

Chapter 2: Liposomal Drug Delivery System

Maitri A. Patel, Dhvani D. Joshi, Meet R. Patel

Department of Pharmaceutical Quality Assurance and Pharmaceutical Chemistry, Nootan Pharmacy College, Sankalchand Patel University, Visnagar, Gujarat, India.

Abstract

Liposomes are spherical, self-assembling vesicular systems composed of one or more phospholipid bilayers surrounding an aqueous core. Owing to their amphiphilic nature, they can encapsulate both hydrophilic and lipophilic therapeutic agents, thereby enhancing solubility, stability, and bioavailability. Since their introduction in the 1960s, liposomes have progressed from simple model membranes to clinically approved nanocarriers with broad therapeutic applications. They provide significant advantages such as targeted delivery, controlled release, reduced systemic toxicity, and improved pharmacokinetic profiles. This chapter provides a comprehensive overview of liposomal technology, including their structural characteristics, classification, and formulation strategies. Various preparation methods such as thin-film hydration, solvent dispersion, extrusion, microfluidics, and detergent removal are critically discussed with respect to scalability, reproducibility, and regulatory compliance. Advances in stealth liposomes, immunoliposomes, and stimuli-responsive systems are highlighted, with emphasis on their clinical relevance. Furthermore, the chapter outlines the current and emerging applications of liposomes in oncology, infectious diseases, ophthalmology, dermatology, vaccine delivery, and gene therapy. Challenges related to stability, large-scale manufacturing, and quality-by-design (QbD) based regulatory considerations are also addressed. Overall, liposomes continue to serve as a cornerstone of nanomedicine, bridging fundamental pharmaceutical science with translational and clinical success.

Keywords: Liposomes; Nanocarriers; Drug delivery systems, Targeted therapy, Controlled release, PEGylation, Pharmaceutical nanotechnology.

2.1 Introduction

Lipo which means "fat" and Soma which means "body" are the Greek terms from which the term liposome is derived. a liposome is a drug delivery system that resembles a colloidal, vesicular structure and is composed of one or more lipid bilayers (the outer layer) with an equal number of aqueous layers (the inner layer) enclosed within. The

References:

1. Kant Shashi, Kumar Satinder, Bharat P. A complete review on: Liposomes. International Research Journal of Pharmacy [Internet]. 2012 Jul 1;3(7). Available from: https://www.researchgate.net/publication/285487882_A_complete_review_on_Liposomes
2. Bozzuto G, Molinari A. Liposomes as nanomedical devices. International Journal of Nanomedicine [Internet]. 2015 Feb;10(1):975. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4324542/>
3. Akbarzadeh A, Rezaei-Sadabady R, Davaran S, Joo SW, Zarghami N, Hanifehpour Y, et al. Liposome: classification, preparation, and applications. Nanoscale Research Letters [Internet]. 2013 Feb 22;8(1). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3599573/>
4. Fujisawa T, Miyai H, Hironaka K, Tsukamoto T, Tahara K, Yuichi Tozuka, et al. Liposomal diclofenac eye drop formulations targeting the retina: Formulation stability improvement using surface modification of liposomes. International Journal of Pharmaceutics. 2012 Oct 1;436(1-2):564–7.
5. Vishvakrama P, Sharma S. Liposomes: An Overview. Journal Of Drug Delivery And Therapeutics. 2014 Jun 25;47:47-55. <https://doi.org/10.22270/jddt.v010.843>
6. Hosseinkhani S, Samadikhah, Majidi, Nikkhah. Preparation, characterization, and efficient transfection of cationic liposomes and nanomagnetic cationic liposomes. International Journal of Nanomedicine. 2011 Oct;2275.
7. Paecharoenchai O, Niyomtham N, Apirakaramwong A, Ngawhirunpat T, Rojanarata T, Yingyongnarongkul BE, et al. Structure–relationship of cationic lipids on gene transfection mediated by cationic liposomes. AAPS PharmSciTech. 2012;13(5):1302–8.
8. Li X, Chen D, Le C, Zhu C, Gan Y, Hovgaard L. Novel mucus-penetrating liposomes as a potential oral drug delivery system: preparation, in vitro characterization, and enhanced cellular uptake. Int J Nanomedicine. 2011;6:3151–62.
9. Ejioogu DC. Formulation and evaluation of etodolac niosomes by modified ether injection technique. Univ J Pharm Res. 2016;1(1):1–6.
10. Sercombe L, Veerati T, Moheimani F, Wu SY, Sood AK, Hua S. Advances and challenges of liposome assisted drug delivery. Front Pharmacol. 2015;6:286. <https://doi.org/10.3389/fphar.2015.00286>
11. Immordino ML, Dosio F, Cattel L. Stealth liposomes: review of the basic science, rationale, and clinical applications, existing and potential. Int J Nanomedicine. 2006;1(3):297–315.
12. Barenholz Y. Doxil®—the first FDA-approved nano-drug: lessons learned. J Control Release. 2012;160(2):117–34. <https://doi.org/10.1016/j.jconrel.2012.03.020>
13. Hou X, Zaks T, Langer R, Dong Y. Lipid nanoparticles for mRNA delivery. Nat Rev Mater. 2021;6:1078–94. <https://doi.org/10.1038/s41578-021-00358-0>
14. Elsaed EH, Dawaba HM, Ibrahim EA, Afouna MI. Investigation of proniosomes gel as a promising carrier for transdermal delivery of glimepiride. Univ J Pharm Res. 2016;1(2):1–18.
15. Sipal AM, Yadav V, Mamatha Y, Prasanth VV. Liposomes: an overview. J Pharm Sci Innov. 2012;1(1):1–5.
16. Sharma VK. Liposomes present prospective and future challenges. Int J Curr Pharm Rev Res. 2010;1(2):18–25.

17. Veena T, Manichandrika D, Madhuri M, Mounika B, Rani B, Ashwini A. Formulation and evaluation of liposomal drug delivery system of decitabine. *Int J Pharm Sci Res.* 2017;6(3):300–6.
18. Karami N, Moghimipour E, Salimi A. Liposomes as a novel drug delivery system: fundamental and pharmaceutical applications. *J Res Pharm Sci.* 2016;11(1):1–8.
19. Bangham AD, Standish MM, Watkins JC. Diffusion of univalent ions across the lamellae of swollen phospholipids. *J Mol Biol.* 1965;13:238–52.
20. Torchilin VP. Recent advances with liposomes as pharmaceutical carriers. *Nat Rev Drug Discov.* 2005;4(2):145–60.
21. Huang C. Studies on phosphatidylcholine vesicles. Formation and physical characteristics. *Biochemistry.* 1969;8(1):344–52.
22. Hope MJ, Bally MB, Webb G, Cullis PR. Production of large unilamellar vesicles by a rapid extrusion procedure. *Biochim Biophys Acta.* 1985;812(1):55–65.
23. Batzri S, Korn ED. Single bilayer liposomes prepared without sonication. *Biochim Biophys Acta.* 1973;298(4):1015–9.
24. Mozafari MR. Liposomes: an overview of manufacturing techniques. *Cell Mol Biol Lett.* 2005;10(4):711–9.
25. Deamer D, Bangham AD. Large volume liposomes by an ether vaporization method. *Biochim Biophys Acta.* 1976;443(3):629–34.
26. Szoka F, Papahadjopoulos D. Procedure for preparation of liposomes with large internal aqueous space and high capture by reverse-phase evaporation. *Proc Natl Acad Sci U S A.* 1978;75(9):4194–8.
27. Kagawa Y, Racker E. Partial resolution of the enzymes catalyzing oxidative phosphorylation. *J Biol Chem.* 1971;246(16):5477–87.
28. Schubert R. Liposome preparation by detergent removal. *Biochim Biophys Acta.* 2003;1611(2):113–6.
29. ICH Q8, Q9, Q10 Guidelines. International Council for Harmonisation (ICH).
30. Allen TM, Cullis PR. Liposomal drug delivery systems: from concept to clinical applications. *Adv Drug Deliv Rev.* 2013;65(1):36–48. <https://doi.org/10.1016/j.addr.2012.09.037>
31. Patil YB, Swaminathan SK, Sadhukha T, Ma L, Panyam J. The use of nanoparticle-mediated targeted gene silencing and drug delivery to overcome tumor drug resistance. *Biomaterials.* 2010;31(2):358–<https://doi.org/10.1016/j.biomaterials.2009.09.033>
32. Zhang H, Zhang W, Zhao L, Li F. Lipid-based nanocarriers for cancer immunotherapy. *Pharmaceuticals.* 2020;13(5):116. <https://doi.org/10.3390/ph13050116>
33. Fang JY, Hwang TL, Huang YL, Fang CL. Enhancement of topical corticosteroid delivery using liposomes and niosomes. *J Control Release.* 2005;102(2):441–52. <https://doi.org/10.1016/j.jconrel.2004.10.020>
34. Goyal R, Macri LK, Kaplan HM, Kohn J. Nanoparticles and nanofibers for topical drug delivery. *J Control Release.* 2016;240:77–92. <https://doi.org/10.1016/j.jconrel.2015.10.049>
35. Mishra GP, Jain NK. Recent applications of liposomes in ophthalmic drug delivery. *Indian J Pharm Sci.* 2011;73(3):255–66. <https://doi.org/10.4103/0250-474X.93507>
36. Strategic advances in liposomes technology: translational paradigm in transdermal delivery for skin dermatosis. *Journal of Nanobiotechnology.* 2025; Article: “Challenges and limitations” section.

37. Peng T, Xu W, Li Q, Ding Y, Huang Y. Pharmaceutical liposomal delivery—specific considerations of innovation and challenges. *Biomaterials Science*. 2023;11(1):62-75.
38. Approaches to Address PK-PD Challenges of Conventional Liposome Formulation with Special Reference to Cancer, Alzheimer's, Diabetes, and Glaucoma. *Current Drug Metabolism*. 2022;23(9)