

Supporting Information

Design and synthesis of biocompatible, hemocompatible and highly selective antimicrobial cationic peptidopolysaccharides *via* click chemistry

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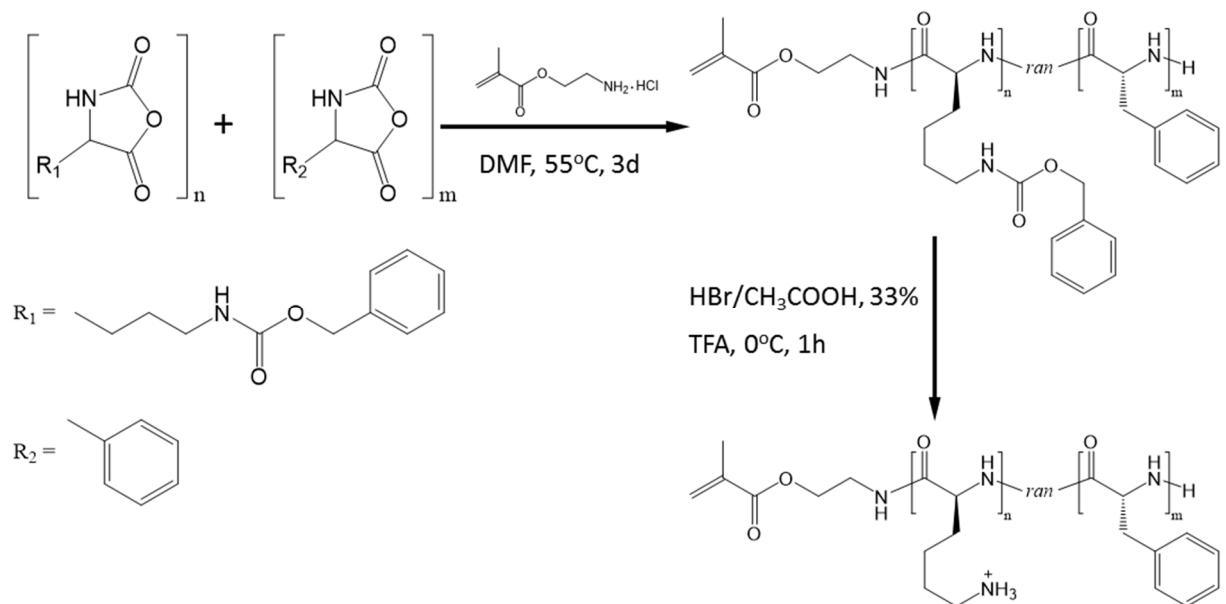
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Scheme S1. Synthesis of metharylate-ended poly-lysine-*random*-phenylalanine (Me-K_nF_m).

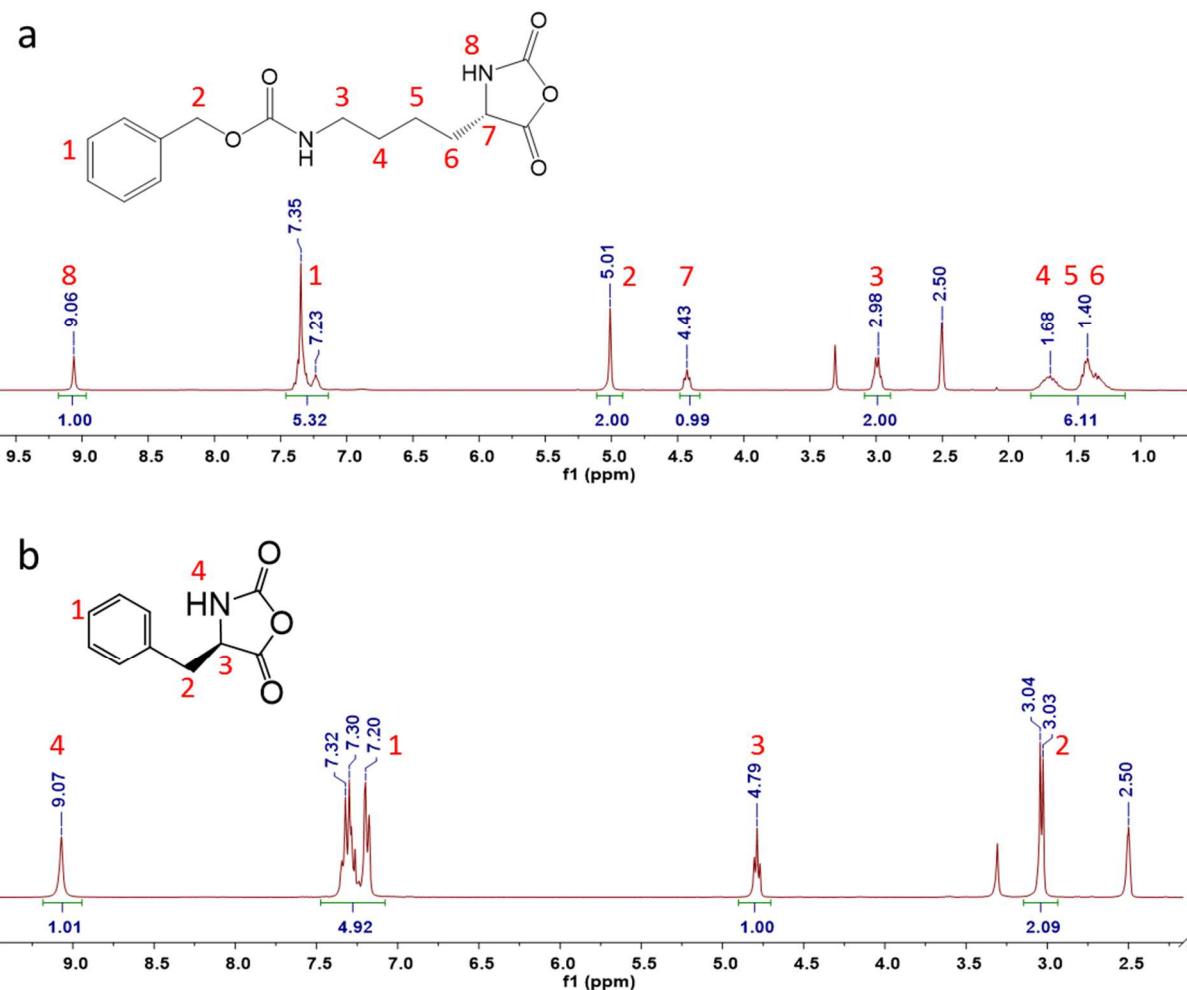


Figure S1. ^1H -NMR spectra of (a) Lys(z)-NCA and (b) Phe-NCA in $\text{DMSO}-d_6$.

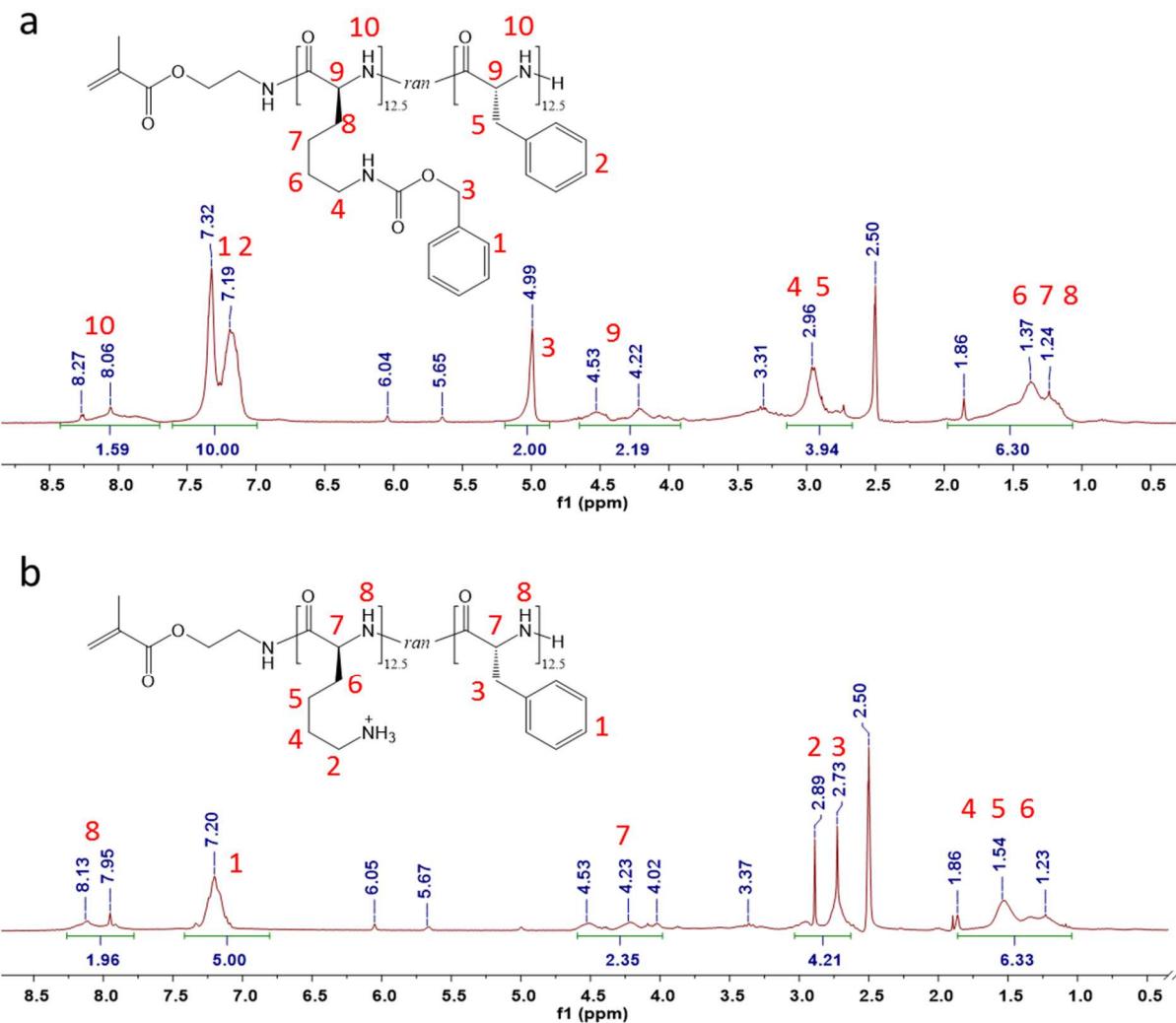


Figure S2. ^1H -NMR spectra of (a) $\text{Me-K}_n\text{F}_m(\text{z})$ and (b) $\text{Me-K}_n\text{F}_m$ in $\text{DMSO}-d_6$.

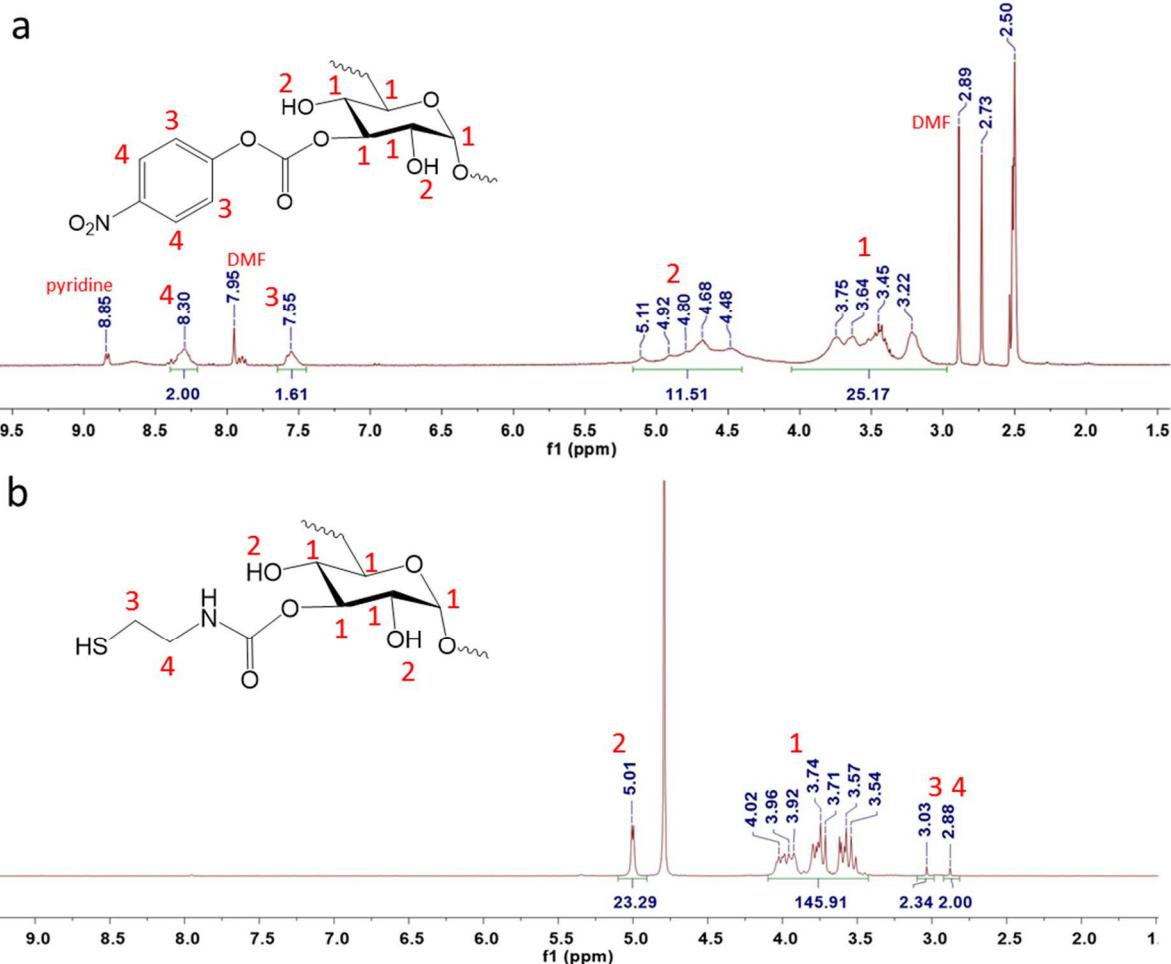


Figure S3. ^1H -NMR spectra of (a) Dex-4NC in $\text{DMSO}-d_6$ and (b) Dex-SH in D_2O .

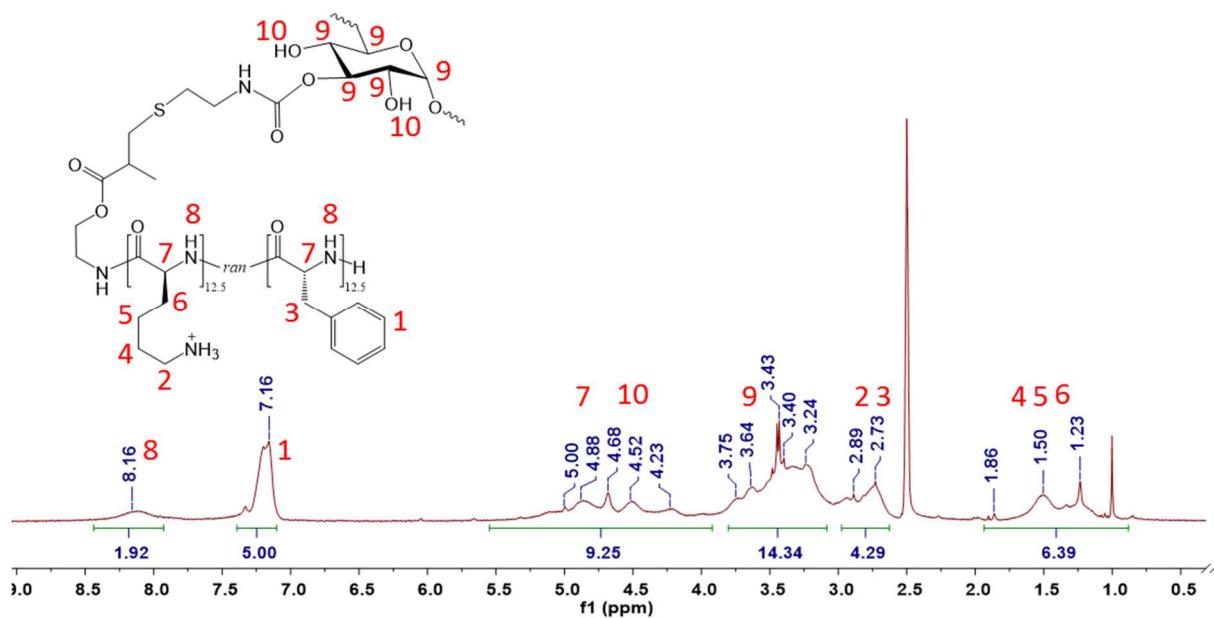


Figure S4. ¹H-NMR spectrum of Dex-g-K_nF_m in DMSO-*d*₆.

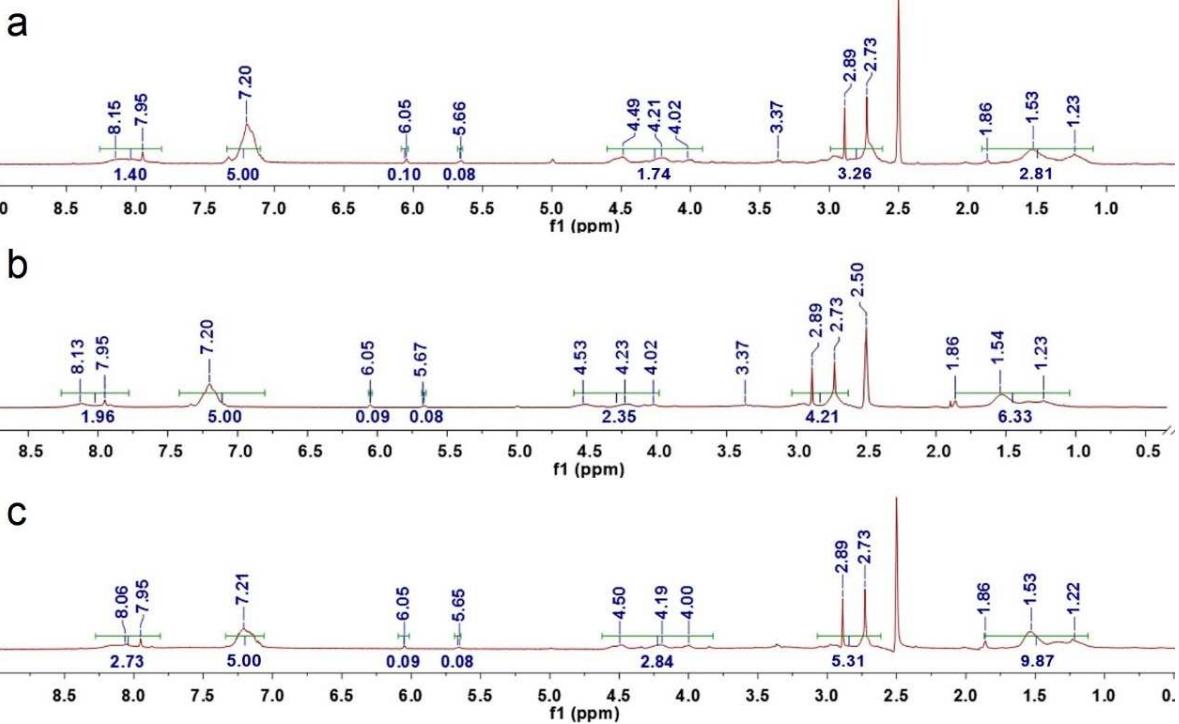


Figure S5. ^1H -NMR spectra of Me- K_nF_m in $\text{DMSO}-d_6$. (a) Me- $\text{K}_5\text{F}_{12.5}$, (b) Me- $\text{K}_{12.5}\text{F}_{12.5}$, and (c) Me- $\text{K}_{20}\text{F}_{12.5}$.

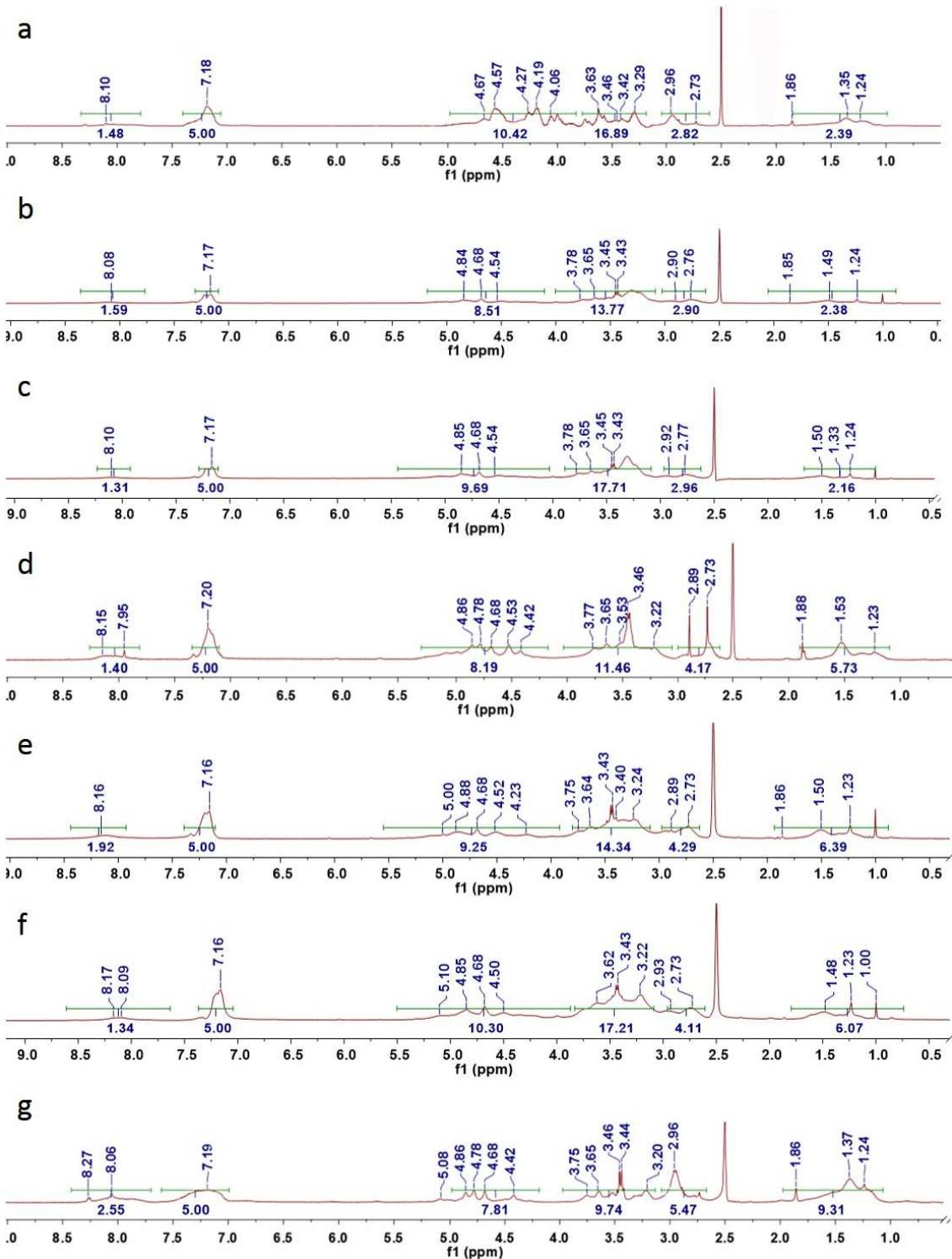


Figure S6. ^1H -NMR spectra of Dex_L-g-K_nF_m in DMSO-*d*₆. (a) Dex_L-g-K₅F_{12.5}-20%, (b) Dex_L-g-K₅F_{12.5}-50%, (c) Dex_L-g-K₅F_{12.5}-80%, (d) Dex_L-g-K_{12.5}F_{12.5}-20%, (e) Dex_L-g-K_{12.5}F_{12.5}-50%, (f) Dex_L-g-K_{12.5}F_{12.5}-80%, and (g) Dex_L-g-K₂₀F_{12.5}-20%.

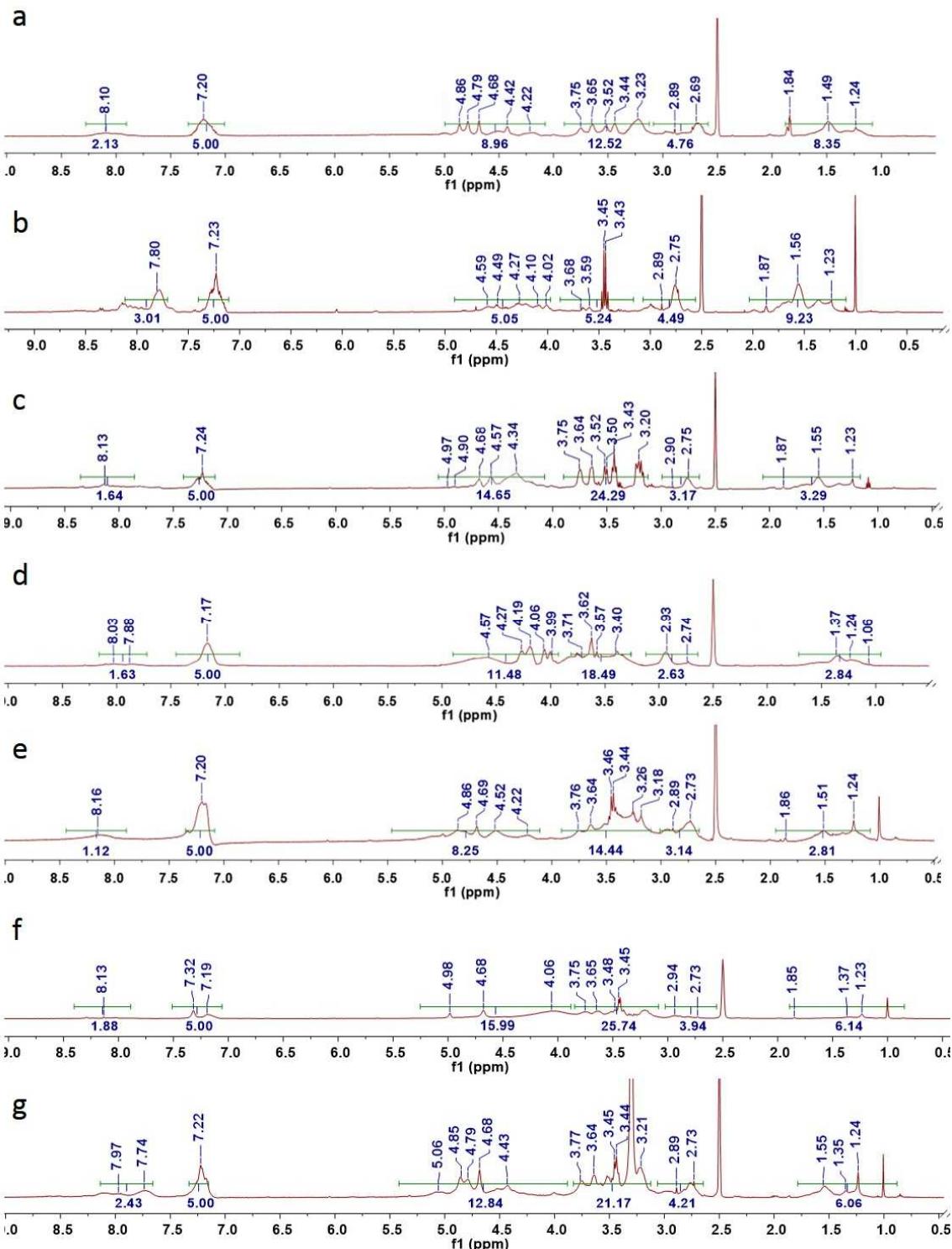


Figure S7. ^1H -NMR spectra of Dex- g -K_nF_m in DMSO- d_6 . (a) Dex_L- g -K₂₀F_{12.5}-50%, (b) Dex_L- g -K₂₀F_{12.5}-80%, (c) Dex_M- g -K₅F_{12.5}-20%, (d) Dex_M- g -K₅F_{12.5}-50%, (e) Dex_M- g -K₅F_{12.5}-80%, (f) Dex_M- g -K_{12.5}F_{12.5}-20%, and (g) Dex_M- g -K_{12.5}F_{12.5}-50%.

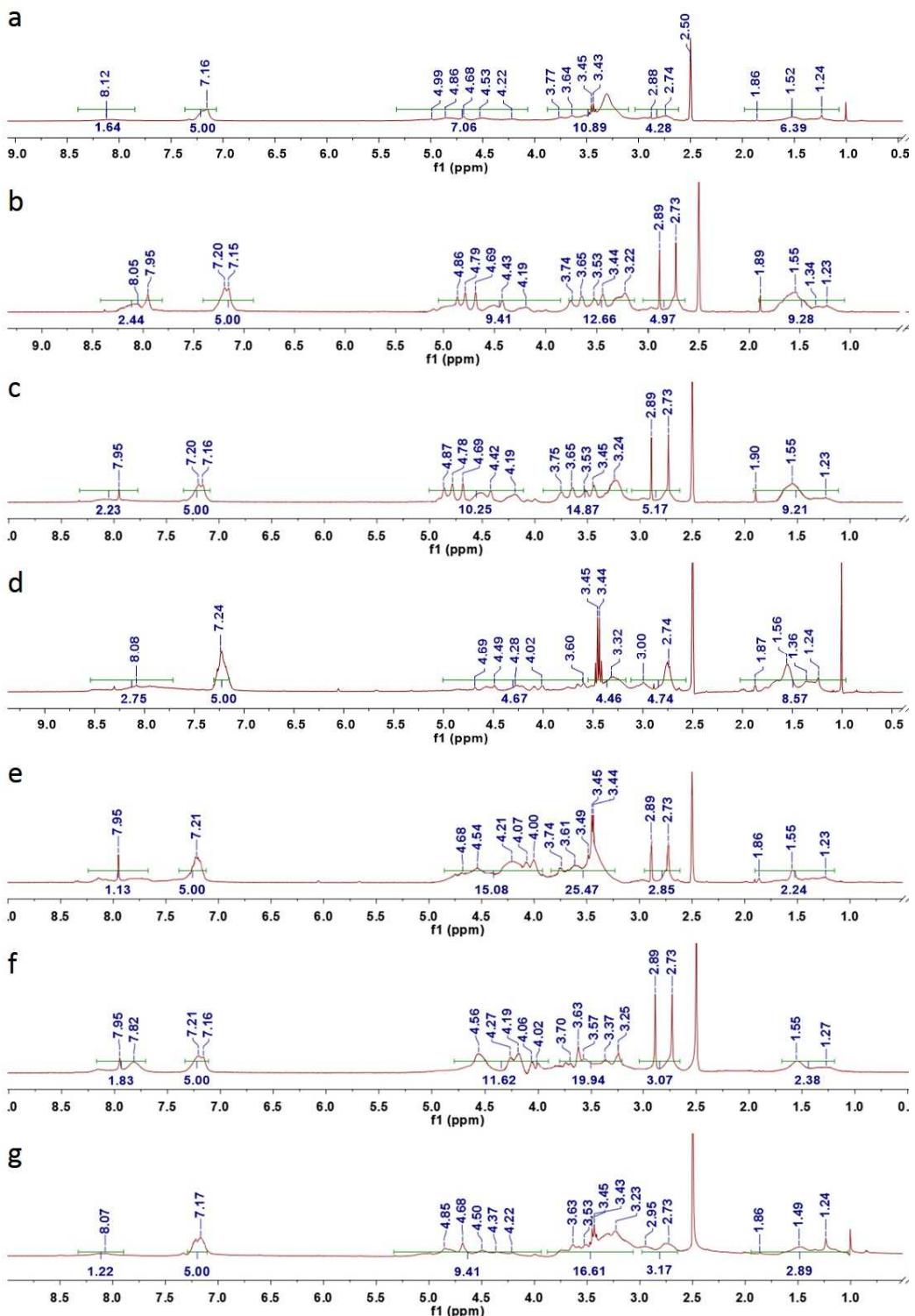


Figure S8. ^1H -NMR spectra of Dex-*g*-K_nF_m in DMSO-*d*₆. (a) Dex_M-*g*-K_{12.5}F_{12.5}-80%, (b) Dex_M-*g*-K₂₀F_{12.5}-20%, (c) Dex_M-*g*-K₂₀F_{12.5}-50%, (d) Dex_M-*g*-K₂₀F_{12.5}-80%, (e) Dex_H-*g*-K₅F_{12.5}-20%, (f) Dex_H-*g*-K₅F_{12.5}-50%, and (g) Dex_H-*g*-K₅F_{12.5}-80%.

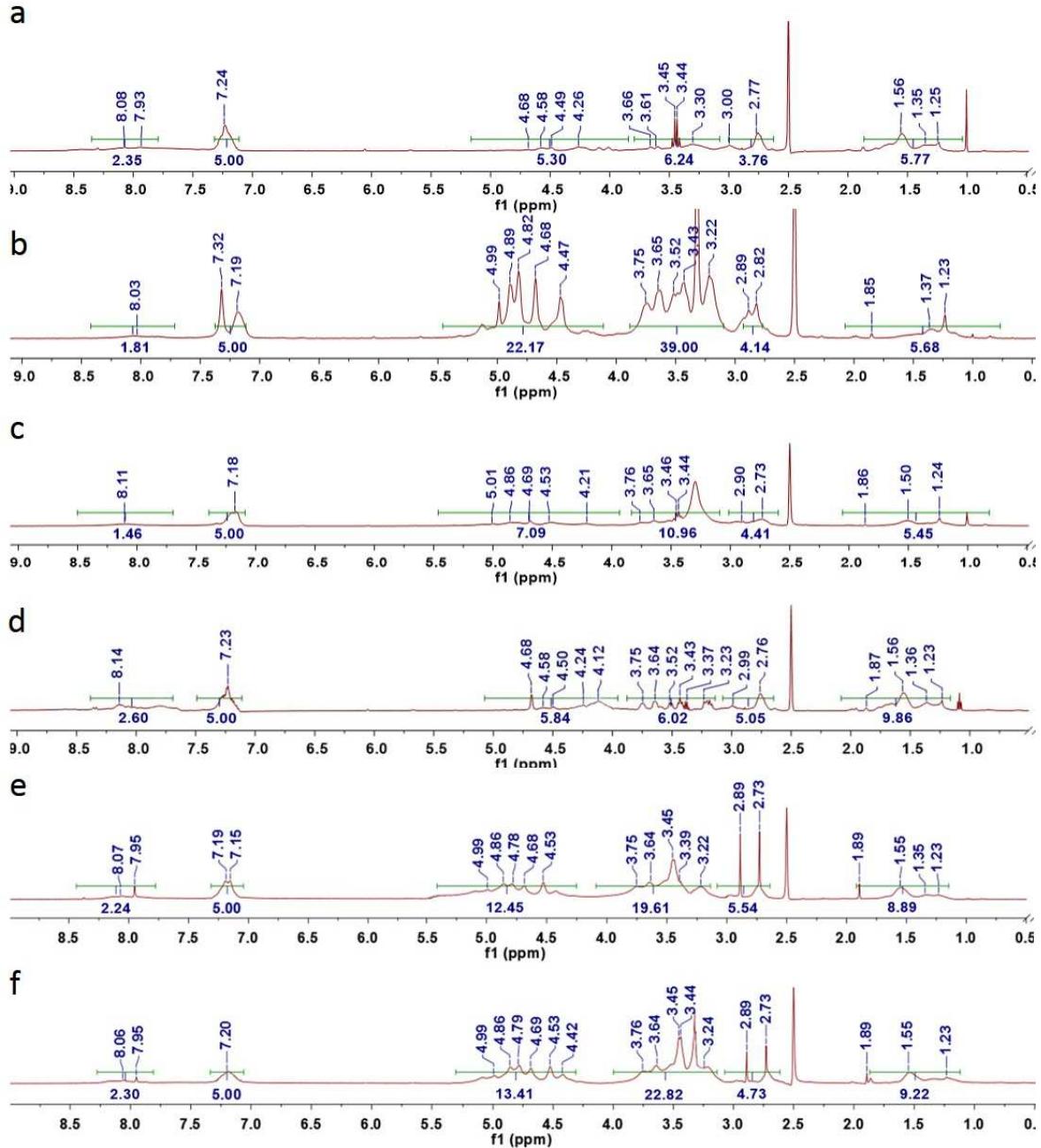


Figure S9. ^1H -NMR spectra of Dex- g -K_nF_m in DMSO-*d*₆. (a) Dex_H- g -K_{12.5}F_{12.5}-20%, (b) Dex_H- g -K_{12.5}F_{12.5}-50%, (c) Dex_H- g -K_{12.5}F_{12.5}-80%, (d) Dex_H- g -K₂₀F_{12.5}-20%, (e) Dex_H- g -K₂₀F_{12.5}-50%, and (f) Dex_H- g -K₂₀F_{12.5}-80%.

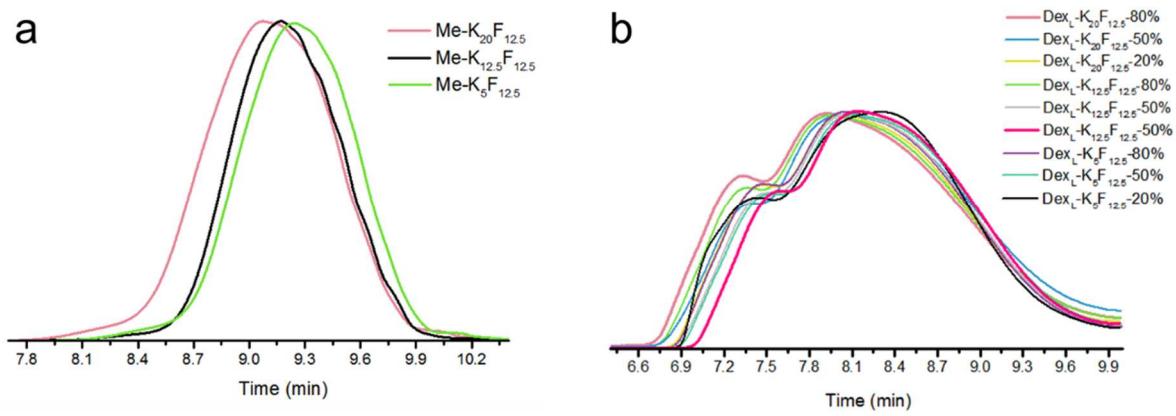


Figure S10. GPC spectra of (a) peptides and (b) Dex-g-K_nF_m peptidopolysaccharides in DMF.

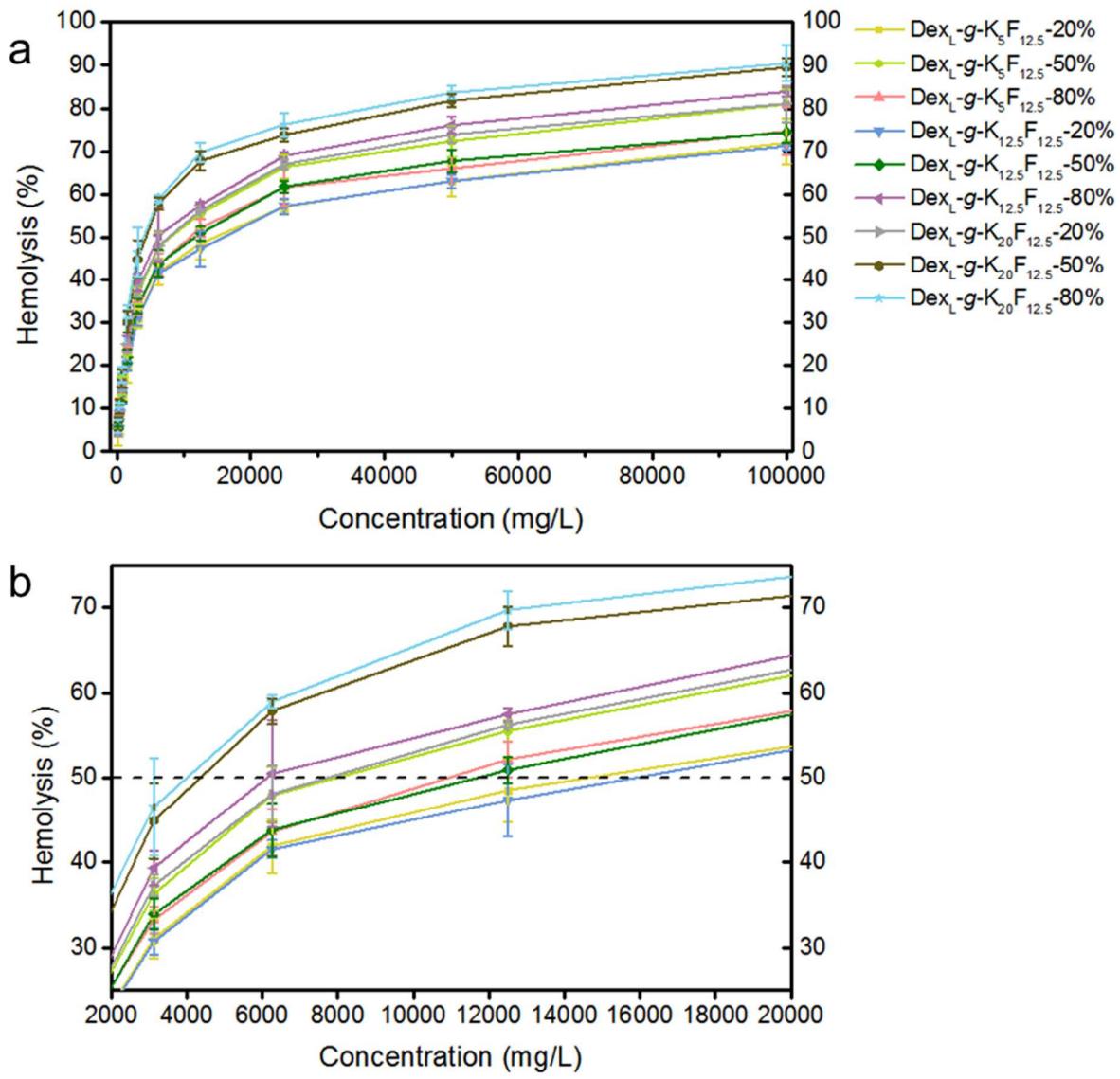


Figure S11. (a) Hemolysis percentage of red blood cells after exposure to various polymers at different concentration for 1h, (b) a partially zoom version of (a).

Table S1. Minimal inhibitory concentration (MIC), minimal lethal concentration (MLC) and hemolytic activity of typical Dex-g-K_nF_m copolymers.

Polymers	MIC ($\mu\text{g}\cdot\text{mL}^{-1}$)/ MLC ($\mu\text{g}\cdot\text{mL}^{-1}$)						Selectivity ^b	
	Gram-positive		Gram-negative		Fungi	$\text{HC}_{50}^{\text{a}}$ ($\mu\text{g}\cdot\text{mL}^{-1}$)		
	<i>S. aureus</i> (MRSA BAA40)	<i>S. epidermidis</i> (ATCC 12228)	<i>E. coli</i> (ATCC 25922)	<i>P. aeruginosa</i> (ATCC 27853)	<i>C. albicans</i> (ATCC 10231)			
Dex _L -g-K ₅ F _{12.5} -20%	125/500	250/500	250/500	500/1000	125/250	12500	50	
Dex _L -g-K ₅ F _{12.5} -50%	62.5/125	125/250	125/250	250/500	62.5/125	6250	50	
Dex _L -g-K ₅ F _{12.5} -80%	62.5/125	125/250	125/250	250/500	62.5/125	6250	50	
Dex _L -g-K ₂₀ F _{12.5} -20%	31.25/62.5	125/250	125/250	125/250	62.5/125	6250	67	
Dex _L -g-K ₂₀ F _{12.5} -50%	31.25/62.5	31.25/62.5	31.25/62.5	62.5/125	62.5/125	3125	71	
Dex _L -g-K ₂₀ F _{12.5} -80%	31.25/62.5	31.25/62.5	31.25/62.5	62.5/125	62.5/125	3125	71	
Dex _M -g-K ₅ F _{12.5} -20%	125/250	250/500	250/250	500/1000	125/250	12500	50	
Dex _M -g-K ₅ F _{12.5} -50%	62.5/250	125/250	125/250	250/500	62.5/125	3125	25	
Dex _M -g-K ₅ F _{12.5} -80%	62.5/125	125/250	125/250	250/500	62.5/125	3125	25	
Dex _M -g-K ₂₀ F _{12.5} -20%	62.5/62.5	125/250	125/250	125/250	62.5/125	6250	62	
Dex _M -g-K ₂₀ F _{12.5} -50%	31.25/62.5	31.25/31.25	31.25/62.5	62.5/125	62.5/125	3125	71	
Dex _M -g-K ₂₀ F _{12.5} -80%	31.25/62.5	31.25/31.25	31.25/62.5	62.5/62.5	62.5/125	3125	71	
Dex _H -g-K ₅ F _{12.5} -20%	250/1000	500/1000	500/1000	500/1000	125/250	6250	17	
Dex _H -g-K ₅ F _{12.5} -50%	62.5/125	125/250	125/250	250/500	62.5/125	3125	25	
Dex _H -g-K ₅ F _{12.5} -80%	62.5/125	125/250	125/250	250/500	62.5/125	3125	25	
Dex _H -g-K ₂₀ F _{12.5} -20%	62.5/125	125/250	125/250	250/500	62.5/125	6250	50	
Dex _H -g-K ₂₀ F _{12.5} -50%	31.25/62.5	31.25/62.5	31.25/125	62.5/125	62.5/125	3125	71	
Dex _H -g-K ₂₀ F _{12.5} -80%	31.25/62.5	31.25/31.25	31.25/62.5	62.5/62.5	62.5/125	3125	71	

^a HC₅₀: the concentration which causes 50% lysis of red blood cells. ^b Selectivity: HC₅₀/MIC (average of five pathogens).

Table S2. Molecular Weight (M_n), polydispersity index (PDI), degree of polymerization (DP) of Me- K_nF_m peptides and degree of substitution (DS) of Dex- g - K_nF_m peptidopolysaccharides.

Polymers	M_n (Da)	PDI	DS (%) or DP
Me- $K_5F_{12.5}$	2624	1.045	$DP_K=5, DP_F=13$
Me- $K_{12.5}F_{12.5}$	3584	1.047	$DP_K=13, DP_F=13$
Me- $K_{20}F_{12.5}$	4544	1.051	$DP_K=19, DP_F=13$
Dex _L - g - $K_5F_{12.5}$ -20%	6288	1.118	DS=10.99
Dex _L - g - $K_5F_{12.5}$ -50%	6365	1.122	DS=13.94
Dex _L - g - $K_5F_{12.5}$ -80%	6576	1.129	DS=15.64
Dex _L - g - $K_{12.5}F_{12.5}$ -20%	6357	1.117	DS=9.97
Dex _L - g - $K_{12.5}F_{12.5}$ -50%	6564	1.121	DS=15.74
Dex _L - g - $K_{12.5}F_{12.5}$ -80%	6703	1.124	DS=15.88
Dex _L - g - $K_{20}F_{12.5}$ -20%	6492	1.118	DS=10.84
Dex _L - g - $K_{20}F_{12.5}$ -50%	6696	1.114	DS=15.33
Dex _L - g - $K_{20}F_{12.5}$ -80%	6970	1.125	DS=16.29
Dex _M - g - $K_5F_{12.5}$ -20%	100238	null ¹	DS=9.08
Dex _M - g - $K_5F_{12.5}$ -50%	100318	null ¹	DS=12.14
Dex _M - g - $K_5F_{12.5}$ -80%	100549	null ¹	DS=15.18
Dex _M - g - $K_{12.5}F_{12.5}$ -20%	100337	null ¹	DS=9.41
Dex _M - g - $K_{12.5}F_{12.5}$ -50%	100525	null ¹	DS=14.66
Dex _M - g - $K_{12.5}F_{12.5}$ -80%	100808	null ¹	DS=16.04
Dex _M - g - $K_{20}F_{12.5}$ -20%	100470	null ¹	DS=10.35
Dex _M - g - $K_{20}F_{12.5}$ -50%	100647	null ¹	DS=14.25
Dex _M - g - $K_{20}F_{12.5}$ -80%	101028	null ¹	DS=15.63
Dex _H - g - $K_5F_{12.5}$ -20%	500275	null ¹	DS=10.48
Dex _H - g - $K_5F_{12.5}$ -50%	500382	null ¹	DS=14.57
Dex _H - g - $K_5F_{12.5}$ -80%	500514	null ¹	DS=16.73
Dex _H - g - $K_{12.5}F_{12.5}$ -20%	500444	null ¹	DS=12.41
Dex _H - g - $K_{12.5}F_{12.5}$ -50%	500586	null ¹	DS=16.36
Dex _H - g - $K_{12.5}F_{12.5}$ -80%	500809	null ¹	DS=16.98
Dex _H - g - $K_{20}F_{12.5}$ -20%	500467	null ¹	DS=10.29
Dex _H - g - $K_{20}F_{12.5}$ -50%	500739	null ¹	DS=16.28
Dex _H - g - $K_{20}F_{12.5}$ -80%	500956	null ¹	DS=17.14

¹ Molecular Weight (M_n) were obtained by 1H -NMR.