

Supporting information

The preparation of liposomal ointment

The formulation of ointment matrix containing deformable liposomes was showed in **Table S1**. During preparation of liposomal ointment, an amount of water was replaced by liposome suspension. Briefly, the oil phase and water phase were heated to 60 °C separately. Then the oil phase was added into water phase with magnetic stirring. The mixture was cooled to 40°C then the liposome suspension was added into it. Finally, the ointment was transferred on ice for further cooling. The final drug content of EGF in ointment was 10µg/g while that of TRA was 0.5mg/g.

Table S1. *Formulation of ointment matrix containing deformable liposomes.*

	Substance	Content (w/w%)
Oil phase	Glycerol monostearate	4
	Cetanol	6
	Miglyol 812	7.5
	Vaseline	25.5
	Tween 60	6.5
Water phase	Propylene glycol	10
	Water	40.45
	Sodium hyaluronate	0.05

Stability study of dual deformable liposomal ointment

In order to elucidate the stability of the dual deformable liposomal ointment, samples of free drug ointment and dual liposomal deformable ointment were stored in 4°C for 1 month, and a comparison between the *in vitro* drug release of the freshly made samples and 1-month-stored samples was carried out following the mentioned method. The results were shown in **Figure S1**. The drug contents of EGF and TRA in 1-month-stored free drug ointment were significantly declined to 75% and 86%. By contrast, 1-month-stored liposomal ointment shared the similar drug release pattern with fresh-made liposomal ointment and the drug contents were relatively retained. Therefore, a conclusion can be reached that the prepared liposomal ointment exhibited satisfactory stability.

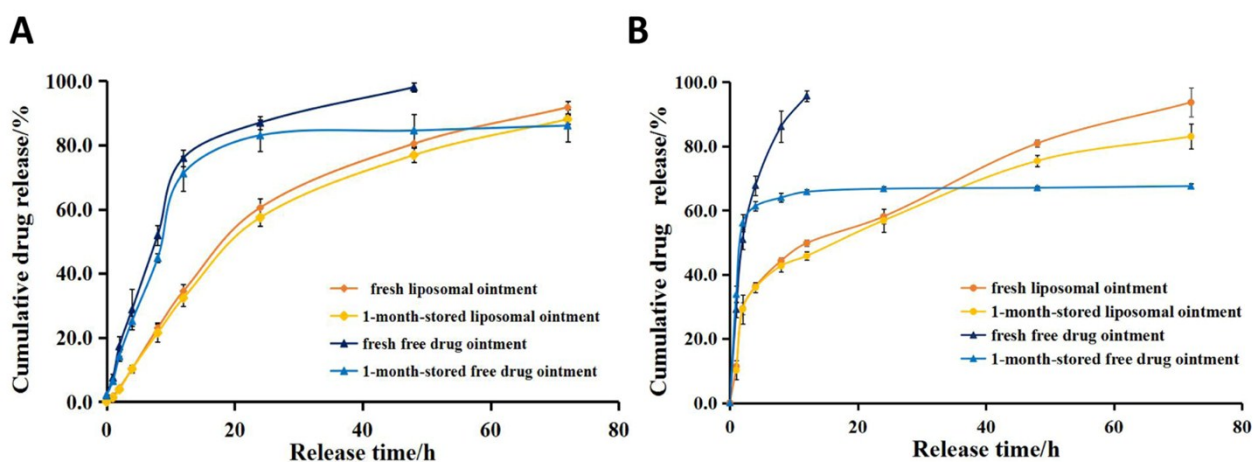


Figure S1. Stability study of dual deformable liposomal ointment. (A) *In vitro* drug release of TRA in fresh and 1-month-stored liposomal ointment; (B) *In vitro* drug release of EGF in fresh and 1-month-stored liposomal ointment.

***In vitro* skin permeation and retention of dual liposomal ointment**

In vitro skin permeation and retention study of dual liposomal ointment was conducted by using Franz diffusion cells, following the similar method mentioned in manuscript. The results are showed in **Figure S2** and **Table S2**. Proceeding from the results, the dual liposomal ointment still retained the high flux and skin retention, being favorable for transdermal drug delivery.

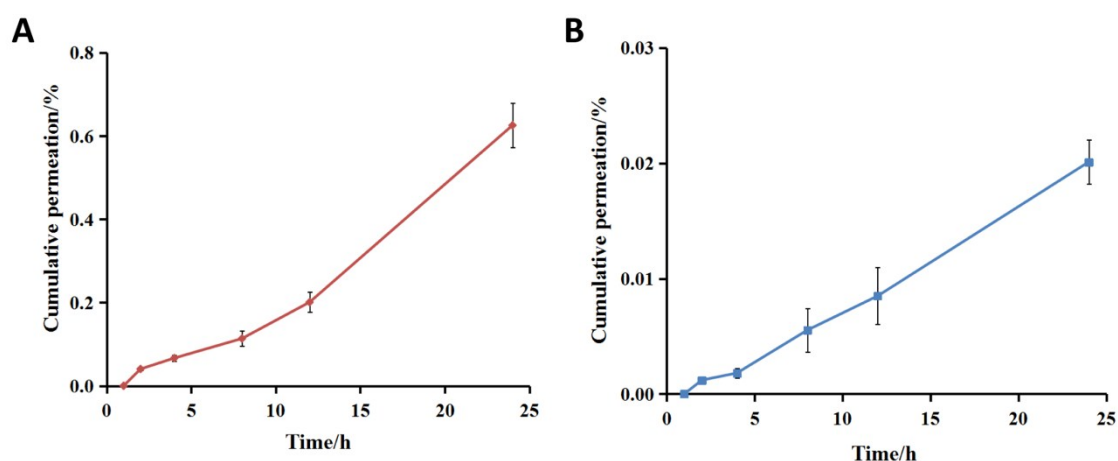


Figure S2. *In vitro* skin permeation and retention study of dual deformable liposomal ointment. (A) *In vitro* skin permeation of TRA in dual deformable liposomal ointment; (B) *In vitro* skin permeation of EGF in dual deformable liposomal ointment.

Table S2. J_{flux} and skin deposition of TRA and EGF in dual deformable liposomal ointment.

Drug	J_{flux}	Skin deposition
TRA	$0.18 \pm 0.02 \mu\text{g}/\text{cm}^2 \cdot \text{h}$	$1.42 \pm 0.07 \mu\text{g}/\text{cm}^2$
EGF	$0.10 \pm 0.01 \text{ng}/\text{cm}^2 \cdot \text{h}$	$8.98 \pm 0.76 \text{ng}/\text{cm}^2$

