THE INCORPORATION OF PROPRANOLOL HYDROCHLORIDE INTO LIPOSOMES

Boglárka Gábor[1], Dorina Gabriella Dobó[1], Ildikó Csóka[1]

[1]Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, H-6720 Szeged, Eötvös u. 6, Hungary
e-mail: gabor.boglarka@szte.hu

Abstract

Liposomes are nano-sized lipid-based vesicles used as drug delivery systems due to their hydrophilic and lipophilic characteristics. Moreover, when the active pharmaceutical agent (API) is incorporated inside the liposome, it protects them from degradation and provides improved targeting and drug release. The side effect is lower compared to other carriers. The properties of the liposomes are influenced by their lipid compositions, surface charge, size and method of preparation [1, 2].

The objective of this study was to successfully incorporate propranolol hydrochloride and to enhance the encapsulation efficiency (EE%). The charge of the phospholipid bilayer can be influenced by membrane additives such as stearylamine (SA) or dicetyl phosphate (DCP). The applied lipids were L-α-phosphatidylcholine (PC), dipalmitoylphosphatidylcholine (DPPC) and 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC). Furthermore, cholesterol (CH) and trehalose were utilised in the synthesis process. The molar ratios of the samples, as determined in a previous study [3], were found to be 8.5:4.5:6.5 for PC:CH:DCP, 12:5:5 for PC:CH:SA, 2.53:0.63:4.06:2.64 for DPPC:DSPC:CH:SA, and 2.53:0.63:1.53:3.96 for DPPC:DSPC:CH:DCP. Trehalose was present at a concentration of 5 w/w%, while propranolol hydrochloride was present at concentrations of 10, 20, or 50 w/w%, as indicated in the composition. The synthesis of liposomes was accomplished through the utilisation of the thin-film hydration method. The ethanol was evaporated from the alcoholic compositions at 100 mbar and 60°C (with the exception of trehalose and propranolol hydrochloride) in a rotary evaporator at 50 rpm. The lipid film was hydrated and ultrasonicated for a period of 30 minutes at a temperature of 60°C. The liposomes were then subjected to vacuum filtration, employing a 0.22 µm membrane filter. Subsequently, the samples were subjected to immediate investigation with regard to their vesicle size, polydispersity and zeta potential in a liquid state. Following this, the samples were lyophilised for the purpose of further investigation. The drug release was examined over a period of one hour.

The size of the particles was found to be between 100 and 250 nm, and the polydispersity index (PdI) was approximately 0.3. The EE% and drug release were measured via HPLC. EE% was 2-36% and the drug release was 60-100%. The structures were examined via FT-IR, Raman and DSC. Further plans are to enhance the EE%.

References

[1] S. Giordani, V. Marassi, A. Zattoni, B. Roda, and P. Reschiglian, "Liposomes characterization for market approval as pharmaceutical products: Analytical methods, guidelines and standardized protocols," *Journal of Pharmaceutical and Biomedical Analysis*, vol. 236, p. 115751, Nov. 2023, doi: 10.1016/j.jpba.2023.115751.

[2] A. Akbarzadeh *et al.*, "Liposome: classification, preparation, and applications," *Nanoscale Res Lett*, vol. 8, no. 1, p. 102, Dec. 2013, doi: 10.1186/1556-276X-8-102.

[3] Z. Németh et al., “Quality by Design-Driven Zeta Potential Optimisation Study of Liposomes with Charge Imparting Membrane Additives,” Pharmaceutics, vol. 14, no. 9, p. 1798, 2022