Plant Cell Biotechnology and Molecular Biology 22(41&42):227-246; 2021 ISSN: 0972-2025

ENDOPHYTES: A STORE HOUSE OF PLANT GROWTH PROMOTERS AND BIOACTIVE COMPOUNDS

SHREYASI BISWAS AND MAHUYA MUKHOPADHYAY[*]
Department of Microbiology, Lady Brabourne College, P1/2 Suhrawardy Avenue, Kolkata 700017, West Bengal, India [SB, MM].
[[*]For Correspondence: E-mail: mahuya.mukhopadhyay@ladybrabourne.com]

Article Information

Editor(s):
(1) Dr. Ravi Kant Chaturvedi, Chinese Academy of Sciences, P.R. China.
Reviewers:
(1) Eduardo Varejão, Universidade Federal de Viçosa, Brazil.
(2) Andrezza Mara Martins Gandini, Federal University of the Valleys of Jequitinhonha and Mucuri, Brazil.

Received: 15 May 2021
Accepted: 21 July 2021
Published: 30 July 2021

Review Article

ABSTRACT

A diverse variety of plants establish relationship with microorganisms. Endophytic microbes whether bacteria or fungi are ubiquitous in most of the plants and colonize inside the plant tissues either localized or systemic way without causing harm on their hosts. Endophytes are most potent phytohormone producers. We have found nitrogen fixing endophytic bacteria, along with phosphate solubilizers and different types of siderophore producers. They even have ACC deaminase activity which actually helps in plant growth promotion by lowering the ethylene level in plants. The endophytes gain entrance in plants by various mechanisms. In ancient period, they were regarded as virulent plant pathogens but after exploring its antagonistic potential against several bacterial and fungal phytopathogens and various plant growth promoting activities, they are used as bioinoculants for the development of plants. As chemical fertilizers, synthetic fungicides are hazardous to plants as well as to human and animals, natural bioactive compounds from endophytes especially from fungi gained attractions of scientists. Several alkaloid, terpeniod, peptide, polyketide derivatives that have antimicrobial properties against plant pathogens have been explored. As in this review, properties of some secondary bioactive metabolites like collectotric acid, phomenone, trichodermin, helvolic acid, pestalachloride A, cryptocin, pyrrocidines A, loline alkaloid, leucinostatin A have been discussed. There are more bioactive compounds from endophytes have been studied in various researches which have antagonistic effects against human pathogens, but not enlisted in this study. We tried to enlist the beneficial roles of endophytes on their host and non-host plants in this review.

Keywords: Endophytic microorganisms; indole acetic acid; gibberellins; ACC deaminase; antimicrobial compounds.

INTRODUCTION

Endophytes are microorganisms live inside the host plant for at least a part of its lifecycle. In this association microbes receive nutrients and protection from host plants while facilitating nutrient uptake and give protection from environmental stresses to the plants [1, 2]. Other beneficial roles of endophytes include increased drought resistance [3], thermal protection [4], survival under osmotic stress [5]. These endophytes were isolated from various wild plants and crops [6, 7].

Chemical fertilizers and pesticides used in agriculture have hazardous effect on mankind [8] and environment [9]. Plant growth promoting bacteria have symbiotic association with their host plants are important to improve productivity and health of plants under various environmental conditions [10,11,12]. Endophytes are gaining attractions owing to their impressive growth promoting potential on plants [13]. Plant growth promotion ability of endophytes includes phytostimulation [14], biofertilization [15], and biocontrolling [16] properties. These microorganisms may produce several phytohormones like auxin, gibberellins, can fix atmospheric nitrogen, solubilize phosphate, and have antimicrobial potentials as well [17,18]. Bacterial endophytes confer stress tolerance to the plants and help in their growth and photosynthesis [19]. The antimicrobial compounds are defined as low molecular weight organic substances produced by microorganisms and are active at low concentrations against other microbes. The endophytes are believed to carry out resistance mechanism against pathogenic invasion by producing secondary metabolites **[**20].

Endophytic fungus from *Ferula sumbul* were reported with their ability to produce various bioactive metabolites like 2-methyl-3-nonyl prodiginine, Bis (2-ethylhexyl) phthalate and preaustinoid A. These secondary metabolites were active against test microorganisms and also had anticancer property against two human melanoma cell lines [21]. Beside this, biofertilizers are those microbes that bring about the enrichment of soil and are most important of sustainable agriculture [22]. The production of healthy crops to meet the demand of world's expanding population relies on chemical fertilizers. So the use of microbes whether rhizosphere or endophytic communities as biofertilizers may be useful for healthy crop production, enhancement of soil fertility and have no negative impacts on human health as well. The endophytic bacteria were also help to promote growth and resulted in an increased biomass of sweet sorghum in heavy-metal contaminated lands. The endosymbiont *Bacillus* sp. SLS18 also help to uptake Mn/Cd from this type of lands and help to grow sweet sorghum for ethanol production. Well this actually reduces the competition between food crops and energy crops for fertile lands [23]. Phytoremediation is the approach based on the ability of plants or plant associated microbes to uptake, remove or lower the environmental pollutants from soil, water or air. Plant growth promoting endophyte *Pseudomonas lurida* strain EOO26 showed an impressive result of ammonia, ACC deaminase production along with multi-metal tolerance. The plants inoculated with this specific strain showed an enhanced Cu uptake by 8.6 fold for roots and by 1.9 fold for leaves than the uninoculated plants, which indicates the phytoremediation ability of plants is boosted up by the endophytes and can be used in to remove environmental contaminants [24]. There were many reports suggested the phytoremediation efficiency of plants for soils contaminated with heavy metals was enhanced greatly by the use of endophytic bacteria [25,26]. So, this review describes the plant growth promoting abilities in a direct and indirect way along with their phytoremediation efficiencies which undoubtedly enlighten the biotechnological application of these beneficial microbes to reduce the environmental pollutions in an eco-friendly manner.

PLANT-ENDOPHYTE ASSOCIATION

The endophytic bacteria are present in each and every plant almost [27]. Both the culture dependent and independent endophytes belong to more than 200 genera of bacteria and these included *Actinobacteria, Acidobacteria, Aquificae, Bacteriodetes, Chloroflexi, Cyanobacteria, Firmicutes, Fusobacteria, Proteobacteria Spirochaetes and Verrucomicrobiae* [28,29,30,31]. There were many reports suggested the plant-endophyte interactions [32,33,34]. The molecular basis of plant growth promotion by endophytes was elucidated by microarray-based gene expression techniques. This would help to identify those genes for example nutrient uptake genes, cell organization, biogenesis genes in plants which were up-regulated during endophyte colonization [35]. Recently the PCR based approach showed lipopeptide genes from endophytic bacteria had antifungal (Iturin D and bacillomycin D) and antibacterial (surfactin) actions against phytopathogens [36]. The interaction between plant and endophyte need an entrance of microorganisms inside the plant tissues. Endophytes enter the plant through various points. These included stomata [37], lenticels [38], tissue wounds [39], root cracks [40] and germination radicles [41]. Apart from this, endophytes use root hair cells [42] and cell wall degradative enzymes [43] to enter in plants. Quadt-Hallmann et al., found that endophytic isolate *Enterobacter asburiae* JM22 was present in roots, cotyledons and stems of cotton plants treated with living bacteria but in ultrathin sections of leaves no bacteria were detected inside the leaf tissues. Not only bacteria but fungi also establish endosymbiotic relation with plants. There are many factors that influence these plant-fungal interactions as for example temperature, humidity, geographic location, age of host plant [44,45,46]. The establishment of plant-endophyte relation begins with colonizing the roots by soil bacteria. In this step various molecules especially proteins played an important role. For an example Methyl-accepting chemotaxis proteins involved in this [47]. Furthermore, biofilm formation is important which helps in the attachment to the roots of plants. Various adhesive components were involved like PAL5 exopolysaccharide, cellulose in biofilm formation and consequent root colonization of microorganisms [48,49]. There are another class of membrane components lipopolysaccharides up-regulated in endophytes during this association [50]. The changes in endophytes are not only the single factor to establish the plant-endophyte association but alteration in plant cell wall was also important. Bacterial endophytes are capable of producing plant cell wall degrading enzymes. It was reported in studies that endoglucanse mutant endophytic strains were unable to colonize the roots of plants, which means endoglucanase are important cell wall degrading enzymes need to be present in the endophytes [51,52].

PLANT GROWTH PROMOTION MECHANISMS BY ENDOPHYTES

Plant growth promoting bacteria, fungi or actinobacteria have several ways to induce growth of plants. Basically there are two methods – direct method and indirect method.

Direct Method

There are multiple mechanism adapted by these endophytes to facilitate the growth of plants directly. They can synthesize phytohormones like auxin, gibberellic acid, cytokinins, and enhance several stages of plant growth. They may fix atmospheric nitrogen and make it available to the plants, as nitrogen is very important for plants. Endophytes are able to produce siderophores which actually can help to sequester iron from soil and supply it to plants. They may also produce an enzyme called ACC deaminase (1-aminocyclopropane-1-carboxylate deaminase) which can lower the plant ethylene level and help in their growth [53,54]. They may solubilize minerals like phosphorus and make readily available to plants. An endophyte especially bacteria or actinobacteria directly affect the plant growth using any one or more of the above mechanisms. Till date, Most of the works on plant growth promotion are focused on phytohormone production ability of these endophytes [55,56, 57].

Indirect Method

The endophytes act as biocontrol agents against phytopathogens which is nothing but an indirect mechanism to promote plant growth. There are several mechanisms like antibiotic or antifungal compounds production, synthesis of cell wall lysing enzymes, induction of systemic resistance in plants. The most common mechanism which is used by endophytes is production of antimicrobial compounds against plant pathogens. In this case endophytic fungi are most potent producers of antimicrobial agents and investigated for many years [58,59,60]. Endophytic actinobacteria are an alternative and novel source of antimicrobial components which have antagonistic potentials documented in investigations [61]. Actinobacteria not only synthesize antimicrobial agents but also can upregulate the defense gene expression. They are able to activate key genes of systemic acquired resistance or jasmonate/Ethylene pathways as for example *Micromonospora* sp. did the same [62]. Endophytic bacteria produce enzymes such as chitinase, lipase, protease which facilitate fungal cell lysis [63]. Other antagonistic bacteria can protect plants from pathogen by out-competing them for niches and nutrients on the root surfaces, therefore they actually prevent phytopathogens from binding and infecting plants [64].

PHYTOHORMONE PRODUCTION BY BACTERIAL ENDOPHYTES

Phytohormones are produced by plants that help to promote their growth in normal and stressed conditions. Auxins, a class of crucial phytohormones that orchestrate almost every aspect of plant growth and development [65,66]. Synthesis of auxin is not limited to any specific tissue of plants rather it was evident from reports that auxins may be synthesized in young leaves, cotyledons, roots and shoots [67,68,69]. Gibberellins (GAs) are tetracyclic diterpenoid growth hormone essential for plant growth. GA deficient mutant plant species exhibit a dwarf phenotype characteristic with an example of *Arabidopsis* having ga1-3 mutant [70]. They induced stem elongation, flowering and germination [71,72,73,74]. Endophytes have potential to produce these phytohormones and play important role in growth promotion of their host plants. Bacterial endophyte *Sphingomonas* sp. LK11 isolated from leaves of *Tephrosia apollinea* observed to produce indole acetic acid and gibberellins [75]. It has been reported that diverse groups of bacterial endophytes can produce these hormones and most of the studies have been focused on IAA (indole acetic acid) production. Endophytic bacteria belongs to phyla *Proteobacteria* have shown to increase in IAA production during in vitro stress conditions and also faster growth and rooting in hybrid Poplar plants (*Populus trimula* x *P.alba*) INRA 717-1B4 [76]. In natural condition, it is quite obvious that mixed type microbial culture give most promising results than the single one, as in mixed type culture some of them are potent auxin producers, some are good nitrogen fixers, some can produce gibberellic acid and induce plant growth [77]. Endophytes belonging to the genus *Paenibacillus* have an intrinsic property to produce IAA, this genus of microorganism with two species *Paenibacillus marcerans* and *Paenibacillus lentimorbus* have shown impressive results in growth promotion to *Cattleya* seedlings during acclimization [78]. Plant growth promotion included an increase in chlorophyll content, plant dry weight, seed germination and endophytes exactly did these. Even they may be used as bioinoculants in agricultural industries which help to improve in crop yield [79]. Endophytic isolates are not only important for crops like maize and rice but also for horticultural plants like rhododendrons and economically important plants like tea, cashew etc. Isolation and plant growth promoting traits of endophytes have been documented in recent investigations [80,81,82].

PRODUCTION OF ACC DEAMINASE BY ENDOPHYTES

ACC deaminase is an enzyme that cleaves ACC the precursor of ethylene in plants into ammonia and α-ketobutyrate. This is a multimeric (homodimeric or homotrimeric), sulfhydryl enzyme having molecular mass of 35-42 kDa. Activity of ACC deaminase is found to be associated with many different soil bacteria [83, 84,85]. Most important thing is how the plant growth promoting bacteria having ACC deaminase activity help to promote plant growth. Well a model was proposed in finding of Glick et al., 1998, which showed that plant growth promoting bacteria even endophytes also bind on the surface of roots or seeds of plants. In response to root exudates, bacteria synthesize indole acetic acid (IAA). The IAA produced by bacteria and endogenous plant IAA together can induce cell proliferation and stimulate the synthesis of ACC Synthase. Due to this some ACC will be produced by the plants and exuded, which is taken up by the ACC deaminase containing bacteria and cleaved into ammonia and α-ketobutyrate. As a consequence of low level of ACC, the amount of

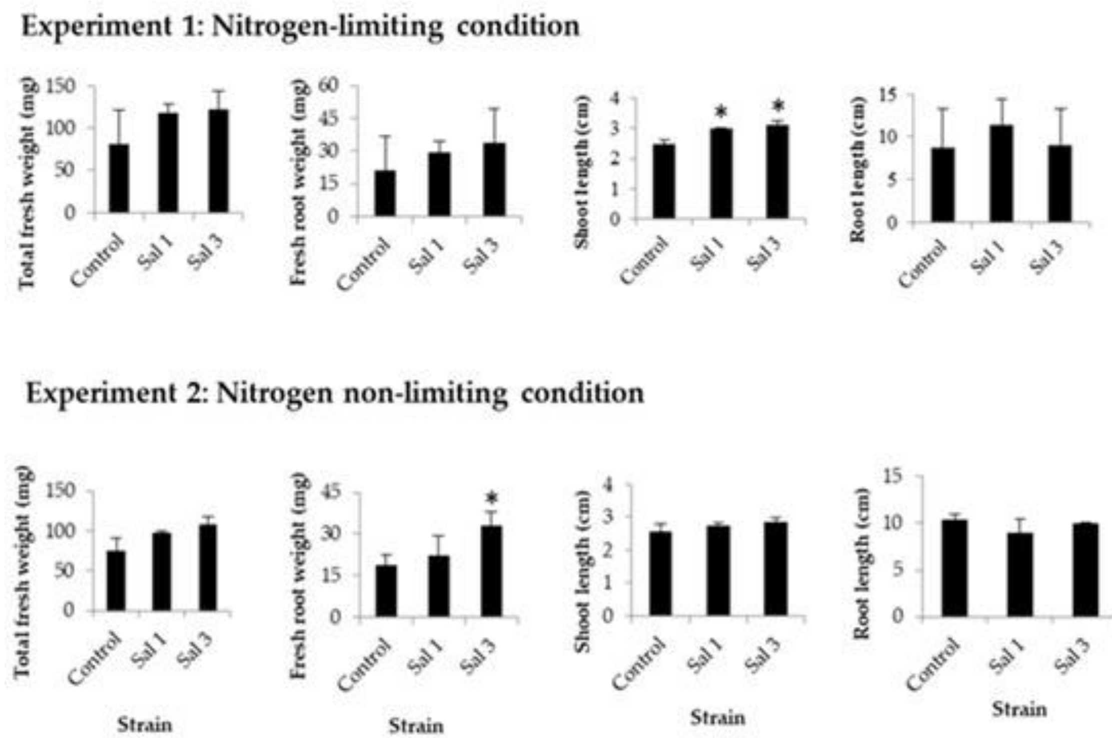

Fig. 1. Effect of Sweet potato endophytes on growth of tomato seedlings in nitrogen-limiting and non-limiting conditions [153]

Note: In nitrogen limiting condition the endophytic strains Sal1 and Sal3 had shown an increased shoot length in tomato seedlings.

ethylene production became reduced. This results in an increased root and shoot length, increase in plant biomass and protect plants from inhibitory effects of ethylene which is produced due to the biotic or abiotic stresses [86]. Long et al., 2008 have shown high levels of ACC deaminase has positive effect on root growth of seedlings of *S. nugum* and in this study, it was also reported that bacterial endophytes isolated from one particular species of plant may not always show similar effect of growth on other plant species like its host plant [87]. Using techniques of Recombinant DNA Technology, it has been reported that deletion of gene *acdS* responsible for ACC deaminase enzyme in endophytic bacteria *Burkholderia phytofirmans* PsJN, which results an altered expression of ACC deaminase along with IAA level and siderophore production and their effect on plants [88]. If salinity increased in agricultural lands, it will affect the crops which is a worldwide problem. Usually in stressed conditions, ethylene level increased in plants [89]. Two wild type endophytic bacteria and their ACC deaminase deficient mutant strains have been investigated for growth promotion in tomato plants, in this work seeds of plants were inoculated with these endophytes in salt stressed condition and showed that ACC deaminase deficient mutant strains inoculated seeds have been reported with lower growth rate than those seeds inoculated with wild type endophytes [90].

NITROGEN FIXATION

Nitrogen is essential for plant growth, but plants cannot get it though percentage of atmospheric nitrogen is 78%. They are not able to fix free nitrogen .There are many reports to suggest that microbes can fix the atmospheric nitrogen and make available to plants [91]. In the year of 1988, Dobereiner *et al.*, had isolated a new type of nitrogen fixing bacteria from roots and stems of sugarcane in Brazil. This new type of N2-fixing endophytic bacteria showed optimal growth with 10% sugar and a pH 5.5 and can fix nitrogen in presence of nitrate. Formerly it was proposed as *Saccharobacter nitrocaptans*, but after DNA/RNA TM values DNA/DNA binding values it was found to be a new species of genus *Acetobacter*, so named *Acetobacter nitropcarpan* [92]. Nitrogen fixing endophytic bacteria were isolated from juice of Japanese sugarcane cv. NiF-8 and based on some biochemical properties 13 isolated endophytes were putative strain of *Acetobacter diazotrophicus*, four isolates showed similarities with *Herbaspirillum seropedicae*, and four isolates had similarities with *Herbaspirillum rubribalbicans* like strains [93]. A new type of nitrogen fixing endophytic bacteria (9C) was reported from internode sap of sugarcane variety ML3-18 along with another nitrogen fixing endophyte (T2) from its roots and based on phylogenetic analysis endophyte designated as 9C was a member of genus *Pantoea* and endophyte T2 was *Gluconobacter diazotrophicus,* both of them reported with nitrogenase activity, but nitrogenase activity in terms of hydrogen production was higher in case of isolate 9C than T2. This 9C strain was able to grow over a wide range of temperature from 20° C to 42°C , pH and salt concentration as well, so can be used in agriculture [94]. There are many reports suggested that endophytes can fix atmospheric nitrogen and make it available to the plants [95,96,97]. Saline based lands can be used for agriculture and the halophytic plants growing in this condition are reservoir of endophytic nitrogen fixers. Endophytic bacteria belonging to *Actinobacteria* were able to grow in nitrogen free medium supplemented with 6% NaCl and had potential to induce plant growth [98]. The crop development was tested by the inoculation with nitrogen fixing endophytic bacteria and rice seedlings had an impressive result in terms of enhanced chlorophyll, nitrogen concentration, fresh and dry weight of root and shoot in rice plants [99]. The inorganic fertilizers though help to speed up the crop production, but they have negative impact on environment. These fertilizers usually contain nitrate, phosphate, ammonium, potassium salts which are important for plants but also have heavy metals. These heavy metals accumulate in the plants and soils and enter in food chain which cause water, soil pollutions [100]. Another drawback of using chemical fertilizers is it can deal with only one matter related to plant growth like either promote growth or protect from phytopathogens. But in case of endophytic application may deal with various prospects of growth promotion of plants. The endophytes can induce growth by fixing nitrogen, producing plant hormones, and same endophytes may also have potentials to combat with phytopathogens along with enhanced fertility of soil. So the use of nitrogen fixing endophytes as biofertilizers can be a substitute of inorganic fertilizers.

PHOSPHATE SOLUBILIZATION

The second most important growth factor is phosphate which is present in soil as mineral salt. Due to unavailability of this insoluble phosphate it can be a growth limiting factor for plants. There are many evidences that endophytic bacteria can solubilize inorganic phosphate and make available to host plants. The strategy behind this phosphate solubilization is organic acid production by endophytes, as organic acids can chelate cations bound to phosphates [101]. Studies have been reported that gluconic acid production leads to solublized phosphates in supernatant [102,103]. *Pseudomonas* strain proved to be a good candidate for phosphate solubilization and can be used as a biofertilizer under phosphate limiting conditions, as *Pseudomonas* strain PSE-1 isolated from *Withania sominifera* (commonly known as Ashwagandha) can solubilize phosphate and enhanced this mineral in soil after its use as a bioinoculant with phosphatase activity at pH10 [104]. Endophytes belongs to genus *Bacillus* obtained from banana tree also have potential to solubilize phosphate when both inorganic and organic phosphate source applied in vitro, Soy lecithin as organic and tricalcium phosphate as inorganic phosphate give positive results whether in case of Ferrous phosphate none of the isolated endophytes can solubilize this phosphate in vitro [105].

SIDEROPHORE PRODUCTION

Siderophores are basically low molecular weight microbial iron chelators, can acquire iron from various soluble and insoluble iron compounds.

Siderophore producing bacteria indirectly promote plant growth as they can sequester iron from limited sources and make it unavailable to plant pathogens [106]. Endophytic bacteria are able to produce them [107]. A research work demonstrated 9 unique endophytic *Actinomycetes* have been isolated from inner tissues of roots of Thai glutinous rice plants (*Oryza sativa* L. cv. RD6) and Thai jasmine rice plants (*Oryza sativa* L. cv. KDML105), among them 5 strains produced siderophores . *Streptomyces* sp. GMKU 3100 with highest siderophore production was identified based on its 16srDNA and showed highest growth promotion to rice and mungbean plant seedlings when ferric citrate was used compared to the untreated and siderophore deficient mutant strain *Streptomyces sp*. GMKU 3100 treated plant seedlings [108]. A diverse siderophore producing endophytic bacterial community has been isolated from *Oryza sativa* cultivated in Uruguayan soil. Among them, isolates I20 and I24 belong to the genera *Burkholderia* and L27, G16 isolates of genus *Pseudomonas* have been reported with strongest siderophore production [109]. Strains of *Gluconacetobacterbacter diazotrophicus* from roots of sugarcane have been tested for different siderophore production and reported to produce catecholate and salicylate type of siderophores. Highest salicylate type (133µg/ml) and catecholate type (126µg/ml) siderophores were recorded in case of isolate L5 of *Gluconacetobacter diazotrophicus* followed by other isolates of this endophyte [110].

ANTAGONISTIC EFFECTS OF ENDOPHYTES

Increasing food production with good nutritional value due to rapid expansion of population in the world is really a challenge for the scientists. But cereal loss is still a problem due to several reasons, specially the plant diseases caused by pathogenic fungi. Synthetic fungicides are mostly applied in agricultural field. But they take much time to degrade which can cause toxicity to humans and animals. That is why a natural biocontrol agent whether endophytic fungi or bacteria are needed which have lower or no toxicity for animals and should have antagonistic effects against phytopathogens [111,112,113]. Apart from this another mechanism, endophytic bacteria and beneficial fungal symbiosis can induce growth of plant and combat against phytopathogens. One such case revealed that endophytic bacteria belonging to the genus *Mycolicibacterium* have positive effect on plant beneficial fungi *Serendipita indica*. Dual Application of endophytic bacterial strain of *Mycolicibacterium* and endophytic fungi *Serendipita indica* have shown to boost up the beneficiary effects of this fungal endophyte on tomato plant and also reduce the symptoms caused by fungal pathogens *Fusarium oxysporum* and *Rhizoctonia solani* [114]. The endophytic bacteria and their antagonistic properties have been widely explored [115, 116, 117]. Actinobacteria are Gram positive in nature with high G+C content that also colonize inside the plant tissues and display biocontrol and plant growth promoting properties. An endophytic actinobacterial strain *Streptomyces* sp. that was closely related to *Streptomyces caeruleatus,* enhanced resistance in tomato seedlings against *Fusarium oxysporum*, a root rot disease causing fungi [118].

- ❖ Few antimicrobial compounds like terpenoids, alkaloids, polyketide, peptide derivatives are mentioned below.

TERPENOIDS

Sesquiterpenes, diterpeniods, triterpenoids are major group of terpenoids isolated from endophytes and discussed below.

Sesquiterpenes

Derivatives are discussed below.

Phomenone

It is an antifungal eremophilane sesquiterpene usually produced by *Xyleria sp*. an endophytic fungus of *Piper aduncum* plant. It has been claimed that Phomenone have antifungal activity against a wheat pathogen *Cladosporium cladosporioides* though supporting evidences were not presented [119]. This compound has been used as natural precursor for synthesis of anticancer ester drugs [120].

Trichodermin

It is member of the 12,13-epoxytrichothecene mycotoxin family, used for synthesis of plant growth regulators and pharmaceutical compounds [121].This sesquiterpene derivative was reported to give protection against two phytopathogens *Alternaria solani* and *Rhizoctonia solani* in vitro [122]. Trichodermin is a potent inhibitor of eukaryotic protein synthesis as well [123].

3, 12-Dihydroxycadalene

This was a cadinane sesquiterpene isolated from *Phomopsis cassia* and this compound have shown inhibitory effect against phytopathogenic fungi *Cladosporium cladosporioides* and *C. sphaerospermum* [124].

Diterpene Derivatives

There are various diterpene derivatives like paclitaxel, sordaricin, scoparasin B, guanacastepene purified from endophytic fungi but most of them showed antagonistic effect against human pathogenic fungi [125,126,127]. Paclitaxel is a tetracyclic diterpenoid found in wild *Taxus* plants. This compound is world's first expensive anticancer drug used to treat breast and ovarian cancer. Endophytes from various plant species were capable to synthesize the taxol [128]. There are numerous endophytic fungal genera produce this bioactive compound like *Botryodiplodia*, *Botrytis*, *Aspergillus*, *Alternaria*, *Ectostroma*, *Fusarium*, *Cladosporium*, *Mucor*, *Metarhizium*, *Pestalotia*, *Pestalotiopsi*, *Pithomyces*, *Taxomyces*, which may be used as an alternative way to produce Taxol. Apart from this, different diterpene derivatives like botryosepharin compounds, acrostalidic acid, acrostalic acid, isocupressic acid were obtained from endophytic fungus *Botryosepharia* sp. MHF colonizes in *Maytenus hookeri*, had antagonistic activity against several bacterial and fungal pathogens [129].

Triterepene Derivative

Helvolic acid

Helvolic acid was isolated from an yeast *Pichia guilliermondii* Ppf9, its asexual form is known as *Candida guilliermondii*, an endophyte of Himalayan medicinal plant *Paris polyphylla*. This compound has an inhibitory effect on spore germination of *Magnaporthe oryzae*, causative agent of rice blast disease [130].

Meroterpenes

The meroterpene derivatives are compounds from mixed biosynthesis having part of terpenoid ring along with quinines or hydroxyquinones. These compounds also have potential antagonistic action against pathogenic microbes. There are various reports that meroterpene compounds were obtained from endophytic fungus associated with mangrove plants [131] and many other plant species. As for an example preaustinoid B2, preaustenoid A3, isoaustinone and austenolide had been isolated from endophytic fungi *Penicillum* sp., [132].

ALKALOIDS

Alkaloids are always being an important bioactive metabolite active against various pathogens. Many reports suggested new alkaloid derivatives have been found in endophytic microorganisms. In the study by Ma et al., new isoquinolone alkaloid 5-hydroxy-8-methoxy-4-phenylisoquinolin-1(2H)-one was isolated from endophytic fungus *Penicillum* sp. R22. This new alkaloid had antifungal potential [133]. Few alkaloids fumigaclavine C and pseurotin A have broad spectrum of activity against pathogens [134]. Numerous studies are there to describe alkaloid derivatives from endophytic origin have beneficial properties for human welfare [135, 136].

Pestalachloride A

This alkaloid derivative was isolated from an endophytic fungus *Pastalotiopsis adusta*. This one had antifungal activity against plant pathogens *Fusarium culmorum*, *Gibberella zeae* and *Verticillium albo-atrum* [137]. This was classified as a new chlorinated benzophenone alkaloid that belongs to amine and amide subclass.

Cryptocin

This alkaloid derivative is a tetremeric acid analog isolated from endophytic fungus *Cryptosporiopsis quercina* associated with stem of a Chinese medicinal plant known as *Tripterygium wilfordii*. Well this compound also have antifungal activity against a wide range of phytopathogens including rice blast pathogen [138].

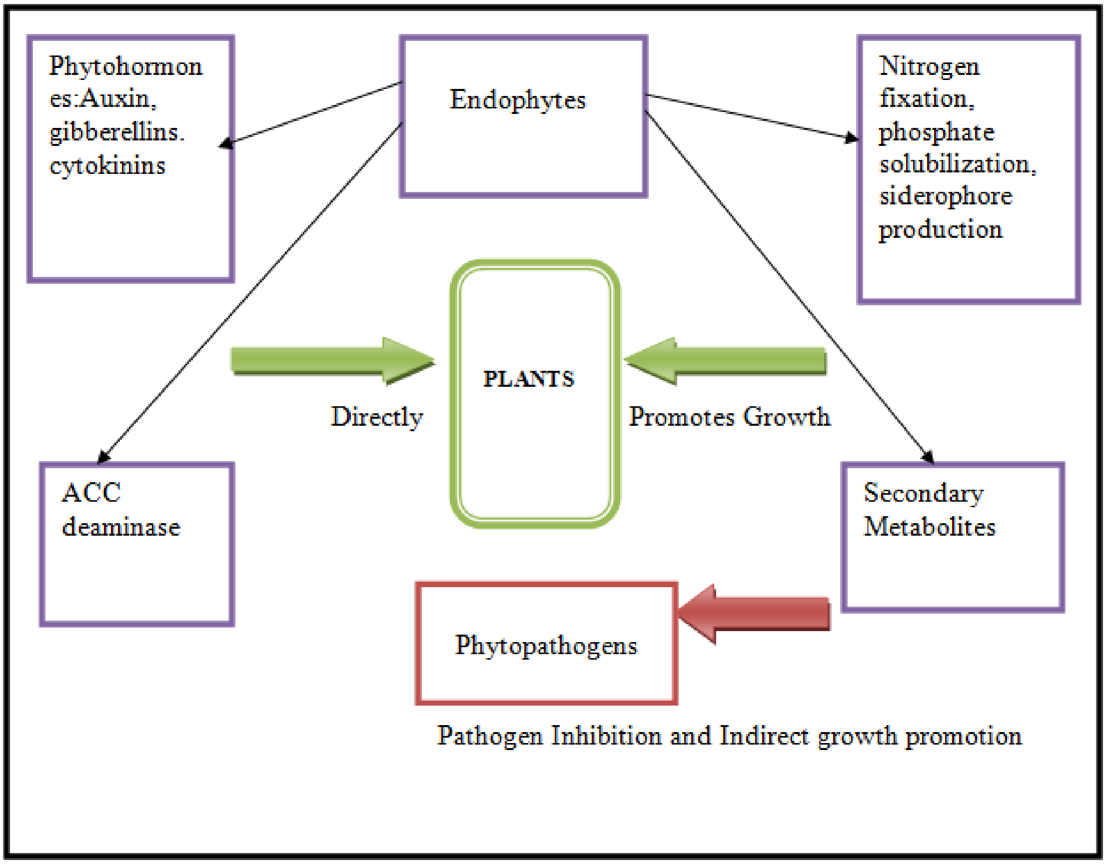

Fig. 2. Schematic diagram of beneficial effect of endophytes on plants

Camptothecin

This is a pentacyclic quinoline alkaloid which was isolated from wood of *Camptotheca acuminate*. It has antineoplastic potential. An endophytic fungus *Fusarium solani* isolated from *Camptotheca acuminate* and *Apodytes dimidiata* can produce 10-hydroxycamptothecin and 9-methoxycamptothecin [139, 140].

INDOLE DERIVATIVE

Loline Alkaloid

This is an indole derivative originated from endophytic fungus *Neotyphodium uncinatum* associated with grass *Festucapratensis* (*Lolium pratense*) [141]. This compound has broad-spectrum of activity against insects and aphids and thereby increasing resistance against insect herbivores in host plants [142]. There was an unique species interaction reported in which loline producing endophytic fungus *Neotyphodium uncinatum* can protect a non-host plant also against plant aphids [143]. The loline encoding genes were also identified in this endophytic fungus and based on this findings, biosynthesis of loline was also proposed using precursor proline and homoserine [144]. But One thing is very important and should be noticed that sexual form *Epichle* of *Neotyphodium uncinatum* (asexual form), is pathogenic for host plant inflorescence, whereas *N. uncinatum* established mutualistic relation with host plant [145].

PHENOLIC COMPOUNDS

There are many phenolic compounds originated from endophytic fungus but here only those derivatives are mentioned that have inhibitory effects against plant pathogens.

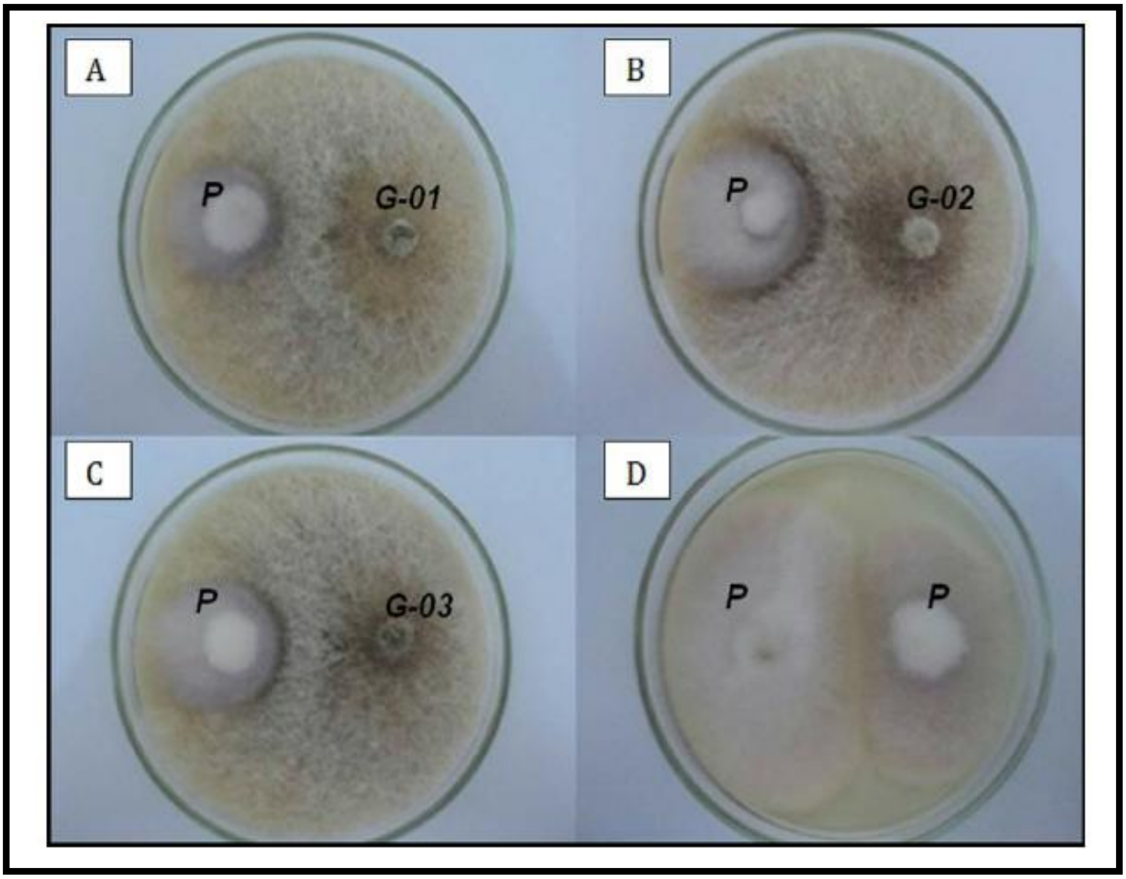

Fig. 3. Endophytic fungal antagonism against plant pathogen [154]

Note: In this figure plant pathogen (P) indicated in this is *Fusarium solani* and the fungal endophytic isolates are G-01, G-02 and G-03. These three foliar endophytic fungal strains from *Mikania glomerata*, have antagonistic property against the test phytopathogen.

2-Methoxy-4-hydroxy-6-methoxymethylbenzaldehyde

This phenolic compound was isolated from an endophytic fungus *Pezicula* strain553. This has shown its antifungal activity against cucumber pathogen *Cladosporium cucumerinum* [146].

Collectotric Acid

It is a tridepside compound originated from an endophytic fungus *Colletotrichum gloeosporioides*, lives inside the stem of Artemisia mongolica .This have antifungal property against a crop pathogenic fungus *Helminthosporium sativum*, and also possesses antibacterial properties against *Bacillus subtilis*, *Sarcina lutea* and *Staphylococcus aureus* [147].

POLYKETIDES

Pyrrocidines A and B

These polyketide amino acid derivatives were isolated from an endophytic fungus called *Acremonium zeae*, colonizes in maize kernels and may protect the kernels in pre-harvest stage against phytopathogens [148]. Pyrrocidine A was a potent inhibitor of ear rot and stalk rot pathogens of maize, as for example *Nigrospora oryzae*, *Rhizoctonia zeae*, and *Stenocarpella maydis* and also has inhibitory effect against seed-rot saprophytes *Eupenicillium ochrosalmoneum*, *Curvularia lunata* (causal agent of fungal leaf spot disease) [149].

Pestalachloride B

This antifungal metabolite was isolated from endophytic fungus *Pestalotiopsis adusta*. This compound exhibited inhibitory action against three plant pathogens *G. zeae* (anamorph *F.graminearum*), and *V.albo-atrum, F.culmorum* [150].

PEPTIDES

Leucinostatin A

This antifungal secondary metabolite isolated from en endophytic fungus *Acremonium* sp. associated with *Taxus baccata*, an evergreen conifer tree. This compound also acts against phytopathofenic fungi *Pythium ultimum*, which causes root rot disease [151].

Cryptocandin

This is a lipopeptide produced by an endophytic fungus *Cryptosporiopsis quercina* , colonizes in Chinese medicinal plant. Well this also have antifungal properties against many phytopathogens like *Sclerotinia sclerotiorum*, which causes white mold disease over 400 plant species and Botrytis cinerea, a necrotic fungus affects grapes [152].

CONCLUSIONS

Plant-endophyte association is an amazing example of symbiotic relation. Today one of the most serious problems is environmental pollution by the use of chemical fertilizers and pesticides etc. The endophytes are able to promote growth and can improve yield of crops and sometimes fast growth also. They can also help in growth of plants under various stress conditions, so they can be used in agriculture. Bioactive secondary metabolites from endophytes have immense value in plant growth and agriculture, but these compounds also have antimicrobial, anticancer properties against human pathogens as well. There are many antimicrobial endophytic derivatives still need to be explored and these new findings may help in agriculture, pharmaceutical industries and in medical science. Till date there are huge data is present about how bioactive metbabolites act against human pathogen. But in case of antagonistic potential of these metabolites against phytopathogens , more investigations are needed on their mode of actions and that can enlighten the path for new research.

ACKNOWLEDGEMENT

The financial support for this work is from University Grants Commission under NET-JRF scheme is duly acknowledged.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Dawwam GE, Elbeltagy A, Emana HM, Abbas IH, Hassan MM. Beneficial effect of Plant growth promoting bacteria isolated from roots of potato plants. Annals of Agricultural Science. 2013;58(2):195-201.
2. Waqas M, Khan AL, Kamran M, Hamayun M, Kang SM, Kim YH, Lee IJ. Endophytic fungi produce gibberellins and indoleacetic acid and promotes during stress. host-plant growth .Molecules. 2012;17:10754-10773.
3. Nowak J, Asiedu SK, Lazarovits G .Enhancement of in vitro growth and transplant stress tolerance of potato and vegetable plantlets co-cultured with a plant growth promoting pseudomonad bacterium. In:Carr F, Chagvardieff P (eds) Proc. International Symposium on Ecophysiology and Photosynthesis in Vitro Culture, Aix-en-Provence, France CEA, Cadarache, 1995;France.173-188.
4. Redman RS, Sheehan KB, Stout RG, Rodriguez RJ. Thermotolerance generated by plant/fungal symbiosis. Science. 2002;298:1581.
5. Creus CM, Sueldo RJ, Barassi C. Water relation in *Azospirillum* inoculated wheat Seedlings under osmotic stress. Can. J. Bot. 1998;76:238-244.

6. Elbeltagy A, Nishioka K, Suzuki H, Sato T, Sato YI, Morisaki H, Mitsui H, Minamisawa K. Isolation and characterization of endophytic bacteria from wild and traditionally cultivated rice varieties. Soil Sci.Plant Nutr. 2000;46(3):617-629.
7. Gayathri S, Saravanan D, Radhakrishnan M, Balagurunathan R, Kathiresan K. Bioprospecting potential of fast growing endophytic bacteria from leaves of mangrove and salt-marsh plant species. Indian Journal of biotechnology. 2010; 9:397-402.
8. Dasgupta S, Meisner C, Wheeler D, Xuyen K, Lam N. Pesticide Poisoning of farm-workers-implication of blood test result from Vietnam. Int J of Hygiene Env Health. 2007;210:121-13
9. Sitaramaraju S, Prasad NVVSD, Chenga R, Vand Narayana E. Impact of pesticides used in crop production on the environment. Journal of Chemical and Pharmaceutical Science. 2014;3:75-79
10. De La T, Neyser VR, Clara IR, Martha R, Carlos A, Federico AG, Héctor P, Reiner R. Effect of plant growth-promoting bacteria on the growth and fructan production of *Agave americana* L. Brazilian J Microbiol. 2016;47:587–596.
11. Abdelaal KAA, Tawfik SF. Response of Sugar Beet Plant (*Beta vulgaris* L.) to mineral nitrogen fertilization and bio-fertilizers. Int J Curr Microbiol Appl Sci. 2015;4:677–688.
12. Abdelaal KAA, Badawy SA, Abdel Aziz RM, Neana SMM. Effect of mineral nitrogen levels and PGPR on morphophysiological characters of three sweet sorghum varieties (*Sorghum bicolor* L. Moench). J Plant Prod. 2015;6:189–203.
13. Taghavi S, Garafola C, Monchy S, Newman L, Hoffman A,Weyers N, Barac T, Vangronsveld J, Lelie D. Genome survey and characterization of endophytic bacteria exhibiting a beneficial effect on growth and development of Poplar trees. Applied and Environmental Microbiology. 2009;75 (3):748-757.
14. Hardoim RR, Van Overbeek LS, Elsas JD. Properties of bacterial endophytes and their their proposed role in plant growth. Trends Microbiol. 2008;16(10):463-471.
15. Balachandar D, Sandhiya GS, Sugitha TCK, Kumar K. Flavinoids and growth hormones influences endophytic colonization and in *Planta* Nitrogen fixation by diazotrophic *Serratia* sp. in rice. World Journal of Microbiology and Biotechnology. 2006;22(7):707-712.
16. Gaiero JR, McCall CA, Thomson KA, Day NJ, Best AS, Dunfield KE. Inside the root microbiome: Bacterial root endophytes and plant growth promotion. Am. J. Bot. 2013;100 (9):1738-1750.
17. Mulhopadhyay M, and Adhikari M . Endophytes of *Catharanthus roseus*: A potential source of plant growth promoters and antimicrobial compounds. Journal of Advanced Scientific Research. 2020;11(2):209-212.
18. Ambawade MS, and Pathade GR Production of gibberellic acid by *Bacillus siamensis* BE 76 isolated from banana plant (Musa sp.). Int. J. Sci. Res. 2013;4:394-398.
19. Win KT, Tanaka F, Okazaki K, Ohwaki Y. The ACC deaminase expressing endophyte *Pseudomonas* spp. Enhances NaCl stress tolerance by reducing stress related ethylene production, resulting in improved growth, photosynthetic performance and ionic balance in tomato plants. Plant Physiology and Biochemistry. 2018;127: 599-607.
20. Tan RX, and Zou WX. Endophytes: a rich source of functional metabolites. Nat Prod Rep. 2001;18(4):448-459.
21. Raza MA, Iqbal T, Naz I, Sehar S, Ahmed S. Isolation of anticancer and antimicrobial metabolites from Epicoccum nigrum;endophyte of *Ferula sumbul*. Microbial Pathogenesis. 2017;110:214-224.
22. Yadav AN. Agriculturally Important Microbiomes: Biodiversity and multifarious PGP attributes for amelioration of diverse abiotic stresses in crops for sustainable agriculture. Biomed J Sci & Tech Res. 2017;BJSTR.MS.ID.000321.

DOI: 10.26717/BJSTR.2017.01.000321

23. Luo S, Xu T, Chen L, Chen J, Rao C, Xiao X, Wan Y, Zeng G, Long F, Liu C, Liu Y. Endophyte-assisted promotion of biomass production and metal-uptake of energy crop sweet sorghum by plant-growth-promoting *Bacillus* sp. SLS18. Applied Microbiology and Biotechnology. 2012;93:1745-1753.
24. Kumar A, Tripti, Voropaeva O, Maleva M, Panikovskaya K, Borisova G, Rajkumar M, Bruno LB. Bioaugmentation with copper tolerant endophyte *Pseudomonas lurida* strain EOO26 for improved plant growth and copper phytoremediation by *Helianthus annuus*. Chemosphere. 2021;vol.266, 128983.
25. Babu AG, Kim JD, Oh BT. Enhancement of heavy metal phytoremediation by *Alnus firma* with endophytic Bacillus thuringiensis GDB-1. Journal of Hazardous Materials. 2013;250-251:477-483.
26. Ma Y, Rajkumar M, Moreno A, Zhang C, Freitas H. Serpentine endophytic bacterium *Pseudomonas azotoformans* ASS1 accelerates phytoremediation of soil metal under drought stress. Chemosphere. 2017;185:75-85.
27. Ryan RP, Germaine K, Franks A, Ryan DJ. Bacterial endophyte: Recent development and application. FEMS Microbiol. 2008;278:1-9.
28. Sun L, Qiu F, Zhang X, Dai X . Endophytic bacterial diversity in rice . (*Oryza sativa* L.) roots estimated by 16S rDNA sequence analysis. Microb Ecol. 2008;55:415-424.
29. Mengoni A, Pini F, Huang LN, Shu WS, Bazzicalupo M. Plant-by-plant variations of bacterial communities associated with leaves of Nickel hyperaccumulator *Alyssum bertolonii* Desv. Microb Ecol. 2009;58:660-667
30. Manter DK, Delgado J, Holm DG, Stong R . Pyrosequencing reveals a highly diverse and cultivar-specific bacterial endophyte community in potato roots. Microb Ecol. 2010;60:157-166.
31. Sessitsch A, Hardoim P, Döring J, Weilharter A, Krause A, Woyke T ,Mitter B, Hauberg-Lotte L, Friedrich F, Rahalkar M, Hurek T, sarkar A, Bodrossy L, Overbeek L, Brar D, Elsas JD, Reinhold-Hurek B. Functional characteristics of an endophyte community colonizing rice roots as revealed by metagenomic analysis. Mol. Plant-Microb. Interac. 2012;25(1):28-36.
32. Suhandono S, Kusumawardhani MK, Aditiawati P. Isolation and molecular identification of endophytic bacteria from Rambutan fruits (*Nephelium lappaceum* L.) cultivar Binjai. Hayati Journal of Biosciences. 2016;33.39-44.
33. Afzal I, Shinwari ZK, Iqrar I. Selective isolation and characterization of agriculturally beneficial endophytic bacteria from wild hemp using Canola. Pak. J. Bot. 2015; 47(5):1999-2008.
34. Anjum N, and Chandra R. Endophytic bacteria: Optimization of isolation procedure from various medicinal plants and their preliminary characterization. Asian J Pharm Clin Res. 2015;8(4):233-238.
35. Vibhuti M, Kumar A, Sheoran N, Nadakkakath AV, Eapen SJ. Molecular basis of endophytic *Bacillus megaterium*-induced growth promotion in *Arabidopsis thaliana*: Revelation by Microarray-based gene expression analysis. Journal of Plant Growth Regulation. 2017;36:118-130.
36. Kumar V, Jain L, Jain SK, Chaturvedi S, Kaushal P. Bacterial endophytes of rice (*Oryza sativa* L.) and their potential for plant growth promotion and antagonistic activities. South African Journal of Botany. 2020;134:50-63.
37. Roos IMM, Hattingh MJ. Scanning electron microscopy *Pseudomonas syringae* pv. Morsprunorum on sweet cherry leaves. Phytopathol Z.1983;108:18-25.
38. Scott RI, Chard JM, Hocart MJ, Lennard JH,Graham DC . Penetration of potato tuber lenticels by bacteria in relation to biological control of blackleg disease. Potato Res. 1996;39:333-334.
39. Agarwhal S and Shende ST. Tetrazolium reducing microbes inside the roots of *Brassica* sp. Curr. Sci. 1987;56:187-188.
40. Sørensen J, and Sessitsch A. Plant-associated bacterial lifestyle and molecular interactions. In:Van elsas JD, Kansson JK,

Trevors JI. (eds). Modern Soil Microbiology.CRC press. 2006;pp.211-236

41. Gagn S, Richard C, Rousseau H, Antoun H .Xylem-residing bacteria in alfalfa roots. Can. J. Microbiol. 1987;33(11):996-1005.
42. Huang J. Ultrastructure of bacterial penetration in plants. Annals. Rev. Phytopathol. 1986;24:141-157
43. Quadt-Hallmann A, Benhamou N, Kloepper JW. Bacterial endophytes in cotton: Mechanism of entering the plant. Can. J. Microbiol. 1997;43:557-582.
44. Song S, Otkur M, Zhang Z, Tang Q. Isolation and characterization of endophytic microorganisms in *Glaycyrrhiza inflat Bat*. from Xinjiang. Microbiology. 2007;5:867–870.
45. Mo L, Kang JC, He J, Cao JJ, Su H. A preliminary study on composition of endophytic fungi from *Gastrodia elata*. J. Fung. Res. 2008;6:211–215.
46. Wu L, Han T, Li W, Jia M, Xue L, Rahman K, Qin, L. Geographic and tissue influences on endophytic fungal communities of *Taxus chinensis* var. mairei in China. Curr. Microbiol. 2013;66:40–48.
47. Balsanelli E, Tadra-Sfeir MZ, Faoro H, Pankievicz VC, de Baura VA, Pedrosa FO, de Souza EM, Dixon R, Monteiro RA. Molecular adaptations of *Herbaspirillum seropedicae* during colonization of the maize rhizosphere. Environ Microbiol. 2016;18(8):2343-2356.
48. Meneses CH, Rouws LF, Simoes-Araujo JL, Vidal MS, Baldani JI. Exopolysaccharide production is required for biofilm formation and plant colonization by the nitrogen-fixing endophyte *Gluconacetobacter diazotrophicus*. Mol Plant Microbe Interact. 2011;24(12):1448-1458.
49. Williams A, Wilkinson A, Krehenbrink M, Russo DM, Zorreguieta A, Downie JA. Glucomannan-mediated attachment of *Rhizobium leguminosarum* to pea root hairs is required for competitive nodule infection. J Bacteriol. 2008;190(13):4706-4715.
50. Kandel SL, Joubert PM, Doty SL. Bacterial endophyte colonization and distribution within plants. Microorganisms. 2017;5(4):77.
51. Reinhold-Hurek B, Maes T, Gemmer S, Van Montagu M, Hurek T. An endoglucanase is involved in infection of rice roots by the not-cellulose-metabolizing endophyte *Azoarcus* sp. strain BH72. Mol. Plant Microbe Interact. 2006;19:181–188.
52. Fan X, Yang R, Qiu S, Cai X, Zou H, Hu F. The Endo-β-1,4-Glucanase of *Bacillus amyloliquefaciens* is required for optimum endophytic colonization of plants. J Microbiol Biotechnol. 2016;26(5):946-952
53. Davison, J. Plant beneficial bacteria. Bio/Technology. 1988;6:282–286.
54. Kloepper JW, Lifshitz R, Zablotowicz RM. 1989. Free-living bacterial inocula for enhancing crop productivity. Trends Biotechnol.1989;7:39–43.
55. Kumar V, Kumar A, Pandey KD, Roy BK. Isolation and characterization of bacterial endophytes from the roots of *Cassia tora* L. Ann Microbiol. 2015; 65:1391–1399.
56. Shi Y, Lou K, Li C. Promotion of plant growth by phytohormone- producing endophytic microbes of sugar beet. Biol Fertil Soils. 2009;45:645–653.
57. Patel HA, Patel RK, Khristi SM, Parikh K, Rajendran G. Isolation and characterization of bacterial endophytes from *Lycopersicon esculentum* plant and their plant growth promoting characteristics. Nepal Journal of Biotechnology. 2012;2(1):37-52.
58. Orlandelli RC, Alberto RN, Almeida TT, Azevedo JL, Pamphile JA. In vitro antibacterial activity of crude extractspProduced by endophytic fungi isolated from *Piper hispidum* Sw. Journal of Applied Pharmaceutical Science. 2012;2(10):137-141
59. Praptiwi, Raunsai M, Wulansari D, Ahmad F, Agusta A. Antibacterial and antioxidant activities of endophytic fungi extracts of medicinal plants from Central Sulawesi. Journal of Applied Pharmaceutical Science. 2018;8(08):069-074.
60. Anjugam M, Bharathidasan R, Shijila Rani AS, Ambikapathy V. Evaluation of antimicrobial activities of endophytic

fungal metabolites against clinical importance microbes. Journal of Pharmacognosy and Phytochemistry. 2019;8(2):1004-1007.

61. Oliveira MF, Silva MG, Van Der Sand ST. Anti-phytopathogen potential of endophytic actinobacteria isolated from tomato plants (*Lycopersicon esculentum*) in southern Brazil, and characterization of *Streptomyces* sp. R18(6), a potential biocontrol agent. Research in Microbiology. 2010;161:565-572.
62. Conn VM, Walker AR, Franco CMM. Endophytic actinobacteria induce defense pathways in *Arabidopsis thaliana*. Molecular Plant-Microbe Interactions. 2008;21(2):208-218.
63. Chet I, and Inbar J. Biological control of fungal pathogens. Appl. Biochem. Biotechnol. 1994;48:37–43.
64. O'Sullivan DJ, and O'Gara F. Traits of fluorescent *Pseudomonas* spp. involved in suppression of plant root pathogens. Microbiol. Rev. 1992;56:662–676.
65. Woodward AW, and Bartel B. Auxin: regulation, action, and interaction. Ann Bot. 2005;95:707–735.
66. Vanneste S and Friml J. Auxin: a trigger for change in plant development. Cell. 2009;136:1005–1016.
67. Muller A, Hillebrand H, Weiler EW. Indole-3-acetic acid is synthesized from L-tryptophan in roots of *Arabidopsis thaliana*. Planta. 1998;206:362–369.
68. Ljung K, Hull AK, Celenza J, Yamada M, Estelle M, Normanly J, Sandberg G. Sites and regulation of auxin biosynthesis in Arabidopsis roots. Plant Cell. 2005;17:1090– 1104.
69. Ljung K, Bhalerao RP, Sandberg G. Sites and homeostatic control of auxin biosynthesis in Arabidopsis during vegetative growth. Plant J. 2001;28:465–474.
70. Koornneef M, van der Veen JH. Induction and analysis of gibberellin sensitive mutants in *Arabidopsis thaliana* (L.) Heynh. Theor Appl Genet. 1980;58:257–63.
71. Aloni R. Role of Auxin and Gibberellin in differentiation of primary phloem fibers. Plant Physiol. 1979;63:609-614.
72. Yang T, Davies PJ, Reid JB. Genetic dissection of their relative roles of auxin and gibberellin in the regulation of stem elongation in intact Light-Crown Peas. Plant Physiol. 1996;110:1029-1034.
73. Cheng H, Qin L, lee S, Fu X, Richards DE, Cao D, Luo D, Harberd NP, Peng J. Gibbrellin regulates *Arabidopsis* floral development via suppression of DELLA protein function. Development. 2004;131(5):1055-1064.
74. Guangwu Z and Xuwen J. Roles of gibberellin and auxin in promoting seed germination and seedling vigor in *Pinus massoniana*. For. Sci. 2014;60(2):367–373.
75. Khan AL, Waqas M, Kang SM, Harrasi AA, Hussain J. Bacterial endophyte *Sphingomona*s sp. LK11 produces gibberellins and IAA and promotes tomato plant growth.The Journal of Microbiology. 2014;52(80):689-695.
76. Khan Z, and Doty A. Characterization of bacterial endophytes of sweet potato plants. Plant and Soil; 2009.
DOI 10.1007/S11104-009-9908-1
77. Dias A, Costa F, Andreote F, lacava P, Teixeira M, Assumpcao L, Araujo W, Azevedo J, Melo I. Isolation of micropropagated strawberry endophytic bacteria and assessment of their potential for plant growth promotion. World J Microbiol Biotechnol. 2009;25:189-195.
78. Faria D, Dias A, Melo I, Costa F . Endophytic bacteria isolated from orchid and their potential to promote plant growth. World J Microbiol Biotechnol. 2013;29:217-221.
79. Singh NP, Singh RK, Shahi JP, Jaiswal HK, Singh T. Application of bacterial endophytes as bioinoculant enhances germination, seedling growth and yield of maize (*Zea mays* L.). Range Mgmt. and Agro forestry. 2013;34(2):171-174.
80. Mukhopadhyay M and Chakraborty S. RICE ENDOPHYTES: A potential source of phytohormones and antimicrobials.

Asian Jr. of Microbiol. Biotech. Env. Sc. 2019;21(2):418-423.

81. Mukhopadhyay M, Thapa M, Firoz A.Potentials of endophytes of *Rhododendron arboreum* for the production of plant growth promoting factors and antimicrobial compounds. Plant Cell Biotechnology and Molecular Biology. 2021;22(23&24):108-115.
82. Shan W, Zhou Y, Liu H, Yu X. Endophytic *Actinomycetes* from tea plants (*Camellia sinensis*): Isolation, Abundance, antimicrobial, and plant-growth-Promoting activities. BioMed Research International.vol 2018;Article ID 1470305.
83. Klee HJ, Hayford MB, Kretzmer KA, Barry GF, Kishore GM. Control of ethylene synthesis by expression of a bacterial enzyme in transgenic tomato plants. Plant Cell. 1991;3:1187–1193.
84. Campbell BG, and Thompson JA. 1-Aminocyclopropane-1-carboxylate deaminase genes from *Pseudomonas* strains. FEMS Microbiol. Lett. 1996;138:207–210.
85. Jacobson CB, Pasternak JJ, Glick BR. Partial purification and characterization of ACC deaminase from the plant growth-promoting rhizobacterium *Pseudomonas putida* GR12-2. Can. J. Microbiol. 1994;40:1019–1025.
86. Glick BR, Penrose DM, Li J. A model for the lowering of plant ethylene concentrations by plant growth promoting bacteria. J. Theor. Biol. 1998;190:63–68.
87. Long HH, Schmidt DD, Baldwin IT. Native bacterial endophytes promote host growth in a species-specific manner;Phytohormone manipulation do not result in common growth responses. Public Library of Science. 2008;3(7):1-29.
88. Sun Y, Cheng Z, Glick BR .The presence of a 1-aminocyclopropane-1-carboxylate (ACC) deaminase deletion mutation alters the physiology of the endophytic plant growth-promoting bacterium *Burkholderia phytofirmans* PsJN. Federation of European Microbiological Societies. 2009;296:131-136.
89. Apelbaum A, and Yang SF. Biosynthesis of stress ethylene induced by water deficit. Plant Physiol. 1981;68:594-596.
90. Ali S, Charles TC, Glick BR. Amelioration of high salinity stress damage by plant growth promoting bacterial endophytes that contain ACC deaminase. Plant Physiology and Biochemistry. 2014;80:160-167.
91. Santos PE, Cristales RB, Mellado JC . *Burkholderia*, a genus rich in plant-associated nitrogen fixers with wide environmental and geographic distribution. Applied and Environmental Microbiology. 2001;67(6):2790-2798.
92. Dobereiner J, and Cavalcante VA. A new acid-tolerant nitrogen fixing bacterium associated with sugarcane. Plant and Soil.1988;108:23-31.
93. Asis Jr. CA, Kubota M, Ohta H, Arima Y, Chebotar VK, Tsuchiya K, Akao S. Isolation and partial characterization of endophytoc diazotrophs associated with Japanese sugarcane cultivar. Soil Science and Plant Nutrition. 2000;46(3):759-765.
94. Loiret FG, Ortega E, Kleiner D, Ortega-Rodes P, Rodes R, Dong Z. A putative new endophytic nitrogen fixing bacterium *Pantoea* sp. from sugarcane. Journal of Applied Microbiology. 2004;97:504-511.
95. Hongrittipun P, Youpensuk S, Rerkasem B. Screening of nitrogen fixing endophytic bacteria in *Oryza sativa* L. Journal of Agriculture Science. 2014;6(6):66-74.
96. Wei CY, Lin L, Luo L, Xing Y, Hu CJ, Yang LT, Li YR, An Q. Endophytic nitrogen fixing *Klebsiella variicola* strain DX120E promotes sugarcane growth. Biol. Fertil. Soils. 2014;50:657-666.
97. Muangthong A, Youpensuk S, Rerkasem B .Isolation and characterization of endophytic nitrogen fixing bacteria in sugarcane. Tropical Life Science Research. 2015;26(1):41-51.
98. Alishahi F, Alikhani HA, Khoshkholgh-Sima NA, Etesami H. Mining the roots of various species of the halophyte *Suaeda* for halotolerant nitrogen-fixing endophytic bacteria with the potential for promoting plant growth. Int Microbiol. 2020;23:415–427.

99. Hongrittipun P, Youpensuk S, Rerkasem B. Screening of nitrogen fixing endophytic bacteria in *Oryza sativa* L. Journal of Agricultural Science. 2014;6(60):66.
100. Aoun M, El Samrani AG, Lartiges BS, Kazpard V, Saad Z. Releases of phosphate fertilizer industry in the surrounding environment: investigation on heavy metals and polonium-210 in soil. J Environ Sci (China). 2010;22(9):1387-1397.
101. Kpomblekou K, and Tabatabai MA. Effect of organic acids on release of phosphorus from phosphate rocks. Soil Science. 1994;158(6):442-453.
102. Oteino N, Lally RD, Kiwanuka S, Lloyd A, Ryan D, Germaine KJ, Dowling DN. Plant growth promotion induced by phosphate solubilizing endophytic *Psudomonas* isolates. Frontiers in Microbiology. 2015;6 (745):1-9.
103. Abreu CS, Figueiredo JEF, Oliveira CA, Santos VL, Gomes EA, Ribeiro VP, Barros BA, Lana UGP, Marriel IE . Maize endophytic bacteria as mineral phosphate solubilizers. Genetics and Molecular Research. 2017;16(1):1-13.
104. Singh R, and Arora NK. Growth enhancement of medicinal plant *Withania somnifera* using phosphate solubilizing endophytic bacteria *Pseudomonas* sp. International Journal of Science, Technology and Society. 2016;2:13-18.
105. Matos ADM, Gomes ICP, Nietsche S, Xavier AA, Gomes WS, Neto JAS, Pereira MCT. Phosphate solubilization by endophytic bacteria isolated from banana trees. Annals of The Brazilian Academy of Science. 2017;89(4):2945-2954.
106. Alexander BD, and Zeeberi DA. Use of chromazurol S to evaluate siderophore production by rhizosphere bacteria. Biol. Fertil. Soils. 1991;2:39-54.
107. Jasim B, Joseph AA, John CJ, Mathew J, Radhakrishnan EK. Isolation and characterization of plant growth promoting endophytic bacteria from the rhizome of *Zingiber officinale*. 3 Boitech. 2014;4:197-204.
108. Rungin S, Indananda C, Suttiviriya P, Kruasuwan W, Jaemsaeng R, Thamchaipenet A. Plant growth enhancing effects by a siderophore-producing endophytic *Streptomycete* isolated from a Thai jasmine rice Plant (Oryza sativa L. cv. KMDL105). Antonie van Leeuwenhoek. 2012;102:463-472.
109. Loaces I, Ferrando L, Scavino AF. Dynamics, diversity and function of endophytic siderophore-producing bacteria in rice. Microb Ecol. 2011;61:606-618.
110. Logeshwaran P, Thangaraju M, Rajasundari K. Hydroxymate siderophores of endophytic bacteria *Gluconacetobacter diazotrophicus* isolated from sugarcane roots. Australian Journal of Basic and Applied Science. 2009;3(4):3564-3567.
111. Ramesh R, Joshi AA, Ghanekar MP . *Pseudomonas*:major antagonistic bacteria to suppress bacterial wilt pathogen, *Ralstonia solanacearum* in egg plant (*Solanum melongena* L.). World Journal Microbiol Biotechnol.2009;25:47-55.
112. Liu CH, Zou WX, Lu H, Tan RX. Antifungal activity of *Artemisia annua* endophyte cultures against phytopathogenic fungi. Journal of Biotechnology. 2001;88:277–282.
113. Kusari P, Kusari S, Spiteller M, Kayser O. Endophytic fungi harbored in *Cannabis sativa* L.: diversity and potential as biocontrol agents against host plant-specific phytopathogens. Fungal Diversity. 2013;60:137–151.
114. del Barrio-Duque A, Ley J, Samad A, Antonielli L, Sessitsch A, Compant S. Beneficial endophytic bacteria- *Serendipita indica* interaction for crop enhancement and resistance to phytopathogens. Front Microbio. 2019;10:2888. DOI:10.3389/fmicb.2019.02888
115. Amaresan N, Jayakumar V, Thajuddin N.Isolation and characterization of endophytic bacteria isolated from chilli (*Capsicum annuum*) grown in costal agricultural ecosystem. Indian Journal of Biotechnology. 2014;13:247-255.
116. Yang CJ, Zhang XG, Shi GY, Zhao HY, Chen L, Tao K, Hou TP. Isolation and identification of endophytic bacterium W4 Against tomato *Botrytis cinerea* and

antagonistic activity stability. African Journal of microbiology Research. 2011;5(2):131-136.

117. Sun ZB, Yuan XF, Zhang H, Wu LF, Liang C, Feng YJ. Isolation, screening and identification of antagonistic downy mildew endophytic bacteria from cucumber. Eur. J. Plant. Pathol. 2013;137:847-857
118. Zamoum M, Goudjal Y, Sabaou N, Barakate M, Mathieu F, Zitouni A. Biocontrol capacities and plant growth-promoting traits of endophytic actinobacteria isolated from native plants of Algerian Sahara. Journal of Plant Diseases and Protection. 2015;122(5/6):215–223.
119. Silva GH, De Oliveira CM, Teles HL, Pauletti PM, Castro-Gamboa I, Silva DHS, Bolzani VS, Young MCM, Costa-Neto CM, Pfenning LH, Berlinck RGS, Araujo AR. Sesquiterpenes from *Xylaria* sp., an endophytic fungus associated with *Piper aduncum* (Piperaceae). Phytochem Lett. 2010;3:164–167.
120. Weerapreeyakul N, Anorach R., Khuansawad T, Yenjai C, Isaka M. Synthesis of bioreductive esters from fungal compounds. Chem Pharm Bull. 2007;55:930–935.
121. Cutler HG, and LeFiles JH. Trichodermin: effects on plants. Plant Cell Physiol. 1978;19:177–182.
122. Chen L, Chen J, Zheng X, Zhang J, Yu X.Identification and antifungal activity of of the metabolite of endophytic fungi isolated from *llex cornuta* [J]. Chinese Journal of Pesticide Science. 2007;9(2):143–150
123. Carter CJ, Cannon M, Smith KE. Inhibition of protein synthesis in reticulocyte lysates by trichodermin. Biochem. J. 1976;154:171–178.
124. Silva GH, Teles HL, Zanardi LM, Marx Young MC, Eberlin MN, Hadad R, Pfenning LH, Costa-Neto CM, Castro-Gamboa I,da Silva Bolzani V, Araujo AR. Cadinane sesquiterpenoids of *Phomopsis cassiae*, an endophytic fungus associated with Cassia spectabilis (Leguminosae). Phytochemistry. 2006;67(17):1964–1969.
125. Zhou X, Zhu H, Liu L, Lin J, Tang K. A review: recent advances and future of taxol-producing endophytic fungi. Appl. Microbiol. Biotechnol. 2010; 86:1707–1717.
126. Pongcharoen W, Rukachaisirikul V, Phongpaichit S, Kühn T, Pelzing M, Sakayaroj J, Taylor WC. Metabolites from the endophytic fungus *Xylaria* sp. PSU-D14. Phytochemistry. 2008;69(9):1900-2.
127. Singh MP, Janso JE, Luckman SW, Brady SF, Clardy J,Greenstein M, Maiese WM. Biological activity of guanacastepene, a novel diterpenoid antibiotic produced by an unidentified fungus CR115. J. Antibiot. 2000;53: 256–261.
128. Strobel GA, Hess WM, Li JY, Ford E, Sears J, Sidhu RS, Summerell B. *Pestalotiopsis guepinii*, a taxol producing endophyte of the Wollemi Pine, *Wollemia nobilis*. Aust J Bot.1997;45:1073–1082.
129. Yuan L, Zhao PJ, Ma J, Lu C.-H, Shen Y.-M. Labdane and tetranorlabdane diterpenoids from *Botryosphaeria* sp. MHF, an endophytic fung *Maytenus hookeri*. Helv. Chim. Acta. 2009;92:1118-1125.
130. Zhao J, Mou Y, Shan T, Li Y, Zhou L, Wang M, Wang J. Antimicrobial Metabolites from the endophytic fungus *Pichia guilliermondii* isolated from *Paris polyphylla* var. yunnanensis. Molecules. 2010;15(11):7961-7970.
131. Mei WL, Zheng B, Zhao YX, Zhong HM, Chen XLW, Zeng YB, Dong WH, Huang JL, Proksch P, Dai HF. Meroterpenes from endophytic fungus A1 of mangrove plant *Scyphiphora hydrophyllacea*. Mar. Drugs. 2012;10:1993-2001.
132. Fill TP, Pereira GK, Santos MG, Rodrigues-Filho E. Four additional meroterpenes produced by *Penicillium* sp. found in association with *Melia azedarach*. Possible biosynthetic intermediates to Austin. Z. Naturforsch. B: Chem. Sci. 2007;62:1035-1044.
133. Ma YM, Qiao K, Kong Y, Li MY, Guo LX, Miao Z, Fan C. A new isoquinolone alkaloid from an endophytic fungus R22 of *Nerium indicum*. Natural Product Research. 2017;31(8):951-958.

134. Pinheiro EA, Carvalho JM, dos Santos DC, Feitosa AD, Marinho PS, Guilhon GM, de Souza AD, da Silva FM, Marinho AM. Antibacterial activity of alkaloids produced by endophytic fungus *Aspergillus* sp. EJC08 isolated from medical plant *Bauhinia guianensis*. Natural product research. 2013; 27(18):1633-1638.
135. Yu Y, Ma BJ, Liu JS, Yue JY, Chen HP, Liang YM, Zhou ZY, Wang GK, Wang G. Two new alkaloid metabolites produced by endophytic fungus *Stagonosporopsis oculihominis* isolated from *Dendrobium huoshanense*. Phytochemistry Letters. 2017;19:266-270.
136. Cruz-Miranda OL, Folch-Mallol J, Martínez-Morales F, Gesto-Borroto R, Villarreal ML, Taketa AC. Identification of a Huperzine A-producing endophytic fungus from *Phlegmariurus taxifolius*. Molecular biology reports. 2020;47(1):489-495.
137. Li E, Jiang L, Guo L, Zhang H, Che Y. Pestalachlorides A– C, antifungal metabolites from the plant endophytic fungus *Pestalotiopsis adusta*. Bioorg. Med. Chem. 2008;16:7894–7899.
138. Li JY, Strobel G, Harper J, Lobkovsky E, Clardy J. Cryptocin, a potent tetramic acid antimycotic from the endophytic fungus *Cryptosporiopsis* cf. quercina. Org. Lett. 2000;2:767–770.
139. KusariS, Zuhlke S, Spiteller M. An endophytic fungus from *Camptothec acuminata* that produces camptothecin and analogues. J Nat Prod. 2009;72:2–7.
140. Shweta S, Zuehlke S, Ramesha BT, Priti V, Mohanakumar P, Ravikanth G, Spiteller M. Endophytic fungal strains of *Fusarium solani*, from *Apodytes dimidiata* E. Mey.ex Arn (*Icacinaceae*) produce camptothecin, 10-hydroxycamptothecin and 9-methoxycamptothecin. Phytochemistry. 2010;71(1):117–122.
141. Blankenship JD, Spiering MJ, Wilkinson HH, Fannin FF, Bush LP, Schardl CL. Production of loline alkaloids by the grass endophyte, *Neotyphodium uncinatum*, in defined media. Phytochemistry. 2001;58: 395–401
142. Wilkinson HH, Siegel MR, Blankenship JD, Mallory AC, Bush LP, Schardl CL. Contribution of fungal loline alkaloids to protection from aphids in a grass-endophyte mutualism. Mol.Plant MicrobeInteract. 2000;13:1027–1033.
143. Lehtonen P, Helander M, Wink M, Sporer F, Saikkonen K. Transfer of endophyte origin defensive alkaloids from a grass to a hemiparasitic plant. Ecol.Lett. 2005;8:1256–1263.
144. Spiering MJ, Moon CD, Wilkinson HH, Schardl CL. Gene clusters for insecticidal loline alkaloids in the grass-endophytic fungus *Neotyphodium uncinatum*. Genetics. 2005;169:1403–1414.
145. Schardl CL. The epichloae symbionts of the grass subfamily Poöideae. Ann. Mo. Bot. Gard. 2010;97: 646–665
146. Schulz B, Sucker J, Aust HJ, Krohn K, Ludewig K, Jones PG, Doring D. Biologically active secondary metabolites of endophytic *Pezicula* species. Mycol. Res. 1995;99(8):1007–1015.
147. Zou WX, Meng JC, Lu H, Chen GX, Shi GX, Zhang TY, Tan RX. Metabolites of *Colletotrichum gloeosporioides*, an endophytic fungus in *Artemisia mongolica*. J Nat Prod. 2000;63(11):1529-1530.
148. Wicklow DT, Roth S, Deyrup ST, Gloer JB. A protective endophyte of maize: *Acremo- nium zeae* antibiotics inhibitory to *Aspergillus flavus* and *Fusarium verticillioides*. Mycol.Res. 2005;109:610–618.
149. Wicklow DT, and Poling SM. Antimicrobial activity of pyrrocidines from *Acremonium zeae* against endophytes and pathogens of maize. Phytopathology. 2009;99:109–115.
150. Li E, Jiang L, Guo L, Zhang H, Che Y. Pestalachlorides A-C, antifungal metabolites from the plant endophytic fungus *Pestalotiopsis adusta*. Bioorg Med Chem. 2008;16(17):7894-7899.
151. Strobel G, Torczynski R, Bol-lon A. *Acremonium* sp. a leucinostatin A producing endophyte of European yew (*Taxus baccata*). Plant Sci. 1997;128:97–108.

152. Strobel GA, Miller RV, Martinez-Miller C, Condron MM, Teplow DB, Hess WM. Cryptocandin, a potent antimycotic from the endophytic fungus *Cryptosporiopsis* cf. *quercina*. Microbiology.1999;145:1919-1926.

153. Adhikari Dhungana S, Adachi F, Hayashi S, Raj Puri R, Itoh K. Plant growth promoting effects of Nepalese sweet potato endophytes. Horticulturae. 2018;4(4): 53.

154. Polonio JC, Almeida TT, Garcia A, Mariucci GEG, Azevedo JL, Rhoden SA, Pamphile JA. Biotechnological prospecting of foliar endophytic fungi of guaco (*Mikania glomerata* Spreng.) with antibacterial and antagonistic activity against phytopathogens. Genetics and Molecular Research. 2015;14(3):7297-7309.
