A Review on *Vitex negundo* L. – A Medicinally Important Plant

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ABSTRACT

Vitex negundo L. (Verbenaceae) is a hardy plant, flourishing mainly in the Indian subcontinent. All parts of the plant, from root to fruit, possess a multitude of phytochemical secondary metabolites which impart an unprecedented variety of medicinal uses to the plant. It is interesting to note that a single plant species finds use for treatment of a wide spectrum of health disorders in traditional and folk medicine; some of which have been experimentally validated. The plant is a component of a number of commercially available herbal formulations and has also shown potential as an effective bio-control agent. Employment of techniques such as cell and tissue culture would provide means of rapid propagation and conservation of the plant species and, from the point of view of phytochemistry, give scope for enhancement of the quality and quantity of the bioactive secondary metabolites occurring in the plant.

Key words: phytochemical; pharmacological; bio-control; herbal formulations; *in vitro* culture

Abbreviations:
BA: 6-Benzyl Amino Purine
CH: Casein Hydrolysate
GA_3: Gibberellic Acid
IAA: Indole-3-Acetic Acid
IBA: Indole-3-Butyric Acid
Kn: Kinetin
MS: Murashige and Skoog
NAA: α-Naphthoxy Acetic Acid
Vn: Vitex negundo

1. INTRODUCTION

1.1. Medicinal Plants

Morgenstern [1] defines ethnobotany as the study of the indigenous uses of plants and the relationship between people and plants. Folk medicines of almost all civilizations of the world abound in herbal remedies. Majority of the traditional medicines used in healthcare are obtained from plants [2]. In spite of several advancements in the field of synthetic drug chemistry and antibiotics, plants continue to be one of the major raw materials for drugs treating various ailments of humans. Clinical and pharmaceutical investigations have in fact elevated the status of medicinal plants by identifying the role of active principles present in them and elaborating on their mode of action in human and animal systems [3].

The world is gradually turning to herbal formulations which are known to be effective against a large repertoire of diseases and ailments. More importantly, they are not known to cause any notable derogatory effects [4]; and are readily availabile at affordable prices [5]. Prajapati et al. [6], however, add a note of caution stating that plant remedies are effective and without side-effects, provided they are selected properly and taken under proper medical supervision. The active component, most often a secondary metabolite, varies in quality and quantity for a given plant species growing in different locations. The market value of such plants depends on their active content rather than merely their luxuriant growth. Purohit and Vyas [7] reckon that close to 70,000 species of the plant kingdom have been used as herbal medicine at one time or other.

1.2. Vitex negundo Linn.

Vitex negundo Linn. (Verbenaceae) is a woody, aromatic shrub growing to a small tree. It commonly bears tri- or penta-foliate leaves on quadrangular branches, which give rise to bluish-purple coloured flowers in branched tomentose cymes. It thrives in humid places or along water courses in wastelands and mixed open forests and has been reported to occur in Afghanistan, India, Pakistan, Sri Lanka, Thailand, Malaysia, eastern Africa and

Madagascar. It is grown commercially as a crop in parts of Asia, Europe, North America and the West Indies [8]. Though *V. negundo* (will henceforth be referred to as *Vn* for sake of convenience) also finds use as a food crop (Facciola, 1990) and a source of timber [9], this review deals only with the medicinal importance and other related attributes of the plant.

2. Phytochemical Constituents

Higher plants are warehouses of assorted bioactive constituents or phytochemicals which find ample use in the pharmaceutical industry. Namdeo [10] states that about a quarter of all prescribed pharmaceuticals in advanced countries contain compounds that are directly or indirectly, derived from plants. Phytochemicals or secondary metabolites usually occur in complex mixtures that differ among plant organs and stages of development [11, 12]. Knowledge of the phytochemical constituents is very essential to enable investigation of the actual effectiveness of the plant in medicine. Table 1 gives the details of the different phytochemical constituents that have been reported from different parts of *Vn*.

Table 1 – Phytochemical constituents of different plant parts of *V. negundo*

PLANT PART	PHYTOCHEMICAL CONSTITUENTS	REFERENCE
Leaves	hydroxy-3,6,7,3′,4′-pentamethoxyflavone	[12]
	6′-p-hydroxybenzoyl mussaenosidic acid; 2′-p-hydroxybenzoyl mussaenosidic acid	[13, 14]
	5, 3′-dihydroxy-7,8,4′-trimethoxyflavanone; 5,3′-dihydroxy-6,7,4′-trimethoxyflavanone	[15]
	viridiflorol; β-caryophyllene; sabinene; 4-terpineol; gamma-terpinene; caryophyllene oxide; 1-oceten-3-ol; globulol	[16]
	betulinic acid [3β-hydroxylup-20-(29)-en-28-oic acid]; ursolic acid [2β -hydroxyurs-12-en-28-oic acid]; n-hentriacontanol; β-sitosterol; p-hydroxybenzoic acid	[17]
	protocatechuic acid; oleanolic acid; flavonoids	[18]
	angusid; casticin; vitamin-C; nishindine; gluco-nonitol; p-hydroxybenzoic acid; sitosterol	[19]
Seeds	3β -acetoxyolean-12-en-27-oic acid; 2α, 3α-dihydroxyoleana-5,12-dien-28-oic acid; 2β,3α diacetoxyoleana-5,12-dien-28-oic acid; 2α, 3β-diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid	[20, 21]
	vitedoin-A; vitedoin-B; a phenylnaphthalene-type lignan alkaloid, vitedoamine-A; five other lignan derivatives	[22]
	6-hydroxy-4-(4-hydroxy-3- methoxy-phenyl)-3-hydroxymethyl-7-methoxy-3, 4-dihydro-2-naphthaldehyde	[23]
	β-sitosterol; p-hydroxybenzoic acid; 5-oxyisophthalic acid; n-tritriacontane, n-hentriacontane; n-pentatriacontane; n-nonacosane	[19]
Roots	2β, 3α-diacetoxyoleana-5,12-dien-28-oic acid; 2α,3α-dihydroxyoleana-5,12-dien-28-oic acid; 2α,3β -diacetoxy-18-hydroxyoleana-5,12-dien-28-oic acid; vitexin and isovitexin	[24]
	negundin-A; negundin-B; (+)-diasyringaresinol; (+)-lyoniresinol; vitrofolal-E and vitrofolal-F	[25]
	acetyl oleanolic acid; sitosterol; 3-formyl-4.5-dimethyl-8- oxo-5H-6,7-dihydronaphtho (2,3-b)furan	[26]
Essential oil of fresh leaves, flowers and dried fruits	δ-guaiene; guaia-3,7-dienecaryophyllene epoxide; ethyl-hexadecenoate; α-selinene; germacren-4-ol; caryophyllene epoxide; (E)-nerolidol; β-selinene; α-cedrene; germacrene D; hexadecanoic acid; p-cymene and valencene.	[27]

2.1. Summary

Extensive biochemical analyses have resulted in the detection and isolation of a wide variety of the phytochemical constituents from different parts of the plant. Application of advanced spectroscopy tools such as NMR, EMR, FTIR along with X- ray crystallography studies would bring to light more such biologically active phytochemicals in different parts of the plant. Use of *in silico* tools to evaluate the efficacy of these phytochemical moieties as drugs would endow an added value to such a study.

3. Medicinal Importance

Herbal medicine, rather than merely curing a particular disease, aims at returning the body back to its natural state of health [28]. The phytochemical components of medicinal plants often act individually, additively or synergistically in improvement of health [29]. After having analyzed the various chemical components present in different parts of *Vn*, it is imperative that focus shifts to the medicinal applications of the plant. Myriad medicinal properties have been ascribed to *Vn* and the plant has also been extensively used in treatment of a plethora of ailments [6]. These properties have been categorized under three heads – traditional medicine, folk medicine and pharmacological evidence.

3.1. Traditional medicine

Traditional medicine mainly comprises of Indian Ayurveda, Arabic Unani medicine and traditional Chinese medicine. In Asia and Latin America, populations continue to use traditional medicine as a result of historical circumstances and cultural beliefs. Traditional medicine accounts for around 40% of all health care delivered in China. Up to 80% of the population in Africa uses traditional medicine to help meet their health care needs [30].

3.1.1. Ayurveda

The plant finds mention in the verses of the *Charaka Samhita* which is unarguably the most ancient and authoritative textbook of Indian Ayurveda. *Vn* has been designated as an anthelminthic (verse *Su:4-15*) and is prescribed as a vermifuge (verse *Vi:7-21*) in the exposition on the *Charaka Samhita* by Sharma [31].

Other Ayurvedic uses of *Vn* are described by Tirtha [32]. People sleep on pillows stuffed with *Vn* leaves to dispel catarrh and headache and smoke the leaves for relief. Crushed leaf poultice is applied to cure headaches, neck gland sores, tubercular neck swellings and sinusitis. Essential oil of the leaves is also effective in treatment of venereal diseases and other syphilitic skin disorders. A leaf decoction with *Piper nigrum* is used in catarrhal fever with heaviness of head and dull hearing. A tincture of the root-bark provides relief from irritability of bladder and rheumatism.

Jadhav and Bhutani [33] report the Ayurvedic use of *Vn* in dysmenorrhea. Patkar [34] refers to the formulations described in *Anubhoga Vaidya Bhaga*, a compendium of formulations in cosmetology, in outlining the use of *Vn* leaves along with those of *Azadirachta indica*, *Eclipta alba*, *Sphaeranthus indicus* and *Carum copticum* in a notable rejuvenation treatment known as *Kayakalpa*.

3.1.2. Unani medicine

Khare [19] outlines the applications of *Vn*, commonly known as *Nisinda* in Unani medicine. The seeds are administered internally with sugarcane vinegar for removal of swellings. Powdered seeds are used in spermatorrhoea and serve as an aphrodisiac when dispensed along with dry *Zingiber officinale* and milk.

3.1.3. Chinese medicine

The Chinese Pharmacopoeia prescribes the fruit of *Vn* in the treatment of reddened, painful, and puffy eyes; headache and arthritic joints [35].

3.2. Folk medicine

Folklore systems of medicine continue to serve a large segment of population, especially those in rural and tribal areas, regardless of the advent of modern medicine [36]. The entries regarding the multifarious applications of *Vn* in folk medicine have been grouped regionally to emphasize the ethnobotanical diversity and ubiquity of the plant; and the details have been laid out in Table 2 and 3.

Table 2 – Uses of *V. negundo* in folk medicine in India

S. NO.	STATE	REGION	LOCAL NAME	USED IN TREATMENT OF	REFERENCES
1	Andhra Pradesh	Puttaparthi	Tella Vaavili	Asthma, Cancer	[37]
				Used as bath for women in puerperal state and for new born children	Unpublished
2	Assam		Pochatia	Jaundice	[38]
				Urticaria, Cellulitis, Abcesses, Carbuncles, Eczema	[39]
				Liver disorders	[40]
3	Himachal Pradesh	Garwahl	Sambhaalu	Kwashiorkor	[4]
		Parvati valley	Bana	Wounds, Body ache	[41]
4	Karnataka	Dharwad	Lakki, Karilakki	Toothache	[42]
		Mysore	Bilenekki	Febrile, catarrhal and rheumatic afflictions	[4]
		Uttara Kanada	Nekki	Migraine	[43]
5	Maharashtra	Konkan	Lingur	Rheumatism	[4]
		Amravati	Samhalu	Encephalitis	[44]
		Chota Nagpur	Nirgundi	Expectorant	[4]
		Satpuda	-	Joint pain	[36]
6	Orissa	Malkangiri	Languni	Jaundice	[45]
7	Tamil Nadu	Southern parts	Notchi	Used as antidote for snake bite	[46]
		Madurai	-	Respiratory disorders, Fever, Headache	[47]
		Kancheepuram	-		[48]
		Salem and Tirucchirappalli	-		[49]
8	Uttar Pradesh	Jaunsar-Bawar hills	Somi	Eye pain	[50]
		Moradabad	Mala	Used as refrigerant for cattle	[51]
		Uttaranchal	-	48 types of ailments	[2]

S. NO.	COUNTRY	REGION	LOCAL NAME	USED IN TREATMENT OF	REFERENCES
1	Bangladesh	Chittagong	-	Weakness, Headache, Vomiting, Malaria, Black fever	[52]
2	China	Guangdong	Buging′iab	Common cold, Flu and Cough	[53]
3	Nepal	Kali Gandaki	Simali	Sinusitis, Whooping cough	[54]
4	Pakistan	Buner	Marvandaey	Chest-pain, Backache Used as toothbrush	[55]
		Kot Manzaray Baba valley	-	Used as anti-allergenic agent	[56]
		Margallah hills	Nirgud	Gum and skin diseases	[9]
		Siran valley	Kalgari	Used as medicine for buffaloes in colic	[57]
5	Philippines		-	Cancer	[58]
6	Sri Lanka		Nilnikka	Eye disease, Toothache, Rheumatism Used as a tonic, carminative and vermifuge	[4]

Table 3 – Uses of *V. negundo* in folk medicine outside India

3.3. Pharmacological evidence

Demands of the scientific community have necessitated experimental evidence to further underline the medicinal importance of *Vn* described above. Taking cue from these traditional and folk systems of medicine, scientific studies have been designed and conducted in order to pharmacologically validate these claims.

3.3.1. Anti-inflammatory and analgesic activity

Yunos et al. [59] and Jana et al. [60] established anti-inflammatory properties of *Vn* extracts in acute and sub-acute inflammation. Anti-inflammatory and pain suppressing activities of fresh leaves of *Vn* are attributed to prostaglandin synthesis inhibition [61], antihistamine, membrane stabilising and antioxidant activities [62].

3.3.2. Effect on oxidative stress

Leaf extracts of *Vn* were determined to possess anti-oxidant potential by [63]. The extracts were useful in decreasing levels of superoxide dismutase, catalase and glutathione peroxidase in Freund's adjuvant induced arthritic-rats [64]. The extracts also possess the ability to combat oxidative stress by reducing lipid peroxidation owing to the presence of flavones, vitamin C and carotene [65]. Rooban et al. [66] evaluated the antioxidant and therapeutic potential of *Vn* flavonoids in modulating solenoid-induced cataract and found it to be effective.

3.3.3. Enzyme-inhibitory activity

Root extracts of *Vn* showed inhibitory activity against enzymes such as lipoxygenase and butyryl-cholinesterase [25]; α-chymotrypsin [67]; xanthine-oxidase [68] and tyrosinase [69]. Woradulayapinij et al. [70] reported the HIV type 1 reverse transcriptase inhibitory activity of the water extract of the aerial parts of *Vn.*

3.3.4. Effect on reproductive potential

The flavonoid rich fraction of seeds of *Vn* caused disruption of the latter stages of spermatogenesis in dogs [71] and interfered with male reproductive function in rats [72]. It must however be noted that these findings are in sharp contrast with the traditional use of *Vn* as aphrodisiac [19]. Hu et al. [73] determined that ethanolic extracts of *Vn* showed estrogen-like activity and propounded its use in hormone replacement therapy.

3.3.5. Histomorphological and cytotoxic effects

Tandon and Gupta [74] studied the histomorphological effect of *Vn* extracts in rats and found the stomach tissue to be unaffected even by toxic doses; while dose-dependent changes were observed in the heart, liver and lung tissues. Cytotoxic effect of leaf extracts of *Vn* was tested and affirmed using COLO-320 tumour cells [75]. On one hand, Diaz et al. [76] found the chloroform extracts of *Vn* leaves to be toxic to a human cancer cell line panel while on the other; Yunos et al. [59] reported that *Vn* extracts were non-cytotoxic on mammary and genito-urinary cells of mice.

3.3.6. Drug potentiating ability

Administration of *Vn* extracts potentiated the effect of commonly used anti-inflammatory drugs such as ibuprofen and phenylbutazone [77]; analgesics such as meperidine, aspirin [78], morphine and pethidine; sedative-hypnotic drugs like pentobarbitone, diazepam [79] and chlorpromazine [80]; anti-convulsive agents such diphenylhydantoin and valporic acid [81].

3.3.7. Other attributes

In addition to the above mentioned activities *Vn* extracts have also been tested for a range of other systemic effects. Leaf extracts of *Vn* were found to possess hepato-protective activity against liver damage induced by d-galactosamine [82], commonly used tubercular drugs [83] and carbon tetrachloride [84, 85]. Villasenor and Lamadrid [86] have provided an account of the anti-hyperglycemic activity of *Vn* leaf extracts. Laxative activity of *Vn* leaf extracts was exhibited in rats by Adnaik et al. [87]. Methanolic root extracts of *Vn* showed antagonization of the lethal activity induced by venom of *Vipera russellii* and *Naja kaouthia* [88]. Immunomodulatory effect of *Vn* extracts has been reported by Ravishankar and Shukla [89].

3.4. Summary

Traditional medicine systems have also been developed throughout history by Asian, African, Arabic, Native American, Oceanic, Central and South American and other cultures. A comprehensive exploration in this regard could bring forth other medicinal applications of *Vn* hitherto unknown.

Ethnobotanical studies open many doors to knowledge that has rarely been cataloged. Such surveys have been conducted and reported from different regions of the Indian subcontinent. The listing of *Vn* in each of them has a novel account in terms of its medicinal use. Similar expeditions in other parts of India and countries where the plant is known to occur would bring to light the unknown aspects regarding this plant and other such plants that continue to remain obscure to the scientific community of the world at large. The lessons learnt from the traditional wisdom of the older generations combined with the modern scientific approach can provide the key to many of the unresolved issues of present-day medicine and open new vistas for the biotechnology industry.

Various other medicinal properties of *Vn* listed in the above sub-sections need to be established by systematic experimental studies before they can actually find their way to the market in the form of herbal-based medication for common ailments and afflictions. Such applications of *Vn*, on entering the pipeline of pharmacological research, could be taken up by the industry for Research and Development of drugs.

4. Commercial products

The pharmacological potential of *Vn* has been exploited effectively in formulating commercial products for treatment of health disorders. Table 4 provides details of such products available in the market which have supporting evidence in the form of scientific publications. Table 5 lists selected herbal products which contain *Vn* extracts, but do not have a backing in the form of readily available research literature.

MANUFACTURER	NAME OF PRODUCT	USED IN
Himalaya Drug Co., Bangalore, India	Antiseptic Cream	Wounds, Burns, Fungal skin infections
	Dental Cream	Tooth ache, Bleeding gums
	Himcolin Gel	Erectile dysfunction
Surya Herbal Ltd., Noida, India	Relieef Cream	Joint and Muscle pain, Stiff back
	Rheumanaad Tablet and Cream	Rheumatic Pain, Sprain
	Ostranil Gel	Osteoarthritis, Lumbago
Ambica Research & Development Pvt. Ltd, New Delhi, India	Amgesic Arthritis Tablets	Arthritis
IndSwift Ltd., Chandigarh, India	Arthrill Capsules and Massage oil	Arthritis, Joint pain, Frozen shoulder, Gout, Cervical spondylitis

Table 4 - Commercial herbal formulations containing *V. negundo*

Table 5 - Commercial herbal formulations containing *V. negundo*

MANUFACTURER	NAME OF PRODUCT	USED IN	REFERENCE
Himalaya Drug Co., Bangalore	Acne-n-Pimple Cream	Acne and skin eruptions	[90]
	JointCare B cream	Rheumatic disorders	[91]
	Muscle and Joint Rub	Muscle strains, musculoskeletal disorders	[92]
	Pilex tablet and cream	Haemorrhoids (Piles)	[93, 94]
	Rumalaya gel and tablets	Inflammatory musculoskeletal disorders	[95-97]
	V-Gel	Vaginitis, Cervicitis	[98]
Hamdard Laboratories, New Delhi, India	Jigrine	Liver ailments	[99, 100]
Dey's Medical, Kolkata, India	Itone Eye Drops	Eye ailments	[101]

5. Biological activity

Plants are known to produce a variety of compounds which have evolved as defence compounds against microbes and herbivores [11]. The elaboration on the biochemically active ingredients and the medicinal properties of *Vn* elicits queries on the effect of the plant extracts on other biological organisms. *Vn* has shown promise as an effective bio-control agent. The extracts of *Vn* possess inhibitory, deterrent or lethal activity on biological agents that cause disease and damage to other organisms. Table 6 summarizes the effect of *Vn* on different pathogens and pests.

Table 6 – Activity of *V. negundo* extracts on biological pathogens and pests

ACTIVITY	**ACTION AGAINST**	**REFERENCE**
Anti-bacterial	*Escherichia coli, Klebsiella aerogenes, Proteus vulgaris*, and *Pseudomonas aerogenes* (Bacteria)	[102]
Anti-feedant	*Spodoptera litura* (Asian army-worm) *Achoea janata* (Castor semi-looper)	[17, 103]
Anti-filarial	*Brugia malayi* (Microfilarial parasite)	[104, 105]
Anti-fungal	*Alternaria alternata, Curvularia lunata Trichophyton mentagrophytes, Cryptococcus neoformans Aspergillus niger, Candida albicans*	[106-108]
Anti-larval	*Cnaphalocrocis medinalis* (Rice leaf-folder)	[109]
Anti-viral	*Plasmodium falciparum* (Virus)	[110]
Insecticidal	C*allosobruchus maculatus* (Pulse beetle)	[111, 112]
	Phthorimaea operculella (Potato-tuber moth)	[113]
	Sitotroga cerealella (Angoumois grain moth)	[114]
	Aphis citricola (Spirea aphid), *Aphis gossypii* (Melon or Cotton aphid), *Myzus persicae* (Green peach aphid)	[115]
Larvicidal	*Anopheles subpictus*, *Culex tritaeniorhynchus* (Mosquitoes)	[116]
	Culex quinquefasciatus (Mosquito)	[117-121]
	Anopheles stephensi (Mosquitoes)	[121]
	Plutella xylostella (Diamond-back moth)	[122]
Mosquito repellant	*Culex tritaeniorhynchus* (Mosquito)	[123]
Mosquito repellant	*Aedes aegypti* (Mosquito)	[124]

6. *In vitro* culture

In vitro culture techniques offer viable means of mass multiplication and germplasm conservation of a multitude of plant species [125] and enhancement of the production of secondary metabolites. Due to poor viability of seeds of *Vn* [126] and slow rate of conventional propagation [127], tissue culture technology has assumed importance as an alternative method for rapid conservation and propagation of this economically important plant species. Additionally, production of plant secondary metabolites *de novo*, by *in vitro* cell culture methods, has assumed importance in the last two decades because the structural complexity of naturally occurring metabolites forms the basis for the chemical synthesis of novel and more potent analogues.

Nodal explants of *Vn* were found to be most effective for *in vitro* studies using Murashige and Skoog (MS) medium [128]. *In vitro* studies conducted to date have been preliminary; involving investigations on the response of explants to different phytohormones and growth supplements on MS medium.

6.1. Shoot initiation and proliferation

6-Benzyl Amino Purine (BA) in combination with α-Naphthoxy Acetic Acid (NAA) was found to be the most efficient in initiation of shoot primordial and formation of multiple shoots. Biotin and Casein Hydrolysate (CH)

[126]; sodium sulphate [129]; Gibberellic Acid (GA_3) [127]; Thidiaruzon [130, 131] and coconut water [131] gave positive results as growth supplements for shoot proliferation and multiple shoot formation. Sharief and Jagadishchandra [126] obtained shoots from stem callus using Kn and NAA in combination. Chandramu et al. [129] observed in vitro flowering with a combination treatment of BA and NAA. Handique [132] reported the use of Woody Plant medium but however found better response of explants in MS medium.

6.2. Root formation and elongation

Root formation and elongation was commonly observed with MS medium fortified with Indole-3-Butyric Acid (IBA) [129, 130, 132], NAA (Afroz et al., 2008), combination of NAA and Indole-3-Acetic Acid (IAA) [126, 131], combination of IAA and IBA [127, 133]. Usha et al. [133] made use of activated charcoal for rooting of *in vitro* plantlets. In contrast to other reports using half strength MS medium to induce rooting, Vadawale et al. [134] used full strength MS medium with IBA.

6.3. Summary

The prospects of rapid multiplication and propagation coupled with enhanced secondary metabolite production bring out with greater emphasis the need for establishment of standardized protocols for *in vitro* culture of medicinal plants, in this case *Vn*. Moreover, *in vitro* technology can potentially overcome common problems such as crop failure due to erratic weather conditions or mineral deficiencies in the soil. It is much simpler to manipulate and monitor the conditions essential for plant growth and development under laboratory conditions. Micropropagation also the advantage of rapid clonal multiplication of desired genotypes. Current approaches to *in vitro* propagation have shown encouraging results only utilizing MS medium as the substrate. Other nutrient media which have been shown to be useful for tissue culture of similar woody type of plants need to be tested, as also the role of other plant growth regulators and supplements.

Although India ranks among the top nations of the world medicinal plant exports, its export of phytochemical derivatives is insignificant in relation to developed countries of the world [135]. It is well-established that plants growing under stress conditions evolve to synthesize variants of commonly produced secondary metabolites. Cell culture provides means of bioconversion of low value compounds into high value products and enhancement of rate of production of these compounds. Application of established protocols using *Agrobacterium rhizogenes* (for hairy root cultures) and optimal elicitors needs to be investigated for enhancement of the yield of secondary metabolites in *Vn*. Additionally, *in vitro* methods can also be exploited to standardize the secondary metabolite content in a given amount of plant material which in turn would provided an added advantage in industrial applications of the plant.

7. CONCLUSION

Uniyal et al. [136] reiterates a popular local quote of the Bhangalis in the Western Himalayan region of India which translates as –"A man cannot die of disease in an area where *Vitex negundo*, *Adhatoda vasica* and *Acorus calamus* are found"; (provided that he knows how to use them). The plant holds great promise as a commonly available medicinal plant and it is indeed no surprise that the plant is referred to in the Indian traditional circles as *'sarvaroganivarini'* – the remedy for all diseases. Considerable amount of literature is available on various aspects of the plant – traditional to biochemical and ethnobotanical to pharmacological; however there many gaps which need to be filled by concurrent researchers in different disciplines. One must make the best use of the naturally available resources which provide valuable raw material for advanced research. Nature has many lessons to teach and the onus is on us to get attuned and grasp whatever is within our reach, before it is too late.

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