Supporting Information

Design and characterization of cyclosporine A-loaded nanofibers for enhanced drug dissolution

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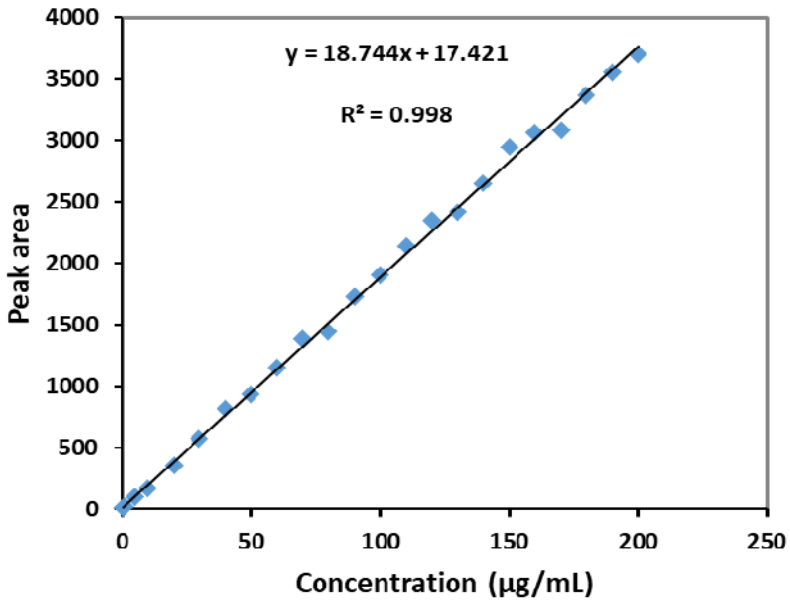
a)



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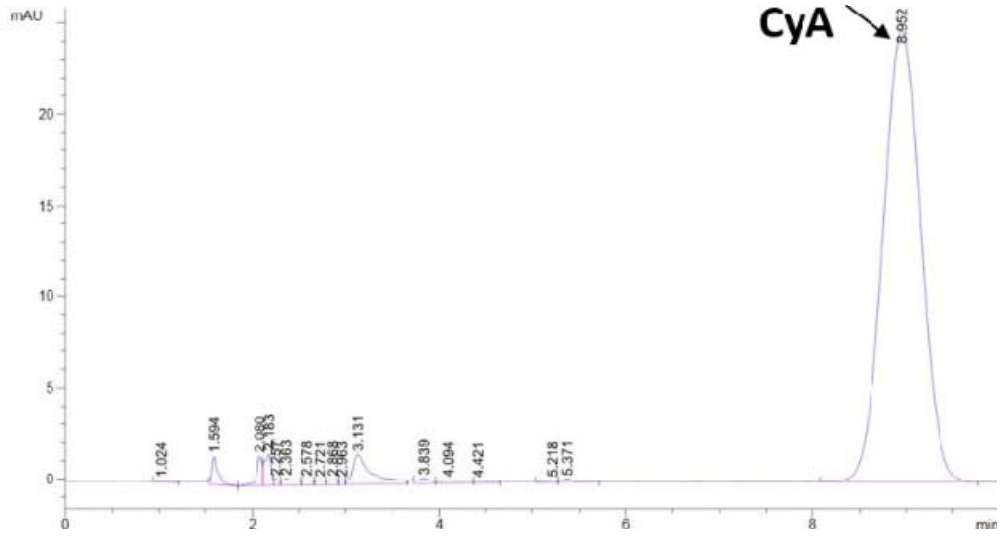

Figure S1: a) Plot of CyA concentration versus peak area obtained by HPLC-UV b) Typical chromatogram for the CyA HPLC-UV analysis at 210 nm

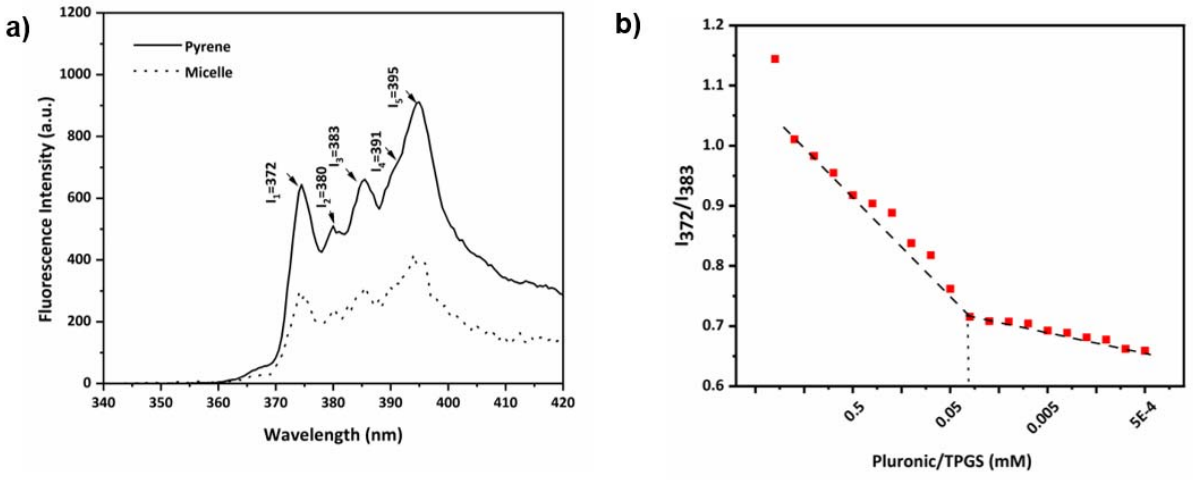

Figure S2: a) Fluorescence spectra of pyrene (0.6 µM) as fluorescence hydrophobic probe alone and in micellar suspension (3:2 F127/TPGS) at 25°C, b) Plot of the fluorescence emission of pyrene at the I372/I383 ratio in the presence of various concentrations (0.0005mM-0.1mM) of copolymers F127/TPGS (3:2 molar ratio).

Surfactants	Ratios	CMC (mM)
TPGS	1:0	0.46
F127	1:0	0.093
F127/TPGS	1:1	0.13
F127/TPGS	1:4	0.023
F127/TPGS	3:2	0.062

Table S1: Critical micelle concentrations (mM) of surfactants Pluronic F127 and TPGS alone, and in combination at a range of molar ratios from 1:0, 1:1, 1:4 and 3:2 respectively.

Surfactants	Concentration (µg/mL)
10mM F127/TPGS	933.8
1mM F127/TPGS	122.3
0.1mM F127/TPGS	73.0
0.0005mM F127/TPGS	52.4
Alone PBS	7.3
PBS+30% Ethanol	12.0
PBS+0.5%Tween	14.0

Table S2: Equilibrium solubility of CyA in relation to molar concentration (0.0005mM-10mM) of surfactant mixture (F127:TPGS; 3:2 molar ratio) in aqueous solution at 37°C.

Functional groups	Wavenumber (cm^{-1}) of CyA	Wavenumber (cm^{-1}) of CyA loaded micelle
n(C-H) alkyl (s)	2960, 2930, 2875	2880
Amine, O-H (b)	3305	-
C=O (s)	1290	1245
CONH	1630	1625
O-H (b)	1475	1465
C-H2 (as)	1410	1415
C-O-C(s)	1205	1235
C-N (s)	1295, 1255	1280, 1240
C-O (s)	-	1340
C-N (s)	1090	1100
C=C (s)	975	965

Table S3: Major vibrational frequencies showed in the IR spectrum of Cyclosporine A alone and on incorporation into 3:2 F127/TPGS micelles (where notation s=symmetric, as= asymmetric and b= bending vibrations).

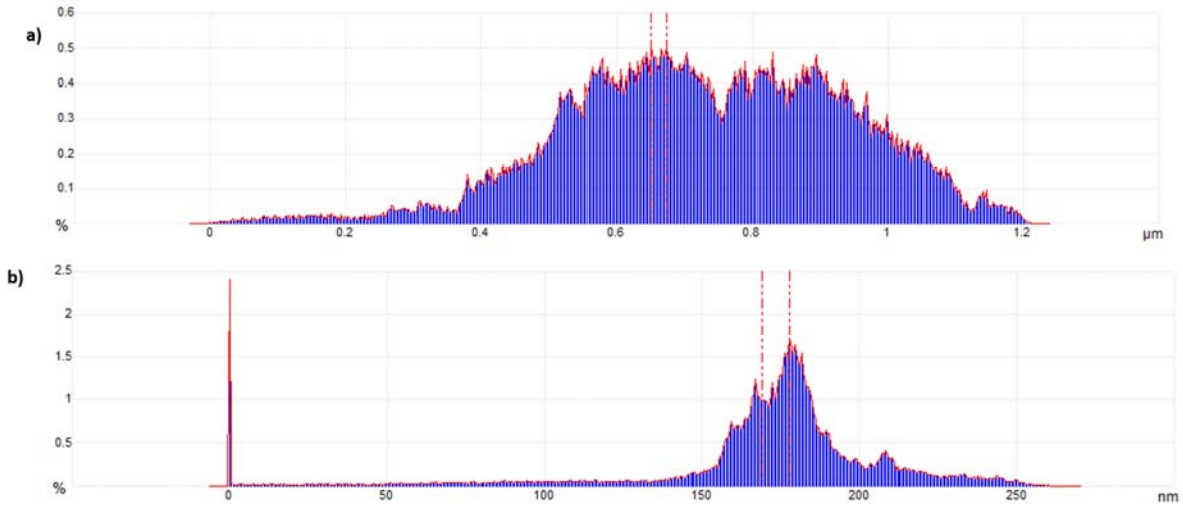

Figure S3: Histogram of a) unloaded PVP nanofibers and b) CyA/micelle loaded nanofibers showing the height distribution for the two sets of samples; analysis performed using AFM Nanoscope analysis software version 1.70.

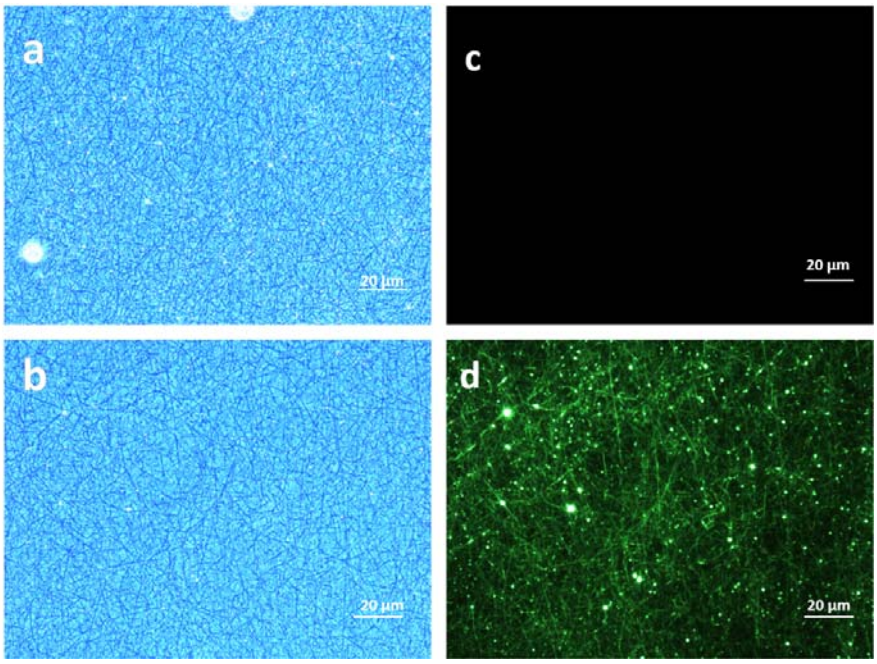

Figure S4: Investigation of micelle loading into nanofibers using fluorescence microscopic imaging: a, c) blank PVP nanofibers under bright field and green fluorescence protein (GFP) filter and b, d) coumarin-6 loaded micelles incorporated into PVP nanofibers under bright field and GFP filters respectively. The images were taken using a 20X objective lens.

Model	Parameter	CyA micelles loaded nanofiber Formulation			Factors
		pH 1.2	pH 7.4	pH 6.8	
Zero order $F_t = k_0 t$	k_0	7.6520	8.154	8.488	k_0-apparent dissolution rate constant.
	R^2_adj	**0.9868**	**0.9943**	**0.9666**	
	AIC	**73.1951**	**62.9757**	**86.9356**	
	MSC	4.1201	5.0192	3.2554	
Korsmeyer-Peppas $F=k_{KP}*t^n$	k_{KP}	11.366	10.034	13.721	n- the diffusional exponent indicating the drug-release mechanism k_{KP} - the release constant incorporating structural and geometric characteristics of the drug-dosage form
	n	0.825	0.908	0.785	
	R^2_adj	**0.9942**	**0.9980**	**0.9927**	
	AIC	**61.5753**	**49.0621**	**66.5040**	
	MSC	**4.9501**	**6.0130**	**4.7148**	
Hopfenberg $F=100*[1-(1-k_{HB}*t)^n]$	k_{HB}	0.062	0.077	0.075	The combined constant, $k_{HB} = k_0/(C_0 \times a_0)$; where k_0 is the erosion rate constant, C_0 is the initial concentration of drug in the matrix, a_0 is the initial radius for a sphere or cylinder or the half-thickness for a slab; n is 1, 2, and 3 for a slab, cylinder, and sphere, respectively
	n	1.507	1.156	1.372	
	R^2_adj	**0.9941**	**0.9958**	**0.9880**	
	AIC	**61.9119**	**59.3787**	**73.4947**	
	MSC	4.9261	5.2761	4.2155	
Comparison result	R2_adj, AIC and MSC of above three model were compared for drug release at different pH. All three model share close R2_adj value for pH 7.4 and 1.2 with difference for pH 6.8. Hence to understand the best fit model AIC was compared as minimum AIC represents best fit, it was observed that at all three pH AIC was minimum for Korsmeyer-peppas model along with high R2_adj value. Further MSC was compared by all the three methods and it was found that highest MSC value were for all the pH with Korsmeyer-peppas model, whereas Hopfenberg model presents closeness in terms of best fit model dissolution behaviour. Hence based on kinetic studies drug follows non-fickian diffusion (nearly n<0.8) along with disintegration of polymeric matrix.				

Table S4: Kinetic models studied for cyclosporine A release from CyA loaded micelle incorporated composite nanofibers at different pH values using DDSolver software. Table shows the best fit models based on comparison of statistical criteria including the adjusted coefficient of determination (Rsqr_adj or R2 adjusted), the Akaike Information Criterion (AIC), and the Model Selection Criterion (MSC). The three closest fit kinetic models were zero order, Korsmeyer-Peppas and Hopfenberg models respectively.