Multiscale approach to investigate self-assembly of telodendrimer based nanocarriers for anticancer drug-delivery

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Supporting Information:

Table S1. Bead types: GROMACS topology file for coarse grained $PEG^{5K}CA_8$ telodendrimer.

nr	type	resnr	residue	atom	cgnr	charge
1	SN0	1	PEG	O1	1	0
2	SN0	1	PEG	O1	2	0
3	SN0	1	PEG	O1	3	0
4	SN0	1	PEG	O1	4	0
5	SN0	1	PEG	O1	5	0
6	SN0	1	PEG	O1	6	0
7	SN0	1	PEG	O1	7	0
8	SN0	1	PEG	O1	8	0
9	SN0	1	PEG	O1	9	0
10	SN0	1	PEG	O1	10	0
11	SN0	1	PEG	O1	11	0
12	SN0	1	PEG	O1	12	0
13	SN0	1	PEG	O1	13	0
14	SN0	1	PEG	O1	14	0
15	SN0	1	PEG	O1	15	0
16	SN0	1	PEG	O1	16	0
17	SN0	1	PEG	O1	17	0
18	SN0	1	PEG	O1	18	0
19	SN0	1	PEG	O1	19	0
20	SN0	1	PEG	O1	20	0
21	SN0	1	PEG	O1	21	0
22	SN0	1	PEG	O1	22	0
23	SN0	1	PEG	O1	23	0
24	SN0	1	PEG	O1	24	0
25	SN0	1	PEG	O1	25	0
26	SN0	1	PEG	O1	26	0
27	SN0	1	PEG	O1	27	0
28	SN0	1	PEG	O1	28	0
29	SN0	1	PEG	O1	29	0
30	SN0	1	PEG	O1	30	0
31	SN0	1	PEG	O1	31	0
32	SN0	1	PEG	O1	32	0
33	SN0	1	PEG	O1	33	0
34	SN0	1	PEG	O1	34	0

35	SN0	1	PEG	O1	35	0
36	SN0	1	PEG	O1	36	0
37	SN0	1	PEG	O1	37	0
38	SN0	1	PEG	O1	38	0
39	SN0	1	PEG	O1	39	0
40	SN0	1	PEG	O1	40	0
41	SN0	1	PEG	O1	41	0
42	SN0	1	PEG	O1	42	0
43	SN0	1	PEG	O1	43	0
44	SN0	1	PEG	O1	44	0
45	SN0	1	PEG	O1	45	0
46	SN0	1	PEG	O1	46	0
47	SN0	1	PEG	O1	47	0
48	SN0	1	PEG	O1	48	0
49	SN0	1	PEG	O1	49	0
50	SN0	1	PEG	O1	50	0
51	SN0	1	PEG	O1	51	0
52	SN0	1	PEG	O1	52	0
53	SN0	1	PEG	O1	53	0
54	SN0	1	PEG	O1	54	0
55	SN0	1	PEG	O1	55	0
56	SN0	1	PEG	O1	56	0
57	SN0	1	PEG	O1	57	0
58	SN0	1	PEG	O1	58	0
59	SN0	1	PEG	O1	59	0
60	SN0	1	PEG	O1	60	0
61	SN0	1	PEG	O1	61	0
62	SN0	1	PEG	O1	62	0
63	SN0	1	PEG	O1	63	0
64	SN0	1	PEG	O1	64	0
65	SN0	1	PEG	O1	65	0
66	SN0	1	PEG	O1	66	0
67	SN0	1	PEG	O1	67	0
68	SN0	1	PEG	O1	68	0
69	SN0	1	PEG	O1	69	0
70	SN0	1	PEG	O1	70	0
71	SN0	1	PEG	O1	71	0
72	SN0	1	PEG	O1	72	0
73	SN0	1	PEG	O1	73	0
74	SN0	1	PEG	O1	74	0
75	SN0	1	PEG	O1	75	0
76	SN0	1	PEG	O1	76	0

77	SN0	1	PEG	O1	77	0
78	SN0	1	PEG	O1	78	0
79	SN0	1	PEG	O1	79	0
80	SN0	1	PEG	O1	80	0
81	SN0	1	PEG	O1	81	0
82	SN0	1	PEG	O1	82	0
83	SN0	1	PEG	O1	83	0
84	SN0	1	PEG	O1	84	0
85	SN0	1	PEG	O1	85	0
86	SN0	1	PEG	O1	86	0
87	SN0	1	PEG	O1	87	0
88	SN0	1	PEG	O1	88	0
89	SN0	1	PEG	O1	89	0
90	SN0	1	PEG	O1	90	0
91	SN0	1	PEG	O1	91	0
92	SN0	1	PEG	O1	92	0
93	SN0	1	PEG	O1	93	0
94	SN0	1	PEG	O1	94	0
95	SN0	1	PEG	O1	95	0
96	SN0	1	PEG	O1	96	0
97	SN0	1	PEG	O1	97	0
98	SN0	1	PEG	O1	98	0
99	SN0	1	PEG	O1	99	0
100	SN0	1	PEG	O1	100	0
101	SN0	1	PEG	O1	101	0
102	SN0	1	PEG	O1	102	0
103	SN0	1	PEG	O1	103	0
104	SN0	1	PEG	O1	104	0
105	SN0	1	PEG	O1	105	0
106	SN0	1	PEG	O1	106	0
107	SN0	1	PEG	O1	107	0
108	SN0	1	PEG	O1	108	0
109	SN0	1	PEG	O1	109	0
110	SN0	1	PEG	O1	110	0
111	SN0	1	PEG	O1	111	0
112	SN0	1	PEG	O1	112	0
113	P5	2	LYS	BB	113	0
114	C3	2	LYS	SC1	114	0
115	P1	2	LYS	SC2	115	0
116	P5	3	LYS	BB	116	0
117	C3	3	LYS	SC1	117	0
118	P1	3	LYS	SC2	118	0

119	P5	4	LYS	BB	119	0
120	C3	4	LYS	SC1	120	0
121	P1	4	LYS	SC2	121	0
122	P5	5	LYS	BB	122	0
123	C3	5	LYS	SC1	123	0
124	P1	5	LYS	SC2	124	0
125	P5	6	LYS	BB	125	0
126	C3	6	LYS	SC1	126	0
127	P1	6	LYS	SC2	127	0
128	P5	7	LYS	BB	128	0
129	C3	7	LYS	SC1	129	0
130	P1	7	LYS	SC2	130	0
131	P5	8	LYS	BB	131	0
132	C3	8	LYS	SC1	132	0
133	P1	8	LYS	SC2	133	0
134	SP5	9	CHOA	OH	134	0
135	SC1	9	CHOA	R1	135	0
136	SC3	9	CHOA	R2	136	0
137	SP5	9	CHOA	O2	137	0
138	SP5	9	CHOA	O3	138	0
139	SC1	9	CHOA	R3	139	0
140	SC1	9	CHOA	C1	140	0
141	SP5	10	CHOA	OH	141	0
142	SC1	10	CHOA	R1	142	0
143	SC3	10	CHOA	R2	143	0
144	SP5	10	CHOA	O2	144	0
145	SP5	10	CHOA	O3	145	0
146	SC1	10	CHOA	R3	146	0
147	SC1	10	CHOA	C1	147	0
148	SP5	11	CHOA	OH	148	0
149	SC1	11	CHOA	R1	149	0
150	SC3	11	CHOA	R2	150	0
151	SP5	11	CHOA	O2	151	0
152	SP5	11	CHOA	O3	152	0
153	SC1	11	CHOA	R3	153	0
154	SC1	11	CHOA	C1	154	0
155	SP5	12	CHOA	OH	155	0
156	SC1	12	CHOA	R1	156	0
157	SC3	12	CHOA	R2	157	0
158	SP5	12	CHOA	O2	158	0
159	SP5	12	CHOA	O3	159	0
160	SC1	12	CHOA	R3	160	0

161	SC1	12	CHOA	C1	161	0
162	SP5	13	CHOA	OH	162	0
163	SC1	13	CHOA	R1	163	0
164	SC3	13	CHOA	R2	164	0
165	SP5	13	CHOA	O2	165	0
166	SP5	13	CHOA	O3	166	0
167	SC1	13	CHOA	R3	167	0
168	SC1	13	CHOA	C1	168	0
169	SP5	14	CHOA	OH	169	0
170	SC1	14	CHOA	R1	170	0
171	SC3	14	CHOA	R2	171	0
172	SP5	14	CHOA	O2	172	0
173	SP5	14	CHOA	O3	173	0
174	SC1	14	CHOA	R3	174	0
175	SC1	14	CHOA	C1	175	0
176	SP5	15	CHOA	OH	176	0
177	SC1	15	CHOA	R1	177	0
178	SC3	15	CHOA	R2	178	0
179	SP5	15	CHOA	O2	179	0
180	SP5	15	CHOA	O3	180	0
181	SC1	15	CHOA	R3	181	0
182	SC1	15	CHOA	C1	182	0
183	SP5	16	CHOA	OH	183	0
184	SC1	16	CHOA	R1	184	0
185	SC3	16	CHOA	R2	185	0
186	SP5	16	CHOA	O2	186	0
187	SP5	16	CHOA	O3	187	0
188	SC1	16	CHOA	R3	188	0
189	SC1	16	CHOA	C1	189	0

Note: The MARTINI bead type for cholic acid beads were changed to SC1 for hydrophobic and SP5 for hydrophilic.

Table S2. Bond lengths: GROMACS topology file for coarse grained $PEG^{5K}CA_8$ telodendrimer.

i	j	funct	length	force
1	2	1	0.33	17000
2	3	1	0.33	17000
3	4	1	0.33	17000
4	5	1	0.33	17000
5	6	1	0.33	17000
6	7	1	0.33	17000
7	8	1	0.33	17000
8	9	1	0.33	17000
9	10	1	0.33	17000
10	11	1	0.33	17000
11	12	1	0.33	17000
12	13	1	0.33	17000
13	14	1	0.33	17000
14	15	1	0.33	17000
15	16	1	0.33	17000
16	17	1	0.33	17000
17	18	1	0.33	17000
18	19	1	0.33	17000
19	20	1	0.33	17000
20	21	1	0.33	17000
21	22	1	0.33	17000
22	23	1	0.33	17000
23	24	1	0.33	17000
24	25	1	0.33	17000
25	26	1	0.33	17000
26	27	1	0.33	17000
27	28	1	0.33	17000
28	29	1	0.33	17000
29	30	1	0.33	17000
30	31	1	0.33	17000
31	32	1	0.33	17000
32	33	1	0.33	17000
33	34	1	0.33	17000
34	35	1	0.33	17000
35	36	1	0.33	17000
36	37	1	0.33	17000
37	38	1	0.33	17000
38	39	1	0.33	17000

39	40	1	0.33	17000
40	41	1	0.33	17000
41	42	1	0.33	17000
42	43	1	0.33	17000
43	44	1	0.33	17000
44	45	1	0.33	17000
45	46	1	0.33	17000
46	47	1	0.33	17000
47	48	1	0.33	17000
48	49	1	0.33	17000
49	50	1	0.33	17000
50	51	1	0.33	17000
51	52	1	0.33	17000
52	53	1	0.33	17000
53	54	1	0.33	17000
54	55	1	0.33	17000
55	56	1	0.33	17000
56	57	1	0.33	17000
57	58	1	0.33	17000
58	59	1	0.33	17000
59	60	1	0.33	17000
60	61	1	0.33	17000
61	62	1	0.33	17000
62	63	1	0.33	17000
63	64	1	0.33	17000
64	65	1	0.33	17000
65	66	1	0.33	17000
66	67	1	0.33	17000
67	68	1	0.33	17000
68	69	1	0.33	17000
69	70	1	0.33	17000
70	71	1	0.33	17000
71	72	1	0.33	17000
72	73	1	0.33	17000
73	74	1	0.33	17000
74	75	1	0.33	17000
75	76	1	0.33	17000
76	77	1	0.33	17000
77	78	1	0.33	17000
78	79	1	0.33	17000
79	80	1	0.33	17000
80	81	1	0.33	17000

81	82	1	0.33	17000
82	83	1	0.33	17000
83	84	1	0.33	17000
84	85	1	0.33	17000
85	86	1	0.33	17000
86	87	1	0.33	17000
87	88	1	0.33	17000
88	89	1	0.33	17000
89	90	1	0.33	17000
90	91	1	0.33	17000
91	92	1	0.33	17000
92	93	1	0.33	17000
93	94	1	0.33	17000
94	95	1	0.33	17000
95	96	1	0.33	17000
96	97	1	0.33	17000
97	98	1	0.33	17000
98	99	1	0.33	17000
99	100	1	0.33	17000
100	101	1	0.33	17000
101	102	1	0.33	17000
102	103	1	0.33	17000
103	104	1	0.33	17000
104	105	1	0.33	17000
105	106	1	0.33	17000
106	107	1	0.33	17000
107	108	1	0.33	17000
108	109	1	0.33	17000
109	110	1	0.33	17000
110	111	1	0.33	17000
111	112	1	0.33	17000
112	119	1	0.33	1200
113	116	1	0.35	1250
116	119	1	0.35	1250
125	128	1	0.35	1250
118	122	1	0.35	1250
121	128	1	0.35	1250
130	131	1	0.35	1250
113	114	1	0.33	5000
116	117	1	0.33	5000
119	120	1	0.33	5000
122	123	1	0.33	5000

125	126	1	0.33	5000
128	129	1	0.33	5000
131	132	1	0.33	5000
114	115	1	0.28	5000
117	118	1	0.28	5000
120	121	1	0.28	5000
123	124	1	0.28	5000
126	127	1	0.28	5000
129	130	1	0.28	5000
132	133	1	0.28	5000
115	140	1	0.368	20000
113	147	1	0.368	20000
125	154	1	0.368	20000
127	161	1	0.368	20000
122	168	1	0.368	20000
124	175	1	0.368	20000
131	182	1	0.368	20000
133	189	1	0.368	20000
134	135	1	0.242	20000
135	136	1	0.26	20000
135	137	1	0.341	20000
137	139	1	0.213	20000
137	140	1	0.544	20000
138	139	1	0.203	20000
139	140	1	0.368	20000
141	142	1	0.242	20000
142	143	1	0.26	20000
142	144	1	0.341	20000
144	146	1	0.213	20000
144	147	1	0.544	20000
145	146	1	0.203	20000
146	147	1	0.368	20000
148	149	1	0.242	20000
149	150	1	0.26	20000
149	151	1	0.341	20000
151	153	1	0.213	20000
151	154	1	0.544	20000
152	153	1	0.203	20000
153	154	1	0.368	20000
155	156	1	0.242	20000
156	157	1	0.26	20000
156	158	1	0.341	20000

158	160	1	0.213	20000
158	161	1	0.544	20000
159	160	1	0.203	20000
160	161	1	0.368	20000
162	163	1	0.242	20000
163	164	1	0.26	20000
163	165	1	0.341	20000
165	167	1	0.213	20000
165	168	1	0.544	20000
166	167	1	0.203	20000
167	168	1	0.368	20000
169	170	1	0.242	20000
170	171	1	0.26	20000
170	172	1	0.341	20000
172	174	1	0.213	20000
172	175	1	0.544	20000
173	174	1	0.203	20000
174	175	1	0.368	20000
176	177	1	0.242	20000
177	178	1	0.26	20000
177	179	1	0.341	20000
179	181	1	0.213	20000
179	182	1	0.544	20000
180	181	1	0.203	20000
181	182	1	0.368	20000
183	184	1	0.242	20000
184	185	1	0.26	20000
184	186	1	0.341	20000
186	188	1	0.213	20000
186	189	1	0.544	20000
187	188	1	0.203	20000
188	189	1	0.368	20000

Table S3. Constraints: GROMACS topology file for coarse grained $PEG^{5K}CA_8$ telodendrimer.

i	j	funct	length
134	136	1	0.493
134	137	1	0.604
136	137	1	0.272
136	138	1	0.346
137	138	1	0.294
138	140	1	0.406
141	143	1	0.493
141	144	1	0.604
143	144	1	0.272
143	145	1	0.346
144	145	1	0.294
145	147	1	0.406
148	150	1	0.493
148	151	1	0.604
150	151	1	0.272
150	152	1	0.346
151	152	1	0.294
152	154	1	0.406
155	157	1	0.493
155	158	1	0.604
157	158	1	0.272
157	159	1	0.346
158	159	1	0.294
159	161	1	0.406
162	164	1	0.493
162	165	1	0.604
164	165	1	0.272
164	166	1	0.346
165	166	1	0.294
166	168	1	0.406
169	171	1	0.493
169	172	1	0.604
171	172	1	0.272
171	173	1	0.346
172	173	1	0.294
173	175	1	0.406
176	178	1	0.493
176	179	1	0.604

178	179	1	0.272
178	180	1	0.346
179	180	1	0.294
180	182	1	0.406
183	185	1	0.493
183	186	1	0.604
185	186	1	0.272
185	187	1	0.346
186	187	1	0.294
187	189	1	0.406

Table S4. Angles: GROMACS topology file for coarse grained $PEG^{5K}CA_8$ telodendrimer.

i	j	k	funct	angle	force
1	2	3	2	130	50
2	3	4	2	130	50
3	4	5	2	130	50
4	5	6	2	130	50
5	6	7	2	130	50
6	7	8	2	130	50
7	8	9	2	130	50
8	9	10	2	130	50
9	10	11	2	130	50
10	11	12	2	130	50
11	12	13	2	130	50
12	13	14	2	130	50
13	14	15	2	130	50
14	15	16	2	130	50
15	16	17	2	130	50
16	17	18	2	130	50
17	18	19	2	130	50
18	19	20	2	130	50
19	20	21	2	130	50
20	21	22	2	130	50
21	22	23	2	130	50
22	23	24	2	130	50
23	24	25	2	130	50
24	25	26	2	130	50

25	26	27	2	130	50
26	27	28	2	130	50
27	28	29	2	130	50
28	29	30	2	130	50
29	30	31	2	130	50
30	31	32	2	130	50
31	32	33	2	130	50
32	33	34	2	130	50
33	34	35	2	130	50
34	35	36	2	130	50
35	36	37	2	130	50
36	37	38	2	130	50
37	38	39	2	130	50
38	39	40	2	130	50
39	40	41	2	130	50
40	41	42	2	130	50
41	42	43	2	130	50
42	43	44	2	130	50
43	44	45	2	130	50
44	45	46	2	130	50
45	46	47	2	130	50
46	47	48	2	130	50
47	48	49	2	130	50
48	49	50	2	130	50
49	50	51	2	130	50
50	51	52	2	130	50
51	52	53	2	130	50
52	53	54	2	130	50
53	54	55	2	130	50
54	55	56	2	130	50
55	56	57	2	130	50
56	57	58	2	130	50
57	58	59	2	130	50
58	59	60	2	130	50
59	60	61	2	130	50
60	61	62	2	130	50
61	62	63	2	130	50
62	63	64	2	130	50
63	64	65	2	130	50
64	65	66	2	130	50
65	66	67	2	130	50
66	67	68	2	130	50

67	68	69	2	130	50
68	69	70	2	130	50
69	70	71	2	130	50
70	71	72	2	130	50
71	72	73	2	130	50
72	73	74	2	130	50
73	74	75	2	130	50
74	75	76	2	130	50
75	76	77	2	130	50
76	77	78	2	130	50
77	78	79	2	130	50
78	79	80	2	130	50
79	80	81	2	130	50
80	81	82	2	130	50
81	82	83	2	130	50
82	83	84	2	130	50
83	84	85	2	130	50
84	85	86	2	130	50
85	86	87	2	130	50
86	87	88	2	130	50
87	88	89	2	130	50
88	89	90	2	130	50
89	90	91	2	130	50
90	91	92	2	130	50
91	92	93	2	130	50
92	93	94	2	130	50
93	94	95	2	130	50
94	95	96	2	130	50
95	96	97	2	130	50
96	97	98	2	130	50
97	98	99	2	130	50
98	99	100	2	130	50
99	100	101	2	130	50
100	101	102	2	130	50
101	102	103	2	130	50
102	103	104	2	130	50
103	104	105	2	130	50
104	105	106	2	130	50
105	106	107	2	130	50
106	107	108	2	130	50
107	108	109	2	130	50
108	109	110	2	130	50

109	110	111	2	130	50
110	111	112	2	130	50
111	112	119	2	130	50
112	119	120	2	130	50
113	116	119	2	134	25
118	122	123	2	100	25
130	131	132	2	100	25
116	113	114	2	100	25
113	116	117	2	100	25
116	119	120	2	100	25
125	128	129	2	100	25
113	114	115	2	180	25
116	117	118	2	180	25
119	120	121	2	180	25
122	123	124	2	180	25
125	126	127	2	180	25
128	129	130	2	180	25
115	140	139	2	130	50
113	147	146	2	130	50
125	154	153	2	130	50
127	161	160	2	130	50
122	168	167	2	130	50
124	175	174	2	130	50
131	182	181	2	130	50
133	189	188	2	130	50

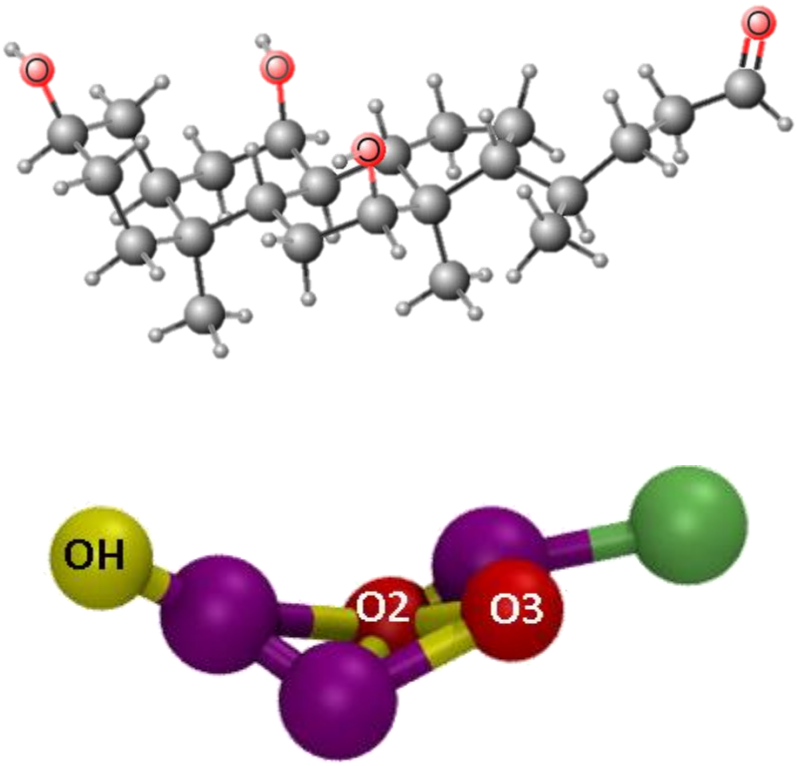

Figure S1. The (a) atomistic and (b) coarse grained structure of cholic acid. The beads labeled as OH (yellow), O2 (red), and O3 (red) in the coarse grained structure provide facial amphiphilicity to cholic acid.

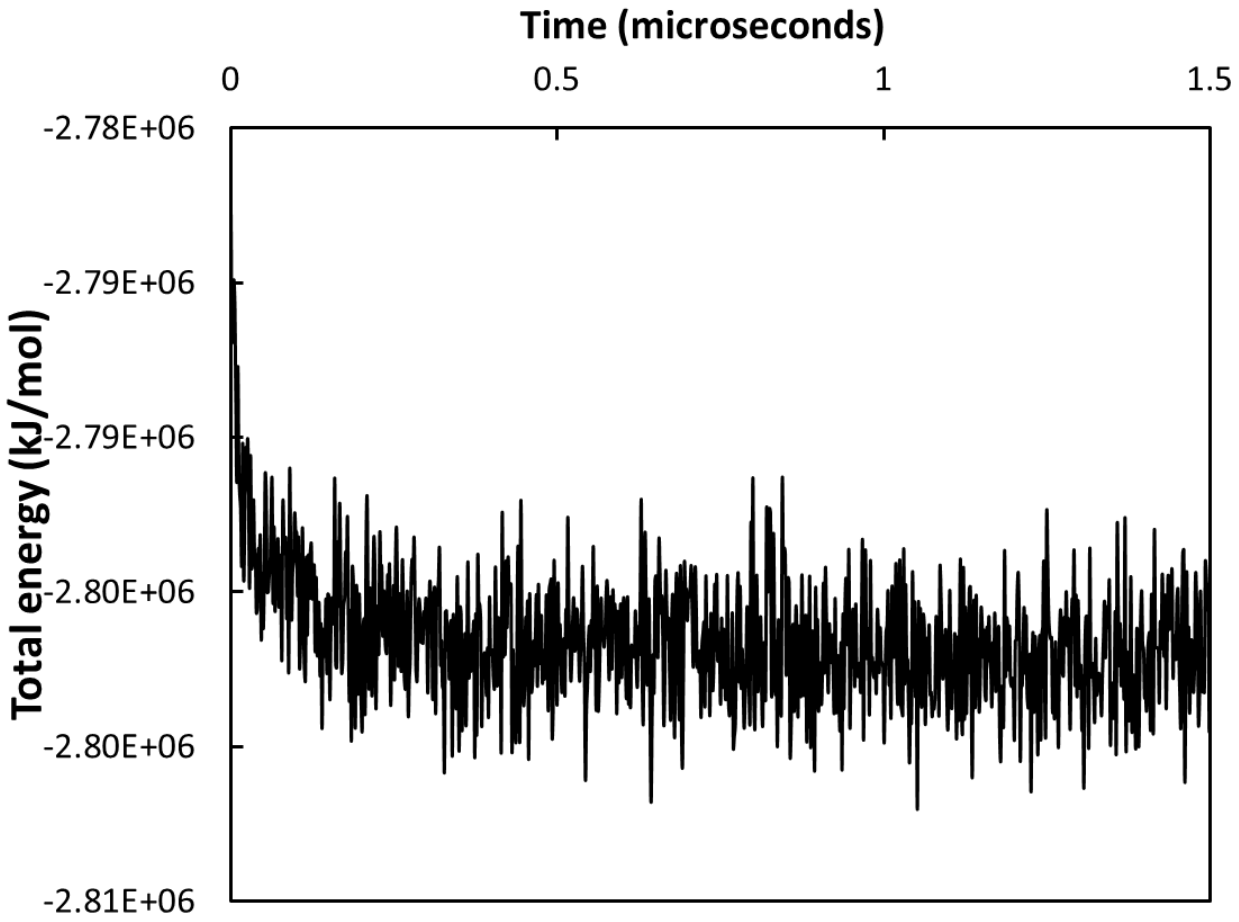

Figure S2. Total energy versus time plot for self-assembly of PTX-PEG^{5K}CA$_8$ 17% (w/w %) system.

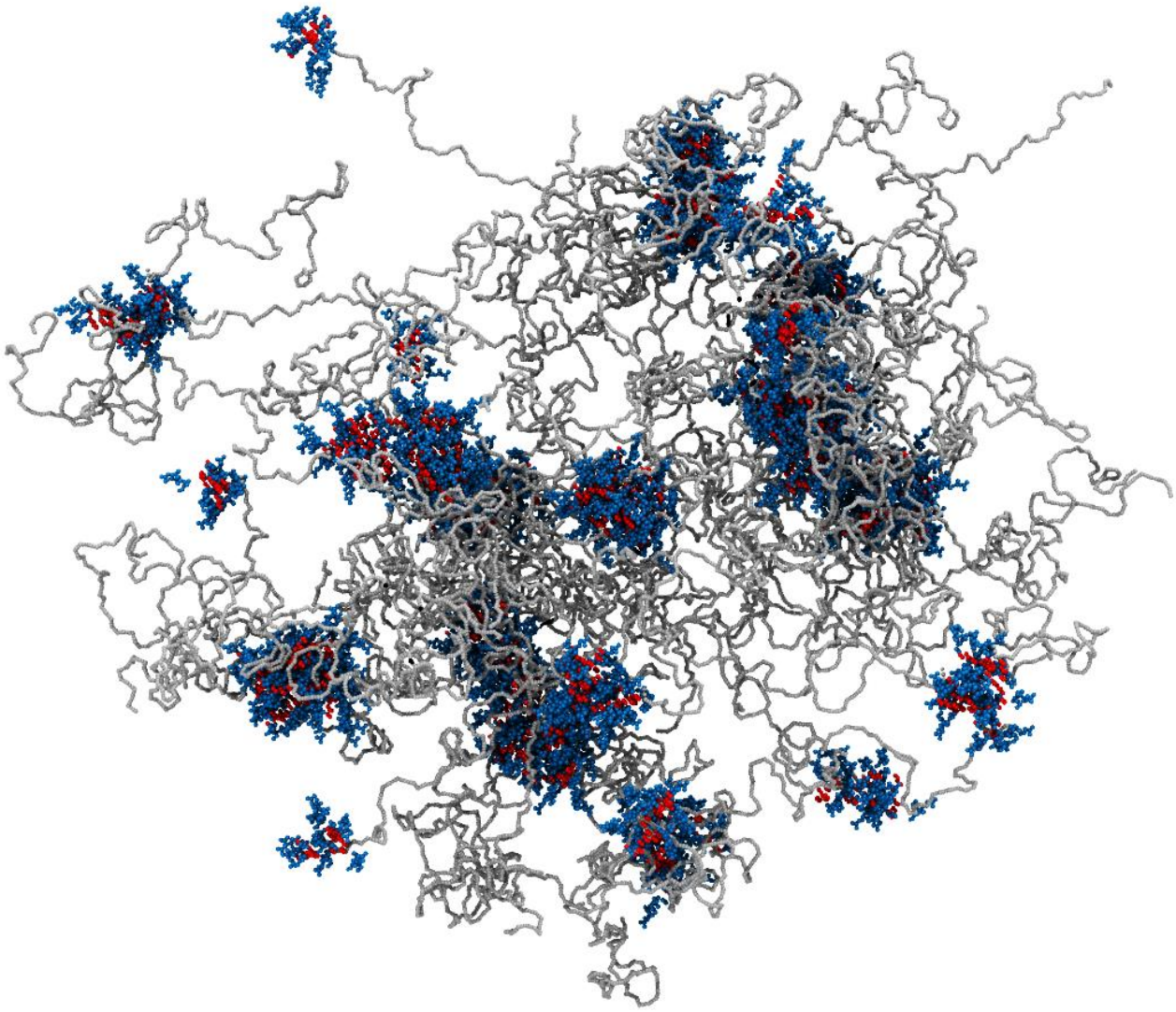

Figure S3. Snapshot of reverse mapped $PEG^{5K}CA_8$ system in a cubic simulation box at 960 ns. Atomistic water molecules are not shown for clarity. Colors: PTX (orange), PEG (gray), Cholic acid (blue) and lysine (red).

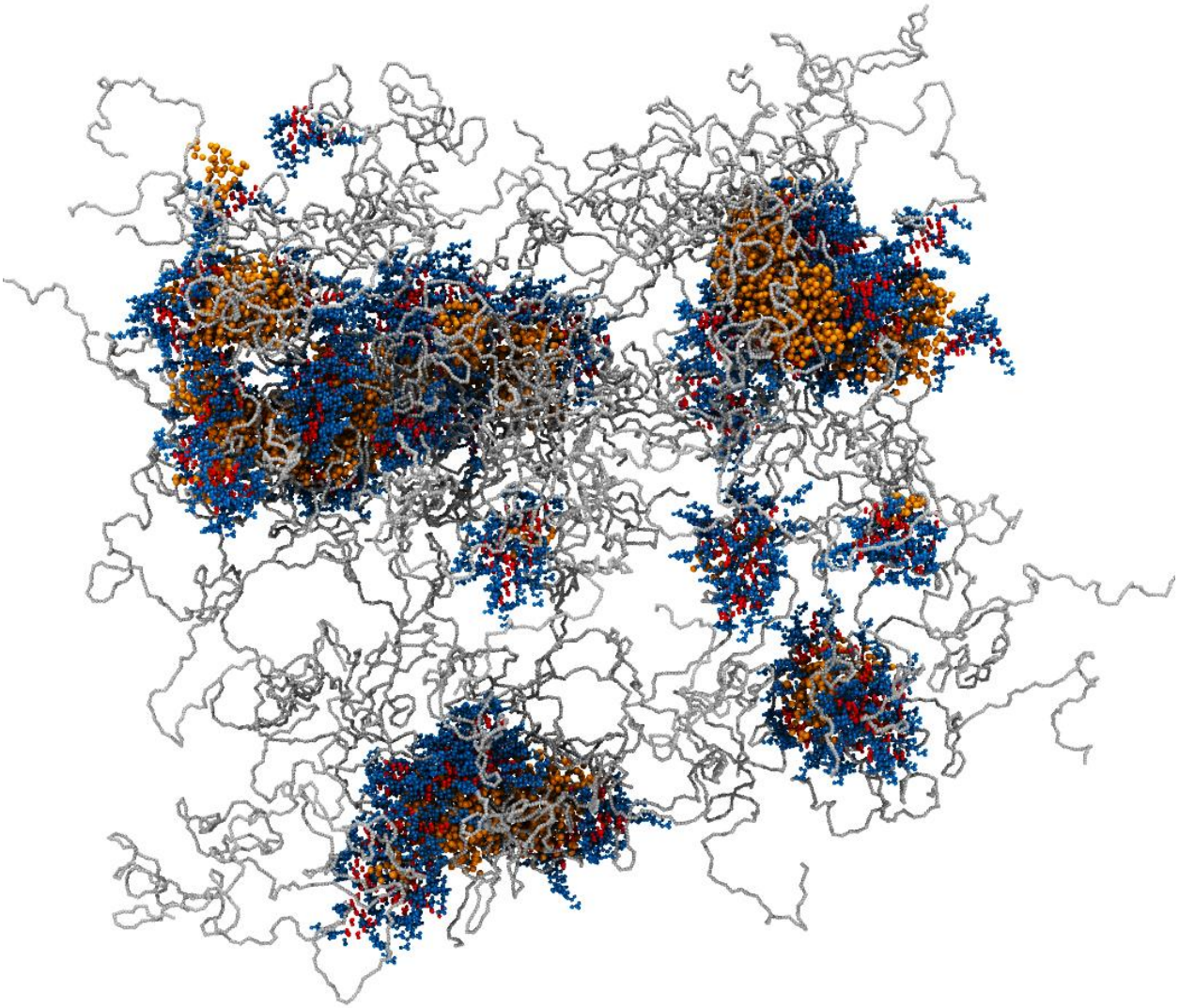

Figure S4. Reverse mapped PTX-PEG^{5K}CA$_8$ system with 17 % (w/w %) drug loading in simulation box at 1.5 µs. Atomistic water molecules are not shown for clarity. Colors: PTX (orange), PEG (gray), Cholic acid (blue) and lysine (red).

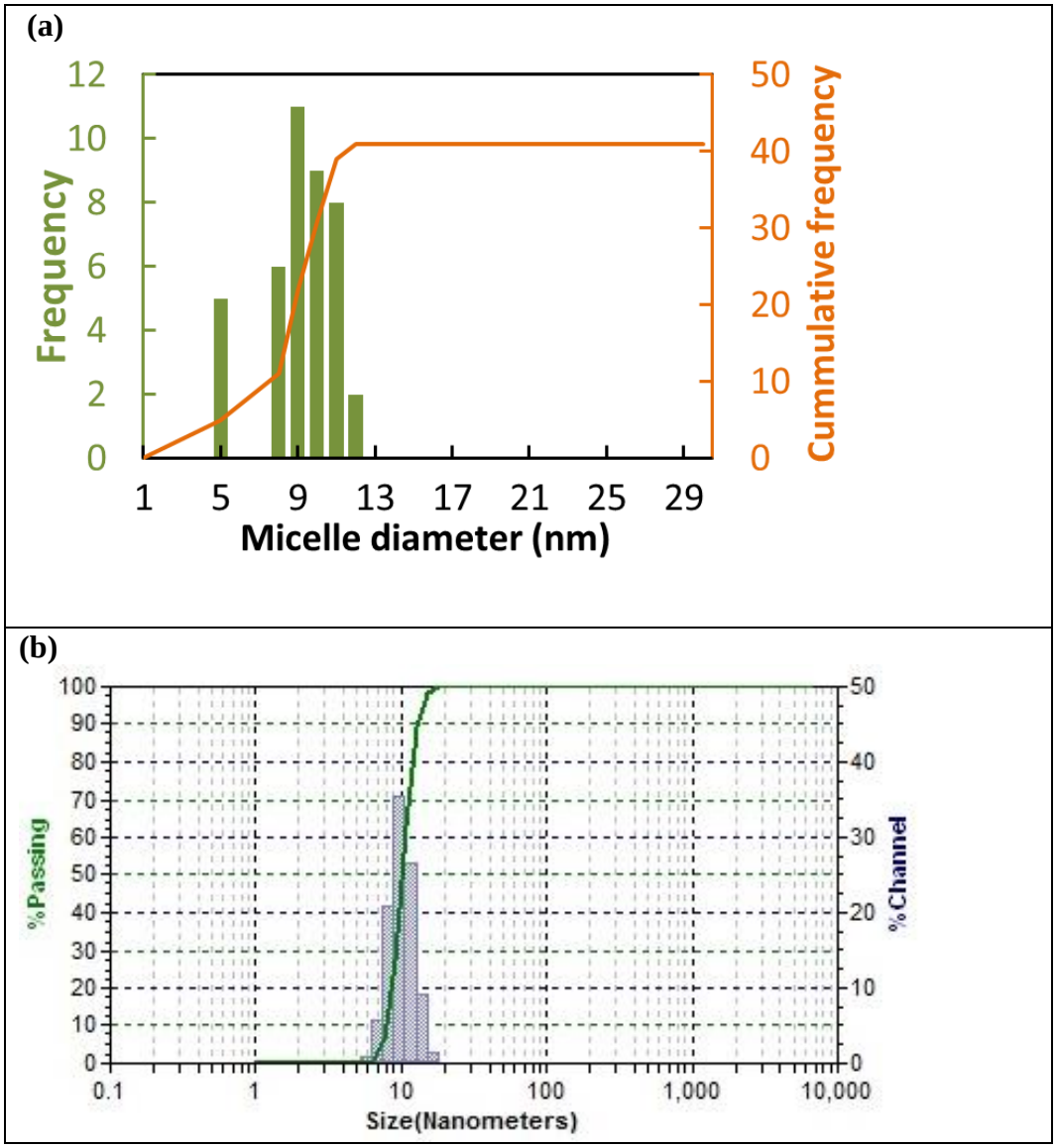

Figure S5. The size distribution of (a) $PEG^{2K}CA_4$ obtained from simulations and (b) experimental data measured by dynamic light scanning

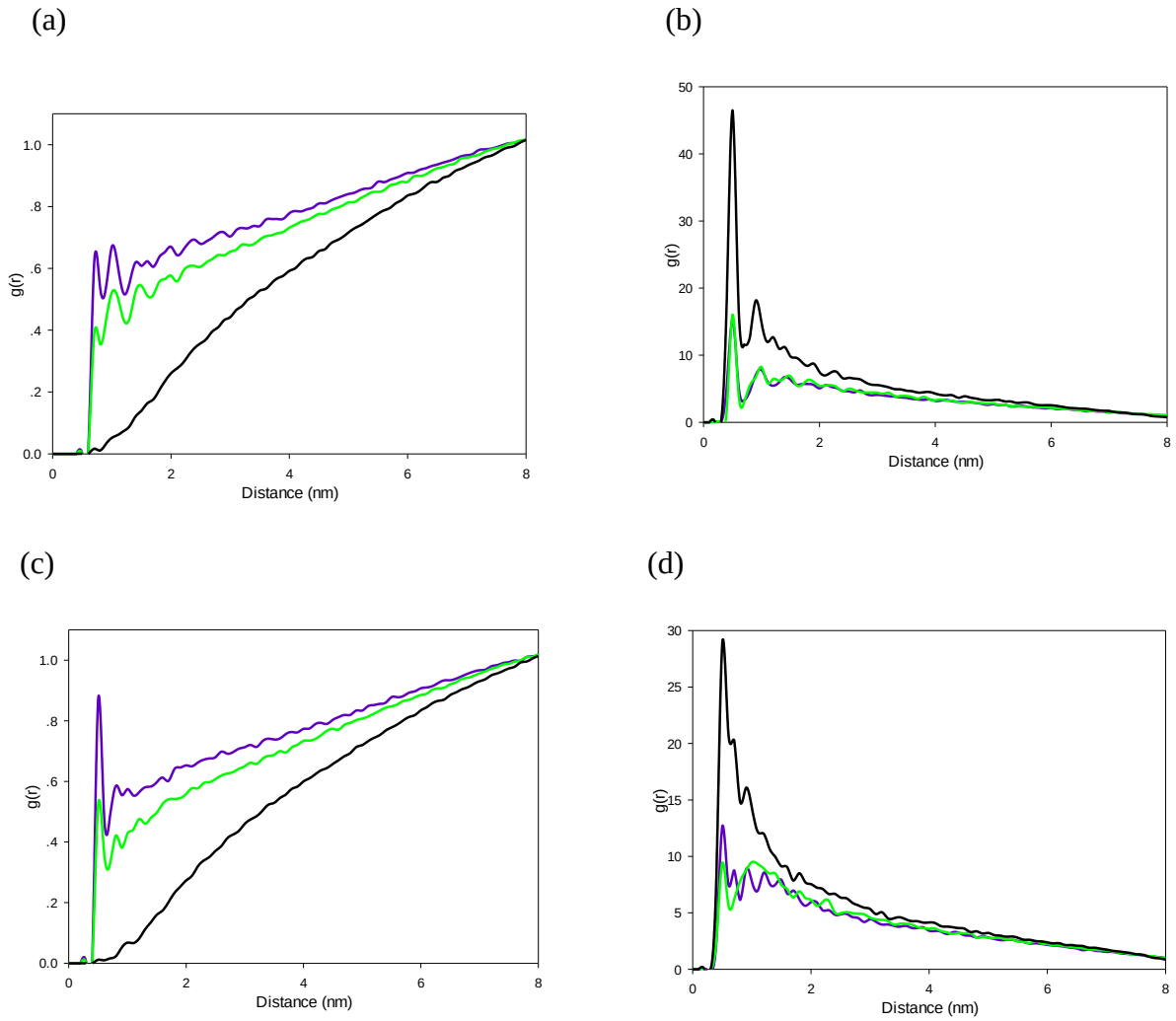

Figure S6. Radial distribution functions of (a) OH-OH (b) O2-water (c) O3-water and (d) O2-O2 cholic acid beads