

Appendix 1. The effect of SLS concentration on the particle size, PDI and ZP of EZ-NS stabilized with PVA (n=3)

SLS (%w/v)	Z_{ave} (nm)	PDI	ZP (mV)
0	311 ± 4.9	0.159 ± 0.06	-14.3
0.01	294 ± 3.7	0.243 ± 0.03	-16.8
0.02	317 ± 5.2	0.225 ± 0.05	-19.3
0.03	322 ± 4.9	0.195 ± 0.07	-18.3
0.05	329 ± 2.8	0.192 ± 0.03	-22.9
0.07	373 ± 4.6	0.178 ± 0.09	-22.5
0.1	394 ± 8.8	0.207 ± 0.05	-20.4

Appendix 2. Model summary statistics for Z_{ave} and PDI

Source	R²		Adjusted-R²		Predicted-R²		PRESS^c	
	Y1 ^a	Y2 ^b	Y1	Y2	Y1	Y2	Y1	Y2
Linear	0.1716	0.2698	-0.0196	0.1013	-0.5626	-0.4114	5.962E+05	0.4301
2FI	0.4940	0.5769	0.1904	0.3230	-0.8863	-0.6870	7.197E+05	0.5141
Quadratic	0.9361	0.8626	0.8540	0.6860	0.4994	0.2482	1.910E+05	0.2291

^aY1: Z_{ave} ; ^bY2: PDI; ^cPRESS: Predicted residual error sum of square

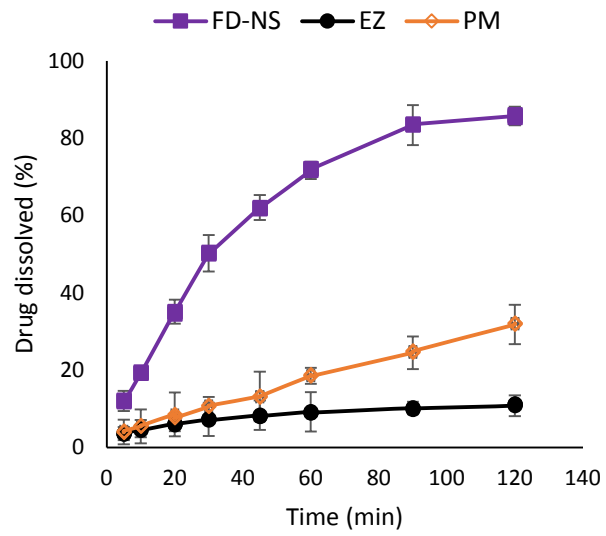
Appendix 3. ANOVA for response surface quadratic model of Z_{ave} (Y1)

Source	Sum of Squares	df ^a	Mean Square	F-value	p-value ^b
Model	3.572E+05	9	39686.61	11.40	<u>0.0021</u>
A-Milling speed	237.62	1	237.62	0.0683	0.8014
B-Milling time	100.54	1	100.54	0.0289	0.8699
C-Stabilizer con.	65117.19	1	65117.19	18.70	<u>0.0035</u>
AB	1.136E+05	1	1.136E+05	32.64	<u>0.0007</u>
AC	3516.49	1	3516.49	1.01	0.3484
BC	5884.42	1	5884.42	1.69	0.2347
A ²	1.638E+05	1	1.638E+05	47.06	<u>0.0002</u>
B ²	91.73	1	91.73	0.0263	0.8756
C ²	1543.69	1	1543.69	0.4434	0.5268
Residual	24370.51	7	3481.50		
Lack of Fit	10591.09	3	3530.36	1.02	0.4705
Pure Error	13779.43	4	3444.86		
Cor Total	3.816E+05	16			

^adf: Degree of freedom; ^bStatistically significant terms are underlined (p-value less than 0.05).

Appendi 4. ANOVA for response surface quadratic model of PDI (Y2)

Source	Sum of Squares	df	Mean Square	F-value	p-value
Model	0.2629	9	0.0292	4.88	<u>0.0242</u>
A-Milling speed	0.0543	1	0.0543	9.08	<u>0.0196</u>
B-Milling time	0.0159	1	0.0159	2.66	0.1467
C-Stabilizer con.	0.0120	1	0.0120	2.01	0.1994
AB	0.0173	1	0.0173	2.89	0.1329
AC	0.0745	1	0.0745	12.46	<u>0.0096</u>
BC	0.0018	1	0.0018	0.2949	0.6039
A ²	0.0279	1	0.0279	4.67	0.0676
B ²	0.0538	1	0.0538	9.00	<u>0.0199</u>
C ²	0.0085	1	0.0085	1.41	0.2731
Residual	0.0419	7	0.0060		
Lack of Fit	0.0113	3	0.0038	0.4952	0.7049
Pure Error	0.0305	4	0.0076		
Cor Total	0.3048	16			



Appendix 5. Dissolution profiles of EZ, FD-NS and related PM in phosphate buffer (pH=6.8) containing 0.1 % SLS (n= 3)

Appendix 6. Dissolution parameters of the intact drug and prepared formulations in phosphate buffer (pH=6.8) containing 0.1 % SLS (mean $\pm$ SD, n=3)

Sample	Q₃₀^a (%)	DE₆₀^b (%)	DE₁₂₀ (%)	MDR^c (%min⁻¹)
EZ	8.77 $\pm$ 1.53	8.29 $\pm$ 0.09	9.62 $\pm$ 0.05	0.39 $\pm$ 0.06
PM	17.92 $\pm$ 0.25	17.75 $\pm$ 0.06	21.98 $\pm$ 0.02	0.53 $\pm$ 0.03
FD-NS	48.25 $\pm$ 0.28	43.68 $\pm$ 0.04	57.77 $\pm$ 0.12	0.99 $\pm$ 0.02

^aQ₃₀: amount of drug dissolved in 30 min; ^bDE: dissolution efficiency; ^cMDR: mean dissolution rate