pharmaceutics

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Supplementary Materials: Improvement of Imiquimod Solubilization and Skin Retention via TPGS Micelles: Exploiting the Co-Solubilizing Effect of Oleic Acid

Martina Ghezzi, Silvia Pescina, Andrea Delledonne, Ilaria Ferraboschi, Cristina Sissa, Francesca Terenziani, De Freitas Rosa Remiro Paula, Santi Patrizia and Nicoli Sara

Table S1. Range of calibration curves, RSD% (relative standard deviation %) and ER% (relative error %) of the fatty acids considered.

Fatty Acid	Concentrations Interval (μg/ml)	RSD%	RE%	LOQ		
				LOQ (μg/ml)	RSD%	RE%
Oleic acid	60–600	< 0.88	< 2.37	60	7.33	2.58
Linoleic acid	3–100	< 2.10	< 2	3	6.6	7
Linolenic acid	5–100	< 5.6	< 5.6	5	2.31	21

Table S2. Hydrogels composition, with their codification, appearance and pH values. The appearance of hydrogels was evaluated after hydration of polymers in water, blank TO20 micelles and IMQ-loaded TO20 micelles. In table only the aspect of water-based and IMQ-loaded TO20-based hydrogels is reported as no difference was observed between hydrogels hydrated in blank TO20 and IMQ-loaded TO20 micelles.

Polymer	Composition	Code	Appearance		pH	
			Water-Based Hydrogels	IMQ-Loaded TO20-Based Hydrogels	Water-Based Hydrogels	IMQ-Loaded TO20-Based Hydrogels
Hydroxyethylcellulose	2%	HEC	transparent	opalescent- whitish – biphasic system	6.75 ± 0.01	4.90 ± 0.05
Xanthan Gum	1%	XG	slightly opalescent	slightly opalescent	5.92 ± 0.68	5.07 ± 0.08
Sodium Carboxymethylcellulose	4%	CMC	transparent/yellowish	opalescent- yellowish	6.66 ± 0.09	6.35 ± 0.72
Carbopol 934	0.5%	CP	transparent	opalescent- whitish	5.71 ± 0.07	6.76 ± 0.04
Sodium Hyaluronate	1%	HA	transparent	transparent	6.72 ± 0.03	4.94 ± 0.02
Polyvinyl Alcohol	15%	PVA	transparent	opalescent- whitish	6.16 ± 0.43	4.82 ± 0.20

Table S3. Size (mean ± SD), intensity and PDI of blank and IMQ-loaded micelles of TP20, TPS20 and TPO20 at 0 days from preparation. Micelles were diluted 1:10 with distilled water prior to analysis.

	Blank			Loaded		
Formulation	Size (nm)	Intensity (%)	PDI	Size (nm)	Intensity (%)	PDI
TP20	12.61 ± 0.34 265.50 ± 24.68	72.53 25.57	1	12.13 ± 0.08 172.67 ± 2.75	68.63 31.37	0.98
TPS20	14.71 ± 0.26 165.83 ± 19.72	41.97 56.20	0.61	65.85 ± 37.82 122.70 ± 0.00	82.53 48.9	0.49
TPO20	13.37 ± 0.36 175.17 ± 2.05	12.97 87.30	0.59	13.07 ± 0.78 249.17 ± 9.77	12.30 87.73	0.65

Table S4. P values obtained from T-test analysis for epidermis, dermis and total amount of the drug in the skin for all formulations tested.

	TO20	TO100	TO20-2	TO20 XG	TO20 HA	IMUNOCARE
TO20	-	0.32; 0.24; 0.16	0.08; 0.52; 0.20	0.29; 0.24; 0.14	0.26; 0.10; 0.09	0.62; 0.81; 0.84
TO100	0.32; 0.24; 0.16	-	**0.04**; 0.23; **0.02**	0.98; 0.67; 0.79	0.92; 0.33; 0.61	0.19; 0.16; **0.03**
TO20-2	0.08; 0.52; 0.20	**0.04**; 0.23; **0.02**	-	**0.02**; 0.24; **0.01**	**0.02**; 0.05; **0.01**	0.37; 0.72; 0.41
TO20 XG	0.29; 0.24; 0.14	0.97; 0.67; 0.77	**0.02**; 0.24; **0.01**	-	**0.90**; 0.08; 0.43	0.16; 0.11; **0.02**
TO20 HA	0.26; 0.10; 0.09	0.92; 0.33; 0.61	**0.02**; 0.05; **0.01**	0.90; 0.08; 0.43	-	0.14; **0.02**; **0.03**
IMUNOCARE	0.62; 0.81; 0.84	0.19; 0.16; **0.03**	0.37; 0.72; 0.41	**0.16**; 0.11; **0.02**	0.14; **0.02**; **0.03**	-

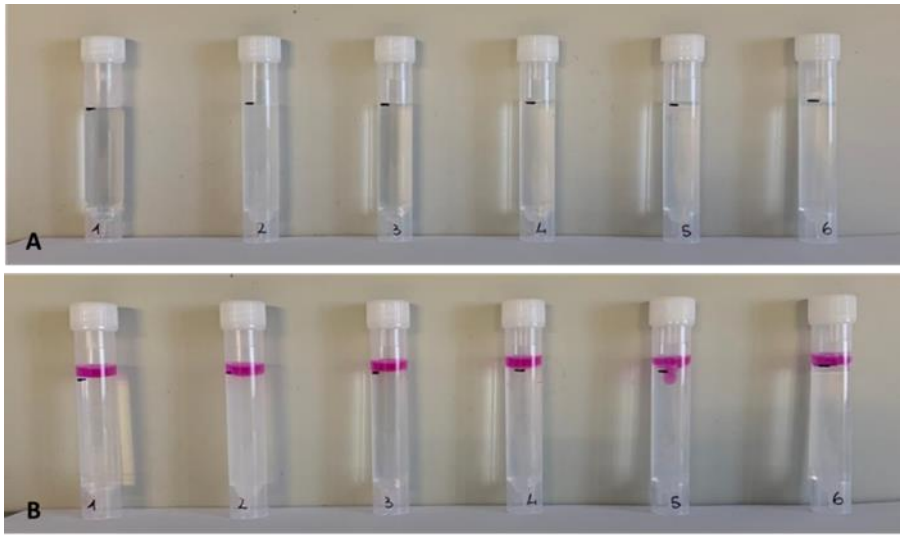


Figure S1. Hydrogels of HEC (1), XG (2), CMC (3), CP (4), HA (5) and PVA (6) before (**A**) and after (**B**) deposition of 200 µl of Nile-Red loaded micellar solution.