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REVIEW ARTICLE

Pathogenic *Ralstonia solanacearum* in Agriculture: A Review of Prevention and Control Strategies Based on Natural Products

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Abstract

Crop diseases are increasingly posing a significant threat to global agriculture, with the geographic extent of affected regions continuing to expand. While chemical pesticides remain widely employed, their use raises substantial concerns regarding toxicity, residue accumulation, pathogen resistance, and environmental degradation. Natural products derived from plants and microbes represent promising eco-friendly solutions. *Ralstonia solanacearum*, the causative agent of bacterial wilt, severely compromises crop yields, yet effective chemical interventions remain elusive. This review systematically evaluates natural compounds derived from plants and microbes for their efficacy against *R. solanacearum*. Relevant literatures on antimicrobial phytochemicals and microbial metabolites were analyzed to elucidate their mechanisms of action (e.g., antibiosis, quorum quenching) and practical applicability. Key findings indicate that plant-derived compounds and microbial metabolites effectively suppress *R. solanacearum* through growth inhibition and virulence disruption. Some compounds also enhance host resistance. However, field efficacy is influenced by varying environmental conditions. Natural compounds offer a sustainable, low-risk alternative for managing bacterial wilt. To provide suggestions for creative, natural disease management strategies, this review investigates the efficacy of natural compounds produced from plants and microorganisms in managing *R. solanacearum*.

Introduction

Bacterial wilt is caused by the soil-borne bacterium *Ralstonia solanacearum*, which is the second most dangerous plant pathogen in the world and a major cause of crop losses worldwide [1]. Compared to seedborne or airborne illnesses, soilborne diseases such as bacterial wilt are far more restricted and account for 10–20% of the loss of crop output each year. *R. solanacearum* affects more than 450 plant species in 54 botanical families and is common around the globe, especially in tropical and subtropical regions [2]. It has a negative effect on crops including eggplant, tomato, pepper, potato, and ginger. Around 1.6 million hectares of potato crops in 78 nations are impacted by the bacteria, which cause an estimated $848 million in losses each year. *R. solanacearum* causes tomato production losses in China that range from 0 to 90%, depending

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on cropping practices, plant cultivars, soil types, climate, and pathogen strains [3].

The majority of strains of *R. solanacearum* enter plants via the soil, traveling to the roots and penetrating at the lateral root emerging sites. After entering, the bacteria move to the root cortex before moving into the xylem, where it uses its own motility and sap flow to propagate throughout the plant. The bacteria use a type III secretion system (T3SS) to transfer different proteins into the host cells, increasing their susceptibility to illness, and releases enzymes to break down the host cell walls during infection. These proteins use intricate molecular processes to suppress the plant's immune response. As the bacteria grow in the xylem, it produces a polysaccharide slime that blocks the flow of sap, causing symptoms including wilting, limited growth, yellowing of the leaves, and eventually plant death [4].

Because of its wide geographic distribution, wide range of hosts, tenacity, and high soil viability, *R. solanacearum* is difficult to control. Chemical treatments, biological agents, resistant plant types, and cultural techniques are some of the strategies used to control bacterial wilt. A biocontrol bacterium employed in potato farming, *Paenibacillus polymyxa*, for example, has shown up to 80% efficacy against bacterial wilt. One well-known natural source of resistance is the tomato cultivar Hawaii 7996 [1]. Soil disinfection, hot water treatment, soil solarization, and crop rotation are further physical control techniques that are cost-effective and efficient in controlling pathogens. Though they may provide some control, synthetic chemicals are linked to environmental pollution, impacting biodiversity, soil, groundwater, and leaving behind harmful residues. This highlights the need for more sustainable alternatives.

Natural products are becoming more and more important in the creation of pesticides because of their distinctive structures and variety of biological activities [2]. This review systematically summarizes the antibacterial activity and mechanisms of plant-derived and microbial-derived natural products against *R. solanacearum*. For plant-derived bioactive compounds, it focuses on the structural characteristics and antibacterial mechanisms of flavonoids, coumarins, terpenoids, and phenols. In terms of the active components from microbial sources, the anti-*R. solanacearum* activities of compounds such as polyketides, pyrones, alkaloids and peptides were analyzed in detail. The findings provide a scientific basis for developing novel and safe anti-*R. solanacearum* agents.

Plant-Derived Antibacterial Active Substances

Adaptation is frequently necessary for life in the competitive natural world, and plants have developed a wide range of secondary metabolites to assist them in coping with environmental stresses. Known for their many biological roles, these secondary metabolites help plants thrive in harsh environments and are extensively used in the food, pharmaceutical, health, and aquaculture sectors. These substances are also essential for internal plant control, which increases the plants'ability to withstand harsh environments. Essential oils and polyphenols found in some plants have the potential to be used as natural insecticides since they are inherently antibacterial. Notable examples of spices with antimicrobial qualities that work against dangerous germs and fungi include clove, oregano, thyme, cinnamon, and cumin. These spices may be used to cure diseases and preserve food [5].

Because of its active chemicals, the Apiaceae family also shows potential in managing pests and diseases [6]. The European Commission has recognized essential oils including those from mint, clove, and thyme as natural pesticides, demonstrating their potential for pest management without the negative effects of synthetic pesticides [7]. A promising strategy for managing plant diseases caused by pathogens like *R. solanacearum*, while simultaneously reducing pesticide residues and overall usage, involves the application of plant-derived natural antibacterial compounds. The natural compounds obtained from plants that effectively suppress the development of *R. solanacearum* will be the main focus of this study (Tables 1, 2, 3, 4, 5, Figs. 1–2).

Flavonoids

The 2-phenylchromenone skeleton of flavonoids, an essential class of secondary metabolites found in plants, connects two benzene rings with a heterocyclic pyran ring. These substances may be produced as a defensive mechanism against microbial assaults and are present in almost every part of plants [8]. Numerous plant species, such as *Populus nigra, P. deltoides, Sapium baccatum, Scutellaria baicalensis*, and *Caragana leucophloea*, have yielded flavones and flavonols (**1**–**11**). While compounds **5**, **8**–**11** had relatively weak antibacterial activity against *R. solanacearum* (MIC > 200 μg/ml), compounds **1**–**4** and **6** showed robust antibacterial activities with MIC value of 12.5–25 μg/ml. While flavonoid glycosides showed less action, the amount of hydroxyl groups and the presence of a methoxyl group at C-3 seem to be related to the antibacterial effectiveness [9–12].

Furthermore, the heartwood of *Dalbergia odorifera* yielded four isoflavanones (**12**–**15**), two flavanones (**16**–**17**), and three additional flavonoids (**18**–**20**), which were then evaluated for antibacterial activity using the diffusion technique. With inhibition zone diameters (IZDs) of 11.19 mm, compound **13** showed more antibacterial effect than other isoflavanones, indicating that the 2'-OH group amplifies isoflavanone action. With IZDs of 16.62 mm and 14.15 mm, respectively. Compounds **18** (an isoflavan) and **19** (a chalcone) demonstrated even stronger antibacterial activity [13].

Table 1 Inhibitory effects of plant-derived flavonoids on *R. solanacearum*

No	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
1	5,7-Dihydroxy-flavonol	$C_{15}H_{10}O_5$	MIC = 15 µg/ml	ATCC 11696	[9]
2	Baicalein	$C_{15}H_{10}O_5$	MIC = 19 µg/ml		[11]
3	3-O-Methylkaempferol	$C_{16}H_{12}O_6$	MIC = 12.5 µg/ml	ATCC 11696	[10]
4	3-O-Methylquercetin	$C_{16}H_{12}O_7$	MIC = 25 µg/ml	ATCC 11696	[10]
5	5,7-Dihydroxyflavone	$C_{16}H_{12}O_4$	MIC > 300 µg/ml	ATCC 11696	[9]
6	Quercetin	$C_{15}H_{10}O_7$	MIC = 25 µg/ml	ATCC 11696	[10]
7	Rhamnazin	$C_{17}H_{14}O_7$	MIC = 150 µg/ml	ATCC 11696	[10]
8	Kaempferol	$C_{15}H_{10}O_6$	MIC > 200 µg/ml	ATCC 11696	[10]
9	Apigenin	$C_{15}H_{10}O_5$	MIC > 200 µg/ml	ATCC 11696	[10]
10	5-Hydroxy-7-methoxyflavone	$C_{16}H_{12}O_4$	MIC > 300 µg/ml	ATCC 11696	[9]
11	Quercetin 3-O-α-L-arabinopyranoside	$C_{20}H_{18}O_{11}$	MIC = 250 µg/ml	SL1944	[12]
12	Sativanone	$C_{17}H_{16}O_5$	IZD = 6.53 mm (1.6 µL, 50 mg/ml)		[13]
13	(3R)-Vestitone	$C_{16}H_{14}O_5$	IZD = 11.19 mm (1.6 µL, 50 mg/ml)		[13]
14	(3R)−2',3',7-Trihydroxy-4'methoxyisoflavanone	$C_{16}H_{14}O_6$	IZD = 8.11 mm (1.6 µL, 50 mg/ml)		[13]
15	(3R)−4'-Methoxy-2',3,7-trihydroxyisoflavanone	$C_{16}H_{14}O_6$	IZD = 9.99 mm (1.6 µL, 50 mg/ml)		[13]
16	Carthamidin	$C_{15}H_{12}O_6$	IZD = 8.34 mm (1.6 µL, 50 mg/ml)		[13]
17	Liquiritigenin	$C_{15}H_{12}O_4$	IZD = 12.23 mm (1.6 µL, 50 mg/ml)		[13]
18	(3R)-Vestitol	$C_{16}H_{16}O_4$	IZD = 16.62 mm (1.6 µL, 50 mg/ml)		[21]
19	Isoliquiritigenin	$C_{15}H_{12}O_4$	IZD = 14.15 mm (1.6 µL, 50 mg/ml)		[13]
20	Sulfuretin	$C_{15}H_{10}O_5$	IZD = 9.10 mm (1.6 µL, 50 mg/ml)		[13]
21	Catechin	$C_{15}H_{14}O_6$	MIC = 18.75 mg/ml	race 3, biovar 2	[14]
22	Epicatechin	$C_{15}H_{14}O_6$	MIC = 9.37 mg/ml	race 3, biovar 2	[14]
23	Daphnodorin A	$C_{30}H_{22}O_9$	IZD = 8.09 mm (5 µl 25 µg/ml)		[15]
24	Daphnodorin B	$C_{30}H_{22}O_{10}$	IZD = 4.04 mm (5 µl,25 µg/ml)		[15]

Compounds **21** and **22** of flavan-3-diols, which were isolated from *Acacia arabica* and *Punica granatum,* showed mild antibacterial activity with MIC values of 18.75 and 9.37 mg/ml, according to further research [14]. Despite having unusual structural configurations, these substances have shown strong antibacterial activity. Conversely, *Daphne acutiloba* compounds **23** and **24** exhibited IZDs of 8.09 mm and 4.04 mm, respectively [15]. Overall, the amount and location of hydroxyl groups in flavonoids, as well as their structural makeup, are strongly linked to their antibacterial action against *R. solanacearum*.

Coumarins

A naturally occurring plant chemical, coumarin (2H-1-benzopyran-2-one) is found in large quantities in the natural world. It is a member of the benzopyrone family and is made up of an α-pyrone ring fused to a benzene ring [16]. Coumarin derivatives have promising antibacterial qualities because they can bind to the *B subunit* of bacterial DNA gyrase and prevent DNA supercoiling by decreasing ATPase activity [17]. The antibacterial properties of eighteen plant-derived coumarins with different substitutions were assessed in studies conducted by Liang Yang and associates. Daphnetin, esculetin, umbelliferone, and xanthotol were the compounds that had the most activity against *R. solanacearum*. Daphnetin was the most potent of these, with MIC values of 64, 192, and 256 mg/L, respectively, compared to coumarin's 384 mg/L. Particularly, hydroxylation at locations C-6, C-7, or C-8 increased the antibacterial ability [18].

Subsequent examination using electron and fluorescence microscopy revealed that umbelliferone, daphnetin, and esculetin may harm *R. solanacearum*'s cell membrane and prevent the production of biofilms. To differing degrees, these substances impacted the expression of bacterial genes: daphnetin caused significant alterations in gene regulation (420 genes were up-regulated, 502 genes were down-regulated), and the suppression of flagellar genes (fliA and flhC) was linked to a strong antibiofilm effect. Additionally, by inhibiting genes such as xpsR, epsE, epsB, and lexM, daphnetin decreased the synthesis of extracellular polysaccharides and the development of biofilms [19].

Furthermore, 7-methoxycoumarin (**44**) demonstrated a MIC value of 75 mg/L against *R. solanacearum*. This compound successfully damaged the bacterial cell membrane and considerably inhibited the development of biofilms

Table 2 Inhibitory effects of plant-derived coumarins on *R. solanacearum*

No	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
25	Daphnetin	$C_9H_6O_4$	MIC = 64 μg/ml	phylotype I, race1, biovar 3	[18]
26	Esculetin	$C_9H_6O_4$	MIC = 192 μg/ml	phylotype I, race1, biovar 3	[18]
27	Umbelliferone	$C_9H_6O_3$	MIC = 256 μg/ml	phylotype I, race1, biovar 3	[18]
28	Xanthotol	$C_{11}H_6O_4$	%IR 80.1%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
29	Coumarin	$C_9H_6O_2$	%IR 50.3%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
30	Scopoletin	$C_{10}H_8O_4$	%IR 32.6%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
31	Scoparone	$C_{11}H_{10}O_4$	%IR 17.3%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
32	Isofraxidin	$C_{11}H_{10}O_5$	%IR 0.7%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
33	4-Methoxycoumarin	$C_{10}H_8O_3$	%IR 54.1%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
34	4-Hydroxycoumarin	$C_9H_6O_3$	%IR 4.9%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
35	Psoralen	$C_{11}H_6O_3$	%IR 57.1%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
36	Xanthotoxin	$C_{12}H_8O_4$	%IR 36.3%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
37	Bergapten	$C_{12}H_8O_4$	%IR 21.9%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
38	3-Acetyl-2H-chromen-2-one	$C_{11}H_8O_3$	%IR 10.7%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
39	Isopimpinellin	$C_{13}H_{10}O_5$	%IR 22.5%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
40	Osthole	$C_{15}H_{16}O_3$	%IR 3.1%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
41	Imperatorin	$C_{16}H_{14}O_4$	%IR 19.1%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
42	Isoimperatorin	$C_{16}H_{14}O_4$	%IR 23.9%, 100 μg/ml	phylotype I, race1, biovar 3	[18]
43	7-Methoxycoumarin	$C_{10}H_8O_3$	MIC = 75 μg/ml	CQPS-1	[21]
44	6-Methylcoumarin	$C_{10}H_8O_2$	%IR 76.79%, 100 μg/ml	CQPS-1	[22]
45	3-Aminocoumarin	$C_9H_7NO_2$	%IR 72.02%, 100 μg/ml	CQPS-1	[22]
46	3-Acetylcoumarin	$C_{11}H_8O_3$	%IR 76.01%, 100 μg/ml	CQPS-1	[22]

Table 3 Inhibitory effects of plant-derived terpenoids on *R. solanacearum*

NO	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
47	Citronellal	$C_{10}H_{18}O$	MIC = 1 μg/ml	phylotype II	[25]
48	Limonene	$C_{10}H_{16}$	MIC = 1 μg/ml		
49	Carvone	$C_{10}H_{16}$	MIC = 5 μg/ml		
50	Camphor	$C_{10}H_{16}O$	MIC = 5 μg/ml		
51	Thymol	$C_{10}H_{14}O$	MIC = 125 μg/ml		
52	Hinokitiol	$C_{10}H_{12}O_2$	MIC = 50 μg/ml		
53	Naphthalenemethanol, decahydro-3-hydroxy-α,α,4a,8a-tetramethyl-8-methylene-, (2S,3S,4aR,8aS)-(ACI)	$C_{16}H_{28}O_2$	IZD = 16.90 mm (50 μL, 10 mg/ml)		
54	(5S, 7S, 9S, 10S)-(+)−9-Hydroxy-selina-3,11-dien-12-al	$C_{16}H_{28}O_2$	IZD = 18.20 mm (50 μL, 10 mg/ml)		[26]
55	(5S, 7S, 9S, 10S)-(+)−9-Hydroxy-eudesma-3,11 (13)-dien-12-methyl ester	$C_{16}H_{24}O_3$	IZD = 10.15 mm (50 μL, 10 mg/ml)		[28]
56	(4αβ,7β,8αβ)−3,4,4α,5,6,7,8,8α-octahydro-7-[1-(hydroxymethyl)ethenyl]−4α-methylnaphthalene-1-car boxaldehyde	$C_{15}H_{22}O_2$	IZD = 8.98 mm (50 μL, 10 mg/ml)		[27]
57	12,15-Dioxo-α-selinen	$C_{15}H_{20}O_2$	IZD = 11.02 mm (50 μL, 10 mg/ml)		
58	Subergorgiol	$C_{15}H_{22}O_2$	MIC = 16 μg/ml		
59	Deoxymikanolide	$C_{15}H_{16}O_5$	MIC = 62.5 μg/ml		
60	Arjungenin	$C_{30}H_{48}O_6$	MIC = 200 μg/ml	ATCC 11696	[83]
61	Betulinic acid	$C_{30}H_{48}O_3$	MIC = 100 μg/ml	race #4	[30]
62	Cycloeucalenol	$C_{30}H_{50}O$	MIC = 25 μg/ml		[32]

Table 4 Inhibitory effects of plant-derived phenols on *R. solanacearum*

No	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
63	Protocatechualdehyde	$C_7H_8O_3$	MIC = 20 µg/ml	phylotype I, race1, biovar 3	[84]
64	Pyrogallol	$C_8H_8O_3$	MIC = 2.34 mg/ml	race 3, biovar 2	[14]
65	Methyl gallate	$C_8H_8O_5$	MIC = 26.0 µg/ml	SL1944	[12]
66	Vanillin	$C_8H_8O_3$	IZD = 11.77 mm 25 µl, 20 mg/ml		[85]
67	Syringaldehyde	$C_9H_{10}O_4$	IZD = 6.24 mm 25 µl, 20 mg/ml		[85]
68	Eugenol	$C_{10}H_{12}O_2$	IZD = 18.5 mm 150 µl 10 mg/ml		[34]
69	Caffeic acid	$C_9H_8O_4$	MIC = 200 µg/ml	CQPS-1	[35]
70	Gallic Acid	$C_7H_6O_5$	MIC = 3 mg/ml	Genbank: KM502217	[36]
71	6-Hydroxy-2-(2-phenylethyl)chromone	$C_{17}H_{14}O_3$	IZD = 6.80 mm 50 µl, 10 mg/ml		[86]
72	Daphneolone	$C_{17}H_{18}O_3$	IZD = 6.72 mm 25 µg/ml		[15]
73	Daphnenone 2	$C_{17}H_{18}O_2$	IZD = 6.00 mm 25 µg/ml		[15]
74	Resveratrol	$C_{14}H_{12}O_3$	MIC = 2 µg/ml	Biovar3, Phylotype I	[37]
75	Alatusol A	$C_{13}H_{18}O_6$	IZD = 6.18 mm 25 µl, 20 mg/ml		[85]
76	Sinapicaldehyde	$C_{11}H_{12}O_4$	IZD = 6.03 mm 25 µl, 20 mg/ml		
77	p-Hydroxycinnamic acid	$C_9H_8O_3$	IZD = 6.01 mm 25 µl, 20 mg/ml		
78	(2S,3S)−2-Hydroxy-3-(4-hydroxy-3-methoxyphenyl)−3-methoxypropyl 4-hydroxybenzenepropanoate	$C_{20}H_{24}O_7$	IZD = 6.03 mm 25 µl, 20 mg/ml		
79	Corilagin	$C_{27}H_{22}O_{18}$	MIC = 31.3 µg/ml	SL1944	[12]
80	Tercatain	$C_{34}H_{28}O_{22}$	MIC = 52.1 µg/ml		
81	Chebulagic acid	$C_{41}H_{30}O_{27}$	MIC = 52.1 µg/ml		
82	Chebulinic acid	$C_{41}H_{32}O_{27}$	MIC = 52.1 µg/ml		
83	3,5-Dihydroxy-4-methoxybenzoic acid	$C_8H_8O_5$	MIC = 0.47 mg/ml	race 3, biovar 2	[14]
84	Gallic acid	$C_7H_6O_5$	MIC = 0.6 mg/ml		
85	3-Hydroxybenzoic acid	$C_7H_6O_3$	MIC = 2.34 mg/ml		
86	2,3,4-Trihydroxybenzoic acid	$C_7H_6O_5$	MIC = 1.17 mg/ml		
87	2,3-Dihydroxybenzoic acid	$C_7H_6O_4$	MIC = 1.56 mg/ml		
88	Vanillic acid	$C_8H_8O_4$	MIC = 1.56 mg/ml		
89	Isovanillic acid	$C_8H_8O_4$	MIC = 2.34 mg/ml		
90	Syringic acid	$C_9H_{10}O_5$	MIC = 1.56 mg/ml		
91	3,4,5-Trimethoxybenzoic acid	$C_{10}H_{12}O_5$	MIC = 4.65 mg/ml		
92	Protocatechuic acid	$C_7H_6O_4$	MIC = 3.12 mg/ml		
93	4,6-Di-O-galloylarbutin	$C_{26}H_{24}O_{15}$	MIC = 0.10 µg/mL	SL1944	[87]
94	2,6-Di-O-galloylarbutin	$C_{26}H_{24}O_{15}$	MIC = 0.08 µg/mL		
95	β-D-Glucopyranose, 2,4,6-tris(3,4,5-trihydroxybenzoate)	$C_{27}H_{24}O_{18}$	MIC = 0.04 µg/mL		
96	1,3,4,6-Tetra-O-galloyl-β-D-glucose	$C_{34}H_{28}O_{22}$	MIC = 0.03 µg/mL		
97	1,2,4,6-Tetra-O-galloyl-β-D-glucose	$C_{34}H_{28}O_{22}$	MIC = 0.03 µg/mL		
98	1,2,3,6-Tetra-O-galloyl-β-D-glucose	$C_{34}H_{28}O_{22}$	MIC = 0.02 µg/mL		

throughout a range of 25–100 mg/L. With relative control efficiencies of 83.61%, 68.78%, and 58.11% at 6, 8, and 10 days post-inoculation, this drug also decreased the severity of tobacco bacterial wilt in pot studies and downregulated virulence-related genes (epsE, hrpG, and popA) [20, 21]**.** Subsequent antibacterial testing revealed that compound **44** had substantial in vitro action, suppressing ftsZ, a crucial bacterial division protein, to reduce bacterial growth by 76.79% at 100 mg/L. This resulted in cell elongation and cell division inhibition. At 10, 11, and 12 weeks following tobacco transplantation, field tests showed that 6-methylcoumarin, another coumarin derivative, had control efficiencies of 35.76%, 40.51%, and 38.99%, indicating its potential for controlling bacterial infections in agricultural settings [22].

Terpenoids

There are around 25,000 identified terpenoids, the most varied class of secondary metabolites found in plants [23]. Terpenes, which are structurally composed of one or

Table 5 Inhibitory effects of other plant-derived compounds on *R. solanacearum*

No	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
99	2,4-Dihydroxy-7-methoxy-1,4-benzoxazine-3-one	$C_9H_9NO_5$	200 μg/ml	phylotype I, race 1, biovar 3	[38]
100	2-Benzoxazolinone	$C_7H_5NO_2$	300 μg/ml		
101	6-Chloro-2-benzoxazolinone	$C_7H_4ClNO_2$	100 μg/ml		
102	2-Mercaptobenzothiazole	$C_7H_5NS_2$	50 μg/ml		
103	Lansiumamide B	$C_{18}H_{17}NO$	MIC = 125 μg/ml		[39]
104	β-Sitosterol	$C_{22}H_{28}O_5$	MIC = 100 μg/ml		[31]
105	γ-Mangostin	$C_{23}H_{24}O_6$	IC_{50} = 34.7 μg/ml		[1]
106	Aristoloxazine C	$C_{19}H_{14}N_2O_6S$	MIC = 0.05 μg/ml		[40]
107	AristoloxazineA	$C_{20}H_{18}N_2O_6S$	0.15 μg/ml		
108	7-Methoxyaristololactam IV	$C_{19}H_{15}NO_6$	6.00 μg/ml		
109	Aristololactam I	$C_{17}H_{11}NO_4$	1.50 μg/ml		
110	Aristololactam IV	$C_{18}H_{13}NO5$	5.00 μg/ml		
111	Aristolochia A	$C_{17}H_{11}NO_7$	6.25 μg/ml		
112	7-Aristolochic acid IVa	$C_{17}H_{11}NO_8$	25.00 μg/ml		
113	9-Ethoxyaristololactam I	$C_{19}H_{15}NO_5$	80.00 μg/ml		
114	9-Ethoxyaristololactam IV	$C_{20}H_{17}NO_6$	50.00 μg/ml		

more five-carbon units, are important for plant defense and ecological communication [24]. Five of these monoterpenes (**47–51**) showed a variety of antibacterial properties when evaluated for activity against *R. solanacearum*. With a MIC value of 1 μg/mL, limonene was the most active compound, whilst thymol was the least active [25]. At a MIC value of 50 μg/mL, hinokitiol (**52**), which is present in the heartwood of *Cupressaceae* species, demonstrated efficacy against *R. solanacearum*. This substance is also well-known for its ability to stimulate plant development and for having broad-spectrum antibacterial qualities.

Additionally, the filter paper disc agar diffusion technique was used to analyze five eudesmane-type sesquiterpenoids (**53–57**) that were isolated from *Aquilaria* species (agarwood). When compared to kanamycin sulfate, the positive control, these substances showed modest antibacterial activity [26]. With a MIC value of 16 μg/mL, subergorgiol (**58**), a sesquiterpene derived from the gorgonian coral *Subergorgia suberosa*, demonstrated potent action against *R. solanacearum* [27, 28]

With a MIC of 62.5 mg/L, deoxymikanolide (**59**), which was isolated from *Mikania micrantha*, had moderate antibacterial activity. By influencing the metabolism of glycan and phosphorus, raising ROS and MDA levels, and suppressing antioxidant enzyme activity, treatment with deoxymikanolide markedly changed the physiology of *R. solanacearum* cells [29]. Additionally, this substance caused cytoplasmic disruption, cell membrane damage, and ultimately cell death [30].

Finally, three triterpenes (**60–62**) were identified in *Erythrophleum suaveolens* and *Terminalia brownii*. With MIC values ranging from 100 to 200 μg/mL, the triterpenes from *T. brownii* had mild antibacterial activity, but the triterpene from *E. suaveolens* showed moderate activity, with a MIC value of 25 μg/mL [30, 32].

Phenols

Essential secondary metabolites of plants, phenolic compounds are well-known for their vast range of functions in plant biology. Among other things, these substances have a role in growth, reproduction, pigmentation, and pathogen defense. There are thousands of known phenolics, which come in a broad range of forms such as monomers, dimers, and polymers [33]. It has been shown that protocatechualdehyde (**63**) may alter the shape and structure of bacterial cells and prevent the development of biofilms. Protocatechualdehyde application has shown efficacy in lowering tobacco bacterial wilt, with a control efficiency of 92.01% nine days after inoculation. By causing damage to bacterial cells, such as flagella loss, cell content leakage, and cavity development, eugenol (**68**) also demonstrates antibacterial action. Eugenol also lowers *R. solanacearum*'s protein levels, hinders the metabolism of carbohydrates, and inhibits enzymes such as succinate dehydrogenase and catalase [34].

Higher quantities of caffeic acid (**69**) have been found in *R. solanacearum*-infected plants than in healthy plants, indicating that it plays a part in the plant's defensive response.

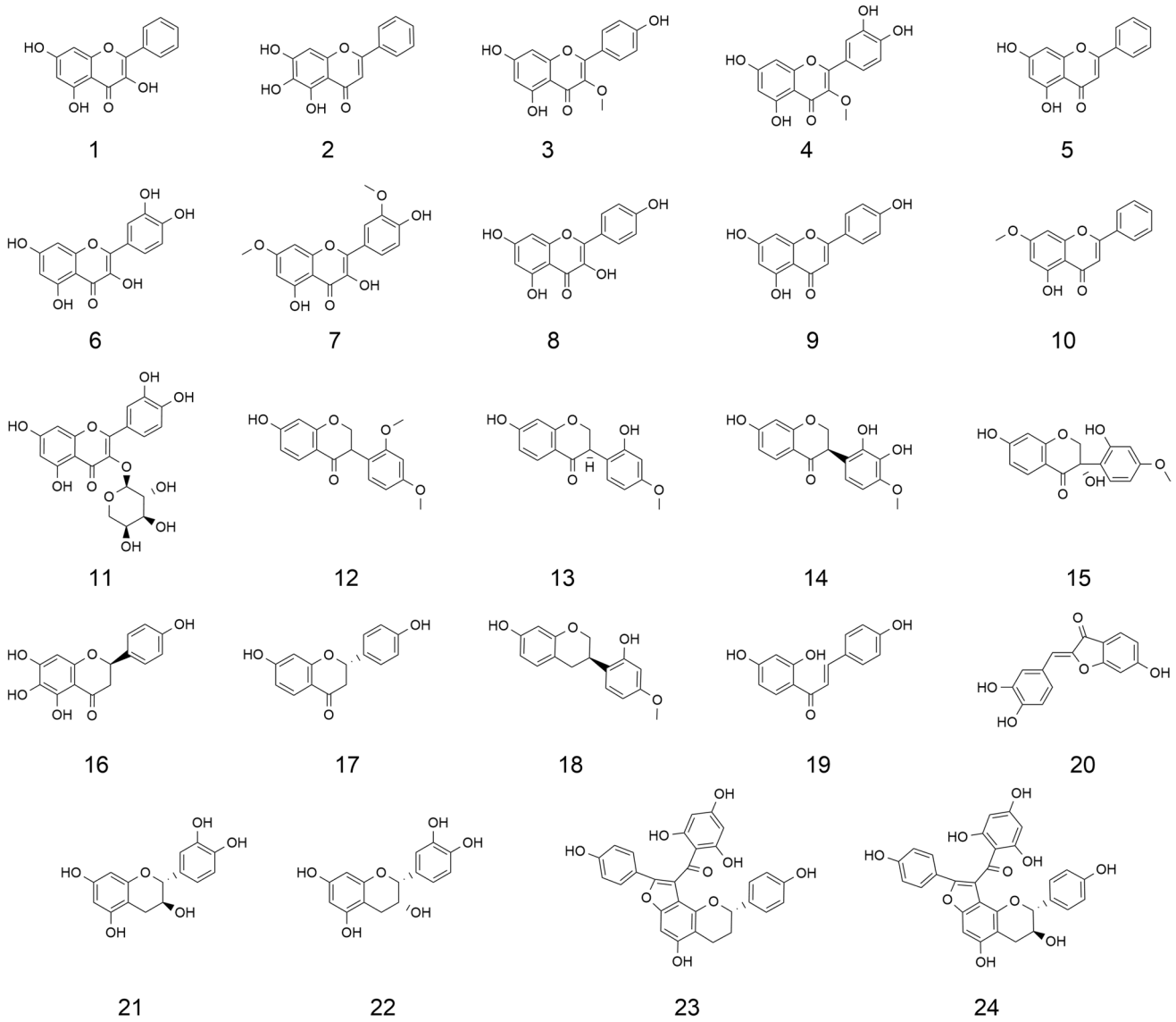

Fig. 1 The structures of plant-derived flavonoids with anti-*R. solanacearum* activity

When applied at a dose of 200 μg/mL, compound **69** significantly damages the cell membrane of *R. solanacearum*, resulting in irregular cavity development and membrane weakening. By downregulating the *lecM* and *epsE* genes, it also lessens the production of biofilms. Compound **69** raises lignin and hydroxyproline levels in vitro by activating enzymes such as phenylalanine ammonialyase and peroxidase. The use of compound **69** effectively postponed and reduced the occurrence of bacterial wilt in tobacco in both field and pot experiments [35]. At 1.5 mg/mL, gallic acid (**70**) reduced mature biofilms by 85% and decreased swimming and twitching motility by 63% and 93%, respectively [36]. With a MIC value of 2 μg/mL, resveratrol (**74**) was similarly effective against *R. solanacearum* [36]. It decreases the production of biofilms, disrupts the bacterial cell membrane, and prevents swarming movement. After 13 days, resveratrol achieved an 85% control efficiency in pot experiments by reducing early bacterial adhesion and colonization on tobacco plants [37].

With MIC values ranging from 0.02 to 0.10 g/L, gallotannins (**93–98**) that were isolated from *Sedum takesimense* showed significant antibacterial activity against *R. solanacearum*. Numerous combinations of these substances increased their total activity by exhibiting partial or synergistic antibacterial activities [38].

Others

Many cereal plants often generate hydroxyamic acids, which are involved in defensive mechanisms against

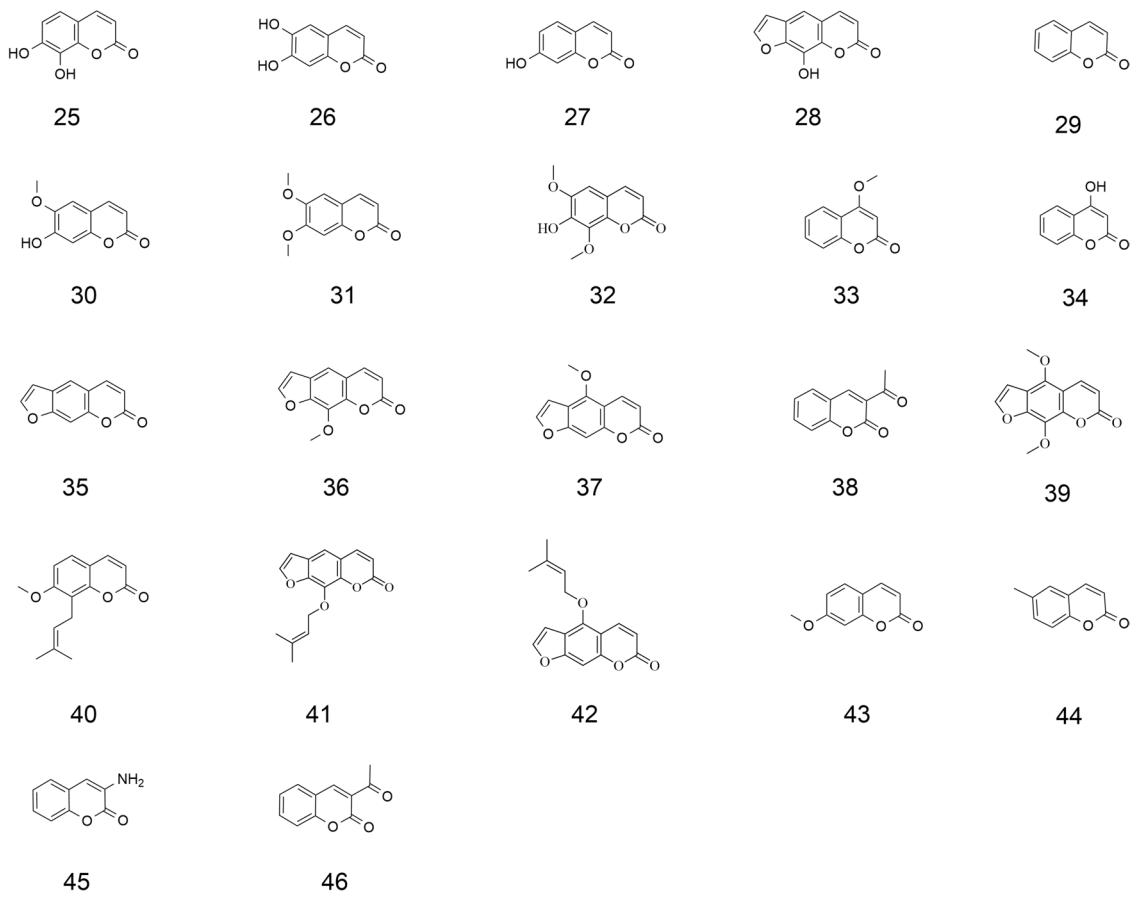

Fig. 2 The structures of plant-derived coumarins with anti-*R. solanacearum* activity

bacteria, fungus, and insect pests. It has been shown that within 24 h, four hydroxamic acids that were separated from Zea mays (corn) dramatically impede swarming motility, limit the development of biofilms, and drastically decrease bacterial growth. Despite these impacts, they did not directly reduce the incidence of bacterial wilt. In contrast to untreated controls, treated plants had greater fresh weight averages and a lower wilt index, suggesting a possible improvement in plant resilience and health [38]. When extracted from *Clausena lansium* seeds, lansiumamide B (**103**) showed a MIC value of 125 μg/mL against bacterial infections. Compound **103** had notable effectiveness in reducing tobacco bacterial wilt in pot experiments. At 7, 14, and 21 days after treatment, its control efficiency was 95.84%, 91.67%, and 86.38%, respectively, when administered at 100 mg/kg by root irrigation. When tested at 21 days, its efficacy was about 40 times greater than that of streptomycin, a common bactericide [39]. γ-Mangostin (**105**), also known as, is a prenyl xanthone that greatly suppresses virulence-related genes including HrpB, FihD, and PilT of *R. solanacearum* at 64 μg/mL and affects bacterial shape at a dosage of 16.0 μg/mL. Furthermore, compound **105** successfully reduces the symptoms of *R. solanacearum*-induced bacterial wilt disease in tomato and tobacco seedlings in vitro [1].

With MIC values ranging from 0.05 to 80 μg/mL, phenolphthalein derivatives (**106–114**) isolated from *Asarum heterotropoides* demonstrate potent antibacterial activity against *R. solanacearum*. Interestingly, compounds **106–111** outperformed the positive control, streptomycin sulfate, in terms of antibacterial activity, with MIC values of less than 10 μg/mL. Aristoloxazine C's (**106**) antibacterial action is mainly ascribed to its capacity to interfere with the construction of the bacterial cell wall [40].

Microbial-Derived Antibacterial Active Substances

In addition to evolving their own defenses and resistance mechanisms to fend against disease invasion, plants have used helpful microbes for increased safety. Over billions of years, this complex interaction has developed, greatly enhancing plant adaptability. Plants draw in helpful microorganisms to inhabit the rhizosphere and even within the plant via chemical signaling and root exudation, giving

these beneficial bacteria vital nutrients like carbohydrates [41]. Up to 40% of the photosynthetic products produced by plants may be released into the rhizosphere as root exudates, according to research. These exudates attract some good microbes to aid in the defense against harmful germs during an assault [42].

In exchange, helpful microbes help control illness and encourage plant development, mostly via the production of antibiotics. Remarkably, the genus *Streptomyces* is the source of almost 80% of antibiotics, with actinomycetes accounting for the majority of these contributions (Tables 6, 7, 8, 9, 10, 11, Figs. 3, 4, 5) [43]. This indicates that a substantial majority of antibiotics originate from microbes, rendering microbial natural products promising candidates for the development of novel agrochemicals.

Polyketides

With the help of certain enzymes called polyketide synthases, acetyl or malonyl units condense to generate polyketides. Because of their many bioactivities, this broad family of natural compounds, which come from both

Table 6 Inhibitory effects of microbial-derived polyketides on *R. solanacearum*

No	From	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
115	*Colletotrichum gloeosporioides*	Sclerone	$C_{10}H_{10}O_3$	MIC = 128 μg/ml		[88]
116	*Colletotrichum gloeosporioides*	Isotalaroflavone	$C_{14}H_{12}O_6$	MIC = 64 μg/ml		[60]
117	*Berkleasmium* sp.	Diepoxins δ	$C_{20}H_{16}O_8$	MIC = 75 μg/ml	ATCC 11696	[46]
118		Palmarumycin C11	$C_{20}H_{14}O_5$	MIC = 37.5 μg/ml		
119		Palmarumycin C12	$C_{20}H_{14}O_6$	MIC = 250 μg/ml		
120		Cladospirone B	$C_{20}H_{14}O_6$	MIC 37.5 μg/ml		
121		Diepoxins δ	$C_{20}H_{16}O_8$	MIC = 75 μg/ml		
122		Diepoxins κ	$C_{21}H_{18}O_8$	MIC = 37.5 μg/ml		
123		Diepoxins ζ	$C_{20}H_{14}O_7$	MIC = 50 μg/ml		
124		Palmarumycin C8	$C_{20}H_{13}ClO_6$	MIC = 25 μg/ml		
125	Aspergillus candidus Bdf-2	3 -Hydroxyterphenyllin	$C_{20}H_{18}O_6$	MIC = 64 μg/ml		[47]
126		3,3''-Dihydroxyterphenyllin	$C_{20}H_{18}O_7$	MIC = 32 μg/ml		
127		Candidusin A	$C_{20}H_{16}O_6$	MIC = 64 μg/ml		
128	*Neohelicosporium griseum*	Neogrisphenol A	$C_{20}H_{16}O_7$	MIC = 15.36 μg/ml		[89]
129	Cosmospora sp.	Pseudoanguillosporin B	$C_{17}H_{26}O_4$	IC_{50} = 42.2 μg/ml		[90]
130	*Aspergillus chevalieri*	Asperglaucin A	$C_{19}H_{26}O_4S$	MIC = 100 μg/ml		[48]
131		Asperglaucin B	$C_{19}H_{26}O_3$	MIC = 50 μg/ml		
132		Tetrahydroauroglaucin	$C_{19}H_{26}O_3$	MIC = 100 μg/ml		
133		Flavoglaucin	$C_{19}H_{28}O_3$	MIC = 100 μg/ml		
134		Isodihydroauroglaucin	$C_{19}H_{24}O_3$	MIC = 50 μg/ml		
135		(3E)−3-Hepten-1-yl-3,6-dihydroxy-5-(3-methyl-2-buten-1-yl)benzaldehyde	$C_{19}H_{26}O_3$	MIC = 50 μg/ml		
136	*Ustilaginoidea virens*	Oxosorbicillinol	$C_{14}H_{16}O_5$	MIC = 64 μg/ml	ATCC11696	[49]
137		Bisvertinolone	$C_{28}H_{32}O_9$	MIC = 4 μg/ml		
138		Demethyltrichodimerol	$C_{27}H_{30}O_8$	MIC = 24 μg/ml		
139		Dihydrotrichodimer ether A	$C_{28}H_{32}O_8$	MIC = 64 μg/ml		
140		Ustisorbicillinol B	$C_{28}H_{34}O_8$	MIC = 64 μg/ml		
141	Serratia plymuthica C1	Serratamid	$C_{28}H_{35}N_3O_5$	MIC = 0.49 μg/ml		[50]
142	*Pestalotipsis* sp. cr014	Pestalotic acid E	$C_{21}H_{26}O_7$	MIC = 100 μg/ml		[51]
143		Pestalotic acid G	$C_{19}H_{26}O_7$	MIC = 0.78 μg/ml		
144		Pestalotic acid H	$C_{19}H_{26}O_7$	MIC = 0.78 μg/ml		
145		Pestalotic acid B	$C_{19}H_{22}O_6$	MIC = 0.78 μg/ml		
146		Pestalotic acid C	$C_{18}H_{25}ClO_5$	MIC = 0.78 μg/ml		
147	Phytohabitans sp. RD003013	Phytohabimicin	$C_{25}H_{32}C_{l2}N_2O_5S$	MIC = 6.3 μg/ml	SUPP1541	[52]
148	*Alternaria alternata* ZHJG5	Verrulactone A	$C_{28}H_{18}O_{12}$	MIC = 4 μg/ml		[60]

prokaryotes and eukaryotes has a lot of economic promise. Cultures of the fungus Berkleasmium sp., an endophyte from the therapeutic herb Dioscorea zingiberensis, were used to extract Spirobisnaphthalenes (**117**–**124**) [44, 45]. These compounds are made up of one decalin unit and one 1,8-dioxynaphthalene unit joined by a spiro-ketal bridge. With a MIC value of 25 μg/mL, palmarumycin C8 (**124**) demonstrated the most potent antibacterial activity against *R. solanacearum* among them [46].

Table 7 Inhibitory effects of microbial-derived pyrones on *R. solanacearum*

No	From	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
149	*Xylaria grammica* KCTC 13121BP	Grammicin	$C_7H_6O_4$	MIC = 500 μg/ml		[54]
150		Patulin	$C_7H_6O_4$	MIC = 7.8 μg/ml		
151	*Hyalodendriella sp.* Ponipo-def12	4-Hydroxymellein	$C_{10}H_{10}O_4$	IC_{50} = 16.24 μg/ml		[57]
152		Botrallin	$C_{16}H_{14}O_7$	IC_{50} = 85.46 μg/ml		
153	*Hyalodendriella sp.* Ponipo-def12	TMC-264	$C_{16}H_{13}ClO_7$	MIC = 25 μg/ml	ATCC 11696	[55]
154	*Alternaria sp.* Samif01	Alternariol 9-methyl ether	$C_{15}H_{12}O_5$	MIC = 75 μg/ml	ATCC 11696	[56]
155	*Alternaria sp.* Samif01	Altenuisol	$C_{14}H_{10}O_6$	MIC = 182.3 μg/ml	ATCC11696	[58]
156	*Rhizopycnis vagum* Nitaf22	Rhizopycnin C	$C_{15}H_{11}ClO_7$	MIC = 50 μg/ml	ATCC11696	[59]
157		Rhizopycnins D	$C_{14}H_9ClO_5$	MIC = 50 μg/ml		
158		Penicilliumolide D	$C_{16}H_{13}ClO_6$	MIC = 50 μg/ml		
159		Alternariol	$C_{14}H_{10}O_5$	MIC = 25 μg/ml		
160	*Hyalodendriella sp.* Ponipo-def12	Palmariol B	$C_{15}H_{11}ClO_5$	IC_{50} = 17.51 μg/ml	ATCC 11696	[57]
161	*Alternaria alternata* ZHJG5	4-Hydroxyalternariol-9-methyl ether	$C_{15}H_{12}O_6$	MIC = 0.5 μg/ml		[83]
162	*Ustilaginoidea virens*	Ustilaginoidin E	$C_{29}H_{24}O_{10}$	MIC = 16 μg/ml	ATCC11696	[60]
163		Ustilaginoidin G	$C_{28}H_{20}O_{10}$	MIC = 64 μg/ml		
164	*Cosmospora sp.*	Cephalochromin	$C_{28}H_{22}O_{10}$	IC_{50} = 27.6 μg/ml		[12]

Table 8 Inhibitory effects of microbial-derived alkaloids on *R. solanacearum*

No	From	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
165	*Chaetomium sp*	Scorpinone	$C_{15}H_{11}NO_4$	IZD = 8.71 mm, 8 μg	ATCC 11696	[61]
166		5-Deoxybostrycoidin	$C_{15}H_{11}NO_4$	IZD = 8.04 mm, 8 μg		
167	*Bacillus velezensis* Hnu24	Bis(1H-indol-3-yl) phenylmethane	$C_{23}H_{18}N_2$	MIC = 50 μg/ml		[91]
168	*Aspergillus candidus* Bdf-2	Fellutanine A	$C_{22}H_{20}N_4O_2$	MIC = 256 μg/ml		[40]
169	*Fusarium sambucinum* TE-6L	Amoenamide C		MIC = 16 μg/ml		[62]
170		Sclerotiamide B	$C_{26}H_{29}N_3O_5$	MIC = 16 μg/ml		
171		Sclerotiamide	$C_{26}H_{29}N_3O_5$	MIC = 8 μg/ml		
172		Notoamide B	$C_{26}H_{29}N_3O_4$	MIC = 16 μg/ml		
173		Notoamide D	$C_{26}H_{31}N_3O_4$	MIC = 32 μg/ml		
174		Speramide A	$C_{26}H_{29}N_3O_4$	MIC = 32 μg/ml		
175	*Penicillium chrysogenum* XNM-12	Decaturin B	$C_{30}H_{35}NO_6$	MIC = 32 μg/ml		[63]
176		Decaturin C	$C_{30}H_{35}NO_5$	MIC = 32 μg/ml		
177		Decaturin F	$C_{30}H_{37}NO_5$	MIC = 16 μg/ml		
178		Oxalicine C	$C_{30}H_{33}NO_7$	MIC = 8 μg/ml		
179		Decaturin D	$C_{30}H_{35}NO_4$	MIC > 64 μg/ml		
180	*Labrenzia* sp.	Labrenzbactin	$C_{32}H_{36}N_4O_{10}$	MIC = 25 μg/ml	SUPP1541	[64]

Table 9 Inhibitory effects of microbial-derived peptides on *R. solanacearum*

No	From	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
181	*Escherichia coli*	Cyclo(L-Pro-D-Ile)	$C_{11}H_{18}N_2O_2$	MIC = 1000 μg/ml	GMI1000	[66]
182		Cyclo(L-Pro-L-Phe)	$C_{14}H_{16}N_2O_2$	MIC = 1000 μg/ml		
183	*Streptomyces sp.*	Cyclo(L-Pro-l-Tyr)	$C_{14}H_{16}N_2O_3$	MIC = 31.25 μg/ml		[67]
184		Cyclo(D-Pro-l-Tyr)	$C_{14}H_{16}N_2O_3$	MIC = 31.25 μg/ml		
185	*Streptomyces* sp. NEAU-HV9	Actinomycin D	$C_{62}H_{86}N_{12}O_{16}$	MIC = 0.6 mg/ml		[68]
186		Iturin	$C_{49}H_{76}N_{12}O_{14}$	MIC = 100 μg/ml	GMI1000	[69]
187	*Paenibacillus ehimensis* MA2012	Polypeptin C	$C_{56}H_{96}N_{12}O_{13}$	MIC = 124 μg/ml	SL 1931	[70]
188	*Bacillus* sp. EA-CB0959	Surfactin	$C_{53}H_{93}N_7O_{13}$	MIC = 128 μg/ml	EAP-009	[71]
189	*Bacillus subtilis* JW-1	Cyclo(L-a-aspartyl-D-leucyl-L-leucyl-3-hydroxy-14-Methyl-pentadecanoyl-L-glutaminyl-L-leucyl-D-leucyl-L-valyl) (ACI)	$C_{54}H_{96}N_8O_{12}$			[72]
190	*Bacillus* sp. EA-CB0959	Fengycin	$C_{72}H_{110}N_{12}O_{20}$	MIC = 32 μg/ml	EAP-009	[71]

Table 10 Inhibitory effects of microbial-derived phenols on *R. solanacearum*

No	From	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
191	*Rhizoctonia solani* Kühn	M-hydroxyphenylacetic acid	$C_8H_8O_3$	IC_{50} = 112.5 μg/ml	ATCC 11696	[73]
192	*Pseudomonas fluorescens* VSMKU3054	2,4-Diacetylphloroglucinol	$C_{10}H_{10}O_5$	MIC = 90 μg/ml		[74]
193	*Aspergillus niger* xj	5-Pentadecylresorcinol	$C_{21}H_{36}O_2$	MIC = 250 μg/ml	race 3, biovar 2	[77]
194	*Aspergillus tabacinus*	Violaceol I	$C_{14}H_{14}O_5$	MIC = 25 μg/ml	SL1944	[75]
195		Violaceol II	$C_{14}H_{14}O_5$	MIC = 25 μg/ml		
196		Diorcinol	$C_{14}H_{14}O_3$	MIC = 30 μg/ml		
197	*Spiromastix* sp.	Spiromastol A	$C_{18}H_{19}C_{l3}O_4$	MIC = 0.5 μg/ml	ATCC 11696	[76]
198		Spiromastol B	$C_{18}H_{18}C_{l4}O_4$	MIC = 4 μg/ml		
199		Spiromastol C	$C_{19}H_{20}C_{l4}O_4$	MIC = 0.5 μg/ml		
200		Spiromastol I	$C_{21}H_{22}O_6$	MIC = 8 μg/ml		
201		Spiromastol J	$C_{20}H_{22}O_7$	MIC = 32 μg/ml		
202		Spiromastol K	$C_{20}H_{22}O_7$	MIC = 32 μg/ml		

Furthermore, three p-terphenyl polyketides (**125**–**127**) were identified from *Aspergillus candidus* strain related with insects [47]. The hydroxyl group was probably the relevant functional group in one of these compounds, which showed considerable antibacterial activity. The quantity of hydroxyl groups seems to be correlated with the antibacterial activity's efficacy. Furthermore, the endolichenic fungus Aspergillus chevalieri yielded six C7-alkylated salicylaldehyde derivatives (**130**–**135**). Among them, compound **130** was found to be a unique natural substance that resembles phthalides and contains sulfur. Asperglaucins A and B (**130** and **131**) had strong antibacterial activity against two plant pathogens, *Bacillus cereus* and *Pseudomonas syringae* pv actinidae, with a MIC of 6.25 μM, but these compounds showed moderate antibacterial activities against *R. solanacearum* [48]. Sporbicillinoids (**136**–**140**) were isolated from the fungus *Ustilaginoidea virens*. With a MIC value of 4 μg/mL, which is equivalent to the positive control, streptomycin sulfate, compound **137** showed the highest potency among these compounds, whereas compounds **136**, **138**, and **140** showed moderate antibacterial activity. Compound **137**, on the other hand, also demonstrated notable phytotoxic effects by preventing the radicle and germ elongation of lettuce and rice seeds [49].

The soil bacteria *Serratia plymuthica* C1 yielded the hybrid non-ribosomal peptide-polyketide antibiotic

Table 11 Inhibitory effects of other microbial-derived compounds on *R. solanacearum*

No	From	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
203	*Aspergillus niger* xj	5-Hydroxymethyl-2-furancarboxylic acid	$C_6H_6O_4$	MIC = 15.65 μg/ml	race 3, biovar 2	[77]
204	*Amphirosellinia nigrospora* JS-1675	(4S, 5S, 6S)−5,6-Epoxy-4-hydroxy-3-Methoxy-5-methyl-cyclohex-2-en-1-one	$C_8H_{10}O_4$	MIC = 62.5 μg/ml		[78]
205	*Rhizoctonia solani* Kühn	3-Methoxyfuran-2-carboxylic acid	$C_6H_6O_4$	IC_{50} = 159.6 μg/ml	ATCC 11696	[73]
206	*Phomopsis sp.* HYP11	(4S, 5S)−5-Hydroxy-4-hexanolide	$C_6H_{10}O_3$	MIC = 50 μg/ml		[92]
207	*Aspergillus sp*. D40	Penicillic acid	$C_8H_{10}O_4$	MIC200 μg/ml		[93]
208	*Colletotrichum gloeosporioides*	Colletolide A	$C_{13}H_{20}O_4$	MIC = 128 μg/ml		[88]
209		Colletolide B	$C_{13}H_{20}O_4$	MIC = 128 μg/ml		
210	*Bacillus megaterium* L2	Phenylacetic acid	$C_8H_8O_2$	MIC = 15.6 μg/ml		[79]
211	*Streptomyces koyangensis* Strain VK-A60	3-Phenyl-3-butenoic Acid	$C_{10}H_{10}O_2$	MIC = 0.5 μg/ml		[80]
212	*Porostereum spadiceum*	3,5-Dichloro-4-methoxybenzaldehyde	$C_8H_6Cl_2O_2$	MIC = 100 μg/ml	MAFF 107633	[94]
213	*Aspergillus Niger* xj	Metazachlor	$C_{14}H_{16}ClN_3O$	MIC = 250 μg/ml		[95]
214		Dimethyl 5-nitroisophthalate	$C_{10}H_9NO_6$	MIC = 250 μg/ml		
215	*Lophiostoma sp.* Sigrf10	(8R,9S)-Dihydroisoflavipucine/(8S,9S)-dihydroisoflavipucine	$C_{12}H_{17}NO_4$	MIC = 150 μg/ml	ATCC 11696	[96]
216	*Streptomyces Parvus* 33	Holomycin	$C_7H_6N_2O_2S_2$	MIC = 0.39 μg/ml		[81]
217	*Streptomyces djakartensis*	Yanglingmycin	$C_{10}H_{11}NO_3$	MIC = 15.6 μg/ml		[97]
218	*Aspergillus persii*	3-Methoxy-5-methyl-4-oxo-2,5-hexadienoic acid	$C_8H_{10}O_4$	MIC = 37 μg/ml		[98]
219	*Rhizoctonia solani* Kühn	(Z)−3-Methylpent-2-en-1,5-dioic acid	$C_6H_8O_4$	IC_{50} = 137.7 μg/ml	ATCC 11696	[73]
220	*Penicillium chrysogenum* XNM-12	Penicierythritol A	$C_{14}H_{20}O_7$	MIC = 4 μg/ml		[63]
221		Penicierythritol B	$C_{12}H_{20}O_6$	MIC > 64 μg/ml		
222	*Aspergillus Niger* xj	Palmitic acid	$C_{16}H_{32}O_2$	MIC = 500 μg/ml		[95]
223	*Bacillus megaterium* L2	Erucamide	$C_{22}H_{43}NO$	MIC = 500 μg/ml		[79]
224		Behenic acid	$C_{22}H_{44}O_2$	MIC = 250 μg/ml		
225	*Aspergillus Niger* xj	Nonacosane	$C_{29}H_{60}$	MIC = 125 μg/ml		[95]
226	*Rhizopycnis vagum*	Rhizoperemophilane K	$C_{15}H_{14}O_5$	MIC = 128 μg/ml		[99]
227		1α-Hydroxyhydroisofukinon	$C_{15}H_{22}O_2$	MIC = 129 μg/ml		
228		2-oxo-3-Hydroxy-eremophila-1(10),3,7(11),8-tetraen-8,12-olide	$C_{15}H_{14}O_4$	MIC = 130 μg/ml		
229	*Septoria rudbeckiae*	Septoreremophilane D	$C_{15}H_{20}O_4$	MIC = 50 μm		[100]
230	*Aspergillus Niger* xj	Cholesta-3,5-dien-7-one	$C_{27}H_{42}O$	MIC = 250 μg/ml		[95]
231	*Septoria rudbeckiae*	(22E)−3β-Hydroxy-26,27-bisnorcholesta-5,22-dien-24-one	$C_{25}H_{38}O_2$	MIC = 50 μm		[100]
232	*Rhizoctonia solani* Kühn	Sitostenone	$C_{29}H_{48}O$	IC_{50} = 188.8 μg/ml	ATCC 11696	[73]
233	*Epicoccum poae* DJ-F	Ganodermaside E	$C_{26}H_{34}O_3$	MIC = 3.3 mM		[101]
234		Ganodermaside F	$C_{28}H_{40}O_3$	MIC = 1.0 mM		
235		Ganodermaside G	$C_{28}H_{40}O_3$	MIC = 0.4–0.9 mM		
236		Ganodermaside H	$C_{28}H_{38}O_3$	MIC = 0.8–1.6 mM		
237	*Aspergillus niger* xj	Ergosterol	$C_{28}H_{44}O$	MIC = 500 μg/ml	race 3, biovar 2	[77]

Table 11 (continued)

No	From	Name	Molecular formula	Activity	Tested *R. solanacearum* strain	References
238	*Epicoccum poae* DJ-F	23R-Hydroxy-(20Z,24R)-ergosta-4,6,8(14),20(22)-tetraen-3-one	$C_{28}H_{38}O_3$	MIC = 2.1 mM		[101]
239	*Aspergillus niger* xj	β-Sitosterol	$C_{29}H_{50}O$	Mic = 250 μg/ml	race 3, biovar 2	[77]
240	*Rhizoctonia solani* Kühn	Ergosterol	$C_{28}H_{44}O$	IC_{50} = 140.9 μg/ml	ATCC 11696	[73]
241	*Simplicillium lamellicola* BCP	Halymecin G	$C_{38}H_{68}O_{16}$	IC_{50} = 75.8 μg/ml	SL1944	[102]
242		Halymecin F	$C_{50}H_{88}O_{20}$	IC_{50} = 73.8 μg/ml		
243	*Hansfordia sinuosae*	Ascotrichalactone A	$C_{40}H_{44}O_{17}$	MIC = 15.62 μM	ATCC11696	[82]
244		Hansforester A	$C_{35}H_{40}O_{14}$	MIC = 15.62 μM		
245		Hansforester B	$C_{39}H_{44}O_{15}$	MIC = 125 μM		
246		Hansforester D	$C_{37}H_{42}O_{15}$	MIC = 62.5 μM		
247		Hansforester E	$C_{39}H_{46}O_{16}$	MIC = 62.5 μM		
248		Hansforester F	$C_{40}H_{48}O_{16}$	MIC = 125 μM		

serratamid (**141**). With a MIC value of 0.49 μg/mL, it demonstrated strong antibacterial activity against *R. solanacearum*, outperforming oxytetracycline, oxolinic acid, and streptomycin sulfate. Furthermore, without having any phytotoxic effects, serratamid efficiently decreased bacterial wilt in tomato seedlings in a dose-dependent way. Its disease control efficiency at 10 μg/mL was much greater than that of streptomycin sulfate, the positive control, at 200 μg/mL [50].

The solid fermentation products of *Pestalotiopsis* sp. cr014 were used to isolate pestalotic acids (**143**–**146**) [51]. With similar MIC values of 0.78 μg/mL, four of these compounds showed strong antibacterial activity against *R. solanacearum*, indicating their potential for both prevention and treatment of bacterial wilt. Phytohabimicin (**147**), a peculiarly modified congener of calcimycin that was isolated from *Phytohabitans* sp. RD003013, has a stereochemically inverted methyl group at C-7, as well as a chlorinated pyrrole and a thiazolecarboxylic acid at both ends of its polyketide backbone. Its biological activity is probably influenced by these structural differences; phytohabimicin has an activity MIC value of 6.3 μg/mL against *R. solanacearum*, but calcimycin is inert [52]. Table 1 and Fig. 1 provide a summary of the chemical compositions and antibacterial properties of other polyketides.

Pyrones

A type of heterocyclic compound that includes oxygen, pyrones come in two isomeric forms in nature: 2-pyrone (α-pyrone) and 4-pyrone (γ-pyrone). The carbonyl group's location in relation to the oxygen atom inside the ring system is indicated by the designations 2 or 4. All three kingdoms of life include pyrone-based natural chemicals, which constitute a significant class of physiologically active substances. Notably, 2-pyrone has antiviral, broad-spectrum antibacterial, and antifungal qualities and is known to bind to certain protein domains in a variety of biological systems [53]. Grammicin (**149**) and patulin (**150**) were extracted from *Xylaria grammica* KCTC 13121BP, an endolichenic fungus. Despite being an isomer of patulin, grammicin and patulin have somewhat different biological functions. Grammicin has very little or no cytotoxicity and a MIC value of 500 μg/mL, indicating modest antibacterial action. Patulin, on the other hand, has significant cytotoxic action (EC_{50} = 4.95 μg/mL against SW.71 cells) and high antibacterial qualities (MIC value of 7.8 μg/mL) [54]. Compounds **152**–**161** are categorized as dibenzo-α-pyrones, which are distinguished by a tricyclic structure formed by a phenolic ring joined to a six-membered carbon ring by a lactone molecule. These substances were extracted from a number of endophytic fungi, such as *Alternaria alternata, Rhizopycnis vagum, Hyalodendriella* sp., and *Alternaria* sp. These compounds'antibacterial properties were evaluated via the use of a modified broth dilution-colorimetric test. Significant antibacterial activity was notably shown by 4-hydroxyalternariol-9-methyl ether (**161**), which had a MIC value of 0.5 μg/mL. The antibacterial properties of other chemicals were moderate to weak. With MIC values of 25.0 and 75.0 μg/mL, respectively, TMC-264 (**153**) and alternariol 9-methyl ether (**154**) demonstrated antibacterial activity against *R. solanacearum*, outperforming the traditional antibiotic streptomycin sulfate, which in two separate investigations reported high MIC values of 50 and 100.0 μg/mL [55, 56]. These findings imply that the strain of *R. solanacearum* can be streptomycin resistant. Furthermore, against this streptomycin-resistant bacterium, compounds **153** and **154** had stronger antibacterial activity than 4-hydroxyalternariol-9-methyl ether [57–60]. The antibacterial activity of

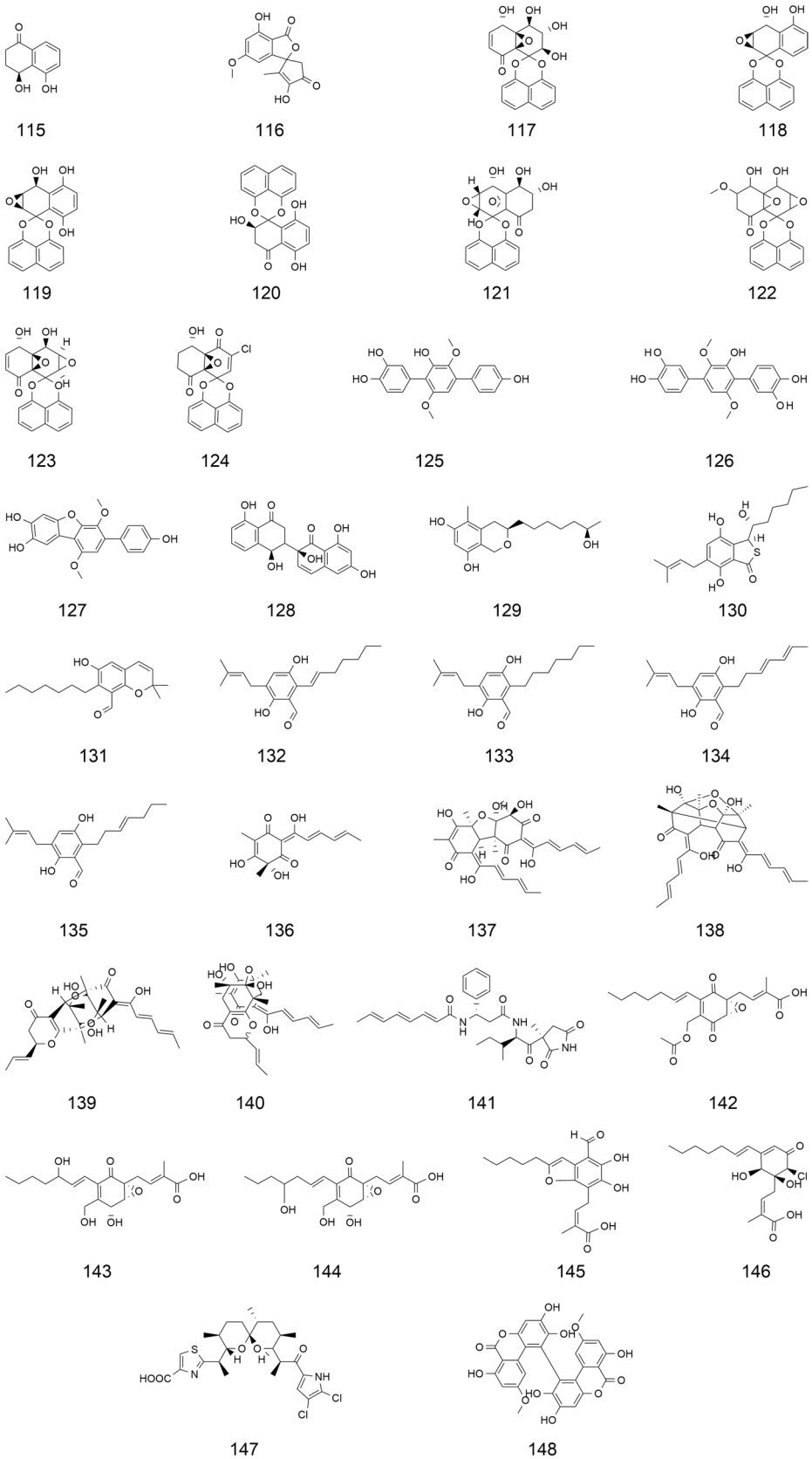

Fig. 3 The structures of microbial-derived polyketides with anti-*R. solanacearum* activity

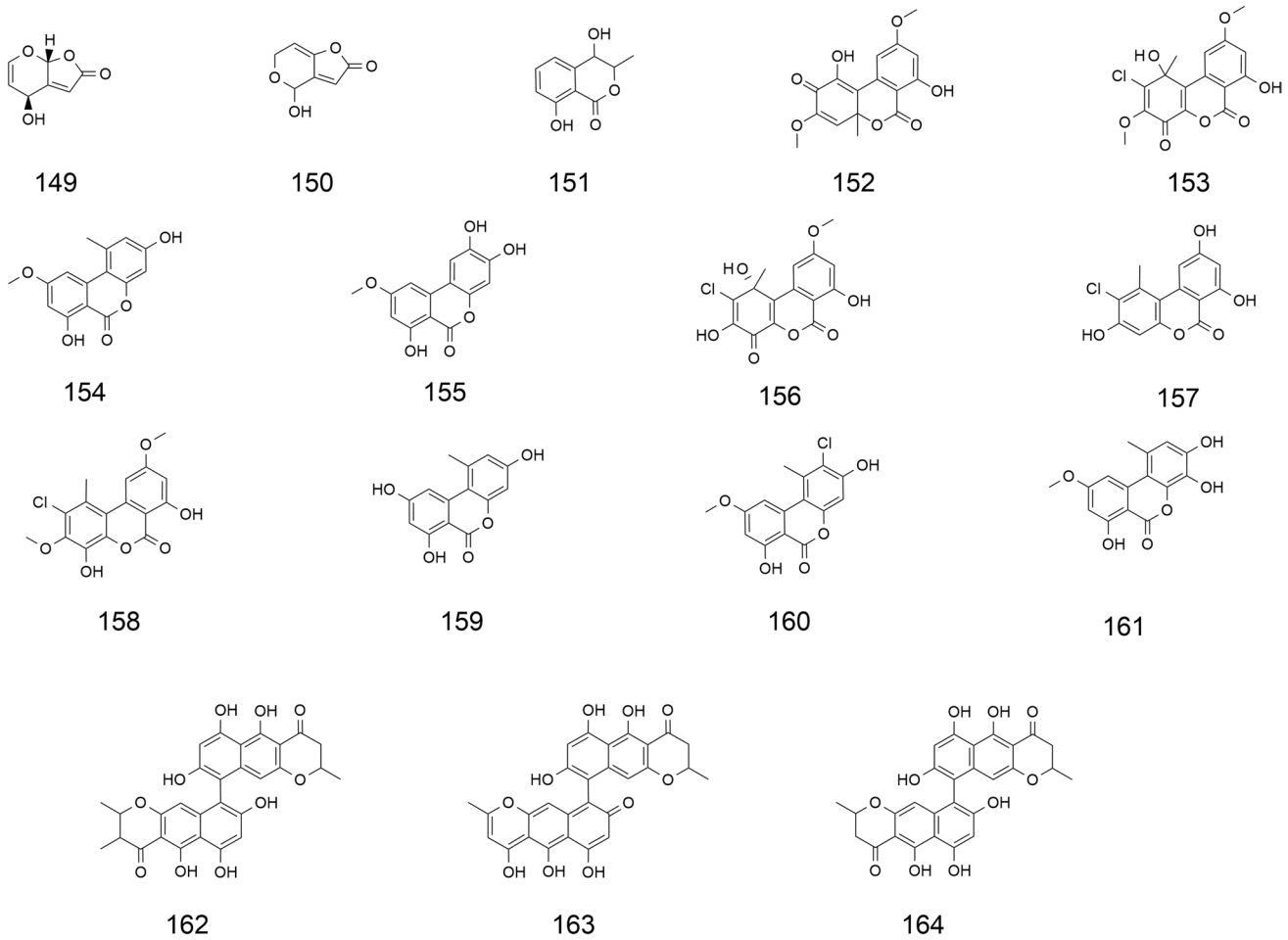

Fig. 4 The structures of microbial-derived pyrones with anti-*R. solanacearum* activity

three bis-naphtho-γ-pyrones (**162–164**) against *R. solanacearum* was assessed; ustilaginoidin E (**162**) showed the greatest antibacterial impact, MIC value of 16 μg/mL.

Alkaloids

The main component of alkaloids, which are made from amino acids, is basic amine nitrogen incorporated into heterocyclic structures. Phenylalanine (Phe), tyrosine (Tyr), tryptophan (Trp), lysine (Lys), and ornithine (Orn) are among the α-amino acids that are their primary source. The processes involved in alkaloid biosynthesis remain unclear despite their importance [45]. Two 2-azaanthraquinone derivatives are synthesized by the endophytic fungus *Lophiostoma* sp. Eef-7, which has poor antibacterial action against *R. solanacearum*. At a dose of 8 μg, the inhibition zone diameters for these derivatives were 8.71 mm and 8.04 mm, respectively. This was less than the inhibition zone diameter for the positive control, which was 13.03 mm at 6.25 μg [61]. Four known biosynthetic congeners (**171–174**) and two new angularly prenylated indole alkaloids with pyrano[2,3-g] indole structures, amoenamide C (**169**) and sclerotiamide B (**170**), were discovered from the endophytic fungus *Fusarium sambucinum* TE-6L. With MIC values ranging from 8 to 32 μg/mL, all compounds showed considerable inhibitory action against *R. solanacearum*. They also showed some damage to zebrafish eggs. Notably, out of all the chemicals examined, sclerotiamide (**171**) had the least effect on embryo hatching but the greatest levels of activity similar to the positive control [62]. The marine algae-derived endophytic fungus *Penicillium chrysogenum* XNM-12 produced five meroterpenoid alkaloids (**175–179**). These compounds have distinct diterpenoid and pyridinyl-α-pyrone substructures that are rare in natural products. Compound **178** had the strongest antibacterial activity against *Penicillium solanum* because it contained one α-pyridine ring with a MIC value of 8 μg/mL [63]. Furthermore, the bactericidal or bacteriostatic actions of siderophores produced by bacteria might restrict the growth potential of competing species by preventing other germs from obtaining

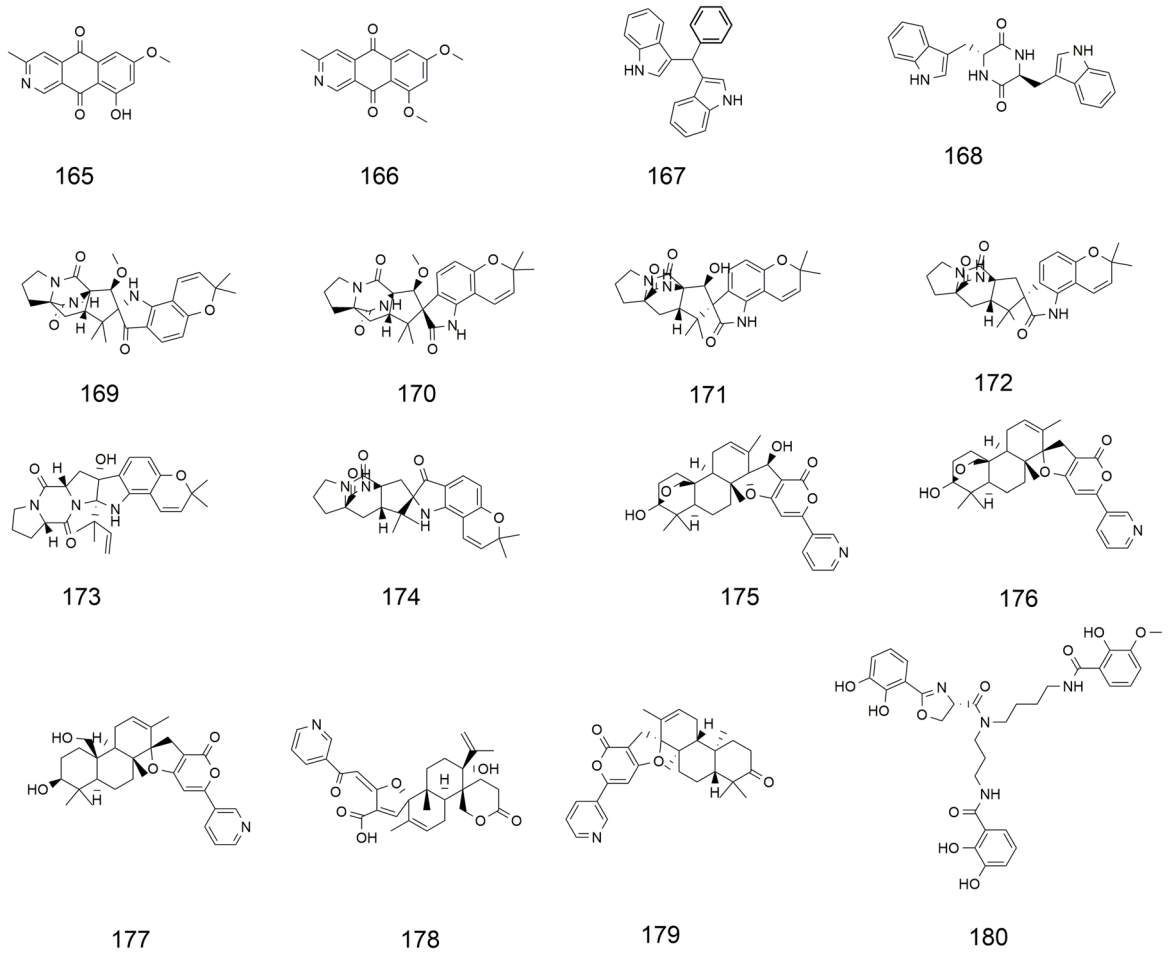

Fig. 5 The structures of microbial-derived alkaloids with anti-*R. solanacearum* activity

iron ions. The fermentation broth of the coral-associated bacteria *Labrenzia* sp. yielded labrenzbactin (**180**), a new catecholate-containing siderophore. This compound's MIC value of 25 μg/mL indicated that it has antibacterial action against *R. solanacearum* [64].

Peptides

A class of tiny peptides known as antimicrobial peptides is usually composed of less than 100 amino acids. They may interact with hydrophobic surfaces and membranes because they typically have an amphiphilic structure and a positive net charge. They have broad-spectrum action against a variety of microorganisms, such as viruses, fungi, and bacteria, because to this property. They work especially well against bacteria that have become resistant to conventional antibiotics and are less likely to spread drug resistance. Antimicrobial peptides thus provide a potential remedy for the expanding problem of antibiotic resistance in harmful microbes [65]. Tomato plants'survival rates were increased and wilt symptoms were lessened by the two cyclic dipeptides. According to in vitro research, both antibacterial substances have a MIC value of 1000 μM. These substances markedly reduced the expression levels of the genes that encode cellulase, pilQ, and hrpB at a dose of 100 μM. The type III secretion system (T3SS), chemotaxis, and the creation of several low molecular weight molecules are all regulated by HrpB. Compound **182** also caused a reduction in the expression of a number of additional genes, such as phcA, epsF, fliT, pilQ, and cheW. PhcA controls the synthesis of cellulose, extracellular polysaccharides, and the AHL quorum sensing system [66]. Cyclo(L-Pro-L-Tyr) and cyclo(D-Pro-L-Tyr), two more cyclic dipeptides, were extracted from *Streptomyces* sp. strain 22–4's culture broth and showed action against *R. solanacearum*, with a MIC value of 31.25 μg/mL [67]. Actinomycin D (**185**) was isolated from *Streptomyces* sp. NEAU-HV9, and its MIC value against *R. solanacearum* was found to be 0.6 mg/L, which is significantly lower than that of other newly reported natural antibacterial agents. This compound demonstrated high efficacy against *R. solanacearum* in tomato seedlings; treatment with actinomycin D at concentrations of 1 × MIC and 2 × MIC resulted in no

disease symptoms among the seedlings, achieving a control efficacy of 100%. In pot culture experiments, actinomycin D (0.6 mg/L) effectively inhibited the progression of bacterial wilt caused by *R. solanacearum*, also achieving a control efficacy of 100% [68]. As biosurfactants, lipopeptides may reduce the surface tension of water, which causes the cytoplasmic membrane of target microorganisms to depolarize and ultimately kill the cell. Four bacterial sources yielded five lipopeptide. Polypeptin C (**187**) shown antibacterial efficacy against a range of fungus and bacteria that cause plant disease. Against *R. solanacearum*, compounds **186**, **188** and **189** may have antagonistic or synergistic effects. Furthermore, Bacillus subtilis JW-1 produces compound **189**, a potent antibacterial agent that efficiently inhibits *R. solanacearum* [69–72]

Phenols

The fermentation cultures of the rice sheath blight pathogen *Rhizoctonia solani* Kühn were used to extract m-hydroxyphenylacetic acid (**191**). When tested against *R. solanacearum*, this chemical showed poor antibacterial activity. Furthermore, it verified the compound's phytotoxin action by showing that it inhibited the radical and prolonged the germination of rice seeds [73]. *Pseudomonas fluorescens* VSMKU3054 generated 2,4-diacetylphloroglucinol (**192**), and its MIC against *R. solanacearum* was determined to be 90 µg/mL. The incidence of bacterial wilt was significantly reduced when *R. solanacearum* cells were treated with this chemical at the MIC level because it reduced cell viability, raised reactive oxygen species levels, and damaged chromosomal DNA [74]. *Aspergillus tabacinus* SFC20160407-M11 culture filtrate was used to isolate dimeric ethers (**194–196**). The MIC values of these compounds ranged from 25 to 50 µg/mL, indicating modest antibacterial activity against *R. solanacearum*. It is impossible to completely rule out the possibility that these substances may harm plants, however, since they are often identified as mycotoxins. Furthermore, it is known that violaceols (**194** and **195**) are harmful byproducts that interfere with oxidative phosphorylation in the mitochondria of rat liver [75]. From the fermentation broth of the fungus *Spiromastix* sp. MCCC 3A00308, six polyphenols (**197–202**) that were identified as spiromastols were extracted. With MIC value ranging from 0.5 to 4 µg/mL, compounds **197–199** showed high inhibitory action against *R. solanacearum*, but compounds **201** and **202** showed moderate inhibition, with an MIC value of 32 µg/mL. The spiromastols'structure–activity connection research showed that alterations on rings A and B affected their antibacterial qualities. While the 2′-methoxylated derivative (**199**) showed greater effects than the 2′-hydroxy homologue (**198**), the inclusion of a dichlorinated ring A increased bacterial inhibition. Furthermore, as not shown in Table 10, analogues with an ester bond between rings A and B (**201** and **202**) were more potent than those with an ether bond or those without a dichlorinated ring A, which had modest antibacterial activity (MICs > 128 µg/mL) [76].

Others

With a MIC value of 15.56 µg/mL, 5-hydroxymethyl-2-furancarboxylic acid (**203**), a bioactive molecule obtained from *Aspergillus* niger xj, showed strong antibacterial activity against *R. solanacearum*. It disrupted intracellular functions, such as membrane osmotic function and the activity of important enzymes, and interfered with bacterial protein production, while it had no effect on the structure and function of the *R. solanacearum* cell membrane [77]. When it came to *R. solanacearum, Amphirosellinia nigrospora* JS-1675 demonstrated potent antibacterial activity in vitro. A derivative of oxygenated cyclohexanone (**204**) was obtained from this fungus and had a MIC value of 62.5 µg/mL. Compound **204** successfully decreased disease symptoms in a dose-dependent manner in trials to control bacterial wilt caused by *R. solanacearum* in four-week-old tomato seedlings. Seven days after inoculation, reductions of 86.4% at 125 µg/mL, 92.3% at 250 µg/mL, and complete suppression (100%) at 500 µg/mL were achieved [78]. Compound **210**, which was isolated from *Bacillus megaterium* L2, showed a MIC value of 15.6 µg/mL and strong antibacterial activity against *R. solanacearum*. Furthermore, it is thought to be a naturally occurring auxin in plants that may increase bud elongation and boost the in vitro regeneration effectiveness of crops like sunflower and chili pepper [79]. *Streptomyces koyangensis* VK-A60 and *Streptomyces parvus* 33 were the strains from which 4-phenol-3-butenoic acid (**211**) and holomycin (**216**) were recovered. With MIC value of 0.5 µg/mL and 0.39 µg/mL, respectively, both substances demonstrated significant antibacterial activity against *R. solanacearum*. Additionally, it was discovered that the MIC value of holomycin was greater than that of ampicillin, the positive control (MIC > 50 µg/mL) [80, 81]. According to Kuo Xu et al., Penicierythritols A (**220**), a derivative of erythritol, is the first substance of its type to be identified from the marine algal-derived endophytic fungus *Penicillium chrysogenum* XNM-12. Compared to the positive control chloromycetin (MIC = 8 µg/mL), this chemical demonstrated substantial inhibitory action against *R. solanacearum*, with a MIC value of 4 µg/mL [63]. Six polyesters (**243–248**) were extracted from the sponge-derived fungus *Hansfordia sinuosae*. Ascotrichalactone A (**243**) and hansforester A (**244**) demonstrated significant inhibitory effects against *R. solanacearum*, with MIC values ranging from 3.9 to 15.6 µM, comparable to the positive control chloramphenicol. Compound **246** exhibited moderate antibacterial activity [82]. Fatty acids, alkanes, steroids, terpenes, and

other substances, on the other hand, showed very little antibacterial activity (Table 11).

Discussion

A major soil-borne bacterial pathogen that significantly reduces agricultural yields globally is *R. solanacearum* [103]. Various elements could play a role in the virulence success of this phytopathogen. These include the existence of enzymes that break down cell walls, the synthesis of exopolysaccharides, and the presence of effector proteins [104]. The drawbacks of using agrochemicals underscore the pressing need for eco-friendly pesticides that may improve crop quality without endangering human health or the environment. Natural goods, which are the outcome of natural selection and biological adaptations, have garnered more attention recently. Plants and microbes create secondary metabolites, which are essential defenses against invaders. It's possible that nature has already found useful substances with strong antibacterial qualities. Natural goods are thus a great way to find possible answers to important agricultural problems. When creating novel bactericides, the isolated chemicals with strong antibacterial properties are very crucial.

Although there are some disadvantages, using natural materials to treat plant diseases has clear benefits. Degradability: Since natural goods are usually made from living things, there is little chance that they will pollute the environment. They don't accumulate since they naturally move about and break down in the environment. High selectivity: The natural products that have been evaluated show specificity in managing illnesses while reducing negative impacts on ecosystems and non-target creatures. Safety: Many natural materials have little effect on the growth and development of plants and have excellent safety ratings for both people and animals.

Of course, it has its limitations. Variability in efficacy: Natural products'degradability may cause instability in their ability to combat illness, which may be impacted by storage conditions, application methods, and environmental factors, producing uneven results. Possible dangers to safety: Even while natural goods are usually harmless, some could be harmful or cause allergies. Cost and technical difficulties: Natural product extraction, processing, and application may be difficult and often need for specific tools and methods. Furthermore, sustainable production and supply may be difficult due to the restricted availability of certain natural components.

In addition to their direct antibacterial activity, the environmental adaptability and ecological impacts of natural products must be carefully evaluated for sustainable agricultural applications. The antimicrobial effects of plant- and microbial-derived compounds are influenced by environmental factors such as soil pH, organic matter content, and microbial diversity, which may alter their stability and bioavailability. Furthermore, while these natural products offer a promising alternative to synthetic pesticides, their long-term use could potentially disrupt soil microbial communities, affecting nutrient cycling and plant–microbe interactions. Studies have shown that certain bioactive compounds may selectively inhibit pathogenic bacteria while promoting beneficial microbes, yet persistent accumulation in soil ecosystems could lead to unintended ecological consequences. Therefore, comprehensive assessments of the environmental fate, degradation pathways, and non-target effects of these natural antimicrobials are essential to ensure their efficacy and ecological safety in integrated pest management strategies.

To sum up, biological approaches that make use of microbial metabolites and natural compounds obtained from plants have a lot of potential for reducing agricultural losses brought on by plant diseases. These substances may be used as lead structures to create new classes of plant protection agents or to combat plant diseases. They may also go through further changes to improve their efficacy. Exploring novel active molecules by structural alterations may provide an effective route to new natural medications, especially with the advances in metabolic control and genetic engineering.

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