Review

From Phytoalexins to Environmental Regulators: An Evolving Understanding of the Role of Coumarins in Regulating Quorum Sensing and Shaping the Soil Microbiome

Alexey S. Vasilchenko * and Aleksandr V. Iashnikov

Posted Date: 17 March 2026

doi: 10.20944/preprints202603.1208.v1

Keywords: quorum sensing; quorum quenching; coumarins; *Ralstonia solanacearum*; type III secretion system; rhizosphere microbiome; context-dependent effects

 doi:10.20944/preprints202603.1208.v1

Review

From Phytoalexins to Environmental Regulators: An Evolving Understanding of the Role of Coumarins in Regulating Quorum Sensing and Shaping the Soil Microbiome

Alexey S. Vasilchenko * and Aleksandr V. Iashnikov

Laboratory of Antimicrobial Resistance, Institute of Environmental and Agricultural Biology (X-BIO), University of Tyumen, Tyumen, Russia

* Correspondence: avasilchenko@gmail.com

Abstract

Quorum sensing (QS) governs microbial virulence, symbiosis, and critical ecosystem processes, such as rhizosphere nitrogen mineralization, positioning QS as both an attractive agricultural target and a potential point of ecological trade-off. This review synthesizes current evidence on coumarins, plant-derived secondary metabolites, that have evolved from being viewed as classical phytoalexins to being recognized as regulators of QS-mediated interaction in the plant-soil system. We synthesize current evidence on the multifaceted mechanisms of coumarin action, from direct antimicrobial effects to selective interference with bacterial QS systems and virulence. Key studies demonstrate that coumarins can suppress phytopathogens while sparing beneficial bacteria, thereby actively editing rhizosphere community composition. However, coumarin effects are profoundly context-dependent, with outcomes ranging from selective microbiome modulation to broad suppression or unintended pathogen enrichment - depending on concentration, plant host and native community structure. Beyond community assembly, coumarin-mediated QS disruption may have functional consequences for QS controlled ecosystem processes such as nutrient cycling. Revealing a potential ecological trade-off between pathogen defense and resource acquisition, this warrants further investigation. Coumarins are versatile compounds that plants use for sensing, communicating with, and actively shaping their microbial environments. Developing the ability to use them precisely and in an environmentally friendly manner represents a promising avenue for sustainable agriculture.

Keywords: quorum sensing; quorum quenching; coumarins; *Ralstonia solanacearum*; type III secretion system; rhizosphere microbiome; context-dependent effects

Introduction

Modern agriculture, even with advances in sustainable practices, grapples with persistent environmental challenges, including emerging microbial diseases, declining soil fertility, and loss of biodiversity. This necessitates a shift towards optimizing agrochemical use and harnessing the power of agricultural microbiology. A particularly promising avenue is targeted management of plant and soil microbiomes to enhance the resilience of agroecosystems. This approach encompasses the development of synthetic microbial consortia and novel delivery methods for beneficial microorganisms and their metabolites (Monica et al., 2025).

Quorum sensing (QS) is a fundamental regulatory mechanism of density-dependent intercellular communication in bacteria, mediated by diffusible chemical signals. First discovered in the 1970s (Nealson et al., 1979) and later termed in the 1990s (Fuqua et al., 1994). QS orchestrates collective behaviors such as virulence, biofilm formation, and symbiosis. Crucially, this cell-to-cell communication system represents a novel and attractive target for microbial control, distinct from

 doi:10.20944/preprints202603.1208.v1

conventional antibiotics. This has led to the "quorum quenching" strategy - interfering with QS signals to disarm pathogens without exerting lethal pressure, thereby potentially mitigating the rise of resistance (Zhu et al., 2023).

In agriculture, QS-targeting strategies have primarily focused on using QQ-active microbes (e.g., *Bacillus* spp. producing AiiA-like lactonases) or designing synthetic anti-QS consortia (Rosa et al., 2024). However, these approaches and much of the underlying QS biology are based on reductionist studies of pure cultures. A critical and understudied area is the ecological role of QS and its manipulation in complex soil and rhizosphere microbiomes (Zhang et al., 2026). Key unanswered questions include the taxonomic diversity of QS-active microorganisms in soils, the specifics of QS regulation in soil-dwelling fungi and bacteria, and the impact of QS modulators on the structure and function of these intricate microbial communities.

Low-molecular-weight quorum sensing inhibitors (QSIs) are produced by a remarkable diversity of life forms, from prokaryotes and fungi to higher plants and mammals (Kalia, 2013). Among these, plants stand out as a particularly rich source of structurally diverse QS-modulating compounds (Viswanathan et al., 2015). This chemical arsenal is believed to play a crucial role in plant-microbe interactions.

Released into the soil via root exudates and plant litter, these phytometabolites exert a profound influence on rhizosphere communities. QS itself governs a plethora of key ecological traits in bacteria and fungi, including biofilm formation, antibiotic production, motility, and stress survival. While these mechanisms are well-characterized in pure cultures, a critical knowledge gap persists. In natural soils, these processes are embedded within complex, cross-kingdom networks involving a vast diversity of culturable and unculturable microorganisms. The ecological consequences of QS modulation in such a context remain largely speculative.

Therefore, bridging this gap requires a model system that connects molecular QS interference with community-level outcomes. Coumarins emerge as appropriate model compounds for such an ecological inquiry. Coumarins are a large family of lactone derivatives of cinnamic acid, comprising over 1300 identified molecules that include simple coumarins, hydroxy-, furano-, and pyranocoumarins (Hoult et al., 1996). They are widely distributed in the plant kingdom. These plant-derived secondary metabolites possess well-documented QS-modulating activity and are naturally and continuously introduced into the soil environment. Studying coumarins offers a unique window into how plants naturally shape their microbial surroundings through chemical interference.

The aim of this review is to analyze current evidence on the impact of coumarins on soil microorganisms and QS-related interkingdom interaction. We will systematically examine the consequences of this interaction at two critical levels: (1) induction of systemic resistance in host plants and (2) modulation of the structure and functional activity of rhizosphere and soil microbial communities. This synthesis positions coumarins as not merely phytoanticipins but as pivotal ecological regulators within the soil-microbiome-plant continuum.

1. The Phenomenon of Quorum Sensing in Microbial World

1.1. Quorum Sensing in Bacteria

The QS phenomenon in bacteria is mediated by a wide range of chemical signals - autoinducers (AIs). The main classes of bacterial AIs include N-acylhomoserine lactones (AHLs), autoinducing peptides (AIPs), furanosyl derivatives (type AI-2), gamma-butyrolactones (GBLs), alkylquinolones (e.g., PQS in *Pseudomonas* spp.) and diffuse signaling factors (DSFs) (Majdura et al., 2023, Coolahan et al., 2025) (Table 1).

 doi:10.20944/preprints202603.1208.v1

Table 1. Interkingdom quorum sensing (QS) communication: bacterial, fungal, and plant participants in QS signal exchange.

QS communication participant	AI-class	Producers	Regulated processes	Relationship with plants	References
Symbiotic and pathogenic bacteria					
Bacillus spp.	AHL (3-oxo-C12-HSL)	No	Degradation of AHL (lactonase AiiA); detoxification; attenuation of pathogen virulence	Biocontrol (e.g. against *Erwinia carotovora*)	Dong et al., 2000; Barbey et al., 2013
Bacillus licheniformis	ComX pheromones	Yes		Inhibitory potential against the crop pathogen *Aspergillus flavus*	Esmaeilishirazifard et al., 2018
Rhodococcus erythropolis	AHL	Not specified	AHL degradation (lactonase activity)	Biocontrol (protection of potatoes from *Pectobacterium)*, root colonization	Dong et al., 2000; Barbey et al., 2013
Ensifer meliloti (and *Ensifer* sp. NGR234)	AHL (3-oxo-C14-HSL)	Yes (symbiont)	Nitrogen fixation, suppression of AHL signals	Nitrogen-fixing symbiont of legumes; priming defense against aphids (*Rhopalosiphum padi*)	Krysciak et al., 2011; Mathesius et al., 2003; Wehner et al., 2021
Pseudomonas putida	AHL (C6-, C8-HSL)	Yes	AHL hydrolysis and production	Rhizobacterium (PGPR); induction of tomato defense against *Alternaria alternata*	Schuhegger et al. 2006
Azospirillum brasilense	AHL (C4-, C12-HSL)	No (most), but there are LuxR solo receptors	AHL degradation, perception of external AHL (LuxR solo)	PGPR; plant growth promotion; root colonization; potential biocontrol	Fukami et al., 2018; Patel et al., 2013; Cassán et al., 2016; Vial et al., 2006; Gualpa et al., 2019

 doi:10.20944/preprints202603.1208.v1

QS communication participant	AI-class	Producers	Regulated processes	Relationship with plants	References
Serratia liquefaciens MG1	AHL (C6-, C8-HSL)	Yes	QS-dependent virulence/interaction	Model organism; induction of tomato defense against *Alternaria alternata*	Schuhegger et al., 2006; Gantner et al., 2006
Serratia plymuthica HRO-C48	AHL (C4-, C6- 3-oxo-C6-HSL)	Yes	Induction of chitinase and antifungal volatile synthesis	Biocontrol of wilt (*Verticillium dahliae*) in rapeseed	Müller et al., 2009
Rhizobium radiobacter F4	AHL (short- and medium-chain)	Yes	Root colonization, growth stimulation, stress resistance	Endophytic PGPR bacterium; closely associated with the plant	Glaeser et al., 2015; Sharma et al., 2008; Alabid et al., 2020
Acidovorax radicis N35	AHL (OH-C10-HSL)	Yes	Root colonization, modulation of plant response (priming vs. defense)	PGPR; beneficial interaction with barley mediated by AHL	Li et al., 20114; Han et al., 2016
Bacterial plant pathogens					
Erwinia carotovora (*Pectobacterium*)	AHL	Yes	Virulence	Pathogen causing soft rot	Põllumaa et al. 2012; Petrova et al. 2023
Pectobacterium spp.	AHL	Yes	Virulence	Pathogen causing soft rot	Barbey et al., 2013
Burkholderia glumae	AHL (C8-HSL, TofI/TofR system)	Yes	Synthesis of toxoflavin	Rice pathogen	Chung et al., 2011
Pseudomonas syringae pv. tomato (Pst)	Not specified (but responds to AHL)	Yes	Virulence	Pathogen of tomato and *Arabidopsis*; susceptible to AHL-induced resistance (ISR)	Shrestha et al., 2020; Schikora et al., 2011

 doi:10.20944/preprints202603.1208.v1

QS communication participant	AI-class	Producers	Regulated processes	Relationship with plants	References
Agrobacterium spp.	AHL	Yes	Virulence/symbiosis, degradation of own AHL	Plant pathogen/symbiont	Zhang et al., 2002
Key recipients of AHL (Plants)					
Medicago truncatula	AHL (3-oxo-C14-HSL, 3-oxo-C16:1-HSL)	No (perceives)	Induction of auxin-sensitive proteins and flavonoid synthesis; secretion of QS mimics	Model legume: early response to symbiont and pathogen signals	Mathesius et al., 2003
Solanum lycopersicum	AHL (C6-, C8-HSL)	No (perceives)	Induction of salicylic acid and defense genes (*PR1a*, chitinase); systemic resistance	Priming protection against fungal pathogen (*Alternaria alternata*)	Schuhegger et al., 2006
Arabidopsis thaliana	AHL (C4-, C6-, C8-, C12-, C14-HSL)	No (perceives)	Stimulation of root growth (GCR1/GPA1), priming of defense (MAPK cascade, oxylipins, SA), induction of detoxification enzymes	Model plant; complex response dependent on AHL chain length; receptor for hydrophobic AHL identified	von Rad et al., 2008; Shrestha et al., 2020; Liu et al., 2012
Barley (*Hordeum vulgare*), wheat (*Triticum aestivum*)	AHL (C6-, 3-oxo-C14-HSL)	No (perceives)	Growth stimulation, hormonal imbalance, priming protection against powdery mildew and aphids	Genetic variation of crops in response to AHL: successful field trials	Shrestha et al., 2019; Moshynets et al., 2019
Rapeseed (*Brassica napus*)	AHL (C4-, C6- 3-oxo-C6-HSL)	No (perceives)	Induction of systemic stability	Protection against *Verticillium dahliae* is mediated by AHL from *S. plymuthica*	Müller et al., 2009
Chickpeas (*Cicer arietinum*)	AHL (C4-HSL)	No (perceives)	Growth promotion, stress tolerance, Fusarium resistance	Positive response to applied AHL	Gupta et al., 2019

 doi:10.20944/preprints202603.1208.v1

QS communication participant	AI-class	Producers	Regulated processes	Relationship with plants	References
			Fungi		
Histoplasma capsulatum (Chemotype II)	Density-dependent phenotypic switch (QS-like)	Yes (α-(1,3)-glucan synthesis)	Hyphae-to-yeast switching; biosynthesis of virulent α-(1,3)-glucan; masking of β-glucans from the dectin-1 receptor	A human and animal pathogen (histoplasmosis). A soil saprophyte that develops into a parasitic yeast form.	Kügler et al., 2000; Sprague et al., 2006; Rappleye et al., 2007; Brown et al., 2001; Marcos et al., 2016
Histoplasma capsulatum (Chemotype I)	Density-dependent phenotypic switch (QS-like)	None or weak (absent α-(1,3)-glucan)	Hyphae → yeast switch; virulence is partly mediated by the *AGS1* gene	A human and animal pathogen	Edwards et al., 2011; Marcos et al., 2016
Aspergillus fumigatus	Farnesol	Yes	Inhibition of hyphae formation, blocking the conidia → hyphae transition; influence on the localization of CWI pathway proteins (AfRho1p, AfRho3p)	Soil saprotroph	Dichtl et al., 2010
Aspergillus nidulans	Farnesol	Yes	Induction of apoptosis through disruption of mitochondria, caspase, and ROS	Demonstration of the interspecies effect of farnesol as a communication molecule	Semighini et al., 2006; Fairn et al., 2007
Aspergillus nidulans	γ-Heptalactone	Yes	Penicillin production	Antagonistic interaction between microbes	Williams et al., 2012
Aspergillus terreus	Butyrolactone I	Yes	Secondary metabolism		Schimmel et al., 1998
Saccharomyces cerevisiae	Farnesol (exogenous)	No (perceives)	Induction of apoptosis through disruption of mitochondria, caspase, and ROS	Demonstration of the interspecies effect of farnesol as a communication molecule.	Fairn et al., 2007

 doi:10.20944/preprints202603.1208.v1

QS communication participant	AI-class	Producers	Regulated processes	Relationship with plants	References
Candida albicans	Farnesol	Yes	Inhibition of hyphae formation (intraspecific QS); inhibition of QS in *P. aeruginosa* (interspecific interaction)	An example of antagonistic interaction between microbes	Cugini et al., 2007; Chung et al., 2010
Various fungi	Ambuic acid	Yes	Inhibition of QS in Gram-positive bacteria	An example of antagonistic interaction between microbes	Nakayama et al., 2009

It has been shown that some antimicrobial metabolites, such as *Bacillus subtilis* surfactin or 2,4-DAPG, can function as antimicrobial agents themselves by regulating the expression of their biosynthetic genes (Wei et al., 2023, Markelova et al., 2025). This interplay between virulence, antibiotic production and QS makes bacterial communication systems an important target for intervention.

1.2. Quorum Sensing in Fungi

The QS phenomenon is also widespread in fungi and regulates key adaptation processes. The first fungal AIs discovered were farnesol, tyrosol, and phenylethanol in the pathogen Candida albicans (Hornby et al., 2001). Subsequently, a wide range of signaling molecules was identified, including oxylipins, peptide pheromones, alcohols (tryptophol, farnesol, etc.), acetaldehydes, and volatiles (Padder et al., 2018, Mehmood et al., 2019). Fungal QS controls physiological functions, such as morphogenesis, spore germination, biosynthesis of secondary metabolites, and secretion of hydrolytic enzymes (Barriuso et al., 2018). Density-dependent regulation has been described for representatives of various taxa, including phytopathogenic *Fusarium oxysporum* (Vitale et al., 2019), *Aspergillus flavus* (Williams et al., 2012), opportunistic *Cryptococcus neoformans* (Lee et al., 2007) and saprotrophic *Neurospora crassa* (Roca et al., 2005), *Penicillium sclerotiorum* (Raina et al., 2010) species, which emphasizes the versatility and ecological significance of this mechanism in the fungal kingdom (Table 1).

2. Plants and QS-Related Molecules

QS signaling molecules are not limited to intra- and interspecific microbial communication. They are also important mediators in the microbe-plant dialogue (Table 1). The first evidence for this was obtained in the work of Mathesius et al. (2003). They showed that AHLs from pathogenic bacteria induce significant changes in the proteome of *Medicago truncatula* roots. These changes affect flavonoid and hormone metabolism, as well as the response to oxidative stress. Further research revealed the dual, structured nature of this influence. Short-chain AHLs (e.g., C6-AHLs) can stimulate root growth and branching by acting as a symbiotic recognition factor (Krumwiede et al., 2020). Long-chain AHLs (e.g., C12-AHLs) that are characteristic of many pathogens often trigger a priming mechanism in plants, a prepared systemic immune response (PSIR). Treatment with these molecules increases plant resistance to subsequent infection, for example by *Pseudomonas syringae*. This correlates with the induction of immune response genes such as *WRKY* and *GST6* (Krumwiede et al., 2020).

 doi:10.20944/preprints202603.1208.v1

Thus, plants have evolved to "eavesdrop" bacterial QS communication, using AI as signals to trigger adaptive responses (Rebolleda-Gómez et al., 2019). The functional significance of QS eavesdropping extends beyond the plant's immediate physiological responses. QS signals also coordinate collective bacterial behaviors that shape the rhizosphere environment itself. DeAngelis et al. (2008) demonstrated that in the rhizospheres of *Avena fatua* L., QS controls the production of extracellular enzymes (chitinases, proteases) that drive nitrogen mineralization from organic matter (DeAngelis et al., 2008). Among 533 bacterial isolates, 24% possessed both AHL production and QS-regulated enzyme activity; disruption of QS abolished enzyme production in seven of the eight tested strains. Thus, QS is not merely a communication system that plants monitor - it is an ecological control point governing nutrient cycling and organic matter decomposition in the rhizosphere. This realization re-frames the plant's chemical response to QS signals.

If plants can detect bacterial QS activity (Mathesius et al., 2003), and if this activity regulates critical ecosystem functions (DeAngelis et al., 2008), then plants may have evolved not only to respond to QS but to intervene in it. This logic provides the conceptual foundation for understanding plant-derived QS inhibitors, particularly coumarins, not as incidental antimicrobials, but as intentional tools for rhizosphere engineering.

 doi:10.20944/preprints202603.1208.v1

3. Coumarin as a Plant Metabolite Regulating Interactions in the "Soil-Plant" System

If bacterial autoinducers serve as signals that plants eavesdrop on, then the response from higher plants is the active secretion of low-molecular compounds into the rhizosphere, which are capable of modulating microbial communication.

One of the key classes of regulatory compounds are coumarins - phenolic secondary metabolites widely distributed in plants, especially in families such as Umbelliferae and Rutaceae (Gutiérrez-Mellado et al., 1996). In addition to their known function in protecting against abiotic stress and herbivores, they play a central role in managing microbial communities in the rhizosphere by interfering with QS systems.

The structural diversity of natural coumarins (simple coumarins, furanocoumarins and pyranocoumarin) determines the range of their biological activities. Simple hydroxy and methoxy derivatives, such as umbelliferone, scopoletin, esculetin and fraxetin are the most common when it comes to interactions with soil microorganisms.

For a long time, their accumulation in root tissues and release into the rhizosphere was considered primarily as part of the antimicrobial response to the invasion of phytopathogens – viruses, bacteria, fungi and oomycetes (Masuda et al., 1998; Dutsadee et al., 2008; Abou Zeid et al., 2008). However, modern data suggest a more complex and selective role for coumarins. They function not simply as broad-spectrum antibiotics, but as signaling molecules that finely regulate the plant's dialogue with the complex soil microbiome. This is supported by the fact that the accumulation of specific coumarins is induced not only by pathogens but also by beneficial rhizobacteria, such as *Pseudomonas fluorescens* (Van de Mortel et al., 2012) и *Paenibacillus polymyxa* (Zhou et al., 2016).

This fact indicates their involvement in establishing mutually beneficial interactions. In an early study predating the molecular characterization of quorum sensing, Shimizu et al. (2005) demonstrated that a non-pathogenic isolate of *Fusarium oxysporum* 101-2 (NPF) induced resistance in morning glory (*Pharbitis nil*) cuttings against pathogenic *F. oxysporum* f. sp. *batatas* O-17 (PF). This induced resistance was accompanied by the rapid activation of phenylalanine ammonia-lyase (PAL) and the accelerated accumulation of the coumarins scopoletin and scopolin in plant tissues. Strikingly, while the non-pathogenic strain consistently induced coumarin synthesis, the pathogenic strain at high inoculum density (10^8 bud-cells/ml) suppressed coumarin accumulation, suggesting that successful pathogens have evolved mechanisms to actively inhibit this protective phenylpropanoid response. The ability of plants to recognize beneficial microorganisms and specifically modify the rhizosphere environment for them is a clear manifestation of this interaction. A striking example is the induction of a specific signaling cascade (MYB72/BGLU42) in response to colonization by beneficial pseudomonads, leading to the secretion of scopoletin, which suppresses pathogens but does not affect inducers (Stringlis et al., 2018). This demonstrates that plants do not passively "eavesdrop" on QS, but actively use their metabolites (coumarins) to create favorable conditions for desired microorganisms.

Thus, plant-secreted coumarins act as ecological regulators: they can suppress the virulence of pathogens by disrupting their coordinated behavior, while simultaneously not hindering and possibly even supporting colonization by beneficial symbionts.

4. Mechanisms of Influence of Coumarins on Soil Microorganisms: From Direct Antimicrobial Action to Community Management Through QS

The influence of coumarins on soil microorganisms is realized at several levels: from direct toxicity, which is characteristic of many phytoalexins, to fine-tuning population dynamics and community composition through modulation of quorum sensing systems. Considering these levels allows us to move from the classical concept of coumarin as antimicrobial agents to a modern paradigm of its role as an ecophysiological regulator.

 doi:10.20944/preprints202603.1208.v1

4.1. Direct Antimicrobial Action of Coumarins

The direct inhibitory effect of coumarins in vitro on a wide range of phytopathogens (fungi, oomycetes, and bacteria) is well documented. For example, scopoletin inhibits the growth of *Botrytis cinerea*, *Alternaria alternata*, and *Pseudomonas syringae* (Stringlis et al., 2019), and furanocoumarins such as psoralen and bergapten exhibit antibacterial activity (Abdul Hamid et al., 2022). Minimum inhibitory concentrations for various coumarins can reach submicromolar values (Kayser et al.,1999), which testifies to the effectiveness of this defense mechanism.

4.2. Coumarins as Quorum Sensing Inhibitors in Phytopathogens

A more specific and ecologically significant mechanism of coumarin action is QS inhibition, which disrupts the coordinated expression of virulence factors without cell death, reducing selective pressure for resistance. The first evidence that coumarins (umbelliferone, esculetin, daphnetin) can suppress the virulence of *R. solanacearum* was obtained by Yang and Chen. They demonstrated a reduction in the expression of the *fliC*/*fliA* motility genes and a decrease in colonization of tobacco roots. However, molecular targets remained unknown and the effect was interpreted in terms of "antivirulent" activity (Yang et al., 2016; Chen et al., 2016).

In the next work, Yang et al. (2017) revealed the mechanism. Umbelliferone inhibits both signaling cascades leading to T3SS activation - HrpG–HrpB and PrhG–HprB. This results in decreased expression of six of the ten key T3SS effectors, while leaving T2SS unaffected. The selectivity of the action indicates the involvement of specific regulatory nodes, rather than general metabolic toxicity. Umbelliferone also inhibits biofilm formation, which is a QS-dependent collective behavior.

But why is the suppression of T3SS and biofilms so critical? The answer is provided by a metagenomic study by Zhang et al. (2026). In the infected rhizosphere, *R. solanacearum*, through its QS systems (eight different pathways), actively suppresses the QS genes of beneficial bacteria and simplifies the microbial network. In this context, the T3SS is not simply a tool for delivering effectors, but a key element of ecological dominance. The pathogen does not attack the plant in isolation. It first restructures the microbial community to suit its needs. By disarming the T3SS and disrupting QS-controlled collective behaviors, coumarins may simultaneously attenuate direct virulence and prevent pathogen-mediated disruption of the protective rhizosphere microbiome.

By disrupting QS communication, coumarins create the preconditions for a profound restructuring of the rhizosphere microbial community. The molecular basis for this effect has been confirmed using bioreporter systems. Coumarins such as bergamottin are able to suppress the production of autoinducers AI-1 and AI-2 in *Vibrio harveyi* (Lee et al., 2014), while for *Pseudomonas aeruginosa* and *Chromobacterium violaceum* the ability of hydroxylated coumarin derivatives to inhibit QS-controlled violacein production was established (D'Almeida et al., 2017). It is important to note that coumarins can selectively influence different QS pathways, without affecting, for example, the expression of the *luxS* synthase gene (AI-2), but suppressing the work of downstream regulons (for example, *lsrA*) (Lee et al., 2014).

4.3. The Influence of Coumarins on the Formation and Functioning of the Rhizosphere Microbial Community

However, in vivo the significance of the direct toxic effect is often limited to the concentrations achieved in the rhizosphere, indicating the leading role of more selective signaling mechanisms.

Key evidence for the selective, controlling effects of coumarins on the microbiome comes from experiments on *Arabidopsis thaliana*. It was shown that root colonization by the beneficial rhizobacteria *Pseudomonas simiae* WCS417 induces plant transcription factor MYB72, which activates biosynthesis and excretion of coumarin scopoletin (Stringlis et al., 2018). Scopoletin exhibits selective antimicrobial activity: it effectively suppresses soil fungal pathogens *Fusarium oxysporum* and *Verticillium dahliae*, but is tolerant to the pseudomonad strains that induce it. Metagenomic analysis revealed that the rhizosphere microbiome composition of scopoletin-producing mutants (F6'H1) was

 doi:10.20944/preprints202603.1208.v1

significantly different from that of the wild type. This demonstrates that a specific coumarin secreted in response to a specific microbial signal acts as a selective factor shaping the composition of the microbial community favoring beneficial symbionts. The impact of coumarins on soil communities is context-dependent and varies with methodology. While some studies demonstrate clear selective effects, others report more nuanced outcomes.

Similar context-dependent outcomes were reported by Yang et al. (2023) in annual ryegrass. At 200 mg/kg, coumarin did not reduce bacterial diversity but significantly shifted community composition, enriching both beneficial bacteria and opportunistic pathogens. This dual outcome: stimulation of symbionts alongside proliferation of pathogens, underscores that coumarin effects are not inherently selective or suppressive; rather, the ecological outcome emerges from the interplay of concentration, plant species, and the native microbial community (Yang et al., 2023).

For instance, in a long-term microcosm experiment aimed at stimulating PCB degradation, coumarin (2 mmol/kg) did not alter the overall microbial community structure assessed by PLFA profiling nor enhance biodegradation (Luo et al., 2007). This suggests that at certain concentrations and in established communities, coumarins may exert subtle functional modulation (e.g., on QS pathways) without causing major taxonomic shifts detectable by broad profiling methods.

In contrast, other microcosm studies report a significant broad-spectrum suppressive effect. The application of coumarin at agriculturally relevant doses (100-150 mg/kg) selectively inhibits weed growth more than wheat and measurably reduces total microbial biomass and genetic diversity of both bacteria and fungi (Niro et al., 2016). Similarly, PLFA analysis has shown that coumarins can significantly decrease total microbial, bacterial and fungal biomass, indicating a potent non-selective pressure that can "reset" the microbial community structure (Li et al., 2013). This duality - specific induction versus broad suppression - highlights that the ecological outcome depends on concentration, soil properties and initial community state (Xiao et al., 2017).

The case of *R. solanacearum* illustrates how these context-dependent effects translate into ecological outcomes. At physiologically relevant concentrations, coumarins such as umbelliferone selectively disarm the pathogen by suppressing its T3SS and QS-regulated collective behaviors (Yang et al., 2016). Direct evidence for pathogen-driven QS restructuring comes from a metagenomic study comparing the rhizosphere microbiomes of healthy tobacco and *R. solanacearum*-infected plants (Zhang et al., 2026). The QS pathway was the most significantly enriched among the 50,960 differentially abundant genes. Overall, QS gene abundance was negatively correlated with *Ralstonia* density ($R^2 = 0.52$), indicating suppression of community quorum sensing as pathogen populations increased. Taxonomic attribution revealed why: while QS genes from most bacteria were depleted, Ralstonia's contribution to QS pathways increased from 2.3% in healthy rhizospheres to 10.4% in diseased ones. Across seven QS subsystems (AI-1, GABA, PapR, NprX, Phr, cCF10, DSF), pathogen-attributed genes were significantly enriched. These findings demonstrate that *R. solanacearum* actively restructures the rhizosphere QS network during infection, suppressing beneficial bacterial communication while enhancing its own QS systems.

Thus, coumarin operates at the intersection of direct virulence inhibition and ecosystem-level intervention: it does not simply kill or weaken pathogens but restores the microbial network integrity that pathogens subvert during infection. This makes coumarin one of the rare classes of plant metabolites that functions as both an anti-virulent agent and a microbiome editor.

4.4. Functional Consequences: Interference with Quorum-Dependent Processes

The ecological significance of coumarin-induced shifts in communities lies in their functional consequences. Key soil processes such as biofilm formation and exoenzyme secretion for organic matter decomposition are controlled by QS, and coumarin inhibition of QS can have far-reaching effects (DeAngelis et al., 2008). Coumarins like scopoletin and esculetin inhibit biofilm formation by pathogens (e.g., *R. solanacearum*) and provide a competitive advantage to non-virulent microorganisms (Pruteanu et al., 2020). Suppressing QS signaling in the soil has also been shown to slow down the mineralization of organic matter (Strickland et al., 2013). By secreting coumarins,

 doi:10.20944/preprints202603.1208.v1

plants not only shape their own microbiome, but also locally modulate carbon and nutrient cycling in the rhizosphere.

5. Challenges and Opportunities for Coumarin-Based Agricultural Strategies

5.1. Ecological Benefit vs. Agronomic Liability

Current agricultural approaches to disrupting quorum sensing fall into two distinct categories, each with inherent strengths and limitations. Microbial quorum quenching relies on live biocontrol agents - typically *Bacillus* or *Rhodococcus* strains expressing AHL-lactonases or other quorum-quenching enzymes. These agents have demonstrated efficacy against soft rot pathogens (*Pectobacterium, Erwinia*) under controlled conditions (Table 1). Their advantages include self-propagation, multifunctionality (some strains also produce antimicrobial agents or promote plant growth), and regulatory familiarity as biopesticides. However, living agents face persistent challenges such as inconsistent establishment in competitive rhizosphere environments, loss of quorum-sensing gene expression in situ, sensitivity to soil physicochemical conditions and short shelf life.

Molecular quorum quenching employs low-molecular-weight QS inhibitors, including plant-derived compounds such as coumarins, flavonoids, and furanones. Coumarins offer a distinct profile: (i) natural origin and biodegradability - they are already present in agroecosystems; (ii) multi-target action - they simultaneously interfere with QS, T3SS, and biofilm formation (Yang et al., 2016); (iii) potential selectivity - differential activity against pathogens vs. beneficial taxa (Stringlis et al.,2018), and (iv) chemical tractability - synthetic analogues can be developed. Yet, molecular approaches face their own challenges, most notably environmental persistence - or rather, lack thereof.

A major obstacle to the use of coumarins is their extremely rapid degradation in soil. The half-life (DT50) of the coumarin can be less than one day, with 90% dissipation within 2–3 days under aerobic conditions (Gamiz et al., 2020). This instability is primarily mediated by microbial metabolism, with sorption to soil organic matter (Kd ~1.04 L/kg) playing a secondary and reversible role. This presents a paradox. From an ecotoxicological perspective, rapid degradation is highly desirable, as coumarins do not persist or bioaccumulate and do not contaminate groundwater, making them "green" by design. However, from an agronomic perspective, a half-life of less than 24 hours means that a single application provides only a transient window for quorum sensing interference, which is insufficient for sustained protection against chronic pathogens or reshaping of established microbial communities.

5.2. Critical Knowledge Gaps

Despite compelling mechanistic evidence in vitro and in model systems, several gaps must be addressed before coumarin-based strategies can be deployed in production agriculture. 1. Dose-response in soil. What concentrations of specific coumarins are actually achieved in the rhizosphere under natural exudation? How do these compare to effective concentrations determined in vitro? The current disconnect between laboratory MIC/QSI values and environmental concentrations is a major barrier to rational formulation design.

2. Non-target effects on beneficial QS functions. QS regulates not only virulence but also symbiotic nitrogen fixation, mycorrhizal establishment, and organic matter decomposition (DeAngelis et al., 2008). Do coumarins, at environmentally relevant concentrations, disrupt these beneficial processes? The trade-off between pathogen suppression and nutrient mineralization remains entirely unexplored.

3. Spectrum of activity across coumarin structural classes. Most studies have focused on a few compounds (umbelliferone, scopoletin, esculetin). How do structural variations (hydroxylation patterns, prenylation, glycosylation) affect QSI potency, selectivity, and environmental fate? A systematic structure-activity-ecotoxicity relationship is urgently needed.

 doi:10.20944/preprints202603.1208.v1

4. Efficacy under realistic field conditions. To date, nearly all evidence for coumarin-mediated QS inhibition and microbiome editing comes from axenic systems, gnotobiotic plants, or laboratory microcosms. Field trials with naturally assembled soil communities, variable weather, and competing microbial processes are the essential next step.

6. Conclusion

Coumarins possess a unique combination of properties - natural origin, ecological relevance, multi-target anti-virulent activity, and demonstrated ability to edit rhizosphere microbial communities - that distinguish them from both live QS agents and synthetic QSI inhibitors. The metagenomic data for Ralstonia's "QS takeover" - increasing its contribution to QS genes from 2.3% to 10.4%, while overall community QS potential decreases (Zhang et al., 2026) - redefines bacterial wilt as not just an infection, but suppression of cooperative interactions in the microbial community. Coumarins, by disarming the pathogen's QS and virulence cascades (Yang et al., 2016), may act as counter-coups, restoring the pre-infection functional network.

Their rapid environmental degradation, although agronomically challenging, is environmentally responsible and can be addressed through structural optimization, and integrated application strategies. The question is no longer whether coumarins can function as agricultural QSI modulators. Mechanistic evidence is compelling, and the question is how to translate this mechanism into reliable, cost-effective, and regulatory acceptable products. This requires convergent research at the intersection of natural product chemistry, soil microbiology, and agriculture.

Funding: This work was supported by the Russian Science Foundation (grant No. 25-26-00720, https://rscf.ru/project/25-26-00720/).

CRediT authorship contribution statement: Alexey S. Vasilchenko: Conceptualization, Writing – original draft, Formal analysis, Funding acquisition. Aleksandr V. Iashnikov: Writing – Formal analysis, Review & editing.

References

1. Abdul Hamid, N.W., Nadarajah, K., 2022. Microbe related chemical signalling and its application in agriculture. Int. J. Mol. Sci. 23, 8998.
2. Abou Zeid, A.H.S., 2002. Stress metabolites from Corchorus olitorius L. leaves in response to certain stress agents. Food Chem. 76, 187-195. https://doi.org/10.1016/S0308-8146(01)00264-3
3. Alabid, I., Hardt, M., Imani, J., Hartmann, A., Rothballer, M., Li, D., Kogel, K.H., 2020. The N-acyl homoserine-lactone depleted Rhizobium radiobacter mutant RrF4NM13 shows reduced growth-promoting and resistance-inducing activities in mono-and dicotyledonous plants. J. Plant Dis. Prot. 127, 769-781. https://doi.org/10.1007/s41348-020-00360-8
4. Barbey, C., Crépin, A., Bergeau, D., Ouchiha, A., Mijouin, L., Taupin, L., Latour, X., 2013. In planta biocontrol of Pectobacterium atrosepticum by Rhodococcus erythropolis involves silencing of pathogen communication by the rhodococcal gamma-lactone catabolic pathway. PLoS One 8, e66642. https://doi.org/10.1371/journal.pone.0066642
5. Barriuso, J., Hogan, D.A., Keshavarz, T., Martínez, M.J., 2018. Role of quorum sensing and chemical communication in fungal biotechnology and pathogenesis. FEMS Microbiol. Rev. 42, 627-638. https://doi.org/10.1093/femsre/fuy022
6. Brown G.D., 2001. Immune recognition. A new receptor for β-glucans. Nature 413, 36-37.
7. Cassán, F., Diaz-Zorita, M., 2016. Azospirillum sp. in current agriculture: From the laboratory to the field. Soil Biol. Biochem. 103, 117-130. https://doi.org/10.1016/j.soilbio.2016.08.020
8. Chen, J., Yu, Y., Li, S., Ding, W., 2016. Resveratrol and coumarin: Novel agricultural antibacterial agent against Ralstonia solanacearum in vitro and in vivo. Molecules 21, 1501.
9. Chung, J., Goo, E., Yu, S., Choi, O., Lee, J., Kim, J., Rhee, S., 2011. Small-molecule inhibitor binding to an N-acyl-homoserine lactone synthase. Proc. Natl. Acad. Sci. U.S.A. 108, 12089-12094. https://doi.org/10.1073/pnas.1103165108

 doi:10.20944/preprints202603.1208.v1

10. Chung, S.C., Kim, T.I., Ahn, C.H., Shin, J., Oh, K.B., 2010. Candida albicans PHO81 is required for the inhibition of hyphal development by farnesoic acid. FEBS Lett. 584, 4639-4645.
11. Coolahan, M., Whalen, K.E., 2025. A review of quorum-sensing and its role in mediating interkingdom interactions in the ocean. Commun. Biol. 8, 179. https://doi.org/10.1038/s42003-025-07608-9
12. Cugini, C., Calfee, M.W., Farrow III, J.M., Morales, D.K., Pesci, E.C., Hogan, D.A., 2007. Farnesol, a common sesquiterpene, inhibits PQS production in Pseudomonas aeruginosa. Mol. Microbiol. 65, 896-906. https://doi.org/10.1111/j.1365-2958.2007.05840.x
13. D'almeida, R.E., Molina, R.D.I., Viola, C.M., Luciardi, M.C., Peñalver, C.N., Bardón, A., Arena, M.E., 2017. Comparison of seven structurally related coumarins on the inhibition of quorum sensing of Pseudomonas aeruginosa and Chromobacterium violaceum. Bioorg. Chem. 73, 37-42. https://doi.org/10.1016/j.bioorg.2017.05.011
14. DeAngelis, K.M., Lindow, S.E., Firestone, M.K., 2008. Bacterial quorum sensing and nitrogen cycling in rhizosphere soil. FEMS Microbiol. Ecol. 66, 197-207.
15. Dichtl, K., Ebel, F., Dirr, F., Routier, F.H., Heesemann, J., Wagener, J., 2010. Farnesol misplaces tip-localized Rho proteins and inhibits cell wall integrity signalling in Aspergillus fumigatus. Mol. Microbiol. 76, 1191-1204.
16. Dong, Y.H., Xu, J.L., Li, X.Z., Zhang, L.H., 2000. AiiA, an enzyme that inactivates the acylhomoserine lactone quorum-sensing signal and attenuates the virulence of Erwinia carotovora. Proc. Natl. Acad. Sci. U.S.A. 97, 3526-3531. https://doi.org/10.1073/pnas.97.7.3526
17. Dutsadee, C., Nunta, C., 2008. Induction of peroxidase, scopoletin, phenolic compounds and resistance in Hevea brasiliensis by elicitin and a novel protein elicitor purified from Phytophthora palmivora. Physiol. Mol. Plant Pathol. 72, 179-187. https://doi.org/10.1016/j.pmpp.2008.09.002
18. Edwards, J.A., Alore, E.A., Rappleye, C.A., 2011. The yeast-phase virulence requirement for α-glucan synthase differs among Histoplasma capsulatum chemotypes. Eukaryot. Cell 10, 87-97.
19. Esmaeilishirazifard, E., Dariush, A., Moschos, S.A., Keshavarz, T., 2018. A novel antifungal property for the Bacillus licheniformis ComX pheromone and its possible role in inter-kingdom cross-talk. Appl. Microbiol. Biotechnol. 102, 5197-5208.
20. Fairn, G.D., MacDonald, K., McMaster, C.R., 2007. A chemogenomic screen in Saccharomyces cerevisiae uncovers a primary role for the mitochondria in farnesol toxicity and its regulation by the Pkc1 pathway. J. Biol. Chem. 282, 4868-4874.
21. Fukami, J., Abrantes, J.L.F., Del Cerro, P., Nogueira, M.A., Ollero, F.J., Megías, M., Hungria, M., 2018. Revealing strategies of quorum sensing in Azospirillum brasilense strains Ab-V5 and Ab-V6. Arch. Microbiol. 200, 47-56. https://doi.org/10.1007/s00203-017-1422-x
22. Fuqua, W.C., Winans, S.C., Greenberg, E.P., 1994. Quorum sensing in bacteria: the LuxR-LuxI family of cell density-responsive transcriptional regulators. J. Bacteriol. 176, 269-275. https://doi.org/10.1128/jb.176.2.269-275.1994
23. Gámiz, B., Velarde, P., Spokas, K.A., Hermosín, M.C., Cox, L., 2017. Biochar soil additions affect herbicide fate: importance of application timing and feedstock species. J. Agric. Food Chem. 65, 3109-3117. https://doi.org/10.1021/acs.jafc.7b00458
24. Gantner, S., Schmid, M., Dürr, C., Schuhegger, R., Steidle, A., Hutzler, P., Dazzo, F.B., 2006. In situ quantitation of the spatial scale of calling distances and population density-independent N-acylhomoserine lactone-mediated communication by rhizobacteria colonized on plant roots. FEMS Microbiol. Ecol. 56, 188-194. https://doi.org/10.1111/j.1574-6941.2005.00037.x
25. Glaeser, S.P., Imani, J., Alabid, I., Guo, H., Kumar, N., Kampfer, P., Hardt, M., Blom, J., Goesmann, A., Rothballer, M., 2015. The endofungal bacterium Rhizobium radiobacter RrF4 colonizes plant roots and exhibits beneficial activity independently of its fungal host Piriformospora indica. ISME J. 9, 871-884. https://doi.org/10.1038/ismej.2015.163
26. Gualpa, J., Lopez, G., Nievas, S., Coniglio, A., Halliday, N., Cámara, M., Cassán, F., 2019. Azospirillum brasilense Az39, a model rhizobacterium with AHL quorum-quenching capacity. J. Appl. Microbiol. 126, 1850-1860. https://doi.org/10.1111/jam.14269

 doi:10.20944/preprints202603.1208.v1

27. Gupta, G.S., Kumar, A., Verma, N., 2019. Bacterial homoserine lactones as a nanocomposite fertilizer and defense regulator for chickpeas. Environ. Sci.: Nano 6, 1246-1258. https://doi.org/10.1039/C9EN00199A
28. Gutiérrez-Mellado, M.C., Edwards, R., Tena, M., Cabello, F., Serghini, K., Jorrín, J., 1996. The production of coumarin phytoalexins in different plant organs of sunflower (Helianthus annuus L.). J. Plant Physiol. 149, 261-266. https://doi.org/10.1016/S0176-1617(96)80119-2
29. Han, S., Li, D., Trost, E., Mayer, K.F., Vlot, A.C., Heller, W., Rothballer, M., 2016. Systemic responses of barley to the 3-hydroxy-decanoyl-homoserine lactone producing plant beneficial endophyte Acidovorax radicis N35. Front. Plant Sci. 7, 1868. https://doi.org/10.3389/fpls.2016.01868
30. Hornby, J.M., Jensen, E.C., Lisec, A.D., Tasto, J.J., Jahnke, B., Shoemaker, R., Nickerson, K.W., 2001. Quorum sensing in the dimorphic fungus Candida albicans is mediated by farnesol. Appl. Environ. Microbiol. 67, 2982-2992. https://doi.org/10.1128/AEM.67.7.2982-2992.2001
31. Hoult, J.R.S., Payá, M., 1996. Pharmacological and biochemical actions of simple coumarins: natural products with therapeutic potential. Gen. Pharmacol. 27, 713-722. https://doi.org/10.1016/0306-3623(95)02112-4
32. Kalia, V.C., 2013. Quorum sensing inhibitors: an overview. Biotechnol. Adv. 31, 224-245. https://doi.org/10.1016/j.biotechadv.2012.10.004
33. Kayser, O., Kolodziej, H., 1999. Antibacterial activity of simple coumarins: structural requirements for biological activity. Z. Naturforsch. C 54, 169-174. https://doi.org/10.1515/znc-1999-3-405
34. Krumwiede, J., Ojiro, I., Grimm, M., Shrestha, A., Schikora, A., 2020. Impact of quorum sensing molecules on plant growth and immune system. Front. Microbiol. 11, 1545. https://doi.org/10.3389/fmicb.2020.01545
35. Krysciak, D., Schmeisser, C., Preuss, S., Riethausen, J., Quitschau, M., Grond, S., Streit, W.R., 2011. Involvement of multiple loci in quorum quenching of autoinducer I molecules in the nitrogen-fixing symbiont Rhizobium (Sinorhizobium) sp. strain NGR234. Appl. Environ. Microbiol. 77, 5089-5099. https://doi.org/10.1128/AEM.00112-11
36. Kügler, S., Sebghati, T.S., Eissenberg, L.G., Goldman, W.E., 2000. Phenotypic variation and intracellular parasitism by Histoplasma capsulatum. Proc. Natl. Acad. Sci. U.S.A. 97, 8794-8798.
37. Lee, H., Chang, Y.C., Nardone, G., Kwon-Chung, K.J., 2007. TUP1 disruption in Cryptococcus neoformans uncovers a peptide-mediated density-dependent growth phenomenon that mimics quorum sensing. Mol. Microbiol. 64, 591-601. https://doi.org/10.1111/j.1365-2958.2007.05666.x
38. Lee, J.H., Kim, Y.G., Cho, H.S., Ryu, S.Y., Cho, M.H., Lee, J., 2014. Coumarins reduce biofilm formation and the virulence of Escherichia coli O157:H7. Phytomedicine 21, 1037-1042. https://doi.org/10.1016/j.phymed.2014.04.008
39. Li, D., Rothballer, M., Schmid, M., Esperschütz, J., Hartmann, A., 2011. Acidovorax radicis sp. nov., a rhizosphere bacterium isolated from wheat roots. Int. J. Syst. Evol. Microbiol. 61, 2589-2594. https://doi.org/10.1099/ijs.0.025296-0
40. Li, X.J., Xia, Z.C., Kong, C.H., Xu, X.H., 2013. Mobility and microbial activity of allelochemicals in soil. J. Agric. Food Chem. 61, 5072-5079.
41. Liu, F., Bian, Z., Jia, Z., Zhao, Q., Song, S., 2012. The GCR1 and GPA1 participate in promotion of Arabidopsis primary root elongation induced by N-acyl-homoserine lactones, the bacterial quorum-sensing signals. Mol. Plant-Microbe Interact. 25, 677-683. https://doi.org/10.1094/MPMI-10-11-0274
42. Luo, W., D'Angelo, E.M., Coyne, M.S., 2007. Plant secondary metabolites, biphenyl, and hydroxypropyl-β-cyclodextrin effects on aerobic polychlorinated biphenyl removal and microbial community structure in soils. Soil Biol. Biochem. 39, 735-743. https://doi.org/10.1016/j.soilbio.2006.09.019
43. Majdura, J., Jankiewicz, U., Gałązka, A., Orzechowski, S., 2023. The role of quorum sensing molecules in bacterial–plant interactions. Metabolites 13, 114. https://doi.org/10.3390/metabo13010114
44. Marcos, C.M., de Oliveira, H.C., de Melo, W.C., da Silva, J.D.F., Assato, P.A., Scorzoni, L., Fusco-Almeida, A.M., 2016. Anti-immune strategies of pathogenic fungi. Front. Cell. Infect. Microbiol. 6, 142.
45. Markelova, N., Chumak, A., 2025. Antimicrobial activity of Bacillus cyclic lipopeptides and their role in the host adaptive response to changes in environmental conditions. Int. J. Mol. Sci. 26, 336. https://doi.org/10.3390/ijms26010336

 doi:10.20944/preprints202603.1208.v1

46. Masuda, T., Takasugi, M., Anetai, M., 1998. Psoralen and other linear furanocoumarins as phytoalexins in Glehnia littoralis. Phytochemistry 47, 13-16. https://doi.org/10.1016/S0031-9422(97)00528-1
47. Mathesius, U., Mulders, S., Gao, M., Teplitski, M., Caetano-Anollés, G., Rolfe, B.G., Bauer, W.D., 2003. Extensive and specific responses of a eukaryote to bacterial quorum-sensing signals. Proc. Natl. Acad. Sci. U.S.A. 100, 1444-1449. https://doi.org/10.1073/pnas.262672599
48. Mehmood, A., Liu, G., Wang, X., Meng, G., Wang, C., Liu, Y., 2019. Fungal quorum-sensing molecules and inhibitors with potential antifungal activity: a review. Molecules 24, 1950. https://doi.org/10.3390/molecules24101950
49. Monica, S., Panneerselvam, S., Rajasekaran, R., Nalliappan, S., Kailappan, A., Rangasamy, A., 2025. Recent advances in bioinoculant formulations and their shelf-life: a review. Curr. Microbiol. 82, 506. https://doi.org/10.1007/s00284-025-04497-3
50. Moshynets, O.V., Babenko, L.M., Rogalsky, S.P., Iungin, O.S., Foster, J., Kosakivska, I.V., Spiers, A.J., 2019. Priming winter wheat seeds with the bacterial quorum sensing signal N-hexanoyl-L-homoserine lactone (C6-HSL) shows potential to improve plant growth and seed yield. PLoS One 14, e0209460. https://doi.org/10.1371/journal.pone.0209460
51. Müller, H., Westendorf, C., Leitner, E., Chernin, L., Riedel, K., Schmidt, S., Berg, G., 2009. Quorum-sensing effects in the antagonistic rhizosphere bacterium Serratia plymuthica HRO-C48. FEMS Microbiol. Ecol. 67, 468-478. https://doi.org/10.1111/j.1574-6941.2008.00635.x
52. Nakayama, J., Uemura, Y., Nishiguchi, K., Yoshimura, N., Igarashi, Y., Sonomoto, K., 2009. Ambuic acid inhibits the biosynthesis of cyclic peptide quormones in gram-positive bacteria. Antimicrob. Agents Chemother. 53, 580-586. https://doi.org/10.1128/AAC.00995-08
53. Nealson, K.H., Hastings, J.W., 1979. Bacterial bioluminescence: its control and ecological significance. Microbiol. Rev. 43, 496-518.
54. Niro, E., Marzaioli, R., De Crescenzo, S., D'Abrosca, B., Castaldi, S., Esposito, A., Rutigliano, F.A., 2016. Effects of the allelochemical coumarin on plants and soil microbial community. Soil Biol. Biochem. 95, 30-39. https://doi.org/10.1016/j.soilbio.2015.11.028
55. Padder, S.A., Prasad, R., Shah, A.H., 2018. Quorum sensing: A less known mode of communication among fungi. Microbiol. Res. 210, 51-58. https://doi.org/10.1016/j.micres.2018.03.007
56. Patel, H.K., Suárez-Moreno, Z.R., Degrassi, G., Subramoni, S., González, J.F., Venturi, V., 2013. Bacterial LuxR solos have evolved to respond to different molecules including signals from plants. Front. Plant Sci. 4, 447. https://doi.org/10.3389/fpls.2013.00447
57. Petrova O, Parfirova O, Gogoleva N, Vorob'ev V, Gogolev Y, Gorshkov V. The Role of Intercellular Signaling in the Regulation of Bacterial Adaptive Proliferation. International Journal of Molecular Sciences. 2023; 24(8):7266. https://doi.org/10.3390/ijms24087266
58. Põllumaa L, Alamäe T, Mäe A. Quorum Sensing and Expression of Virulence in Pectobacteria. Sensors. 2012; 12(3):3327-3349. https://doi.org/10.3390/s120303327
59. Pruteanu, M., Hernández Lobato, J.I., Stach, T., Hengge, R., 2020. Common plant flavonoids prevent the assembly of amyloid curli fibres and can interfere with bacterial biofilm formation. Environ. Microbiol. 22, 5280-5299. https://doi.org/10.1111/1462-2920.15216
60. Raina, S., Odell, M., Keshavarz, T., 2010. Quorum sensing as a method for improving sclerotiorin production in Penicillium sclerotiorum. J. Biotechnol. 148, 91-98. https://doi.org/10.1016/j.jbiotec.2010.04.009
61. Rappleye, C.A., Eissenberg, L.G., Goldman, W.E., 2007. Histoplasma capsulatum α-(1,3)-glucan blocks innate immune recognition by the β-glucan receptor. Proc. Natl. Acad. Sci. U.S.A. 104, 1366-1370.
62. Rebolleda-Gómez, M., Wood, C.W., 2019. Unclear intentions: eavesdropping in microbial and plant systems. Front. Ecol. Evol. 7, 385. https://doi.org/10.3389/fevo.2019.00385
63. Roca, A., Cabeo, M., Enguidanos, C., Martínez-Checa, F., Sampedro, I., Llamas, I., 2024. Potential of the quorum-quenching and plant-growth promoting halotolerant Bacillus toyonensis AA1EC1 as biocontrol agent. Microb. Biotechnol. 17, e14420. https://doi.org/10.1111/1751-7915.14420
64. Roca, M.G., Arlt, J., Jeffree, C.E., Read, N.D., 2005. Cell biology of conidial anastomosis tubes in Neurospora crassa. Eukaryot. Cell 4, 911-919. https://doi.org/10.1128/EC.4.5.911-919.2005

 doi:10.20944/preprints202603.1208.v1

65. Schikora, A., Schenk, S.T., Stein, E., Molitor, A., Zuccaro, A., Kogel, K.H., 2011. N-acyl-homoserine lactone confers resistance toward biotrophic and hemibiotrophic pathogens via altered activation of AtMPK6. Plant Physiol. 157, 1407-1418. https://doi.org/10.1104/pp.111.180604
66. Schimmel, T.G., Coffman, A.D., Parsons, S.J., 1998. Effect of butyrolactone I on the producing fungus, Aspergillus terreus. Appl. Environ. Microbiol. 64, 3707-3712. https://doi.org/10.1128/AEM.64.10.3707-3712.1998
67. Schuhegger, R., Ihring, A., Gantner, S., Bahnweg, G., Knappe, C., Vogg, G., Hutzler, P., Schmid, M., Van Breusegem, F., Eberl, L., Hartmann, A., Langebartels, C., 2006. Induction of systemic resistance in tomato by N-acyl-L-homoserine lactone-producing rhizosphere bacteria. Plant Cell Environ. 29, 909-918. https://doi.org/10.1111/j.1365-3040.2005.01471.x
68. Semighini, C.P., Hornby, J.M., Dumitru, R., Nickerson, K.W., Harris, S.D., 2006. Farnesol-induced apoptosis in Aspergillus nidulans reveals a possible mechanism for antagonistic interactions between fungi. Mol. Microbiol. 59, 753-764.
69. Sharma, M., Schmid, M., Rothballer, M., Hause, G., Zuccaro, A., Imani, J., Kogel, K.H., 2008. Detection and identification of bacteria intimately associated with fungi of the order Sebacinales. Cell. Microbiol. 10, 2235-2246. https://doi.org/10.1111/j.1462-5822.2008.01202.x
70. Shimizu, B.I., Miyagawa, H., Ueno, T., Sakata, K., Watanabe, K., Ogawa, K., 2005. Morning glory systemically accumulates scopoletin and scopolin after interaction with Fusarium oxysporum. Z. Naturforsch. C 60, 83-90.
71. Shrestha, A., Elhady, A., Adss, S., Wehner, G., Böttcher, C., Heuer, H., Schikora, A., 2019. Genetic differences in barley govern the responsiveness to N-acyl homoserine lactone. Phytobiomes J. 3, 191-202. https://doi.org/10.1094/PBIOMES-03-19-0015-R
72. Shrestha, A., Grimm, M., Ojiro, I., Krumwiede, J., Schikora, A., 2020. Impact of quorum sensing molecules on plant growth and immune system. Front. Microbiol. 11, 1545. https://doi.org/10.3389/fmicb.2020.01545
73. Sprague, G.F., Winans, S.C., 2006. Eukaryotes learn how to count: quorum sensing by yeast. Genes Dev. 20, 1045-1049.
74. Strickland, M.S., McCulley, R.L., Bradford, M.A., 2013. The effect of a quorum quenching enzyme on leaf litter decomposition. Soil Biol. Biochem. 64, 65-67.
75. Stringlis, I.A., Yu, K.E., Feussner, K., de Jonge, R., Van Bentum, S., Van Verk, M.C., Pieterse, C.M., 2018. MYB72-dependent coumarin exudation shapes root microbiome assembly to promote plant health. Proc. Natl. Acad. Sci. U.S.A. 115, E5213-E5222. https://doi.org/10.1073/pnas.1722335115
76. Van de Mortel, J.E., de Vos, R.C., Dekkers, E., Pineda, A., Guillod, L., Bouwmeester, K., Raaijmakers, J.M., 2012. Metabolic and transcriptomic changes induced in Arabidopsis by the rhizobacterium Pseudomonas fluorescens SS101. Plant Physiol. 160, 2173-2188.
77. Vial, L., Cuny, C., Gluchoff-Fiasson, K., Comte, G., Oger, P.M., Faure, D., Wisniewski-Dyé, F., 2006. N-acyl-homoserine lactone-mediated quorum-sensing in Azospirillum: an exception rather than a rule. FEMS Microbiol. Ecol. 58, 155-168. https://doi.org/10.1111/j.1574-6941.2006.00153.x
78. Viswanathan, P., Rathinam, P., Suneeva, S.C., 2014. Plant quorum sensing inhibitors: food, medicinal plants, and others, in: Quorum Sensing vs Quorum Quenching: A Battle with No End in Sight. Springer India, New Delhi, pp. 269-281. https://doi.org/10.1007/978-81-322-1982-8_22
79. Vitale, S., Di Pietro, A., Turrà, D., 2019. Autocrine pheromone signalling regulates community behaviour in the fungal pathogen Fusarium oxysporum. Nat. Microbiol. 4, 1443-1449. https://doi.org/10.1038/s41564-019-0456-z
80. von Rad, U., Klein, I., Dobrev, P.I., Kottova, J., Zazimalova, E., Fekete, A., Durner, J., 2008. Response of Arabidopsis thaliana to N-hexanoyl-DL-homoserine-lactone, a bacterial quorum sensing molecule produced in the rhizosphere. Planta 229, 73-85. https://doi.org/10.1007/s00425-008-0811-4
81. Wehner, G., Schikora, A., Ordon, F., Will, T., 2021. Priming negatively affects feeding behaviour and aphid biomass of Rhopalosiphum padi on barley. J. Pest Sci. 94, 1237-1247. https://doi.org/10.1007/s10340-021-01329-8

 doi:10.20944/preprints202603.1208.v1

82. Wei, Y., Dong, B., Wu, X., Zhao, M., Wang, D., Li, N., Zhang, Q., Zhang, L., Zhou, H., 2023. RpoZ regulates 2,4-DAPG production and quorum sensing system in Pseudomonas fluorescens 2P24. Front. Microbiol. 14, 1160913. https://doi.org/10.3389/fmicb.2023.1160913
83. Williams, H.E., Steele, J.C., Clements, M.O., Keshavarz, T., 2012. γ-Heptalactone is an endogenously produced quorum-sensing molecule regulating growth and secondary metabolite production by Aspergillus nidulans. Appl. Microbiol. Biotechnol. 96, 773-781. https://doi.org/10.1007/s00253-012-4065-5
84. Xiao, Z., Le, C., Xu, Z., Gu, Z., Lv, J., Shamsi, I.H., 2017. Vertical leaching of allelochemicals affecting their bioactivity and the microbial community of soil. J. Agric. Food Chem. 65, 7847-7853. https://doi.org/10.1021/acs.jafc.7b01581
85. Yang, L., Ding, W., Xu, Y., Wu, D., Li, S., Chen, J., Guo, B., 2016. New insights into the antibacterial activity of hydroxycoumarins against Ralstonia solanacearum. Molecules 21, 468.
86. Yang, L., Li, S., Qin, X., Jiang, G., Chen, J., Li, B., Yao, X., Liang, P., Zhang, Y., Ding, W., 2017. Exposure to umbelliferone reduces Ralstonia solanacearum biofilm formation, transcription of type III secretion system regulators and effectors and virulence on tobacco. Front. Microbiol. 8, 1234. https://doi.org/10.3389/fmicb.2017.01234
87. Yang, Y., Xu, J., Li, Y., He, Y., Yang, Y., Liu, D., Wu, C., 2023. Effects of coumarin on rhizosphere microbiome and metabolome of Lolium multiflorum. Plants 12, 1096. https://doi.org/10.3390/plants12051096
88. Zhang, B., Liu, Y., Zhou, D., Lv, Y., Cao, M., Li, H., Meng, D., 2026. The role of quorum sensing in rhizosphere community regulation during bacterial wilt pathogen invasion. Front. Plant Sci. 17, 1685007. https://doi.org/10.3389/fpls.2026.1685007
89. Zhang, H.B., Wang, L.H., Zhang, L.H., 2002. Genetic control of quorum-sensing signal turnover in Agrobacterium tumefaciens. Proc. Natl. Acad. Sci. U.S.A. 99, 4638-4643. https://doi.org/10.1073/pnas.022056699
90. Zhou, C., Guo, J., Zhu, L., Xiao, X., Xie, Y., Zhu, J., Wang, J., 2016. Paenibacillus polymyxa BFKC01 enhances plant iron absorption via improved root systems and activated iron acquisition mechanisms. Plant Physiol. Biochem. 105, 162-173.
91. Zhu, X., Chen, W.-J., Bhatt, K., Zhou, Z., Huang, Y., Zhang, L.-H., Chen, S., Wang, J., 2023. Innovative microbial disease biocontrol strategies mediated by quorum quenching and their multifaceted applications: A review. Front. Plant Sci. 13, 1063393. https://doi.org/10.3389/fpls.2022.1063393