Supporting Information

Nano-in-Nano Dendrimer Gel Particles for Efficient Topical Delivery of Antiglaucoma Drugs into the Eye

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Table S1. Conditions for making dendrimer gel particles of various sizes.

	µDHP10	**µDHP3**	**nDHP**
Surfactant tween80/span80 (w/w)	1/5	1/5	4.5/5
Oil phase surfactant/hexane (v/v)	1/70	1/70	3.7/70
Water phase	DH-G5-10%	DH-G5-10%	DH-G5-10%
O/W (v/v)	10/1	35/1	762/1
Emulsion formulation	Disperser, 30 000 rpm	Disperser, 30 000 rpm	Stirrer, 700 rpm
Processing	2 h at 500 rpm	2 h at 500 rpm	2 h at 500 rpm

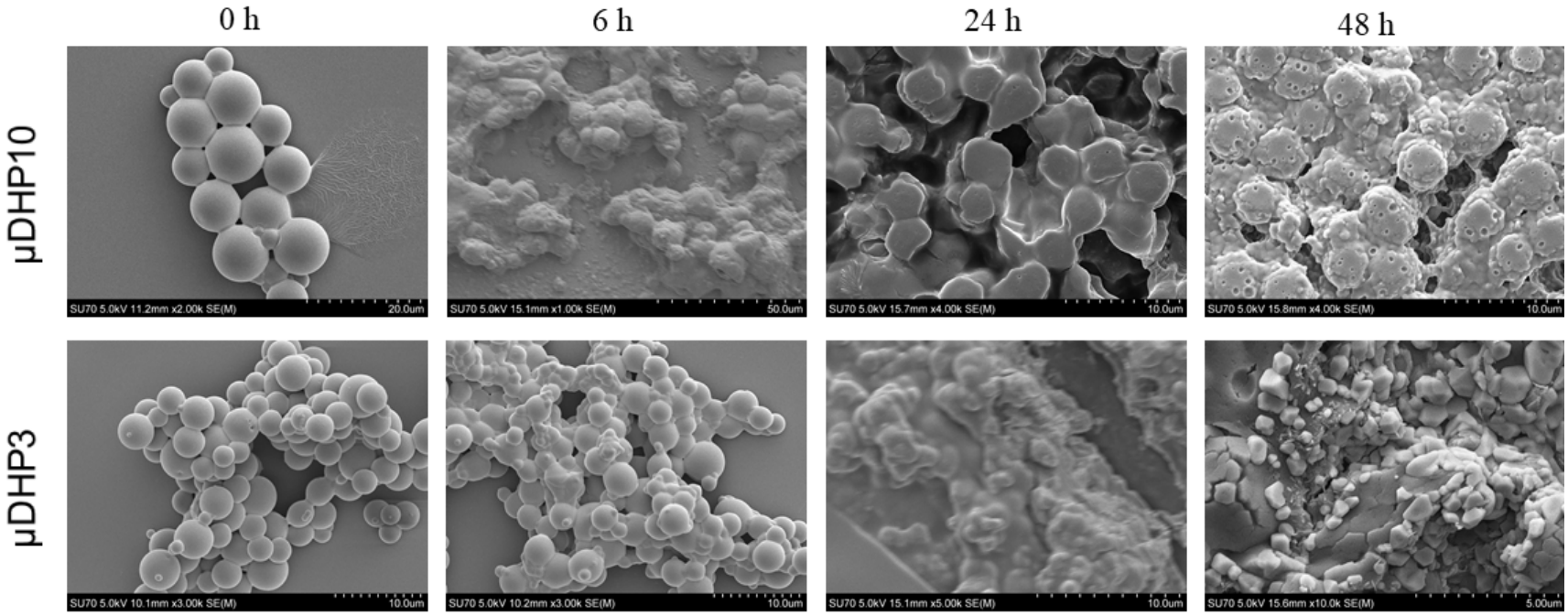

Figure S1. SEM images of μDHPs after incubation for different lengths of time in contrived tears incubated at 37 ℃.

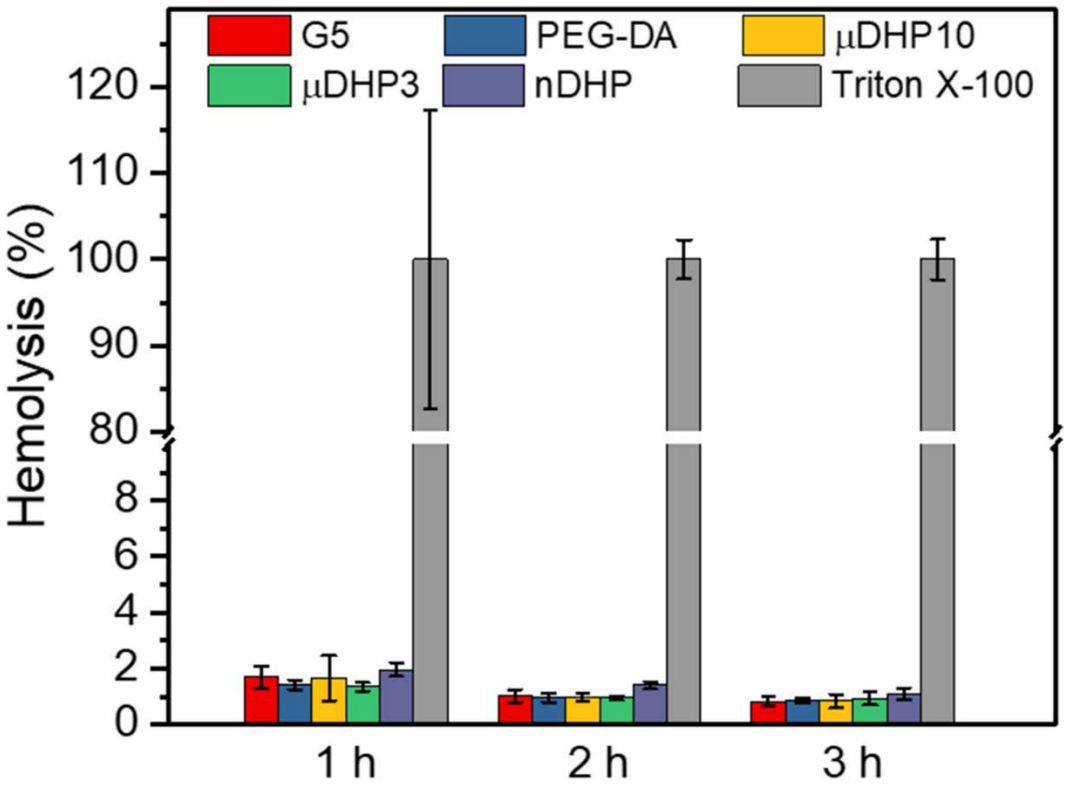

Figure S2. Hemolytic effect of μDHP10, μDHP3, nDHP, G5 and PEG-DA on rabbit red blood cells at 37 °C for 1, 2 and 3 h. Triton X-100 was served as positive control and PBS (pH 7.4, 1×) as negative control.

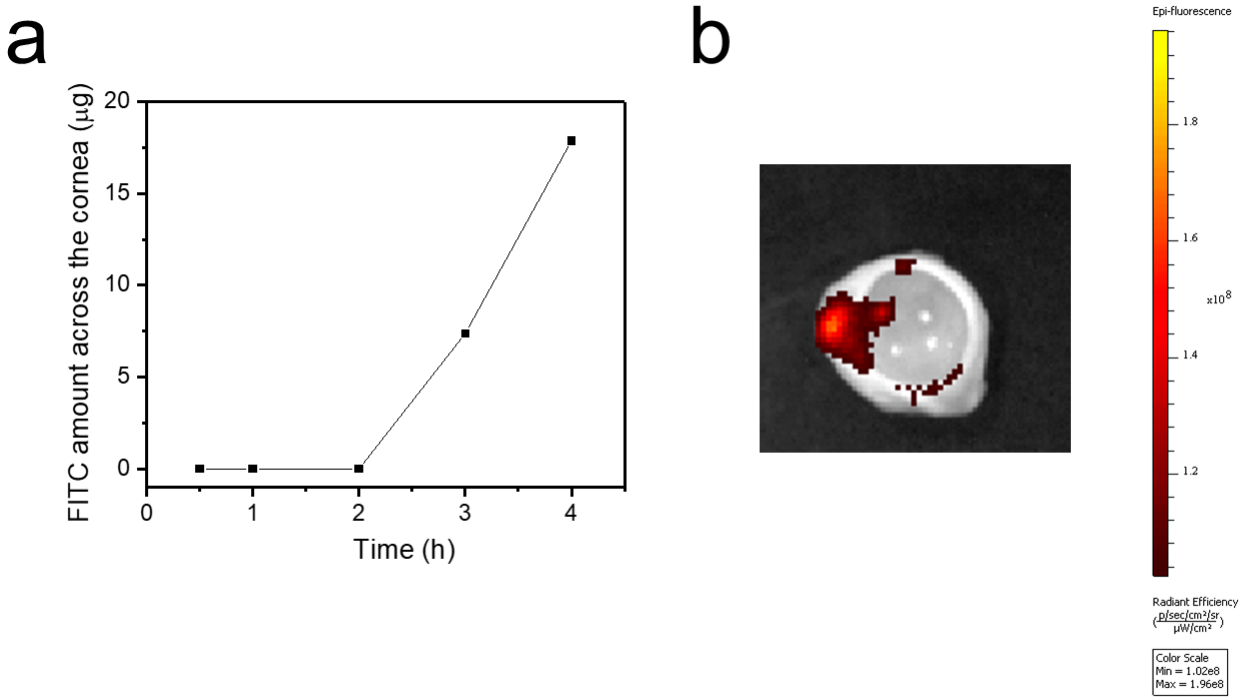

Figure S3. *Ex vivo* permeation of μDHP3. a) Corneas were extracted from fresh rabbit eyes and mounted in a Franz diffusion cell system. The receiver chamber was filled with PBS. FITC-labeled microgel ($\mu DHP3^{FITC}$, 200 μL) was loaded to the donor chamber. At pre-determined time points up to 4 h, an aliquot of 500 μL from the receiver chamber was withdrawn and analyzed with UV-Vis. Fresh PBS (500 μL) was added to the receiver chamber following each sampling. The concentration of FITC for each sampling and those remained in donor chamber were detected by UV-Vis based on a standard curve of FITC. b) The NiR dye labeled μDHP3 was topical administrated on the rabbit eye globe ex vivo. After stored at RT for 48 h, the globe surface was washed gently by PBS, and then imaged on IVIS-200. The DiR signals showed on the cornea after 48 h, indicating the retention of the particles on the cornea.

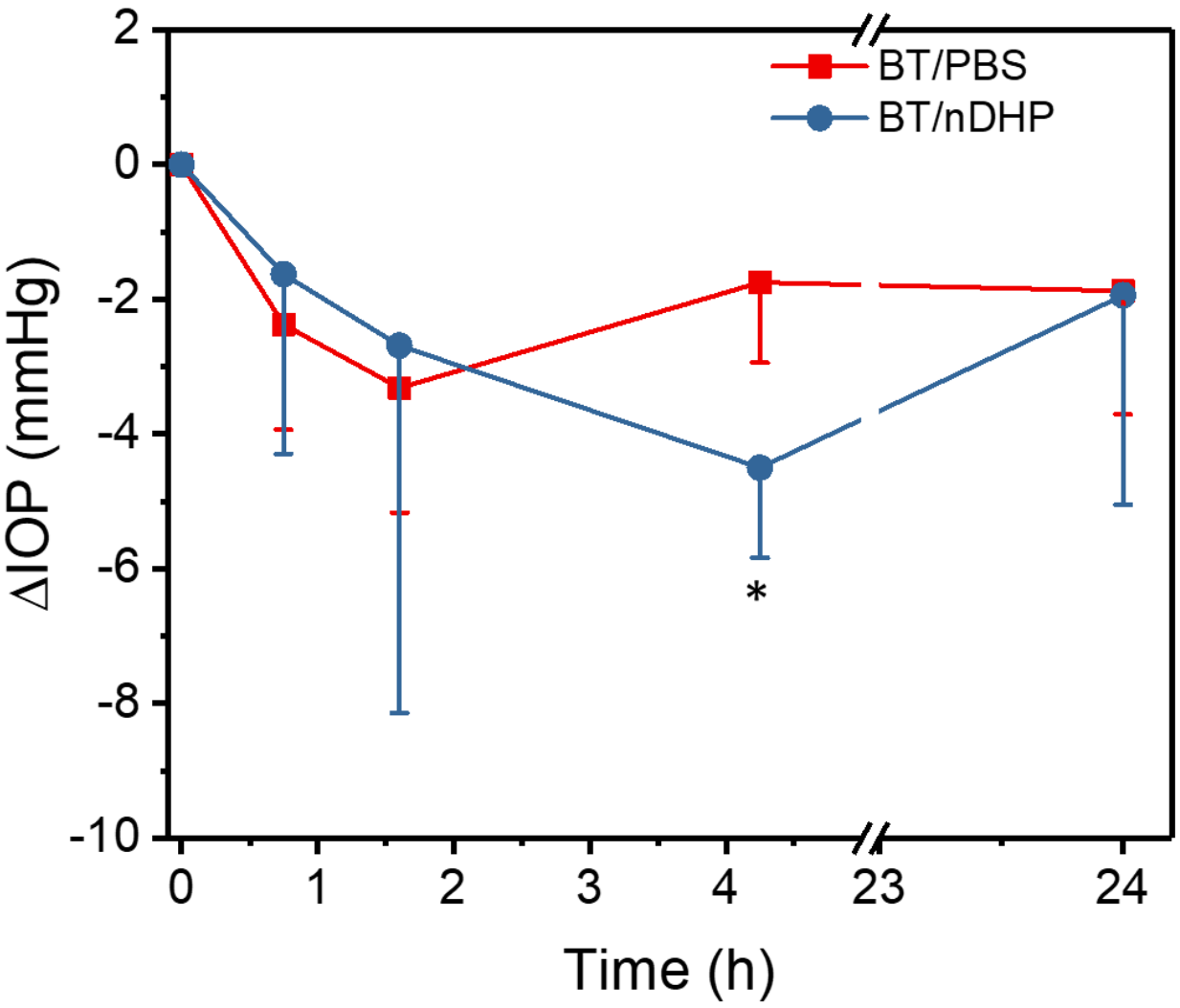

Figure S4. In vivo IOP-lowering effect of BT/nDHP and BT/PBS in normotensive rats after one-time topical administration. * $P < 0.05$.

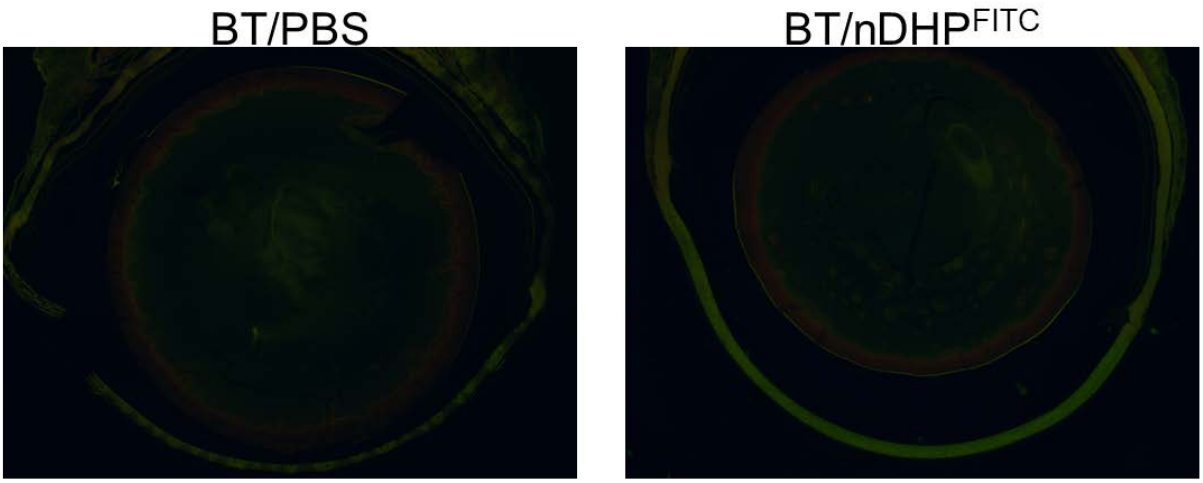

Figure S5. Fluorescent imaging of whole-mount globes. Following once-daily instillation of BT/PBS and BT/nDHP^{FITC} for 7 days, there is retention of FITC-labeled nDHP in the fibrous tunic, including the cornea.