Supporting Information for

Lysine-derived, pH-sensitive and Biodegradable Poly(Beta-aminoester Urethane) Networks and Their Local Drug Delivery Behaviour

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Mathematical models for the mechanism of drug release

For better understanding the release mechanism of doxycycline hyclate (DH), its *in vitro* release data were fitted to different mathematical equations.

Zero-order kinetic model: This model characterizes the systems where the rate of drug release is not related to its concentration and can be explained by Equation S1, [1,2]

$$Q_t = Q_0 + K_0 t \qquad (S1)$$

where Q_0 and Q_t are the initial quantity of drug in solution and the quantity of released drug at time "t", respectively, K_0 is the constant of zero order release and t is the time in hours. The initial amount of drug in the solution is mostly zero (Q_0=0).

First-order kinetic model: This model can be used when the rate of drug release is linearly related to the amount of unreleased drug from the network and can be described as Equation S2, [1,3]

$$\log Q_t = \log Q_0 - \frac{K_1 t}{2.303} \qquad (S2)$$

where Q_0 and Q_t are the initial quantity of the drug in solution and the released quantity of drug at time "t", K_1 is the constant of first order release and t is the time in hours.

Table S1. Swelling parameters of LPBAEU networks fitted to Voigt Model and Korsmeyer-Peppas power-law equation at pH 7.4 and pH 5.6. (Results represented are mean ± SD, n=3)

Sample	pH 7.4				pH 5.6			
	τ	$Kx10^3$ / s^{-1}	n	R^2	τ	$Kx10^3$ / s^{-1}	n	R^2
LPBAEU-A1	47.0 ± 2.5	1.149	0.725	0.9980	39.3 ± 1.2	1.366	0.741	0.9985
LPBAEU-A2	54.9 ± 1.5	2.859	0.627	0.9940	56.5 ± 2.1	2.116	0.652	0.9917
LPBAEU-T1	60.0 ± 3.2	5.187	0.576	0.9992	63.1 ± 3.6	2.740	0.609	0.9998
LPBAEU-T2	70.0 ± 2.9	6.113	0.535	0.9989	105.6 ± 2.6	3.072	0.588	0.9982

Table S2. The results of DH release data fitting to Korsmeyer-Peppas and Kopcha model at pH 7.4 and pH 5.6.

pH : 7.4				
Sample	**Korsmeyer-Peppas Model**	**Kopcha Model**		
	n	**A**	**B**	**A/B**
LPBAEU-A1	0.73	15.23	19.47	0.78
LPBAEU-A2	0.63	7.13	15.05	0.47
LPBAEU-T1	0.54	8.82	17.86	0.49
LPBAEU-T2	0.60	3.78	10.53	0.36
pH : 5.6				
LPBAEU-A1	0.55	11.65	59.74	0.20
LPBAEU-A2	0.57	10.45	32.64	0.32
LPBAEU-T1	0.59	14.06	37.4	0.38
LPBAEU-T2	0.73	8.89	11.65	0.76

Table S3. Diffusion coefficient values of LPBAEU networks that were calculated by fitting the drug release data to Korsmeyer-Peppas model at pH 7.4 and pH 5.6.

Sample	Drug release $Dx10^{8}$ / cm^{2} s^{-1}	
	pH 7.4	**pH 5.6**
LPBAEU-A1	8.5971	10.6260
LPBAEU-T1	5.3276	6.3679
LPBAEU-A2	5.7883	5.1743
LPBAEU-T2	0.4416	0.5934

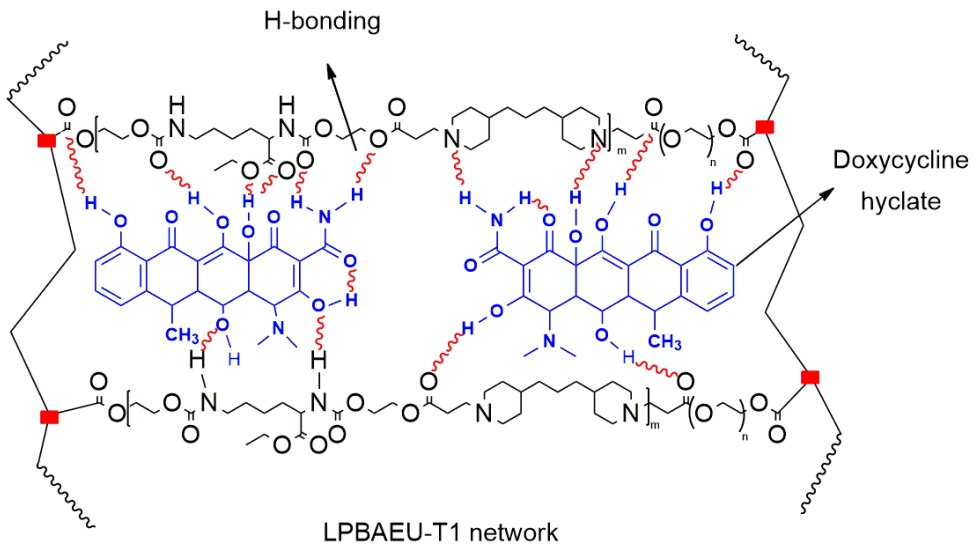

Fig. S1 Probable hydrogen bonding interactions between LPBAEU-T1 network and doxycycline hyclate (DH). DH, which has a highly hydrophilic structure, can form hydrogen bonds with the networks through their polar amino, hydroxyl and amide functional groups.

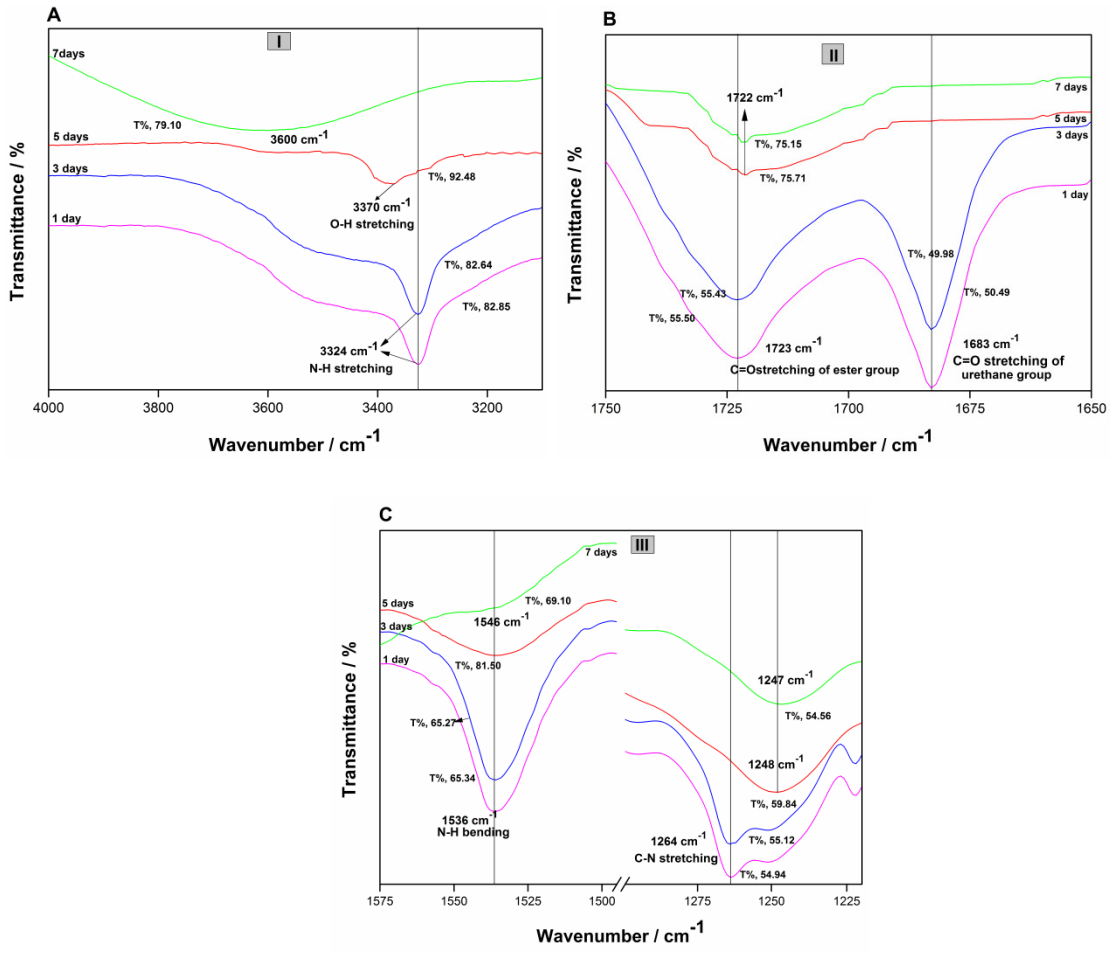

Fig. S2 ATR-FTIR spectra of LPBAEU-T1 network during degradation: (A) I region of spectra, (B) II region of spectra and (C) III region of spectra. The spectra were shifted vertically for better understanding. These spectra are the chemical verification of that the network is losing parts of its chemical structure via hydrolysis of ester and urethane linkages. Briefly, LPBAEU-T1 network was immersed in distilled water and kept at 37 °C in a shaker. At predetermined time intervals sample was taken from the medium and dried under vacuum to constant weight. Then ATR-FTIR spectrum was collected.

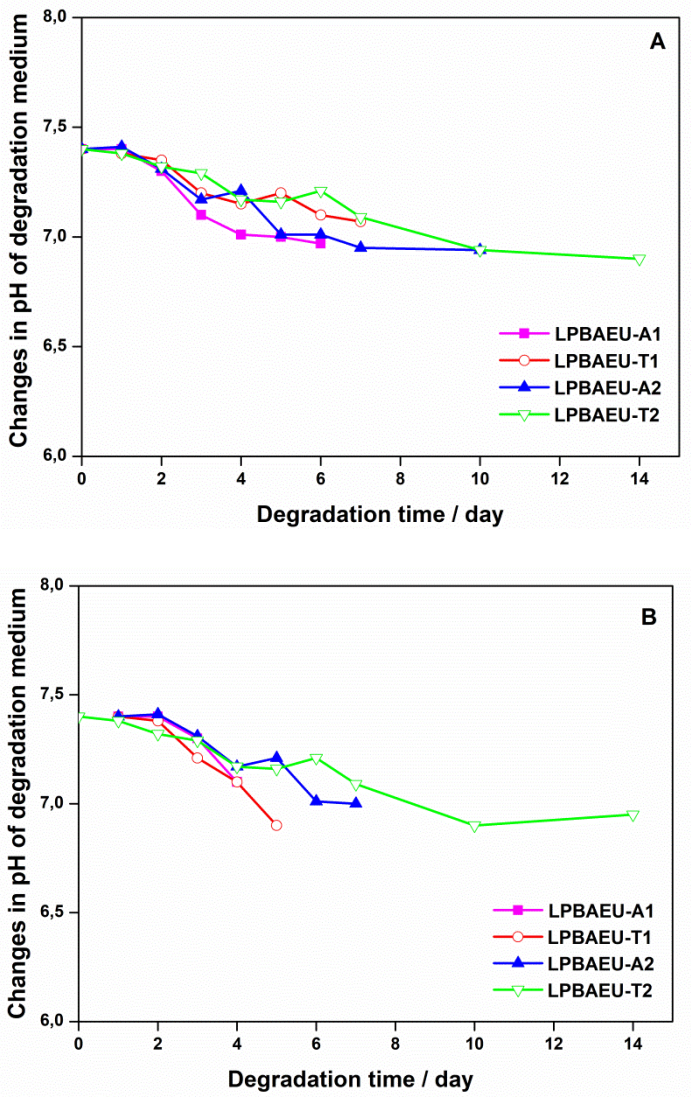

Fig. S3 Changes in pH of the medium during the degradation of LPBAEU networks: (A) PBS solution, and (B) lipase containing PBS solution.

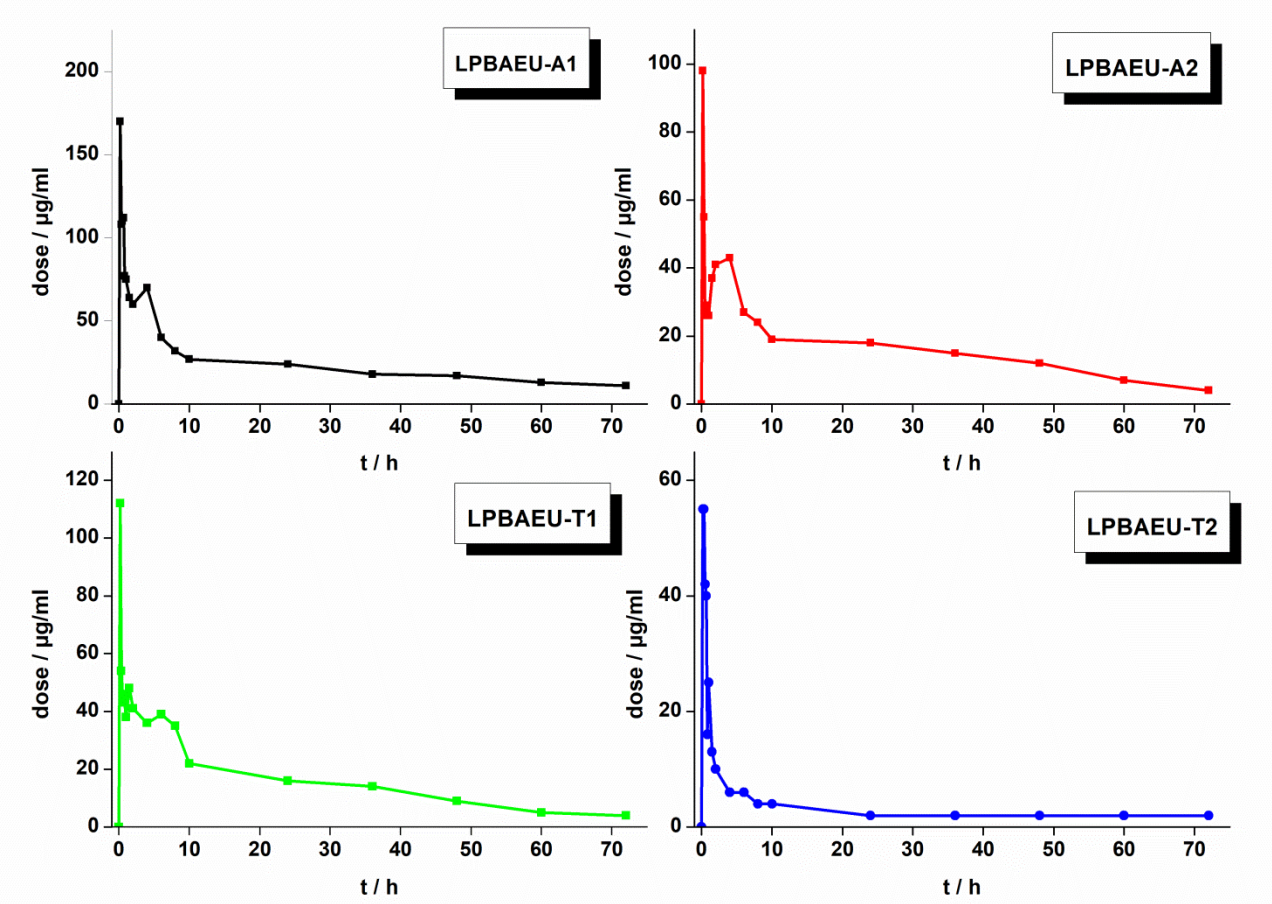

Fig. S4 Daily doses of doxycycline hyclate released from LPBAEU networks during 72 hours at pH 7.4.

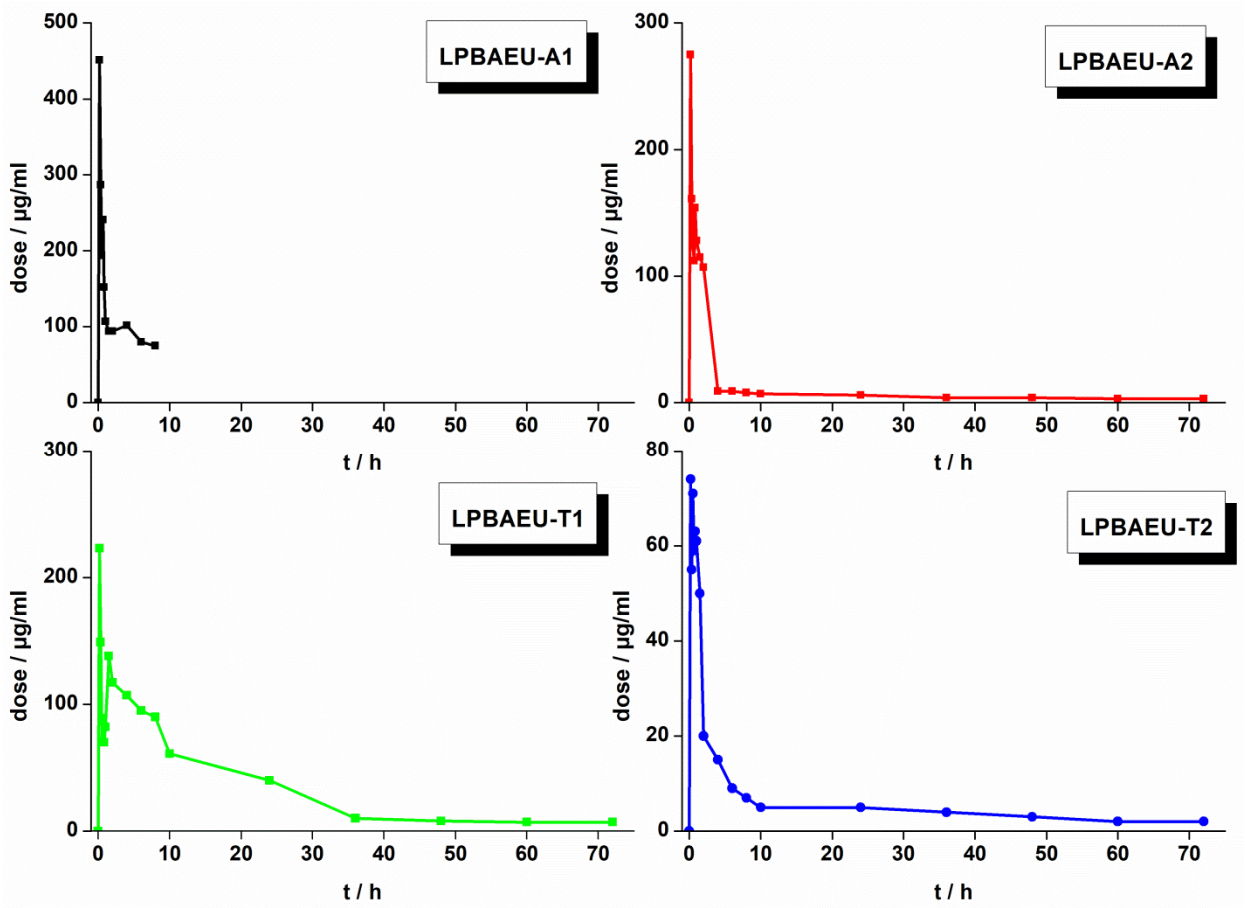

Fig. S5 Daily doses of doxycycline hyclate released from LPBAEU networks during 72 hours at pH 5.6.

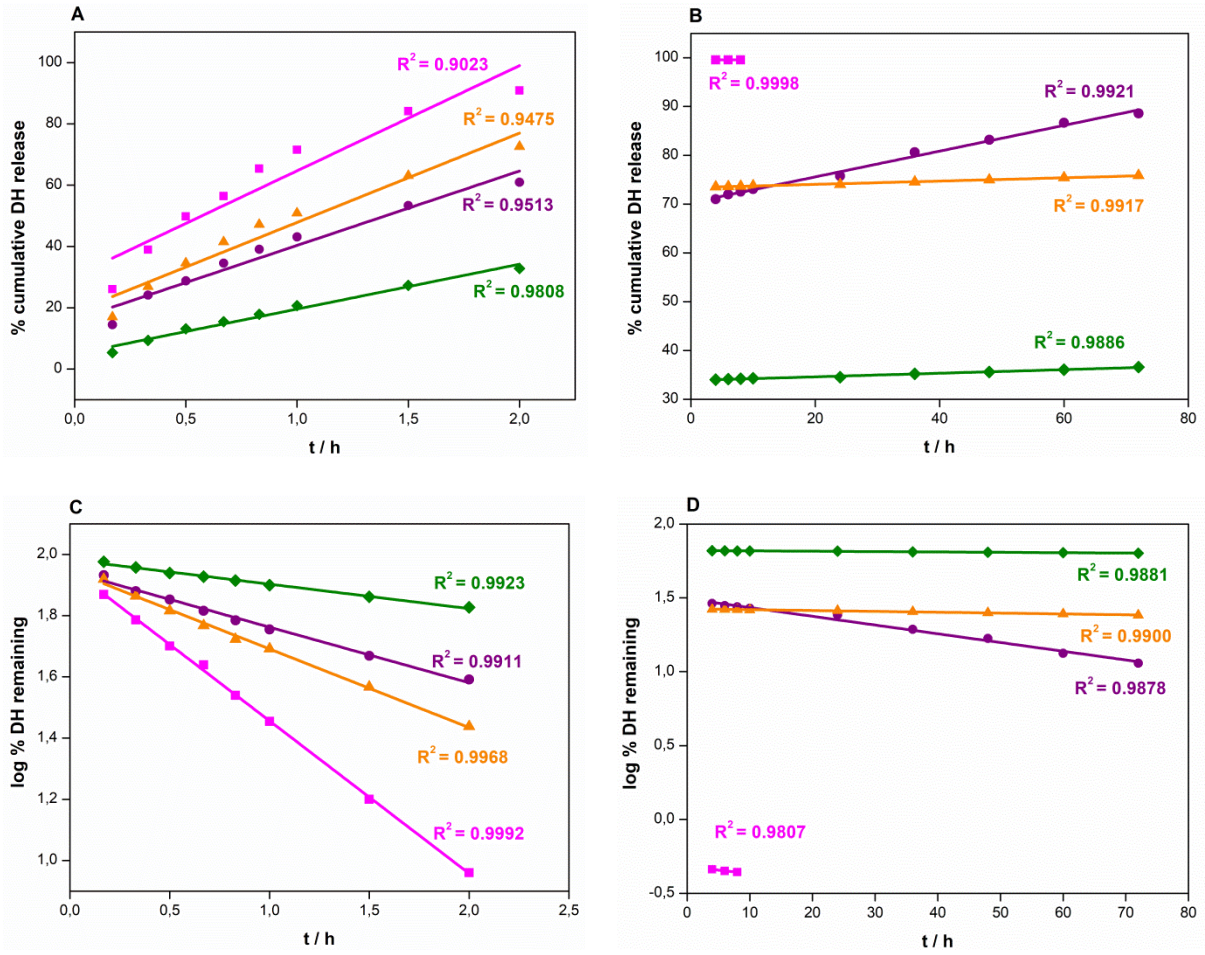

Fig. S6 Fitting the *in-vitro* DH release data to zero-order and first-order kinetic models at pH 5.6: (A) early time and (B) late time zero-order release; (C) early time and (D) late time first-order release. ■: LPAEU-A1, ●: LPAEU-T1, ▲: LPAEU-A2, ♦: LPAEU-T2.

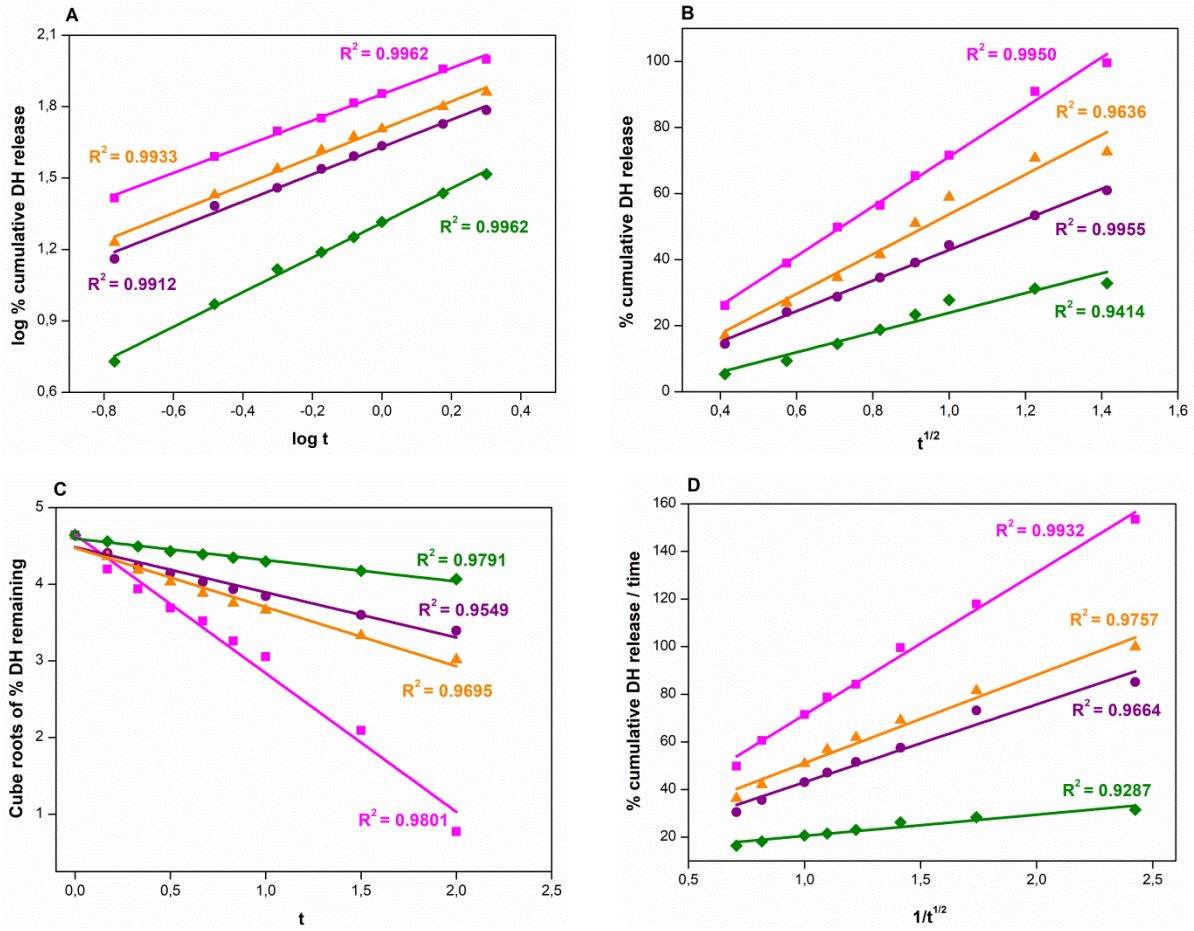

Fig. S7 Fitting the *in-vitro* DH release data to different mathematical models at pH 5.6: (A) Korsmeyer-Peppas model, (B) Higuchi model, (C) Hixon-Crowell model, and (D) Kopcha model. The unit of time is hour. ■: LPAEU-A1, ●: LPAEU-T1, ▲: LPAEU-A2, ♦: LPAEU-T2.

References

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