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Chemical Compounds and Bioactivities of *Vertex negundo* Linn: A review

Khaled Rashed*

Department of Pharmacognosy, National Research Centre, 33 El-Bohouthst-Dokki, Giza, P.O.12622, Egypt

Abstract

Vertex negundo is large aromatic shrub. Phytochemical analysis showed the presence of volatile oil, triterpenes, diterpenes, sesquiterpenes, lignan, flavonoids, flavones, glycosides, iridoid glycosides and stilbene derivative. It is good for disease of the eye, consumption, inflammation, leucoderma, enlargement of the spleen, bronchitis, asthma, biliousness, painful teething of children. It is expectorant, carminative, digestive, anodyne, antiseptic, antipyretic, diuretic, depurative, rejuvenating, ophthalmic, vulnerary and tonic.

Keywords: *Vertex negundo* Linn, chemical compounds, plants, bioactivities.

***Correspondence Info:**
Dr. Khaled Rashed
Department of Pharmacognosy,
National Research Centre,
33 El-Bohouthst.-Dokki, Giza, P.O.12622, Egypt

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1. Introduction

Plants have a great potential for producing new drugs for human benefit. Plants used in traditional medicine contain a vast array of substances that can be used to treat chronic and even infectious diseases. According to a report of World Health Organization, more than 80% of world's populations depend on traditional medicine for their primary health care needs [1]. *Vertex negundo* Linn. (Verbenaceae family) occurs in different parts of Pakistan, such as Rawalpindi hills, Murree, Muzaffarabad, Mirpur, Lower Hazara, Kurram, and Swat [2]. It is locally known as ''Nirgandi'' and commonly as ''Lagundi''. It is a small tree with an irregular trunk and branches covered with thin grey bark. Phytochemical analysis of the plant revealed the presence of casticin, isoorientin, chrysophenol D, luteolin, p-hydroxybenzoic acid, and fructose [3]. Additionally, alkaloids, glycosides, flavonoids, sterols, resins, tannins, dimethyl ethers of delphinidin and leucocyanidin, rhumano-glucosides, and flavones glycosides. A new diterpenoid, negundol was reported from the seeds of *V. negundo* [4]. Pharmacologically, the plant has been reported as hepatoprotective [5], antibacterial [6], hypnotic [7], antioxidant [8], analgesic and anti-histaminic [9], anticancer [10], antiandrogenic [11], and anti-inflammatory [12]. The extract of *V. negundo* in guinea-pig tracheal smooth muscle was investigated and found that it inhibits the release of histamine and products of arachidonic acid metabolism, which are responsible for tracheals mooth muscle contraction [13]. The alcoholic extract of *V. negundo* has a bronchodilator effect against histamine and acetylcholine induced bronchospasm[14]. Recently, we have investigated the functional nature of the antidiarrheal and antispasmodic activities of the extract of *V. negundo*[15]. This review summaries the chemical compounds and bioactivities of *V. negundo*.

2. Chemical Compounds

2.1 The Leaves

The various chemical constituents present in leaves of *Vertex negundo* Linn leaves are Friedelin, vitamin-C, carotene, casticin, artemetin[8], 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, vitexicarpin, viridiflorol [16-19], 4, 4″-dimethoxy-trans-stilbene, 5, 6, 7, 8, 3′4′5-heptamethoxy, 5-hydroxy-6, 7, 8, 3′4′-pentamethoxy(5-Odesmethylnobiletin), 5-hydroxy-6, 7, 8, 3′, 4′, 5-hexamethoxy (gardenin A), 5-hydroxy-6, 7, 8, 4′-tetramethoxy(gardenin B), 5-hydroxy-7, 3′, 4′, 5′-tetramethoxyflavone (corymbosin)[20-23], terpinen-4-ol, α-copaene, β-caryophyllene, β-elemene, camphene, α-thujene, α-pinene, sebinene, linalool, stearic acid and behenic acid [24], 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 [25-29], 2′-p-hydroxybenzoylmussaenosidic acid, agnuside, lagundinin, aucubin and nishindaside [30], 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-trimethoxyflavanone, p-hydroxybenzoic acid, 3, 4 – dihydroxybenzoicacid, luteolin-7-glucoside, isoorientin [31], 3′-benzoyloxylhydroxy-3, 6, 7, 4-tetramethoxyflavone, 5, 3′-dibenzoyloxy-3, 6, 7, 4-teramethoxyflavone, 5, 3′-Dipropanyloxy- 3, 6, 7, 4′-tetramethoxyflavone, 5, 3-Dibutanoyloxy3, 6, 7, 4-tetramethoxyflavone, 5, 3′- Dipenty4enoyloxy-3, 6, 7, 4′tetramethoxyflavone, 5, 3-Dihexanoyl 3, 6, 7, 4-tetramethoxyflavone [25], betulinic acid, ursolic acid [32], dimethoxyflavonone, 5, 3′-dihydroxy-7, 8, 4′-trimethoxyflavonone, 7, 8-Dimehylherbacetin-3-rhamnoside, vitegnoside [33], 1, 4a, 5, 7a tetrahydro1β Dglucosyl (3′, 4′dihydroxy benzoyl oxymethyl)-5-ketocyclopenta[c] pyran-4- carboxylic acid, luteolin-7-O-β-D-glucosid[28], 6′-p-hydroxybenzoylmussaenosidic acid [34].

2.2 The Roots

Vitexoside, agnuside, R-dalbergiphenol [45, 46], negundin A, negundin B, vitrofolal E, (+)- lyoniresinol, (+)-lyoniresinol-3α-O-β-d-glucoside, (+)-(−)-pinoresinol, and (+)-diasyringaresinol [35], 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 [36], acetyl oleanolic acid, sitosterol, 3-formyl-4.5-dimethyl-8- oxo-5H-6, 7-dihydronaphtho (2, 3-b) furan (a new furanoeremophilane) [37].

2.3 The Stem and bark

The various chemical constituents present in the stem and bark are 3, 6, 7, 3′, 4′-Pentamethoxy-5-Oglucopyranosyl-rhamnoside, vitexincafeate, 4′-O-methyl myricetin- 3-O-[4′-O-β-D-galactosyl]- β-D-galactopyranoside [38], β-amyrin, epifriedelinol and oleanolic acid [41], Hepta methyl- phenyl-cyclotetrasiloxane, Cycloheptasiloxane, tetradecamethyl Nona methyl, phenyl- cyclopentasiloxane, Cyclooctasiloxane, hexadeca methyl, Borazine, 2, 4, 6-tripheny-l1, 3, 5- tryophl, Nonamethyl, phenyl-cyclopentasiloxane , Tetracosamethylcyclododecasiloxane, penta methyl phenyl-Disilane, Heptasiloxane, Octadecamethyl, cyclononasiloxanes Cyclooctasiloxane, hexadeca methyl [39], p-hydroxy benzoic acid, β-sitosterol [40], 5-hydroxy-3, 6, 7, 3′4′- pentamethoxy flavone, 5-hydroxy-3′dihydroxy-7, 8, 4′-trimethoxy flavanone, 3β-acetoxy-olean-12-en-27-oic acid, 3β-hydroxy-olean-5, 12-dien-28-oic acid [41].

2.4 The Seeds

The seeds of Vitexnegundo Linn have chemical constituents such as n-Tritriacontane, n- hentriacontanol, n-hentricontane, n-pentatricontane, n-nonacosane, β-sitosterol, phydroxybenzoic acid and 5-oxyisophthalic acid, 3, 4-dihydroxybenzoic acid [42-44], artemetin [45], 3β-acetoxyolean-12-en-27-oic acid, 5β-hydro-8, 11, 13-abietatrien-6α-ol, 2α, 3α-dihydroxyoleana- 5, 12-dien-28-oicacid, 2β, 3α-diacetoxyoleana-5, 12-dien-28-oicacid and 2α, 3β-diacetoxy-18- hydroxyoleana-5, 12-dien-28-oic acid [46, 47], vitedoin A, vitedoamine A, vitedoin B [36, 37], 5, 7, 3′-trihydroxy 6, 8, 4′-trimethoxy [38], 6-hydroxy-4-(4-hydroxy-3- methoxy-phenyl)-3- hydroxymethyl-7-methoxy-3, 4-dihydro-2-naphthaldehyde [48].

2.5 Essential oil of fresh leaves, flowers and dried fruits

The various chemical constituents of essential oil of from leaves, flowers and dried fruits are 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 [49], viridiflorol (19.55%), β-caryophyllene (16.59%), sabinene (12.07%), 4-terpineol (9.65%), γ-terpinene(2.21%), caryophyllene oxide (1.75%), 1-oceten-3-ol (1.59%), and globulol (1.05%) [50].

3. Activities

3.1 Cytotoxic effect

The methanolic, petroleum ether and carbon tetrachloride leaf extract of *Vertex negundo* Linn were screened for antibacterial and cytotoxic activity using disc diffusion method and brine shrimp lethality bioassay respectively. Antibiotic kanamycin and anti-tumor agent vincristine sulphate were used as standard and the fractions screened for anti-bacterial activity showed prominent zone of inhibition against *Bacillus megatrium*, *Bacillus subtilis*, *Salmonella typhi*, *Vibrio mimicus*, *Aspergillus niger*. When compared to methanolic extract, the petroleum ether and carbon tetrachloride extract showed significant cytotoxic activity [51]. In vitro cytrotoxic activity of hydroalcoholic

extracts of aerial parts of *Vertex negundo* Linn was studied against DAL (Dalton's ascites lymphoma) and EAC (*Ehrlich ascites* carcinoma) cell lines. Trypan blue dye exclusion technique on cell counting in vitro was used and hydro alcoholic extracts of *Vertex negundo* Linn showed good *in vitro* cytotoxic activity [52].

3.2 Anti-HIV activity

The anti-HIV activity of ethanolic leaf extract of *Vertex negundo* Linn was studied against HIV-1 reverse transcriptase. Using a non-radioactive HIV-RT colorimetric ELISA kit and with recombinant HIV-1 enzyme it was evaluated *in vitro*. The study concluded that the ethanolic extract exhibits anti HIV activity and the flavonoids as anti-viral agents [53].

3.3 Antinociceptive activity

The antinociceptive activity of ethanolic *Vertex negundo* Linn leaf extract was performed by tail flick test in rats and writhing test induced by acetic acid in mice. In tail flick test meperidine was used as a standard control, aspirin used as a standard control in writhing test which was compared to the effect of *Vertex negundo* Linn extract. Mechanism of central analgesic action was studied by the interaction of naloxone hydrochloride. *Vertex negundo* extract has both central and peripheral analgesic activity [54].

3.4 Larvicidal activity

The larvicidal activity of flavonoid extract of different parts of *Vertex negundo* Linn and *Andrographis paniculata* is performed against the late III or IV in star larvae of *Aedes aegypti* and *Anopheles stephensi* and the two plants showed good larvicidal activity and can be used to synthesis eco-friendly insecticide [55]

3.5 Anti snake venom activity

Snake venom neutralization by the methanolic roots extracts of *Vertex negundo* Linn and *Emblica officinalis* was performed against the *Viper arusselli* and *Najak authia* venom induced lethal activity both *in-vivo* and *in-vitro* and since no precipitating bands were found between the plants extract and snake venom which revealed that these plants extracts have potent anti snake venom activity [56].

3.6 Anti-amnesic activity

The anti-amnesic activity of *Vertex negundo* extract was studied against scopolamine induced amnesia in rats. Based on the stages of memory accquisition, consolidation and retention the scopolamine was given that different stages and anti amnesic activity of *Vertex negundo* Linn was compared with standard donepezil and study proved that the groups treated with *Vertex negundo* Linn extract showed decrease the phenomenon of amnesia through the antioxidant effect thus increases memory [57-60].

3.7 Antipyretic activity

The yeast induced hyperpyrexia method was used to evaluate the antipyretic activity of methanolic and petroleum ether extract of *Vertex negundo* Linn leaves in groups of male rabbits. Paracetamol was used as the positive standard and 1% CMC was used as control. Compared to petroleum ether extract, methanolic extract has excellent antipyretic activity [61-64].

4. Conclusion

Vertex negundo Linn is a popular medicine for human kind. It has phytochemical constituents which makes it very effective antimicrobial, cytotoxic, analgesic, anti-inflammatory, anti-arthritic, anxiolytic, anti amnesic, antidote for snake venom.

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