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Decoding the Structure of Drug Loaded Silk Fibroin Nanoparticles Surrounded by a Complex Lipid Shell

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Targeted drug delivery plays a vital role in advancing cancer treatment, particularly for cancer types that exhibit strong resistance to chemotherapy. Silk fibroin protein can self-assemble into biocompatible, biodegradable nanoparticles, that have demonstrated high encapsulation efficacy for hydrophobic drugs. However, morphology and thus the properties of silk fibroin nanoparticles (sfNPs) could be strongly affected by preparation conditions, they are hydrophobic, prone to aggregation in aqueous solutions, and require enhanced targeting specificity. In our work, we vary the preparation methods of sfNPs with encapsulated drug and modify their surface using synthetic lipids and extracellular vesicles to improve their stability and targeting efficacy. Using small-angle X-ray scattering and Fourier-Transform Infrared Spectroscopy we demonstrated that loading of a hydrophobic curcumin into nanoparticles affects the roughness of their surface, while the shape of the nanoparticles could be affected by solubilization technique. Moreover, the lipid layer around sfNPs can significantly enhance their interaction with biomimetic membranes, thus promoting cellular uptake of the nanoparticles. Variation of the lipid composition allows us to control properties of the resulting lipid shell such as membrane morphology, thickness, and stability.