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REVIEW ARTICLE OPEN ACCESS

Eco-friendly Management of Plant Pathogens through Secondary Metabolites Released by Fluorescent *Pseudomonads*

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Abstract

Concerning sustainable agriculture, plant growth promoting rhizobacteria (PGPR), which are a subgroup of "fluorescent *Pseudomonads*," are crucial. They are widely known for supporting plant health through a variety of methods. The use of fluorescent *Pseudomonads* in agri-biotechnology has gained traction due to their potential for safeguarding plants from a variety of phytopathogens. Fluorescent *pseudomonads* being commercialized as bioinoculants for the treatment of various plant diseases is currently regarded as highly successful on a global scale. Fluorescent *Pseudomonads* are being employed as efficient bio-control agents (BCAs) against an array of phytopathogens. Due to their capacity to generate a wide range of secondary metabolites, they offer enormous promise as BCA. Thus, this review's goal is to outline and evaluate the functions of fluorescent *Pseudomonads*' secondary metabolites in reducing phytopathogens and improving plant health. Prominent secondary metabolites linked to biocontrol through fluorescent *Pseudomonads* include phenazines (PHZ), 2, 4-diacetylphloroglucinol (DAPG), pyoluteorin (PLT), pyrrolnitrin (PRN), cyclic lipopeptides (CLPs), and volatile organic compounds (VOCs), including hydrogen cyanide (HCN). The antifungal, antibacterial, antiviral, antitumor, and antinematicidal effects of these metabolites are well-established.

Keywords: Bio-control Agent (BCA), Eco-friendly Management, Fluorescent *Pseudomonads*, Phytopathogens, Secondary Metabolites

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INTRODUCTION

Phytopathogens have taken advantage of crop plants at different phases of their development ever since agriculture began. There are many different agrochemicals on the market for controlling diseases and pests, and some of them are harmful for the environment. Demands for safer-to-consume organic products have increased recently on the global market.[1] A closer examination of plant diseases reveals a long history of agricultural losses brought on by phytopathogens. Phytopathogens are the primary cause of a number of serious epidemics that have resulted in a significant loss of human life. For instance, *Phytophthora infestans* caused potato blight epidemics known as the "Great Irish Famines" (1739 and later 1845-1849) claimed 750,000 lives and drove two million others to immigrate to United States.[2]

An estimated 10-20% of the world's agricultural output is impacted by phytopathogens, depriving 800 million people of a sufficient diet.[3] Diseases brought on by bacteria, nematodes that parasitize plants, fungus, and viruses inflict billions of dollars' worth of losses in terms of economic damage annually. Pests and diseases cause more than 25% of crop loss globally, according to estimates from the Food and Agriculture Organization (FAO) more recently.[4] Due to agriculture's primary role in these countries' economic growth, A decrease in production is more likely to occur in developing nations.[5] With differing degrees of effectiveness, many strategies for managing phytopathogens have been developed for more than a century. Nonetheless, the cornerstone of crop protection among them has remained chemical control based on synthetic agents. Synthetic insecticides gained traction as efficient ways to manage a wide range of pests due to their rapid efficacy and simplicity of usage. But its unrestrained usage also caused harm to human health and ecological collapse.[6] Nevertheless, the impact of bacteria on plant phenotype—which is linked to modifications in the secondary metabolite profiles of plants—has not been well examined in many theoretical or experimental research.[7] Therefore, in modern agriculture, protecting crops from harmful phytopathogens and eliminating them using more environmentally friendly methods is of utmost importance. Numerous different types of microbes live in and communicate with one another in the soil, which is a living system. The "rhizosphere," which is the region immediately surrounding a plant's roots, is thought to have the greatest influence on microbial interactions.[8] Numerous PGPRs, or beneficial rhizobacteria, have their home in the rhizosphere.[9] These bacteria actively colonize plant roots and play a major part in plant growth promotion (PGP).[10] Many genera of bacteria, such as *Serratia, Arthrobacter, Acinetobacter, Burkholderia, Enterobacteria, Pseudomonas, Rhizobium,* and *Azospirillum*[11,12] as well as representatives from a wide range of bacterial taxa are included in PGPR.[13] For the past few decades, Many of these PGPR have been used as biocontrol agents (BCA), particularly in formulations that are cell-based. Eco-friendly methods of controlling phytopathogens to preserve the sustainability of agro-ecosystems are largely supported. Poor shelf life and inconsistent performance are the main causes. There is a dearth of information regarding the functioning of the real biocontrol factors, such as the metabolites generated by PGPR in field conditions. The capacity of "Fluorescent *pseudomonas*" to suppress a broad range of phytopathogens sets them apart from other members of the PGPR group.[14] Due to their advanced biocontrol capabilities, these rhizosphere bacteria are utilized to create bioinoculants that protect crops against various phytopathogens.[15] Signals from the environment and the plant host help microorganisms and plants to create complex connections. Both harmful and helpful bacteria can have an indirect or direct impact on these interactions, and the intricate chemical signaling also has an impact on the growth and development of plants.[16]

Because they have evolved the ability to biosynthesize a variety of secondary chemicals, they have an advantage over other rhizospheric bacteria in the selection process. The fluorescent *pseudomonas* must be taken advantage of in order to manage the phytopathogens with their variety of secondary metabolites. Understanding the mechanisms of action of these metabolites while accounting for environmental, ecological, and gene regulatory factors is crucial for this Thus, the focus of this work is on fluorescent

pseudomonas' secondary metabolites, investigating their production, structures, and physiological roles in connection to the biological control of phytopathogens.

About the Fluorescent *pseudomonas*

Pseudomonas is a member of the gammaproteobacteria class and the *Pseudomonads* family (Order: Pseudomonadales), which includes 236 species that have been scientifically described. Plants that are resistant to disease react to biotic stress caused by microorganisms by boosting the activity of antioxidant enzymes like peroxidase (POD) and superoxide dismutase (SOD) to lessen oxidative stress linked to disease. Under a range of stress situations, malondialdehyde (MDA) is a potent indication of cell damage resulting from membrane lipid peroxidation, and its concentration might indirectly represent the extent of peroxide damage.[17] The name's origin was first recorded as Greek pseudo meaning "false" and monas meaning "a single unit" in the 7th edition of Bergey's Manual. Consequently, single-celled organisms were referred to as "monas" in the early history of microbiology.[18] Nevertheless,[19] named the typed species "*Pseudomonas aeruginosa*" after seeing that this strain may be identified by its ability to manufacture colors (aerugo is the Latin word for verdigris, the blue-greenish copper rust). Therefore, it is thought that one distinguishing characteristic shared by all fluorescent *pseudomonas* is the production of luminous pigment. Typically found in agricultural soils, saprophytic fluorescent *pseudomonas* interacts with plants in a variety of ways.[9] Medium chain length polyhydroxy alkenoates (mcl-PHA) are accumulated by numerous species in the genus as a carbon store material. Fluorescent *pseudomonas'* antagonistic action is mostly associated with the synthesis of lipopeptides, lytic enzymes, antibiotic chemicals, and siderophores. Fluorescent *pseudomonas* also synthesizes a variety of volatile organic chemicals, including several types of molecules involved in antagonistic interactions with other species and in inducing systemic reactions in plants.[20] The genus includes rod-shaped, Gram-negative, nonspore-forming, catalase-positive organisms that can breathe aerobically (some strains can also breathe anaerobically using nitrate as the terminal electron acceptor and/or fermenting arginine)[21]; They also have a high genomic G+C content (59-68%) and metabolic flexibility. *pseudomonas aeruginosa, P. aureofaciens* (now *P. chlororaphis*), *P. cichorii, P. fluorescens, P. putida, P. syringae*, and *P. viridiflava* were among the bacteria listed in Bergey's Manual of Systematic Bacteriology.[22] Among them are *P. aeruginosa*, an opportunistic human pathogen, and *P. syringaea*, a phytopathogen that has been detected in a variety of crop plant species.[23,24] Study by Palleroni et al.[25] verified that *pseudomonas* is multigeneric. They separated the genus into five distantly related groupings known as rRNA groups (rRNA groups I–V) by evaluating rRNA:DNA hybridization. However, the phylogenetic distribution of the *Pseudomonads* was previously ascertained using 16S rRNA sequence analysis, rRNA-DNA hybridization, and polyphasic taxonomic research (including DNA: DNA hybridization) data. At the moment, multilocus sequence analysis (MLSA), which is based on the sequence analysis of the four housekeeping genes (16S rRNA, gyrB, rpoB, and rpoD), is the most trustworthy technique for identifying and categorizing *pseudomonas* strains.[26] Currently limited to the rRNA group I, the genus *pseudomonas* has 57 true *Pseudomonas* species that resemble the type species *P. aeruginosa* in both genomic and morphological traits.[27] Most other species have been reclassified as belonging to the family *Comamonodaceae*, which include the genera *Burkholderia, Ralstonia, Brevundimonas, Sphingomonas, Xanthomonas*, and *Stenotrophomonas*, as well as the genera *Acidovorax, Comamonas*, and *Hydrophagaga*.[28] See the reviews by Gomila et al [29] and Garrido-Sanz[30] for further information on the phylogenomics and systematics of *pseudomonas*.

Role of secondary metabolites in biocontrol produced by fluorescent *pseudomonas*

Effective BCA need to possess the capacity to generate secondary metabolites possessing antimicrobial properties against an array of phytopathogens. This is one of their desired characteristics. It has been demonstrated that this bacterium has antibiotic activity against oomycetes, fungi, and pathogenic bacteria.[31] According to Budziliewicz,[32] secondary metabolites are naturally occurring chemicals that are created as byproducts of primary metabolism and are not

Table 1. Fluorescent Pseudomonads released secondary metabolites against phytopathogens

No.	Secondary metabolites	Effective in	Fluorescent Pseudomonads	Plant pathogens	Ref.
1	Hydrogen Cyanamide (HCN)	Many cultivated crops	*Pseudomonas* sp. P76, P124	*Sclerotium rolfsii*	37
		Under laboratory condition only	*P. mediterranea* and *P. corrugata*	*Botrytis cinerea*	38
		Under laboratory condition only	*Pseudomonas* CF1 and CF5	*Macrophomina phaseolina*	39
		Tomato	*Pseudomonas* sp.	*Clavibacter michiganensis*	40
2	Hydrogen Cyanamide and volatile compounds	Under laboratory condition only	Pseudomonas donguensis	*Rhizoctonia solani* and *Pythium ultimum*	41
3	Pyrrolnitrin (PRN)	Tomato	*Pseudomonas chloraphis*	*Rhizoctonia solani*	42
		Soyabean	*Pseudomonas fluorescens*	*Pythium ultimum*	43
		Under laboratory condition	*Pseudomonas cepacia*	*Colletotrichum truncatum*	44
		Sugarbeet	*Pseudomonas cepacia*	*Aphanomyces*	45
4	Phenazine-1-carboxylic acid (PCA)	Under laboratory condition	*Pseudomonas* sp.	*Fusarium oxysporum*	46
		Wheat	*Pseudomonas* sp.	*Rhizoctonia solani*	47
		Pigeon pea and chickpea	*Pseudomonas aeruginosa*	*Fusarium udum, F. ciceri*	48
		Wheat	*Pseudomonas fluorescens*	*Gaeumannomyces graminis* var. *tritici*	49
5	2,4-Diacetyl-phloroglucinol	Groundnut	*Pseudomonas fluorescens*	*Aspergillus niger*	50,51
		Wheat	*Pseudomonas fluorescens* VUPf5	*G. graminis* var. *tritici*	52
		Tomato	*Pseudomonas* sp. LBUM300	*C. michiganensis* subsp. *michiganensis*	40
		Under laboratory condition only	*P. brassicacearum* J12	*Ralstonia solanacearum*	53
		Banana	*P. aeruginosa*	*Fusarium cubens*	54
		Rice	*Pseudomonas* sp.	*Xanthomonas oryzae* pv. *oryze*	55
		Wheat	*P. aurantiaca*	*F. oxysporum*	56
6	Cyclic lipopeptides (CLPs)	Groundnut	*Pseudomonas* SH-C52	*Sclerotium rolfsii*	57
		Tomato	*Pseudomonas fluorescens*	*Phytophthora infestans*	58
		Sugarbeet	*Pseudomonas fluorescens*	*R. solani* and *P. ultimum*	59-60

useful as reserves or sources of energy. Despite having a less evident function in the organism's internal economy, their importance for survival functions cannot be overstated.[33] The prolonged effectiveness of micro-volatile compounds is significantly impacted by their high volatility and poor water solubility. High concentrations of particular volatiles can be synthesized by microbial strains through the use of engineered strategies.[34] The identification of particular micro-volatile compounds may offer a novel diagnostic tool to detect the presence of a given species in infected wounds, as evidenced by the identification of species-specific molecules from both mixed and pure cultures of single species.[35] Numerous volatile chemicals that are released by bacteria contribute to interactions across different kingdoms of fungus, plants, and animals. Secondary metabolites are the principal method of antagonism that fluorescent *pseudomonas* uses against plant diseases, same like other powerful biocontrol PGPR (Table 1 and Figure 1). Phloroglucinol, HCN, PHZ, PLT, PRN,

and CLPs are examples of secondary metabolites that drive the antagonistic relationship between fluorescent *pseudomonas* and phytopathogens. Although the impact of various bacterial volatile chemicals on population dynamics in polymicrobial communities is poorly understood, they do change the physiology and stress responses of bacteria. It has found that volatile hydrogen cyanide (HCN), which inhibits the growth of a wide range of pathogens under *in vitro.*[36]

A diverse range of plant-beneficial bacteria may colonize the rhizosphere of various plant species and create biofilms, thanks to the fluorescent *pseudomonas* group.[61] The rhizosphere and soil microbiomes play a major role in suppressing plant disease by synthesising antagonistic secondary compounds. However, the processes governing the degree of pathogen control remain poorly understood. Numerous *pseudomonas* species are linked to the microbiomes of soil and rhizosphere, and there is ample evidence of their capacity to inhibit pathogens.[62]

HCN (Hydrogen Cyanamide)

Among the inorganic volatile compounds that inhibit the growth of insects, nematodes, and plant pathogens is HCN. In many *pseudomonas* species, HCN synthase converts glycine into it.[63] Most fluorescent *Pseudomonads*, certain fluorescent *Pseudomonads*, and a small number of species of the genus *Chromobacterium, Burkholderia*, certain *Rhizobia*, and *Cyanobacteria* all report that cyanide synthesis in bacteria occurs frequently.[64] Fluorescent *pseudomonas* produce varying amounts of hydrogen cyanide in the rhizosphere, depending on environmental variables.[65] According to Nandi et al,[66] glycine is the direct metabolic precursor of cyanide and is decarboxylated into HCN and CO_2 when HCN synthase is present.[67] HCN synthase as an oxygen-sensitive, membrane-associated enzyme involved in cainogenesis that is the result of the HCN ABC synthase gene cluster. Because it inhibits cytochrome c oxidase, HCN generated by fluorescent *Pseudomonads* has demonstrated toxicity against phytopathogens.[68] However, RhdA, a thiosulfate known as cyanide sulfur

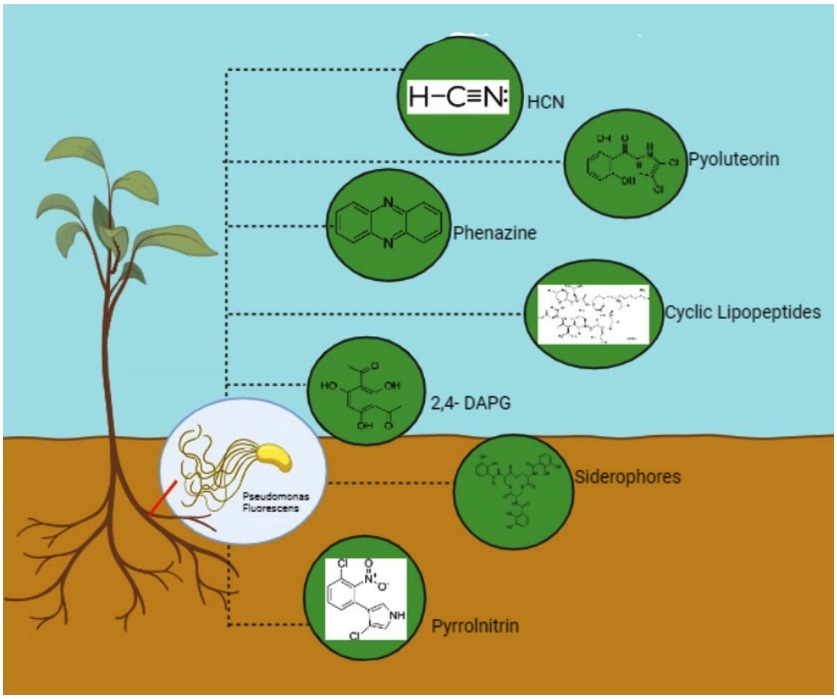

Figure 1. Depicting *Pseudomonas fluorescences* released secondary metabolites in rhizosphere

transferase (rhodanese), which changes cyanide into a less lethal thiocyanate, makes fluorescent *Pseudomonads* immune to cyanide. According to estimates, several *pseudomonas* species may produce up to 300 µM cyanide through the oxidative decarboxylation of glycine. According to reports, in microaerophilic settings, cyanide production peaks between 34 and 37°C.[69] While the majority of previous research has indicated a clear function for HCN in phytopathogen biocontrol, more recent investigations have cast doubt on this idea. According to Rijavec and Lapanje,[70] HCN has less to do with the biological control of phytopathogens and more to do with the chelation of metals, which makes more phosphate available to the plant.

PHZ (Phenazines)

It is a broad class of heterocyclic rings consisting nitrogen that have been found in the archaeal phylum Euryarcheotic, the bacterial phyla *Actinobacteria*, and *Proteobacteria*.[71] More than 6000 compounds with phenazine as a key component have been synthesized, and more than 100 unique natural PHZ structural variations have been identified for their antibacterial properties.[72] The role of secondary metabolites in management of plant pathogen showed in Figure 2.

According to Guttenberger et al,[73] there are actually more than 180 PHZ-based compounds that have anti-tumor, anti-fungal, insecticidal and other anti-pathogenic properties. According to Briard et al,[74] Phenazine-1-carboxylic acid (PCA), phenazine-1-carboxamide (PCN), and pyocyanin (PYO) all have blue coloration in PHZ isolated from *pseudomonas* species, while 1-hydroxyphenazine (1-HP) has an orange coloration. Substitutes at different locations also affect a substance's redox potential, solubility, and biological activity.[75] It is occasionally stated that a single species has many derivatives.[76] All other PHZ begin with phenazine-1-carboxylic acid (PCA), which is derived from chorismic acid.[77] The seven-gene operon phzABCDEFGen encodes the structural proteins needed for fluorescent *pseudomonas* to convert chorismic acid into PCA.[78] Two different enzymes (PhzM and PhzS) that alter PCA produce PYO, while PhzH converts PCA into PCN. According to the majority of research, reactive oxygen species (ROS) produced by PHZ are mostly responsible for

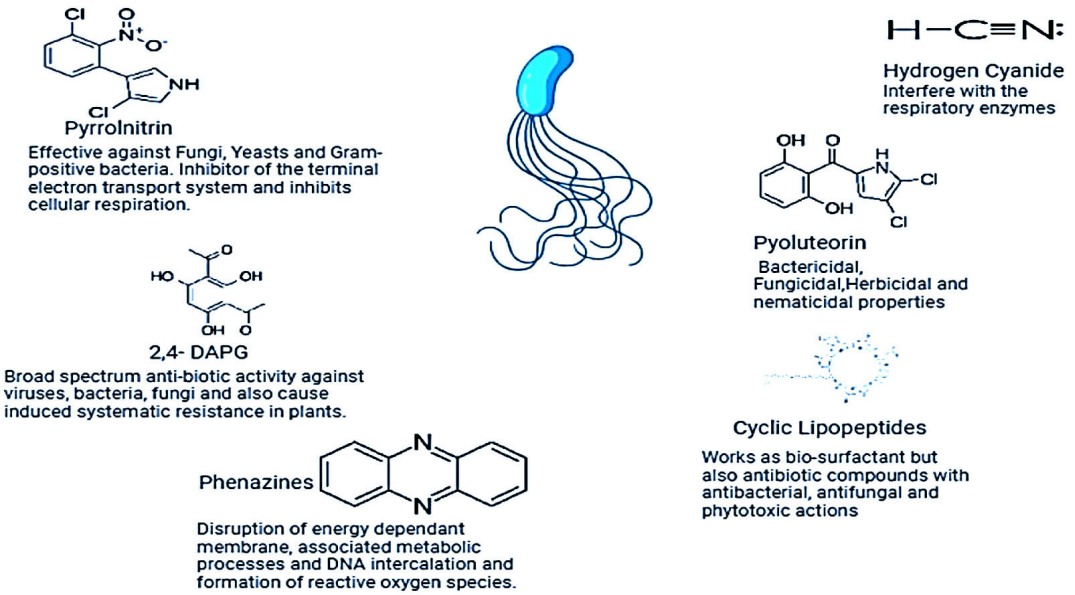

Figure 2. Depicting Fluorescent Pseudomonas with their mode of action

their antibacterial properties.[79,80] *Pseudomonas* strain PCL1391 produces PCA and PCN, which are known to stimulate several ABC transporters in *Botrytis cinerea*.[81] It has been discovered that PCA and PYO phenazines work incredibly well to treat fungal infections. While most PHZ compounds are efficient in biocontrol of many bacterial and fungal infections, they frequently failed to stop the growth of co-occurring immediate competitor microorganisms.[82,83] Additionally, PHZ are crucial for the uptake of iron, cell communication, gene expression modulation, biofilm formation, and bacterial survival. Enzymes participating in major metabolic pathways may change PHZ as a result of its reaction with primary metabolites. These characteristics imply a potential involvement for them in primary cell metabolism, namely in the cell's ability to survive under stressful situations. PHZ function as an electron shuttle and are involved in energy metabolism and transmission.[84] There have been recent reports of new developments on the manufacturing of substituted PHZ.[85] It is unknown if and how the secondary metabolites of the host plant affect the relationship between the bacteria and their host plant. Numerous investigations into how various biotic variables alter the phenotypic of plants have been documented.[86,87] Secondary metabolites (SMs) produced by bacteria are essential to microbial interactions. Even while many natural products' structures, biosynthesis, and roles have been clarified with great progress, little is still known about what happens to SMs when they are released into a particular niche.[88]

Phloroglucinol

According to Loper et al,[87] Phenologlucinol (1,3,5-benzenetriol or 1,3,5-trihydroxybenzene) and its derivatives are phenolic compounds with a wide spectrum of antiviral, antibacterial, antifungal, antihelminthic, and phytotoxic properties. More than 700 naturally occurring phloroglucinol compounds have been identified from a range of natural sources, including microorganisms, plants, and marine life.[88] Nonetheless, fluorescent *pseudomonas* is a highly conserved microorganism with the capacity to make phloroglucinol and its derivatives.[14] According to Troppens et al.,[89] DAPG is a well-known kind of phloroglucinol derivative that fluorescent *Pseudomonads* manufacture. Numerous experimental investigations have confirmed that DAPG is a significant antibacterial metabolite that suppress the growth of plant pathogens.[90] Studies show that the antibiotic DAPG is only produced by *pseudomonas* found worldwide. According to reports, *pseudomonas* isolated from a variety of geographic regions share the same DAPG biosynthesis locus.[91] Polyketide synthases (PKSs) catalyse the decarboxylative condensation of monomers such as acetyl coenzyme A (acetyl-CoA), propionyl-CoA, malonyl-CoA, and methylmalonyl-CoA to produce phenolglucinol and its derivatives, which are categorised as secondary metabolites in the polyketides class.[92] There are three different types of PKSs that have been approved.[93] Three regulatory genes (phlF, phlG, and phlH) and six structural genes (phlA, phlC, phlB, phlD, phlE, and phlI) regulate the synthesis of DAPG.[94]

While the majority of fluorescent *pseudomonas* retained the DAPG biosynthesis gene cluster, evolution has caused many strains to lose this ability.[95,96] It was demonstrated by Landa et al.[96] that genotypes that produce DAPG may be crop-specific. According to Picard and Bosco,[97] the biosynthetic gene phlD is essential for the synthesis of the precursor of DAPG and a trustworthy marker for DAPG producers. The selection of a growth medium, stressors brought on by a high concentration of salt, or heat shock can all increase the production of DAPG.[98] It has been observed that employing metabolically modified *Escherichia coli* improves the production of phloroglucinol. Recently, attempts have also been made to express the bacterial phlD gene in plants in an attempt to boost the commercial production of phloroglucinol and its specific derivatives, such as DAPG.[99]

Pyoluteorin (PLT)

PLT is a phenolic polyketide that was initially identified in *P. aeruginosa* and subsequently in other fluorescent *Pseudomonads*. It is made up of a substance connected to bichlorinated pyrrole.[100]

PLT has antifungal, antibacterial, and herbicidal properties.[101] PLT biosynthesis requires the pltLABCDEFG gene cluster.[102] Reportedly, PLT functions as an auto-inducer and an intercellular signalling mechanism among multiple co-occurring

bacterial cell types in the rhizosphere.[103] According to a recent study, phloroglucinol affects PLT production in *P. protegens* and the expression of the genes that make PLT in a concentration-dependent manner.[104] Phloroglucinol has been shown to induce two unique metabolites (DAPG and PLT) with separate processes and targets that are phytopathogens at various concentrations.

Pyrrolnitrin (PRN)

Burkholderia pyrrocinia is the source of PRN, which is halogenated aryl pyrrole.[105] A small variety of Gram-negative bacteria, including *pseudomonas* species, are known to make PRN.[106-108] According to Jani et al.,[109] PRN generated by fluorescent *pseudomonas* exhibits antagonistic activity against yeast, fungus, and Gram-positive bacteria. Inhibition of glycerol kinase, which results in glycerol buildup and leakage in the cell membrane, is the mechanism of PRN activity.[110] The oxidation of amino-pyrrolnitrin to PRN is a crucial step that is catalyzed by the prnD gene.[111] According to Steinberg et al.,[112] there have been numerous reports of fluorescent pseudomonad-containing genes from suppressive soils. These genes are specifically recognized for their ability to inhibit *Rhizoctonia solani*. Wide spread distribution of PRN-producing, highly genotypically linked *pseudomonas* from European soils with widespread anti-fungal action was described by Costa et al.[113] Phenylpyrroles, chemical derivatives of PRN, are successfully employed as seed and foliar treatments to guard against fungal phytopathogens and are produced on a commercial scale. An efficient phenylpyrrole analog, fludioxonil, is employed against a variety of fungal phytopathogens. Since fludioxonil has been on the market for more than 25 years, there hasn't been any resistance noted. There hasn't been a developed analog of PRN other than these two derivatives, which are both successful in the field and on the commercial front.[114]

Cyclic lipopeptides (CLPs)

According to Raaijmakers et al,[115] the short oligopeptides known as CLPs are produced by a range of bacteria and fungi and have a linked fatty acid tail. A brief oligopeptide is cycled by the formation of a lactone ring between two amino acids. However, variability in CLPs is caused by differences in the amount of fatty acids, the manner in which amino acids are changed, and the arrangement of the lactone ring.[115,116] Mycoplasmas, enveloped viruses, and Gram-positive bacteria are only a few of the pathogenic microorganisms against which CLPs have demonstrated antibacterial activity in the last few years since their recognition as biosurfactants.[115,117,118] Records state that CLPs from fluorescent *Pseudomonads* actively participate in seed and root colonisation, swarming motility, biofilm formation, pathogenicity, and Many CLPs are produced by fluorescent *Pseudomonads*, some of which require thorough characterization.[119] The viscosin, amphisin, tolaasin, and syringomycin families contain the most investigated CLPs.[120] Non-ribosomal peptide synthetases (NRPSs) are responsible for the biosynthesis of CLPs. NRPSs are large multienzymes that produce linear or cyclic peptides by sequentially coupling amino acids in an assembly line fashion.[121] According to Olorunleke et al.,[122] CLPs derived from *pseudomonas* are presently classified into eight distinct structural groupings based on the length and makeup of the oligopeptide and fatty acid tail. The capacity of CLPs to disrupt cellular membranes is thought to be the mechanism behind their antibacterial activity. The tolaasin and syringomycin groups of CLPs function as cellular poisons by forming pores or tunnels. It was recently found that the supposedly generated CLP orfamide by *P. protegens* has insecticidal effects.[123] In fluorescent *pseudomonas*, the two-component GacS/GacA regulatory mechanism is crucial for controlling the production of CLP. The possible roles of new regulatory genes required for the synthesis of CLPs in a number of fluorescent *pseudomonas* species and strains were emphasised.[124] The generation and regulation of CLPs are directly influenced by the quorum sensing (QS) system; further research is necessary in this area to fully use the biocontrol potential of fluorescent *Pseudomonads* that produce CLPs. It has been noted that the QS system mediates the synthesis of CLPs such as putisolvin, viscosin, cormycin, and corpeptins. Cell density is required for *P. corrugata* and *P. mediterranea* to make cormycin and corpeptin CLPs, and it is controlled by the QS regulatory system.[125-127] The QS mechanism plays a crucial role in *P. fluorescence* producing the biosurfactant

Table 2. Effects of secondary metabolites released by Fluorescent Pseudomonas in crop plants

No.	Metabolites	Observed in			
		Mechanism	Ref.	Other	Ref.
1	VOC (Volatile compounds)	Having antibacterial and antifungal property	145, 146	Helps in plant growth promotion	147, 148
2	Phenazines	Inhibit conidial germination and mycelial suppression	74, 149	Signaling and promote plant growth	150-156
3	CLPs	Disruption of cell membrane and cell wall	157, 158	Having biosurfactant property	159, 160
4	2,4-DAPG	Suppress disease symptoms and disruption of cell membrane	161, 162	Signaling and co-regulation	144, 163, 164
5	HCN	Inhibits cytochrome c oxidase	68, 165	Signaling and chelation of metals	166, 167
6	PLT	Disruption of cell membrane	110, 168	Auto-induction and as signal molecule	104, 169
7	PRN	Interfere to electron transport system	170	Interferes with osmotic Signal transduction	171

viscosin only when the cell density is high enough to overwhelm the host.[128] provided evidence of the connection between QS and *P. putida* putisolvin synthesis. Thus, in coordinating the expression of CLPs throughout the fluorescent *Pseudomonads* population, the QS system is extremely important. This can also be used to allow CLPs to produce fluorescent *pseudomonas* and colonize plant roots.

Effective use of secondary metabolites in agriculture

It is commonly recognized that certain soils have antimicrobial properties that prevent phytopathogen growth even in the presence of host plants. Numerous studies have demonstrated the important impact fluorescent *Pseudomonads* play in suppressing illness in these types of soils.[129,130] Such suppressive soil mixtures were used in fields with high disease incidence, especially those caused by fungal phytopathogens. Given that it helped spread biocontrol agents to sensitive soil and resulted in phytopathogen control, this could be considered one of the earliest uses of bioformulations for phytopathogen suppression. Over the past few decades, research has demonstrated the critical function that fluorescent pseudomonad secondary metabolites play in suppressing phytopathogens in soils that are susceptible to them (Table 1). Fluorescent *Pseudomonads*, possessing a plethora of secondary metabolites, are currently frequently utilized as biopesticides.[131] They are marketed as bioinoculants over the world to treat various plant diseases, and they are thought to be quite successful.[132,133] The commercial usage of fluorescent pseudomonad bioformulations is relatively young, having begun in the 1970s, when compared to the use of biopesticides produced from *Bacillus thuringiensis* or biofertilizers made of other microbes like cyanobacteria and rhizobia.[134] Previous studies[135] have confirmed that bioformulations containing antagonistic fluorescent *pseudomonas* were effective in suppressing take-all disease in wheat and barley. Packing houses are also using fluorescent *pseudomonas*-based bioformulations, Bio-Save®10LP and Bio-Save®11LP, registered with the U.S. Environmental Protection Agency and containing *P. syringae* ESC-10 and ESC-11 strains, to prevent postharvest fungal diseases during the storage of citrus, pome, and stone fruits.[136] *P. fluorescens* A506 strain is present in a separate formulation called Blight Ban A506, which is used to control fire blight caused by *Erwinia amylovora* in pear and apple.[137] In addition to Cedemon, other biocontrol agents for other phytopathogens include FROSTBAN and AtEze, primarily utilized in the United States.

In a similar way, fluorescent *Pseudomonads* have been used in the development of other formulations that are currently in commercial use worldwide. Shenqinmycin, a biopesticide with PCA as its primary ingredient that is generated from *P. aeruginosa* PA1201, has been registered in China to suppress *Xanthomonas oryzae* pv. *oryzae* and *R. solani* K hn, the agents responsible for bacterial blight and rice sheath blight, respectively. Fluorescent *Pseudomonads* that produce numerous metabolites and have broad activity against phytopathogens are generally preferred in agriculture. Recent research has shown that the treatment of wheat plants with phenazine-1-carboxylic acid (PCA), cyclic lipopeptide (CLP), and lahorenoic acid A, which generates in variable amount from the strains of *P. chlororaphis* and *P. aurantia*, dramatically enhanced the growth and development.[138] According to a study by Sharifazizi et al,[139] fluorescent pseudomonad strain Ps170 has the ability to regulate *E. amylovora,* which causes fire blight in pears, and can also produce PCA, DAPG, PRN, and PLT. The application of fluorescent *pseudomonas* metabolites is currently expanding its scope to inhibit protozoa and diseases.[140-142] Additionally, recent studies have suggested the use of formulations based on metabolite(s) from fluorescent pseudomonad, either in conjunction with or independently of cells, for biocontrol and a number of other purposes, such as cell signaling, cell protection, gene regulation. In this regard, field testing has demonstrated the extraordinary success of bioformulations based on rhamnolipid and exopolysaccharides (from fluorescent *pseudomonas*) (Table 2).[142,143] According to Yan et al,[144] phloroglucinol at nanomolar concentrations is sufficient to initiate PLT synthesis by *P. protegens*, which effectively inhibits *E. amylovora*. While the use of luminous pseudomonad metabolites in bioformulations rather than synthetic compounds is an emerging trend that is showing great promise, more extensive field trials are needed to ensure the wider applicability of these techniques.

Future scope

Despite the fact that bioformulations and biopesticides have numerous benefits, especially for environmentally friendly agriculture, they still fall well short of chemical pesticides in terms of quality, shelf life, and other concerns as well as uneven performance and narrow spectrum. Future success will hinge on resolving these problems and understanding how biocontrol microorganisms, like fluorescent *Pseudomonads*, function and how their metabolites are regulated in soil environments. Molecular screening techniques can significantly speed up the basic steps involved in choosing strong antagonistic fluorescent *Pseudomonads*. Additionally, it is critical to look into novel secondary metabolites from fluorescent *pseudomonas* that are either already known to exist or have not yet been discovered, as genomic sequencing of even the most studied microbes has confirmed that we have not yet been able to identify products of most of the gene clusters responsible for secondary metabolites synthesis.[172,173] This implies that we still need to comprehend the chemical, environmental, and biological factors that lead to gene clusters expressing secondary biomolecules that have already been identified. This will support the creation of more effective bioformulations as well as the large-scale synthesis of secondary metabolites. In this regard, metabolic approaches can be highly helpful in identifying new compounds as well as figuring out how stimuli or gene expression affect the production of metabolites that are already known. Metabolomics can therefore be used to support molecular methods like gene sequencing and identification, opening the door for more research on secondary metabolites and the development of reliable bioformulations made from them. These are combined with bioinformatics technologies, which could greatly advance secondary metabolite research in the future. Finding biosynthetic gene clusters for secondary metabolites in bacterial genomes and metagenomes is the aim of the Integrated Microbial Genomes Atlas of Biosynthetic Gene Clusters (IMG-ABC) data mart.[174] The NCBI's verified gene clusters and their secondary metabolites provide even more value to this resource. IMG-ABC can be very helpful in the investigation of both known and new metabolites from fluorescent *Pseudomonads* and other PGPR. Numerous fluorescent *Pseudomonads* are known to produce a range of metabolites with the capacity to inhibit one or more phytopathogens. Further research is required on these multi-secondary metabolites-producing fluorescent *pseudomonas*

because these strains will be more effective in treating soils damaged by numerous diseases and will be able to demonstrate a larger host range. It has previously been documented that multifaceted strains of fluorescent *pseudomonas* can be created via recombinant DNA technology, and this technique can be applied even more successfully in the future. When Yang et al.[175] found that the recombinant strain that produced the combination of metabolites (CLP and PCA) inhibited *G. graminis* far more efficiently than the wild strain after introducing the gene for PCA synthesis from *P. synxantha* into *P. fluorescens*. The creation of recombinant fluorescent *pseudomonas* strains with appropriate metabolite genes can be aided using the IMG-ABC data base. Additionally, precursors and intermediates might be included in formulations to increase secondary metabolite synthesis.[175] Phloroglucinol, an intermediary of DAPG biosynthesis, can also be employed to control PLT production in the instance of fluorescent *pseudomonas*. The use of such intermediates at very low concentrations for the large-scale synthesis of secondary metabolites may prove advantageous for the development of low-cost metabolite-based bioformulations in the future.[176] Formulations based on metabolites will be especially helpful in the case of fluorescent *pseudomonas*, such *P. aeruginosa*, which is known to produce a range of anti-fungal metabolites and is a potential human pathogen. Because of its potential therapeutic repercussions, *P. aeruginosa* should not be used as a biocontrol agent. Additionally, authorities and experts are very concerned about the use of this bacteria in biopesticides. In the future, though, we should be able to extract the needed metabolite from fluorescent *Pseudomonads* by using more advanced methods, understanding how to stimulate the creation of secondary metabolites through the ecology of gene expression, and access to inexpensive nutritional sources. To employ fluorescent *Pseudomonads* in large-scale secondary metabolite production for agricultural bioformulations in the future, production technology needs to be carefully examined. Fluorescent pseudomonad secondary metabolites are today regarded as highly significant bioproducts with a variety of applications in the medical (anti-microbial, anti-cancer) and other industries.[177] But further investigation is needed to find out how they could be applied to sustainable agriculture, particularly as strong natural anti-phytopathogenic agents.

CONCLUSION

Even after much research, the proportion of microbial dependent biocontrol products in global plant health management is still quite small when compared to synthetic chemicals. Additionally, there are extremely few registered biopesticide products that contain fluorescent *pseudomonas* or their metabolites. The development of bioformulations using PGPR metabolites is still in its early stages. Without a question, fluorescent *pseudomonas* are an effective biological control agent for phytopathogens because of their ability to produce dependable bioproducts. Nevertheless, there is still room for improvement in the way these amazing creatures are used. This can be accomplished by employing a comprehensive strategy that combines improved or innovative production techniques with metabolomic, molecular, and bioinformatics tools to investigate and use fluorescent *pseudomonas* and their metabolites for the creation of new bioformulations.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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ETHICS STATEMENT

This article does not contain any studies on human participants or animals performed by any of the authors.

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