Supporting Information

Supramolecular Eutectogel Based on THDESs as Skin Penetrating Carrier for Effective Transdermal Delivery of Hydrophobic Drug Curcumin

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Table S1: Criteria for the evaluation of the primary irritation test proposed by the ICDRG.

Reaction	Result	Grade
No reaction	Negative (–)	0
Mild erythema	Doubtful (?)	1
Clear erythema	Positive (+)	2
Erythema + edema + papules	Positive (++)	3
Erythema + edema + papules + vesicles	Positive (+++)	4

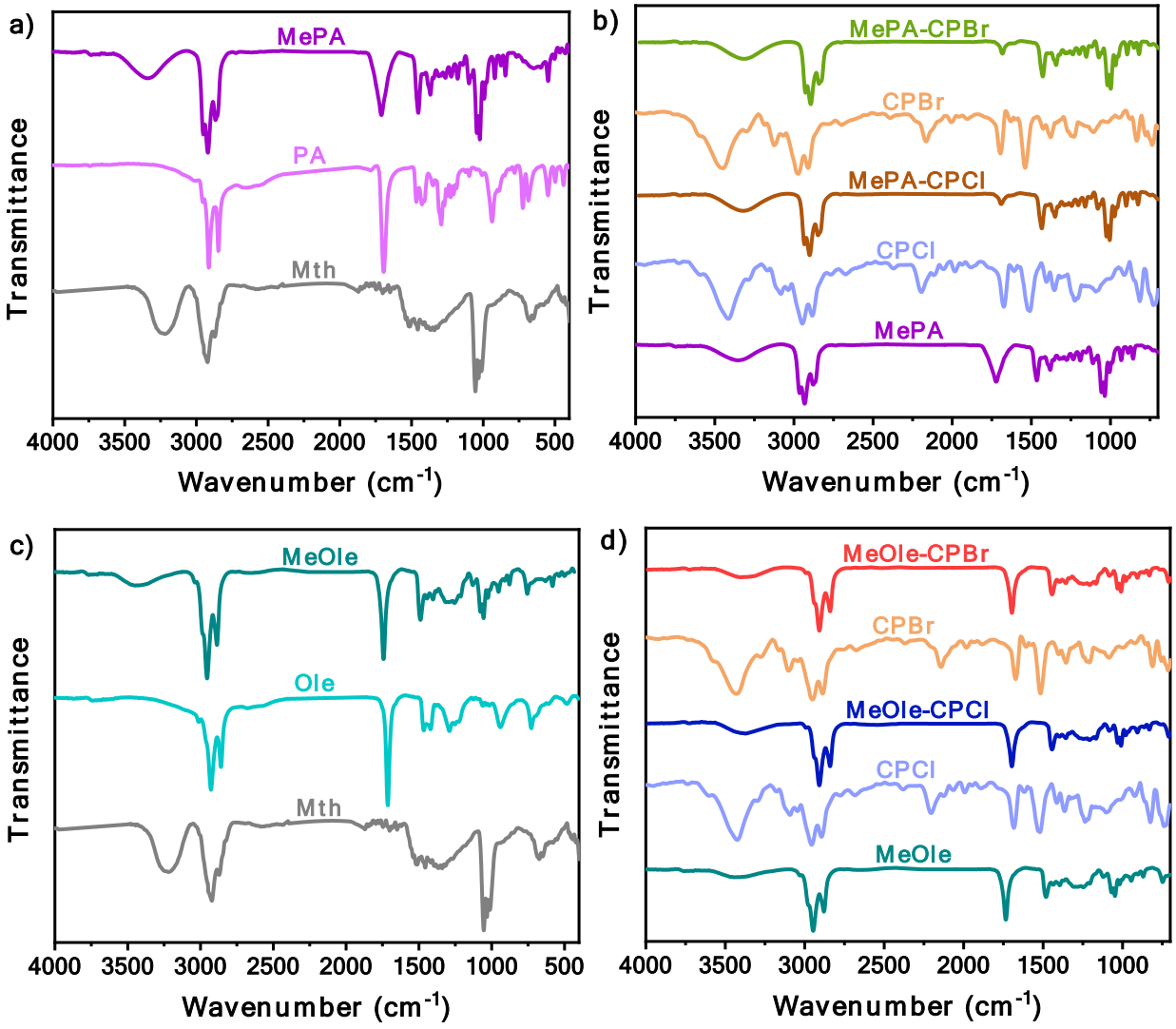

Figure S1: FTIR spectra of **a, c)** individual components (Mth, PA, Ole) and their comparison with the respective DESs (MePA, MeOle); **b, d)** individual surfactants (CPCl, CPBr), DESs (MePA, MeOle) and their corresponding gels.

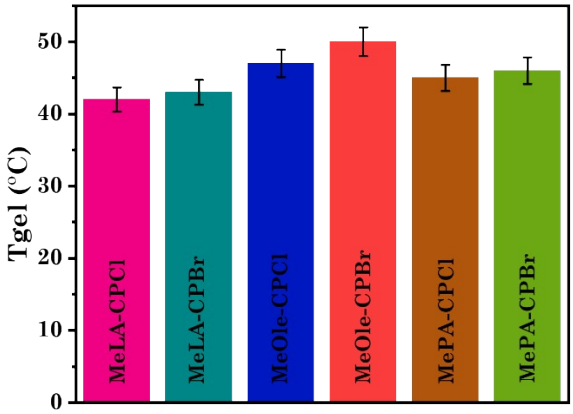

Figure S2: Transition temperature (Tgel) of the investigated supramolecular eutectogels.

Table S2: Crossover data of studied eutectogel through rheological strain sweep measurement.

Sr. No.	Eutectogel	γ_c (%)
1	MeLA-CPCl	4.7
2	MeLA-CPBr	5.3
3	MePA-CPCl	5.6
4	MePA-CPBr	6.1
5	MeOle-CPCl	12.5
6	MeOle-CPBr	12.1

Table S3: Drug loading efficiency of studied eutectogels. The solubility advantage values are written in brackets alongside the obtained drug loading values.

Gelator	**THDESs**		
	MeLA	MePA	MeOle
CPCl	11.6 ± 0.6 (19,334)	14.0 ± 0.4 (23,334)	19.4 ± 0.6 (32,333)
CPBr	11.1 ± 0.7 (18,500)	13.7 ± 0.5 (22,833)	19.7 ± 0.5 (32,833)

Table S4: Comparative encapsulation efficiency of curcumin in our studied eutectogels with other systems reported in the literature.

System	Curcumin encapsulation	Reference
MeLA CPCl/CPBr	11.6/11.1 mg/g	**Present work**
MePA CPCl/CPBr	14.0/13.7 mg/g	**Present work**
MeOle CPCl/CPBr	19.4/19.7 mg/g	**Present work**
Choline chloride:sorbitol (1:1)	1.29 mg/ml	1
Choline chloride:Fructose (1:1)	3.11 mg/ml	1
Choline chloride:glucose (1:1)	2.90 mg/ml	1
Choline chloride:sucrose (1:1)	0.27 mg/ml	1
Choline chloride:maltose (1:1)	1.17 mg/ml	1
Choline chloride: glycerol (1:1)	7.15 mg/ml	1
Choline chloride: Citric acid- CPBr gel	0.73 mg/g	2
Choline chloride: Oxalic acid- CPBr gel	0.58 mg/g	2

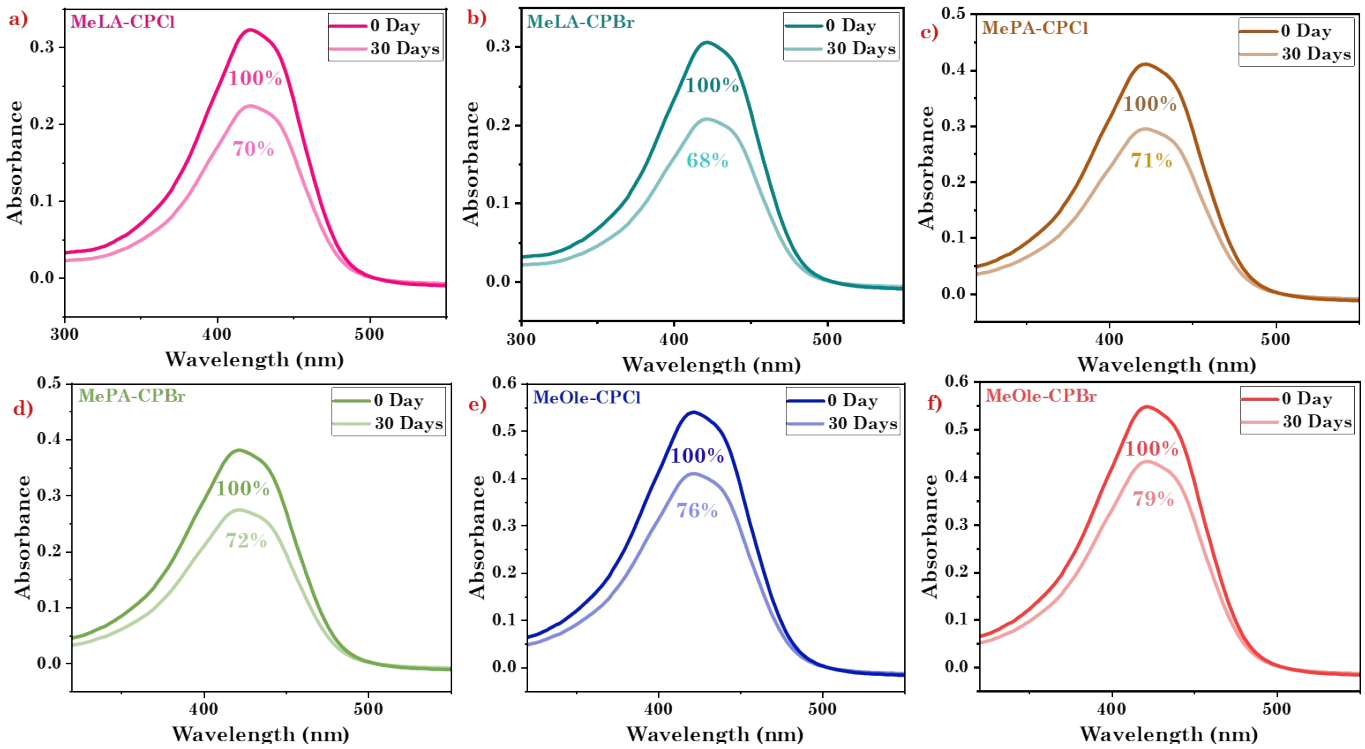

Figure S3: Absorbance of curcumin in eutectogels on Day 0 (100%; No degradation) and after 30 Days at room temperature: **a)** MeLA-CPCl, **b)** MeLA-CPBr, **c)** MePA-CPCl, **d)** MePA-CPBr, **e)** MeOle-CPCl, and **f)** MeOle-CPBr.

Table S5: Flux (J) and permeability coefficient (Kp) of drug from various eutectogel samples.

Eutectogel	Flux (J) (μg/cm²/h)	Permeability Coefficient (Kp) (cm/h)
MeLA-CPCl	103.17	0.206
MeLA-CPBr	101.95	0.2039
MePA-CPCl	111.1	0.2222
MePA-CPBr	112.36	0.2247
MeOle-CPCl	114.7	0.2294
MeOle-CPBr	115.19	0.2304

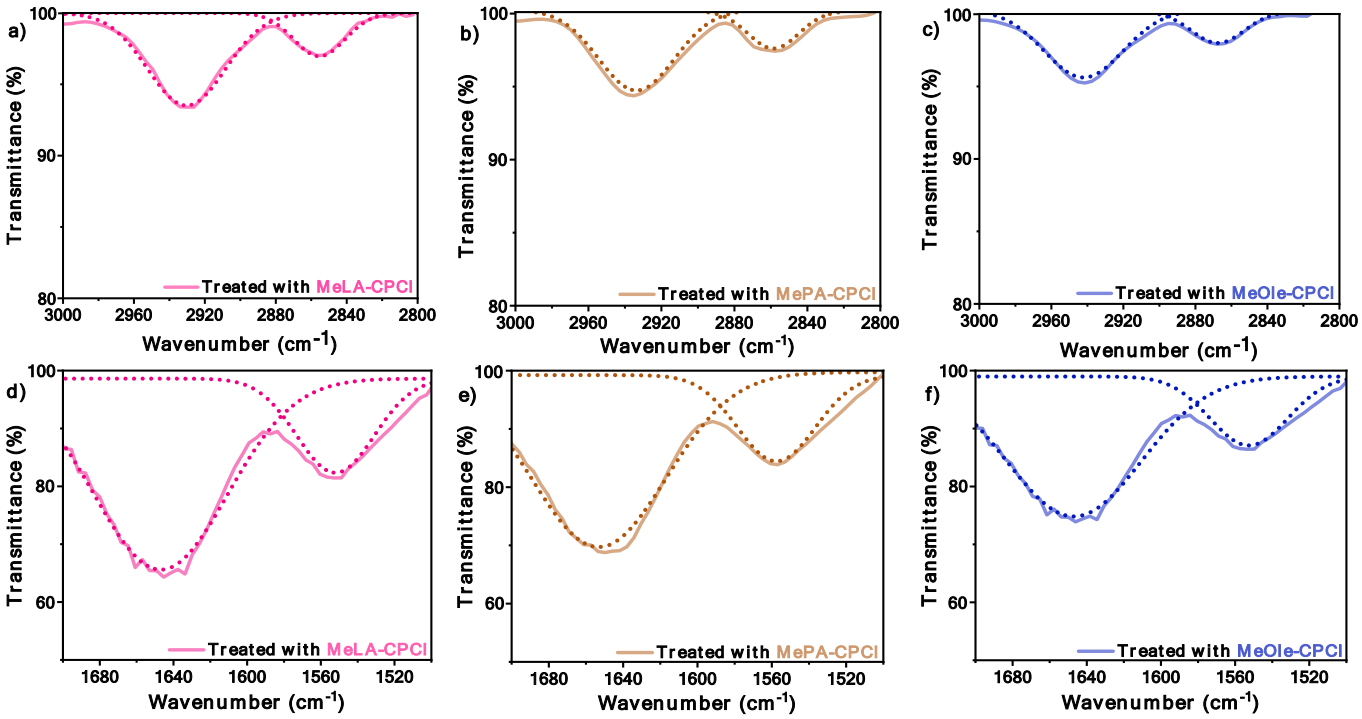

Figure S4: FTIR spectra (solid line) of the skin after treatment with MeLA-CPCl, MePA-CPCl and MeOle-CPCl. Deconvoluted FTIR spectra (dotted lines) highlight regions indicative of lipids (**a, b, c**) and proteins (**d, e, f**). The changes in lipid content ($\nu_a CH_2$ and $\nu_s CH_2$) and protein content (νC=O and □N-H) of the skin as assessed by the peak area.

Table S6: IC_{50} values of curcumin loaded eutectogels in A431 cell line.

Sr. No.	Eutectogels	IC_{50} value (µM)
1	MeLA-CPCl	15.39
2	MeLA-CPBr	15.30
3	MePA-CPCl	14.93
4	MePA-CPBr	15.01
5	MeOle-CPCl	14.34
6	MeOle-CPBr	14.09

REFERENCES

(1) Jeliński, T.; Przybyłek, M.; Cysewski, P. Natural Deep Eutectic Solvents as Agents for Improving Solubility, Stability and Delivery of Curcumin. Pharm Res 2019, 36 (8), 116.

(2) Parsana, N.; Kumar, S.; Aswal, V. K.; Seoud, O. El; Malek, N. I. Self-Healable, Injectable, and Conductive Supramolecular Eutectogel for the Encapsulation and Sustained Release of the Anticancer Drug Curcumin. ACS Applied Engineering Materials 2023, 1 (1), 380–393.