

Supplementary data

Indomethacin Incorporated Microemulsion-Laden Contact Lenses for Improved Ocular Drug Delivery and Therapeutic Efficacy

Kashvi Panchal¹, Yashkumar Patel¹, Harshilkumar Jani¹, Mittal Dalal², Vijay R Chidrawar³, Deepanjan Datta⁴, Popat Mohite⁵, Abhijeet Puri⁵, Ketan Ranch^{1*} and Sudarshan Singh^{6,7*}

¹Department of Pharmaceutics and Pharmaceutical Technology, L. M. College of Pharmacy, Ahmedabad, Gujarat 380009, India [KP: kashvi38@gmail.com;

KR: ranchketan@gmail.com; YP: yash.patel@lmcp.ac.in; HJ: harshil.jani@lmcp.ac.in]

²Department of Pharmacology, L. M. College of Pharmacy, Ahmedabad, Gujarat 380009, India [MD: mittal.dalal@lmcp.ac.in]

³School of Pharmacy and Technology Management, SVKM's Narsee Monjee Institute of Management Studies (NMIMS), Deemed-to-University, Green Industrial Park, TSIIC, Jadcherla, Hyderabad 509301, India [VRC: vijay.chidrawar@gmail.com]

⁴Department of Pharmaceutics, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal, Karnataka 576104, India [DD: deepanjandtt@gmail.com]

⁵AETs St. John Institute of Pharmacy and Research, Palghar, Maharashtra 401404, India [PM: mohitepb@gmail.com; AP: abhijeetp@sjpr.edu.in]

⁶Office of Research Administration, Chiang Mai University, Chiang Mai 50200, Thailand

⁷Faculty of Pharmacy, Chiang Mai University, Chiang Mai 50200, Thailand [SS: sudarshan.s@cmu.ac.th]

***Correspondence:** sudarshan.s@cmu.ac.th; ranchketan@gmail.com

Supplementary data

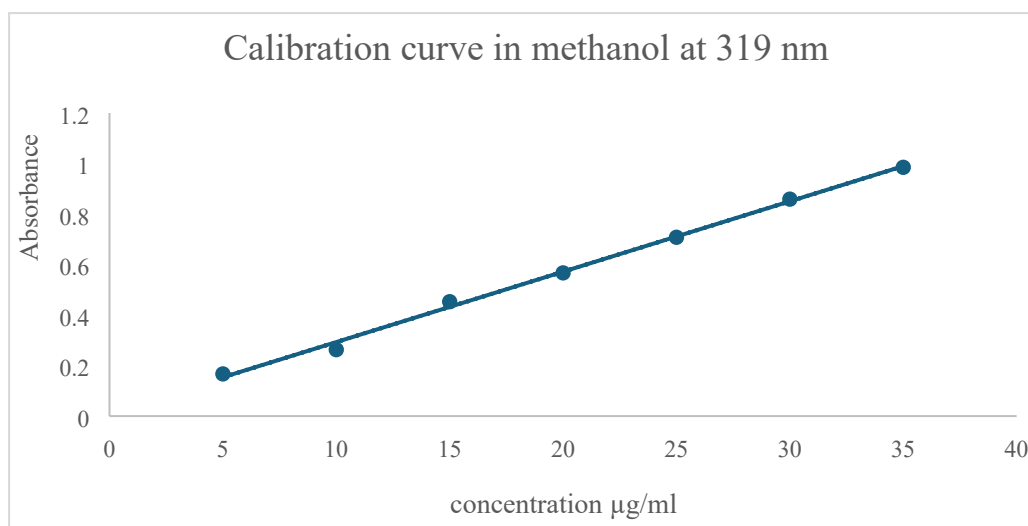


Figure S1. Calibration curve of IND in methanol using UV-Vis Spectrophotometer

Supplementary data

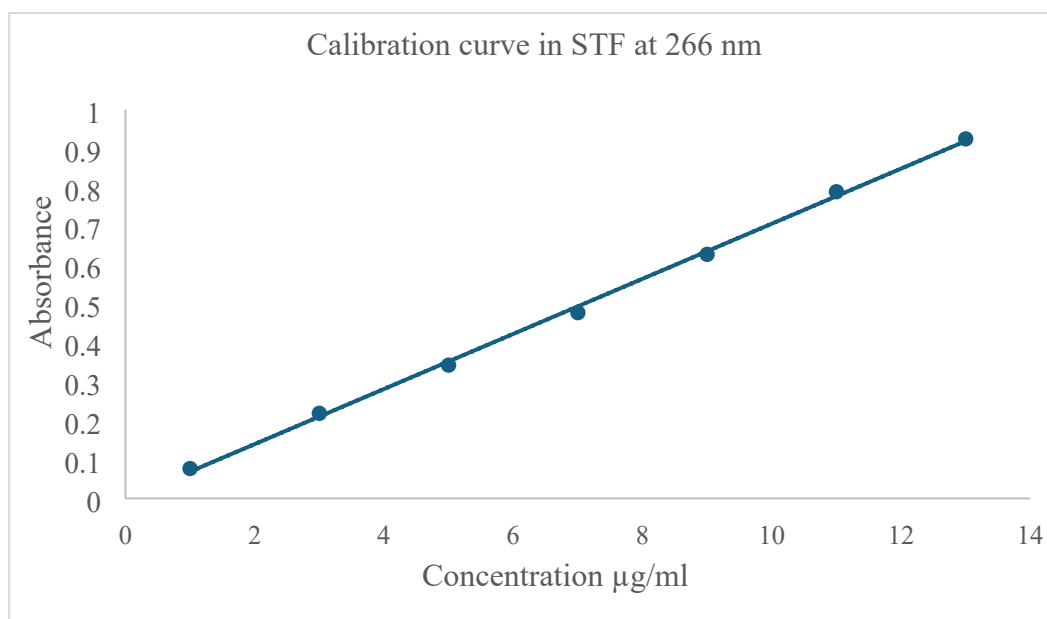


Figure S2. Calibration curve of IND in methanol using UV-Vis Spectrophotometer

Supplementary data

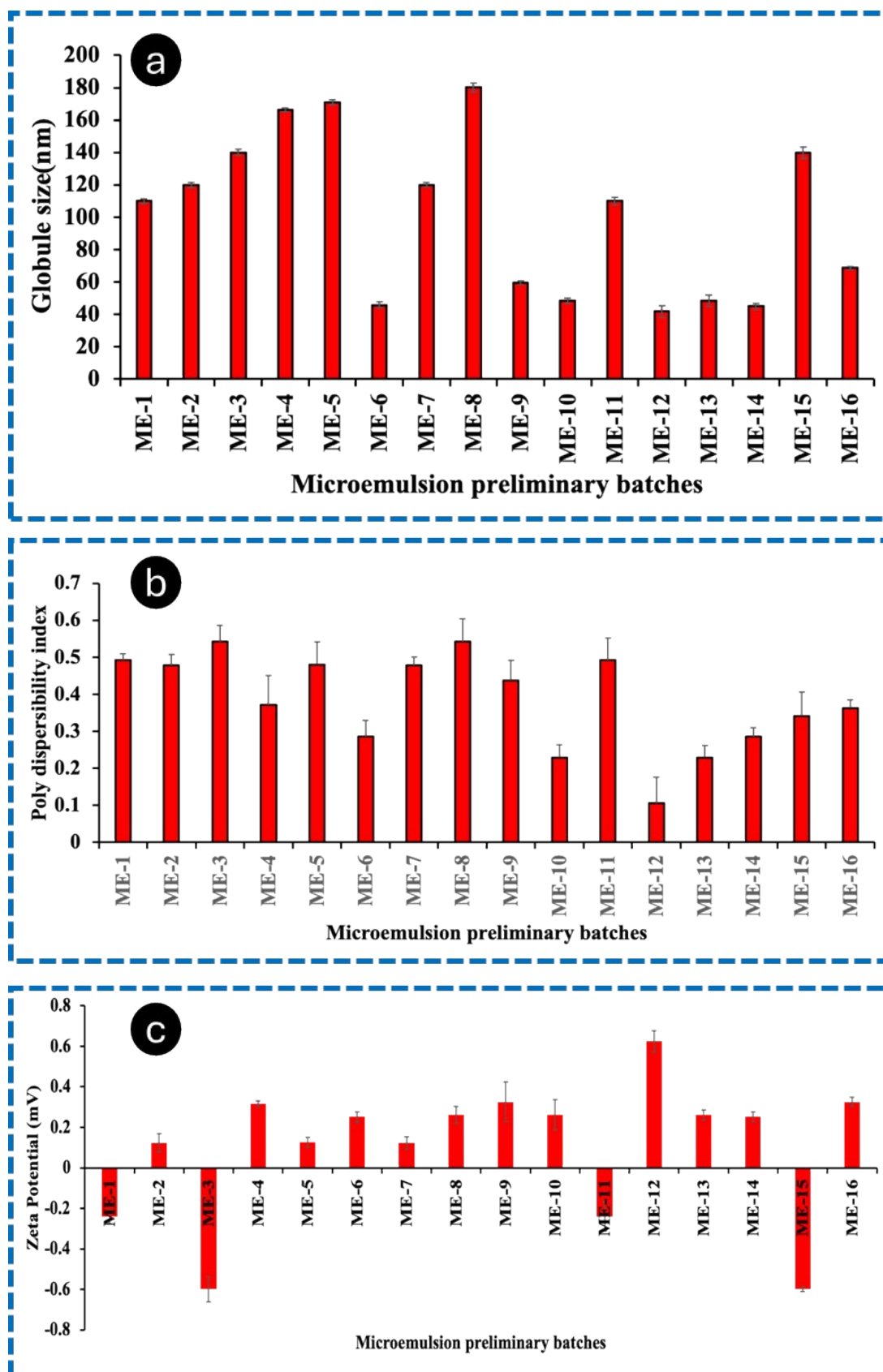


Figure S3. Globule size of Me (a), poly dispersibility index of Me (b), and ZP (c) of Me.

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Figure S4. Globule size (a) and ZP (b) of optimized checkpoint batch.

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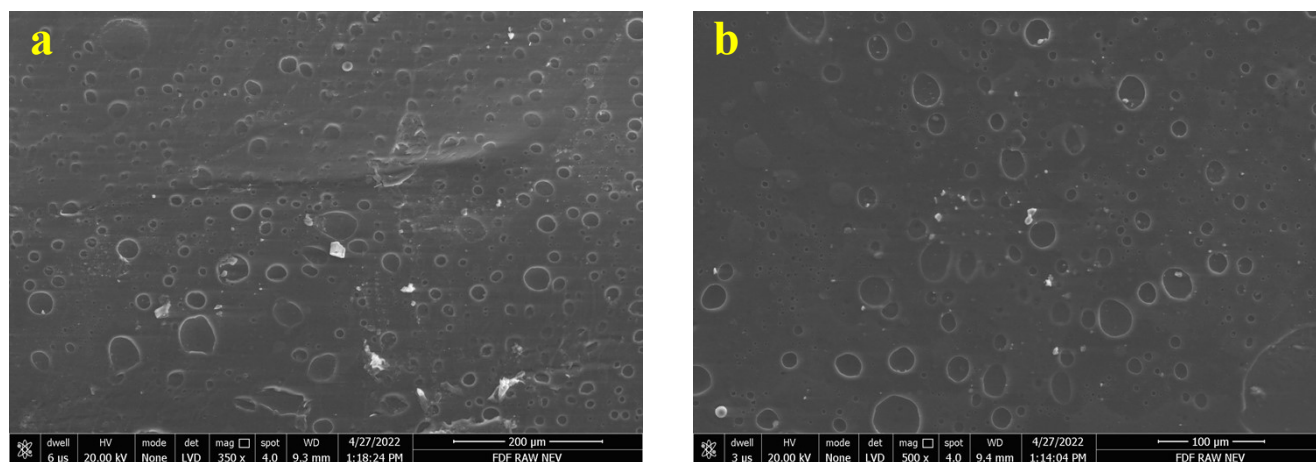


Figure S5. Transmission electron microscopy of optimised formulation at 350 x (b) and 500 x (b)

Supplementary data

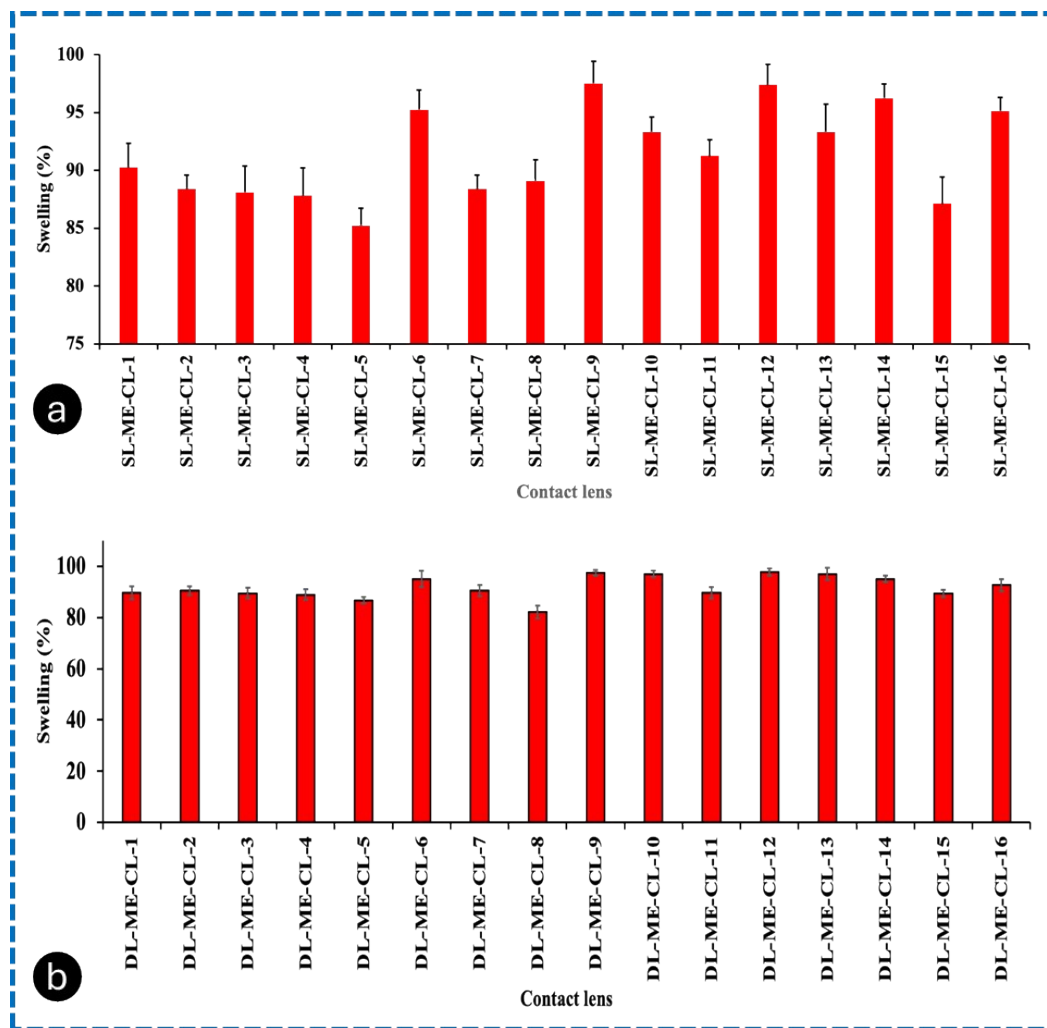


Figure S6. Swelling study (%) of CLs prepared by soaking technique (a), and direct loading technique (b).

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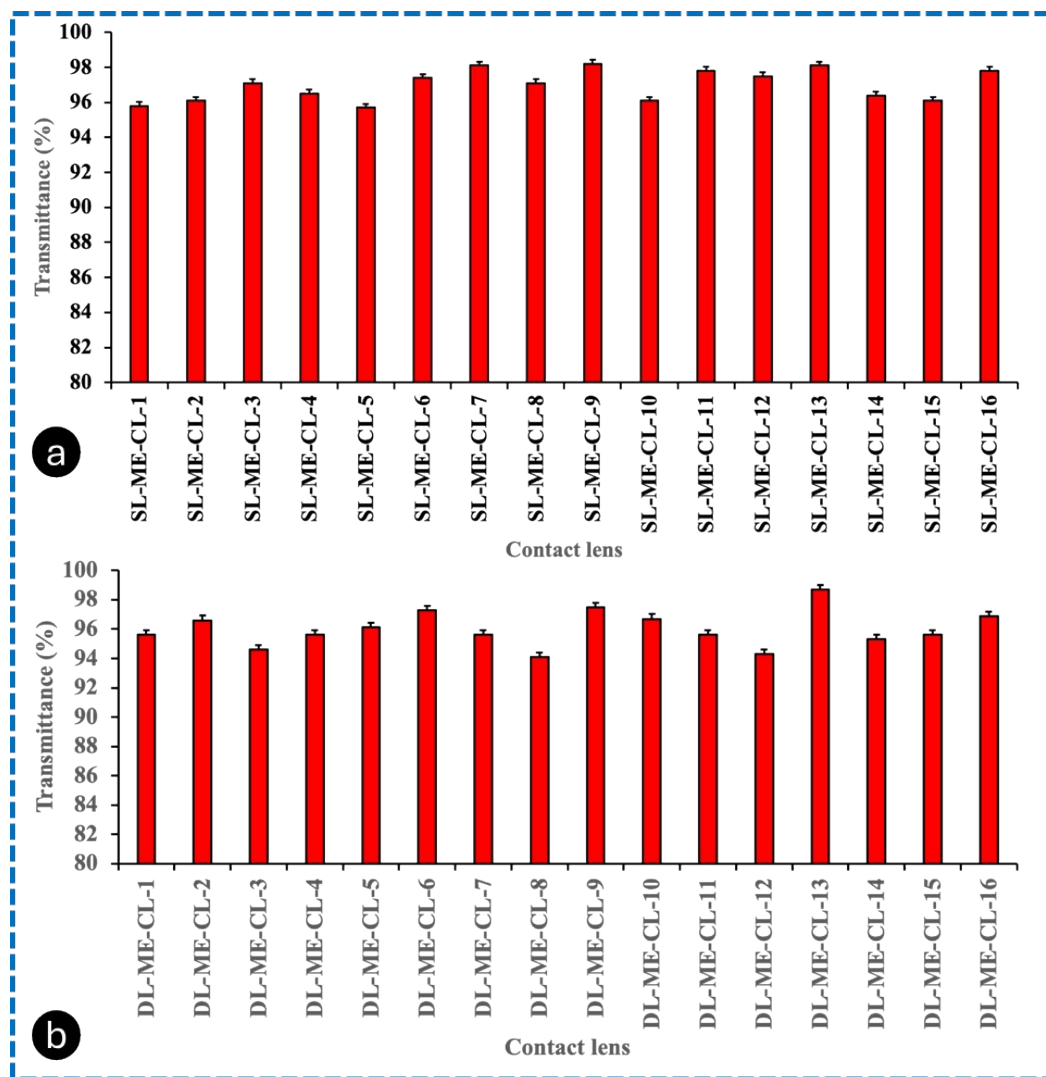


Figure S7. Transmittance (%) studies of CLs prepared by soaking technique (a), and direct loading technique (b)

Supplementary data

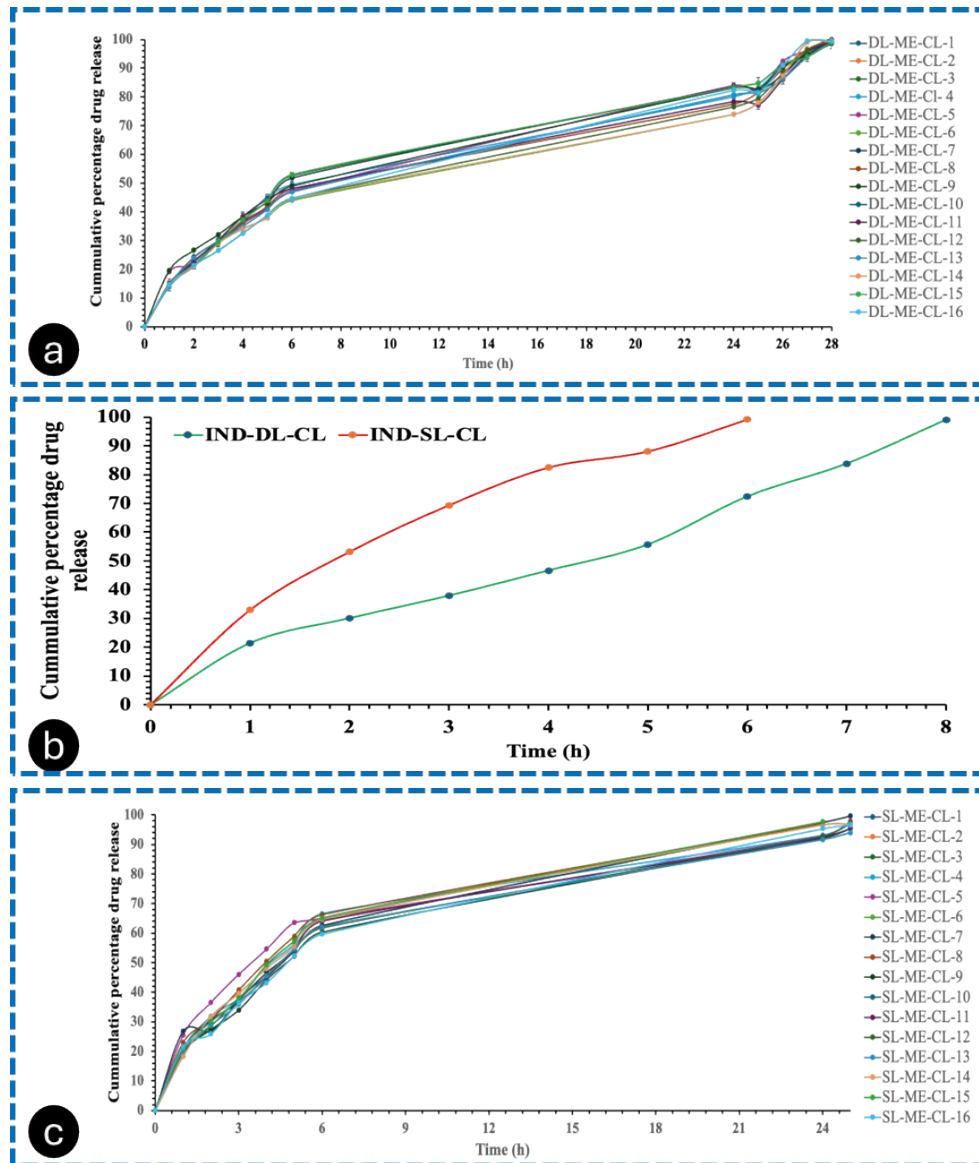


Figure S8. Cumulative drug release (%) from Me-laden CLs (direct loading technique) (batch DL-ME-1 to DL-ME-8) (a); cumulative drug release (%) from drug-loaded CLs fabricated by direct loading and soaking technique (b); and cumulative drug release (%) from Me-laden CLs (soaking method) (batch SL-ME-1 to SL-ME-8) (c).

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Table S1. Calibration curve of IND in methanol using UV-Vis Spectrophotometer

Concentration (µg/ml)	Absorbance at 319nm			Average Absorbance	Standard Deviation (n=3)
5	0.163	0.177	0.172	0.167	0.004
10	0.260	0.260	0.270	0.263	0.005
15	0.429	0.520	0.411	0.453	0.058
20	0.573	0.568	0.561	0.567	0.006
25	0.749	0.697	0.678	0.708	0.036
30	0.861	0.928	0.790	0.859	0.006
35	0.935	0.985	0.983	0.985	0.001

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Table S2. Calibration curve of IND in STF using UV-Vis Spectrophotometer

Concentration (µg/ml)	Absorbance at 266nm			Average Absorbance	Standard Deviation (n=3)
1	0.077	0.078	0.078	0.077	0.0005
3	0.219	0.218	0.220	0.219	0.001
5	0.343	0.342	0.344	0.343	0.001
7	0.478	0.477	0.479	0.478	0.001
9	0.628	0.627	0.629	0.628	0.001
11	0.788	0.789	0.79	0.789	0.001
13	0.925	0.924	0.926	0.925	0.001

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Table S3. Batches of D-optimal mixture design

	Oil (mL)	S_{mix} (2:1) (Tween 80/Iso propyl alcohol)	Water (mL)
ME-1	0.229	0.535	0.235
ME-2	0.322	0.572	0.104
ME-3	0.323	0.350	0.326
ME-4	0.437	0.350	0.212
ME-5	0.550	0.350	0.100
ME-6	0.100	0.573	0.326
ME-7	0.322	0.572	0.104
ME-8	0.436	0.463	0.100
ME-9	0.173	0.426	0.400
ME-10	0.100	0.350	0.550
ME-11	0.229	0.535	0.235
ME-12	0.100	0.800	0.100
ME-13	0.100	0.350	0.55
ME-14	0.100	0.573	0.326
ME-15	0.323	0.350	0.326
ME-16	0.125	0.676	0.197

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Table S4. ANOVA table and regression analysis for response (Y1)

Source	Sum of squares	df	Mean square	F-value	p-value	
Model	36011.36	9	4001.26	110.77	< 0.0001	significant
Linear	33746.59	2	16873.29	467.11	< 0.0001	
Mixture						
AB	148.09	1	148.09	4.10	0.0893	
AC	481.23	1	481.23	13.32	0.0107	
BC	0.0091	1	0.0091	0.0003	0.9879	
ABC	308.55	1	308.55	8.54	0.0265	
AB(A-B)	739.97	1	739.97	20.49	0.0040	
AC(A-C)	149.14	1	149.14	4.13	0.0884	
BC(B-C)	576.12	1	576.12	15.95	0.0072	
Residual	216.73	6	36.12			
Lack of fit	16.73	1	16.73	0.4184	0.5463	not significant
Pure error	200.00	5	40.00			
Cor total	36228.09	15				
Regression analysis of response (Y1)						
R²	0.9940					
Equation						
Full model	$Y1 = 170.39 X1 + 41.28 X2 + 48.30 X3 + 49.91 X1X2 + 81.19 X1X3 - 0.353X2X3 + 484.90 X1X2X3 + 356.29 X1X2(X1-X2) + 137.92 X1X3(X1-X3) + 291.28 X2X3(X2-X3)$					
Reduced model	$Y1 = 170.39 X1 + 41.28 X2 + 48.30 X3 + 81.19 X1X3 + 484.90 X1X2X3 + 356.29 X1X2(X1-X2) + 291.28 X2X3(X2-X3)$					

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Table S5. ANOVA table and regression analysis of response (Y2)

Source	Sum of squares	df	Mean square	F-value	p-value	
Model	20046.53	5	4009.31	6.63	0.0057	significant
Linear mixture	16147.29	2	8073.64	13.35	0.0015	
AB	1366.02	1	1366.02	2.26	0.1638	
AC	3348.82	1	3348.82	5.54	0.0404	
BC	106.96	1	106.96	0.1769	0.6830	
Residual	6047.26	10	604.73			
Lack of fit	4062.76	5	812.55	2.05	0.2252	not significant
Pure error	1984.50	5	396.90			
Cor Total	26093.79	15				
Regression analysis of response (Y2)						
R²	0.7682					
Equation						
Full model	$(Y2) = 23.66 X1 + 102.73 X2 + 102.55 X3 - 130.69 X1X2 - 194.64 X1X3 - 35.42 X2X3$					
Reduced model	$(Y2) = 23.66 X1 + 102.73 X2 + 102.55 X3 - 194.64 X1X3$					

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Table S6. ANOVA Table and regression analysis for response (Y3)

Source	Sum of squares	df	Mean square	F-value	p-value	
Model	111.65	5	22.33	17.40	0.0001	significant
Linear mixture	45.77	2	22.89	17.83	0.0005	
AB	31.56	1	31.56	24.59	0.0006	
AC	38.74	1	38.74	30.18	0.0003	
BC	5.80	1	5.80	4.52	0.0594	
Residual	12.84	10	1.28			
Lack of Fit	12.84	5	2.57			Non-significant
Pure error	0.0000	5	0.0000			
Cor total	124.49	15				
Regression analysis of response (Y3)						
R²	0.8969					
Equation						
Full model	$(Y3) = 46.40 X1 + 44.84 X2 + 47.17 X3 + 19.87 X1X2 + 20.93 X1X3 - 8.25 X2X3$					
Reduced model	$(Y3) = 46.40 X1 + 44.84 X2 + 47.17 X3 + 19.87 X1X2 + 20.93 X1X3$					

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Table S7: Coefficient table

Response	A:	B: S_{mix}	C:	AB	AC	BC	ABC
	oil		water				
globule size (Y1)	170.39	41.28	48.30	49.91	81.19	-0.353	484.9
p-values	<	<	<	0.08	0.010	0.987	0.026
	0.0001	0.0001	0.0001				
Transmittance	23.65	102.72	102.54	-130.68	-194.63	-35.42	-
(%)(Y2)							
p-values	0.0015	0.0015	0.0015	0.16	0.040	0.68	-
Drug release (%)	46.40	44.84	47.17	19.86	20.93	-8.24	-
(Y3)							
p-values	0.0005	0.0005	0.0005	0.0006	0.0003	0.059	-

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Table S8. Result of thermodynamic stability study

Batch no.	Centrifugation test	Heating cooling cycle	Freeze Thaw cycle
ME-1	Stable	Stable	Stable
ME-2	Stable	Stable	Stable
ME-3	Stable	Stable	Cracking
ME-4	Stable	Phase separation	-
ME-5	Stable	Phase separation	-
ME-6	Stable	Stable	Stable
ME-7	Stable	Stable	Stable
ME-8	Stable	Stable	Phase separation
ME-9	Stable	Stable	Stable
ME-10	Stable	Stable	Stable
ME-11	Stable	Stable	Stable
ME-12	Stable	Stable	Stable
ME-13	Stable	Stable	Stable
ME-14	Stable	Stable	Stable
ME-15	Stable	Stable	Cracking
ME-16	Stable	Stable	Stable

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Table S9. Transmittance study (%) and dilution test of batches of microemulsion

Batch no.	Components			Transmittance (%) of microemulsion	Transmittance (%) after 10 times dilution
	Oil	S _{mix}	Water	(%)	(%)
ME-1	0.229	0.535	0.235	91.2	11.1
ME-2	0.322	0.572	0.104	90.2	12.2
ME-3	0.323	0.350	0.326	89.8	14.3
ME-4	0.437	0.350	0.212	92.6	16.6
ME-5	0.550	0.350	0.100	91.4	17.8
ME-6	0.100	0.573	0.326	97.3	97.8
ME-7	0.322	0.572	0.104	90.3	75.2
ME-8	0.436	0.463	0.100	93.2	18.2
ME-9	0.173	0.426	0.400	97.5	95.6
ME-10	0.100	0.350	0.550	96.7	96.2
ME-11	0.229	0.535	0.235	91.2	11.1
ME-12	0.100	0.800	0.100	98.0	98.2
ME-13	0.100	0.350	0.550	96.7	96.2
ME-14	0.100	0.573	0.326	97.2	97.8
ME-15	0.323	0.350	0.326	89.8	14.7
ME-16	0.125	0.676	0.197	97.1	97.4