

Looking for the optimal coating for mucoadhesive isoniazid-liposomes for pulmonary infections: Chitosan vs ϵ -PLL

Forte J.^{1,2*}, Fabiano M. G.², D'Intino E.², Rinaldi F.², Marianecci C.², Carafa M.²

¹Catholic University of Sacred Heart, Department of Basic Biotechnological Sciences, Intensivological and Perioperative Clinics - Rome, 00168, Largo Francesco Vito 1, Italy.

²Sapienza University of Rome, Department of Drug Chemistry and Technology - Rome, 00185, Piazzale Aldo Moro, Italy.

Pulmonary infections remain among the leading causes of mortality worldwide. Lung route of administration offers the opportunity to directly deliver drugs to the diseased tissue. In this context, liposomes, represent a promising strategy to enhance drug stability, retention, and targeted.

The limited stability of liposomes, combined with the fragility and permeability of the lipid bilayers, restricts their applicability. Modifying the surface properties of liposomes by coating them with mucoadhesive polymers, which is able to improve their stability and pharmacokinetic properties. The aim of this study was firstly to prepare and characterize DPPG-HSPC liposomes, encapsulating isoniazid (INH), a first-line anti-TB drug, and then decorated their surface with two distinct cationic polymers: chitosan (Chit) and ϵ -poly-L-lysine (ϵ -PLL), investigating whether such coating could influence or improve the characteristics of the liposome itself.

All samples preserved optimal particle size (<300 nm) compatible with pulmonary administration, low polydispersity, and suitable ζ -potential, ensuring colloidal stability. Fluorescence anisotropy and entrapment efficiency remained unchanged after coating, confirming the integrity of the lipid bilayer. Mucoadhesion assays, using mucin, demonstrated that both coatings significantly increased mucin binding, with ϵ -PLL showing slightly higher affinity. Stability studies confirmed that all samples maintained a good stability, in terms of size and ζ -potential, for 60 days at both 4°C and room temperature. Notably, INH encapsulated within the nanocarrier exhibited enhanced stability compared to the free drug.

Both polymers enhanced physicochemical stability, mucus interaction, and intracellular antimicrobial activity, supporting their suitability for pulmonary delivery.

Furthermore, ϵ -PLL emerges as a promising and underutilized alternative to Chit for the development of next-generation aerosolizable nanocarriers for tuberculosis therapy.

Corresponding author's contact and billing information:

- Full name of the institution: Catholic University of Sacred Heart, Rome.
- Full address: Largo Francesco Vito 1, 00168, Rome, Italy.
- E-mail: jacopo.forte@unicatt.it
- PEC/SDI code: jacopoforte@pec.it