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Importance of conserving *Vitex peduncularis*: A depleting forest resource with immense ethno pharmacological uses

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Abstract

Vitex peduncularis, vernacularly known as 'Charaigorwa' is a large evergreen tree having numerous ethnopharmacological uses and belongs to the family Lamiaceae. The species is globally known for its usage to cure multifarious human health issues in traditional as well as contemporary medicines. The species exerts high bioactivity due to the presence of several secondary metabolites, including flavonoids, Vitexin, iridoid glycosides, pachypodol, ursolic acid, 2-hydroxy-ursolic acid terpenoids. Due to the high demands of *V. peduncularis* in pharmaceutical industries, the species is being exploited indiscriminately, pushing it towards the abyss of extinction. Immediate conservation measures are required to sustain the available natural population through multidisciplinary scientific interventions. This article cumulates the importance of the species directing towards its specialized pharmacological characteristics and its therapeutic uses. It also highlights the research gaps needed to be filled up for judicial use of the species conserving its depleting genetic resources.

Keywords: *Vitex*, Charaigorwa, lamiaceae, flavonoids, vitexin

Introduction

Plants serve as the primary source of basic amenities for sustaining human livelihood and health security^[1]. These plants also play a key role in traditional medicine practices since the prehistoric period. The majority of the medicines are derived from plant resources having anti-cancerous, immune-stimulating, antiviral, anti-inflammatory, and antibacterial properties^[2]. The use of plants as remedial measures against human health challenges is rapidly increasing owing to easy accessibility, bioactive components, and their impactful presence in indigenous traditional knowledge since time immemorial. Since the past few decades, the world's healthcare system is being highly influenced by medicinal and aromatic plants representing a crucial source in pharmaceuticals. India is rich in medicinal plant bio-diversity, and over 75% of the native population still relies on traditional knowledge and herbal remedies for curing various ailments^[3]. Compounds with proven therapeutic effects are developed from several medicinal plants since the pre-historic ages^[4]. According to a survey by the World Health Organization, up to 80% of people throughout the world remain dependent on conventional healthcare for their basic medical requirements^[5, 6]. Ecological and anthropogenic pressures along with the introduction of exotic species have caused several therapeutic plants to become rare, endangered, or prone to vulnerability^[7]. If overexploitation continues at the present rate due to the spike in demand; the ecological equilibrium of the ecosystem will be disturbed and as a result, these important medicinal plants might run to the verge of extinction^[8]. The genus *Vitex* has about 270 species, mostly trees and shrubs, the majority growing in tropical and subtropical environments; with a few species in temperate zones^[9, 10, 11]. Almost all of the species of *Vitex* have got medicational recommendations in conventional medicine. Numerous diseases can be cured by using plants and the chemical substances they provide. Fruits of some *Vitex* species are incredibly beneficial for low-income populations as food sources owing to their high nutritional values^[12]. Nevertheless, high dependence on the genus can jeopardize the biological balance of the environment where they typically flourish; rendering the availability of these plants untenable in several cases^[13]. Hence, both the socio-economic and ecological significance of *Vitex* cannot be denied.

Vitex peduncularis Wall. Ex Schauer belongs to the family Lamiaceae and it is traditionally consumed for health reasons throughout Southeast Asia and India [14]. It is a tree of medium to big size with an average height of 6-12 m, generally growing in moist deciduous forests at altitudes up to 1000 m elevation [15, 16, 17]. Similar to the other species in the genus *Vitex*, *V. peduncularis* is also over-exploited in its natural habitat and may eventually be extinct [18]. The species is already listed as 'Rare' in different states of India [19] and as 'Threatened' in the country Bangladesh [20]. The leaves of the species are lanceolate or narrowly elliptic in shape, with a length of 5–15 cm, whole, long acuminate, and base cuneate, and have infrequently four foliations [21] and winged petiole in immature leaf [22]. The flowers are 15-20 cm long, peduncled, and yellowish, and they grow on axillary panicles with many flowers from March to June [23]. The globular drupe fruits mature attaining the size of black pepper and ripen up to September. An enlarged calyx encloses fruit, and seeds are exalbuminous [21]. The species has numerous vernacular or regional names, e.g., Chang Xu Jing in China, Korobaong in Bengali, Horina in Chittagong [24], Charaiygorwa in Hindi ('charai' means bird and 'gorwa' means leg) [25] and Goda in Bangladesh [21, 26]. The hard-coated seed of *V. peduncularis* is naturally propagated from the seed despite having a very low natural germination rate. Ancient cultures employed *Vitex* to treat a variety of illnesses, such as digestive issues, and inflammatory disorders, and to alleviate the symptoms associated with psychological conditions [27, 28, 29, 30]. The wood of *Vitex* was used to manufacture furniture in ancient civilizations and the tree was respected for its ability to treat a wide range of medical problems. The historical significance of *Vitex* is well versed in the literature of a reputed historians like Pliny, Banckes, Madaus, etc. Owing to its high medicinal usage, commercially, *Vitex* is still available under the brand name 'Agnolyt'.

Distribution pattern

V. peduncularis is generally found throughout the tropical and subtropical climates and seldom in temperate regions, the species has a wide distribution range encompassing countries like China, Nepal, Myanmar, Cambodia, Pakistan, Sri Lanka, Eastern Africa, Madagascar, Sri Lanka, Thailand, Afghanistan, India, and Laos [23, 31, 32]. In India, its natural distribution is found in the states of Andhra Pradesh, Kerala, Odisha, West Bengal, Tamil Nadu, Jharkhand, Assam, Tripura, Mizoram, Odisha, Madhya Pradesh, Bihar, Utter Pradesh [33, 34]. It flourishes in moist conditions or by rivers and streams in squatter areas and mixed open woodlands. In some regions of Asia, Europe, North America, and the West Indies, it is cultivated economically as a crop [35]. However, only thirteen species of the *Vitex* genus are found in India [36, 37, 112] among which *Vitex agnus-castus*, *Vitex negundo*, *Vitex peduncularis*, *Vitex pubescens*, and *Vitex trifolia* are some of the most economically and ethnobotanical important species [4].

Conventional applications

Plants contain several distinct bioactive compounds with the potential to inhibit the growth of bacteria or fungi. It is well known that plants contain distinct bioactive compounds that interact with other environmental species to inhibit the growth of bacteria or fungi [30]. *V. peduncularis* is widely used in ethno pharmacology to treat various human health issues caused by insects, snakes, and poisonous spiders [38], and even in gynecological diseases [39]. The plant shows acaricidal properties against various mites and pests [40]. A broad range of secondary metabolites found in the leaves of the species promote defense against several diseases [41]. The juvenile barks of the stem, leaves, and leaves infusion of this plant have been employed for centuries in conventional herbal treatments for malaria and blackwater fever [42, 43, 44, 45, 46, 47, 48, 49], diabetes [24], chest pain, joint pain [50, 51], typhoid, [52], urethritis, visceral leishmaniasis [53], jaundice [21,25]. The roots are used for reducing painful periods [30]. An oral dosage of extract produced from a leaf, root, or bark is administered to cure malaria in states like Mizoram and Jharkhand [54, 45, 55]. During the wintertime, the infusion of the plant's leaves is consumed as a tea by native dwellers in several states, viz., Orissa, Jharkhand, Chhattisgarh, etc. [10]. Bark on stems and leaves both have antifungal, antibacterial, antioxidant, antidepressant [56], insecticidal effects [10], larvicidal efficacy against *A. stephe* and *C. quinquefasciatus* [57, 58], thrombolytic and cytotoxic properties [26]. Kirtikar and Basu [59] reported that in Chota Nagpur regions, localities use its bark to address aches and pains.

Many compounds such as peduncularaside, iridoidanguside, Vitexin, triterpenoids, and flavonoids [60, 61, 62, 11, 63, 64, 65], pachypodol, ursolic acid, and 2-hydroxy-ursolic acid [66, 41, 67, 68], crisimartin, 3 α -friedelinol, genkwanin, and, 3 β -friedelinol [24] are present in the leaves. Researchers have already examined the various parts of *V. peduncularis* for exploring bioactive substances and evaluated their efficacy [69]. However, it is necessary to carry out further in-depth research studies on the species to identify its significant pharmacogenetic abilities [9].

Ethno-pharmacological Importance: Several species in *Vitex* have been linked to a variety of energy attributes; in certain instances, these properties were described with the development of Traditional Chinese Medicine [11]. Different plant parts of *V. negundo* L [70, 71, 72, 73, 74], *V. trifolia* L [75, 76, 77, 78, 79], and *V. agnus-castus* L. [80, 81, 82, 83, 84] are reported to have medicinal uses against several health issues. Numerous phytochemicals that were extracted from *V. peduncularis* have been studied for their potential as analgesic [85], anti-inflammatory [14], sedative, antioxidant, anxiolytic anti-nociceptive, anthelmintic [24], and antibacterial [86, 9] activities. In 2015, Dr. Kaushal Kumar was granted a patent for his drug 'BAU Birsin', based on the antipyretic and analgesic characteristics of *V. peduncularis* and could potentially be employed for the treatment of fever, coughing, and aches and pains [87]. It is produced from the bark and leaves of this tree.

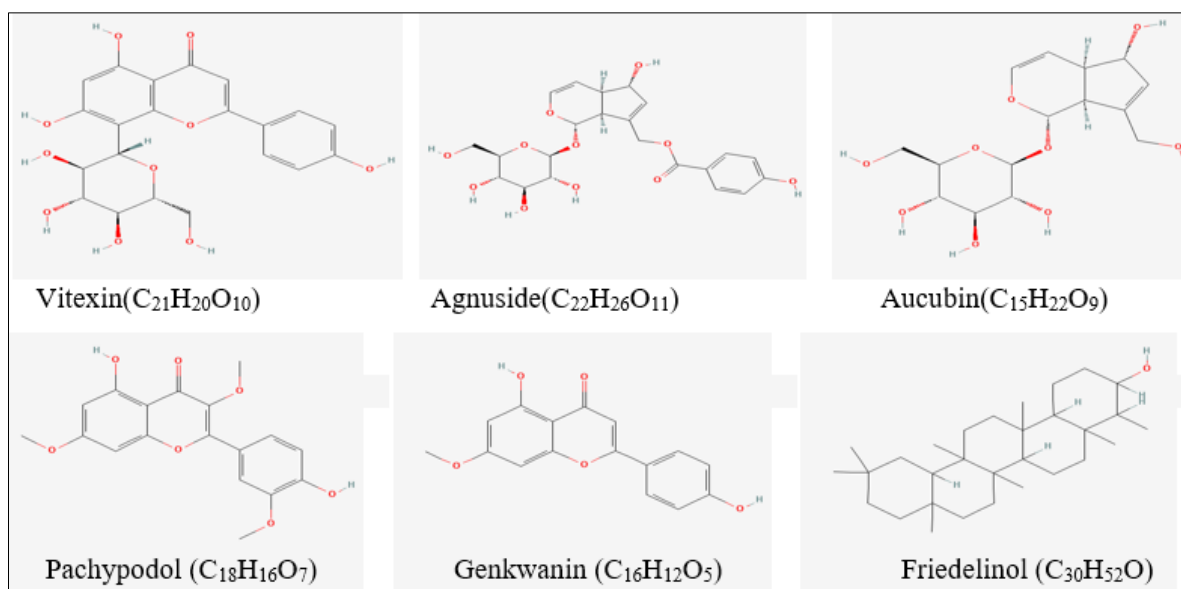


Fig 1: The chemical constituents of *V. peduncularis* Wall

The fruits comprise 20% 1,8-cineole, 22% sabinene, and 6% pinene and consist of 1.3–1.6% extractable volatile oils. Kastrak *et al.* [88] indicated that oil extracted from the fruits of species had antibacterial properties. According to Kuruuzum-Uz *et al.* [89], it encompasses flavonoids and iridoid glycosides. Recently, Azarnia *et al.* [90] evaluated the iridoid glycosides and determined that these compounds consist of agnoside 0.6%, aucubin 0.3%, and eustroside 0.07%. With IC₅₀ values of 0.026–0.015 mg/ml, iridoid agnoside-2, and pedunculariside were extracted with BuOH extract from stem bark which indicated potential anti-inflammatory activity by inhibiting the activity of proinflammatory enzymes like COX-2. Besides, it also showed moderate COX-1 inhibitory properties [62]. Iridoids like agnoside as well as aucubin may be employed as chemotaxonomic agents. Agnoside is used to treat premenstrual problems as well as to manage menopause [91]. At an intake of 80 mg/kg intraperitoneally, aucubin was reported to have liver-protective characteristics and can prevent liver damage caused by exposure to carbon tetrachloride or alpha-amanitin [92]. The methanolic extraction of the leaf and stem of the species showed the highest level of effectiveness against *Staphylococcus aureus* and *Enterobacter aerogens*, as well as antifungal activities against the species of *Candida* and *Rhizopus* [9].

The flavone C-glycoside *Vitexin* (apigenin-8-C-β-D-glucopyranoside) is extracted from the leaves and root bark and exhibits analgesic, antidepressant characteristics [20], and cardioprotective, anti-inflammatory, anti-microbial, anti-cancer, and neuron-protective properties [93, 94, 95]. *Vitexin* increases cells' defense against oxidative stress inducers, which in turn promotes cell survival and minimizes tissue damage. The protective effects of *Vitexin* depend on the concentrations of malondialdehyde, or MDA, and the presence of reactive oxygen species (ROS) inside cells [93, 96, 97]. It prevents the transcription factor NF-κB from being activated and the consequent synthesis of TNF- and IL-1, mitigating cardiac ischemia or reperfusion [98].

The dried roots serve as an expectorant, astringent, as well as antipyretic, while the steaming water solution from the fruit performs as a vermifuge [99]. Significant antileishmanial activity against *Leishmania donovan* was reported by

Rudrapaul *et al.* [100] through induction of iNOS expression. Several researches conducted on its phytochemistry have shown that it contains sterols, flavonoids, and iridoids [101, 102]. According to Nathan *et al.* [103], due to its potent enzyme inhibition properties, the plant extract can be used as an insecticide for combating the rice leaf folder (*Cnaphalocrocis medinalis*).

Kannathasan *et al.* [31] reported the isolation of epifriedelinol from the methanol extract of leaves and its antibacterial activity, crystal structure, and molecular makeup. A suspension of leaves, root bark, or immature stem tissue is effectively administered to treat both malaria and black water fever [4]. It is possible to effectively treat hypoxia-induced oxidative damage with plant products as a dietary supplement or in conjunction with other bioproducts [104].

In vitro propagation

V. peduncularis is naturally propagated through seeds or root suckers. However, both methods are not very effective in producing a large quantity of planting stocks because of the low germination rate, and naturally propagated plantlets grow slowly depending on age and season. In India, natural tree stands are rapidly disappearing because of indiscriminate use [105]. Traditional ways to propagate *Vitex* species, such as seeds or branch cuttings, are inadequate for mitigating the ever-growing demand for this plant in the pharmaceuticals and medicine industries [106, 18]. Although, the plant is classified as Least Concerned (LC) on the IUCN Red List [107], the current propagation techniques are insufficient to meet its ever-growing demand, leading the species towards severe ecological pressures. Where, other propagation techniques potentially hasten plant's large-scale proliferation, development, and conservation, tissue culture techniques made it possible to quickly produce large quantities of plants [13]. *In vitro* propagation is a biotechnological technique that is useful for the mass reproduction of medicinally important plants [108, 109, 110], including cryopreservation and genetic alteration [111]. Hence, *In vitro* propagation techniques can readily be used to mass-proliferate *V. peduncularis* which is yet to be explored for its conservation purposes.

Conclusion and prospects

The *Vitex peduncularis* has a wide range of medicinal properties, particularly owing to the antibacterial and antifungal effects of various bio-active compounds present in different parts of the species. In a nutshell, the present review of the therapeutic effects and chemistry of *V. peduncularis* is aimed to offer a cumulative overview on the existing investigations and recommend opportunities for additional analysis. The genus *Vitex* has drawn a major interest in the health sector market due to the phytochemicals existing in the plant tissue possessing pharmacological potential. *In vitro* propagation techniques have been established for very few *Vitex* species with the majority of the research concentrating on *V. negundo* and *V. trifolia*. To develop *in vitro* development methods appropriate for clonal improvement, cryogenic preservation, and modification of genes; it is crucial to provide suitable, comprehensive knowledge regarding *in vitro* environments for research to be implemented. To isolate the several crucial components from the extracts of its leaves, bark, and root, further research must be done. The chemical compositions associated with the Lamiaceae family might be used in subsequent investigations on the medicinal potential of the species. The *V. peduncularis* leaf tissue is a potential substrate for a variety of biological processes. It is possible to do more studies on them to ascertain their potential efficacy, support their usage as conventional medications, and potentially even assist in the discovery of innovative lead compounds in the future. *In vivo*, models must be utilized for additional analyses to evaluate the potential of the bioactive chemicals expressed in *V. peduncularis* as well as other species in the genus. The prospect of this article lies in the future usage of the concerned species in the advancements of medical care and the exploration of new areas for further investigation.

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