A Comprehensive Investigation of Chitosan/tripolyphosphate Nanoparticles Using Artificial Neural Networks

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Abstract

Chitosan/tripolyphosphate (CS/TPP) nanoparticles have been widely investigated in many applications. Many experimental studies evaluated effective parameters on CS/TPP nanoparticles without a comprehensive study to explain the influence of parameters on nanoparticles. The purpose of present work was to build a mathematical model capable of predicting the particle size and zeta potential of CS/TPP nanoparticles using seven significant factors, including CS and TPP concentrations, deacetylation degree of CS (DD), the molecular weight of CS, pH of CS solution and temperature, and their interactions on the size and zeta potential of CS/TPP nanoparticles. A model was built using artificial neural network including properties of nanoparticles as input with particle size and zeta potential as output. Artificial neural networks (ANN) models were used based on 8 experimental works consisting 160 data to estimate the variation tendency of size and zeta potential. The established model successfully predicted particle size and zeta potential of nanoparticles covering a range of 50-1000 nm. All parameters had significant effects on the size, the interaction between parameters changed the relationship pattern between them. In addition, results indicated that the main reason for the unexplained difference in previous works is the interactions between parameters. In addition, there is a relationship between size and zeta potential, which is due to the attractive and repulsive electrostatic charges, ionic interactions, CS chain length and viscosity. The ANN models in this work were valid for other papers.

Full Text

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Tables

Table 1 Employed references for this work

	Name of reference	Authors
1	Modulation of surface charge, particle size and morphological properties of chitosan–TPP nanoparticles intended for gene delivery	Gan et al. [24]
2	Formation mechanism of monodisperse, low molecular weight chitosan nanoparticles by ionic gelation technique	Fan et al. [31]
3	Depolymerized Chitosan Nanoparticles for Protein Delivery: Preparation and Characterization	Janes et al. [44]
4	Chitosan-tripolyphosphate nanoparticles: Optimization of formulation parameters for improving process yield at a novel pH using artificial neural networks	Hashad et al. [25]
5	Preparation, characterization and evaluation of selenite-loaded chitosan/TPP nanoparticles with or without zein coating	Luo et al. [29]
6	Preparation and properties of ionically cross-linked chitosan nanoparticles	Liu & Gao [27]
7	Antifungal Activity of Chitosan Nanoparticles and Correlation with Their Physical Properties	Ing et al. [28]
8	Chitosan nanoparticles as a novel delivery system for ammonium glycyrrhizinate	Wu et al. [36]

Table 2 Range of employed data.

Parameters	Range	Set point
CS concentration (mg/ml)	0.5- 9	1
TPP concentration (mg/ml)	0.1-2.91	0.5
CS molecular weight (kDa)	6.632- 620	50
Degree of deacetylation (%)	80- 95	87
CS/TPP mass ratio (dimensionless)	2.5- 9	5
pH of CS solution	1- 6.2	4.7
CS temperature (°C)	20- 60	25

Table 3 Experimental and predicted NPs’ size and zeta potential for “training”, “testing” and “validation” data.

Sample number		NP size (nm)		Sample number		Zeta potential (mV)	
	Experimental	Predicted	Error		Experimental	Predicted	Error
1	196	191.392	4.608	1	25	24.915	0.085
2	255	194.9054	60.0946	2	26.1	26.1931	-0.0931
3	259	200.0812	58.9188	3	23.9	23.0341	0.8659
4	220	233.6774	-13.6774	4	23.3	24.6697	-1.3697
5	253	238.9213	14.0787	5	26	25.8526	0.1474
6	245	244.4032	0.5968	6	43.3	43.693	-0.393
7	276	322.0349	-46.0349	7	45.5	45.5591	-0.0591
8	337	322.2837	14.7163	8	47.6	46.5735	1.0265
9	335	322.1547	12.8453	9	45.9	46.3906	-0.4906
10	358	320.4057	37.5943	10	24	23.0341	0.9659
11	219	233.6774	-14.6774	11	23.5	24.6697	-1.1697
12	254	238.9213	15.0787	12	26	25.8526	0.1474
13	247	244.4032	2.5968	13	27	26.7377	0.2623
14	253	258.9107	-5.9107	14	39.6	36.9604	2.6396
15	172.6341	170.2033	2.4308	15	38.6	37.6109	0.9891
16	165.0244	162.6582	2.3662	16	38	37.6501	0.3499
17	160.5854	156.7379	3.8475	17	36.7	37.2112	-0.5112
18	149.1707	152.1048	-2.9341	18	36.4	36.4185	-0.0185
19	144.7317	148.4936	-3.7619	19	35	35.3787	-0.3787
20	137.7561	145.6965	-7.9404	20	34.05	34.1809	-0.1309
21	135.2195	143.5508	-8.3313	21	33.5	32.8986	0.6014
22	135.8537	141.9284	-6.0747	22	32.4	31.59	0.81
23	133.3171	140.7284	-7.4113	23	30	30.2991	-0.2991
24	148.5366	139.8704	8.6662	24	26	29.0576	-3.0576
25	237.3171	139.2902	98.0269	25	50.13889	49.826	0.312889
26	150.3371	158.8149	-8.4778	26	47.91667	48.5997	-0.68303
27	167.5281	163.4473	4.0808	27	46.94444	47.1095	-0.16506
28	168.5393	170.092	-1.5527	28	46.66667	45.351	1.315667
29	176.6292	179.948	-3.3188	29	43.75	43.3394	0.4106
30	184.7191	195.4498	-10.7307	30	42.77778	41.1081	1.669678
31	193.8202	220.901	-27.0808	31	48.75	48.0715	0.6785
32	159.4382	172.4194	-12.9812	32	46.25	45.7064	0.5436
33	173.5955	172.1487	1.4468	33	42.5	42.9819	-0.4819
34	178.6517	174.2484	4.4033	34	41.52778	39.9952	1.532578
35	188.764	179.867	8.897	35	39.58333	36.8655	2.717833
36	202.9213	191.3284	11.5929	36	44.30556	44.3411	-0.03554
37	178.6517	178.3189	0.3328	37	35	34.9762	0.0238
38	250.4494	211.8399	38.6095	38	48.3	45.6423	2.6577
39	136.2	144.7588	-8.5588	39	44.2	43.5762	0.6238
40	142.3	140.2824	2.0176	40	41	41.4341	-0.4341
41	152.9	142.9023	9.9977	41	39.7	39.2897	0.4103
42	171.2	154.8362	16.3638	42	37.3	37.2066	0.0934

43	190.3	180.5335	9.7665	43	33.3	33.3747	-0.0747
44	312.7	309.0546	3.6454	44	31.6	31.639	-0.039
45	429.6	431.6663	-2.0663	45	28.2	28.4072	-0.2072
46	712.4	723.6779	-11.2779	46	26.9	26.8353	0.0647
47	800	825.2271	-25.2271	47	25.2	25.2536	-0.0536
48	900	887.45	12.55	48	43.9	43.3508	0.5492
49	145.3	142.1561	3.1439	49	40.3	40.7971	-0.4971
50	150.5	149.6152	0.8848	50	39.1	38.1255	0.9745
51	165.2	166.7953	-1.5953	51	37.2	35.4157	1.7843
52	182.3	197.1717	-14.8717	52	37.7	37.9471	-0.2471
53	155	149.7363	5.2637	53	34.8	34.5576	0.2424
54	188.9	171.5868	17.3132	54	49.2	48.602	0.598
55	143.2	152.58	-9.38	55	46.8	47.3145	-0.5145
56	152.1	152.3497	-0.2497	56	45.6	45.84	-0.24
57	159.2	156.8669	2.3331	57	44.3	44.2108	0.0892
58	172.8	168.6003	4.1997	58	42.7	42.4832	0.2168
59	181.9	191.366	-9.466	59	39.4	39.0259	0.3741
60	273.2	293.5664	-20.3664	60	37.1	37.4327	-0.3327
61	387.2	381.6207	5.5793	61	36.8	35.9872	0.8128
62	519.6	485.676	33.924	62	34.2	34.6968	-0.4968
63	604	587.5001	16.4999	63	33.3	33.5423	-0.2423
64	692.1	673.518	18.582	64	32.7	32.4857	0.2143
65	726.6	741.3184	-14.7184	65	30.8	30.48	0.32
66	846.7	838.0157	8.6843	66	30	29.4489	0.5511
67	858.9	873.6001	-14.7001	67	28.5	28.3657	0.1343
68	893.6	902.4185	-8.8185	68	26.7	27.2266	-0.5266
69	908.7	924.8605	-16.1605	69	26.2	26.0438	0.1562
70	938.7	941.5162	-2.8162	70	46.8	46.971	-0.171
71	156.1	155.1256	0.9744	71	44.4	44.6003	-0.2003
72	163.7	155.9636	7.7364	72	40.3	42.1262	-1.8262
73	170.7	163.4231	7.2769	73	39.8	39.7173	0.0827
74	181.5	179.1901	2.3099	74	37.8	37.5069	0.2931
75	192.2	206.4231	-14.2231	75	33.8	33.91	-0.11
76	310.2	318.1746	-7.9746	76	32.7	32.5017	0.1983
77	427.5	413.6756	13.8244	77	32.1	31.2852	0.8148
78	546.3	529.2565	17.0435	78	30.4	30.1968	0.2032
79	654.3	644.1477	10.1523	79	29	29.179	-0.179
80	721.5	739.4754	-17.9754	80	28.6	28.1878	0.4122
81	783.2	810.1916	-26.9916	81	27.5	27.196	0.304
82	848.3	860.7398	-12.4398	82	25.3	26.1929	-0.8929
83	881	897.0587	-16.0587	83	25.1	25.1817	-0.0817
84	936.8	923.3845	13.4155	84	24.8	24.1746	0.6254
85	988.6	942.3268	46.2732	85	41.3	38.4777	2.8223
86	162.7	158.6043	4.0957	86	37.4	37.4541	-0.0541

87	176.1	167.7879	8.3121	87	33.2	33.6508	-0.4508
88	257	294.1863	-37.1863	88	32.6	32.6465	-0.0465
89	362.3	368.0349	-5.7349	89	31.8	31.5815	0.2185
90	478	468.344	9.656	90	29.5	29.2775	0.2225
91	697.3	702.8856	-5.5856	91	26.3	26.8587	-0.5587
92	828	860.1881	-32.1881	92	25.9	25.6697	0.2303
93	898.5	902.948	-4.448	93	23.2	24.5275	-1.3275
94	976.8	931.0267	45.7733	94	14.43	15.9199	-1.4899
95	166.48	256.0483	-89.5683	95	15.89	16.109	-0.219
96	252	268.8835	-16.8835	96	16.62	16.1109	0.5091
97	260.75	276.563	-15.813	97	16.2	15.9545	0.2455
98	289.8	277.6585	12.1415	98	19.34	17.4885	1.8515
99	278.35	284.1268	-5.7768	99	16.71	17.7676	-1.0576
100	317.8	316.7133	1.0867	100	17.92	17.7017	0.2183
101	374.94	345.8189	29.1211	101	18.65	17.7819	0.8681
102	173.13	261.7309	-88.6009	102	18.7	18.8987	-0.1987
103	386.98	314.0635	72.9165	103	20.8	19.716	1.084
104	420.26	371.2113	49.0487	104	19.9	20.0569	-0.1569
105	469.56	429.3081	40.2519	105	20.12	19.8889	0.2311
106	487.56	483.7737	3.7863	106	15.8	17.1213	-1.3213
107	162.7	165.9455	-3.2455	107	18.52	17.3425	1.1775
108	174.55	176.0433	-1.4933	108	18.71	17.2485	1.4615
109	184.03	185.2919	-1.2619	109	17.54	16.9169	0.6231
110	200.05	193.2886	6.7614	110	18.16	18.3356	-0.1756
111	169.94	169.7467	0.1933	111	20.06	19.0711	0.9889
112	198.57	190.205	8.365	112	19.31	18.5602	0.7498
113	232.7	260.3307	-27.6307	113	19.82	19.2969	0.5231
114	184.52	192.5311	-8.0111	114	20.9	21.6878	-0.7878
115	299.49	265.9476	33.5424	115	21.7	22.0144	-0.3144
116	317.39	311.2215	6.1685	116	20.4	21.6979	-1.2979
117	331.03	361.0367	-30.0067	117	17.16	18.0042	-0.8442
118	170.08	172.3376	-2.2576	118	18.78	18.2235	0.5565
119	204.1	189.0351	15.0649	119	20.01	18.0644	1.9456
120	217.75	206.6799	11.0701	120	17.62	17.6373	-0.0173
121	231.68	225.0128	6.6672	121	17.14	17.095	0.045
122	244.66	243.7135	0.9465	122	18.75	19.6547	-0.9047
123	170.58	195.2295	-24.6495	123	22.3	20.5348	1.7652
124	207.93	218.4398	-10.5098	124	19.87	20.5911	-0.7211
125	264.2	270.6047	-6.4047	125	19.62	19.9186	-0.2986
126	278.28	298.7621	-20.4821	126	20.21	21.1927	-0.9827
127	205.68	210.4188	-4.7388	127	24.31	23.0349	1.2751
128	227.38	236.3225	-8.9425	128	24.6	24.2875	0.3125
129	293.25	265.3291	27.9209	129	23.4	24.7834	-1.3834
130	300.86	297.2615	3.5985	130	25.46	24.5356	0.9244

131	312.32	331.7607	-19.4407	131	45	44.903	0.097
132	321	328.1618	-7.1618	132	43.46	43.6767	-0.2167
133	295.3125	308.4113	-13.0988	133	42.3077	42.1983	0.1094
134	286.5625	281.7256	4.8369	134	41.5384	40.0817	1.4567
135	280	265.3859	14.6141	135	32.6923	32.7148	-0.0225
136	242.8125	271.4428	-28.6303	136	27.154	27.1563	-0.0023
137	210	305.4505	-95.4505	137	50.077	50.1289	-0.0519
138	300	302.8641	-2.8641	138	55.461	55.1454	0.3156
139	337.5	302.8956	34.6044	139	50.692	53.5997	-2.9077
140	387.5	366.2959	21.2041	140	41.123	41.0912	0.0318
141	406.25	427.5018	-21.2518	141	37.092	37.1099	-0.0179
142	556.25	548.3783	7.8717	142	42.7693	44.5296	-1.7603
143	50	67.6593	-17.6593	143	45.8031	44.8246	0.9785
144	90	105.7002	-15.7002	144	45.8659	45.001	0.8649
145	195.57	204.8164	-9.2464	145	46.4085	47.6326	-1.2241
146	318.83	267.9977	50.8323	146	44.2302	44.2602	-0.03
147	299.28	316.0222	-16.7422	147	35	35.001	-0.001
148	265.15	323.6264	-58.4764	148	43	43.0203	-0.0203
149	260.2	280.4688	-20.2688	149	47	55.0586	-8.0586
150	235.46	217.1329	18.3271	150	38	38.0012	-0.0012
151	121.02	158.263	-37.243				
152	154.032	159.2983	-5.2663				
153	155.044	159.9223	-4.8783				
154	179.203	180.1228	-0.9198				
155	220.21	221.2323	-1.0223				
156	101	104.6727	-3.6727				
157	169	197.132	-28.132				
158	348	340.3201	7.6799				
159	136	236.3055	-100.306				
160	276	289.3115	-13.3115				

Table 4 Investigation of model validity with other references.

Reference	CS concentration (%) (w/v)	TPP concentration (%) (w/v)	CS Mw (kDa)	DD (%)	CS/TPP mass ratio	pH	Temperature (°C)	Size(nm)			Zeta (mV)	
								Experimental	Predicted	Error (%)	Experimental	Predicted
Grillo et al. ⁵⁷	1	1	27	80	4	4.7	25	320	348.512	8.91	44.7	43.11
Hussain and Sahudin ²⁶	2	1	100	85	5	4.8	25	227	205.8908	9.29	38	35.74

Figures

Figure 1
The topology of the ANN structure

Figure 2

Actual versus predicted particle size from network and regression for training, test, validation, and all data sets.

Figure 3
effect of CS concentration and CS/TPP on the size and zeta potential.

Figure 4
effect of TPP concentration and CS/TPP mass ratio on the size and zeta potential

(a)

(b)

Figure 5

Effect of CS Mw on the size and zeta potential

(a)

(b)

Figure 6

Effect of DD and TPP concentration on the size and zeta potential

Figure 7

Effect of pH on the size and zeta potential

a) TPP concentration and pH

b) pH and CS Mw

c) Degree of deacetylation and pH

d) pH and CS/TPP mass ratio

Figure 8

(a)

(b)

Figure 9

Effect of temperature on the size and zeta potential

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