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BIOLOGICAL MEDIATED MANAGEMENT OF BACTERIAL DISEASES IN CROP-PLANTS: A REVIEW

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A B S T R A C T

Biological control is described as the suppression of one or more populations of plant pathogens using introduced or resident living species rather than disease-resistant host plants. This can be accomplished by the use of microbial biological control agents (MBCAs) where they biologically control plant pathogens interacting with their hosts via a range of modes of action. Overuse of pesticides has had a negative impact on the climate in recent decades that gave rise to human health issues. This posed a dire need to explore alternative strategies that are comparatively safe, environmental, and monetarily feasible. The employment of MBCAs is found to be a highly effective way to regulate several diseases of the exiting flora caused mainly by nematode infestation and bacterial or fungal pathogens. Microbial inoculants suppress a particular form of plant disease or regulate soils so that plant-associated species and native soil can work together to suppress the disease. Microbes, such as bacteria, protozoa, algae, and fungi, frequently interact with plants in several ways including protocooperation, mutualism, commensalism, rivalry, neutralism, amensalism, predation, and parasitism. These interactions are cascades of highly regulated metabolic events that combine various kinds of action. Compounds such as enzymes, signaling compounds, and other interfering metabolites are released in situ at low levels during the interaction. *Pseudomonas*, *Erwinia*, *Bacillus*, *Agrobacterium*, *Rahnella*, *Lysobacter*, *Myxobacteria*, *Enterobacter*, and *Streptomyces* are some of the bacterial genera that have major biocontrol potential to mitigate crop plant diseases. Several species, including *P. fluorescens*, *P. putida*, *P. cepacia*, *P. aureofaciens*, P. tolaasii, *P. fluorescens* (strains A1, BK1, TL3B1, A506, and B10), *Erwinia herbicola*, *B. cereus* (strain UW85), *Agrobacterium radiobacter* (strain K84), *Rahnella aquatilis* have been proved beneficial against various crop diseases. Likewise, *Trichoderma harzianum*, *Glomus fasciculatum*, *G. macrocarpum, and Pisolithus tinctorius* are known to induce plant defense response against phytotoxic effects caused by different pathogenic strains. This review highlights the role of MBCAs against pathogenic microorganisms and their mode of action in terms of the ability to enhance plant defense systems for their improved growth.

Keywords: Microbes, Bacteria, Disease suppression, Biocontrol, Bacterial diseases.

INTRODUCTION

Plant diseases must be managed to maintain the balance of food, feed, and fiber provided by different stakeholders all across the globe (Di Francesco et al., 2017). There are numerous ways to mitigate plant diseases, which include cultural, physical, chemical, and behavioral practices, enabling the farming community to combat dilemmas of agricultural worlds (Kohl et al., 2019). Normally, growers depend on the use of chemicals in the form of pesticides, fertilizers, nematicides, fungicides, and bactericides which are being practiced for over a hundred years. However, in the modern era, the trend is being changed from chemical to biological control of pathogens to improve crop productivity under various

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biotic and abiotic stresses (Elad, 2000). According to world organizations (UN, FAO, UNICEF, UNESCO, and USDA), aiming at sustainable agricultural development, the use of agrochemicals exerts adverse environmental effects. Furthermore, the excessive use of hazardous chemicals on edible flora renders it unsuitable for human consumption (European Food Safety Authority [EFSA], 2017). Keeping in view the undesirable effects of agrochemicals, there is a dire need of adopting alternative strategies to control plant diseases.

Microbe's relationship with host plants helps reduce pathogen attachment to plant surface and their parts. Using green manures, composts, and cover crops to manipulate agricultural processes may also help improve endogenous levels of general suppression. Therefore, biological-mediated management is the best way to improving crop production by controlling plant diseases and insect pests. (Rahman et al., 2018; O'Brien, 2017). Different plant diseases can be controlled through biological management by using plant-associated microbes. The isolation, identification, and characterization of these organisms are performed to screen and culture the most suitable microbial strains (Glare et al., 2012). The best example of this is *Pseudomonas*. This bacterium is produced an antibiotic compound which is known as 2,4-diacetylphloroglucinol. A decrease in various soil-borne pathogens was observed by the introduction of *P. fluorescens* into the soil (Weller et al., 2002). Similarly, microbial isolates (*Pseudomonas* spp.) or fungal antagonists (*Trichoderma asperellum*) producing increased amounts of siderophores having high iron affinity also cause disease suppression (van Loon, 2000; Whipps, 2001; Lugtenberg and Kamilova, 2009; Segarra et al., 2010).

What is Biological Control?: The term "Biological Control" (abbreviated as "Biocontrol") refers to the use of living organisms to control the population of plant pathogens. (Heimpel and Mills, 2017). Biological control agents (BCA) can be defined as organisms that have the ability to suppress pathogens or pests of a crop. In a broader perspective, applications of biological control agents involve the extraction and fermentation of natural products from biological sources. These formulations may be both simple and complex mixtures, where the former constitutes of natural ingredients with specific effects and the latter with multiple effects on the host and its pathogen (Olorunleke et al., 2015). To deal with the increasing population of plant pathogens and insect pests on various crops, antagonists (fungi, bacteria, and nematodes spp.) should be exploited to protect humans and the environment from the damages caused by the chemicals (Arseneault and Filion, 2017). Similarly, it is the need of the hour to practice host-specific microbial pathogens to mitigate the weed population. Based on primary benefits provided to the host plant, bio-pesticides or bio-fertilizers are the preferred nomenclatures since they imitate the behaviour of living organisms (Pieterse et al., 2014).

Based on biotechnological developments, Biological control is defined as "the use of natural or modified organisms, genes, or gene products to reduce the effects of undesirable organisms and to favour desirable organisms such as crops, beneficial insects, and microorganisms" by members of the United States National Research Council., but this definition is still considered to be too broad by many scientists and has started new debates in the science of biocontrol. Since the term "Biological Control" can refer to a whole variety of diversities, one needs to define the width of this spectrum when reviewing in a certain aspect (Ren et al., 2013). Definitions of biological control may differ based on various aspects i.e. number, source and type of biological agents, the target of suppression, and the degree of human intervention. The disease suppression can be incurred in many ways depending on the plant disease type, e.g. the use of crop rotation and plantation of different resistant cultivars or, in a narrower perspective, utilizing resident living organisms could also be regarded as biological control (Larkin and Brewer, 2020).

Types of interactions contributing to biological control: There is a chain of interactions between plants, pathogens, and other microorganisms, and these interactions are made throughout their lives. Plant growth is directly affected by these interactions in various ways (Moh Tariq et al., 2020). Proto-cooperation, mutualism, commensalism, competitiveness, neutralism, parasitism, amensalism, and predation are some examples of these interactions. (Odum, 1953). Although the term was established for macroecology, both at macroscopic and microscopic level but these kinds of connections are in regular flora and fauna prevailing in nature while the development of plant diseases includes plants, pathogens, time, their interactions, and relationship among themselves which could be studied at multiple levels during whole cropping period or in any time of their life. While discussing plant diseases, Odum

(1953) described biological control as a natural phenomenon maintaining equilibrium in nature.

Mechanisms of biological control: Many scientists have worked to determine the mechanisms of biological control. Most pathogens are irritated by the existence and movement of other organisms that they come upon while a diverse mechanism of antagonism happened across and among a range of interspecies with a specificity of the contact (Kohl et al., 2019; Sachana, 2018). Although in plant pathogens, hyperparasitism by obligate parasites is the most non-stop form of antagonism due to the achievements of another individual, it is necessary to apply a suppressive outcome, antagonism results from bodily contact and/or high choosiness for the pathogen by the appliances expressed by the BCA (s), whereas Achievements that do not involve the BCA(s) guessing or guiding pathogen results in unplanned antagonisms (Romanazzi et al., 2016). The non-pathogenic BCA(s) incentive of plant host defense pathways produces the strongest secondary type of antagonism. Although, in the perspective of the regular environment, utmost defined tools of pathogen reduction will be regulated by the comparative existence of organisms other than the pathogen (Spadaro and Droby, 2016).

Numerous studies have looked into the role of specific biocontrol mechanisms in different pathosystems; however, the mechanisms described below are likely to be active to some extent in both natural and advanced ecologies. The best real BCAs tested to date seem to fight pathogens through various mechanisms. For example, Pseudomonads produced the antibiotic 2,4-diacetylphloroglucinol (DAPG) which activates the host's defensive response (Iavicoli et al., 2003). Furthermore, the microbes which produce DAPG may have the ability to colonize the roots aggressively. This may enhance the ability of plants to defeat pathogen action over the natural nutrient competition (Weller and Raaijmakers, 2002).

Hyperparasites and predation: Hyperparasitism, refers to specific biological control agents attack the specific pathogen that kills it or its propagules e.g., hypoviruses are hyperparasite, although there are four major types of hyperparasites in broad-spectrum, they are: 1) obligate bacterial pathogens, 2) predators, 3) hypoviruses, and 4) facultative parasites (McNeely et al., 2017; Kohl et al., 2019). This phenomenon could be better understood by the fungus producing chestnut blight, infecting the *Cryphonectria parasitica* by a virus, hence, affecting its hypovirulence and decreasing the ability of the pathogen to cause the disease. In this way, the occurrence of chestnut blight has been controlled in several places (Milgroom and Cortesi, 2004).On the base of the interaction between tree, virus, fungus, and climate determines whether hypovirulence is achieved or not. (Zheng et al., 2017). Several fungi are parasites of plant pathogens, including those that cause sclerotia outbreaks and others that parasitize living hyphae, or even several hyperparasites, attack a single fungal pathogen, such as *Cladosporium oxysporum, Ampelomyces quisqualis*, and *Gliocladium virens*, which are among the few fungi that can parasitize powdery mildew pathogens (Kiss 2003). Although a few hyperparasites make plant-pathogenic nematodes as their target during their early stages of life. Examples of such hyper parasites are *Paecilomyces lilacinus* and *Dactylella oviparasitica*).while in hyperparasitism target is nonspecific and their range of predation is wide.Therefore disease control is also lower in hyperparasitism (Jeffries, 1995). So, BCAs display predatory actions under nutrient-limited situations while on the contrary, under distinctive growing circumstances such movement is not conveyed. As we see many species of *Trichoderma* contain a broad variety of enzymes that target only cell walls of fungi and do not directly infect plant pathogens, such as Rhizoctonia solani. whereas equally, fresh bark is recycled in manures. Then in disintegrating bark, the attention of voluntarily existing fiber decreases. They activate *Trichoderma spp*. chitinase genes, which generate chitinase to parasitize *R. solani*. (Benhamou and Chet 1997). In a soil food web, the living beings in soil cooperate while the food web base is containing organic matter - this arises from living and dead plants, plant roots (which leak a lot of nutrients), dead animals of all sizes, and waste products of animals, hence, members of the soil food web are the microbes - like bacteria, fungi, protozoa, etc (Karlsson et al., 2017; Nygren et al., 2018)

Antibiotic-mediated suppression: Microorganisms can cause disease in the plants and it is assumed that some microbes produce and secrete effective antibiotic compounds at different concentrations which kill the pathogenic fungi, bacteria, or nematode naturally whereas release of less amount of antibiotic toxins near the pathogen is severely damaging for the growth of pathogen which is being done by various biocontrol agents (Thomashow et al., 2002). In line with this discussion, it is assumed that to estimate antibiotic effective quantities and their expression on infection sites vary from pathogen to pathogen because different microbes possess different associations with the plant they infect or cure, many studies are being carried out to develop a suitable method to estimate the production of antibiotic by biocontrol agent for the suppression of pathogen in question (Notz et al., 2001). Furthermore, the production of antibiotics by different biocontrol bacteria is unlike, and in the same way, it manipulates the behavior of one or more genes for the production of the antibiotic compound by the BCA, e.g., some mutant strains produce phenazines while others phloroglucinols while both can colonize the rhizosphere. Some biocontrol strains are producing many antibiotics to control more than several pathogens, e.g., *Bacilluscereus* strain UW85 produce zwittermycin and kanosamine and they can control different classes of the pathogen by producing multiple antibiotics but the pathogen is suppressed in the field by antibiotic compounds produced by Pseudomonas putida WCS358r strains that produce only DAPG and phenazine. (Silo-Suh et al., 1994; Keel et al., 1992; Thomashow and Weller, 1988).

The 'black box' and the 'silver bullet' approach: The phenomenon of disease suppressive soils has made Plant pathologists interested for decades. Suppressive soils are referred to those soils in which a particular pathogen can not survive even under ideal conditions, or the pathogen develops but can not cause disease, or where the disease occurs but is controlled by a normal monoculture of the same crop. They have been observed in many locations around the world (Lugtenberg et al., 2017). Even the phenomenon of fumigation and heat-sterilization of the soil is thought to be biological. But people did not know it reduces the suppressive effect of soil and disease is gone to its extreme level if the pathogen is reintroduced at that site. The soil suppressive to wheat's take-all disease is a classic example (Kohl et al., 2019). Initially, with each successive wheat crop, the take-all disease worsens, but the disease is stabilized at a low level by continued monoculture. Suppressive soils are living laboratories where the intricate interactions between microorganisms that contribute to disease suppression can one day be discovered. Some researchers have turned to individual microorganism strains as biocontrol agents because of the difficulties in recognizing the complex interactions of the 'black box' approach to biological regulation. (Raaijmakers and Mazzola, 2012). Although simplistic, this "silver bullet" approach has resulted in the production of many commercially available biopesticide products and has yielded several realistic solutions to plant disease problems. Although the mode of action for only a few biocontrol systems is known, research with unique antagonists has led to important biocontrol mechanism discoveries.

Destructive Mycoparasitism and nutrient competition: Destructive mycoparasitism is also a biocontrol in which one fungus is inhibited by another fungus, ultimately reduces the nutrient uptake, and break the hyphal strand of the pathogenic fungus (Ghorbanpour et al., 2018). The mycoparasitism produced antibiotics to control the growth of the pathogen e.g., *Trichoderma* spp. are used to inhibit the pathogenic fungus which competes for the food and nutrients. In nutrient competition two organisms compete with each other for the nutrients e.g., *Pseudomonas fluorescens* is used commercially to control the growth of the *Pseudomonas tolaasii*. The other antibiosis component Kodiak (Gustafson, TX) is produced by the *Bacillus subtilis* and used to control the growth of the fungus (Mauch-Mani et al., 2017).

Lytic enzymes, other byproducts of microbial life, and competition for food: Biocontrol agents secrete metabolites that inhibit pathogen growth and other activities. For example, various polymeric compounds, such as hemicellulose, cellulose, chitin, proteins, and DNA are hydrolyzed by lytic enzymes. Similarly, *Serratia marcescens* controlled *Sclerotium rolfsii* by chitinase expression (Karlsson et al., 2017; Ordentlich et al. 1988). Biocontrol activities of *Lysobacter enzymogenes* strain C3 are significantly enhanced by the contribution of 1,3 Beta glucanase protein(Palumbo et al. 2005). The amount of carbon or nitrogen contributes towards the suppression of the disease. The multiplication of the enzyme can help to control disease production. For example that is a biodegradable non-toxic polymer of beta-1,4-glucosamine. Chitosan is made from chitin by alkaline deacylation and used to suppress the infection of the root rot of the tomato caused by *Fusarium oxysporum* f. sp. *radicis-lycopersici*. Resistance of the host plant against diseases can be enhanced by Chitosan treatment. Surfaces of living plants and soils are mostly considered as nutrient-deficient habitats from a microbial perspective (Reithner et al., 2011).

Soil-borne pathogens are more susceptible to competition from other soil and plant-associated microbes which are infected through mycelial contact of *Fusarium* and *Pythium* as compared to those pathogens that germinate directly on the surfaces of the plant and infect via appressoria. An association was observed by Anderson et al. (1988) between the ability of *P. putida* to colonize the root system and the development of a specific plant glycoprotein called agglutinin. *P. putida* mutants lacking this ability had a lower ability to colonize the rhizosphere and a lower ability to inhibit Fusarium wilt in cucumbers (Tari and Anderson, 1988; Nygren et al., 2018). These microorganisms suppress the pathogens by the metabolites. These microorganisms colonize places like secondary root walking out points, injured epidermal compartments, root mucilage, and nectaries where water and carbon-holding nutrients are abundant. To survive in such an environment, siderophores are secreted by iron-binding ligands of organisms. They have a strong affinity for iron in the atmosphere, where all microorganisms develop siderophores of the hydroxamate and catechol types(Neilands 1981). Kloepper et al. (1980) was firstly studied the importance of siderophore assembly produced by a biological control mechanism of *Erwinia carotovora*. Many strains of *Pseudomonas fluorescens* such as A1, BK1, and TL3B1which stimulate plant growth, depend on this mechanism. A direct correlation was observed in vitro between synthesis of siderophore in *pseudomonads fluorescent* and their ability to minimize the production of chlamydospores of *F. oxysporum* (Elad and Baker 1985, Sneh et al. 1984; Keel et al. 1989, Loper and Buyer 1991). In commensal microorganisms uptake of iron is increased and is considered to be a major factor to violently colonize plant roots and spread of micro-organism from the initial infection point.

EXAMPLES OF BIOLOGICAL CONTROL OF BACTERIAL DISEASES

Biological control of bacteria through bacteria: Bio control of crown gall disease by *Agrobacterium radiobacter* strain K84: In crown gall disease, the first symptom appears as galls on roots or base of plants such as stone (e.g., Apricot) and pome fruits. In ornamental woody crop, crown galls are also formed e.g., *Marguerite daisies*, and *Chrysanthemum* spp. in addition to grapevines and raspberries. These plants become systemically infected when infection occurs. In field crops, galls have been observed such as cotton, tomatoes, bean, and alfalfa but this does affect so much economically (Borges et al., 2019). The causal organism of crown gall is *Agrobacterium tumefaciens,* which is gram-negative bacteria and normally causes symptoms on roots. In many soils, these bacteria remain alive where good aeration and crown plants are also available. In some orchard weeds, bacterium survives on the root surface when a suitable host plant is not available. By experimental inoculation, it is demonstrated that 93 plant families are susceptible to crown gall. Highly susceptible plants to crown galls are Jimson weed *(Datura stramonium*) and sunflower (*Helianthus annuus*) and used as indicator hosts for analysis of the degree of virulence of *A. tumefaciens* (Moore et al., 2001; Tzfira et al., 2004).

A. tumefaciens is a rhizoplane-non-fastidious bacterium that can recognize the phenolics of plant and, in tumor-inducing plasmid have virulence gene which is situated in the Ti plasmid and expressed and form the flexuous filament that is long known as T-pilus (Puławska et al., 2006). Motility of circumthecal flagella is shut off by the activation of VirA, apparently when bacteria *A. tumefaciens* cells bind to plant cells, attachment is required for initiation of the relocation or transfer of the T-DNA into the plant cell, have an important role in virulence. According to some differences, *A. tumefaciens* isolates were initially categorized into three biotypes or biovars e.g., 3-ketosugars are produced by Biotype 1 and normally have extensive host choice. Whereas hairy root-forming organisms are classified in Biotype II (A. *rhizogenes)* while some isolates are confined to grapevines are reported in Biotype III which produce polygalacturonase. By cultural practices including accidental and localized injury wounds occur by moving machines to control the weeds in orchards or fields. For the initiation of this disease, wounds work as an invitation for the bacterium (Magori and Citovsky, 2012).

Besides, injured tissues are susceptible to infection, where *A. tumefaciens* lives systematically all over the plant, such as in grapevines, where small tumors are found in the vascular system of infected plants. First of all, galls originated on subterranean parts from infected stock and then these wounds are susceptible to crown gall infection that occurred due to grafting and pruning. Firstly, crown gall tumors are hard but after one year they appear complicated with cavities and insect resides in these cavities while in aged galls, it is very difficult to isolate and remove the *A. tumefaciens*. When a young plant is infected with crown gall, it directly damages the yield and promotes the stunting of the plants (Munoz-Galvan et al., 2013).

The use of *A. radiobacter* strain K84 or its genetically modified type K1026 for control of the crown gall bacterium *A. tumefaciens* is the best example of biological control. This saprophytic bacterium that lives in the soil is closely related to *A. tumefaciens*, but it lacks the tumor-inducing (Ti) plasmid. *A. radiobacter* is a strong root colonizer (better than *A. tumefaciens*) and produces Agrocin 84, a bacteriocin that is toxic to *A. tumefaciens*, the crown gall bacterium. Unlike most other bacteriocins, this one is an adenine-based nucleotide rather than a protein. A plasmid named pAgK84 contains the genes for producing the bacteriocin (Ongena and Jacques, 2008). Only strains of A. tumefaciens that contain the opine compounds nopaline and agrocinopine are susceptible to the bacteriocin. Bacteriocin-insensitive strains that produce octopine and agropine are present in the latter case. By dipping peach and cherry roots in a saprophyte suspension, up to 90% control was achieved in the United States and Australia. Plant cells develop agrocinopine when nopaline-producing strains of *A. tumefaciens* are present. The pathogen's Ti plasmid codes for a particular agrocinopine permease that allows agrocinopine uptake. Agrocin 84 is mistakenly taken up by this permease in the *A. tumefaciens* cell and inhibits DNA synthesis and cell growth in the pathogen as a nucleotide analog (Fischer et al., 2008). Due to genetic exchange with *A. radiobacter*, *A. tumefaciens* strains can become immune to the bacteriocin. The broad plasmid pNOC found in *A. radiobacter* will spread itself and the small plasmid pAgK84 to other *A. radiobacter* cells as well as *A. tumefaciens*. As a result, genetically modified *A. radiobacter* strains have been created by removing the transfer genes from the broad plasmid, preventing it from transferring bacteriocin resistance (strain K1026). Agrobacterium strains that are resistant to *A. vitis* have also been discovered. Plants are covered against Agrocin-84 susceptible pathogen strains by dipping the root system into an *A. radiobacter* K84 suspension before planting in infested fields. In several areas, biological regulation of crown gall has proven to be a highly effective method of controlling the disease (Gohlke et al., 2013).

Bio control of bacterial wilt of brinjal by *Pseudomonas fluorescens:* The most important and cultivated vegetable in Pakistan is brinjal (*Solanum melongena* L.) for poor people, providing food security to the lower class in society and contributing and poverty elevation (Eltayeb, 2017). The eggplant is a local dish vegetable and used as a cooking vegetable or also used for medical sources. The bacterial wilt disease caused by *R. solanacearum*, a gram-negative proteobacterium (Bacterial wilt), which adversely affects the brinjal production had spread across the tropical, subtropical, and high-temperature regions of the world, infecting more than 200 species of plants. (Buddenhagen 1962; Yabuuchi *et al*., 1996). Bacteria survive on infected parts of the plant, water, and soil and move with the help of water, soil, and infected equipment. The pathogen enters into the plant's cell through wounds, stomata, emerging point of roots, and made colonies shapes in the intercellular spaces of the vascular system. The pathogen dissolves the cell wall of the plant cell by the highly polymerized polysaccharides that increase the damage of the cell wall, hence, wilt causes blockage of the vessel of the plant. *R. solanacearum* possesses a variety of races and strains that it has made impossible for the breeders to make any genetically modified variety having resistance against the bacterium (Girlanda et al., 2001). Since bacteria can live in soil, various soil treatments are successful in reducing bacterial development in host plants. Changing in pH of soil, heat treatment through hot water and solarization, and chemical treatment with plant essential oils (e.g., Thymol), bleaching powder application, and plant resistance inducers (e.g., Acibenzolar -S-methyl). There has always been a dire need for the (affordable, effective, and with a high degree of food safety) control of this bacterium with minimum environmental risks. Biological control techniques, in this context, can either assist in the creation of alternative management measures or be combined with other practices for successful disease management in the field (Hernandez-Leon et al., 2015; Lwin and Ranamukhaarachchi 2006). Several *Pseudomonas fluorescens* strains are effective at inhibiting soil-borne diseases (O'Sullivan and O'Gara 1992). *P. fluorescens* improve the growth of the plant and increase plant resistance with the decrease in pathogen infection (Hoffland *et al*., 1996).

Bio control of Bacteria-Mediated Frost Injury by *Erwinia herbicola:* When the temperature decreases below 0°C, it causes injury to the plant tissues. *E. herbicola* is reported as a biological control agent which is used to increase the plant's resistance during infection of those bacteria which survive on ice temperature and cause infection in the plant. *P. syringae*, *P. fluorescens*, and *E. herbicola* are the three strains of these bacteria that are used to control infection (McNeely et al., 2017). This helps in protecting the plants from low-temperature injury, but untreated may face harsh injuries. Another antagonist, saprophytic *Pseudomonas* spp. has been used in the control of *Pseudomonas* in *Agaricus bisporus* (Mushroom) whereas strains of *Pseudomonas* like *P. savastanoi* reduces the production of indole acetic acid and play a very effective role against the olive knot in olives. But for *Erwinia amylovora*, *P. fluorescens* act as an antagonist which is very effective and existing commercially (Kohl et al., 2019. Moreover, many antagonist bacterial strains include *Bacillus subtilus* and *Rahnella aquatilis* which have proved their vitality against many pathogens. Growers can be persuaded to use strain A506 for a variety of reasons, including its ability to control fire blight while also limiting frost injury and russeting on pears. It is the only biocontrol microbe that can be used in orchards with streptomycin-resistant strains of the microbe due to its natural resistance to the antibiotic. When antibiotic resistance prohibits the use of antibiotics and the host does not have durable resistance, bacteriophages have been used to monitor pathogens, such as *X. vesicatoria* in tomatoes.

Bio control of soil-borne bacterial diseases by *Bacillus subtilis* strain A13.: A study was conducted by (Raaijmakers and Mazzola, 2012) revealed Priming of cereal (sweet corn) and carrot seeds with slurries, water suspensions, or powders containing Bacillus subtilis (strain A13) or Streptomyces sp. protected the plants from root pathogens and increased yield. Similarly, a significant increase in plant growth, yield, and a decrease in various diseases such as damping-off, soft rot, and bacterial wilts was observed when seeds, seed fragments, and plant roots were treated with *Pseudomonas rhizobacteria* of *P. fluorescens*, *P. putida*, *P. cepacia*, and *P. aureofaciens* classes (Raaijmakers and Mazzola, 2012). Similarly, two bacterial species *B. subtilis* and *P. fluorescens* are formulated at a commercial scale and traded with the name of Kodiak and Dagger G respectively. Results of both are substantial at small-scale trials but have shown mixed results on large-scale trials. Some studies have shown that treated potato seed tubers yield 5-33% more. Likewise, the treated sugar beet seed has yielded 4-6 tonnes more per hectare increasing to 955-1,227 kg of sugar per acre. Similarly, seeds of radish which were treated with these bacteria showed 60 to 144 percent more root weight as compared to untreated seeds, and treated seed of wheat also showed 27 percent more yield in soil which was infested with *Gaeumannomyces graminis* var. *tritici* (take-all of wheat) as compared to untreated seeds (Pieterse et al., 2014). Damping-off and root rot are the most common soil-borne diseases which are caused by various pathogens such as *oomycetes, Pythium*, *Phytophthora*, *Rhizoctonia*, *Fusarium*, and *Gaeumanno myces*. *Bacillus cereus* strain especially UW85F is the most effective biocontrol agent in the management of damping-off diseases of legumes. Three species of *pseudomonas fluorescent* and one species of *Pantoea* were used in lonely and combination form through wheat seed treatment. A decrease in seedling death caused by *Fusarium culmorum* and increased crop stand and yield at a higher level was observed as compared to fungicides. It is still unclear that which mechanism is present behind these plant-growth-promoting rhizobacteria throughout they improve yield. Competition for iron or inhibition of dangerous, toxic microorganisms and soil-borne pathogens by antibiotics, appears to be associated with at least some of the determinants of their efficacy (Schenk et al., 2010).

Bio control of aerial plant parts bacterial diseases by *Erwinia herbicola:* During the early growing season, bacterial pathogens that are present on the aerial surfaces of plants are mainly saprophytic gram-negative bacteria belonging to the genera of *Pseudomonas*, *Erwinia*, and *Xanthomonas*. Similarly some gram-positive bacteria are also present which belongs to the genera *Lactobacillus*, *Bacillus*, and *Corynebacterium* (McNeely et al., 2017). Some bacterial pathogens live epiphytically on buds, leaves, and other surfaces of the plant before causing infection and disease. *Pseudomonas syringae* pv. *morsprunorum*, *P. syringae* pv. *syringae*, *P. syringae* pv. *glycinea*, *Erwinia carotovora,* and *E. amylovora* are some examples of such bacteria. In certain cases, a significant reduction or decrease was observed in various fungal and bacterial infections by spraying surfaces of leaves with saprophytic bacteria preparations or avirulent pathogenic bacteria. Similarly, *Erwinia herbicola* spray was used to control fire blight disease of apple blossoms caused by E. amylovora. Sprays of *Erwinia* and *Pseudomonas* isolates were used to control bacterial leaf streak of rice which is caused by *Xanthomonas translucens* pv. *Oryzicola* (Kohl et al., 2019). There have been some accounts of epiphytic bacteria being introduced to plants to prevent fungi from infecting them. *P. fluorescens* spray was used in grass plants to manage the *Drechslera (Helminthosporium) dictyoides* infection and a significant decrease was observed in infection. as well as the infection was also reduced when apple leaves were sprayed with *Nectria galligena* and grapes with *Eutypa lata*. *Cercospora* and *Alternaria* leaf spot of peanut and tobacco plants was also controlled by spraying these hosts with *P. cepacia* or *Bacillus* sp. (McNeely et al., 2017).

Bio control of post-harvest bacterial diseases by *Pseudomonas syringae:* The pear was an easy victim of various rots. Now pear is protected from several rots by the use of *Pseudomonas* bacteria. Two strains of *P. syringae* have been licensed with the trade name of Bio-Save to control the postharvest losses in oranges, apples, and pears(Robinette and Matthysse, 1990). Many types of stone fruit, such as nectarines, apricots, peaches, and plums can be saved for at least nine days from brown rot which is caused by the fungus *Monilinia fructicola* by the treatment of antagonistic bacterium *Bacillus subtilis* suspensions after harvest. While avocado fruit was also covered from rot in storage by the same bacteria (Lee et al., 2009).

Biological control of bacteria through fungi: "Ascopyrone P", a novel antibacterial derived from fungi: As the growth medium is deprived of carbon sources, fungi's carbon storage polymer, glycogen, is degraded to glucose. In the case of normal growth conditions, glucose reaches the glycolysis pathway, supplying energy and building blocks. However, under stress conditions which may be biotic or abiotic, glycogenolysis pathway is diverted. 1,5-anhydro-D-fructose (1,5-anhydro-D-arabino-hex-2-ulose, AF) and other many secondary metabolites are formed instead of glucose forming and such phenomenon is called Anhydrofructose Pathway of glycogenolysis. The conversion of glycogen to AF can be catalyzed with the help of the A-1,4-glucan lyase(EC 4.2.2.13) enzyme (Baute et al. 1988; Yu et al. 1995, 1997, 1999). Ascopyrone P (1,5-anhydro-4-deoxy-D-glycero-hex-1-en-3-ulose, APP) can be prepared from AF by catalyzation of a dehydratase (Baute et al. 1993). Firstly developed pyrolysis products of amylopectin, amylose, and cellulose was APP with a yield of less than 3% (Shafizadeh et al. 1978). Its crystal structure has been determined and it has been further characterized (Stevenson et al. 1981). While the position of APP and its functionality is still unrevealed. Just two Staphylococcus strains and one Escherichia coli strain have been screened for anti-APP activity with a minimum inhibitory concentration of 250 and 500 mg ^{ml} (Baute et al. 1993). A study was conducted to investigate the antimicrobial activity of APP against various microorganisms, such as gram-negative and gram-positive bacteria, molds, and yeasts. Food-borne and food spoiling pathogens were chosen as research strains. Ascopyrone P (APP) with an antimicrobial property is produced as a secondary metabolite in various microorganisms such as *Anthracobia melaloma*, *Plicaria anthracina*, *Plicaria leiocarpa*, and *Peziza petersi*. At high concentrations, APP inhibited the growth of Gram-positive and Gram-negative bacteria according to in vitro research using a good diffusion technique (approximately 5 percent). After incubation for 24 hours at 30 C, growth curve analysis using an automated microbiology reader revealed that complete or substantial inhibition of bacteria was observed at a concentration of 2000–4000 mg /L. While at a higher concentration (1000–2000 mg l) of APP inhibited the growth of certain yeast strains and stimulated the growth of some other certain yeast strains. At a concentration (2000 mg l), no effect was observed at *Clostridium* or fungal strains of APP. After 2 hours, there was no major cidal impact against *Escherichia coli* or *Listeria monocytogenes.* If the APP samples were made enzymatically or chemically, the findings were the same. APP inhibited the growth of a wide range of bacteria at a concentration of 2000 mg^{ml}, but not yeasts or molds.

Biological control of bacteria through nematode: "Nematophin", a novel antibacterial substance produced by *Xenorhabdus nematophilus:* Bacteria of the genus *Xenorhabdus* are lived symbiotically with entomopathogenic *Steinemema* nematodes which are soil-dwelling (Akhurst 1983). When these bacteria are parasite insects or cultured in vitro, they produce various metabolites of which some have antimicrobial properties (Forst and Nealson 1996). There are two types of compounds which are known as proteinaceous and non-proteinaceous compounds. Xenorhabdins, indoles, and xenocoumacins are non-proteinaceous compounds while xenorhabdincin and chitinases are proteinaceous compounds. Gram-positive bacteria and a few fungi are more susceptible to nonproteinaceous groups than Gram-negative bacteria. Only *Xenorhabdus sp*. bacteria are susceptible to the proteinaceous xenorhabdincin (Chen et al., 1996). The nematophin was discovered as a new antibiotic in all Xenorhabdus nematophilus strains tested after being isolated from Xenorhabdus nematophilus strain BC1. Extensive spectroscopic analysis has confirmed its structure as 3-indoleethyl (3'-methyl-2'-0xo) pentanamide. The strain form and culture conditions affect nematophin development. The compound has a high degree of bioactivity in vitro against several bacteria (Raaijmakers and Mazzola, 2012, McInerney et al. 1991a, 1991b).

Biological control of bacteria through a mixture of bacteria and fungi: Disease suppression mechanisms vary between fungal and bacterial biocontrol agents. In general, fungal antagonists depend on their physical contact with pathogens as compared to bacteria which depend on antibiotics to destroy their pathogens. The majority of research on plant-pathogen biological control concentrates on a single biocontrol agent acting as an antagonist to a single pathogen. Bio control agents have some degree of host specificity, even at the subspecies level, this may account for some of the recorded inconsistent performance of bio control agent preparations (Bardin et al., 2015; Heimpel and Mills, 2017; ; Li et al. 1995). In all soil environments and against all pathogens that target the host plant, a single bio control agent is unlikely to be effective. Rather than massive populations of a single antagonist, most cases of naturally occurring biological regulation are triggered by mixtures of antagonists. In disease-suppressive soils, antagonist mixtures are thought to be responsible for defense. As a result, using a mixture of an added biological agent would more closely resemble a natural scenario and could expand the range of possible outcomes. Mixtures of fungi, fungi and bacteria, bacteria and bacteria, and mixtures of fungi and bacteria have all been used in previous research on biocontrol agents against various plant diseases (Glare et al., 2012; Akhurst and Dunphy, 1993). A majority of these studies on biocontrol agents in combination found that combining antagonists increased disease control. However, some studies indicate that combining biocontrol agents does not enhance disease suppression as opposed to using individual antagonists. Coinoculants incompatibility can occur because these bio-agents can inhibit each other as well as the target pathogen (Kohl et al., 2019; Akhurst and Dunphy, 1993; Thaler et al., 1995). For the efficient development of strain mixtures, compatibility of co-inoculated microorganisms is usually an essential requirement. Testing of the efficacy of mixed formulations of compatible and most effective fungal (*Trichoderma*) and bacterial (*Pseudomonas*) biocontrol agents against significant plant bacterial diseases.

Induction of host resistance through biological control agents: There are only a few environmental stimuli whom plant respond. Some enzymes of PR proteins are enhanced the host defense system against various types of infections by directly lyse invading cells, strengthen cell wall boundaries, or cause localized cell death. Jasmonic acid (JA) and ethylene are involved in another phenotype known as induced systemic resistance (ISR) which is produced after some nonpathogenic rhizobacteria (Larkin et al., 2020; Kohl et al., 2019, Mauch-Mani et al., 2017; Reithner et al., 2011). Amazingly, the ISR pathway may be antagonistic because some bacterial pathogens use this to avoid SAR. *Pseudomonas syringae* which is a pathogenic strain produced JA-like compound called coronatine to avoid the SA-mediated pathway (He et al. 2004). Since different microbes and insect feeding can trigger different host-resistance pathways to varying degrees, the plant may be constantly receiving and processing multiple stimuli. As a result, the extent and length of host security induction will almost certainly change over time. Host resistance can be enhanced only through the completely overwhelming of endogenous signals. Many strains of root-colonizing microbe have been stated as plant host defense elicitors. A few biocontrol strains of *Pseudomonas* sp. and *Trichoderma* sp are considered as strong plant host defense elicitors (Haas and Defago 2005). There are various diseases caused by different pathogens such as angular leaf spot (*Pseudomonas syringae pv. lachrymans*), anthracnose (*Colletotrichum lagenarium*), and bacterial wilt (*Pseudomonas syringae* pv. *la Erwinia tracheiphila*) have been successfully controlled by inoculations with plant-growth-promoting *rhizobacteria* (PGPR). After inoculation, the PGPR strains can produce many chemical elicitors of SAR and ISR such as siderophore, salicylic acid, 2,3-butanediol, lipopolysaccharides, and many other volatile substances (Van Loon et al., 1998; Ongena et al., 2004; Ryu et al., 2004). Such molecules can play an important role in various tasks like blurring the lines between direct and indirect antagonistic interactions. A large number of microbial products have been recognized as plant host defense elicitors which continuously stimulated the plant defense system during the plant life cycle. Examples of such products are lipopolysaccharides and flagellin from gram-negative bacteria; cold shock proteins from various bacteria; transglutaminase, elicitins, and -glucans from *Oomycetes*; invertase from yeast; chitin and ergosterol from all fungi; and xylanase from *Trichoderma* (Numberger et al. 2004; Nygren et al., 2018). The fact that microbiological and chemical inducers do not often succeed in improving plant health or productivity in the field highlights the significance of such interactions (Vallad and Goodman, 2004).

Microbial diversity and disease suppression: Plants are mostly surrounded by a large number of mesofauna and microbial organisms, some of them work as a biological control to manage various plant diseases.Competitive saprophytes, facultative plant symbionts, and facultative hyperparasites are the microbes whose contribution is much more in controlling plant diseases (van Lenteren et al., 2018). These organisms can survive on dead plant material but they can also colonize plant tissues and express biocontrol activities. Phylogenetically, few fungi are closely related to plant pathogens but they have a lack of virulence elements which causes disease for many of the plant hosts from which they can be recovered.Examples of such fungi are avirulent *Fusarium oxysporum* and *binucleate Rhizoctonia. Pythium oligandrum* is also recognized as distinct species (Wiesel et al., 2014).Some bacterial genera such as *Burkholderia, Bacillus*, *Lysobacter*, *Pseudomonas*, *Pantoea* and *Streptomyces* and some fungal-like *Ampelomyces*, *Coniothyrium*, *Dactylella*, *Gliocladium*, *Paecilomyces*, and *Trichoderma* genera have got the attention of researchers towards themselves because of their easily cultured ability (Segarra et al., 2010; Zheng et al., 2017). Other microbes have also been thoroughly studied that are resistant to culture in vitro. Some mycorrhizal fungi, such as *Pisolithus* and *Glomus* spp. can control succeeding infections, as *Pasteuria penetrans* which is a plant pathogen hyperparasites of root-knot nematodes.In some cases, weakly virulent pathogens make a cause of suppression of more virulent pathogens. Because they activate the plant defense system before attacking more virulent pathogens on the plant.Finally, there are various general micro- and mesofauna predators are present whose herbivorous activities may reduce biomass of pathogen while also minimizing infection by stimulating plant host defenses.Examples of such genera are collembolan, protists, mites, annelids, insect larvae, and nematodes (Rahman et al., 2018). While many epiphytes and endophytes may play an important role in biological regulation.The widespread presence of mycorrhizae deserves special devotion.A mutual symbioses relationship between fungi and plants formed Mycorrhizae.Fungi make ubiquitous root colonies which help plant nutrients uptakes from the soil. The vesicular-arbuscular mycorrhizal fungi (VAM) are also known as endomycorrhizal fungi.VAM are members of Zygomycota having only.one order.The order is Glomales which is consisting of six genera and 149 species (Morton and Benny, 1990). Aseptate fungi are involved in arbuscular mycorrhizae, which are named after root cortex structures like arbuscles and vesicles.Arbuscules are formed as a result of repeated dichotomous branching of fungal hyphae root penetration into the cortical cell of the plant. Arbuscules are considered to be the fungus's point of contact with the host. Vesicles are considered the storage organ of VAM. Vesicles are hyphal swellings produced in the cortex cell of the root and contained lipids and cytoplasm. These structures can be found both intracellularly and intercellularly.The older roots forms thick walls and these thick-walled structures may work as propagules (Biermann and Linderman 1983). By reducing access sites and stimulating host defense during colonization, VAM fungi may escape root infections. Root-knot nematode occurrence is decreased by VAM fungi (Linderman 1994). VAM fungi can enhance plant tolerance against disease stress through various mechanisms.VAM fungi formed a complex web of hyphae around the plant's roots and protect roots from various pathogens attack. Apple replant disease caused by phytotoxic myxomycetes was controlled by inoculation of apple seedlings with VAM fungi especially with *Glomus fasciculatum* and *G. macrocarpum* (Catska 1994). Similarly, tomato losses due to *Pseudomonas syringae* can be significantly decreased by the colonization of tomato plants with mycorrhizae (Garcia-Garrido and Ocampo 1989). Physical defense, chemical reactions, and indirect effects are involved in such types of interactions (Fitter and Garbaye 1994).VAM fungi indirectly control or minimize the pathogen growth in two ways.First, it created morphological changes in the roots of the plant by increasing the process of lignification.Second, it alters the chemical composition of plant tissues (Morris and Ward 1992; Linderman, 1994).While *ectomycorrhizae* formed a sheath onto the outer surface of the root called a mantle. It is composed of a mass of root and hyphae and its surrounds to the roots of the host tree. Antibiosis, fungistatic compound synthesis by plant roots in response to mycorrhizal infection, and a physical shield of the fungal mantle around the plant root are all possible mechanisms of ectomycorrhizal fungi to enhance plant resistance against diseases (Duchesne 1994). Root rot of red pine caused by *Fusarium oxysporum* and *Fusarium* *moniliforme* was effectively managed through ectomycorrhizal fungi such as *Paxillus involutus.* The diseases of *Phytophthora cinnamomi* were managed by inoculating sand pine with an ectomycorrhizal fungus known as *Pisolithus tinctorius* (Ross and Marx 1972).Researchers are struggling to classify the species of various microbes that are used as biological control agents.The need for this is come because of the involvement of more than one microbes in disease suppressing.This has historically been achieved mainly through the isolation, characterization, and application of single species. This method focuses on particular types of disease suppression by design. Specific suppression is caused by the behaviour of one or a few microbial antagonists. When a biocontrol agent is inoculated and results in high levels of disease suppression, this type of suppression is thought to occur. It'll likely show up in natural systems at some stage. *Pseudomonas fluorescens*, for example, can kill several soil-borne pathogens by producing the antibiotic 2,4-diacetylphloroglucinol (Weller et al. 2002). However, when the targeted pathogens are actively threatening plant health, specific agents must compete with other soil- and root-associated microbes to survive, spread, and expression of their antagonistic ability.General suppression is more widely used to understand why plant diseases aren't as frequent or as serious. Pathogens have fewer ecological niches to compete for food because high soil organic matter supports a diverse population of microbes. The amount and type of organic matter present in the soil will have a direct impact on the overall suppression level (Hoitink and Boehm 1999). The functional redundancy of microbes to deplete the available soil nutrients is faster as compared to a pathogen.So in the presence of a microbial community, a pathogen cannot easily proliferate the nutrients and cant trigger the disease (McKellar and Nelson 2003). Various organic matters viz., cover crops, composts and green manures are being used to raise endogenous levels of general suppression in agricultural systems.

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