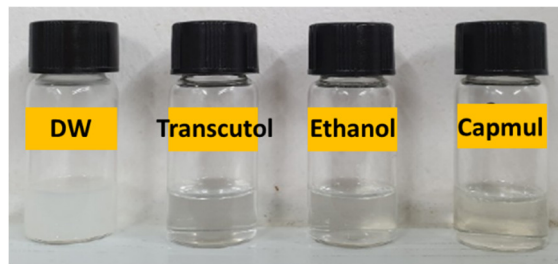


1 Article

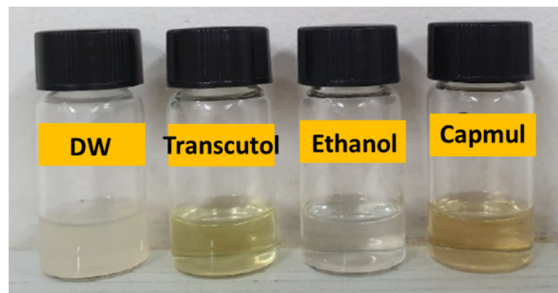
2 **Supplementary Materials: Lipid Nanoparticles for**
3 **Enhancing the Physicochemical Stability and Topical**
4 **Skin Delivery of Orobol**

5 Min-Hwan Kim, Yae-Eun Jeon, Soobeen Kang, Jae-Young Lee, Ki Won Lee, Ki-Taek Kim and
6 Dae-Duk Kim

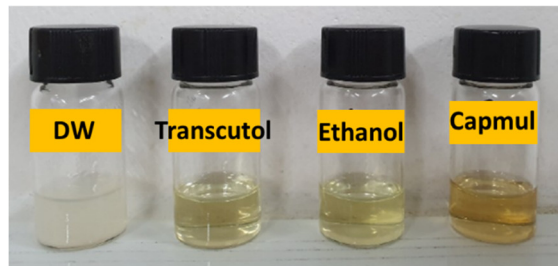
(a)



(b)

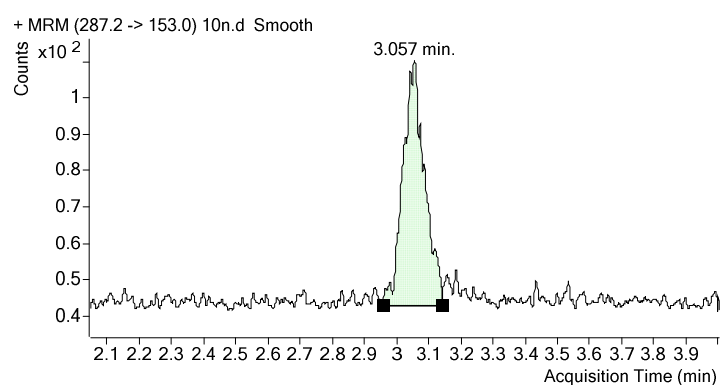


(c)

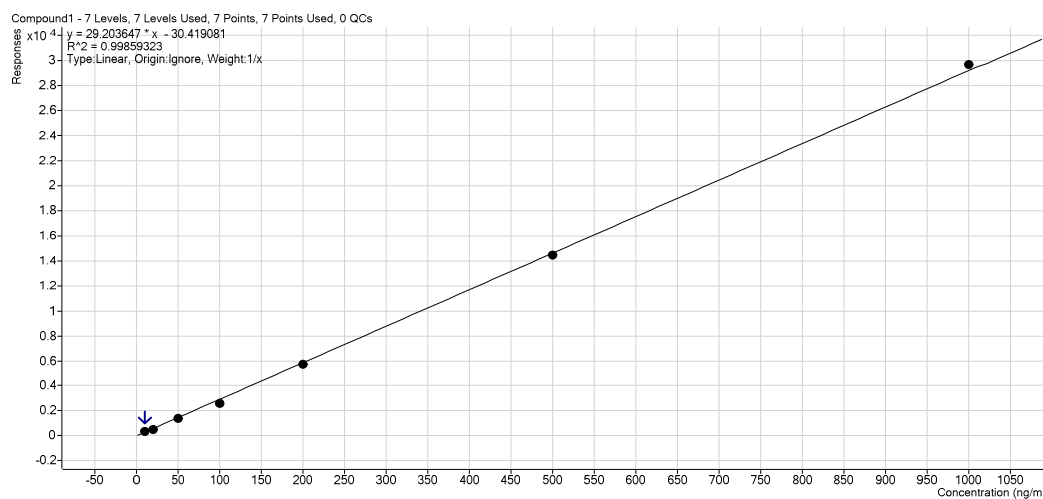


7 **Figure S1.** The color change of orobol (0.05%, *w/w*) in various vehicles. (a) Samples immediately after
8 the preparation; (b) samples stored at room temperature for 14 days without sunlight exposure; (c)
9 samples stored at room temperature for 14 days with sunlight exposure.

(a)

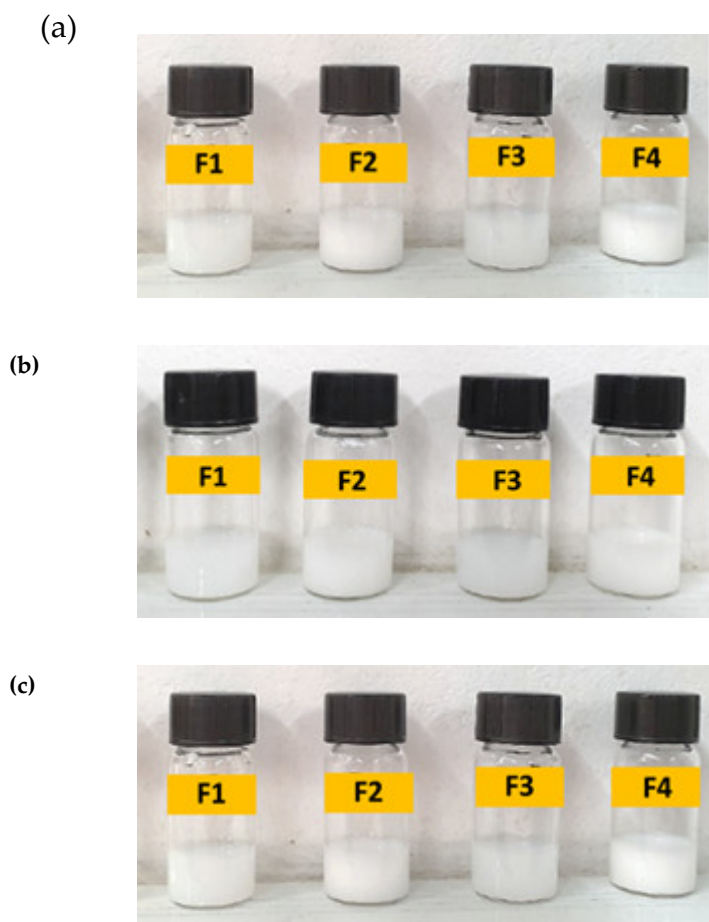


(b)

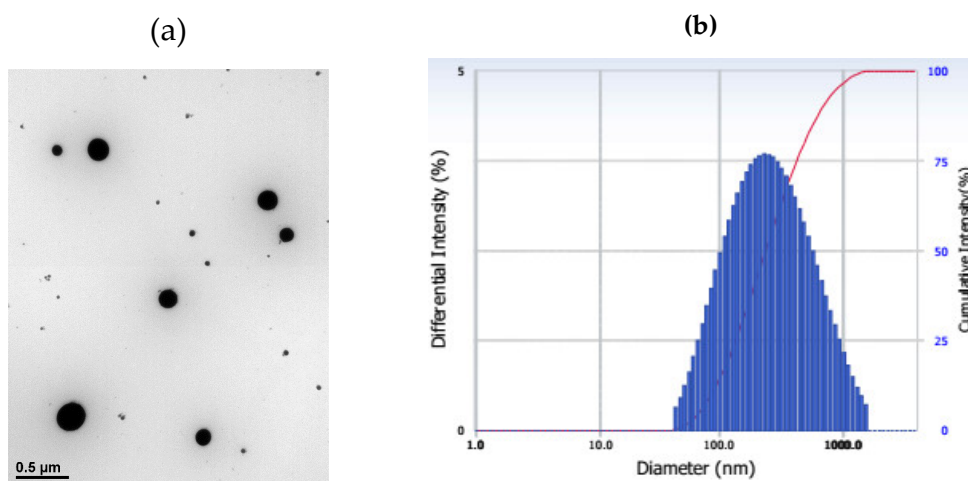


10 **Figure S2.** (a) The LC-MS/MS peak of orobol at a concentration of the lower limit of quantification
11 (10.0 ng/mL); (b) The calibration curve of orobol at a final concentration range of 10.0 – 1000 ng/mL.

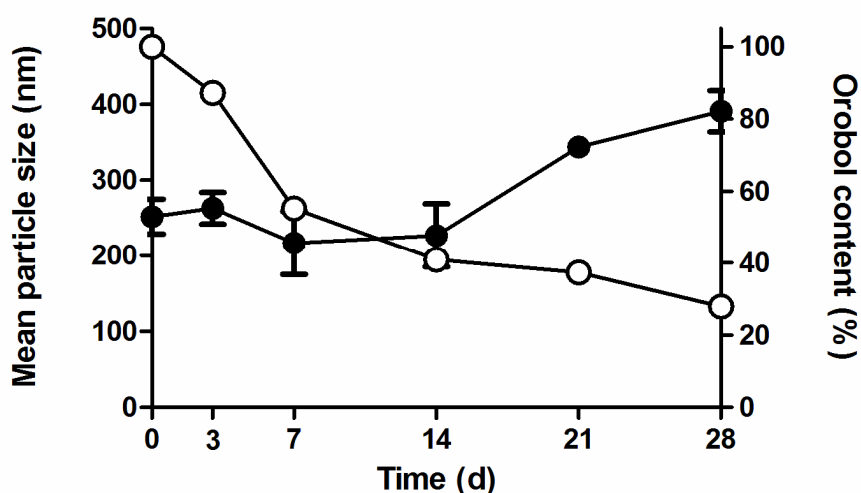
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13 **Figure S3.** The color change of the orobol-loaded formulations. (a) Samples immediately after the
 14 preparation; (b) Samples stored at room temperature for 14 days without exposure to sunlight; (c)
 15 Samples stored at room temperature for 14 days with exposure to sunlight.



16 **Figure S4.** (a) Morphological shapes of *o/w* ME formulation by TEM and (b) its size distribution. The
 17 scale bars represent 0.5 μm.



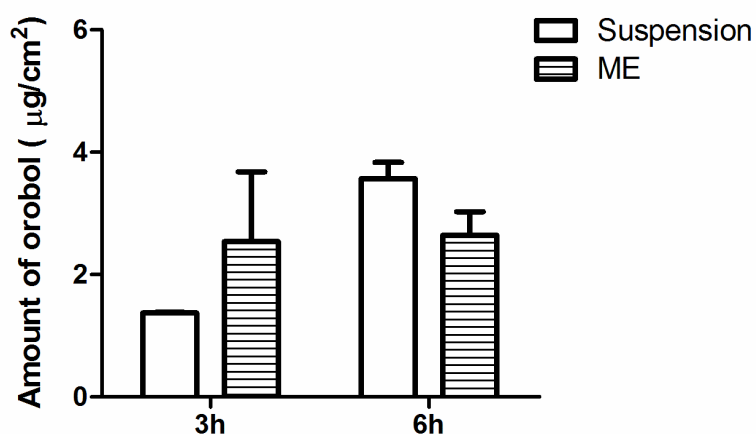
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Figure S5. The change of mean particle size (left Y-axis; ●) and content (% of initial concentration; right Y-axis; ○) in *o/w* ME formulation at room temperature on day 0 (initial state after the preparation), day 3, 7, 14, 21, and 28.



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Figure S6. In vitro deposition of orobol into a Strat-M membrane after applying orobol-loaded *o/w* ME formulation at the concentration of 0.5 mg/mL for 3 h and 6 h.

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Table S1. Criteria of the skin irritation score system by the guideline of the International Contact Dermatitis Research Group (ICDRG) and the Personal Care Products Council (PCPC).

| Score | Criteria for Skin Irritation |
|-------|---|
| 0 | No signs of irritation |
| 0.5 | Doubtful or slight reaction |
| 1 | Slight erythema |
| 2 | Moderate erythema with or without partial edema |
| 3 | Moderate erythema with diffusive edema |
| 4 | Intense erythema with diffusive edema containing vesicles |

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29 **Table S2.** The standard procedure dermal classification system by the Environmental Protection
30 Agency (EPA).

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| Skin Irritation Index | Classification of Skin Irritation |
|-----------------------|-----------------------------------|
| 0.00–0.02 | No irritancy |
| 0.02–0.25 | Low irritancy |
| 0.25–1.00 | Slight irritancy |
| 1.00–2.50 | Moderate irritancy |
| >2.50 | Severe irritancy |

32 **Table S3.** Skin irritation scores of the blank nanostructured lipid carrier (NLC) formulation (blank F4)
33 and the orobol-loaded NLC formulation (F4) at 30 min, 24 h, and 48 h after topical application of the
34 samples to human volunteers for 24 h.

| Human Subject | Not-Treated | | | Blank F4 | | | F4 | | |
|---------------|-------------|------|------|----------|------|------|--------|------|------|
| | 30 min | 24 h | 48 h | 30 min | 24 h | 48 h | 30 min | 24 h | 48 h |
| No. 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 11 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 14 | 0 | 0 | 0 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| No. 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 17 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 18 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 19 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 20 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 21 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 22 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 23 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 24 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 26 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 27 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 28 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 29 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| No. 30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

35 **Table S4.** Composition of o/w ME formulation (w/w %) containing 0.05(w/w %) of orobol.

| Phase | Vehicle | ME Formulation |
|------------|---------------|----------------|
| Oil | Capmul MCM EP | 20 |
| Surfactant | Transcutol | 28.7 |
| | Labrasol | 14.3 |
| Water | DW | 36.95 |

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