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Plant bacterial endophytes as a potent source of plant growth promoters and other bioactive compounds: A Review

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ABSTRACT

The global climate is drastically changing. Climate change factors such as enhanced CO_2 levels, increased temperature and drought affect all plant-microorganism interactions. Plants are associated with a variety of microorganisms which can occur as epiphytes or endophytes. Endophytes are present inside the host plants whereas epiphytes are present on the surface of host plants. Endophytes are known to be reservoirs of novel bioactive compounds such as phenolic acids, alkaloids, terpenoids and steroids that has properties such as anti-microbial, anticancer and anti-insect. They are also known to enhance the growth of host plants and provide resistance to several diseases, biotic and abiotic stresses. This review aims to discuss the various functions and behavior of endophytes and the effect of climatic changes on their activities.

***Key words:** Endophytes, Bioactive compounds, Climate change, Biotic stress, Abiotic stress*

Introduction

Due to several natural and anthropogenic activities the global climate is drastically changing. Concentration of atmospheric CO_2 and global surface temperatures has increased steadily leading to decreased soil water content which in turn increased drought in several areas of the world. Climate change is known to affect all kinds of macroorganisms as well as microorganisms. All investigated plant taxa have well established symbiosis with microorganisms (Nicolson, 1967; Brundrett, 2009). The associations can be neutral, pathogenic or beneficial to the host (de Bary, 1879).

Endophytes are a group of microorganisms that colonize the inter- and/or intracellular locations of plants. (Pimentel *et al*., 2011; Singh and Dubey, 2015). All or part of their lifecycle occurs within their host, without causing any diseases. They are ubiquitous in nature. Endophytes provide various benefits to the host plants such as growth enhancement, nutrient gain, tolerance of various abiotic and biotic stress, insect and pest resistance. They produce a wide array of bioactive compounds (Joseph *et al.*, 2011; Parthasarathi *et al*., 2012; Compant *et al.*, 2010). These microorganisms greatly influence the survival and health of the host plants. This relationship is thought to have evolved 60 million years ago and provides benefits for both the partners. It has played an important role in land ecosystems (Arora *et al.*, 2018). Endophytes are also sources of novel natural products which are used in medicine, agriculture and industry (Maela *et al*., 2019). Climatic changes leads to altered environmental conditions which induce several changes in physiology and root exudation of plants. Factors such as elevated

CO_2 levels, elevated temperature and drought lead to changes in the abundance, composition or activity of plant associated microorganisms. Thus, it will also affect the interactions of endophytes with their host plants (Compant *et al*., 2010).

Endophytes

De Bary introduced the term endophyte and defined it as any organism that grows within plant tissues. One or more endophytes can be present in a single plant. They can colonize various structures of a plant such as the stem, roots, leaves, petioles, seeds and buds (Oldroyd *et al*., 2011; Turner *et al*., 2013; Andreote *et al*., 2014). The population of endophytes in a plant is variable. It depends on various factors such as host species, host developmental stage, climatic conditions and inoculum density (Gouda *et al.*, 2016).

Endophytes can be 'obligate' or 'facultative' (Rosenblueth and Martínez- Romero, 2006). Obligate endophytes are those that depend on the metabolism of plants for their survival, being spread by different types of vectors or by vertical transmission (Hardoim *et al*., 2008). Facultative endophytes are those that can survive outside the body of the host during a certain stage of their lifecycle (Abreu-Tarazi *et al*., 2010). Endophytes are present in various forms such as bacteria (actinomycetes or mycoplasma) or fungi. More than 200 genera of bacterial species have been known to be associated with endophytes. Most of the species belong to the phyla Actinobacteria, Proteobacteria and Firmicutes (Golinska *et al*., 2015). Gram negative to gram positive bacteria such as *Achromobacter, Acinetobacter, Agrobacterium, Bacillus, Brevibacterium, Pseudomonas, Xanthomonas* etc. are present as endophytes (Sun *et al*., 2013) Bacterial endophytes produce various bioactive metabolites that act as antimicrobial and anticancer compounds (Berdy, 2012).

Actinomycetes belong to the phylum Actinobacteria and possess fungal like mycelium and spores. Endophytic actinomycetes are known to produce many chemical entities of medical importance such as antimicrobial compounds (Chaudhary *et al*., 2013; Barka *et al*., 2016; Gayathri and Muralikrishnan, 2013; Singh and Dubey, 2015). Compounds such as munumbicins (A and B), naphthomycin (A and K), clethramycin and coronamycin have been isolated from *Streptomyces* sp. Other compounds have also been isolated from *Kitasatospora* sp. and *Emblica officinalis* (Zhao *et al*., 2011; Gangwar *et al*., 2014; Golinska *et al*., 2015).

Endophytic mycoplasma are known to be in a symbiotic relationship with some red algae such as *Bryopsis pennata* and *B. hypnoides* (Hollants *et al*., 2011)

Endophytic fungi include clavcipitaceous and non-clavicipitaceous endophytes. They produce the most widely used anticancer drugs and antibiotics. *Penicillium* sp. produces penicillenols which is cytotoxic to various cell lines. Taxol produced by *Taxomyces andreanae*, Clavatol (*Torreya mairei*), sordaricin (*Fusarium* sp.), jesterone (*Pestalotiopsis jester*) possess antibacterial ad antifungal properties against many foodborne infectious agents (Jalgaonwala *et al*., 2011).

Colonization of plants by endophytes

The colonization process is similar for both bacterial and fungal endophytes but their mode of colonization is different. Fungal colonization is intercellular and intracellular, while bacterial colonization is only intercellular. Endophytes penetrate the plant tissues through root hairs and epidermis by the production of pectin degrading enzymes without causing any harm to the plant (Maela *et al.*, 2019).

Bacterial endophytes colonize plants by passive invasion in the roots through open root sites or wounds. Bacteria possess certain traits known as colonization traits which regulate the whole plant colonization process. It also regulates the communication between the plant and bacterial endophytes and vice versa (Schulz and Boyle, 2006; Dutta *et al*., 2014). Bacterial endophytes contain cell wall degrading enzymes such as cellulase, pectinases, endoglucanases and exoglucanases that actively hydrolyze the exodermal cell walls of the plant host (Singh *et al*., 2017). There is a limited concentration of nutrients in the upper parts of fruits, seeds, flowers, shoots and leaf apoplast, hence only a small fraction of bacterial endophytes colonize there.

In addition to plant roots, bacterial endophytes enter the plants through aerial tissues that are above the ground through passive or active mechanisms. It allows the endophytes to travel from the rhizhoplane into the cortical cell layers (Hardoim *et al*., 2015; Dutta *et al*., 2014; Frank *et al*., 2017). Upon entering the plant tissues, the bacteria get transported by the xylem vascular system resulting in systematic colonization by endophytes of internal tissues within the host plant. Depending on the host species and the strain, bacterial endophytes also use different mechanisms such as motility, chemotaxis and quorum sensing to enter the host plant (Maela *et al*., 2019; Frank *et al*., 2017).

The process of colonization begins with the bacterial endophytes first attaching to the plant roots or other opening sites using type IV pili. Bacterial cells synthesize exopolysaccharides (EPS) and lipopolysaccharides which also aid in the attachment and colonization process. Type III Protein Secretion Systems (TTSS) regulate the recognition of bacterial endophytes by host plants (Ibá-ez, 2017). The endophytic bacteria are able to form biofilms which have unique properties based on the type of tissue that has been colonize. In *Gluconacetobacter diazotrophicus,* a gene cluster gumD was required for plant colonization and biofilm formation (Kandel *et al*., 2017).

Bacteria interact within the plant tissues by active motility, surface proteins, polysaccharides and adhesions. Flavonoids stimulate colonization process. It regulates various bacterial genes such as genes for phytoalexin resistance, genes for synthesizing lipopolysaccharides and type III secretion (Dutta *et al*., 2014; Rosenblueth *et al*., 2006).

Regulation of host plant's immune system by endophytes

In order to colonize the host plant, endophytes have to pass through the defense of the plant's immune system. This process involves the recognition of certain conserved molecules known as microbe- or pathogen-associated molecular patterns (MAMPs or PAMPs) by the host plant's pattern recognition receptors (PRRs) on the plant cell surface. Some of the most worked upon MAMPs include flagellin, elongation factor TU, lipopolysaccharide, bacterial superoxide dismutase and peptidoglycan. Endophytic bacteria produce their own MAMPs that are not recognized by PRRs of the host plant or they elicit a weak defense reaction compared to pathogenic interactions. Some fungal endophytes avoid recognition by the plant as they produce chitin deacetylases that deacetylate chitosan oligomers (Newman *et al*., 2013; Vandenkoornhuyse *et al*., 2015; Arora *et al*., 2018).

Enzymes like superoxide dismutases (SOD), catalases (CatA), glutathione S-transferases(GSTs), peroxidases (POD) and alkyl hydroperoxide reductases (AhpC) produced by endophytes aids in their protection from the defense mechanism of plants, which involve processes such as generation of reactive oxygen species (ROS) or oxidative bursts (Zeidler *et al*., 2004). The plant immune system can also be modulated by protein secretion systems (SSs) in bacteria. Type III (T3SS) and type IV (T4SS) secretion systems deliver effector proteins by pathogenic bacteria into plants. Although in certain rhizobial strains T3SS is important for nodulation of legumes, these are generally either absent or present in low quantity in endophytic bacteria (Green and Mecsas, 2016; Liu *et al*., 2017).

Endophytes and Climate Change

The mechanisms by which endophytes influence plant growth and mitigation of biotic and abiotic stresses were discussed. Endophytes depend on root exudates and plant metabolites and are influenced by altered environmental conditions due to climate change. Hence the endophytic communities are also affected by the physiological changes of the plant.

Effect of enhanced CO_2 levels: 'Free Air CO_2 Enrichment (FACE)' experiment performed in Switzerland provide most information on the effects of increased CO_2 levels on plant associated bacteria (Hebeisen *et al*., 1997).According to this experiment elevated CO_2 increased the interaction between legumes and rhizobia which fixed nitrogen and formed 17% more nodules than rhizobia growing in ambient CO_2 concentration. It also enhanced plant growth (Schortemeyer *et al*., 1996; Marilley *et al*., 1999; Montealegre *et al*., 2000). Some plants under elevated CO_2 levels favors some *Rhizobium leguminosarum* strains over others. Moreover, reduced nitrogen concentration in tissues of common beans were also reported. It can be due to increased root exudation and enhanced plant-microbial nitrogen completion in the rhizosphere.

Enhanced CO_2 levels also exerted positive effects on antibiotic producing genes of *Pseudomonas* and *Burkholderia* sp. However, strong antibiotic producers such as *Actinomycetes* and *Bacillus* sp. remained unaffected by enhanced CO_2 levels. In rye plants, increased dominance of *Pseudomonas* sp. and in white clover, increased dominance of *Rhizobium* sp. were reported. In some plants, the inhibition of HCN- producing *Pseudomonas* sp. which inhibits root parasitic fungi were noted. While siderophore and nitrate dissimilating strains increased in number. Thus, elevated levels of CO_2 have differential impacts on endophytes (Compant *et al*., 2010).

Effect of temperature: Endophytic bacteria can alleviate temperature stress on plants by inducing a systemic response (Yang *et al*., 2009). Some are capable of growing under extreme conditions due to special adaptions. The performance and growth of bacteria are affected by temperature and soil type. Certain genotypes prefer certain environmental conditions. *Mycobacterium*, a *Pseudomonas fluorescens* and a *Pantoea agglomerans* strain were found to increase the shoot and root growth of winter wheat at 16ºC when compared with that at 26ºC in loamy sand. However, *Mycobacterium phlei* MbP18 and *Mycoplasma bullata* MpB46 showed good performance under both conditions. Physiological distinction were observed in strains belonging to the same species and bacteria colonizing different sites also react differentially to environmental conditions. The endophyte *Burkholderia phytofirmans* PsJN exhibited reduced colonization in tomato rhizosphere but endophytic abundance was not affected when the temperature was increased from 10 to 30ºC. Hence by taking into account the effect of temperature change on colonization and plant growth promotion, such strains can be used in agriculture (Egamberdiyeva and H¨oflich, 2003; Pillay and Nowak, 1997).

Effects of drought: Drought stress leads to change in endophytes and other plant associated communities. In sunflower cultivated under drought or under irrigation management, different subpopulations of endophytic bacteria were isolated. Endophytic bacteria isolated from sunflower cultivated under drought showed better plant growth promotion when compared with plants cultivated with irrigation. Certain strains of bacteria such as *Achromobacter* was found only under drought stress (Forchetti *et al*., 2007).

Azospirillium strains improve plant growth under drought stress by trehalose accumulation which is an osmoprotectant and decreases osmotic stress (Rodríguez-Salazar *et al*., 2009). Other bacterial genera such as *Burkholderia phytofirmans* PsJN, *Paenibacillus polymyxa* and *Actinobacteria* are known to alleviate drought stress by callose accumulation, cell wall lignification of sieve cells and higher osmotic pressure of plant cells (Hasegawa *et al*., 2004, 2005).

Endophytes induce many responses in plants under drought stress such as increased cell division in roots, increased number of root hairs and decreased distance between root hairs and root tip which enables enhanced nutrient and water uptake by plant roots (Michiels *et al*., 1989). Reduction in oxidative stress and osmotic stress via modulating gene expression was also observed. In addition, endophytes also regulate levels of stress related hormones such as abscisic acid and ethylene by the production of ACC deaminase (Aroca and Ruiz-Lozano, 2009; Glick, 2005).

Beneficial Roles of Endophytes

Factors such as fertile soil and stable climate are important in agriculture sector. Recently, agriculture sector is facing grave issues due to environmental pollution, plant diseases, pest problems and climatic changes. Global climate changes exacerbated abiotic stresses such as drought, increasing temperature, soil salinity, oxidative and osmotic stress. The commonly used approaches to mitigate stress include mutational selection and genetic modification which have limited field success (Tester and Bacic, 2005; Yamaguchi and Blumwald, 2005). However, the ability of endophytes to exist within plant tissues increases the potential for successful application to boost crop production (Hardoim *et al*., 2008).

Plant growth promoting abilities of endophytes via production of phytohormones such as IAA, ADCC, siderophore production and phosphate solubilization enhances water and nutrient uptake (Singh *et al*., 2017).

The production of antimicrobials and enhancement of the plant immune system by endophytes confer resistance against emerging pathogen attacks. The use of chemical fertilizers and pesticides which cause environmental pollution can be considerably reduced as endophytes can be used as biofertilizers and also confer pest resistance (Maela *et al*., 2019).

In the era of changing climatic conditions, the advantages of developing crops with tolerance to abiotic stresses such as drought, salinity and high temperature is enormous. Stress tolerance offered by endophytes are much larger than the tolerance offered by the plant genome (Arora *et al*., 2018).

Regulation of plant growth by endophytes

A wide variety of compounds are produced by endophytes which regulate the growth of host plants. Bacterial endophytes produce phytohormones which enhances water and nutrient uptake of the plants through the modification of the root system. Most plant growth promoting bacteria (PBPB) display certain properties such as synthesis of indole-3-acetic acid (IAA), 1-aminocyclopropane-1-carboxylate deaminase (ACCD), phosphate solubilisation and siderophore production.

Indole-3-acetic acid (IAA): IAA has been found as a crucial phytohormone that contains a carboxyl group which is attached to the third carbon of the indole group (Jasim *et al*., 2014). It plays an essential role in plant nutrition and development as it influences cell division, cell elongation and cell differentiation in plants (Jasim *et al*., 2013). Many root associated microorganisms such as *Pseudomonas* sp., *Enterobacter* sp. and *Azospirillium sp.* are known to produce IAA (Etesami *et al*., 2015). Plant abnormalities can be induced by high levels of IAA production by bacteria whereas low levels of IAA stimulates root elongation (Bal *et al*., 2013; Ali *et al*., 2009).

1-Aminocyclopropane-1-Carboxylate Deaminase (ACCD): Ethylene is known to inhibit plant growth. ACCD is a pyridoxal phosphate independent enzyme that promote plant growth by reducing ethylene levels. It promotes plant growth and reduce the effect of ethylene as it hydrolyses 1-aminocyclopropane-1-carboxylic acid (ACC) which is a precursor of ethylene (Singh *et al*., 2015; Bal *et al*., 2013). The precursor of ACC is also hydrolyzed into ammonia and a-ketobutyrate which are again metabolized by bacteria (Numan *et al*., 2018).

The bacterial communities that are involved in the synthesis of ACCD is also involved in phytoremediation, rhizodegradation and detoxification of heavy metals. It is also known to confer protection against plant pathogens, environmental stress and delay senescence. ACC enzyme was purified from *Pseudomonas putida* HS-2 which enhanced growth of tobacco plants (Rodriguez *et al*., 2009; Singh *et al*., 2015; Ma *et al*., 2011).

Phosphate solubilization: After nitrogen, phosphorus is the most essential nutrient needed by plants. It is usually found in soils as mineral salts or organic compounds (Lin *et al.*, 2013; Gull *et al.*, 2004). Plants are unable to utilize phosphate present in the soil as it is insoluble and has poor mobility (Ramanuj and Shelat, 2018). Various organic acids such as acetic, citric, succinic and oxalic acid are secreted by microorganisms to convert insoluble phosphate into soluble mono- and di- basic ions which can be utilized by plants (Nautiyal, 1999). Phosphate-Solubilizing Bacteria (PBS) are known to transform insoluble phosphate into soluble phosphate by the process of acidification, formation of polymeric substances, exchange reactions and chelation. Several bacteria such as *Pseudomonas* and *Bacillus* are known to be PBS. Such bacteria decrease the need for phosphate fertilizers in agriculture (Glick, 2012; Nautiyal, 1999; Lin *et al.,* 2013).

Siderophore production: Siderophores are low molecular weight metabolites produced by bacteria and fungi which have a high iron chelating affinity (Etesami *et al*., 2015; Lacava *et al*., 2008). Based on their structure, functional group and the kind of ligand, siderophores can be classified into four groups which are carboxylates, hydroxamates, catecholates and mixed types. Insoluble iron present in the soil is made available to plants by bacteria through the production of siderophores. It solubilizes iron by binding ferric ions and transporting it into cells or by the expression of certain proteins by the bacteria (Arora and Verma, 2017; Schwyn *et al*., 1987). The production of siderophores not only promotes plant growth but also inhibits plants pathogens by limiting iron (Jasim *et al.,* 2013; Etesami *et al.,* 2015; Lacava *et al.,* 2008). Such bacteria may also be used in bioremediation as it helps in the binding of toxic heavy metals like chromium, lead and mercury (Rajkumar *et al.,* 2010; Loaces *et al.,* 2011).

Chrome Azurol Sulphonate (CAS) assay is used for the determination of siderophore producing microorganisms (Arora and Verma, 2017; Schwyn *et al.,* 1987). Using this method, two endophytic bacterial strains *Bacillus subtilis* (KDRE01) and *Bacillus megaterium* (KCRE25) exhibited positive reactions for siderophore production under iron limiting conditions (Louden *et al.,* 2011).

Regulation of host genetic and phenotypic expression

Resistance to biotic stress

Endophytes possess the ability to suppress the growth of phytopathogens. They also induce ISR against phytopathogens. The host genetic expression can be regulated thus affecting plant physiological responses and defensive pathways (Kloepper and Ryu, 2006; Van Bael *et al*., 2012; Estrada *et al*., 2013; Salam *et al*., 2017). Endophytic bacteria produce volatile organic compounds (VOCs) which have broad-spectrum antimicrobial activity against phytopathogens (Sheoran *et al.*, 2015). Gibberellin-producing endophytes increase resistance against phytopathogens and insects through salicylic acid and jasmonic acid pathways. High cellulose content, lamina density and high leaf toughness has been reported in plants containing endophytes. Thus endophytes increase resistance against phytopathogens by inducing host response or by the production of antagonistic metabolites. Both endophytes and plants work together to protect the plant from biotic stress (Arora *et al.*, 2018).

Resistance to abiotic stress

Drought, extreme temperatures, salinity, heavy metal toxicity and oxidative stress are some of the abiotic stresses that affect plants (Wang *et al*., 2003; Khare and Arora, 2015). Endophytes induce the expression of stress responsive genes, generation of scavenger molecules and synthesis of antistress metabolites as molecular mechanisms against stress (Lata *et al*., 2018). Phytohormones such as abscisic acid (ABA) mediates stomatal closure and plant growth regulation. The presence of beneficial microorganisms modulates the ABA biosynthesis and ABA mediated signaling pathways (Wani *et al*., 2016; Waqas *et al*., 2012). Certain endophytes such as *Trichoderma harzianum* mediates the upregulation of aquaporin, dehydrin and malonialdehyde genes in lessening abiotic stress in rice. Extracellular precipitation, intracellular accumulation, sequestration or biotransformation of toxic metals to less toxic forms are some of the mechanisms of endophytic bacteria in the reduction of metal phytotoxicity. Endophytes also modulate the activity of plant antioxidant enzymes to prevent oxidative damage induced by heavy metals. Herbicide resistance and metabolizing genes present in *Pseudomonas punonensis* D1-6 confer herbicide resistance to the host (Pandey *et al*., 2016; Arora *et al*., 2018)

Bioactive compounds from endophytes

Endophytes are known to produce a wide array of bioactive metabolites which can be used as drugs for the treatment of various diseases. It also has applications in the field of agriculture, pharmaceutical, food and cosmetics industries (Gouda *et al*., 2016). Bioactive compounds produced by endophytes are much more advantageous than those that are produced by plants alone. Some of the bioactive compounds include antibiotics, alkaloids, phenols, terpenoids, nanoparticles, phytohormones, various enzymes, anticancerous compounds, antioxidants and antiviral compounds. The antimicrobial agents are effective against multi-drug resistant pathogenic microbes. Amines and amides can be used as insecticidal agents. They also confer disease resistance to the host plants (Singh *et al*., 2017).

Phenols: Phenols possess biological properties such as anti-carcinogenic, antioxidant or antimicrobial activities. Phenolic compounds are produced via the shikimate pathway (Kyselova 2011; Valdes *et al*., 2015; Lunardelli *et al*., 2016; Lai Thi Ngoc Ha, 2016). Endophytic bacteria such as *Pseudomonas fluorescens* Endo2 and Endo32 are known to confer systemic resistance against dry root rot of black gram (*Vigna mungo* L.) caused by *Macrophomina phaseolina.* In addition to phenolics and lignin, the bacterized black gram plants showed increased activities of peroxidase, polyphenol oxidase and phenylalanine ammonia lyase (Karthikeyan *et al.,* 2005).

Terpenoids: Terpenes are derived from isoprene units and nearly 50,000 terpenoid metabolites have been isolated from plants, fungi and bacteria. Only a minor fraction of these metabolites have been discovered in prokaryotes (Yamada *et al*., 2015). Some well-known volatile odoriferous microbial metabolites of *Streptomyces* are geosmin, tricyclic α, β-unsaturated ketone, albaflavenone and 2-methylisoborneol. More than 30 species of *Streptomyces* are known to produce the sesquiterpenoid antibiotic, pentalenolactone (Takahashi *et al.,* 1983). *A. lancea*, is a Chinese medicinal plant that contains oxygenous sesquiterpenoids. *Pseudomonas fluorescens* ALEB7B is known to generate reactive oxygen species (ROS) in this plant that leads to increased oxygenous sesquiterpenoid content (Zhou *et al*. 2015).

Alkaloids: Alkaloids are low molecular weight, nitrogen containing compounds. They possess high biological activities due to which they are important in pharmaceutical industries (Silva *et al*. 2007). They act as antifungal, antiviral and anti-cancer agents. Endophytic bacteria that produces alkaloids include, *Bacillus cereus, Aranicola proteolyticus, Serratia liquefaciens, and Bacillus thuringiensis and Bacillus licheniformis* (Liu *et al*., 2015).

Antimicrobial compounds: Endophytes produce several secondary metabolites that possess antimicrobial properties. They belong to different structural groups such as peptides, steroids, alkaloids, phenols and flavonoids (Guo *et al*., 2008; Yu *et al*., 2010). Novel antimicrobial compounds produced by endophytes are alternatives to chemically synthesized ones and are highly effective against multi drug resistant strains (Ferlay *et al.*, 2010; Taechowisan *et al.*, 2012).

Nanoparticles also act as antimicrobial compounds and are effective against various kinds of cancer. Silver nanoparticles also act against HIV-1, hepatitis B virus, herpes simplex virus and respiratory syncytial virus. Endophytic Bacillus sp. are known to synthesize silver nanoparticles by the reduction of silver nitrate (Sunkar and Nachiyar, 2012; Sun *et al.*, 2005; Taylor *et al.*, 2005; Lu *et al.*, 2008).

Anti-cancerous compounds: Many bioactive compounds isolated from endophytes show activity against cancer (Firakova *et al.*, 2007). Ginseng (Panax *ginseng*) produces ginsenosides that have anti-cancer property. The transformed endophytic bacterium *Paenibacillus polymyxa* showed high ginsenoside concentration in Ginseng plants (Gao *et al.,* 2015). Exopolysaccharides (EPS) are of high therapeutic value for cancer. It induces morphological abnormalities in cells as an anti-tumoral mechanisms of action linked with the dysfunction of mitochondria of the treated cells. The first discovered anti-tumoral EPS was from *Bacillus* sp (Chen *et al.*, 2013). *B. licheniformis, B. pseudomycoides* and *Paenibacillus denitriformis* produced L- asparaginase which catalyzes the conversion of L-asparagine needed for the function of some neoplastic cells such as lymphoblasts (Joshi and Kulkarni, 2016; (Jakubas *et al*., 2008).

Anti-biotics: Microorganisms produce certain secondary metabolites that inhibit or kill other microorganisms. Endophytic bacteria produce a range of antibiotics including ecomycin, pseudomycins and kakadumycins (Christina *et al*., 2013). Ecomycin is usually produced by *Pseudomonas viridiflava*. It is commonly used in the treatment of eye, skin, gut, respiratory and urinary tract infections (Miller *et al*., 1998). A chlorine containing ansamycin, naphthomycin K exhibited cytotoxicity against P388 and A-549 cell lines. Endophytic Streptomyces produces approximately 80% of the total antibiotics including coronamycin, spectinomycin, treponemycin, doxorubicin and monensin which displays wide range of biological activities (Singh *et al.,* 2017).

Conclusion

The plant microbiome is a treasure trove of endophytic bacteria. Endophytes are an ecofriendly choice for plant growth promotion and for serving as reservoirs of novel bioactive compounds. Plant growth promotion takes place directly via the production of phytohormones, acquisition of environmental resources such as iron, phosphorus and nitrogen. Indirect plant growth promotion is via resistance against biotic and abiotic stresses.

They are widely used in various fields such as medical, food, pharmaceutical and cosmetics. They are particularly used in the production of antimicrobial, antifungal, antiviral, antioxidant, anti-inflammatory and anticancer drugs. Several bioactive compounds produced by endophytes can be utilized in agriculture, bioremediation and biodegradation. They are also used in the manufacture of nanoparticles.

It provides effective ways of sustaining the agricultural sector. They can be utilized to develop biofertilizers, stress protection products and for biocontrol. It is also important in the prevention of outbreak of plant diseases or critical human pathogens associated with plants

Climate change affects all kinds of plant-microbe interactions. Several studies indicated a variable effect of enhanced CO_2 levels on endophytic bacteria. However, growth of endophytic fungi was increased. The response to increase in temperature by endophytic bacteria was variable and it depends on the adaptations of the microbe and plant to the environment. Drought decreases the colonization of plants by bacteria but the endophytes reduce drought stress and enhance plant growth.

The invasion and colonization of plants by endophytes depend on the availability of certain compounds, root exudation or certain metabolite patterns. Climate change such as elevated CO_2, increased temperature and drought effect the metabolite patterns and exudates of plants and in turn microbial activities are affected. Altered colonization behavior can be observed as endophytes have to compete with other microbial communities. Such changes would result in altered communities or induction of different plant responses. Alterations in plant microbial communities influence plant diversity and the diversity and functioning of soil microbiota. Selection of adapted plant cultivars will be required in agriculture. The use of cultivars not completely adapted to changing environmental conditions could be aided by making use of PGPB. However, endophytes are an invaluable tool in climate change mitigation.

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