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Review on the therapeutic potential of Vitex negundo Linn.

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ABSTRACT

Medicinal plants have been widely used to treat a variety of infectious and non-infectious ailments. According to one estimate, 25% of the commonly used medicines contain compounds isolated from plants. *Vitex negundo* Linn. (VN), belonging to family Verbenaceae, is a small aromatic plant that flourishes abundantly in wastelands and is widely distributed in tropical to temperate regions, being a native of South Asia, China, Indonesia, and the Philippines. It contains many polyphenolic compounds, terpenoids, glycosidic iridoids and alkaloids. In the ayurvedic system of medicine it is used as a drug of choice to manage pain, inflammation and other related diseases. The review highlights the various potential therapeutic feature of *Vitex negundo* which can be used in the drug designing process to find solution for the unsolved infectious and non-infectious deformities without side effects.

Key words: Medicinal plants; *Vitex negundo*: Polyphenolic compounds; Deformities

INTRODUCTION

*Vitex negundo* Linn., Verbenaceae, known as Nirgundi in Hindi, grows gregariously in wastelands and is also planted as a hedge-plant. The Sanskrit word nirgundi literally means that which protects the body from diseases. It is one of the herbs mentioned in all Samhitas of Ayurveda, and has various synonyms like sinduka, sephali, sitabhiru, vanaka, bhutakesi, anilamanjiri. It is an erect, 2–5 m in height, slender tree with quadrangular branchlets. The leaves have five leaflets in a palmately arrangement, which are lanceolate, 4–10 cm long, hairy beneath and pointed at both ends. The bluish purple flowers are numerous. The fruit is succulent, black when ripe, rounded and about 4 mm in diameter [1]. Although all parts of *Vitex negundo* are used as medicine in the indigenous system of medicine, the leaves are the most preferred for medicinal use. It is used for treatment of eye-disease, toothache, inflammation, leucoderma, enlargement of the spleen, skin-ulcers, in catarrah fever, rheumatoid arthritis, gonorrhoea, and bronchitis. They are also used as tonics, vermifuge, lactagogue, emmenagogue, antibacterial, anti-pticritic and antihistaminic agents [2]. Furthermore, *Vitex negundo* has been reported to display high estrogen-like activity, and could be useful in hormone replacement therapy (HRT) in clinical practice [3]. The fresh mature leaves are used internally and externally in Ayurveda medicine as anti-inflammatory, analgesic and anti-itching agents [4].

Aqueous extract and oil of seeds possess anti-oxidant property. Flavonoids, iridoids, terpenes, and steroids are the major classes of compounds present in this plant [5]. The ethanolic extract of the seeds of *Vitex negundo* has been shown to possess hepatoprotective action against carbon tetrachloride-induced liver damage [6]. So it is clearly evident that *Vitex negundo* has good therapeutic potential. This review critically analyses the therapeutic potential of *Vitex negundo* in different prospective applications.

Antioxidant properties of *Vitex negundo*

In the past few years, many plant extracts and pure phytochemicals have been reported to have both anti-inflammatory and free radical scavenging property [7]. Reactive oxygen species (ROS) produced in vivo includes superoxide radicals (O-2-) and hydrogen peroxide (H2O2), which on reaction with transition metals yields a highly reactive oxidizing species, the hydroxyl radical (OH) [8]. These ROS can initiate or propagate many diseases, such as inflammation, cancer, liver injury and cardiovascular disease [9].

Leaf of *Vitex negundo* had the antioxidant potential to scavenge the ROS produced. Tiwari et al. (2007) have studied the antioxidant capacity of different fractions of *Vitex negundo* by employing various established in vitro systems [10]. Different fractions of *Vitex negundo* leaves exhibited a potent scavenging activity for ABTS (2,2’-azino-bis-(3-ethylbenzthiazoline-6-sulphonic acid)) radical cations in a concentration dependent manner [10]. This property may be attributed to the presence of polyphenolics and flavonoids in the leaf of *Vitex negundo*. Inhibition of lipid peroxidation has also been reported due to the antioxidant properties of *Vitex negundo* in rats, by using ethanol induced oxidative stress model [11]. Munasinghe et al. (2001) have shown the antioxidant potential of the total alcoholic extract of root of *Vitex negundo* on different systems [12]. Studies also revealed that methanolic and aqueous extracts of entire *Vitex negundo* plant have high antioxidant potential (as consistently established by the diverse in vitro test systems) which simultaneously inhibits H2O2-induced oxidative toxicity to Hep3B human hepatic carcinoma cells. These properties of both the extracts are due to their diverse phenolic constituents [18]. It is thus clear that the leaf of *Vitex negundo* contain a number of antioxidant compounds, which can effectively scavenge various reactive oxygen species and free radicals under in vitro conditions. They have shown mild metal chelation properties [10].

Anti-inflammatory and analgesic activities of *Vitex negundo*

Inflammation may start in every part of our body. Any time when the word describing a disease ends with -itis, it’s an inflammatory disease. Dermatitis means an inflammation of the skin, an arthritis an inflammation of joints, an othitis an inflammation of the ear. Thus anti-inflammatory activity of a compound is considered to be a valuable feature.

The leaves of *Vitex negundo* possess anti-inflammatory activity. Experimental investigations revealed that the mature fresh leaf of *Vitex negundo* have dose-dependent activity against inflammation as revealed in the carrageenan and formaldehyde models. Mature fresh leaf extract of *Vitex negundo* also demonstrated a dose-dependent prostaglandin (PG) synthesis inhibition, membrane stabilising and antihistamine activities. The inverse dose--response relationship shown by acute anti-inflammatory, antihistamine, PG synthesis inhibition and membrane stabilising activities may be due to reduction of the effectiveness of the active principle at its high concentrations [13].

Sedatives and stress are responsible for producing analgesia [14,17]. There was no sign of stress observed in the rats treated with the mature fresh leaves extract of *Vitex negundo* [13]. Mature fresh leaves extract of *Vitex negundo* is effective against the establishment of chronic inflammation which happens at the later stage of acute inflammation [13,16]. Moreover treatment with the
mature leaf extracts of *Vitex negundo* in rats did not show a gastric lesion which is an advantage when compared with the use of modern NSAIDs [13]. Treatment of mature fresh leaves extract of *Vitex negundo* for 14 days in rats orally did not produce detectable toxic effect in terms of body weight, serum concentrations of urea, creatinine, glucose and serum activity of ALT [13]. This is a very important criterion that favours the use of this extract for medicinal purposes.

The anti-inflammatory and analgesic activities of the leaves did not disappear after flowering of the tree in contrast to *Anisomeles indica* which lost these activities after flowering of the plant [13,15]. These studies provide evidence for the anti-inflammatory and analgesic properties of mature fresh leaves of *Vitex negundo* claimed in Ayurveda medicine. Further studies are still in progress to correlate the pharmacological activities with the chemical constituents.

### Antifungal and Antibacterial properties of *Vitex negundo*

Resistance to antimicrobial agents has become a global problem since last three decades. About 2 million people in US acquire bacterial and fungal infections each year, of the 65% patients have resistance to at least one drug [19,20]. A similar cause of concern in other countries including UK that leads to repeated use of antibiotic and insufficient control of the disease [21]. Second adequate treatment of mycotic infections is difficult since fungi are eukaryotic organisms with a structure and metabolism that is similar to those of eukaryotic host. For this reason, substantial researches in the field of anti-infectives are now desperately needed to develop new prototype antimicrobial agents to avert this situation. Development of new drugs from plants is not a new phenomenon. Plants and plant derived agents have long history to clinical relevance as source of potential chemotherapeutic agents [22]. Continuous efforts are taken to identify antifungal agents from plant sources.

The extract of *Vitex negundo* leaves and twigs was reported to show antibacterial activity against *Micrococcus pyogenes* and *Escherichia coli* [23]. Sathiamoorthy et al. (2007) isolated six compounds from the powdered leaf extracts of *Vitex negundo*. The isolated compounds were evaluated for antifungal and anti-bacterial activity (Table 1). The structure of the isolated compounds is given in Fig 1 [5].

The isolated compounds possess potent anti-fungal activities and compounds 4 and 5 were very active when compared to other isolated compounds. Significant antifungal
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Flavonoids of Vitex negundo offer protection against cataract development

Oxidative stress has been identified as one of the major causes of age-related diseases including cataract [26]. Selenite-induced cataract (oxidative stress model) is an extremely rapid and convenient model of nuclear cataract in rats [24]. Major events of selenite cataract are loss of calcium homeostasis, reactive oxygen species generation, lipid peroxidation, calpain activation, insolubilization of proteins, decreased water soluble proteins and GSH [25]. Lens antioxidant status and lipid peroxidation products have been implicated in human cataract [27].

Preventive protection as a therapeutic approach against cataract has generated considerable interest in recent years. Rooban et al. (2009) have used selenite-induced cataract as a model to evaluate the therapeutic efficacy of flavonoids isolated from the leaf of Vitex negundo [28]. He has demonstrated with the use Neonatal rat pups of Sprague-Dawley strain initially weighing 10–12 g on the 8th day. Animals were grouped as G I Control (normal laboratory diet), G II (normal laboratory diet + sodium selenite), G III (normal laboratory diet + sodium selenite + quercetin) and G IV (normal laboratory diet + sodium selenite+ flavonoid) with eight rats in each group. Preliminary studies were done to assess the toxicity of the plant material and to fix the dose before the main experiment. Evaluation of toxicity parameters – activities of Glutamate Oxaloacetate Transaminase (GOT) and Glutamate Pyruvate Transaminase (GPT) – which are common indicators of toxicity in serum and liver confirmed flavonoid isolated from Vitex negundo was non-toxic. In flavonoid treated group, lower levels of calcium and higher levels of Ca3ATPase activity were observed attributing to its protective effect [28].

Previous studies on cataract using Disulfiram and Verapamil hydrochloride have shown similar effects [29]. Supplementation of GSH or maintenance of its level in lens may help to maintain its protective ability against oxidative stress and lead to slower age-related loss of antioxidant activity of lens and eventually to delay the onset of cataract [30]. It is also found that flavonoid treatment prevents the above process and maintained the GSH in its active form. Similar results were reported with the use of antioxidant therapy in streptozotocin-induced diabetic cataract [31] and selenite cataract [32].

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Although, herbal (medicinal plants) preparations are widely used in several parts of the world, individually or in combination, data about the interactions of medicinal plants on living system is non-existent. It is only experience of the indigenous people using a particular plant and phytochemical product for treating an ailment. This review discussed the therapeutic potential of Vitex negundo attributing to its anti-oxidant, anti-inflammatory, analgesic, antimicrobial and its preventive medicinal activities. More in vivo studies of these species are required, and more advanced systematic investigation of these anti-oxidant rich species is needed before they can be used as preventive medicine.

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