

Supplementary Figures

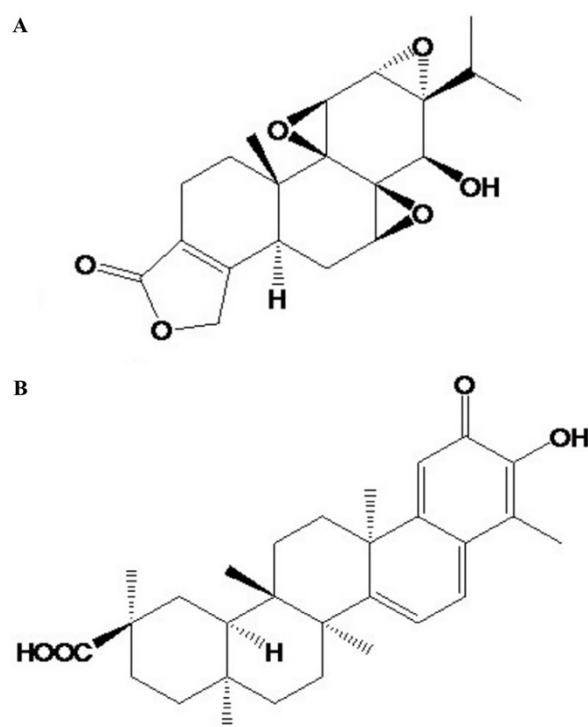


Fig. S1. The chemical structures of A. TPL B. CL.

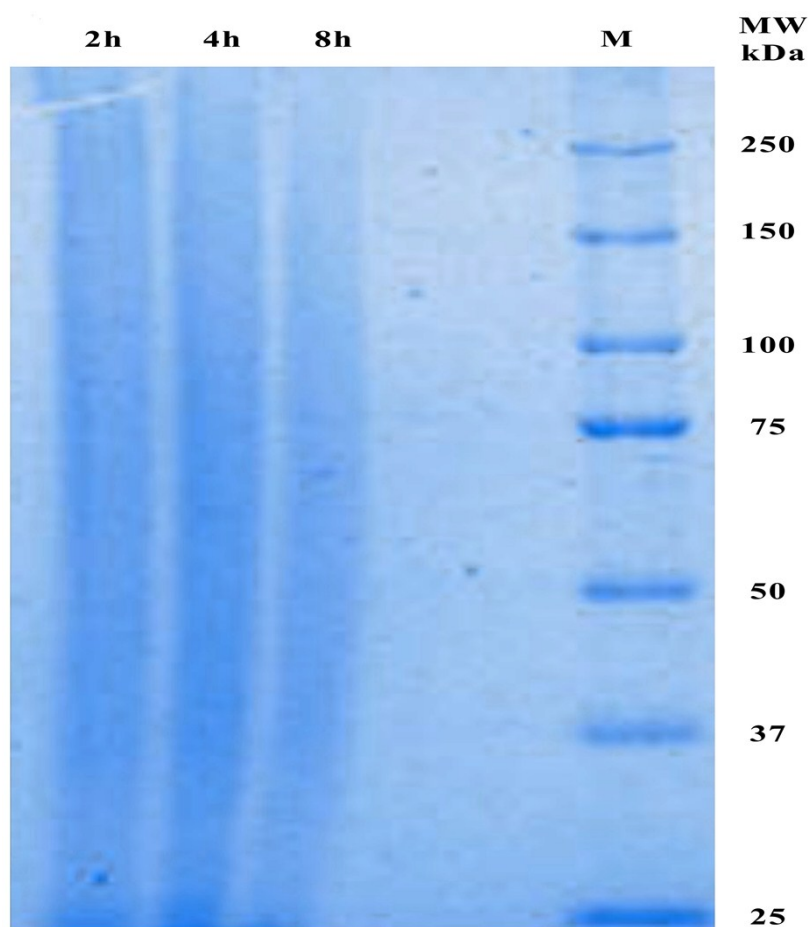


Fig. S2. SDS-PAGE analysis of SF dissolved by $\text{CaCl}_2 \cdot \text{CH}_3\text{CH}_2\text{OH} \cdot \text{H}_2\text{O}$ ternary system where (M) are the molecular weight markers. The concentration of the separating gel was 8%.

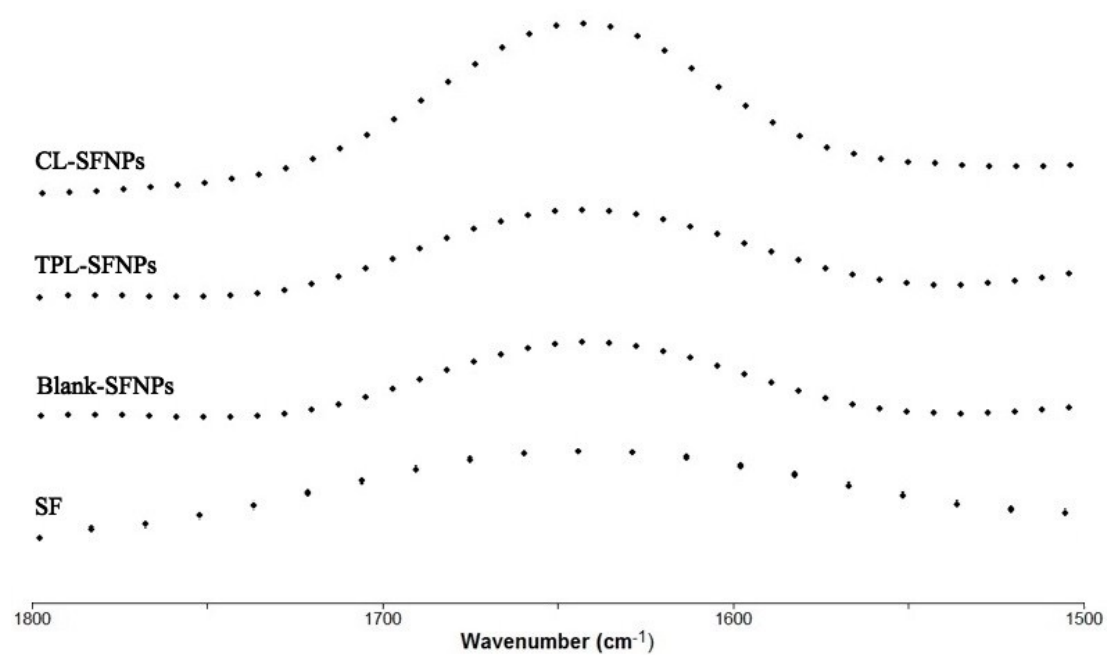


Fig. S3. Amide I (1700-1600 cm^{-1}) regions of FTIR spectra of SF, Blank-SFNPs, TPL-SFNPs and CL-SFNPs.

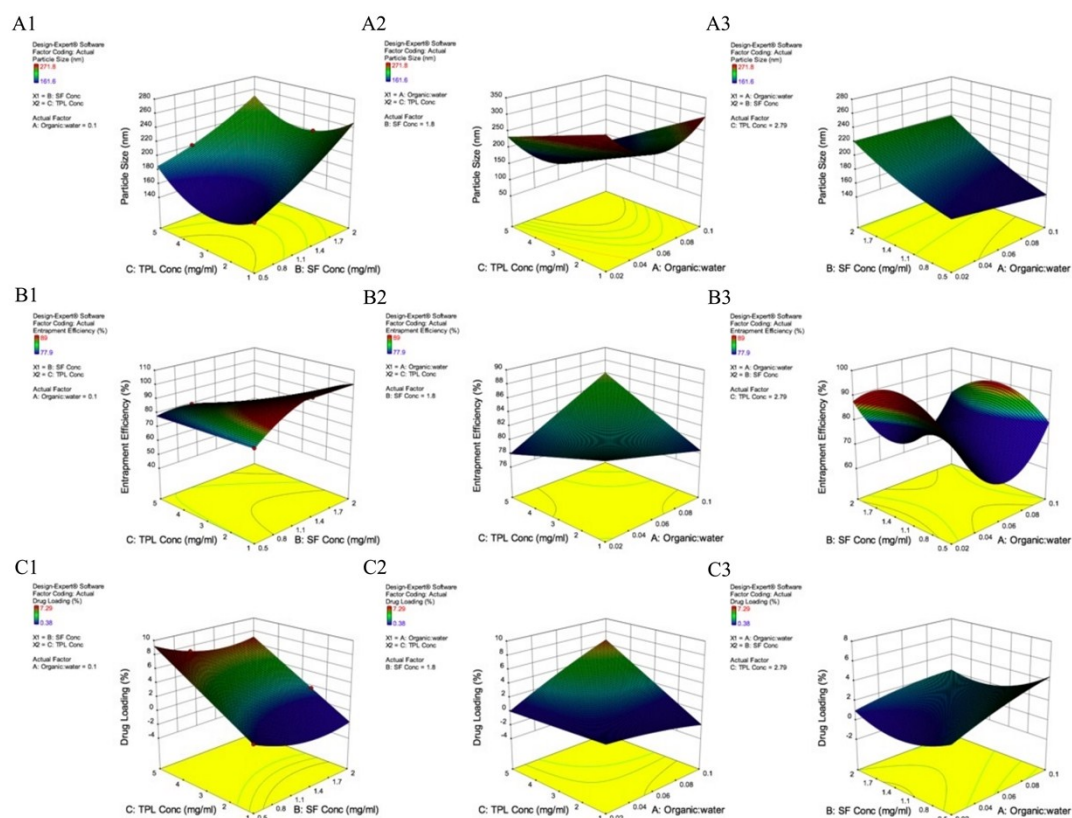


Fig. S4. Response surface plots showing the effect of selected factors on particle size (A1-A3), entrapment efficiency (B1-B3), and drug loading (C1-C3) of TPL-SFNPs analyzed using Design Expert® Software.

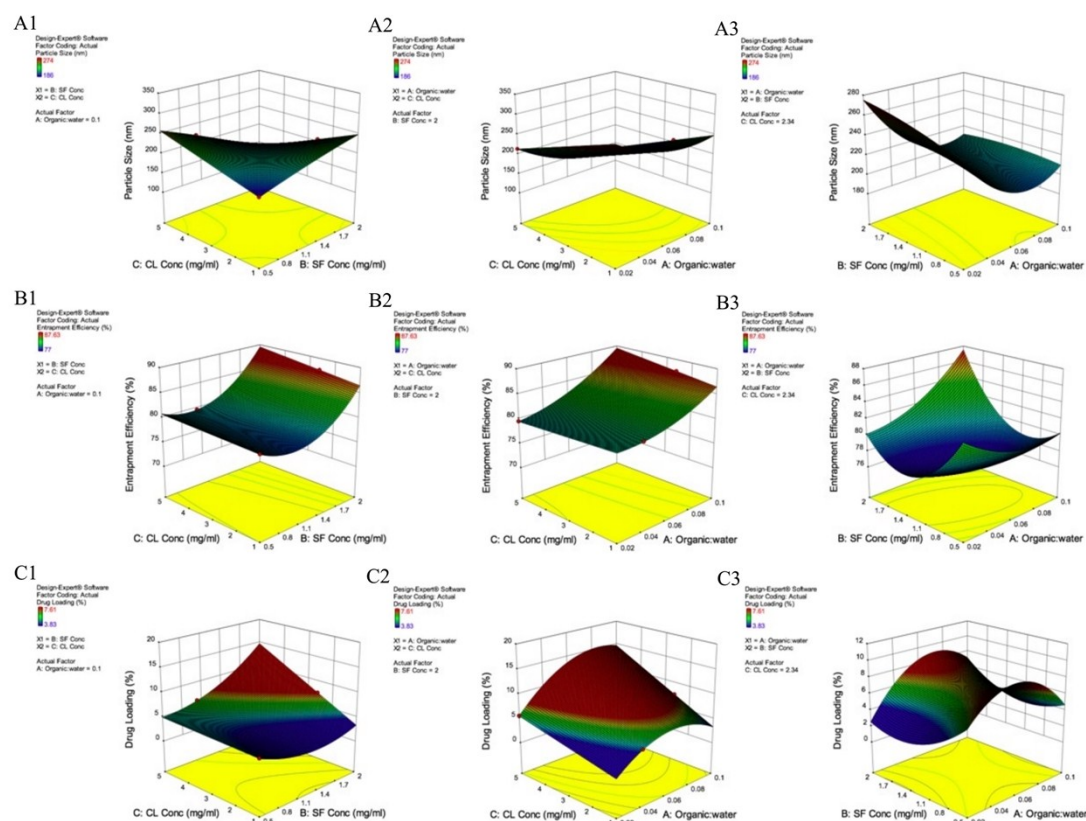


Fig. S5. Response surface plots showing the effect of selected factors on particle size (A1-A3), entrapment efficiency (B1-B3), and drug loading (C1-C3) of CL-SFNPs analyzed using Design Expert® Software.

Supplementary Tables

Table S1. Factors and coded levels selected for TPL-SFNPs and CL-SFNPs formulation development and optimization

Levels	Factor		
	Organic : SF solution (V/V)	C _{SF} (mg/ml)	C _{TPL/CL} (mg/ml)
1	1:10	0.5	1.0
2	1:25	1.0	2.5
3	1:50	2.0	5.0

Table S2. Experimental design factoring dose range and dose density of TPL and CL for drug combination analysis

Sample	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5
TPL/TPL-SFNPs	0.25 X (IC ₅₀) ₁	0.5 X (IC ₅₀) ₁	X (IC ₅₀) ₁	2X (IC ₅₀) ₁	4X (IC ₅₀) ₁
CL/CL-SFNPs	0.25 X (IC ₅₀) ₂	0.5 X (IC ₅₀) ₂	X (IC ₅₀) ₂	X (IC ₅₀) ₂	4X (IC ₅₀) ₂
Combination	(fa) _{1,2}	(fa) _{1,2}	(fa) _{1,2}	(fa) _{1,2}	(fa) _{1,2}

Table S3. Taguchi's L9 orthogonal array experimental design for TPL-SFNPs and CL-SFNPs formulation optimization (factors and responses

No	Factor			Responses					
	Organic : SF solution (V/V)	C _{SF} (mg/ml)	C _{TPL/CL} (mg/ml)	TPL-SFNPs			CL-SFNPs		
				Particle size (nm±s.d)	EE (%)	DL (µg/mg)	Particle size (nm±s.d)	EE (%)	DL (µg/mg)
1	1:10	0.5	1.0	161.6 ± 0.8	80.0	6.5	186.2 ± 1.6	80.0	45.4
2	1:25	1.0	2.5	178.7 ± 1.1	77.9	7.9	228.1 ± 0.9	77.0	59.1
3	1:50	2.0	5.0	214.1 ± 1.4	79.6	6.6	214.5 ± 3.0	79.6	56.0
4	1:10	0.5	1.0	201.3 ± 2.1	79.7	72.9	221.0 ± 3.0	79.7	62.1
5	1:25	1.0	2.5	271.8 ± 8.5	80.7	8.0	271.5 ± 1.4	80.7	44.6
6	1:50	2.0	5.0	170.7 ± 1.3	83.2	14.8	250.7 ± 0.1	83.2	58.2
7	1:10	0.5	1.0	221.1 ± 2.6	83.5	16.8	207.4 ± 2.8	87.6	74.7
8	1:25	1.0	2.5	174.1 ± 1.4	80.0	33.0	274.1 ± 2.0	80.0	54.7
9	1:50	2.0	5.0	230.6 ± 12.4	89.0	3.8	249.2 ± 2.6	79.0	37.4

Table S4. Validation of optimized formulation parameters recommended by Design Expert® Software for TPL-SFNPs and CL-SFNPs

Formulations	Factors			Predicted Value			Experimental Value			Desirability
	Organic : SF solution (V/V)	C _{SF} (mg/ml)	C _{CL/TPL} (mg/ml)	Particle size (nm)	EE (%)	DL (µg/mg)	Particle size (nm±s.d)	EE (%±s.d)	DL (µg/mg)	
TPL-SFNPs	1:10	1.8	2.79	164	81	62	155.7 ± 5.1 3.1	81.6 ± 3.1	56.6 ± 2.6	0.971
CL-SFNPs	1:10	2.0	2.34	211	85	65	170.5 ± 2.3 1.1	87.0 ± 1.1	63.5 ± 3.8	0.904