pharmaceutics

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Supplementary Material

Antibacterial Efficacy of Liposomal Formulations Containing Tobramycin and *N*-acetylcysteine against Tobramycin-Resistant *Escherichia coli*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii*

Reem E. Alarfaj [1,2], Manal M. Alkhulaifi [1], Ahmed J. Al-Fahad [3], Shokran Aljihani [4], Alaa Eldeen B. Yassin [5], Majed F. Alghoribi [2,*] and Majed A. Halwani [4,*]

[1] Department of Botany and Microbiology, College of Science, King Saud University, Riyadh 11451, Saudi Arabia; reemalarfaj.95@gmail.com (R.E.A.); manalk@ksu.edu.sa (M.M.A.)
[2] Infectious Diseases Research Department, King Abdullah International Medical Research Center, King Saud bin Abdulaziz University for Health Sciences, National Guard Health Affairs, Riyadh 11481, Saudi Arabia
[3] National Center for Biotechnology, Life Science & Environment Research Institute, King Abdulaziz City for Science and Technology (KACST), Riyadh 12354, Saudi Arabia; ajlfahad@kacst.edu.sa
[4] Nanomedicine Department, King Abdullah International Medical Research Center, King Saud bin Abdulaziz University for Health Sciences, National Guard Health Affairs, Riyadh 11481, Saudi Arabia; sh.aljihani@gmail.com (S.A)
[5] Pharmaceutical Sciences Department, College of Pharmacy, King Saud bin Abdulaziz University for Health Sciences, National Guard Health Affairs, Riyadh 11481, Saudi Arabia; yassina@ksau-hs.edu.sa
* Correspondence: halawanima@ngha.med.sa (M.A.H.); alghoribima@ngha.med.sa (M.F.A.); Tel.: +96-61-1429-4433 (M.A.H.)

Table S1. MIC of *E. coli* isolates by VITEK.

Isolate ID	EC_057	EC_068	EC_077	EC_083	EC_089	EC_162	EC_219
Specimen type	Urine	Urine	Urine	Urine	Urine	Urine	Urine
SAM	>=32	>=32	>=32	>=32	>=32	>=32	>=32
	R	R	R	R	R	R	R
TIM	>=128	64	64	>=128	>=128	>=128	>=128
	R	I	I	R	R	R	R
TZP	8	<=4	8	8	8	8	>=128
	S	S	S	S	S	S	R
CAZ	>=64	16	16	<=1	4	16	16
	R	R	R	R	R	R	R
FEP	>=64	4	4	<=1	2	8	>=64
	R	R	R	R	R	R	R
ATM	>=64	16	16	<=1	16	>=64	16
	R	R	R	R	R	R	R
ETP	<=0.5	<=0.5	<=0.5	<=0.5	<=0.5	<=0.5	<=0.5
IMP	S	S	S	S	S	S	S
	<=0.25	<=0.25	<=0.25	<=0.25	<=0.25	<=0.25	<=0.25
	S	S	S	S	S	S	S
MEM	<=0.25	<=0.25	<=0.25	<=0.25	<=0.25	<=0.25	<=0.25
	S	S	S	S	S	S	S
AMK	<=2	4	4	8	4	8	8
	S	S	S	I	S	I	I
GEN	>=16	>=16	>=16	4	4	>=16	<=1
	R	R	R	R	R	R	S

TOB	8	>=16	>=16	>=16	>=16	>=16	>=16
	R	R	R	R	R	R	R
CIP	>=4	>=4	>=4	>=4	>=4	1	>=4
	R	R	R	R	R	S	R
LVX	>=8	>=8	>=8	>=8	>=8	1	>=8
	R	R	R	R	R	S	R
MIN	4	2	2	<=1	<=1	<=1	>=16
	S	S	S	S	S	S	R
TGC	<=0.5	<=0.5	<=0.5	<=0.5	<=0.5	<=0.5	<=0.5
	S	S	S	S	S	S	S
SXT	>=320	>=320	>=320	>=320	>=320	>=320	>=320
	R	R	R	R	R	R	R

S: Sensitive, R: Resistant, I: Intermediate.

Table S2. MIC of *K. pneumoniae* isolates by VITEK.

Isolate ID	**KP_002**	**KP_017**	**KP_019**	**KP_026**	**KP_050**	**KP_057**	**KP_059**	**KP_086**	**KP_095**
Specimen	Fluid	Wound	Urine	Rectal	Blood	Urine	Blood	Sputum	Wound
AMP	R	R	R	R	R	R	R	R	R
	>=32	>=32	>=32	>=32	>=32	>=32	>=32	>=32	>=32
AMC	R	R	R	R	R	R	R	R	R
	>=32	>=32	>=32	>=32	>=32	>=32	>=32	>=32	>=32
PIP/TAZ	R	R	R	R	R	R	R	R	R
	>=128	>=128	>=128	>=128	>=128	>=128	>=128	>=128	>=128
CF	R	R	R	R	R	R	R	R	R
	>=64	>=64	>=64	>=64	>=64	>=64	>=64	>=64	>=64
FOX	R	R	R	R	R	R	R	R	R
	>=64	>=64	>=64	>=64	>=64	>=64	>=64	16	>=64
CAZ	R	R	R	R	R	R	R	R	R
	>=64	>=64	>=64	>=64	>=64	>=64	>=64	>=64	>=64
CRO	R	R	R	R	R	R	R	R	R
	>=64	>=64	>=64	>=64	>=64	>=64	>=64	>=64	>=64
FEP	R	R	R	R	R	R	R	R	R
	>=64	>=64	>=64	>=64	>=64	>=64	>=64	>=64	>=64
IMP	R	I	R	R	I	R	R	R	R
	>=16	2	>=16	>=16	8	>=16	>=16	>=16	>=16
MEM	R	R	R	R	R	R	R	R	R
	>=16	>=16	>=16	>=16	>=16	>=16	>=16	8	>=16
AMK	R	R	R	I	R	R	R	R	R
	>=64	>=64	>=64	32	>=64	>=64	>=64	>=64	>=64
GEN	I	R	I	R	R	R	R	S	I
	4	>=16	4	>=16	>=16	>=16	>=16	<=1	4
CIP	R	R	R	R	R	R	R	R	R
	>=4	>=4	>=4	>=4	>=4	>=4	>=4	>=4	>=4
TGC	R	R	R	R	R	R	R	R	S
	>=8	4	>=8	8	>=8	>=8	>=8	4	<=0.5
NIT	R	R	R	R	R	R	R	R	R
	128	256	256	256	256	256	128	128	128
TMP	R	R	R	R	R	R	R	R	R
TMP-SMX	R	R	R	R	R	R	R	R	R

>=320	>=320	>=320	>=320	>=320	>=320	>=320	>=320	>=320

S: Sensitive, R: Resistant, I: Intermediate.

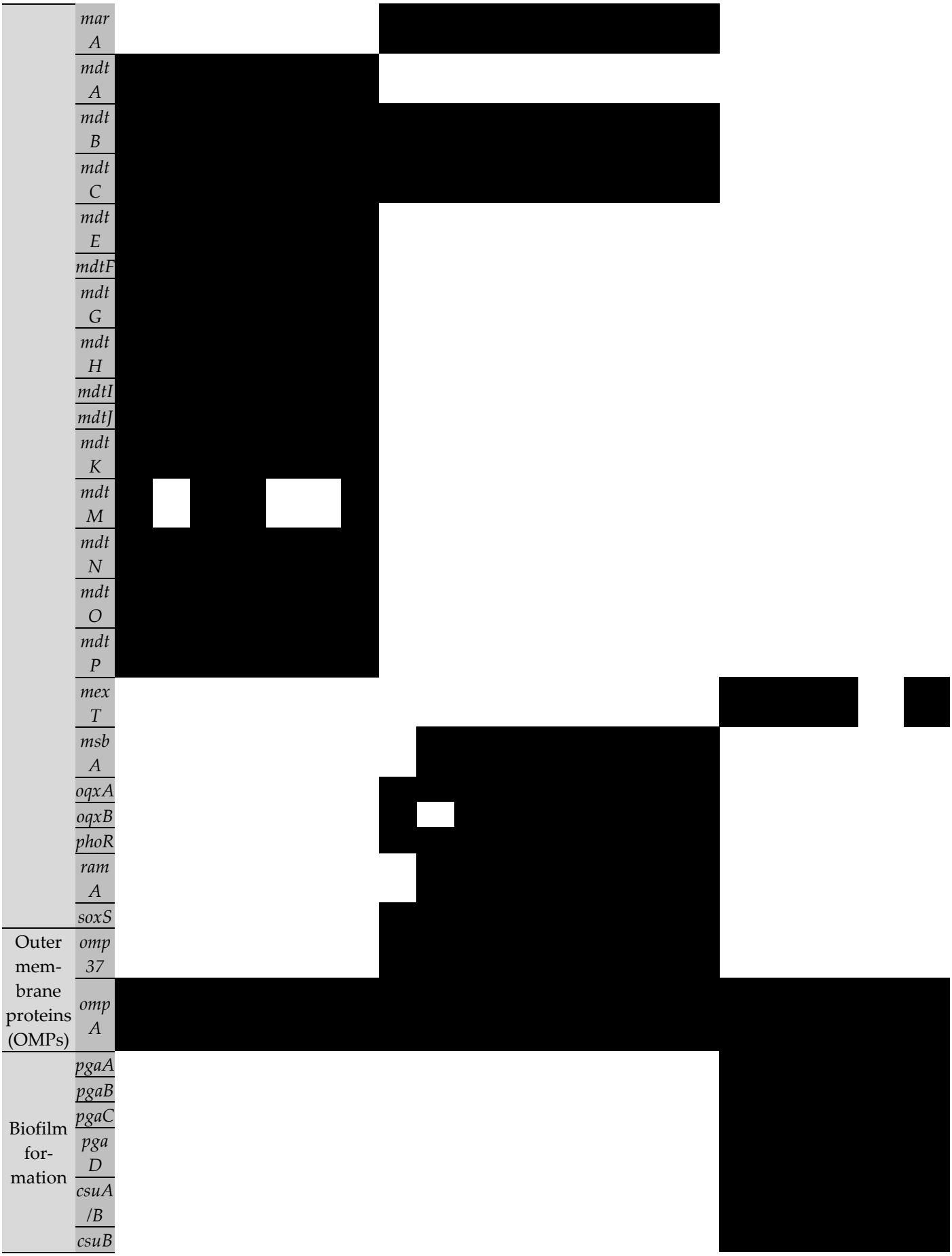
Table S3. MIC of *A. baumannii* isolates by VITEK.

Isolate ID	**RAB_005**	**RAB_009**	**RAB_014**	**RAB_030**	**RAB_055**
Specimen	Respiratory	Respiratory	Respiratory	Urine	Respiratory
SAM	R	R	R	R	R
	>=32	16	>=32	16	>=32
TIM	R	R	R	R	R
	>=128	>=128	>=128	>=128	>=128
TZP	R	R	R	R	R
	>=128	>=128	>=128	>=128	>=128
CAZ	R	R	R	R	R
	>=64	>=64	>=64	>=64	>=64
FEP	R	R	R	R	R
	>=64	>=64	>=64	>=64	>=64
IMP	R	R	R	R	R
	>=16	>=16	>=16	>=16	>=16
MEM	R	R	R	R	R
	>=16	>=16	>=16	>=16	>=16
GEN	R	R	R	R	R
	>=16	>=16	>=16	>=16	>=16
TOB	R	R	R	R	R
	>=16	>=16	>=16	>=16	>=16
CIP	R	R	R	R	R
	>=4	>=4	>=4	>=4	>=4
LVX	R	R	R	R	R
	>=8	4	>=8	>=8	>=8
MIN	I	S	I	I	I
	8	4	>=16	>=16	>=16
TGC	2	2	4	>=8	4
	S	S	I	R	I
SXT	<=20	<=20	>=320	>=320	<=20
	S	S	R	R	S
	2	>=16	2	<=0.5	<=0.5
	S	R	S	S	S

S: Sensitive, R: Resistant, I: Intermediate.

Table S4. Detected efflux pumps, outer membrane, and biofilm formation genes in *E. coli, K. pneumoniae*,and *A. baumannii.*

Category	Genes	*Escherichia coli*							*Klebsiella Pneumoniae*								*Acinetobacter baumannii*				
		EC_057	EC_068	EC_077	EC_083	EC_089	EC_162	EC_219	KP_002	KP_017	KP_019	KP_026	KP_050	KP_057	KP_059	KP_086	KP_095	RAB_005	RAB_009	RAB_014	RAB_030	RAB_055
Efflux pumpS (EPS)	*abeM*																	■	■	■	■	■
	abeS																	■	■	■	■	■
	acrA	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■					
	acrB	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■					
	acrD	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■					
	acrE	■	■	■	■	■	■	■														
	acrF	■	■	■	■	■	■	■														
	acrS	■	■	■	■	■	■	■														
	adeA																	■	■	■	■	■
	adeB																	■	■	■	■	■
	adeC																	■	■	■	■	■
	adeI																	■	■	■	■	■
	adeK																	■	■	■	■	■
	adeL																	■	■	■	■	■
	adeN																	■	■		■	
	adeR																	■	■	■	■	■
	adeT1																	■	■	■	■	■
	adeT2																	■	■	■	■	■
	amvA																	■	■	■	■	■
	asmA									■	■	■	■	■	■	■	■					
	baer								■	■	■	■	■	■	■	■	■					
	cpxar								■	■	■	■	■	■	■	■	■					
	crp								■	■	■	■	■	■	■	■	■					
	emrB								■	■	■	■	■	■	■	■	■					
	emrD								■	■	■	■	■	■	■	■	■					
	emrR								■	■	■	■	■	■	■	■	■					
	hns									■	■	■	■	■	■	■	■					
	kdeA								■	■	■	■	■	■	■	■	■					
	kdpE	■	■	■	■	■	■	■														
	kmrA								■	■	■	■	■	■	■	■	■					
	kpn								■	■	■	■	■	■	■	■	■					
	kpnE								■	■	■	■	■	■	■	■	■					
	kpnF								■	■	■	■	■	■	■	■	■					
	kpnO								■	■	■	■	■	■	■	■	■					


marA
mdtA
mdtB
mdtC
mdtE
mdtF
mdtG
mdtH
mdtI
mdtJ
mdtK
mdtM
mdtN
mdtO
mdtP
mexT
msbA
oqxA
oqxB
phoR
ramA
soxS
Outer membrane proteins (OMPs)
ompA
Biofilm formation
pgaA
pgaB
pgaC
pgaD
csuA/B
csuB



The black highlight ( ) indicates the presence of the gene.

Table S5. Detected Aminoglycosides modifying enzymes, 16S rRNA methyltransferases, and other genes in *E. coli, K. pneumoniae* and *A.baumannii.*

Species	Isolate	Aminoglycosides modyfing enzymes (AMEs)												16S rRNA methyl-transferases		Miscellane-ous		
		N-acetyltransferases					O-nucleotidyl-transferases		Aminoglycoside_O-phosphotransferases									
		aac3	*aac(3)-IIa*	*aac(6′)-Ib3*	*aac(6′)-Ib-Hangzhou*	*aac(6′)-Ib-cr*	*ant(2′′)-Ia*	*ant3-dprime*	*aph(3′)-Ia*	*aph3-prime*	*aph(3′)-VI*	*aph(3′)-VIb*	*aph(6)-Id*	*aph(3′′)-Ib*	*armA*	*rmtF*	*aadA1*	*aadA2*	*aadA5*
Escherichia coli	EC_057	■	■			■		■											■
	EC_068	■	■			■		■											■
	EC_077	■	■			■		■											■
	EC_083					■	■										■		
	EC_089							■					■	■					
	EC_162	■	■			■		■											■
	EC_219					■													
Klebsiella Pneumoniae	KP_002					■		■		■			■			■	■	■	
	KP_017				■	■		■								■		■	
	KP_019					■				■		■	■	■					
	KP_026			■		■		■			■		■	■	■				
	KP_050			■		■		■					■	■	■		■	■	

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