Supporting Information

Co-delivery of Loaded 4-Butylresorcinol and Licochalcone A Supramolecular for Synergistic Permeation and Whitening Effects

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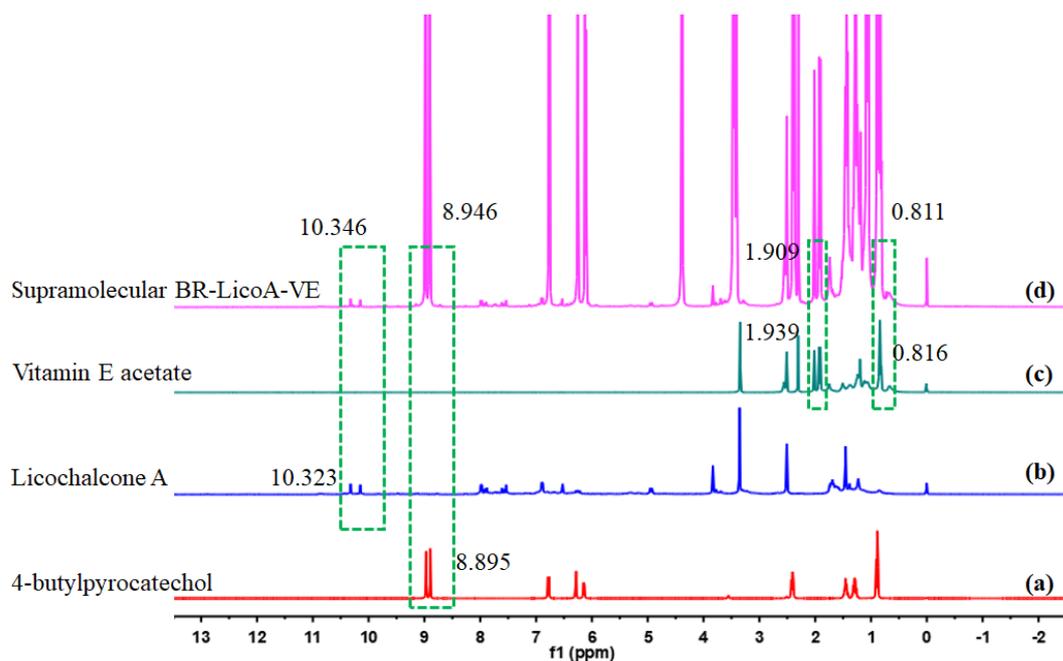zhangjiaheng@hit.edu.cn (Jiaheng Zhang)

Figure S1. ^{1}H NMR spectra of 4-butylpyrocatechol (BR), licochalcone A (LicoA), vitamin E acetate (VE) and supramolecular BR-LicoA-VE.
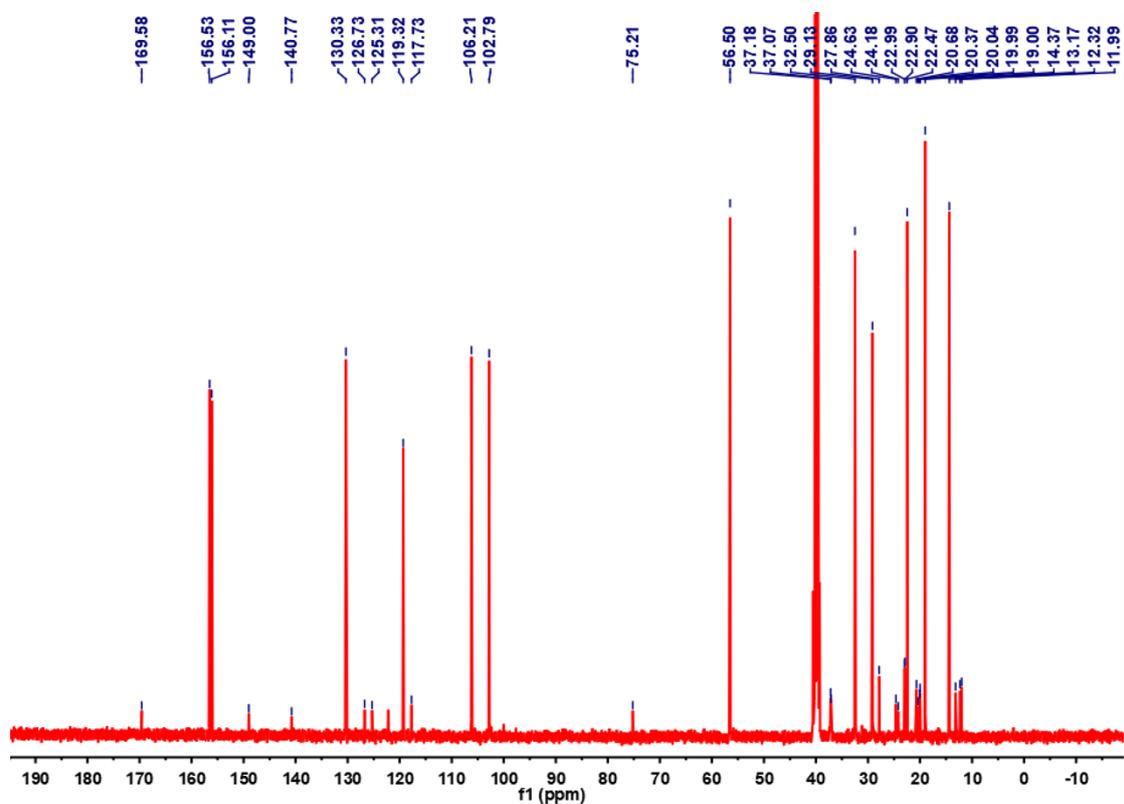

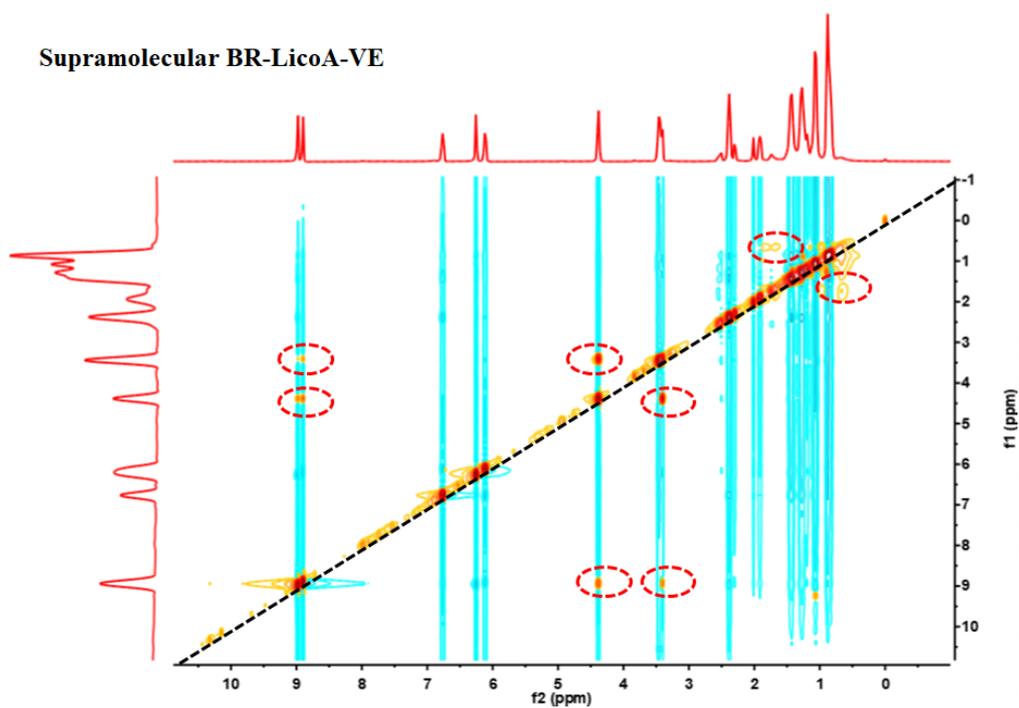**Figure S2.** ^{13}C NMR spectrum of supramolecular BR-LicoA-VE.

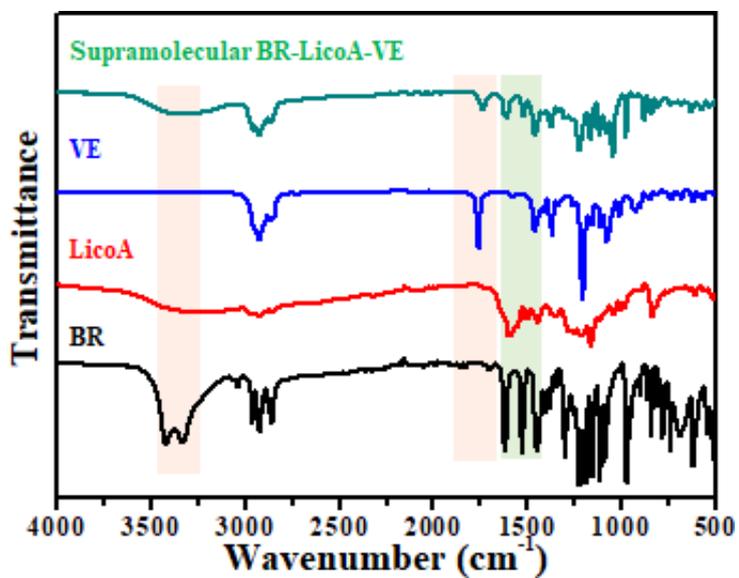**Figure S3.** NOESY spectrum of supramolecular BR-LicoA-VE.

Figure S4. FTIR spectra of BR, LicoA, VE and supramolecular BR-LicoA-VE.
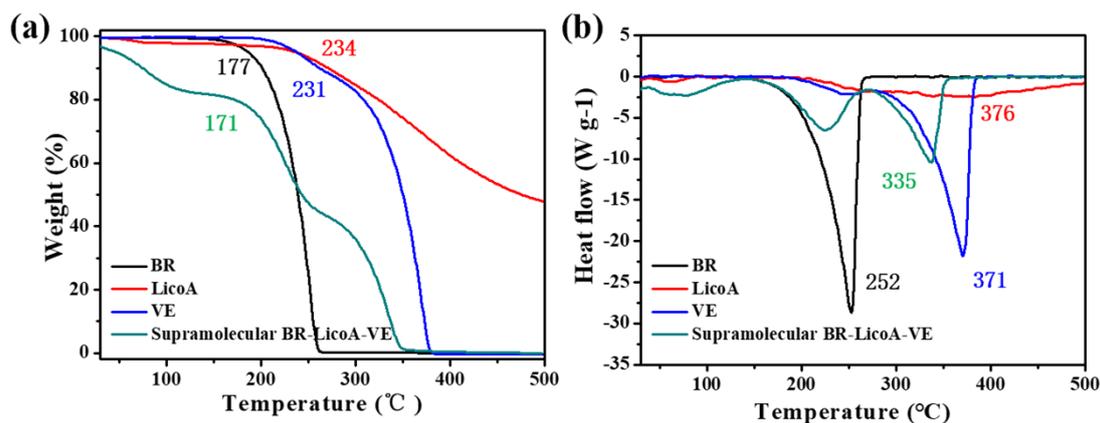
Figure S5. (a) TGA and (b) DSC images of BR, LicoA, VE, and supramolecular BR-LicoA-VE.
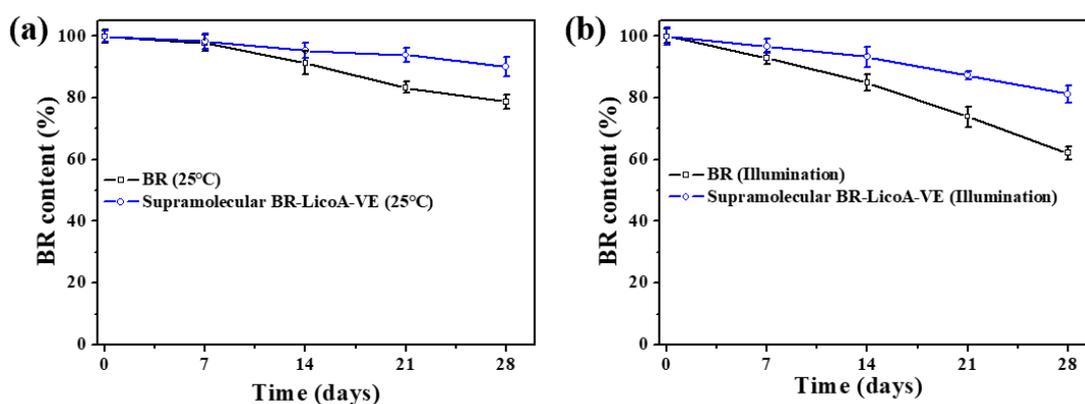

Figure S6. The stability of BR and supramolecular BR-LicoA-VE after 28 days of storage at (a) room temperature (25°C) and (a) under illumination conditions.
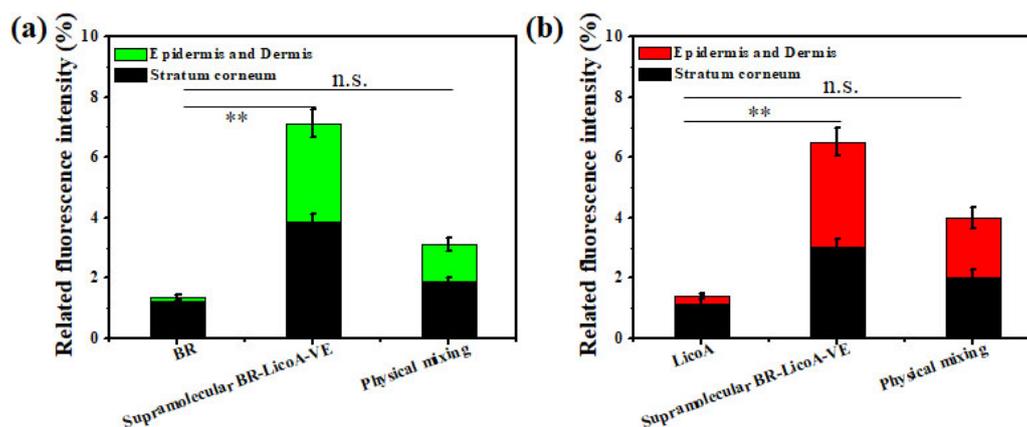

Figure S7. Relative fluorescence quantitative plots of (a) BR and (b) LicoA transdermal penetration of in supramolecular BR-LicoA-VE for 24h. (n=6; *$p < 0.05$, **$p < 0.01$ and n.s. represent no significance).
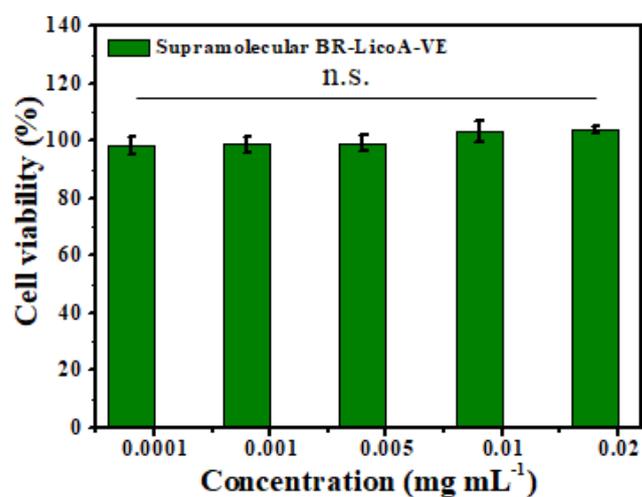
Figure S8. Cell viability of supramolecular BR-LicoA-VE in different concentrations (n=6; *p* < 0.05 and **p* < 0.01).

Table S1. Experimental results of the supramolecular BR-LicoA-VE patch test

Group	Number of subjects	Observation time	Number of people with different skin reactions in the patch test [a]				
			0	1	2	3	4
Control	34	0.5	34	0	0	0	0
		24	34	0	0	0	0
		48	34	0	0	0	0
BR	34	0.5	34	0	0	0	0
		24	34	0	0	0	0
		48	34	0	0	0	0
LicoA	34	0.5	34	0	0	0	0
		24	34	0	0	0	0
		48	34	0	0	0	0

VE	34	0.5	34	0	0	0	0
		24	34	0	0	0	0
		48	34	0	0	0	0
Supramolecular BR-LicoA-VE	34	0.5	34	0	0	0	0
		24	34	0	0	0	0
		48	34	0	0	0	0

[a]: 0 represents a negative reaction, 1 represents an able reaction, only weak erythema, 2 represents a weak positive reaction, erythema reaction, 3 represents a strong positive reaction, herpes reaction, 4 represents an extremely strong positive reaction, fusion herpes reaction.

Table S2. Binding energy of supramolecule BR-LicoA-VE to proteins

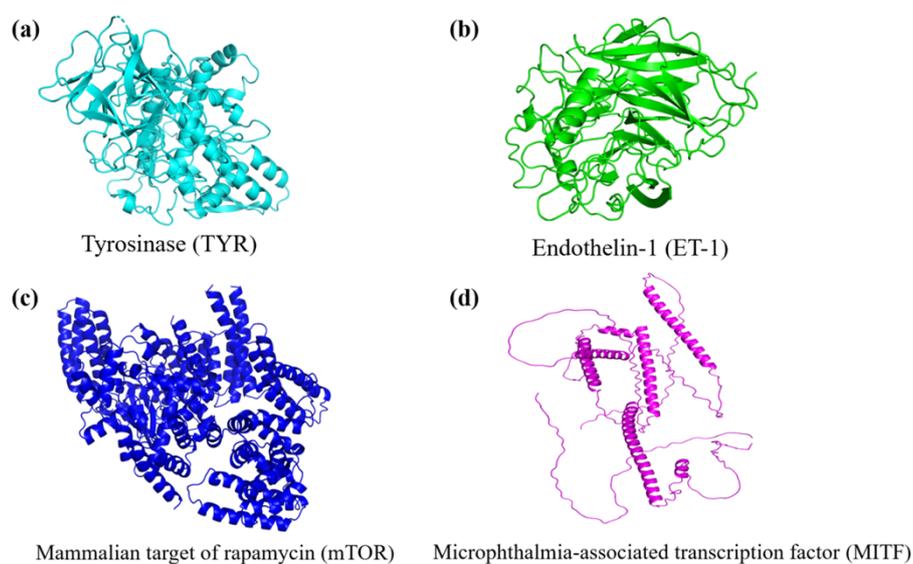| Group	Binding energy (kcal/mol)			
	TYR	ET-1	mTOR	MITF
BR	-5.095	/	/	/
LicoA	/	-7.388	/	/
Supramolecular BR-LicoA-VE	-8.024	-8.404	-8.531	-5.433

Figure S9. Three-dimensional structural diagram of (a) tyrosinase protein, (b) endothelin-1 protein, (c) mammalian target of rapamycin (mTOR) protein, (d) microphthalmia-associated transcription factor (MITF) protein.

Table S3. Experimental results of the supramolecular BR-LicoA-VE formula patch test

Group	Number of subjects	Observation time	Number of people with different skin reactions in the patch test [a]				
			0	1	2	3	4
Control	34	0.5	34	0	0	0	0
		24	34	0	0	0	0
		48	34	0	0	0	0
BR formula	34	0.5	34	0	0	0	0
		24	34	0	0	0	0
		48	34	0	0	0	0
PR formula	34	0.5	34	0	0	0	0
		24	34	0	0	0	0
		48	34	0	0	0	0
Supramolecular BR-LicoA-VE formula	34	0.5	34	0	0	0	0
		24	34	0	0	0	0
		48	34	0	0	0	0

[a]: 0 represents a negative reaction, 1 represents an able reaction, only weak erythema, 2 represents a weak positive reaction, erythema reaction, 3 represents a strong positive reaction, herpes reaction, 4 represents an extremely strong positive reaction, fusion herpes reaction.
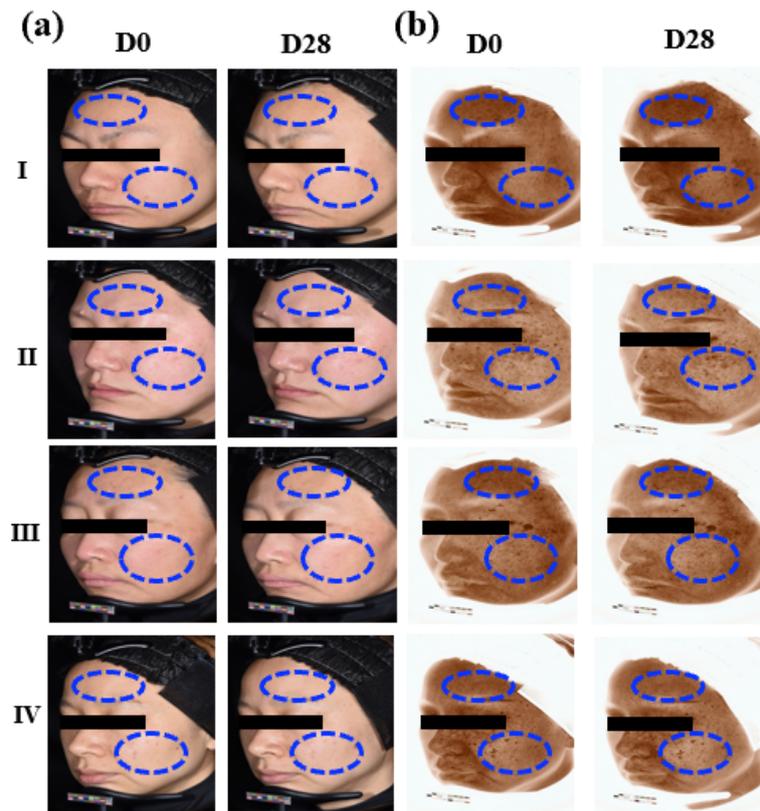
Figure S10. (a) Positive white light diagram and (b) brown spot diagram of the skin after 0 and 28 days of use of the sample. (n=12; *$p < 0.05$ and **$p < 0.01$).