

Supplementary Information

***Burkholderia* as a Source of Natural Products**

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Table S1. Natural products isolated from *Burkholderia sensu lato*

Class	Compound	Source	Discovery method	Bioactivity	Reference(s)
Nonribosomal peptides	Pyochelin	<i>B. cepacia</i>	Bioactivity-guided	Iron chelating	[1-3]
	Aeruginaldehyde	<i>B. cepacia</i>	Other	Antifungal, byproduct of pyochelin biosynthesis	[4,5]
	Fragin	<i>B. cenocepacia</i>	Genome mining	Antifungal, metal chelating	[6]
	Valdiazin	<i>B. cenocepacia</i>	Genome mining	Other (Quorum sensing signaling molecule)	[6]
	BTH-II0204-207:A	<i>B. pseudomallei</i> K96243	Genome mining	Other (PDE4 inhibitor)	[7]
	Sulfazecin	<i>P. acidophila</i> G-6302	Bioactivity-guided	Antibacterial	[8,9]
	Glidopeptin A	<i>Burkholderiales</i> strain DSM 7029	Genome mining	Cytotoxic	[10]
	Rhizomide A	<i>B. rhizoxinica</i> HKI 454	Genome mining	Cytotoxic	[10]
	Icosalides	<i>B. gladioli</i> HKI 0739	Genome mining	Antibiotic	[11]
	Ornibactins	Bcc	Bioactivity-guided	Iron chelating	[3,12-14]
	Rhizonins	<i>B. endofungorum</i> HKI456	Bioactivity-guided	Toxin (Hepatotoxic)	[15-17]
	Heptarhizin	<i>B. rhizoxinica</i> HKI454	Genome mining	Unknown	[18]
	FR900359	<i>Candidatus B. crenata</i>	Genome mining	Other (Gq-signaling inhibitor)	[19,20]
	Haereogladsins and burriogladsins Haereoglumin A and burrioglumin A	<i>B. gladioli</i> pv. <i>agaricicola</i> <i>B. glumae</i>	Genome mining	Swarming and biofilm formation	[21]
	AFC-BC11*	<i>B. cepacia</i> BC11	Bioactivity-guided	Antifungal	[22]
	Xylocandins	<i>B. cepacia</i> ATCC 39277	Bioactivity-guided	Antifungal	[23,24]
	Gramibactin	<i>P. graminis</i> C4D1M	Genome mining	Iron chelating	[25]
	Malleonitrone	<i>B. thailandensis</i> E264	Other	Iron chelating, antibacterial	[26]
Malleobactins	<i>B. pseudomallei</i> group	Bioactivity-guided	Iron chelating	[27-31]	

		<i>P. xenovorans</i> LB400	Genome mining		
	Cepaciachelin	<i>B. cepacia</i> and <i>B. ambifaria</i> PHP7	Bioactivity-guided	Iron chelating	[12,32]
	Holrhizin	<i>B./P. rhizoxinica</i> HKI 454	Genome mining	Swarming and biofilm formation (Biosurfactant)	[33]
	Burkholdines	<i>B. ambifaria</i> 2.2N	Bioactivity-guided	Antifungal	[34,35]
	Occidiofungins	<i>B. contaminans</i> MS14	Bioactivity-guided	Antifungal	[36-41]
	Cepacidines	<i>B. cepacia</i> AF 2001	Bioactivity-guided	Antifungal	[42-44]
	Endolides	<i>B. contaminans</i>	Bioactivity-guided	Other (Vasopressin and serotonin receptor)	[45-47]
	Onychocin D	<i>B. contaminans</i>	Genome mining	Not reported	[45]
	Cyclo[N-(Lys-Phe)-Orn-Val]	<i>B. cepacia</i>	Other	Not reported	[48]
Other/Unknown	3-[L-alanyl-L-homoserinyl-L-aspartyl-β-carboxy]-4-hydroxy-5-oxopyrazole	<i>B. glumae</i>	Bioactivity-guided	Antibacterial	[49]
	Kirkamide	<i>Candidatus B. kirkii</i>	Genome-mining	Cytotoxic, insecticidal	[50]
	(+)-Streptol glucoside & (+)-Streptol	<i>Candidatus B. kirkii</i>	Bioactivity-guided	Other (Plant growth inhibitor)	[51]
	Sinapigliadoside	<i>B. gladioli</i> Lv-StA	Genome-mining	Antifungal	[52]
	Bulgecin A	<i>P. acidophila</i> G-6302ATTC 31363	Bioactivity-guided	Antibacterial	[53-55]
	Rhizobitoxine	<i>B. andropogonis</i> strains	Bioactivity-guided	Other (Ethylene biosynthesis inhibitor)	[56-58]
	Iminopyrrolidines	<i>B. plantarii</i> 9424	Bioactivity-guided	Antibacterial	[59]
	Cepaciamide A	<i>B. cepacia</i> D-202	Bioactivity-guided	Antifungal	[60,61]
	Cepabactin/BN-227	<i>B. cepacia</i> ATCC 25416, <i>B. sp.</i> BN-227	Bioactivity-guided	Antibacterial, iron-chelating	[62-64]
	Toxoflavin	<i>B. glumae</i> , <i>B. gladioli</i> HDXY-02	Bioactivity-guided	Phytotoxic	[65-67]
	Arsinothricin	<i>B. gladioli</i> strain GSRB05	Bioactivity-guided	Not reported	[68]
	4-(2-hydroxyethoxy)-phenol	<i>B. cenocepacia</i>	Other	Not reported	[69]

	Maculosin	<i>B. cenocepacia</i>	Other	Not reported	[⁶⁹]
	Methyl Myristate	<i>B. cenocepacia</i>	Other	Not reported	[⁶⁹]
	Acylhomoserine lactones	<i>B. spp.</i>	Other (Structure-guided)	Other (Quorum sensing signal)	[⁷⁰⁻⁷⁵]
	Cepacian exopolysaccharide*	Bcc	Other	Other (Protects bacterial cells, virulence)	[^{76,77}]
	2-O- α -L-rhamnopyranosyl- α -L-rhamnopyranosyl- α -(R)-3-hydroxytetradecanoyl-(R)-3-hydroxytetradecanoate (RL-2,214)	<i>B. plantarii</i>	Bioactivity-guided	Toxin (Endotoxin)	[⁷⁸]
Hybrid polyketide-nonribosomal peptides	Thailandepsin A, also called Burkholdac B	<i>B. thailandensis</i> E264	Genome mining	Cytotoxic (HDAC inhibitor, antitumor)	[^{70,79-84}]
	Spiruchostatin C	<i>B. thailandensis</i> E264	Bioactivity-guided	Cytotoxic (HDAC inhibitor)	[⁸⁵]
	FK228	<i>B. thailandensis</i> MSMB43	Genome mining	Cytotoxic (Anticancer)	[⁸⁶]
	Spliceostatins (FR901464 and FR901465, spliceostatin A)	<i>B. sp.</i> FERM BP-3421	Bioactivity-guided	Cytotoxic (mRNA splicing inhibitor, antitumor)	[⁸⁷⁻⁹²]
	Thailanstatin A	<i>B. thailandensis</i> MSMB43	Genome mining	Cytotoxic (mRNA splicing inhibitor, antitumor)	[^{91,93,94}]
	Glidobactin A	<i>Burkholderiales strain</i> DSM 7029	Bioactivity-guided	Cytotoxic, antifungal	[^{95,96}]
	Cepafungin I	<i>B. cepacia</i>	Bioactivity-guided	Cytotoxic, antifungal	[⁹⁷⁻⁹⁹]
	Bactobolins	<i>B. thailandensis</i> E264	Genome mining	Antibacterial	[^{70,100,101}]
	Malleilactone / Burkholderic acid	<i>B. thailandensis</i> E264	Genome mining	Cytotoxic, antibacterial, other (virulence factor, quorum-sensing regulation)	[^{102, 103}]
	WF-1360F (rhizoxin precursor)	<i>B. rhizoxinica</i> HKI454, <i>P.</i>	Bioactivity-guided	Cytotoxic (Anticancer, tubulin inhibitor)	[¹⁰⁴⁻¹¹⁴]

		<i>endofungorum</i> HKI456, and <i>Burkholderia</i> sp. B1, B2, B3, B4, B7, B8			
	Thailandamides	<i>B. thailandensis</i> E264	Genome mining	Antibacterial (fatty acid biosynthesis inhibitor), Cytotoxic	[¹¹⁵⁻¹¹⁹]
	Lagriamide	<i>B. gladioli</i> Lv-StB	Bioactivity-guided	Antifungal	[¹²⁰]
	Enacyloxin IIa	<i>B. ambifaria</i> AMMD	Bioactivity-guided	Antibacterial	[¹²¹⁻¹²⁴]
Shikimate Pathway Derived	Tropolone	<i>B. plantarii</i> MAFF301723	Bioactivity-guided	Phytotoxin, antibacterial, antifungal	[^{125,126}]
	Salicylic acid (formerly azurechelin)	<i>B. cepacia</i>	Bioactivity-guided	Iron-chelating	[^{3,127}]
	Pyrrolnitrins	<i>B. cepacia</i> K87	Bioactivity-guided	Antifungal	[¹²⁸]
	Iodinin	<i>P. phenazinium</i>	Bioactivity-guided	Cytotoxic	[¹²⁹⁻¹³³]
	Pityriacitrin	<i>B. sp.</i> NBF227	Bioactivity-guided	Cytotoxic	[^{134,135}]
	2-hydroxymethyl- chroman-4-one	<i>Burkholderia</i> sp. MSSP	Bioactivity-guided	Antifungal	[¹³⁶]
	Burkholone	<i>B. sp.</i> QN15488	Bioactivity-guided	Cytotoxic	[¹³⁷]
	4-hydroxy-3-methyl-2- (2-nonenyl)-quinoline (HMNQ)	<i>B. thailandensis</i> E264	Bioactivity-guided	Antibacterial	[¹³⁸]
	2-heptyl-4(1H)- quinolone N-oxide (HQNO)	<i>B. thailandensis</i> E264	Bioactivity-guided	Antibacterial	[¹³⁸]
	2-alkylquinolones	<i>B. sp.</i> MBAF1239	Bioactivity-guided	Antibacterial	[¹³⁹]
	<i>N</i> -acyl-anthranilic acids	<i>B. thailandensis</i> E264	Other	Cytotoxic, Other	[^{70,140}]
	4-Flavanone*	<i>B. gladioli</i> pv. <i>agaricicola</i>	Bioactivity-guided (detected by GC- MS only)	Antifungal	[¹⁴¹]
Polyketides	Gladiolin	<i>B. gladioli</i> BCC0238	Bioactivity-guided	Antibacterial (antituberculosis)	[^{142,143}]
	Bongkrekiic Acid	<i>B. gladioli</i> pv. <i>cocovenenans</i>	Bioactivity-guided	Other (Mitochondrial ATPase inhibitor)	[¹⁴⁴⁻¹⁴⁷]
	Lagriene	<i>B. gladioli</i> Lv-StA	Genome mining	Antibacterial	[⁵²]

Ribosomally Synthesized and Posttranslationally Modified Peptides (RiPPs)	Capistruin	<i>B. thailandensis</i> E264	Genome mining	Antibacterial (RNA polymerase inhibitor)	[¹⁴⁸⁻¹⁵⁰]
	Burhizin*	<i>B. rhizoxinica</i> HKI 454	Genome mining, Detected only by LC/MS	Not reported (compound not isolated)	[^{151,152}]
Polyynes	Cepacins	<i>B. cepacia</i> SC11783	Bioactivity-guided	Antibacterial	[^{153,154}]
	Caryoynencin	<i>B. caryophylli</i> DSM50341 <i>B. gladioli</i> pv. <i>cocovenenans</i> DMS11318	Bioactivity-guided	Antibacterial	[^{155,156}]
Terpenes	Hopanoids	<i>B. caryophylli</i> DSM 50341 <i>B. gladioli</i> DSM 4245 <i>Burkholderia</i> spp. strains G-21019, G-21027, G-22034, G-22009, G-22037, G-21032	Other (Biomarkers for chemotaxonomy)	Not reported	[¹⁵⁷]
	d-limonene (1-methyl-4-(1-methylethenyl)-cyclohexene)*	<i>B. gladioli</i> pv. <i>agaricicola</i>	Bioactivity-guided (detected by GC-MS only)	Antifungal	[¹⁴¹]

* Denotes that chemical structure was not elucidated or that the compound was detected by mass spectrometry only.

Table S2. Natural product BGCs detected in *Paraburkholderia* genomes

<i>Paraburkholderia</i> strains and NCBI RefSeq assembly accession codes	GC content (%)	size (Mb)	Number of chromosomes	Number of plasmids	Number of natural product BGCs	BGCs per Mb of genome
Complete genomes						
<i>P. aromaticivorans</i> BN5 GCF_002278075.1	62.9	8.9	2	6	10	1.12
<i>P. caribensis</i> Bcrs1W GCF_001611015.1	62.3	9.3	3	0	12	1.29
MBA4 GCF_00522545.2	62.5	9.5	2	1	13	1.37
<i>P. phenoliruptrix</i> BR3459a GCF_000300095.1	63.1	7.7	2	1	9	1.17
<i>P. phymatum</i> STM815 GCF_000020045.1	62.2	8.7	2	2	11	1.26
<i>P. phytofirmans</i> PsJN GCF_000020125.1	62.3	8.2	2	1	11	1.34
<i>P. sprentiae</i> WSM5005 GCF_001865575.1	63.2	7.8	2	3	7	0.90
<i>P. xenovorans</i> LB400 GCF_000013645.1	62.6	9.7	2	1	10	1.03
Complete and draft genomes						
<i>P. caledonica</i> NBRC 102488 GCF_000685095.1	62.0	7.3	draft genome		9	1.23
PHRS4 GCF_003330745.1	61.9	7.2	2	1	7	0.97
<i>P. fungorum</i> ATCC BAA-463 GCF_00961515.1	61.8	9.1	3	1	11	1.21
NBRC 102489 GCF_000685055.1	61.8	8.6	draft genome		14	1.63
<i>P. graminis</i> PHS1 GCF_003330785.1	62.8	7.5	2	1	8	1.07
C4D1M GCF_000172415.1	62.9	7.5	draft genome		8	1.07
<i>P. hospita</i> DSM 17164 GCF_002902965.1	62.8	11.5	6 replicons		13	1.13
mHSR1 GCA_003330805.1	61.9	10.8	3	1	12	1.11
<i>P. terrae</i> DSM 17804 GCF_002902925.1	61.9	10.1	3	1	11	1.09
NBRC 100964 GCF_000739835.1	62.0	9.9	draft genome		11	1.11
Draft genomes						
<i>P. acidipaludis</i> NBRC 101816 GCF_000684975.1	65.2	6.5	draft genome		12	1.85
<i>P. aspalathi</i> LMG 27731 GCF_900116445.1	61.1	9.9	draft genome		13	1.31
<i>P. bannensis</i> NBRC 103871 GCF_000685015.1	64.0	8.6	draft genome		16	1.86
<i>P. bryophila</i> 376MFSHa3.1 GCF_000383275.1	61.9	7.7	draft genome		10	1.30
<i>P. caballeronis</i> TNe-841 GCF_900104845.1	67.0	7.1	draft genome		10	1.41
<i>P. diazotrophica</i> LMG 26031 GCF_900108945.1	63.0	8.6	draft genome		11	1.28
<i>P. dilworthii</i> WSM3556 GCF_000472525.1	61.8	7.7	draft genome		10	1.30
<i>P. eburnea</i> JCM 18070 GCF_002917095.1	64.1	6.9	draft genome		13	1.88
<i>P. ferrariae</i> NBRC 106233 GCF_000685035.1	64.9	7.9	draft genome		17	2.15

<i>P. ginsengiterrae</i> DCY85-1 GCF_001645135.1	62.5	8.5	draft genome	7	0.82
<i>P. ginsengisoli</i> NBRC 100965 GCF_000739735.1	63.6	6.5	draft genome	10	1.54
<i>P. heleia</i> NBRC 101817 GCF_000739775.1	64.6	8.0	draft genome	16	2.00
<i>P. kururiensis</i> M130 GCF_00341045.1 NBRC 107107 GCF_000739795.1	65.1	6.8	draft genome	10	1.47
	65.0	7.1	draft genome	13	1.83
<i>P. megapolitana</i> LMG 23650 GCF_900113825.1	62.1	7.6	draft genome	16	2.11
<i>P. mimosarum</i> LMG 23256 GCF_000472825.1 STM 3621 GCF_000472845.1	63.9	8.4	draft genome	18	2.14
	63.9	8.6	draft genome	16	1.86
<i>P. monticola</i> JC2948 GCF_001580545.1	63.8	7.8	draft genome	6	0.77
<i>P. oxyphila</i> NBRC 105797 GCF_000685075.1	64.1	10.6	draft genome	17	1.60
<i>P. nodosa</i> CNPSO 1341 GCF_001718195.1 DSM 21604 GCF_000519185.1	64.1	9.6	draft genome	16	1.67
	64.2	8.6	draft genome	16	1.86
<i>P. phenazinium</i> LMG 2247 GCF_900100735.1	62.3	8.6	draft genome	19	2.21
<i>P. ribeironis</i> STM7296 GCF_900019265.1	62.5	7.3	draft genome	9	1.23
<i>P. sacchari</i> LMG 19450 GCF_000785435.1	64.0	7.3	draft genome	14	1.92
<i>P. sartisoli</i> LMG 24000 GCF_900107685.1	63.5	5.9	draft genome	9	1.53
<i>P. tropica</i> P-31 GCF_001673675.1	64.7	8.9	draft genome	14	1.57
<i>P. tuberum</i> WSM4176 GCF_000372945.1	62.9	9.1	draft genome	8	0.88
Average	63.1	8.3		12	1.43
Range	61.1– 67.0	5.9– 11.5		6–19	0.77–2.21

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