Electronic Supplementary Material (ESI) for Natural Product Reports.

SUPPLEMENTARY INFO

Bacterial Pathogens: Threat or Treat?
(A review on bioactive natural products from bacterial pathogens)

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Table 1. Bioactive natural products identified from bacterial pathogens

Compound	Producing Organism	Biosynthesis	Target	Activity	MIC (μM)[a]	Ref
Burkholderia spp. – phytopathogen and human pathogen						
AFC-BC11	*B. cepacia* BC11	NRPS	unknown	fungi	0.01-15	[1]
Bactobolin A-C	*B. ambifaria* *B. thailandensis*	Hybrid *cis*-AT PKS-NRPS	Ribosome, L2 protein	G^+, G^-, VISA	0.5-261	[2,3]
Bongkrekic acid	*B. gladioli*	*trans*-AT PKS	adenine nucleotide translocase (ANT)	G^+, G^-, fungi	-	[4–7]
Burkholdines	*B. ambifaria*	Hybrid *cis*-AT PKS-NRPS	unknown	fungi	0.3-26	[8,9]
Caryoynencins A-C	*B. caryophilli* *B. gladioli* Lv-StA	other	unknown	G^+, G^-, fungi	<0.07-89	[10–13]
Cepabactin / BN-227	*B. cepacia* *Pseudomonas sp. BN-227*	other	unknown	G^+, G^-	10-325	[14,15]
Cepaciamide A	*B. cepacian* D-202	unknown	unknown	fungi	-	[16]
Cepacidines (also called xylocandins)	*B. cepacia*	NRPS	unknown	fungi	0.01-0.32	[17,18]
Cepacin A-B	*B. cenocepacia*	unknown	unknown	G^+, G^-	0.3-175	[19]

Compound	Producing Organism	Biosynthesis	Target	Activity	MIC (μM)[a]	Ref
Cepafungin I, II, III (Cepafungin II is also known as glidobactin A)	*B. cepacia* *P. luminescens*	unknown	proteasome	fungi	3.0-23.4[b]	[20–22]
Enacyloxin IIa	*B. ambifaria* *B. gladioli*	PKS-NRPS	Elongation factor Tu ribosome	G^+, G^-	4.3-10.7	[23,24]
Fragin	*B. cenocepacia H111*	NRPS	Metal chelation	G^+, fungi	20[e]	[25,26]
Gladiofungin A-B	*B. gladioli*	PKS	unknown	fungi	9.9	[27]
Gladiolin	*B. gladioli* BCC0238	*trans*-AT PKS	RNA polymerase	G^+, G^-, fungi	5.1-82.0	[28]
Glidobactins (Glidobactin A is also known as cepafungin II)	*Burkholderia sp.* *P. luminescens* *P. asymbiotica*	PKS-NRPS	proteasome	fungi	2.9-46	[22,29,30]
Icosalide	*B. gladioli* Lv-StA *B. gladioli BCC0238 s*	NRPS	unknown	G^+, fungi	11-22.0	[31,32]
Lagriamide	*B. gladioli*	PKS	unknown	fungi	-	[33]
Lagriene	*B. gladioli* Lv-StA	PKS	unknown	G^+, fungi	-	[13]
Occidiofungin A-B	*B. contaminans* *B. pyrrocinia*	Hybrid *cis*-AT PKS-NRPS	Cell wall	fungi	0.4-26.7	[34–36]
Pyrrolnitrin	*Burkholderia sp.* *Pseudomonas sp.* *Serratia sp.*	other	Respiratory electron transport system	G^+, G^-, fungi	0.04-62	[37]
Rhizoxin	*B. rhizoxinica* *P. fluorescens*	Hybrid *trans*-AT PKS-NRPS	microtubuli	fungi	-	[38–40]
Sinapigladioside	*B. gladioli* Lv-StA	other	unknown	fungi	-	[13]
Xylocandins (also called cepacidines)	*B. cepacia* ATCC 39277	NRPS	unknown	fungi	0.09-23	[41,42]
Clostridium puniceum **- phytopathogen**						
Clostrubin A	*C. puniceum*	PKS	unknown	G^+	0.047-0.97	[43,44]
Clostrubin B	*C. puniceum*	PKS	unknown	G^+	0.14-0.27	[43]
Dickeya spp. **- phytopathogen**						
Oocydin A	*Dickeya sp.* *S. marcescens*	PKS	unknown	fungi	0.04-0.79	[45–47]
Zeamine Zeamine II	*D. zeae* strain EC1 *S. plymuthica* RVH1	PKS-NRPS	Cell membrane	G^+, G^-	0.36-59	[48–51]
Erwinia amylovora **- phytopathogen**						

Compound	Producing Organism	Biosynthesis	Target	Activity	MIC (µM)[a]	Ref
6-thioguanine	*Erwinia species*	other	DNA, RNA	G^-	0.25[c]	52–55
2,5-dihydrophenylalanine	*E. amylovora* *Streptomyces spp.* *P. luminescens* *Pseudomonas sp.*	other	unknown	G^+, G^-, fungi	30-300	56–59
Nocardia spp. – animal and human pathogens						
Brasilidine A	*N. brasiliensis*	others	unknown	G^+, G^-, fungi	1.57-403	60
Brasilinolide A-C	*N. brasiliensis* IFM0406	PKS	unknown	fungi	2.6-21	61–65
Brasiliquinone A-D	*N. brasiliensis*	PKS	unknown	G^+	0.77-49	66,67
Erythromycin E	*N. brasiliensis* IFM 0466	PKS	50s RNA	G^+, G^-	0.04-43	64,68,69
Nabscessin A-C	*N. abscessus*	other	unknown	*C. neoformans*	35-77[d]	64,70,71
Nocarasin A-C	*N. brasiliensis*	unknown	unknown	G^+	1.5-96	66
Nocardicyclin A-B	*N. pseudobrasiliensis*	PKS	unknown	G^+	1.33-43	64,72
Nocardithiocin	*N. pseudobrasiliensis* IFM 0757	RiPP	unknown	G^+, rifampicin-resistant *Mycobacteria* strains	<0.0065-5.2	64,73
Nocavionin	*N. terpenica*	PKS-NRPS	unknown	G^+	-	64,74
PC-766B	*N. brasiliensis*	PKS	unknown	G^+, *C. neoformans*	2-16	64,75,76
SF2457	*N. brasiliensis* SF2457	other	unknown	G^+, G^-	2.6-169	64,77
SO-075R1	*N. brasiliensis*	PKS	unknown	G^+	<0.36-5.6	64,78,79
Transvalencin A, Z	*N. transvalensis*	unknown	unknown	G^+	<0.34-44	64,80,81
Paenibacillus larvae – honeybee pathogen						
paenilamicins	*P. larvae*	NRPS	unknown	*P. larvae*	0.3-20	82,83
Paenilarvins A-C	*P. larvae*	PKS-NRPS	unknown	fungi	1.89-30.0	84
sevadicin	*P. larvae*	NRPS	unknown	*B. megaterium*	62.5[e]	85
Photorhabdus spp. - entomopathogen						
Benzaldehyde	*P. temperata* M1021	other	Cell membrane	G^+, G^-	6-10	86
Cepafungin 1	*P. luminescens* *B. cepacia*	unknown	proteasome	fungi	3-23	21,87
Darobactin	*P. khanii*	RiPP	BamA	G^-	2.0-16.0	88
Duotap-520	*P. luminescens*	PKS	Nrf2	G^+	4.1-6.5	89
Flesusides A-B	*P.* PB45.5-*Δhfq*	NRPS	unknown	G^+, G^-, fungi	-	90
Glidobactins (Glidobactin A is also known as cepafungin II)	*P. luminescens,* *P. asymbiotica* *Burkholderia sp.*	PKS-NRPS	proteasome	fungi	2.9-46	22,29,30

Compound	**Producing Organism**	**Biosynthesis**	**Target**	**Activity**	**MIC (µM)[a]**	**Ref**
Indigoidine	*P. luminescens*	NRPS	unknown	G^+, G^-, fungi	-	[91,92]
Lumiquinone A	*P. luminescens*	PKS	unknown	G^+, fungi	50[e]	[93]
Photoditritide	*P. temperata* Meg1	NRPS	unknown	G^+	3.0-24	[94]
Photorhabdicins	*Photorhabdus sp.*	RiPP	unknown	G^-	-	[95,96]
Silathride	*P.* PB45.5-*Δhfq*	NRPS	unknown	G^+, G^-, fungi	-	[90]
Stilbenes	*P. luminescens,* *P. temperata*	PKS	unknown	G^+, fungi	27-50.5	[89,97]
Tapinarof	*Photorhabdus spp.*	PKS	AhR and Nrf2 genes	G^+	27-50.5	[89]
Pseudomonas spp. – phytopathogen and human pathogen						
2-Heptyl-4-hydroxyquinoline-N-oxide	*P. aeruginosa*	other	Cytochrome B	G^+	-	[98]
L-2-Amino-4-methoxytrans-3-butenoic acid (AMB)	*P. aeruginosa*	NRPS	PLP-dependent enzymes	G^-	-	[99,100]
Phenazine-1-carboxylic acid / G26A	*P. aeruginosa*	other	Generation of reactive oxygen species	fungi	22-223	[101–103]
Pseudomycin A-C	*P. syringae*	unknown	Cell membrane	fungi	0.05-5	[104,105]
Pyocins S1, S2, S3, S8, S9, S10, AP41	*P. aeruginosa*	RiPP	DNA	G^-	-	[106–108]
F-type Pyocins	*P. aeruginosa*	RiPP	Unknown	G^-	-	[106,108]
R-type Pyocins	*P. aeruginosa*	RiPP	Cell membrane	G^-	-	[106,108,109]
Pyocins S4, S11, S12	*P. aeruginosa*	RiPP	tRNA	G^-	-	[106–108]
Pyocins S5	*P. aeruginosa*	RiPP	Cell membrane	G^-	-	[106,108,110]
Pyocins S6, S7	*P. aeruginosa*	RiPP	rRNA	G^-	-	[106,108]
Pyocins M1, M4	*P. aeruginosa*	RiPP	Lipid II	G^-	-	[108]
Pyocyanin	*P. aeruginosa*	other	Cell membrane respiratory chain	G^+, G^-, fungi	-	[111,112]
Syringomycin E	*P. syringae*	NRPS	Cell membrane	G^+, fungi	0.8-6.4	[113–118]
Syringopeptins	*P. syringae*	NRPS	Cell membrane	G^+, fungi	1.8-14.4	[115,116,118]
Syringostatin A-B	*P. syringae*	unknown	Cell membrane	fungi	2.1-34	[117,119,120]
Syringotoxin	*P. syringae*	unknown	Cell membrane	fungi	0.7-22	[117,120]
Tabtoxin	*P. syringae*	other	Glutamine synthetase	*E. coli* expressing β-	<0.031-16	[118,121]

Compound	Producing Organism	Biosynthesis	Target	Activity	MIC (µM)[a]	Ref
				lactamases		
Tabtoxinine-β-lactam	*P. syringae*	other	Glutamine synthetase	*E. coli* expressing β-lactamases	-	121
Serratia marcescens – entomopathogen and human pathogen						
Althiomycin	*S. marcescens* Db10	NRPS-PKS	Peptidyl transferase	G+, G-	1.6-200	122–124
Carbapenem / carbapenams	*S. marcescens* *Serratia sp.* *Erwinia sp.* *P. luminescens* TT01	other	Peptidoglycan transpeptidases	G+, G-	-	125,126
Oocydin A	*S. marcescens* *Dickeya* sp.	*trans*-AT PKS	unknown	fungi	0.04-0.79	45–47
Prodigiosin	*S. marcescens*	Hybrid *cis*-AT PKS-NRPS / other	DNA damage	G+, G-	0.9-6.0[f]	127,128
Serrawettin W1 or serratamolide A	*S. marcescens*	NRPS	cell membrane	G+, G-, fungi	12-97.3	129,130
Serrawettin W2	*S. marcescens*	NRPS	unknown	G+, G-, fungi	12-97.3	129,130
Stephensiolides	*S. marcescens*	NRPS	unknown	G+	6-200	130–132
Staphylococcus spp. – human and animal pathogen						
Aureocin A53	*S. aureus* A53	RiPP	Cell membrane	G+, MRSA	0.0015	133,134
Aureocin A70	*S. aureus*	RiPP	unknown	G+	-	134–136
BacCH91	*S. aureus* CH91	RiPP	unknown	G+	0.0025-6.0	137
BacSp222	*S. pseudintermedius*	RiPP	unknown	G+	0.11-7.80	138
Capidermicin	*S. capitis*	RiPP	unknown	G+	0.6-7.3	139
Epicidin 280	*S. epidermidis* BN280	RiPP	unknown	G+	0.06-22	140
Epidermicin N101	*S. epidermidis* 224	RiPP	unknown	G+	0.01-0.66	141–143
Epidermin	*S. epidermidis* Tü3298	RiPP	Lipid I, II, III, IV	G+, G-	0.12-59	144–147
Epilancin 15X	*S. epidermidis* 15X154	RiPP	unknown	G+	-	145,148
Epilancin K7	*S. epidermidis* K7	RiPP	unknown	G+	-	145,149
Gallidermin	*S. gallinarum* F16/P57 Tü3298	RiPP	Lipid I, II, III, IV	G+, G-	0.12-59	147,150,151
Hominicin	*S. hominis* MBBL2–9	RiPP	unknown	G+	0.05-3.9	152,153
Hyicin 3682	*S. hyicus* 3682	RiPP	unknown	G+	-	146,154
Hyicin 4244	*S. hyicus* 4244	RiPP	unknown	G+	-	155,156

Compound	Producing Organism	Biosynthesis	Target	Activity	MIC (µM)[a]	Ref
Lugdunin	*S. lugdunensis*	NRPS	DNA, RNA, protein and cell wall	G^+, MRSA, VRE, GISA	1.9-15	157–159
Nisin J	*S. capitis* APC2923	RiPP	unknown	G^+	0.03	145,160,161
Pep5	*S. epidermidis* 5	RiPP	unknown	G^+, MRSA, CNS	0.0003-5.4	134,140,144–146,162,163
Warnericin RB4	*S. warneri* RB4	RiPP	unknown	G^+	-	164
Streptococcus mutans **– human pathogen**						
Mutacins	*S. mutans*	RiPP	unknown	G^+, G^-	0.02-14 (0.004-31)[g]	165–173
Mutanobactins	*S. mutans*	PKS-NRPS	unknown	*C. albicans*	5.3-910[h]	174,175
Mutanocyclin	*S. mutans*	PKS-NRPS	unknown	-	-	176
Reutericyclins	*S. mutans*	PKS-NRPS	Cell membrane	G^+, mupirocin-, vancomycin-, linezolid-, clindamycin-resistant MRSA strains	0.03-19	176–180
Streptomyces **spp. - phytopathogen**						
Borrelidin	*S. sp.* GK18	PKS	threonyl-tRNA synthetase	G^+, G^-	0.51-65	181,182
Bottromycin	*S. scabiei* *S. bottropensis* *Streptomyces spp.*	RiPP	tRNA	G^+, MRSA, VRE	0.61-2.4	183–186
Vibrio parahaemolyticus **– fish pathogen**						
2,2-di(3-indolyl)-3-indolone	*V. parahaemolyticus*	other	unknown	G^+	275[e]	187
N-(3-methyl-1,2,4-oxadiazol-5-yl)-1-Pyrrolidinecarboximidamide	*V. parahaemolyticus*	unknown	unknown	G^+, G^-	-	188
Nonyl-phenol	*V. parahaemolyticus*	unknown	unknown	G^+, G^-	-	188
Phenol, 4-(1,1,3,3-tetramethyl butyl)	*V. parahaemolyticus*	unknown	unknown	G^+, G^-	-	188
Phenyl acetic acid	*V. parahaemolyticus*	unknown	unknown	G^+, G^-	-	188
Pyrrolo-(1,2-a)pyrazine-1,4- dione, hexahydro-3(2-methylpropyl)	*V. parahaemolyticus*	unknown	unknown	G^+, G^-	-	188
Tetramethyl pyrazine	*V. parahaemolyticus*	unknown	unknown	G^+, G^-	-	188

Compound	Producing Organism	Biosynthesis	Target	Activity	MIC (µM)[a]	Ref
Vibrindole A	*V. parahaemolyticus*	other	unknown	G^+, fungi	385[e]	[187]
Xanthomonas spp. - phytopathogen						
Albicidin	*X. albilineans*	PKS-NRPS	DNA gyrase	G^+, G^-	0.037-19	[189–191]
Glycinecin A	*X. campestris*	RiPP	Cell membrane	G^-	-	[192,193]
Xenorhabdus spp. - entomopathogen						
Amicoumacins	*X. bovienii*	Hybrid *cis*-AT PKS-NRPS	Ribosome (E-site)	G^+, G^-, MRSA	3.3-47	[194,195]
Benzylideneacetone	*X. nematophila*	unknown	unknown	G^-	-	[196]
Cabanillasin	*X. cabanillasii*	unknown	unknown	fungi	1.5-25[d]	[197]
Cuidadopeptide	*X.* KJ12.1-*Δhfq*	NRPS	unknown	G^+, G^-, fungi	-	[90]
Fabclavines	*X. budapestensis,* *X. szentirmaii* *X. indica* *X. cabanillasii* *X. hominicki* *X.* KJ12.1 *X. stockiae* *X.* KK7.4 *X. innexi*	Hybrid PUFA synthase-like assembly line/*cis*-AT PKS/NRPS	unknown	G^+, G^-, fungi	74[e]	[198,199]
Lipopetides	*X. szentirmaii-Δhfq*	NRPS	unknown	G^+, G^-, fungi	-	[90]
Nematophin	*X. nematophila*	NRPS	unknown	G^+, MRSA, fungi	0.5-44.0	[200,201]
Nemaucins	*X. cabanillasii*	unknown	unknown	fungi	0.04-1.2	[202]
Odilorhabdins	*X. nematophila*	NRPS	30S subunit	G^+, G^-	3.0-12.0	[203]
PAX peptides	*X. nematophila,* *X. caballinasii,* *X. khoisanae SB10*	NRPS	unknown	G^+, G^-, fungi	-	[204,205]
Szentirazine	*X. szentirmaii-Δhfq*	NRPS	unknown	G^+, G^-, fungi	-	[90]
Xenematide	*X. budapestensis,* *X. nematophila*	NRPS	unknown	G^+, G^-	15-60.4	[206,207]
Xenobactin	*Xenorhabdus* sp. PB30.3	unknown	unknown	*M. luteus*	85	[208]
Xenobovide A-C	*X. bovienii*	unknown	unknown	G^+	62-65	[209]
Xenocin	*X. nematophila*	RiPP	unknown	G^-	-	[210]
Xenocoumacins	*X. nematophila* *X. khoisanae SB10*	Hybrid *cis*-AT PKS-NRPS	Arginyl-tRNA synthetase	G^+, G^-, fungi	0.27-1.1	[205,211,212]

Compound	Producing Organism	Biosynthesis	Target	Activity	MIC (μM)[a]	Ref
Xenomins	*X. bovienii*	unknown	unknown	G^+, fungi	16.6-33	[213,214]
Xenorhabdicin	*X. nematophila*	RiPP	membrane	G^-	-	[215,216]
Xenorhabdins	*X. nematophila* *X. bovienii*	Hybrid FAS/NRPS	RNA polymerase	G^+, G^-	-	[217,218]
Xenorxides	*X. bovienii*	unknown	unknown	G^+, fungi	2.4-79.0	[219]
Yersinia ruckeri – fish pathogen						
holomycin	*Y. ruckeri*	NRPS	RNA, FbaA	G^+, G^-	0.93	[220–225]

[a] Minimum inhibitory concentration (in μM) of the NP against bacteria and/or fungi. All MIC values in μg/mL reported in literature were converted to μM concentration
[b] MIC (in μM) of cepafungins using the complex of components I, II and III
[c] complete growth inhibition of E. coli at 24h for 0.25 μM thiogunanine
[d] IC_{50} (in μM) after 24h incubation
[e] Lowest concentration (in μg) of the natural product used in disc diffusion test against bacteria and/or fungi
[f] Concentration of NP (in μM) that causes 30% growth rate reduction of *C. albicans* and *S. aureus*
[g] MIC of mutacin B-Ny266 expressed as the median (range)
[h] IC_{50} (in μM) expressed as the concentration of compound required to cause a 50% reduction in biofilm formation
G^+ Gram positive bacteria
G^- Gram negative bacteria

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