Medicinal uses and biological activities of *Vitex negundo*

Vishal R Tandon
Post Graduate Department of Pharmacology and Therapeutics
GMC, Jammu-180 001, Jammu & Kashmir, India
E-mail: dr_vishaltandon@yahoo.com
Correspondence address: Plot 5/B, Near Arya Samaj
Bakshi Nagar, Jammu-Tawi - 180 001, Jammu & Kashmir, India

Abstract

***Vitex negundo* Linn.** is credited with innumerable medicinal activities like analgesic, anti-inflammatory, anticonvulsant, antioxidant, bronchial relaxant, hepatoprotective, etc. The ethanolic extract of leaves has been found safe as LD_{50} dose (by oral route) of it was recorded in non-toxic dose range. Larger trials are required to prove its all activities before it is recommended in future for clinical use, but it carries a great potential to be developed as a drug by the pharmaceutical industry. In this paper general medicinal uses and pharmacological activities of various parts of the plant have been reviewed.

Keywords: *Vitex negundo*, *Sambhalu*, *Nirgundi*, Medicinal uses, Analgesic, Antiinflammatory, Anticonvulsant, Antioxidant, Insecticidal, Pesticidal.

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Introduction

Herbal medicine is the oldest form of healthcare known to mankind and it will not be an exaggeration to say that use of herbal drug for human healthcare is probably as ancient as mankind. A perfect example of medicinal plant credited with innumerable medicinal qualities validated by modern science and used since ancient times is ***Vitex* Linn.** (Family — *Verbenaceae*). The genus consists of 250 species of which about 14 species are found in India and some have commercial and medicinal importance. ***Vitex negundo* Linn.**, commonly known as Five-leaved Chaste tree or Monk's Pepper (Hindi — *Sambhalu*, *Nirgundi*) is used as medicine fairly throughout the greater part of India and found mostly at warmer zones and ascending to an altitude of 1500m in outer Western Himalayas (Wealth of India — Raw Materials, 1976; Chopra *et al*, 1956).

The *Nirgundi* plant is a large aromatic shrub or sometimes a smaller slender tree with quadrangular, densely whitish tomentose branchlets up to 4.5-5.5m in height. Bark thin, yellowish grey; leaves 3-5 foliolate; leaflets lanceolate; terminal leaflets 5-10 ×1.6-2.3 cm, lateral one smaller, all nearly glabrous. Upper surface of the leaves are green and the lower surface are silvery in colour. Flower bluish purple, black when ripe, whereas roots cylindrical, long woody, tortuous with grey brown colour (Prasad & Wahi, 1965). The plant can grow on nutritionally poor soil.

Medicinal Uses

Plant is bitter, acrid, astringent, cephalic, stomachic, antiseptic, alterant, thermogenic, depurative, rejuvenating, ophthalmic, anti-gonorrhoeic, antiinflammatory, antipyretic and useful in bronchitis, asthma and enlargement of spleen. Roots are tonic, febrifuge, anti-rheumatic, diuretic, expectorant and are useful as a demulcent in dysentery, in cephalalgia, otalgia, colic, uropathy, wound and ulcers. Bark is useful in odontalgia, verminosis and ophthalmopathy. Leaves are aromatic, bitter, acrid, astringent, anodyne, anti-inflammatory, antipyretic or febrifuge, tranquillizer, bronchial smooth muscle relaxant, anti-arthritic, antihelmintic and vermifuge. Flowers are cool, astringent, carminative, hepatoprotective, digestive, febrifuge, vermifuge and are useful in haemorrhages and cardiac disorders. Fruit is nervine, cephalic, aphrodisiac,

emmenagogue and vermifuge (Husain *et al*, 1992; Chopra *et al*, 1956).

Chemical Constituents

Leaves contain an alkaloid nishindine, flavonoids like flavones, luteolin-7- glucoside, casticin, iridoid glycosides, an essential oil and other constituents like vitamin C, carotene, gluco-nonital, benzoic acid, β-sitosterol and C-glycoside (Husain *et al*,1992). Seeds contain hydrocarbons, β-sitosterol, benzoic acid and phthalic acid (Husain *et al*, 1992), antiinflammatory diterpene, flavonoids, artemetin and triterpenoids (Chawla *et al*, 1991, 1992). Fatty acids, β-sitosterol, vanillic acid, *p*-hydroxybenzoic acid and luteolin have been isolated from bark (Husain *et al*, 1992). Stem bark yields leucoanthocyanidins (Husain *et al*, 1992; Chopra *et al*, 1956).

Pharmacological Activities

Analgesic activity

Ravishankar *et al* (1985, 1986) found that interperitoneal (I.P.) administration of some leaf and root extracts using different solvents showed analgesic activity. Ethanol and cold aqueous leaf extract showed only weak effect in acetic acid writhing test. Whereas, chloroform and toluene leaf extracts raised the threshold of tail-flick response moderately. While studying the root extract of the plant, ethanol extract significantly increased threshold of tail-flick response. The chloroform extract showed moderate, butanol and cold aqueous root extract produced marked effects in acetic acid induced writhing method. In another study the methanolic leaf extract when given by I.P. route has been found to possess analgesic properties. It also potentiated Morphine and Pethidine induced analgesia significantly in dose dependent manner in mice using hot plate method as an experiment (Gupta *et al*, 1999). Telang *et al* (1999) evaluated the analgesic activity of aqueous methanol leaf extract on oral administration and results showed both central and peripheral analgesic action in acetic acid writhing and tail immersion test comparable to Salicylate and Pethidine hydrochloride, respectively. In rat uterus preparation, they noticed the inhibitory action of extract on prostaglandin (PG) biosynthesis and thereby confirming non-steroidal anti-inflammatory (NSAID's) like activity. In their study they also observed that leaves (crude basis) also contain 1.30% flavonoid compounds. Recently, Gupta and Tandon (2004) also suggested that ethanolic leaf extract of this plant possesses analgesic activity, which appears to be due to PG inhibition and reduction of oxidative stress. They suggested in their study that sub-therapeutic doses of this plant could potentiate the analgesic action of standard drugs like Aspirin and Meperidine. Moreover, they indicated that Naloxone did not reverse the analgesia induced by the extract, indicating that central analgesic action is not mediated through opioid receptors.

Vitex negundo

Antiinflammatory activity

The experimental studies using various animal models have demonstrated that different parts of the plant especially leaves, fruits, roots and seeds possess anti-inflammatory and anti-arthritic activity (Chaturvedi & Singh, 1965; Ravishankar *et al*, 1985, 1986; Chawla *et al*, 1991, 1992; Tamhankar & Saraf, 1994; Jana *et al*, 1999). However, possible mechanism of antiinflammatory activity was indicated (Telang *et al*, 1999) as an inhibitory action on prostaglandin biosynthesis. Recently, Dharmasiri *et al* (2003) suggested that leaves have antiinflammatory and analgesic properties mediated via PG synthesis inhibition, antihistamine, membrane stabilizing and antioxidant activities. ***V. negundo***, which is known to act by prostaglandin inhibition, may be expected to cause gastric damage but on the contrary it produced no histomorphological changes in the stomach even in toxic doses (Tandon & Gupta, 2004). This may be due to a selective COX-2 inhibition that might be responsible for its NSAID's like activity. However, this aspect still needs to be established.

Anticonvulsant activity

The plant has been studied for its anticonvulsant activity. The petroleum and butanol leaf extracts have shown

protection, whereas, none of root extract has shown protection against maximal electro shock (MES) seizures. Petroleum root extract could only provide protection against Leptazole induced convulsions (Ravishankar *et al*, 1985, 1986) whereas, methanolic leaf extract showed significant protection against Strychnine and Leptazole induced convulsions (Gupta *et al*, 1999). Gupta and Tandon (2002) not only suggested anticonvulsant activity of ethanolic leaf extract of this plant but also indicated that it can potentiate the effects of standard anticonvulsants, which may help to reduce dose and dose related side effects of standard anticonvulsants.

Antioxidant activity

The antioxidant activity of the plant was studied using free radical scavenging activity effect on hydroxyl radical mediated damage to deoxyribose and *in vivo* lipid peroxidation assay but did not show any significant effect (Munasinghe *et al*, 2001). However, recently Tandon and Gupta (2005) observed reduction of oxidative stress produced by leaf extract in albino rats. It produced significant reduction in MDA (malondialdehyde) levels after 14 days treatment in only higher dose (500mg/kg/po). Although non-significant marginal rise of SOD (superoxide dismutase) in this dose was observed. In ethanol induced oxidative stress model, however, it significantly reduced only MDA levels in both moderate and higher doses and the effect on SOD were non-significant.

Other Activities

Ethanolic leaf extract has been found to possess anti-histaminic/mast cell stabilizing activity and bronchial smooth muscle relaxing activity (Nair & Saraf, 1995). Similarly various parts especially leaf and root extracts have shown activity against rheumatism (Bhattacharya, 1981) and poliomylities (Nair *et al*, 1988). It has been found to be hepatoprotective (Avadhoot & Rana, 1991), diuretic (Vohora & Khan, 1981), antifilarial (Parveen, 1991), antibacterial (Perumal Samy *et al*, 1998), antimalarial (Pushpalata & Muthukrishnan, 1995) and antiandrogenic/antifertility (Lal *et al*, 1992) agent.

Insecticidal and Pesticidal activities

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

Acute Toxicity Study

Preliminary acute toxicity study of ethanolic leaf extract in albino rats by oral route carried out by Tandon and Gupta (2004) indicated it to be practically nontoxic, as its LD_{50} dose recorded was 7.58g/kg/wt. The stomach showed no histomorphological changes in any of the doses of the extract studied. However, dose dependant histomorphological changes were observed in the specimens of the heart, liver and lung. The specimens of the heart showed vascular dilatation and haemorrhage. Liver showed nonspecific portal dilatation and lung showed edema and congestion microscopically. Dyspnoea noticed mostly after 12 hours of the administration of the extract likely to have been caused by cardiac toxicity in the form of vascular dilatation and haemorrhage appears to be major cause of mortality in their study.

Recommended Dosage

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

Conclusion

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

References

1. Avadhoot Y and Rana AC, Hepatoprotective effect of *Vitex negundo* against carbon tetrachloride induced liver damage, *Arch Pharm Res*, 1991, **14**(1), 96-98.

2. Bhattacharya C, Clinical experiences with *Nirgundi* (*Vitex negundo*), *Rheumatism*, 1981, **16**(3), 111-117.

3. Chaturvedi GN and Singh RH, Experimental studies on anti-arthritic effect of certain indigenous drugs, *Indian J Med Res,* 1965, **53**(1), 71-80.

4. Chaudhari RD, Herbal Drug Industry, A practical approach to industrial pharmacognosy (Eastern Publisher, New Delhi), 1st edn, 1996, 467.

5. Chawla AS, Sharma AK, Handa SS and Dhar KL, Chemical investigation and anti-inflammatory activity of *Vitex negundo* seeds, *Indian J Chem,* 1991, **30B,** 773-776.

6. Chawla AS, Sharma AK, Handa SS and Dhar KL, Chemical investigation and anti-inflammatory activity of *Vitex negundo* seeds, *J Nat Prod,* 1992, **55**(2), 163-167.

7. Chopra RN, Nayar SL and Chopra IC, Glossary of Indian Medicinal Plants (Publications and Information Directorate, Council of Scientific & Industrial Research, New Delhi), 1956, 256-257.

8. Deshmukh PB, Chavan SR and Renapurkar DM, A study of Insecticidal activity of twenty indigenous plants, *Pesticides,* 1982, **16**,7.

9. Dharmasiri MG, Jayakody JR, Galhena G, Liyanage SS and Ratnasooriya WD, Antiinflammatory and analgesic activities of mature fresh leaves of *Vitex negundo*, *J Ethnopharmacol*, 2003, **87**(2-3), 199-206.

10. Dictionary of Indian Medical Plants by Akhtar Husain and others (Central Institute of Medicinal and Aromatic Plants, Lucknow), 1992, 491.

11. Gupta M, Mazumdar UK and Bhawal SR, CNS activity of *Vitex negundo* Linn. in mice, *Indian J Exp Biol,* 1999, **37**, 143-146.

12. Gupta RK and Tandon V, An experimental evaluation of anticonvulsant activity of *Vitex negundo*, Proceeding of 48th Annual Conference, Dec 17-20, 2002 in CME Programme in Physiology and Pharmacology, Lucknow (Abstract), *In*: *Indian J Physiol Pharmacol*, 2002, **46**(5S), 82.

13. Gupta RK and Tandon VR, Antinociceptive activity of *Vitex negundo* Linn. leaf extract, Proceedings of 35th Annual Conference of the Indian Pharmacological Society, Nov. 26-29, 2002, Gwalior (Abstract), *In: Indian J Pharmacol*, 2004, **36**(1), 54.

14. Hebbalkar DS, Hebbalkar GD, Sharma RN, Joshi VS and Bhat VS, Mosquito repellent activity of oils from *Vitex negundo* Linn. leaves, *Indian J Med Res*, 1992, **95**, 200-203.

15. Jana U, Chattopadhyay RN and Shaw BP, Preliminary studies on antiinflammatory activity of *Zingiber officinale* Rosc, *Vitex negundo* Linn. and *Tinospora cordifolia* (Willd.) Miers. in albino rats, *Indian J Pharmacol,* 1999, **31**(3), 232-233.

16. Lal B, Udupa KN and Tripathi VK, Study of the Antifertility effect of Nirgundi (*Vitex negundo*)-A preliminary trials, *J Res Ayurv Siddha,* 1992, **13**(1-2), 89-93.

17. Munasinghe TCJ, Seneviratne CK, Thabrew MI and Abeysekera AM, Anti-radical and antilipoperoxidative effect of some plant extracts used by Sri Lankan traditional medical practitioner for cardioprotection, *Phytother Res*, 2001, **15**, 519-523.

18. Nair AM and Saraf MN, Inhibition of antigen and compound 48/80 induced contractions of Guinea pig trachea by ethanolic extract of the leaves of *Vitex negundo* Linn., *Indian J Pharmacol,* 1995, **27**, 230-233.

19. Nair PR, Vijayan NP, Madhavikotty P and Nair CNB, Clinical evaluation of *Sahacharadi* and *Nirgundi taila* in *saisaveeyavata* (poliomyelitis), *Ancient Sci Life,* 1988, **8**(1), 25-29.

20. Parveen N, Anti-Filarial activity of *Vitex negundo* against *Seloria cervi*, *Fitoterapia,* 1991, **62**(2), 163-165.

21. Perumal Samy SR, Ignacimuthu S and Sen A, Screening of 34 Indian medicinal plants for antibacterial property, *J Ethnopharmacol,* 1998, **62**(2), 173-182.

22. Prakash A and Mathur KC, Active principles on plant products used in insect pest management of stored grains, *Bull Grain Technol*, 1985, **23**,102.

23. Prasad S and Wahi SP, Pharmacognostic study of leaf of *Vitex negundo* Linn. (Nirgundi), *J Res Indian Med*, 1965, **72**, 208-211.

24. Pushpalatha E and Muthukrishnan J, Larvicidal activity of a few plant extracts against *Culex quinque-fasciatus* and *Anopheles stephensi*, *Indian J Malariol,* 1995, **32**(1), 14-23.

25. Ravishankar B, Bhaskaran NR and Sasikala CK, Pharmacological evaluation of *Vitex negundo* (Nirgundi) leaves, *Bull Medico-Ethno-Bot Res,* 1985, **6**(1), 72-92.

26. Ravishankar B, Bhaskaran NR and Sasikala CK, Pharmacology of *Vitex nugundo* Linn. (Nirgundi) root, *J Res Ayurv Siddha,* 1986, **7**(1-2), 62-77.

27. Tandon V and Gupta RK, Histomorphological changes induced by *Vitex negundo* in albino rats, *Indian J Pharmacol,* 2004, **36**(3), 176-177.

28. Tandon V and Gupta RK, Effect of *Vitex negundo* on oxidative stress, *Indian J Pharmacol*, 2005, **37**(1), 38-40.

29. Tamhankar CP and Saraf MN, Anti-arthritic activity of *Vitex negundo* Linn., *Indian J Pharm Sci*, 1994, **56**(1), 158-159.

30. Telang RS, Chatterjee S and Varshneya C, Studies on analgesic and anti-inflammatory activities of *Vitex negundo* Linn., *Indian J Pharmacol,* 1999, **31**(5), 363-366.

31. The Wealth of India: A Dictionary of India Raw Materials and Industrial Products — Raw Material Series (Publications and Information Directorate, Council of Scientific & Industrial Research, New Delhi), Vol. X, 520-525, 1976, reprint, 1998.

32. Vohora SB and Khan MSY, Diuretic studies on plant principles, *Indian Drugs Pharm Ind*, 1981, **16**(1), 39-40.