

Supplementary Information

Bioadhesive glycosylated Nanoformulations for Extended Trans-Cornea Drug

Delivery to Suppress Corneal Neovascularization

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Scheme S1. Synthetic route of p(AAPBA-*r*-GEA) glycopolymer

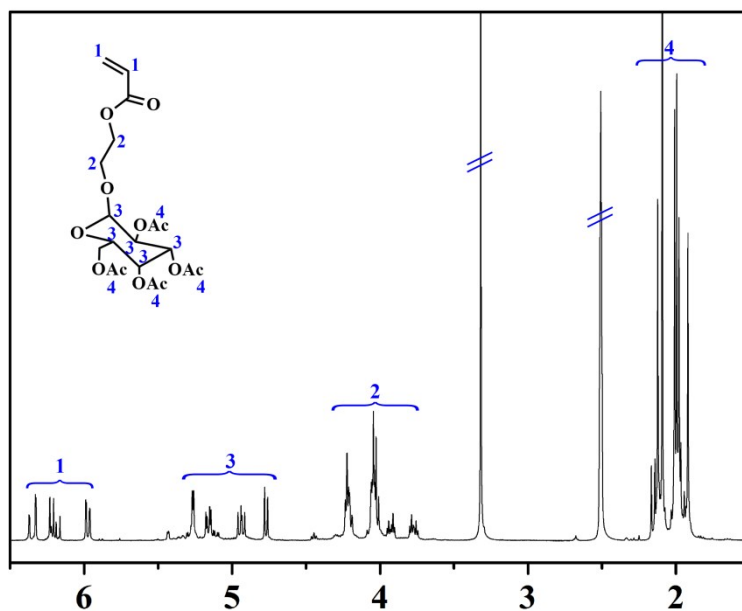
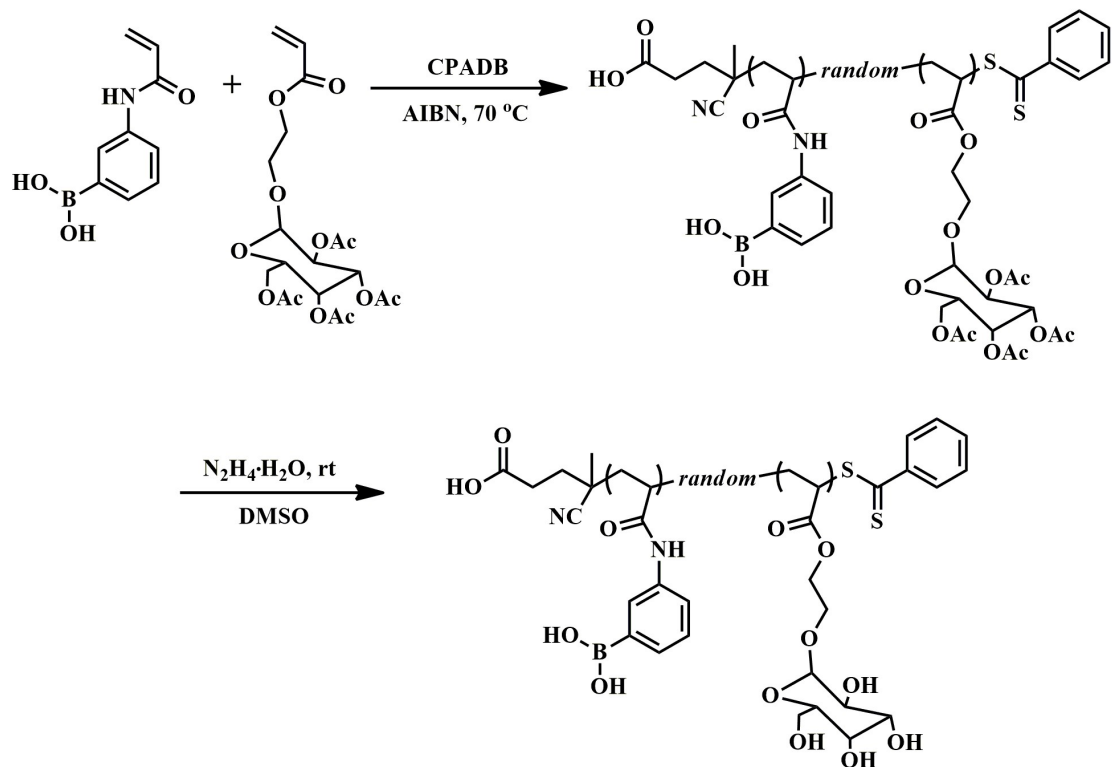


Fig. S1 1H NMR spectrum of AcGEA in $DMSO-d_6$ at 25 °C.

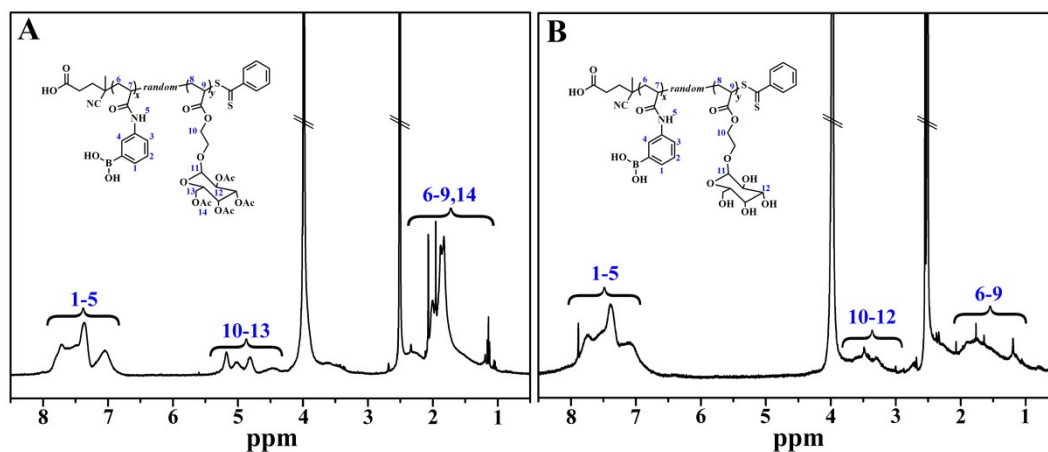


Fig. S2 ^1H NMR spectra of glycopolymer (A) p(AAPBA-*r*-AcGEA) and (B) p(AAPBA-*r*-GEA) in $\text{DMSO-}d_6/\text{D}_2\text{O}$ (v/v, 4/1) at 25 °C.

Table S1. Constitution of p(AAPBA-*r*-AcGEA) glycopolymers

Sample	Monomer	RAFT agent	Conv (wt %) ^b	AAPBA/AcGEA (mol/mol)	
				Theory ^a	^1H NMR ^b
p(AAPBA ₆₀ - <i>r</i> -AcGEA ₄₀)	AcGEA	AAPBA	77.96 ± 6.98	1.5	2.1 ± 0.45
p(AAPBA ₈₀ - <i>r</i> -AcGEA ₄₀)	AcGEA	AAPBA	93.29 ± 7.85	2	2.9 ± 0.51
p(AAPBA ₁₀₀ - <i>r</i> -AcGEA ₄₀)	AcGEA	AAPBA	73.13 ± 6.26	2.5	3.4 ± 0.42
<i>p</i>			< 0.05		> 0.05

^aThe theoretical molar ratio of AAPBA/AcGEA; ^bThe approximate polymerization conversion and copolymer compositions were measured on the basis of the integral intensity of the ^1H NMR spectra.

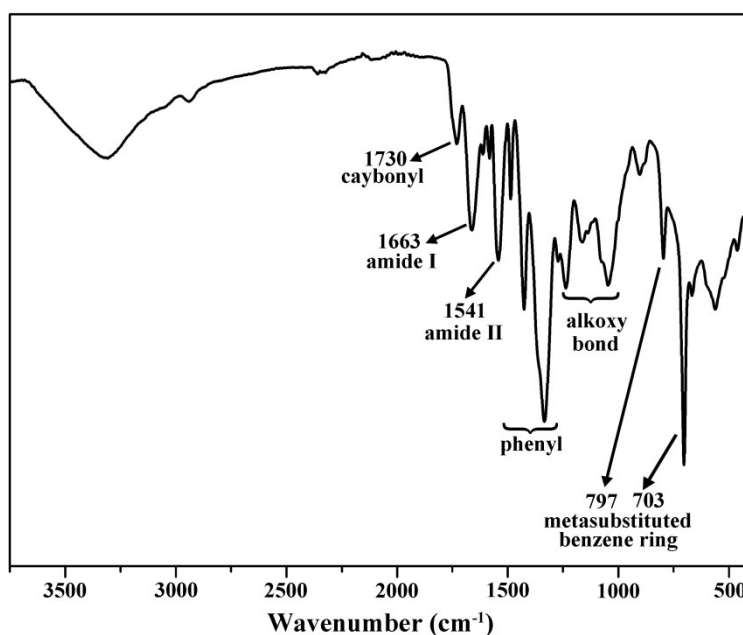
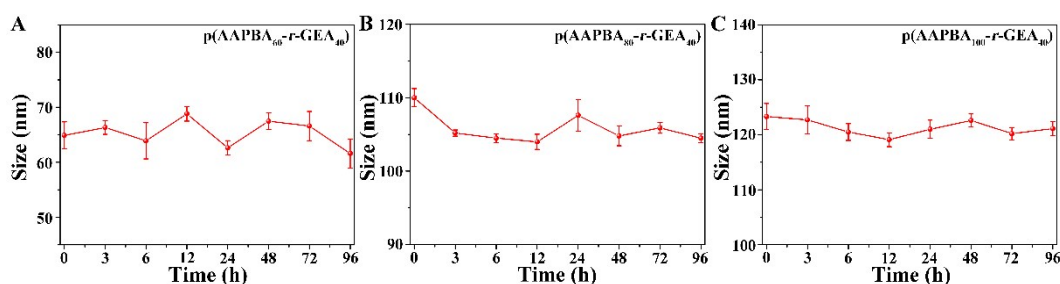
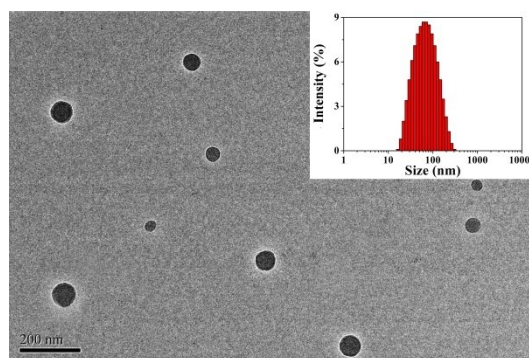


Fig. S3 FT-IR spectrum of p(AAPBA-*r*-AcGEA).

Table S2. D_H , PDI, and zeta potential of p(AAPBA-*r*-GEA) nanoparticles^a

Sample	D_H (nm)	PDI	Zeta potential (mV)
p(AAPBA ₆₀ - <i>r</i> -GEA ₄₀)	65.6 ± 3.7	0.12 ± 0.03	-20.5 ± 3.4
p(AAPBA ₈₀ - <i>r</i> -GEA ₄₀)	110.0 ± 4.3	0.09 ± 0.02	-29.7 ± 3.9
p(AAPBA ₁₀₀ - <i>r</i> -GEA ₄₀)	123.3 ± 5.4	0.22 ± 0.04	-15.5 ± 2.5
<i>p</i>	< 0.05	< 0.05	< 0.05

^a Each experiment was performed in triplicate and the results were reported as mean ± SD.

**Fig. S4** Colloidal stability of (A) p(AAPBA₆₀-*r*-GEA₄₀) nanoparticles; (B) p(AAPBA₈₀-*r*-GEA₄₀) nanoparticles; (C) p(AAPBA₁₀₀-*r*-GEA₄₀) nanoparticles.**Fig. S5** TEM micrograph and size distribution measured by DLS of DEX-loaded p(AAPBA-*r*-GEA) NPs.**Table S3. EE and LC of the DEX-loaded p(AAPBA-*r*-GEA) nanoparticles^a**

Sample	D_H (nm)	PDI	Zeta potential (mV)	EE (%)	LC (%)
NP1@DEX	68.3 ± 2.6	0.25 ± 0.04	-19.0 ± 1.4	56.2 ± 1.5	7.8 ± 0.8
NP2@DEX	83.7 ± 2.2	0.23 ± 0.03	-21.5 ± 1.5	63.1 ± 2.1	8.6 ± 1.1
NP3@DEX	116.8 ± 2.9	0.24 ± 0.01	-25.0 ± 2.3	72.0 ± 1.9	9.8 ± 1.2
<i>p</i>	< 0.05	> 0.05	< 0.05	< 0.05	> 0.05

^a Each experiment was performed in triplicate and the results were reported as mean \pm SD.

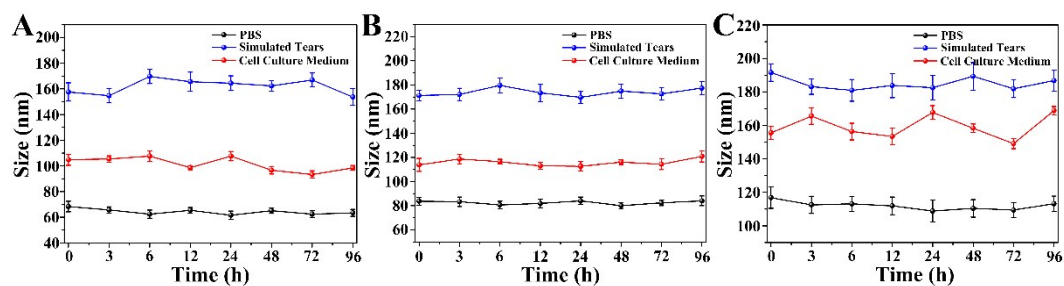


Fig. S6 Colloidal stability of (A) NP1@DEX, (B) NP2@DEX and (C) NP3@DEX in PBS, simulated tears and cell culture medium.

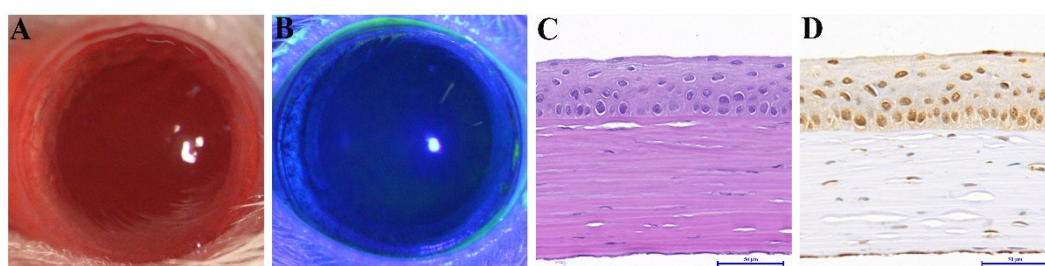


Fig. S7 Slit lamp examination, H&E and TUNEL staining of the corneas of rats treated with p(AAPBA-r-GEA) nanoparticles (A: slit-lamp photograph; B: corneal fluorescein staining; C: H&E staining; D: TUNEL staining).

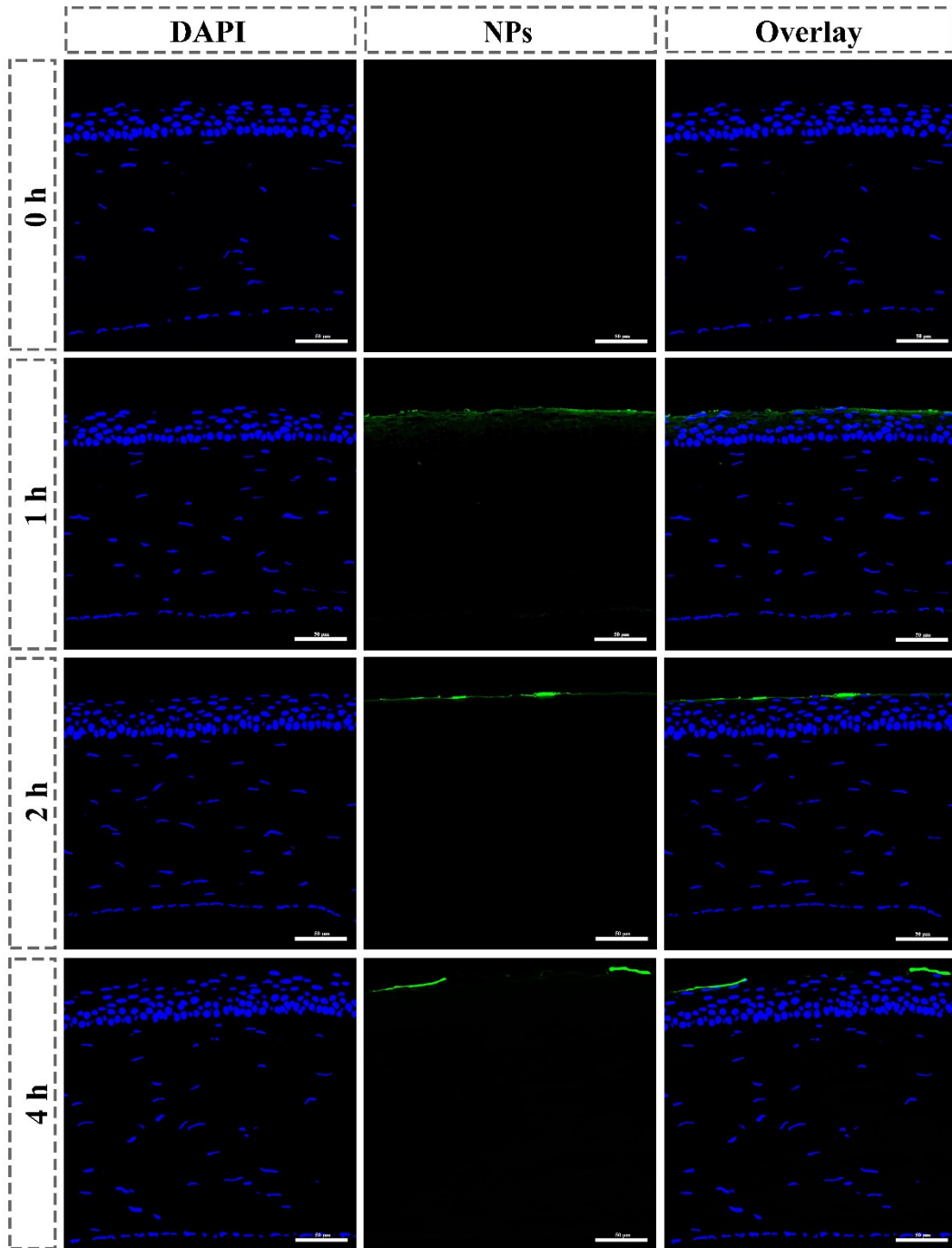


Fig. S8 Inverted fluorescence micrographs of corneal penetration and persistence of BODIPY-labeled fluorescent nanoparticles after topical administration in the healthy cornea.

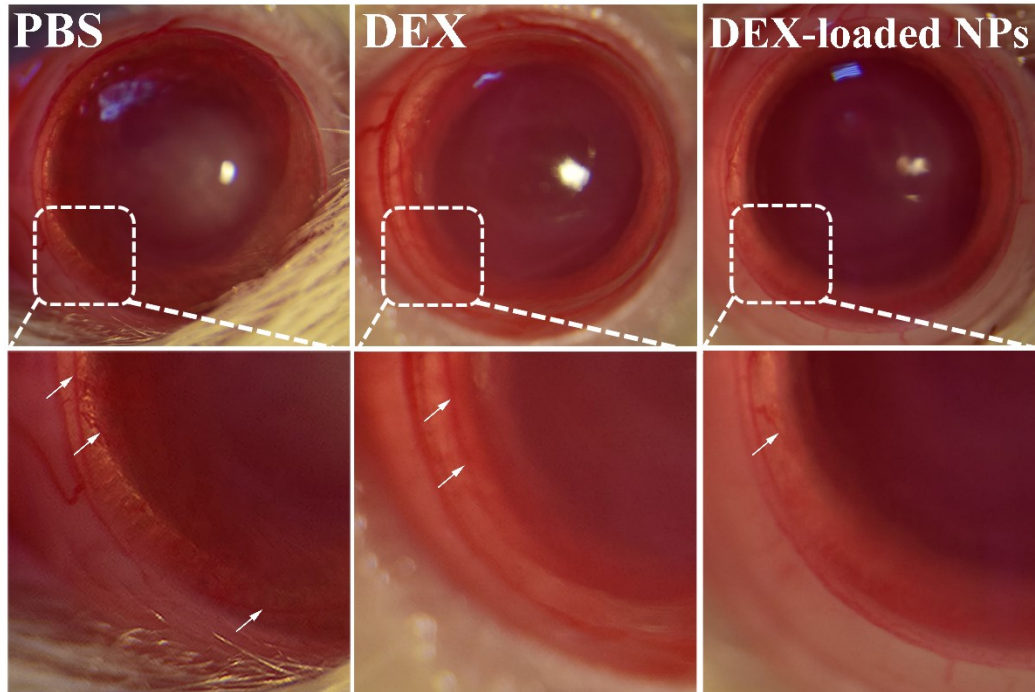


Fig. S9 Representative images of CNV at 7 days posttreatment. The white arrows indicate CNV. * $p < 0.05$.

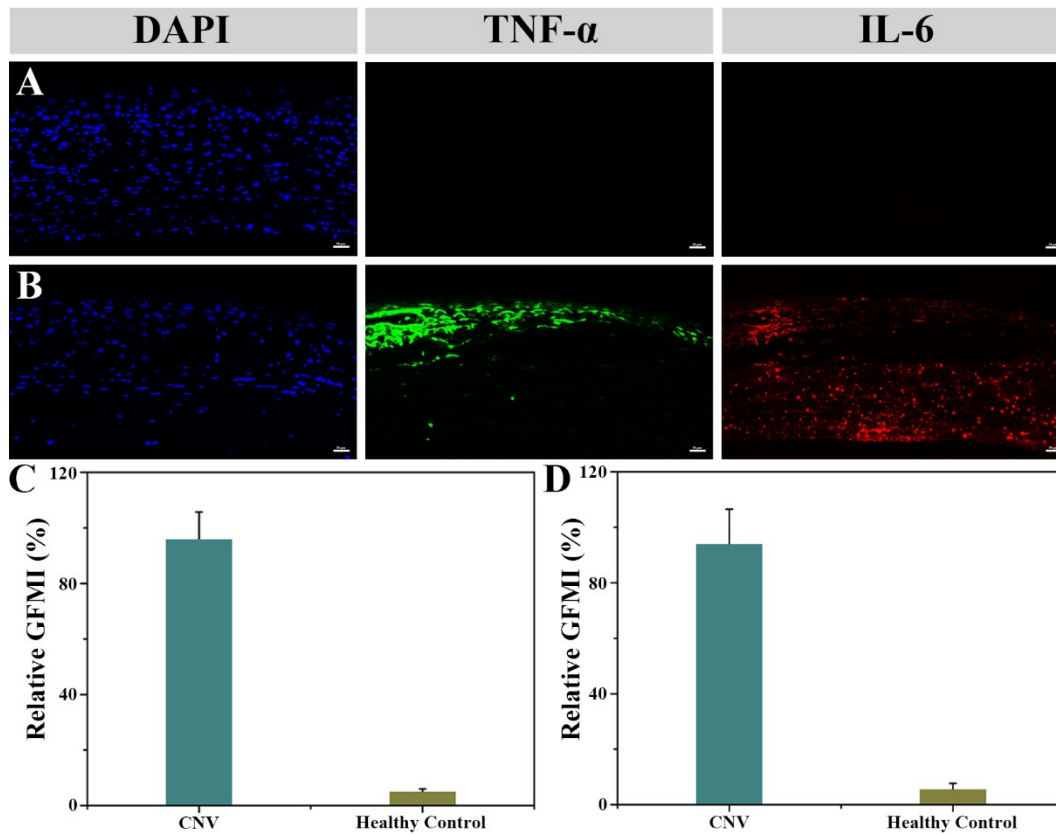


Fig. S10 (A-B) Representative images of double-color immunofluorescence analysis of IL-6 and TNF- α in the corneas of healthy (A) and CNV (B) group after treatment with NP1. (C-D) GMFI analysis of TNF- α (C) and IL-6 (D) by Image J software.