

Supplementary Materials

Supplementary Table 1

Effects of DHA27 (32, 64, and 128 $\mu\text{g/mL}$) on daunorubicin (DNR) accumulation in clinical isolates of *Pseudomonas aeruginosa* (PA)

isolates name	FICI	Incubation time after adding daunorubicin								
		10 min			20 min			30 min		
		DHA27(32)	DHA27(64)	DHA27(128)	DHA27(32)	DHA27(64)	DHA27(128)	DHA27(32)	DHA27(64)	DHA27(128)
PA05	<0.13	↓↓	↓↓	↓↓	↓↓	↓↓	↓↓	↓↓	↓↓	↓↓
PA16	<0.13	↓	↓	↓	↑↑	—	↓↓	↓↓	—	—
PA01	<0.19	—	↓	↓	↑↑	—	—	↑↑	—	—
PA06	<0.19	—	—	↓↓	—	↓	↓↓	—	—	↓↓
PA07	<0.19	—	—	↓↓	↓↓	↓↓	↓↓	—	↑	↓
PA08	<0.19	↓	↓↓	↓↓	—	↓	↓↓	↓↓	—	↓↓
PA13	<0.19	↑↑	↑↑	↑↑	↑↑	—	↓↓	↑↑	↑↑	↑↑
PA17	<0.19	—	↑↑	—	—	↑↑	↑↑	↓	—	↑↑
PA04	<0.25	↑↑	↑↑	↑↑	—	↓↓	↑↑	↑↑	↓↓	↓↓
PA09	<0.25	—	↓	↓↓	—	↓↓	↓↓	↓↓	↓↓	↓↓
PA02	<0.31	↑↑	—	—	↓↓	↑↑	↓↓	↑↑	↑↑	↑↑

PA19	<0.31	↑↑	↑↑	↑↑	↑↑	↑↑	↑↑	↓	↑↑	↑
PA20	<0.38	—	—	—	↑↑	—	↓↓	↓↓	—	↓↓

FICI, fractional inhibitory concentration index. ↑↑, the increase in the DHA27 group compared with the DNR

group was statistically different; ↑, Compared with the DNR group, DHA27 group showed an upward trend but

no statistically significant difference; —, DHA27 group showed no upward trend compared with the DNR

group; ↓↓, compared with the DNR group, the DHA27 group showed a statistically significant decrease; ↓, the

DHA27 group showed a decreasing trend compared with the DNR group, but there was no statistically

significant difference.

Supplementary Table 2

Effect of DHA27 antibacterial sensitization and tobramycin (TOB) resistance on 16S rRNA methyltransferase (16S-RMtases) in *Pseudomonas aeruginosa*

Isolate name	MIC		FICI	16S rRNA	Effect on 16S-RMtases	
	TOB	DHA27			TOB	TOB+DHA27
PA05	512	>1024	<0.13	<i>armA</i>	↑↑	↓
				<i>rmtA</i>	↑↑	↓↓
				<i>rmtB</i>	↑↑	↓↓
				<i>rmtC</i>	↓	↑↑
				<i>rmtD</i>	↑↑	↑
				<i>armA</i>	↑↑	↓
PA16	1024	>1024	<0.13	<i>rmtA</i>	↑↑	↓
				<i>rmtB</i>	×	×
				<i>rmtC</i>	↑	↓↓
				<i>rmtD</i>	↑↑	↓↓
				<i>armA</i>	↑↑	↓↓
				<i>rmtA</i>	↑↑	↓

				<i>rmtB</i>	↑↑	↑↑
				<i>rmtC</i>	↑	↑
PA01	1024	>1024	<0.19	<i>rmtD</i>	↑↑	↓↓
<hr/>						
				<i>armA</i>	↑↑	↑↑
				<i>rmtA</i>	↑↑	↑↑
				<i>rmtB</i>	↑	↑↑
				<i>rmtC</i>	×	×
PA06	512	>1024	<0.19	<i>rmtD</i>	↑↑	↓
<hr/>						
				<i>armA</i>	↑↑	↓
				<i>rmtA</i>	↑↑	↓↓
				<i>rmtB</i>	×	×
				<i>rmtC</i>	↓↓	↓
				<i>rmtD</i>	↑↑	↑
PA07	256	>1024	<0.19			
<hr/>						
				<i>armA</i>	↑↑	↑↑
				<i>rmtA</i>	↑	↑
				<i>rmtB</i>	↑↑	↑↑

PA08	256	>1024	<0.19	<i>rmtC</i>	↓↓	↑
				<i>rmtD</i>	↑↑	↑
<hr/>						
PA13	>1024	>1024	<0.19	<i>armA</i>	↑↑	↑
				<i>rmtA</i>	↑↑	↓↓
				<i>rmtB</i>	↑↑	↓
				<i>rmtC</i>	↑↑	↓
				<i>rmtD</i>	↑↑	↓↓
<hr/>						
PA17	1024	>1024	<0.19	<i>armA</i>	↑↑	↑↑
				<i>rmtA</i>	↑↑	↑↑
				<i>rmtB</i>	↓↓	—
				<i>rmtC</i>	↓↓	↑↑
				<i>rmtD</i>	↑	↑
<hr/>						
PA04	512	>1024	<0.25	<i>armA</i>	↑↑	↑
				<i>rmtA</i>	↑↑	↑
				<i>rmtD</i>	↑↑	↑
<hr/>						
				<i>armA</i>	↑↑	↑

PA09	1024	> 1024	< 0.25	<i>rmtA</i>	↑	↑↑
				<i>rmtB</i>	×	×
				<i>rmtC</i>	↓	↓
				<i>rmtD</i>	↑	↑↑

PA02	1024	> 1024	< 0.31	<i>armA</i>	↓	↑↑
				<i>rmtA</i>	↓↓	↑↑
				<i>rmtB</i>	×	×
				<i>rmtC</i>	↓↓	↑↑
PA19	1024	> 1024	< 0.31	<i>rmtD</i>	↓↓	↑↑

				<i>armA</i>	↓↓	↓↓
				<i>rmtA</i>	↓	↓
PA19	1024	> 1024	< 0.31	<i>rmtB</i>	↓↓	↓↓
				<i>rmtC</i>	×	×
				<i>rmtD</i>	↓	↓

PA19	1024	> 1024	< 0.31	<i>armA</i>	↑	↓↓
				<i>rmtA</i>	↑↑	↓
				<i>rmtB</i>	×	×
				<i>rmtC</i>	↑↑	↑

PA20

1024

>1024

<0.38

rmtD

↑↑

↓

FICI, fractional inhibitory concentration index

(1) ↓↓, Compared with the TOB group, the drug combination group showed a statistically significant difference; ↓, the drug combination group showed a downward trend compared with the TOB group, but there was no statistically significant difference; -, compared with the TOB group, the drug combination group showed no downward trend; ↑, the drug combination group showed an upward trend compared with the TOB group, but there was no statistically significant difference; ↑↑, compared with the TOB group, the drug combination group showed a statistically significant upward trend; ×, some results did not come out:

(2) ↓↓, Compared with the broth group, the TOB group showed a statistically significant decrease; ↓, the TOB group showed a decreasing trend compared with the broth group, but there was no statistically significant difference; -, compared with the broth group, the TOB group showed no downward trend; ↑, the TOB group showed an upward trend compared with the broth group, but there was no statistically significant difference; ↑↑, compared with the broth group, the TOB group showed a statistically significant upward trend; ×, some results did not come out

Supplementary Table 3

Effect of DHA27 antibacterial sensitization and tobramycin (TOB) resistance on the mRNA

expression of aminoglycoside-modifying enzymes (AMEs) in *Pseudomonas aeruginosa*

strain name	MIC		FICI	AMEs	Drug effects on AMEs	
	TOB	DHA27			TOB	TOB+DHA27
PA05	512	>1024	<0.13	<i>aac(3)-I</i>	↑ ↑	↓
				<i>aac(3)-II</i>	↑	↓
				<i>aac(3)-IV</i>	↑ ↑	↓ ↓
				<i>aac(6')-Ib</i>	↑ ↑	↓ ↓
				<i>aac(6')-II</i>	↑ ↑	↓ ↓
				<i>ant(2'')-Ia</i>	↑ ↑	↓ ↓
				<i>ant(2'')-I</i>	↑	↑
				<i>ant(3'')-I</i>	↑ ↑	↑
				<i>aph(3')-Ia</i>	↑ ↑	↓
				PA16	1024	>1024
<i>aac(3)-II</i>	↑ ↑	↓				
<i>aac(3)-IV</i>	↑ ↑	↓ ↓				
<i>aac(6')-Ib</i>	↑ ↑	↓				
<i>aac(6')-II</i>	↑ ↑	↓ ↓				
<i>ant(2'')-Ia</i>	↑ ↑	↓				
<i>ant(2'')-I</i>	↑ ↑	↓				
<i>ant(3'')-I</i>	↑	↑ ↑				
<i>aph(3')-Ia</i>	↑ ↑	↑				
PA01	1024	>1024	<0.19			
				<i>aac(3)-II</i>	↑ ↑	↓ ↓
				<i>aac(3)-IV</i>	↑ ↑	↓ ↓
				<i>aac(6')-Ib</i>	↓	↓ ↓
				<i>aac(6')-II</i>	—	↓
				<i>ant(2'')-Ia</i>	↑ ↑	↓
				<i>ant(2'')-I</i>	↑ ↑	↓ ↓
				<i>ant(3'')-I</i>	↑ ↑	↓

				<i>aph(3')-Ia</i>	×	×
				<i>aac(3)-I</i>	↓	↓
				<i>aac(3)-II</i>	↓	↑
				<i>aac(3)-IV</i>	↑	↓
				<i>aac(6')-Ib</i>	↓	—
PA06	512	>1024	<0.19	<i>aac(6')-II</i>	↓	↓
				<i>ant(2'')-Ia</i>	↑ ↑	↑
				<i>ant(2'')-I</i>	↑	↓
				<i>ant(3'')-I</i>	↑ ↑	↓ ↓
				<i>aph(3')-Ia</i>	↑	↑
				<i>aac(3)-I</i>	↑	↑
				<i>aac(3)-II</i>	↑	↑
				<i>aac(3)-IV</i>	↑ ↑	↓
				<i>aac(6')-Ib</i>	↑ ↑	↓
				<i>aac(6')-II</i>	↓ ↓	↓
PA07	256	>1024	<0.19	<i>ant(2'')-Ia</i>	↑ ↑	↓ ↓
				<i>ant(2'')-I</i>	↓	↑
				<i>ant(3'')-I</i>	↑	↑
				<i>aph(3')-Ia</i>	×	×
				<i>aac(3)-I</i>	↑	↑ ↑
				<i>aac(3)-II</i>	—	↑
				<i>aac(3)-IV</i>	↑	—
				<i>aac(6')-Ib</i>	↓	↑
PA08	256	>1024	<0.19	<i>aac(6')-II</i>	↓ ↓	↑ ↑
				<i>ant(2'')-Ia</i>	↑ ↑	↑ ↑
				<i>ant(2'')-I</i>	↓ ↓	↑ ↑
				<i>ant(3'')-I</i>	↑	↑
				<i>aph(3')-Ia</i>	↑	↓
				<i>aac(3)-I</i>	↑ ↑	↓ ↓
				<i>aac(3)-II</i>	↑ ↑	↓ ↓
				<i>aac(3)-IV</i>	↑	↓
				<i>aac(6')-Ib</i>	↑ ↑	↓ ↓
PA13	>1024	>1024	<0.19	<i>aac(6')-II</i>	↑ ↑	↓
				<i>ant(2'')-Ia</i>	↑ ↑	↓ ↓
				<i>ant(2'')-I</i>	↑ ↑	↓ ↓
				<i>ant(3'')-I</i>	↑ ↑	↓

				<i>aph(3')-Ia</i>	↑ ↑	↑
				<i>aac(3)-I</i>	↑	—
				<i>aac(3)-II</i>	↑	↑
				<i>aac(3)-IV</i>	↑ ↑	↑
				<i>aac(6')-Ib</i>	↑ ↑	↑
PA17	1024	>1024	<0.19	<i>aac(6')-II</i>	↑ ↑	↑
				<i>ant(2'')-Ia</i>	↑ ↑	↑ ↑
				<i>ant(2'')-I</i>	↑	↑
				<i>ant(3'')-I</i>	↑ ↑	↑
				<i>aph(3')-Ia</i>	↑	↓
				<i>aac(3)-I</i>	—	↑
				<i>aac(3)-II</i>	↑ ↑	—
				<i>aac(3)-IV</i>	↑ ↑	—
				<i>aac(6')-Ib</i>	↑ ↑	↑ ↑
PA04	512	>1024	<0.25	<i>aac(6')-II</i>	↑ ↑	↓
				<i>ant(2'')-Ia</i>	↑ ↑	↑
				<i>ant(2'')-I</i>	↑	↓
				<i>ant(3'')-I</i>	↑ ↑	↓
				<i>aph(3')-Ia</i>	↑ ↑	↑
				<i>aac(3)-I</i>	↑ ↑	↑ ↑
				<i>aac(3)-II</i>	↑ ↑	↓
				<i>aac(3)-IV</i>	↓	↑
				<i>aac(6')-Ib</i>	↓	↑ ↑
PA09	1024	>1024	<0.25	<i>aac(6')-II</i>	↓	↑
				<i>ant(2'')-Ia</i>	↑	↑ ↑
				<i>ant(2'')-I</i>	↓ ↓	↑ ↑
				<i>ant(3'')-I</i>	↑	↓
				<i>aph(3')-Ia</i>	↑ ↑	↑ ↑
				<i>aac(3)-I</i>	↑ ↑	↑ ↑
				<i>aac(3)-II</i>	↓	—
				<i>aac(3)-IV</i>	↑ ↑	↑
				<i>aac(6')-Ib</i>	↓ ↓	↓
PA02	1024	>1024	<0.31	<i>aac(6')-II</i>	↑ ↑	—
				<i>ant(2'')-Ia</i>	↓ ↓	↑ ↑
				<i>ant(2'')-I</i>	↓ ↓	↓
				<i>ant(3'')-I</i>	—	↑ ↑

				<i>aph(3')-Ia</i>	↑	↑
				<i>aac(3)-I</i>	↓ ↓	↓ ↓
				<i>aac(3)-II</i>	↓	↑
				<i>aac(3)-IV</i>	↑ ↑	↓ ↓
				<i>aac(6')-Ib</i>	↓ ↓	↓ ↓
PA19	1024	>1024	<0.31	<i>aac(6')-II</i>	↑	↓
				<i>ant(2'')-Ia</i>	↓ ↓	↓ ↓
				<i>ant(2'')-I</i>	—	—
				<i>ant(3'')-I</i>	↓	↓
				<i>aph(3')-Ia</i>	↑	↓
				<i>aac(3)-I</i>	↑ ↑	↓
				<i>aac(3)-II</i>	↑ ↑	↑
				<i>aac(3)-IV</i>	↑ ↑	—
				<i>aac(6')-Ib</i>	↑ ↑	↓
PA20	1024	>1024	<0.38	<i>aac(6')-II</i>	↑ ↑	↓
				<i>ant(2'')-Ia</i>	↑ ↑	↓ ↓
				<i>ant(2'')-I</i>	↑ ↑	↓
				<i>ant(3'')-I</i>	↑ ↑	↑ ↑
				<i>aph(3')-Ia</i>	↑ ↑	↑

(1) ↓↓, Compared with the TOB group, the drug combination group showed a statistically significant difference; ↓, the drug combination group showed a downward trend compared with the TOB group, but there was no statistically significant difference; —, compared with the TOB group, the drug combination group showed no downward trend; ↑, the drug combination group showed an upward trend compared with the TOB group, but there was no statistically significant difference; ↑↑, compared with the TOB group, the drug combination group showed a statistically significant upward trend; ×, some results did not come out.

(2) ↓↓, Compared with the broth group, the TOB group showed a statistically significant decrease; ↓, the TOB group showed a decreasing trend compared with the broth group, but there was no statistically significant difference; —, compared with the broth group, the TOB group showed no downward trend; ↑, the TOB group showed an upward trend compared with the broth group,

but there was no statistically significant difference; ↑↑, compared with the broth group, the TOB group showed a statistically significant upward trend; ×, some results did not come out.