

SUPPORTING INFORMATION

PEGylation of Polyethylenimine Lowers Acute Toxicity While Retaining Anti-Biofilm and β -Lactam Potentiation Properties Against Antibiotic Resistant Pathogens

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Results from the maximum tolerable dose study using ICR mice

600 Da BPEI

Group	n	Treatment	Conc. mg/kg	Route	Schedule	Animal Deaths					Total Death	% Death
						Day 0	Day 1	Day 2	Day 3	Day 4		
						10/17/17	10/18/17	10/19/17	10/20/17	10/21/17		
1	3	600 Da BPEI	6.25	SC	QD Day 0, 1, 2	0	0	0	0	0	0	0%
2	3	600 Da BPEI	12.5	SC	QD Day 0, 1, 2	0	0	0	0	0	0	0%
3	3	600 Da BPEI	25	SC	QD Day 0, 1, 2	0	0	0	0	0	0	0%
4	3	600 Da BPEI	50	SC	QD Day 0, 1, 2	3					3	100%

600 Da BPEI

Group	n	Treatment	Conc. mg/kg	Route	Schedule	Observations									
						Day 0			Day 1		Day 2		Day 3		Day 4
						10/17/17			10/18/17		10/19/17		10/20/17		10/21/17
						15 min	30 min	2 hour							
1	3	600 Da BPEI	6.25	SC	QD Day 0, 1, 2	N	N	N	N	N	N	N	N	N	
2	3	600 Da BPEI	12.5	SC	QD Day 0, 1, 2	N	N	N	N	N	N	N	N	N	
3	3	600 Da BPEI	25	SC	QD Day 0, 1, 2	L	N	N	N	N	N	N	N	N	
4	3	600 Da BPEI	50	SC	QD Day 0, 1, 2	D									

N: Normal L: Lethargic D: Dead

PEG350-BPEI

Group	n	Treatment	Conc. mg/kg	Route	Schedule	Animal Deaths					Total Death	% Death
						Day 0	Day 1	Day 2	Day 3	Day 4		
						10/17/17	10/18/17	10/19/17	10/20/17	10/21/17		
1	3	PEG350-BPEI	6.25	SC	QD Day 0, 1, 2	0	0	0	0	0	0	0%
2	3	PEG350-BPEI	12.5	SC	QD Day 0, 1, 2	0	0	0	0	0	0	0%
3	3	PEG350-BPEI	25	SC	QD Day 0, 1, 2	0	0	0	0	0	0	0%
4	3	PEG350-BPEI	50	SC	QD Day 0, 1, 2	0	0	0	0	0	0	0%
5	3	PEG350-BPEI	100	SC	QD Day 0, 1, 2	3					3	100%
6	3	PEG350-BPEI	75*	SC	QD Day 0, 1, 2	0	0	0	0	0	0	0%

** Dose reduced to 75 mg/kg after deaths in Group 5 were observed*

PEG350-BPEI

Group	n	Treatment	Conc. mg/kg	Route	Schedule	Observations									
						Day 0			Day 1		Day 2		Day 3		Day 4
						10/17/17			10/18/17		10/19/17		10/20/17		10/21/17
						15 min	30 min	2 hour							
1	3	PEG350-BPEI	6.25	SC	QD Day 0, 1, 2	N	N	N	N	N	N	N	N		
2	3	PEG350-BPEI	12.5	SC	QD Day 0, 1, 2	N	N	N	N	N	N	N	N		
3	3	PEG350-BPEI	25	SC	QD Day 0, 1, 2	N	N	N	N	N	N	N	N		
4	3	PEG350-BPEI	50	SC	QD Day 0, 1, 2	N	L	N	N	N	N	N	N		
5	3	PEG350-BPEI	100	SC	QD Day 0, 1, 2	L	D								
6	3	PEG350-BPEI	75*	SC	QD Day 0, 1, 2	L	L	L	L	N	N	N	N		

N: Normal L: Lethargic D: Dead

** Dose reduced to 75 mg/kg after deaths in Group 5 were observed*

Figure S1. Animal survival and observations in response to dosing with 600 Da BPEI or (PEG-350)₁-(BPEI-600)₁.

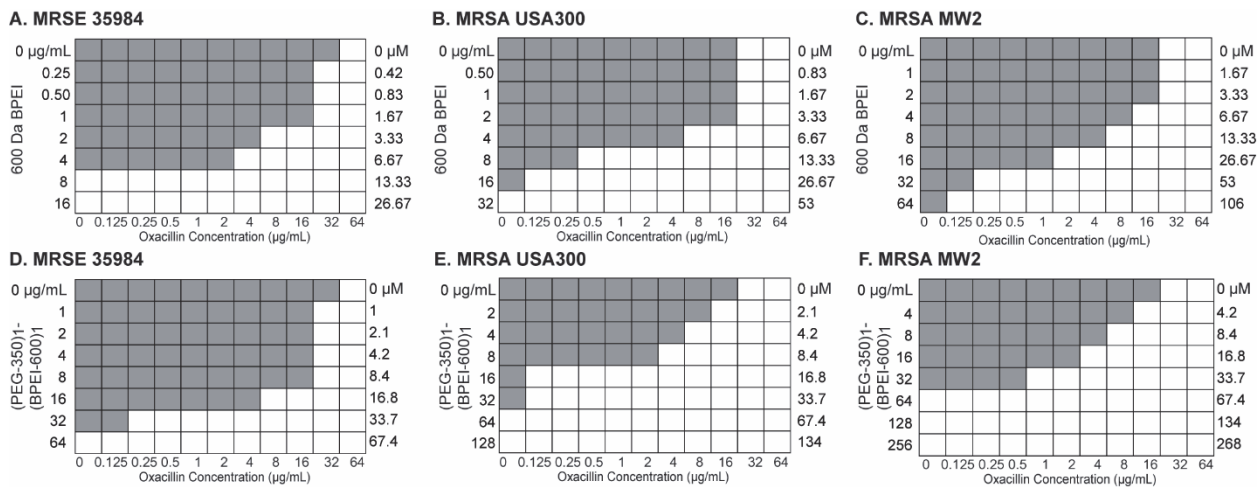


Figure S2. Checkerboard assays of MRSE 35984, MRSA USA300, and MRSA MW2 show a reduction in oxacillin MIC when mixed with 600 Da BPEI (Panels A-C) or (PEG-350)₁-(BPEI-600)₁ (Panels D-F). Each assay was performed in triplicate and presented as the average change in optical density at 600 nm (OD₆₀₀).

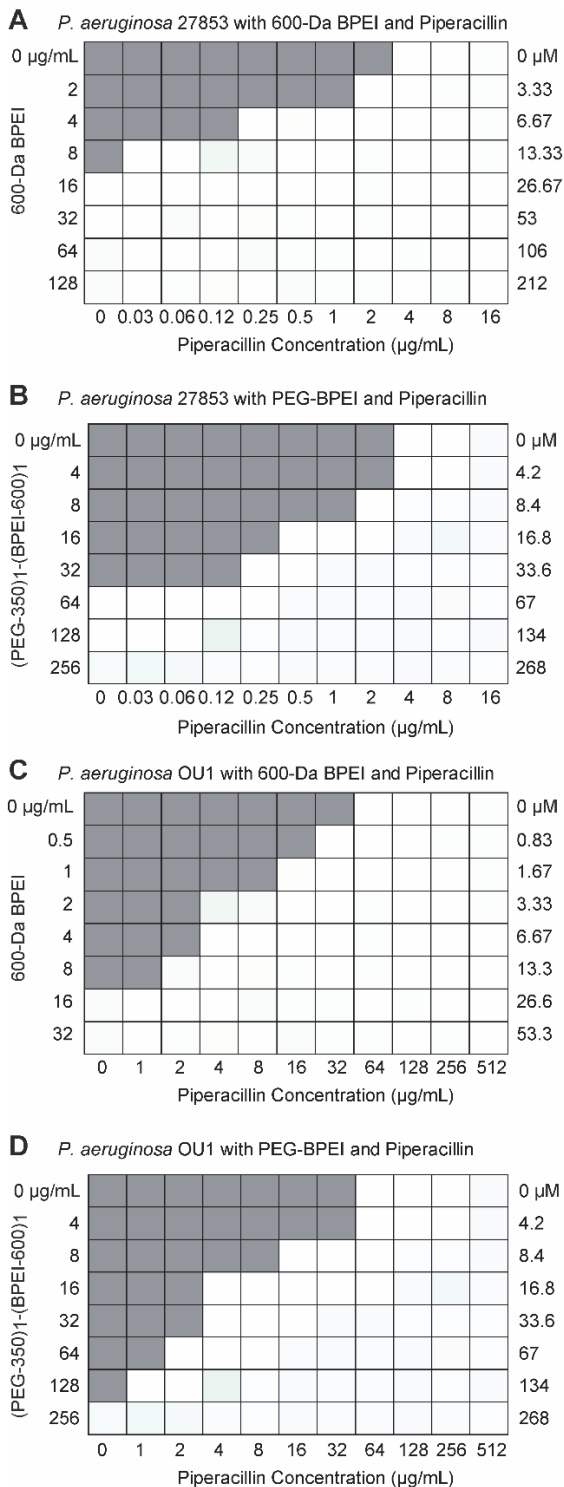


Figure S3. Although *P. aeruginosa* 27853 is susceptible to piperacillin (MIC \leq 16 $\mu\text{g/mL}$) both 600 Da BPEI and (PEG-350)₁-(BPEI-600)₁ improve piperacillin efficacy (A and B, respectively). For a clinical isolate with piperacillin resistance, *P. aeruginosa* OU1, antibiotic resistance can be overcome in the presence of 600 Da BPEI and (PEG-350)₁-(BPEI-600)₁ as shown in C and D, respectively. Each assay was performed in triplicate and presented as the average change in OD₆₀₀.

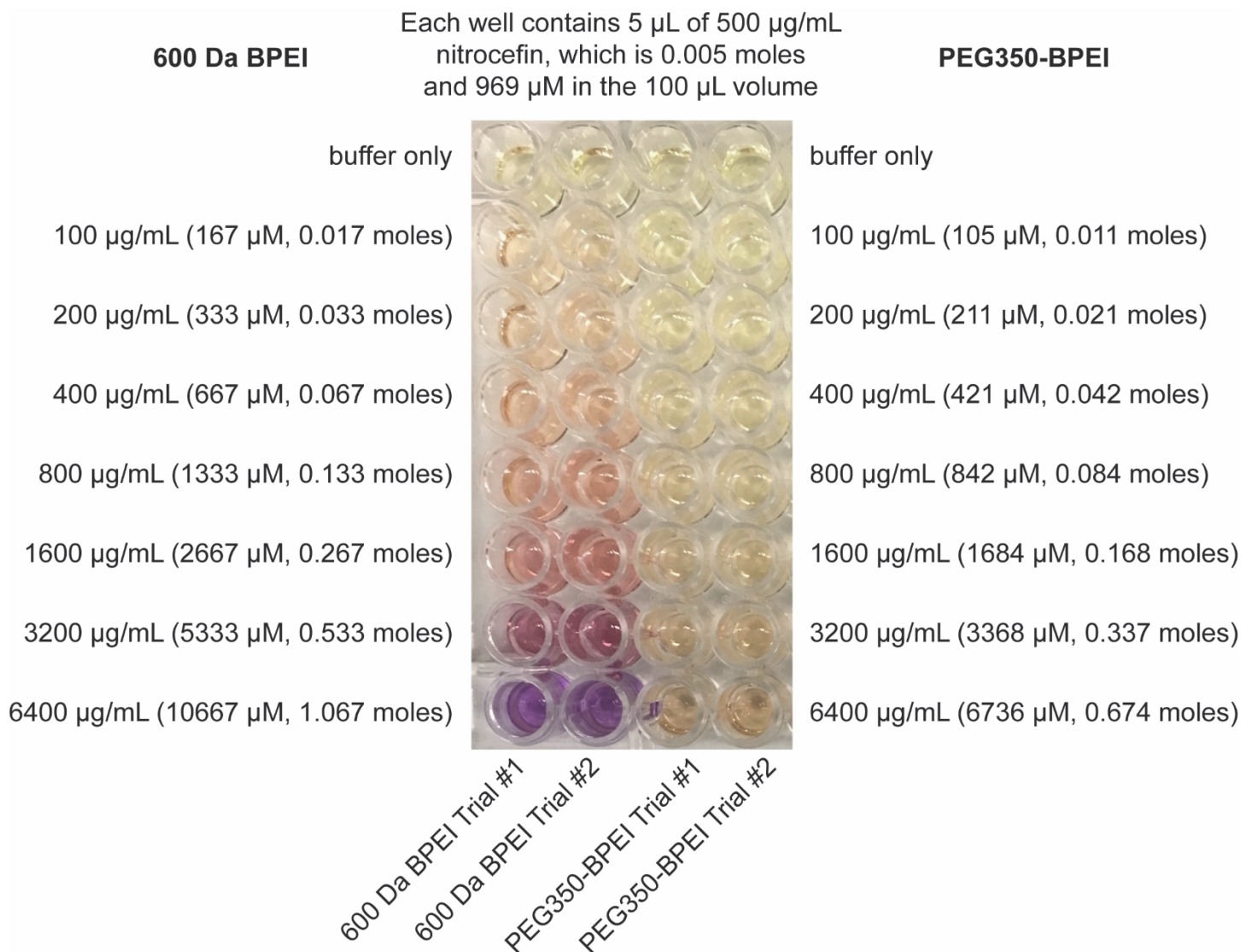


Figure S4. Photograph of the nitrocefin β -lactam ring hydrolysis assay results. Various amounts of 600 Da BPEI or PEG-BPEI were distributed in the wells of a 96-well plate. Each well contains the same amount of nitrocefin (0.005 moles). After 30 minutes, hydrolysis causes the yellow color of nitrocefin to become red. From these data, nitrocefin is 100-times less susceptible to hydrolysis from PEG-BPEI compared to the unmodified 600 Da BPEI. Photograph courtesy of one of the co-authors, Erika Moen.