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CLUSTAL O(1.2.4) multiple sequence alignment

HFB4      GPCSSGVTTNNVPKCCGTGVLDDLKLTPTQATSVLNPLSAVCGRVGLQAKCCTAGIGS 60
HFB1      NVCPPGLF-SNPQCCATQVLGLIGLCKVPSQNVYDGTDFRNVCAKTGAQPLCCVAPVAG 59
HFB2      AVCPTGLF-SNPLCCATNVLDLIGVDCPTPTIAVDTGAIQAHCAKSGSKPLCCVAPVAD 59
          *  * : . * * * . * * : : * * * : . : * . * : * * . : ..

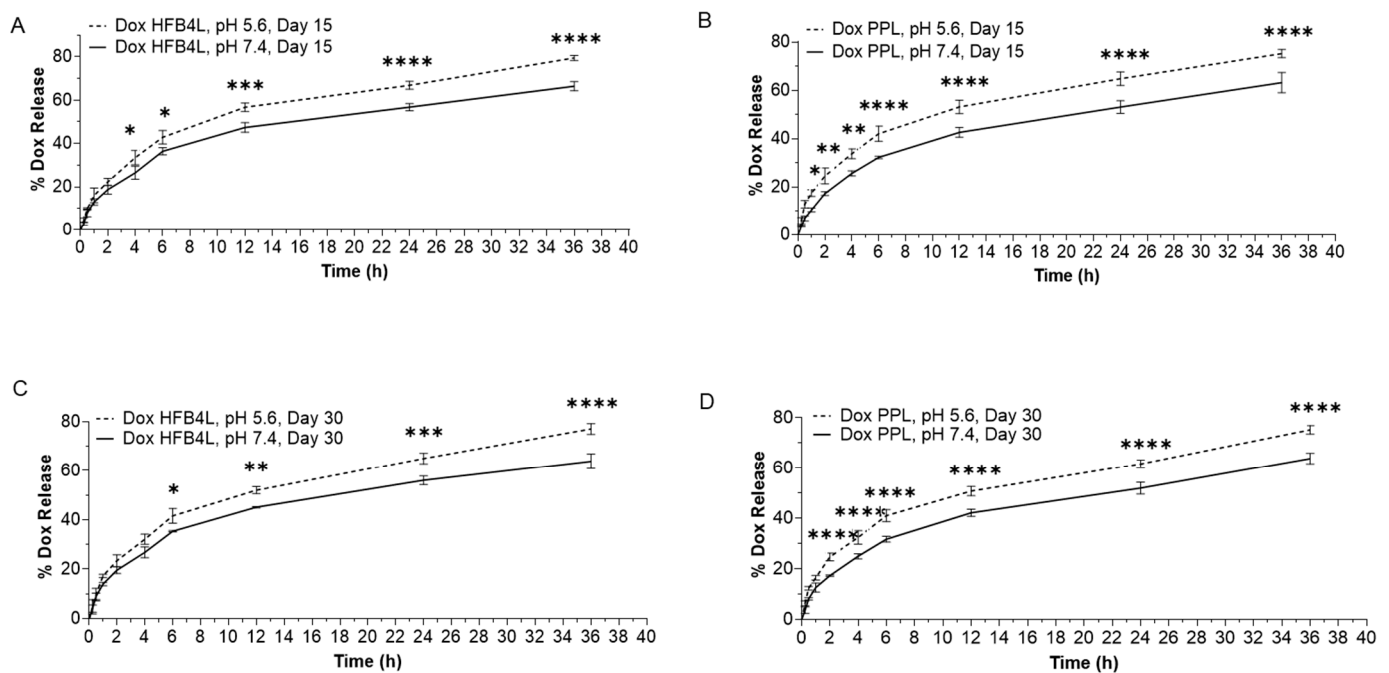
HFB4      LGVLC 65
HFB1      QALLC 64
HFB2      QALLC 64
          . : * *
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B

Reference sequence (1): HFB4  
Identities normalised by aligned length.  
Colored by: identity

	cov	pid	1
1 HFB4	100.0%	100.0%	GPCSSGVTTNNVPKCCGTGVLDDLKLTPTQATSVLNPLSAVCGRVGLQAKCCTAGIGS 65
2 HFB1	98.5%	36.9%	NVCPPGLF-SNPQCCATQVLGLIGLCKVPSQNVYDGTDFRNVCAKTGAQPLCCVAPVAG 64
3 HFB2	98.5%	38.5%	AVCPTGLF-SNPLCCATNVLDLIGVDCPTPTIAVDTGAIQAHCAKSGSKPLCCVAPVAD 64
consensus/100%			ssCsslh.ssp.CCultvslhldCKsso.ss.shs.hpshCuphs.pshCCsaslus.ulLC
consensus/90%			ssCsslh.ssp.CCultvslhldCKsso.ss.shs.hpshCuphs.pshCCsaslus.ulLC
consensus/80%			ssCsslh.ssp.CCultvslhldCKsso.ss.shs.hpshCuphs.pshCCsaslus.ulLC
consensus/70%			ssCsslh.ssp.CCultvslhldCKsso.ss.shs.hpshCuphs.pshCCsaslus.ulLC

**Figure S1.** Multiple Sequence Alignment of HFB1, HFB2 and HFB4 with Clustal Omega. (A) Mview visualisation of MSA exhibiting conserved residues (B).



**Figure S2.** Release profiles of Dox-HFB4L Day 15 (A), Dox-PPL Day 15 (B), Dox-HFB4L Day 30 (C), Dox-PPL Day 30 for pH 5.6 and pH 7.4 at different time points. One-way ANOVA using Tukey's multiple comparison tests was conducted for each time point;  $p < 0.05$  was accepted as statistically significant. Each experiment was performed in triplicate. \* $p = 0.0103$ ; \*\* $p = 0.0035$ ; \*\*\* $p = 0.0007$ ; \*\*\*\* $p < 0.0001$ .

**Table S1.** The average particle size, particle size distribution (PDI), and zeta potential of Dox-HFB4L without lyophilization.

	Day 0 at 4 °C		Day 3 at 4 °C	
	Particle size (nm)	PDI	Particle size (nm)	PDI
Dox-HFB4L	213.90 ± 2.12	0.19 ± 0.06	341.23 ± 13.55	0.27 ± 0.03
Dox-HFB4L (1 min vortex)	-	-	316.60 ± 19.54	0.26 ± 0.01
Dox-HFB4L (2 min vortex)	-	-	249.73 ± 5.06	0.24 ± 0.01