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Endophytes: Extent of Their Importance

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Abstract

Asymptomlessly residing organism within the plant body are called Endophytes. (Tejesvi *et al.* 2007). They are known to produce a number of active compounds possessing utility in the improvement of host plant body as well as human health. They may be used as natural agents controlling the pest and also useful in soil remediation by improving the factors responsible for the endophytic colonization. A single endophytic fungal strain may produce multiple bioactive compounds including alkaloids, steroids, terpenoids and peptides (Tan & Zou 2001)

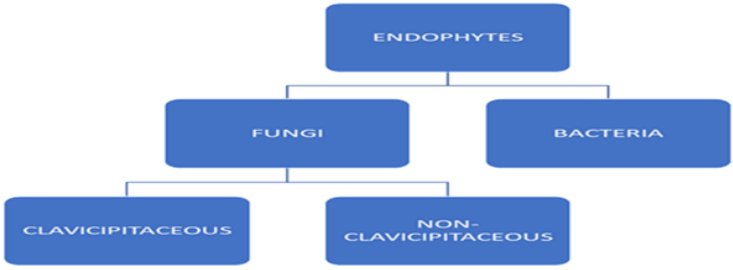
Endophytes are the bacterial and fungal forms of organisms living within the plant system causing no ill effects to the host. They are known to produce a range of metabolites of utility in treating various disorders in humans and also produce chemicals of utility in agriculture such as growth regulators and pesticides, in several economically important plants. The present review is focused on diversity of endophytes, current national and international bioactive secondary metabolite scenario and future prospects

Key words: Endophytes; Secondary metabolites; colonization factor; biocontrol agents.

INTRODUCTION:

Heinrich Friedrich Link in 1809 named microorganisms residing in plants as “entophytae”; In 1866, de Bary describes endophytes as the any organism that grows within plant tissues. In 1887 by Galippe, (1889) Laurent, (2011)considered that the microorganisms inhabiting plants, derive from soil environment and migrate into the

plant, where they might play a beneficial role for the host plant are endophytes. Endophyte word is self-explanatory, this word comprises of mainly two words:'Endo' means inside/within & 'phyta' means plants (Lata *et.al*.2018).Therefore, these are the micro-organisms which reside within plant tissue, without causing any negative effect(Sun, Z.-H *et al*.2016). No negative effect shown by the endophytes,apparently because no phytopathogenicity assays are normally performed (Hardoim *et al*. 2015; Andreea *et al*.2019). Endophyte-host relationship could be termed as a balanced antagonism(Istifadah and Suganda 2010)and the secondary metabolites could be a contribution of the endophytic partner to this mutualistic relationship (Elad Y *et al.* 2009).



Endophyte micro-organism may be either bacterial strains or fungus species(El-Tarabily *et al.* 2009). Majorly the fungal endophytes reported belongs to Ascomycetes & Basidiomycetes. Clavicipitaceous fungal endophytic strains

mainly infect grasses of cool regions. Non -clavicipitaceous fungal species infect mainly non -vascular plants to Angiospermic plants(El-Tarabily*et al*.2020).

Use of fertilizers & pesticides cause a lot of problem as they are not feasible for everyone & also causes a high degree of damage to the environment. So, there is a need for an alternative option(El-Tarabily *et al*.2020).Endophyte may be considered as that alternative option because endophyte can be readily isolated from any microbial and plant growth medium. Endophytes are the reservoir of novel bioactive secondary metabolites and also the source of novel drug discovery (Chutulo,Chukalo and Chalannavar,2018).

Generallyendophytes are considered as non-pathogenic but in conditions of extremities,they may behave as saprophytes(activates the saprotrophic program in root endophyte *Piriformospora indica* (Mengistu 2020) or sometimes pathogenic (Vedashreeet.al.2013). Plant and endophytic sp. allow one another in their proximity mainly because of nutrient exchange, if there is any kind of nutrient imbalance, the endophyte changes its lifestyle from endophytic to parasitic mode due to changes in the genetic and biochemical base of a endophytic lifestyle (Mengistu2020).Plant cells supply Fe ions to the endophytic sp. for siderophore production (Sessitsch *et al*.2004; Lacava2018).Endophytic sp. may be cultivable and non-cultivable. The cultivable sp. can be grown in in-vitro condition to obtain rapid biomass accumulation, and extraction of large quantity of secondary metabolites (Puri *et.*

al.2006)

Rosenblatt & Martinez Romero(2006), categories endophyte in sub- group: obligate endophyte & facultative endophyte.Certain fungi have been found to be well adapted for endophytic mode of life in wide varieties of plants. This includes *Phoma sp., Chaetomium sp., Curvularia sp., Fusarium sp.*(Fisher & Petrini(1987);Rajagopal (1999)). These fungi are more successful in occupying the niche as endophytes.Endophytes live in intercellular space or inside cells and vascular tissue of host plant in various organs:Pseudostems-*Neotyphodium* in tall fescue,Leaves-Chaetomiumsp., Phomasp. from wheat, Roots-*Burkholderia ambifaria,*in corn*Fusarium oxysporum* in tomatoStems -*Bacillus subtilis* in chestnut tree, Seed-*Neotyphodium* in tall fescue.The evolutionary thought regarding the endophytes is, symbiotic endophytes developed machinery to biosynthesize and tolerate high levels of secondary metabolites in order to better compete and survive in association with the medicinal plant. (Strobel *et al*.2003; Liu*etal*.2019).

In the past few decades natural and biological control of insect-pests and diseases affecting cultivated plants has gained much attention. Diseases resistant sp. harbours high colonization frequency of endophytic sp.(Gaynor and Hunt, 1983).Point of attraction in endophytic research are the tropical tree endophytes, because they can be used to control pest-insect and plant diseases. (Lacava and Azevedo 2014).Enzymes like hydroperoxide, superoxide dismutase, catalase, etc; are released by endophytes like *Enterobacter*

sp. which to cope up the oxidative stress during colonization. (Mengistu 2020)

Factors determining the endophytic colonization:

Observation is that different plant sp. growing on the same soil harbours a distinct group of endophytes, it means genotypic differences can foster different endophytic communities. With the change in plant age & health endophytic composition changes because of change in plant's physiology(Gaiero *et al*.2013). Plant -microbe signalling could be a prominent cause of endophytic colonization as plants show different chemical responses when interacting with PGPBEs(plant growth promoting bacterial endophytes)& non beneficial bacteria (Rocha *et al.* 2007). Multiple studies have shown that plants secrete compounds that specifically stimulate or inhibit AHL-(N-acyl homoserine (acetone)) dependent QS responses through interaction with microbial AHL receptors (Gao and Teplitski 2003).

Normally more than one kind of endophytic community is found within a plant tissue. Possibly soil factor, microbial factor and plant factor are the drivers of endophytic community colonization within a plant(Murphy *et al.*2018). Some passenger endophytes get entry in the internal tissue of plants just by chance or accidently even in the absence of any factor. (Murphy, *et al.*2018; Hardoim and Pablo2008). By analyzing the role of factors or drivers of the endophytic community, researchers may develop methodologies that minimize the pathogen population while enhancing the beneficial population. Genes detected byAli et al., 2014a, Ali

et al., 2014b are experimentally seen to be involved to promote endophytic lifestyle. Such findings support the thought that bacterial endophytes have a different genomic framework than that of rhizospheric colonising bacteria.(Santoyo *et al.2016*).

Endophytes have evolved ways to use plant signalling pathways to their advantage. Endophytes can effectively reprogram the plant signalling pathways & therefore influences endophyte community structure. Type of soil, plant & neighbouring microbial community are local scale factors determining the endophytic community structure. Organic, loamy soil has chances of finding more endophytes as compared to sandy & mineral soil type. Large scale factors like geography, climate provide external control on endophytic communities as these factors affect plant's physiology which in turn affects endophytic communities (Santoyo 2018). One should know about these factors if trying to inoculate plants to improve plant health.

Beneficial Role of Endophytes

1.Catalysis the plant growth activities:

Plant-endophytic relationship may be considered as mutualistic or symbiotic relationship(Houng*et al.* (2008). e.g.,IAA(Auxin) involved in host-endophytic interactions(Arnold and Lutzoni 2020). In *Trapa japonica, Galactomyces geotrichum* an endophyte is responsible for enhanced IAA production (Wages *etal.2014).Cucumber* roots, *Phoma glomerata, Penicillium sp.*are responsible for more gibberellin & IAA production.*Alternaria alternate,* in rice plants

produce Auxin (Khan *et al.2015*). *Paecilomyces formosus & F. proliferatum* produces gibberellin in *Physalis alkekengi* (Khan *eta.l*2011). *Aspergillus, Cladosporium,Talaromyces* obtained from soybean plant proved to be responsible for gibberellin synthesis. (Humayun *et al*. 2009; Khan *et al.* 2011). IAA can also be obtained from *Burkholderia vietnamiensis,* the endophyte of *Populus trichocarpa (*wild cotton plant).The use of PGPBEs(Plant Growth Promoting Bacterial Endophytes) as fertilizer treatment for *Zea mays* reduced the need for 'P' application by 50% without significant loss in grain yield (Yazdani *et al.*2009)

Siderophores are low molecular weight, Fe binding molecules produced by microorganism under low Fe condition. They are also component of virulence of micro -organism infecting man, animals & plants. Seven endophytic fungi belonging to *Colletotrichum lasiodiplodia & Fusarium* showed siderophore zone >30mm on CAS(Casein Digest agar) agar (Aramsirijiwet *et al*. 2016). *Phialocephala fortinii* may prove sources of large-scale production of siderophore like ferricrocin, ferrirubin,ferrochrome, but their production depends on pH & Fe(iii) concentration of culture media.

2.Role of endophyte in stress tolerance:

Plants can bypass stress situations if they allow endophytes to reside within them. Endophytes are responsible for release of Defence Signalling substances which induces defence related protein biosynthesis (Lata R 2018)and protective secondary metabolites. Certain bacterial endophytes release ACC deaminase enzyme which reduces

ethylene production in host plant tissue, resulting in plant growth enhancement. Strains of *Phoma glomerata & Penicillium sp.* help the host plant to withstand under stress condition, also help in increase in plant biomass,assimilation of essential nutrients & reduces sodium toxicity (Clayand Holah 1999).Metabolite products like amines & amides have found to be toxic to insects but not to the mammals (Gehlot *et al.*2018).

Indole Diterpenes, ergot alkaloids, per amine are 2^0 metabolites produced by endophytes that are highly toxic against phytophagous insects & mammalian herbivores *Pirijormospora indica* endophyte protect barely from salt stress. *Curvularia sp. & Dichanlhelium lanuginosum* can help plants to withstand up to 65 ^{0}C. .Bacterial endophytes are able to colonize an ecological niche similar to that of vascular wilt pathogens that favors them as potential biocontrol agents against wilt diseases (Puri 2006).

Phosphate solubilization under salt stress condition by *Fusarium verticilloides, Humicola sp.,* (Radhakrishnan *etal*.2015). *P. sclerotiorum, P. chrysogenum, F. oxysporum, endophytes* of *Camellia sinensis* responsible for ‘P’, ‘N’ & ‘Zn’ solubilization(Nath et.al 2015).Low molecular weight acids released by endophytes allows the chelation of the metal carbon attached to ‘P’ making it more accessible to plants(Kpomble andTabatabai 2003).

3.Endophyte as Biocontrol agent:

Endophyte and pathogenic micro-organism occupy almost same niche;therefore, endophytes succeed in

competitive exclusion of pathogens from host plant body(Eljounaidi 2016).Endophytes also compete with phytopathogens for trace elements (White*et al* 2019)Endophytes also produce anti-microbial metabolites like 2,4 -diacetylphloroglucinol (DAPG) which enhances disease suppression in plant(Robert *et al*.2008).Ramesh et.al (2008) reduces the egg – plant wilting by 70% after seeds were inoculated with DAPG (2,4-diacetylphloroglucinol) producing endophytic isolates.Endophytes are responsible for reduction of disease reduction(Hallman2006).Different endophytes isolated from healthy cereal plants like Pseudomonas inhibits colonization of *Gaeumannomyces graminis ;Rhizoctonia solani; Pythium. Bacillus & Paenibacillus sp. strains* of potato(Robert *et al.2008).Tectona grandis Samanea saman* shows bioactivity against broad spectrum of pathogenic micro-organism as 18 endophytes isolates from them can produce inhibitory substances against *Bacillus subtilis, Staphylococcus aureus, E. coli,Candida albicans* in in-vitro conditions 9S(Chareprasert *et al.*2006)

4.Role of Endophyte in Phytoremediation:

Heavy metal contaminated soil can be treated by using those endophytes which are capable of degrading organic compounds(Hai-Yan Li*etal*.2012).Therefore, these are very much useful in practical application for soil remediation practices(Khan and Doty 2011) Use of endophytes for modern, cheap, and promising solutions to decrease emission of greenhouse gases into the Earth's atmosphere.The mechanisms of bioremediation depend on the mobility,

solubility, degradability, and bioavailability of contaminant (Stępniewska and Kuźniars 2013).Five different colonies of endophytic bacteria were isolated from Poplar tree & characterise them as *Cellulomonas, Clavibactor, Curtobacterium, Pseudomonas, Microbacterium*, and all these were involved in phytoremediation of BTEX I.E, 2,4,6 trinitro-toluene, ethylene benzene, xylene(Robert*etal.*2008).

Commercial importance of endophytes:

Taxol, potent anticancer drug obtained from *Taxus sp.*plant, but actually it is metabolic product of inhabiting endophytes within the Taxus *plant*. *Taxomyces andreanea, Pestalotiopsis microspore, Gliocladium sp., Guignardia mangiferae, Fusarium culmorum* etc., can be commercially exploited for anticancer drugs without harming biodiversity (Strobel 2003).Endophytes are responsible for production of important compounds like Taxol, Cryptocin, Pseudomycin, Ambuic acid, Testerone, Oocydin, Cryptocandin, as antifungal agent. Isopestacin as antioxidant munumbicinea wide spectrum antibiotic & kakadumycin as antioxidant. Topotecan & irinotecan are two clinically useful anti-cancer drugs & their precursor Camptothecin &10- hydroxy camptothecin can be obtained from endophyte *Fusarium solani* (Rai *et al.*2012). Diabetes mellitus, a major concern. This human hyperglycaemic problem is drastically increasing worldwide. According to WHO, it's proportion may rise up to 35% by2025 !Endophytic exploration is required to discover novel drugs for anti-arthritic, anti-microbial, and anti-cancer, anti-diabetic, anti-insect, immunosuppressant activities(Gouda *et al.* 2016).

Pezicula cinnamomea	*Tripterygium wilfordii*		*Candida albican* *Pyricularia oryzae*	Lie et.al (2000) Doley Jha (2010)
Taxomyces andreanea	*Taxus brevifolia*	Taxol	Anti- cancerous	Stierle et.al (1995)
Pestalotiopsis microspora	*Taxus wallichiam*	Taxol	Anti-cancerous	Wang et.al
Gliocladium sp.	*Taxus baccata*	Taxol	Anti-cancerous	Sreekanth et.al (2009) Garyali et.al (2013)
Guignardia mangiferae	*Taxus media*	Taxol	Anti-cancerous	Xiong et .al (2013)
Fusarium culmorum	*Tinospora*	Taxol	Anti-cancerous &Anti-Myobacterium tuberculosis	Sonaimuthu et.al (2010) Thangaraj et.al (2017)
Fusarium sp.	Banana Plant		*Cosmopolits sordidus Rhadopholus sp.* (Nematode)	
Phomopsis oblonga	Elm tree	Coronamycin p-aminoacetophenomic acids Fusaricidine A-D	*Ceratocystis ulmi*	
Metarhizium anisopliae	Bark of *Taxus*	Taxol (paclitaxel)	Anti-cancerous	
Kitasatospora sp.	*Taxus baccata Emblica officinalis*	Paclitaxol Tyrosol	Anti-Cancerous Food-borne microbes	
Penicillium &Penicillium	Symphonis globulifera		antiplasmodial	Joël E. T. Ateba et.al
Chaetomium chsiversii	*Ephedra fasciculate*	Radicicol	Antifungal, antimalarial	Turbyville TJ (2006)
Hypoxylon genus	Taxodium distichum		hydrocarbon fuels or volatile organic compound	Yuemin Wang and James K. Harper*
Diaporthe Strains	Catharanthus roseus		Antifungal Activities	Dong-Hui Yan et.al
Cryptosporiopsis quercina	Tripterigium wilfordii	cryptocandin	antimycotic	Strobel et al., 1999a
Colletotrichum gloeosporioides	A. mongolica	colletotric acid	antifungal metabolite	Zou et al., 2000).

Serratia marcescens	Rhyncholacis penicillata	oocydin A	antioomycetous	(Strobel et al., 1999b)
Pseudomonas viridiflava	Grass	Ecomycins B and C	Antimicrobial	Miller et al. (1998)
Streptomyces sp.	Monstera sp.	Coronamycin	Antimalarial antifungal	Ezra et al. (2004)
Serratia marcescens	Rhyncholacis penicillata	Oocydin A	Antifungal	Strobel et al. (2004)
Paenibacillus polymyxa	Wheat	Fusaricidin A–D	Antifungal	Beck et al. (2003)
Phomopsis sp	Mangrove	Phomopsin A, B, C; cytosporone B	Antifungal	Huang Z et al (2008)

Fig: Endophytic sp.: Host plant:Metabolite from endophyte: Activity of metabolite

Yadav J.P.2013 isolated 17 fungi isolate in four solvents like aqueous (hyphal strained/ unidentified fungus), methanol (Aspergillus *sp. JP1* & *Aspergillus sp. JP2)*, Acetone (*Phoma sp*.). It was found that the fungal extract (2,6 di-tert-butyl p-cresol) extracted from these strains are very much safe up to 1000 mg/Kg by wt. if consumed through an oral route. >80% of natural drugs in the market are bioactive compounds & 2^0 metabolites of medicinal plants & their endophytes(Singh and Dubey 2015).

Endophytes can be used as microbial inoculation in place of fertilizers & pesticides i.e., they are important in sustainable agricultural practices(Horrigan*etal.*2002). To make a plant disease resistant, a mixture of endophytic communities could be the better option than treating the plant with a single endophytic species because different sp. may

fulfil different ecological niches in place of pathogenic organisms.

Fungal chitinase helps in cycling of 'C' &'N' from chitin molecules. Endophytes can be commercially exploited for production of enzymes(Hardoim *et al*. 2015). Amylase, Cellulase, Protease, Lipase, Xylanase, production in endophytic fungi of medicinal plants of Meghalaya (Bhagobstyand Joshi 2012).

Bioactive compounds from endophytic fungi originate by various biosynthetic pathways like PKS/NRPS(polyketide synthases (PKS) or non-ribosomal peptide synthetases (NRPS))These compounds belong to diverse structural groups such as alkaloids, benzopyranones, chinones, cytochalasines, depsipeptides, enniatines,flavonoids,furandiones, isocumarines peptides, polyketones, phenols, quinols, terpenoids, tetraloans, & xanthones. All these compounds were characterized by NMR mass spectrometry, X-ray crystallography etc. (Hardoim *et al*. 2015) Red pigment from *P. purpurogenum, (*endophyte of *Ginkgo biloba)* can be used as food colourant.(Ruisheng *et.al* (2010) Pigment from endophytic fungi *Monodictyscastaneae* can inhibit few human pathogenic bacteria *Staphylococcus aureus, Klebsiella pneumonia, Salmonella typhi, Vibrio cholera* & these endophytic fungi proved more active than Streptomycin.(Nair and Padmavathy2014).

Endophytes associated with Moraceae Family

Taxonomical Classification:

Kingdom Plantae –Plants (Fic)

Subkingdom- Tracheobionta

Superdivision- Spermatophyta

Division- Magnoliophyta

Class -Magnoliopsida

Subclass- Hamamelidae

Order- Urticales

Family- Moraceae

Lot of endophytic research has been done over agriculturally important plants (Compant *et al*.2005), but not so much eye on endophytes associated with woody trees. (Wang *et al*.2006). Ficus, the largest woody genera and the key-stone sp. of tropics because they provide year-round food source for many frugivorous animals. Genus Ficus (Moraceae) found in tropical and sub-tropical regions over the globe, constitutes more than 800 species of trees, epiphytes, and (Singh *et al*.2011). Out of 800, 500 sp. are found in south-eastern region of the globe (The Asian–Australasian region is the richest and most diverse). It is a promising candidate in pharmaceutical biology for the development/ formulation of new drugs and future clinical uses. Ethnomedical have been used traditionally for more than 40 types of disorders. ailments such as anaemia, cancer, diabetes, leprosy, liver diseases, paralysis, skin diseases, and ulcers. Other important activities are: (1) Bioactive components in Mulberry protects brain damage. (2) Phenolic phytochemistry (3)Antioxidant potential (4)Fruit extract role on memory impairment and brain damage in animal proved in model of

vascular dementia (4) Alzheimer disorder(Kuk*etal.*2014) (5) Mulberry extract used in depression by down regulation of serine/ threonine protein phosphatase 5 levels (6)Anti-aging effect (Zhang*etal*.2014).(7)Anticonvulsant activity (8) Mulberry extract proved useful in Parkinson disease.

Mulberry (Morus spp.) is a fast growing, deciduous woody tree species of Moraceae family with perennial nature and origin in Himalayan foothills of India and China(Rohela *et al.*2020).Mulberry having long list of beneficial roles like able to grow in broader range of geographical conditions (Khan *et al.* 2013; Sarkar *et al.*2017), bioremediation and eco-restoration of damaged land cover, improves air quality by 'C' sequestration, medicinal and industrial role, because of presence of pharmacokinetic compounds found in leaf, stem and root parts. The best-known area is sericulture along with bio-fuel production and nanoparticle synthesis. Hence, this plant may be considered as a multi-purpose plant or plant for sustainable future. In India, mulberry is known as 'Kalpavriksha' as all the parts of it used in traditional system of ayurvedic medicine

As almost every plant sp. harbours less or more endophytic sp., mulberry plant is also known for having endophytic sp. in its various plant parts. Gram-positive, endospore-forming bacterium (ZJU1)(a novel strain of *Bacillus amyloliquefaciens*)was frequently isolated from healthy mulberry leaves showing antagonism against pathogens *B. cinerea* and pests by inducing plant systematic defence and by producing diverse secondary metabolites, including high expression levels of mulberry disease resistance genes also biosynthesis of toxins, particularly the crystal (Cry) proteins (similar to the Cry10Aa gene from *B. thuringiensis*) that target herbivorous insects(Xie*et.al*.2020). In another experiment eight endophytic bacterial *Bacillus* strains were found to stimulate the growth of mulberry seedlings at different levels and root fresh weight increased by 217.70% and shoot length by 83.37% (Weifang2019). FEF(Foliar Endophytic Fungi) assemblage depends upon: (i) host phylogeny, (ii)evolutionary & ecological processes, (iii)horizontal transmission (Rodriguage*et.al*2009). (iv)host-specific leaf chemistry (Liu 2019).

Sericulture (the silkworm industry) gave economic empowerment. The benefits from sericulture are very much benefitted by the endophytes. Silkworm rearing requires quality feed, standard rearing conditions, protection from diseases and pests to the host plant as well as to the insect. In Mulberry plants healthy leaves are very important as *Bombyx mori* feeds on them. Bombax *mori* are the vital raw material of silk industry(J. Justin Kumar 2011; Ji, *et al*.,

(2008)). Mulberry leaves face wilting, because of a soil borne bacteria *Ralstonia solanacearum* (Smith). This wilting can be prevented by the application of *Bacillus subtilis* strain Lu144when it was applied to sterile or non-sterile soil before the infection by the pathogens. In Mulberry leaves, colonizing an antagonistic bacterium *Burkholderia cepacia* strain Lu10-1, isolated by acupuncturing, seed soaking, root soaking and leaf daubing. This strain can play an important role in the biological control of mulberry diseases(J. Justin Kumar 2011). Another threat to the sericulture is Mulberry anthracnose, caused by *Colletotrichum dematium*, is a commonly observed disease (Liu 2019) and thus a major problem in mulberry cultivation. The use of fungicide or bactericidal or other kinds of agrochemicals to treat the disease could be hazardous to the worms.(Ji *et al*.2010). Natural biocontrol agent, *B. cepacia* strains have proved useful as antagonists of plant pests and in increasing the yield of several crop plants(Luigi etal. 1998). From leaves of *Ficus racemosa* by ITS2 sequence-secondary structure-based analysis 88 fungal endophytes were isolated (Kumar*etal*.2019). These are divided in to 7 clades belonging to the two classes Sordariomycetes and Dothideomycetes extending in seven orders of Ascomycota (Botryosphaeriales, Capnodiales, Diaporthales, Glomerellales, Hypocreales, Pleosporales and Xylariales).

Ficus benghalensis (The banyan) depicts the ‘Trimurti: Vishnu, Brahma and Shiva in Hindu mythology. It is mainly found in South-Asiatic region (Maheswari and Rajagopal 2011). Tree is ethnomedical very much important

as it possesses anti-inflammatory activity, anti-helminthic, anti-stress, anti-allergic, anti-oxidant, anti-microbial, anti-fungal, anti-diarrhoeal, analgesic and antipyretic, allelopathic, hyperlipidaemic activity, immunomodulatory activity, wound healing, insulin sparing (Rebai *etal*.2017; Rajagopal 2008). The colonization frequency of petiolar endophytes is more as compared to lamilar(Bernstein and Caroll 1977) and least colony found in aerial roots ,horizontal transfer of endophytes may be the cause(Rebai *et al*.2017).

Ficus religiosa possess hypoglycaemic activity. From this plant 21 endophytic fungi isolated mainly belong to

Aspergillus sp. Plant based medicines for diabetes are under limited use. *Aspergillus sp.* shows inhibition for alpha-amylase inhibition assay (91%+- 0.06), alpha glucosidase inhibition assay (42%+-0.01) (Tiwari et al. 2017).

In *Ficus carica, Aspergillus tamarii* was isolated. *A. tamarii* having cytotoxic and antibiotic cyclic pentapeptide. Endophytic fungi found more in leaves than in bark; belonging to Hyphomycetes> Coelomycetes >Sterile fungi.*F. religiosa* having more endophytic fungi than the *F. benghalensis.*

Future prospect: The microbiota which is associated with the host plant sp. is very much responsible for the plant's health, its phenotype, and they may be considered as bio-factories because of production of secondary metabolites such as drugs, pesticides and other industrial bioproducts. They are also responsible for the enhancement of the ecophysiology of the host plant. Now research work

emphasizes not only the type and extent of active metabolite production by the endophytes, but also focuses on the mechanism of these metabolite production. Earlier mainly bacterial and fungal species were discovered as endophytes but today algae, archaebacteria, amoeba is also found inhabiting the internal plant tissues(Müller & Döring 2009).These plant microbiome gives new ideas regarding the plant evolution (Balansiaceous endophytes)(Coşoveanu and Cabrera 2019).To overcome the problem of multiple drug resistance in pathogens and pest would be solved by more extensive research in the field of endophytes. In majority of cases, endophyte-host relationship is of mutual type. Both the interacting species are benefitted by each other. Goal of sustainable agriculture could be achieved by commercialization of endophytes and their products. There is more need to focus on the ecology of endophytes, how endophytes synergise or antagonise one another in similar niche is also an important factor. Genetic engineering can be employed to improve endophytic strains (till now less recorded success)(Shahid *et al.*2012).Signalling pathways followed by the endophytes needs clear demonstration starting from the precursor to the end product in a consistent manner. Identification and isolation of new metabolites from the biodiversity of endophytic strains and those metabolites may be used as new drugs for effective treatment of disease in humans, plants, and animals. Which genes of endophytic organisms are required to enter, compete, colonize the plant, suppress pathogens and generally survive within the plant?

Molecular basis of interaction between plants and endophytic bacteria can be detected using techniques IVET (in vivo expression technology); RIVET (recombination in vivo expression technology)(Preston *et al.*2001;Zhang *et al.* 2006). Comprehensive screens for antiviral compounds from bacterial endophytes have yet to be reported. The design & development of bacteria and higher plants able to accumulate PHAs(Polyhydroxyalkanoates) may also help to streamline cost-effective production and to produce novel heteropolymers for a range of applications(Aldorand Keasling 2003).

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