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Ethnobotany, phytochemistry and pharmacological potential of *Vitex negundo* L. (five-leaved chaste tree): An updated review

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ABSTRACT

In the past two decades, a shift in paradigm has been observed in the development of new drugs from the plants for the treatment of diseases. Many scientists are focusing on the evidence based use of medicinal plants to develop pharmacotherapy for various human ailments. An important medicinal plant that has caught the attention of researchers all over the globe is *Vitex negundo* Linn. This plant is commonly used in various traditional systems of medicine like Ayurveda, Chinese, Siddha and Unani to treat various diseases and has been the subject of extensive research studies lately. Its roots and leaves are widely used in various disorders and illnesses such as skin eczema, ringworm, liver disorders, spleen enlargement, rheumatic pain, gout, abscess, backache etc. Seeds are also used as folklore medicine in bronchitis, eye disorders, female reproductive disorders, cold, dropsy, malarial fever and as demulcent. The current article is an effort to compile an updated review to disseminate knowledge and information among the scientific fraternity covering the progress made in the pharmacology and phytochemistry of this useful medicinal plant. This review on a very important traditional medicine, *Vitex negundo* L. can serve as a reference to the scientific community for their future research on this plant.

1. Introduction

The concept of using plants in pharmacotherapy is not new to humankind. Available evidences clearly indicate that mankind has used plants to prevent and treat various diseases since ancient time. For example, Materia Medica documented by Hippocrates (about 460-370 BC) states the use of certain plants like *Mentha piperita*, *Papaver somniferum*, *Ruta graveolens*, *Verbena officinalis*, etc. which are presently used as medicines[1]. In the present world scenario too, the use of plants as medicinal agents is evident. Moreover, in the past two decades there has been a boom in the use of plants or their isolates as drugs. This shift in paradigm from synthetic based medicines to natural products might be due to cost,

over use and side effects associated with the use of almost all the synthetic drugs. Also majority of the world population still does not have an easy access to the most commonly used synthetic drugs[2]. Approximately 25% of the total drugs available worldwide to treat and manage the human ailments are of plant origin. Out of 252 essential drugs as identified by World Health Organization (WHO), approximately 11% are derived from plants[2]. WHO has recognized the importance of plants as medicinal agents and therefore, decided to document detailed information on selected medicinal plants in 28 standard pharmacopoeia[1,3]. Because of such massive use of plants as therapeutic agents, systematic scientific evaluation of such plant based products on the basis of their medicinal properties becomes indispensable.

One such plant that has been used traditionally over centuries to treat various acute as well as chronic diseases is *Vitex negundo* L (*V. negundo*). *V. negundo* is popularly known as nirgundi and belongs to the family Verbenaceae. In Sanskrit language, the word "nirgundi" word is used for plant or any substance that protects the body from the diseases. The vernacular names of *V. negundo* are as follows; Assamese: Aslok; Bengali: Nirgundi, Nishinda; English: Five-leaved chaste tree; Gujarati: Nagod; Hindi: Nirgundi, Sambhalu,

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Shambalu; Kannad: Lakkigida, Nekka, Nakkilu, Nakkigida; Malayalam: Indranee, Karunacci; Marathi: Nirgundi; Punjabi: Sambhalu, Banna; Tamil: Vellai-nocohi, Nirkkundi, Venmochi and Urdu: Sambhalu.

This plant is credited with innumerable therapeutic actions like anti-inflammatory, anti-asthmatic, analgesic, etc.

1.1. Botanical description

V. negundo is a large woody aromatic shrub that grows in humid conditions. Its leaves are 3-5 foliate, minutely hairy on dorsal side, densely pubescent ventrally, shallow, blunt toothed margin with long leaf stalks. The leaflets have a short petiole, lanceolate nearly glabrous above, covered with a fine white tomentum beneath and acute base. The plant bears bluish-white to bluish-purple flowers, 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, lanceolate caduceus. Calyx is 0.8–1 mm long, white tomentose and teeth triangular. The berry is of pea size and coloured black. Fruits are four valved and capsulated; ovary glabrous; style glabrous and stigma forked[4,5].

1.2. Ecology and distribution

V. negundo is native to India and Philippines and occurs as exotic species in United Kingdom. The species is also cultivated in Europe, Asia and West Indies. It is a water loving plant and found abundantly along river banks, in humid conditions and in open wastelands. Nirgundi is one of the commonly used hedge plant which is planted along roads and between fields. It grows best up to an altitude of 2000 m, requires a mean annual rainfall of 600 to 2000 mm and can tolerate alkaline and saline soils[6,7].

1.3. Propagation and management

Stem cutting is the usual method for the propagation of nirgundi. In the month of May–June, the stems are planted in nursery beds and transplanted two months later. The plant is managed by coppicing with a rotation of every two years[6]. Nirgundi seeds are recalcitrant and losses viability in about 3 weeks' time. Vadawale *et al.*, were able to generate fully functional flowers in Murashige and Skoog (MS) medium rich in benzylaminopurine and naphthalene acetic acid supplements to overcome the poor viability problem[8]. However, the best *in-vitro* rooting was obtained with MS supplemented with indole-3-butyric acid[8]. Afroz *et al.*, established an efficient protocol for *in-vitro* shoot propagation and found that MS fortified with benzyladenine was the most effective for inducing multiple shoots from nodal explants[9]. In another study, leaf explants cultured on MS with different concentrations of 2,4 dinitrophenyl acetic acid

and indole acetic acid in combination with benzylaminopurine showed shoot regeneration and nearly 90% survival of *in-vitro* plants[10]. Chandramu *et al.*, were also successful in producing *in-vitro* flowering in MS medium enriched with benzyladenine and naphthalene acetic acid[11].

2. Medicinal importance

2.1. Uses of *V. negundo* in traditional system of medicine

As stated earlier, nirgundi has been used since ancient time for large number of clinical conditions and is still being used. In early times in Roman society, *V. negundo* leaves were used to reduce sexual desire. Also, monks used to chew nirgundi berries for the same purpose and hence the name Monk's berry or Monk's pepper was assigned to it[12]. In homoeopathic system of medicine the herb is used to treat reproductive system related disorders like depression of vital power, self contempt for the sexual abuse, feeble erection without libido, emission of prostatic fluid during stool, painful, hard, cold, swollen testicles, etc.[7]. Plant may also be used to reduce hot flashes due to reduced progesterone production during menopause and to regulate ovulatory cycles[12]. In South East Asian countries *viz.* Cambodia, Laos and Vietnam, *V. negundo* is used as herbal medicine to heal wounds, and to treat beriberi and paralysis. Some of its uses in various traditional systems of medicines practiced all over the world were listed in Table 1.

2.2. Uses of *V. negundo* in folklore medicine

In developing countries, folklore medicines play a vital role. Because of lack of knowledge and limited modern health facilities people tend to find natural cure for various diseases. India is one such country where a large population depends on natural healers. Folklore uses of *V. negundo* were presented in Table 2.

Apart from India, in other countries especially Indian subcontinent, nirgundi forms a greater part in the locally used medicines. For instance, in Bangladesh and Iran, its leaves are used to enhance memory and to control diabetes[14,35-39]. Its leaves and flowers are used in Sri Lanka as febrifuge, vermifuge, in rheumatism, toothache, eye diseases, etc.[13]. Decoction of nirgundi leaves is applied locally by Nepalese to combat inflammation, scabies and bacterial infections[40,41]. In Pakistan, leaves as well as seeds are indicated to treat cholera and skin diseases[42-45].

3. Phytochemical profile

Rates (2001) states that about 2/3rd of the anti-neoplastic and antimicrobial drugs currently under clinical trials or available in the market are of plant origin[2]. Not only do the plants serve as a direct mode of treatment, but sometimes natural compounds can also act as

Table 1
Use of *V. negundo* in various traditional systems of medicine

System of medicine	Uses
Ayurvedic system of medicine[4,7,12,13]	Analgesic, anthelmintic, demulcent in diarrhoea and piles, rheumatism, female reproductive disorders, tranquilizer, sinusitis, neck swellings and ulcer
Unani system of medicine[7,13-15]	Contraceptive, dropsy, aphrodisiac, malarial fever and spermatorrhoea
Chinese system of medicine[7,13,16-18]	Antacid, stomach-ache, arthritis, bronchitis, asthma, cold, eye disorders, indigestion, diarrhea, gallstone and hernia
Siddha system of medicine[19]	Joint inflammation swelling

Table 2
Ethnobotanical uses of *V. negundo* in different states of India.

State	Region/Tribe	Local name	Part used	Ailment	Method of usage	Reference
Andhra Pradesh	Sriharikota Island	Vavilli chettu	Twigs	Toothache	-	[20]
		Tella vavilli	Leaves	Mouth ulcers	Paste applied locally	
	Puttaparthi			Asthma	-	[12]
Assam	Dibrugarh district (Mishings tribe)	Pochotia	-	Cancer	-	
	Sonitpur district	Pochotia	-	Eczema	-	[21]
Himachal Pradesh	Guddi and Gujjar tribe	Banna	Shoots	Joint pain	-	[22]
		Nirgundi Sambhalu	Leaves	Internal injury	Decoction is taken internally; leaves are tied around the area of internal injury for relief	[23]
Jharkhand	Bihore tribe	Sindwar	Bark	Muscular pain, headache	Boiled with milk and taken	[24]
Karnataka	Shimoga district	Lakki gida	Leaves	Cold	Mix or ground with fruits of <i>Sapindus laurifolius</i> , leaves of <i>Leucas aspera</i> , pepper, garlic and inhaled	[25]
	Dharwad	Lakki Karilakki	-	Toothache	-	[12]
Madhya Pradesh	Chhindwara Betul district	Nirgundi	Leaves	Rheumatism	Decoction of leaves is taken	[26]
Meghalaya	Jaintia tribe	Tohtihdkhar	Root	Epilepsy	Paste with liquor is applied over neck	[27]
			Leaves	Arthritis	Warm leaf applied topically	
Orissa	Kalahandi district	Nirgundi	Leaves	Cold	Mix of leaf decoction + <i>Piper longum</i> powder + honey taken orally	[28]
	Malkangiri district	Languni	-	Rheumatism	Warm leaves applied as hot massage	[12]
Rajasthan	Udaipur	Negad	Leaves	Veterinary use in foot and mouth disease	-	[29]
	Meena community	Nirgundi	Leaves	Joint pain	Decoction used as fomentation	[30]
Tamil Nadu	Salem region	Nochi	Leaves	Animal poison bite, headache, running nose	-	[31]
	Southern regions	Notchi	-	Antidote for snake bite	-	[12]
Uttarakhand	Kancheepuram district	Notchi	Leaves	Cold, cough	Boiled in water and the vapour is inhaled twice a day to get relief	[32]
	Haridwar	Nirgundi Mehla	-	Swelling, conjunctivitis, cataract	-	[33]
Uttar Pradesh	Bhoxas tribe	Muhalu	Root	Piles	Powdered root taken with boiled water internally	[34]
	Jaunsar-Bawar hills	Sinwalu Somi	Leaves	Piles	Paste applied locally on piles	[34]
West Bengal	Bankura district	Nishinda	-	Eye pain	-	[12]
			Boan	Leaves	Gout, ulcer	-
		Boan	Flowers	Inflammation, fever	-	[35]
				Diarrhea	-	

lead compounds and help in rational drug design. Many a times these natural products lead to the discovery of new therapeutic targets and development of synthetic or semi synthetic analogues possessing interesting pharmacological actions[2,46].

The therapeutic action(s) of a medicinal plant to provide specific biological benefits in humans are attributed to the secondary plant metabolites i.e. phytochemicals present in it. The qualitative and quantitative phytochemical analysis of *V. negundo* L. have resulted in the identification of various compounds ranging from iridoids to terpenes. The various phytochemicals previously isolated from *V. negundo* L. are given in Table 3.

4. Pharmacological properties

Nirgundi plant is reported to possess a large number of diverse pharmacological activities, thus making it to be a useful drug in the treatment of various ailments. Some of its commonly explored pharmacological properties by *in vivo/in vitro* experiments either in order to validate its use in traditional medicine or to identify lead molecules for the drug discovery have been discussed below.

4.1. Antioxidant activity

Enormous literature is available documenting the antioxidant activity of *V. negundo* both *in vivo* and *in vitro* models[70-72].

Kulkarni *et al.* (2008) evaluated the radical scavenging activity of methanolic leaf extract of *V. negundo* by 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay and lipid peroxidation inhibitory activity[73]. EC₅₀ value of 18.70 µg/mL was obtained against the value of 2.85 µg/mL for ascorbic acid. The extract also exhibited a concentration dependent inhibition of formation of thiobarbituric acid reacting substances. Alam *et al.* in 2009 reported that ethanolic extract of *V. negundo* L. leaves exhibits a dose dependent antioxidant effect in DPPH and hydrogen peroxide scavenging assays[74]. For DPPH assay IC₅₀ value for ethanolic extract was found to be 178.43 µg/mL and for hydrogen peroxide scavenging assay IC₅₀ value was 158.93 µg/mL[74]. Zargar *et al.* (2011) evaluated the antioxidant activity of methanol extract, hexane extract and essential oil of *V. negundo* L. leaf by three different assay methods[75]. Authors found that methanol extract exhibited higher antioxidant activity in terms of DPPH free radical scavenging capacity, ferric ion antioxidant power and β-carotene-linoleic acid as compared to hexane extract. A study done by Huang *et al.* (2012) revealed that the leaves essential oil of *V. negundo* also possess good antioxidant potential[76]. IC₅₀ value of essential oil by DPPH assay was 103.85 µg/mL and for 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid) assay was 19.94 µg/mL. There are several studies which have evaluated and described the antioxidant action of total alcoholic extract of root[77,78], supercritical extract as well as different solvent extracts of leaves by *in-vivo* and *in-vitro* methods[79-83].

Table 3Phytochemicals isolated from different parts of *V. negundo*.

Phytochemical	Plant part	Reference
Aliphatic alcohol/phenol	n-hentriaconatol	Leaves, [47-49]
	p-hydroxybenzoic acid	seed
	3,4 dihydroxybenzoic acid	Seed [47-49]
	5-oxyisophthalic acid	
	Linalool	Leaves [17]
Alkaloids	Vanillic acid	Bark [50]
	Nishindine	Leaves [50]
Amino acid	Guanine, alanine, valine, leucine	Seed [17]
Flavonoids	5,6,7,8,3', 4', 5' heptamethoxy flavone,	Leaves [51-53]
	5-O- desmethoxynobioletin flavone,	
	Gardenin A, gardenin B, corymbosin,	
	Vitexicarpin, 5-hydroxy 3,6,7,3'4	
	pentamethoxy flavone	
	Casticin, artemitin	Leaves [53,54]
	Vitexoside	Root [52,55,56]
	Luteolin	Bark, [50,57]
	4,4-dimethoxy trans stilbene (Stilbene derivative)	leaves [58-61]
	Acerosine	
	Leucoanthocyanidin	Bark [1]
Glycoside	Luteolin-7-glucoside	Leaves [50]
	Leucocyanidin-7-O-rhamnoglucoside	Bark [17]
Hydrocarbon	n-Tritriacontane, n-hentriacontane,	Seed [47-49]
	n-pentatriacontane	
	n-Nonacosane	
Iridoid glycoside	2-p-hydroxybenzoyl mussaenosidic acid	Leaves [53,62]
	Agnuside, Lagundinin, Aucubin,	
	Nishandaside	
	4',5,7-trihydroxy-3'-O-β-D-glucuronic acid-6"-methyl ester	[52]
Lignans (Phenyl dihydronaphthalene type)	Negundoside	[17]
	Vitedoin A, Vitedoamine A, Vitexdoin A	Seed [63-65]
	Vitedoamine B	
	Vitexdoin B-E (Phenylnaphthalene type)	
Fatty acids	Negundin A, Negundin B	
	vitrofolal E	Root [66]
Fatty acids	Lionelic acid, Oleic acid, Stearic acid	Seed [53,67]
	Palmitic acid	Seed, fruit [17,53,67]
Phytosterol	β-sitosterol	Seed [47-49]
Terpene	Monoterpene	Leaves [17]
	α-Pinene, camphene, citral, sabinene	
Sesquiterpene	p-Cymene	Flower [17]
	Viridiflorol	Leaves [53]
Furanoeremophilane	β-Carophyllene	Root [17]
	β-Salinene	
	α-Cedrene	Leaves [17]
	Germacrene D	Fruit, [17]
	Germacren-4-ol	flower
	Nerolidol, valencene	Fruit [17]
Diterpene	Flower [17]	
	Vitedoin C (trinorlabdane type)	Seed [63,64]
	Negundol	Seed [68]
Triterpenes	Vitexilactone	Leaves [53]
	Betulinic acid, ursolic acid	Leaves [54]
	Friedelin	Leaves [53]
	Squalene, β-amyirin, Epifriedelinol	Heartwood [69]

4.2. Anti-inflammatory activity

Various studies are available to support the anti-inflammatory activity of *V. negundo* in different models. Jana *et al.* (1999)[84] and Yunos *et al.* (2005)[85] demonstrated anti-inflammatory properties of *V. negundo* extracts in acute and sub-acute inflammation. The effect is due to the inhibitory action on prostaglandin synthesis[50,86]. Moreover, few other studies suggest that the anti-inflammatory potential of leaves of *V. negundo* might be due to the inhibition of prostaglandin synthesis, anti-histaminic, membrane stabilizing and antioxidant activity[50,87]. Vinuchakkaravarthy *et al.* (2011) isolated a novel anti-inflammatory compound Tris(2,4-di-tert-butylphenyl) phosphate from the leaves of *V. negundo* which reduced the carrageenan-induced raw paw oedema volume at both the tested doses (50 mg/kg and 70 mg/kg body weight) significantly[88]. Choksi *et al.*, (2012) tested different extracts from

the plant combined with oil for their anti-inflammatory activity[89]. Their finding revealed that methanolic extract was better than the other extracts. Kumar *et al.* (2013) recently confirmed the anti-inflammatory action of ethanolic extract in carrageenan induced paw oedema and cotton pellet in Albino rats[90].

4.3. Antibacterial activity

The volatile oils obtained from leaves, flowers and seeds of *V. negundo* L. are reported to possess antibacterial activity. The main chemical constituents identified in leaves which are chiefly responsible for their antibacterial activity includes; guaiene, carryophyllene epoxide and ethylhexadecenoate; in flower -selinene, germacren-4-ol, carryophyllene epoxide and (E)-nerolidol while in fruit β-selinene, β-cedrene, germacrene D and hexadecanoic acid[7]. Jeyaseelan *et al.* in 2010 showed that ethyl acetate extract of flower of *V. negundo* is quite active against *Pseudomonas solanacearum* and *Xanthomonas axonopodis* pv. *citri*[91]. The *V. negundo* leaves extract and twigs extract is also reported to exhibit antimicrobial activity against pathogens such as *Micrococcus pyogenes* and *Escherichia coli*[77,92]. Panda *et al.* (2011)[93] studied the antibacterial effect of five different polarity solvent extracts of bark and leaf of *V. negundo* on eleven microorganisms. All extracts showed good antibacterial activity with zone of inhibitions ranging from 9.6–15.6 mm for bark and 9.3–14.3 mm for leaf. Another study concluded that the ethanolic leaf extracts of *V. negundo* possess the spectrum to inhibit the growth of *Salmonella paratyphi*[94]. Recently, in 2013 Kamruzzaman *et al.* reported that methanol extract of *V. negundo* leaves possess potent bactericidal activity against diverse multidrug resistant enteric bacterial pathogens making it an ideal candidate for further studies in hope of developing a potent antibacterial agent[95].

4.4. Hepatoprotective activity

Avadhoot and Rana have reported the protective effect of alcoholic extract of *V. negundo* seeds on carbon-tetrachloride induced hepatotoxicity[96]. A dose of 250 mg/kg (1/6 of LD₅₀) of the extract was found to be effective. Hepatoprotective activity of *V. negundo* ethanolic leaf extract was also investigated against hepatotoxic anti-mycobacterial drugs *viz.* isoniazid, rifampin and pyrazinamide. Its hepatoprotective effect was evident at doses 250 and 500 mg/kg. The protective action was further confirmed by histological examination of liver section[97]. Tasduq *et al.* were successful in confirming the hepatoprotective action of negundoside when tested in carbon-terachloride induced toxicity[98]. Authors proposed that the hepatoprotective action could be due to inhibition of lipid peroxidation, followed by an improved intracellular calcium homeostasis and inhibition of calcium-dependent proteases. Kadir *et al.* investigated the therapeutic effect of ethanolic extract of *V. negundo* in thioacetamide induced liver fibrosis in adult male rats for twelve weeks[99]. The hepatoprotective action of nirgundi extract was found to be comparable with standard drug silymarin at dose level of 100 mg/kg and 300 mg/kg body weight. The outcome of this study suggests that *V. negundo* could be used to prevent drug induced hepatotoxicity[99].

4.5. Analgesic activity

Several studies have showed that essential oil, leaf and other parts of *V. negundo* possess significant peripheral and central analgesic activity in experimental animals[100-103]. Further, it was also suggested that sub-therapeutic doses of *V. negundo* plant can possibly potentiate the effect

of analgesic drugs such as aspirin, meperidine *etc.*, and thus may be used as an adjunct to analgesic therapy[50].

4.6. Anticonvulsant activity

The leaf extracts of the plant of varying polarity have showed protection against maximal electroshock seizure and pentylenetetrazole induced seizures in Albino mice. Though, its anticonvulsant activity was not at par with the standard antiepileptic drugs but it can potentiate the action of diphenylhydantoin and valproic acid[104,105]. Recently, Khokhra *et al.*, evaluated the anticonvulsant activity of essential oils isolated from dried fruits, fresh leave and flowers of *V. negundo* Linn. The activities of oils were compared with phenytoin in MES and diazepam in pentylenetetrazole induced seizures. Essential oil isolated from leaves showed exhibited excellent protection against pentylenetetrazole induced clonic seizures only while all oils at 200 mg/kg dose found to potentiate the anticonvulsant activity of phenytoin and diazepam standard drugs[106].

4.7. Memory enhancer activity

This plant is used in Indian traditional system of medicine as a brain tonic and to improve learning and memory[107]. Hydroalcoholic leaves extract of *V. negundo* is shown to decrease brain lipid peroxidation and increase brain glutathione in scopolamine induced cognitive deficit mice, and thereby improve learning and memory processes. The authors suggested that this action could be due to acetylcholinesterase inhibition, antioxidant effect, and/or increase in cholinergic transmission[108].

4.8. Anti-HIV activity

Kannan *et al.* evaluated the effects of 85% ethanolic leaf extract of *V. negundo*. HIV-1 reverse transcriptase activity by using a non-radioactive HIV-RT colorimetric ELISA kit. The plant extract significantly inhibited the HIV-1 RT activity by 92.8% at a concentration of 200 µg/ml. The anti-HIV activity of the plant might be due to the presence of high quantity of kaempferol, quercetin and myricetin[109].

4.9. Other pharmacological actions

Due to the antioxidative action of flavonoids of *V. negundo*, the plant extract can also be used in the treatment of cataract. Rooban *et al.* from their research concluded that flavonoids of *V. negundo* can successfully modulate senite induced cataractogenesis in rats by altering lens proteins and lens structure[110,111]. Furthermore, Pai *et al.* have reported cardioprotective action of aqueous extract of *V. negundo* leaves which showed positive inotropic and negative chronotropic effect in comparison to digxin[112]. Some other interesting pharmacological actions of *V. negundo* include anti-acne[113-116], antiasthmatic[117], anthelmintic[118,119], antihyperpigmentation[120], anxiolytic[121], central nervous system depressant[105], hypoglycemic[122,123], laxative[124], cytotoxic[7,13,51,82,125-128] and ulcerative colitis[129], *etc.*

5. Drug interactions

Very limited literature data is available on drug interactions as not much work has been done on this front. Padmalatha *et al.* reports the alerted pharmacological action of steroidal drugs like norethindrone, ethinyl estradiol, drospirenone, levonorgestrel when taken with *V. negundo*[130]. *In vitro* study also reveals that due to dopaminergic activity of the plant, it may also alter the effect of psychotropic drugs

like selegeline, amantadine, carbidopa, levodopa, bromocriptine, pergolide, *etc*[130,131]. A study by Tripathi *et al.* pointed out a significant drug interaction with paracetamol. An appreciable decline in the plasma concentration of paracetamol was observed when both were administered together[132]. Thus it can be concluded that *V. negundo* extract or its ayurvedic formulation should not be taken concurrently with paracetamol or if co-administered with paracetamol, then the dose of paracetamol should be adjusted to achieve desired therapeutic response.

6. Acute toxicity study

It is non-toxic and LD₅₀ of its ethanolic leaf extract determined *p.o.* in Albino rats was found to be 7.58 g/kg body weight[50].

7. Conclusion

The review discusses the traditional uses and pharmacological potentials of *V. negundo*. Its mention in *Charaka Samhita* is one such evidence of its use since ancient time. Ethnobotanical claims have also been clearly presented suggesting that the plant has served all sections of the world.

It is clear from the review that the immense biological actions of *V. negundo* have been investigated scientifically to a large extent through experimental studies. The plant is used as antioxidant, anti-inflammatory, analgesic, anticarcinogenic agent in the treatment of vast range of diseases. Only very few clinical trials for various activities have been conducted in the past but more clinical trials are required to evaluate its safety and clinical efficacy in humans.

Conflict of interest statement

We declare that we have no conflict of interest.

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