

Classification and Multifaceted potential of secondary Metabolites

Produced by *Bacillus subtilis* group: A Comprehensive Review

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Table S1: NRPs from *B. subtilis* group.

NRPs class	Sub-class	Metabolites	Antimicrobial activity				References
			Antibacterial		Antifungal	Other	
			Gram +ive	Gram -ive			
Cyclic lipopeptide	Fengycin	Agrastatin A	-	-	+	-	[1]
Cyclic lipopeptide	Fengycin	Fengycin	-	-	+	-	[2,3,4]
Cyclic lipopeptide	Fengycin	Fengycin A	-	-	+	-	[5]
Cyclic lipopeptide	Fengycin	Fengycin B	-	-	+	-	[6]
Cyclic lipopeptide	Fengycin	Fengycin C, D, S	-	-	+	-	[5]
Cyclic lipopeptide	Fengycin	Plipastatin	-	-	+	-	[7]
Cyclic lipopeptide	Iturin	Bacillomycin	-	-	+	-	[8,9]
Cyclic lipopeptide	Iturin	Bacillomycin D	-	-	+	-	[10]
Cyclic lipopeptide	Iturin	Bacillomycin F	-	-	+	-	[11]
Cyclic lipopeptide	Iturin	Bacillomycin L	-	-	+	-	[12]
Cyclic lipopeptide	Iturin	Bacillomycin Lc	-	-	+	-	[13]
Cyclic lipopeptide	Iturin	Bacillomycin R	+	-	+	-	[13]
Cyclic lipopeptide	Iturin	Eumycin	-	-	+	-	[13]
Cyclic lipopeptide	Iturin	Iturin	-	-	+	-	[2,14]
Cyclic lipopeptide	Iturin	Iturin A	-	-	+	-	[6,12]
Cyclic lipopeptide	Iturin	Iturin C	-	-	+	-	[14]
Cyclic lipopeptide	Iturin	Iturin D, E	-	-	+	-	[13]
Cyclic lipopeptide	Iturin	Mycosubtilin	+	-	+	-	[12,15]
Cyclic lipopeptide	Iturin	Subtulene A	+	+	+	-	[16]
Cyclic lipopeptide	Surfactin	Bamylocin A	-	-	+	-	[11,17,18]
Cyclic	Surfactin	Lichenysin	+	+	+	-	[19]

lipopeptide							
Cyclic lipopeptide	Surfactin	Lichenysin A	+	+	-	-	[20]
Cyclic lipopeptide	Surfactin	Locillomycin	+	+	-	Antiviral	[21]
Cyclic lipopeptide	Surfactin	Pumilacidin A-G	+	+	-	Antiviral	[22]
Cyclic lipopeptide	Surfactin	Surfactin	+	+	+	-	[2,23,24]
Cyclic lipopeptide	Surfactin	fengycin	-	-	+	-	[22,25,26,27]
Cyclic lipopeptide	Surfactin	Surfactin like peptide	+	+	+	-	[28,29]
Cyclic lipopeptide	-	Gageopeptine	-	-	+	-	[30]
Cyclic lipopeptide	-	Bacilotetrins A and B	+	-	-	-	[30]
Cyclic lipopeptide	Nonapeptide	Locillomycins	+	+	-	Antiviral	[21]
Linear lipopeptide	Gageopeptide	Gageotetrine A-C	-	-	+	-	[30]
Linear lipopeptide	-	Gageostatins	-	-	+	-	[30]
Linear lipopeptide	Siderophore	Bacillibactin	-	-	+	+	[31]
Other NRPs	Dipeptide	Bacilysin	+		+	-	[32]
Other NRPs	cyclohexenone	Chlorotetain	-	-	+	-	[33]
Other NRPs	Polypeptide	Bacitracin A, F	-	+	-	-	[34]
Other NRPs	Polypeptide	Mycobacillin	-	-	+	-	[35]
Other NRPs	Dipeptide	Rhizocticin A	-	-	+	-	[36]

Table S2: Ribosomal peptides (RPs) from *B. subtilis* group.

RPs Class	Sub-class	Metabolite	Antimicrobial activity			References
			Antibacterial activity		Antifungal activity	
			Gram +ive	Gram -ive		
Modified peptides	Lanthibiotics	Entianin	+	-	-	[37,38,39,40]
Modified peptides	Lanthibiotics	Ericin A	+	-	-	[41]
Modified peptides	Lanthibiotics	Ericin S	+	-	-	[41,42]
Modified peptides	Lanthibiotics	Subtilin	+	-	-	[41,43]
Modified peptides	Lanthibiotics	Mersacidin	+	-	-	[44]
Modified peptides	Lanthibiotics	Sublancin 168	+	-	-	[45]

Modified peptides	Lanthibiotics	Lichenicidin	+	-	-	[46]
Modified peptides	Lanthibiotics	Subtilisin A	+	+	-	[47,48,49]
Modified peptides	Lanthibiotics	Subtilomycin	+	+	+	[50,51]
Others	Bacteriocin like peptides	Lichenin	+	-	-	[48]
Non-modified peptides	Large antimicrobial peptides	Bac 14B	+	+	+	[49]
Non-modified peptides	Large antimicrobial peptides	Baciamin	-	-	+	[50]
Modified peptides	Cyclized peptides	Amylocyclicin	+	-	-	[52]
Modified peptides	LAP	Sonorensin	+	+	-	[53]
Modified peptides	LAP	Plantazolicin	+	-	-	[52]
Non-modified peptide	Large antimicrobial peptide	CAMT2	+	+	-	[51]
Non-modified peptide	Large antimicrobial peptide	Bacisubin	-	-	+	[54]
Modified peptides	Lanthibiotics	Amylolysin	+	+	+	[55]

Table S3: PolyKetides (PKs) from *B. Subtilis*

PKs Class	Sub-class	Metabolite	Antibacterial activity		Antifungal activity	Other	References
			Gram +ive	Gram -ive			
Polyene	Macrolactin	7-O-6'(2"-acetylphenyl)-5'-hydroxyhexanoate macrolactin A	-	+	-	-	[56]
Polyene	Macrolactin	7-O-2'E-butenoyl-macrolactin A	-	-	+	-	[5]
Polyene	Macrolactin	Lactones with 3 diene moieties in the carbon	+	-	-	Antiviral	[8]

		backbone					
Polyene	Macrolactin	Gageomacrolactins	+	-	-	-	[30]
Polyene	Macrolactin	7- <i>O</i> -methyl-5'-hydroxy-3'-heptenoate-macrolactin A	+	+	-	-	[56]
Polyene	Macrolactin	7- <i>O</i> -malonyl-macrolactin A	+	+	+	-	[8]
Polyene	Macrolactin	7- <i>O</i> -succinyl-macrolactin F	+	+	-	-	[57]
Polyene	Macrolactin	7- <i>O</i> -succinyl-macrolactin A	+	+	+	-	[57]
Polyene	Macrolactin	Macrolactin A	+	+	+	-	[58]
Polyene	Macrolactin	7- <i>O</i> -2' <i>E</i> -butenoyl macrolactin A	-	-	+	-	[5]
Polyene	Macrolactin	Macrolactin B and C	+	-	-	-	[59]
Polyene	Macrolactin	Macrolactin D	+	+	+	-	[21]
Polyene	Macrolactin	Macrolactin F-M	+	-	-	-	[57]
Polyene	Macrolactin	Macrolactin N	+	+	-	-	[31]
Polyene	Macrolactin	Macrolactin Q	+	+	-	-	[60]
Polyene	Macrolactin	Macrolactin S	+	+	+	-	[61]
Polyene	Macrolactin	Macrolactin T	+	-	+	-	[5]
Polyene	Macrolactin	Macrolactin W	+	-	-	-	[60]
Polyene	-	Aurantinin B-D	+	-	-	-	[62]
Polyene	-	2-(8-butyl-3-ethyl-3,4,4a,5,6,8a-hexahydro-2H-chromen-6-yl)-ethyl benzoate	-	+	-	-	[56]
Polyene	-	methoxycarbonyl)-4-(5-(2-ethylbutyl)-5,6-dihydro-3-methyl-2H-pyran-2-yl)-butyl benzoate	-	+	-	-	[56]
Polyene	Difficidin	Macrocyclic	+	+	-	-	[63]

		polyene lactone phosphate ester					
Polyene	Difficidin	Difficidin	+	+	-	-	[63]
Polyene	Difficidin	Oxydifficidin	+	+	-	-	[64]

Table S4: Hybrid (NRP/PK) metabolites from *B. Subtilis*.

Class	Sub-class	Metabolite	Antibacterial activity		Antifungal activity	Other activity	References
			Gram +ive	Gram -ive			
Hybrid.	Bacillaene.	Bacillaene A.	+	+	+	-.	[65]..
Hybrid.	Isocoumarins.	N-acetylated amicoumacin B.	-.	+	-.	-.	[59] ..
Hybrid.	Isocoumarins.	Amicoumacin A.	+	-.	-.	Anticancer, Antiulcer and Anti-inflammatory.	[5]..
Hybrid.	Isocoumarins.	Amicoumacin A B, C.	+	-.	-.	Anti-inflammatory.	[59]..
Hybrid.	Isocoumarins.	AI-77s.	+	-.	-.	Gastro protective .	[66] ..
Hybrid.	Isocoumarins.	Baciphelacin.	+	+	-..		[67] ..
Hybrid.	Isocoumarins.	Bacilosarcons A and B.	+	+	-.	herbicidal.	[68]..
Hybrid.	Isocoumarins.	Damxungmacin A and B.	+..		-.	Anticancer.	[69]..
Hybrid.	Isocoumarins.	PM-94128.	-.	-.	-.	Anticancer.	[70]..
Hybrid.	Isocoumarins.	Hetiamacin A (PJS).	+	-.	-.	-.	[54]..
Hybrid.	Isocoumarins.	Hetiamacin B.	+	-.	-.	-.	[54]..
Hybrid.	Isocoumarins.	Lipoamicoumacins A-D.	+	+	-.	Anticancer.	[5]..

Table S5: Volatile metabolites from *B. subtilis* group.

Class	Sub-class	Metabolite	Antifungal activity	Antibacterial activity	References
Organic metabolite	Acids	Butanoic acid, 3-methyl	+	-	[37]
Organic metabolite	Acids	Gentisic acid	+	-	[38]
Organic metabolite	Acids	n-Hexanoic acid	-	+	[39]
Organic metabolite	Acids	n-Hexadecanoic acid	+	-	[38]

Organic metabolite	Acids	Octadecanoic acid, Propanoic acid, 4-hexen-1-yl ester	+	-	[54]
Organic metabolite	Acids	Oleic acid	-	+	[39]
Organic metabolite	Acids	Propanoic acid, 2-methyl	+	-	[37]
Organic metabolite	Acid	Isovaleric acid	+	-	[71]
Organic metabolites	Acid	2-methylbutyric acid	+	-	[32]
Organic metabolites	Alcohols	Ethanol	+	-	[72]
Organic metabolite	Alcohols	3,4-dimethyl-5-hexen-3-ol, Heptanol	+	-	[54]
Organic metabolite	Alcohol	1-decanol	+	-	[73]
Organic metabolite	Alcohols	2-Undecanol	+	-	[22]
Organic metabolite	Alcohols	1-Butanol	+	-	[37]
Organic metabolite	Alcohols	1-Butanol, 3-methyl-	+	-	[37,54]
Organic metabolite	Alcohols	Hexanol,2-ethyl	+	-	[63]
Organic metabolite	Alcohol	Isoamyl alcohol/3-methyl-1-butanol	+	-	[71]
Organic metabolite	Alcohol	1-dodecanol	+	-	[73]
Organic metabolite	Alcohol	2-ethylhexanol	+	-	[74]
Organic metabolite	Aldehyde	2,4-Heptadienal, (E,E)-, 2-Decenal, (E)-, 2-Heptenal, (Z)-, 2-Nonenal, (E)-, 2-Octenal, (E)-, 2-Undecenal, 2,4-Decadienal, Octanal	+	-	[54]
Organic metabolite	Aldehyde	Decanal	+	-	[58]
Organic metabolite	Aldehyde	Nonanal	+	-	[39]
Organic metabolites	Hydrocarbon	5-methyl-2-heptanone	+	-	[72]
Organic metabolite	Hydrocarbon	Eicosane, 10-methyl-	+	-	[63]
Organic metabolite	Hydrocarbon	Heneicosane	+	-	[38]
Organic metabolite	Hydrocarbon	Heptadecane	-	+	[39]
Organic metabolite	Hydrocarbon	Heptadecane, 2,6,10,15-tetramethyl-	+	-	[63]
Organic metabolite	Hydrocarbon	Heptane, 2-methyl-7-oxabicyclo[2.2.1]	+	-	[54]
Organic metabolite	Hydrocarbon	Hexadecane, 2,6,11,15-tetramethyl-	+	-	[63]
Organic metabolite	Hydrocarbon	Nonadecane, 9-methyl-	+	-	[63]
Organic metabolite	Hydrocarbon	Nonadecane,10-methyl-	+	-	[63]
Organic metabolite	Hydrocarbon	Pentadecane	+	-	[75]
Organic metabolite	Hydrocarbon	Pentadecane, 8-hexyl-	+	-	[63]

Organic metabolite	Hydrocarbon	Tetradecane	+	-	[75]
Organic metabolite	Hydrocarbon	Tetradecane, 2,6,10-trimethyl-	+	-	[63]
Organic metabolite	Hydrocarbon	Undecane,1,2-methyl	+	-	[75]
Organic metabolite	Hydrocarbon	1H-indene, 1-methylene-	+	-	[54]
Organic metabolite	Hydrocarbon	1,3-butadiene	+	+	[76]
Organic metabolite	Hydrocarbon	8-methyl-1-decene	+	-	[54]
Organic metabolite	Htdrocarbon	m-tolunitrile	+	-	[74]
Organic metabolite	Hydrocarbon	1,3- pentadiene	+	-	[77]
Organic metabolite	Hydrocarbon	6-methyl-2-heptanone	+	-	[74]
Organic metabolite	Benzenoids	β-Benzeneethanamine	+	-	[38]
Organic metabolite	Benzenoids	1,2-Benzisothiazol-3(2H)-one	-	+	[76]
Organic metabolite	Benzenoids	2,4-bis(2-Methylpropyl)-phenol	+	-	[63]
Organic metabolite	Benzenoids	2-Phenylethanol	-	+	[39]
Organic metabolite	Benzenoids	4-Hydroxybenzaldehyde	+	+	[76]
Organic metabolite	Benzenoids	Benzene, 1,2,4,5-tetramethyl	+	-	[63]
Organic metabolite	Benzenoids	Benzene, 1,2,4-trimethyl	+	-	[58]
Organic metabolite	Benzenoids	Benzene, 1-methyl-4-(1-methylethyl)-	+	-	[58]
Organic metabolite	Benzenoids	Benzene, 2-propenyl	+	-	[75]
Organic metabolite	Benzenoids	Benzene,1,4-dichloro	+	-	[75]
Organic metabolite	Benzenoids	Benzothiazole	+	-	[74]
Organic metabolite	Benzenoids	Butylated hydroxytoluene	+	-	[38]
Organic metabolite	Benzenoids	Ethylbenzene	+	-	[58]
Organic metabolite	Benzenoids	Phenol, 2,4-bis(1,1-dimethylethyl)	+	-	[7]
Organic metabolite	Benzenoids	Phenol, 4,4'-(1-methylethylidene) bis-	-	+	[39]
Organic metabolite	Benzenoids	Phenol, 4-chloro-3-methyl	+	-	[7]
Organic metabolite	Benzenoids	Phenol,2,3,6-trimethyl-	+	-	[58]
Organic metabolite	Benzenoids	P-xylene	+	-	[58]
Organic metabolite	Benzenoids	Styrene	+	-	[22]
Organic metabolite	Benzenoids	Toluene	+	-	[39]
Organic metabolite	Benzenoids	Phenol	+	-	[73]
Organic metabolite	Benzenoids	2,4-di- <i>tert</i> -butylphenol	+	+	[7]
Organic metabolite	Benzenoid	Benzylacetone	+	-	[74]
Organic metabolite	Esters	Ethyl acetate	+	-	[37]
Organic metabolite	Ester	Butyl formate	+	-	[71,78]

Organic metabolite	Ester	Isopentyl acetate	+	-	[79]
Organic metabolite	Furans	2-pentyl-furan	+	-	[54]
Organic metabolite	Ketone	2-nonanone	+	-	[74,80]
Organic metabolite	Ketone	Acetophenone	+	-	[74]
Organic metabolites	Ketone	Methyl isobutyl ketone	+	-	[72]
Organic metabolite	Ketone	Acetoin	+	-	[77]
Organic metabolite	Ketone	2-heptanone	+	-	[79,80]
Organic metabolite	Ketone	Butan-2-one	+	-	[37]
Organic metabolite	Ketone	Butanone, 3-hydroxy-2-	+	-	[37]
Organic metabolite	Ketone	Dodecan-2-one	+	-	[38]
Organic metabolite	Ketone	Ethanone, 1-(4-methylphenyl)	+	+	[39]
Organic metabolite	Ketone	Pentanone, 2,2,4-trimethyl-3-	-	+	[5]
Organic metabolite	Ketone	Propan-2-one	+	-	[37]
Organic metabolite	Ketone	Tridecan-2-one	+	-	[39]
Organic metabolite	Ketone	5-methyl-2-hexanone	+	-	[74]
Organic metabolite	Nitrogen-containing	1-ethyl-1H-imidazole	+	-	[54]
Organic metabolite	Nitrogen-containing	Ammonium acetate	+	-	[63]
Organic metabolite	Nitrogen-containing	2,5-dimethyl Pyrazine	+	-	[78]
Organic metabolite	Nitrogen-containing	2-ethyl-3,5-dimethyl Pyrazine	+	-	[37]
Organic metabolite	Nitrogen-containing	Tetramethyl-Pyrazine	+	-	[63]
Organic metabolite	Nitrogen-containing	2,3,5,6-tetramethyl Pyrazine	+	-	[37]
Organic metabolite	Nitrogen-containing	S-(-)-2-methylbutylamine	+	-	[72]
Organic metabolite	Nitrogen-containing	2,3-dimethyl pyrazine	+	-	[71]
Organic metabolite	Sulphur-containing	Carbon disulphide	-	+	[37]
Organic metabolite	Sulphur-containing	Dimethyl trisulfide	+	-	[81]
Organic metabolite	Hydrocarbon	Nonane	+	-	[71]
Organic metabolite	Aldehyde	Benzaldehyde	+	-	[73]
Organic metabolite	Ketones	Diacetyl/Butane-2,3-dione	+	-	[71]
Organic metabolite	Sulphur-containing	Thiophene	+	-	[77]

Inorganic metabolite	-	Hydrogen sulfide	+	-	[32]
Inorganic metabolites	-	Hydrogen cyanide	+	-	[73,81]

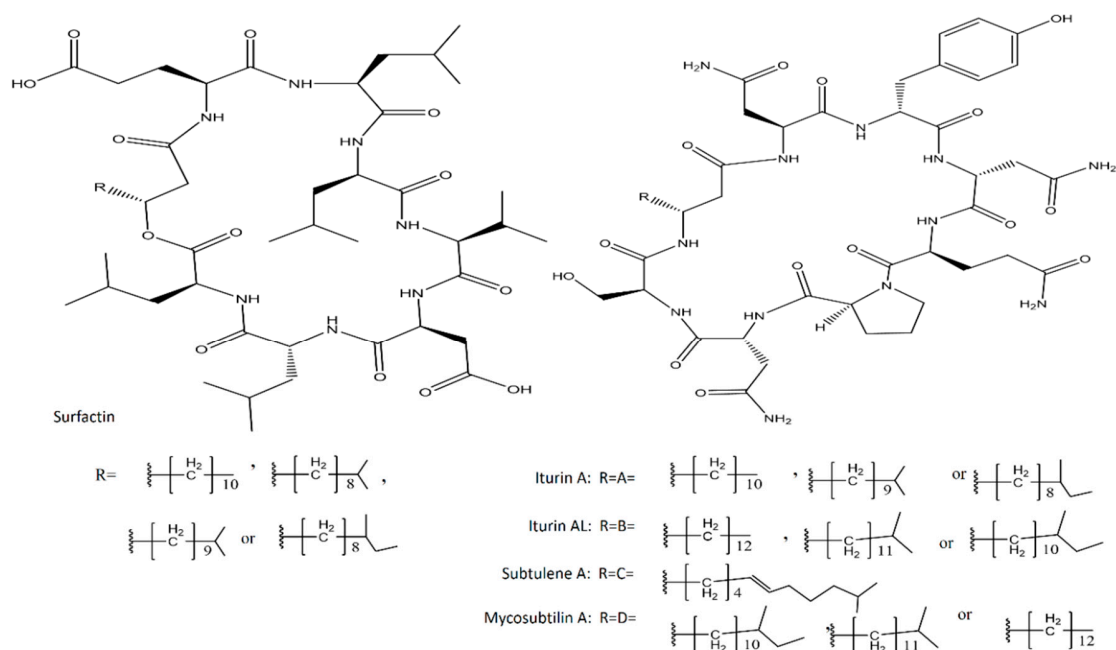


Figure S1. Showing various confirmations of surfactin and iturin cyclic lipopeptides.

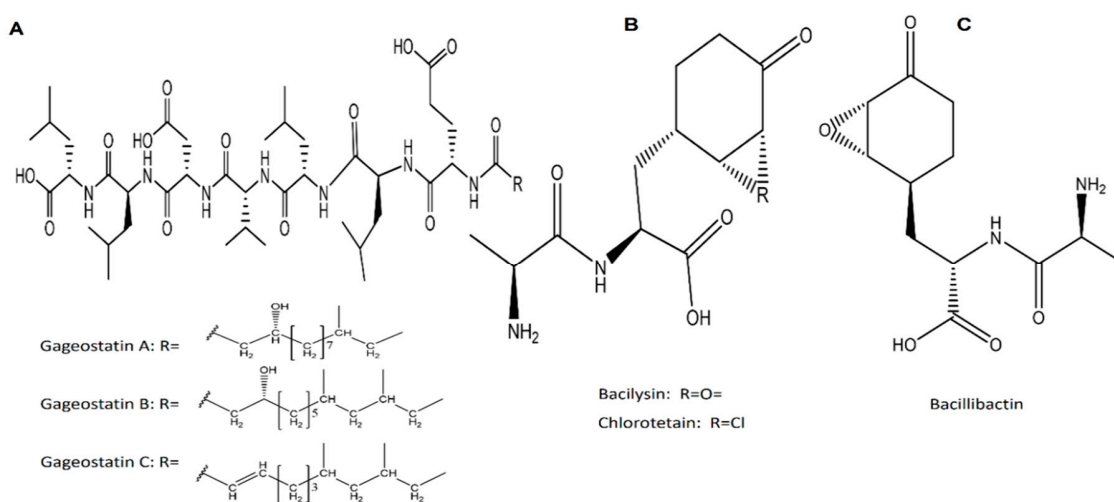


Figure S2. Showing molecular structure of gageopeptide (gageostatin A, B and C) (**A**) and siderophore (bacilysin, chlorotetain, and bacillibactin) linear lipopeptide (**B and C**).

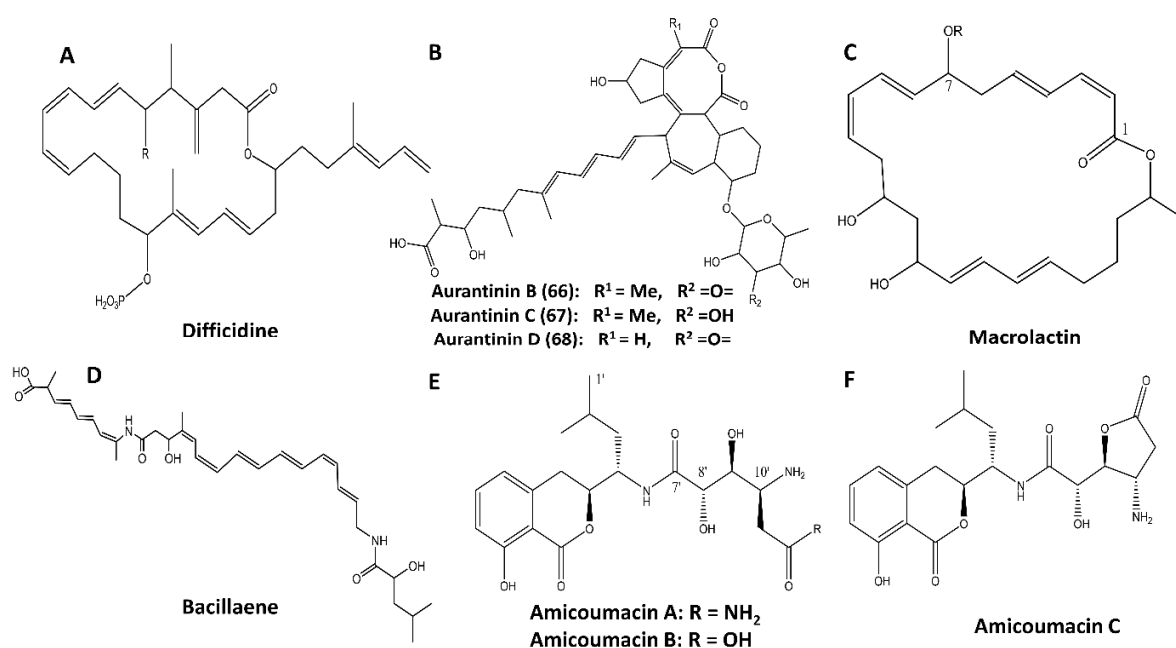


Figure S3. Chemical structure of polyketides (PKs), difficidine (A), aurantin (B) and macrolactin (C) and Hybrid NRPs/PKs metabolites bacillaene (D) and amicoumacin A and B (E) and amicoumacin C (F).

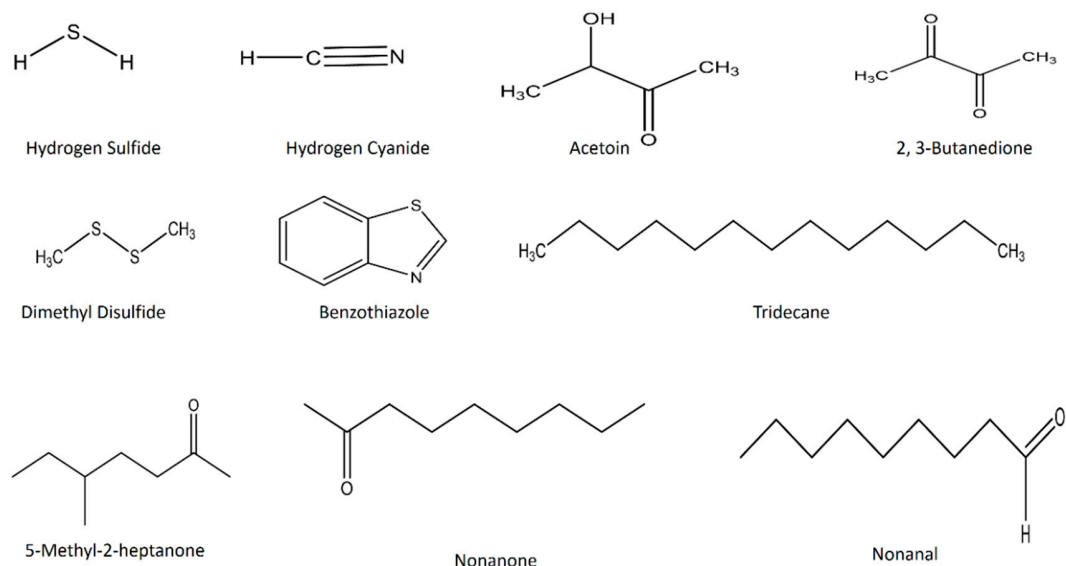


Figure S4. Representing structure of volatile bioactive metabolites produced by *B. subtilis* group.

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