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A REVIEW ON PHARMACOLOGICAL ACTIVITIES AND PHYTOCONSTITUENTS OF *VATERIA INDICA* LINN. (SARJA)

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Abstract:
Vateria indica Linn is an endangered tree that belongs to Dipterocarpaceae family. These species are most common in moist evergreen forests and different parts of Southern Western Ghats of India from the states of Kerala, Karnataka and Tamil Nadu and a 'Tree flora of Kerala'2 listed 26 other reports concerning V. indica[1]. It is a versatile tree which has commercial and medicinal significance. It is known as Sarja rasa in Ayurveda, resin from V. indica is known as white dammar. The resin which is extensively used in Indian medicine is credited with tonic, carminative and expectorant properties. It is also used in the treatment of chronic bronchitis, throat troubles, wounds, boils, rheumatism, urinary discharges, piles, gonorrhea and syphilis. Most of the studies accounts on its pharmacological activities such as anti-inflammatory, anthelmintic, anti-ulcer, anti-tumor activity and anticancer potential[2]. According to the comprehensive investigation of chemical constituents in the leaves of V. indica contains several secondary metabolites which include alkaloids, flavonoids, saponins, terpenoids, steroids, glycosides, tannins, volatile oils polyphenol compounds etc., are used for curing many diseases.

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INTRODUCTION:

Reinvigoration with therapeutic plants is as ancient as mankind itself. Knowledge of medicinal plants practice is a result of the many years of efforts against illnesses due to which man learned how to isolate drugs in barks, seeds, fruit bodies, and other parts of the plants in order to treat health disorders and to preclude the diseases including epidemics. The traditional medicine practice is prevalent in China, India, Japan, Pakistan, Sri Lanka and Thailand. It has been approximated that the acceptable therapy is accessible only for one third of the known human ailments. Therefore, the fight against diseases must be conceded on persistently. Medicinal plants or their extracts have been used by humans since time long-established for different ailments and have provided effective drugs such as analgesics (morphine), antitussives (codeine), antihypertensives (reserpine), cardiotonics (digoxin), antineoplastics (vinblastine and taxol) and antimalarials (quinine and artemisinin). Compared with chemical synthesis, plant derived natural products represent an attractive source of biologically active agents since they are natural and available at affordable prices. The 19th century evident the isolation of abundant alkaloids from plants used as drugs, namely, atropine (*Atropa belladonna*), caffeine (*Coffea arabica*), cocaine (*Erythroxylum coca*), ephedrine (Ephedra species), morphine and codeine (Papaver somniferum), pilocarpine (*Pilocarpus jaborandi*), physostigmine (*Physostigma venenosum*), quinine (*Cinchona cordifolia*), salicin (Salix species), theobromine (*Theobroma cacao*), theophylline (*Camellia sinensis*) etc. Most natural products are compounds derived from primary metabolites such as amino acids, carbohydrates and fatty acids and are commonly characterized as secondary metabolites[3]. Secondary metabolites are reflected products of primary metabolism and are generally not involved in metabolic activity viz. alkaloids, phenolics, essential oils and terpenes, sterols, flavonoids, lignins, tannins, etc. Secondary metabolites are yielded either as a result of the organism acclimating to its surrounding environment or are produced to act as a potential defense mechanism against predators to aid in the endurance of the organism. Traditional medicine is the sum total of the knowledge, skills and practices based on the concepts, principles and experiences indigenous to different cultures used in the maintenance of health, anticipation of diseases and improvement of physical and mental illness. Ethno botanical and traditional practice of medicinal plants serves as a source of evidence for the isolation of active compounds. About 40% of the total medicinal consumption is attributed to traditional tribal medicines alone by China. Contagious diseases signify an important root of morbidity and mortality amongst the population, intensely in developing countries. In current existences, there has been emergent interest in alternative therapies and the therapeutic use of natural products, exclusively those derivatives from plants. Plants are considered as one of the main sources of biologically active resources. It is estimated that 60 % of anti-tumor and anti-infectious drugs already on the market or enduring clinical trials are of natural origin. Phytochemical investigation of medicinal plants has influenced a prodigious deal for the discovery of new drugs. Verification of the safety, eminence, and adequacy of therapeutic plants and natural products has now turned into a crucial issue in industrialized and in developing nations. Medicinal plants have been utilized for a significant number of years to flavor, essence and preserve food, these therapeutic plants are the vivid source of constituents which can be utilized as a part of medication synthesis and advancement. Medicinal plant drug discovery endures to provide new and influential leads against innumerable pharmacological targets including cancer, malaria, cardiovascular diseases and neurological disorders. The genus *Vateria* belongs to the Dipterocarpaceae family, these were well known as rich sources of various resveratrol (3, 5, 4′-trihydroxystilbene) oligomers and consists of three species, namely, *V. indica*, *V. macrocarpa*, and *V. copallifera*. *V. copallifera* (Retz.) Alston is a plant endemic to Sri Lanka, locally known as “Hal”. In the traditional system of medicine,[4] a decoction of the *V. copallifera* bark has been used in the treatment of diarrhea, ulcers, rheumatic pains, and diabetes mellitus. It is also a hopeful basis for unique bioactive secondary metabolites with distinct chemical structures. Two resveratrol trimers, copalliferol A and copalliferol B, together with stemonoporol, which is isomeric with copalliferol A, have been testified from the acetone extract of the bark of *V. copallifera*. *Vateria macrocarpa* is an Evergreen trees, to 30 m high, bark grey, mottled with white and green, smooth; exudation resinous, pale yellowish-white. Sarja (*V. indica* Linn.) is one such Indigenous & Widespread plant species to the Western Ghats, which requires an imperative awareness to be conserved. *V. indica* is recorded as critically endangered on the 2013 IUCN Red List based on its overexploitation for its timber and its habitat loss of more than 80%[5]. This species is cogitated suitable for restoration of degraded wet evergreen rain forests due to its high survival and fast growth, the tree is slow-growing species, endemic & found primarily in the South west coast evergreen forests, up to an altitude of 750 m, and also occasionally in secondary evergreen dipterocarp forest found in the state of Karnataka, Kerala and Tamil Nadu. It is a multipurpose tree which has economic and medicinal significance. It was found to be over exploited & highly destroyed for the purpose of making Plywood’s. Histological parameters concealed the bark was rough with cork

patches, greyish-green in color with longitudinal gaps and wrinkles on outer surface but inner surface was smooth, light brown in color with longitudinal patterns [6]. This exploration is an effort to record macro-microscopic features of *V. indica*. Fruits along with physico-chemical characterization of seed and butter. On an average, a fully matured tree yields about 400 to 500 kg of fruits, the fruits quickly germinate in the rainy season [7] and need a facility for quick collection, transportation, decortication, drying and storage. Analytical specifications of *V. indica* butter has shown saponification value and iodine value as 112.43 and 8.82 respectively. Phytochemical analysis of *V. indica* showed the presence of glycosides and coumarins as main functional groups. Discovery of endophytes from medicinal plants plays crucial role in the production of novel secondary metabolites with valuable biological activity, which also influences to the diversity of microbes in the natural environment. Sampling and characterization of fungal endophyte diversity is an emergent challenge, which leads to the discovery of new species producing new compounds and a better supportive of their role in ecosystems. In the present study fungal endophytes were isolated from surface sterilized leaf [8]. From literature survey it was discovered that the resinous exudates from *V. indica* can be used to treat lipid disorders but no peculiar studies were done on its antiobesity activity. Hence an attempt was made to assess its antiobesity activity against HFD induced obesity. The preliminary phytochemical study performed on aqueous extract exposed the presence of reducing sugar, flavanoids, resins, tannins and saponins. The acute oral toxicity studies showed that the aqueous extract of *V. indica* was found to be safe till 2000mg/kg body weight. Extract was given to animals using three different doses i.e. 100, 200 and 400 mg/kg body weight. The anti-obesity effect was assessed in terms of serum total cholesterol, triglycerides, HDL, LDL, VLDL. The body weight and organ weights were also assessed in both the models. The extract treated groups showed significant reduction in the serum lipids [9]. The total ash was found to be 3.5%, acid insoluble ash 2% and water-soluble ash were 2.5% w/w of dried powder. The water soluble, ethanol soluble and ether soluble extractive values were obtained 25.4% w/w, 3.6% w/w, 0.4% w/w respectively. Tannin content of stem bark powder of *V. indica* was found to be 35 % w/w. phytochemical studies were carried out on ethanol and water extracts indicated the presence of tannins, phytosterols, Phenol, flavonoid, alkaloid and carbohydrates [10]. The phytochemical estimation of drug, dried powdered bark (5 g) was extracted in a Soxhlet apparatus with petroleum ether (60-80), benzene, chloroform, ethanol, and distilled water successively. The extracts were evaporated to dryness under vacuum. These extracts were used for testing of different phyto-constituents such as alkaloids, carbohydrates, phenols, flavonoids, proteins, amino acids, saponins, gums, mucilages and resins

Properties of *V. indica* Stem bark powder with different chemical reagents.

Sl. No.	Treatment	Colour/ ppt	Constituents
1	Powder + Mg-HCl	Magenta	Flavonoid present
2	Powder + 1N H_2SO_4	Reddish-brown	Sterols/ Triterpenoids present
3	Powder + 1N HNO_3	Yellow	-
4	Powder + 1N Aq. NaOH	Blackish green	Flavonoid present
5	Powder + Picric acid	No Precipitation	Alkaloids absent
6	Powder + 5% $FeCl_3$	Brown	Tannin present
7	Powder + Iodine	Dark yellow	Starch absent
8	Powder + 5% KOH	No change	Anthracene glycoside absent
9	Powder + Acetic acid	Blackish-purple	-

It is obligatory to determine standard parameters for the precise identification of the plants and purity. Pharmacognostical and phyto-chemical screening study on the particular plant will set up standard for its identification among closely related species of plant and to find out its adulteration.

MORPHOLOGY

A large elegant perennial tree, grows up to 30 m. high, with a clean, cylindrical trunk of 15 m. and a girth of 4.5 m.

Bark: Rough, whitish to grey, peeling off in thick round flakes.

Leaves: Coriaceous, Ovate to Oblong, entire (Leaf falls in March, new foliage appears in April May, the second flush of foliage starts after rains, in October to December.)

Flowers: White, fragrant, in terminal Corymbose Panicles (Flowering – January to March)

Fruits: Capsules, ovoid, pale brown, fleshy, 8 to 11cm long, and 3.5 to 6 cm in Diameter. 1 seeded, Reddish white, filled with fat. Ripens during June to July.

Botanical classification

The botanical classification is done is the following ways.

Kingdom	Plantae
Family	Dipterocarpaceae
Genus	Vateria
Species	*V. indica*
Synonyms	*V. malabarica*

Sarja as it is termed in Ayurveda, Raala in Unani, Vellai Kungiliyamin Siddha systems of medicines, is highly ideal in confined healing traditions for curing many diseases. Although the status of this species is critical, very few healthy populations remain.

MEDICINAL EVALUATION– IN GENERAL

The timber is in much requirement for marketable first-class plywood making. It is sold in the name of "Malabar White Pine". It has been found to be corresponding to Oregon Pine of USA [11]. Resin: Piney Resin, White Dammar or Dhupa of Trade is obtained from this tree. Generally used in production home Varnishes, Incense sticks, Torches & candles with coconut oil. Also finds massive use in Indian Medicine.

The Resin comes in 3 forms:

1. Compact form: Solid lumps and considered as the finest quality. It is very hard and bright orange to dull yellow, with a glassy fracture, and amber like appearance.
2. Cellular form: Occupied of air bubbles and provides a cellular structure.
3. Dark-colored form: Appears in cavities of old and moribund trees or dead trees and of low-grade quality.

Tallow Piney, Malabar Tallow or Dhupa fat in the conventional method of isolating the Dhupa fat also called as Piney Tallow, the seeds are crushed and boiled in water till the melted fat rises to the surface, which is semi-solid in reliability. The same fat is also extracted by hydraulic press which yields high. The Tallow is used for edible purposes after refining, used in and as an adulterant of ghee. Also been suggested for use in blends with cocoa butter or as its substitute. The fat is being used in making candles and Soaps [12].

Figure 1*: V. indica* Linn.

CHEMICAL CONSTITUENTS:

The Phytochemical evaluation of *V. indica* stem bark suggests the existence of carbohydrate, tannin, phenols and flavonoid in aqueous and ethanolic extract, as well as the bark is used to control fermentation in when making alcoholic beverages such as arrack and toddy. The leaves and roots comprises bergenin, it is a trihydroxybenzoic acid glycoside commonly called as paashanbhed and it also shows potent immunomodulatory effect and hopeaphenol, it is a crucial stilbenoid, It illustrates an opposite effect to vitisin A (Vitisin A is a natural phenol found in red wines.) on apoptosis of myocytes isolated from adult rat heart. The stem is identified to yields biological active compounds such as oligostilbenoids and monoterpenes. Seeds are tough and brittle and have a faded aromatic fragrance, and it contain up to 50% of solid oil called as piney resin or white dammar or Dhupa fat and is commercially imperative as an aromatic drug. It is used for the edible purpose, confectionery and as an adulterant of ghee. In addition to this therapeutically it is utilized as a local application in rheumatism and allied afflictions. The review on phenolic constituents in *V. indica* afforded five resveratrol tetramers (it is a part of group of compound called polyphenols, acts like antioxidant, protects brain, increases insulin sensitivity, ease joint pain and also it has a positive effect on blood fat), resveratrol

chemo preventive and therapeutic polyphenol found in grape skin or dipterocarpaceous plants, it is the most famous phytochemical compound currently under investigation [13]. High-performance liquid chromatography (HPLC) analysis showed that the extract contains bergenin, hopeaphenol, vaticanol B, vaticanol C, and ε-viniferin.

Figure 2: *V. indica* Linn. Leaves

Vaticanol B is a tetramer of resveratrol that shields against endoplasmic reticulam stress – induced cell death, vaticanol B also influences a strong anti-inflammatory activity. Vaticanol B is a novel anti-inflammatory agent that improves the ER environment by decreasing the protein load on the ER and by maintaining the membrane integrity of the endoplasmic reticulam. Enhanced endoplasmic reticulum (ER) stress has been concerned in various pathological circumstances including inflammation. During exploration for compounds that regulate ER stress, we identified vaticanol B [14]. Production of a diversity of inflammatory modulators such as tumor necrosis factor-alpha, nitric oxide, and prostaglandin E(2) was inhibited by vaticanol B to a much better extent than by monomeric or dimeric resveratrol after exposure of cells to lipopolysaccharide. Further studies to determine the common mechanisms underlying the regulation of ER stress and inflammation by vaticanol B disclosed an important role for vaticanol B in regulation of basic gene expression and in anticipation of the protein leakage from the ER into the cytosol in both conditions

Vaticanol C is a resveratrol tetramer and was stated to exert various pharmacological properties, including antiproliferative, antioxidant, anti-inflammatory, and anticancer properties having cytotoxicity against tumor cell lines which induces the *in vitro* apoptosis and suppression of cell proliferation in various human cancer cells as evaluated by morphological changes, nucleosomal DNA fragmentation and elevated activities of caspases (which are executional factor of apoptosis). Although tumor growth was alike between control and vaticanol C treated group, collections of lymph node and lungs metastasis were drastically lowered only in animals receiving the high dose (200ppm) of vaticanol C overall metastasis to any organ also decreased, but not to statistically substantial degree over control. Cell proliferation inclines to decrease in mammary tumor with exposure to vaticanol C in a dose dependent method, but again the decrease was statistically irrelevant [13]. Breast cancer is one of the fatal cancers in humans and mortality is generally due to metastasis, typically to lungs, lymph nodes liver and bone. Since lymph node involvement is the most important prognostic factor in breast cancer patients. The antimetastatic activity of vaticanol C may be of clinical consequence.

ε-Viniferin was first isolated from *Vitis vinifera* (Vitaceae), is classified as a model for its biosynthesis from resveratrol a naturally occurring phenol, it can found in many plant families including *Vitaceae*, grape vines (*Vitis*), it is a protective phytochemical found in several plant families. It also concerned attention as a phytoalexin and was conveyed to have antifungal, antibacterial, and antiviral activities belonging to the stilbenoids family. It is a resveratrol dimer. Many reviews of ε-viniferin are about the antioxidant and anticancer activities. The antioxidant activity of ε-viniferin is vital in the prevention of oxidative damage or chemical-induced cancer by inhibiting cancer initiation and progression, it also revealed the direct cytotoxicity to numerous cancer cells. It was reported that ε -viniferin could kill C6, Hep G2, HeLa, and MCF-7 cancer cell lines in a dose-dependent method. Viniferin, and resveratrol both exert the antiproliferative and proapoptotic effect [15]. Further analyses on the multiple myeloma cell line directed that viniferin and resveratrol could control cell cycle by affecting diverse targets. In this model, viniferin induced apoptosis by arresting cell cycle in G2/M, while cells treated with resveratrol were accumulated in S phase, and both of them induced apoptosis in a caspase-dependent manner by disrupting normal mitochondrial membrane potential.

Hopeaphenol is a resveratrol tetramer isolated from *Dipterocarpaceae* like *Shorea ovalis* and wines from North Africa, it also repressed the growth of human cancer cells SW-480 and HL-60 and murine leukemia cells P-388 It controlled potent cytotoxicity against the human epidermoid carcinoma of the nasopharynx hepatoma and also

illustrated anti-inflammatory antimicrobial and HIV-inhibitory activities [15].

Bergenin, a natural secondary metabolite, has been isolated from diverse portions of a number of plants [16]. It is one of dynamic constituents in herbal and ayurvedic formulations. It reveals antiviral, antifungal, antiplasmodial, antiinflammatory, antihepatotoxic, antiarrhythmic, antitumor, antiulcerogenic, antidiabetic and wound healing properties. It has been examined and estimated in different plant extracts, blood and drug samples using chromatographic techniques, and pharmacokinetic studies have been made. Several bergenin derivatives were isolated and synthesized and were found to hold pharmacological activities. Ethnomedicinal significance of bergenin comprising plant materials is also emphasized. This ample review specifies information on the potentiality of bergenin and its derivatives for therapeutic usages.

Endophytes of *V. indica*

Endophytic microbes (bacteria and fungi) reside in plant tissues without affecting any symptoms of disease in the host. It can colonize in the stem, roots, petioles, leaf segments, inflorescences of weeds, fruit, buds, seeds and also dead and hollow hyaline cells of plants The initiation of fungal endophytic organizations inside roots can vary the mineral nutrient composition, the phytohormonal balance [17]. Current studies validated that endophytic fungi can yield phytohormones, particularly gibberellins (GAs), to enhance crop growth certain fungal endophytes have also been described to produce various classes of auxins, such as indole acetic acid (IAA).The chemical constituents of root exudates, and protect the plant against abiotic and biotic stresses. Therapeutic companies have modified their awareness towards the first two pathways. These pathways exploit the latest innovations in three-dimensional X-ray crystallography, drug-docking tools, and other computer-aided methodologies [18] which drastically cut the development time of a compound, from compound synthesis to market delivery. Most bioactive natural products have the competence to target specific proteins coded by essential genes [19]. While it is recognized that this property cannot be fully employed for human genetically linked diseases due to the more complex human protein-protein interactions. [20] Endophytic fungi have been renowned as sources for unique secondary metabolites with effective medicinal properties. Interest in fungal endophytes is mainly due to their chemical diversity. Since of their abilities to produce bioactive metabolites, endophytic fungi can also ease oxidative stress. The production of radicals can hamper cellular functions. The anti- oxidative role of endophytic fungi might be due to the secretion of phenolic and flavonoid compounds into the growth medium. These suggest a virtually unexploited source of chemical reservoir that finds applications in agriculture and therapeutics. Sampling and characterization of fungal endophyte diversity is an emergent challenge, [8] which leads to the discovery of new species producing new compounds and a better understanding of their role in ecosystems. It is well known that diverse endophytes colonize internal tissue of plants. Recently, endophytic fungi inhabiting in medicinal plants have gained clear attention, thus requiring their systematic documentation and description. Endophytes, especially those from medicinal plants have become the focus of research for bioactive the reason for this is high diversity of endophytes, easy to apply statistics, Explorations on the fungal endophytes associated with tropical evergreen trees are confined. When a plant species disappears, so too does its entire group of associated endophytes. The endophytes retrieved belong to class *Ascomycetes* and *Hyphomycetes* i.e. *Aspergillus* spp. *Colletotrichum spp. Fusarium spp.* And *Penicillium spp.* higher number of isolates was recovered from the bark of the plants than from twigs[21] . Bacterial endophytes are distinct in nature and are known to produce unique bioactive metabolites that act as antimicrobial and anticancer compounds. There are a number of bioactive compounds, such as camptothecin, diosgenin, hypericin, paclitaxel, podophyllotoxin, and vinblastine, which have been commercially produced by diverse endophytic fungi present in respective plants and they are of both agricultural as well pharmaceutical importance [22]**.** The frequency dominant genera were *Coniothyrium* sp (96.5%), *Trichoderma* sp. (84.5%), *Mortierella* sp. (36.75%), *Phyllosticta* sp. (19%) and *Acremonium* sp. (21.5%).The frequency dominant genera were *Coniothyrium sp* (96.5%), *Trichoderma* sp. (84.5%), *Mortierella* sp. (36.75%), *Phyllosticta* sp. (19%) and *Acremonium* sp. (21%).

Ascomycetes: Many bioactive constituents of *Ascomycetes* have been extracted comprising nucleoside, polysaccharide, sterol, protein, amino acid, and polypeptide. In addition, these constituents' corresponding pharmacological actions were also shown in the study such as anti-inflammatory, antioxidant, antitumour, antiapoptosis, and immunomodulatory actions[23]. Therefore can use different effects of Ascomycetes against different diseases and impart reference for the study of *Ascomycetes* in the future.

Hyphomycetes: *Hyphomycetes* are wide spread and well known soil-borne pathogens in nature, with a wide range of insect hosts, and are deliberated excellent biological control agents [24]. Evaluations of entomopathogenic fungi

noticeably are absent from previous research on control of *G. uzeli* [25] and in recent reviews [26].

Aspergillus: During the last decades, around 1,300 bioactive compounds have been reported from marine sources that show diverse biological activities including, antitumor, antibacterial, anticoagulant, anti-inflammatory, antifungal, and antiviral activities [27] [28]. Many of these metabolites are noted for their exceptional potencies [29] and show cytotoxic activity toward human cancer cell lines and inhibit tubulin polymerization by interacting with the colchicine-binding site.

***Colletotrichum*:** *Colletotrichum* spp. often serves as models in studies varying from pathogenic progress and differentiation to plant-microbe interactions. During organization and colonization of host plants, members of this genus distinctively procure nutrients via biotrophy and necrotrophy [30]. *Colletotrichum* species thus are experimentally attractive organisms to study the molecular, biochemical and cellular origin of fungal pathogenicity, development and signal transduction [31] [32].

Fusarium spp: The genus *Fusarium* was first termed in the early 19th century. In 1935, Wollenweber and Reinking used morphological variances to consolidate the genus into 16 sections with 65 species, 55 varieties, and 22 forms. *Fusarium* has an effective efflux mechanism to eliminate xenobiotics from its cells [33] and this may also moderate azole sensitivity. Amphotericin B, second-generation broad spectrum triazoles (fluconazole, itraconazole, voriconazole, and posaconazole), antimetabolites (5-fluorocytosine), and echinocandins (caspofungin, anidulafungin, and micafungin) all have limited activity against *Fusarium* species. High-level cross-resistance to fluconazole and itraconazole was reported in almost all *Fusarium* species. Cross-resistance has been observed among the three echinocandins in *Fusarium* species [34].

Penicillium spp: *Penicillin* is one of the most commonly used antibiotics in the world, as it has a wide range of clinical indications. Penicillin is effective against many different types of infections involving gram-positive cocci, gram-positive rods. *Penicillin* administration can be either intravenously or intramuscularly [35]. Penicillin has a small risk of toxicity. Compared to other biologically-active substances, clinicians can administer these drugs at relatively high doses without harm to patients. Estimates are that it would take 5g/kg body weight intravenously to cause convulsions [36]**.**

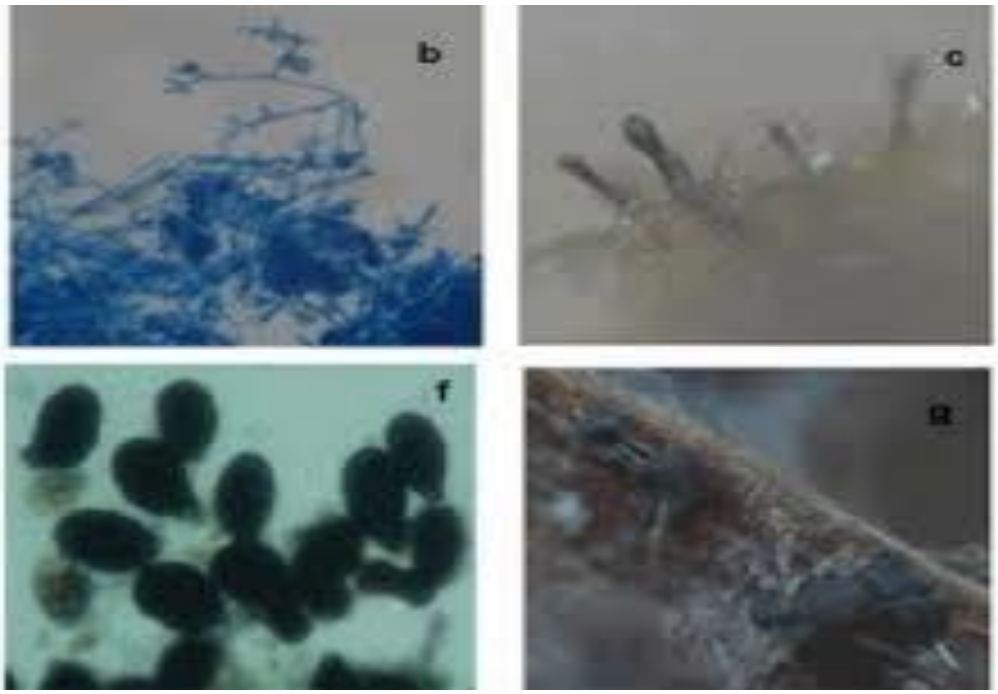

Figure 3 : Different types of endophytes with conidial characteristics (Diversity of Fungal Endophytes from Two Endemic Tree Species *Artocarpus hirsutus* Lam. And *V. indica* Linn. Of Western Ghats, India [22].)

REFERENCES:

1. Dr. Ambar Siddiqui, Dr. Tabassum K., Dr. Aisha Anjum A. Pharmacological activities of Kahruba (*Vateria indica* Linn.)– A literary review. Available online at: www.ijarnd.com © 2019, www.IJARND.com All Rights Reserved.
2. Shrijani JK, Karunakar Hegde and Shabaraya AR. A review on pharmacological activities of *Vateria Indica* LINN. Department of Pharmacology, Srinivas College of Pharmacy, Valachil, Post- Farangipete, Mangalore- 574 143, Karnataka, India
3. Suresh Kumar, Surender Paul, Yogesh Kumar Walia, Aditya Kumar and Parul Singhal Therapeutic Potential of Medicinal Plants: A Review J. Biol. Chem. Chron. 2015, 1(1), 46-54 ISSN (Print): 2454 – 7468 ISSN (Online): 2454 – 7476.
4. Saroopa P. Samara divakara, Radhika Samara sekera, Shiroma M. Handunnetti, Jagathpriya Weerasena O. V. D. S, Ayad A. Al-Hamashi, James T. Slama, William R. Taylor, Qasim Alhadidi, Zahoor A. ShahLalith Perera, and . Viranga Tillekeratne L. M A Bioactive Resveratrol Trimer from the Stem Bark of the Sri Lankan Endemic Plant *Vateria copallifera.* Journal of natural products, 81(8), 1693–1700. https://doi.org/10.1021/acs.jnatprod.7b00892.
5. Ismail, S.A., Ghazoul, J., Ravikanth, G. et al. Fragmentation Genetics of *Vateria indica*: implications for management of forest genetic resources of an endemic dipterocarp. Conserv Genet 15, 533–545 (2014). https://doi.org/10.1007/s10592-013-0559-7
6. Venkateshwarlu G, Shantha T R, Shiddamallayya N, Kishore K and Sridhar B N Priliminary physiochemical evaluation of Sarja rasa (resin of *Vateria indica* Linn. And its traditional medicinal formulation ISSN 2229-3566 IJRAP 2011, 2 (2) 334-337.
7. Rajmohan, Mallya Suma, Mohammed Faisal, Sunil Kumar KN, and Ravishankar B. Traditional method of preparation and development of quality standards for an edible vegetable fat Malabar tallow (*Vateria indica* L. seed butter). Indian Journal of Natural Products and Resources Vol. 9(1), March 2018, pp. 60-65
8. Bharathi T.R and Prakash H.S Endophytic fungi isolation and identification from Memecylon species of Western Ghats, India DOI: https://doi.org/10.7439/ijpp.v8i1.4464 Accepted: 10/01/2018 IJPP | Volume 8 | Issue 1 | 2018
9. Shanal Smitha Alva, Himanshu Joshi, Gururaja M. P, Prasanna Shama K, Ullas P D'souza. Anti-Obesity Activity of *Vateria indica* linn. Stem Bark in Rats. Research J. Pharm. and Tech 2018; 11(12): 5238-5242. DOI: 10.5958/0974 360X.2018.00955.1. Accepted on 28.07.2018 © RJPT All right reserved
10. Richard Lobo, Nilesh Gupta, Reshma K. K. Pharmacognostical and phytochemical study of *Vateria indica* linn. stem bark. WORLD Journal Of Pharmacy and Pharmaceutical Sciences Volume 4, Issue 08, 972-979 Research Article ISSN 2278 – 4357
11. Venkatesh K. R. Hari, Sushrutha C.K. Flora of concern endangered medicinal plants - part i *Vateria indica* linn, dipterocarpaceae – A REVIEW IJRAP 2010, 1 (1) 1-7
12. Rajmohan, Mallya Suma, Mohammed Faisal, Sunil Kumar KN, and B Ravishankar. Traditional method of preparation and development of quality standards for an edible vegetable fat Malabar tallow (*Vateria indica* L. seed butter) Indian Journal of Natural Products and Resources Vol. 9(1), March 2018, pp. 60-65
13. Masa-Aki Shibata, Yukihiro Akao and Munekazu Iinuma. A novel resveratrol tetramer Vaticanol C from stem bark acts as an antimetastatic action in mouse mammary cancer model Shibata, *et al*., Altern Integ Med 2015
14. Yoshiyuki Tabata, Katsura Takano, Tetsuro Ito, Munekazu Iinuma, Tanihiro Yoshimoto, Hikari Miura, Yasuko Kitao, Satoshi Ogawa and Osamu Hori Vaticanol B, a resveratrol tetramer, regulates endoplasmic reticulum stress and inflammation 01 JUL 2007https://doi.org/10.1152/ajpcell.00095.2007
15. You-Qiu Xue, Jin-Ming Di, Yun Luo, Ke-Jun Cheng, Xing Wei, and Zhi Shi Resveratrol Oligomers for the Prevention and Treatment of Cancers Review Article Open Access Volume 2014 |Article ID 765832 | 9 pages | https://doi.org/10.1155/2014/765832
16. Gan B. Bajracharya, Diversity, pharmacology and synthesis of bergenin and its derivatives: Potential materials for therapeutic usages Received 16 October 2014, Revised 1 January 2015, Available online 13 January 2015.
17. Abdul L Bajracharya atif Khan, Syed Abdullah Gilani, Muhammad Waqas, Khadija Al-Hosni, Salima Al-Khiziri, Yoon-Ha Kim, Liaqat Ali, Sang-Mo Kang, Sajjad Asaf, Raheem Shahzad, Javid Hussain, In-Jung Lee, Ahmed Al-Harrasi J Zhejiang Univ Sci B. 2017 Feb; 18(2): 125–137. doi: 10.1631/jzus.B1500271
18. Müller, 2009 B.A. Müller Imatinib and its successors–how modern chemistry has changed drug development. Current Pharmaceutical Design, 15 (2009), pp. 120-133.
19. Kingston, 2011 D.G.I. Kingston Modern natural products drug discovery and its

relevance to biodiversity conservation. Journal of Natural Products, 74 (2011), pp. 496-511.
20. Alfonsus Alvin Kristin I. Miller Brett A. Neilan. Exploring the potential of endophytes from medicinal plants as sources of antimycobacterial compounds. Microbiological Research. Volume 169, Issues 7–8, July–August 2014, Pages 483-495.
21. Karmakarruma, Sekhar Shailashree, Kumar KK Sampath, Siddapura Ramachandrappa Niranjana and Harishchandra Sripathy Prakash. Diversity of fungal endophytes from two endemic tree species *Artrocarpus hirsutus* Lam. And *Vateria indica* Linn. Of Western ghats of India. World journal of agricultural sciences 7(5):577-582, 2011 IDOSI publications, 2011.
22. Sushanto Gouda, Gitishree Das, Sandeep K. Sen, Han-Seung Shin, and Jayanta Kumar Patra Endophytes: A Treasure House of Bioactive Compounds of Medicinal Importance Front Microbiol. 2016; 7: 1538. Published online 2016 Sep 29. doi: 10.3389/fmicb.2016.01538
23. Yi Liu, Jihui Wang, Wei Wang, Hanyue Zhang, Xuelan Zhang, and Chunchao Han The Chemical Constituents and Pharmacological Actions of *Cordyceps sinensis*. Volume 2015 |Article ID 575063 | https://doi.org/10.1155/2015/575063
24. S. Gouli, V. Gouli, M. Skinner, B. Parker, J. Marcelino, and M. Shternshis 2008. Mortality of western flowers thrips, *Frankliniella occidentalis*, under influence of single and mixed fungal inoculations. J. Agr. Techn. 4: 37–47.
25. D. W. Held, D. Boyd, T. Lockley, and G. B. Edwards. 2005. *Gynaikothrips uzeli* Zimmerman (Thysanoptera: Phlaeothripidae) in the southeastern United States: Distribution and review of biology. Florida Entomol. 88: 538–540.
26. Claudio Rios-Velasco, Jhonathan Cambero-Campos, Rita Valenzuela-García, Gabriel Gallegos-Morales, Carlos Carvajal Cazola, Luis Aguirre-Uribe 1 December 2011 Biological Activity of Hyphomycete Entomopathogenic Fungi Against *Gynaikothrips uzeli* (Thysanoptera: Phlaeothripidae).
27. Aqil F, Zahin M, El Sayed KA, Ahmad I, Orabi KY, Arif JM (2011) Antimicrobial, antioxidant, and antimutagenic activities of selected marine natural products and tobacco cembranoids. Drug Chem Toxicol 34:167–179
28. Mayer AMS, Gustafson KR (2003) Marine pharmacology in 2000: antitumor and cytotoxic compounds. Int J Cancer 105:291–299.
29. Lee, Y.M., Kim, M.J., Li, H. *et al*. Marine-Derived Aspergillus Species as a Source of Bioactive Secondary Metabolites. Mar Biotechnol 15, 499–519 (2013). https://doi.org/10.1007/s10126-013-9506-3
30. Martin B. Dickman. Department of Plant Pathology. University of Nebraska. Lincoln. USA J. W. Kronstad (ed.), Fungal Pathology, 127-148. © 2000 Kluwer Academic Publishers.
31. Bailey, J. A. and Jeger, M. J. (1992). *Colletotrichum*: Biology, Pathology and Control. Wallingford: CAB International.
32. Prusky, D., Freeman, S., Dickman, M. B. (1999). *Colletotrichum*: Host Specificity, Pathology and Host Pathogen Interactions. APS Press, St. Paul, Minnesota (in press).
33. Berthiller F, Crews C, Dall'Asta C, Saeger SD, Haesaert G, *et al.* (2013) Masked mycotoxins: a review. Mol Nutr Food Res 57: 165–186. 10.1002/mnfr.201100764
34. Al-Hatmi AM, Meis JF, de Hoog GS. Fusarium: Molecular Diversity and Intrinsic Drug Resistance. PLoS Pathog. 2016; 12(4):e1005464. Published 2016 Apr 7. doi:10.1371/journal.ppat.1005464.
35. Derek W. Yip, Valerie Gerriets Penicillin May 12, 2020.
36. STEWART GT. TOXICITY OF THE PENICILLINS. Postgrad Med J. 1964 Dec; 40: SUPPL:160-9.