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Endophytes and their benefits

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Abstract: Endophytes are the microorganisms which reside inside the plant parts causing no symptom of diseases. These endophytes can be easily identified with the morphological and molecular studies. These endophytes are beneficial in terms of human health as well as in terms of production of certain compounds which are required for human welfare. These endophytes are capable of producing metabolites which are of clinical significance. Endophytes are capable in mimicking the properties of their host and due to this property, they happen to produce beneficial compounds which are also found in plants, specifically the medicinal ones. Endophytes have potent medicinal prospective which includes anticancer, antidiabetic, antihypertensive, antibacterial, antifungal and antioxidant effects.

Keywords: Endophytes, microorganisms, beneficial, medicinal.

Introduction:

Microorganisms that commonly live within plants without causing any disease symptom are termed as endophytes (Bacon, 2000). These microorganisms have the capability to interact with the host plant, and consecutively, the plants to some point adapt the metabolic process of these endophytes to generate molecules that might manifest defensive functions towards the microbe and the host (Kusari et al., 2012). These organisms also exhibit interspecies interaction through chemical signals (Kusari et al., 2012) and such signaling molecules could sometimes become important for host's survival fitness. In recent times, endophytic fungi have gained impulsion because of their vast prospective property to construct a myriad of medicinally significant metabolites (Eyberger et al., 2006; Chakravarthi et al., 2008). Consequently, exploring endophytic fungi that reside in plant species with medicinal properties would offer plenty of opportunities to ascertain new metabolites with prospective bioactivity (Huang et al., 2007).

A remarkably diverse, ubiquitous group of eukaryotes are endophytic fungi which are known to synthesize secondary metabolites of clinical significance. The presence of such endophytes is

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advantageous in terms of the growth and health of host plants under duress. These also are regarded as a source of various medicinal compounds since the discovery of taxol, which is an important anti-cancer drug (Gangadevi and Muthumary, 2008). In the prior art, their therapeutic potential, such as, cancer cytotoxicity, immunomodulatory, anti-parasitic and anti-pathogenic prospective have also been studied. The studies related to genomics, metagenomics, transcriptomics, proteomics and metabolomics of endophytic fungi are also reviewed. Applications of omics-based studies on these mutualistic biotrophs have been influential in breakthrough of many unreciprocated and novel aspects of their biosynthetic potential and overall biology. The constant growth of data reservoir over the past decades on fungal endophytes is providing a paving path for future examination of these advantageous organisms in the field of therapeutics, biology and evolution through emergent and evolving modes of analysis like machine learning and more (Chetia et al., 2019).

Endophytic fungal metabolites and their benefits:

The secondary metabolites of these endophytic fungi suggest by their structural and complexity and chemical diversity that they are useful in terms of drug discovery (Shukla et al., 2014). *Terminalia* species have been reported in such cases where the diversity and biological activities of endophytic fungi is studied. Consequently, a discussion on the influence of seasons, locations, and also the plant species on the diversity of endophytic fungi, as well as their biological activities and secondary metabolites isolated from potent strains are also reported. Endophytic population in *Terminalia* species is extremely diverse and influenced by the season, location, and host plant species which is reported and discussed. These fungal endophytes possibly will be potential producers of rich and reliable source of bioactive and chemically novel compounds for prospective use in medicine, agriculture, and industry. In fact, it is reported and discussed that endophytes from *Terminalia* spp. might produce vastly potent and extensively acclaimed metabolites such taxol, isopestacin, and pestacin. In addition, it is also reported that bioprospecting endophytes from *Terminalia* species have the potential to reveal more metabolites of value for therapy. Although *Terminalia* represents one of the most significant genera of medicinal plants with diverse biological activity, still it is regarded as one of the most unexplored biomes with reference to fungal endophyte community. According to a study, it is

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revealed that among the 200–250 *Terminalia* species described, only thirteen species have been studied so far for their endophytic fungi content (Kouipou and Boyom, 2019).

It is suggested that more than 47 fungi genera have been studied from the *Terminalia* species, and metabolites which are produced by some of these fungi exhibited diverse biological activities which includes antimicrobial, antioxidant, antimalarial, anti-inflammatory, anti-hypercholesterolemic, anticancer, and biocontrol varieties. Furthermore, it is reported that more than 40 compounds with eighteen newly described secondary metabolites were described; among which some metabolites are the well-known anticancer drugs, a group that includes taxol, antioxidant compounds, isopestacin, and pestacin (Kouipou and Boyom, 2019). Therefore, these studies provide considerable diversity and biological potential of fungal endophytes of the *Terminalia* species and also provide a vision into significant findings while paving the way for future researches.

Perspective endophytes and their study:

According to one of the reports it is found that one of the fungal isolate *Chaetomium nigricolor* exhibited significant cytotoxic, apoptotic and antioxidant potential. The study involved diversity and bioactivity of the endophytic fungal community from *Catharanthus roseus* inhabiting the coastal region. The study was conducted based on the hypothesis that the in coastal regions the microbial communities would tolerate a range of abiotic stress such as salinity, humidity, temperature and soil composition, and it possibly will produce new metabolites, which may possess bioactive property. As a result in the study, cytotoxicity and free radical scavenging prospective of the fungal organic extracts was discussed. Furthermore, in the study the apoptotic and the antioxidant prospective of the fungus that exhibited the best activity in first round screening were also discussed (Dhayanithy et al., 2019).

It is reported in the previous studies that *Catharanthus roseus (C. roseus),* which is an extensively widespread herb is an inhabitant of the subtropical area and belongs to the family Apocynaceae. The plant is a producer of numerous secondary metabolites and until now around 130 alkaloids alone have been recognized (Das and Sharangi, 2017). Various medicinal prospective ranging from anticancer, antidiabetic, antihypertensive, antibacterial, antifungal and antioxidant effects is been studied in such plants (Segelman and Farnsworth, 1974). Traditionally

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this plant is reported to be used in the treatment of fever, rheumatism and fatigueness. Blood coagulation is another property of this plant which is discussed in the prior art (Das and Sharangi, 2017). Numerous phenolic compounds of such plant are also reported to exhibit in vitro antioxidant potential (Ferreres et al., 2008). Two significant indole alkaloids isolated from this plant are vincristine and vinblastine which are used to treat leukemia and Hodgkin's lymphoma (Neuss et al., 1964). It is reported that the endophytes that reside inside the plants have the potential to produce host-specific metabolites, this is the reason vincristine and vinblastine could be found in endophytes isolated from such plants (Palem et al., 2013; Palem et al., 2015). Lately, it has also been described that the organic extracts of endophytic fungi that inhabit *C. roseus* plant presented important cytotoxicity against the selected cell lines (Khiralla et al., 2016). Furthermore, endophytic fungi from *C. roseus* have also been described to produce some novel compounds with prospective cytotoxic activities. The endophytic actinomycetes that inhabit *C. roseus* plant have also been discussed for their antioxidant activity (Jasmine and Agastian, 2013). This study provided vision into the diversity of endophytic fungal community isolated from *C. roseus* growing in the coastal regions which is the first report to be carried out where studies on the diversity of endophytic fungus inhabiting *C. roseus* plant growing in coastal region (Dhayanithy et al., 2019).

On the other hand, in a study twenty endophytic fungal isolates were identified from diverse parts of the plant using internal transcribed spacer region analysis. Based on the colonization frequency, the dominant genera were found to be *Colletotrichum, Alternaria* and *Chaetomium* with colonization frequency % of 8.66, 7.00 and 6.33, respectively. It was detected that the species diversity and richness was the maximum in bark followed by leaf and stem regions of the plant. On further screening the fungal ethyl acetate extracts for cytotoxicity against the HeLa cells, the *Chaetomium nigricolor* extract were found to exhibit effective cytotoxic activity of 92.20% at $100\,\mu g\,mL^{-1}$ concentration. A Comparative study between the different organic extracts (ethyl acetate, chloroform, dichloromethane and hexane) of *Chaetomium nigricolor* mycelial and culture filtrate was also carried out and it was found that the mycelial as well the culture filtrate ethyl acetate extracts and the culture filtrate hexane extract showed substantial cytotoxic perspective against the HeLa and MCF-7 cells, respectively. In this study illustrations on the apoptotic- and mitochondrial membrane depolarisation-induction potential of

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the *Chaetomium nigricolor* ethyl acetate extract is also been done. Additionally, the screening of antioxidant potential of the ethyl acetate fungal extracts using DPPH scavenging assay displayed that *Chaetomium nigricolor* extract exhibited potential activity with a substantial EC_{50} value of $22\,\mu g\,mL^{-1}$. The ethyl acetate extract of *Chaetomium nigricolor* also exhibited superoxide radical scavenging possibilities (Venieraki et al., 2017).

It is well known that medicinal plants have been used for thousands of years now, in folk medicines and still are used for their health benefits. Earlier report on medicinal plants shows that these are exploited for the isolation of plant-derived drugs as they are very effective and have comparatively less or no side effects. Nevertheless, the natural resources of medicinal plants have progressively exhausted and access to plant bioactive compounds is challenged by the low levels at which these products hoard in native medicinal plants. With this regard, this review aims to highlight the fact that endophytic fungi residing in medicinal plants are capable to biosynthesize pharmacologically active secondary metabolites similar or identical to those produced by their host medicinal plant (Bedi and Deshmukh, 2018).

Conclusion:

Emergence of endophytes as advantageous sources of bioactive compounds is known, since after the discovery of taxol from *T. andreanae*. The secondary metabolites of endophytes have been used significantly for the sustainable production of therapeutically vital compounds. The restricted availability of bioactive values in plant sources might be surpassed by manipulating the chemical entities in the endophytes. With the recounting information of the properties of endophytes and existing technological advancements in “omics” and fermentation, endophytic fungi could play a significant role in providing a persistent supply of chemotherapeutics with maximum target specificity and minimal side effects at an inexpensive cost. Endophytes as possible drug sources for the coming generation could be taken into account by putting efforts in genetic manipulations, overexpressing of the genes that are crucial for the production of the precise bioactive metabolite, and other optimization approaches which may contribute to the strain improvement. Hence, exploring and manipulation of metabolites from endophytes in

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terrestrial, mangrove, and marine environments possibly will provide an excellent path for the discovery of drug candidates against deadly human diseases.

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