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Supplementary Information

Enhanced Transdermal Efficiency of Curcumin-loaded Peptide-modified Liposomes for Highly Effective Antipsoriatic Therapy

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1. Supplementary Methods

S1.1 In vitro curcumin release under physiologically simulated conditions

The curcumin formulations were placed in a shaker with a speed of 150 rpm at 37°C. The samples were collected at predetermined time points and centrifuged at 1000 rpm for 15 min. Then, the supernatant was removed and the precipitate was dissolved with DMSO. The curcumin release rate was calculated according to the UV absorbance.

S1.2 Analysis of quantitative cellular uptake by flow cytometry

HaCaT cells were seeded in a 6-well plate at a density of 2×10^5 cells/well and cultured for 24 h at 37°C in an incubator. Then, TNF-α was added (the final concentration was 100 ng/mL) and the incubation lasted for 2 h. Next, CRC-Lip or CRC-TD-Lip in DMEM without FBS was added to the experimental group (the final curcumin concentration was 10 μg/mL) and the incubation continued for 30 min. Finally, the cells were trypsinized, washed twice with PBS and resuspended in 0.5 mL of PBS. The average fluorescence intensity of CRC in the cells was measured using a flow cytometer (CytoFLEX, Beckman, USA).

S1.3 In vivo skin permeation distribution and depth

In experiments, the back hair of the health female BALB/c mice was removed with an electric hair shaver; the mice were anesthetized and fixed on a constant temperature plate, with a cylindrical silicone tube (inner diameter: 1 cm) adhered to the back skin (200 μL of curcumin formulations was loaded); after 8 h, the mice were sacrificed and the skin receiving curcumin formulations was carefully cut off, washed with saline, and scanned using the z-axis of the confocal laser scanning microscope to obtain the penetration distribution and depth of the drug in the skin.

2. Supplementary Figures

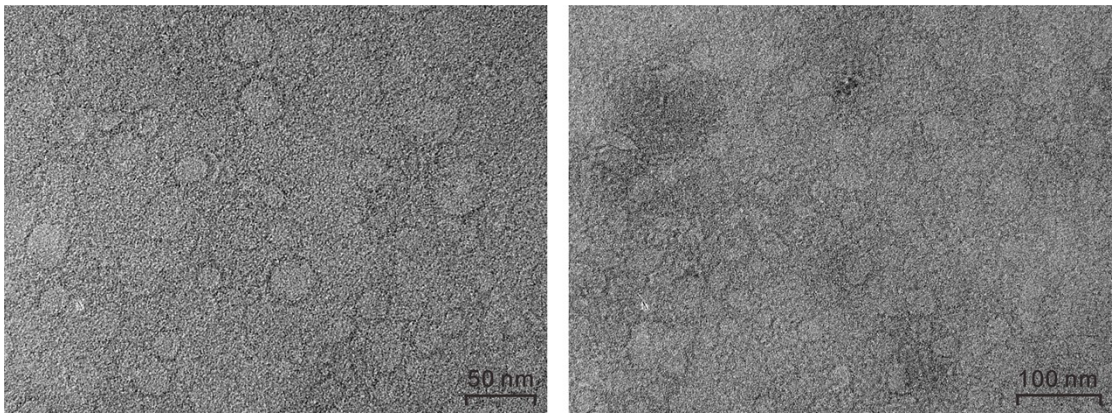

Figure S1. TEM micrographs of CRC-TD-Lip.

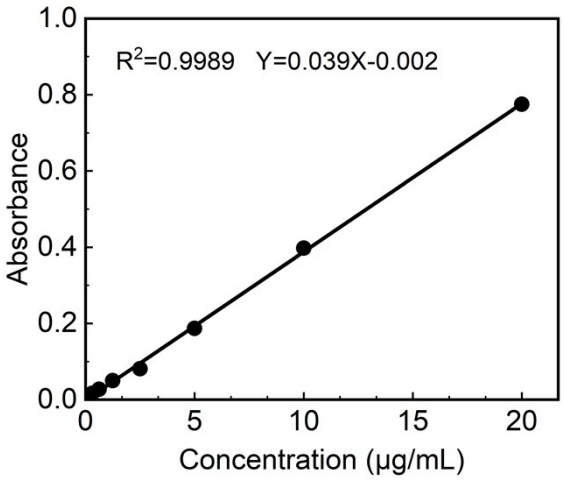

Figure S2. Standard absorbance curve of curcumin dissolved in DMSO.

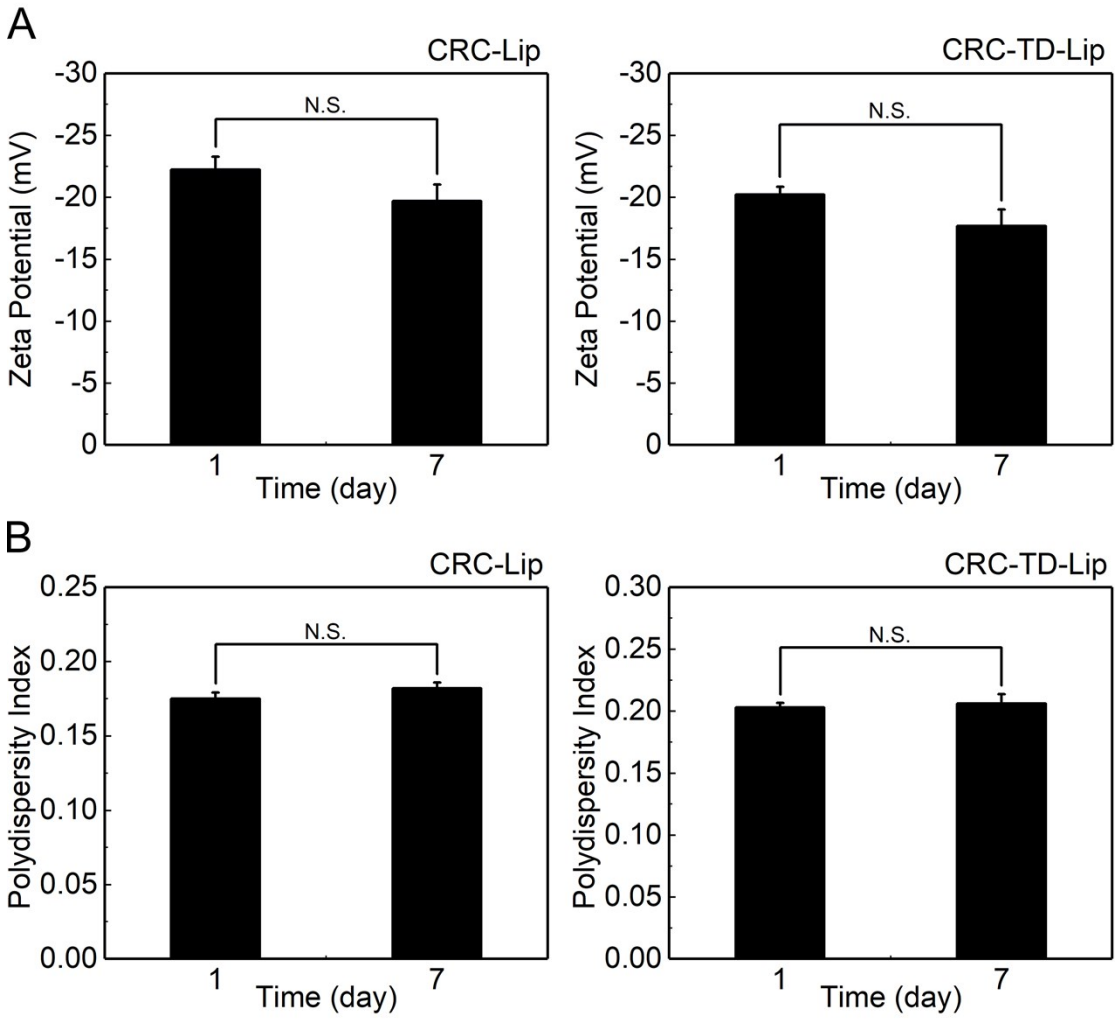

Figure S3. Zeta potentials (A) and polydispersity indexes (B) of CRC-Lip and CRC-TD-Lip.

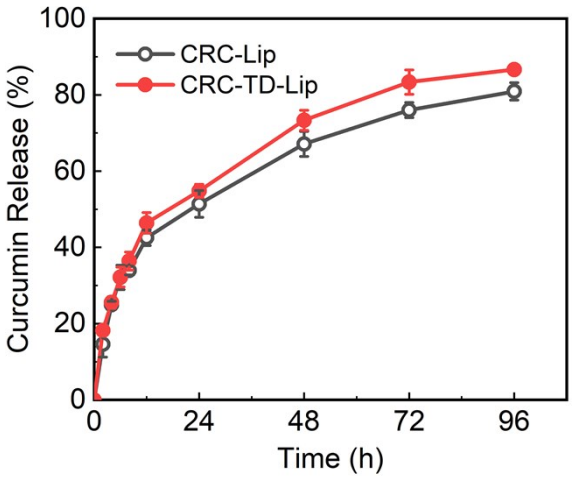

Figure S4. In vitro curcumin release of CRC-Lip and CRC-TD-Lip within 96 h.

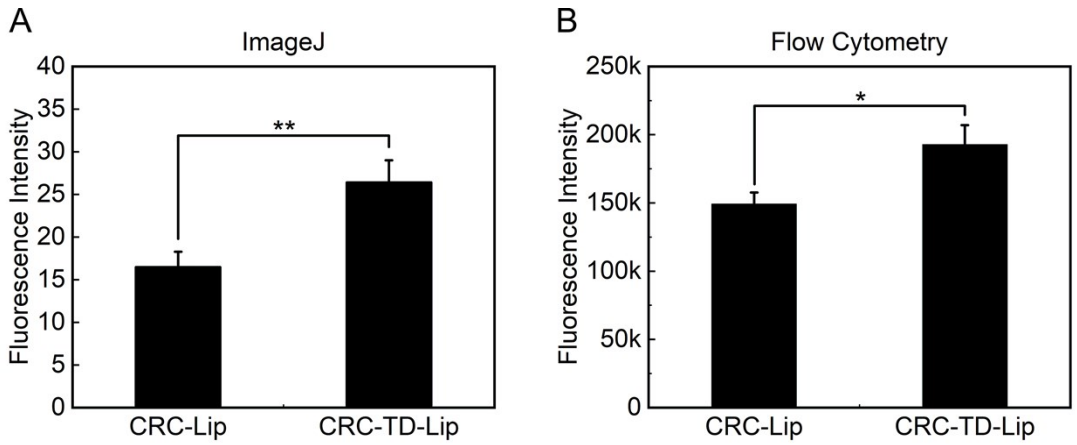

Figure S5. Fluorescence intensity of curcumin in HaCaT cells treated with CRC-Lip or CRC-TD-Lip measured by ImageJ (A) or flow cytometry (B). *$p < 0.05$, **$p < 0.01$.

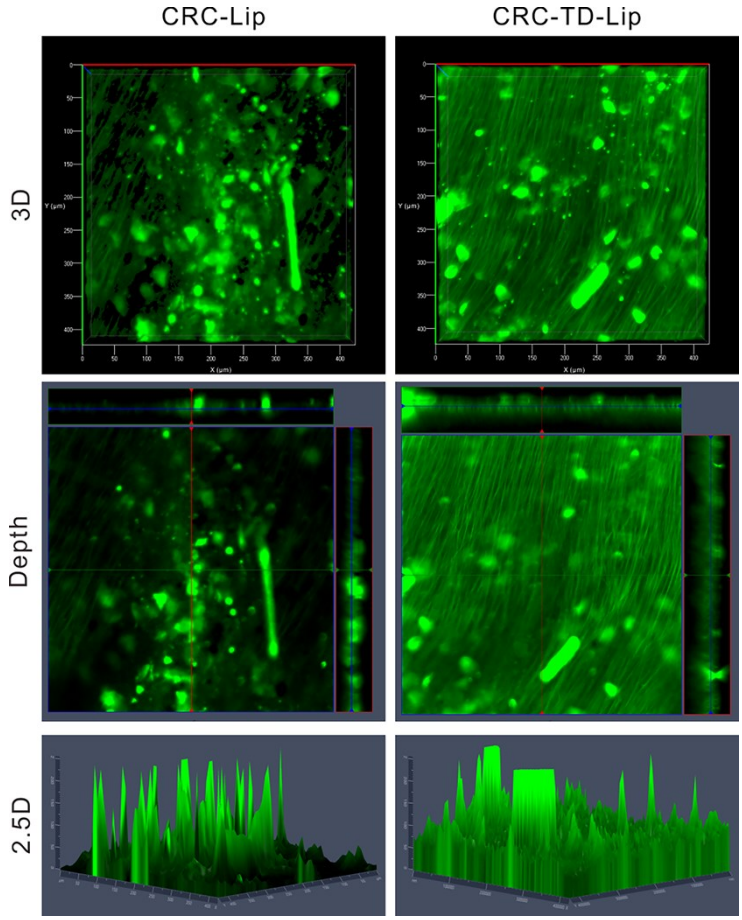

Figure S6. Comparison of the in vivo permeation distribution of CRC between CRC-Lip and CRC-TD-Lip after 8 h (the skin permeation depth in 2.5D images was approximately 30 μm; green denotes curcumin).

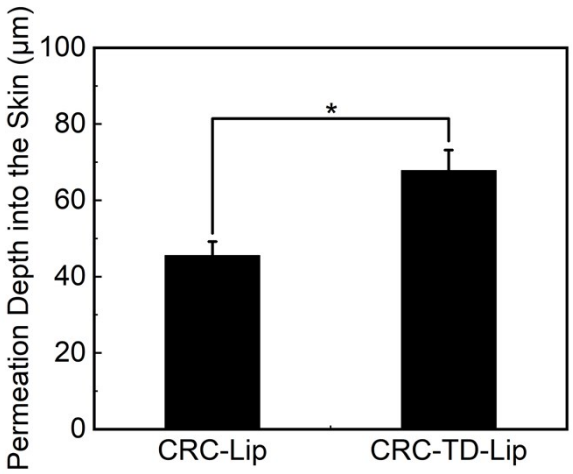

Figure S7. Comparison of the in vivo permeation depth of CRC between CRC-Lip and CRC-TD-Lip (*$p < 0.05$).

3. Supplementary Tables

Table S1. Compositions of various formulations

Composition	CRC-TD-Lip	CRC-Lip	CRC-DMSO	TD-Lip
Curcumin (%, w/v)	0.1	0.1	0.1	/
Lecithin (%, w/v)	1.6	1.6	/	1.6
DSPE-PEG-NHS (%, w/v)	0.8	0.8	/	0.8
Cholesterol (%, w/v)	0.8	0.8	/	0.8
Tween-80 (%, v/v)	0.5	0.5	/	0.5
TD (%, w/v)	0.16	/	/	0.16
DMSO (%, v/v)	/	/	100	/

Table S2. Primer sequences for quantitative real-time PCR (qPCR)*

Primer	Base sequence
L-17A-F	GTCCAAACACTGAGGCCAAG
IL-17A-R	TCTTCATTGCGGTGGAGAGT
IL-17F-F	CCAGGGCTGTTCTAATTCC
IL-17F-R	TTGTATGCAGCGTTGTCAG
IL-22-F	CTTCTCATTGCCCTGTGG
IL-22-R	ATAAAGGTGCGGTTGACG
IL-1β-F	GAAGAAGAGCCCATCCTCTG
IL-1β-R	TCATCTCGGAGCCTGTAGTG
TNF-α-F	GAAACACAAGATGCTGGGA
TNF-α-R	TTGCAGAACTCAGGAATGG
β-actin-F	ACCCTAAGGCCAACCGTGAAA
β-actin-R	ATGGCGTGAGGGAGAGCATA

*The cytokines, IL-17A, IL-17F, IL-22, IL-1β and TNF-α, are related to the hyper-proliferation of keratinocytes in skin psoriatic inflammation. IL-17A, IL-17F and IL-22 induce the proliferation of keratinocytes resulting in psoriatic skin damage (Dyring-Andersen et al., British Journal of Dermatology, 2017, 177: e321-e322; Ekman et al., Journal of Investigative Dermatology, 2017, 139: 1564-1573); TNF-α is mainly secreted by activated T lymphocytes, monocytes and macrophages, which affect the keratinocyte proliferation and apoptosis, and induce inflammation (Dowlatshahi et al., British Journal of Dermatology, 2013, 169: 266-282); IL-1β promotes the secretion of IL-17 and amplifies the inflammatory response of psoriasis (Cai et al., Journal of Investigative Dermatology, 2019, 139: 146-156.). Here, qPCR was used to evaluate the expression levels of the abovementioned cytokines in the back skin slices of mice.