Supplementary Information

Microfluidic Fabrication of Dexamethasone-Loaded Silk Fibroin Microspheres for Targeted Pulmonary Drug Delivery

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Principles of Aerodynamic Diameter Measurement Methods

Aerodynamic diameter (d_{ae}) quantifies particle behavior in airflow and is measured through distinct physical principles. Inertial impaction—employed by cascade impactors like the Andersen and Next Generation Pharmaceutical Impactor (NGI)—separates particles by size through staged nozzles, where d_{ae} is derived from Stokes number (St) calculations: $St=\frac{\rho_{ae}C_{ae}d_{ae}^2U}{9\mu W}$, with the 50% collection efficiency point defining the stage-specific cut-off diameter (d_{50}). Time-of-flight (TOF) analyzers determine d_{ae} by measuring particle transit time between laser beams in accelerated flow ($d_{ae}\propto\sqrt{transit\ time}$), while laser diffraction (LD) computes volume-equivalent diameter (d_v) from light scattering patterns, converting to d_{ae} via $d_{ae}=d_v\sqrt{\frac{\rho_p}{\chi\rho_0}}$.

The NGI represents a significant advancement in inertial impaction technology, featuring seven horizontally aligned collection cups and a micro-orifice collector (MOC) to minimize particle bounce and enable automated analysis. Its design allows operation across 15-100 L/min flow rates, with stage-specific d_{50} values calibrated using the power-law equation $D_{50,1}=A(\frac{Q_{ref}}{Q_1})^b$, thereby accounting for gravitational effects on particles >5 μm. The NGI delivers pharmacopeial -compliant mass-weighted d_{ae} distributions through direct chemical assay of active pharmaceutical ingredients (APIs), outperforming optical methods (e.g., LD, TOF) in API specificity and clinical relevance for inhaler quality control.

Curing method	SF concentration	Oil-to-water phase flow rate ratio	Particle size/nm	PDI
Direct stirring curing	2 wt%	1:5	355.2±15.6	0.123±0.027
	2 wt%	1:3	401.6±17.2	0.138±0.023
	5 wt%	1:5	530.9±19.4	0.224±0.032
	5 wt%	1:3	707.3±24.1	0.192±0.019
Anhydrous ethanol curing	2 wt%	1:5	210.1±14.5	0.298±0.034
	2 wt%	1:3	339.5±16.4	0.262±0.029
	5 wt%	1:5	317.5±13.3	0.255±0.026
	5 wt%	1:3	495.4±19.1	0.293±0.031
25% glutaraldehyde curing	2 wt%	1:5	609.4±25.5	0.128±0.018
	2 wt%	1:3	710.4±28.7	0.136±0.023
	5 wt%	1:5	822.7±32.9	0.190±0.021
	5 wt%	1:3	1149±42	0.217±0.023

Table S1. Characterization of particles synthesized by the emulsion method (n = 3)

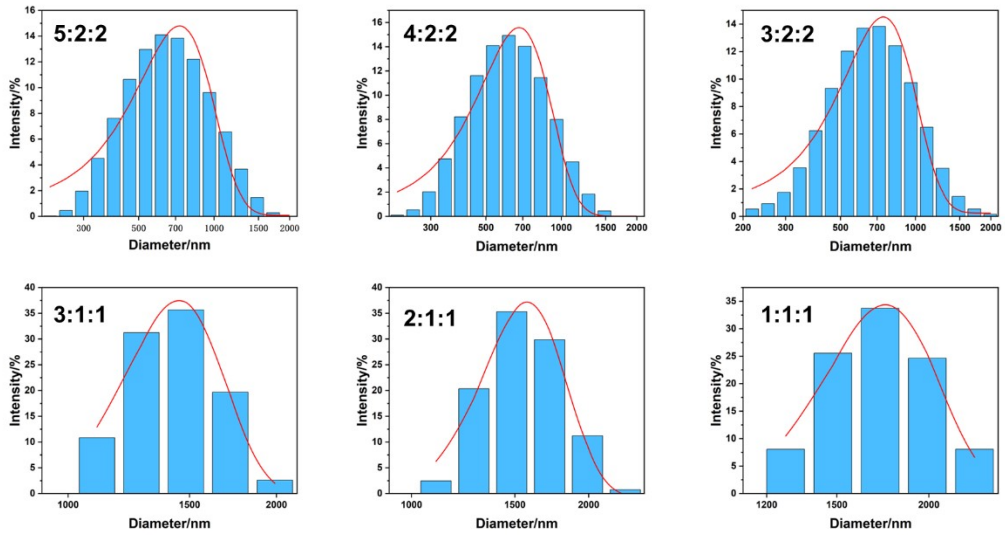

Figure S1. Particle size distribution of microspheres at different flow rates

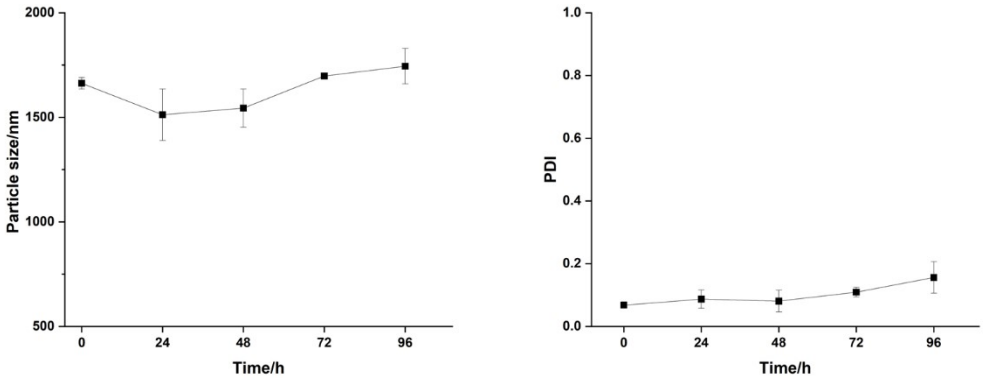

Figure S2. Time-dependent studies on the stability of SFP in water at room temperature

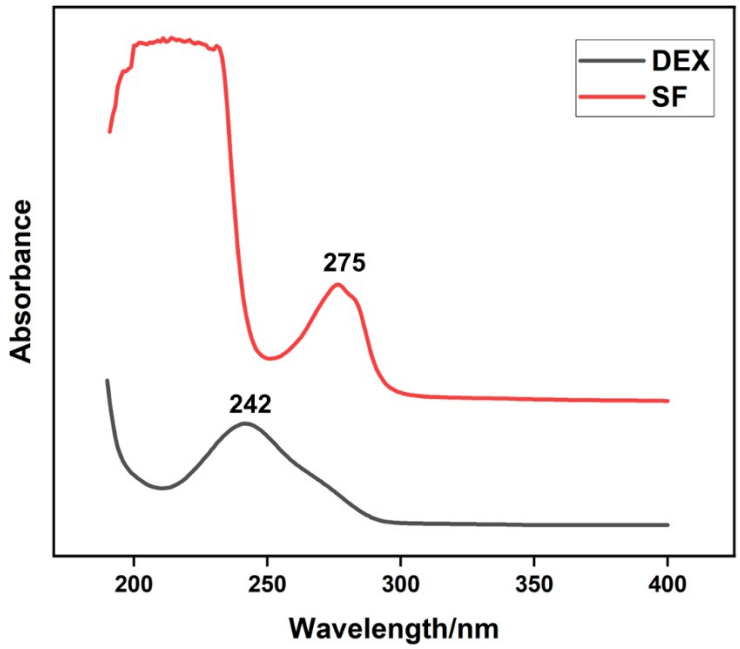

Figure S3. UV absorption spectra of dexamethasone and silk fibroin

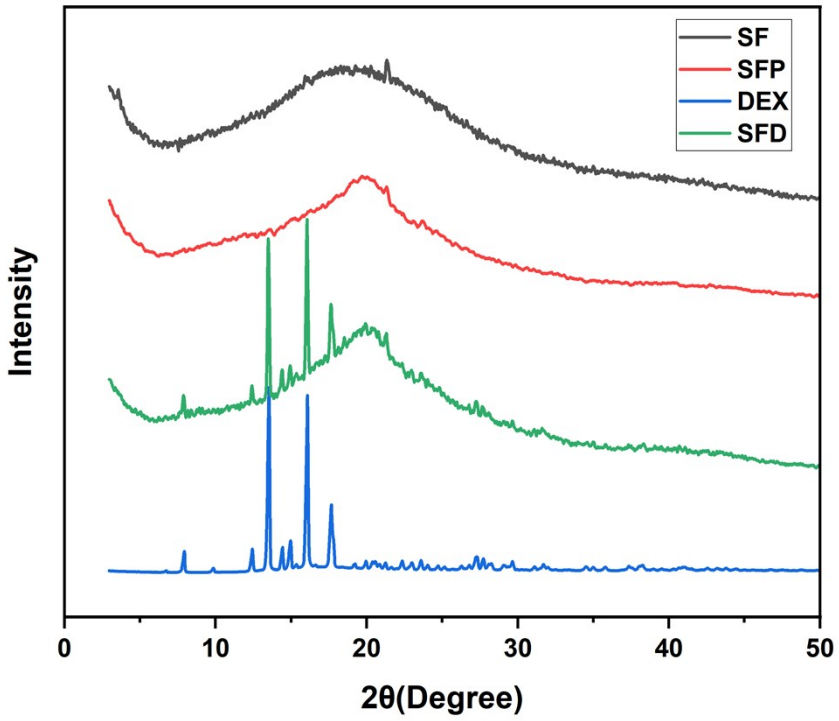

Figure S4. XRD spectra of lyophilized silk fibroin, SFP, dexamethasone, and SFD