F-1511

Antimicrobial Activity and Spectrum of a Seachaid Pharmaceuticals Investigational Compound (SP2078) Tested against Gram-positive Pathogens

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ABSTRACT

Background: *Staphylococcus aureus* and *S. epidermidis* isolates have become important causes of serious nosocomial infections, including bacteremia. In addition, multidrug-resistant (MDR) *Enterococcus faecium* isolates have challenged the antimicrobial therapies available. The activity of a new glycopeptide was assessed against Gram-positive strains, including MDR subsets.

Methods: 262 clinical Gram-positive strains were selected for this study. Susceptibility testing for SP2078 and comparator agents were performed by CLSI methods (M07-A9 and M100-S22). SP2078 was tested in 96-well plates containing polysorbate-80 (0.002%). MICs were quality assured using QC strains. MIC interpretations for comparators were based on CLSI (M100-S22) and EUCAST (2012) criteria.

Results: SP2078 showed potent activity when tested against methicillin-resistant (MRSA) and -susceptible *S. aureus* (MSSA; $MIC_{50/90}$, 0.06/0.06 μg/mL, for both groups). Similar SP2078 MIC values were obtained against heterogeneous vancomycin-intermediate *S. aureus* (hVISA; $MIC_{50/90}$, 0.06/0.06 μg/mL) and VISA strains (MIC_{50}, 0.12 μg/mL). SP2078 displayed higher MIC values when tested against vancomycin-resistant *S. aureus* (VRSA; MIC_{50}, 2 μg/mL). SP2078 was at least 4- and 8-fold more potent than comparators when tested against MRSA and MSSA, and hVISA and VISA, respectively. Low $MIC_{50/90}$ results were obtained for SP2078 when tested against *S. epidermidis* ($MIC_{50/90}$, 0.03/0.06 μg/mL), as well as against vancomycin-susceptible *E. faecalis* ($MIC_{50/90}$, 0.06/0.12 μg/mL) and vancomycin-susceptible *E. faecium* ($MIC_{50/90}$, 0.03/0.03 μg/mL). VanB-*E. faecalis* ($MIC_{50/90}$, 0.12/0.12 μg/mL) and -*E. faecium* ($MIC_{50/90}$, 0.015/0.03 μg/mL) were also susceptible to SP2078, while higher MIC results were obtained against VanA enterococci ($MIC_{50/90}$, 4-8/8 μg/mL). Potent SP2078 MIC values were noted against *S. pneumoniae*, including MDR strains ($MIC_{50/90}$, 0.015/0.03 μg/mL) and β-hemolytic streptococci ($MIC_{50/90}$, 0.03/0.06 μg/mL).

Conclusions: SP2078 showed potent activities against Gram-positive strains, including MDR challenge subsets. This drug was less active against VRSA and VanA enterococci. These *in vitro* data warrant further investigations for potential clinical development of this compound.

INTRODUCTION

Antimicrobial resistance increases the morbidity, mortality and associated costs of treating infectious diseases. The threat from resistance, particularly dispersion of successful clones of multidrug resistant (MDR) bacteria is becoming more common, often via the movement of people or contaminated materials. Several organisms, such as methicillin-resistant *Staphylococcus aureus* (MRSA), *Staphylococcus epidermidis* and *Enterococcus faecium* continue to be a clinical and therapeutic problem and have been increasingly associated with nosocomial infections, especially in the treatment of critically ill patients found in intensive care units.

Vancomycin has been the agent of choice for infections caused by MRSA and other Gram-positive bacteria, and until recently, all isolates were uniformly susceptible. The isolation of staphylococci with intermediate susceptibility or resistance to teicoplanin, as well as vancomycin, has now been reported with increasing frequency. In addition, more than 70% of *E. faecium* isolates in USA hospitals are resistant to glycopeptides. Studies have suggested that vancomycin may not be the best therapeutic option for treating certain infections, due to suboptimal efficacy. A novel glycopeptide agent (SP2078; see poster F-1510 for additional information) is in pre-clinical development for the treatment of complicated Gram-positive infections. In this study, the *in vitro* spectrum of activity of SP2078 was assessed against Gram-positive species, including MDR subsets.

MATERIALS AND METHODS

Bacterial strain collection. Isolates included in this investigation are as follows: *S. aureus* (22 wildtype methicillin-susceptible [MSSA]; 22 MRSA; 10 heterogeneous vancomycin-intermediate *S. aureus* [hVISA]; five VISA and six vancomycin-resistant *S. aureus* [VRSA]); *Staphylococcus epidermidis* (21 wildtype methicillin-susceptible; and 22 methicillin-resistant); *E. faecium* (21 wildtype; 10 vancomycin-resistant VanA- and 10 vancomycin-resistant VanB-type strains); *E. faecalis* (23 wildtype; 11 vancomycin-resistant VanA- and 12 vancomycin-resistant VanB-type strains); *E. gallinarum* (11); *E. casseliflavus* (11); *S. pneumoniae* (11 wildtype and 11 MDR); β-hemolytic streptococci (11 *Streptococcus pyogenes* and 12 *Streptococcus agalactiae*).

Antimicrobial susceptibility test methods. Isolates were tested for susceptibility by broth microdilution methods following the Clinical and Laboratory Standards Institute (CLSI; M07-A9, 2012) document. Solvent, diluents and dilution procedures utilized for SP2078 investigational compound followed the CLSI recommendations for water-insoluble agents (Table 7B; M100-S22, 2012). Susceptibility testing was performed in cation-adjusted Mueller-Hinton broth (CA-MHB) using customized frozen-form 96-well panels. CA-MHB was supplemented with a surfactant polysorbate-80 (final well concentration, 0.002%). Quality assurance was performed by concurrent testing of CLSI-recommended (M100-S22, 2012) quality control (QC) strains: *E. faecalis* American Type Culture Collection (ATCC) 29212 and *S. aureus* ATCC 29213. Interpretation of MIC results obtained for comparator agents tested against QC strains was in accordance with published CLSI (M100-S22) criteria.

RESULTS

- SP2078 inhibited all MRSA and MSSA strains at ≤0.12 μg/mL ($MIC_{50/90}$, 0.06/0.06 μg/mL), and exhibited MIC_{50} results four- to eight-fold lower than the direct comparators daptomycin (MIC_{50}, 0.25 μg/mL), vancomycin (MIC_{50}, 0.5 μg/mL) and teicoplanin (MIC_{50}, 0.5 μg/mL; **Table 1**).
- Similarly, all hVISA and VISA strains were inhibited by SP2078 at ≤0.12 μg/mL (MIC_{50} values of 0.06 and 0.12 μg/mL, respectively; **Table 1**). SP2078 displayed MIC_{50} values eight-fold lower than daptomycin (MIC_{50}, 0.5-1 μg/mL) and 16- to 64-fold lower than vancomycin (MIC_{50}, 1-4 μg/mL) and teicoplanin (MIC_{50}, 2-8 μg/mL) when tested against hVISA and VISA, respectively.
- Higher MIC values were observed for SP2078 when tested against VRSA strains (MIC_{50}, 2 μg/mL), while daptomycin remained *in vitro* active (MIC_{50}, 0.25 μg/mL; **Table 1**).
- SP2078 ($MIC_{50/90}$, 0.03/0.06 μg/mL) was eight-fold more potent than daptomycin ($MIC_{50/90}$, 0.25/0.5 μg/mL), and 32- to 64-fold more potent than vancomycin ($MIC_{50/90}$, 1/2 μg/mL) and teicoplanin ($MIC_{50/90}$, 2/4 μg/mL) tested against *S. epidermidis* (**Table 1**).
- Overall, the SP2078 compound exhibited higher MIC results ($MIC_{50/90}$, 8/8 μg/mL) when tested against vancomycin-resistant VanA-type *E. faecalis* (**Table 2**); while daptomycin ($MIC_{50/90}$, 1/2 μg/mL) and linezolid ($MIC_{50/90}$, 1/1 μg/mL) remained very active.
- When tested against vancomycin-resistant VanB-type *E. faecalis*, SP2078 ($MIC_{50/90}$, 0.12/0.12 μg/mL) demonstrated *in vitro* activity comparable to the wildtype vancomycin-susceptible control strains ($MIC_{50/90}$, 0.06/0.12 μg/mL; **Table 2**).
- SP2078 was active when tested against vancomycin-susceptible ($MIC_{50/90}$, 0.03/0.03 μg/mL) and -resistant (VanB) *E. faecium* ($MIC_{50/90}$, 0.015/0.03 μg/mL; **Table 3**). However, SP2078 was less active against vancomycin-resistant (VanA) *E. faecium* strains ($MIC_{50/90}$, 4/8 μg/mL).
- Enterococcal isolates intrinsically harboring the *vanC* gene were very susceptible to SP2078 ($MIC_{50/90}$, 0.06/0.25 μg/mL; **Table 4**). In addition, teicoplanin and daptomycin ($MIC_{50/90}$, 1/2 μg/mL for both) showed MIC_{50} values 16-fold higher than SP2078, whereas the vancomycin MIC_{50} value obtained ($MIC_{50/90}$, 4/4 μg/mL) was 64-fold higher than SP2078.
- SP2078 ($MIC_{50/90}$, 0.03/0.06 μg/mL) was four-fold more potent than teicoplanin ($MIC_{50/90}$, 0.12/0.25 μg/mL) and daptomycin ($MIC_{50/90}$, 0.12/0.25 μg/mL), and eight-fold more active than vancomycin ($MIC_{50/90}$, 0.25/0.5 μg/mL) when tested against β-hemolytic streptococci (**Table 5**).
- *S. pneumoniae* clinical isolates were very susceptible to SP2078 ($MIC_{50/90}$, 0.015/0.03 μg/mL), regardless of MDR phenotype (**Table 5**). When the activity of SP2078 was compared with those of teicoplanin (MIC_{50}, 0.12 μg/mL), daptomycin (MIC_{50}, 0.12 μg/mL) and vancomycin (MIC_{50}, 0.25 μg/mL) tested against *S. pneumoniae*, SP2078 displayed MIC_{50} results eight- to 16-fold lower than those comparators.

Table 1. MIC distribution of SP2078 and comparator compounds when tested against *S. aureus* and *S. epidermidis* strains.

Organism[a] (no. tested)/ Compound	MIC (μg/mL) 50%	MIC (μg/mL) 90%	Number (cumulative %) of isolates inhibited at each MIC (μg/mL)[b] 0.015	0.03	0.06	0.12	0.25	0.5	1	2	4
MSSA (22)											
SP2078	0.06	0.06	0(0.0)	5(22.7)	**16(95.5)**	1(100.0)					
Vancomycin	0.5	1	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**17(77.3)**	5(100.0)		
Teicoplanin	0.5	1	NT	0(0.0)	0(0.0)	0(0.0)	8(36.4)	**11(86.4)**	3(100.0)		
Daptomycin	0.25	0.5	NT	0(0.0)	0(0.0)	1(4.6)	**18(86.4)**	3(100.0)			
Linezolid	1	1	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**20(90.9)**	2(100.0)	
MRSA (22)											
SP2078	0.06	0.06	0(0.0)	1(4.6)	**19(90.9)**	2(100.0)					
Vancomycin	0.5	1	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**13(59.1)**	9(100.0)		
Teicoplanin	0.5	0.5	NT	0(0.0)	0(0.0)	0(0.0)	7(31.8)	**15(100.0)**			
Daptomycin	0.25	0.5	NT	0(0.0)	0(0.0)	0(0.0)	**13(59.1)**	8(95.5)	1(100.0)		
Linezolid	1	1	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(9.1)	**20(100.0)**		
hVISA (10)											
SP2078	0.06	0.06	0(0.0)	1(10.0)	**8(90.0)**	1(100.0)					
Vancomycin	1	1	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**10(100.0)**		
Teicoplanin	2	2	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(20.0)	0(20.0)	**8(100.0)**	
Daptomycin	0.5	0.5	NT	0(0.0)	0(0.0)	0(0.0)	3(30.0)	**6(90.0)**	1(100.0)		
Linezolid	1	1	NT	0(0.0)	0(0.0)	0(0.0)	1(10.0)	1(20.0)	**8(100.0)**		
VISA (5)											
SP2078	0.12	–	0(0.0)	0(0.0)	0(0.0)	**5(100.0)**					
Vancomycin	4	–	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**5(100.0)**
Teicoplanin	8	–	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(20.0)
Daptomycin	1	–	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**3(60.0)**	2(100.0)	
Linezolid	1	–	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	**3(80.0)**	1(100.0)	
VRSA (6)											
SP2078	2	–	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(33.3)	**3(83.3)**	1(100.0)
Daptomycin	0.25	–	NT	0(0.0)	0(0.0)	0(0.0)	**4(66.7)**	2(100.0)			
Linezolid	1	–	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(33.3)	**4(100.0)**		
S. epidermidis (43)											
SP2078	0.03	0.06	2(4.7)	**22(55.8)**	19(100.0)						
Vancomycin	1	2	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**30(69.8)**	12(97.7)	1(100.0)
Teicoplanin	2	4	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(4.7)	**12(32.6)**	**12(60.5)**	13(90.7)
Daptomycin	0.25	0.5	NT	0(0.0)	0(0.0)	0(0.0)	**30(69.8)**	13(100.0)			
Linezolid	0.5	1	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(4.6)	**33(81.4)**	8(100.0)	

a. MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; hVISA, heterogeneous vancomycin-intermediate *S. aureus*; VISA, vancomycin-intermediate *S. aureus*; and vancomycin-resistant *S. aureus*.
b. Modal MIC values are in bold. NT, concentration not tested.

Table 2. MIC distribution of SP2078 and comparator compounds when tested against *E. faecalis*.

Organism (no. tested)/ Compound	MIC (μg/mL) 50%	MIC (μg/mL) 90%	Number (cumulative %) of isolates inhibited at each MIC (μg/mL)[a] 0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	≥32
Vancomycin-susceptible (23)													
SP2078	0.06	0.12	1(4.4)	**12(56.5)**	10(100.0)								
Vancomycin	1	2	0(0.0)	0(0.0)	0(0.0)	0(0.0)	7(30.4)	**11(78.3)**	5(100.0)				
Teicoplanin	0.5	0.5	0(0.0)	0(0.0)	0(0.0)	10(43.5)	**13(100.0)**						
Daptomycin	1	2	0(0.0)	0(0.0)	1(4.4)	1(8.8)	6(34.8)	**12(87.0)**	3(100.0)				
Linezolid	1	1	0(0.0)	0(0.0)	0(0.0)	1(4.4)	6(30.4)	**16(100.0)**					
Vancomycin-resistant VanA (11)													
SP2078	8	8	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(18.2)	**9(100.0)**		
Vancomycin	>64	>64	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**11(100.0)**
Teicoplanin	64	>64	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**11(100.0)**
Daptomycin	1	2	0(0.0)	0(0.0)	0(0.0)	0(0.0)	4(36.4)	**6(90.9)**	1(100.0)				
Linezolid	1	1	0(0.0)	0(0.0)	0(0.0)	0(0.0)	4(36.4)	**7(100.0)**					
Vancomycin-resistant VanB (12)													
SP2078	0.12	0.12	1(8.3)	4(41.7)	**7(100.0)**								
Vancomycin	>64	>64	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**12(100.0)**
Teicoplanin	0.5	1	0(0.0)	0(0.0)	1(8.3)	0(8.3)	**9(83.3)**	2(100.0)					
Daptomycin	0.5	1	0(0.0)	1(8.3)	0(8.3)	0(8.3)	5(50.0)	**6(100.0)**					
Linezolid	1	1	0(0.0)	0(0.0)	0(0.0)	0(0.0)	4(33.3)	**8(100.0)**					

a. Modal MIC values are in bold.

Table 3. MIC distribution of SP2078 and comparator compounds when tested against *E. faecium*.

Organism (no. tested)/ Compound	MIC (μg/mL) 50%	MIC (μg/mL) 90%	Number (cumulative %) of isolates inhibited at each MIC (μg/mL)[a] 0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	≥32
Vancomycin-susceptible (21)														
SP2078	0.03	0.03	**10(47.6)**	**10(95.2)**	1(100.0)									
Vancomycin	0.5	1	NT	0(0.0)	0(0.0)	0(0.0)	1(4.8)	**14(71.4)**	5 (95.2)	1(100.0)				
Teicoplanin	1	2	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**9(42.9)**	**9(85.7)**	3(100.0)				
Daptomycin	2	2	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	5(23.8)	**16(100.0)**				
Linezolid	1	2	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(4.8)	**15(76.2)**	5(100.0)				
Vancomycin-resistant VanA (10)														
SP2078	4	8	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(10.0)	1(20.0)	**6(80.0)**	2(100.0)		
Vancomycin	>64	>64	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**10(100.0)**
Teicoplanin	64	>64	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**10(100.0)**
Daptomycin	2	2	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	4(40.0)	**6(100.0)**				
Linezolid	1	1	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**9(90.0)**	1(100.0)				
Vancomycin-resistant VanB (10)														
SP2078	0.015	0.03	**5(50.0)**	**5(50.0)**										
Vancomycin	64	>64	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**10(100.0)**
Teicoplanin	1	1	NT	0(0.0)	0(0.0)	0(0.0)	1(10.0)	2(30.0)	**6(90.0)**	1(100.0)				
Daptomycin	2	2	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	4(40.0)	**6(100.0)**				
Linezolid	1	1	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(10.0)	**9(100.0)**					

a. Modal MIC values are in bold. NT, concentration not tested.

Table 4. MIC distribution of SP2078 and comparator compounds tested against *vanC*-carrying *E. gallinarum* (11 strains) and *E. casseliflavus* (11 strains).

Organism (no. tested)/ Compound	MIC (μg/mL) 50%	MIC (μg/mL) 90%	Number (cumulative %) of isolates inhibited at each MIC (μg/mL)[a] 0.015	0.03	0.06	0.12	0.25	0.5	1	2	4
VanC enterococci (22)											
SP2078	0.06	0.25	0(0.0)	3(13.6)	**12(68.2)**	4(86.4)	3(100.0)				
Vancomycin	4	4	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	3(13.6)	**19(100.0)**
Teicoplanin	1	2	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	8(36.4)	**11(86.4)**	3(100.0)	
Daptomycin	1	2	NT	1(4.6)	1(9.2)	2(18.2)	0(18.2)	2(27.3)	**9(68.2)**	5(90.9)	2(100.0)
Linezolid	1	2	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(4.6)	**16(77.3)**	5(100.0)	

a. Modal MIC values are in bold. NT, concentration not tested.

Table 5. MIC distribution of SP2078 and comparator compounds when tested against β-hemolytic streptococci and *S. pneumoniae*.

Organism (no.tested)[a]/ Compound	MIC (μg/mL) 50%	MIC (μg/mL) 90%	Number (cumulative %) of isolates inhibited at each MIC (μg/mL)[b] ≤0.008	0.015	0.03	0.06	0.12	0.25	0.5	1
β-hemolytic streptococci (23)										
SP2078	0.03	0.06	0(0.0)	0(0.0)	**18(78.3)**	4(95.7)	1(100.0)			
Vancomycin	0.25	0.5	NT	NT	0(0.0)	0(0.0)	0(0.0)	**18(78.3)**	5(100.0)	
Teicoplanin	0.12	0.25	NT	NT	0(0.0)	2(8.7)	**15(73.9)**	6(100.0)		
Daptomycin	0.12	0.25	NT	NT	0(0.0)	8(34.8)	5(56.5)	**10(100.0)**		
Linezolid	1	1	NT	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(4.3)	**22(100.0)**
Wildtype *S. pneumoniae* (11)										
SP2078	0.015	0.03	0(0.0)	**7(63.6)**	4(100.0)					
Vancomycin	0.25	0.5	NT	NT	0(0.0)	0(0.0)	1(9.1)	**7(72.7)**	3(100.0)	
Teicoplanin	0.12	0.12	NT	NT	0(0.0)	3(27.3)	**8(100.0)**			
Daptomycin	0.12	0.25	NT	NT	0(0.0)	0(0.0)	**9(81.8)**	2(100.0)		
Linezolid	1	1	NT	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	3(27.3)	**8(100.0)**
MDR *S. pneumoniae* (11)										
SP2078	0.015	0.03	1(9.1)	**5(54.5)**	**5(100.0)**					
Vancomycin	0.25	0.25	NT	NT	0(0.0)	1(9.1)	0(9.1)	**9(90.9)**	1(100.0)	
Teicoplanin	0.12	0.12	NT	NT	0(0.0)	2(18.2)	**9(100.0)**			
Daptomycin	0.12	0.25	NT	NT	0(0.0)	0(0.0)	**9(81.8)**	2(100.0)		
Linezolid	0.5	1	NT	NT	0(0.0)	0(0.0)	0(0.0)	0(0.0)	**8(72.7)**	3(100.0)

a. MDR, multidrug-resistant strains. All *S. pneumoniae* showed a resistance phenotype to penicillin (MIC, >0.25 μg/mL), erythromycin (MIC, >8 μg/mL) and clindamycin (MIC, >2 μg/mL), while 63.6, 36.4 and 81.8% of strains were also non-susceptible to ceftriaxone (MIC, >0.5 μg/mL), tetracycline (MIC, >8 μg/mL) and levofloxacin (MIC, >4 μg/mL), respectively.
b. Modal MIC values are in bold. NT, concentration not tested.

CONCLUSIONS

- Overall, SP2078 exhibited *in vitro* antimicrobial activity greater than comparator agents when tested against clinically relevant and contemporary Gram-positive isolates, including MDR challenge subsets. SP2078 was less active when tested against *S. aureus* (VRSA) and enterococci carrying *vanA*.
- These *in vitro* data for SP2078 warrant further investigations for establishing additional clinical and pharmacological parameters to determine if the findings described in this study reflect important therapeutic advantages.

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