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MICROBIOLOGÍA

THE IMPORTANCE OF ANTIMICROBIAL COMPOUNDS PRODUCED BY BENEFICIAL BACTERIA ON THE BIOCONTROL OF PHYTOPATHOGENS

Importancia de compuestos antimicrobianos producidos por bacterias benéficas en el biocontrol de fitopatógenos

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ABSTRACT

Bacteria produce antimicrobial compounds to compete for nutrients and space in a particular habitat. Antagonistic interactions can be evaluated by several methodologies including the double-layer agar and simultaneous inhibition assays. Among the well-known inhibitory substances produced by bacteria are the broad-spectrum antibiotics, organic acids, siderophores, antifungal, and bacteriocins. The most studied bacterial genera able to produce these inhibitory substances are *Enterococcus*, *Lactococcus*, *Streptomyces*, *Bacillus*, *Pseudomonas*, *Klebsiella*, *Escherichia*, and *Burkholderia*. Some beneficial bacteria can promote plant growth and degrade toxic compounds in the environment representing an attractive solution to diverse issues in agriculture and soil pollution, particularly in fields with damaged soils where pesticides and fertilizers have been indiscriminately used. Beneficial bacteria may increase plant health by inhibiting pathogenic microorganisms; some examples include *Gluconacetobacter diazotrophicus*, *Azospirullum brasilense*, *Pseudomonas fluorescens*, *Pseudomonas protegens*, and *Burkholderia tropica*. However, most studies showing the antagonistic potential of these bacteria have been performed *in vitro*, and just a few of them have been evaluated in association with plants. Several inhibitory substances involved in pathogen antagonism have not been elucidated yet; in fact, we know only 1 % of the bacterial diversity in a natural environment leading us to assume that many other inhibitory substances remain unexplored. In this review, we will describe the characteristics of some antimicrobial compounds produced by beneficial bacteria, the principal methodologies performed to evaluate their production, modes of action, and their importance for biotechnological purposes.

Keywords: Antagonism, antibiotic, competition, inhibition, PGPR.

RESUMEN

Las bacterias producen compuestos antimicrobianos para competir por nutrientes y espacio en un hábitat particular. Las interacciones antagónicas pueden evaluarse mediante varias metodologías, incluido el agar de doble capa y los ensayos de inhibición simultánea. Las sustancias inhibidoras mejor conocidas producidas por bacterias incluyen antibióticos, ácidos orgánicos, sideróforos, antifúngicos y bacteriocinas. Entre los géneros bacterianos más estudiados que producen sustancias inhibidoras se incluyen *Enterococcus*, *Lactococcus*, *Streptomyces*, *Bacillus*, *Pseudomonas*, *Klebsiella*, *Escherichia* y *Burkholderia*. Algunas bacterias beneficiosas tienen la capacidad de promover el crecimiento de las plantas y degradar compuestos tóxicos en el ambiente, por lo que podrían incrementar el rendimiento de los cultivos y disminuir problemas de contaminación del suelo, especialmente donde los pesticidas y fertilizantes han sido utilizados

indiscriminadamente. Algunas bacterias beneficiosas pueden aumentar la salud de las plantas al inhibir microorganismos patógenos, por ejemplo, *Gluconacetobacter diazotrophicus*, *Azospirullum brasilense*, *Pseudomonas fluorescens*, *Pseudomonas protegens* y *Burkholderia tropica*. Sin embargo, la mayoría de los estudios que muestran el potencial antagónico de estas bacterias se han realizado *in vitro*, y pocos de ellos se han evaluado en asociación con plantas. Varias sustancias inhibitorias implicadas en el antagonismo de los patógenos aún son desconocidas; de hecho, sabemos que solo se ha aislado el 1 % de la diversidad bacteriana en un ambiente natural, lo que sugiere que hay muchas otras sustancias inhibitorias que no han sido exploradas. En esta revisión describimos las características de algunos compuestos antimicrobianos producidos por bacterias beneficiosas, las principales metodologías usadas para evaluar su producción, modos de acción y su importancia para fines biotecnológicos.

Palabras clave: Antagonismo, antibiótico, competencia, inhibición, PGPR.

INTRODUCTION

Microbial communities interact in different ways, either synergistically or antagonistically. To survive the adversities and coexist with other microorganisms, bacteria are continually fighting for nutrients and niche space (Hibbing *et al*., 2010). When it comes to bacterial antagonism, it is essential to define a producer strain as the one capable of producing toxic compounds that inhibit the growth of other non-producing strains, generally sensitive to the substance (Russel *et al*., 2017). Competition between bacteria can be influenced by the production of these toxic substances and producer strains are benefited compared to non-producing or sensitive strains by dominating the niche in which they are located (Khare and Tavazoie, 2015). However, producer and sensitive strains interact differently when they are in a structured environment than in an unstructured one (Kelsic *et al*., 2015; Chacón *et al*., 2018). In an unstructured environment where a population of sensitive strains has been established, producers are not able to invade because they pay the price for toxin production (i.e., energetic cost of plasmid carriage, production, and resistance to the molecule), decreasing their growth compared to the growth experienced by the sensitive strains. In a structured environment such as the surface of an agar plate, producers and sensitive strains grow in separate colonies and toxins diffuse from the producing colony towards the sensitive neighbors making resources more available to the producer strains, due to their excessive accumulation. Therefore, producer strains numbers increase compared to the sensitives, even if their growth rate is lower (Stubbendieck *et al*., 2016).

Different inhibitory substances produced by bacteria have been reported. Some of them include broad-spectrum antibiotics, organic acids, siderophores, and volatile organic compounds, antifungals, bacteriocins, among others (Riley, 2009; Li *et al*., 2013; Meena and Kanwar, 2015; Sindhu *et al*., 2016). Several inhibitory substances have not been elucidated yet; in fact, we only know 1 % of the bacterial diversity in a natural environment, leading us to assume that many other inhibitory substances remain to be explored. In this review, we will begin by describing the principal methodologies used to evaluate the production of these inhibitory substances. Next, we will provide some examples of diverse bacterial inhibitory substances including (i) bacteriocins, (ii) siderophores and (iii) other metabolites such as broad-spectrum antibiotics, covering their structural characteristics and modes of action. Finally, given the importance of the inhibitory substances for biotechnological purposes, their applications, as well as the use of beneficial bacteria as bio-inoculants, will be discussed.

METHODS TO EVALUATE MICROBIAL ANTAGONISM

Different methods can evaluate microbial inhibition, the most used comprise the double-layer agar and simultaneous inhibition assays (Molina-Romero *et al*., 2017a; b). Assays in liquid media have also been frequently reported and represent a variant of simultaneous active interaction (Kreth *et al*., 2008). All those methods have been used to evaluate the antagonism among bacterial or fungal strains, however, to determine the antagonism against nematodes and viruses other methodologies have been developed; one example is the microscopic observation to evaluate the paralysis of nematodes with inhibitory substances and diminution of disease symptoms produced by virus when the plant was inoculated with a beneficial bacteria (Wong *et al*., 2016; Su *et al*., 2017a; b) . This review only describes the most common methodologies used to evaluate microbial inhibition.

Double-layer agar

In the double-layer agar method bacteria never interact between them; however, bacteria explored as sensitive should be able to grow in the presence of metabolites previously produced by the antagonistic strain grown on the first agar-layer (Mukherjee and Ghosh, 2014). The double-layer agar method consists of growing a producer strain on the surface of an agar-medium during 24-48 h. After incubation time, producer colonies are removed with a sterile glass slide and the remain cells are killed by exposing the glass Petri dish to the vapor of chloroform during 1.5 h. Plates are left in a laminar flow cabinet until the residual chloroform is evaporated and the second layer of soft agar inoculated with the indicator strain is poured over the first layer of agar, where the producer strain had grown

previously. Plates are incubated at the optimal temperature for each microorganism analyzed. Inhibition halos formed in the upper layer are considered indicative of antibacterial activity (see Fig. 1).

Simultaneous inhibition

In the simultaneous inhibition assay, both bacterial species are co-interacting all the time during the assay. For this methodology, overnight cultures of strains explored as sensitive are placed over the surface of an agar plate by the spread-plating method (Sanders, 2012; Molina-Romero *et al*., 2017b), and a 20 µl-drop of the producer strain is placed on the middle of the agar plate. After the drop dried, Petri plates are inverted and incubated at the right temperature for the microorganism analyzed. Surrounding halos of the producer strain are indicative of antibacterial activity (see Fig. 2).

Antagonism in liquid media

In this assay, the producer and the sensitive strains are grown in a defined liquid media, both separately and together in co-culture. Bacterial growth observed in the mixed culture is compared to the observed in the individual culture. When a producer bacterium inhibits the growth of a sensitive strain, the bacterial number of the sensitive strain decreases sharply in the mixed culture. In this experiment, the bacterial number is determined by counting CFU/ml using a selective medium, the media selection play an essential role in the screening of co-interacting strains (Muñoz-Rojas *et al*., 2005).

It is essential to highlight that the production of an inhibitory substance could be different in each bacterial growth conditions, growth phase and the kind of culture media used for this assay (Anacarso *et al*., 2014). This could be because gene expression depends on environmental and nutrient-availability conditions (McArthur and Bibb, 2008). Though, some strains can produce their inhibitory substances constitutively independently of the growth conditions (Muñoz-Rojas *et al*., 2005).

INHIBITORY SUBSTANCES PRODUCED BY BACTERIA

The most studied bacterial genera capable of producing inhibitory substances are *Enterococcus*, *Lactococcus*, *Streptomyces*, *Bacillus*, *Pseudomonas*, *Klebsiella*, *Escherichia,* and *Burkholderia*, and several articles have been published (Khabbaz *et al*., 2015; Sekhar and Thomas, 2015; Tontou *et al*., 2016; Huo *et al*., 2018). In this section, we will focus on some inhibitory substances produced by beneficial bacteria.

Siderophores

Iron, unlike other elementary nutritional sources such as nitrogen, phosphorus, potassium, among others, is not freely available in host organisms and is, therefore, an important limiting factor for the growth of microorganisms. Production of siderophores confers producing microorganisms a competitive advantage over other bacteria in the environment, excluding them from their ecological niche (Beneduzi *et al*., 2012).

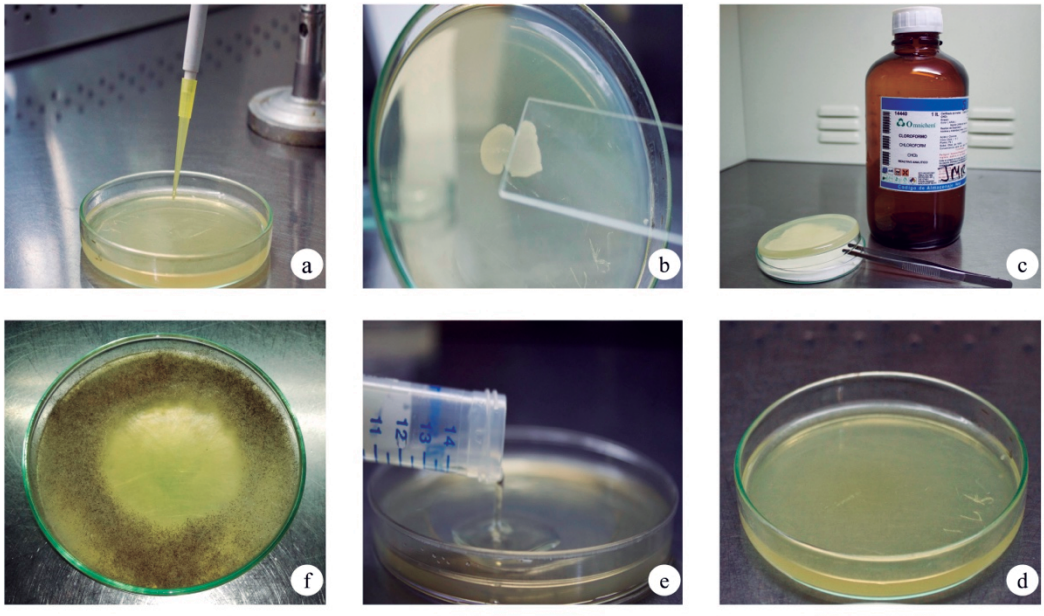

Figure 1. Double-layer agar assay. In this process the producer strain is grown in the middle of a glass plate with a specific culture media (a). After incubation of 48 h bacterial colonies are removed (b) and killed under chloroform vapors (c). Once the remaining chloroform is evaporated (d), a double layer of soft agar (inoculated with an indicator strain) is poured (e). Once more the plates are incubated to look for an inhibition halo (f).

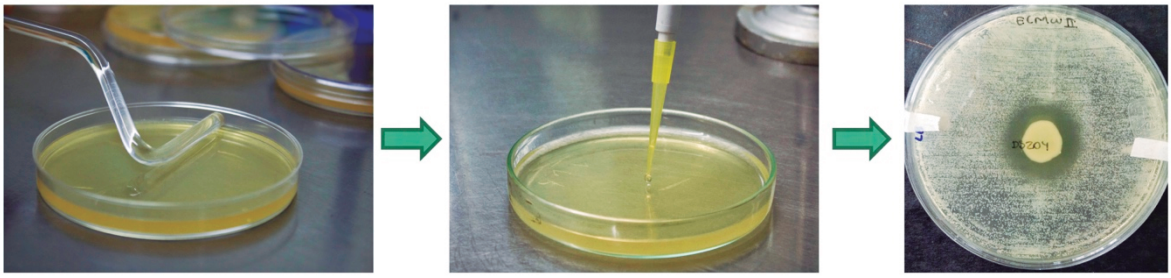

Figure 2. Simultaneous inhibition assay. An indicator strain is massively grown on the surface of an agar plate and a drop of the producer strain is placed in the middle of the plate. Once the drop dried, plates are incubated and the inhibition halo surrounding the producer strain is observed as shown in the last step.

Siderophores are small molecules (< 1500 Da) produced under iron-limited conditions and secreted to chelate iron from the environment. By diffusion, siderophores can attract the ferric ion with high affinity into the cell and also return it to the cell surface (Aguado-Santacruz *et al*., 2012). These molecules are mainly produced by Gram-negative bacteria, fungi, yeast and some graminaceous plants (phytosiderophores). Bacterial siderophores have been classified into different families according to their functional group: hydroxamates, catecholates, phenolates, and carboxylates. Additionally, there are some groups of siderophores that contain a mix of the main functional groups (Beneduzi *et al*., 2012; Ahmed and Holmström, 2014).

Some bacteria produce only one class of siderophores; however, other bacteria can secrete different types of siderophores, making them more efficient to colonize different environments. For example, some species of the genus *Pseudomonas* produce hydroxamates as ferribactine and pseudobactin, and other species produce molecules denominated pyoverdines of the type catechol (Pahari *et al*., 2017). About 270 siderophores have been structurally characterized, and their mechanism of transport has been described, and some variations have been found between Gram-positive and Gram-negative bacteria. For example, in Gram-positive bacteria, the Fe (III)-siderophore complex is bound to a periplasmic binding protein (that is anchored to the cell membrane) and eventually the complex is transported to the cytoplasm by ATP-dependent transporter systems. In contrast, Gram-negative bacteria carry out a more complicated process due to the presence of the outer membrane; involving TonB-dependent outer membrane receptors which recognize Fe (III)-siderophore complexes (Krewulak and Vogel, 2008). Once the complex binds to the outer membrane receptor at the cellular surface, it crosses the membrane through an energy-dependent mechanism carried out by membrane receptor proteins, periplasmic binding proteins, and inner membrane transport proteins; then, the complex is released into the periplasmic space and transported across the cytoplasmic membrane, where the complex is separated via reduction of Fe(III) to Fe (II) (Ahmed and Holmström, 2014).

It has been reported that siderophore-producing bacteria exert extensive biocontrol action against soil and root borne phytopathogens through the release of siderophores (Sah *et al*., 2017), Therefore, siderophore-producing bacteria protect plants from phytopathogens by acting as competitors, reducing the iron availability necessary for the pathogen growth (Beneduzi *et al*., 2012). Siderophore-producing bacteria also benefit plants by supplying them with iron when its availability is low in the environment, promoting plant-growth and improving phytoremediation (Chen *et al*., 2017). Siderophores produced by bacteria could be able to chelate other metals such as Cu, Cd, Ni, Zn, and others (Johnstone and Nolan, 2015; Chen *et al*., 2017). Moreover, bacterial siderophores have shown that protect plants by triggering induced systemic resistance (ISR) (Trapet *et al*., 2016). Some crops that have benefited from siderophore-producing bacteria include potato, sunflower, sorghum, oat, cotton, peanut, pigeon pea and cucumber (Dimkpa, 2016).

Several studies have reported the role of siderophores in biological control (Sayyed and Patel, 2011). *Pseudomonas* sp. strain B10 was the first bacteria showing biocontrol of plant pathogens. In particular, the synthesis of siderophores by fluorescent *Pseudomonas* promote plant growth and inhibit the growth of phytopathogens such as *Erwinia carotovora*, *Ralstonia solanacearum*, and *Fusarium oxysporum*. Pyoverdines, mainly produced by *Pseudomonas aeruginosa* and *Pseudomonas fluorescens*, have demonstrated to be adequate to control *Pythium* and *Fusarium* species. *Pseudomonads* also produce pyochelin, which is thought to contribute to the protection of tomato plants from *Pythium*, as reported in *Pseudomonas aeruginosa* 7NSK2 (Siddiqui, 2006).

It has been reported that some strains of *Pseudomonas putida* produce siderophores increasing yield and biosynthesis of the major essential oil components when they are inoculated to *Mentha piperita* (peppermint) (Santoro *et al*., 2015).

Burkholderia species are known to produce siderophores that inhibit multiple phytopathogens, for example, *Paraburkholderia tropica* (formerly *Burkholderia tropica*) (Tenorio-Salgado *et al*., 2013). Other strains such as *Azospirullum brasilense* have also shown biocontrol properties. This bacterium produces catechol type siderophores having *in vitro* activity against the fungus *Colletotrichum acutatum*, one of the most critical pathogens in strawberry crop (Tortora *et al*., 2011). *Rhizobium* species also produce catecholates, inhibiting the growth of fungal pathogens including *Fusarium oxysporum*, *Fusarium solani*, *Ustulina zonata*, and *Fomes lamonensis*. Indeed, using *Rhizobium* strains in pea production has helped to decrease the presence of *Fusarium oxysporum* in infested soils, improving crop growth (Siddiqui, 2006). Rhizobactin from *Rhizobium meloti* is another example; although it is not known if this siderophore participates in biocontrol, agronomically is very interesting since it allows the bacteria to be more competitive in the environment (Saha *et al*., 2016). Species of *Azotobacter* also produce different siderophores including aminochelin, azotochelin, protochelin and azotobactin which protect crops from pathogens such as *Aspergillus*, *Alternaria*, *F. oxysporum*, among others (Baars *et al*., 2015).

Bacteriocins

These molecules belong to the most abundant and diverse class of antimicrobial agents, constituting an unusual microbial weapon. At first, bacteriocins were defined as ribosomally synthesized peptides directed against bacteria closely related to the producer strain (Silva *et al*., 2018), differing from traditional antibiotics precisely to their "relatively" narrow spectrum; however, later in this review we will describe some examples of bacteriocins with broad-spectrum activity showing that beyond inhibiting only related strains, bacteriocins may inhibit other prokaryotes and also fungi or parasites (De la Fuente-Salcido *et al*., 2015). For this reason, we propose to define them as antimicrobial peptides that may or may not act on strains related to the producer bacterium, which may also be active against other bacterial genera, fungi and/or parasites.

It is believed that 99 % of all bacteria may produce at least one bacteriocin and the only argument why we do not know more bacteriocins is because they are poorly studied (Klaenhammer, 1988). Before studying a bacteriocin *per se* it is necessary to find a producer strain which is possible by performing antagonism assays (Muñoz-Rojas *et al*., 2005), and once the producer strain is found these molecules can be isolated and purified by diverse methodologies. We will notice that the chemical nature and biosynthesis mechanisms of bacteriocins may vary significantly so characterize a bacteriocin could become complicated. For example, in many studies it is only possible to obtain a partially-purified preparation because the activity or the concentration of the bacteriocin is lost after the purification steps (Gálvez *et al*., 2007); a bacteriocin recombinantly produced could be highly concentrated in only two steps of purification but the characterization may turn out unsatisfactory due to difficulties presented in the following assays, as was the case with the crystallization and X-ray assays of the bacteriocin LlpA (Parret *et al*., 2004). Consequently, in most of the cases, the structure or modes of action are not described, which encourages us to intensify the study of these intriguing molecules.

Several classifications of bacteriocins have been proposed; in this review we show them as bacteriocins from Gram-positive and Gram-negative bacteria (see Fig. 3), choosing the primary examples and mechanisms of action such as nisin, colicins, tailocins, pyocins, among others (Rebuffat, 2016; Silva *et al*., 2018).

Gram-positive bacteriocins

Bacteriocins produced by Gram-positive bacteria are generally cationic, amphiphilic, membrane permeabilizing proteins, with an approximate size ranging from < 5 to > 30 kDa. Several classifications of these bacteriocins have been proposed mainly according to their biochemical characteristics (Kemperman *et al*., 2003). The mechanism of action of Gram-positive bacteriocins is still under investigation, but it is accepted that they disrupt membranes through electrostatic interactions or by interacting with anionic membrane phospholipids causing pore formation (e.g. wedge-like and barrel-steve complexes), which results in the rapid efflux of the cytoplasmic compounds. In bacteriocins such as nisin and enterocin, it has been proposed that the antimicrobial activity is due to the presence of two structural domains (one located at N-terminus and one at C-terminus) where N-terminal rings play an essential role in binding the lipid II (main peptidoglycan transporter) preventing the correct synthesis of the cell wall (Gillor *et al*., 2009).

Members of the genus *Bacillus* are known to produce different bacteriocins, especially the lipopeptide type (Abriouel *et al*., 2011). The well-known bacteriocins produced by the genus *Bacillus* are subtilin and coagulin. Regarding this genus, *Bacillus licheniformis* ZJU12 was found to produce a bacteriocin-like peptide with a broad antagonistic spectrum. This peptide was able to inhibit the growth of some pathogenic microorganisms such as *S. aureus*, *M. flavus,* and some fungal phytopathogens such as *Fusarium oxysporum*; an interesting fact is that no adverse effects to mice have been detected in toxicity tests, which indicate a great prospect to use for biocontrol (He *et al*., 2006). *Bacillus thuringiensis* was considered as a model organism for producing antimicrobial compounds. Most of the bacteriocins synthesized by *B. thuringiensis* have a broad-spectrum, inhibiting phytopathogens such as *Aspergillus* and *P. aeruginosa,* being employed mainly for the control of plagues (Ugras *et al*., 2013; Salazar-Marroquín *et al*., 2016). In a recent study, it was reported a bacteriocin produced by an insect originated bacterium, *Bacillus thuringiensis* subsp.

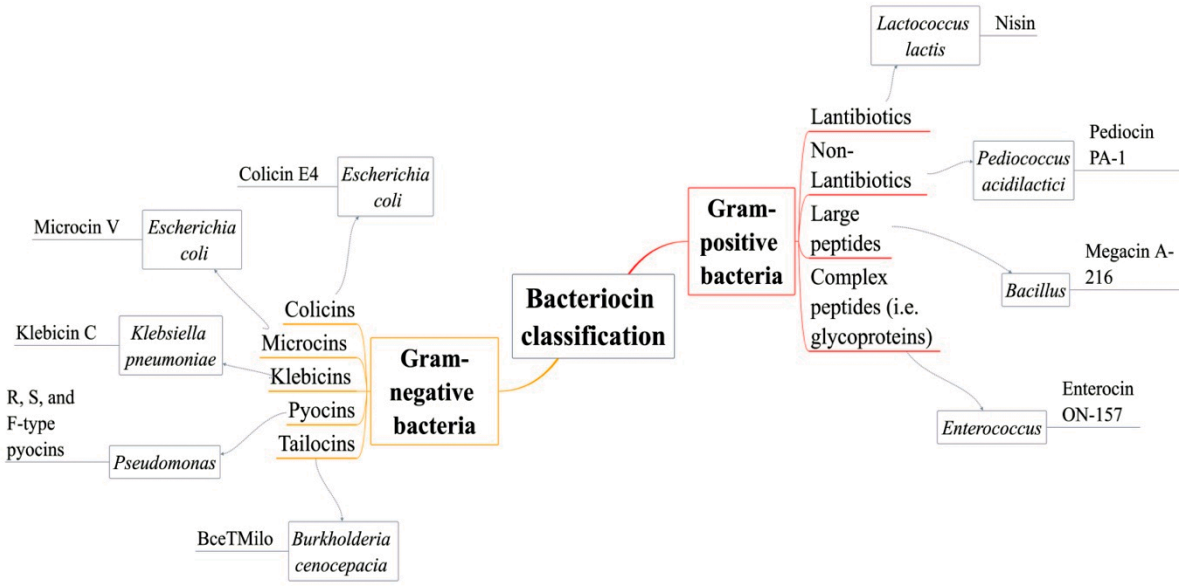

Figure 3. Bacteriocins classification. This figure shows the main examples of bacteriocins produced by Gram-positive and Gram-negative bacteria.

kurstaki Bn1; this bacteriocin was named as thuricin Bn1 and inhibits the growth of *P. syringae*, a plant pathogen (Ugras *et al*., 2013).

Gram-negative bacteriocins

Unlike bacteriocins from Gram-positive bacteria, Gram-negative bacteriocins are more extensive and carry out different mechanisms of action. One of the most known and extensively studied bacteriocin from Gram-negative bacteria is colicin, identified in *E. coli* (Riley and Wertz, 2002). Colicins are plasmid-encoded antimicrobial peptides secreted by *E. coli* and other related enterobacterial strains; their molecular weight varies between 20 kDa and 60 kDa and inhibit closely related strains such as *Salmonella* and other strains of *E. coli*. Production of colicins occurs mainly during times of stress like nutrient or oxygen depletion (Kaur and Kaur, 2015).

Structures of colicins are organized in three different domains: the translocation domain (T) N-terminally located, the receptor binding (R) located in the central region, and the cytotoxic domain (C) located at C-terminus, allowing to perform diverse mechanisms to kill bacterial cell (Cursino *et al*., 2002; Yang *et al*., 2014). Colicins target cells specifically through cell surface receptors so they can bind the outer membrane proteins by interacting with Tol or Ton complex periplasmic proteins and kill the sensitive strain, mainly through pore-formation, non-specific DNA degradation, murein and lipopolysaccharide biosynthesis inhibition (by interfering with lipid carrier regeneration), and inhibition of protein biosynthesis (Riley, 2009; Kaur and Kaur, 2015).

Other examples of bacteriocins produced by Gram-negative bacteria are microcins. These molecules are hydrophobic, low molecular weight, and ribosomally synthesized antimicrobial peptides. Their production is through a precursor peptide, including an N-terminal leader peptide and core peptides that may or may not undergo post-translational modifications. Microcins are characterized by showing heat, pH, and proteases tolerance, and do not require a lysis process to be secreted outside; indeed, they are secreted through the type I ABC (ATP binding cassette) transporter secretion system. Their mechanisms of action include pore-forming, DNase or RNase functions, and inhibitors of protein synthesis (Yang *et al*., 2014; Kaur and Kaur, 2015).

The genus *Pseudomonas* is also characterized for producing bacteriocins, well-known as pyocins. Pyocins target cells through specific receptors. Based on their structure, pyocins are classified as R, F or S-types. R-type pyocins are nuclease-protease resistant and it is thought that they have evolved from phage tails because their structure resembles non-flexible and contractile tails of bacteriophages. Their mechanism of action is through depolarization of the cytoplasmic membrane by pore formation. F-type pyocins are high molecular weight protease-resistant proteins which structure is similar to R-type pyocins, except for the flexible and non-contractile rod-like structure. S-type pyocins are colicin-like, protease-sensitive, and their structure consists in two components: the more significant component executes the killing activity (DNase, tRNase or channel-forming activities) while the smaller component, by showing sequence homology with colicin E2, is considered as an immunity protein. S-type pyocins cause cell death by DNA breakdown (pyocin AP41, S1, S2, S3) and pore formation (pyocin S5) (Michel-Briand and Baysse, 2002; Parret and De Mot, 2002).

Pyocins have shown a limited spectrum against other *Pseudomonas* species, in particular, they target *Burkholderia cepacia* complex strains; however, R-type pyocins have been shown to kill a diversity of *P. aeruginosa* strains as well as *Campylobacter* species, *Neisseria gonorrhea*, *Neisseria meningitides*, *Haemophilus ducreyi*, *Pseudomonas fluorescens*, and *Pseudomonas putida* (Naz *et al*., 2015). Another example is putadicin T01 produced by *Pseudomonas putida* which has shown a broad-spectrum against not only Gram-negative but also Gram-positive bacteria like *Bacillus megaterium* and *Enterococcus faecalis*, representing another opportunity for the treatment of pathogenic bacteria (Ghrairi *et al*., 2014).

Similar phage tail-like bacteriocins have been reported, particularly in plant-associated pseudomonad species. These molecules known as "tailocins", are large bactericidal structures with contractile (myotailocins) and flexible tails (siphotailocins) (Ghequire and De Mot, 2015; Yao *et al*., 2017). Both carry out a mechanism similar to phage infection: first, they reproduce the initial steps of the infection cycle by binding a cell receptor, and then the cytoplasmic membrane is punctured, where massive ion release occurs.

Recent studies have revealed that tailocins are not restricted to the genus *Pseudomonas*. For example, *Burkholderia cenocepacia* BC0425 produces a broad-spectrum tailocin (BceTMilo); it is suggested that BceTMilo binds to a D-glucose receptor for its adsorption through the *Pseudomonas aeruginosa* cell surface (Yao *et al*., 2017).

Other inhibitory compounds produced by bacteria

Bacteria also produce other metabolites such as volatile compounds and broad-spectrum antibiotics. Volatile compounds are vital in bacterial communication processes, but recent research indicates that these compounds, when secreted by bacteria, could perform antagonism over other microorganisms (Chaurasia *et al*., 2005; Kai *et al*., 2016). One of the volatile compounds produced by bacteria, mainly from the genus *Pseudomonas*, is hydrocyanic acid and it has been demonstrated that it participates in diverse antibiotic activities; evidence of this is the biocontrol of *Thielaviopsis basicola* (Matilla and Krell, 2017). Other volatile organic compounds (VOCs) produced by bacteria have been described; however, the biological role of most of them remains to be deciphered (Tyc *et al*., 2017).

Metabolites such as broad-spectrum antibiotics may have antibacterial and/or antifungal properties. Some of them include lipopeptides, generally produced by strains of the genus *Bacillus*. These molecules have been characterized by having an amphiphilic structure, which consists of the binding of a hydrophilic cyclic peptide to a fatty acid chain that can range from 12 to 14 carbon atoms (Meena and Kanwar, 2015). A very interesting feature of these molecules is the diversity of their structures which can influence their antimicrobial activity. In fact, their effectiveness to inhibit the growth of microorganisms has been proved, demonstrating that some of them only have activity against fungi, as is the case of iturines (Rojas-Solís *et al*., 2013); on the other hand, lipopeptides such as surfactins do have activity against bacteria and fungi (Meena and Kanwar, 2015). Other antibiotics described are the polyketides (PK) which contain in their structure multiple β-hydroxyketone or β-hydroxyaldehyde as functional groups. Some of them have a broad-spectrum antibacterial activity such as andrimid (Matilla *et al*., 2016) but others are only effective against fungi, for example, pyoluteorin and amphotericin B (Gomes *et al*., 2013; Matilla and Krell, 2017) (see table 1).

A new family of antibacterial proteins was recently discovered, defined as lectin-like bacteriocins. These molecules are characterized by containing two carbohydrate-binding domains of the monocot mannose-binding lectin (MMBL) family. Some lectin-like bacteriocins from *P. putida*, *P. syringae*, and *P. fluorescens* were described: putidacin L1 or LlpABW from *P. putida*; LlpAPss642 from *P. syringae*; and LlpA1Pf-5 from *P. fluorescens*. These lectin-like bacteriocins can kill several *Pseudomonas* species but they are not active outside this genus (Parret *et al*., 2005). Similarly, the lectin-like bacteriocin LlpAXcm761from *Xanthomonas citri* pv. *malvacearum* LMG 761 can inhibit diverse species within the genus *Xanthomonas* (McCaughey *et al*., 2014).

PLANT-ASSOCIATED BENEFICIAL BACTERIA

In nature, interactions between microorganisms and plants may occur. For example, plant growth-promoting bacteria (PGPB) enhance plant growth through different mechanisms that include: direct mechanisms such as biological nitrogen fixation, phytohormone production, production of 1-Aminocyclopropane-1-carboxylate deaminase (ACC), phosphate solubilization and production of volatile organic compounds; and indirect mechanisms such as induction of systemic resistance (ISR), production of lytic enzymes and pathogen inhibition through the production of inhibitory substances (Lucy *et al*., 2004; Lugtenberg and Kamilova, 2009; Rojas-Solís *et al*., 2013; Molina-Romero *et al*., 2015). Other beneficial bacteria can degrade toxic compounds from contaminated soil, and several strains have shown the capability to biodegrade toxic compounds (Dvořák *et al*., 2017). It is noteworthy that inoculation of beneficial bacteria in plants could diminish the damage produced by chemical fertilizers on the environment and the cost of production (Baez-Rogelio *et al*., 2017; Pazos-Rojas *et al*., 2018). Moreover, beneficial microorganisms allow an increase in the size of roots, a better nutrient absorption, and diminution in the lixiviation level of combined nitrogen. Therefore, the addition of chemical fertilization could be diminished because the plant improves the efficiency to take the combined nitrogen (Dobbelaere *et al*., 2002a; Fuentes-Ramírez and Caballero-Mellado, 2005).

Depending on the colonization site of the plant, beneficial bacteria have been classified in rhizospheric,

Table 1. Antibiotics produced by bacteria and their antimicrobial spectrum. Novel antibiotics with antibacterial, antifungal, antihelmintic and antioomycete activity are included.

Antibiotic	Type of molecule	Activity	Producer strain	Reference
Surfactin	Lipopeptide	Antibacterial and antifungal	*B. subtilis, B. amyloliquefaciens*	(Meena and Kanwar, 2015)
Iturin	Lipopeptide	Antifungal	*Bacillus subtilis*	(Rojas-Solís *et al*., 2013)
Fengycin	Lipopeptide	Antifungal	*B. subtilis, B. amyloliquefaciens*	(Meena and Kanwar, 2015)
Novel lipopeptide	Lipopeptide	Broad-spectrum antibacterial	*Streptomyces amritsarensis* sp. nov.	(Sharma *et al*., 2014)
Polymixin	Lipopeptide	Antibacterial	*Bacillus polymyxa*	(Velkov *et al*., 2010)
Chromobacto mycin	Lipopeptide	Antifungal	*Chromobacterium* sp.	(Meena and Kanwar, 2015)
Amphotericin B	Polyketide	Antifungal	*Streptomyces nodosus*	(Gomes *et al*., 2013)
Pyoluteorin	Polyketide	Antifungal, antioomycete	*Pseudomonas fluorescens* Pf5	(Matilla and Krell, 2017)
2,4, diacetylphloro glucinol	Polyketide	Antibacterial, antifungal, antihelmintic	*Pseudomonas protegens* sp. nov.	(Weller *et al*., 2007)
Zwittermycin A	Non-ribosomal peptide	Antifungal, antioomycete	*Bacillus cereus* UW85	(Matilla and Krell, 2017)
Andrimid	Hybrid PK/Non-ribosomal peptide	Broad-spectrum antibacterial	*Serratia plymuthica* A153	(Matilla *et al*., 2016)

endophytic, epiphytic, bacteria from rhizoplane, and others. In the rhizosphere, region of the soil where diverse microbial communities live and are influenced by plant root exudates (Sylvia *et al*., 2005), bacteria are the most abundant microorganisms able to colonize and compete against the microflora of the roots, causing a neutral, detrimental or beneficial effect to the plant, specifically plant growth; these beneficial bacteria have been termed as plant growth promoting rhizobacteria (PGPR) (Vejan *et al*., 2016).

The main mechanism of the competition of PGPR is through the production of inhibitory substances (Beneduzi *et al*., 2012), resulting in an advantage for the elimination of phytopathogens.

ANTAGONISM OF RHIZOBACTERIA AGAINST PHYTOPATOGENS

Among the PGPR able to eliminate phytopathogens are included *Gluconacetobacter diazotrophicus* (Muñoz-Rojas *et al*., 2005), *Azospirullum brasilense* (Méndez *et al*., 2014), *Pseudomonas fluorescens* (Laue *et al*., 2000), *Pseudomonas protegens* (Ramette *et al*., 2011) and *Burkholderia tropica* (Bolívar-Anillo *et al*., 2016); and some *Bacillus* strains are also known for protecting plants from phytopathogens (Subramanian and Smith, 2015). For example, *Gluconacetobacter diazotrophicus* has shown in antagonism assays its ability to inhibit important phytopathogens such as *F. oxysporum*, *F. solani*, *C. fimbriata* and *C. falcatum* possibly due to the production of pyoluteorin (Logeshwaran *et al*., 2011).

Recently, it was described a new bacteriocin from *Gluconacetobacter diazotrophicus,* PAL5, named Gluconacin which has an antagonistic effect against phytopathogens such as *X. albilineans* (which produce leaf scald of sugarcane plants), and *X. vasicola* pv. *vasculorum* (causal agent of gumming disease of sugarcane and leaf streak of corn) (Oliveira *et al*., 2018).

Although *Azospirillum* is not well known as a typical biocontrol agent, some possible mechanisms to reduce damage by pathogens have been described; for example, the production of phenylacetic acid. One report also showed the ability of *A. brasilense* to produce siderophores with antifungal activity *in vitro* against *Colletotrichum acutatum* M11, preventing the anthracnose caused by this fungus (Tortora *et al*., 2011).

Some plant-associated *Pseudomonas* inhibit several phytopathogens such as *Xanthomonas* spp. (Garza-Ramos *et al*., 2015) and diverse bacteriocins produced by this genus have been isolated and characterized. For example, *P. syringae* pv. *ciccaronei* NCPPB2355 produces a bacteriocin that inhibits *P. syringae* subsp. *savastanoi*, the causal agent of olive knot disease (Lavermicocca, 1999); *P. fluorescens* strain BC8 produces the bacteriocin fluoricin-BC8 that inhibits *P. solanacearum* under *in vitro* conditions; *Pseudomonas aeruginosa* RsB29 cause suppression of *Fusarium* wilt and rot of chickpea (Sindhu *et al*., 2016); *P. protegens* CHA0 produces diverse secondary metabolites that include hydrogen cyanide, 2,4-diacetylphloroglucinol, pyoluteorin, and pyrrolnitrin to inhibit diverse phytopathogens such as *Thievaloviopsis basicola*

and *Pythium ultimum* in tobacco and cucumber (Jousset *et al*., 2014; Sindhu *et al*., 2016).

Burkholderia species also inhibit essential phytopathogens. For example, *Burkholderia tropica* produces siderophores and volatile compounds that act as bio-controllers of phytopathogens such as fungi and nematodes, making it an excellent candidate to be used as a bio-inoculant in crops. The ability to inhibit the growth of phytopathogenic fungi by *Burkholderia tropica* was proven against *Colletotrichum gloeosporioides, Fusarium culmorum, Fusarium oxysporum* and *Sclerotium rolffsi* by producing 18 volatile compounds that included α-pinene and limonene (Bolívar-Anillo *et al*., 2016). *Burkholderia gladioli* strains have also shown inhibitory activity *in vitro* and *in planta* against *T. ptyseos*, a pink disease causative agent (Marín-Cevada *et al*., 2012).

Bacillus strains such as *Bacillus thuringiensis* ssp. *tochigiensis* HD868 and *Bacillus thuringiensis* ssp. *entomocidus* HD9 (Subramanian and Smith, 2015) have been potentially accepted for protection against phytopathogens as *Aspergillus niger, Aspergillus fumigatus, Aspergillus flavus, Cryphonectria parasitica, Fusarium oxysporum, Penicillium digitatum,* among others. *B. thuringiensis* NEB17 produces the bacteriocin thuricin 17 (Th17) whose application in leaves soybean and corn stimulates the growth and it is the only bacteriocin studied extensively for plant growth promotion; it also participates as a bacterial signal compound and is able to increase phytohormones production and response to salt stress in *Arabidopsis thaliana* (Abriouel *et al*., 2011). *B. amyloliquefaciens* strain RC-2 produces a bacteriocin-like substance able to inhibit *C. dematium* and other phytopathogens such as *R. necatrix, P. oryzae, A. tumefaciens,* and *X. campestris* pv. *campestris* (Abriouel *et al*., 2011). *Bacillus subtilis* 14B reduced the percentage of infection in plants caused by *Agrobacterium tumefaciens* and it was proposed for biocontrol of crown gall disease in tomato plants (Hammami *et al*., 2009).

APPLICATION OF ANTAGONISTIC PGPB AS BIO-INOCULANTS

Beneficial bacteria have shown diverse potential functions when used in intensive agriculture, for example, plant growth. Furthermore, their ability to produce inhibitory compounds represents a potential for biological control. The strategy commonly used to kill phytopathogens is the use of chemical compounds such as pesticides. Nevertheless, reducing the use of pesticides is truly important since they have been implied in ecological, environmental and human health damages (Baez-Rogelio *et al*., 2017).

Although antagonistic interactions in rhizosphere for biocontrol purposes have not been intensively studied, it has been proposed that PGPR interactions with other soil microorganisms (fungal or bacteria) could be potentially used in plants of agricultural interest by developing mixed bio-inoculants or using their inhibitory substances *per se* (Ramamoorthy, 2001). Many reports have shown the biocontrol potential of PGPR, but most of the assays are only performed *in vitro,* and their direct application in crops has been little explored.

Mono-inoculants have been developed for commercial agriculture and are already being commercialized in several countries, mainly in Mexico and Argentina (Molina-Romero *et al*., 2015). One of the most explored bacteria in crops has been *Azospirillum brasilense*, which has been used in various crops showing successful results in more than 70 % of cases (Dobbelaere *et al*., 2002b). Other bacteria used for the development of these inoculants are *Rhizobium etli*, *Pseudomonas fluorescens, Bradyrhizobium* sp., *Mesorhizobium cicerii, Sinorhizobium meliloti, Rhizobium legumonisrum biovar trifoli* and *Bradyrhizobium japonicum* (Vivanco-Calixto *et al*., 2016).

The co-inoculation of microorganisms has already been reported and has apparently been more compelling, perhaps because of the synergistic effect that occurs when they are in co-interaction (Atieno *et al*., 2012; Zoppellari *et al*., 2014); for example, the co-inoculation of lettuce with *Bacillus* sp. and *Glomus intraradices* (Vivas *et al*., 2003) and co-inoculation of pea with *Rhizobium* and *Bacillus megaterium* (Elkoca *et al*., 2010). Few formulations containing more than three species of microorganisms in consortium have also been studied (Molina-Romero *et al*., 2015), one of them is the inoculation of sugarcane with a mixture of five diazotrophic bacteria (*Gluconacetobacter diazotrophicus, Herbaspirillum seropedicae, H. rubrisubalbicans, Azospirillum amazonense, Burkholderia tropica*) (Oliveira *et al*., 2009). Although mono and co-inoculations have resulted excellent for crops, all these formulations have been marketed mainly to promote plant growth and not for biocontrol purposes; examples of this are *Bradyrhizobium* spp. or *A. brasilense* inoculants which have been commercialized for years to increase the yield of diverse crops (Fukami *et al*., 2016). For this reason, designing new formulations of mono or multi-inoculants with beneficial bacteria capable of eliminating phytopathogens is a challenge.

The design, formulation and optimization of a compelling mixture of bacteria to be used as inoculants is not an easy task; it requires studies of adhesion to seeds and colonization in plants (Sundaramoorthy *et al*., 2012; Singh *et al*., 2014; Baez-Rogelio *et al*., 2017). Also, antagonistic assays among the microbial strains of the mixture should be performed before the design and application of a multi-species inoculant, because some antagonistic effects could occur among bacteria (Molina-Romero *et al*., 2017b). It also requires assays to guaranty the coexisting of bacterial strains when they are in the formulation and associated with plants and verify the plant growth promotion effectiveness (Muñoz-Rojas *et al*., 2013). Several polymicrobial formations contain microbial strains capable of coexisting without antagonizing each other with the capability of eliminate pathogens (Oliveira *et al*., 2009; Muñoz-Rojas *et al*., 2013; Baez-Rogelio *et al*., 2017; Molina-Romero *et al*., 2017b; Pérez-Santos

et al., 2017a; b) and some of these formulations contain desiccation-tolerant bacteria, making them more efficient in environments with low water availability (Molina-Romero *et al*., 2017b; Pérez-Santos *et al*., 2017a; Pazos-Rojas *et al*., 2018).

Some bacterial inoculants are commercially available for promoting growth in crops and are also useful for biocontrol; however, some of them inhibit pathogens due to the presence of fungicides (Crovo and Clemente, 2015) such as metalaxyl, fludioxonil or benomyl which may cause health damages.

Recently, in the Laboratory of Ecology and Survival of Microorganisms from the Center of Research in Microbiological Sciences (Sciences Institute, University of Puebla, Puebla, Mexico) multispecies inoculants have been developed, fulfilling the challenge of containing strains capable of coexisting without antagonizing each other and also able to eliminate phytopathogens (Muñoz-Rojas *et al*., 2013). Other examples of mono and multi-inoculants that inhibit the growth of phytopathogens include Enerbac from the company "Agrícola Inovación-Mexico", Fungikiller® from Bio-Iliberis R&D, and Serenade ASO® from Bayer CropScience, among others (Matilla and Krell, 2018).

Microbes often exist in complex multispecies communities in the environment, but the molecular mechanisms through which such communities develop and persist, despite significant antagonistic interactions between species, are not well understood (Wong *et al*., 2016). It would be interesting to perform research related to the effect of beneficial antagonistic bacteria on rhizosphere bacterial communities and evaluate if multispecies formulations influence is stronger than mono-inoculants. Plant microbiomes are fundamental to understanding how to improve the health of plants and crops production (Berg *et al*., 2014; Busby *et al*., 2017). In this context, studies of microbial diversity are critical to the prevention of diseases and can be implemented as a biomarker in plant protection strategies (Berg *et al*., 2017). An effective biocontrol should be based on the knowledge of the microbiomes present in healthy and thriving plants.

CONCLUSIONS

By producing diverse antimicrobial compounds, beneficial bacteria play a very important role in different areas, particularly in agriculture. The use of these microorganisms as bio-inoculants represents a great strategy to fight against phytopathogens since their production is cheaper than any other chemical fertilizer and they have positive effects on plants. Moreover, reducing the use of chemical fertilizers and toxic compounds such as pesticides and herbicides is a critical factor to preserve the environment and human health. Although many bacterial inoculants have been designed, marketing formulations with bacterial consortiums, especially those with the capability to inhibit the growth of diverse kind of pathogens, is still in development. Having them available will contribute to sustainable agriculture by reducing the use of toxic compounds without affecting agricultural productivity.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

Abriouel H, Franz CMAP, Omar N Ben, Galvez A. Diversity and applications of Bacillus bacteriocins. FEMS Microbiol Rev. 2011;35(1):201–32. Doi: https://doi.org/10.1111/j.1574-6976.2010.00244.x

Aguado-Santacruz G, Moreno-Gómez B, Jiménez-Francisco B, García-Moya E, Preciado-Ortiz R. Impact of the microbial siderophores and phytosiderophores on the iron assimilation by plants: a synthesis. Rev Fitotec Mex . 2012;35(1):9–21.

Ahmed E, Holmström S. Siderophores in environmental research: Roles and applications. Microb Biotechnol. 2014;7(3):196–208. Doi: https://doi.org/10.1111/1751-7915.12117

Anacarso I, Bondi M, Mura C, Niederhäusern S De, Iseppi R, Messi P, *et al*. Plant Pathology & Microbiology Culture Compounds which are Able to Increase the Growth and the Production of Bacteriocins by Two Different LABS. Plant Pathol Microb. 2014;5(3):1–8. Doi: https://doi.org/10.4172/2157-7471.1000234

Atieno M, Herrmann L, Okalebo R, Lesueur D. Efficiency of different formulations of Bradyrhizobium japonicum and effect of co-inoculation of Bacillus subtilis with two different strains of Bradyrhizobium japonicum. World J Microbiol Biotechnol. 2012;28(7):2541–2550. Doi: https://doi.org/10.1007/s11274-012-1062-x

Baars O, Zhang X, Morel FMM, Seyedsayamdost MR. The Siderophore Metabolome of *Azotobacter vinelandii*. Appl Environ Microbiol. 2015;82:27–39. Doi: https://doi.org/10.1128/AEM.03160-15

Baez-Rogelio A, Morales-García YE, Quintero-Hernández V, Muñoz-Rojas J. Next generation of microbial inoculants for agriculture and bioremediation. Microb Biotechnol. 2017;10(1):19–21. Doi: https://doi.org/10.1111/1751-7915.12448

Beneduzi A, Ambrosini A, Passaglia LM. Plant growth-promoting rhizobacteria (PGPR): Their potential as antagonists and biocontrol agents. Genet Mol Biol. 2012;35:1044–1051. Doi: https://doi.org/10.1590/S1415-47572012000600020

Berg G, Grube M, Schloter M, Smalla K. The plant microbiome and its importance for plant and human health. Front Microbiol. 2014;5:1-4.

Berg G, Köberl M, Rybakova D, Müller H, Grosch R, Smalla K. Plant microbial diversity is suggested as the key to future biocontrol and health trends. FEMS Microbiol Ecol. 2017;93(5):1-9. Doi: https://doi.org/10.1093/femsec/fix050.

Bolívar-Anillo HJ, Contreras-Zentella ML, Teherán-Sierra LG. Burkholderia tropica una bacteria con gran potencial para su uso en la agricultura. TIP Rev Espec en Ciencias Químico-Biológicas. 2016;19(2):102–8. Doi: https://doi.org/10.1016/j.recqb.2016.06.003

Busby PE, Soman C, Wagner MR, Friesen ML, Kremer J, Bennett A, *et al*. Research priorities for harnessing plant microbiomes in sustainable agricultura. PLoS Biol. 2017;15(3):1-14. Doi: https://doi.org/10.1371/journal.pbio.2001793.

Chacón JM, Möbius W, Harcombe WR. The spatial and metabolic basis of colony size variation. ISME J. 2018;12:669-680. Doi: https://doi.org/10.1038/s41396-017-0038-0

Chaurasia B, Pandey A, Palni LMS, Trivedi P, Kumar B, Colvin N. Diffusible and volatile compounds produced by an antagonistic Bacillus subtilis strain cause structural deformations in pathogenic fungi in vitro. Microbiol Res. 2005;160(1):75–81. Doi: https://doi.org/10.1016/j.micres.2004.09.013

Chen Y, Yang W, Chao Y, Wang S, Tang YT, Qiu RL. Metal-tolerant *Enterobacter* sp. strain EG16 enhanced phytoremediation using *Hibiscus cannabinus* via siderophore-mediated plant growth promotion under metal contamination. Plant Soil. 2017; 413(1-2):203-216. Doi: https://doi.org/10.1007/s11104-016-3091-y

Crovo V, Clemente G. Eficacia de fungicidas de Síntesis y biológico en base a Trichoderma harzianum para controlar patógenos de Semillas de soja. Rev FAVE Ciencias Agrar. 2015;14(2):1–13.

Cursino L, Šmarda J, Chartone-Souza E, Nascimento AMA. Recent updated aspects of colicins of Enterobacteriaceae. Brazilian J Microbiol. 2002;33:185–95. Doi: https://doi.org/10.1590/S1517-83822002000300001

De la Fuente-Salcido NM, Castañeda-Ramírez JC, García-Almendárez BE, Bideshi DK, Salcedo-Hernández R, Barboza-Corona JE. Isolation and characterization of bacteriocinogenic lactic bacteria from M-Tuba and Tepache, two traditional fermented beverages in México. Food Sci Nutr. 2015;3(5):434–42. Doi: https://doi.org/10.1002/fsn3.236

Dimkpa C. Microbial siderophores: Production, detection and application in agriculture and environment. Endocytobiosis Cell Res. 2016;27(2):7–16.

Dobbelaere S, Croonenborghs A, Thys A, Ptacek D, Vanderleyden J, Dutto P, *et al*. Responses of agronomically important crops to inoculation with *Azospirillum*. Funct Plant Biol. 2002a;28(9):871-879 Doi: https://doi.org/10.1071/pp01074

Dobbelaere S, Croonenborghs A, Thys A, Ptacek D, Okon Y, Vanderleyden J. Effect of inoculation with wild type *Azospirillum brasilense* and *A. irakense* strains on development and nitrogen uptake of spring wheat and grain maize. Biol Fertil Soils. 2002b;36(4):284–297. Doi: https://doi.org/10.1007/s00374-002-0534-9

Dvořák P, Nikel PI, Damborský J, de Lorenzo V. Bioremediation 3.0: Engineering pollutant-removing bacteria in the times of systemic biology. Biotechnol Adv. 2017;35(7):845–866. Doi: https://doi.org/10.1016/j.biotechadv.2017.08.001

Elkoca E, Turan M, Donmez MF. Effects of single, dual and triple inoculations with Bacillus subtilis, Bacillus megaterium and Rhizobium leguminosarum bv. phaseoli on nodulation, nutrient uptake, yield and yield parameters of common bean (Phaseolus vulgaris l. cv. 'Elkoca-05'). J Plant Nutr. 2010;33(14):2104–2119. Doi: https://doi.org/10.1080/01904167.2010.519084

Fuentes-Ramírez LE, Caballero-Mellado J. Bacterial biofertilizers. PGPR: Biocontrol and Biofertilization. 2006, p. 143-172. Doi: https://doi.org/10.1007/1-4020-4152-7_5

Fukami J, Nogueira MA, Araujo RS, Hungria M. Accessing inoculation methods of maize and wheat with Azospirillum brasilense. AMB Express. 2016;6(1):1–13. Doi: https://doi.org/10.1186/s13568-015-0171-y

Gálvez A, Abriouel H, López RL, Omar N Ben. Bacteriocin-based strategies for food biopreservation. Int J Food Microbiol. 2007;120(1–2):51–70. Doi: https://doi.org/10.1016/j.ijfoodmicro.2007.06.001

Garza-Ramos U, Silva-Sánchez J, Martínez-Romero E, Tinoco P, Pina-Gonzales M, Barrios H, *et al*. Development of a Multiplex-PCR probe system for the proper identification of *Klebsiella variicola*. BMC Microbiol. 2015:1–14. Doi: https://doi.org/10.1186/s12866-015-0396-6

Ghequire MGK, De Mot R. The Tailocin Tale: Peeling off Phage Tails. Trends Microbiol. 2015;23(10):587–590. Doi: https://doi.org/10.1016/j.tim.2015.07.011

Ghrairi T, Braiek O Ben, Hani K. Detection and characterization of a bacteriocin, putadicin T01, produced by *Pseudomonas putida* isolated from hot spring water. APMIS. 2014:260–268. Doi: https://doi.org/10.1111/apm.12343

Gillor O, Giladi I, Riley MA. Persistence of colicinogenic Escherichia coli in the mouse gastrointestinal tract. BMC Microbiol. 2009;7:1–7. Doi: https://doi.org/10.1186/1471-2180-9-165

Gomes ES, Schuch V, Lemos EG de M. Biotechnology of polyketides: New breath of life for the novel antibiotic genetic pathways discovery through metagenomics. Brazilian J Microbiol. 2013;44(4):1007–1034. Doi: https://doi.org/10.1590/S1517-83822013000400002

Hammami I, Rhouma A, Jaouadi B, Rebai A, Nesme X. Optimization and biochemical characterization of a bacteriocin from a newly isolated Bacillus subtilis strain 14B for biocontrol of Agrobacterium spp. strains. Lett Appl Microbiol. 2009;48(2):253–60. Doi: https://doi.org/10.1111/j.1472-765X.2008.02524.x

He L, Chen W, Liu Y. Production and partial characterization of bacteriocin-like pepitdes by *Bacillus licheniformis*. Microb Res. 2006;161:321–326. Doi: https://doi.org/10.1016/j.micres.2005.12.002

Hibbing ME, Fuqua C, Parsek MR, Peterson SB. Bacterial competition: surviving and thriving in the microbial jungle. Nat Rev Microbiol. 2010;8(1):15–25. Doi: https://doi.org/10.1038/nrmicro2259.Bacterial

Huo Y, Kang JP, Kim YJ, Yang DC. *Paraburkholderia panacihumi* sp. nov., an isolate from ginseng-cultivated soil, is antagonistic against root rot fungal pathogen. Arch Microbiol. Springer Berlin Heidelberg; 2018;200(8):1–8. Doi: https://doi.org/10.1007/s00203-018-1530-2

Johnstone TC, Nolan EM. Beyond iron: Non-classical biological functions of bacterial siderophores. Dalt. Trans. 2015;14:6320-6339. Doi: https://doi.org/10.1039/c4dt03559c

Jousset A, Schuldes J, Keel C, Maurhofer M, Daniel R, Scheu S, *et al*. Full-Genome Sequence of the Plant Growth-Promoting Bacterium *Pseudomonas protegens* CHA0. Genome Announc. 2014;2(2):1. Doi: https://doi.org/10.1128/genomeA.00322-14

Kai M, Effmert U, Piechulla B. Bacterial-plant-interactions: Approaches to unravel the biological function of bacterial volatiles in the rhizosphere. Front Microbiol. 2016;7:108. Doi: https://doi.org/10.3389/fmicb.2016.00108

Kaur S, Kaur S. Bacteriocins as potential anticancer agents. Front Pharmacol. 2015;6:1–11. Doi: https://doi.org/10.3389/fphar.2015.00272

Kelsic ED, Zhao J, Vetsigian K, Kishony R. Counteraction of antibiotic production and degradation stabilizes microbial communities. Nature. 2015;521(7553):516–519. Doi: https://doi.org/10.1038/nature14485

Kemperman R, Kuipers A, Karsens H, Nauta A, Kuipers O, Kok J. Identification and characterization of two novel clostridial bacteriocins, circularin A and closticin 574. Appl Environ Microbiol. 2003;69(3):1589–1597. Doi: https://doi.org/10.1128/AEM.69.3.1589-1597.2003

Khabbaz SE, Zhang L, Cáceres LA, Sumarah M, Wang A, Abbasi PA. Characterisation of antagonistic *Bacillus* and *Pseudomonas* strains for biocontrol potential and suppression of damping-off and root rot diseases. Ann Appl Biol. 2015;166(3):456–471. Doi: https://doi.org/10.1111/aab.12196

Khare A, Tavazoie S. Multifactorial Competition and Resistance in a Two-Species Bacterial System. PLoS Genet. 2015;11(12):e1005715 Doi: https://doi.org/10.1371/journal.pgen.1005715

Klaenhammer TR. Bacteriocins of lactic acid bacteria. 1988;70(11171):337–349.

Kreth J, Zhang Y, Herzberg MC. Streptococcal antagonism in oral biofilms: *Streptococcus sanguinis* and *Streptococcus gordonii* interference with *Streptococcus mutans*. J Bacteriol. 2008;190(13):4632–4640. Doi: https://doi.org/10.1128/JB.00276-08

Krewulak KD, Vogel HJ. Structural biology of bacterial iron uptake. Biochim Biophys Acta - Biomembr. 2008;1778(9):1781–1804. Doi: https://doi.org/10.1016/j.bbamem.2007.07.026

Laue BE, Jiang Y, Chhabra SR, Jacob S, Stewart GSAB, Hardman A, *et al*. The biocontrol strain Pseudomonas fluorescens F113 produces the Rhizobium small bacteriocin, N-(3-hydroxy-7-cis-tetradecenoyl) homoserine lactone, via HdtS, a putative novel N-acylhomoserine lactone synthase. Microbiology. 2000;146(10):2469–80. Doi: https://doi.org/10.1099/00221287-146-10-2469

Lavermicocca P. Bacteriocin production by Pseudomonas syringae pv. ciccaronei NCPPB2355. Isolation and partial characterization of the antimicrobial compound. J Appl Microbiol. 1999;86(2):257–65. Doi: https://doi.org/10.1046/j.1365-2672.1999.00656.x

Li W, Rokni-zadeh H, Vleeschouwer M De, Ghequire MGK, Sinnaeve D. The Antimicrobial Compound Xantholysin Defines a New Group of Pseudomonas Cyclic Lipopeptides. PLoS One. 2013;8(5):1–16. Doi: https://doi.org/10.1371/journal.pone.0062946

Logeshwaran P, Thangaraju M, Rajasundari K. In Vitro Suppression of Soil Borne Pathogenic Fungi and Pyoluteorin Production by Gluconacetobacter Diazotrophicus. J Basic Appl Sci Res. 2011;1(3):150–156.

Lucy M, Reed E, Glick BR. Applications of free living plant growth-promoting rhizobacteria. Antonie Van Leeuwenhoek. 2004;86(1):1–25. Doi: https://doi.org/10.1023/B:ANTO.0000024903.10757.6e

Lugtenberg B, Kamilova F. Plant growth promoting Rhizobacteria. Annu Rev Microbiol. 2009;63:541–556. Doi: https://doi.org/10.1146/annurev.micro.62.081307.162918

Marín-Cevada V, Muñóz-Rojas J, Caballero-Mellado J, Mascarúa-Esparza MA, Castañeda-Lucio M, Carreño-López R, *et al*. Antagonistic interactions among bacteria inhabiting pineapple. Appl Soil Ecol. 2012:230–235. Doi: https://doi.org/10.1016/j.apsoil.2011.11.014

Matilla MA, Nogellova V, Morel B, Krell T, Salmond GPC. Biosynthesis of the acetyl-coA carboxylase-inhibiting antibiotic, andrimid in Serratia is regulated by hfq and the LysR-type transcriptional regulator, admX. Environ Microbiol. 2016;18(11):3635–3650. Doi: https://doi.org/10.1111/1462-2920.13241

Matilla MA, Krell T. Bacterias rizosféricas como fuente de antibióticos. Alianzas y Tendencias. 2017;2(1):14–21.

Matilla MA, Krell T. Plant Growth Promotion and Biocontrol Mediated by Plant-Associated Bacteria. In: Egamberdieva D., Ahmad P. (eds) Plant Microbiome Stress Response Microorganisms for Sustainability, vol 5. Singapore: Springer. 2018. p. 45-80.

McArthur M, Bibb MJ. Manipulating and understanding antibiotic production in Streptomyces coelicolor A3(2) with decoy oligonucleotides. Proc Natl Acad Sci. 2008;105(3):1020–1025. Doi: https://doi.org/10.1073/pnas.0710724105

McCaughey LC, Grinter R, Josts I, Roszak AW, Waløen KI, Cogdell RJ, *et al*. Lectin-Like Bacteriocins from Pseudomonas spp. Utilise D-Rhamnose Containing Lipopolysaccharide as a Cellular Receptor. PLoS Pathog. 2014;10(2):1–15. Doi: https://doi.org/10.1371/journal.ppat.1003898

Meena KR, Kanwar SS. Lipopeptides as the antifungal and antibacterial agents: Applications in food safety and therapeutics. Biomed Res Int. 2015;2015. Doi: https://doi.org/10.1155/2015/473050

Méndez M, Mercado EC, Pineda EG. *Azospirillum* una rizobacteria con uso potencial en la agricultura. Biológicas . 2014;16(1):11–18.

Michel-Briand Y, Baysse C. The pyocins of *Pseudomonas aeruginosa*. Biochimie. 2002;84(5–6):499–510. Doi: https://doi.org/10.1016/S0300-9084(02)01422-0

Molina-Romero D, Bustillos-Cristales M del R, Rodríguez-Andrade O, Morales-García YE, Santiago-Saenz Y, Castañeda-Lucio M, *et al*. Mecanismos de fitoestimulación por rizobacterias , aislamientos en América y potencial biotecnológico. Biológicas. 2015;17(2):24–34.

Molina-Romero D, Baez A, Quintero-Hernández V, Castañeda-Lucio M, Fuentes-Ramírez LE, Bustillos-Cristales M del R, *et al*. Compatible bacterial mixture, tolerant to desiccation, improves maize plant growth. PLoS One. 2017a;12(11):1–21. Doi: https://doi.org/10.1371/journal.pone.0187913

Molina-Romero D, Baez A, Quintero-Hernández V, Castañeda-Lucio M, Fuentes-Ramírez LE, Bustillos-Cristales M del R, *et al*. Antagonism assays to identify bacterial strains producing antimicrobial compounds. Protoc PLoS One. 2017b;12(11):1–2. Doi: https://doi.org/10.17504/protocols.io.j4mcqu6

Mukherjee A, Ghosh K. Antagonism against fish pathogens by cellular components and verification of probiotic properties in autochthonous bacteria isolated from the gut of an Indian major carp, Catla catla (Hamilton). Aquac Res. 2014;47(7):1–13. Doi: https://doi.org/10.1111/are.12676

Muñoz-Rojas J, Fuentes-Ramírez L, Caballero-Mellado J. Antagonism among *Gluconacetobacter diazotrophicus* strains in culture media and in endophytic association. FEMS Microbiol Ecol. 2005;54:57–66. Doi: https://doi.org/10.1016/j.femsec.2005.02.011

Muñoz-Rojas J, Morales-García YE, Juárez-Hernández D, Fuentes-Ramirez LE, Munive JA. Formulación de un inoculante multiespecies para potenciar el crecimiento de plantas. 2013:1–36.

Naz SA, Jabeen N, Sohail M, Rasool SA. Biophysicochemical characterization of pyocin SA189 produced by Pseudomonas aeruginosa SA189. Brazilian J Microbiol. 2015;46(4):1147–1154. Doi: https://doi.org/10.1590/S1517-838246420140737

Oliveira ALM, Stoffels M, Schmid M, Reis VM, Baldani JI, Hartmann A. Colonization of sugarcane plantlets by mixed inoculations with diazotrophic bacteria. Eur J Soil Biol. 2009;45(1):106–113. Doi: https://doi.org/10.1016/j.ejsobi.2008.09.004

Oliveira MM, Ramos ETA, Drechsel MM, Vidal MS, Schwab S, Baldani JI. Gluconacin from *Gluconacetobacter diazotrophicus* PAL5 is an active bacteriocin against phytopathogenic and beneficial sugarcane bacteria. J Appl Microbiol. 2018:1812–1826. Doi: https://doi.org/10.1111/jam.14074

Pahari A, Pradhan A, Nayak S, Mishra B. Bacterial Siderophore as a Plant Growth Promoter. In: Patra JK, Vishnuprasad CN, Das G, editors. Microb Biotechnol Vol 1 Appl Agric Environ. Singapore: Springer Singapore; 2017 p. 163–180.

Parret AHA, De Mot R. Bacteria killing their own kind: Novel bacteriocins of Pseudomonas and other γ-proteobacteria. Trends Microbiol. 2002;10(3):107–112. Doi: https://doi.org/10.1016/S0966-842X(02)02307-7

Parret AHA, Wyns L, De Mot R, Loris R. Overexpression, purification and crystallization of bacteriocin LlpA from Pseudomonas sp. BW11M1. Acta Crystallogr Sect D Biol Crystallogr. 2004;60(10):1922–4. Doi: https://doi.org/10.1107/S0907444904020153

Parret AHA, Temmerman K, De Mot R. Novel lectin-like bacteriocins of biocontrol strain Pseudomonas fluorescens Pf-5. Appl Environ Microbiol. 2005;71(9):5197–5207. Doi: https://doi.org/10.1128/AEM.71.9.5197-5207.2005

Pazos-Rojas LA, Rodríguez-Andrade O, Muñoz-Arenas LC, Morales-García YE, Corral-Lugo A, Quintero-Hernández V, *et al*. Desiccation-Tolerant Rhizobacteria Maintain their Plant Growth- Promoting Capability after Experiencing Extreme Water Stress. SciFed J. Appl. Microbiol. 2018;1(1):1-13.

Pérez-Santos JLM, Alatorre-Cruz JM, Bustillos-Cristales MDR, Morales-García YE, Hernández-Tenorio AL, Baez-Rogelio A, *et al*. Multi-species formulation to improve the growth of plants from semi-desertic zones. 2017a.

Pérez-Santos JLM, Santiago-Saenz YO, Hérnandez-Tenorio AL, Morales-García YE, Quintero-Hernández V, Baez-Rogelio A, *et al*. Method for obtaining potato plants from the extraction of induced sprouts in controlled conditions. 2017b.

Ramamoorthy V. Induction of systemic resistance by plant growth promoting rhizobacteria in crop plants against pests and diseases. Crop Prot. 2001;20(1):1–11. Doi: https://doi.org/10.1016/S0261-2194(00)00056-9

Ramette A, Frapolli M, Saux MF Le, Gruffaz C, Meyer JM, Défago G, *et al*. Pseudomonas protegens sp. nov., widespread plant-protecting bacteria producing the biocontrol compounds 2,4-diacetylphloroglucinol and pyoluteorin. Syst Appl Microbiol. Elsevier GmbH.; 2011;34(3):180–188. Doi: https://doi.org/10.1016/j.syapm.2010.10.005

Rebuffat S. Microcins and Other Bacteriocins: Bridging the Gaps Between Killing Stategies, Ecology and Applications. In: Dorit RL, Roy SM, Riley MA, editors. Bacteriocins Curr Knowl Futur Prospect. U.K.: Caister Academic Press; 2016 p. 11–34.

Riley MA, Wertz JE. Bacteriocins: Evolution, Ecology, and Application. 2002;56:117–37. Doi: https://doi.org/10.1146/annurev.micro.56.012302.161024

Riley MA. Bacteriocins, Biology, Ecology, and Evolution. Encycl Microbiol. 2009:32–44

Rojas-Solís D, Contreras-Pérez M, Santoyo G. Mecanismos de estimulación del crecimiento vegetal en bacterias del género *Bacillus*. Biológicas. 2013;15(2):36–41.

Russel J, Røder HL, Madsen JS, Burmølle M, Sørensen SJ. Antagonism correlates with metabolic similarity in diverse bacteria. Proc Natl Acad Sci. 2017;114(40):10684-10688. Doi: https://doi.org/10.1073/pnas.1706016114

Saha M, Sarkar S, Sarkar B, Sharma BK, Bhattacharjee S, Tribedi P. Microbial siderophores and their potential applications: a review. Environ Sci Pollut Res. 2016;23(5):3984–3999. Doi: https://doi.org/10.1007/s11356-015-4294-0

Sah S, Sahgal M, Singh R. Concomitant Ability of Siderophore Against Iron Paucity and Fusarium wilt in Lycopersicon esculentum. Biosci Biotechnol Res Asia. 2017;14(1):319-328

Salazar-Marroquín EL, Galán-Wong LJ, Moreno-Medina R, Reyes-López MÁ, Pereyra-Alférez B. Bacteriocins synthesized by Bacillus thuringiensis: generalities and potential applications. Rev Med Microbiol. 2016;27:95–101. Doi: https://doi.org/10.1097/MRM.0000000000000076

Sanders ER. Aseptic Laboratory Techniques: Plating Methods. J Vis Exp. 2012(63):1–18. Doi: https://doi.org/10.3791/3064

Santoro MV, Cappellari LR, Giordano W, Banchio E. Plant growth-promoting effects of native Pseudomonas strains on Mentha piperita (peppermint): An in vitro study. Plant Biol. 2015;17(6):1218–1226. Doi: https://doi.org/10.1111/plb.12351

Sayyed RZ, Patel PR. Biocontrol Potential of Siderophore Producing Heavy Metal Resistant Alcaligenes sp. and Pseudomonas aeruginosa RZS3 vis-à-vis Organophosphorus Fungicide. Indian J Microbiol. 2011;51(3):266–272. Doi: https://doi.org/10.1007/s12088-011-0170-x

Sekhar AC, Thomas P. Isolation and Identification of Shoot-Tip Associated Endophytic Bacteria from Banana cv. Grand Naine and Testing for Antagonistic Activity against *Fusarium oxysporum* f. sp. cubense. Am J Plant Sci. 2015;06(07):943–954. Doi: https://doi.org/10.4236/ajps.2015.67101

Sharma D, Mandal SM, Manhas RK. Purification and characterization of a novel lipopeptide from *Streptomyces amritsarensis* sp. nov. active against methicillin-resistant *Staphylococcus aureus*. AMB Express. 2014;4(1):50. Doi: https://doi.org/10.1186/s13568-014-0050-y

Siddiqui ZA. PGPR: Biocontrol and biofertilization. Netherlands: Springer. 2006:1–318. Doi: https://doi.org/10.1007/1-4020-4152-7

Silva CCG, Silva SPM, Ribeiro SC. Application of bacteriocins and protective cultures in dairy food preservation. Front Microbiol. 2018;9:594. Doi: https://doi.org/10.3389/fmicb.2018.00594

Sindhu SS, Sehrawat A, Sharma R, Dahiya A. Biopesticides: Use of Rhizosphere Bacteria for Biological Control of Plant Pathogens. Def Life Sci J. 2016;01(2):135–148.

Singh A, Jain A, Sarma BK, Upadhyay RS, Singh HB. Rhizosphere competent microbial consortium mediates rapid changes in phenolic profiles in chickpea during Sclerotium rolfsii infection. Microbiol Res. 2014;169:(5-6). Doi: https://doi.org/10.1016/j.micres.2013.09.014

Stubbendieck RM, Vargas-Bautista C, Straight PD. Bacterial communities: Interactions to scale. Front Microbiol. 2016;7:1234. Doi: https://doi.org/10.3389/fmicb.2016.01234

Su L, Shen Z, Ruan Y, Tao C, Chao Y, Li R, *et al*. Isolation of antagonistic endophytes from banana roots against meloidogyne javanica and their effects on soil nematode community. Front Microbiol. 2017a;8:1-11. Doi: https://doi.org/10.3389/fmicb.2017.02070

Su P, Tan X, Li C, Zhang D, Cheng J, Zhang S, *et al*. Photosynthetic bacterium *Rhodopseudomonas palustris* GJ-22 induces systemic resistance against viruses. Microb Biotechnol. 2017b;10(3):612-624. Doi: https://doi.org/10.1111/1751-7915.12704

Subramanian S, Smith DL. Bacteriocins from the rhizosphere microbiome - from an agriculture perspective. Front Plant Sci. 2015;6:909. Doi: https://doi.org/10.3389/fpls.2015.00909

Sundaramoorthy S, Raguchander T, Ragupathi N, Samiyappan R. Combinatorial effect of endophytic and plant growth promoting rhizobacteria against wilt disease of *Capsicum annum* L. caused by *Fusarium solani*. Biol Control. 2012;60(1):59-67. Doi: https://doi.org/10.1016/j.biocontrol.2011.10.002

Sylvia D, Fuhrmann J, Hartel P, Zuberer D. Principles and Applications of Soil Microbiology. 2nd ed. U.K: Pearson Prentice Hall; 2005.

Tenorio-Salgado S, Tinoco R, Vazquez-Duhalt R, Caballero-Mellado J, Perez-Rueda E. Identification of volatile compounds produced by the bacterium *Burkholderia tropica* that inhibit the growth of fungal pathogens. Bioengineered. 2013;4(4):236–243. Doi: https://doi.org/10.4161/bioe.23808

Tontou R, Gaggia F, Baffoni L, Devescovi G, Venturi V, Giovanardi D, *et al*. Molecular characterisation of an endophyte showing a strong antagonistic activity against *Pseudomonas syringae* pv. actinidiae. Plant Soil. 2016;405(1–2):97–106. Doi: https://doi.org/10.1007/s11104-015-2624-0

Tortora ML, Díaz-Ricci JC, Pedraza RO. *Azospirillum brasilense* siderophores with antifungal activity against *Colletotrichum acutatum*. Arch Microbiol. 2011;193(4):275–286. Doi: https://doi.org/10.1007/s00203-010-0672-7

Trapet P, Avoscan L, Klinguer A, Pateyron S, Citerne S, Chervin C, *et al*. The Pseudomonas fluorescens Siderophore Pyoverdine Weakens *Arabidopsis thaliana* Defense in Favor of Growth in Iron-Deficient Conditions. Plant Physiol. 2016;171(1):675-693. Doi: https://doi.org/10.1104/pp.15.01537

Tyc O, Song C, Dickschat JS, Vos M, Garbeva P. The Ecological Role of Volatile and Soluble Secondary Metabolites Produced by Soil Bacteria. Trends Microbiol. 2017;25(4):280–292. Doi: https://doi.org/10.1016/j.tim.2016.12.002

Ugras S, Sezen K, Kati H, Demirbag Z. Purification and characterization of the *Bacteriocin thuricin* Bn1 produced by *Bacillus thuringiensis sub*sp. kurstaki Bn1 isolated from a hazelnut pest. J Microbiol Biotechnol. 2013;23(2):167–176. Doi: https://doi.org/10.4014/jmb.1209.09056

Vejan P, Abdullah R, Khadiran T, Ismail S, Nasrulhaq Boyce A. Role of plant growth promoting rhizobacteria in agricultural sustainability-A review. Molecules. 2016;21(5). Doi: https://doi.org/10.3390/molecules21050573

Velkov T, Thompson PE, Nation RL, Li J. Structure-activity relationships of polymyxin antibiotics. J Med Chem. 2010;53(5):1898–1916. Doi: https://doi.org/10.1021/jm900999h

Vivanco-Calixto R, Molina-Romero D, Morales-García YE, Quintero-Hernández V, Munive-Hernández A, Baez-Rogelio A, *et al*. Reto agrobiotecnológico: inoculantes bacterianos de segunda generación. Alianzas y Tendencias. 2016;1:9–19.

Vivas A, Marulanda A, Ruiz-Lozano JM, Barea JM, Azcón R. Influence of a *Bacillus* sp. on physiological activities of two arbuscular mycorrhizal fungi and on plant responses to PEG-induced drought stress. Mycorrhiza. 2003;13(5):249–256. Doi: https://doi.org/10.1007/s00572-003-0223-z

WellerDM,LandaBB,MavrodiOV.,SchroederKL,DeLaFuenteL, Blouin Bankhead S, *et al*. Role of 2,4-diacetylphloroglucinol-producing fluorescent *Pseudomonas* spp. in the defense of plant roots. Plant Biol. 2007;9(1):4–20. Doi: https://doi.org/10.1055/s-2006-924473

Wong MJQ, Liang X, Smart M, Tang L, Moore R, Ingalls B, *et al*. Microbial Herd Protection Mediated by Antagonistic Interaction in Polymicrobial Communities. Appl Environ Microbiol. 2016;82(23):6881-6888. Doi: https://doi.org/10.1128/aem.02210-16.

Yang SC, Lin CH, Sung CT, Fang JY. Antibacterial activities of bacteriocins: Application in foods and pharmaceuticals. Front Microbiol. 2014;5:1–10. Doi: https://doi.org/10.3389/fmicb.2014.00241

Yao GW, Duarte I, Le TT, Carmody L, LiPuma JJ, Young R, *et al*. A Broad-Host-Range Tailocin from Burkholderia cenocepacia. Appl Environ Microbiol. 2017;83(10). Doi: https://doi.org/10.1128/AEM.03414-16

Zoppellari F, Malusa E, Chitarra W, Lovisolo C, Spanna F, Bardi L. Improvement of drought tolerance in maize (*Zea mays* L.) by selected rhizospheric microorganisms. Ital J Agrometeorol Ital Di Agrometeorol. 2014;19(1):5–18.