



Using some microorganisms as biocontrol agents to manage phytopathogenic fungi: a comprehensive review

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Abstract

Globally, phytopathogenic fungi infections cause crop diseases, resulting in crop yield and quality loss. Extensive use of chemical fungicides leads to resistance and high costs for growers as well as environmental pollution; thus, researchers are exploring a more sustainable approach using biological control tactics. This review highlights the critical processes involved in biological control by bacteria, fungi, viruses, and archaea, i.e., the synthesis of various metabolites, enzymes, and signaling molecules, as well as competitive tactics or soil suppressiveness that can effectively control the phytopathogenic fungi. The global increase in registrations for biological products reflects the rising demand and requirement for more organic agriculture and achieving some sustainable development targets. Understanding the complicated interplay between microorganisms in this environment can aid in managing soil diversity and inhibiting phytopathogenic fungi without chemical residues. Therefore, microorganisms are recommended as a sustainable alternative biological control.

Keywords Biological control · Crop Diseases · Fungal plant Infections · Microorganisms · Metabolites

Abbreviations

FAO	Food and Agriculture Organization of the United Nations
DMDS	dimethyl disulfide
VOCs	volatile organic compounds
DMHDA	dimethyl hexadecylamine
PGPB	plant growth-promoting bacteria
PGPR	plant growth-promoting rhizobacteria
NRPS	non-ribosomal peptide synthetases
PKS	polyketide synthetases
SAR	systemic acquired resistance
ISR	induced systemic resistance
JA	jasmonic acid
SA	salicylic acid
ET	ethylene
PR1, 2	pathogenesis-related gene
Chit-1	the plant defensive chitinase
Glu-2	1,3-glucanase
dsRNA	Double-stranded RNA

CHV	Cryphonectria hypovirulence viruses
SsNSRV-1	S. sclerotiorum negative-stranded RNA virus 1
SsHV2	S. sclerotiorum hypovirus 2
SsPV1	S. sclerotiorum partitivirus 1

Introduction

Plant diseases yearly cost the world economy more than 220 billion USD, according to The Food and Agriculture Organization of the United Nations (FAO) reports; moreover, phytopathogenic fungi cause an effective loss in crops worldwide (Jantasorn et al. 2016). They are responsible for approximately 30% of all agricultural plant diseases, including rice, wheat, maize, barley, soybean, cotton, bananas, coffee, etc. (Figuroa et al. 2021). The significant economic effects of fungal plant diseases result from declining agricultural output and quality (Bonaterra et al. 2022; Bhat et al. 2023). Their exportability is at stake, and the expense of disease surveillance and possible fungicide spraying can increase (Palm 2001; Fisher et al. 2012; Brauer et al. 2019; Jain et al. 2019).

Agriculture has increased its use of pesticides, e.g., herbicides, insecticides, and fungicides, to increase production

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(Grützmacher et al. 2008), but the extensive usage of these pesticides has polluted the ecosystems. Nowadays, the focus has shifted to microorganisms with the potential to control pathogenic fungi. Therefore, microbial agents may be viewed as an alternate technique for disease control because it is ecologically benign and simultaneously reduces the potentially harmful effects of chemical fungicides (Moreira et al. 2002; Khunnamwong et al. 2020). Along with the life-cycles of plants and diseases, one may see dynamic interactions with other creatures. These interactions are known to impact plant health in various ways. It is feasible to manage fungal plant diseases through the various actions of biocontrol-active microorganisms. Biological management of plant diseases is still moving at a snail's pace, mostly because of its inconsistent efficacy under various climatic circumstances (Heydari and Pessarakli 2010).

Numerous microbes generate and release one or more antimicrobial compounds. In low quantities, these substances are microbial poisons that can harm or kill bacteria and others (El-Tarabily et al. 1996; El-Saadony et al. 2022; Gómez-Godínez et al. 2023). Numerous biocontrol-active bacteria create compounds that can inhibit the development and activity of pathogens. Lytic enzymes are metabolites that degrade polymeric materials, such as DNA, chitin, proteins, cellulose, and hemicellulose (El-Tarabily et al. 1997; Anderson et al. 2004). This characteristic enables these microbes to have a range of biocontrol uses (Badalyan 2001). It is feasible to mention hyperparasitism, predation, antibiosis, cross-protection, competition concepts for location and/or resources, and induced resistance among the several recognized microbial biocontrol effects. According to Heydari and Pessarakli (2010), the presence and actions of other microorganisms that a pathogen encounters are always detrimental. Mejía et al. (2008) stated that biological controller microorganisms must be effective colonizers. They have a combined growth rate and antibiosis action, indicating the significance of integrating field data with in vitro experiments to get good results when selecting biological pesticides (Elnahal et al. 2022; Bonaterra et al. 2022).

Moreover, in many instances, a single microbe cannot suppress the appearance of the disease; a community of microorganisms can play a crucial role in regulating soil-borne diseases. In search of a more sustainable option in agriculture, this method has exploded in popularity worldwide. In light of this, it is necessary to study some under-developed parts of biocontrol to build more effective biological control tactics in the future (De Vrieze et al. 2020; Elnahal et al. 2022). The biocontrol of plant diseases has a bright and hopeful future. With the increasing demand for biocontrol products among farmers, it is conceivable to employ biological control as an effective way to manage plant diseases, boost crop yields, and safeguard the environment and

biological resources as we move toward a more sustainable agricultural system (Heydari and Pessarakli 2010; Daranas et al. 2019; Legein et al. 2020; Bonaterra et al. 2022).

Endophytic microorganisms as a source of potential antifungal compounds

Endophytic bacteria are plant-beneficial bacteria that exist within plants and can enhance plant development under normal and demanding environmental circumstances. The capacity of certain microorganisms, mostly bacteria and fungi, to create secondary metabolites relevant to the food, pharmaceutical, and agricultural sectors has been studied (Gao et al. 2017). Diverse sources exist for isolating and characterizing microorganisms of biotechnological relevance; however, endophytic microbes provide a new reservoir of novel metabolites (Rana et al. 2020). Endophytes are a category of microorganisms that may infiltrate plant tissues without having detrimental effects (Duong et al. 2021). According to Ali et al. (2020), endophytes are rhizosphere microorganisms that connect effectively with their host plants. Endophytic microbes can be used to isolate and characterize natural compounds.

Bacteria and fungi isolated from plants have the potential to create antibiotics, antifungals, anthelmintics, and anticancer compounds (Daranas et al. 2019; Montes-Osuna et al. 2021). In addition, they can increase the defenses of plants and exhibit antagonistic features, such as the creation of antibiotics, siderophores, HCN, and several enzymes (Duong et al. 2021; Sabra et al. 2022; Saad et al. 2022; Ashry et al. 2022). Multiple plants were chosen as sources for isolating bacteria with antibiotic properties. Most research focuses on the production of antimicrobials with therapeutic significance or the separation of endophytes from plants with medicinal qualities (Musa et al. 2020). In recent years, however, there has been a growing interest in discovering and characterizing microorganisms with valuable antibacterial capabilities for agriculture. The utilization of endophytes as biocontrol agents is advantageous since the evolutionary process has already chosen microorganisms that compete ecologically for the same niche, such as fungi and phytopathogenic bacteria (Rojas-Solís et al. 2018; Bungtongdee et al. 2019).

Certain secondary metabolites generated by bacterial and fungal strains, such as dimethyl disulfide (DMDS), which can promote systemic resistance. In a greenhouse experiment, Huang et al. (2012) revealed that *Bacillus cereus* C1L elicited a defensive immunity against *Botrytis cinerea* and *Cochliobolus heterostrophus* by developing systemic resistance in maize and tobacco plants. Some investigations try to discover bacterial strains capable of inhibiting the growth

of phytopathogenic fungi. By isolating 282 bacteria from the leaves, stems, and roots of chilli pepper plants (*Capsicum annum* L.), four isolates can prevent the growth of phytopathogenic fungus *Alternaria panax*, *B. cinerea*, *Colletotrichum acutum*, *Fusarium oxysporum*, and *Phytophthora capsici* could be identified. *Bacillus tequilensis* (CNU082075), *Burkholderia cepacia* (CNU082111), and *Pseudomonas aeruginosa* were the designations given to these bacterial strains (CNU082137 and CNU082142). Another 18 strains inhibited at least one of the examined phytopathogenic fungi (Fig. 1), demonstrating the significance of chilli pepper isolates in isolating microorganisms of agricultural significance (Pei et al. 2019). *Bacillus subtilis* SC1.4, isolated from sugar cane leaves, inhibits the development of many phytopathogenic fungi, including *Alternaria*, *Cochliobolus*, *Curvularia*, *Fusarium*, *Neodeightonia*, *Phomopsis*, and *Saccharicola*. The secondary metabolites in chloroform and methanol extracts of bacterial strains confirmed their antifungal activity (Fig. 1).

Surfactin and other volatile organic compounds (VOCs) may inhibit fungal development and, as a result, exert antifungal action (El-Tarabily 2003; Hazarika et al. 2019). The use of endophytic microbiota as a biocontrol agent can still

present as an additional characteristic in promoting plant growth, such as the bacterium *Arthrobacter agilis* UMCV2 that generates metabolite dimethyl hexadecylamine (DMHDA), which is characterized as an antagonist against phytopathogenic fungi *B. cinerea* and the oomycete *Phytophthora cinnamomic*. Selim et al. (2017) demonstrated the antifungal ability of three bacterial strains, namely *P. aeruginosa* H40 (isolated from the roots of *Pisum sativum* L.), *Stenotrophomonas maltophilia* H8 (isolated from the roots of *Brassica oleracea* L.), and *B. subtilis* H18 (isolated from the stem of *Cicer arietinum* L.) (Selim et al. 2016). The three examined strains inhibited the development of the disease in cotton cultivars caused by the fungus *Rhizoctonia solani*, based on the inoculum of the bacterial strains in the soil. Thus, it may be emphasized that the protective ability mediated by endophytes might be conferred by the presence of the microbe in the soil and not necessarily by entry into the plant tissues (Fig. 2). Additionally, crop yield increased, resulting in higher dry and fresh weight and shoot length (Legein et al. 2020; Bonaterra et al. 2022; El-Mageed et al. 2022; Elsayed et al. 2023).

Although several endophytic fungal strains are known for suppressing phytopathogenic fungi, most research focus

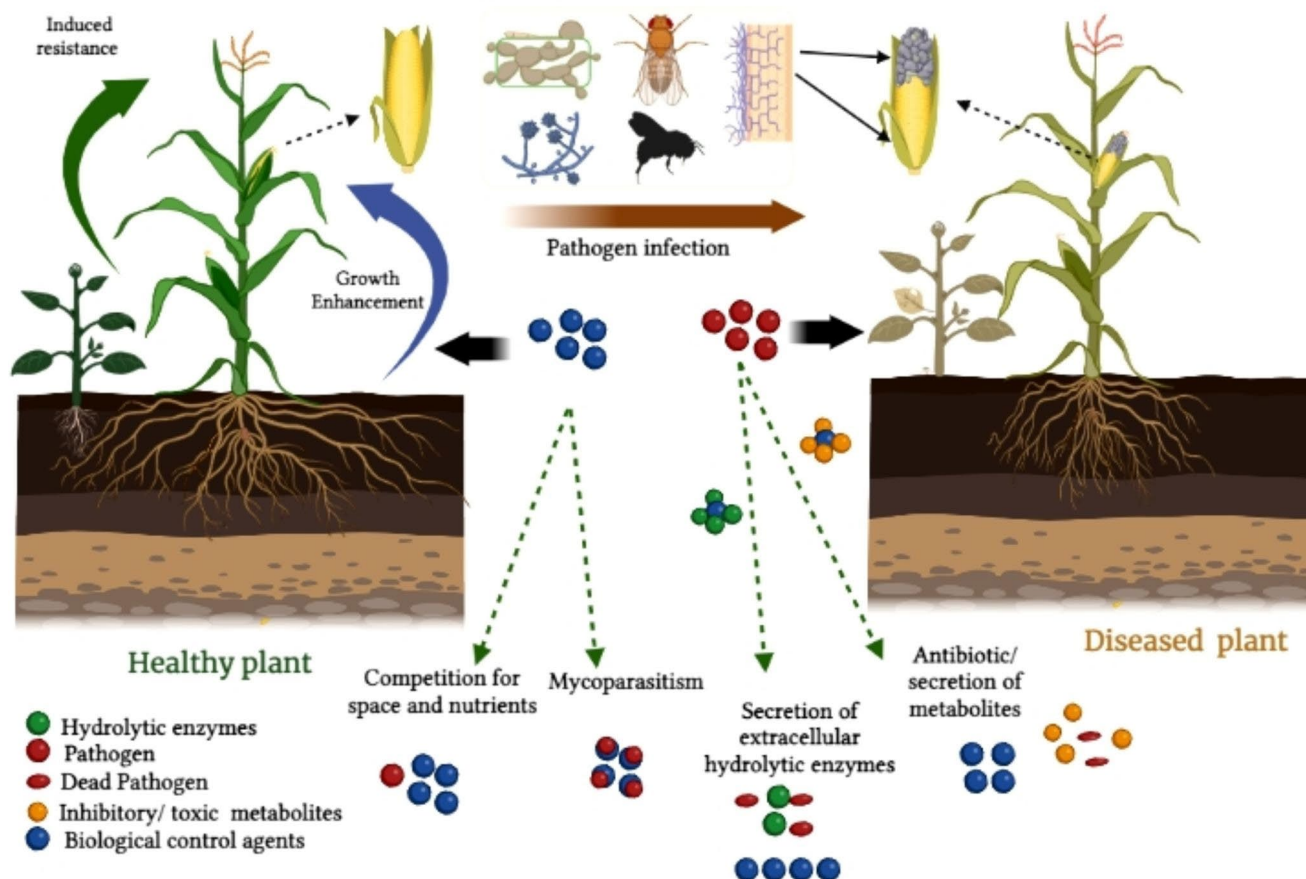


Fig. 1 Principal biological pathways involved in the bio-control of plant diseases by fungal inhibitors

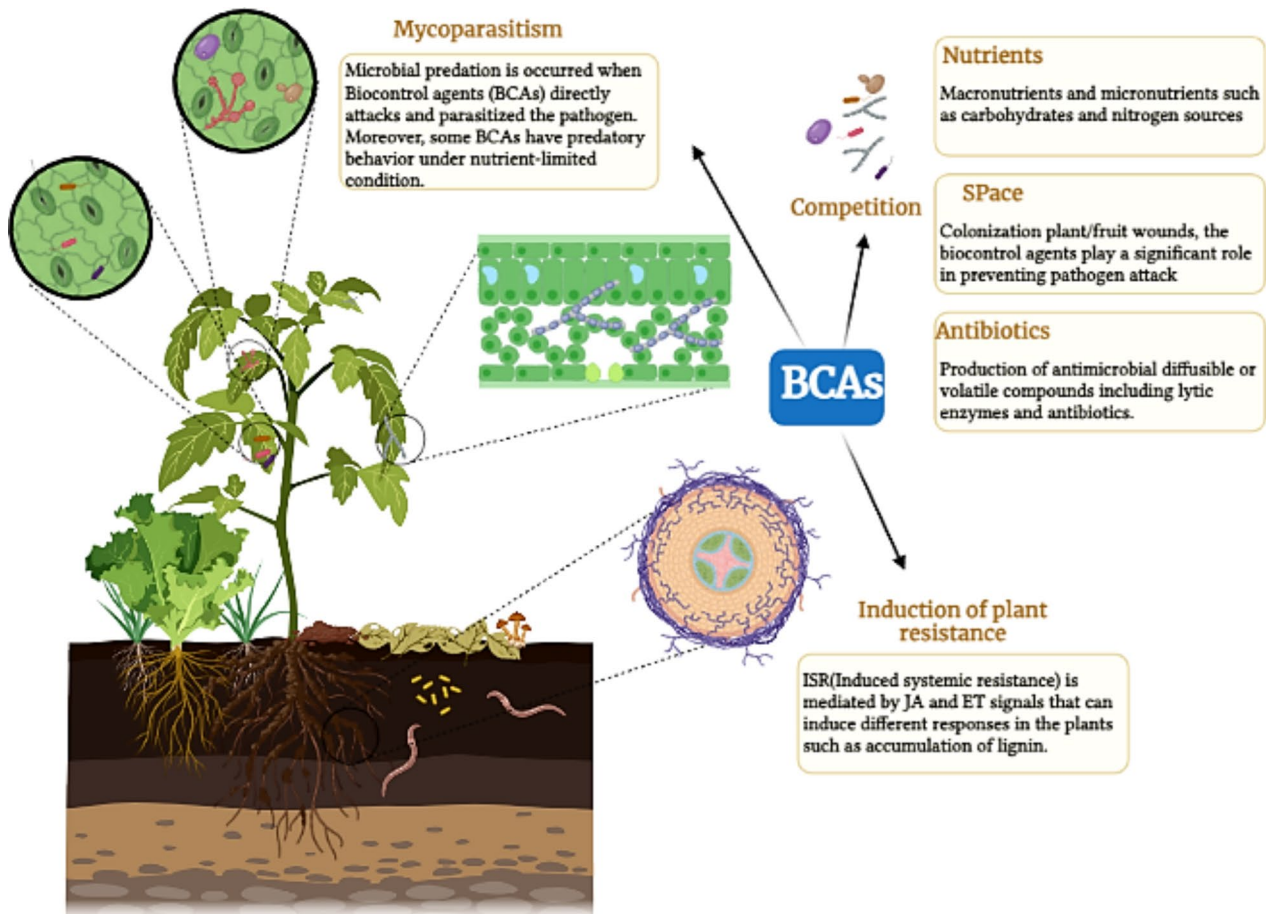


Fig. 2 The primary mechanism of biocontrol agents (BCAs) against plant pathogenic diseases, ethylene (ET) and jasmonic acid (JA)

on isolating fungi for their agricultural significance (Hassan et al. 2021; El-Mageed et al. 2022; de Andrade et al. 2023). *Ginkgo biloba* is a plant with therapeutic applications; nonetheless, it was used to isolate endophytic fungi, which were then evaluated for their capacity to prevent the growth of phytopathogenic fungi such as *Fusarium graminearum*, *Sclerotia sclerotiorum*, and *Phytophthora capsici*. Twelve of the 80 isolated endophytic fungal strains could inhibit at least one of the analyzed fungi, with *Chaetomium globosum* CDW7 being the most effective because producing 1,2-benzenedicarboxaldehyde-3,4,5-trihydroxy-6-methyl (flavin), which can protect the development of phytopathogenic fungi (in vivo, Fig. 1) and has healing properties for symptoms caused by pathogenic fungi (Xiao et al. 2013; El-Saadony et al. 2021; Alblooshi et al. 2022).

Lutfia et al. (2020) noted that medicinal plants are often distinguished by their capacity to suppress human infections. However, these microorganisms can also be employed for phytopathogenic fungus characterization. Seven endophytic fungi of *Etilingera elatior* were isolated,

described, and evaluated for their capacity to inhibit *F. oxysporum*, *Ganoderma boninense*, and *Rigidoporus lignus* in their investigation (Elnahal et al. 2022; de Andrade et al. 2023). Given the potential of benefit from the endophytic plant interaction, using endophytic microorganisms in the control of phytopathogens is contingent on several factors, including host specificity, moving in plant tissues, inducing systemic resistance, adaptation to environmental conditions, and adaptation to the physiological state of the plant (Fig. 1). However, using these specific microorganisms can benefit economically and environmentally since bacteria and fungi can produce cheaper costs and less environmental harm than chemical fungicides. In addition to controlling phytopathogens, developing biotechnological techniques that manipulate endophytic microbes may promote plant growth (El-Saadony et al. 2022; Elnahal et al. 2022) (Fig. 2).

Bacteria as antifungal biocontrol agents

Many environmental bacteria inhabiting soil and rhizosphere are sources of antifungal secondary metabolites (Desoky et al. 2022; Ahmed et al. 2022; Abdelkhalik et al. 2023). These chemicals are useful in human and animal therapy and plant protection against phytopathogens (Hasan et al. 2021; de Andrade et al. 2023; Elsayed et al. 2023). The secondary metabolism is not engaged in survival but provides producers with adaptive benefits (Katz and Baltz 2016). Most bacteria that generate bioactive natural chemicals are actinomycetes, known as actinobacteria in recent years. Among them, soil-dwelling filamentous *Streptomyces* are most frequently associated with producing antibiotic chemicals (Saeed et al. 2017; Kamil et al. 2018; Al Hamad et al. 2021; Al Raish et al. 2021; Alwahshi et al. 2022). In addition to antibacterial chemicals, actinomycetes produce

natural molecules with insecticide and anticancer characteristics (Table 1). Competition, protection, and signaling-mediated host interaction can account for the developing antimicrobial chemicals found mostly in soil bacteria (El-Tarabily and Sivasithamparam 2006; Hutchings et al. 2019).

Phytopathogenic fungi such as *Fusarium*, *Colletotrichum*, *Ceratocystis*, and *Rhizoctonia*, among others, can cause illnesses in different crops such as vascular wilt (Ma et al. 2013), anthracnose (Yan et al. 2018), black rot (Stahr and Quesada-Ocampo, 2020), and sheath blight (Rao et al. 2019), respectively. Biological control is an indirect plant growth-promoting strategy that occurs when an organism kills or halts the growth of pathogens through competition for space or resources, induction of plant systemic resistance, or antibiosis mediated by the creation of secondary metabolites (Olanrewaju et al. 2017). Beneficial microorganisms that colonize plants and promote plant development are

Table 1 Some bacteria and fungi strain as biocontrol agent against phytopathogenic fungi

Biocontrol Agent	Commercial name	Crop	Pathogen group	References
<i>Bacillus subtilis</i> QST 713	Cease®	Ornamentals and Vegetable i.e., potatoes.	For foliar/soilborne diseases, bio fungicides and bio bactericides.	(Bertuzzi et al. 2022)
<i>Bacillus subtilis</i> GB03	Companion®	Legumes, grasses, ornamentals	Bio fungicide, bio bactericide, biochemical pesticide	(Ni and Punja 2019)
<i>Bacillus amyloliquefaciens</i> D747	Ethos® XB Biofungicide	Sweet corn	Bio-fungicides	(Conrad 2022; Conrad and Telenko 2023)
<i>Bacillus amyloliquefaciens</i> MBI600	Integral®	Ornamentals, legumes i.e. Soybean and vegetables	Biological liquid fungicide	(Beris et al. 2018)
<i>Aspergillus flavus</i>	Afla-Guard® GR	Peanuts and different types of corn	Using biofungicide to lower aflatoxin contamination	(Pedro et al., 2013)
<i>Coniothyrium minitans</i>	Contans® WG	Soybean, beans, sunflower, vegetables	Biopesticide and biofungicide	(Conrad and Telenko 2023)
<i>Streptomyces lydicus</i>	Actinovate® AG	Tomatoes, dry legumes and corn	Bio fungicide effective against several soilborne and bacterial infections, as well as some foliar pathogens	(Sanogo and Lujan, 2022)
<i>Pasteuria nishizawae</i>	Clariva® pn	Soybean, sugarbeets	Bio-nematicide	(Lund et al. 2018)
<i>Burkholderia sp</i>	Majestene®	Vegetables e.g., Potatoes, tomatoes, fruits, apples, legumes, i.e., soybean, and i.e., grasses, Alfalfa, wheat	Bio-nematicide	(Eberl and Vandamme 2016)
<i>Bacillus firmus</i>	Poncho®/VOTiVO®	Sweet and field Corn sorghum, soybeans, and sugar beet.	Bio-nematicide, Soybean Cyst Nematode	(Hussain et al. 2022)
<i>Reynoutria spp.</i> extract	Regalia® Rx	Wheat, Corn, soybean,	Biofungicide; biobactericide-induced systemic resistance against fungi and bacteria	(Pavela and Vrchotová 2008)
<i>Bacillus subtilis</i> QST 713	Rhapsody®	Multiple cereals, grasses, legumes, and ornamental crops	Bio-fungicide and bio-bactericide	(Rotolo et al., 2016)
	Serenade®	Corn, soybeans, veggies, and potatoes	Bio-fungicides, bio-bactericides, Rhizoctonia root rot, grey and white mold, bacterial spores	(Bertuzzi et al. 2022)
<i>Bacillus subtilis</i>	Xanthion®	Field and sweet corn	Biological fungicide used in conjunction with chemical	(Milijašević-Marčić et al. 2017)
<i>Trichoderma harzianum</i>	Rootshield®	Multiple crops, veggies, and landscaping	Biofungicide for root pathogen prevention	(Ahluwalia et al. 2015; Khan et al. 2020)

plant growth-promoting bacteria (PGPB). The use of PGPB as biofertilizers in agriculture has increased in recent years, with *Pseudomonas*, *Bacillus*, *Enterobacter*, *Klebsiella*, *Azobacter*, *Azospirillum*, and *Rhizobium*, among others, being the predominant organisms (Vejan et al., 2016).

Bacterial secondary metabolites

Diffusible antifungal substances

Secondary metabolites with effective antifungal action include phenazine (phenazine-1-carboxylic acid), pyrrolnitrin, surfactin, iturin, fengicin, and hydrogen cyanide (Fig. 3). The plant growth-promoting rhizobacteria (PGPR), *Pseudomonas* spp. strain ST-TJ4, was able to effectively suppress 6 phytopathogenic fungi in agriculture and forestry, including *Botryosphaeria berengeriana*, *Colletotrichum tropicale*, *Fusarium oxysporum*, *Fusarium graminearum*, *Phytophthora cinnamomic*, and *Rhizoctonia solani*. The production of phenazines, pyrrolnitrins, and hydrogen cyanide was associated with aggressive action (Kong et al. 2020).

Pseudomonas spp., were also discovered to produce ecomycins, pseudomonic acid, pyoluteorin, oomycin A, cepaciamides, butyrolactones, aerugines, azomycins, rhamnolipids, cepafungins (Goswami et al. 2016). *Bacillus* spp., are significant producers of antifungal metabolites, including fengycin, iturin, and surfactin, which are bioactive against, among others, *Monilinia fructicola*, *S. sclerotiorum*, *Phoma medicaginis*, *F. oxysporum*, *Penicillium expansum*, and *Aspergillus flavus* (Penha et al. 2020). *Bacillus velezensis* HC6 has antagonistic activity against *Aspergillus* and *Fusarium* in maize by suppressing mycelial growth and lowering toxin generation via lipopeptides release (Liu et al. 2020).

Bacillus metabolites are often generated from the ribosome or non-ribosomal peptide synthetases (NRPS) and polyketide synthetases (PKS). Examples include bacilysin, bacillaene, chlorotetain, sublancin, subtilisin, and subtilin, in addition to fengycin, iturin, and surfactin (Olanrewaju et al. 2017) (Table 2). The species of this genus are promising for the biocontrol of fungi that have already been marketed to control various diseases in a vast array of crop cultures.

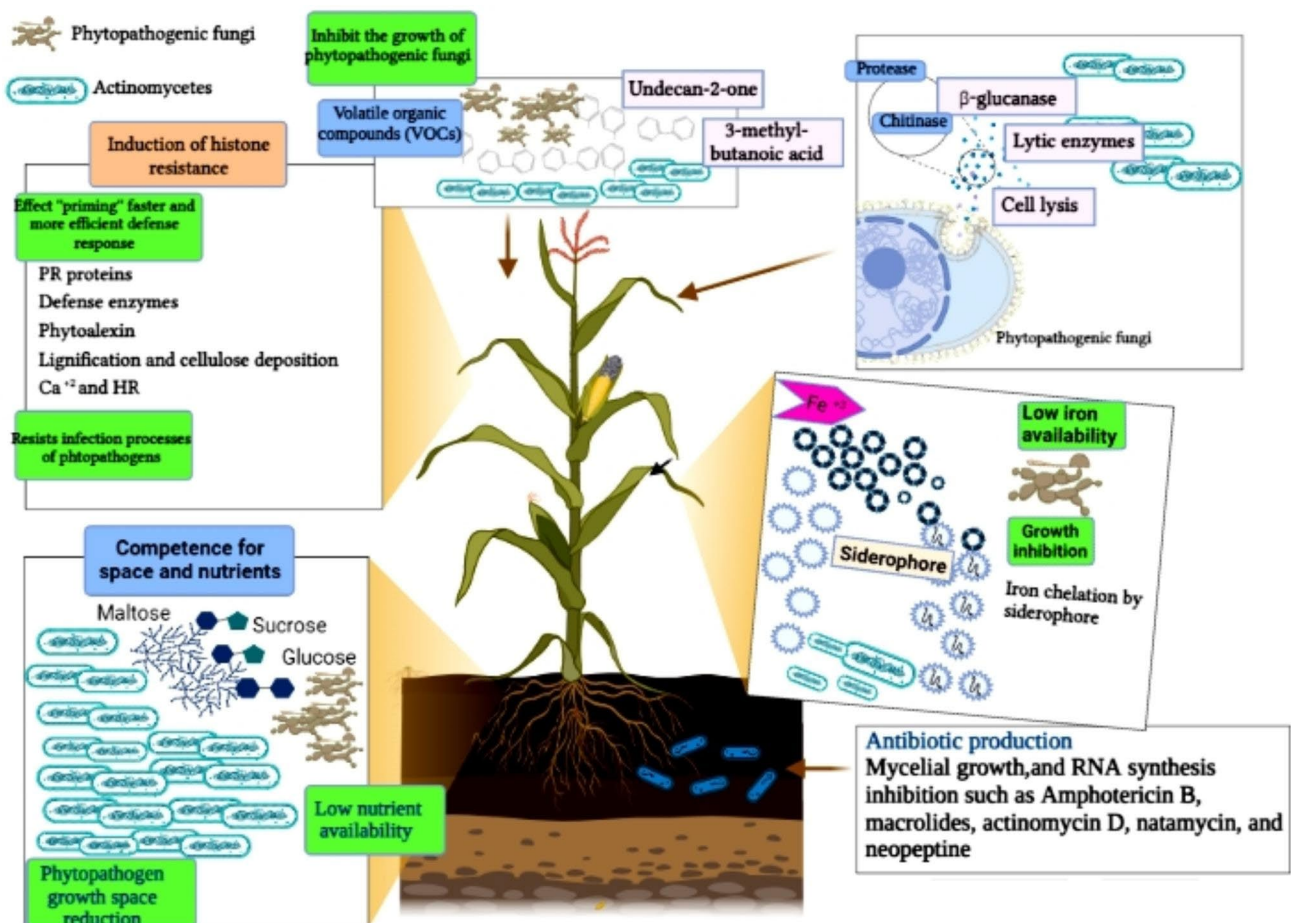


Fig. 3 Principal phytopathogen-antagonistic strategies of actinomycetes, Pathogenesis-related (PR) proteins, HR lysine demethylase and nuclear receptor corepressor

Table 2 Antifungal activity of some secondary metabolites in biocontrol agents against phytopathogenic bacteria

Biocontrol agent	Secondary metabolites	Target pathogen	References
<i>Pseudomonas</i> spp. strain ST-TJ4	phenazine-1-carboxylic acid), pyrrolnitrin, surfactin, iturin, fengycin, and hydrogen cyanide	<i>Botryosphaeria berengeriana</i> , <i>Colletotrichum tropicale</i> , <i>Fusarium oxysporum</i> , <i>Fusarium graminearum</i> , <i>Phytophthora cinnamomic</i> , and <i>Rhizoctonia solani</i>	(Kong et al. 2020)
<i>Pseudomonas</i> spp.	Ecomycins, pseudomonic acid, pyoluteorin, oomycin A, cepaciamides, butyrolactones, aeruginosins, azomycins, rhamnolipids, cepafungins	<i>Fusarium oxysporum</i> , <i>Fusarium graminearum</i> , <i>Phytophthora cinnamomic</i>	(Goswami et al. 2016)
<i>Bacillus</i> spp.	Fengycin, iturin, and surfactin, bacilysin, bacillaene, chlorotetain, sublancin, subtilosin, and subtilin	<i>Monilinia fructicola</i> , <i>Sclerotinia sclerotiorum</i> , <i>Phoma medicaginis</i> , <i>Fusarium oxysporum</i> , <i>Penicillium expansum</i> , and <i>Aspergillus flavus</i>	(Penha et al. 2020)
<i>Bacillus velezensis</i> HC6	Lipopeptides	<i>Aspergillus</i> and <i>Fusarium</i> species	(Liu et al. 2020)
<i>Bacillus pumilus</i> GB34	Fengycin, iturin, and surfactin, bacilysin, bacillaene, chlorotetain, sublancin, subtilosin, and subtilin	<i>Rhizoctonia</i> , <i>Pythium</i> , and <i>Fusarium</i>	(Lopes et al. 2018)
<i>Bacillus velezensis</i> strain ZSY-1	2,5-dimethylpyrazine, benzothiazole, 4-chloro-3-methyl-phenol, and 2,4-bis(1,1-dimethylethyl)-phenol	<i>Alternaria solani</i> and <i>Botrytis cinerea</i>	(Gao et al. 2017)
<i>Burkholderia</i> spp. with	Pyrrolnitrin	<i>Botrytis cinerea</i> , <i>Rhizoctonia solani</i> , <i>Sclerotinia sclerotiorum</i> , and <i>Verticillium dahlia</i>	(Kanchiswamy et al. 2015)
<i>Burkholderia cenocepacia</i> ETR-B22	Dimethyl trisulfide, indole, methyl anthranilate, methyl salicylate, and benzyl propionate	<i>Aspergillus</i> and <i>Fusarium</i> species, <i>Rhizoctonia</i> , <i>Pythium</i> , and <i>Fusarium</i>	(Chen et al. 2020)
<i>Staphylococcus sciuri</i> MarR44	Mesityl oxide	<i>Colletotrichum nymphaeae</i>	(Alijani et al. 2019)
<i>Sinorhizobium fredii</i>	Chitinases and β -glucanases	<i>Fusarium</i> spp., and <i>Rhizoctonia solani</i>	(Vejan et al., 2016)
<i>Azospirillum brasilense</i> REC2, REC3, and PGPB	Catechol-type siderophores	<i>Colletotrichum acutatum</i>	(Tortora et al. 2011)
<i>Brevibacillus laterosporus</i> A60	Protein elicitor PeBL2	<i>Botrytis cinerea</i>	(Jatoi et al. 2019)
<i>Trichoderma asperellum</i>	chitinase and cellulase	<i>Fusarium oxysporum</i> on rooted cuttings of <i>Stevia rebaudiana</i>	(Díaz-Gutiérrez et al. 2021)
<i>Diatrype palmicola</i>	8-methoxynaphthalen-1-ol	<i>Athelia rolfsii</i>	(Tanapichatsakul et al. 2020)
<i>Nodulisporium</i> spp.	2-ethyl-2-hexenal and 2,4-dimethyl-1,3-cyclopentanedione	<i>Penicillium digitatum</i>	(Yeh et al. 2021)
<i>Aspergillus flavus</i> , <i>Aspergillus niger</i> , <i>Penicillium citrinum</i> , <i>Penicillium chrysogenum</i> , and <i>Trichoderma koningiopsis</i>	Pathogenesis-related gene (PR1, 2), the plant defensive chitinase (Chit-1), and β -1,3-glucanase (Glu-2)	<i>Rhizoctonia solani</i> R43	(El-Maraghy et al. 2020)
<i>Sulfolobus</i> and <i>Haloarchaea</i> <i>Archaea</i>	Amphiphilic peptides, archaeocins	<i>Penicillium citrinum</i> , <i>Aspergillus niger</i> , and <i>Aspergillus flavus</i>	(Adebayo and Aderiyé 2010)
	halocins HalH1, HalH4, HalH6, HalS8, HalC8	<i>Candida</i> spp.	(Roschetto et al. 2018)
	Antimicrobial peptide (VLL-28)	<i>Candida tropicalis</i> , <i>Candida albicans</i> , <i>Candida parapsilosis</i> , and <i>Candida glabrata</i> , except <i>Candida krusei</i>	(Roschetto et al. 2018)

Bacillus pumilus GB34 is a component of Bayer Crop Science's (United States) Yield Shield product with antifungal action against *R. solani* and *Fusarium* spp., in soybean crops. The Bio-Yield (3Bar Biologics, USA) is another example of a *Bacillus*-based inoculant that targets *Rhizoctonia*, *Pythium*, and *Fusarium* in bedding plants (El-Tarabily 2006; El-Tarabily et al. 2009; Lopes et al. 2018).

Fungi resistance to the active fungicides used on crops is evolving daily, and the utilization of alternate natural resources, such as beneficial bacteria, is increasing (Lamichhane et al. 2016). *B. cinerea* is a fungus that infects most greenhouse crops, and its global resistance to conventional fungicides is growing. Three strains of *Pseudomonas* (*P. protegens* AP54, *P. chlororaphis* 14B11, and *P. fluorescens*

89F1) were able to reduce *B. cinerea* infection in petunia under greenhouse conditions, so providing a viable solution to the fungicide-resistance issue (South et al. 2020).

Volatile organic compounds

The VOCs generated by microorganisms may travel great distances, facilitating indirect interaction between organisms even at low concentrations, limiting the development of phytopathogenic fungi, and establishing systemic resistance in plants (Fig. 3; Table 2). VOCs have smaller molecules than non-volatile chemicals, allowing for easy dispersion in soil and air (Chen et al. 2020). *Bacillus*, *Arthrobacter*, *Pseudomonas*, *Serratia*, and *Stenotrophomonas* are examples of bacteria that generate VOCs that affect plant development (Vejan et al., 2016).

Many molecules, including acetaldehyde, butanoic acid, camphene, camphor, methanol, geosmin, propanoic acid, 5-hydroxy-methyl-furfural, and caryophyllene can be emitted as VOCs (Kanchiswamy et al. 2015). Several studies demonstrated that bacterial volatile organic compounds inhibit phytopathogenic fungi. *B. velezensis* strain ZSY-1 generates the volatile organic compounds 2,5-dimethylpyrazine, benzothiazole, 4-chloro-3-methyl-phenol, and 2,4-bis(1,1-dimethylethyl)-phenol, which manages tomato fungal infections by inhibiting *Alternaria solani* and *B. cinerea* (Gao et al. 2017) (Fig. 3; Table 2).

Pyrrolnitrin is a volatile organic compound generated by *Burkholderia* spp. with efficacy against significant *B. cinerea*, *R. solani*, *S. sclerotiorum*, and *Verticillium dahlia* are examples of phytopathogens (Kanchiswamy et al. 2015). *Pseudomonas* spp. ST-TJ4 (1-undecene) can prevent the growth of phytopathogenic fungi, such as *C. tropicale*, *F. oxysporum*, *P. cinnamomic*, and *R. solani*, by emitting volatile organic compounds. VOCs inhibited more fungal growth than the diffusible chemicals in the culture media (Kong et al. 2020). *Burkholderia cenocepacia* ETR-B22 produces 32 distinct volatile organic compounds, including dimethyl trisulfide, indole, methyl anthranilate, methyl salicylate, and benzyl propionate, with potent antagonistic action against 12 fungal phytopathogens (Chen et al. 2020). *Staphylococcus sciuri* MarR44 decreased anthracnose disease at post-harvest on strawberries by 72.17%, caused by *Colletotrichum nymphaeae* detected VOCs, mesityl oxide (81.4%) being the most prevalent (Alijani et al. 2019).

Hydrolytic enzymes

Multiple PGPBs can generate protease, lipase, chitinase, and cellulase. Enzymes generated by bacteria can degrade phytopathogenic fungus cell walls, preventing their growth. Due to the presence of chitin and b-glucan in fungal cell

walls, the bacterial enzymes chitinases and b-glucanases can impede fungal growth (Ali et al., 2020). *Pseudomonas* spp. and *Sinorhizobium fredii* are examples of hydrolytic enzyme makers that can inhibit *Fusarium* spp., and *R. solani* (Vejan et al., 2016) (Fig. 3; Table 2).

The mechanism of killing phytopathogenic fungi

Competition

Struggle for nutrients or space and competition for binding sites on roots hinder the phytopathogen's ability to reach and colonize the plant. This rivalry is often tied to biocontrol processes, such as releasing secondary metabolites (Olanrewaju et al. 2017). Primarily in soil, VOCs have a role in competitive interactions between bacteria and fungi. A collective volatile-mediated antagonism of soil bacteria against invading fungi is an integral approach for bacteria to fight invading fungi for nutritional locations (Li et al. 2020) (Fig. 3).

Some bacteria create a siderophore, a tiny molecular weight molecule whose role is to bind the iron in the environment and transfer it to the cell interior, providing a competitive advantage to the organism (Hutchings et al. 2019). The siderophore pyoverdine produced by *P. aeruginosa* is essential for combating *Aspergillus fumigatus* (Sass et al. 2018).

Strains REC2, REC3, and PGPB of *A. brasilense* release catechol-type siderophores that are efficient against the phytopathogen *Colletotrichum acutatum*, hence protecting strawberry crops against anthracnose disease (Tortora et al. 2011). Studies conducted in vitro with the siderophore producer *Acinetobacter calcoaceticus* HIRFA32 from wheat rhizosphere indicated a significant reduction of *F. oxysporum* mycelium growth (Maindad et al. 2014).

Induced systemic resistance (ISR)

Several PGPBs can be protective agents by generating ISR, activating the plants' resistance to certain diseases. Signaling chemicals, such as salicylic acid, released by PGPB, which may protect the plant from phytopathogens, coordinate the process (Olanrewaju et al. 2017). Rhizobacteria produced systemic resistance to *F. oxysporum* in chickpeas, safeguarding the plant (Kumari and Khanna 2020). By releasing the protein elicitor PeBL2, *Brevibacillus laterosporus* A60 can generate systemic resistance to *B. cinerea* in tobacco (Jatoi et al. 2019). Beneficial bacteria and rhizobacteria can protect plants from phytopathogenic fungi through several processes. Using microorganisms or their metabolites

in agriculture is a more ecologically friendly alternative to chemical fungicides that must be progressively implemented to maintain sustained crop yield (Fig. 3; Table 2).

Fungi as biological control agents

Because they occupy a similar ecological niche, some fungi can regulate phytopathogenic fungi by competing for resources, creating antagonistic chemicals, and developing plant resistance (Schardl and Phillips 1997; Hallmann et al. 1998; Peixoto Neto et al. 2002). Thus, Santos et al. (2019) revealed that an endophytic fungus (*Diaporthe*) isolated from *Sapindus saponaria* L. leaves may inhibit phytopathogenic fungi in vitro. Several phytopathogens, including *Fusarium solani*, *Glomerella* spp., and *Monilophthora perniciosa*, had their growth reduced by touch, showing that competition for space was part of the inhibitory process (Table 1).

Mycoparasitism, in which fungi colonize the surface of the phytopathogen colony, is another method utilized by fungicides to inhibit the proliferation of phytopathogenic fungi. Wall-degrading enzymes are essential antagonists in this process (De Vrieze et al. 2020; Montes-Osuna et al. 2021; Díaz-Díaz et al. 2022). Since most phytopathogenic fungi have cell walls consisting of complex polymers, glucanases, chitinases, and proteases are primarily extra cellular enzymes responsible for the destruction of cell walls (Silva et al. 2019; Khunnamwong et al. 2020; Peters et al. 2020). *Trichoderma* species are recognized for their ability to generate lytic enzymes, which play crucial functions in the cell wall (da Silva Ribeiro et al. 2018), making this genus a significant biological control agent. Khatri et al. (2017) examined the effectiveness of 12 soil-isolated species of *Trichoderma* against fungal plant diseases, including *A. niger*, *F. oxysporum*, and *Sclerotium rolfsii*.

Trichoderma viride was shown to be the most effective antagonist against fungal plant diseases among the examined species, generating three important cell wall degrading enzymes (chitinase, protease, and glucanase) and playing a significant part in the adversary process. In a separate investigation, Díaz-Gutiérrez et al. (2021) evaluated the growth inhibition capacity of rhizospheric *Trichoderma asperellum* against *F. oxysporum* on rooted cuttings of *Stevia rebaudiana* L. *T. asperellum* prevented the development of *F. oxysporum* and five other pathogenic fungi, demonstrating the capacity to hydrolyze chitin and cellulose by releasing chitinase and cellulase. Antimicrobial secondary metabolites are an additional mode of action utilized by fungi against phytopathogenic organisms (Köhl et al. 2019). In this instance, endophytic fungi have attracted interest due to their mutualistic interaction with plants, which produces bioactive chemicals (de Almeida et al. 2018).

Using a crude hexane extract of the fungal mycelium from the endophytic fungus *Diatrype palmicola*, isolated from the medicinal plant *Polyscias fruticosa*, Tanapichatsakul et al. (2020) observed significant antifungal activity, with a 64.71% inhibition rate, against the common tomato infected by *Athelia rolfsii*. The bioactive chemical generated by *D. palmicola* has been discovered as 8-methoxynaphthalen-1-ol, suggesting that this substance, which inhibits the growth of *A. rolfsii*, may be a viable alternative for managing this phytopathogen (Table 2). The endophytic fungus can also form combinations of carbon-based molecules known as volatile organic compounds (VOCs) have shown promise as antifungal plant defenses (Kaddes et al. 2019).

Yeh et al. (2021) subjected volatile organic compounds from the endophytic fungus *Nodulisporium* spp., isolated from the medicinal plant *Peperomia dindygulensis*, to inhibitory assays. The isolated fungus was cultivated in various media to yield active compounds tested against *Penicillium digitatum*, the fungus responsible for citrus green mould. 2-ethyl-2-hexenal and 2,4-dimethyl-1,3-cyclopentanedione were the substances produced by the fungus cultivated in bagasse that reduced the prevalence of green mold, indicating that *Nodulisporium* spp. might be employed as a bioagent to control *P. digitatum*.

Like bacteria, fungi may reduce plant diseases via two kinds of induced resistance: systemic acquired resistance (SAR) and induced systemic resistance (ISR). They produce signaling chemicals such as jasmonic acid (JA), salicylic acid (SA), ethylene (ET), phytoalexins, protein-related chitinases, and glucanases (Hermosa et al. 2012; Nawrocka and Małolepsza 2013; Desoky et al. 2020; Olowe et al. 2020). El-Maraghy et al. (2020) investigated the capability of plant growth-promoting fungi (PGPF) strains to produce ISR against wilt disease caused by *R. solani* R43 in wheat (*Triticum aestivum* L.). According to their findings, the PGPF *A. flavus*, *A. niger*, *Penicillium citrinum*, *Penicillium chrysogenum*, and *Trichoderma koningiopsis* were identified from the rhizosphere of *Triticum aestivum* (ISR) infected with *R. solani* R43 and resistant to wilt disease.

This was accomplished by activating the pathogenesis-related gene (PR1, 2), the plant defensive chitinase (Chit-1), and -1,3-glucanase (Glu-2) genes and increasing the *R. solani*-specific plant-specific defensive proteins. Consequently, biological management against phytopathogenic organisms employing fungus has been demonstrated to be a potential solution for managing some plant diseases. These microorganisms employ diverse modes of action against the pathogen, making them helpful in developing novel and more effective pesticides, improving cropping systems, reducing the use of chemically synthesized pesticides, and diminishing the latter's environmental impact (Mckenna et

al. 2001; De Vrieze et al. 2020; Montes-Osuna et al. 2021; Díaz-Díaz et al. 2022).

Virus as biological control agents

Hyper-parasitism by obligatory parasites of a plant pathogen would be regarded as the most direct mechanism since no other organism's activities would be necessary to provide a suppressive impact (Harman et al. 2004). Four critical categories of hyperparasites, including hypoviruses, facultative parasites, obligate bacterial pathogens, and predators, have been identified. Mycoviruses are fungal viruses, and most have dsRNAs as their genome. There are at least 12 families of mycoviruses; some resemble plant and animal viruses, while others comprise their own families (Marzano and Domier 2016; Nerva et al. 2016). *Partitiviridae*, *Totiviridae*, *Chrysoviridae*, and *Endornaviridae* are the primary families into which double-stranded RNA (dsRNA) mycoviruses fall. However, it has been suggested that newly found mycoviruses should be placed into a new genus and family (Ghabrial et al. 2015). In general, dsRNA mycoviruses consistently infect the host fungus, are propagated vertically during host cell division, and cause asymptomatic infections (Osaki et al. 2006).

In the worst-case scenario, viruses can infect plant-associated fungi with an incidence rate ranging from a few percentage points to 90%. Even though most viral infections are asymptomatic, phenotypic changes can be damaging or advantageous to the host fungus. This review will cover harmful interactions between viruses and hosts, including hypovirulence and debilitation in various phytopathogenic fungi (Marzano and Domier 2016; Nerva et al. 2016). Hypovirulence is a prime example of a negative interaction in which several viruses diminish the virulence of fungi (Ghabrial et al. 2015). Additionally, it is frequently accompanied by additional phenotypic abnormalities, such as diminished pigmentation, sporulation, and growth problems (Hillman et al. 2018). Due to their parasitic nature, viruses cannot create secondary metabolites that can serve as antifungal substances. Therefore, if fungal viruses infect harmful plant fungi, they might serve as biocontrol agents (Yu et al. 2013).

Numerous studies have found fungal viruses that infect agriculturally significant phytopathogenic fungi; hence, a subset of these viruses might serve as biological control agents for fungal crop diseases (Xie and Jiang 2014; García-Pedrajas et al. 2019). However, hypovirulence-associated viruses have a variety of phenotypes that affect fungal properties and reproductive performance, such as reduced growth and fertility, together with modified pigment and metabolite synthesis, can render infected fungus fewer

competitive than untreated fungi or less able to facilitate viral transmission (Nuss 2005).

In a small number of plant endophytic and pathogenic fungi, beneficial interactions are identified when heat tolerance and virulence are improved (Marzano and Domier 2016; Nerva et al. 2016). Despite viral infection, certain fungal plant diseases are biologically controlled by viruses with harmful RNA. For instance, in the chestnut blight (*Cryphonectria parasitica*), take-all disease (*Gaeumannomyces graminis*), *Sclerotinia* moulds (*Sclerotinia* spp.), and Dutch elm disease (*Ophiostoma novoulmi*) pathosystems, viruses are responsible for natural disease suppression under field conditions, and research is currently being conducted to utilize this hypovirulence phenomenon (Duffy and Weller 1996; Zhou and Boland 1998; Brasier 2001).

The viral infection of *C. parasitica* is a prominent example of hypo-parasitism when it causes hypovirulence, or a reduction in the pathogenicity of the pathogen, hence reducing chestnut blight in several locations (Milgroom and Cortesi 2004). Based on the infection system between plant disease fungi and viruses, there are possible *in vitro*-control agents to determine if they infect plant pathogen fungi, such as the hypo viruses, to manage the chestnut blight in Europe (Rigling and Prospero 2018).

Notably, the most well-described mycoviruses responsible for affecting the phytobiome (as the American Phytopathological Society defines plant pathology as “plants and their environments”, and the related groups of organisms”) are the *C. parasitica* hypovirulence-inducing viruses. Several critical historical texts Anagnostakis (1982); Heiniger and Rigling (1994); Nuss (2005) describe chestnut blight and hypovirulence viruses. Chestnut blight fungus was first described in North America in 1906 by Merkel apud Schoelz and Stewart and in Europe in 1946 by Biraghi with devastating effects (Schoelz and Stewart 2018). Hypovirulent strains were first identified in Italy when Biraghi discovered chestnut trees (*Castanea sativa*) healing from cankers (Biraghi 1953). Subsequently, Day (1977) identified dsRNAs in hypo-virulent strains, and these dsRNAs were ultimately shown to be viral.

Anagnostakis (1982) outlined how more hypovirulent strains were subsequently discovered on American chestnut and how, over time, several viruses associated with *C. parasitica* hypovirulence of diverse viral lineages were discovered (Nuss 2005). The *Cryphonectria* hypovirulence viruses 1–4 (CHV1–4) are infectious clones of CHV1 (Chen and Nuss 1999). From 1982 to 2005, the biocontrol of chestnut disease in North America was less effective than anticipated, although it looked more influential in Europe (Heiniger and Rigling 1994). This may be because the biocontrol does not proliferate effectively in the less dense American chestnut trees and because the mating kinds (regulated by six vic loci)

of chestnut disease are incompatible with the mating types of biological control in North America are more diverse and complex than in Europe. There may be susceptibility variations between the host trees (American and European chestnut) (Anagnostakis 1982).

In addition to *Cryphonectria hypoviruses*, other hypoviruses for other phytopathogenic fungi, such as *Rhizoctonia*, dollar spot, Dutch elm, Victoria blight on oats, and white root rot pathogens, have been identified. The majority of hypovirulence-associated viruses found so far belong to the families *Totiviridae*, *Chrysoviridae*, and *Reoviridae* or are unclassified viruses; viruses of phytopathogenic fungi also include *Endornaviridae*, *Partitiviridae*, and *Hypoviridae* viruses (Nuss 2005; Ghabrial and Suzuki 2009).

Xie and Jiang (2014) discussed the bottlenecks in using these viruses as biocontrol tools. They suggested they are comparable to those for *Cryphonectria hypovirulence* viruses (CHV), such as establishing knowledge about the related virus-causing hypovirulence and discovering effective, sustainable delivery strategies to resolve vegetative incongruence and other dispersion obstacles. Also, *S. sclerotiorum* is a crucial plant-pathogenic fungus for which the viruses with the highest hypovirulence were found (Xie and Jiang 2014). Notably, it was the first report of a Gemini-like SsDNA virus, SsHADV1, and a mono-negavirus, *S. sclerotiorum* negative-stranded RNA virus 1 (SsNSRV-1), linked with hypovirulence (Yu et al. 2010; Liu et al. 2014).

Sclerotinia sclerotiorum hypovirus 2 (SsHV2) (Marzano et al. 2015) and Sclerotinia sclerotiorum partitivirus 1 (SsPV1) (Xiao et al. 2014) cause hypovirulence in *S. sclerotiorum*. The latter is notable because most partiti-viruses, whether plants or fungi cause asymptomatic infections in their hosts. There are a large number of hypovirulence-causing viruses from a variety of viral families. Host fungi exhibiting hypo-virulent phenotypes are primarily limited to Ascomycota, and virtually little is known about viral or host mechanisms causing the phenotypic alterations generated by these viruses (Hillman et al. 2018).

The interactions between species in natural systems are many and intricate. One of the field's most significant challenges is sorting out the numerous little connections constituting a complicated tapestry of interconnected interactions. Schoelz and Stewart (2018) stated that, similar to bacteria, viruses may be bio-prospected and utilized for bio-controlling projects or other valuable objectives. They thought it was conceivable owing to the hypovirulence factor's potential but detecting these interactions is not yet simple.

The research on using viruses to control the effects of various biotic and abiotic stressors has just begun (Schoelz and Stewart 2018). Sustainable agriculture is a movement supported in most Latin American nations, intending to profit from the increased usage of registered viral pesticides, novel

viral products undergoing registration, and other products in the applied research pipeline (Haas and Défago 2005). The baculovirus family (Baculoviridae) was regarded to have produced the most commercial viral biopesticides among natural insect viruses (Haase et al. 2015) (Fig. 4).

In the 1930s, the very first well-documented introduction of a baculovirus to the environment led to the efficient eradication of a pest when an NPV specific for the spruce sawfly *Diprion hercyniae* was accidentally introduced along with a parasitoid imported from Europe to the United States and Canada to control the spruce sawfly (Bird and Elgee 1957). They are deemed safe for vertebrates; no incidences of baculovirus pathogenicity in vertebrates have been identified (Black et al. 1997).

In addition, its host-specificity is often restricted to a particular insect species. Several effective baculovirus-based pest management programs have been implemented in Latin American nations, as (Haase et al. 2015) described in detail (Fig. 4).

Baculovirus-based pesticides are a potential example of virus-based biocontrol agents; once they are compatible with integrated pest management systems, their use will substantially minimize the dangers associated with synthetic chemical insecticides. Given the high host-specificity of baculoviruses and their restricted use without causing any harm to vertebrates, it is believed that the naturally isolated fungal RNA virus represents a potential biocontrol tool for improved agricultural management, causing little harm to non-target creatures, such as beneficial fungi, vertebrates, and plants.

Archaea: a possible source of antimicrobial compounds

Archaea is a significant domain that could serve as an alternative method to increase agricultural production due to their unique characteristics, particularly their prominent role in nutrient (nitrogen, sulfur, and carbon) recycling in agricultural productions when the plant requires these nutrients in large quantities (Odelade and Babalola 2019). Chelius and Triplett (2001) have documented the presence of archaea in the rhizospheres of plant roots. In addition, archaea act as hosts for a unique class of potentially beneficial antibiotics. In general, bacteriocins are ribosomally generated, tiny (10 kDa), bactericidal, heat-stable, antibiotic-like compounds, amphiphilic peptides, or proteins produced by bacteria that may kill the same strain or closely related strains of bacteria (Cascales et al. 2007).

Moreover, bacteriocins show antifungal efficacy against three spoilage fungi (*P. citrinum*, *A. niger*, and *A. flavus*), as described (Adebayo and Aderiyi 2010). The archaea

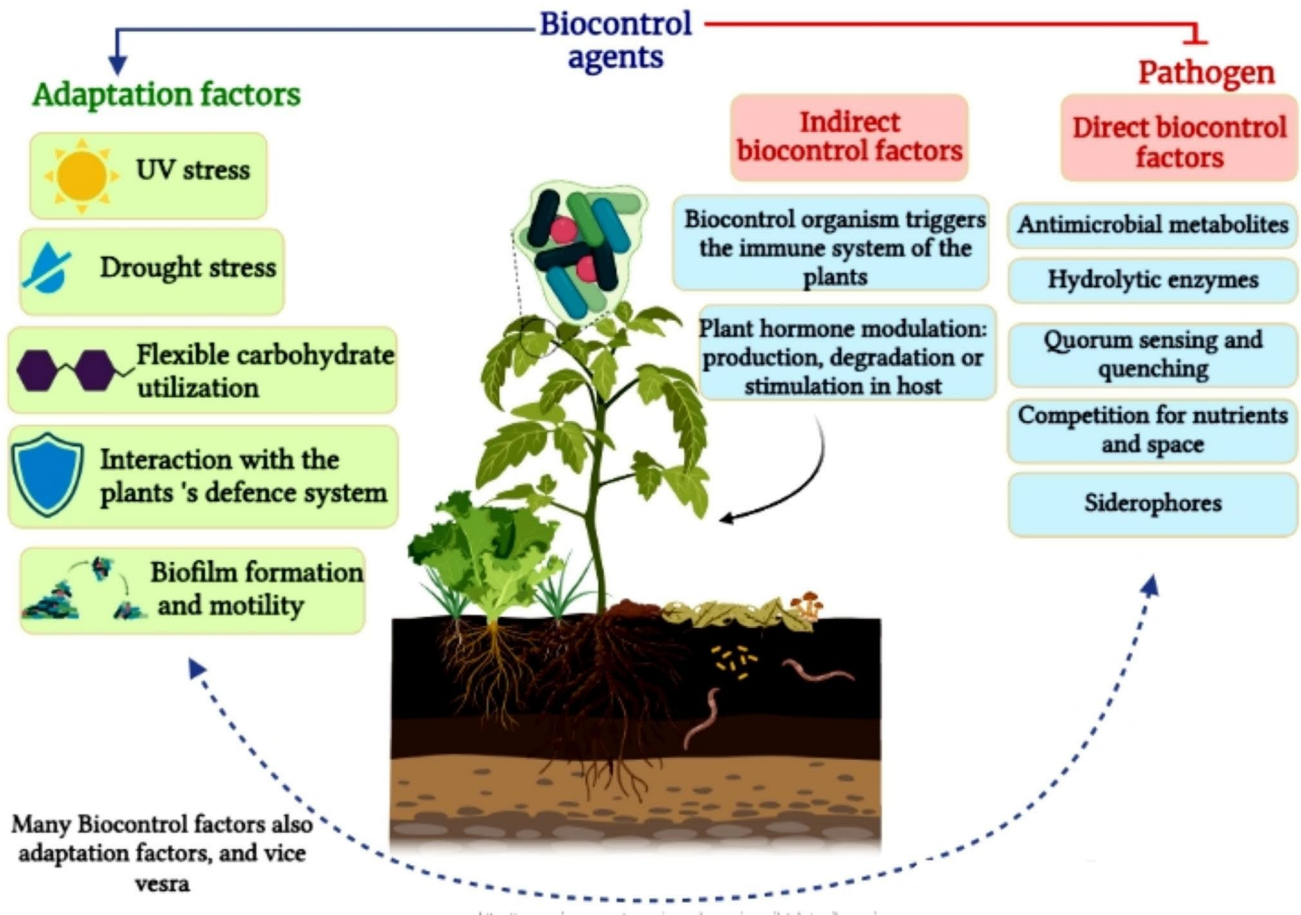


Fig. 4 General factors affected the biocontrol agent mechanism. An effective biocontrol agent contains both biocontrol and adaptability aspects. Biocontrol factor interactions can be categorized as either direct or indirect. These are interactions between the biocontrol agent (blue) and the pathogen (red). Indirect connections are interactions

generate their own separate family of bacteriocin-like antimicrobial peptides called archaeocins; they have been found and described in the *Sulfolobus* and *Haloarchaea* classes of archaea, but it is estimated that one hundred more archaeocins exist (Shand and Leyva 2008). The word “archaeocin” was employed to distinguish peptide- and protein-based antibiotics produced by archaea from those produced by bacteria (Kumar and Tiwari 2017). The first archaeocin found was halocin S8 from *Haloarchaea*, a short hydrophobic peptide of 36 amino acids. The cells create these chemicals when they enter the stationary phase. When bacteria deplete a local environment’s resources, the producer strain lyses the target cells by secreting archaeocins, lowering competition (Heng et al. 2007; El-Tarabily et al. 2009, 2010).

Because these chemicals differ structurally from antibiotics generated by bacteria, their mechanism of action may be unique. In the molecular biology of archaea, it is possible to produce new selectable markers for application (Shand and

between the biocontrol agent and the host plant that result in the host plant’s greater resistance to pathogen infection. Adaptation factors are variables necessary to adapt to the particular phyllosphere circumstances, such as elevated levels of UV stress, inadequate water availability, nutrients, and host immune system responses

Leyva 2008). Archaeocins generated by *Haloarchaea*, a type of euryarchaea that are severe halophiles, are called “halocins,” whereas the crenarchaeal genus *Sulfolobus*, which is an aerobic hyperthermophile, generates “sulfolobocins” (Quehenberger et al. 2017). Halocins (Hal) have a broad spectrum of action against *Haloarchaea* and *Halobacteriaceae* (Mazguene et al. 2018) (Table 2).

Rani et al. (2021) provided a comprehensive assessment of antimicrobial compounds generated by various microbes, including archaea; in their review, no authors presented any evidence, however scant, of archeocins as possible bioactive agents against the development of fungi. Rani et al. (2021) evaluated the reported halocins HalH1, HalH4, HalH6, HalS8, HalC8, HalR1, and sulfolobocins, which all exhibited anti-archaeal action. It is uncertain if there is no bioactivity against plant disease fungi because archeocin compounds do not inhibit their growth or if there is no evidence because no one has tested archeocins against this fungal group (Table 2). Archaea-produced bioactive

antifungal chemicals (against plant pathogen species of fungus) against plant pathogen fungi have not been demonstrated to exist. Despite this, Roscetto et al. (2018) discovered antifungal activity from the first cryptic antimicrobial peptide generated by an archaeon against clinical isolates of *Candida* spp., worldwide, *Candida* species are the most common opportunistic fungal infections. *Candida* spp., as commensal fungi colonizes the skin, oral cavities, and gastrointestinal and genitourinary systems of most healthy individuals (Calderone and Fonzi 2001).

The antifungal activity of an antimicrobial peptide (VLL-28) generated from an archaeal transcription factor was demonstrated against 10 clinical isolates of *Candida* spp., *Candida* forms biofilm through cell adhesion on the host cell tissues or abiotic surfaces. VLL-28 was found to inhibit biofilm formation by interfering with cell viability at sub-MIC doses, hence drastically lowering biofilm viability for *C. tropicalis*, *C. albicans*, *C. parapsilosis*, and *C. glabrata*, except *C. krusei* isolates, for which no inhibition of cell adhesion was observed. Through the fluoresceinated derivative of this peptide, Roscetto et al. (2018) discovered that VLL-28 attaches to the surface of planktonic *Candida* spp., cells with no evidence of internalization. In this instance, it was determined that VLL-28 operates as a typical cationic antimicrobial peptide (CAMP) by causing damage to the cell membrane and cell wall, hence reducing the possibility of strain resistance.

The most significant contribution of this research is that VLL-28 is the first example of an archaeal antimicrobial peptide active against *Candida* spp., a member of the kingdom of fungi. Rossetti et al. (2018) thought that the antifungal function of VLL-28 indicates that archaeal microbes may be a source of new antifungal drugs. In this way, a great deal of hope could be placed in the potential application of peptides produced by archaeons demonstrating bioactivity against human opportunistic pathogenic fungi such as *Candida* spp. or even other pathogens, such as phytopathogens that cause so much damage to agriculture; however, the field of study is vast, and there is still much to learn (Table 2). Regarding the archaeal source of antifungal chemicals, the findings of (Roscetto et al. 2018) represent merely the tip of the iceberg.

Advantages and disadvantages of using microorganisms as biocontrol

The secondary metabolites from PGBR microbes are naturally occurring and gaining importance in plant disease management. Considering its frequency, dominance, and potential as an agrochemical, it could be marketed commercially (Pang et al. 2022). Less harmful and eco-friendly;

Targets the specific organism and decomposes quickly; Supplies micronutrients and balances the soil nutrient cycle; Regulates plant metabolism against diseases; efficient colonizer of roots and supports colonization of mycorrhiza. However, disadvantages related to the lack of commercially accessible and effective BCA hinder the widespread application of biological control. Future BCA research should focus on finding new and better BCAs, and learning more about how they work. This will help us develop new and more effective ways to use BCAs to treat diseases and improve human health.

Future prospective and economics

Recent years have witnessed significant advancements in BCA knowledge for developing commercial therapies for controlling bacterial and fungal diseases. However, the lack of commercially accessible and effective BCA hinders the widespread application of biological control. Future developments should involve the discovery of innovative BCA and necessitate efficient and effective screening approaches appropriate for evaluating many candidates. In addition, comprehensive research of model BCA utilizing comparative genome analysis, genome, transcriptome, and proteome analysis will provide a helpful foundation for a comprehensive examination of the biological processes of BCA and the development of ways to enhance its positive effect. In addition, this multi-omics technique will analyze bacterial application's effect on plants' indigenous microbiome. This study would permit studying the environmental impact of BCA, ensuring its biosafety, and understanding how to regulate the microbiota to enhance the efficacy of biocontrol.

Conclusion

The biocontrol of phytopathogenic fungi can be carried out directly by bacteria, fungus, viruses, and archaea; by the many metabolites, enzymes, and signaling molecules these microorganisms can create; by competitive tactics; or even by soil microbiomes. Extensive usage of different fungicides results in resistance; thus, researchers are pursuing a more sustainable alternative using biological control. The rise in biological product registrations globally demonstrated its widespread use. Understanding the intricate interplay between microorganisms can also aid in managing soil diversity and inhibiting phytopathogenic fungi without chemical residues.

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