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Smart Poly(amidoamine) Dendrons Functionalized Magnetic Graphene Oxide for Cancer Therapy

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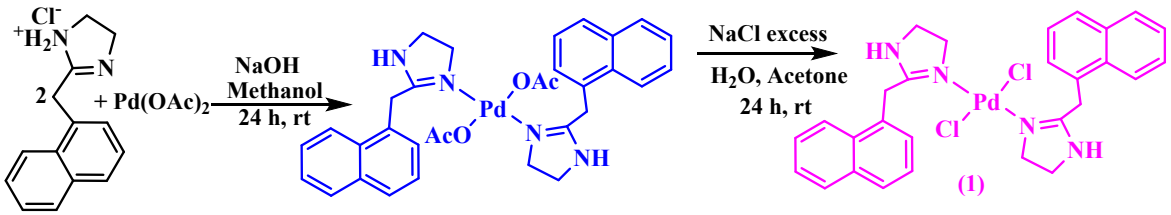
1. Synthesis of *trans*-[Pd(Naph)$_2$(Cl)$_2$] (Pd(II) complex)

In order to synthesize *trans*-[Pd(Naph)$_2$(Cl)$_2$], Naphcon (2 mmol) was added to solution of Pd(OAc)$_2$ (1 mmol) followed by the addition of NaOH solution (2 mmol). The obtained solution was stirred at room temperature for 24 h. The resulted orange solid was dissolved in acetone and an aqueous NaCl solution was supplemented to it, stirred for 24 h at ambient temperature and air dried. The obtained yellow precipitate (*trans*-[Pd(Naph)$_2$(Cl)$_2$]) was washed with distilled water to the remove excess NaCl. The yellow precipitate was recrystallized in ethanol.

Naphcon: FT-IR (KBr, cm^{-1}): ν (C-H $_{aromatic}$)= 3053, ν (C-H$_{aliphatic}$)= 2810-2922, ν (-NH$_2^+$)= 2688, ν (C=N)= 1620, ν (C=C$_{aromatic}$)= 1489. ^{1}H NMR (500.13 MHz, DMSO-d$_6$, ppm): δ= 3.79 (s, 4H, CH$_2$), 4.41 (s, 2H, CH$_2$), 7.5-8.11 (7H, aromatic rings), 10.52 (s, 2H, NH$_2^+$).

***Trans*-[Pd(Naph)$_2$(Cl)$_2$]**: Yield: 73%, Anal. Calc. for C$_{28}$H$_{28}$Cl$_2$N$_4$Pd (%): C, 56.25; H, 4.72; N, 9.37. Found: C, 55.98; H, 4.65; N, 9.23. FT-IR (KBr, cm^{-1}): ν (N-H)= 3407, ν (C-H$_{aromatic}$)= 3052, ν (C-H$_{aliphatic}$)= 2850-2927, ν (C=N)= 1609, ν (C=C$_{aromatic}$)= 1520. ^{1}H NMR (500.13 MHz, DMSO-d$_6$, ppm): δ= 11.93 (br s, -NH), 7.36-8.38 (m, 14H, aromatic rings), 4.42 (s, 2H, -CH$_a$), 4.24 (s, 2H, -CH$_{a'}$), 3.86 (t, 2H, -CH$_2$, ^{3}J= 10 Hz), 3.72 (t, 2H, -CH$_2$, ^{3}J= 10 Hz), 3.54 (t, 2H, -CH$_2$, ^{3}J= 10 Hz), 3.41 (t, 2H, -CH$_2$).



Scheme. S1: Synthetic procedure of the Pd(II) complex (1)

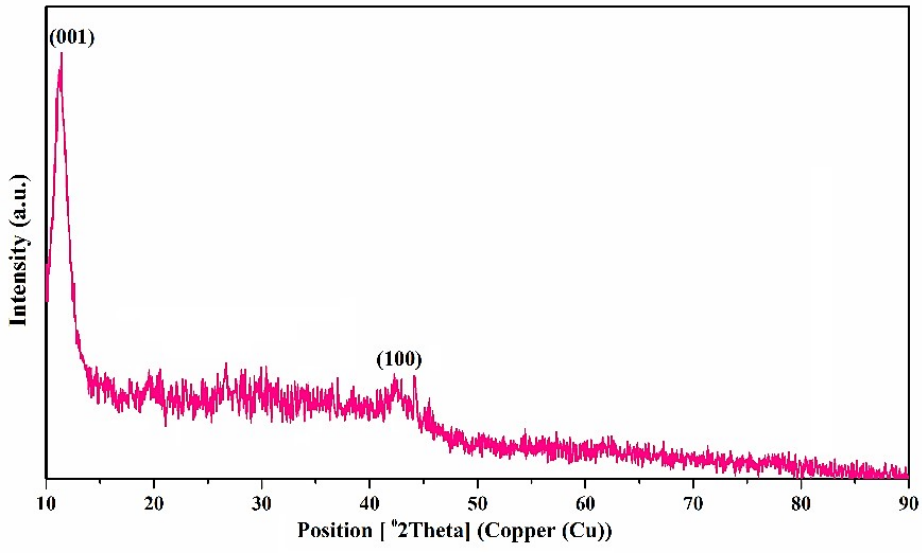


Fig. S1: XRD pattern of GO

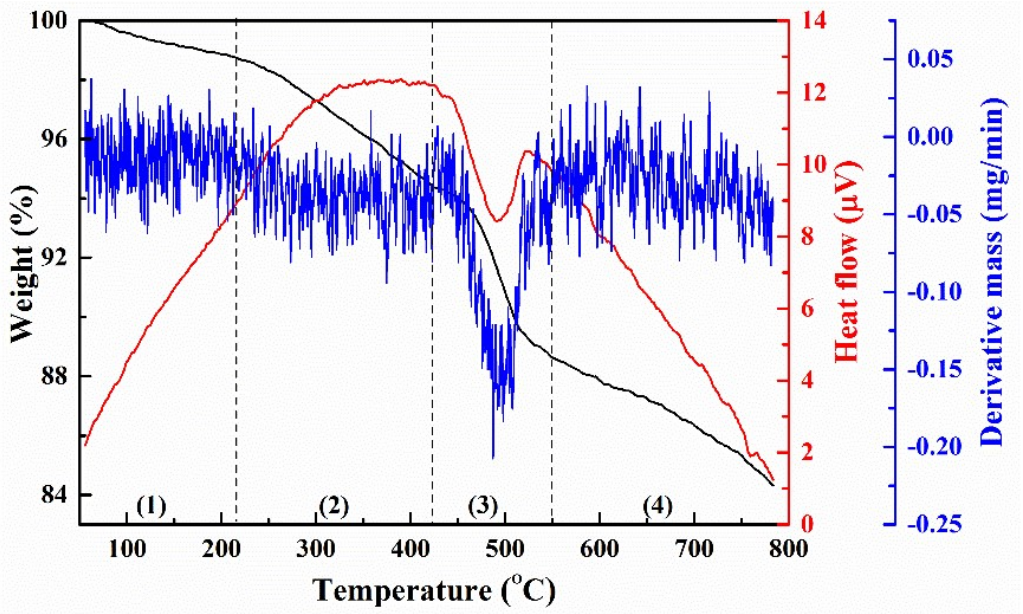


Fig. S2: TG/DTG/DTA curves of mG-NH_2 nanocomposite under argon flow and heating rate of 10 ℃ min^{-1}

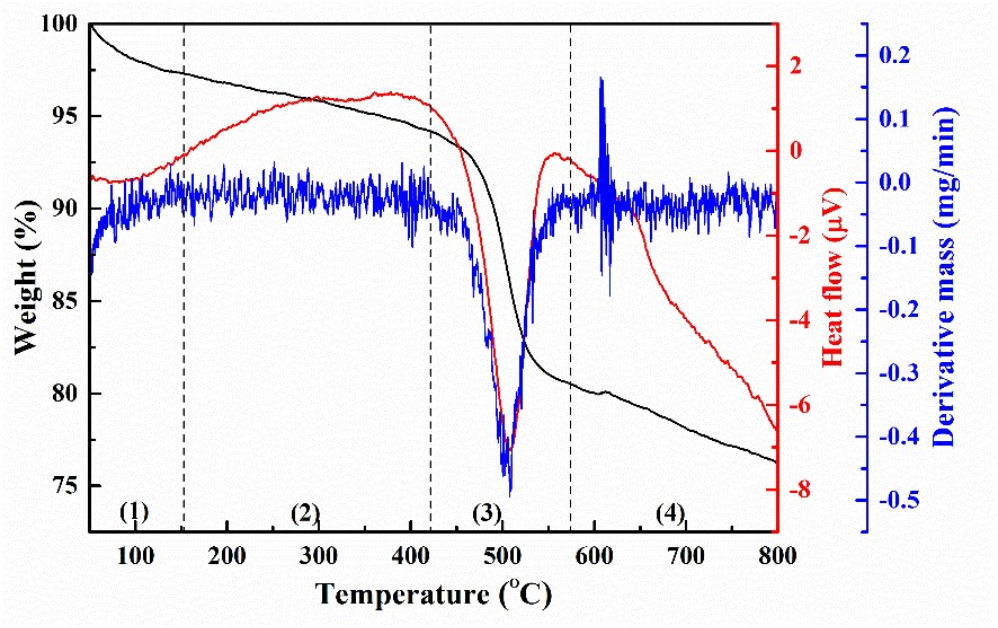


Fig. S3: TG/DTG/DTA curves of mGG3 nanocomposite under argon flow and heating rate of 10 ℃ min^{-1}

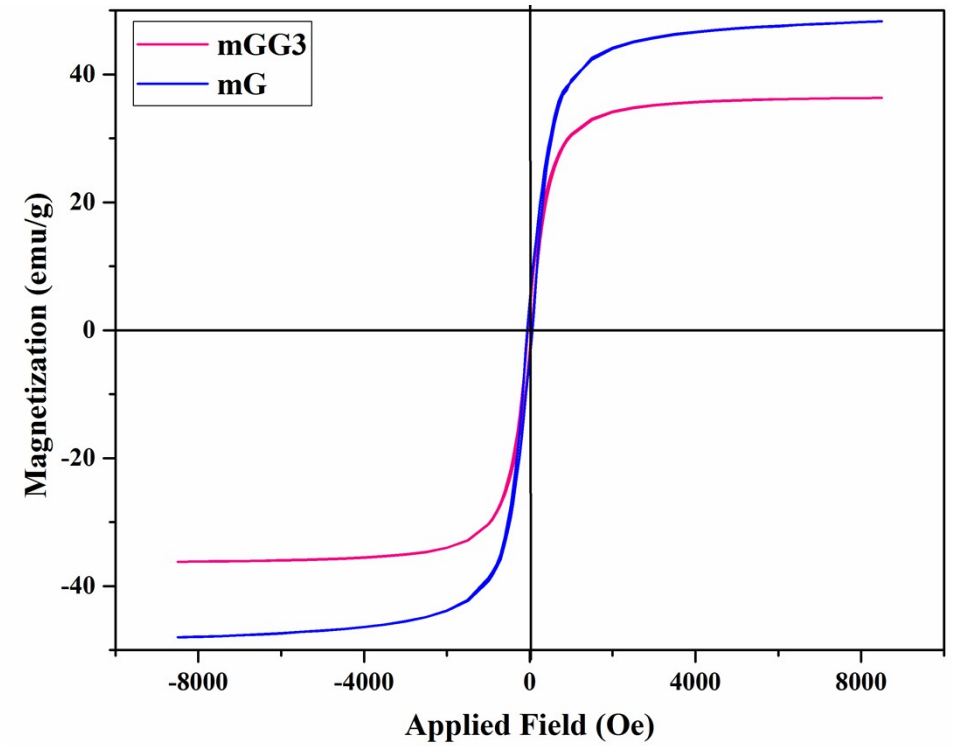


Fig. S4: Magnetization as a function of the applied magnetic field of the mG and mGG3 nanocomposites

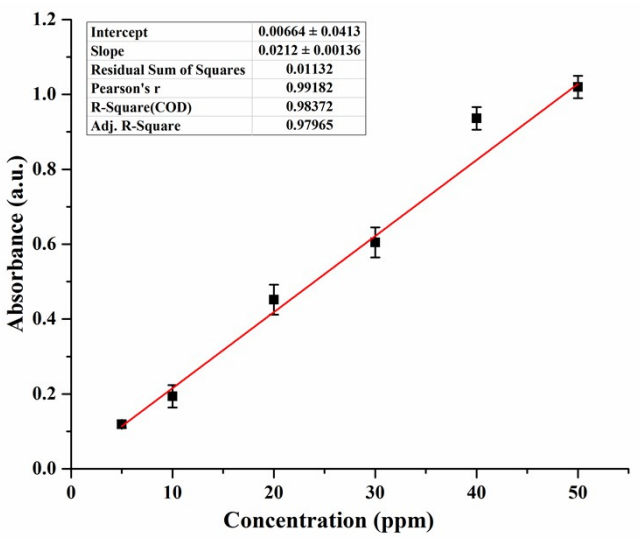


Fig. S5: Calibration curve of Pd(II) complex in water for optimizing loading condition

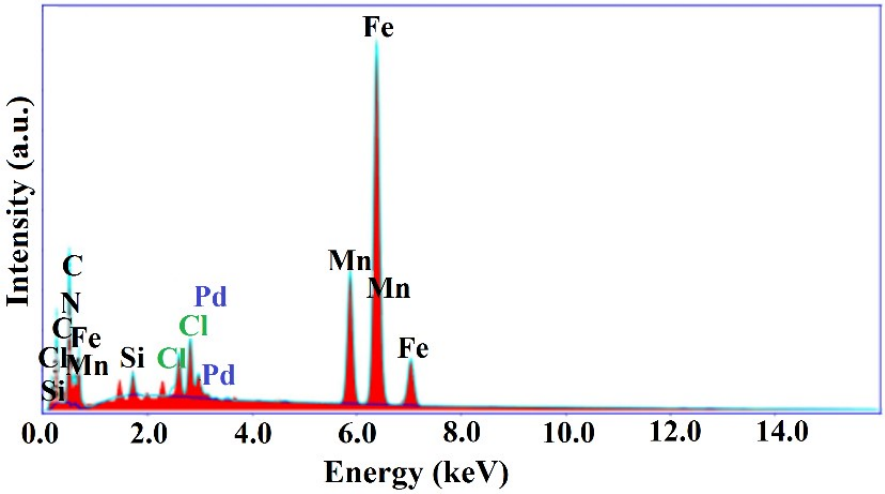


Fig. S6: EDAX spectrum of Pd(II) complex@mGG3F system

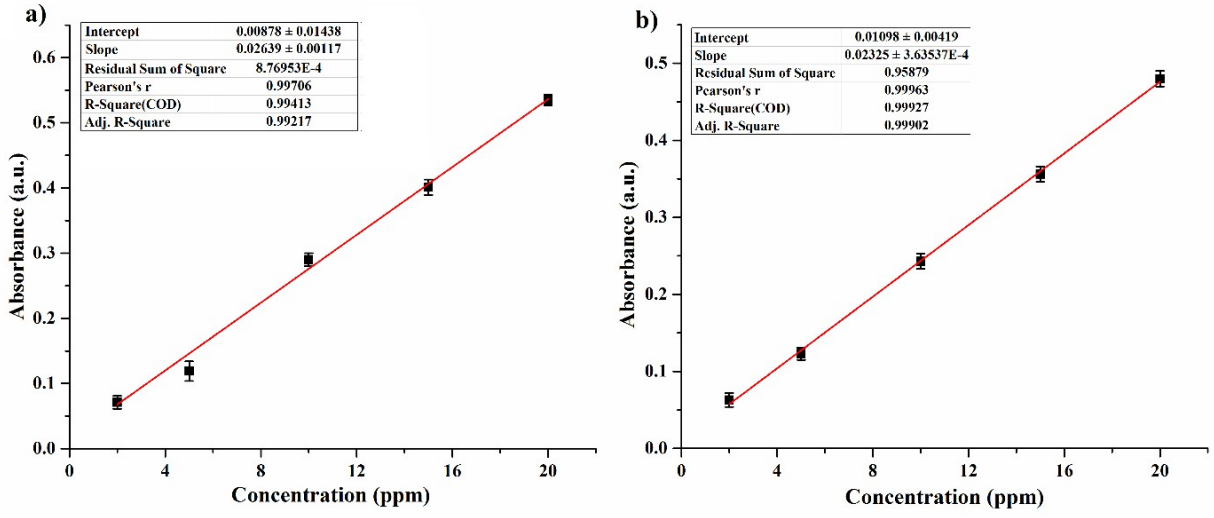


Fig. S7: Calibration curves of Pd(II) complex in PBS a) pH=7.2 and b) pH= 5.4 for *in vitro* release studies

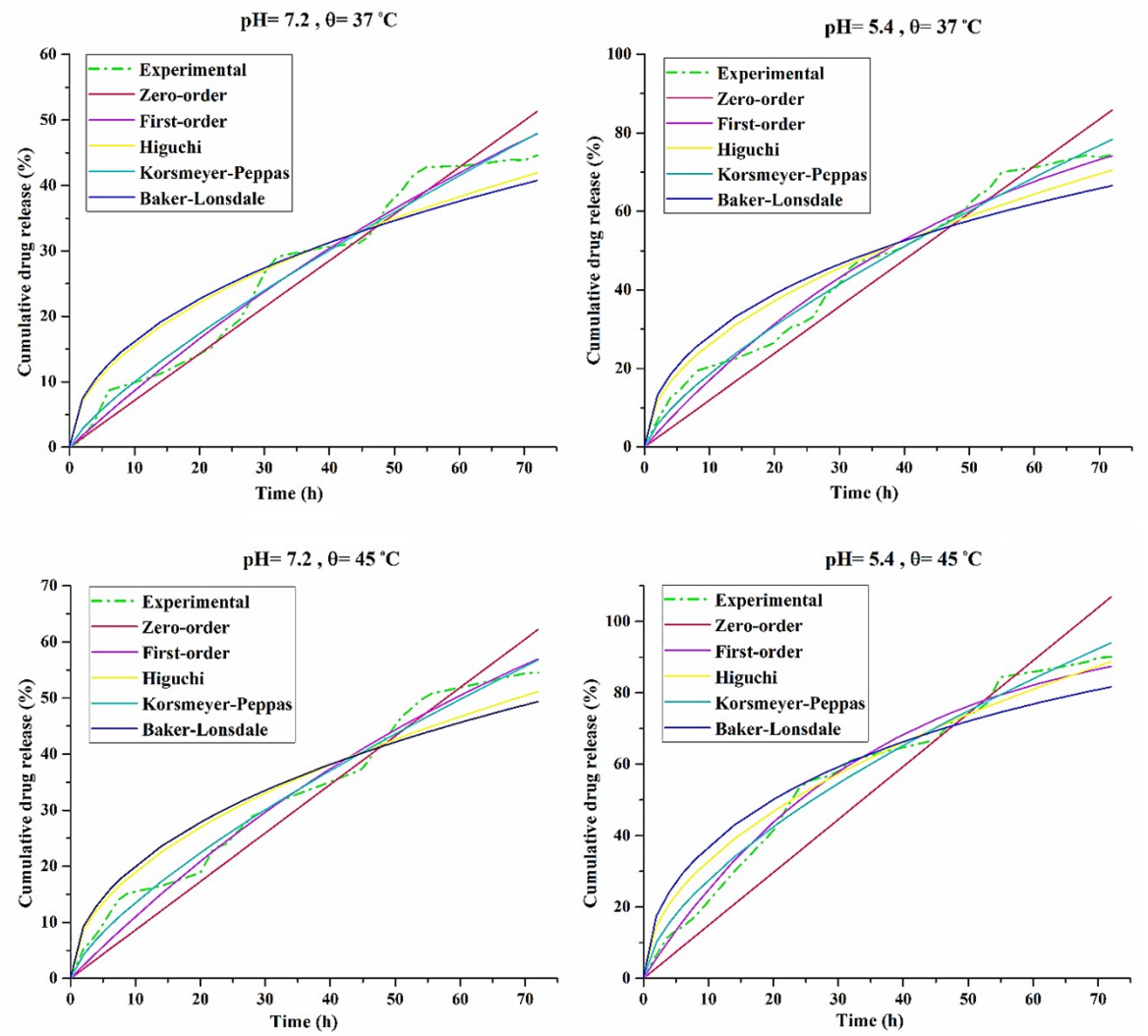


Fig. S8: Experimental (green dashed line) and predicted models (colored lines) of the cumulative release

- Equations of different kinetic models:

(1) Zero-order: $F = k_0.t$

(2) First-order: $F = 1 - \exp(-k_1 t)$

(3) Higuchi: $F = k_H.t^{0.5}$

(4) Korsmeyer–Peppas: $F = k_{KP}.t^n$

(5) Baker-Lonsdale: $3/2[1-(1-F)^{2/3}]$

$-F=k_{BL}.t$

In these equations, k_0, k_1, k_H, k_{KP} and k_{BL}, t and F are parameter of models, time and cumulative release, respectively.

Table. S1: Data of the optimization loading condition

Optimized factor	amount	LC (%)	EE (%)
concentration (ppm)	80	5.00	62.63
	160	11.71	73.32
	200	14.76	73.93
	240	17.71	73.95
	280	19.30	69.05
time (h)	12	9.96	41.57
	24	17.72	73.97
	48	15.31	63.89
	72	2.71	11.32
temperature (°C)	27	17.70	73.93
	35	16.89	70.36
	45	6.50	27.16
	55	2.53	12.59

Table. S2: Experimental and predicted cumulative release values for various kinetic models at pH=7.2 and temperature 37 °C

Time (h)	CDR (%)					
	Experimental	predicted				
		zero-order	first-order	Higuchi	Korsmeyer-Peppas	Baker-Lonsdale
0	0	0.00	0.00	0.00	0.00	0.06
2	1.19617	1.43	1.79	6.99	2.79	7.44
4	4.21351	2.85	3.56	9.88	4.84	10.45
6	8.67922	4.28	5.29	12.11	6.68	12.72
8	9.24541	5.70	6.99	13.98	8.39	14.62
14	11.2	9.98	11.90	18.49	13.08	19.12
20	14.20553	14.26	16.56	22.10	17.36	22.65
22	15.27411	15.68	18.06	23.18	18.72	23.69
24	17.95354	17.11	19.53	24.21	20.06	24.67
26	19.08592	18.53	20.97	25.20	21.37	25.61
28	22.62659	19.96	22.39	26.15	22.67	26.51
30	26.62978	21.39	23.78	27.07	23.94	27.38
32	29.10984	22.81	25.15	27.96	25.20	28.21
39	30.52	27.80	29.75	30.86	29.48	30.91
45	31.23105	32.08	33.46	33.15	33.03	33.00
47	33.38416	33.50	34.66	33.88	34.19	33.66
49	37.16407	34.93	35.83	34.59	35.34	34.30
51	39.01415	36.36	36.98	35.29	36.48	34.93
53	41.6856	37.78	38.11	35.98	37.61	35.54
55	42.80202	39.21	39.22	36.65	38.73	36.14
61	43	43.48	42.44	38.60	42.05	37.86
68	43.92643	48.47	45.97	40.75	45.83	39.73
70	43.86263	49.90	46.94	41.35	46.90	40.25
72	44.58033	51.33	47.89	41.93	47.96	40.75

Table. S3: experimental and predicted cumulative release values for various kinetic models at pH=5.4 and temperature 37 °C

Time (h)	CDR (%)					
	Experimental	predicted				
		Zero-order	First-order	Higuchi	Korsmeyer -Peppas	Baker-Lonsdale
0	0	0.00	0.00	0.00	0.00	0.06
2	6.80581	2.38	3.69	11.75	5.78	13.23
4	12.47672	4.77	7.24	16.62	9.57	18.46
6	15.44405	7.15	10.66	20.36	12.85	22.38
8	19.37327	9.54	13.96	23.51	15.84	25.62
14	22.5	16.69	23.13	31.10	23.80	33.17
20	26.55113	23.84	31.33	37.17	30.85	38.95
22	30.23534	26.22	33.86	38.98	33.07	40.63
24	31.26075	28.61	36.30	40.72	35.23	42.22
26	33.20267	30.99	38.65	42.38	37.34	43.73
28	38.80158	33.37	40.91	43.98	39.41	45.16
30	41.32427	35.76	43.09	45.52	41.44	46.53
32	46.60558	38.14	45.19	47.01	43.43	47.83
39	50.2	46.48	51.95	51.90	50.16	52.02
45	55.60739	53.63	57.07	55.75	55.66	55.21
47	57.96674	56.02	58.65	56.98	57.45	56.20
49	59.89959	58.40	60.18	58.18	59.22	57.16
51	63.66547	60.79	61.65	59.35	60.97	58.10
53	65.67091	63.17	63.06	60.51	62.70	59.01
55	69.96311	65.55	64.42	61.64	64.41	59.89
61	71.5	72.71	68.22	64.91	69.45	62.40
68	74.31883	81.05	72.13	68.54	75.17	65.10
70	73.74714	83.43	73.16	69.54	76.77	65.83
72	74.50031	85.82	74.15	70.52	78.36	66.54

Table. S4: experimental and predicted cumulative release values for various kinetic models at pH=7.2 and temperature 45 °C

Time (h)	CDR (%)					
	Experimental	Predicted				
		Zero-order	First-order	Higuchi	Korsmeyer-Peppas	Baker-Lonsdale
0	0	0.00	0.00	0.00	0.00	0.06
2	5.18341	1.73	2.31	8.52	4.21	9.23
4	7.80202	3.46	4.58	12.06	6.97	12.94
6	11.54206	5.19	6.79	14.77	9.35	15.74
8	14.95513	6.91	8.94	17.05	11.52	18.07
14	16.5	12.10	15.12	22.55	17.30	23.56
20	18.83073	17.29	20.88	26.96	22.41	27.83
22	23.17682	19.02	22.71	28.27	24.02	29.09
24	24.01415	20.74	24.50	29.53	25.58	30.28
26	26.45434	22.47	26.25	30.74	27.11	31.41
28	28.9344	24.20	27.96	31.90	28.61	32.50
30	29.85944	25.93	29.62	33.02	30.08	33.54
32	31.5899	27.66	31.25	34.10	31.52	34.53
39	34.6	33.71	36.66	37.65	36.39	37.75
45	37.33153	38.90	40.96	40.44	40.37	40.23
47	40.78448	40.62	42.33	41.33	41.67	41.02
49	43.4958	42.35	43.66	42.20	42.95	41.78
51	46.64572	44.08	44.97	43.05	44.21	42.52
53	48.64732	45.81	46.24	43.88	45.46	43.24
55	50.67284	47.54	47.49	44.71	46.70	43.95
61	52.1	52.73	51.05	47.08	50.35	45.97
68	53.91845	58.78	54.90	49.71	54.48	48.16
70	54.42084	60.51	55.95	50.43	55.64	48.76
72	54.51654	62.23	56.97	51.15	56.79	49.35

Table. S5: experimental and predicted cumulative release values for various kinetic models at pH=5.4 and temperature 45 °C

Time (h)	CDR (%)					
	Experimental	predicted				
		Zero-order	First-order	Higuchi	Korsmeyer-Peppas	Baker-Lonsdale
0	0	0.00	0.00	0.00	0.00	0.06
2	6.66969	2.97	5.59	14.79	10.19	17.49
4	12.3406	5.94	10.87	20.92	15.66	24.29
6	14.39777	8.91	15.86	25.62	20.14	29.34
8	17.39868	11.88	20.56	29.59	24.07	33.48
14	30	20.78	33.16	39.14	34.05	42.99
20	41.32518	29.69	43.76	46.78	42.48	50.13
22	47.57472	32.66	46.91	49.07	45.07	52.18
24	53.47944	35.63	49.88	51.25	47.56	54.11
26	55.85422	38.60	52.68	53.34	49.99	55.92
28	56.44133	41.57	55.33	55.35	52.34	57.64
30	57.92681	44.54	57.83	57.30	54.62	59.27
32	61.23625	47.51	60.18	59.17	56.85	60.82
39	64.3	57.90	67.45	65.33	64.27	65.71
45	66.85966	66.81	72.61	70.17	70.24	69.36
47	71.21266	69.77	74.14	71.71	72.16	70.48
49	73.36057	72.74	75.59	73.22	74.04	71.56
51	74.61919	75.71	76.95	74.70	75.90	72.61
53	77.23897	78.68	78.24	76.16	77.74	73.62
55	84.42318	81.65	79.46	77.58	79.54	74.59
61	86.2	90.56	82.72	81.70	84.82	77.32
68	88.54932	100.95	85.87	86.26	90.73	80.19
70	89.82609	103.92	86.66	87.52	92.37	80.95
72	90.10104	106.89	87.41	88.76	94.00	81.69

Table. S6: Goodness of fit values for release process at pH=7.2 and temperature 37 °C

Parameter	Mechanism models				
	Zero-order	First-order	Higuchi	Korsmeyer-Peppas	Baker-Lonsdale
N-observed	24	24	24	24	24
DF	23	23	23	22	23
R_obs-pre	0.9809	0.9881	0.9739	0.9866	0.9685
Rsqr	0.9491	0.9758	0.9017	0.9731	0.8806
Rsqr_adj	0.9491	0.9758	0.9017	0.9719	0.8806
MSE	11.3917	5.4220	22.0008	6.2842	26.7062
MSE_root	3.3752	2.3285	4.6905	2.5068	5.1678
Weighting	1	1	1	1	1
SS	262.0082	124.7058	506.017	138.2526	614.2436
WSS	262.0082	124.7058	506.017	138.2526	614.2436
AIC	135.6410	117.8230	151.437	122.2980	156.0894
MSC	2.7598	3.5022	2.1016	3.3157	1.9077
Model parameter	k_0=0.713	k_1= 0.009	k_H= 4.942	k_{KP}= 1.611 n= 0.794	k_{BL}= 0.000

Table. S7: Goodness of fit values for release process at pH=5.4 and temperature 37 °C

Parameter	Mechanism models				
	Zero-order	First-order	Higuchi	Korsmeyer-Peppas	Baker-Lonsdale
N-observed	24	24	24	24	24
DF	23	23	23	22	23
R_obs-pre	0.9878	0.9901	0.9818	0.9930	0.9693
Rsqr	0.9389	0.9799	0.9370	0.9860	0.8953
Rsqr_adj	0.9389	0.9799	0.9370	0.9854	0.8953
MSE	33.5739	11.0274	34.6140	8.0402	57.5681
MSE_root	5.7943	3.3207	5.8834	2.8355	7.5874
Weighting	1	1	1	1	1
SS	772.2005	253.6291	796.1210	176.8839	1324.0665
WSS	772.2005	253.6291	796.1210	176.8839	1324.0665
AIC	161.5819	134.8610	162.3140	128.2118	174.5231
MSC	2.5511	3.6645	2.5206	3.9415	2.0119
Model parameter	k_0=1.192	k_1= 0.019	k_H= 8.311	k_{KP}= 3.488 n= 0.728	k_{BL}= 0.002

Table. S8: Goodness of fit values for release process at pH=7.2 and temperature 45 °C

Parameter	Mechanism models				
	Zero-order	First-order	Higuchi	Korsmeyer-Peppas	Baker-Lonsdale
N-observed	24	24	24	24	24
DF	23	23	23	22	23
R_obs-pre	0.9884	0.9928	0.9819	0.9932	0.9746
Rsqr	0.9388	0.9797	0.9382	0.9863	0.9127
Rsqr_adj	0.9388	0.9797	0.9382	0.9856	0.9127
MSE	17.5776	5.8319	17.7762	4.1260	25.0974
MSE_root	4.1926	2.4149	4.2162	2.0313	5.0097
Weighting	1	1	1	1	1
SS	404.2855	134.1334	408.8517	90.7722	577.2395
WSS	404.2855	134.1334	408.8517	90.7722	577.2395
AIC	146.0509	119.5720	146.3205	112.2005	154.5982
MSC	2.5484	3.6517	2.5372	3.9588	2.1923
Model parameter	k_0=0.864	k_1= 0.012	k_H= 6.028	k_{KP}= 2.548 n= 0.726	k_{BL}= 0.001

Table. S9: Goodness of fit values for release process at pH=5.4 and temperature 45 °C

Parameter	Mechanism models				
	Zero-order	First-order	Higuchi	Korsmeyer-Peppas	Baker-Lonsdale
N-observed	24	24	24	24	24
DF	23	23	23	22	23
R_obs-pre	0.9671	0.9952	0.9911	0.9919	0.9829
Rsqr	0.8648	0.9901	0.9650	0.9831	0.9214
Rsqr_adj	0.8648	0.9901	0.9650	0.9824	0.9214
MSE	107.4380	7.8903	27.8178	14.0041	62.4775
MSE_root	10.3652	2.8090	5.2743	3.7422	7.9043
Weighting	1	1	1	1	1
SS	2471.0744	181.4760	639.8090	308.0902	1436.9815
WSS	2471.0744	181.4760	639.8090	308.0902	1436.9815
AIC	189.4978	126.8270	157.0681	141.5294	176.4872
MSC	1.7364	4.3477	3.0877	3.7351	2.2786
Model parameter	k_0= 1.485	k_1= 0.029	k_H= 10.461	k_{KP}= 6.629 n= 0.620	k_{BL}= 0.003