Electronic Supplementary Material (ESI) for RSC Advances.

Extended-Release of Opioids using Fentanyl-based Polymeric Nanoparticles for Enhanced Pain Management

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^{1}H NMR spectra of fentanyl initiators

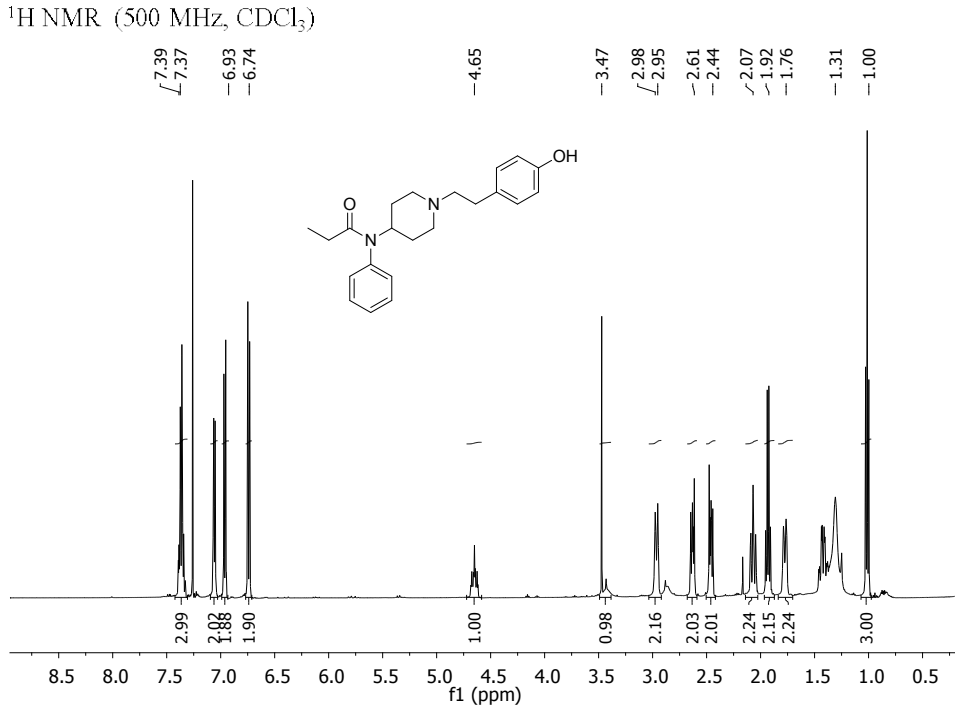

Figure S1. ^{1}H NMR spectrum of Fen-OH.

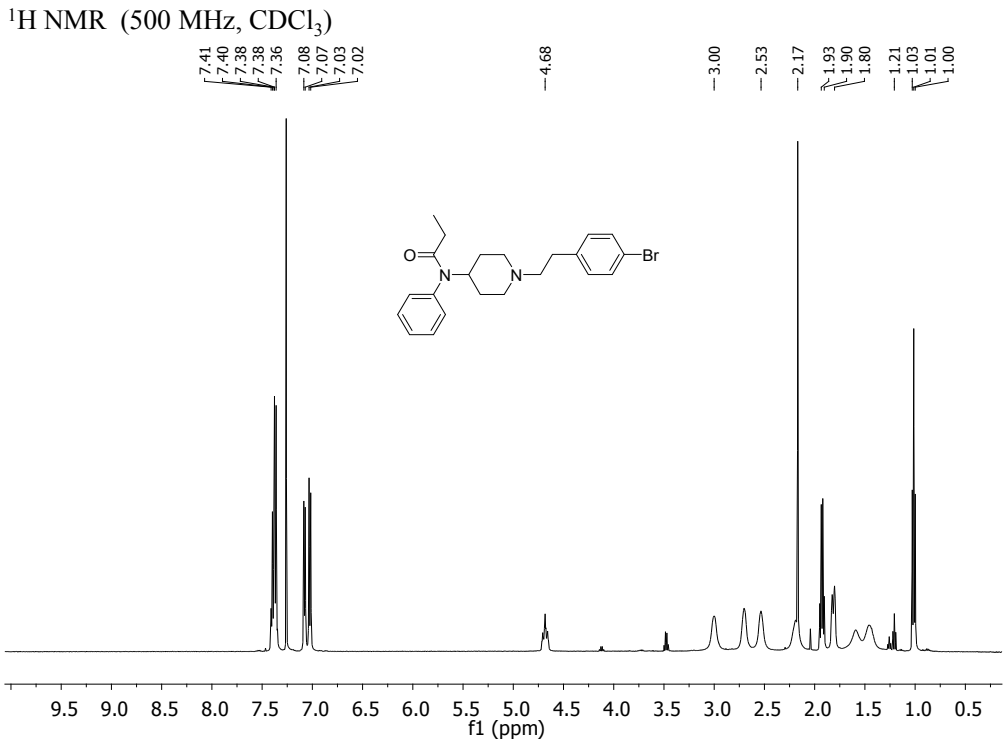

Figure S2. ^{1}H NMR spectrum of Fen-Br.

^{1}H NMR (500 MHz, $CDCl_3$)

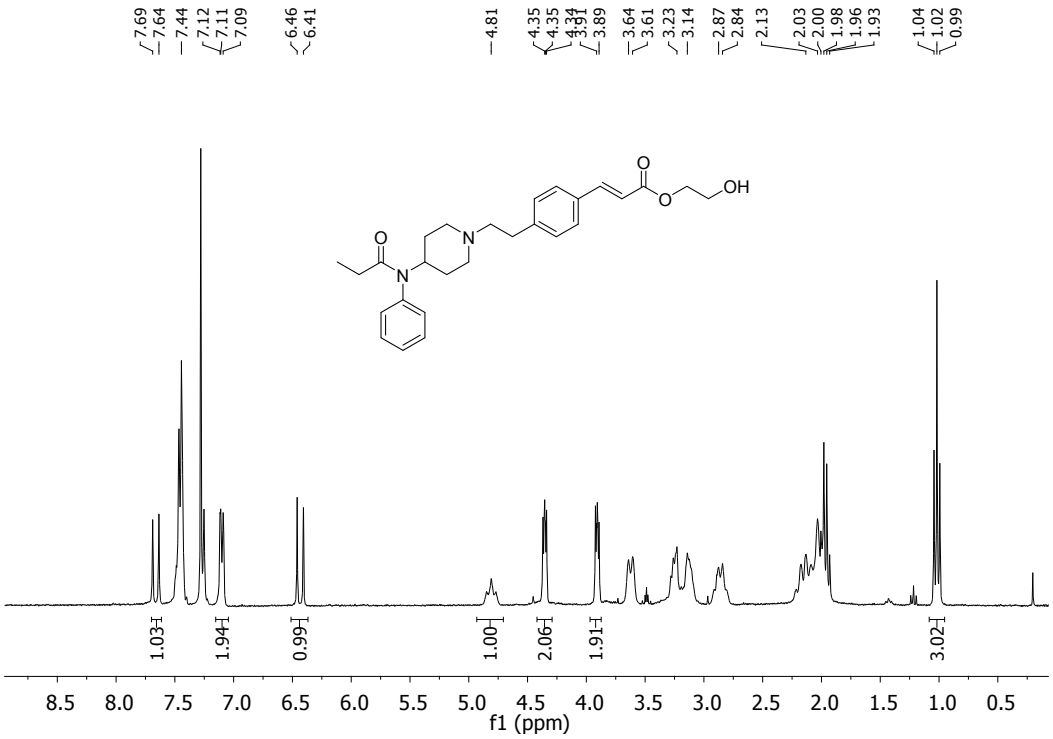

Figure S3. ^{1}H NMR spectrum of Fen-Acry-EtOH.

HPLC spectra of fentanyl initiators

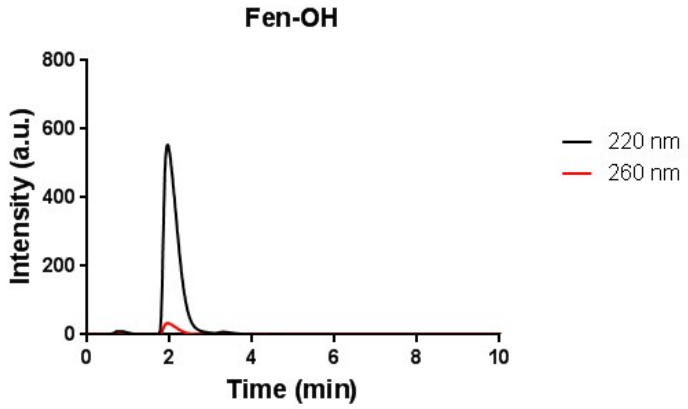

Figure S4 Chromatographic profile of Fen-OH.

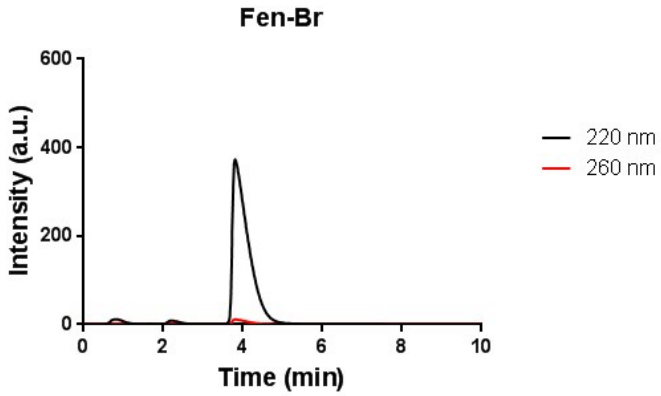

Figure S5 Chromatographic profile of Fen-Br.

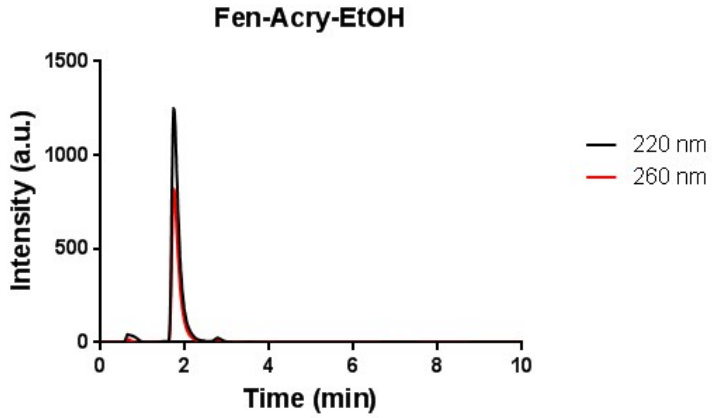

Figure S6 Chromatographic profile of Fen-Acry-EtOH.

^{1}H NMR spectra of fentanyl polymers

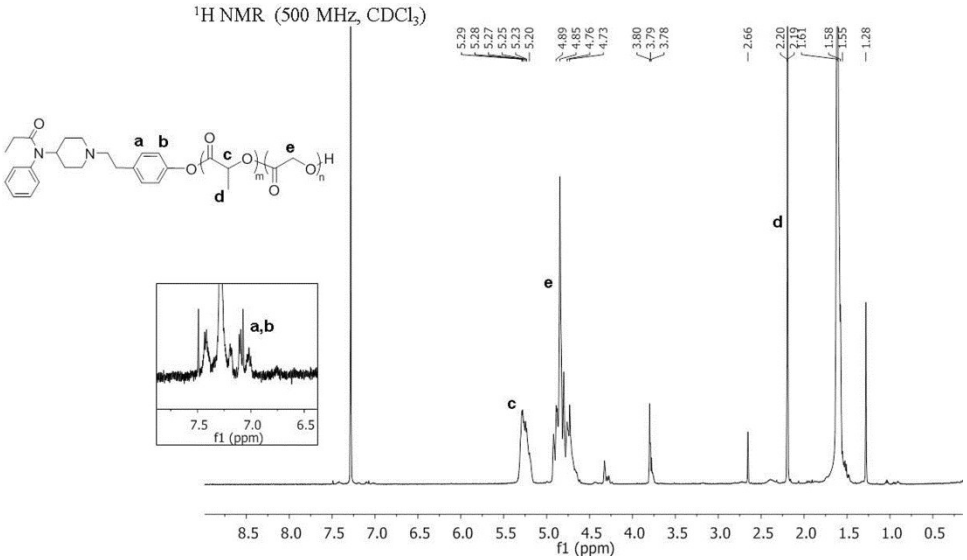

Figure S7 ^{1}H NMR spectrum of Fen-PLGA.

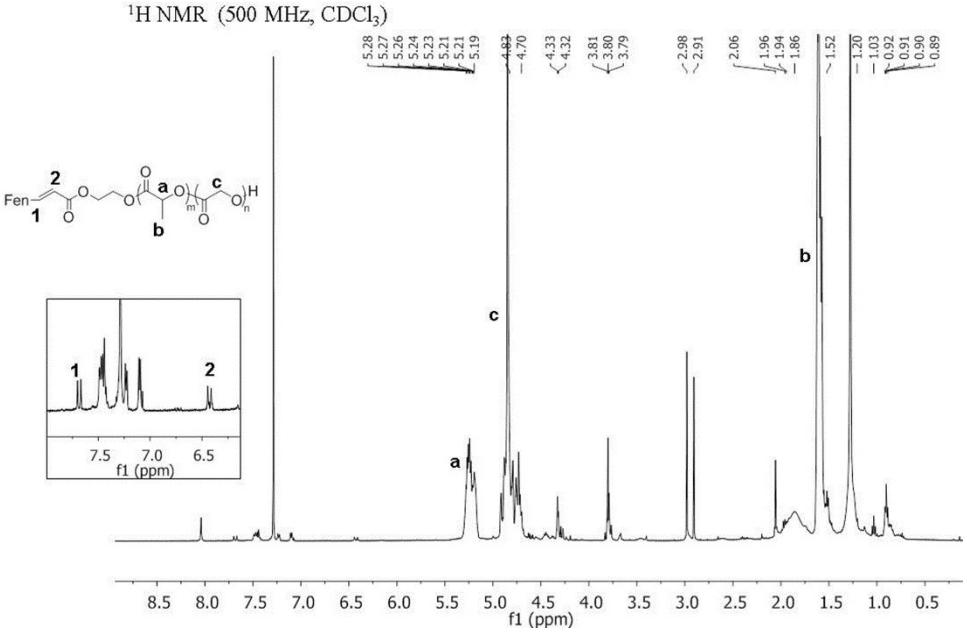

Figure S8 ^{1}H NMR spectrum of Fen-Acry-PLGA.

GPC traces

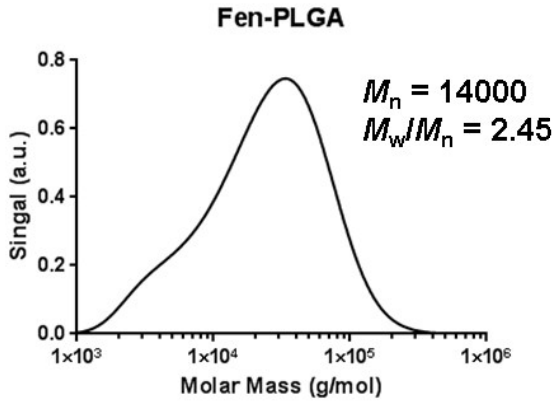

Figure S9 GPC trace of Fen-PLGA.

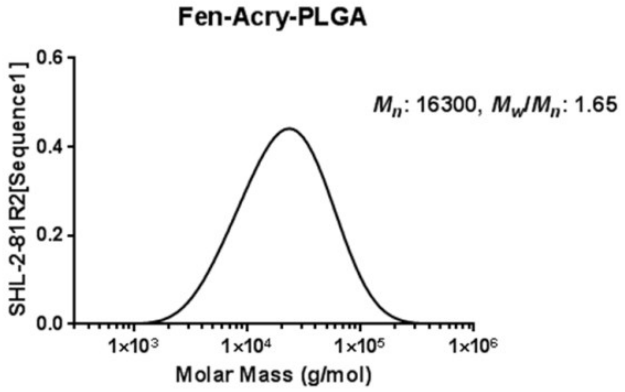

Figure S10 GPC trace of Fen-Acry-PLGA.

DLS traces

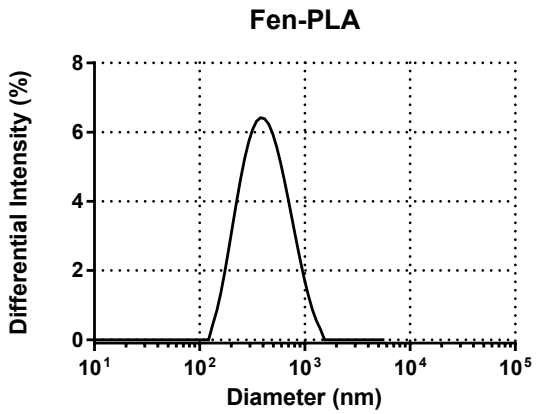

Figure S11 Size distribution of Fen-PLA NPs measured by DLS.

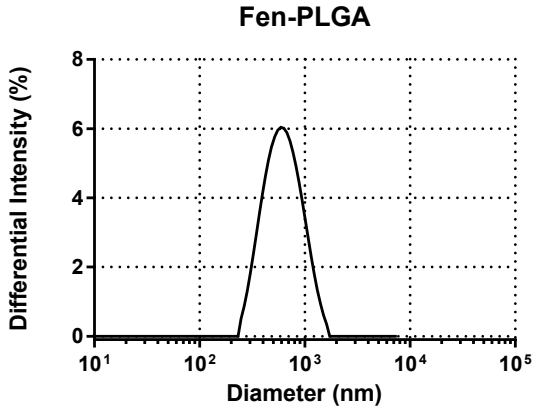

Figure S12 Size distribution of Fen-PLGA NPs measured by DLS.

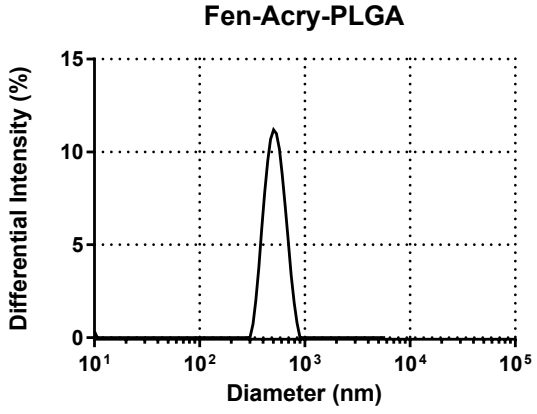

Figure S13 Size distribution of Fen-Acry-PLGA NPs measured by DLS.

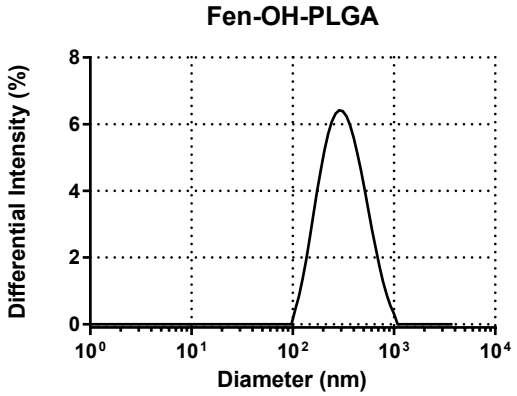

Figure S14 Size distribution of Fen-OH-PLGA NPs measured by DLS.

Zeta potential

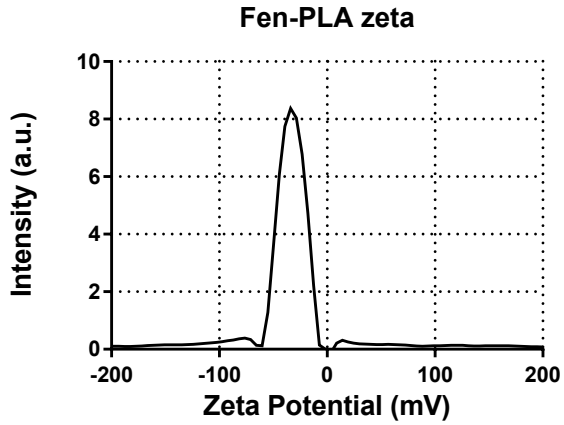

Figure S15 Intensity distribution of the zeta potential of Fen-PLA NPs.

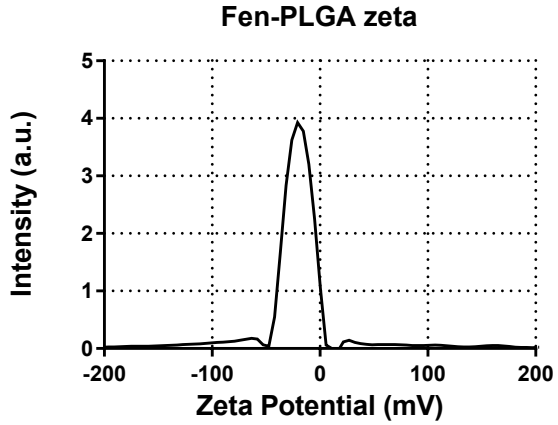

Figure S16 Intensity distribution of the zeta potential of Fen-PGLA nanoparticles.

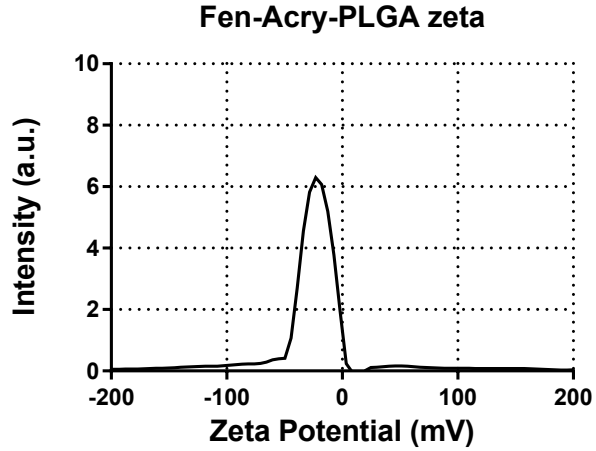

Figure S17 Intensity distribution of the zeta potential of Fen-Acry-PGLA nanoparticles.

ESEM images

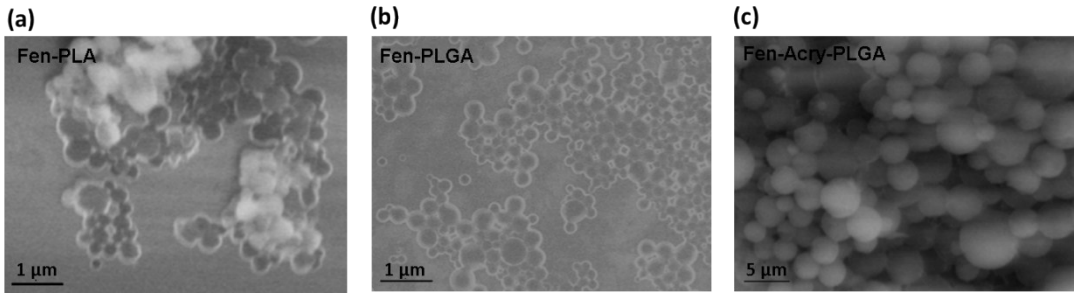

Figure S18 ESEM images: (a) Fen-PLA, Fen-PLGA, Fen-Acry-PLGA.

In vivo activity

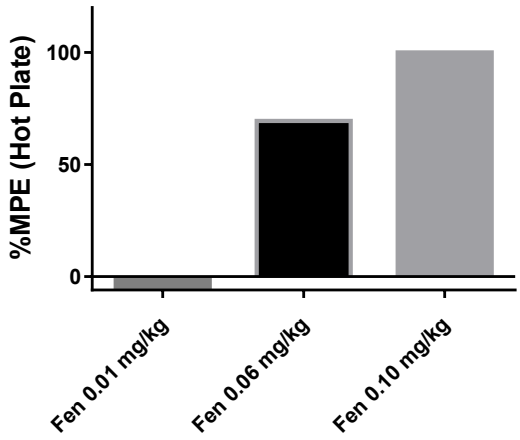

Figure S19 Hot plat test: each point shows the % of MPE induced by fentanyl at different concentrations.

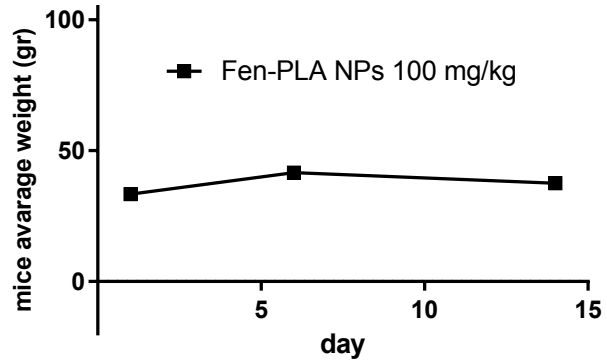

Figure S20 The change in mouse weight throughout the testing period.

Dissolvable microneedle arrays (MNA)

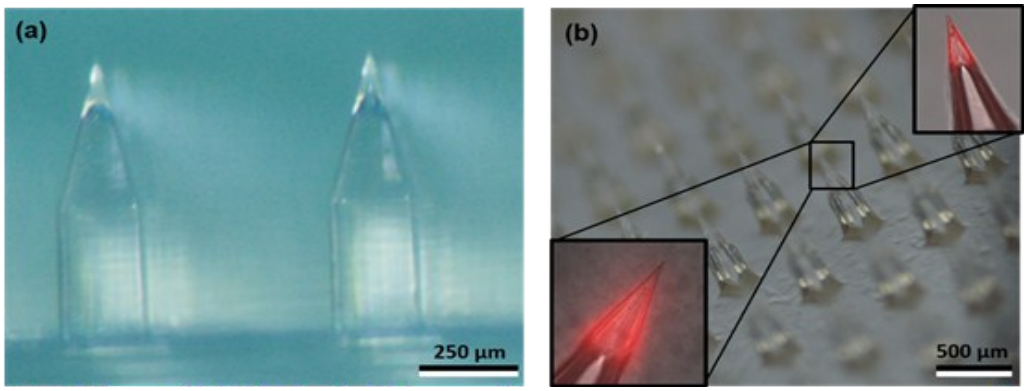

Figure S21 Tip-loaded dissolvable MNAs created using the micromilling/elastomer molding/spin-casting technique for patient-friendly delivery of opioid biohybrids in skin: (a) Optical microscope images of the elastomer mold after tip loading with the NPs; and (b) bright field microscope images of the tip-loaded dissolvable MNAs along with merged bright field and fluorescence microscope image of the tip portion of the individual microneedle.