

Review



Plant Growth-Promoting Rhizobacteria (PGPR): Approaches to Alleviate Abiotic Stresses for Enhancement of Growth and Development of Medicinal Plants

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Abstract: Plants are constantly exposed to both biotic and abiotic stresses which limit their growth and development and reduce productivity. In order to tolerate them, plants initiate a multitude of stress-specific responses which modulate different physiological, molecular and cellular mechanisms. However, many times the natural methods employed by plants for overcoming the stresses are not sufficient and require external assistance from the rhizosphere. The microbial community in the rhizosphere (known as the rhizomicrobiome) undergoes intraspecific as well as interspecific interaction and signaling. The rhizomicrobiome, as biostimulants, play a pivotal role in stimulating the growth of plants and providing resilience against abiotic stress. Such rhizobacteria which promote the development of plants and increase their yield and immunity are known as PGPR (plant growth promoting rhizobacteria). On the basis of contact, they are classified into two categories, extracellular (in soil around root, root surface and cellular space) and intracellular (nitrogen-fixing bacteria). They show their effects on plant growth directly (i.e., in absence of pathogens) or indirectly. Generally, they make their niche in concentrated form around roots, as the latter exude several nutrients, such as amino acids, lipids, proteins, etc. Rhizobacteria build a special symbiotic relationship with the plant or a section of the plant's inner tissues. There are free-living PGPRs with the potential to work as biofertilizers. Additionally, studies show that PGPRs can ameliorate the effect of abiotic stresses and help in enhanced growth and development of plants producing therapeutically important compounds. This review focuses on the various mechanisms which are employed by PGPRs to mitigate the effect of different stresses in medicinal plants and enhance tolerance against these stress conditions.

Keywords: PGPRs; biostimulants; phytohormones; priming; abiotic stress

1. Introduction

Since the colonization of the terrestrial environment, plants have always been exposed to different types of biotic and abiotic stresses. Generally, stress is defined as an extrinsic factor which affects the growth of the plant. These conditions challenge the plants' growth and development and restrict their potential to reproduce and pass their genes to the next generation. In maximum scenarios, stress is measured in terms of crop yield, plant survival, biomass accumulation or CO_2 and minerals uptake. In nature, stress conditions can be caused by both biotic as well as abiotic factors. Biotic stress caused by nematodes, viruses, bacteria, fungi, insects such as white flies and various other groups of living organisms can challenge the survival of plants. Additionally, various abiotic stresses related to temperature, such as cold and heat stress, water-associated stresses like drought and flood



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Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). conditions, salinity and heavy metals, beyond a certain level exerts negative impact on plants growth and development [1]. To mitigate the stress condition, plants induce specific responses that lead to reprogramming at genetic, molecular, etc. levels for protection against these stresses. On a cellular level, it leads to changes in cell division and cell cycle, in addition to changes in endomembrane system, vacuolization of cells and changes in structure of the cell wall. Plants also modify their metabolisms in order to accommodate the various environmental stresses at the biochemical level. In recent years, there have been many studies on the association of stress response with genetic composition of a plant [1]. Often, the defense mechanism in plants is aided by external assistance from microbial communities. The migration of plants from water to land established a role for microorganisms, which included the protection of plants against different stress conditions [2]. The soils surrounding the roots are found to be hotspots for microbes as root exudates of varying chemical composition act as reduced carbon source for supporting microbial growth. Additionally, plants produce signals for the growth of specific microbial communities and then regulate their genetic and biochemical activity [3]. Harboring bacterial communities in the rhizosphere plays an important role in the growth and development of plants. These rhizobacteria, termed PGPR, help plants in acquisition of nutrition [4], stress management or mediate induced systemic resistance (ISR) in plants which is phenotypically similar to pathogens-induced systemic acquired resistance (SAR) [4,5]. In order to suppress disease in plants, rhizobacteria induce a mechanism known as ISR. This process enhances the capabilities of plants in tackling disease. This phenomenon was first reported by Van Peer et al. [6] where they witnessed the systemic resistance in plants by Pseudomonas fluorescens strain WCS417r against Fusarium oxysporum f. sp. dianthi. Again in 1991, rhizobial activity was seen in cucumbers, where it protected plants from anthracnose causing Colletotrichum orbiculare [7]. On the other hand, SAR provides resistance to non-affected plant parts from pathogens such as viruses, bacteria, fungus, insects and nematodes [5] and it is comparatively more effective than ISR [8]. Together, they provide better results than performing alone [9]. Both ISR and SAR follow different signaling pathways. ISR requires a jasmonic acid (JA) and ethylene (ET) signaling pathway while SAR follows salicylic acid (SA) for its induction. Additionally, by various other mechanisms such as by secretion of osmoprotectants, exopolysaccharides (EPS) and volatile organic compounds (VOCs) as well as promoting the release of phytohormones, PGPRs alleviate stress conditions in plants. Furthermore, studies show that PGPRs produce siderophores which help in acquisition of nutrients like iron [10,11].

To increase the demand of pharmaceutical constituents there are several methods that have been investigated to develop the high yields of medicinal plants under abiotic stress. To study the tolerance of the medicinal plants under adverse conditions, gene expression study is required [12]. Apart from abiotic stress signalling (phosphoinositol-induced Ca^{2+} changes, receptor-coupled phosphorelay, mitogen-activated protein kinase cascades, etc.), there are several stress-responsive genes that also have been reported to combat abiotic stress followed by transcriptional activation [13–15]. Abiotic stresses are responsible for the synthesis and accumulation of amino acids, proteins, nucleic acids and carbohydrates which causes stimulus to the cells as signalling cascade through plasmodesmata [16,17]. The stress-inducible genes encode proteins (chaperons) as well as the signal transduction to express enzymes (phosphatases, protein kinases), transcription factors and phospholipid metabolism enzymes for cell protection [18,19]. The expression of the genes leads by DNA methylation and RNA polymerase II [20–22]. Several sequencing reports of the plant genome stated that many transcription factors coding genes (10% in Arabidopsis thaliana and 5% in soybean) are also expressed as the stress responsive genes [23–25]. The manuscripts fill the scientific gap. by explaining the uses of PGPRs in terms of medicinal plants. Though the general physiology of plants remains the same, the economic importance of plants differs on the basis of metabolites present in it. The presence of medicinally important metabolites makes a plant important for use in ayurveda practices and by traditional

healers. This manuscript explains in detail about all the possible routes by which abiotic stress is mitigated in plants.

2. Amelioration of Abiotic Stress in Medicinal Plants

Due to their sessile nature, plants have to endure various types of abiotic stresses such as drought, heat, toxic heavy metals, salinity, etc. which impede their growth and development. They obtrude injurious effects on various physiological processes such as photosynthesis, floral development, and seed germination, as well as induce stomatal closure, etc. [26–30]. The quality of medicinal plants is defined by their active ingredients and their concentrations. However, under stressed conditions, the metabolite constitution of these plants gets altered. In a study on effect of drought stress on *Thymus vulgaris*, it was that found that stress affects the different compound levels of metabolite of medicinal plants such as γ -terpinene, carvacrol, p-cymene, etc. as well as decreasing essential oils [31]. To overcome the drought stress, medicinal plants produce bioactive ingredients and induce genetic factors. Salinity causes water reduction as well ionic toxicity which directly affects the growth reduction due to nutrient deficiency in medicinal plants such as Matricaria necati, Aloe vera, and T. vulgaris. Salinity also increases the essential oils contents in medicinal plants such as T. vulgaris, Salvia officinalis, etc. Heavy metal stress causes protein denaturation and lipid peroxidation by interacting with phytochelatins, organic molecules and glutathione. High concentration of nickel reduces the production of hypericin and hyperforin in *Hypericum perforatum*. Ramankutty et al. [32] reported that approximately 12% of the earth's surface can be used for the agricultural practices due to cold stress. Cold stress affects the physiological, metabolic and genetic processes in plants. Under cold stress, plants produce protective compounds like inositol, sorbitol, rebitol, sucrose, trehalose, raffineur, glucose, proline, glycinebetaine, and phenolic compounds. Under heat stress, plants increase the activity of antioxidative enzymes to remove reactive oxygen species. High temperature induces the production of pseudohypericin, hypericin and hyperforin in medicinal plants. PGPR employs various methods for tackling the stress conditions and promoting the growth and development of plants (Figure 1).



Figure 1. Different mechanisms employed by PGPRs to overcome the abiotic stress and enhance the growth of plants.

2.1. Production of ACC (1-Aminocyclopropane-1-Carboxylate) Deaminase

Ethylene has been considered to be one of the most important plant hormone(s) which is secreted during stress conditions. However, the elevated level of ethylene or "stress ethylene" in plants has been found to have a negative role in plant growth. In a study, it was found that overproduction of ethylene in *Arabidopsis thaliana* resulted in dwarfness of plant and the inhibition of normal growth [33]. PGPR plays an imperative role by inhibiting the negative effects of ethylene stress [34]. PGPR with enhanced ACC deaminase activity

reduces the concentration of endogenous ethylene by cleaving 1-aminocyclopropane-1carboxylate, the precursor of ethylene, in ammonia and α -ketobutyrate [34–36]. Zarei and colleagues [37] studied sweet corn (*Zea mays* L. *var. saccharata*) and concluded that under osmotic stress/drought condition, crop yield could be increased by using *P. fluorescens*. Under stress conditions, it enhanced the nutrient acquisition, reduced the endogenous ethylene concentration and ameliorated physiological condition of plants to increase the overall productivity of the plant [37]. ACC deaminase production in PGPR *Achromobacter piechaudii* ARV8 elevated the dry and fresh weights in pepper and tomato under water stress [38,39]. It was found out that PGPR did not affect the plants' water content but with the supply of water, it improved the plants' health. ACC deaminase not only provides protection towards drought stress but flooding stress as well.

In a study, a tomato plant was inoculated with ACC deaminase producing PGPRs such as *Enterobacter cloacae* CAL2, *Pseudomonas putida* UW4, *P. putida* (ATCC17399/pRKACC) or *P. putida* (ATCC17399/pRK415) which demonstrated resistance against flooding stress [40]. In the study, when a plant was accompanied with ACC deaminase producing PGPR, it showed normal development in salinity stress. It has been determined that if we employ ACC deaminase producing PGPR in natural soil and plant systems, it proves to be more economical, feasible, and environmentally friendly. On commercial levels in floriculture, the shelf life of flowers can be increased by treatment with PGPRs which release ACC deaminase. ACC deaminase producing PGPR strains plays a better role at biocontrol than do strains without this enzyme. In addition to that, they also help in phytoremediation of soil with heavy metals such as *Kluyvera ascorbata*; SUD165 shows normal growth in *Brassica napus* under high levels of CrO₄²⁻, Ni²⁺, Pb²⁺ and Zn²⁺ [41].

2.2. Secretion of Osmoprotectants (Proline, Choline and Trehalose)

In the course of evolution in the terrestrial environment, plants and bacteria developed symbiotic relationships to fulfill different essential requirements for survival. One of the major benefits which plants derive from bacteria is protection against various environmental abiotic stresses. Under osmolality fluctuation conditions in the environment, microbes accumulate large quantities of solutes in their cytosol which acts as an osmoprotectant [42]. During osmotic stress, synthesis of solutes like proline, trehalose and choline is found to be quicker in microbes than in plants. During salinity and drought stress, these solutes are absorbed by plant roots and increase the osmolyte concentration in plants, and ameliorate stress conditions [43–45]. In a whole genome study on eight different PGPR isolated from halophytes, it was found that they contain genes which play crucial roles in abiotic stress response [46]. Environmental perturbations such as drought stress lead to decreases in metabolite concentration in plants, and thus hamper the normal physiological process. Khan et al. [47], in their studies demonstrated in chickpeas that, under stressed conditions, the level of sugar, amino acid (histidine, tyrosine, and methionine) and some organic acids like tartaric acid and citric acid were decreased. Decreased sugar levels lead to reduced chlorophyll content and hence resulted in dropped photosynthetic efficiency of plants. However, treating the chickpea plants with PGPR and PGR consortium led to increased sugar levels in plants and consequently, attainment of the normal photosynthetic efficiency of the plants [47].

2.3. Secretion of Volatile Compounds for Tolerance against Stress

PGPR stimulates tolerance against stress in plants in various ways. One of the most common mechanisms by which PGPR mediates abiotic stress tolerance in plants is production of volatile as well as non-volatile compounds which facilitate plant development. In 2003, for the first time, Ryu et al. [48] in a study showed that PGPR releases a mixture of volatile compounds which enhance development and growth of *Arabidopsis thaliana*. Volatile compounds have been found to induce arrays of response in plants like increases in biomass, tolerance against different types of stresses and resistance against disease. However, the induction of tolerance in plants by PGPR is not much studied and needs

more investigation. Volatile compounds secreted by PGPR are absorbed by plant roots, which regulate different aspects of physiological processes and induce systemic tolerance in plants (Figure 2). In a study, Li et al. [49] demonstrated that the overall salt tolerance in Robinia pseudoacacia was increased during exposure to volatile compounds which had been secreted by Rahnella aquatilis JZ-GX1. The seeds exposed to volatile compounds released by JZ-GX₁ had well-developed lateral root systems and biomass. Volatile compounds released by PGPR into inter-soil root pores are sensed by roots and act as important communication signals when roots are not directly in contact with bacteria. JZ-GX₁ volatile compounds, by enhancing the quaternary root formation, aid plants in better absorption of nutrients and water [49]. Salt stress conditions lead to increased hydrogen peroxide (H_2O_2) and reactive oxygen species (ROS; O_2^{-}). ROS is an important signal molecule at low concentration and plays an important role in programmed cell death, regulation of cell cycle, etc. but at higher concentration, it confers deleterious effects on plants. It leads to damage to cells and overall growth of plants [50] and inhibits development of roots by reducing the size of root meristems [51]. However, treating plants with PGPR leads to reduced levels of ROS and alleviates salt stress in plants. JZ-GX₁ produced volatile organic compounds (VOCs) that induced activity of antioxidant enzymes in plants and prevented oxidative damage caused by ROS through enzymatic and non-enzymatic systems [49]. Based on present research findings, under salt stress Azotobacter enhances the antioxidative enzyme activity by inhibiting H₂O₂ and malondialdehyde in Glycyrrhiza glabra L. (medicinal and industrial plant) to relieve salt stress [52]. It was also observed that treating the plants with PGPR led to decreased levels of malondialdehyde, which is an indicator of membrane disintegration and plasma membrane damage [53].



Figure 2. Role of VOCs in enhancement of plant growth and mitigation of abiotic stress. (FIT1, Fe-deficiency induced transcriptional factor 1; HKT1, high affinity K⁺ transporters; PEAMT, phosphoethanolamine N-methyltransferase; ROS, reactive oxygen species; VOCs, volatile organic compounds; SA/ABA, salicylic acid/abscisic acid).

Salinity stress results in increased concentration of sodium (Na⁺) ions and Na⁺/K⁺ imbalance into cytoplasm. Potassium (K⁺) ion is important for functioning of plant metabolism and overall physiological process. K⁺ is considered a "master switch" which regulates the transition from "normal state" to "hibernated state" during stress conditions [54,55]. Previous studies demonstrate that the high K⁺/Na⁺ cytosolic levels in plants are a prerequisite for salt tolerance. However, due to high physico-chemical similarities between K⁺ and Na⁺, Na⁺ competes with binding sites of K⁺ ions, and interrupts the normal functioning

of enzymes. Volatile compounds secreted by certain PGPRs are shown to reduce the Na⁺ level in plant roots and shoots. HKT (high affinity K⁺ transporter) is a member of IMPs (integral membrane proteins) and plays a crucial role in transport of cation across plasma membranes in plant cells [56]. It plays a pivotal role in plants under salt stress. Sodium transporter (HKT) is expressed in xylem parenchyma and is responsible for exclusion of Na⁺ from leaves by removing Na⁺ from xylem sap [57,58]. In *Arabidopsis thaliana*, it was observed that the plant exposed to Bacillus subtilis GB03 VOCs accumulated less Na⁺ in both root and shoots. AtHKT restricts Na⁺ into roots, which leads to higher root-to-shoot Na⁺ ratio. B. subtilis GB03 released VOCs, repressing the activity of AtHKT in root while increasing its activity in shoot. This mechanism of recirculation of Na⁺ from shoot to root by modulating the activity of AtHKT explains the role of VOCs in alleviating salt stress [48,57]. In different studies, it was observed that VOCs induced systemic tolerance against drought in plants. Acetoin and 2,3-butanediol released from Pseudomonas chlororaphis O6 and Bacillus amyloliquefaciens FZB42 induced stomatal closure in Arabidopsis thaliana and Nicotiana benthamiana by invoking the SA/ABA signaling pathway [59,60]. 2,3-Butanediol and its precursor acetoin produced by B. subtilis GB03 and B. amyloliquefaciens IN937 promoted the growth and yield in cucumbers, peppers, and tomatoes. VOCs produced by many PGPRs also elevate the manufacture of essential oils in Mentha piperita Huds [61].

Volatile compounds released by PGPRs also mediate the iron uptake by plants. Because of its presence in soil as oxyhydroxide polymers, iron becomes biologically unavailable for uptake and leads to iron deficiency in plants. It was observed that *B. subtilis* GB03 VOCs, in normal growth condition, would elevate Fe levels in *Arabidopsis thaliana* by transcriptional upregulation of FIT1 (Fe-deficiency induced transcriptional factor 1) and its target gene ferric reduction oxidase 2 (*FRO2*) and iron transporter gene (*IRT1*). However, *fit1* knockdown mutants lacked any enhancement in iron levels and photosynthetic efficiency, thus indicating the crucial role of FIT1 in iron uptake. Additionally, iron uptake is also facilitated by VOCs mediated rhizosphere acidification which upregulates the activity of FRO2 [57]. VOCs have been found to induce tolerance against osmotic stress in plants by upregulating the synthesis of osmoprotectants. It was found that the transcriptional upregulation of PEAMT (phosphoethanolamine N-methyltransferase) by VOCs led to synthesis of osmoprotectants choline and glycine betaine. In dehydration condition, the osmoprotectants elevate the osmotic pressure of the cell and lower the free water potential of the cell to prevents water loss [51,62].

2.4. PGPRs as Biostimulants

The various substances or microorganisms which stimulate the plant productivity through natural processes are known as biostimulants. This word has been coined by horticulturists and some of them identified humic acid and seaweed extract as biostimulants. It principally includes amino-acid-containing products (AACP), hormone-containing products (HCP) and humic substances (HS) [63]. PGPR as biostimulants are placed under the category of biofertilizers, biopesticides and phyto-stimulators [64]. They monitor the life cycle of plants from germination of seeds to maturity by increasing the stress tolerance, nutrient accumulation, improving properties of soil and providing a healthy environment to other microorganisms within the soil [65]. In addition to that, PGPR has the ability to modify the cell wall composition of the plant and accumulate a high quantity of solutes since they increase the water retention and provide protection against ionic and osmotic stress [66,67]. PGPR also has shown an effective role in tackling the salinity, drought, high temperatures and pH due to high quantity of indole-3-acetic acid (IAA) which relieves the salt stress and also maintains the production of exopolysaccharides (EPS) in order to the sustain the hydration around the roots under water scarcity [68].

2.5. Secretion of Exopolysaccharides (EPS)

Exopolysaccharides are usually long chains of polysaccharides constructed with sugar units such as galactose, sugar and rhamnose in diverse fractions. Microbial EPS are categorized into two kinds, homopolysaccharides and heteropolysaccharides. EPS has an acyl group, hence, it exhibits anionic properties and, in addition to that, this group also elevates the lipophilicity of compounds, which eventually affects their relationship with other cations and polysaccharides. EPS secretion helps the bacteria to sustain in harsh environments and tolerate abiotic stress. For instance, in A. brasilense Sp245 a capsular material with complex carbohydrates has been found which protects this bacteria against drought [69]. PGPR releases more EPS in circumstances of stress than non-stress scenarios. There has been much research which supports this claim, such as the finding that when stress conditions formed guanine cyclase in cell, it leads to the production of EPS [40]. The secretion of EPS by bacteria helps in colonizing around the roots and prevents its dehydration. Different bacteria produce EPS with variety of composition depending upon the circumstances and accessibility of nutrients. The general make-up of bacterial EPS encompasses a water-soluble diversified blend of lipids, nucleic acid, polysaccharides and proteins. They protect the bacteria during drought stress by hydrating the microenvironment and diffusing the carbon sources. PGPR such as Azospirillum, Bacillus spp. and Pseudomonas, as well as EPS production, changes the soil structure and accumulates the properties which help in the serene uptake of minerals and water [70]. With the help of innumerable processes such as anion adsorption, cation bridges, hydrogen and Van der waal bonds, PGPR-released EPS gets absorbed on the soil surface and permits development and preservation of aggregates [48]. Under drought stress, EPS producing bacterial strains induce antioxidants enzymes such as catalase (CAT), peroxidase (POD) and superoxide dismutase (SOD), which removes ROS and increases plant resistance [71]. During drought conditions, secretion of EPS expands the growth of roots, shoots, and dry weight of plants. In Pseudomonas sp., it forms a hydrophilic biofilm on the root surface in order to prevent root hardening [70]. In study, it was found out that EPS AK-1 produced by *Pseudomonas* sp., bound with Na⁺ and made them unavailable for soybeans [72]. Lipids and polysaccharides found in EPS act as emulsifiers and also hunt free radicals, since they have harmful effects on the growth of plants [70]. According to the study conducted by Mohammed [73], NaCl concentration and EPS secretion are directly proportional to each other, resulting in the formation of biofilm. Under salt stress, EPS and biofilm protect the bacterial cell wall from the rhizosphere. It has also been found that heavy metal tolerant-PGPRs release EPS which binds with toxic trace elements, leading to the formation of organic metal complexes and hence increases the tolerance in plants against heavy metal stress [40]. Apart from being beneficial for the growth of the plants, EPS of several plant pathogens such as Ralstonia solanacearum suppress the MAMP-triggered immunity by sequestration of calcium ions apoplastically [74]. EPS was also considered as virulence factor for several plant pathogenic bacteria and shows variations in the chemical structures [75].

2.6. Release of Phytohormones

According to Maheshwari et al. [76], phytohormones are defined as organic substances which are synthesized in minute quantities in one part of the plant's body and transported to another part, where they influence specific physiological processes. Traditionally, it has been known that the development of plants is modulated by five plant hormones: auxins, gibberellins, cytokinins, ethylene, and abscisic acid. Although, recently other substances have also been found, such as the brassinosteroids, jasmonic acid, the polypeptide systemin, plant steroids and salicylic acid [1] which are considered as crucial hormones for functioning of plant metabolism. PGPRs generally secrete major phytohormones like auxin, gibberellins, cytokinins and abscisic acid [77–79]. According to several studies, these bacteria improve the overall health of plants and also maintain the hormonal level inside the plants during drought stress. Under water stress, PGPR releases phytohormones in the root domain which cause modification in endogenous hormone levels of plants. PGPR with the same strains have the capacity to produce different phytohormones under different growth conditions. The nature of the phytohormone released by PGPR will also vary with the kind of host plants [78]. In the orchid rhizosphere, an IAA producing *My*-

cobacterium species has been found, and Azospirillum, Azotobacter, Cellulomonas, Mycoplasma and Rahnella were reported in the rhizosphere of wheat. In research, it has been found that Bacillus cereus, Bacillus megaterium, Bacillus subtilis, Escherichia coli, Halomonas desiderata and P. fluorescens G20-18 produce cytokinins. PGPRs such as, B. cereus, B. megaterium, Klebsiella pneumoniae, Phaseolus vulgaris and Proteus mirabilis synthesize abscisic acid [79]. *Bradyrhizobium japonicum* E109 synthesizes IAA, GA_3 , ethylene, ABA and zeatin in addition to low levels of jasmonic acid and salicylic acid [80]. Phytohormones secreting bacteria are gaining wide popularity all over the globe due to their agricultural applications. The phytohormones producing PGPRs are either free living or sustained in a community which pose positive effects on the growth and development of plants, repress disease causing microorganisms and maintain the proper nutrient level in the soil [81]. They also help in defeating the density-dependent and density-independent stress within the rhizosphere. The density-dependent stress is caused by pathogenic pathogens such as bacteria, fungi and viruses; on the other hand, density-independent stress happens because of abiotic components of environments like pH, salinity, temperature, water, etc. IAA producing PGPR was isolated from Leptochloa fusca (L.) Kunth which had been grown in soil with high salinity [82]. The interconnection of plants and PGPR facilitates chlorophyll content, leaf area, hydraulic activity, nutrient uptake and root-shoot development. In addition, they also lower the ethylene concentration of the plant, which retards the root length of the seedling. In a study, it was found out that Pseudomonas sp. RDV 108 not only inhibited the development of harmful bacteria but also expanded the root-shoot length along with germination of seeds. In another study, when spinach was inoculated with nitrogen fixing and phytohormones producing bacteria, it led to an increase in its growth [76]. The microbial-produced phytohormones are better at functioning than chemically produced phytohormones because in the latter the threshold between stimulatory level and inhibitory level is low [77].

2.7. Production of Siderophores under Iron Deficiency Condition

Under saline stress conditions, one of the major changes that occur in soil are nutritional imbalance and thus its unavailability to plants. One of such important micronutrients whose level drops dramatically in saline stress is iron (Fe). Iron plays a crucial role in metabolism of plants and is important for DNA synthesis, chlorophyll production, respiration, photosynthesis and other developmental processes [40,83]. Additionally, it is an important constituent for many enzymes and thus its deficiency impedes normal metabolic processes in plants. However, many studies show that the PGPR plays an important role in iron sequestration by production of chelating agents and hence increases the availability of iron for both plants and itself. Iron, in soil, is mainly found in its unavailable state Fe^{3+} . The Fe^{2+} undergoes rapid oxidation in presence of oxygen and neutral pH which converts it to Fe³⁺ and reduces its solubility in soil rendering it biologically inaccessible to plants as well as rhizobacteria. However, rhizobacteria produce low molecular weight (400–1000 Da) peptides known as siderophores, which act as chelating agents and bind to Fe^{3+} ions with high affinity [84–86]. Siderophores are water soluble compounds and can be divided into extracellular and intracellular siderophores [87]. Siderophores bind to Fe^{3+} ions and form a complex which is later transported to cytoplasm. However, the method of transportation of this complex varies into gram positive and gram negative bacteria. In gram negative bacteria, the siderophore-Fe³⁺ complex bind to OMTs (outer membrane transporters) and are transported to the periplasm. However, this transportation of complex into periplasm requires activation of OMTs, which is done by TonB machinery. TonB machinery is composed of TonB-ExbB-ExbD complexes which are anchored to the cytoplasmic membrane (CM) [88]. The binding of siderophore-Fe³⁺ complex to OMT brings conformational change which leads to trapping of siderophore-Fe³⁺ complex in its binding site. The next step in translocation of complex into periplasm is induced by Ton mediated activation of transporters. In periplasm, siderophore- Fe^{3+} complex bind with periplasmic SBP (siderophore binding proteins) which is an important part of the Fe transport system

in bacteria [89–91]. The final translocation of siderophore-Fe³⁺ complex in cytoplasm is mediated by ABC transporters. Siderophorepermeases-ATPase system provides a channel for transportation of siderophore-Fe³⁺ complex into cytoplasm and is an ATP-dependent process. Once inside the cytoplasm, ferric iron reductase reduces the Fe³⁺ to Fe²⁺ and releases it inside the cell (Figure 3A). However, in gram positive bacteria, the mechanism of iron uptake is different as they lack outer membrane, OMTs and TonB machinery. The siderophore-Fe³⁺ complex directly bind to SBP anchored to fatty acid groups on cellular membrane. The iron complex is transported directly into cytoplasm by ABC transporters (Figure 3B) [10,85,92].



Figure 3. (**A**) Iron uptake mechanism by gram negative bacteria and (**B**) iron uptake mechanism by gram positive bacteria.

In different studies, it was found that PGPRs make iron available for themselves as well as plants. An Indian pennywort, *Centella asiatica* use in Indian and Chinese traditional medicines having properties to heal wound, neuroprotective, anti-aging potential by producing medicinally active compound asiaticoside (trisaccharide triterpene). *Piriformospora indica* (an endophytic fungus) successfully enhances asiaticoside production by colonizing roots of *C. asiatica* [83]. Under salinity stress, siderophore enhances biomass production in *Arabidopsis thaliana* when treated with different strains of *Bacillus* [93].

2.8. Enhancement of Abiotic Stress in Plants by Priming

Priming can be defined as preconditioning of plant immunity and defense with beneficial bacteria for better stress tolerance in plants. This state of preconditioning leading

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to preparedness against different abiotic stress is called 'primed state' [94,95]. This state leads to robust and rapid response to abiotic stress faced by plants and thus ameliorates tolerance in them compared to non-primed state plants [96].

3. Amelioration of Abiotic Stress by PGPRs in Medicinal Plants

Medicinal plants include all those plants of which either one or more than one part is used in herbalism and/or for the production of therapeutic drugs [97]. These plants have played an important role in developing the healthcare system since time immemorial. Not only in the development of the healthcare system but herbal plants have also boosted the global economy, especially after COVID-19. The global market of herbal medicines, which was US\$110.2 bn in 2019, is expected to boost up to US\$178.4 bn in 2026 [98]. With such a promising market and an important aid to the healthcare system, medicinal plants are an important asset to any nation. However, climate change and increasing global temperature along with many other abiotic stresses imposed detrimental effects on growth and development of these plants as well as reduced the quality of medicinally useful metabolites [99]. To overcome these abiotic stresses and continue optimum growth and development, medicinal plants have developed symbiotic relationships with microbes residing in the rhizosphere. These microbes, termed PGPRs, alleviate the abiotic stress by different mechanisms like nutrition acquisition [4], phytohormone production, siderophores production and many others, helping plants to thrive in the stress conditions [100,101]. PGPR treatments have been also found to be efficacious for enhancing the vigor of seeds. In a study on Asparagus officinalis L. in greenhouse conditions, Liddycoat et al. [102] found that under drought or flooding stresses, the *Pseudomonas* sp. was able to rescue seeds from the detrimental effect of stress and exert a positive effect on the growth of seeds. The following table summarizes different studies that have described various mechanisms which have been employed by PGPRs to attenuate the abiotic stress effects on medicinal plants (Table 1).

Table 1. Various mechanisms which have been employed by PGPRs to attenuate the abiotic stress effects on medicinal plants.

Plant	PGPRs	Type of Stress Alleviated	Mechanism Employed by PGPRs	Effect of PGPRs	References
Capsicum annuum L.	Arthrobacter sp. (EZB4), Bacillus sp. (EZB8)	Osmotic stress	ACC-deaminase activity, production of phytohormone IAA, P-solubilization, production of siderophores, increased proline concentration	Reduced upregulation and even downregulation of stress inducible genes CaACCO and CaLTPI	[103]
	Achromobacter piechaudii	Drought stress	ACC-deaminase activity	Reduced production of ethylene	[104]
Lactuca sativa L.	Bacillus sp.	Drying soil	Production of cytokinin	Increased shoot biomass due to expansion of leaves	[105]
	Azospirillum sp.	Salt stress	Production of phytohormones like GAs, osmoprotectants like proline and glutamate	Increased fresh and dry biomass in the aerial portion of plants	[106]
Ocimum basilicum L.	Consortium of Bacillus lentus, Azospirillum brasilens, Pseudomonades sp.	Water stress	Regulation of antioxidative enzymes like APX (ascorbate peroxidase) and photosynthetic activity	ROS scavenging, Increased chlorophyll content and antioxidants activity needed to mitigate stress effect	[107]
Glycyrrhiza glabra L.	Azotobacter sp.	Salt stress	Induced polyphenol oxidase (PPO), peroxidase (POD) and phenylalanine ammonia-lyase (PAL) activity	Induced the antioxidative enzyme defense activity under salinity	[52]
Dalbergia sissoo Roxb.	Bradyrhizobium (Ds Rhz-9) and Glomus fasciculatum	Overall stress in arid and semi-arid conditions	Increased phosphorus and nitrogen acquisition, production of phytohormone IAA	Increase in growth, dry weight and nodulation of seedling as well as increased nitrogen fixation efficiency of seedling	[108]
Cicer arietinum L.	Pseudomonas putida and Pseudomonas pseudoalcaligenes	Saline stress	Siderophore and phytohormone IAA production, phosphate solubilization	Overall increase in vegetative as well as reproductive traits like flower and fruit formation were increased	[109]
Abelmoschus esculentus L.	Agrobacterium and Bacillus sp.	Saline stress	Production of phytohormones and phosphatases	Increased overall yield	[110]

4. Conclusions and Future Perspective

In the past few years, climate change and the population explosion has resulted in increased demand for food crops as well as medically important crops all over the globe. To fulfill these demands, various practices have been adopted such as crop breeding, genetic engineering and increased usage of fertilizers. All these practices have related pros and cons. However, the major concerns with these practices are that they are time consuming processes and an increased usage of fertilizers has shown a negative impact on the health of the soil. Thus, to promote sustainable agricultural practices, microorganisms such as PGPRs are employed which accomplish more than an increase in soil fertility. Various studies demonstrate that inoculation of plants with PGPRs enhanced growth, enzyme activity and transcription activity. These observations have also been found true for medicinal plants where PGPRs protect them from abiotic stresses through various metabolic mechanisms. Additionally, usage of PGPRs in growth of medicinally important plants also showed increased metabolite production which has been used in traditional healing practices. PGPRs not only positively regulate the growth and development of plants, but also reduce the effect of plant diseases directly by interfering with the growth of pathogens inside plants called antagonists. Antagonistic activities are summarized as: (i) they produce hydrolytic enzymes such as protease, chitinase, lipases and glucanases which dissolve the fungal cells, (ii) compete for nutrients and form niches around the root surface, (iii) manage the level of ethylene with the help of ACC deaminase enzyme in case of pathogenic stress, and (iv) produce antibiotics and siderophores. In addition to this they also produce phytohormones which regulate the roots and shoots development along with facilitating nutrient uptake. Additionally, they also act as biostimulants, which can be classified into biofertilizers, biopesticides and phytostimulators.

Thus, it can be concluded that PGPRs, by various mechanisms, mitigate the abiotic stress conditions and make the environment suitable for the growth of plants. Furthermore, in medicinally important plants, they were also found to elevate the metabolite level of economically important compounds in addition to alleviating stress conditions. This dual benefit makes them a suitable alternative to promote the sustainable agricultural practices for cultivation of medicinal plants in stressed environment and to improve the soil health. PGPRs in optimized consortium or alone can function as biofertilizers and biopesticides and can be used when excesive use of inorganic fertilizers are already causing harm to soil, rhizomicrobiome and associated population of plants. This review provides information about possible mechanism used by different PGPRs in optimization of different medicinal plant growth. However, there is a gap which still persists in our knowledge about exact pathways and molecular mechanism which is modulated by the PGPRs for imaprting these effects. Omics approaches as well as metabolic engineering can be a tool of great use for deciphering different pathways which are being orchestrated by these PGPRs. Overall, future study should be focused on PGPR-based metabolite engineering, exploration of beneficial strains of PGPRs and identification of target genes to promote plant growth under stress condition through biotechnology.

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Abbreviations

PGPR, plant growth promoting rhizobacteria; ISR, induced systemic resistance; SAR, systemic acquired resistance; JA, jasmonic acid; ET, ethylene; SA, salicylic acid; ACC, 1-aminocyclopropane-1-carboxylate; PGR, plant growth regulation; H₂O₂, hydrogen peroxide; ROS, reactive oxygen species; VOCs, volatile organic compounds; Na⁺, sodium ion; K⁺, potassium ion; HKT, high affinity K⁺ transporters; IMPs, integral membrane proteins; FIT1, Fe-deficiency induced transcriptional factor 1; FRO2, ferric reduction oxidase 2; PEAMT, phosphoethanolamine N-methyltransferase; AACP, amino acid-containing products; HCP, hormone-containing products; HS, humic substances; IAA, indole-3-acetic acid; EPS, exopolysaccharides; CAT, catalase; POD, peroxidase; SOD, superoxide dismutase; OMTs, outer membrane transporters; CM, cytoplasmic membrane; SBP, siderophore binding proteins.

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