Potentiation of Gram-positive specific antibiotics against Gram-negative bacteria through outer membrane disruption

Wesseling, C.M.J.

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Promotores:	Prof. dr. Nathaniel I. Martin
	Prof. dr. Suzan H.M. Rooijakkers (UMC Utrecht)
Doctorate committee:	Prof. dr. Gilles P. van Wezel
	Prof. dr. Dennis Claessen
	Prof. dr. Sander I. van Kasteren
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“Cruciaal is dat je jezelf overhaalt om van de wereld te houden. Als je de schoonheid ziet van de breekbare menselijke soort, van bouwkunst, sport, staatsrecht, gastronomie en al die andere manieren die we verzonnen hebben om ons biologische repertoire te verfijnen, dan pas kun je je eigen bijdrage, hoe klein ook, naar waarde schatten. Dat is een grote troost als je weet dat alles doorgaat als jij er niet meer bent.”

- René Gude

Table of contents

List of abbreviations

ΔF	α,β-didehydrophenylalanine
AA	amino acid
Ac_2O	acetic anhydride
AcOH	acetic acid
ACS	American Chemical Society
alle	D-*allo*-isoleucine
AMP	antimicrobial peptides
AMR	antimicrobial resistance
ATCC	American Type Culture Collection
Bip	biphenylalanine
BPEI	branched polyethylenimine
BPI	bactericidal/permeability-increasing protein
Boc	tert-butyloxycarbonyl
tBu	tert-butyl
tBuOH	tert-butanol
Boc	tert-butyloxycarbonyl
BOP	(benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate
C6	hexanoyl
C8	octanoyl
C10	decanoyl
CBr_4	carbon tetrabromide
Cbz	benzyloxycarbonyl
$CDCl_3$	deuterated chloroform
Cha	cyclohexylalanyl
CLSI	Clinical & Laboratory Standards Institute
Dab	2,4-diaminobutyric acid
DAPB	deacylpolymyxin B
DIC	N,N-Diisopropylcarbodiimide
DIPEA	N,N-diisopropylethylamine
DMF	N,N-dimethylformamide
dUSCL	dilipid ultrashort cationic lipopeptide
dUSTBP	dilipid ultrashort tetrabasic peptidomimetic
EDTA	ethylenediaminetetraacetate
ESBL	extended spectrum β-lactamase
EtOAc	ethyl acetate
EtOH	ethanol
FICI	fractional inhibitory concentration index
Fmoc	fluorenylmethyloxycarbonyl
H_2SO_4	sulfuric acid
HCl	hydrogen chloride
HFIP	1,1,1,3,3,3-hexafluoro-2-propanol
HMP	hexametaphosphate
HPLC	high-performance liquid chromatography
HTS	high throughput screening
LB	Lysogeny Broth
LPS	lipopolysaccharide
MAC	membrane attack complex
MDR	multidrug-resistant
MeOH	methanol
MIC	minimum inhibitory concentration
MOX	moxifloxacin
MSC	minimum synergistic concentration
MTBE	methyl tert-butyl ether

Na_2SO_4	sodium sulfate
Nal	β-naphthylalanine
NDM-1	New Delhi β-lactamase 1
NEB	nebramine
NMP	1-(1-naphthylmethyl)-piperazine
NPN	N-phenyl-napthalen-1-amine
NR	no data reported
OAK	oligo-acyl-lysyl
OM	outer membrane
Oxyma	ethyl cyanohydroxyiminoacetate
PAR	paroxetine
Pbf	2,2,4,6,7-pentamethyldihydrobenzofuran-5-sulfonyl
PEDES	PEptide DEscriptors from Sequence
PG	phosphatidylglycerol
PMB	polymyxin B
PMBH	polymyxin B heptapeptide
PMBN	polymyxin B nonapeptide
PMBO	polymyxin B octapeptide
PPh_3	triphenylphosphine
SAR	structure-activity relationship
SM	squalamine mimics
THF	tetrahydrofuran
TIS	triisopropylsilane
TOB	tobramycin
TPP	tetraphenylphosphonium
$TriA_1$	Tridecaptin A_1
Trt	trityl
UTBLP	ultrashort tetrabasic lipopeptide
WHO	World Health Organization

Amino acids

Ala	A	Alanine
Arg	R	Arginine
Asn	N	Asparagine
Asp	D	Aspartic acid
Cys	C	Cysteine
Glu	E	Glutamic acid
Gln	Q	Glutamine
Gly	G	Glycine
His	H	Histidine
Ile	I	Isoleucine
Leu	L	Leucine
Lys	K	Lysine
Met	M	Methionine
Phe	F	Phenylalanine
Pro	P	Proline
Ser	S	Serine
Thr	T	Threonine
Trp	W	Tryptophan
Tyr	Y	Tyrosine
Val	V	Valine