Figure S1. Statistical analysis of formulation variables on C888-SLN characteristics: Pareto charts (top), main-effect plots (middle), and interaction plots (bottom) for (A) particle size (Y_1), (B) PDI (Y_2), (C) zeta potential (Y_3), and (D) encapsulation efficiency (Y_4).

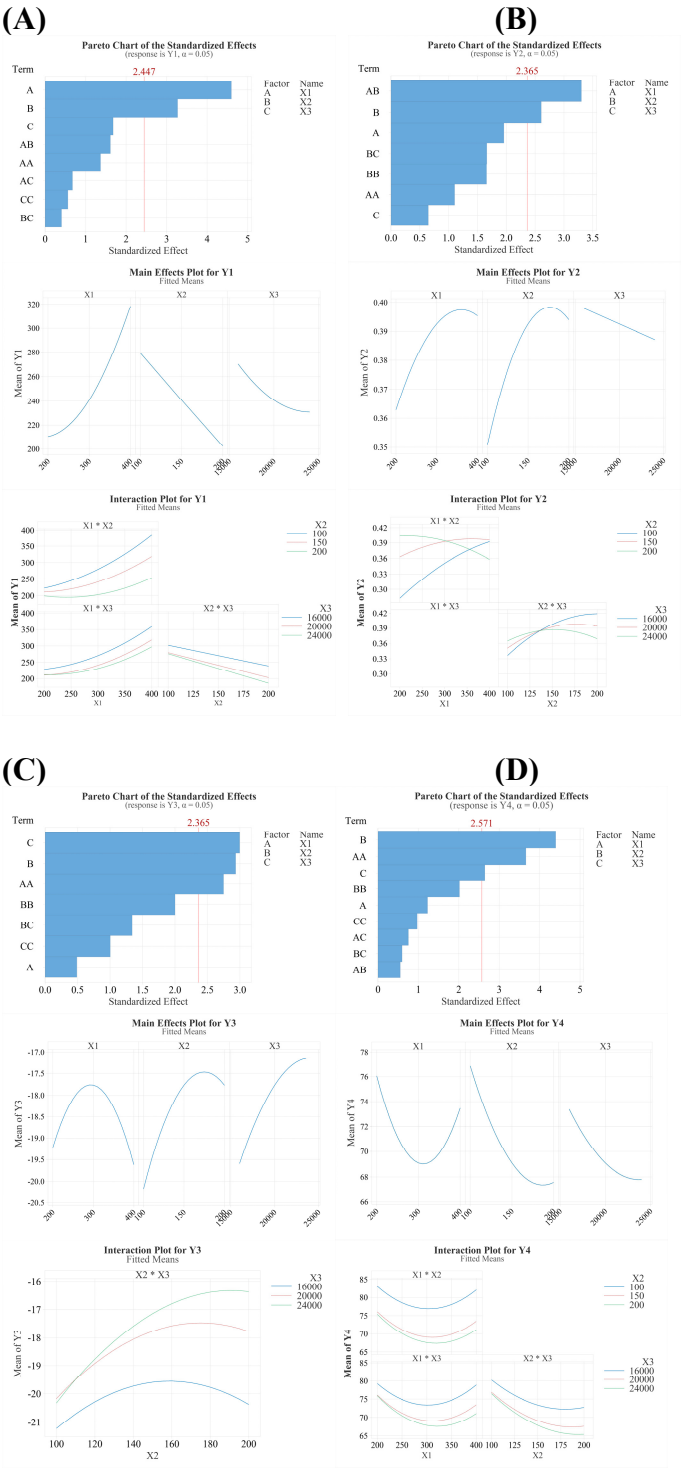


Figure S2. Statistical analysis of formulation variables on CHD5-SLN characteristics: Pareto charts (top), main-effect plots (middle), and interaction plots (bottom) for (A) particle size (Y_1), (B) PDI (Y_2), (C) zeta potential (Y_3), and (D) encapsulation efficiency (Y_4).

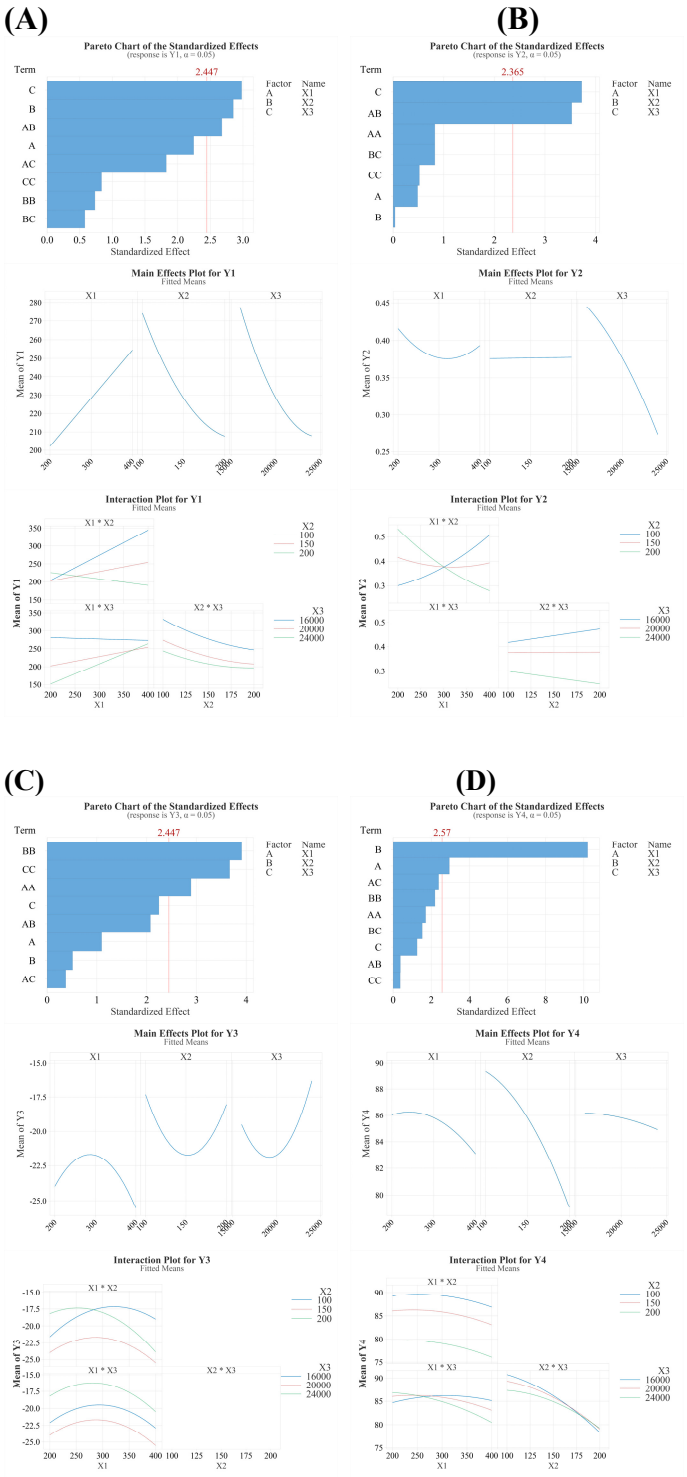


Figure S3. Statistical analysis of formulation variables on St.a-SLN characteristics: Pareto charts (top), main-effect plots (middle), and interaction plots (bottom) for (A) particle size (Y_1), (B) PDI (Y_2), (C) zeta potential (Y_3), and (D) encapsulation efficiency (Y_4).

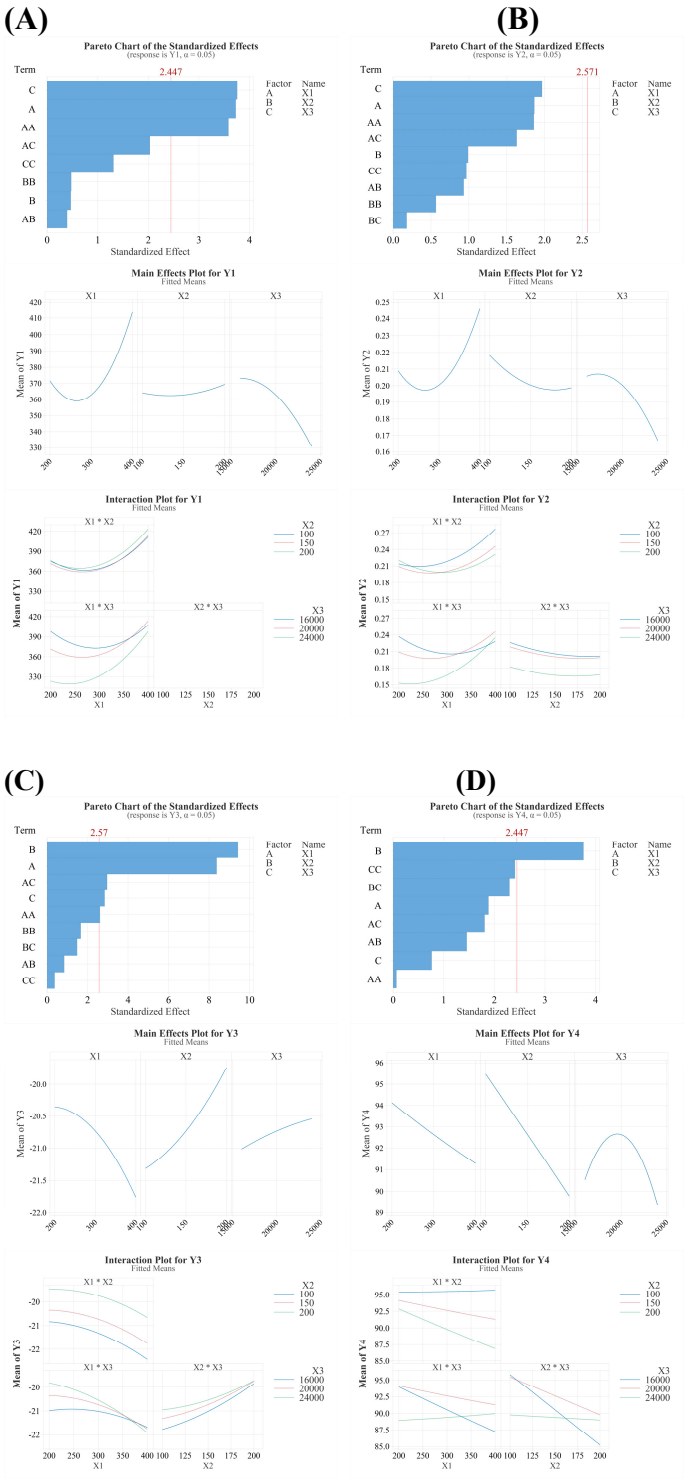


Table S1. Box-Behnken design matrix and experimental responses for C888-SLN.

X_1	X_2	X_3	Y_1	Y_2	Y_3	Y_4
Amount of lipids (mg)	**Amount of surfactant (mg)**	**Homogenization (rpm)**	**Particle size (nm)**	**PDI**	**Zeta potential (mV)**	**Encapsulation Efficiency (%)**
200	100	20000	241.1	0.292	-22.2	85.5
400	100	20000	408.3	0.41	-23.1	82.4
200	200	20000	177	0.38	-19.3	75.1
400	200	20000	237.2	0.343	-17.9	68.6
200	150	16000	249.3	0.39	-21.4	79.2
400	150	16000	373.9	0.41	-21.3	81.0
200	150	24000	193.8	0.349	-17.6	73.8
400	150	24000	273.5	0.378	-19.8	71.1
300	100	16000	263.7	0.31	-20.3	77.8
300	200	16000	241.2	0.425	-21.1	73.1
300	100	24000	276.3	0.364	-19.6	76.1
300	200	24000	226.9	0.401	-17.3	67.8
300	150	20000	231.7	0.388	-17.3	68.7
300	150	20000	234.7	0.397	-17.9	67.0
300	150	20000	250.2	0.382	-18.1	71.6

Table S2. Box-Behnken design matrix and experimental responses for CHD5-SLN.

X_1	X_2	X_3	Y_1	Y_2	Y_3	Y_4
Amount of lipids (mg)	**Amount of surfactant (mg)**	**Homogenization (rpm)**	**Particle size (nm)**	**PDI**	**Zeta potential (mV)**	**Encapsulation Efficiency (%)**
200	100	20000	202.7	0.328	-20	90.2
400	100	20000	378.6	0.572	-19.6	87.7
200	200	20000	200.2	0.48	-17.6	78.7
400	200	20000	199.8	0.266	-25.5	75.1
200	150	16000	290.9	0.465	-24	85.2
400	150	16000	247.6	0.394	-22.6	85.6
200	150	24000	186.4	0.355	-18.5	86.3
400	150	24000	263.3	0.307	-18.6	80.0
300	100	16000	328.5	0.421	-14.8	89.4
300	200	16000	267.3	0.555	-14.5	78.8
300	100	24000	215.1	0.231	-13.2	86.9
300	200	24000	192	0.258	-12.9	80.7
300	150	20000	246.8	0.406	-21.8	86.7
300	150	20000	197.4	0.331	-19.8	85.8
300	150	20000	223.2	0.366	-23.6	85.0

Table S3. Box-Behnken design matrix and experimental responses for St.a-SLN.

X_1	X_2	X_3	Y_1	Y_2	Y_3	Y_4
Amount of lipids (mg)	**Amount of surfactant (mg)**	**Homogenization (rpm)**	**Particle size (nm)**	**PDI**	**Zeta potential (mV)**	**Encapsulation Efficiency (%)**
200	100	20000	360.4	0.203	-20.9	97.2
400	100	20000	420.2	0.29	-22.6	95.4
200	200	20000	366.4	0.207	-19.3	93.1
400	200	20000	438.8	0.242	-20.6	85.1
200	150	16000	412.3	0.241	-21.1	94.2
400	150	16000	397.8	0.208	-21.7	89.5
200	150	24000	333.1	0.173	-19.8	86.6
400	150	24000	383.3	0.231	-21.8	89.7
300	100	16000	378.4	0.233	-21.6	93.8
300	200	16000	371.1	0.211	-19.9	84.7
300	100	24000	335.1	0.173	-20.9	90.3
300	200	24000	338.9	0.161	-19.9	91.0
300	150	20000	367.4	0.225	-20.7	91.9
300	150	20000	369.3	0.213	-21	93.6
300	150	20000	351.7	0.163	-20.5	92.3