One-pot functionalization of liposomes with gold nanoparticles: combining electrostatic and covalent strategies for tailored biological interactions

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Surface modification is a key strategy for tailoring the physicochemical and biological performance of nanocarriers in biomedical applications. Gold-modified liposomes (LipoAuNPs) represent a versatile class of hybrid nanostructures with promising potential not only as drug delivery systems but also as functional platforms for biochemical sensing, thermal imaging, and combined anticancer therapy. In addition to providing a functionalizable surface that enables signal amplification, supports electrochemical signal generation, and can be readily integrated with sensing platforms, the liposomal matrix can reduce the tendency of gold nanoparticles to aggregate, thereby improving their colloidal stability. Moreover, anchoring AuNPs on the liposomal surface alters their optical properties, including the maximum absorption wavelength, enabling fine-tuning of plasmonic characteristics to match specific diagnostic or therapeutic needs.

In this work, we present a facile, one-step approach to engineer liposomal surfaces with gold nanoparticles (AuNPs), yielding LipoAuNPs that combine the high drug encapsulation capacity of liposomes with the unique optical and electronic properties of AuNPs. The attachment of AuNPs is achieved through a synergistic mechanism involving electrostatic attraction between permanently cationic liposomes and negatively charged AuNPs, as well as covalent anchoring via thiol-containing lipids. Formation of LipoAuNPs was confirmed using ζ-potential analysis, dynamic light scattering (DLS), transmission electron microscopy (TEM), and voltammetric measurements at the electrified liquid–liquid interface. Surface modification significantly altered the biological interactions of the liposomes: flow cytometry revealed enhanced cellular uptake by cancer cells, while confocal microscopy demonstrated reduced colocalization with acidic compartments, suggesting improved endosomal escape. These findings highlight how nanoscale surface engineering can profoundly influence nanocarrier behavior, offering a versatile platform for designing next-generation drug delivery systems, multifunctional biosensing interfaces, and theranostic nanomaterials.

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