

Article

Preparation and Characterization of Chitosan-Alginate Microspheres Loaded with Quercetin

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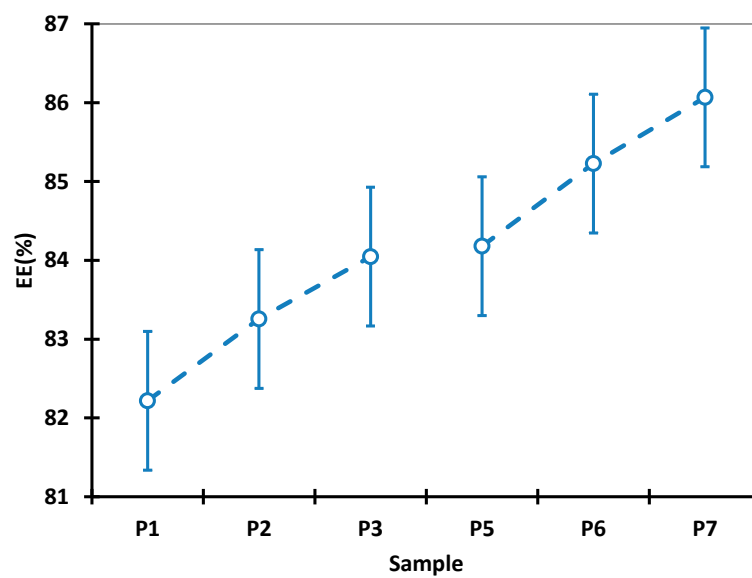
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Supplementary Figure S1. Interval plots of the microspheres' entrapment efficiency (EE(%)) for sample factor levels

Supplementary Table S1. Percentage of swelling index (idxSWL (%)) from microspheres
The results belong to the Time factor levels

Time	idxSWL (%)
1h	1797.265h ±1550.706
2h	3603.814g ±2826.160
3h	5063.423f ±3736.602
4h	6165.873e ±4319.882
5h	6922.697d ±4663.962
6h	7470.614c ±4892.880
7h	7790.508b ±5021.012
8h	7941.329a ±5082.533

Note: Different letters that follow the means prescribe statistically significant means. Results were calculated with post-hoc Duncan ($P = 0.05$) multiple comparisons test, within the two-way ANOVA test ($P = 0.05$).

Supplementary Table S2. Percentage of swelling index (idxSWL (%)) from microspheres
The results belong to the Sample*pH interaction factor levels

pH	P1	P2	P3	P4	P5	P6	P7	P8
1.2	1473.425ah ±538.853	1427.960ai ±539.484	1404.273aj ±542.794	1528.835ag ±564.444	1307.667al ±496.099	1130.668am ±402.629	979.569an ±343.418	1365.924ak ±528.571
3	2275.329z ±881.996	2218.219aa ±843.629	2112.933ab ±794.380	2401.298y ±882.953	1783.587ad ±800.941	1745.538ae ±788.417	1690.836af ±778.962	1935.494ac ±841.999
5	6113.748r ±2723.801	5847.415s ±2622.650	5435.710t ±2514.804	6561.800q ±2730.620	4945.600v ±2379.324	4701.554w ±2306.529	4312.221x ±2065.922	5087.868u ±2456.338
6.8	10074.148j ±2983.065	9590.240k ±3099.716	8993.680l ±2941.007	10548.054g ±3193.720	8401.038n ±2888.310	8052.005o ±2917.265	7544.502p ±2795.821	8672.039m ±2982.315
7.4	12730.665b ±3802.067	12091.470c ±3822.017	11447.610d ±3564.082	13154.598a ±3894.450	10855.442f ±3475.770	10481.360h ±3318.026	10291.154i ±3382.006	11062.138e ±3486.226

Note: Different letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).

Supplementary Table S3. Percentage of swelling index (idxSWL (%)) from microspheres

The results belong to the Sample*Time interaction factor levels

Time (h)	P1	P2	P3	P4	P5	P6	P7	P8
1	2111.586bb ±1708.746	1977.970bc ±1648.481	1863.390bd ±1570.016	2173.230ba ±1740.397	1636.347bf ±1415.783	1533.027bg ±1355.169	1390.005bh ±1252.721	1692.562be ±1465.031
2	4314.516as ±3284.754	3809.003au ±2761.908	3576.851av ±2638.858	4588.448aq ±3402.536	3218.112ax ±2506.902	3089.102ay ±2459.149	2858.531az ±2297.026	3375.949aw ±2606.158
3	5847.523ai ±4227.424	5419.997al ±3776.339	5071.436an ±3551.664	6180.719ag ±4299.870	4646.097ap ±3450.504	4349.597ar ±3266.790	4211.661at ±3227.409	4780.357ao ±3462.475
4	6876.459y ±4674.870	6611.087ab ±4437.5961	6259.761ae ±4227.238	7348.459r ±4879.085	5716.531aj ±4009.670	5443.489ak ±3892.903	5218.928am ±3817.495	5852.271ai ±4053.975
5	7680.065m ±5036.429	7400.024q ±4833.197	6975.384w ±4538.154	8097.092h ±5232.432	6458.980ac ±4331.477	6204.656af ±4222.779	5935.447ah ±4170.873	6629.931aa ±4399.728
6	8261.844g ±5295.406	8019.329i ±5159.513	7485.099p ±4768.962	8541.580d ±5423.352	7040.053v ±4540.720	6771.981z ±4448.116	6440.157ad ±4374.256	7204.868t ±4613.712
7	8534.763e ±5368.766	8265.205g ±5224.243	7787.080 ±4876.678	8824.191b ±5550.553	7402.509q ±4742.855	7123.249u ±4614.031	6766.793z ±4533.979	7620.270n ±4807.913
8	8640.945c ±5406.801	8377.873f ±5256.6826	8011.727j ±4971.906	8957.618a ±5649.230	7550.705o ±4800.800	7262.703s ±4678.650	6887.728x ±4609.238	7841.332k ±4850.132

Note: Different letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).

Supplementary Table S4. Percentage of swelling index (idxSWL (%)) from microspheres

The results belong to the Sample factor levels

Sample	idxSWL (%)
P1	6533.463b ±5033.793
P2	6235.061c ±4838.292
P3	5878.841d ±4554.464
P4	6838.917a ±5206.396
P5	5458.667f ±4376.188
P6	5222.225g ±4251.799
P7	4963.656h ±4154.492
P8	5624.693e ±4448.765

Note: Different letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05)

Supplementary Table S5. Percentage of swelling index (idxSWL (%)) from microspheres

The results belong to the P1*pH*Time interaction factor levels

Time (h)	P1_pH1.2	P1_pH3	P1_pH5	P1_pH6.8	P1_pH7.4
1	456.777ic ±0.424	645.287hw hx ±0.525	1198.023he ±0.469	3521.980eq ±1.367	4735.863ec ±0.719
2	856.900hp ±0.699	1323.027ha ±0.555	2997.160fb ±0.497	7442.653cv ±95.926	8952.840ca ±0.537
3	1246.487hd ±0.755	1832.407gj ±0.390	4679.867ee ±4.621	9547.803br ±0.600	11931.053ap ±2.901
4	1547.333gt ±0.396	2292.380fu fv ±0.933	6209.833dm ±1.601	10853.383bd ±0.978	13479.363uv ±0.882
5	1741.553go ±0.681	2676.103fj ±0.792	7480.103cu ±1.104	11767.100aq ±0.940	14735.467l ±0.685
6	1894.560gh ±0.479	2998.780fb ±0.455	8430.207cg ±1.576	12225.417al ±1.046	15760.257g ±1.038
7	1995.650ge ±0.540	3175.783ew ±0.568	8910.327cb ±1.129	12547.567af ±1.489	16044.487d ±1.790
8	2048.137gb ±0.830	3258.867eu ± 27.955	9004.460bz ±1.263	12687.277ad ±1.079	16205.987c ±1.913

Note: Different group letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).

Supplementary Table S6. Percentage of swelling index (idxSWL (%)) from microspheres

The results belong to the P2*pH*Time interaction factor levels

Time (h)	P2_pH1.2	P2_pH3	P2_pH5	P2_pH6.8	P2_pH7.4
1	435.303id ±1.211	631.933hx hy ±0.875	978.100hl ±0.829	3275.893et ±1.271	4568.620ef ±1.081
2	806.050hq ±1.315	1302.777hb ±0.964	2896.567fd ±1.162	6185.953dn ±1.099	7853.670co ±2.227
3	1175.643hf ±1.505	1826.553gj gk ±0.741	4575.710ef ±0.962	8767.513cc ±1.081	10754.563be ±1.496
4	1480.757gw ±0.919	2272.223fw ±1.038	6054.140dp ±0.868	10452.983bh ±1.727	12795.333ac ±1.001
5	1684.350gp ±0.671	2621.343fl ±0.942	7174.140cz ±1.148	11385.107av aw ±1.911	14135.180q ±1.288
6	1854.713gi ±1.044	2871.620fe ±1.327	8066.483cl ±1.060	12047.663an ±1.161	15256.163i ±1.656
7	1958.990gg ±0.703	3063.430fa ±0.516	8447.027cf ±0.940	12275.613ak ±1.806	15580.963h ±2.100
8	2027.873gd ±0.753	3155.870ex ±1.506	8587.157ce ±1.076	12331.197aj ±2.122	15787.267f ±2.295

Note: Different group letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).

Supplementary Table S7. Percentage of swelling index (idxSWL (%)) from microspheres

The results belong to the P3*pH*Time interaction factor levels

Time (h)	P3_pH1.2	P3_pH3	P3_pH5	P3_pH6.8	P3_pH7.4
1	416.917ie ±0.601	613.850hz ±0.205	857.050hp ±0.764	3080.260ez ±0.821	4348.873ei ±1.137
2	784.763hr ±1.123	1248.227hd ±0.831	2485.083fp ±0.784	5938.040dr ±0.772	7428.143cw ±0.797
3	1128.477hg ±0.838	1786.767gn ±0.487	4155.423ej ±1.086	7973.410cn ±1.045	10313.103bj ±1.591
4	1448.620gx ±47.773	2153.520fy ±0.694	5711.593dt ±1.114	9536.800br ±1.300	12448.270ag ±0.928
5	1667.210gq ±1.271	2467.757fq ±0.619	6784.837df ±1.317	10498.870bg ±1.250	13458.247w ±0.776
6	1815.150gk gl ±1.066	2693.327fi ±0.876	7514.070cs ±1.150	11255.170ay ±1.539	14147.780q ±1.590
7	1954.657gg ±0.646	2888.133fd ±0.792	7862.407co ±0.996	11681.263ar ±2.068	14548.940n ±2.765
8	2018.393gd ±0.681	3051.880fa ±1.283	8115.217cj ±1.055	11985.623ao ±2.127	14887.520k ±1.954

Note: Different group letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).

Supplementary Table S8. Percentage of swelling index (idxSWL (%)) from microspheres

The results belong to the P4*pH*Time interaction factor levels

Time (h)	P4_pH1.2	P4_pH3	P4_pH5	P4_pH6.8	P4_pH7.4
1	474.700ib ±0.403	696.883hu ±0.590	1201.290he ±0.610	3728.180en ±0.885	4765.097eb ±0.872
2	874.710ho ±0.764	1448.537gx ±0.389	3554.980ep ±0.700	7516.130cs ±0.787	9547.883br ±0.576
3	1288.293hb hc ±0.320	2043.430gc ±0.767	5459.497du ±0.496	9765.663bp ±0.534	12346.710ai ±0.830
4	1603.033gr ±0.338	2491.790fp ±0.707	7129.957db ±1.318	11373.147aw ±0.974	14144.367q ±0.951
5	1803.737gl gm ±0.558	2822.287ff ±0.935	8215.717ci ±0.863	12425.110ah ±1.096	15218.610j ±0.897
6	1956.170gg ±0.328	3116.957ey ±0.728	8742.110cd ±1.524	12946.800aa ±0.765	15945.863e ±0.662
7	2093.567ga ±0.696	3288.410et ±0.380	9029.650by ±1.934	13223.477z ±1.492	16485.853b ±1.527
8	2136.473fz ±0.488	3302.093es ±0.926	9161.203bv ±1.979	13405.923x ±1.846	16782.397a ±0.716

Note: Different group letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).

Supplementary Table S9. Percentage of swelling index (idxSWL (%)) from microspheres

The results belong to the P5*pH*Time interaction factor levels

Time (h)	P5_pH1.2	P5_pH3	P5_pH5	P5_pH6.8	P5_pH7.4
1	384.983if ±0.418	445.157ic id ±0.289	784.587hr ±0.283	2618.067fl fm ±0.570	3948.940el ±0.255
2	732.370ht ±0.835	894.810hn ±0.485	2178.903fx ±0.406	5229.780dx ±0.584	7054.697dc ±0.230
3	1078.823hi ±0.776	1288.540hb hc ±0.721	3591.763eo ±0.565	7498.550ct ±0.687	9772.807bp ±0.525
4	1365.343gy gz ±0.658	1684.603gp ±0.278	4959.020dz ±0.428	9093.400bw ±1.003	11480.290au ±0.964
5	1572.137gs ±0.593	2060.910gb ±0.632	6056.623dp ±0.701	9979.607bm ±0.752	12625.623ae ±0.836
6	1729.663go ±1.223	2451.150fr ±1.549	6992.553de ±0.429	10536.827bf ±0.752	13490.070u ±0.9070
7	1794.250gm gn ±0.478	2641.250fk ±0.446	7443.593cv ±1.513	10983.810ba ±2.091	14149.643q ±1.351
8	1803.763gl gm ±0.435	2802.273fg ±0.835	7557.760cr ±2.066	11268.263ay ±1.857	14321.463p ±0.341

Note: Different group letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).

Supplementary Table S10. Percentage of swelling index (idxSWL (%)) from microspheres

The results belong to the P6*pH*Time interaction factor levels

Time	P6_pH1.2	P6_pH3	P6_pH5	P6_pH6.8	P6_pH7.4
1h	379.303if ±0.202	407.220ie ±1.874	649.597hw ±0.225	2481.540fp ±0.185	3747.473em ±0.371
2h	678.393hv ±0.462	854.020hp ±0.673	2057.203gb gc ±0.248	4867.977ea ±0.543	6987.917de ±0.636
3h	928.083hm ±0.160	1281.093hc ±0.103	3396.293er ±0.272	6724.627dg ±0.702	9417.887bs ±0.605
4h	1174.967hf ±0.158	1677.577gp gq ±0.681	4693.370ed ±0.957	8382.453ch ±0.275	11289.077ax ±0.362
5h	1360.163gz ±0.335	2048.117gb gc ±0.706	5756.450ds ±1.019	9593.530bq ±0.929	12265.020ak ±0.531
6h	1454.693gx ±0.678	2384.230fs ±0.520	6652.060dh ±0.931	10434.770bi ±0.518	12934.150aa ±5.181
7h	1521.520gu ±0.215	2588.487fn ±0.376	7145.203da ±1.778	10886.183bc ±1.025	13474.850v ±1.343
8h	1548.223gt ±0.224	2723.563fh ±0.314	7262.257cy ±0.545	11044.960az ±1.075	13734.510r ±1.117

Note: Different group letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).

Supplementary Table S11. Percentage of swelling index (idxSWL (%)) from microspheres

The results belong to the P7*pH*Time interaction factor levels

Time (h)	P7_pH1.2	P7_pH3	P7_pH5	P7_pH6.8	P7_pH7.4
1	308.770ig ±0.387	387.670if ±0.653	626.213hy hz ±0.284	2094.073ga ±0.737	3533.300eq ±0.256
2	596.240ia ±0.159	802.433hq ±0.403	1901.897gh ±0.285	4445.310eg ±0.675	6546.773dj ±0.543
3	853.373hp ±0.119	1205.470he ±0.343	3237.780ev ±0.455	6485.967dk ±0.392	9275.717bu ±0.586
4	1041.837hj ±0.413	1612.200gr ±0.255	4394.020eh ±0.725	7994.533cm ±1.052	11052.050az ±1.378
5	1166.590hf ±0.273	2004.283ge ±0.556	5301.637dw ±0.349	9049.467bx ±1.014	12155.257am ±0.907
6	1248.843hd ±0.440	2346.220ft ±0.236	5990.780dq ±1.082	9828.100bo ±0.744	12786.843ac ±0.192
7	1297.750hb ±0.385	2561.877fo ±0.419	6428.593dl ±1.169	10198.543bl ±0.740	13347.203y ±1.054
8	1323.147ha ±1.537	2606.533fm ±0.111	6616.847di ±0.661	10260.023bk ±1.305	13632.090t ±1.579

Note: Different group letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).

Supplementary Table S12. Percentage of swelling index (idxSWL (%)) from microspheres

The results belong to the P8*pH*Time interaction factor levels

Time (h)	P8_pH1.2	P8_pH3	P8_pH5	P8_pH6.8	P8_pH7.4
1	410.690ie ±0.608	449.950ic ±0.338	802.647hq ±0.329	2720.317fh ±0.620	4079.207ek ±0.251
2	769.073hs ±0.307	993.303hk ±0.414	2293.713fu ±0.574	5441.483dv ±0.913	7382.173cx ±0.739
3	1095.507hh ±0.260	1498.203gv ±0.833	3753.277em ±0.175	7640.420cq ±0.848	9914.377bn ±0.651
4	1376.493gy ±0.368	1892.430gh ±0.245	5010.570dy ±0.896	9325.203bt ±1.426	11656.660as ±0.436
5	1612.373gr ±0.539	2279.257fv fw ±0.691	6082.457do ±0.564	10318.707bj ±1.146	12856.863ab ±47.953
6	1796.710gm gn ±0.559	2591.740fn ±4.789	7013.023dd ±1.283	10949.133bb ±1.019	13673.733s ±0.344
7	1894.040gh ±0.400	2803.477fg ±0.713	7655.807cp ±1.248	11393.470av ±0.956	14354.557o ±0.445
8	1972.503gf ±0.478	2975.593fc ±0.721	8091.447ck ±0.871	11587.580at ±1.675	14579.537m ±0.847

Note: Different group letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).

Supplementary Table S13. Percentage of QUE released (mQrel (%)) from microspheres

The results belong to the Sample*Time interaction factor levels

Time (h)	P1	P2	P3	P5	P6	P7	QUE
0.25	0.150bh ±0.008	0.290bh ±0.014	0.387bh ±0.013	0.120bh ±0.008	0.117bh ±0.013	0.130bh ±0.008	1.820bg ±0.269
0.5	11.187bc ±0.017	14.473bb ±0.005	15.067ba ±0.033	6.963bf ±0.029	7.480be ±0.008	8.187bd ±0.013	24.467av ±0.314
0.75	22.460aw ±0.028	26.347at ±0.021	28.780ar ±0.025	16.377az ±0.013	17.853ay ±0.029	18.937ax ±0.033	41.477am ±0.338
1	35.143ap ±0.009	38.053ao ±0.017	42.090al ±0.008	25.177au ±0.033	28.167as ±0.013	30.353aq ±0.029	55.440ae ±0.385
2	59.517ai ±0.033	63.357ag ±0.042	67.810af ±0.008	44.717ap ±0.013	49.573an ±0.029	56.087ak ±0.013	76.073y ±0.707
3	77.850ac ±0.022	81.843aa ±0.021	85.193x ±0.021	64.687aj ±0.013	69.277ah ±0.042	74.643ad ±0.029	89.107t ±0.522
4	85.103w ±0.034	87.917u ±0.017	90.227r ±0.017	71.547ae ±0.033	76.270ab ±0.008	80.347y ±0.042	96.217n ±0.682
5	90.337rs ±0.013	92.417o ±0.039	94.917l ±0.033	77.540z ±0.008	80.783w ±0.029	85.140u ±0.008	97.320h ±0.650
6	92.830l ±0.008	94.347j ±0.009	96.483g ±0.021	81.777v ±0.013	84.907t ±0.013	88.443q ±0.029	97.337b ±0.725
8	96.143g ±0.009	96.140e ±0.008	97.733c ±0.021	84.597s ±0.013	87.377p ±0.013	90.913l ±0.029	97.347a ±0.723
12	47.273e ±0.041	51.097d ±0.031	54.307b ±0.013	35.120o ±0.008	38.850lm ±0.008	43.377i ±0.033	66.847a ±0.473
24	69.647b ±0.009	74.387b ±0.009	78.017a ±0.039	55.133m ±0.029	60.357k ±0.033	66.450f ±0.008	84.050a ±0.611

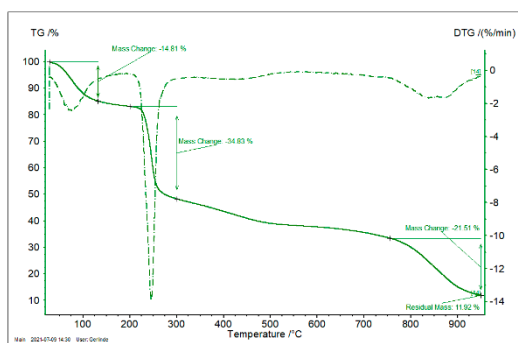
Note: Different letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).

Supplementary Table S14. Percentage of QUE released (mQUErel (%)) from microsphere

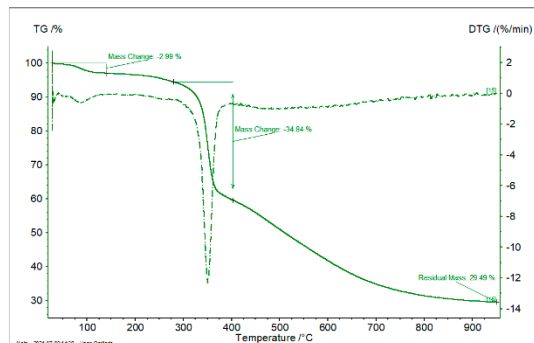
The results belong to the Time interaction factor levels

Time (h)	mQUErel_t (%)
0.25	0.430l ±0.584
0.5	12.546k ±5.732
0.75	24.604j ±8.065
1	36.346i ±9.484
2	48.124h ±9.829
3	59.590g ±9.912
4	69.720f ±9.316
5	77.514e ±8.046
6	83.947d ±7.867
8	88.350c ±6.855
12	90.875b ±5.528
24	92.893a ±4.900

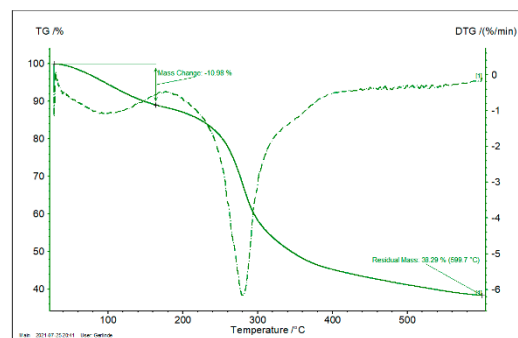
Note: Different letters that follow the means prescribe statistically significant means. Results were calculated with *post-hoc* Duncan (P = 0.05) multiple comparisons test, within the two-way ANOVA test (P = 0.05).



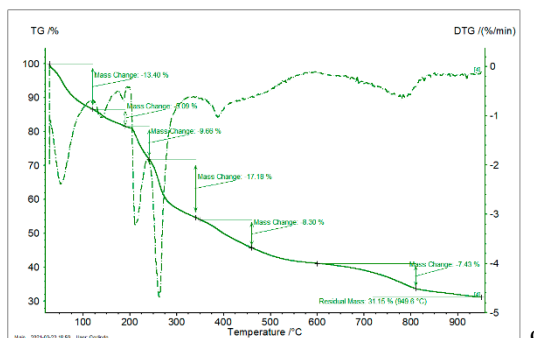
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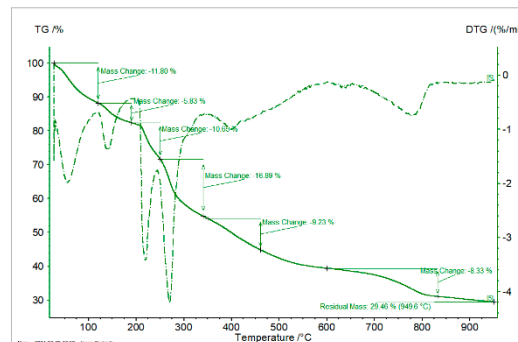
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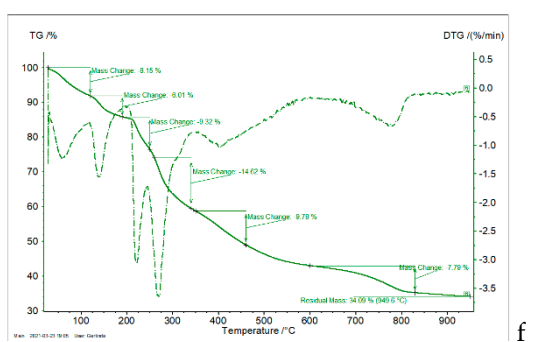
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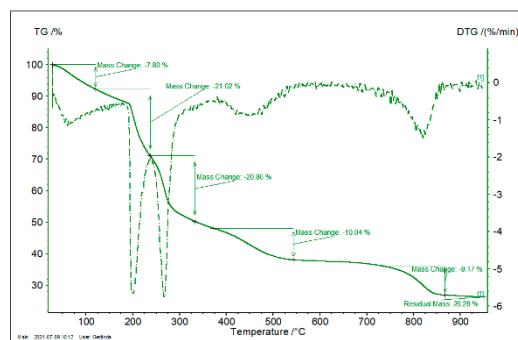
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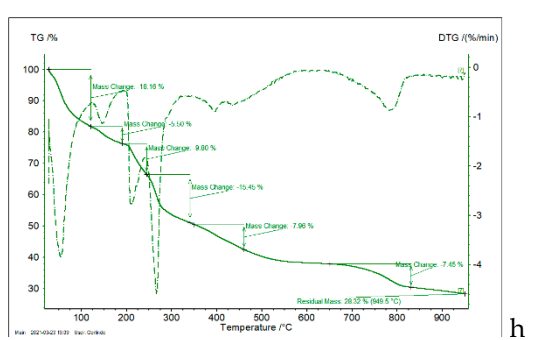
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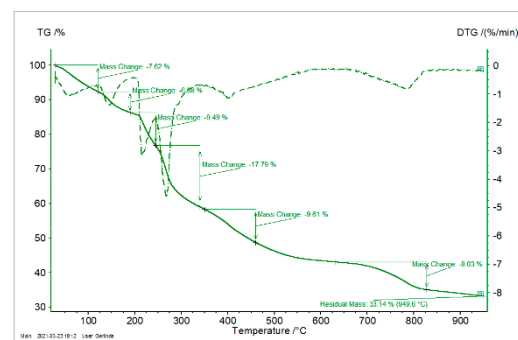
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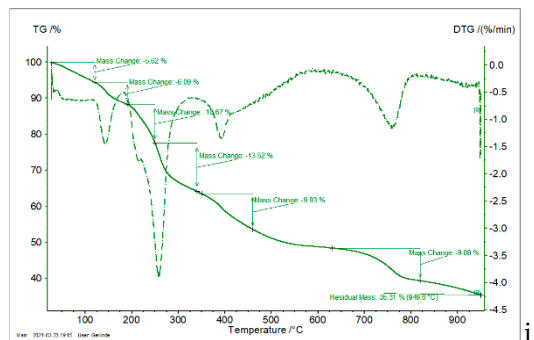
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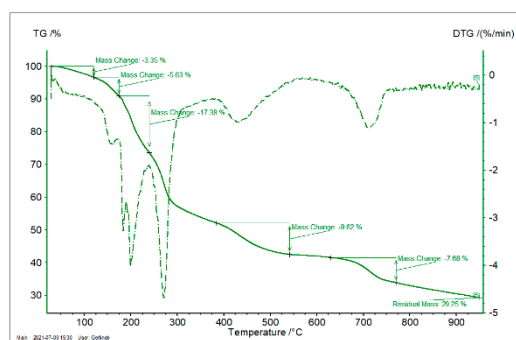
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i

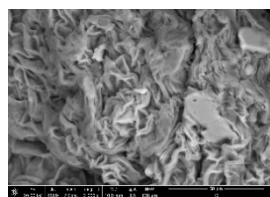
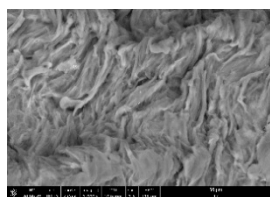
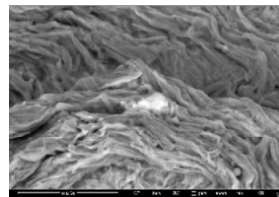
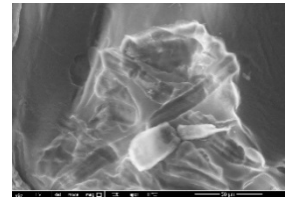
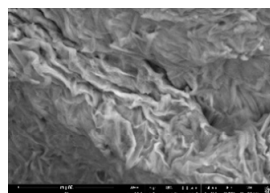
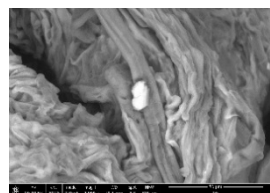
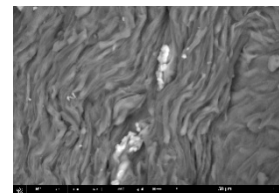
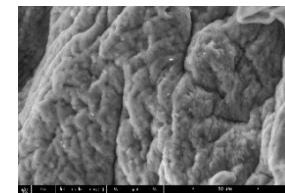
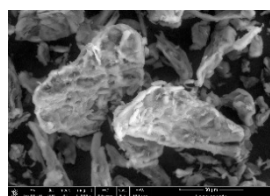
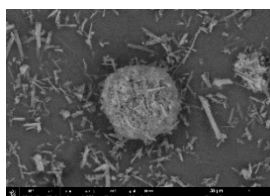
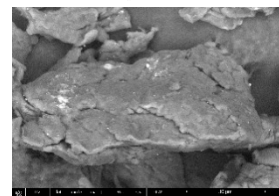


j



Supplementary Figure S2. TG and DTG for: a - Na-Alg, b - QUE, c - Ch, d - P1, e - P2, f - P3, g - P4, h - P5, i - P6, j - P7, k - P8.

k

**P1****P2****P3****P4****P5****P6****P7****P8****Sodium alginate****Quercetin****Chitosan**

Supplementary Figure S3. SEM analysis of quercetin micro-spheres.

Supplementary Table S15. Results of the non-linear regression of the idxSWL (%) time series for sample P1 and all pH factor levels

P1	pH 1.2	pH 3	pH 5	pH 6.8	pH 7.4
Best-fit values					
Ymax	2504	4322	14554	13546	17490
K	0.2281	0.1872	0.1332	0.3863	0.3629
HalfLife	3.039	3.704	5.203	1.794	1.910
Std. Error					
Ymax	55.18	113.3	1342	201.3	185.0
K	0.009860	0.008634	0.01854	0.01598	0.01022
95% Confidence Intervals					
Ymax	2390 to 2619	4087 to 4557	11770 to 17337	13129 to 13963	17106 to 17873
K	0.2076 to 0.2485	0.1692 to 0.2051	0.09477 to 0.1717	0.3532 to 0.4195	0.3417 to 0.3841
HalfLife	2.789 to 3.338	3.380 to 4.096	4.038 to 7.314	1.652 to 1.963	1.804 to 2.028
Goodness of Fit					
Degrees of Freedom	22	22	22	22	22
R square	0.9940	0.9952	0.9792	0.9873	0.9944
Adjusted R square	0.9937	0.9950	0.9783	0.9867	0.9941

Supplementary Table S16. Results of the non-linear regression of the idxSWL (%) time series for sample P2 and all pH factor levels

P2	pH 1.2	pH 3	pH 5	pH 6.8	pH 7.4
Best-fit values					
Ymax	2583	4036	13517	13813	17603
K	0.2036	0.2017	0.1395	0.3239	0.3136
HalfLife	3.405	3.437	4.969	2.140	2.211
Std. Error					
Ymax	60.68	90.59	1318	272.3	200.0
K	0.008796	0.008283	0.02091	0.01569	0.008563
95% Confidence Intervals					
Ymax	2457 to 2709	3848 to 4224	10784 to 16251	13248 to 14378	17188 to 18017
K	0.1853 to 0.2218	0.1845 to 0.2188	0.09614 to 0.1829	0.2913 to 0.3564	0.2958 to 0.3313
HalfLife	3.125 to 3.740	3.167 to 3.757	3.791 to 7.210	1.945 to 2.379	2.092 to 2.343
Goodness of Fit					
Degrees of Freedom	22	22	22	22	22
R square	0.9951	0.9957	0.9744	0.9867	0.9957
Adjusted R square	0.9949	0.9955	0.9733	0.9861	0.9955

Supplementary Table S17. Results of the non-linear regression of the idxSWL (%) time series for sample P3 and all pH factor levels

P3	pH 1.2	pH 3	pH 5	pH 6.8	pH 7.4
Best-fit values					
Ymax	2655	3819	13490	13406	16322
K	0.1886	0.2036	0.1261	0.2977	0.3300
HalfLife	3.675	3.404	5.495	2.328	2.100
Std. Error					
Ymax	74.87	63.60	1652	152.5	216.8
K	0.009393	0.006237	0.02283	0.007861	0.01092
95% Confidence Intervals					
Ymax	2499 to 2810	3687 to 3951	10064 to 16917	13090 to 13723	15873 to 16772
K	0.1691 to 0.2081	0.1907 to 0.2165	0.07880 to 0.1735	0.2814 to 0.3140	0.3074 to 0.3527
HalfLife	3.331 to 4.099	3.201 to 3.635	3.995 to 8.796	2.207 to 2.463	1.966 to 2.255
Goodness of Fit					
Degrees of Freedom	22	22	22	22	22
R square	0.9943	0.9975	0.9698	0.9964	0.9933
Adjusted R square	0.9941	0.9974	0.9684	0.9962	0.9930

Supplementary Table S18. Results of the non-linear regression of the idxSWL (%) time series for sample P4 and all pH factor levels

P4	pH 1.2	pH 3	pH 5	pH 6.8	pH 7.4
Best-fit values					
Ymax	2647	4070	12183	14486	17862
K	0.2204	0.2297	0.1978	0.3644	0.3750
HalfLife	3.146	3.018	3.504	1.902	1.848
Std. Error					
Ymax	60.33	100.1	853.0	199.4	207.8
K	0.009658	0.01112	0.02509	0.01339	0.01190
95% Confidence Intervals					
Ymax	2521 to 2772	3862 to 4277	10413 to 13952	14072 to 14899	17431 to 18293
K	0.2003 to 0.2404	0.2066 to 0.2527	0.1458 to 0.2499	0.3366 to 0.3922	0.3504 to 0.3997
HalfLife	2.883 to 3.460	2.743 to 3.355	2.774 to 4.754	1.767 to 2.059	1.734 to 1.978
Goodness of Fit					
Degrees of Freedom	22	22	22	22	22
R square	0.9942	0.9925	0.9657	0.9907	0.9926
Adjusted R square	0.9939	0.9922	0.9641	0.9902	0.9923

Supplementary Table S19. Results of the non-linear regression of the idxSWL (%) time series for sample P5 and all pH factor levels

P5	pH 1.2	pH 3	pH 5	pH 6.8	pH 7.4
Best-fit values					
Ymax	2304	5592	15307	12887	15957
K	0.2140	0.09050	0.09334	0.2809	0.3068
HalfLife	3.239	7.659	7.426	2.467	2.259
Std. Error					
Ymax	81.97	378.7	2502	281.7	160.0
K	0.01440	0.008136	0.02043	0.01372	0.007288
95% Confidence Intervals					
Ymax	2134 to 2474	4806 to 6377	10119 to 20495	12303 to 13471	15625 to 16289
K	0.1842 to 0.2439	0.07362 to 0.1074	0.05098 to 0.1357	0.2525 to 0.3094	0.2917 to 0.3219
HalfLife	2.842 to 3.764	6.456 to 9.415	5.108 to 13.60	2.240 to 2.745	2.153 to 2.376
Goodness of Fit					
Degrees of Freedom	22	22	22	22	22
R square	0.9874	0.9955	0.9749	0.9894	0.9969
Adjusted R square	0.9869	0.9953	0.9738	0.9889	0.9968

Supplementary Table S20. Results of the non-linear regression of the idxSWL (%) time series for sample P6 and all pH factor levels

P6	pH 1.2	pH 3	pH 5	pH 6.8	pH 7.4
Best-fit values					
Ymax	1874	5275	15774	13464	15122
K	0.2387	0.09519	0.08428	0.2353	0.3211
HalfLife	2.904	7.281	8.224	2.946	2.158
Std. Error					
Ymax	40.97	381.6	2977	304.3	175.4
K	0.01051	0.009273	0.02072	0.01063	0.009104
95% Confidence Intervals					
Ymax	1789 to 1959	4483 to 6066	9599 to 21950	12833 to 14095	14758 to 15485
K	0.2169 to 0.2605	0.07596 to 0.1144	0.04131 to 0.1273	0.2133 to 0.2573	0.3023 to 0.3400
HalfLife	2.661 to 3.196	6.058 to 9.125	5.447 to 16.78	2.694 to 3.250	2.039 to 2.293
Goodness of Fit					
Degrees of Freedom	22	22	22	22	22
R square	0.9931	0.9943	0.9743	0.9931	0.9953
Adjusted R square	0.9928	0.9940	0.9732	0.9928	0.9951

Supplementary Table S21. Results of the non-linear regression of the idxSWL (%) time series for sample P7 and all pH factor levels

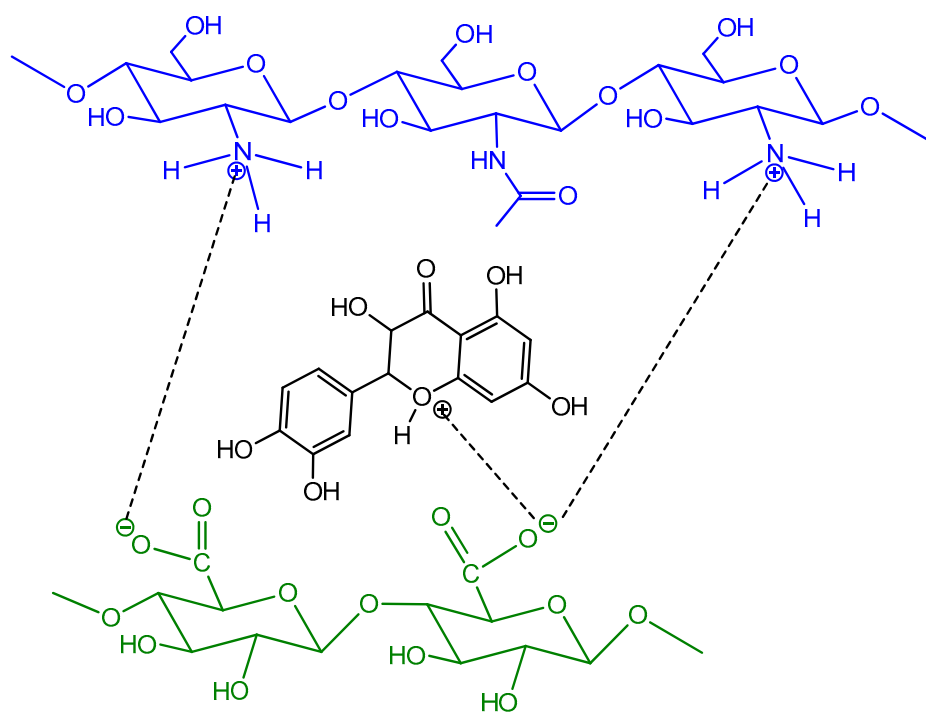
P7	pH 1.2	pH 3	pH 5	pH 6.8	pH 7.4
Best-fit values					
Ymax	1552	5373	12765	12579	15279
K	0.2622	0.08933	0.09905	0.2378	0.3009
HalfLife	2.644	7.759	6.998	2.914	2.303
Std. Error					
Ymax	33.22	601.3	1932	405.2	240.5
K	0.01199	0.01322	0.02043	0.01541	0.01107
95% Confidence Intervals					
Ymax	1483 to 1621	4126 to 6620	8758 to 16773	11738 to 13419	14781 to 15778
K	0.2373 to 0.2870	0.06191 to 0.1168	0.05669 to 0.1414	0.2059 to 0.2698	0.2780 to 0.3239
HalfLife	2.415 to 2.921	5.937 to 11.20	4.901 to 12.23	2.569 to 3.367	2.140 to 2.494
Goodness of Fit					
Degrees of Freedom	22	22	22	22	22
R square	0.9916	0.9885	0.9752	0.9862	0.9930
Adjusted R square	0.9912	0.9880	0.9740	0.9856	0.9927

Supplementary Table S22. Results of the non-linear regression of the idxSWL (%) time series for sample P8 and all pH factor levels

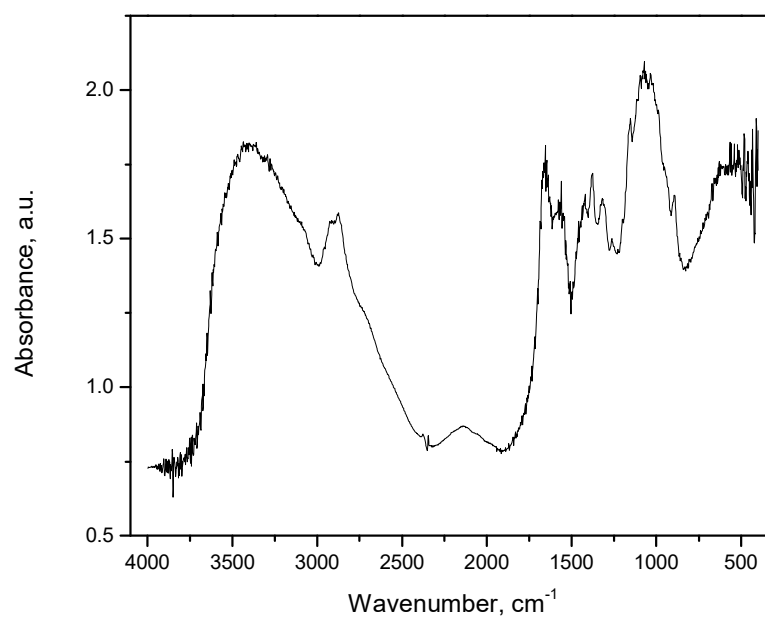
P8	pH 1.2	pH 3	pH 5	pH 6.8	pH 7.4
Best-fit values					
Ymax	2622	4938	18164	13352	16089
K	0.1836	0.1197	0.07759	0.2786	0.3142
HalfLife	3.775	5.791	8.933	2.488	2.206
Std. Error					
Ymax	61.55	239.8	2695	279.0	117.4
K	0.007509	0.008425	0.01469	0.01293	0.005518
95% Confidence Intervals					
Ymax	2494 to 2750	4441 to 5435	12575 to 23752	12773 to 13930	15845 to 16332
K	0.1680 to 0.1992	0.1022 to 0.1372	0.04713 to 0.1081	0.2518 to 0.3054	0.3028 to 0.3257
HalfLife	3.480 to 4.125	5.053 to 6.781	6.415 to 14.71	2.270 to 2.753	2.128 to 2.289
Goodness of Fit					
Degrees of Freedom	22	22	22	22	22
R square	0.9963	0.9953	0.9865	0.9905	0.9982
Adjusted R square	0.9962	0.9951	0.9859	0.9900	0.9981

Supplementary Table S23. Results of the non-linear regression of the QUE *in vitro* release time series for samples P1-P7 and QUE

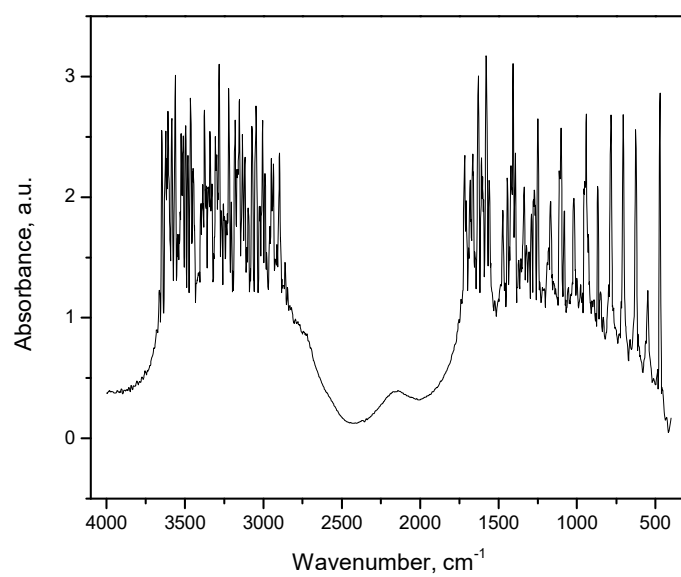
mQUErel (%)	P1	P2	P3	P5	P6	P7	P1
Best-fit values							
Ymax	95.69	95.91	97.37	85.88	88.30	91.50	97.85
K	0.3412	0.3877	0.4217	0.2698	0.2967	0.3255	0.6390
HalfLife	2.032	1.788	1.644	2.569	2.336	2.130	1.085
Std. Error							
Ymax	1.342	1.276	1.374	1.244	1.275	1.229	1.392
K	0.01356	0.01550	0.01857	0.009974	0.01140	0.01213	0.03356
95% Confidence Intervals							
Ymax	92.96 to 98.42	93.31 to 98.51	94.57 to 100.2	83.35 to 88.41	85.71 to 90.89	89.00 to 94.00	95.02 to 100.7
K	0.3136 to 0.3687	0.3562 to 0.4192	0.3839 to 0.4595	0.2495 to 0.2901	0.2735 to 0.3199	0.3008 to 0.3501	0.5708 to 0.7073
HalfLife	1.880 to 2.210	1.654 to 1.946	1.509 to 1.805	2.390 to 2.778	2.167 to 2.534	1.980 to 2.304	0.9800 to 1.214
Goodness of Fit							
Degrees of Freedom	34	34	34	34	34	34	34
R square	0.9886	0.9880	0.9852	0.9906	0.9897	0.9903	0.9754
Adjusted R square	0.9882	0.9877	0.9848	0.9903	0.9894	0.9901	0.9747



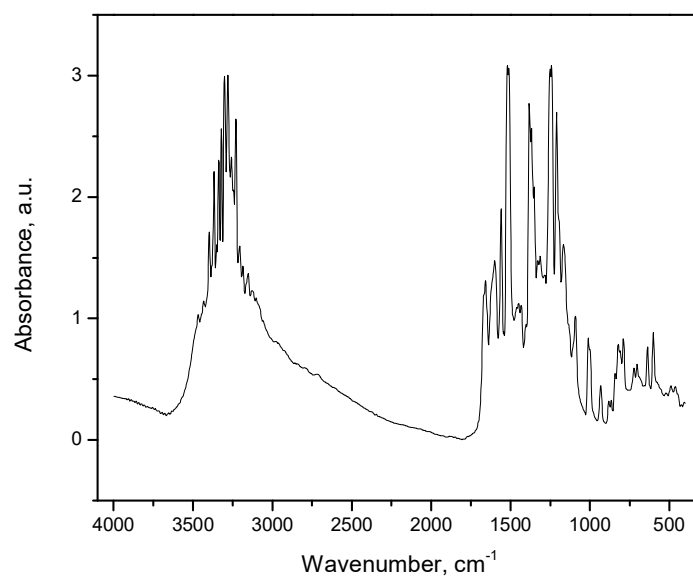
Supplementary Figure S4 – Interactions established during microsphere formation and drug loading.



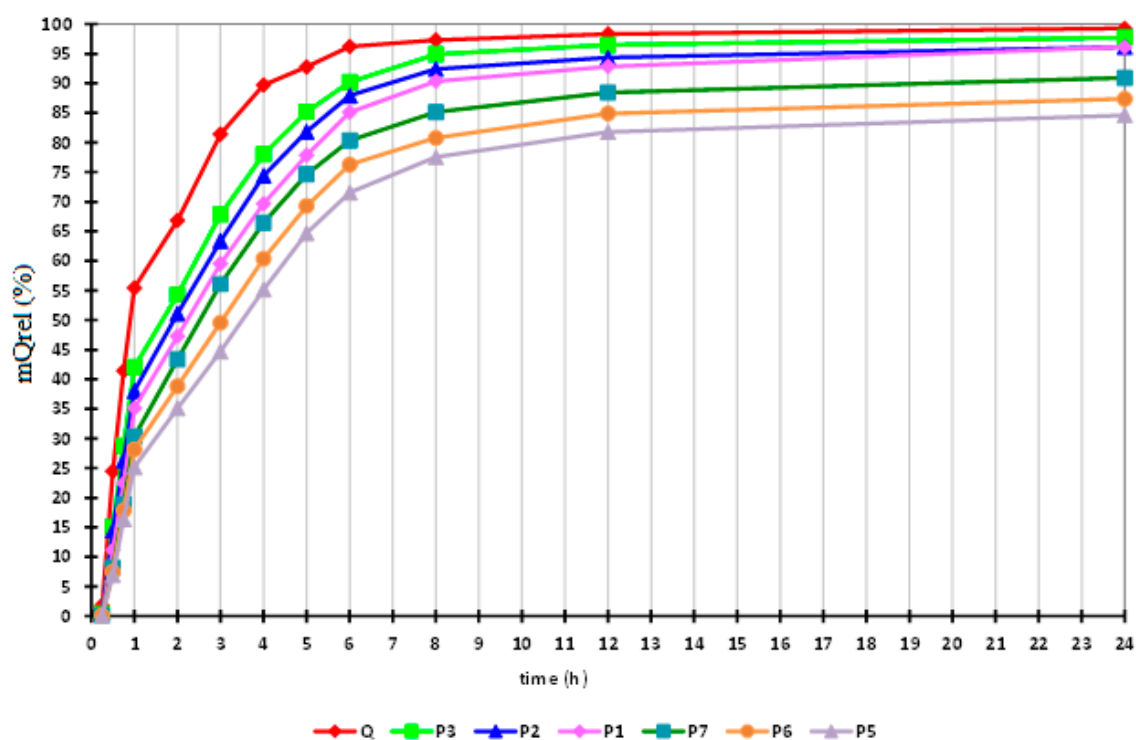
Supplementary Figure S5 – Ch FT-IR spectra



Supplementary Figure S6 – Na-Alg FT-IR spectra



Supplementary Figure S7 – QUE FT-IR spectra



Supplementary Figure S8 - Interval plots of the microspheres' percentage of Q released (mQrel (%)) from microspheres for Sample*Time interaction factor levels