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## Therapeutic uses of *Vitex negundo* leaves in glycaemia control

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### Abstract

Diabetes mellitus (DM) is a metabolic disorder described via an excessive blood glucose degree. *Vitex negundo* leaves extract phytochemicals to have the extremely good capability of healing diabetes. *Vitex negundo* belongs to the family Verbenaceae found in almost all parts of Asian countries, *V. negundo* leaf extract has a significant impact on glycoprotein metabolism. The phytochemical extracts of the leaf contain many other antidiabetic compounds like Friedelin, carotene, B-Pinene, Linalool, Camphor, and Nerolidol. In the present report, we have discussed the geographical distribution, different phytochemicals present in the plant, and their therapeutic uses. An herbal approach is highly needed to treat diabetes to minimize the adverse effect of allopathic medicine. Further studies are needed to find the potential target of diabetes and to convert the antidiabetic potential of *Vitex negundo* into the form of an herbal drug.

**Keywords:** Diabetes, vitex, antidiabetic, iridoids

### Introduction

Diabetes mellitus (DM) is a metabolic disorder described via an excessive blood glucose degree. Chronic hyperglycemia is considered a long-term disease, disorder, and dysfunction of diverse organs, like nerves, eyes, heart, kidneys, and various blood vessels. There are various forms of DM, however, the two commons are type 1 and type 2. Type 1 DM is an insulin-dependent disorder (autoimmune disorder) that results from the loss of pancreatic cells that produce insulin, and those who have it are dependent on exogenous insulin injections. Type 2 DM occurs due to insulin secretion by damaged Pancreatic  $\beta$ -cell, which commonly happens in the condition of pre-current hyperglycemic agent resistance. Pancreatic  $\beta$ -mobile disorder performs a vital function within the pathogenesis of each type of diabetes. Insulin is the important regulator of metabolism which is produced by  $\beta$ -cells. several vitamins and amino acids involved in glucose-triggered insulin secretion <sup>[1]</sup>.

Diabetic sufferers are anticipated to increase in numbers to 300 million by 2025 in line with the World Health Organization. It is roughly calculated that there are about 33 million adults and 70 million total individuals suffering from diabetes in India. This data is expected to boom to fifty-seven for adults by the year 2025. It is a reality that diabetes can't be cured completely because it has never been stated that someone had recovered absolutely from it. The traditional antidiabetic drugs are both high-priced and frequently related to adverse effects. To overcome the adverse effects, Ayurvedic herbs are always a better choice for the treatment of any disease. The use of herbal therapies to combat diabetes has also been supported by the World Health Organization <sup>[2]</sup>

After covid pandemic, medicinal plants are appearing yet again very promising to cure many diseases effectively. Diabetes is a very common disease nowadays and is highly needed to find an herbal drug for curing it and helps to reduce side effects. Earlier studies found many traditional drugs in medicinal vegetation. Metformin is an effective oral glucose-decreasing drug. Its manufacturing is totally based on the usage of *Galega officinalis* (wealthy in guanidine, the hypoglycemic aspect) to deal with diabetes <sup>[3]</sup>. Here in this review, we tried to highlight the role of *Vitex negundo* plant compounds and their roles against diabetes. We also spotlight the significance of *V. negundo* leaf as a promising supply of natural antioxidants for controlling the glycemic condition.

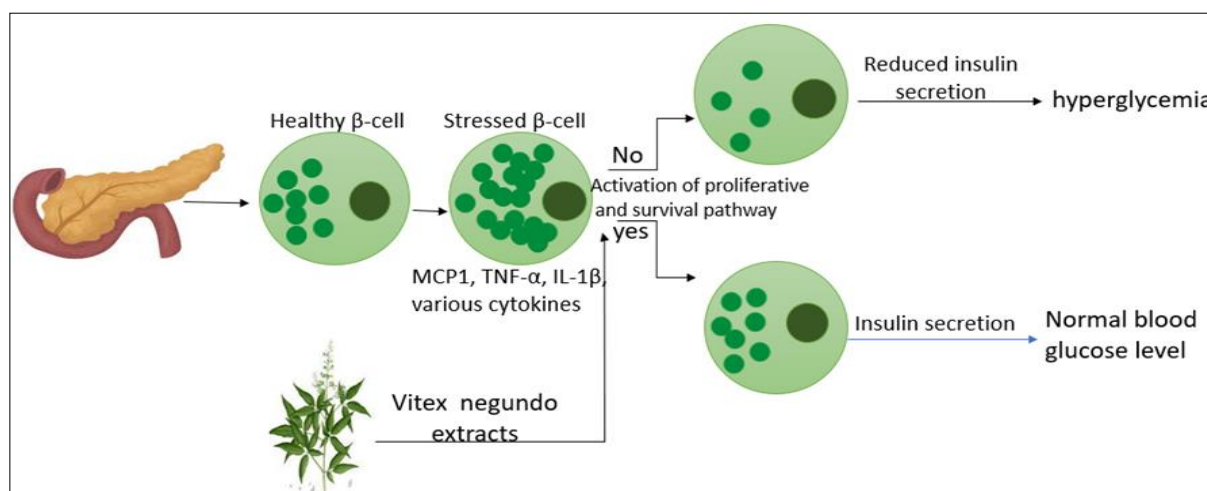
**Morphology and geographical distribution of *Vitex negundo***

It belongs to the family *Verbenaceae* which incorporates 5 Genera and almost 250 species; generally small timber growing from 6 to 27 ft in peak. Its leaves are digitated, with 5 or with 3 leaflets. per leaflet is nearly 3.8 to 10.2 cm (1.5 to 4 in) in duration, the first leaflet is the most important and possesses a stalk, It is a woody fragrant shrub that has a bitter, stinky, astringent flavor [4]. Commonly discovered all through the Indian subcontinent and riverbanks, moist localities, and deciduous forests. The shrubs develop approximately 2-4 m in peak. *Vitex negundo* is used by people as a remedy in a maximum of the states of India, Bangladesh, and Southeast Asia. The leaves are maximum robust for medicinal use. *Vitex negundo* has been used for numerous ailments inclusive of, irritation, antihistaminic, analgesic, eye sickness, fever, allergies, sinuses, headache, toothache, ulcers, digestion troubles, bronchitis, antibacterial, antipyretic, diabetes, insecticidal, antidote for snake bite, and many others. [5]. The leaves of those flowers were proven mosquito repellent

consequences as well as an ant. The plant additionally has anticancer, rheumatoid arthritis healing, and hepatoprotective potentials. The leaves are used for treating infection, pores and skin ulcers, gonorrhea, and bronchitis, diabetes. They are also used as tonics, and vermifuge to treat catarrhal fever. Oral management of the leaves claims to have antihyperglycemic, antibacterial, antipyretic, antihistaminic agents, and anti-implantation hobby [6].

**Herbal approach towards management of Diabetes**

Although several powerful allopathic medicines are present for the treatment and control of diabetes, there is still a need to create a herbal solution with fewer side effects and a lower cost. It is of utmost necessity to understand the molecular mechanism for making any drug that targets the disease. Several studies have been done so far to understand the pathway which is impaired in diabetes (Reference Fig 1) shows the possible herbal approach to target the disease,



**Fig 1:** Possible Therapeutic effect of different compounds of vitex-negundo plant in Diabetes

**Phytochemicals and therapeutic uses of *Vitex negundo***

*Vitex negundo* is usually acknowledged for its function within the regulation of cell activities such as apoptosis, cellular-

cycle, sperms motility, polycystic ovary disease, and menstrual-cycle (Table 1)

**Table 1:** Phytochemicals and therapeutic uses of *Vitex negundo*

Sr. No	Components	Cellular events	Roles	Reference
1	Flavonoids, vitamin C and carotene	Anti-Oxidative stress	Responsible for the reduction of lipid peroxidation production, which results inanity-oxidant potential.	[8]
2	Flavone Vitexicarpin	Anticancer	exhibits anticancer property	[9]
3	Coumarin glycosides Vitexnegheteroins I-J iridoid glycosides, vitexnegheteroins K-L.	Antioxidant	VN extracts components are used as a powerful antioxidant.	[10]
4	6-hydroxy-three-hydroxymethyl-7-methoxy-three,4-dihydro-2-Naphthaldehyd, Vitexin-6 (VB6) and Vitexin EVn-50	Apoptosis	VN extract Vitexin- 6 induces apoptosis in most cancer cells with the aid of cleavage of poly (ADP- ribose) polymerase and caspase-3.	[11]
5	Phytoestrogens and vitexin	Menstrual cycle	Vitexin increases the level of progesterone and minimizes the level of estrogen in the pituitary gland. Also, increasing the concentration of prolactin hormones and luteinizing hormones increases and decreases Follicle stimulating hormone (FSH).	[12]
6	Vitexin	Polycystic ovary syndrome (PCOS)	Vitexin reduces the production of prolactin, luteinizing hormone, and testosterone. Treating with vitexin can regulate the manner of ovulation and increase metabolic hormone profile and fertility.	[13]
7	4,6,8'-trimethoxy 5,7,3'-trihydroxy, flavone	Viability of sperms	Alienate the male reproductive system's extrinsic testosterone androgen movement, and it increases the viability and motility of sperm in male mice.	[14]

### Medicinal uses of *Vitex negundo* leaves extract

The *Vitex negundo* leaves have several medicinal uses such as Antibacterial, and critical in harsh, medicinal, drugs, Tonic and Vermifuge. They are helpful in treating joint swelling brought on by severe rheumatism. Juice from *Vitex negundo* leaves is used to treat ulcers and eliminate foul discharges, while an oil mixture made with leaf juice is used to treat swelling, and lesions on the side of the neck. *Vitex negundo* leaves extracts have been proven for use in bactericidal and antitumor anti-parasitical, fragrant, vermifuge, pain relief, and insect repellents. Additionally, it helps with rheumatic swellings. Leaf extracts are employed as a fumigant and an insecticide [15].

### Anti-diabetic effect

Beyond its antihyperglycemic activity, *V. negundo* leaf extract has a significant impact on glycoprotein metabolism. Iridoid glucoside has a similar anti-diabetic effect to *glipalamide*, a known hyperglycemic medication with anti-diabetic effects [16]. Hepatocellular carcinoma can be fought using vitexin that is derived from the *V. negundo*'s seeds. By stopping the cell cycle, vitexin inhibits Hep3B, HepG2, and Huh-7 cell proliferation at G1/G0 and prevents both anchorage-based and independent HepG2 mobile growth. Additionally, vitexin lowers VEGF release, which prevents the development of endothelial tubes. Vitexin treatment of the HepG2 cells reduced the phosphorylation of FOXO3 and Akt. Additionally, silencing FOXO3a by using siRNA downstream of the expression level resulted in a greater growth inhibition when Akt1 was knocked down by small interfering RNA (siRNA) [18]. Akt (protein kinase B) controls the decreasing of proteins which include mTOR which is an instantaneous goal to the signaling of insulin, for this reason forming the link

toward diabetes and cancer.

The list of the compound showed anti-diabetic properties extracted from *Vitex negundo* leaves.

Table no. 2 shows the antidiabetic compounds These are the compounds that have been seen controlling glycemic conditions, these compounds are the source of different plants and are present in *Vitex negundo* plant leaves also, the compounds are - Friedelin, Carotene, B-pinene, and a-pinene, Linalool, Camphor, Nerolidol, and Iridoids which are showing diabetic effects and are present in the *Vitex negundo* plant Leaves.

The phytochemical screening of extracts from *Vitex negundo* L. Leaves confirmed the presence of many derivatives. These bioactive substances have interest in antibacterial, anticancer, anti-inflammatory, antioxidant, and antidiabetic properties. Below are certain phytochemical components discovered in *Vitex negundo* plant leaves.:

The various chemical parts present are Friedelin,  $\alpha$ -element, diet-C, casticin, Iridoids, terpineol, vitexicarpin, Globule, Farnese, Farnesol, Viridiflorol, Ethyl phenol,  $\alpha$ , $\beta$ -pinene, Linalool, Garden in-A, Garden in-B, Terpinen-4-ol,  $\alpha$ copaene, Camphene, Spatulous,  $\alpha$ -thujene, Sabinene, Agnosies, Carotene, Stearic and behenic acid,  $\alpha$ -element, Luteolin-7-O- $\beta$ -D-glucosides, Camphor, Camphene, Careen, phellandrene,  $\alpha$ - guanine, Neural, Geranial, Bornyl acetate, Nerolidol,  $\beta$ bisabolol, Cedrol, 2'-p-hydroxy benzoyl lmusnaenosidic acid, laudanine, Aucoin and Ntshangase [19], Squalene, Flavones, p-hydroxybenzoic acid, Heptamethoxyflavone, Botulinic-acid, Ursolic-acid, Dimethoxyflavone, Vitegnoside, Pyran-4-carboxylic-acid, 6'p-hydrox- benzoyl-mussaenosidic-acid [20], Negundo side, glycosidic iridoids,  $\gamma$ -tocopherol,  $\beta$ -caryophyllene, and vitexin,  $\beta$ -sitosterol and tocoquinone [21].

**Table 2:** Shows the antidiabetic compounds

Compounds	Diabetes impact	Model use	Reference
Friedelin	Friedelin has an anti-diabetic impact through an insulin-established signaling cascade mechanism.	STZ-induced Diabetic Rat	[22]
Carotene	$\alpha$ -carotene and $\beta$ -carotene are used to reduce diabetes Mellitus type-2.	Male mice	[23]
B-pinene	when compared to those of the control group, pinene decreased plasma levels of glucose, triglycerides, VLDL, LDL, and HDL.	Male Wistar rats	[24]
a-pinene	Capable of lessening the fast of blood glucose tiers.	alloxan-induced diabetic mice	[25]
Linalool	Linalool reduces the hazard of developing diabetes vascular headaches. Linalool has shown positive results in diabetes treatment, it helps in the metabolism of lipids and glucose.	Diabetic mice	[26]
Camphor	It shows an Antidiabetic effect.	alloxan-induced diabetic rats	[27]
Nerolidol	Nerolidol considerably decreased the blood glucose in diabetic rats and levels of plasma insulin while additionally, it reduces the enzyme activity that metabolizes the carbohydrate.	type 2 diabetic rats	[28]
Iridoids	Iridoid glucoside possesses antidiabetic and antioxidant ability	Mice	[29]

### Conclusion

Diabetes is a huge public fitness issue nowadays. Diabetes is growing unexpectedly in India, mainly in cities, and is now a matter of concern. Morbidity and mortality are also increasing in diabetes. It demands Early identification of the symptom and good remedies at the grassroots level. Drug treatment is the mainstay of managing diabetes, even when mixed with supplements and remedies. It is largely controllable but not completely curable. Although there are currently a number of medicines available, none of them haven't any facet effects. The protection and tolerability of an overdose of many antidiabetic tablets is also a hassle. Many effective medicinal drugs come from plant assets and proved very useful in the treatment of diabetes with minimum adverse effects. *Vitex*

*negundo* has the potential for the development of a drug against diabetes as many studies show the safety and efficacy of *Vitex negundo* or its compounds if used in unique doses. *Vitex negundo* leaves extract phytochemicals had the extremely good capability of healing diabetes. Further studies are needed to find the potential target of diabetes and to study the antidiabetic potential of *Vitex negundo*. Cited Literature discovered that *Vitex negundo* Linn is a famous remedy for humankind since it is important to investigate whether or not *Vitex negundo* nutritional complement may be a useful preventive or nutritional mitigation technique to lessen diabetes's consequences.

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