

Minimum inhibitory concentration evaluation of BWC0977, a novel bacterial topoisomerase inhibitor, against recent drug resistant clinical isolates

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P2317

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INTRODUCTION

Current trend of increased emergence and spread of antimicrobial resistance poses serious challenges in the health care sector making even treatment of simple infections difficult. BWC0977 is a novel bacterial topoisomerase inhibitor, with broad spectrum anti-bacterial activity. In order to assess the potency, spectrum and cross-reactivity of BWC0977, it is essential to test its *in vitro* anti-bacterial property against multiple clinical isolates from different infections possessing varying antibiotic susceptibility profiles. At IHMA, different sets of isolates were tested, including random consecutive isolates and resistant isolate collection separately.

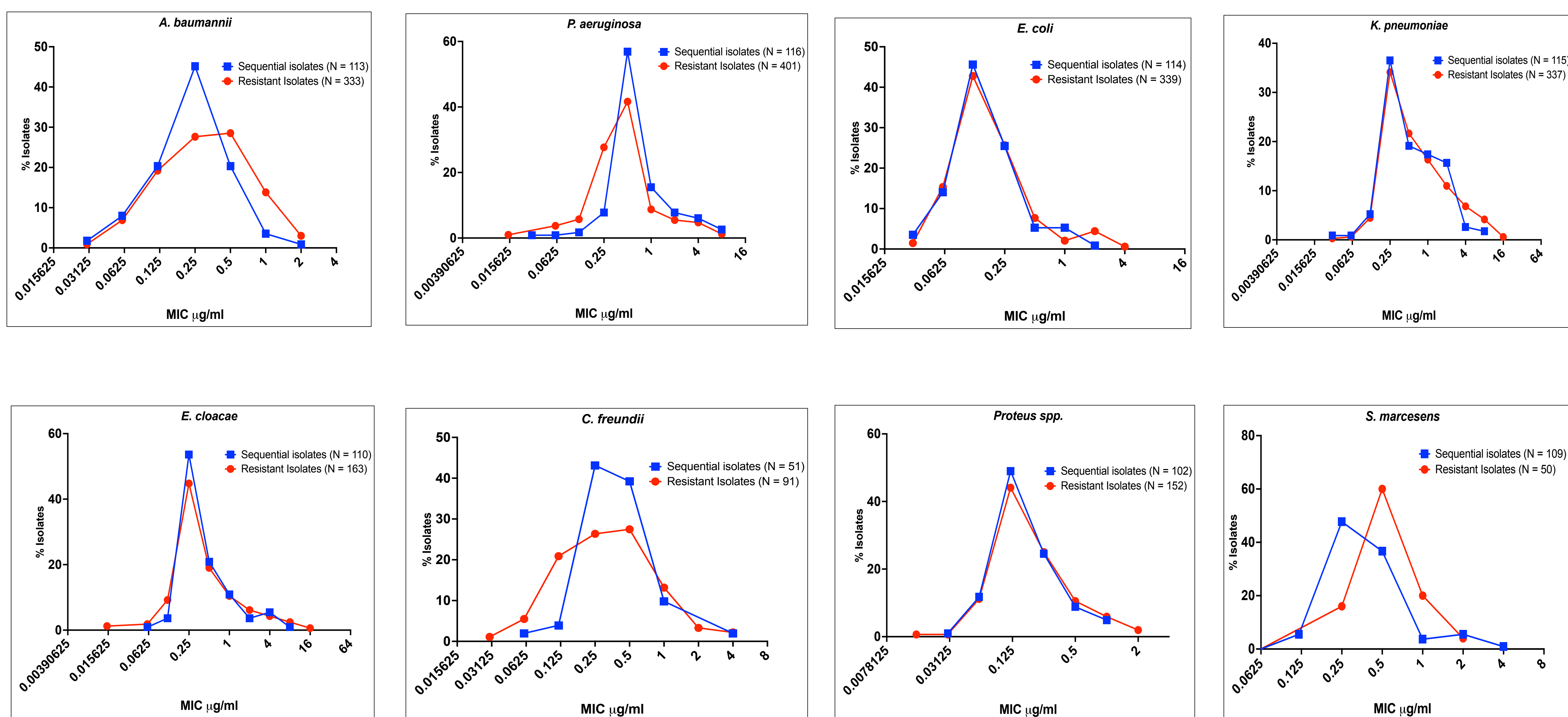
METHODS

MICs were determined according to Clinical and Laboratory Standards Institute methodology and guidelines and MIC₉₀ deduced to evaluate its potency *in vitro*. BWC0977 was dissolved in DMSO to make initial stock solutions and for broth microdilution, further diluted into cation-adjusted Mueller-Hinton broth (CAMHB) for the sequential dilutions in the test panels. Comparator compounds were dissolved according to CLSI specifications.

MICs of consecutive isolates (community and hospital-associated sources, and included skin and soft tissue, respiratory, blood, urinary tract, and gastrointestinal infections) collected in 2017-2018 from global medical centres were determined at IHMA with no specific bias on the pre-existing resistance profiles. MICs were also determined at IHMA of two sets of diverse multi-drug resistant isolates collected from global medical centres in 2016-2018 & 2019 respectively from infections of blood, intra-abdominal, reproductive organs, respiratory tract, skin and soft tissue and urinary tract.

RESULTS

Frequency Distribution of Isolates Across the BWC0977 MIC Range
 Sequential Isolates (2017-2018) and Selected MDR (2016-2019) Isolates



MIC₉₀ retained across sensitive & drug resistant (ESBL, CRE, CRAB, FQ^r) clinical isolates indicating lack of cross resistance

MIC₉₀ vs MDR Gram negative Pathogens

MIC₉₀ vs MDR Gram positive Pathogens

	<i>A. baumannii</i>	<i>P. aeruginosa</i>	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>E. cloacae</i>	<i>S. maltophilia</i>	<i>Citrobacter spp.</i>	<i>Proteus spp.</i>	<i>M. morgani</i>	<i>S. marcescens</i>	<i>N. gonorrhoeae</i>
N	333	401	339	337	163	150	151	152	42	50	90
BWC0977	1	1	0.5	2	2	0.25	1	0.5	1	1	0.016
Ciprofloxacin	>32	16	ND	>32	ND	16	ND	ND	ND	ND	>1
Levofloxacin	>32	32	16	>32	64	8	2	8	16	1	ND
Cefiderocol	4	2	2	2	4	2	2	0.5	1	1	ND
Cefepime	>32	>32	>32	>32	64	>32	>32	16	>32	>32	ND
Cefpodoxime	ND	ND	>32	>32	64	ND	>32	>32	>32	>32	0.06
Ceftazidime	>32	>32	64	>64	128	>32	>64	2	16	8	ND
Avycaz	ND	>16	0.25	1	2	ND	0.5	0.06	0.125	1	ND
Aztreonam	ND	>16	>64	>64	128	ND	64	0.5	16	32	ND
Azt/Avi	ND	>16	0.125	0.25	0.5	ND	0.25	0.016	0.06	0.25	ND
Pip/Tazo	>128	128	ND	ND	0.06	>128	ND	ND	ND	ND	ND
Meropenem	>64	32	0.06	32	8	>64	0.06	0.125	0.125	0.125	ND
Vabomere	>32	32	0.03	16	0.25	>32	0.03	0.125	0.06	0.125	ND
Colistin	0.5	1	0.25	0.5	2	>32	0.5	>32	64	>32	ND
Amikacin	>64	64	8	32	4	>64	4	4	8	8	ND
Gentamicin	>32	>32	>32	>32	1	>32	8	16	64	16	ND
Doxycycline	64	32	32	32	16	4	16	>32	64	16	ND
Tetracycline	>32	32	ND	ND	ND	32	ND	ND	ND	ND	ND
Eravacycline	ND	ND	0.25	1	ND	ND	0.5	2	1	2	ND
Tobramycin	>32	>32	16	>32	32	>32	8	8	16	32	ND
Plazomicin	ND	ND	1	0.5	0.5	ND	0.5	4	8	2	ND

Organism	<i>S. aureus</i>	<i>E. faecalis/ E. faecium</i>	<i>S. pneumoniae</i>	<i>S. pyogenes</i>	Coagulase negative Staph.
N	301	152	149	149	152
BWC0977	0.03	0.06	0.03	0.03	0.03
Azithromycin	>32	>32	>32	4	>32
Clindamycin	>32	>32	>32	0.125	>32
Daptomycin	0.5	2	0.125	0.06	0.5
Levofloxacin	32	>32	1	1	16
Linezolid	2	2	1	1	1
Vancomycin	1	32	0.5	0.5	2
Doxycycline	1	16	8	8	4
Penicillin	>32	>32	2	0.03	>32

Data presented here demonstrates BWC0977 as a potent broad spectrum antibacterial agent that lacks cross resistance to current antibiotics and thus holds promise as a novel agent that could be used for treating wide variety of drug resistant infections

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ACKNOWLEDGEMENTS AND DISCLAIMER: Research reported in this presentation is supported by CARB-X. CARB-X's funding for this project is sponsored by the Cooperative Agreement Number IDSEP160030 from ASPR/BARDA and by awards from Wellcome, Germany's Federal Ministry of Education and Research, and the UK Global Antimicrobial Resistance Innovation Fund (GAMRIF) funded by the UK Government Department of Health and Social Care (DHSC). The content is solely the responsibility of the authors and does not necessarily represent the official views of CARB-X or any of its funders