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VITEX ALTISSIMA LINN: A COMPREHENSIVE REVIEW ON PHYTOCHEMICAL COMPOSITION AND PHARMACOLOGICAL ACTIONS

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Abstract:
Vitex altissima L, belonging to the Verbanaceae family, is available in India's Eastern Ghats and Deccan plateau. They were traditionally used to treat rheumatism. Six Iridoid glycosides and two Iridoids agunoside and negunoside with potent antioxidant potential were isolated, and Lignan altisonin, flavonoid 2-o-hydroxybenzoylorientin, were found in leaves. The compounds showed high binding energy with reverse transcriptor protein and exhibited antiviral action comparable with zidovudine, and stavudine. GC-MS analysis revealed the presence of n-hexadecanoic acid, 12-octadecadienoic acid, and squalene. HPTLC fingerprinting analysis was developed to quantify and identify the marker compounds. Leaf methanolic extracts exhibited antibacterial activity against five strains of Gram-positive and Gram-negative bacteria. The sesquiterpenoid compounds were found to exhibit anticancerous and antioxidant action. The *V.altissima* was proved to have promising acts so could be further explored for their pharmacological actions and formulated.

Keywords: *Vitex altissima*, HPTLC, GC-MS, Isolated compounds.

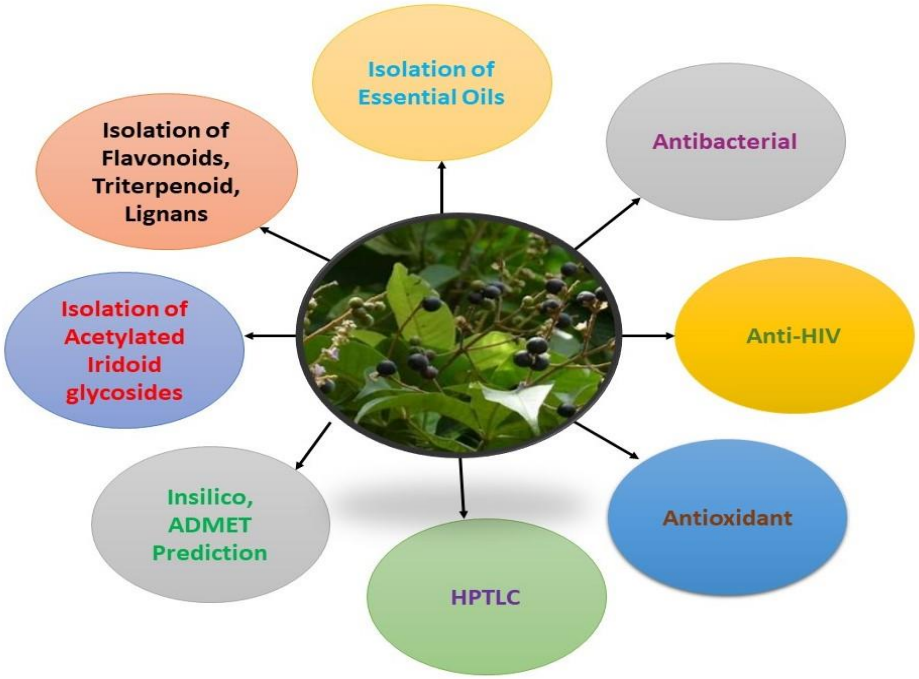

Fig.1 Graphical Abstract

Introduction:

Vitex altissima Linn. belongs to the family Verbenaceae and is a huge deciduous tree that may grow to a height of up to forty metres and can be found practically everywhere in Indochina, Sri Lanka and Westren. Greyish lenticellate scaly bark. It also has a blazing yellowish colour. The young branches are quadrangular and pubeatecent, and Leaves are typically trifoliate or, on rare occasions, 5-foliate (with two tiny leaflets), opposite, and decussate. The midrib is pulvinate, petiole is winged, and minorly pubescent[1]. The leaflets are sessile, 7-17x2-6.5 cm, narrowly elliptic, apex acuminate, serrate or entire margin, 10-20 pairs of secondary nerves and reticulate tertiary nerves. There are zygomorphic flowers that have a bluish-white hue, and the blooms are minutely pubescent. The flowers are inflorescence terminal panicles. The fruits and seeds are drupes, smooth, globose, and 0.9 centimetres wide. They are dark purple in colour and contain seeds that are firm.[3,4] In Ayurvedic medicine, the plant is supposed to alleviate a variety of conditions includes urinary system diseases, stomatitis, emaciation, postpartum troubles, inflammation, wounds, ulcers, allergies, eczema, pruritus, worm infestations, and vitiated kapha and vata. anti-inflammatory effects, as well as antibacterial and antioxidant activities[2].

Methods:

Literature survey:

The scientific results on *Vitex altissima* were obtained using a variety of search engines and databases, including Google Scholar, ScienceDirect, PMC, Research Gate, and Scopus. The information on pharmacological activities, botany, nanotechnology, traditional applications, bioactivity, phytoconstituents, and phytochemistry was obtained from research publications, review papers, book chapters, and proceeding papers.

Fingerprinting Analysis:

Using the high-performance thin-layer chromatography (HPTLC) method, the study aimed to detect the biocompounds present in the hydroalcoholic extract of *Vitex altissimo* leaves. The extract was examined for a wide range of phytoconstituents. The HPTLC system that was used was an HPTLC (CAMAG) system that was outfitted with a LINOMAT applicator. Different compositions of vehicles were used in order to accomplish the goal of creating a high level of separation[5]. The findings of a preliminary screening confirmed the existence of phytochemicals. The analysis of the extract revealed the existence of thirteen distinct kinds of flavonoids, each of which had a unique Rf value that fell anywhere between 0.019 and 0.97. The findings of the saponin experiment demonstrated that there are twelve different varieties of saponins, each of which has a different Rf value that ranges from 0.01-0.92. The phenolic profile's findings demonstrated the existence of fifteen different types of phenolic compounds, each of which had a single Rf value that fell somewhere between 0.02 and 0.94. However, the outcomes of the steroid outline revealed the existence of seven different kinds of steroids, each of which had seven divergant Rf values that ranged from 0.02 to 0.52. In order to accurately identify and quantify marker molecules, HPTLC fingerprint analysis was developed. New medications may be developed to treat a variety of ailments by isolating and identifying the marker molecules.[6,7]

Establishment of New acylated iridoid glucosides via Isolation :

Six novel iridoid glucosides—6'-O-trans-feruloylnegundoside (1), 6'-O-trans-caffeoylnegundoside (2), 2'-O-p-hydroxybenzoyl-6'-O-trans-caffeoylgardoside (3), 2'-O-p-hydroxybenzoyl-6'-O-trans-caffeoyl-8-epiloganic acid (4), 2'-O-p-hydroxybenzoyl gardoside (5), and (6), which were separated from the *Vitex altissima* leaves ethyl acetate extractive[8]. Additionally, Agnuside and negundoside, two recognised iridoids, have been found to be present in the extractive[9]. The compositions of these substances' structures were deduced

using spectrum data interpretation. Superoxide and the DPPH-assay approaches have shown a significant amount of antioxidant activity for compounds (2-4)[10].

Isolation of Triterpenoids, Lignan, and Flavonoids from Vitex altissima

Altissinone (1), a novel tetrahydrofuranoid lignan, and 2″-O-p-hydroxybenzoylorientin (2), an acylated flavone C-glucoside, were extracted from the leaves of *Vitex altissima*, together with other recognized triterpene acids and flavonoids. The compound structures were identified by analysing the data from high-resolution nuclear magnetic resonance (HMQC, HMBC, and NOESY) spectrums. In the rat paw edoema model, the ethylacetate extract shown significant anti-inflammatory activity. The antioxidant and 5-lipoxygenase enzyme inhibitory activity of flavonoids and triterpene acids were moderate.

Comparative analysis of *V.altissima* and *V.trifolia* L, capacity for wound healing:

To evaluate the efficacy, excision, incision, and dead space wound models were used for V. *trifoliata* L. and *V. altissima* L.ethanolic extracts in terms of their ability to restore wound healing. Either of them showed potent wound healing activity based including reduction in period of epithelialization, an improvement in the ratio of contraction of wound, breaking strength of skin, granulation tissue and its dry weight, content of hydroxyproline. This was demonstrated by the fact that the epithelialization period was shortened. Compared with the animals in the control group, the histopathological examination of the granulation tissue revealed increased collagenation. Compared to the leaf extract of *V. altissima*, the ethanol leaf extract of *V. trifolia* had the highest level of wound healing efficacy among the two extracts. On the other hand, and in contrast to the control group, it was discovered that both leaf extracts have a high capacity for wound healing[11].

***Insilico* and Anti HIV analysis, compounds identified in *Vitex altissima* and *Vitex Leucoxylon*:**

India's traditional plant knowledge has been accumulated over millennia by our ancient ancestors. Over 5000 years of fighting illnesses and preserving moral, mental, and physical health have made the Siddha System of Medicine also known as the Traditional Tamil System of Medicine the best medical system in the world. Vitex species were used in Siddha for several years for their anti-viral activity. The Human Immunodeficiency Virus, on the other hand, is the subject of the current investigation due to the fact that it is both complicated and responsible for death. Twenty-one and seventeen bioactive chemicals were discovered to exist in *Vitex leucoxylon* L. and *Vitex altissima* L. respectively, according to the results of an FTIR study. Molecular docking and bioinformatics tools were utilised in order to conduct

additional research on these compounds in order to investigate their binding affinity mechanism against reverse transcriptase, which is a target protein of the Human Immunodeficiency Virus (HIV). This protein is responsible for cause of virulence in the virus. In order to calculate the interaction rate between bioactive chemicals and the protein target, the binding free energy needs were taken into consideration. Zidovudine, Stavudine and Nevirapine, which are all commercially available medications, were also subjected to molecular docking in order to determine their effectiveness of binding to target Protein[12]. When the results of the bio-compounds found in the Vitex sps were compared with the formulations that are available for commercial use, it became it was evidently far more effective for the bioactive chemicals than the available medications making them acceptable in order to cure AIDS. As a result, this research would serve as foundation for promoting therapeutically lead compounds derived from medicinal plants. These molecules will not only bring back the ancient practises but will also reduce the undesirable side effects[13].

***Invitro* antibacterial potential of Vitex species:**

The following species of *Vitex* are *Vitex altissima (V. altissima), Vitex diversifolia (V. diversifolia), Vitex negundo (V. negundo), Vitex peduncularis (V. peduncularis), and Vitex trifolia*, leaf methanol extracts were tested for antibacterial activity (*V. trifolia*). The disc diffusion method was used to find the minimum bactericidal concentrations (MBC) and minimum inhibitory concentrations (MIC) for five and seven Gram+ve and Gram-ve pathogens[14]. Among all of the bacteria that were examined, *V. peduncularis* had the highest level of activity. In addition, it produced a inhibitiory zone in the range from (11.000 0.577) to (22.670 0.667) mm, MIC values that ranged from 62.5 to 10000.0 g/mL, and MBC values that ranged from 125.0 to 20000.0 g/mL. Based on the findings of this investigation, it is suggested that *V. peduncularis* be used to identify antibacterial compounds accountable for action against the evaluated human pathogenic bacterial strains[15, 16].

Profiling of phytochemicals and research on biological processes:

The primary goal of this research is to conduct phytochemical profiling, chemical composition quantification, and biological investigations on *V. altissima*. JNTBGRI in Thiruvananthapuram was the source of the collected plant leaves. The dried plant material extracted using various solvents. After that, the extract was subjected to phytochemical screening so that the metabolites could be qualitatively examined. Flavonoids, Carbohydrates, phenolic acids, saponins and terpenoids were discovered in the screening findings. HPTLC analysis was used to profile these compounds in leaf extracts. *V. altissima*

leaf extracts exhibit significant antibacterial activity in Agar Well Diffusion assays using hexane and chloroform extracts. In the DPPH radical scavenging experiment and the Protein denaturation test, the methanolic extract exhibits antioxidant properties and anti-inflammatory[17,18]

Biological activities of Essential oils:

The purpose of this work is to use molecular-docking to test the efficiency of a few active chemicals isolated from *Vitex altissima*. Chemical profiling was accomplished using GC/MS and GC/FID. MTT test was used by the use of an *in vitro* investigation of possible anticancer effects utilising the cancer cell line DLD-1 and the normal cell line L929. This was accomplished by docking all of the bioactive compounds to phosphoinositide-3 kinase with the help of the Auto Dock 4.2.6 programme (PI3K). There were a total of 22 compounds that were discovered, with allo-aromadendrene accounting for 29.82 percent, E-phytol for 16.08 percent, α-humulene for 14.04 percent, β-caryophyllene for 4.18 percent, α-santol for 3.64 percent, and panthenol for 2.23 percent. The oil has antioxidant and anticancer properties, according to the research. Following the treatment with Vitex altissima leaf oil, apoptosis tests revealed that the cells were necrotic. Inhibition of the PI3K enzyme's activation is linked to a variety of malignancies. The pharmacokinetic features of the various drugs are revealed by their ADMET properties. All substances docked fulfilled Lipinski's rule of five, suggesting their potential for application as medications taken orally [19,20].

Vitex species- Larvicidal activity of Fatty acid methyl esters (FAME):

FAME of *V.negundo, V. altissima* and *V.trifolia* larvicidal action on 4th instar Culex quinquefasciatus was investigated. The Gas chromatography was used to examine the lipid composition. Palmitic acid, lauric, stearic, oleic and linolenic acid were some of the acids that were found in the maximum concentrations in *V. negundo.* Linolenic acid is found in the highest quantity in the leaves of the *V. trifolia* plant. LC_{50} of 9.25 ppm was found that *V. trifolia* FAME extract, exhibited the prominent larvicidal effectiveness. This was succeeded by the FAME extract of *V. negundo*-18.64 ppm and *V. altissima* -14.82 pp[21].

Conclusion:

Based on the reports of *V.altissima,* it was discovered to have potential phytocompounds and beneficial pharmacological effects. Thus, it may be further investigated to assess the plant's pharmacokinetic and therapeutic characteristics.

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