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Bacterial strategies for suppression and evasion of plant immunity: Molecular and cellular aspects

M. V. Patyka*, ***, S. H. Khablak**, L. M. Bondareva***, T. I. Patyka*, M. M. Dolia***, V. M. Spychak**, Y. V. Lykholat****

**Qufu Normal University, Qufu, China*
***Institute of Food Biotechnology and Genomics of the National Academy of Sciences of Ukraine, Kyiv, Ukraine*
****National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine*
*****Oles Honchar Dnipro National University, Dnipro, Ukraine*

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Qufu Normal University, Faculty of Life Sciences, No 57 West Road Jingxuan, Qufu, China. E-mail: npatyka@gmail.com

Institute of Food Biotechnology and Genomics of the National Academy of Sciences of Ukraine, Baida-Vyshnevetsky st., 2A, Kyiv, 04123, Ukraine. E-mail: sergeyhab211981@gmail.com

National University of Life and Environmental Sciences of Ukraine, Heroiv Oborony st., 15, Kyiv, 03041, Ukraine. E-mail: lnubip69@gmail.com

Oles Honchar Dnipro National University, Gagarin av., 72, Dnipro, 49010, Ukraine. E-mail: lykholat2006@ukr.net

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The review analyzes current data on the molecular mechanisms employed by bacteria to suppress and evade plant defense responses. It presents the strategies used by various pathogenic bacteria to overcome protective barriers associated with the cell wall and cytoplasmic components, including the cytoskeleton, which play a crucial role in plant immune responses to pathogens. Particular attention is given to bacterial effector proteins translocated into plant cells via the Type III Secretion System (T3SS), aimed at suppressing plant innate immunity and interfering with additional defense-related cellular processes such as proteasome-mediated protein degradation, phytohormone signaling, cytoskeleton organization, vesicular trafficking, and gene expression. Promising chemical compounds and innovative strategies for the control of bacterial plant diseases are also discussed.

Keywords: cell wall; bacterial pathogens; plant immunity; defense responses; effector proteins.

Introduction

The plant cell wall serves as the primary physicochemical barrier that phytopathogens must overcome to colonize plant tissues successfully. The nature of the interaction with the cell wall and the extent of its degradation after breaching the cuticular layer are determined by the pathogen's nutritional strategy. For instance, necrotrophic fungi cause extensive cell wall destruction using a complex of degrading enzymes. In contrast, biotrophic fungi require more localized and controlled degradation to maintain host cell viability and to form specialized feeding structures. Similarly, bacteria and nematodes degrade the plant cell wall at specific stages of the infection process to gain access to nutrients essential for their growth and reproduction (Bellincampi et al., 2014).

The Type III Secretion System (T3SS) is one of the most extensively studied bacterial secretion systems due to its central role in bacterial pathogenesis and plant infection. Foundational insights into its function in disease development in both animals and plants were established over three decades ago. Subsequent research has revealed the involvement of T3SS in symbiotic interactions between bacteria and plants, broadening our understanding of its ecological significance. The T3SS enables the translocation of a wide array of bacterial effectors into various host organisms, including plants, animals (vertebrates and nematodes), and insects (Alvarez-Martinez et al., 2020).

Pathogenic bacteria cause severe plant diseases, the control of which is often complicated by the limited effectiveness of traditional fungicides that primarily target fungal infections. Classical approaches to managing bacterial diseases include the use of antibiotics (such as streptomycin, oxytetracycline, gentamicin, oxolinic acid, and kasugamycin) and copper-based compounds. However, the use of copper-containing agents is currently restricted in many countries due to their environmental toxicity, while the growing application of antibiotics in crop production promotes the emergence of resistant strains of phytopathogenic bacteria and contributes to the broader problem of antibiotic resistance among human pathogens. Each year, an increasing number of bacterial strains resistant to antibacterial agents are reported, undermining the efficacy of treatment strategies in both human and plant disease management (Puigvert et al., 2019).

Given the rising issue of antibiotic resistance, an urgent task is to develop novel strategies to combat phytopathogens by targeting bacterial virulence rather than viability. Unlike antibiotics, virulence inhibitors do not exert direct bactericidal activity, which may slow down the development of resistance. These compounds reduce the pathogenic potential of bacteria and can promote the activation of plant immune responses. Such responses include various defense mechanisms: reinforcement of the cell wall via protein cross-linking and deposition of secondary metabolites (such as lignin, suberin, and callose); accumulation of toxic phenolic compounds and pathogenesis-related (PR) proteins at the infection site; degradation of damaged proteins via the 26S proteasome; activation of RNA interference (RNAi) as a defense against foreign genetic elements; and the hypersensitive response (HR), leading to localized programmed cell death. Understanding these fundamental defense pathways, as detailed by Khablak & Spychak (2024) in the context of resistance to parasitic plants, is critically important, as many of these mechanisms represent universal responses to various biotic stressors, including bacterial pathogens. These pathways often become targets of bacterial immune evasion factors.

Given the relevance of this research area, this review aims to analyze recent advances in the study of mechanisms by which pathogenic bacteria modulate and suppress host cell defense responses. Such an analysis is essential for a deeper understanding of bacterial virulence factors that play a critical role during infection and immune evasion in plants, as well as for the development of innovative strategies to control bacterial diseases. This review provides a detailed overview of the mechanisms used by bacteria to overcome plant defense responses, including their need to degrade the plant cell wall at specific stages of infection to acquire nutrients, and discusses the prospects of applying novel chemical compounds and biological control agents in the management of bacterial plant diseases.

Diversity of bacterial pathogens

Approximately 1,600 bacterial species are known to cause plant diseases. However, bacteria capable of infecting healthy plants are limited to a relatively small number of genera, including the gram-negative *Erwinia*, *Pseudomonas*, *Xanthomonas*, *Xylella*, and *Agrobacterium*, as well as the gram-positive *Clavibacter* (formerly *Corynebacterium*) and *Streptomyces*. Research into the pathogenicity of gram-negative bacteria has advanced significantly compared to other groups. Many gram-negative phytopathogens are readily cultured under laboratory conditions and can be easily used for artificial inoculation of plants. In contrast, the limited understanding of gram-positive bacteria is partly due to the technical challenges associated with their cultivation (Mansfield et al., 2012).

Two main types of bacterial plant diseases are distinguished: systemic bacterial blight, characterized by the pathogen's entry into the plant's vascular system and its subsequent spread through the conductive tissues and neighboring cells, resulting in disrupted water transport; and localized bacterial blight, which is manifested by damage to the parenchymal tissues of specific plant organs (Table 1).

Table 1
Diversity of plant bacterial pathogens

Pathogen and disease	Bacterial type	Infection type	Symptoms	Host plants	Entry route	Lifestyle	Infection source	Control class / method
Pseudomonas syringae – bacterial canker, leaf spots	gram-negative	localized / systemic	necrosis, spots, wilting	tomato, cucumber, stone fruits	stomata, wounds, water	facultative parasite	water droplets, plant debris	copper-based compounds, antibiotics (streptomycin)
Xanthomonas campestris – black rot of crucifers	gram-negative	systemic	vascular necrosis, wilting, and chlorosis	cabbage, radish, rapeseed	stomata, hydathodes	facultative parasite	seeds, soil	copper-based bactericides, seed heat treatment
Erwinia amylovora – fire blight of fruit trees	gram-negative	systemic	blackening of blossoms and shoots, wilting	apple, pear, quince	damaged tissues, insects	facultative parasite	insects, water droplets	antibiotics (oxytetracycline), sanitary pruning
Ralstonia solanacearum – bacterial wilt	gram-negative	systemic	vascular browning, wilting	tomato, eggplant, pepper	roots (via soil)	facultative parasite	soil, water	phytosanitary isolation, crop rotation
Xylella fastidiosa – Pierce's disease	gram-negative	vascular systemic	chlorosis, leaf scorch, dieback	grapevine, citrus, almond	xylem vessels via insects	obligate parasite	leafhopper vectors	vector control, quarantine
Clavibacter michiganensis – tomato bacterial canker	gram-positive	systemic	necrosis, wilting, pale spots	tomato, pepper	wounds, seeds	facultative parasite	seeds, plant debris	seed disinfection, removal of infected plants
Streptomyces scabies – common scab of potato	gram-positive	localized	rough lesions on tubers	potato, beet	through the soil (during drought)	facultative saprophyte	soil	crop rotation, soil acidification

Note: bacterial type (Gram-positive or Gram-negative) is important for diagnosis and selection of appropriate control measures; type of infection – localized (parenchymal tissues) or systemic (vascular system).

The primary symptoms of bacterial infections include wilting, necrosis, chlorosis, and rotting (Nazarov et al., 2020). Among phytopathogenic bacteria, the most widespread and economically significant diseases are caused by *Clavibacter michiganensis*, *Pseudomonas syringae* (bacterial canker, bacterial spot), *Xanthomonas campestris* (vascular bacterial wilt – black rot of crucifers, citrus canker), *Erwinia amylovora* (fire blight of fruit trees), *Erwinia carotovora*, *Ralstonia solanacearum* (bacterial wilt), *Xylella fastidiosa* (Pierce's disease of grapevine, citrus variegated chlorosis), and *Pantoea stewartii* (Abramovitch et al., 2006).

Comparison of the cell wall structure of gram-positive and gram-negative bacteria and the role of PAMPs in plant immunity

Based on structural characteristics of the cell wall, bacteria are classified as gram-positive or gram-negative. The structural characteristics of cell walls are a key factor distinguishing between gram-positive and gram-negative bacteria. Specifically, the cell wall of gram-positive bacteria is characterized by the presence of a cytoplasmic membrane directly adjacent to a significantly thickened peptidoglycan layer. This peptidoglycan layer, whose primary structural element is multilayered murein, also integrates various components such as proteins, lipids, as well as teichoic and teichuronic acids, which play an important role in cell wall function. In contrast, gram-negative bacteria have evolved with a more complex double-membrane architecture. Their cell wall includes an inner cytoplasmic membrane and an outer membrane, between which a relatively thin layer of peptidoglycan is located. A significant distinguishing feature of the outer membrane of gram-negative bacteria is the presence of lipopolysaccharides (LPS) and porins, whereas teichoic and lipoteichoic acids are absent from it (Mansfield et al., 2012). Some components, such as peptidoglycans, are shared by both bacterial groups, while others are specific. For example, lipopolysaccharide (LPS) is an exclusive component of gram-negative bacteria, whereas lipoteichoic acid (LTA) is characteristic of gram-positive bacteria (Szentirmai et al., 2021) (Tables 2, 3).

Table 2
Structural components of the bacterial cell wall: types, localization, and immunological significance

Component	Bacterial type	Localization	Description	Note / Immunological significance
Peptidoglycan (PG)	gram-positive and gram-negative	cell wall	mesh-like murein polymer; provides mechanical strength	thick layer in gram +, thin in gram –
Murein	both types	part of pg	the main structural component of pg	forms the rigid scaffold of the cell wall
Teichoic acids (TA)	gram-positive	cell wall	anionic polymers linked to peptidoglycan or lipids	specific to gram +; modulate wall charge
Lipoteichoic acid (LTA)	gram-positive	membrane → pg	anchored in the membrane, extends into pg	recognized by tlr2 as a PAMP
Lipopolysaccharide (LPS)	gram-negative	outer membrane	composed of lipid a, core oligosaccharide, and o-antigen	strong PAMP; activates tlr4
Lipid A (part of LPS)	gram-negative	outer membrane	conserved toxic portion of lps	primary immunogenic structure of lps
Porins	gram-negative	outer membrane	channel proteins for the transport of small molecules	unique to gram –; considered a PAMP
Flagellin	both types	flagellum	the main protein of the bacterial flagellum	recognized by fls2 (plants), tlr5 (animals)
EF-Tu	both types	cytosol; exposed upon lysis	conserved translation elongation factor	recognized as a PAMP (e.g., by EFR in plants)
sBLP (surface bacterial lipoproteins)	mainly gram-positive	membrane	surface-exposed lipoproteins	recognized by tlr2/1 or tlr2/6

Table 3
Comparative characteristics of the cell wall of gram-positive and gram-negative bacteria and their PAMPs

Characteristic	Gram-positive bacteria	Gram-negative bacteria	Major PAMPs
Peptidoglycan	thick layer (~20–80 nm)	thin layer (~2–7 nm)	peptidoglycan (PGN) – present in both types
Lipoteichoic acid (LTA)	present (in the cell wall)	absent	LTA – specific to gram-positive bacteria
Outer membrane	absent	present (contains LPS, porins)	lipopolysaccharide (LPS) – gram-negative only
Other wall components	teichoic acids	porins, lipoproteins, exotoxins	flagellin, porins – mostly gram-negative
Functional features	rigid, resistant to physical damage	dual membrane layers – antibiotic resistance	all PAMPs are recognized by the host immune system

Note: Gram-positive bacteria have a thick peptidoglycan layer that provides mechanical strength and contain lipoteichoic acids (LTA), which act as PAMPs recognized by the immune system; They lack an outer membrane; Gram-negative bacteria possess a thin peptidoglycan layer but additionally have an outer membrane containing lipopolysaccharide (LPS), a highly potent PAMP; this outer membrane also includes porins – protein channels – and can produce various exotoxins; PAMPs (pathogen-associated molecular patterns) are molecular signals recognized by immune receptors in plants and animals, triggering immune responses; the most important bacterial PAMPs include peptidoglycan, LTA (in gram-positive bacteria), LPS, flagellin, and porins (in gram-negative bacteria).

The Gram staining type – gram-positive or gram-negative – is a fundamentally important characteristic reflecting profound biochemical and structural differences between major groups of bacterial phytopathogens. Gram-positive bacteria possess a thick cell wall primarily composed of peptidoglycan and lack an outer membrane. Upon Gram staining, they appear violet or purple. This group notably includes *Clavibacter* spp. and *Streptomyces* spp. (Schaad et al., 2001).

In contrast, gram-negative bacteria have a thinner peptidoglycan layer located between two membranes, with the outer membrane containing lipopolysaccharides (LPS) – potent virulence factors that contribute to pathogenicity and resistance to chemical control agents (Pfeilmeier et al., 2016; Laforest et al., 2019). These bacteria stain pink or red. Gram-negative phytopathogens of particular importance include the genera *Pseudomonas*, *Xanthomonas*, *Erwinia*, *Ralstonia*, and *Xylella*.

From a phytopathologist's perspective, determining the Gram type of a pathogen is critical both at the stage of initial diagnosis and in selecting an effective control strategy (Sundin et al., 2016). Gram-negative bacteria more frequently cause systemic vascular infections, whereas gram-positive bacteria are typically limited to localized tissue lesions. Moreover, the efficacy of antibacterial treatments, including biopreparations and copper-based fungicides, depends significantly on the structure of the bacterial cell envelope. The outer membrane of gram-negative bacteria acts as an additional barrier to the penetration of chemical and biological agents, resulting in higher resistance compared to gram-positive bacteria, which lack this membrane (Hayward, 2000).

Gram-negative phytopathogenic bacteria possess several structural and functional features that enhance their ability to penetrate the plant vascular system and cause systemic infections. A key characteristic is the presence of a thin peptidoglycan layer combined with an outer membrane rich in lipopolysaccharides (LPS) (Table 4). This architecture provides resistance to pH fluctuations, toxic plant metabolites, and antimicrobial compounds, and also allows evasion of immune detection by the plant. In contrast, gram-positive bacteria, with their thick peptidoglycan layer and absence of an outer membrane, are generally more sensitive to physical and chemical stressors such as pH shifts, redox changes, and nutrient limitation. Many gram-negative pathogens harbor a type III secretion system (T3SS), which facilitates the delivery of effector proteins into plant cells, suppressing immune responses and enabling systemic colonization. Additionally, traits such as biofilm formation, motility via flagella, secretion of cell wall-degrading enzymes, and exotoxins contribute to effective colonization of the xylem, a vascular tissue characterized by limited immune surveillance (Puigvert et al., 2019). Consequently, gram-negative bacteria exhibit greater ecological plasticity and pathogenic efficiency than gram-positive bacteria, particularly in the context of vascular plant infections.

Table 4
Gram-negative bacteria capable of causing systemic vascular infections in plants

Pathogen	Systemic disease	Host crops
Ralstonia solanacearum	bacterial wilt	tomato, potato, eggplant
Xanthomonas campestris pv. *campestris*	black rot of crucifers	cabbage, broccoli, brassicas
Pseudomonas syringae pv. *actinidiae*	bacterial canker of kiwifruit	kiwifruit (*actinidia*)
Xylella fastidiosa	Pierce's disease, olive quick decline syndrome	grapevine, olive, citrus
Dickeya spp., *Pectobacterium* spp.	soft rot, vascular wilts	potato, carrot, celery
Erwinia amylovora	fire blight	pear, apple

In horticulture, vegetable production, field crops, and perennial plantations – where the use of antibiotics is strictly limited – the Gram type also determines the availability of effective control options. For example, streptomycin-based products (e.g., Kasumin) are primarily effective against gram-positive pathogens (McManus et al., 2002). Knowing the Gram type allows agronomists to assess potential risks of resistance development and to optimize the use of biocontrol agents such as antagonistic strains of *Bacillus* or *Pseudomonas* (Compant et al., 2005). Thus, the Gram staining type of a bacterial pathogen is not merely a taxonomic or morphological trait but a practically relevant factor that directly influences agronomic decisions related to diagnosis, treatment, and prevention of bacterial diseases in agriculture (Tables 5, 6).

Table 5
The importance of bacterial Gram type in the diagnosis of plant diseases

Aspect	Relevance of gram type
Microscopy	enables rapid identification of pathogen type via gram staining
Cultivation	gram-positive bacteria (e.g., *Streptomyces*) are generally more difficult to culture
Molecular diagnostics	primers and probes often differ between gram-positive and gram-negative bacterial groups
Symptomatology	systemic bacterial diseases are more frequently caused by gram-negative pathogens

Table 6
Impact of bacterial Gram type on the effectiveness of plant disease control measures

Criterion	Gram-positive	Gram-negative
Resistance to copper-based compounds	often lower	often higher
Sensitivity to antibacterial agents	more sensitive to streptomycin and biocontrol products	some are resistant due to the outer membrane barrier
Efficacy of biological control agents	less studied	more widely targeted by antagonists (*Bacillus*, *Pseudomonas*)
The cell wall as a target	more susceptible to enzymatic products	the outer membrane complicates the penetration of control agents

A wide range of diverse molecules, including glycans and glycoconjugates, can function as PAMPs (pathogen-associated molecular patterns). Flagellin is another important PAMP, recognized by TLR5 (toll-like receptor 5) through its conserved D1 domain. Bacterial lipopolysaccharides (LPS) – also known as endotoxins – are located on the outer membrane of gram-negative bacteria and are considered a prototypical class of PAMPs. The lipid component of LPS, lipid A, consists of a diglucosamine backbone with multiple acyl chains. This conserved structural motif is recognized by the TLR4-MD2 complex. Bacteria employ two major strategies to modulate LPS-mediated immune responses: masking lipid A or targeting LPS to immunomodulatory receptors. Peptidoglycan (PG), also present in the cell walls of gram-negative bacteria, is recognized by TLR2, which typically functions as a heterodimer with TLR1 or TLR6 (Raetz & Whitfield, 2002). Lipoteichoic acid (LTA) of gram-positive bacteria, bacterial lipoproteins (sBLPs), phenol-soluble modulins from *Staphylococcus epidermidis*, and zymosan (a component of yeast cell walls) are recognized by the TLR2–TLR1 or TLR2–TLR6 heterodimers. However, LTA induces a weaker immune response compared to lipopeptides, as it is recognized solely by TLR2, and not by a heterodimer (Cot et al., 2011) (Table 7).

Bacterial organisms synthesize specific molecules known as microbe-associated molecular patterns (MAMPs) or induce the plant's production of signaling compounds – damage-associated molecular patterns (DAMPs). Such signals include, among others, flagellin, chitin, volatile organic compounds (VOCs), and siderophores. These molecular patterns are perceived by pattern recognition receptors (PRRs) that are integrated into plant cell membranes. Upon activation, PRRs initiate diverse signaling cascades that, among other functions, can serve as precursors for the biosynthesis of phytohormones, which, in turn, trigger defense pathways. Furthermore, these kinase cascades are capable of phosphorylating transcription factors, thereby modulating the expression of early and late response genes (Lahlali et al., 2022).

Table 7
Major plant PRR receptors for recognition of bacterial pathogens

Receptor Name	PRR Type	Recognized PAMP	PAMP Source	Mechanism / Notes
FLS2 (FLAGELLIN SENSING 2)	RLK (receptor-like kinase)	Flg22 (flagellin epitope)	bacterial flagellin	forms a complex with BAK1 to activate the immune response
EFR (EF-Tu Receptor)	RLK	elf18 (EF-Tu epitope)	elongation factor Tu	recognizes the N-terminal peptide of EF-Tu
LYM1 / LYM3 + CERK1	RLP + RLK	peptidoglycan	PG from the bacterial cell wall	heterodimeric receptor complex for binding peptidoglycan
LORE (LipoOligosaccharide-specific Reduced Elicitation)	RLK	3-OH medium-chain fatty acids	gram-negative bacterial LPS	specific receptor for lipid A
PEPR1 / PEPR2	RLK	DAMPs (danger peptides: Pep1, Pep2)	endogenous plant peptides	enhance PTI after PAMP recognition
WAK1 (Wall-Associated Kinase 1)	RLK	Oligogalacturonides (DAMPs)	cell wall degradation products	activates the immune response
CERK1 (Chitin Elicitor Receptor Kinase 1)	RLK	chitin	fungi (not bacteria)	included for contrast with peptidoglycan recognition

During biotic stress caused by bacteria, plant cells recognize PAMPs such as flagellin and elongation factor Tu (EF-Tu) via PRRs. One of the most well-studied plant PRRs is the receptor-like kinase (RLK) Flagellin-Sensing 2 (FLS2) in *Arabidopsis*, which recognizes a conserved epitope of bacterial flagellin consisting of 22 amino acids (flg22). Flagellin is the main protein of bacterial flagella and a well-characterized PAMP recognized by the FLS2 receptor in *Arabidopsis*. It is believed that plasma membrane-localized FLS2 plays a key role in the early stages of bacterial interaction with the plant by recognizing and binding flagellin (Sun et al., 2020).

Infection pathways of plants by phytopathogenic bacteria

The process of plant infection by pathogenic bacteria is multi-stage and may include survival on the leaf surface (epiphytic phase) and biofilm formation; directed migration using flagella to natural openings or wounds (apoplastic entry sites); release of phytotoxins to neutralize defense reactions such as stomatal closure; induction of ice nucleation to damage cell surfaces; secretion of extracellular enzymes to degrade cell walls and injure plant tissue; as well as secretion of phytotoxins that manipulate the physiology, metabolism, and immune responses of the host plant (Pfeilmeier et al., 2016) (Table 8).

Table 8
Entry pathways of phytopathogenic fungi and bacteria

Feature / Pathogen	Phytopathogenic bacteria	Phytopathogenic fungi
Entry sites	- stomata - hydathodes - wounds	- stomata - cuticle (direct penetration) - wounds
Active penetration	passive or via natural openings/damage	formation of appressoria, enzymatic degradation, and mechanical pressure
Dependence on moisture	yes (moisture needed for movement and stomatal opening)	yes (required for spore germination and appressoria formation)
Mobility	motile via flagella, chemotaxis	non-motile; spread by spores or hyphae
Penetration through stomata	frequent, facilitated by coronatine or effectors	possible (especially in hemibiotrophs like *Magnaporthe*)
Effect on stomata	active opening (coronatine, AvrB, syringolin A)	no direct activation, but can enter through open stomata
Cell wall degradation	limited (enzymes involved, but not the main entry route)	major mechanism – pectinases, cellulases, hemicellulases
Formation of specialized structures	none	appressoria, haustoria, infectious hyphae
Secretion of toxins/signaling molecules	coronatine, syringolin, AHLs, effectors	phytotoxins, autoxins, effectors
Secretion systems	well-developed (T3SS, T2SS, T6SS)	different types: exocytosis, vesicles, invaginations
Type of infection	often localized or vascular	Can be localized or systemic

Note: bacteria predominantly utilize natural openings for entry and modulate plant immunity through molecules such as coronatine; fungi can penetrate without natural openings by breaching the cuticle using enzymes and mechanical pressure; both groups are capable of causing biotrophic, necrotrophic, or hemibiotrophic infections, although the underlying mechanisms differ.

The leaf surface is a harsh environment for pathogenic microorganisms, where bacteria are regularly exposed to desiccation, ultraviolet radiation, temperature fluctuations, mechanical damage, and wind. The ability of bacteria to survive and persist on the plant surface is considered an important component of their virulence strategy, playing a significant role in subsequent stages of the infection process. Metabolic adaptations to cold and osmotic stress, as well as desiccation tolerance, substantially contribute to the survival of epiphytic po-

pulations (Djonović et al., 2013). Exopolysaccharide (EPS) production plays a critical role in the epiphytic survival of bacteria. Various EPS molecules, including well-studied polymers such as xanthan, levan, and alginate, facilitate colonization of plant surfaces and infection. EPS molecules are associated with numerous functions in plant-microbe interactions, most of which aim to ensure epiphyte survival, induce resistance to freeze-thaw cycles, desiccation, and osmotic stress, maintain microbial populations, and participate in immune evasion mechanisms. The formation of biofilms on both external and internal plant surfaces at different stages of infection is a crucial factor for bacterial survival (Freeman et al., 2013).

Epiphytic existence on plant leaves is a complex and dynamic process during which pathogens continuously "decide" whether to activate genes required for survival on the surface or genes necessary to overcome the epidermal barrier and penetrate the apoplast for subsequent colonization of the intercellular space or vascular system. This decision-making process is a critical factor in pathogenicity, virulence, and persistence of plant infections, and it is largely mediated by signaling pathways based on small molecules. These systems regulate motility, biofilm formation, virulence gene expression, and intercellular communication both within and between bacterial species. A large number of signaling systems have been described in plant pathogens, among which the quorum sensing (QS) system and secondary messenger pathways such as cyclic diguanylate monophosphate (c-di-GMP) signaling are key (Pfeilmeier et al., 2016). Bacteria use QS to exchange information and assess population density by producing small signaling molecules called autoinducers, which are detected by neighboring bacteria and influence gene expression once a threshold concentration, reflecting a critical cell density, is reached. In phytopathogenic bacteria, the main characterized QS signals are N-acyl homoserine lactones (AHLs), diffusible signal factor (DSF), and Ax21 (Pierce et al., 2014).

Many pathogenic bacteria respond to contact with the leaf surface by activating mechanisms that promote survival until favorable conditions for apoplast entry arise. Once such conditions emerge or are immediately present, in the case of some less-adapted epiphytes, pathogens activate various motility systems to migrate across the leaf surface toward stomata, wounds, or other entry points into the plant's internal tissues. Flagellum-mediated motility gives *Pseudomonas syringae* a competitive advantage in epiphytic adaptation and is critically important for surface colonization and effective virulence (Yu et al., 2013).

While the plant cuticle and cell wall can be penetrable by some fungal pathogens, most bacteria are unable to directly breach the epidermis. Instead, the majority of phytopathogenic bacteria remain in the intercellular space (apoplast). To enter the plant, bacteria exploit natural openings such as hydathodes, nectaries, lenticels, and most importantly, stomata. In addition, wounds caused by insects, herbivores, wind, or rain provide further routes for infection.

Beyond physical barriers, plants constitutively produce antimicrobial compounds collectively known as phytoanticipins that inhibit pathogen growth. These compounds include defense-related proteins and certain secondary metabolites, such as glucosinolates and their derivatives (Makandar, 2024) (Table 9).

The ability of certain bacteria to infect plants and proliferate within their tissues depends on the secretion of proteins such as adhesins, toxins, and cell wall-degrading enzymes. In addition, bacterial pathogens often deliver effector proteins directly into plant cells. These effectors interfere with plant immune responses, including PAMP-triggered immunity (PTI) and effector-triggered immunity (ETI), as well as with mitogen-activated protein kinase (MAPK) signaling pathways, proteasome-dependent protein degradation, phytohormone signaling, photosynthesis, gene expression, and cytoskeleton organization. Effectors from various pathogens employ both general and pathogen-specific strategies to undermine plant immunity and promote bacterial survival. Bacterial virulence factors are delivered via specialized protein secretion systems, which are classified into at least six types (from type I to type VI) (Costa et al., 2015). Additionally, virulence-associated proteins can be secreted through outer membrane vesicles (OMVs), which facilitate the transport of a wide range of proteins from the periplasm of gram-negative bacteria into the extracellular environment (Bonnington & Kuehn, 2014).

To initiate infection, free-living bacterial pathogens must overcome the surface defense mechanisms of the plant and penetrate the apoplast. One of the most accessible routes of entry for bacteria is through the stomata. However, plants close their stomatal pores as part of their innate immune response to prevent bacterial invasion. In response, many phytopathogens, such as *Xanthomonas campestris* pv. *campestris* (Xcc) and various pathovars of *Pseudomonas syringae* produce and secrete phytotoxins that overcome stomatal immunity. A variety of pathogen-secreted molecules act as stomatal-opening factors, including the well-studied toxins coronatine and syringolin A. In each case, these phytotoxins function by interfering with NPR1-dependent salicylic acid (SA) signaling (Xin & He, 2013). The type III effector AvrB from *P. syringae* can substitute for coronatine in inducing jasmonic acid (JA)-dependent genes and promoting stomatal reopening (Tables 10–12).

The process of stomatal opening regulation in plants involves the function of auto-inhibited plasma membrane H^+-H-ATPases, such as AHA1 and AHA2, which are responsible for actively pumping protons from the cytosol into the apoplast. This proton transport, in turn, establishes an electrochemical proton gradient that serves as the driving force for channel and carrier proteins, mediating the uptake of charged solutes into the guard cells. Consequently, the accumulation of these solutes increases osmotic pressure, leading to water influx and elevated turgor, which ultimately results in stomatal opening. It has been shown that the induction of stomatal opening by the bacterial effector AvrB depends on the activity of the F-box protein COI1 and the immune regulator RIN4, which directly interacts with AvrB. Furthermore, RIN4 is known to associate with AHA1, enhancing its functional activity.

Table 9
Stages of plant infection by pathogenic bacteria

Infection stage	Bacterial mechanisms	Target in the plant	Virulence factors / Molecules	Example bacteria / Disease
1. Epiphytic survival phase	production of exopolysaccharides, biofilm formation	protection from stress, surface colonization	xanthan, alginate, levan, EPS	*Pseudomonas syringae* – bacterial speck; *Xanthomonas campestris* – black rot of cabbage
2. Environmental sensing and signaling	quorum sensing (QS), c-di-GMP signaling	population coordination, virulence induction	AHL, DSF, Ax21, c-di-GMP	*Xanthomonas campestris* – black rot of cabbage
3. Movement to entry sites	flagella, chemotaxis	access to stomata, hydathodes, wounds	flagellin, motor proteins	*Pseudomonas syringae* – bacterial speck
4. Plant entry	activation of openings, tissue damage	entry into apoplast	phytotoxins (coronatine, syringolin A)	*P. syringae* – bacterial speck; *X. campestris* – black rot
5. Evasion of stomatal immunity	suppression of salicylic acid (SA) signaling	reopening of stomata	coronatine, AvrB, syringolin A	*Pseudomonas syringae* – bacterial speck
6. Apoplastic colonization	secretion of enzymes, adhesins	cell wall degradation, retention in apoplast	cellulases, pectate lyases, and adhesins	*Xanthomonas campestris* – black rot of cabbage
7. Immune suppression	PTI/ETI interference, MAPK signaling	inactivation of immune responses	type III effectors (T3SS), AvrB, Hop proteins	*P. syringae* – bacterial speck; *X. campestris* – black rot
8. Tissue spread	vascular colonization, motility	systemic infection	secretion systems (I–VI), outer membrane vesicles (OMVs)	*Xanthomonas campestris* – black rot of cabbage

Table 10
Virulence factors of plant pathogenic bacteria

Virulence Factor	Type / Example	Function / Mechanism of action
Type III secretion system (T3SS)	Hrp pilus (e.g., *Pseudomonas*, *Xanthomonas*)	injection of effector proteins directly into host plant cells
Effectors	AvrPto, AvrBs2, HopM1	suppression of plant immunity, signaling interference, promotion of pathogenicity
Toxins	coronatine (*P. syringae*), tabtoxin	mimicry of phytohormones (e.g., JA), stomatal reopening, suppression of SA signaling
Phytohormones / hormone mimics	IAA (Indole-3-acetic acid)	plant growth stimulation, weakening of plant defenses
Exopolysaccharides (EPS)	xanthan, alginates	biofilm formation, xylem blockage, protection from environmental stress
Cell wall–degrading enzymes	cellulases, pectinases	breakdown of plant cell walls, facilitation of tissue penetration
Type VI secretion system (T6SS)	*Ralstonia solanacearum*	competition with other microbes, injection of toxic proteins into neighboring cells

Table 11
Sites of bacterial entry and mechanisms of overcoming barriers

Entry Site	Mechanism of entry	Facilitating factors
Stomata	entry through open stomatal pores	coronatine (JA mimic), HopM1, suppression of stomatal closure
Hydathodes (water pores)	passive entry via guttation fluid	high humidity, capillary action
Wounds, micro-injuries	passive entry through damaged tissues	rain, wind, and insect activity
Root hairs	entry through apoplast or lateral cracks	increased turgor pressure, pH shifts
Cuticle vulnerability	penetration through softened or thin cuticle	cellulases, pectinases, and localized wall-degrading enzymes
Vascular system	systemic spread following initial entry	biofilms, EPS production, flagellar motility, and pressure reduction mechanisms

Table 12
Comparative characteristics of plant pathogenic bacteria

Disease (pathogen)	Type of infection	Infection mechanism	Effectors / Virulence factors
Bacterial speck (*Pseudomonas syringae*)	localized	entry through stomata, effector injection via T3SS	AvrPto, HopM1, coronatine
Black rot of cabbage (*Xanthomonas campestris*)	localized / systemic	T3SS delivery, active secretion, and cell surface attachment	AvrBs2, HpaA, TAL effectors
Bacterial wilt (*Ralstonia solanacearum*)	systemic	root penetration, spread via xylem vessels	PopP2, T6SS, HrpB
Crown gall (*Agrobacterium tumefaciens*)	localized	T-DNA transfer to host cell, tumor induction via T4SS	VirE2, VirF, VirD2
Tomato bacterial canker (*Clavibacter michiganensis*)	systemic	entry through wounds, enzymatic tissue degradation	cellulases, pectinases, phytotoxins
Fire blight of apple (*Erwinia amylovora*)	systemic	entry via wounds, nectaries, vascular movement	DspA/E (T3SS), exopolysaccharides, biofilms

Transient expression studies in *Nicotiana benthamiana* revealed that AHA1, RIN4, and AvrB collectively initiate the degradation of JA proteins, indicating a mechanistic link between jasmonic acid (JA) signaling, RIN4-AvrB interaction, and the process of stomatal opening (Zhou et al., 2015).

In addition to stomatal entry, phytopathogens can infiltrate the apoplast through epidermal damage in plant tissues. To achieve this, many pathogens produce cell wall-degrading enzymes and other proteins that facilitate tissue penetration. Several pathovars of *Pseudomonas syringae* produce ice nucleation-active (INA) proteins, and INA gene loci have also been identified in other plant pathogens such as *Xanthomonas campestris* and *Pantoea ananatis*. The size, membrane association, and aggregation propensity of INA proteins currently hinder efforts to resolve their three-dimensional structures. However, it is hypothesized that INA proteins order water molecules into ice-like clathrate lattices, thereby raising the ice nucleation temperature and triggering ice formation at relatively mild subzero temperatures. Frost damage caused by INA-mediated ice nucleation can facilitate pathogen entry into plant tissues. Genes conferring resistance to freeze-thaw stress are widespread among epiphytic bacteria, supporting their survival under abiotic stress as well as pathogen-induced frost injury. This aligns with the hypothesis that intentional frost damage represents a common virulence strategy among phytopathogens (Garnham et al., 2011).

In contrast to the epiphytic lifestyle observed in early infection stages of *Xanthomonas* and *Pseudomonas* spp., other bacterial phytopathogens, such as *Xylella fastidiosa* and phytoplasmas, rely on insect vectors that feed on plant sap to penetrate host tissues and facilitate transmission (Pfeilmeier et al., 2016).

Cell wall-degrading enzymes and phytotoxins of phytopathogenic bacteria

Phytopathogens also secrete numerous degradative enzymes, primarily via type II secretion systems (T2SS), which break down structural components of the plant cell wall and hydrolyze the middle lamella between individual cells. This degradation provides both a carbon source for the pathogen and a mechanism for apoplastic spread within plant tissues. These extracellular enzymes are structurally and functionally diverse and include proteases, cellulases, pectinases, and xylanases (Korotkov et al., 2012).

In addition to cell wall-degrading enzymes, phytopathogenic bacteria produce small secreted phytotoxins that enhance bacterial virulence by disrupting host defense responses and exacerbating tissue chlorosis and necrosis. Some phytotoxins cause direct cellular damage, while others modulate host metabolism and signaling pathways in ways that favor the pathogen. Examples of the first group include lipodepsipeptide toxins such as syringomycin and syringopeptin, which are synthesized by nonribosomal peptide synthetases during *Pseudomonas syringae* infection. These amphiphilic compounds cause tissue necrosis by forming pores in the plant plasma membrane. Modified peptide toxins like phaseolotoxin, mangotoxin, and tabtoxin are produced by various *P. syringae* pathovars and induce chlorosis and necrosis. These toxins target key enzymes involved in amino acid biosynthesis, inhibiting their function and thereby disrupting nitrogen metabolism. The accumulation of nitrogen-containing intermediates resulting from enzyme inhibition can then be exploited by the pathogen as a nutrient source. The toxic moiety of tabtoxin is released via hydrolysis inside the plant cell and induces chlorophyll degradation, leading to visible chlorosis due to the irreversible inhibition of glutamine synthetase (Pfeilmeier et al., 2016) (Tables 13 and 14).

Coronatine, syringomycin, syringopeptin, tabtoxin, and phaseolotoxin are the most intensively studied phytotoxins produced by the gram-negative bacterium *Pseudomonas syringae*, which causes bacterial diseases in a wide range of plants. Each of these phytotoxins plays a crucial role in enhancing bacterial virulence. For instance, coronatine partly functions as a molecular mimic of methyl jasmonate, a plant hormone synthesized in response to biotic stress. Syringomycin and syringopeptin lead to the formation of pores in the plasma membranes, causing electrolyte leakage from cells. In turn, tabtoxin and phaseolotoxin demonstrate potent antimicrobial activity by inhibiting glutamine synthetase and ornithine carbamoyltransferase, respectively. Genetic studies have revealed the molecular mechanisms responsible for the biosynthesis of these toxins. Coronatine biosynthesis requires the coordinated action of polyketide synthases and peptide synthases to assemble fragments of coronafacic acid and

coronamic acid, respectively. Tabtoxin is produced through modification of lysine biosynthesis intermediates, while the biosynthesis of syringomycin, syringopeptin, and phaseolotoxin depends on peptide synthases. The activation of phytotoxin synthesis is regulated by various environmental factors, including plant signaling molecules and temperature (Bender et al., 1999).

Table 13
Degradative enzymes of phytopathogenic bacteria

No.	Enzyme type	Plant target	Mechanism of action	Examples of bacteria and diseases
1	Pectinases (PL)	cell wall pectin	breakdown of polygalacturonic acid	*Pectobacterium carotovorum* – potato soft rot
2	Pectate lyases (Pel)	pectate	degradation by β-elimination	*Dickeya dianthicola* – potato blackleg
3	Cellulases	cellulose	hydrolysis of β-1,4-glucosidic bonds	*Clavibacter michiganensis* – bacterial canker of tomatoes
4	Hemicellulases	xyloglucans, arabinans	destruction of cell wall polymers	*Pectobacterium atrosepticum* – soft rot, blackleg
5	Proteases	PR proteins, membrane proteins	breakdown of protective proteins	*Ralstonia solanacearum* – bacterial wilt of tomatoes
6	Phospholipases / Lipases	cell membranes	plasmalemma lysis, cell rupture	*Xanthomonas campestris* – black rot of cabbage

Table 14
Phytotoxins of phytopathogenic bacteria

No.	Toxin name	Target / effect	Mechanism of action	Examples of bacteria and diseases
1	Coronatine	stomata, chloroplasts	mimics jasmonic acid, causing necrosis	*Pseudomonas syringae* pv. tomato – bacterial speck of tomatoes
2	Phaseolotoxin	mitochondria	inhibits ATP synthase	*Pseudomonas syringae* pv. *Phaseolicola* – halo blight of beans
3	Tabtofen	cell membranes	membrane lysis	*Xanthomonas campestris* – black rot of cabbage
4	Rizotoxin	aminoacyl-tRNA synthetase	blocks protein synthesis	*Pseudomonas andropogonis* – sorghum leaf spot
5	Serinol	growth regulators	disrupts amino acid metabolism	*Pseudomonas fuscovaginae* – sheath rot of rice
6	Glycoalkaloids (derivatives)	cell membranes	oxidative stress disrupts permeability	*Ralstonia solanacearum* – bacterial wilt of solanaceous plants

Pathogens actively interfere with the hormonal physiology of their hosts to maximize virulence, overcome plant defense mechanisms, and manipulate internal signaling pathways. Many phytotoxic molecules produced by pathogenic microbes share both structural and functional similarities with auxin and other plant hormones. A prominent example is the polyketide toxin coronatine, which, in addition to inducing stomatal opening, promotes apoplastic bacterial proliferation and exacerbates disease symptom development. Coronatine is recognized by the plant receptor complex COI1/JAZ and stimulates jasmonic acid (JA) signaling in the plant, which in turn suppresses salicylic acid (SA)-mediated defenses. Many biological effects of coronatine closely resemble those of jasmonates, including stimulation of chlorosis, anthocyanin production, root growth inhibition, and induction of various JA-responsive genes. Coronatine's activity is also linked to several virulence phenotypes independent of JA/SA antagonism. It contributes to chlorosis and leaf yellowing by stimulating the plant *STAYGREEN* gene and induces necrotic cell death by increasing reactive oxygen species production (Xin & He, 2013).

Pseudomonas syringae is best characterized as a locally infecting hemibiotrophic pathogen. It primarily infects the aboveground parts of plants, such as leaves and fruits. The infection is often confined to only a few millimeters around the initial infection sites and does not typically spread to other parts of the plant. In a successful disease cycle, *P. syringae* strains generally undergo two spatially and temporally linked phases of their life cycle: an initial epiphytic phase after landing on the surface of a healthy plant, and an endophytic phase within the apoplastic space following penetration through natural openings or accidental wounds. Under favorable environmental conditions, such as heavy rain, high humidity, and moderate temperatures, *P. syringae* can proliferate aggressively within a susceptible host plant. The most intense bacterial multiplication occurs without visible host cell death. However, at the later stages of pathogenesis (often after the bacterial population has nearly peaked in infected tissues), host cells begin to die, and the infected tissues show significant necrosis. This mode of pathogenesis differs from strictly biotrophic pathogens, which derive nutrients from living host cells without causing their death, and from strictly necrotrophic pathogens, which kill host cells early in infection as their primary nutrient acquisition strategy (Ishiga et al., 2012).

Factors limiting the aggressive proliferation of *P. syringae* during PTI (PAMP-triggered immunity) or ETI (effector-triggered immunity) remain not fully elucidated, but are generally thought to involve a complex of defense responses. These include callose deposition to reinforce cell walls at the infection site, synthesis of antibacterial phytoalexins, generation of reactive oxygen species (ROS), apoplastic pH changes, and restriction of nutrient availability. Additionally, ETI is often accompanied by a hypersensitive response (HR) at the infection site, which involves programmed cell death. The accumulation of the defense hormone salicylic acid (SA) is critical for the full manifestation of both PTI and ETI at infection sites and surrounding tissues in response to biotrophic and hemibiotrophic pathogens. Local immune signals at infection sites can subsequently lead to the induction of systemic resistance against *P. syringae* throughout the plant, an effect known as systemic acquired resistance (SAR). SA accumulation is a central factor in the development of SAR. In contrast to SA, the plant hormone jasmonic acid (JA), best known for its role in defense against insect herbivores and necrotrophic pathogens, generally promotes *P. syringae* infection due to the antagonistic interaction between the SA and JA signaling pathways (Xin & He, 2013).

Two-tiered plant defense system (PTI and ETI) against pathogenic bacteria

Plants generally defend themselves against microbial attacks through a two-tiered immune response system: PTI (PAMP-triggered immunity) and ETI (effector-triggered immunity). PTI serves as one of the first lines of defense and is activated upon recognition of conserved microbial molecules (PAMPs) by pattern recognition receptors (PRRs) located on the plant cell surface. PTI responses include the production of reactive oxygen species (ROS), callose deposition in the cell wall, stomatal closure, activation of defense-related genes, and limitation of survival and proliferation of non-adapted bacteria. PTI may also reduce the efficiency of type III secretion system (T3SS)-dependent translocation of effector proteins, indicating active interference by the plant with T3SS gene expression or the protein delivery process itself (Zipfel et al., 2014). PAMPs are evolutionarily conserved microbial molecules such as flagellin, bacterial elongation factor Tu (EF-Tu), lipopolysaccharides, peptidoglycan, chitin, or oligosaccharides derived from cell walls, which are essential for pathogen viability or adaptation.

PTI defenses can be overcome by translocated type III effector proteins that interfere with PTI signaling components and promote bacterial virulence. However, these effector proteins, or their activity, may be recognized by the second layer of defense ETI, which is activated by products of plant resistance genes (R-genes) upon detection of specific effector proteins (Cui et al., 2015) (Table 15).

Type III effectors: tools for inducing and suppressing plant defense responses

Depending on the final destination of the T3S substrates, protein transport into the extracellular space is called "secretion," whereas transport into the cytosol of the eukaryotic cell is referred to as "translocation".

Table 15
Components of plant immune response to pathogenic bacteria

Immunity level	Molecule / complex type	Examples	Function / role	Suppression by bacterial effectors
PTI (PAMP-triggered immunity)	PAMPs	flg22 (flagellin), elf18 (EF-Tu), lipopolysaccharides, chitin	recognition of conserved microbial molecules	–
	PRRs (pattern recognition receptors)	FLS2, EFR, CERK1	binding PAMPs, signal initiation	FLS2 inhibited by AvrPto; degradation via AvrPtoB
	Co-receptors	BAK1 (BRI1-associated kinase 1)	complex formation with PRRs	inhibited by HopF2, AvrPphB, AvrAC
	Cytosolic kinases	BIK1 (botrytis-induced kinase 1)	phosphorylation of RBOHD, MAPK activation	inhibited by HopAO1, AvrAC
	MAPK cascades	MKK5, MPK3/6	signal transduction to the nucleus	inactivated by HopAI1, HopF2
	Ion channels / ROS production	RBOHD	production of reactive oxygen species (oxidative burst)	partially suppressed
	G-proteins	XLG2, AGB1, AGG1/2	regulation of BIK1 and RBOHD stability	not well defined
	Hormonal pathways	SA, JA	activation of programmed cell death (SA) or defense against necrotrophs (JA)	effectors can interfere
ETI (effector-triggered immunity)	R proteins (NLR)	RPM1, RPS2, SUMM2	effector recognition, activation of hypersensitive response (HR)	some effectors evade recognition
	Type III effectors	AvrPto, AvrPtoB, HopAO1, AvrAC, HopF2, HopAI1, AvrB	suppression of PTI/ETI, inhibition of PRRs, MAPKs, protein degradation	some are recognized by R proteins, triggering ETI

Notes: PAMP – pathogen-associated molecular patterns; PRR – pattern recognition receptors, often RLK/RLP types; R proteins – mostly NLR receptors (CNL/TNL); ROS – reactive oxygen species, one of the earliest signals in PTI; ETI is usually stronger and leads to PCD (programmed cell death).

Phytopathogenic bacteria translocate effector proteins through the Type III Secretion System (T3SS) directly into the cytoplasm of plant cells (Büttner, 2016). In resistant plants, specific effectors are recognized directly or indirectly by corresponding plant R proteins or activate R-genes, leading to the induction of strong ETI defense responses. Some Type III effectors can suppress both PTI and ETI. Translocated bacterial Type III effectors interfere with cellular PTI defense responses by targeting cytoskeleton organization, MAPK signaling cascades, gene expression, proteasome-dependent protein degradation, and hormone signaling pathways.

PTI defense responses are triggered upon recognition of bacterial PAMPs by pattern recognition receptors (PRRs). These responses not only limit pathogen survival but may also interfere with T3S-mediated effector protein delivery (Böhm et al., 2014). The perception of microbe-associated molecular patterns (PAMPs) is mediated by pattern recognition receptors (PRRs), which typically consist of three functional parts: an extracellular PAMP-binding domain, a transmembrane domain, and an intracellular kinase domain. Upon binding to the corresponding PAMP, PRRs initiate the activation of downstream signaling components such as receptor-like cytoplasmic kinases (RLCKs) and mitogen-activated protein kinase (MAPK) cascades. Among the well-studied plant PRRs are EFR (EF-Tu receptor), the chitin receptor CERK1 (chitin elicitor receptor kinase 1), and FLS2 (flagellin-sensitive 2), a member of the receptor-like kinase (RLK) family responsible for detecting flagellin. Common PTI elicitors used to activate FLS2 and EFR are flagellin-derived peptides (flg22) and EF-Tu-derived peptides (elf18), respectively (Wu et al., 2014).

Upon binding of flg22, the receptor FLS2 forms a complex with the membrane-associated RLK BAK1 (BRI1-associated receptor kinase 1), which also interacts with the RLCK BIK1 (*Botrytis*-induced kinase 1). BAK1 phosphorylates BIK1, which in turn phosphorylates both FLS2 and BAK1, then dissociates from the FLS2-BAK1 complex and activates downstream signaling pathways, including MAPK cascades. BIK1 also phosphorylates the NADPH oxidase RBOHD (respiratory burst oxidase homolog D), promoting the production of reactive oxygen species (ROS). In addition to BIK1, FLS2-mediated signaling involves heterotrimeric G-proteins. The Gα subunit XLG2, Gβ subunit AGB1, and Gγ subunit AGG1/2 from *Arabidopsis* suppress the proteasome-dependent degradation of BIK1. BIK1 interacts with and phosphorylates XLG2; after flg22 perception, XLG2 dissociates from BIK1, interacts with RBOHD, and contributes to the regulation of the oxidative burst. ROS can act as direct toxins against invading pathogens, participate in signaling during defense activation, trigger autophagy to remove pathogens or metabolically altered cytoplasmic content, and isolate damaged mitochondria, generating superoxide anions to maintain cellular and energy homeostasis. They also deactivate reactive oxygen radicals generated under stress. However, excessive ROS or nitrogen species accumulation or overactive autophagy may result in cell death (Kadota et al., 2014). SA-dependent responses are associated with massive ROS accumulation and result in programmed cell death (PCD), providing an effective defense against biotrophic pathogens. In contrast, necrotrophic pathogens and herbivorous insects are effectively countered by JA-dependent signaling, which triggers the secretion of phytoalexins such as flavonoids and terpenes that act as direct toxins to the pathogen (Doehlemann & Hemetsberger, 2013).

Given their inhibitory effect on bacterial pathogens, successful pathogens have evolved strategies to counteract PTI defense responses in order to establish themselves within plant tissues. Several type III effectors, such as AvrPto, AvrPtoB, and HopAO1 (Hrp-dependent outer protein AO1), specifically target PRRs and associated proteins. Effector proteins actively disrupt the functions of PRRs and MAPK cascades. These virulence-crucial proteins are capable of interacting with elements of the plant immune system, such as FLS2, BAK1, BIK1, and EFR. For instance, the effector AvrPto demonstrates the capacity to suppress the kinase activity of FLS2 and EFR receptors. Concurrently, the E3 ubiquitin ligase AvrPtoB initiates the degradation of PRRs, including FLS2 and CERK1. The tyrosine phosphatase HopAO1, for its part, impedes the phosphorylation of the EFR receptor. Additional effectors produced by *Pseudomonas syringae* and *Xanthomonas campestris* pv. *campestris*, such as the mono-ADP-ribosyltransferase (mADP-RT) HopF2, the cysteine protease AvrPphB, and the uridyltransferase AvrAC, specifically target the PRR-associated proteins BAK1 and BIK1. A multitude of these effectors also modify PTI responses by disrupting the function of downstream PTI-associated MAPK signaling cascades (Zhou et al., 2014).

PRR-mediated immune responses typically involve the initiation of MAPK cascades. These signaling pathways are appealing targets for type III effectors, as they play a central role in integrating defense signals into a diverse array of cellular reactions. Effectors that interfere with MAPK signaling and SUMM2-mediated defenses include HopF2, HopAI1, and AvrB from *P. syringae*. For example, the ADP-RT HopF2 inactivates MAP2K MKK5, while HopAI1 suppresses overall MAPK activity. Interestingly, AvrB, conversely, stimulates the activation of MAPK MPK4. Consequently, effector proteins like AvrB can exert contrasting effects on MAPK signaling cascades, depending on the specific cellular context (Zhang et al., 2012).

MAPK signaling is initiated by MAP kinase kinase kinases (also known as MAP3Ks or MEKKs), which are directly or indirectly activated by receptor proteins, including PRRs. MAP3Ks are serine/threonine kinases that activate MAP2Ks (also referred to as MEKs) through phosphorylation. Subsequently, MAP2Ks phosphorylate

threonine and/or tyrosine residues on MAPKs, leading to their activation. Among the well-characterized plant MAPKs involved in immune responses are MPK3, MPK4, and MPK6. MPK3 and MPK6 are part of a signaling cascade activated by MAP3K MEKK1 and two MAP2Ks – MKK4 and MKK5. A second major signaling cascade encompasses MAP3K MEKK1, MAP2Ks MKK1 and MKK2, and MPK4. Known substrates of MPK4 include its interacting partners RIN4, the MAP3K MEKK2 (also known as SUMM1), and MKS1 (MPK4 substrate 1), which forms a nuclear complex with MPK4 and the transcription factor WRKY33. Phosphorylation of MKS1 by MPK4 leads to the release of WRKY33, which activates the expression of its target genes and initiates PTI responses. MAPK activation directly or indirectly triggers the release of transcription factors (TFs), which promote the expression of defense-related genes (Kong et al., 2012).

The eukaryotic 26S proteasome, responsible for degrading superfluous or defective proteins through proteolysis into short peptides, holds a central role in numerous cellular processes, including hormone signaling and defense responses, and represents a key virulence target for several type III effectors. Certain effectors (e.g., AvrPtoB, HopM1, XopL, and GALA proteins) bind to E3 ubiquitin ligases or operate as E3 ligases themselves, leveraging the proteasomal pathway to degrade specific plant target proteins. Other effectors, such as XopD from *Xanthomonas* spp., can indirectly destabilize plant proteins by cleaving the small ubiquitin-like modifier (SUMO). SUMO is structurally analogous to ubiquitin and can reversibly modify proteins, thereby altering their localization, stability, or activity. In contrast to effectors that promote protein degradation, type III effectors from the predicted cysteine protease or YopJ-like acetyltransferase family (YopJ: *Yersinia* outer protein J), such as XopJ and HopZ4, inhibit proteasome activity. A comparable inhibitory effect is achieved by the bacterial tripeptide-derived toxin syringolin, produced by specific strains of *Pseudomonas syringae* (Singer et al., 2013).

Signaling mediated by various plant hormones, such as auxin, jasmonic acid (JA), ethylene (ET), and salicylic acid (SA), involves proteasome-mediated degradation of transcriptional repressors, leading to the liberation or activation of transcription factors and subsequent hormone-induced gene expression. Research in the model plant *Arabidopsis thaliana* has demonstrated that JA, SA, and ET function as pivotal regulators of plant defense against microbial pathogens. While SA is typically associated with resistance to biotrophic and hemibiotrophic pathogens, including pathogenic bacteria, JA and ET often act antagonistically to SA and foster resistance against necrotrophic pathogens. Due to this antagonistic interplay, the activation of JA-dependent defenses frequently suppresses SA-induced signaling pathways, which are commonly triggered during biotrophic pathogen infections. SA-dependent responses are critical for plant resistance to biotrophic pathogens, whereas JA-dependent defense is activated in response to necrotrophs. SA and JA signaling pathways frequently operate antagonistically and possess the capacity to mutually suppress one another (Kazan & Lyons, 2014).

Type III effectors from biotrophic or hemibiotrophic pathogens often manipulate this hormonal crosstalk by activating JA signaling and repressing SA-mediated defenses through translocated type III effector proteins (Gimenez-Ibanez & Solano, 2013). SA-dependent defense responses rely on the pivotal regulatory protein NPR1 (nonexpressor of PR genes 1), which persists in an inactive oligomeric state in the absence of salicylic acid (SA). Upon SA accumulation, NPR1 monomerizes and translocates into the nucleus, where it engages with transcription factors (such as TGAs) to activate them, thereby initiating the expression of SA-responsive genes, including pathogenesis-related (PR) genes. Type III effectors HopD1 and HopI1 from *P. syringae* diminish SA levels, whereas the bacterial toxin syringolin and the effector XopJ from *Xanthomonas campestris* pv. *vesicatoria* impede NPR1 degradation. The jasmonic acid (JA) signaling pathway encompasses JAZ (Jasmonate ZIM-domain) proteins and the SCFCOI1 complex (Skp1-Cullin-F-box protein COI1). The bacterial toxin coronatine and type III effectors such as AvrB, HopX1, and HopZ1 from *P. syringae* facilitate the degradation of JAZ repressors, thereby stimulating JA-responsive gene expression (Gimenez-Ibanez et al., 2014).

Pathogenic bacteria generate phytohormone mimics to disrupt host hormone signaling pathways. A notable instance is the phytotoxin coronatine, synthesized by various *P. syringae* pathovars, which structurally and functionally emulates the bioactive form of JA-jasmonoyl-isoleucine (JA-Ile). Beyond producing hormone mimics, phytopathogenic bacteria deliver type III effectors to manipulate plant hormone signaling. Effectors targeting JA signaling include the cysteine protease HopX1, the acetyltransferase HopZ1a, and AvrB from *P. syringae*. Furthermore, the cysteine protease AvrRpt2 from *P. syringae* interferes with auxin signaling, while XopD from *X. campestris* pv. *campestris* modulates gibberellic acid (GA) and ethylene (ET) signaling pathways (Zhou et al., 2015). One of the effective strategies employed by type III effectors to disrupt plant cellular processes involves the manipulation of gene expression at either the transcriptional or post-transcriptional level. Effector proteins that are directly imported into the nucleus and bind either to DNA or to components of the host transcriptional machinery include the TAL (Transcription Activator-Like) effectors from *Xanthomonas* spp. and the HsvG effector from *Pantoea agglomerans*. Type III effectors that specifically target plant transcription factors and RNA-binding proteins include XopD from Xanthomonas spp., PopP2 from *Ralstonia solanacearum*, and HopU1, HopD1, and HopM1 from *P. syringae* (Yang et al., 2014).

The monumental discovery of the TAL-DNA binding code inaugurated a new era in genome engineering, leading to the conception of diverse genome-editing tools (e.g., TALENs, or TAL effector nucleases) that enable precise targeting of DNA-modifying enzymes using modular TAL repeats as customizable DNA-binding domains (Mahfouz et al., 2014). The precise mechanisms by which TAL effectors activate the transcription of host genes are not yet fully elucidated. Interaction studies suggest that TAL effectors not only bind DNA but also form associations with RNA polymerase II and with negative regulators of RNA polymerases II and III, respectively. Consequently, TAL effectors not only function as direct DNA-binding proteins but also engage with components of the plant transcriptional machinery to instigate the expression of their target genes. The plant cytoskeleton, primarily composed of actin filaments and microtubules, plays an indispensable role in numerous cellular processes, including cell division and growth, organelle movement, vesicular trafficking, endocytosis, stomatal regulation, and plant defense responses against pathogens. The reorganization of actin filaments – specifically, their enhanced bundling and increased density – constitutes a pivotal component of PAMP-triggered immunity (PTI). The translocation of bacterial type III effector proteins (e.g., HopW1, HopG1) into the cytoplasm results in the depolymerization or disruption of actin filament organization. Infiltration of latrunculin B, an inhibitor of actin polymerization, escalates the susceptibility of *Arabidopsis* leaves to bacterial infection and promotes the augmented growth of *P. syringae* pv. *tomato*. The actin network also contributes to effector-triggered immunity (ETI). For example, actin-depolymerizing factor 4 (ADF4), which facilitates the severing and disassembly of F-actin, is indispensable for the expression of the resistance gene RPS5 (Henty-Ridilla et al., 2014).

In addition to actin filaments, microtubules are involved in plant defense against bacterial infection. Treatment of *Arabidopsis* plants with oryzalin, a microtubule-disrupting agent, enhances the growth of *P. syringae* pv. *tomato*, but not of a T3S-deficient mutant, suggesting that microtubules are direct targets of bacterial effectors. Type III effector proteins from *P. syringae* such as HopE1 and members of the YopJ family, including HopZ1a interfere with microtubule formation and stability, thereby promoting bacterial virulence (Lee et al., 2012).

The use of novel compounds and biocontrol agents in managing bacterial plant diseases

There is a limited number of effective treatment options for bacterial plant diseases, such as bacterial wilt caused by *Ralstonia solanacearum* and bacterial speck of tomato caused by *P. syringae* pv. *tomato*. Traditionally, management strategies have relied on antibiotics (e.g., streptomycin, oxytetracycline, gentamicin, oxolinic acid, kasugamycin) and copper-based compounds. However, the use of

copper compounds is currently restricted in many countries due to environmental concerns, while widespread antibiotic application has led to the emergence and dissemination of resistant bacterial strains.

There is an urgent need to develop and implement new strategies aimed at disarming phytopathogenic bacteria by inhibiting their virulence factors, rather than eliminating them outright. In contrast to traditional bactericidal agents, virulence inhibitors do not kill the pathogen but rather suppress its ability to cause disease, which theoretically slows down the development of antimicrobial resistance (Puigvert et al., 2019). This approach aligns with the concept that enhancing the plant's innate immune responses rather than directly targeting the pathogen can offer a more sustainable and resilient solution to disease management. As highlighted by Khablak & Spychak (2024), modulation of host defense mechanisms may provide effective protection, allowing plants to counteract infection through activation of endogenous resistance pathways (Table 16).

The induction of systemic acquired resistance (SAR) or induced systemic resistance (ISR) in plants through the application of chemical inducers such as the commercially available compound acibenzolar-S-methyl (ASM), a synthetic analog of salicylic acid, represents a major success in translating fundamental plant immunity research into practical crop protection strategies. This "priming" approach, involving foliar application of ASM to prepare plants for potential pathogen attack, has been successfully employed to control bacterial canker of tomato, tomato bacterial wilt and blight, as well as citrus canker on young grapefruit trees. Although ASM alone is generally insufficient to achieve full disease control, its integration into broader plant protection programs has been shown to significantly improve efficacy, enabling reductions in the use of conventional agrochemicals such as copper-based products and antibiotics (Li et al., 2016).

Table 16

Modern strategies for the control of bacterial plant diseases: mechanisms of action and examples of control agents

Strategy	Type of agent / approach	Mode of action	Examples of compounds / agents	Target pathogens / diseases
Traditional chemical control	antibiotics	inhibit growth or kill bacterial cells	streptomycin, gentamicin, oxytetracycline, kasugamycin	*Pseudomonas syringae* – bacterial speck, *Ralstonia solanacearum* – bacterial wilt
	copper-based compounds	antiseptic action, destabilization of pathogen membranes	copper hydroxide, copper oxychloride	*Xanthomonas* spp. – bacterial spot, *Clavibacter michiganensis* – bacterial canker
Virulence inhibition	T3SS inhibitors	block T3SS function, suppress effector translocation	synthetic HrpB inhibitors, compounds targeting the Hrp pilus	*P. syringae*, *Xanthomonas* spp., *R. solanacearum* – various bacterial diseases
Plant defense induction (SAR/ISR)	synthetic elicitors	mimic salicylic acid, activate SAR pathways	acibenzolar-S-methyl (ASM), Benzothiadiazole (BTH)	*P. syringae* – leaf spot, *X. campestris* – black rot, *R. solanacearum* – wilt
	PGPR / PGPF microorganisms	induce ISR via jasmonic acid and ethylene signaling	*Bacillus* spp., *Pseudomonas* spp., *Trichoderma* spp.	broad-spectrum bacterial diseases: wilts, leaf spots, soft rots
Use of natural compounds	phenolic compounds	modulate T3SS gene expression, trigger host defense signaling	*o*-Coumaric acid (OCA), *t*-Cinnamic acid (TCA)	*Dickeya dadantii* – soft rot, *Ralstonia* spp. – wilt
Inorganic elements	silicon	reinforce cell walls, induce defense-related signaling	SiO_2, silicates	*R. solanacearum* – wilt, *Xanthomonas* spp. – spots, rots
Biological control agents	antagonistic bacteria	competition, production of antimicrobial metabolites	*Bacillus subtilis*, *Pseudomonas fluorescens*, *Streptomyces* spp.	*P. syringae* – speck, *Clavibacter michiganensis* – canker
Genetic approaches (future)	effector / T3SS target inhibition	repress *hrpB* transcription/effector gene expression	RNA-based inhibitors, CRISPR-editing (experimental)	*R. solanacearum*, *P. syringae* – wilt, speck

The use of ISR (Induced Systemic Resistance) involves the activation of plant defense mechanisms through the action of specific rhizosphere bacteria and fungi that promote plant growth (PGPR/PGPF), including *Bacillus* spp., *Pseudomonas* spp., *Trichoderma* spp., and others. This type of resistance is mediated by hormone-dependent signaling, often involving jasmonic acid (JA) and ethylene (ET). ISR is an effective strategy in controlling various bacterial pathogens, including *P. syringae*, *X. oryzae* pv., and *R. solanacearum* (Pieterse et al., 2014).

Other strategies aimed at enhancing plant defense against bacterial pathogens such as *R. solanacearum* include the application of inorganic elements, particularly silicon. Silicon contributes to the formation of reinforced structural barriers against pathogen invasion and also induces resistance through hormone-regulated signaling pathways similar to those involved in ISR (Wang et al., 2022).

An effective virulence strategy of both plant and animal pathogens is the delivery of effector proteins or DNA into the host cell to overcome its defense systems. Phytopathogenic bacteria possess three main types of secretion systems involved in this process. The Type II secretion system, identified in members of the genus *Erwinia*, is used to secrete cell wall-degrading enzymes that cause soft rot, while the Type IV secretion system facilitates the transfer of proteins and DNA in *Agrobacterium* species. The third type, the Type III secretion system (T3SS), characteristic of *Pseudomonas* pathovars and many other gram-negative bacteria, secretes effector proteins directly into plant cells. T3SS is a multi-protein complex phylogenetically related to the bacterial flagellum. In T3SS, bacteria located in the apoplastic space form a specialized structure, the pilus (or Hrp-pilus), to inject effector proteins into the plant cell cytoplasm (Grennan, 2006).

The Type III secretion system (T3S) functions as a molecular "syringe" or needle-like apparatus that allows pathogens to translocate effector proteins directly from the bacterial cytoplasm into the host cell cytoplasm. This translocation suppresses host defense responses, with part of the T3SS (the translocon complex) embedded as a pore-forming complex in the plant plasma membrane. These secreted effectors inhibit the host immune response and play a crucial role during bacterial infection. Plant pathogenic bacteria typically possess a large arsenal of diverse effector proteins. Genome sequence analyses of *P. syringae* strains have revealed 94 effector families, with individual strains containing between 9 and 39 effectors. *R. solanacearum* strains harbor 60 to 75 effectors belonging to 57 families, including 32 "core" effectors present in most strains. In *Xanthomonas* spp., the core effector set is limited to only 3 out of 32 known effectors, as recently identified by comparative genome sequence analysis (Büttner, 2016).

Type III secretion systems (T3SS) are found not only in plant and animal pathogenic bacteria but also in certain non-pathogenic and symbiotic bacterial species, specifically in members of the genus *Rhizobium*. This indicates that the presence of T3SS is not an exclusive characteristic associated with pathogenicity. Phylogenetic analysis demonstrates that the T3SS of phytopathogenic bacteria can be grouped into distinct families. These include the Hrp1 family (hypersensitive response and pathogenicity 1), which is characteristic of *P. syringae* and *Erwinia* species. The Hrp2 T3SS systems are identified in *R. solanacearum*, *Xanthomonas* spp., *Acidovorax*, and *Burkholderia*. In addition to the Hrp1 T3SS, some *P. syringae* strains also possess a rhizobium-like T3SS system designated as Hrp3 (Gazi et al., 2012).

In plant pathogenic bacteria, T3SS is encoded by hrp genes (hypersensitive response and pathogenicity), named for their key role in inducing the hypersensitive response (HR) as well as pathogenicity. HR is a form of programmed cell death that occurs locally in plants upon pathogen recognition at the infection site and serves as an effective defense mechanism. In the model phytopathogen *R. solanacearum*, the regulator HrpB directly activates the transcription of genes

encoding the structural components of T3SS and associated effectors. Among the genes controlled by HrpB is *hrpY*, which encodes a major structural component of the T3SS Hrp-pilus. Since T3SS is essential for the pathogenesis of many gram-negative bacterial pathogens, this system is an attractive target for the development of antimicrobial compounds aimed at inhibiting pathogenicity within novel strategies for controlling bacterial plant diseases (Puigvert et al., 2019) (Table 17).

Table 17
Key components of the Type III Secretion System (T3SS) in phytopathogenic bacteria, targets for inhibitors, and crop hosts

T3SS component	Function	Example proteins	Inhibitor targets / type	Pathogen / species (disease)	Target crop	Potential inhibition effect
Transcription regulators	initiation of *T3SS* gene expression	HrpL, HrpB	INP1750, flavonoids	*Pseudomonas syringae* (bacterial spot), *Ralstonia solanacearum* (bacterial wilt)	tomato, pepper, potato	blocking T3SS cascade activation
Basal structure	anchoring in the bacterial membrane, the secretion channel	HrcC, HrcJ	salicylates, phenolic compounds	*Xanthomonas campestris* (black rot of cabbage), *Erwinia amylovora* (fire blight of apple)	cabbage, apple	disruption of the secretion apparatus assembly
Pilus / Needle apparatus	effector transport through the cell wall	HrpA, HrpZ	cinnamic acid, retinol-like molecules	*P. syringa*e pv. tomato (tomato spot), *X. vesicatoria* (pepper spot)	tomato, pepper	blocking effector penetration into the plant cell
Chaperones	stabilizing effectors before secretion	HpaB, SicA	small molecules disrupting the chaperone-effector complex	Salmonella-like T3SS in *P. syringae* (bacterial spot)	tomato	destabilization of effectors, reduced virulence
Energy components	ATP-dependent energy for protein export	HrcN, InvC	DNP, ATP synthase inhibitors	*Ralstonia solanacearum* (bacterial wilt), *P. syringae* (leaf spot)	potato, eggplant	blocking effector transport
Effectors	molecules suppressing plant immunity	AvrPto, AvrBs2, HopM1	RNA inhibitors, protein-protein interaction blockers	*P. syringa*e (spot), *X. campestris* (black rot), *X. vesicatoria* (pepper spot)	tomato, pepper, cabbage	preventing pathogen-induced immune suppression
Signaling molecules	activation of T3SS in response to plant signals	hrp-inducing signals	phenolics blocking HRP activation	*Pseudomonas* spp. (spot), *Xanthomonas* spp. (bacterial diseases)	cereals, vegetable crops	reducing T3SS activation upon plant contact
Intermediate components	control of the timing and amount of protein secretion	HpaC, YscP	allosteric inhibitors	*Ralstonia* (wilt), *Erwinia* (fire blight), *Pseudomonas* (spot)	potato, apple, eggplant	disruption of effector secretion timing

Two plant phenolic compounds, o-coumaric acid (OCA) and t-cinnamic acid (TCA), have been identified as inducers of T3S gene expression in *Dickeya dadantii*. OCA and TCA are biosynthetic precursors of the plant defense hormone salicylic acid (SA) and also play certain roles in plant protection. This finding suggests that plant phenolic compounds may represent a promising source for identifying potential T3S inhibitors (Yang et al., 2008). A collection of phenolic compounds was screened for their ability to inhibit the expression of the hrpA gene, which encodes the major structural component of the Type III secretion (T3S) pilus in *D. dadantii*. This approach led to the identification of a new phenolic compound, p-coumaric acid (PCA), as a T3S inhibitor. PCA is an intermediate in the biosynthesis pathway of phenylpropanoids. Phenylpropanoids are a group of secondary metabolites produced by plants, functioning as protective molecules in response to microbial attack (Li et al., 2009).

The identification of PCA as a potential T3S inhibitor was further leveraged to enhance inhibitory efficacy through chemical modification of the compound. Subsequent screening of a PCA derivative library led to the discovery of trans-4-hydroxycinnamohydroxamic acid (TS103), which exhibited an eightfold higher inhibitory activity against structural and regulatory T3S genes compared to PCA. PCA derivatives, including the phenolic T3S inhibitors trans-4-phenylcinnamic acid and trans-3-fluorocinnamohydroxamic acid, reduced fire blight symptoms in apple blossoms caused by *E. amylovora* with effectiveness comparable to kasugamycin (Li et al., 2015). Other studies have demonstrated that salicylidene acylhydrazides (e.g., SAH1–3) are potent inhibitors of the T3S system in *R. solanacearum*. These SAH-type compounds suppress T3SS gene expression and disrupt bacterial proliferation within plants (Puigvert et al., 2019).

The formation of biofilms provides bacteria with robust protection against adverse environmental conditions, the action of antimicrobial agents, and host defense mechanisms. This process represents a crucial virulence factor for numerous phytopathogenic bacteria. The development of biofilm formation inhibitors for controlling bacterial infections has become a promising research area. Biofilm development generally consists of three main stages: surface attachment, biofilm maturation, and biofilm dispersion (Kostakioti et al., 2013). Currently, most developed anti-biofilm inhibitors, such as d-amino acids and indole derivatives, target the prevention of early biofilm formation, leading to reduced disease symptoms caused by animal and plant pathogens and increased bacterial sensitivity to conventional antibiotics and copper-based compounds. Promising compounds that inhibit biofilm formation in bacterial plant pathogens include 2-aminoimidazole (2AI), 3-indoleacetonitrile, D-leucine, and N-acetylcysteine (Worthington et al., 2012; Sundin et al., 2016). The development of effective biofilm inhibitors could represent a significant breakthrough, particularly in combating foliar pathogens, as biofilm formation can markedly affect the efficacy of bactericides. Biofilm inhibitors do not necessarily have to be developed as standalone products but could potentially be used effectively as adjuvants or components of tank mixes to enhance the efficacy of existing bactericides (Nadar et al., 2022) (Table 18).

Table 18
Promising chemical inhibitors of bacterial virulence factors

Chemical compound	Physiological effect	Reference
p-Coumaric acid (PCA)	T3SS inhibitor	Li et al. (2009)
o-Coumaric acid (OCA)	T3SS inducer/inhibitor (context-dependent)	Yang et al. (2008)
t-Cinnamic acid (TCA)	T3SS inducer/inhibitor (context-dependent)	Yang et al. (2008)
Acibenzolar-S-methyl (ASM, synthetic SA analog)	Inducer of systemic acquired resistance (SAR)	Li et al. (2016)
Silicon	Structural barrier formation induces ISR/SAR	Wang et al. (2022)
trans-4-Hydroxycinnamohydroxamic acid (TS103)	T3SS inhibitor	Li et al. (2015)
Salicylidene acylhydrazides (e.g., SAH1–3)	T3SS inhibitor	Puigvert et al. (2019)
trans-4-Phenylcinnamic acid and trans-3-Fluorocinnamohydroxamic acid	T3SS inhibitors	Li et al. (2015)
D-amino acids and indole derivatives	Biofilm formation inhibitors	Worthington et al. (2012); Sundin et al. (2016)
2-Aminoimidazole (2AI), 3-indoleacetonitrile, D-leucine, N-acetylcysteine	Bacterial antibiofilm inhibitors	Worthington et al. (2012); Sundin et al. (2016)

Conclusions

An optimal and environmentally sustainable strategy for managing plant diseases, including bacterial infections, should focus on targeted manipulation and enhancement of the host plant's defense mechanisms. Pathogenic bacteria translocate numerous effector proteins into plant cells, primarily via the Type III secretion system (T3SS), to suppress innate plant immunity and interfere with key cellular defense processes such as proteasome-dependent protein degradation, phytohormone signaling, cytoskeleton dynamics, vesicular transport, and gene expression regulation. The growing body of research centered on the molecular biology and pathogenesis of phytopathogenic bacteria has led to a deeper understanding of Type III effector proteins and their molecular targets within plant cells. This knowledge broadens the horizon for identifying novel compounds and developing innovative strategies for the treatment and control of bacterial plant diseases based on the complex interactions between pathogen and host. Further studies in this field, particularly employing systems biology approaches and genome editing technologies, are critically important for creating effective and durable plant protection solutions.

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