Supplemental Information

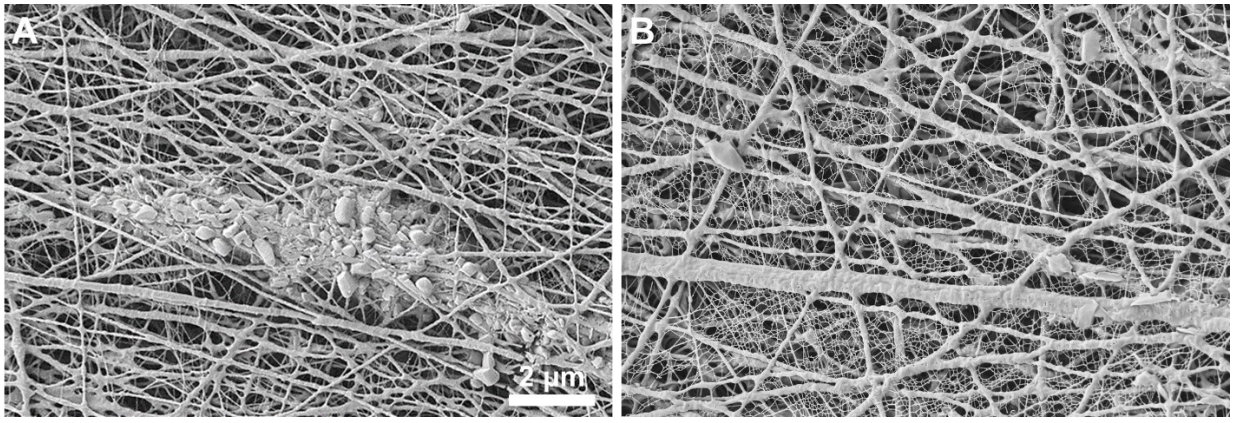
Supplemental Information SI-1

Preparation of standard curve for DS release study: The standard curve of diclofenac sodium was prepared before the release study. In brief, the standard stock solution of DS was prepared by dissolving 10 mg of DS in 10 mL of 1× DPBS. Stock solution was subsequently diluted to get the concentration of 2 µg, 4 µg, 6 µg, 8 µg, and 10 µg/mL. The absorbance of diluted solutions was measured by a UV spectrometer (CLARIOstar Plus, BMG LABTECH Inc., Cary, NC, USA) at 277 nm. All measurements were performed in triplicate.

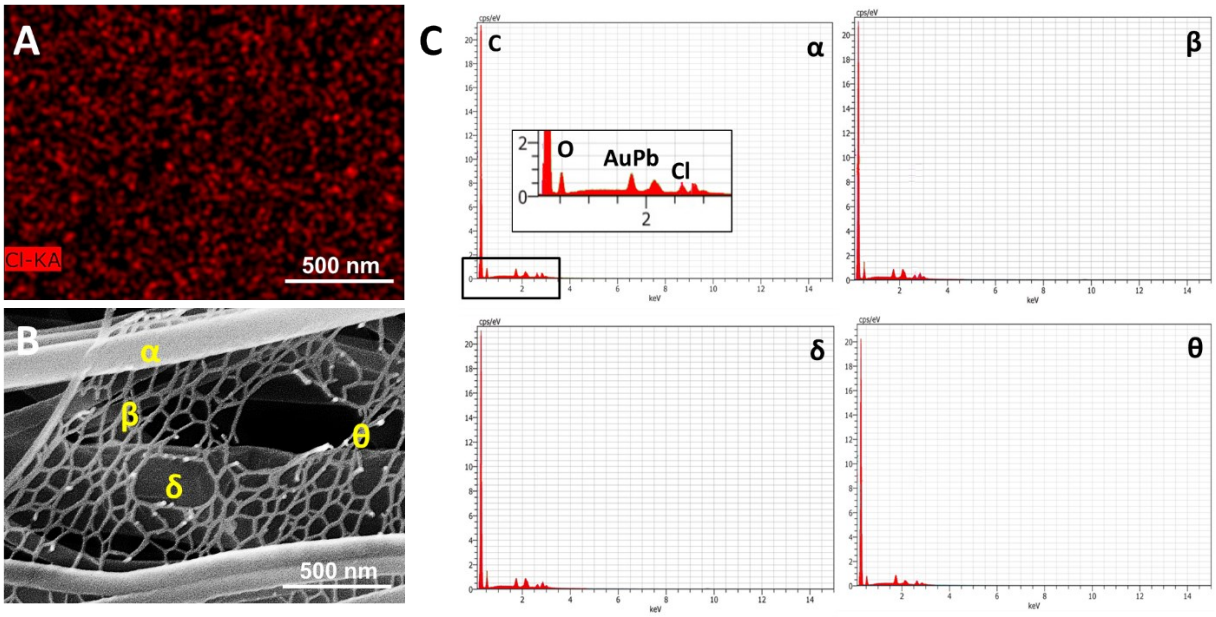
Supplemental Information SI-2

Preparation of free drug solution for cell viability study: 2 mg of diclofenac sodium was dissolved in 20 mL cell culture media (Dulbecco's modified Eagle's medium (DMEM) (Life Technologies, Grand Island, NY) supplemented with 10% fetal bovine serum (FBS) and 1% antibiotics (10,000 units/mL of penicillin and 10,000 µg/mL of streptomycin) as stock solution. Then stock solution was subsequently diluted to get the concentration of 50 µg, 100 µg and 200 µg /mL.

Supplemental Figure SF-1. SEM analysis of PC-25 mesh. Fiber meshes were cut in small pieces and placed in carbon tape. Samples were then sputter-coated (Leica EM ACE200, IL, USA) with gold-palladium (Au-Pd) for 5 nm in height before imaged in SEM (Zeiss Auriga FIB/FESEM, Carl Zeiss Microscopy, LLC, NY, USA) to avoid the accumulation of charge. SEM images were taken with an accelerating voltage of 3 kV. Fibers were very inconsistent throughout different regions of the mesh. Both nanonet fibers and precipitates of the excess DS crystal were observed (Fig. A and B).



Supplemental Figure SF-2. SEM + EDS mapping analysis of DS-NNEM (PC-12). Sample was prepared as described earlier in S1. Additionally, the elemental composition of the samples was analyzed by energy-dispersive X-ray spectroscopy (Quantax 70, Bruker Corporation, Billerica, MA, USA) equipped with SEM instrument (Zeiss Auriga FIB/FESEM, Carl Zeiss Microscopy, LLC, NY, USA). Elemental mapping for chlorine (Cl) (A) obtained from SEM image (B). Since Cl is one of the elements in the chemical structure of DS it indicates the presence and distribution of DS through the fiber mesh. Elemental compositions were analyzed by EDS at four different points (i.e. α, β, δ, and θ) of image B. Spectra of these four points are demonstrated in (C). Supplemental Table 1 shows the relative percentage of elements at these selected positions.

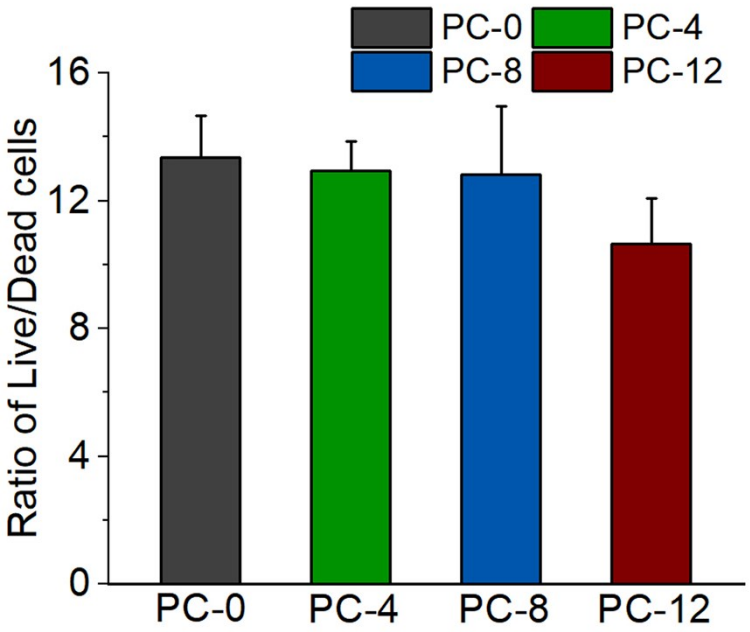


Supplemental Table ST-1:

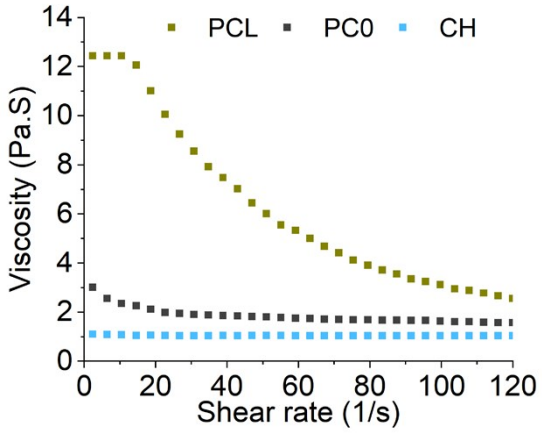
Relative percentage of elements at the three positions shown in ***Supplemental Fig. SF-2.***

Position	Percentage (%)		
	Cl	C	O
α	1.41	90.69	7.89
ß	1.33	89.86	8.80
δ	1.31	89.19	9.50
Θ	1.17	88.38	8.12

Supplemental Figure SF-3. Ratio of live cells to dead cells. Live cells (stained green) and dead cells (stained red) were counted from the fluorescence images taken on day 3. Three images (n=3) were analyzed from each DS-NNEMs sample (PC-0, PC-4, and PC-12) compare to control (PC-0). Images were analyzed by ImageJ 1.53c software (NIH, Bethesda, MD, USA). In brief, images were splitted in green and red color channels which were further converted into pixel area calculation mood by adjusting the threshold values. Least possible area was selected and cells were counted accordingly. No significant difference in the ratio was observed between the control and the experimental samples.



Supplemental Figure SF-4. Viscosity measurement of PCL, chitosan, and PCL-CH solution. Viscosity of the solutions was measured using a viscometer (Brookfield DV3T, AMETEK Brookfield, MA, USA) with a thermosel spindle at 5-250 rpm. Equilibrium time (t = 10 sec) was set for each measurement point and 2 mL of the solution was used under room temperature. Data were analyzed with RheocalT software (AMETEK Brookfield, MA, USA) and shear viscosity was plotted as a function of shear rate in OriginPro software (Origin Lab, Northampton, MA, USA). PCL solution showed significantly high viscosity compare to the CH solution at a low shear rate. This is the typical nature of shear-thinning properties of a viscoelastic PCL solution. The blend of PCL-CH showed much lower viscosity compare to PCL alone. The viscosity of CH and PCL-CH showed not much different as the shear rate increases.



Supplemental Figure SF-5. Solubility of DS in electrospinning solvent with different concentrations.1 to 4% DS (w/w) with respect to 6% CH (w/w) were mixed in TFA/DCM (70/30) solvent system. DS powder was added first for homogenous dispersion and CH was added afterward. Red marker line was drawn on a white paper and placed behind the DS solution containing vials, 1% (A), 2% (B), 3% (C), and 4% (D). Digital camera pictures were taken from the front side before adding CH. The red line was opaque with the vial of 1% DS whereas the visibility of the line increased with other vials indicates solubility of the drug increased with higher concentration.