Electronic Supplementary Material (ESI) for Nanoscale Advances.

Supplementary Information

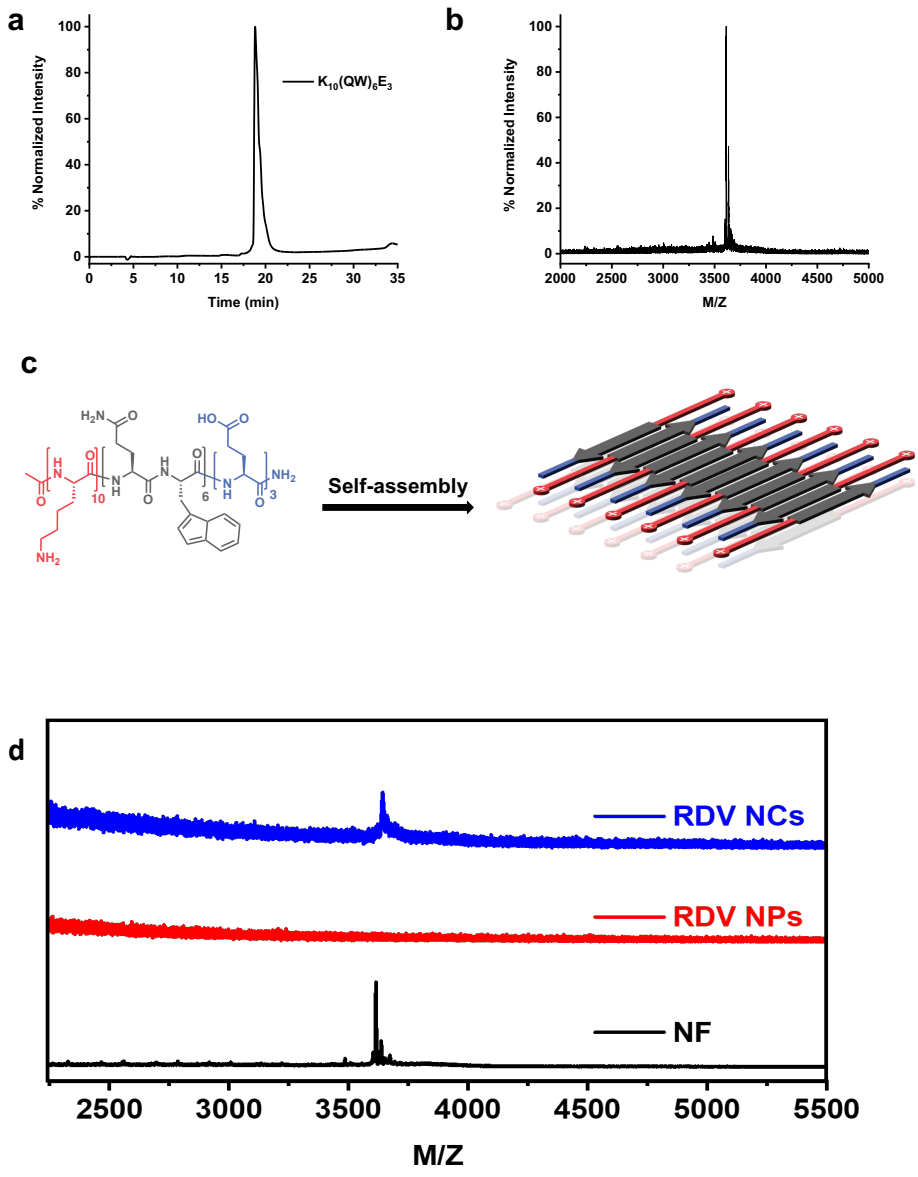

Figure S1.(a) (a) The HPLC chromatogram and (b) MALDI spectra of the peptide (calculated mass: 3614.22: experimental mass: 3614.36), demonstrate the successful synthesis . (c). A schematic representation illustrates the self-assembly of the peptide into a sandwich-like b-sheet structure, forming nanofibers (NF). (d)Stacked MALDI spectra of the NF (calculated mass: 3614.22: experimental mass: 3614.36), MALDI spectra of RDV-NPs showing the absence of NF, and MALDI spectra of RDV-NCs showing the presence of NF.

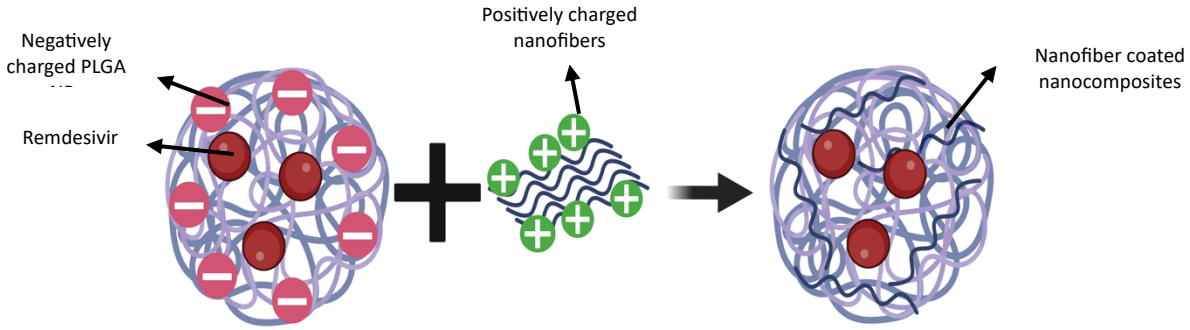

Figure S2. Schematic of nanocomposites. Positively charged nanofibers electrostatically interact with negatively charged PLGA NPs loaded with Remdesivir forming nanocomposites with enhanced cell penetrating abilities and drug delivery.

Table S1. Characterization of Nanocomposites

Particle group	Size (nm)	Zeta Potential (mV)	Polydispersity index (PDI)
Blank PLGA	150 ± 40	-23 ± 2	0.15
RDV NPs	210.47 ± 70	-26.3 ±1	0.212
RDV NCs	230 ± 77	31.09 ± 1	0.223

Table S2. Remdesivir (RDV) release kinetics during wash steps

Test study/Group	1st Wash (Indirect method)	2nd Wash (Indirect method)	3rd Wash (Indirect method)	4th Wash (Indirect method)	5th Wash (Indirect method)	Total drug lost (ug) in 4 mg NPs	Total drug loaded inside NPs
Remdesivir drug lost (Indirect method)	28 ug	7 ug	4 ug	6 ug	3 ug	48 ug	272 ug
Pellet (Direct method)	220 ug						

Table S3. Primer sequences used to study nanocomposite immune responses

Primer	Forward 5'-3'	Reverse 5'-3'
hIL-1β	CCT CCA GGG ACA GGA TAT GG	ACA CGC AGG GGT ACA GA
HiL-6	TAG CCT CAA TGA CGA CCTA AG	GTG GGG CTG ATT GGA AAC CT
hTNF-α	CTC TTC TGC CTG CTG CAC TTT G	ATG GGC TAC AGG CTT GTC ACTC
hIL-10	TCT CCG AGA TGC CTT CAG CAG A	TCA GAC AAG GCT TGG CAA CCC A

Preparation of Nanofibers: The peptides for this study were synthesized using standard solid-phase peptide synthesis. After synthesis, the crude peptide underwent purification using High-Performance Liquid Chromatography (HPLC) and mass was confirmed using Matrix-Assisted Laser Desorption/Ionization (MALDI) as shown in FigureS1. The peptide's chemical design

(Sequence: K10(QW)6E3) involves a core with alternating hydrophilic (Q: glutamine) and hydrophobic (W: tryptophan) sequence, leading to the formation of sandwich-. In this structure, the hydrophobic side faces the assembly's core, while the hydrophilic side faces the solvents. The presence of a flexible cationic domain (K: lysine) ensures effective interaction with cell membranes. Glutamic acids are added to the C-terminus to promote self-assembly equilibrium in the presence of the long cationic domain. Transmission Electron Microscopy (TEM) was used to characterize nanofiber formation, revealing higher-order assemblies (figure 2a). The excess positive charge along the long fiber axis grants these nanofibers exceptional cell-penetrating activity.