



Integrative Approaches to Control Plant Pathogens- A Comprehensive Review

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ABSTRACT

The growing human population worldwide, declines in land and water availability, and challenging climatic changes are problematic factors in global food production. However, the major limiting factor in agricultural food production is plant diseases. Plant diseases need to be controlled to maintain the quality and abundance of food, feed, and fiber produced by growers around the world. Different approaches may be used to prevent, mitigate or control plant diseases. Beyond good agronomic and horticultural practices, growers often rely heavily on chemical fertilizers and pesticides. Such inputs to agriculture have contributed significantly to the spectacular improvements in crop productivity and quality over the past 100 years. However, the environmental pollution caused by excessive use and misuse of agrochemicals, as well as fear-mongering by some opponents of pesticides, has led to considerable changes in people's attitudes towards the use of pesticides in agriculture. Additionally, the spread of plant diseases in natural ecosystems may preclude successful application of chemicals, because of the scale to which such applications might have to be applied. Consequently, some pest management researchers have focused their efforts on developing alternative inputs to synthetic chemicals for controlling pests and diseases. The most effective plant disease management approach requires an integrated strategy that utilizes biological control agents. This review highlights various biocontrol approaches used in current scenario to ascertain sustainable agriculture on a global scale.

Keywords:- Integrated Disease Management, Phytopathogens, Biological Control

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INTRODUCTION

Sustainable agriculture is defined as an integrated system of plant production practices having a site-specific application that will, over the long term satisfy human food and fiber needs; improve environmental quality and the natural resources based upon which the agricultural economy depends; make the best use of non-renewable resources and on-farm resources and integrate where appropriate, natural biological cycles and controls; sustain the economic viability of farm operations and enhance the quality of life for farmers and society as a whole [1]. New technology in all areas has improved agricultural production, thus its sustainability. Plant disease has been a major factor influencing food production and human societal development over thousands of years [1]. Plant diseases caused by a variety of causal agents such as fungi, bacteria, viruses, phytoplasmas and nematodes reduces crop yields worldwide [2]. The diversity of pathogens harmful to crops is large. Crops can be attacked at different growth stages: at seedling establishment (root and seed rots), young seedlings (root and collar rots, seedling blights, wilts), pre-flowering (wilts, leaf blights, yellowing and mottling of the foliage, stunting), flowering (bud rots, flower blight), post flowering (rusts, blights) and at post-harvest stage (fruit rots). The same disease can induce diverse symptoms at different growth stages. Man-made activities such as crop intensification and introduction of new crops or new cultivars of existing crops to new regions as well as changes in cropping practices, including plant breeding led to the development of serious epidemics around the globe, mainly because such activities could disturb the balance, which naturally existed for many generations [3].

Despite the contribution of scientific and technological advances to significant reductions in the frequency and intensity of epidemics in recent times, 20–30% of actual production is still lost due to plant diseases per year [4].

BIOLOGICAL CONTROL OF PLANT PATHOGENS

Biological control of plant pathogens has become an integral component of pest management in light of the environmental and health issues attributed to the use of fungicides in agriculture. The term biological control applies to the use of microbial antagonists to suppress plant diseases as well as the use of host-specific pathogens to control weed populations. In both fields, the organism that suppresses the pest or pathogen is referred to as the biological control agent (BCA)[5]. These specialized fungi and bacteria are microorganisms that normally inhabit most soils. Several biocontrol agents have been recognized and are available as bacterial agents for example *Pseudomonas*, *Bacillus*, and *Agrobacterium*, and as fungal agents such as *Aspergillus*, *Gliocladium*, *Trichoderma*, *Ampelomyces*, *Candida*, and *Coniothyrium*[6,7]. In their native habitat, the BCAs compete with other microorganisms for space and food by producing toxic substances that parasitize and/ or kill other soil inhabiting microorganisms such as *Pythium* sp., *Phytophthora* sp., *Rhizoctonia* sp. and other plant pathogens [8]. There are four different mechanisms by which biocontrol agents control other microorganisms; direct antagonism, which results from physical contact and/or a high-degree of selectivity for the pathogen by the mechanism(s) expressed by the BCA(s); antibiosis, where the biocontrol agent produces an antibiotic or some type of toxin that kills or has some detrimental effect on the target organism; predation or parasitism of the target organism, where the biocontrol agent can attack and feed directly on the target organism or the biocontrol agent can produce enzymes and some sort of toxins that kills the target organism and then the biocontrol agent feeds on the dead target; and lastly by induced resistance of the host plant, where it has been known for the decades that once a plant is infected with the pathogen, that infection triggers some sort of reaction in the infected host plant that helps keep it from being infected with other pathogens. The infected plant becomes more resistant to other infections [8].

Fluorescent *Pseudomonas* are the most frequently used bacteria for biological control and plant growth promotion, but *Bacillus* and *Streptomyces* species have also been commonly used. *Trichoderma*, *Gliocladium* and *Coniothyrium* are the most commonly used fungal biocontrol agents [9]. Competition has been exploited by many researchers with soilborne plant pathogens as with the pathogens on the phylloplane. Baek et al. [10] used nonpathogenic strains of *Fusarium oxysporium* to control wilt diseases caused by *Fusarium* spp. The most common bacteria that have been used for the control of diseases in the phyllosphere include *Pseudomonas syringae*, *P. fluorescence*, *P. cepacis*, *Erwinia herbicola* and *Bacillus subtilis*. Fungal genera that have been used for the control include *Trichoderma*, *Ampelomyces* and the yeasts *Tilletiopsis* and *Sporobolomyces*[11].

SIDEROPHORES IN BIOLOGICAL CONTROL

Iron is an essential nutrient for almost all microorganisms. Ferrous iron (Fe^{+2}) is highly soluble up to a concentration of 100 mM at pH 7. However, the ferric form of iron (Fe^{+3}), which is needed for growth by organisms, is soluble at biological pH only to a concentration of 10^{-9} M, which makes the bioavailability of iron very low. Fe^{+3} is not readily consumed by living organisms because of its extremely low solubility; this restriction means that iron bioavailability is a major limiting factor for living organisms. At neutral pH, iron bioavailability is much more limited and leads to competition among microorganisms for limited nutrients. This competition for iron nutrition is one of the mechanisms of biological control for both bacterial and fungal phytopathogens. Siderophore, coined by Lankford in 1973 is present in one of the major mechanisms of bacteria that is involved in the biological control of plant diseases. These siderophores are produced in iron-limited conditions to sequester the less-available iron from the environment and thereby deprive the pathogen of iron, which ultimately leads to inhibition. Both plant pathogenic fungi and bacteria have been found to be inhibited by siderophore-producing biocontrol agents [12]. In agriculture, siderophores are used to improve soil fertility and biocontrol [13]. Kloepper et al. [14] demonstrated the importance of siderophore pseudobactin production by the biocontrol agent *Pseudomonas fluorescens* against *Erwinia carotovora*.

QUORUM SENSING AS A BIOCONTROL METHOD

Quorum sensing is the regulation of gene expression in response to fluctuations in cell-population density. Quorum Sensing has been used by many plant-associated microorganisms as part of their pathogenic or symbiotic life cycle. de Kievit and Iglewski [15] suggested that the ability to block or promote these Quorum Sensing or Quorum Quenching systems may reveal new strategies for managing

plant diseases and increasing crop yield. Dong *et al.* [16] demonstrated first application of QQ strategy in protection against plant disease by transforming *aiiA* gene into the phytopathogen *Erwinia carotovora* to attenuate its pathogenicity in Chinese cabbage.

CYANOBACTERIA AND ALGAE AS BIOCONTROL AGENTS

Cyanobacteria and algae have been reported to produce unique antibacterial and antifungal bioactive metabolites that are eco-friendly and may be used for the control of phytopathogens. The wide spectrum of cyanobacterial secondary metabolites include 40.2% lipopeptides, 5.65 amino acids, 4.2% fatty acids, 4.2% macrolides and 9.4% amides [17]. The efficacy of two commercial cyanobacterial metabolites, Weed-Max and Oligo-Mix, against some soil-borne pathogens was evaluated by El-Mougy and Abdel-Kader [18]. These algal compounds, when supplemented in the growth medium, inhibited the growth of root rot pathogens *Alternaria solani*, *Fusarium solani*, *Fusarium oxysporum*, *Rhizoctonia solani*, *Sclerotium rolfsii* and *Sclerotinia sclerotiorum*. These compounds have been reported to reduce root rot disease and improve crop yields when combined with bioagents *Trichoderma harzianum* or *Bacillus subtilis* as integrated soil treatments of vegetable plants.

Application of seaweed extracts have been found to exert protection against pathogens [19]. Abetz and Young [20] also demonstrated that when an algal extract of *Ascophyllum nodosum* (L.) was sprayed on lettuce plants (*Lactuca sativa* L.) during the growing stage, it reduced plant sensitivity from 18% (in unsprayed plants) to 12% against diseases. Raghavendra *et al.* [21] evaluated the effect of a commercial product of seaweed, *Sargassum wightii* (Dravya), on bacterial blight caused by phytopathogen *Xanthomonas campestris* in cotton. In another study, soil application of liquid seaweed extracts to cabbage (*Brassica oleracea* var. *capitata*) reduced the incidence of damping-off disease in seedlings caused by *Pythium ultimum* [22].

ARBUSCULAR MYCORRHIZAE FUNGI IN PLANT DISEASE CONTROL

The negative antagonistic interaction of the Arbuscular Mycorrhizae Fungi with various soil-borne plant pathogens is one of the main reasons that it has potential to be used as a biocontrol agent [23]. The Arbuscular Mycorrhizae Fungi (AMF) play an important function in the reduction of plant pathogens, such as *Rhizoctonia solani* and *Pythium ultimum* and *Phytophthora* species. The ability of AMF to control plant diseases improves with the application of organic amendments. AMF stimulates the activity of beneficial microorganisms in the rhizosphere that are antagonistic to bacterial plant pathogens. Most plant pathogenic bacteria alter the host plants' physiology as well as its biochemical activities, which may be lethal effects. AMF, however, have the ability to reduce the defects in host plants caused by pathogenic bacteria [24]. Different mechanisms have been reported to explain bio-control by AMF including biochemical changes in plant tissues, microbial changes in rhizosphere, nutrient status, anatomical changes to cells, changes to root system morphology and stress alleviation [25]. Mycorrhizal fungi provide a very effective alternative method of disease control, especially for pathogens that affect below-ground plant parts. AMF have enormous potential to control the plant pathogenic bacteria that cause soil-borne diseases, because root diseases are the most difficult to manage and lead to losses in disturbing proportions. Moreover, mycorrhizal symbiosis substantially influences plant growth under a variety of stressful conditions; their role in biological control of soil/root-borne pathogens is therefore of immense importance in both agricultural systems and forestry [26].

PLANT GROWTH PROMOTING RHIZOBACTERIA AS BIOCONTROL AGENTS

Several studies have shown that the consortia of plant-growth-promoting rhizobacteria could enhance biological control for multiple plant diseases through the induced systemic resistance or antagonism. PGPR suppress plant pathogenic bacteria by the secretion of antibiotics, bacteriocins, and siderophores, and the induction of systemic resistance. Jagadeesh [27] reported that bacterial wilt caused by *Rhizobium solanacearum* was controlled by rhizobacteria in tomato, whereas inoculation of three strains of fluorescent *Pseudomonas* resulted in suppression. Several researchers have reported the different types of antimicrobial compounds produced by bacteria which include volatiles (HCN, aldehydes, alcohols, ketones, and sulfides), nonvolatile polyketides (diacetyl phloroglucinol [DAPG] and mupirocin), heterocyclic nitrogenous compounds (phenazine derivatives: pyocyanin, phenazine-1-carboxylic acid; PCA, PCN, and hydroxy phenazines), phenylpyrrole antibiotic (pyrrolnitrin) and lipopeptide antibiotics (iturins, bacillomycin, surfactin, and Zwittermicin A) [28,29,30]. Fluorescent pseudomonads and *Bacillus* species have also been found to be active in the suppression of plant pathogens. These bacterial antagonists enforce suppression of plant pathogens by the secretion of the abovementioned extracellular inhibitory metabolites [31].

BACTERIOPHAGES AS BIOCONTROL AGENTS

Bacteriophages are natural non-phytopathogenic strains that have the potential to be used in biocontrol. The use of phages in biocontrol was first reported in 1896 by Ernest Hankin, who observed antibacterial activity against *Vibrio cholera* [32]. Phage therapy has been found to be an effective tool for the control of several phytopathogenic bacteria, including *Xanthomonas* spp. [33], *Pseudomonas* spp. [34], *Erwinia* spp. [35], *Pantoea* spp. [36], *Ralstonia* spp. [37], *Streptomyces* spp. [38], *Dickeya* spp. [39] and *Pectobacterium* spp. [40]. Phages have been found to have several potential advantages in disease control; bacteriophages can be readily isolated from bacteria that occur in a range of locations, including soil, water, plants, animals and humans, as well as hydrothermal vents [41]. Phages are self-replicating and self-limiting; they reproduce only as long as the host bacterium is present in the environment and quickly degrade in its absence [42]. Phages target only the bacterial receptors that are essential for pathogenesis; therefore, the resistant mutants of bacterial strains are attenuated in virulence [43]. Bacteriophages are not only nontoxic to eukaryotic cells but also are specific [44]. Phage formulations are inexpensive to produce and can be stored at 4°C in complete darkness for months without a significant reduction in titer [45].

ENZYMES AS BIOCONTROL AGENTS

Plants have evolved chitinases, peroxidases (POs), and polyphenol oxidases (PPOs) are defense enzymes that are induced in plants during pathogenesis [46]. Chitinases are defense proteins with antimicrobial activity. Some chitinases have also been found to possess lysozymal activity [47] and thus responsible for conferring resistance to bacterial pathogens. Peroxidases create a physical barrier to limit pathogen invasion in host tissues by catalyzing the cross-linking of cell wall components in response to pathogen infection [48], where such enzymes have been implicated in the oxidation of phenols [49], lignifications [50], plant protection [51] and elongation of plant cells [52]. Polyphenol oxidases use molecular oxygen to oxidize common ortho-diphenolic compounds (e.g., caffeic acid and catechol) to their respective quinones [53].

ANTIMICROBIAL PEPTIDES AS BIOCONTROL AGENTS

Endogenous antimicrobial peptides have emerged as potential biocontrol agents for the protection of crops against pathogenic bacteria [54]. These peptides have been found in a variety of mammals, amphibians, insects, and plants, and play an important role in host defense systems and innate immunities [55]. Natural antimicrobial peptides exhibit a broad spectrum of activity against bacteria and fungi. They are lytic, and have synergistic activity with conventional antibiotics. When Ferre et al [56] synthesized short peptides and evaluated them against *Erwinia amylovora*, *Ps. syringae*, and *X. vesicatoria*, bactericidal activity at micromolar concentrations was observed.

NANOPARTICLES AS ANTIMICROBIALS

Nanoparticles are particles with at least one dimension within the 1–100-nm range. Particles within this size range have unique physical and chemical properties, including large surface to mass ratio, high reactivity and unique interactions with biological systems [57]. Some of the above properties make them excellent antimicrobials, and some properties make them ideal carriers/delivery systems for other antimicrobials. The antimicrobial activities of most nanoparticles result from three major aspects: photocatalysis, physical damage to the microbial cell envelope and the release of toxic metal ions. Nanoparticles with photocatalysis activity are mostly metal oxides, such as CuO, TiO₂, ZnO and Fe₃O₄ [58], and metals, such as Ag [59]. During photocatalysis, reactive oxygen species (ROS) are generated in the form of hydrogen peroxide, hydroxyl radicals and peroxide [60]. These ROS are toxic to microorganisms, as they can damage cellular constituents, such as DNA, lipids and proteins, resulting in bactericidal and bacteriostatic effects [61]. In one study, a nanoparticle formulation of titanium dioxide (TiO₂) induced photocatalysis, resulting in antimicrobial effects against the bacterial spot pathogen *Xanthomonas perforans* [62]. ZnO and Ag NPs have also been found to exhibit promising antimicrobial activity against [63]. The association of nanoparticles with a support material has been shown to possess promising antimicrobial effects. Bare nanoparticles tend to form agglomerations that weaken the antimicrobial activity [64]. Graphene oxide (GO) has been used as support material to grow Ag NPs, significantly reducing agglomeration and enhancing the antimicrobial activity against the bacterial spot pathogen *X. perforans* [64]. In addition to antimicrobial activities, nanoparticles have also been reported to be efficient delivery systems for many other antimicrobial compounds. Multiple nanoparticle delivery systems, such as hydrogel, dendrimers, liposomes, carbon nanotubes, micelles, and micro and nanoemulsions, have been studied for the delivery of various active ingredients [65]. Among them, nano-emulsions have shown promising delivery of an agriculturally important herbicide [66] and a nano-emulsion formulation was

reported to enhance the permeability of the antibiotic ampicillin through the citrus cuticle into the phloem via a foliar spray targeted against Huanglongbing disease [67]. As the plant cuticle (wax, cutin and pectin) acts as the major barrier preventing antimicrobial compounds from penetrating into plant tissues, and as many plant-pathogenic bacteria infect the phloem and xylem tissues, the development of antimicrobial delivery technology which penetrates through the cuticle may have wide applications in the control of bacterial plant diseases. In summary, Nanoparticles possess many desirable traits that may make them excellent antimicrobials for the management of microbial plant diseases in the future.

CHALLENGES AND FUTURE PERSPECTIVES

To meet the challenge, plant disease management strategies, current agricultural practices and plant disease management strategies must change. Three components (society, economics and ecology) should be considered in future plant disease management strategies. Providing safe and adequate food for society is always the most important task of plant disease management. Plant disease management should strike to ensure food security and social stability by increasing crop productivity, reducing food contamination by microbial toxins, and guaranteeing the supply of diverse and reasonable priced foods.

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