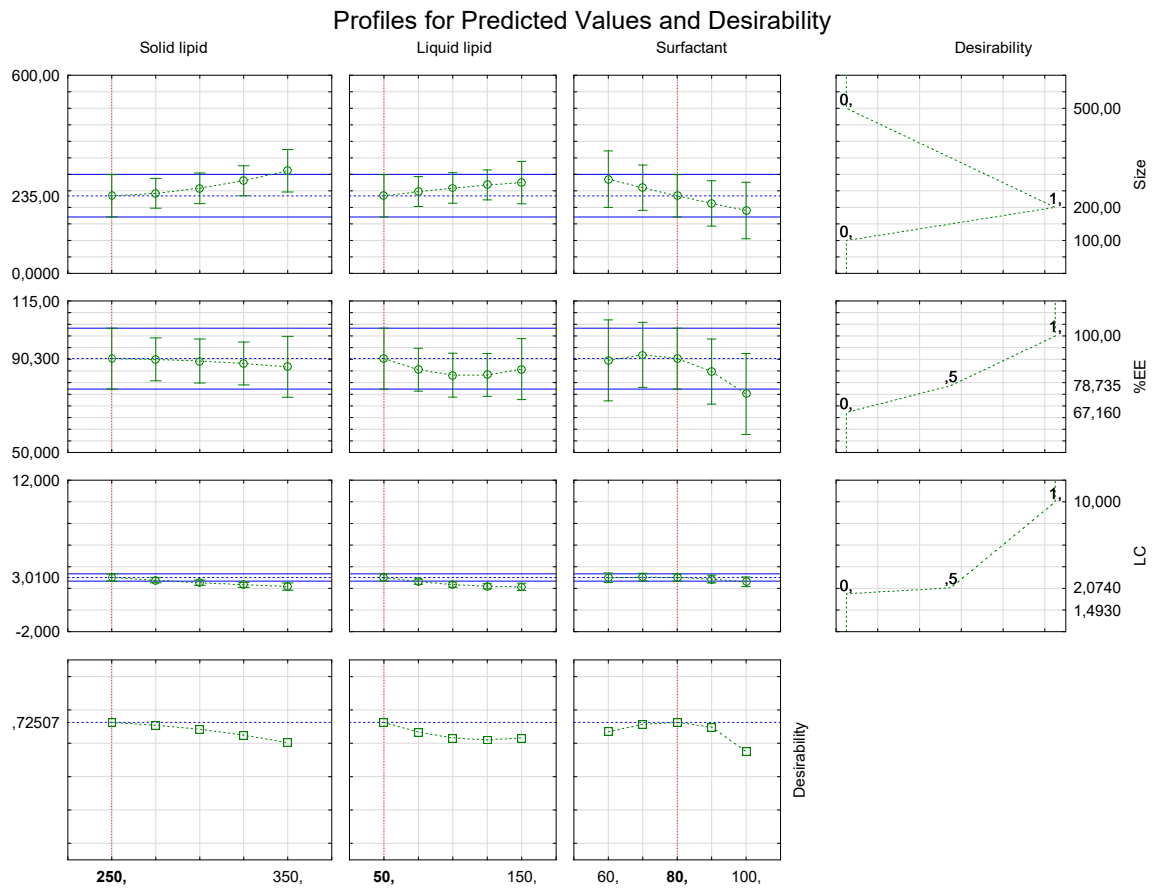|	Sum of squares	df	Mean square	F-value	p-value
X_1	**6845.00**	**1**	**6845.000**	**30.69507**	**0.031068**
X_1^2	612.06	1	612.058	2.74465	0.239426
X_2	1960.20	1	1960.200	8.79013	0.097423
X_2^2	87.75	1	87.750	0.39350	0.594534
X_3	**6552.20**	**1**	**6552.200**	**29.38206**	**0.032390**
X_3^2	36.06	1	36.058	0.16169	0.726505
X_1X_2	72.25	1	72.250	0.32399	0.626622
X_1X_3	1369.00	1	1369.000	6.13901	0.131513
X_2X_3	225.00	1	225.000	1.00897	0.420931
Error	446.00	2	223.000		
Total SS	18691.73	14			
R^2	0.976				
Adj.R^2	0.833				

Supplementary Table 1. Analysis of variance for particle size (Y_1). Statistically significant parameters (p-value < 0.05 with a 95% confident interval) are highlighted in bold.

	Sum of squares	df	Mean square	F-value	p-value
X_1	16.0205	1	16.0205	1.73695	0.318234
X_1^2	10.7231	1	10.7231	1.16261	0.393691
X_2	57.1220	1	57.1220	6.19321	0.130578
X_2^2	6.9385	1	6.9385	0.75228	0.477191
X_3	66.2480	1	66.2480	7.18265	0.115580
X_3^2	**233.6078**	**1**	**233.6078**	**25.32791**	**0.037288**
X_1X_2	3.2400	1	3.2400	0.35128	0.613476
X_1X_3	89.3025	1	89.3025	9.68224	0.089616
X_2X_3	**193.2100**	**1**	**193.2100**	**20.94796**	**0.044570**
Error	18.4467	2	9.2233		
Total SS	748.9773	14			
R^2	0.975				
Adj.R^2	0.828				

Supplementary Table 2. Analysis of variance for encapsulation efficiency (Y_2). Statistically significant parameters (p-value < 0.05 with a 95% confident interval) are highlighted in bold.

	Sum of squares	df	Mean square	F-value	p-value
X_1	**0.695645**	**1**	**0.695645**	**115.3003**	**0.008562**
X_1^2	0.000108	1	0.000108	0.0180	0.905671
X_2	**0.856980**	**1**	**0.856980**	**142.0409**	**0.006967**
X_2^2	0.028001	1	0.028001	4.6410	0.164033
X_3	0.040500	1	0.040500	6.7127	0.122247
X_3^2	**0.163478**	**1**	**0.163478**	**27.0957**	**0.034981**
X_1X_2	0.016900	1	0.016900	2.8011	0.236175
X_1X_3	0.042025	1	0.042025	6.9655	0.118568
X_2X_3	**0.122500**	**1**	**0.122500**	**20.3039**	**0.045888**
Error	0.012067	2	0.006033		
Total SS	2.054373	14			
R^2	0.994				
Adj.R^2	0.959				

Supplementary Table 3. Analysis of variance for loading capacity (Y_3). Statistically significant parameters (p-value < 0.05 with a 95% confident interval) are highlighted in bold.

Supplementary Figure 1. Response desirability profile of the optimized formulation. The prediction and profiling function of STATISTICA 10 (Statsoft[1]. Inc.) software was used to obtain the response desirability profile. The factors were settled as particle size in the optimum value of 200 nm, the maximum encapsulation efficiency, and the maximum loading capacity.