-dien-28-oic acid



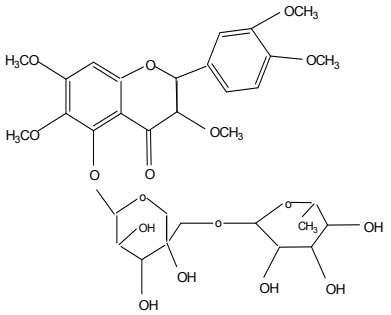
2β, 3α-diacetoxyolean-5, 12-dien-28-oic acid



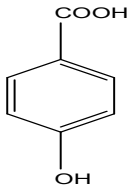
2α, 3β-diacetoxy-18-hydroxy olean-5,12-dien-28-oic acid



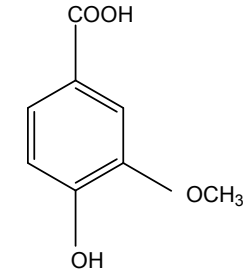
6-hydroxy-4-[4-hydroxy-3-methoxyphenyl] -3-hydroxymethyl-7-methoxy-3, 4-dihydro -2-naphthaldehyde



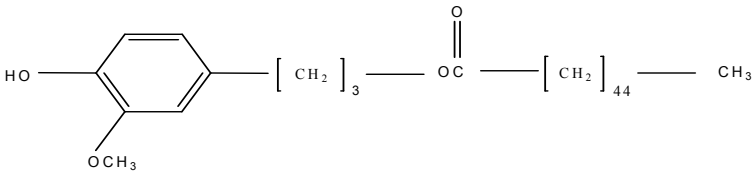
3, 6, 7, 3', 4'-pentamethoxy-5-O-glucopyranosyl rhamnoside



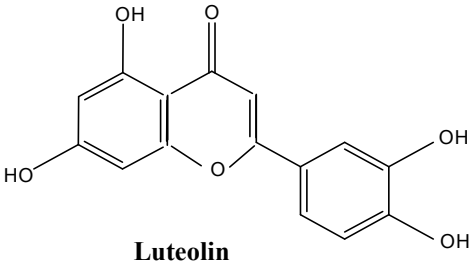
p - hydroxy benzoic acid



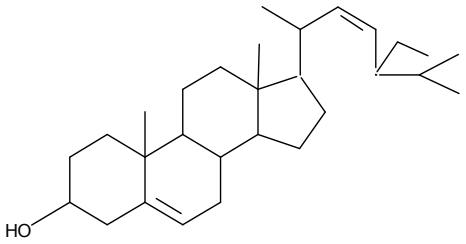
Vanillic acid



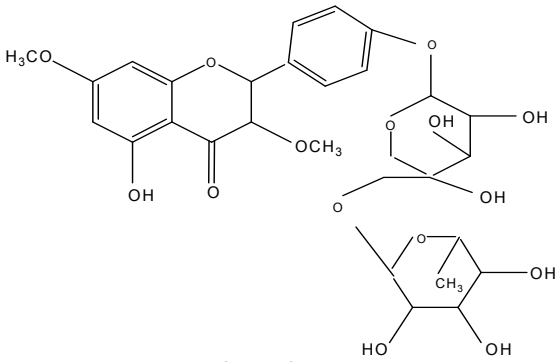
Hexatetracontanoic acid derivative



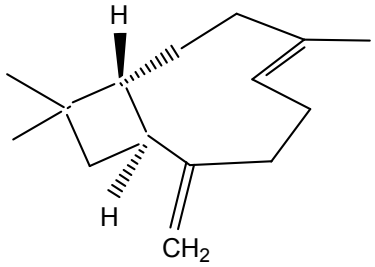
Luteolin



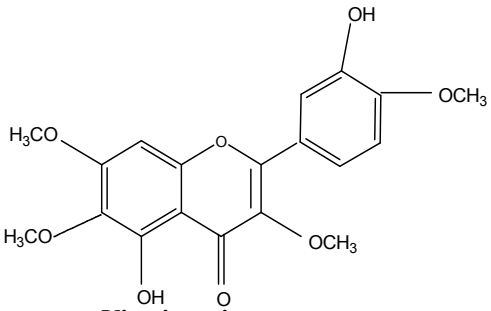
Stigmasterol



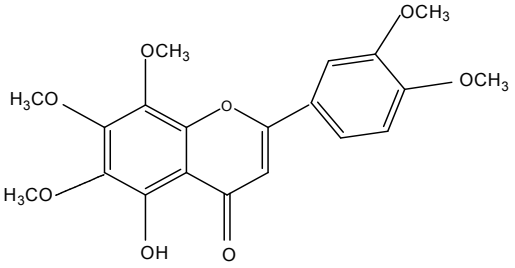
Vitexoside



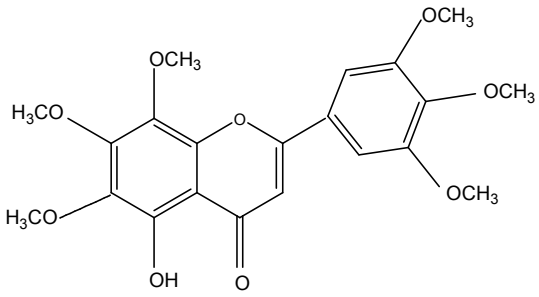
β – caryophyllene



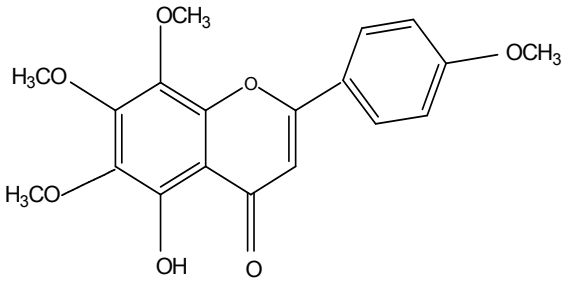
Vitexicarpin



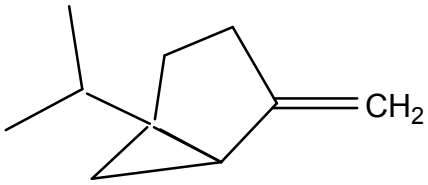
5-hydroxy-6, 7, 8, 3', 4'-pentamethoxy flavone



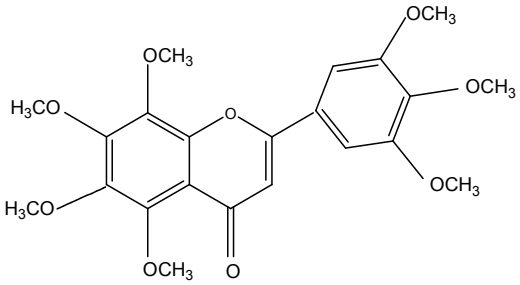
Gardenin A



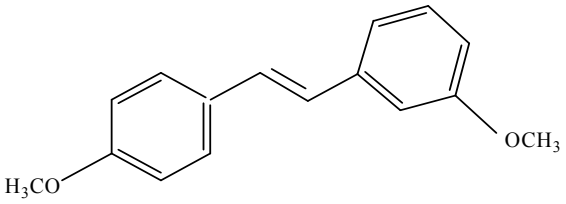
Gardenin B



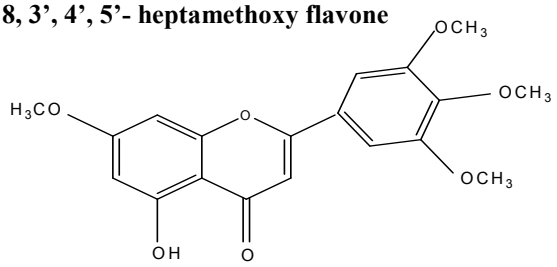
Sabinene



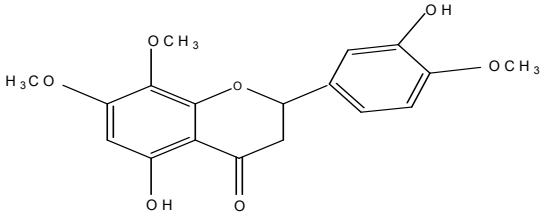
5, 6, 7, 8, 3', 4', 5'- heptamethoxy flavone



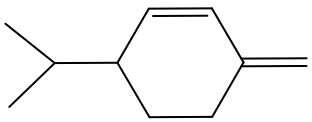
4, 4' – dimethoxy trans stilbene



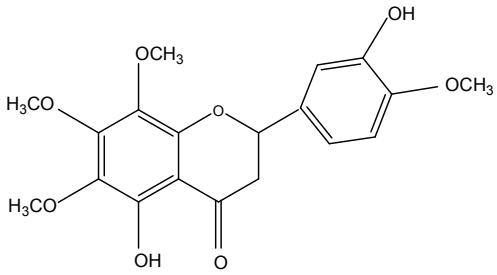
Corymbosin



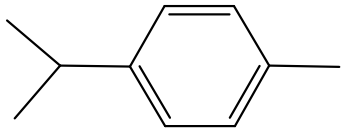
5, 3'-dihydroxy-7, 8, 4'-trimethoxy flavanone



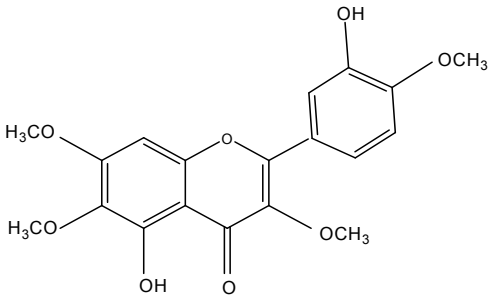
β - phellandrene



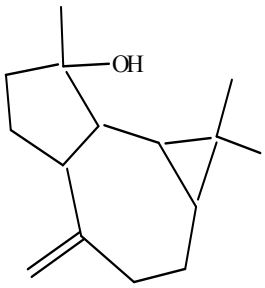
5, 3'-dihydroxy-6, 7, 4'-trimethoxy flavanone



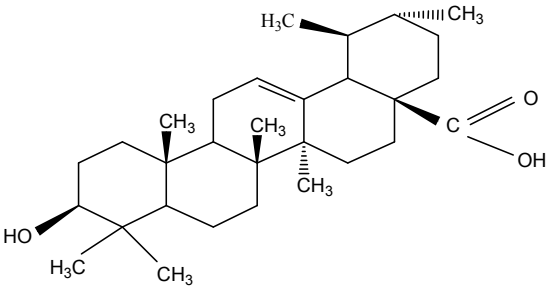
p - cymene



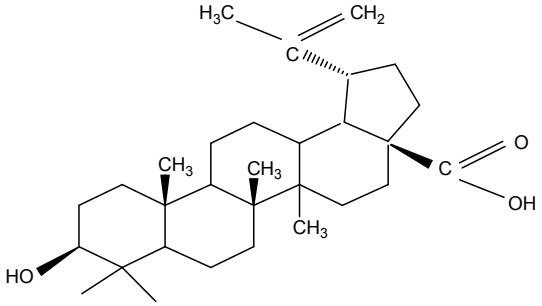
Casticin



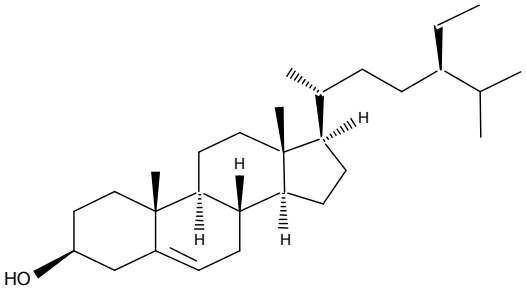
Spathulenol



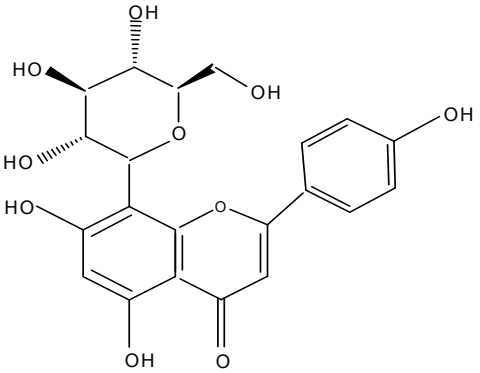
Ursolic Acid



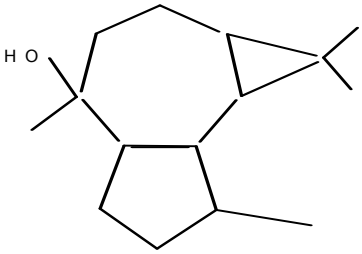
Betulinic acid



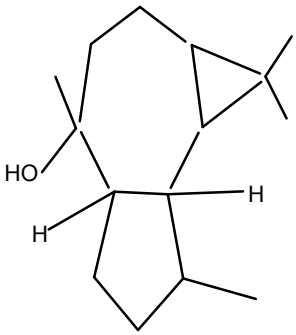
β - Sitosterol



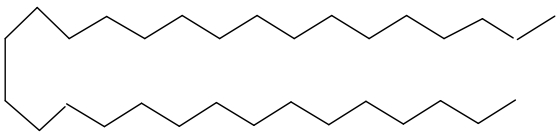
Vitexin



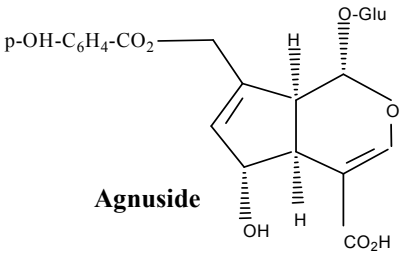
Viridifloral



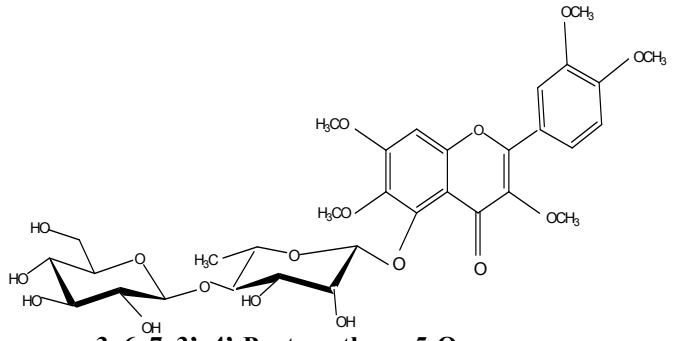
Globulol



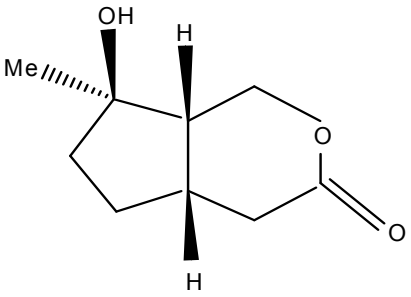
Hentriacontane



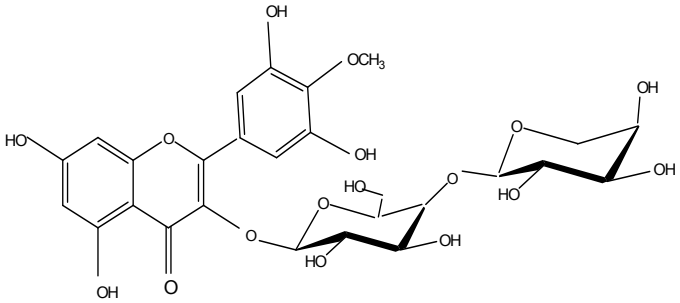
Agnuside



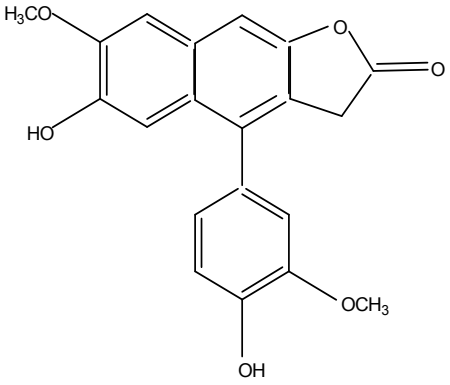
3, 6, 7, 3', 4'-Pentamethoxy-5-O-glucopyranosyl-rhamnoside



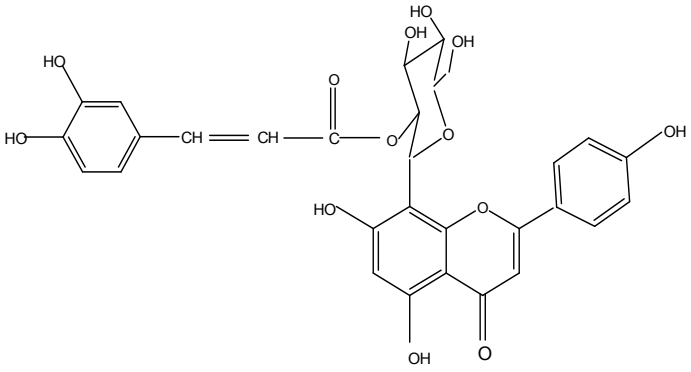
Lagundinin



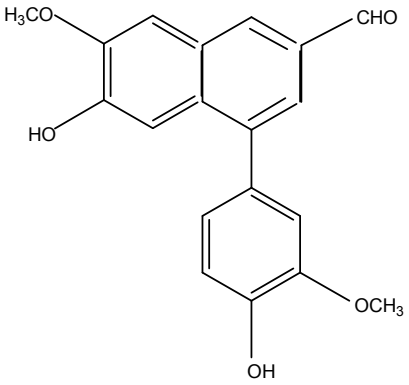
4'-O-methyl myricetin-3-O-[4''-O-β-D-galactosyl]-β-D-galactopyranoside



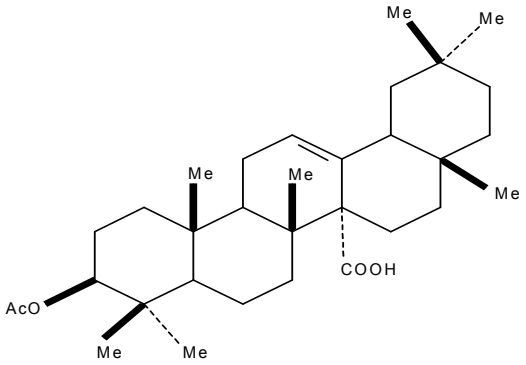
Negundin A

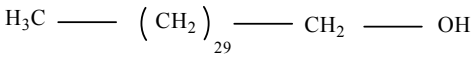


Vitexin caffeate

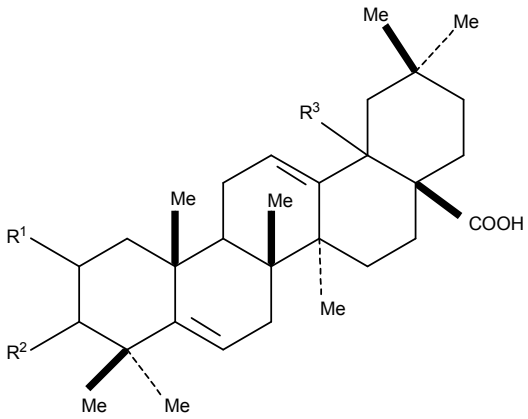


Vitrofolal E





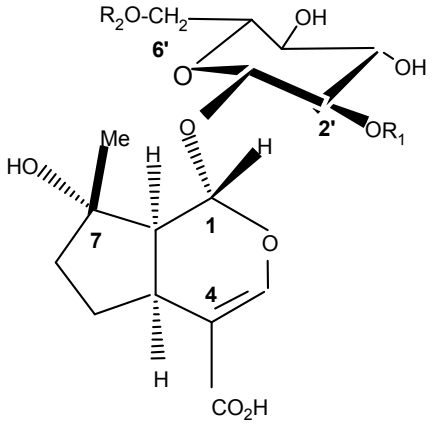
3β-acetoxyolean-12-en-27-oic acid **n-Hentriacontanol**



$R^1 = R^2 = \alpha$-OH, R^3 = H → 2α, 3α-dihydroxyoleana-5, 12-diene-28-oic acid

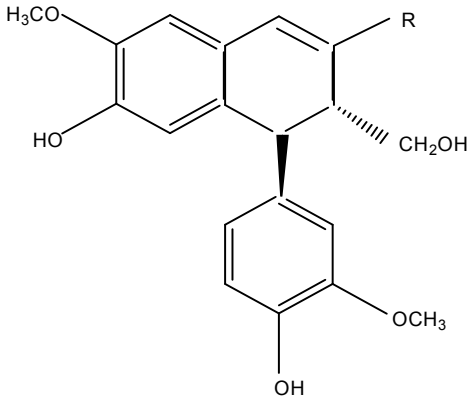
$R^1 = \beta$-OAc, $R^2 = \alpha$-OAc, R^3 = H → 2β, 3α-diacetoxyoleana-5, 12-dien-28-oic acid

$R^1 = \alpha$-OAc, $R^2 = \beta$-OAc, R^3 = OH →2α, 3β-diacetoxy-18-hydroxyoleana-5, 12-diene-28-oic acid



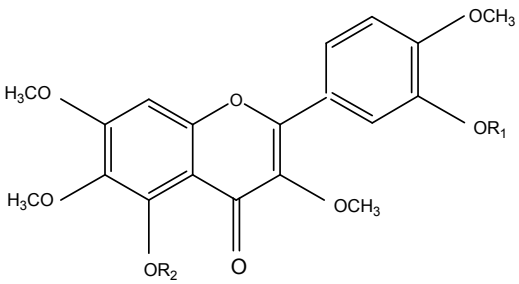
R_1 = COC_6H_4OH (para), R_2 = H → 2'-p-Hydroxybenzoyl mussaenosidic acid

R_1 = H, R_2 = COC_6H_4OH (para) → 6'-p-Hydroxybenzoyl mussaenosidic acid



R = CH_2OH → Negundin B

R = CHO → 6-hydroxy-4-(4-hydroxy-3-methoxy)-3-hydroxymethyl-7-methoxy-3, 4-dihydro-2-naphthaldehyde



(1) $R_1 = CH_3$, $R_2 = CH_3$ → methylated derivative of Vitexicarpin

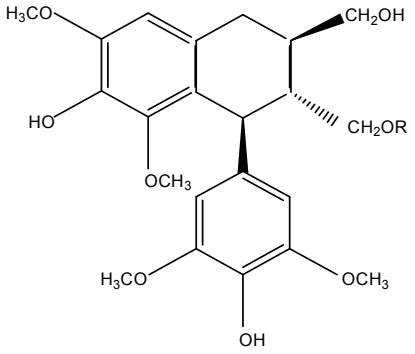
(2) $R_1 = CH_3CO$, $R_2 = CH_3CO$ → acetylated derivative of Vitexicarpin

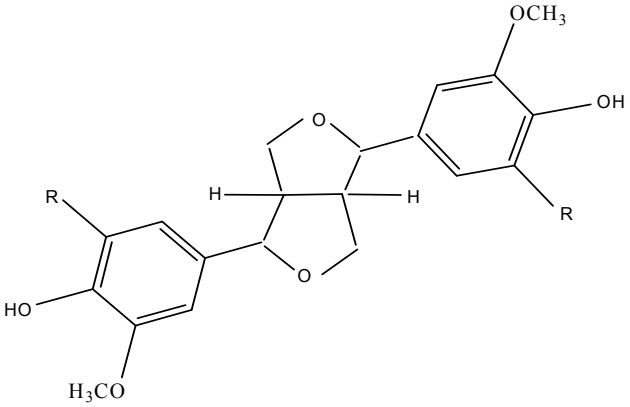
(3) $R_1 = C_6H_5CO$, $R_2 = H$, (4) $R_1 = C_6H_5CO$, $R_2 = C_6H_5CO$, (5) $R_1 =$

CH_3CH_2CO, $R_2 = CH_3CH_2CO$, (6) $R_1 = CH_3(CH_2)_2CO$, $R_2 = CH_3(CH_2)_2CO$,

(7) $R_1 = CH_2 = CH(CH_2)_2CO$, $R_2 = CH_2 = CH(CH_2)_2CO$, (8) $R_1 = CH_3$

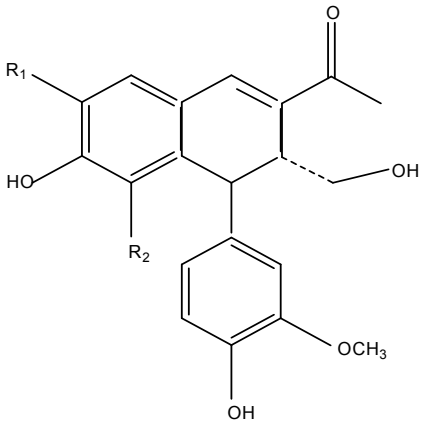
$(CH_2)_4CO$, $R_2 = CH_3(CH_2)_4CO$ → acylated derivatives of Vitexicarpin

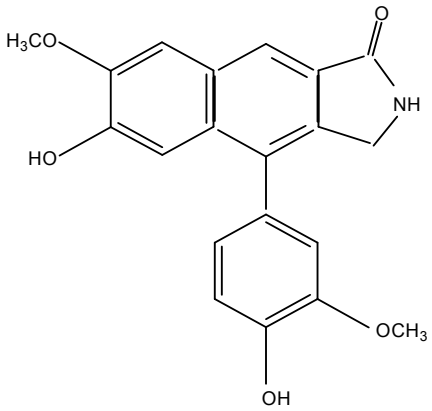




R = H → (+)-(−)-pinoresinol
R = OCH_3 → (+)-diasyringaresinol

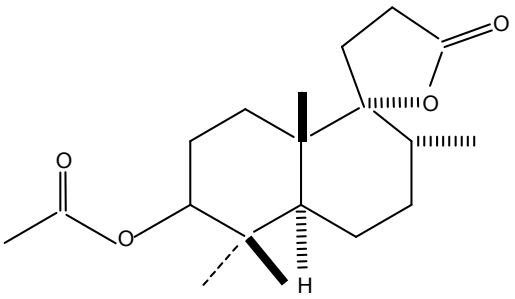
R = H → (+)-lyoniresinol
R = β-D-Glucose → (+)-lyoniresinol- 3α-O-β-D-glucoside



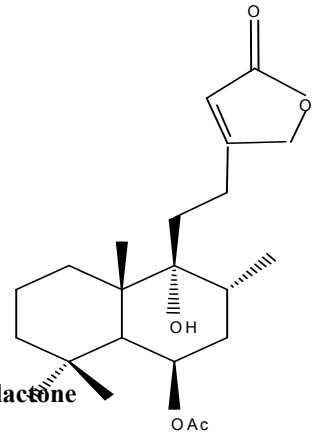


$R_1 = H$, $R_2 = OCH_3$ → Vitedoin A

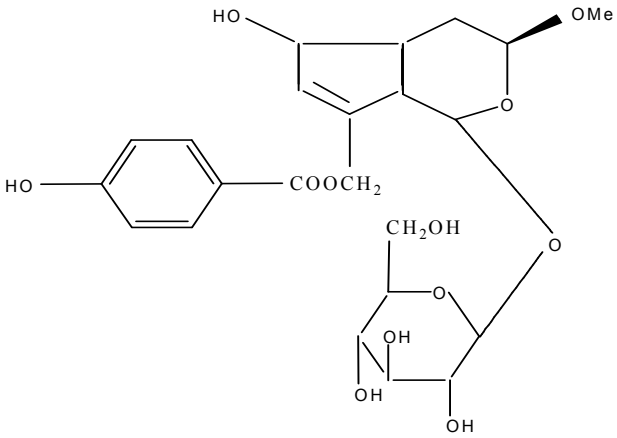
Vitedoamine



Vitedoin B



Vitexilactone



Nishindaside

Structures of various phytoconstituents isolated from *Vitex negundo*

Pharmacological Profile

Anticancer Activity

F. Diaz *et al.* **(2003)** evaluated cytotoxicity of flavones isolated from the chloroform extract of *Vitex negundo* leaves. Vitexicarpin, a flavone was investigated for its cytotoxic action in human cancer cell line.[40]

Antifeedent Activity

S.S. Sharma *et al*. **(2001)** & K. Srinivas & M.B.V. Raju **(2002)** reported anti-feedent activity of betulinic acid and ursolic acid against castor semilooper.[53, 54]

R.D. Manohar *et al.* **(2003)** reported antifeedent activity of Betulinic acid, Ursolic Acid, n-hentriacontanol, β-sitosterol and p-hydroxy benzoic acid from the methanolic extract of *Vitex negundo* leaves against the larvae of *Achoea janata* using a no-choice laboratory assay.[41]

V. Singh *et al.* **(2003)** investigated anti-feedent activity of Viridifloral in a dose dependent manner against *Sitophilus oryzae* and ovipositional activity against *Callosobruchus chinensis*.[39]

Antimicrobial Activity

J.A. Rideout *et al.* **(1999)** reported antibacterial & antifungal activity of Vitexilactone & Casticin from the chloroform extract of *Vitex negundo* leaves against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans* & *Aspergillus niger* using agar plate method.[37]

V. Alagarsamy *et al.* **(1999)** reported antibacterial & antifungal activity of *Vitex negundo* leaves. Antibacterial & antifungal activity of chloroform, methanol and water extracts were evaluated by Agar cup plate method at concentrations of 10 mg/ml, 20 mg/ml and 30 mg/ml against *E.coli*, *P. aeruginosa*, *S. aureus & Candida albicans* employing co-trimoxazole & amphotericin as a reference standards for said screenings.[55]

V.S. Rana & R. Dayal **(2003)** & R.D. Kaushik *et al.* **(2003)** reported anti-microbial activity of hexane and methanolic extracts of *Vitex negundo* leaves. The extracts were active against *Mycogene perniciosa*, *Rhizoctonia solani*, *Bacillus megaterium*, *Pseudomonasa fluorescens*, *Staphylococcus* species and *Xanthomonas* species.[56, 57]

K.H. Shin *et al.* **(1997)**, C.K. Lee *et al.* **(1998)** & Z. Iqbal *et al.* **(2002)** & E. Nyligira *et al.* **(2004)** reported anti-microbial activity from the chloroform extract of *Vitex negundo* leaves containing Vitexilactone and Casticin and were active against *Candida albicans*, *Aspergillus niger*, *F. chlamdosporum*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*.[58, 59, 60, 61, 62]

V. Loganathan *et al.* **(2004)** investigated antibacterial activity from the methanolic and chloroform extracts of *Vitex negundo* leaves against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus albus*, *Bacillus subtilis*, *E.coli*, *Klabsiella aerogens*, *Proteus vulgaris* and *Pseudomonas aeruginosa* using agar plate method.[63]

Pradeep Singh *et al.* (2010) reported antibacterial and antifungal activity of volatile oil against *S. aureus, E. coli, K. pneumoniae, B. subtilis, M. luteus* and *Candida albicans* using ciprofloxacin and chloramphinicol as reference.[23]

Anti-inflammatory Activity

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.[32]

U.K. Rao *et al.* **(1977)**, M.B. Ahmad *et al.* **(1989)**, A.S. Chawla *et al.* **(1991)**, & E. Nyligira *et al.* **(2004)** reported anti-inflammatory activity of bark, seeds, seed oil and essential oil of *Vitex negundo*.[12, 64, 31, 62] U. Jana *et al.* **(1999)** reported preliminary anti-inflammatory activity of *Vitex negundo* in albino rats along with *Zingiber officianale* and *Tinospora cordifolia*.[65]

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.[66]

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.[67]

Pradeep Singh *et al.* **(2009)** reported anti-inflammatory activity of ethanolic extract of roots.[84]

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.[44]

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.[68] J.L. Suri *et al.* reported immunostimulatory potential of two iridoid glucosoides from *Vitex negundo* leaves.[69]

Antioxidant Activity

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

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 benzothiazioline-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.[73]

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.[46, 47]

CNS Activity

M. Gupta *et al.* **(1997 & 1999)** evaluated CNS activity & anti-convulsant activities of petroleum ether & methanolic extracts of *Vitex negundo* in mice.[74,75]

Anti-androgenic Activity

S.K. Bhargava **(1984, 1986)** & R.P. Samy *et al.* **(1998)** reported anti-androgenic 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.[76, 77, 78]

Anti-histaminic Activity

M.A. Rimando *et al*. **(1987)** & G. Stylian **(1996)** tested anti-histaminic property of methanolic extract of *Vitex negundo* leaves. The said extract was found to be active against histamine release from mast cells.[79, 80]

M.N. Saraf *et al.* **(1994)** reported mast cell stabilizing potential of *Vitex negundo*. Ethanolic extract of the leaves on degranulation of male Wistar rat peritoneal mast cells induced by Compound 48/80 and Egg albumin was examined. The inhibitory effect of the extract was stronger in immunologically induced degranulation of mast cells.[81]

Enzyme Inhibition Activity

A. Haq *et al.* **(2004)** reported anti- lipoxygenase and anti - butyrylcholinesterase potential of two lignans Negundin B and Vitrofolal F.[82]

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).[66]

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.[83]

Conclusion

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, hepatopropective, 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.

Acknowledgement

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1. Paarakh PM. *Nigella sativa* Linn.-A comprehensive review. Indian Journal of Natural Products and Resources 2010; 1(4), 409-429.
2. Sahare KN, Anandhraman V, Meshram VG, Meshram SU, et al. Anti-microfilarial activity of methanolic extract of *Vitex negundo* and *Aegle marmelos* and their phytochemical analysis. Indian Journal of Experimental Biology 2008; 46: 128-131.
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