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ISSN: 0975-7538
Review Article

Endophytic fungi a novel source of bioactive compounds for Pharmaceutical industry

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ABSTRACT

Over the past two decades, remarkable progress has been made to further elucidate the significances of endophytic fungi. The prime focus being the treasure of products which are of medically important. They are found to be anticancer, antioxidants, antifungal, etc. Similarly, in recent years a tremendous progress has been made on developing them into an important medical tool in the therapy of various medical conditions. In this article, we will address some of the more prominent and recent researches and make suggestions for further studies to be performed in near future. Fungal endophytes which are ubiquitous, reside in the internal tissue of living plants. Endophytic fungi that spread out from tropic to arctic have enormous potential in terms of secondary metabolic production. Apart from this the fungal bio synthesis which leads to pharmaceutically valuable chemical subsidies will also be taken into account for discussion.

Keywords: Endophytes; Symbiotic; Xerophytes; Bioactive Compounds; Antimicrobial compounds; secondary metabolites.

INTRODUCTION

Endophytic fungi belong to mitosporic and meiosporic classification of fungal kingdom. This ascomycete resides asymptomatically and lives within the internal tissues of the host plant below the epidermal cell layer. They commonly colonize within them as healthy living tissue through calm, quiet and innocent infections. (Bacon & White 2000). Endophytes are omnipotent, limited to exist as an integrated and known for their diversity and host specificity.

This review explores the enhanced interaction of endophytes in xerophytic plants. The plants which are described as xerophytic are not like hydrophytes and mesophytes. They distinctly live in an environment with little water and require a unique mechanism in terms of curtaining the water loss. They differ with storage of water which is accounted as an essential tool to beat the water crisis in extreme conditions for plants in desert or similar soil. Under these extreme conditions, endophytes help the host plants in water uptake so as to survive. The peculiar nature of these xerophytic plants with the integrated presence of endophytes is seemingly amazing, especially to grow with the available sources. These drought evaders live symbiotically to accommodate endophyte–host interaction to continue very smoothly.

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Received on: 17-08-2017
Revised on: 20-09-2017
Accepted on: 25-09-2017

Diversity of endophytic fungi

It is observed that the endophytic fungal species have various special features. Among them a few to mention, are one that over a million endofungal species present ubiquitously in this planet. Secondly they are divided into three main ecological types such as Mycorrhizal, Balansicaeous or pasture endophytic fungi and non-pasture endophytic fungi (Stanley Faeth & William Fagan, 2002). It is importantly noticed that the various bioactive essential compounds evaluated by these endophytic fungi are also host specific. They are very important to increase the adaptability of both endophytic fungi and their host plants such as the tolerance to biotic and abiotic stresses (Zhang *et al.*, 2006, Suryanarayanan, 2017; Rajagopal, 1999 and Rodriguez, *et al.*, 2009). It is equally noted that some of the bioactive compounds could not be verified whether the active metabolites are produced by the host plant or by the endophytic fungi. It is also said that some of the metabolites are presented equally by both the fungus and host plants.

Various studies have stated that they are mostly symbiotic; in certain conditions they are opportunistic. In certain conditions they are poisonous too but not to the extent of killing the host plant but to protect them from external injuries. These conflicting issues have made the researchers to go further and prove that they are truly symbiotic. And the important available bioactive compounds are made useful for the future generation in various aspects.

Above all, these essential components of bioactive radicals are found to be of eminent use for the modern era of pharmaceuticals and other branches of medicine (Monnanda Somaiah Nalini *et al*., 2014). These are found to produce plethora of known as well as novel biologically alert and active secondary metabolites. These active secondary metabolites are exploited and applied by human resources as important components with medicinal properties.

In contrast to the above said findings it is also observed in some of the rare representations that colonization of endophytic fungi is an incidental opportunity because of the chemotaxis (Ravindra Kharwar *et al,*. 2008). This statement has given a suggestion that endophytes are not host specific. The factors elicited so far, have given a conclusion that single endophyte can invade a wide range of hosts. Further these studies contribute that some strains of same fungi isolated from different parts of the same host differ in their ability to utilize different substances. It is therefore concluded that endophytes isolated from different plants belong to different families and classes. It is also noted that these endophytic fungi especially in xerophytic plants which live symbiotically in terms of helping each other give us enormous amount of conclusive and concrete informative indications.

Bioactivity of endophytes

The fungal endophytes are of diverse in nature. Their associations are omnipotent presenting throughout the plant kingdom. These endophytes provide indirect defense in the host plant. It has been established by various studies and researches that some of the so called chemical defenses once confirmed to be produced by the host plants are synthesized by endophytic fungi only (Wang *et al*. 2016)

By means of various research studies this has been estimated that there are secondary metabolites produced by fungi which may also affect the behavior of natural enemies like herbivorous species in a so called multi tropic defense association (Park *et al.,* 2012). It is very peculiar that the various multitrophic interactions will have a battery of cascading consequences for the entire plant kingdom. It is important to note that these conditions will vary widely but not always with rare exceptions depending on the combination of fungal species infecting a given plant under abiotic condition. This alters the biochemical equation of the plants with equal impacts on their herbivores. A novel study has brought an important note that altering the carbon and nitrogen ratio in certain parts of plants, leads to a situation wherein there is a less efficient source of protein and this plays a vital role here. Thus the endophytic fungus uses the plant nitrogen to form nitrogen secondary metabolites such as alkaloids which are considered to be a general effect of apoplastic concentrations.

It is importantly observed that endophytic fungi produce various antibiotics as secondary metabolites. *Penicillium* species produces Penicillia which is useful as antibiotics for animals and human beings. Salicliyx produced by *Salix* species (willow) is used as analgesic. Lovastatin which helps to lower the cholesterol level in the body is produced by *Aspergillus terreus*. There is also another important antibiotic Vanomycin *which is released by Nocardia orientalis*.

Endophytic fungi as anti-cancerous compounds

The endophytes produce several anti-cancerous compound forexample in the family Taxaceae produce taxol, which has an enormous potential as antitumor activity in many occasions (Strobel & Daisy, 2003). This has given ample opportunity to utilize these metabolites in cases of ovarian, uterine and breast cancers (Bharadwaj*, et al.*2016). These findings have thrown a light on other endophytic fungi and their metabolites which could be used as rewarding drugs for different ailments.

Fungal endophytes – metabolites as antioxidant compounds

The plant *Terminalia morobensis* and *Pestalotiposis microspora* produce Isopestacin and Pestacin which are extensively studied and found to be of great value as antioxidant compounds (Khan *et al.,* 2016).

Fungal endophytic metabolites as antiviral compound

The endophytic fungus *Cytonaema* species produces cytonic acid A and B. These have been extensively investigated and found to be of great value as antiviral compound.

Fungal metabolites as antibacterial compound

Considerable studies through different modalities on the endophytic fungi producing secondary metabolites such as alkaloids, terpenoids, phenols, quinines, flavonoids and steroid, have shown antimicrobial activities. These are used extensively in the medical field for different clinical conditions as antibacterial compounds (Jamith Basha, 2016)

Fungal endophytes- metabolites- as antifungal compounds

Recent researches have clearly shown that some of the antifungal agents are now available for the critical care of various life threatening dreaded fungal infections (Meenambiga, 2017).

Table 1: Bioactive compounds from endophytic fungi

S.No	Endophytic fungi	Plant Source	Bioactivity
1.	*Curvularia* sp. *Fusarium* sp. *Alternaria* sp. *Penicilliium* sp.	*Ipomoea carnia*	Antifungal and antibacterial
2.	*Curvularia clavata* *Curvularia lunata* *Curvularia pallescens* *Fusarium oxysporum*	*Ocimum sanctum*	Antimicrobial
3.	*Fusarium oxysporum* *Fusarium pallidoroseum* *Fusarium verticillioides* *Cladosporium herbarum*	Maize roots	Fungicides
4.	*Puccinia recondite*	Wheat leaf	Antifungal property against plant pathogenic fungi
5.	*Phyllosticta spinarum*	*Cupressus sp*	Anticancerous
6.	*Aspergillus fumigates*	Juniper plant	Antibacterial property
7.	*Rhizopus* *Aspergillus* *Scedosporium conidia*	*Camptotheca acuminata*	Antifungal

Impacts on the host plant

The recent studies have augmented the fact that the-host plants which are harboring the endophytes are suffering lesser damage and herbivores feeding on infected plants are less productive. But it is also equally noted that the chemical defenses produced by fungal endophytes are not universal (Fernando Vega *et al.* 2008). Only in few among these, endophytic symbiosis has been proved to be an effective defense mutualism. The endophytic fungi which exert an effective defense service to the host plant (Martin *et al*., 2015) in some occasions elicit a pressure, coined as selective pressure. This favoring association enhances the level of fitness related to the uninfected host plants.

A bird eye view of researches

It has been interesting to note that these omnipotent, ubiquitous endophytic fungi in xerophytic plants exert enormous effects on the chemical composition of the plant. Various researches and studies have shown that there has been greater impact on agricultural products and livestock for centuries. First they were identified as poisons. Subsequently they were distilled and distracted and found to be of more valuable medicinal values (Huang, *et al*., 2008). By means of various continuing descriptive studies on the effects of infections by defense of mutualistic fungal endophytes, there have been many epic researches which have opened various doors for further studies on the ecology of plant-fungus association. The researches dealt with various means by which a plant physiology has been altered and the series of chemical reactions in delivering volatile biomedical components are waiting to be answered further to find out solutions for the lacuna present in the path (Massimo *et al.,* 2015).

Aspects of importance

The combined endophytic fungal associations are also found to be harmful to mammals including live stocks and humans. Human losses are also reported in some occasions. But the environmental representation of fungal resistance to herbivores has given a reasonable success in agricultural applications. The so called metabolites produced from the endophyte-plant interactions, especially the secondary metabolites have been isolated either in raw or derived forms. These are used to manufacture a variety of drugs. These drugs are essentially helpful to treat various health conditions in human beings. Starting from ergot alkaloids to the latest anticancer drugs especially Taxol, are worth to be mentioned. The revelation of bio pesticides is noteworthy. Interestingly the highly debated soil conservation is also one of the vital topics wherein the host and fungal combinations play a highly selective role (Kumar, 2004). This is happening in a situation where water is scarce, temperature is volatile and nutrition is poor in terms of morphological as well as bio chemical adaptations (Neha Chadha *et al.,* 2015). This microbial symbiosis plays a vital role in bringing out a concrete solution so as to ensure viability and utility. Whether the combination of host plant and the endophytic fungi agree to live together either in active status throughout the life time or for an extended period of time or with a latent status of activity, the importance cannot be under estimated (Rajagopal *et al*., 2017- Communicated).

CONCLUSION

The analysis of various recent studies clearly show that the strength, structure and the distribution of endophytic fungi, in terms of geographical and biochemical nature vary extremely. The resultant effect is to produce metabolites either primary or secondary that are helpful for the fungi themselves, the host plant as well as the human race at large. This review essentially enlightens the importance of host–plant factors, geographical, environmental conditions and their importance. They are totally dependent on the factors such as taxonomy, host, genetic environment and the tissues of the host plant. The above mentioned factors highly influence the investigation of bioactive substances which are considered to be the focus of the review of these articles. It is clearly evident that ubiquitous, environment friendly, essentially mutual fungi promote seed growth of many host plant species. These signifying factors that increase the opportunity of growth of those seeds that cannot germinate under normal conditions are widely discussed.

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