IJHSR
ijhighschoolresearch.org
REVIEW ARTICLE

Application of Liposomes as a Cancer Drug Delivery Vehicle for Various Therapies

Nandini Sipani

Sancta Maria International School, Survey No. 106, 107, Dubey Colony Road, Serilingampalle (M), Hyderabad, Telangana, 500019, India; nandini.sipani@gmail.com

ABSTRACT: Cancer is fast approaching as one of the leading causes of mortality in humans. Various treatment plans are available, with conventional ones being surgery, chemotherapy, and radiation, depending on the type of cancer. While effective, such treatment plans not only treat cancer cells but also adversely affect healthy tissues of the body, leading to a long-lasting, sometimes permanent, impact on the quality of life. Liposomes offer an effective drug delivery vehicle that delivers medicines to only specific tumor cells, significantly reducing the effect of these potent drugs on healthy cells. Liposomes consist of hydrophobic phospholipid vesicles with an aqueous core. With the versatility of their design and customization, liposomes are considered useful delivery systems for various types and sizes of drugs. With these nano-structures being adaptable, they can be tailored to address specific cancers. Numerous studies have been published that explore the biosynthesis of liposomes, making them compatible with the bodies of living beings, and several reports are available on the application of liposomes in drug delivery. In this paper, the author will provide a review of the manufacturability of liposomes, followed by an overview of their broad applications, focusing on cancer drug delivery.

KEYWORDS: Biochemistry, Medical Biochemistry, Liposome, Cancer Drug Delivery, Nano.

Introduction

Cancer is the second leading cause of mortality in the world.[1] As per the World Health Organization (WHO) report published in 2024, 20% of people will develop cancer in their lifetime. Moreover, only about 40% of countries currently actively address and fund testing.[2] Apart from the health impact, the global economic cost of cancer is estimated to be $25.2 trillion in international dollars in the 30 years from 2020 to 2050.[3] This suggests an accelerated necessity to invest in preventive as well as treatment plans for cancer. Due to cytotoxicity towards fast-growing cells (cancerous and non-cancerous), conventional cancer treatment methods, such as chemotherapy and radiotherapy, could have a multitude of undesirable side effects.[4-9] Immunotherapy has emerged as a targeted treatment providing precision in drug delivery; however, it also leads to an overstimulated immune system, which can lead to other side effects such as inflammation and fatigue affecting healthy tissues.[10-13] One upcoming technique of bio-delivery systems is through liposomes. Liposomes find a wide variety of applications in various treatments, such as vaccination, gene delivery, and even in cosmetics and the food industry.[14] In particular, liposome-based therapy delivery systems are known to be very effective in targeted drug delivery, thereby improving the efficacy of treatment.[15-18] The term liposome (also known as spherules) is derived from the Greek words lipos (fat) and soma (body), described for the first time by British biophysicist Alec Douglas Bangham in 1963. Liposomes are phospholipid vesicles, varying between 50nm and 5μm in diameter. As their name suggests, liposomes may be formed of multiple layers, with an outer shell composed of fat and an inner core of aqueous polarity. This versatile constitution makes them ideal components for the delivery of not only hydrophilic, but also hydrophobic compounds.[19,20] This type of useful structural design of liposomes facilitates the entrapment of targeted drugs, followed by delivery at the desired location of the organ, resulting in an improved outcome of treatment.[21] While many review articles on liposomes exist, none have provided a comprehensive review on liposomes as this paper does. In this paper, the focus is on using liposomes as drug delivery vehicles to treat tumors.

Their structures and classifications, as well as synthesis methods, along with wide-ranging applications, are provided. Finally, a brief overview of how the use of Artificial Intelligence (AI) and Machine Learning (ML) is revolutionizing the design of liposomes to further improve the efficacy of cancer treatment is given.

Liposome Structure and Classification

Liposomes are multi-layered spherical structures made of phospholipids in aqueous solutions. These phospholipids have a hydrophilic nano-spherical head and hydrophobic tail, resulting in an amphiphilic structure, as shown in Figure 1. Since these are formed in aqueous solution, the surrounding phospholipid bilayer outer shell of the liposome is lined with hydrophilic heads on the inside and outside layers, whereas the hydrophobic tail composes the inside of the shell. This also results in the core of the liposome being aqueous. This unique design facilitates the delivery of both hydrophobic drugs (carried inside the outer shell) and hydrophilic drugs (carried in the aqueous core of the liposome).[22] Based on their physical design and size, liposomes may broadly be classified as Unilamellar Vesicles (ULV), which may be small and below 100nm

DOI: 10.36838/v8i1.70

or large and greater than 100nm in diameter; and Multilamellar Vesicles (MLV). As the name suggests, ULVs have a single phospholipid bilayer, whereas an MLV has multiple concentric layers surrounding it. One other variation is the presence of multiple vesicles inside one large vesicle, leading to the formation of a Multi-Vesicular Vesicle (MVV).[23] Studies on a few drug systems have shown that the extent of availability of the drug in liposome formulations of smaller size is typically higher than that of liposomes of larger size, and therefore, the preferred size of these liposomes is 50-150nm.[24]

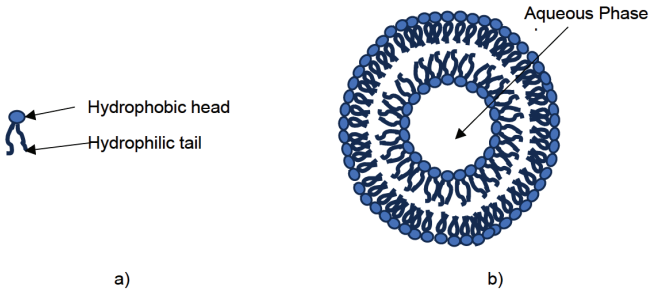

Figure 1: a) Phospholipid unit of a liposome, b) Cross-sectional image of a simple liposome structure.

Liposome Syntheses

There are various methods available for synthesizing liposomes. One very popular and simple to implement method is the lipid film hydration method (the Bangham method), where a thin film of liposomes is manufactured by dissolving lipids in an organic solvent and then evaporating the solvent. This thin film is then transferred into an aqueous medium to form a liposome.[25] Other commonly known methods in literature are the ethanol/ether injection method, the Reverse Phase Evaporation method, the Detergent Depletion method, and Emulsification. Each of these methods comes with its advantages and limitations and is used depending on the type of drug to be administered, stability, expected performance, and target cancers.[26,27]

The biggest issue in most of the traditional methods for liposome synthesis is poor encapsulation efficiency, which is defined as the overall concentration of lipids in the solution. Additionally, the stability is also quite poor, which limits the effectiveness of clinical applications of liposomes. To improve these factors, a variety of novel technologies have been studied and developed,[27-31] such as Lyophilization, also known as the freeze-drying method, supercritical fluid-assisted methods using dense gas technology, microfluidic methods, and the membrane contactor method. For bio-applications, which is the focus of this paper, the supercritical fluid-assisted methods, such as Supercritical Anti-Solvent (SAS), Rapid Expansion of a Supercritical Solution (RESS), and Supercritical Assisted Liposome Formation (SuperLip), are more suitable. These methods provide reliability in production, control of particle size, and *in situ* sterilization, and their use in cancer drug delivery justifies the high costs.

Liposome Stability and Applicability

Enabling liposome stability is a key research area to enable the incorporation of these nanostructures in drug delivery systems. During the synthesis, various physical factors, such as temperature, pH, and particle size, and chemical factors, such as lipid composition, oxidation, and presence of metal ions, affect the stability of liposomes. Once injected and until the drug is delivered to the desired tissues or cancer cells, biological factors such as the environment, biological barriers, etc., will affect its stability.[32] As the liposomes transit through the body, the conditions that they encounter vary, leading to disruption of their fidelity. Therefore, a thorough evaluation and experimentation of their structure is required before incorporating them for medical applications.[32-35]

The phase transition temperature of liposomes, T_m, one of the more important factors affecting liposome stability, is the temperature at which liposomes' lipid components transition from a gel-like ordered state to a crystalline disordered state.[36] Having a detailed understanding of this temperature for selected lipid chains is crucial to selecting appropriate lipids for biological systems as well as drugs. The phase transition understanding determines the performance of the liposomes, such as their permeability, rigidity, stability, and impact of biological constituents.[37]

Liposomes are preferred drug delivery vehicles due to their tendency to accumulate in the region of the tumor as compared to normal tissue. This characteristic is referred to as the Enhanced Permeability and Retention (EPR) effect and is the primary reason for adopting liposomes in cancer treatment. This is because fast-growing cells in the tumor region do not allow the blood vessels to develop fully, and endothelial cells lining the blood vessels have gaps between them, allowing direct accessibility for liposomes to permeate through these openings and transfer the drugs to the affected region.[38] This method of drug transfer is known as passive targeting[39] since it is dependent on the inherent characteristics of liposomes as well as the target tumor site (active targeting will be covered in the Gene Therapy section of this paper).

Liposomes – Prominent Applications

Liposomes are versatile and may be used in multiple functions for cancer treatment. Some of the more prominent applications are discussed here.

Types of Cancer Delivery Drugs:

Nanoparticle-based drug delivery systems allow significant advantages[40,41] over traditional chemotherapy treatments, primarily by avoiding harmful side effects on healthy cells and by being highly efficient in treating the cancer cells. These nanoparticles include liposomes, polymer nanoparticles, gold nanoparticles, carbon nanotubes, quantum dots, and others.[42-44] In this review paper, the focus is only on liposomes as cancer delivery drugs. Liposomes find utility in delivering a variety of drugs and related biocompatible compounds. Additionally, liposomes can also deliver nucleic materials used in gene therapy and immunotherapy.[45] They can be used to enhance gene therapy via the delivery of nucleic agents, designed to

combat the disease, at the site of mutated cells. Similarly, it was found that when liposomes were used as a carrier for immunomodulatory agents, they increased the therapeutic payload and therefore increased the capability of these drugs to target the disease more effectively.[46] Liposomes also offer precision in transferring photo-thermal therapeutic medicines to cancer cells.[47] All these versions of therapies are typically combined to improve the outcome of the treatment.

Chemotherapy:

Since liposomal nanoparticles encapsulate the drugs, they are known to be low in toxicity as compared to the traditional chemotherapy drugs. The liposomes may be further modified to give them a controlled transfer rate and increased grafting tendencies, thereby increasing the efficacy of the transported drugs. Depending on the type of cancer (location, size, stage), a combination of liposomes may be used to target these specific cancer cells.[48] Typically, healthy cells are known to have a tight interface that does not allow large particles to pass through them. However, the mutated cancer cells have weak intercellular resistance, and therefore, encapsulated drugs in liposomes can permeate through the walls of tumors more easily at these target sites.[49] This is an example where liposomes find utility in chemotherapy. Doxorubicin and paclitaxel are very specialized chemotherapy drugs for breast and lung cancer, and liposomes have been tested to be a useful vehicle for their delivery.[50] Doxorubicin works by blocking a specific enzyme that is known to lead to cancer cell multiplication. Encapsulating this drug in liposomes has been shown to keep the drug in the bloodstream longer. This research indicated that liposomes provided enhanced treatment results with these drugs compared to direct delivery of these medicines.

Gene Therapy:

Gene therapy refers to the delivery and assimilation of a specific gene into a system, with the intention of treatment. Various studies are being conducted to develop a model for a variety of lipids used in gene delivery.[51] Liposomes make a good vehicle for this transfer owing to their controllable size and lipid profile, matching the gene type being transferred. Several studies have discussed the benefits of DNA-mediated or mRNA delivery through liposomes.[52-54] Another type of genetic material that is used is short hairpin RNA (shRNA), which is used to silence specific gene expression via a method known as RNA interference (RNAi), the effects of which last for a long time when delivered via liposomes.[55] Another such genetic material widely used for gene therapy is small interfering RNA (siRNA). It is a double-stranded RNA that is vital in the regulation of genes. Similar to shRNA, siRNA works by thwarting the expression of certain genes.[56] To enable such biological material delivery systems, a thorough review is required to address interaction with serum, intercellular transportation properties, and targeted impact. Many successful tests have been completed for the delivery of virus vaccination, and currently, non-viral biomaterial delivery for cancer is being tested.[57,58] Non-viral methods, such as through liposomes, of delivering genetic tools are preferred owing to their low risk, biocompatibility, and immunogenicity. Additionally, metal complexes, such as ligands, may further functionalize liposomes to improve their selectivity to diseased cells; this is known as active targeting.[59]

Photothermal Therapy:

Photothermal therapy (PTT), as the name implies, uses light on photosensitized medicines, which in turn releases thermal energy to destroy the cancer cells.[60] Photothermal therapy has been in use for various treatments for many years now. This therapy finds utility as it is a minimally disruptive treatment. In this method, nanoparticles carrying drugs that are sensitized by light are delivered in the bloodstream. These drugs may be activated at a given spectrum of wavelengths of light only. Once administered, the target location of treatment can be mildly irradiated with the specific wavelength of light, leading to the emission of heat at that location.[61] Typically, gold-based nanoparticles are used for this therapy as they tend to easily absorb near-infrared (NIR) light through surface plasmon resonance.[62-64] There are various other studies available using novel materials such as carbon nanotubes, carbon dots, graphene, and quantum dots.[65] Liposomes enhance the impact of this treatment by delivering certain photosensitive dyes safely to the target site. Indocyanine-green is one such popular dye due to its very sharp light absorption characteristic in the NIR region.[66] Various reports also provide detailed fundamental characterization of these drugs to determine their efficiency and stability.[67]

T Cell Immunotherapy:

As per the American Cancer Society (ACS), immunotherapy can be defined as a method in which a living being's immune system can be harnessed to attack the cancer-causing cells.[68] Immunotherapy is gaining precedence as it improves the immune system and may proactively address cancer spread.[69] To realize immunotherapy, it is important to understand the significance of T cells. As per standard cancer terminology, T cells constitute the immune system and are responsible for developing stem cells in the body. They not only boost immunity but also help fight the occurrence of cancer by producing specific antigens.[70] T cell immunotherapy, also sometimes referred to as adoptive cell therapy (ACT), is a method where autologous (patient's own cells) or allogenic (cells derived from donor plasma) T cells are introduced into the body to eliminate the cancer cells.[65,71] T cell immunotherapy may be broadly classified into two categories: tumor-infiltrating lymphocytes (TIL) and chimeric antigen receptor (CAR) T cell therapy.[72] Both therapies work by extracting T cells and augmenting them externally in a lab, followed by reintroducing them into the body. TIL therapy extracts T cells from the tumor itself and separates the ones that recognize tumor cells, whereas CAR T may include the modification of T cells to teach them to recognize tumor cells. Liposomes may be used for the delivery of these specified T cells to a precise site and boost natural immunity in the body. In an upcoming area of research, as part of immunotherapy, liposomes may also be used for the delivery of cancer-associated antigens. [73]

DOI: 10.36838/v8i1.70

Targeted therapies:

Since liposomes are customizable, they make for impressive drug delivery vehicles for targeted therapy. Various studies have been conducted where liposomes are used for delivering specific drugs to specific tissues, such as the lung, breast, and pancreas. Additionally, the surface of the liposomes can be modified with various functional groups to enhance their efficacy.[74] One such example is stimulus-responsive liposome treatment, which triggers drug release in response to a very targeted stimulus. Such stimuli could be based on certain specific enzymes, pH-sensitive, to name a few.[75] This leads to targeting the treatment to very localized cells, rather than conventional methods that are detrimental to all cells. An additional advantage of liposomes is that they may be used to deliver both chemotherapy and immunotherapy drugs together, without their interference.

Toxicity:

The natural lipid constitution of liposomes makes them low in intrinsic toxicity. These lipids are biologically inactive, with their constituents being derived from natural food sources such as egg yolk, soybean, milk, or they may be synthetically created from low-toxicity lipids. This makes them ideal transport vehicles for drug delivery for cancer and other drugs.[48] Certain negatively charged dicetyl phosphate-based liposomes, however, may be toxic.[76] This is a field where more exploration is underway to determine the bio-feasibility of liposomes.

■ Liposome Design: An AI/ML Approach

AI and ML are further accelerating the development of template drugs as well as delivery systems. For example, liposomes can now be efficiently designed by effectively performing predictive modeling and process optimization. ML-driven advanced algorithms are accelerating the formulation processes and enabling personalized cancer therapies.[77-79] By analyzing large data sets, supervised learning models are generated, and key parameters such as encapsulation efficiency, particle size, and drug loading efficiency are optimized. More importantly, liposome-based drug delivery systems are then optimized for targeted cancer cell growth and customized for individuals, making them significantly more effective than the conventional liposome-based cancer drugs both in terms of improving the recovery and minimizing the side effects. The future is indeed bright for the AI/ML-based precision medicine.

■ Conclusions and the Future

As illustrated in this review paper, research is being carried out on using liposomes as a cancer drug delivery vehicle at an accelerated pace. Various avenues are in the process of being explored with promising results. There are several liposome systems that are in the research phase today for multiple medicines, targeting different cancers. Apart from the type of drugs, there are various types of therapy systems being explored, such as gene therapy and different versions of immunotherapy. Each of these therapies comes with its specific conditions in which they are most effective. For example, certain therapies may work at a very specific pH, concentration in the bloodstream, or time of availability near the tumor site for controlled interaction time. While liposomes are an upcoming field and have gained recent recognition as cancer drug delivery systems, more focused studies are required to develop and assimilate them into becoming the standard treatment plan. In addition to the requirement of more research and evaluation, as well as approval by the Food and Drug Administration (FDA), additional constraints of throughput, consistent manufacturing, supply, and cost also exist. Functionalization of liposomes to increase their targeting properties and overall efficacy requires multiple manufacturing steps, making high-volume manufacturing challenging. Clinical trials are underway where various combinations of liposomes and drugs are being explored. With AI accelerating the pace of sequencing therapeutic drugs that are customized to match with patient's biological constitution, it is expected that quicker and more effective progress will be seen in the coming decade. In conclusion, while there are various challenges, the outlook for the incorporation of liposomes as part of the standard plan of treatment is strong, and with continued research efforts and funding, liposomes are expected to become an integral part of the standard treatment plan for cancers.

■ Acknowledgments

I would like to acknowledge Kalyani Eswar, Prime Minister's Research Fellow, from the P-Nanospace Lab at the Indian Institute of Technology, Hyderabad, for her constant guidance and support, as well as for giving me insight into the world of liposomes and the revolutionary way they are changing cancer treatment. I would also like to call out Dr. Aravind Rengan, Associate Professor, Indian Institute of Technology, Hyderabad, and Dr. Prakriti Tayalia, Professor, Indian Institute of Technology, Bombay, for inspiring me with their research work on cancer therapies. Finally, I would like to thank my family for their encouragement in my pursuit of studies and biotechnology research.

■ References

1. Leading Causes of Death; Centers for Disease Control and Prevention, National Center for Health Statistics. https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm (accessed 2025-04-30)
2. Global cancer burden growing, amidst mounting need for services. *News Release*. World Health Organization, February 1, 2024. https://www.who.int/news/item/01-02-2024-global-cancer-burden-growing--amidst-mounting-need-for-services
3. Kreier, F. Cancer will cost the world $25 trillion over next 30 years. Nature, March 07, 2023. Cancer will cost the world $25 trillion over next 30 years
4. Cheng, Z.; Huang, H.; Yin, M.; Liu, H. Applications of liposomes and lipid nanoparticles in cancer therapy: current advances and prospects. *Experimental Hematology & Oncology* **2025**, 14 (11). DOI: 10.1186/s40164-025-00602-1
5. Monsuez, J. J.; Charniot, J. C.; Vignat, N.; Artigou, J. Y. Cardiac side-effects of cancer chemotherapy. *International Journal of Cardiology* **2010**, 144 (1), 3-15. DOI: 10.1016/j.ijcard.2010.03.003
6. Van den Boogaard, M. C.; Komninos, D. S. J.; Vermeij, W. P. Chemotherapy Side-Effects: Not All DNA Damage Is Equal. *Cancers* **2022**, 14 (3), 627. DOI: 10.3390/cancers14030627

7. Barazzuol, L.; Coppes, R. P. Prevention and treatment of radiotherapy-induced side effects. *Molecular Oncology* **2020**, 14 (7), 1538-1554. DOI: 10.1002/1878-0261.12750
8. Dieckmann, K.; Widder, J.; Pötter, R. Long-Term Side Effects of Radiotherapy in Survivors of Childhood Cancer. *Normal Tissue Reactions in Radiotherapy and Oncology*; Dörr, W., Engenhart-Cabillic, R., Zimmermann, J. S., Eds.; Frontiers of Radiation Therapy and Oncology, Vol. 37; Karger, 2002; pp 57-68.
9. Löbrich, M.; Kiefer, J. Assessing the likelihood of severe side effects in radiotherapy. *International Journal of Cancer* **2006**, 118 (11), 2652-2656. DOI: 10.1002/ijc.21782
10. Esfahani, K.; Roudaia, L.; Buhlaiga, N.; Del Rincon, S. V.; Papneja, N.; Miller Jr., W. H. A review of cancer immunotherapy: From the past, to the present, to the future. *Current Oncology* **2020**, 27 (S2), 87-97. DOI: 10.3747/co.27.5223
11. Florian, S.; Raffaele, R.; Philippe, B. Side effects of immunotherapy: a constant challenge for oncologists. *Current Opinion in Oncology* **2019**, 31 (4), 280-285. DOI: https://doi.org/10.1097/CCO.0000000000000541
12. Kroschinsky, F.; Stölzel, F.; von Bonin, S.; Beutel, G.; Kochanek, M.; Kiehl, M.; Schellongowski, P. New drugs, new toxicities: severe side effects of modern targeted and immunotherapy of cancer and their management. *Critical Care* **2017**, 21, 89. DOI: https://doi.org/10.1186/s13054-017-1678-1
13. Li, S.; Zhang, Z.; Lai, W. F.; Cui, L.; Zhu, X. How to overcome the side effects of tumor immunotherapy. *Biomedicine & Pharmacotherapy* **2020**, 130, 110639. DOI: https://doi.org/10.1016/j.biopha.2020.110639
14. Lasic, D. D. Applications of Liposomes. *Neuro-informatics and Neural Modelling (Handbook of Biological Physics)*; Moss, F.; Gielen, S., Eds.; Elsevier, 1995; pp 491-519. DOI: 10.1016/S1383-8121(06)80027-8
15. Gu, Z.; Da Silva, C. G.; Van der Maaden, K.; Ossendorp, F.; Cruz, L. J. Liposome-Based Drug Delivery Systems in Cancer Immunotherapy. *Pharmaceutics* **2020**, 12 (11), 1054. DOI: 10.3390/pharmaceutics12111054
16. Lian, T.; Ho, R. J. Y. Trends and Developments in Liposome Drug Delivery Systems. *Journal of Pharmaceutical Science* **2001**, 90 (6), 667-680. DOI: 10.1002/jps.1023
17. Sercombe, L.; Veerati, T.; Moheimani, F.; Wu, S. Y.; Sood, A. K.; Hua, S. Advances and Challenges of Liposome Assisted Drug Delivery. *Frontiers in Pharmacology* **2015**, 6, 286. DOI: 10.3389/fphar.2015.00286
18. Alavi, M.; Karimi, N.; Safaei, M. Application of Various Types of Liposomes in Drug Delivery Systems. *Advanced Pharmaceutical Bulletin* **2017**, 7 (1), 3-9. DOI: 10.15171/apb.2017.002
19. Furneri, P. M.; Petronio, G. P.; Fuochi, V.; Cupri, S.; Pignatello, R. Nanosized devices as antibiotics and antifungals delivery: past, news, and outlook. *Nanostructures for Drug Delivery (Nanostructures in Therapeutic Medicine Series)*; Andronescu, E., Grumezescu, A. M., Eds.; Elsevier, 2017; pp 697-748. DOI: 10.1016/B978-0-323-46143-6.00023-3
20. Duzgunes, N.; Gregoriadis, G. Introduction: The Origins of Liposomes. *Methods in Enzymology* **2005**, 319, 1-3. DOI: 10.1016/S0076-6879(05)91029-X
21. Birhanu, G.; Javar, H. A.; Seyedjafari, E.; Zandi-Karimi, A. Nanotechnology for delivery of gemcitabine to treat pancreatic cancer. *Biomedicine & Pharmacotherapy* **2017**, 88, 635-643. DOI: 10.1016/j.biopha.2017.01.071
22. Akbarzadeh, A.; Rezaei-Sadabady, R.; Davaran, S.; Joo, S. W.; Zarghami, N.; Hanifehpour, Y.; Samiei, M.; Kouhi, M.; Nejati-Koshki, K. Liposome: classification, preparation, and applications. *Nanoscale Research* Letters **2013**, 8 (102). DOI: 10.1186/1556-276X-8-102
23. Nsairat, H.; Khater, D.; Sayed, U.; Odeh, F.; Al Bawab, A.; Alshaer, W. Liposomes: structure, composition, types, and clinical application. *Heliyon* **2022**, 8 (5), e09394. DOI: 10.1016/j.heliyon.2022.e09394
24. Ong, S. G. M.; Ming, L.C.; Lee, K. S.; Yuen, K. H. Influence of the encapsulation efficiency and size of liposome on the oral bioavailability of griseofulvin-loaded liposomes. *Pharmaceutics* **2016**, 8 (3), 25. DOI: 10.3390/pharmaceutics8030025
25. Tomnikova, A.; Orgonikova, A.; Krizek, T. Liposomes: preparation and characterization with a special focus on the application of capillary electrophoresis. Chemical Monthly 2022, 153, 687-695 *Monatshefte für Chemie* **2022**, 153, 687-695. DOI: 10.1007/s00706-022-02966-0
26. Andra, V. V. S. N. L.; Pammi, S. V. N.; Bhatraju, L. V. K. P.; Ruddaraju, L. K. A Comprehensive Review on Novel Liposomal Methodologies, Commercial Formulation, Clinical Trials and Patents. *Bionanoscience* **2022**, 12 (1), 274-291. DOI: 10.1007/s12668-022-00941-x
27. Lombardo, D.; Kiselev, M. A. Methods of Liposomes Preparation: Formation and Control Factors of Versatile Nanocarriers for Biomedical and Nanomedicine Application. *Pharmaceutics* **2022**, 14(3), 543-591. DOI: 10.3390/pharmaceutics14030543
28. Patil, Y. P.; Jadhav, S. Novel methods for liposome preparation. *Chemistry and Physics of Lipids* **2014**, 177, 8-18. DOI: 10.1016/j.chemphyslip.2013.10.011
29. Has, C.; Sunthar, P. A comprehensive review on recent preparation techniques of liposomes. *Journal of Liposome Research* **2020**, 30(4), 336-365. DOI: 10.1080/08982104.2019.1668010
30. Panahi, Y.; Farshbaf, M.; Mohammadhosseini, M.; Mirahadi, M.; Khalilov, R.; Saghfi, S.; Akbarzadeh, A. Recent advances on liposomal nanoparticles: synthesis, characterization and biomedical application. *Artificial Cells, Nanomedicine, and Biotechnology* **2017**, 45(4), 788-799. DOI: 10.1080/21691401.2017.1282496
31. Mozafari, M. R. Liposomes: An Overview of Manufacturing Techniques. *Cellular & Molecular Biology Letters* **2005**, 10, 711-719.
32. Jyothi, V. G. S. S.; Bulusu, R.; Rao, B. V. K.; Pranothi, M.; Banda, S.; Bolla, P. R.; Kommineni, N. Stability characterization for pharmaceutical liposome product development with focus on regulatory considerations: An update. *International Journal of Pharmaceutics* **2022**, 624, 122022. DOI: 10.1016/j.ijpharm.2022.122022
33. Chowdhary, P.; Mahalakshmi, L.; Dutta, S.; Moses, J. A.; Anandharamakrishnan, C. Strategies for stabilization and preservation of liposomes. *Liposomal Encapsulation in Food Science and Technology* **2023**, 223-237. DOI: 10.1016/B978-0-12-823935-3.00014-X
34. Pasarin, D.; Ghizdareanu, A. I.; Enascuta, C. E.; Matei, C. B.; Bilbie, C.; Paraschiv-Palada, L.; Veres, P. A. Coating Materials to Increase the Stability of Liposomes. *Polymers* **2023**, 15, 782-811. DOI: 10.3390/polym15030782
35. Yadav, A. V.; Murthy, M. S.; Shete, A. S.; Sakhare, S. Stability Aspects of Liposomes. *Indian Journal of Pharmaceutical Education and Research* **2011**, 45(4), 402-413.
36. Jing, Y.; Trefna, H.; Persson, M.; Kasemo, B.; Svedhem, S. Formation of supported lipid bilayers on silica: relation to lipid phase transition temperature and liposome size. *Soft Matter* **2014**, 10, 187-195. DOI: 10.1039/C3SM50947H
37. Chen, J.; He, C.; Lin, A.; Gu, W.; Chen, Z., Li, W.; Cai, B. Thermosensitive liposomes with higher phase transition temperature for targeted drug delivery to tumor. *International Journal of Pharmaceutics* **2014**, 475(1-2), 408-415. DOI: 10.1016/j.ijpharm.2014.09.009
38. Tan, A.; Jeyaraj, R.; De Lacey, S. F. Nanotechnology in neurosurgical oncology. *Nanotechnology in Cancer*; Mathur, A. B.; Ed.; Elsevier, 2017; pp 139-170. DOI: 10.1016/B978-0-323-39080-4.00007-0

DOI: 10.36838/v8i1.70

39. Alavi, M.; Hamidi, M. Passive and active targeting in cancer therapy by liposomes and lipid nanoparticles. *Drug Metabolism and Personalized Therapy* **2019**, 34(1), 20180032. DOI: 10.1515/dmpt-2018-0032
40. Ajith, S.; Almomani, F.; Elhissi, A.; Husseini, G. A. Nanoparticle-based materials in anticancer drug delivery: Current and future prospects. *Heliyon* **2023**, 9(11), e21227. DOI: 10.1016/j.heliyon.2023.e21227
41. Dang, Y.; Guan, J. Nanoparticle-based drug delivery systems for cancer therapy. *Smart Materials in Medicine* **2020**, 1, 10-19. DOI: https://doi.org/10.1016/j.smaim.2020.04.001
42. Dandia, H. Y.; Pillai, M. M.; Sharma, D.; Suvarna, M.; Dalal, N.; Madhok, A. Ingle, A.; Chiplunkar, S. V.; Galande, S.; Tayalia, P. Acelluar scaffold-based approach for in situ genetic engineering of host T-cells in solid tumor immunotherapy. *Military Medical Research* **2024**, 11(1), 3-22. DOI: 10.1186/s40779-023-00503-6
43. Singh, A.; Tayalia, P. Three-dimensional cryogel matrix for spheroid formation and anti-cancer drug screening. *Journal of Biomedical Materials Research Part A* **2020**, 108(2), 365-376. DOI: 10.1002/jbm.a.36822
44. Dalal, N.; Dhandapani, H.; Ingle, A.; Sharma, D.; Tayalia, P. Functionalized Poly(ethylene Glycol) Diacrylate Scaffolds for In Situ Immunomodulation of Dendritic Cells Targeting Melanoma Tumor. *ACS Biomaterials Science & Engineering* **2025**, 11(4), 2396-2407. DOI: 10.1021/acsbiomaterials.4c02036
45. Hamad, I.; Harb, A. A.; Bustanji, Y. Liposome-Based Drug Delivery Systems in Cancer Research: An Analysis of Global Landscape Efforts and Achievements. *Pharmaceutics* **2024**, 16 (3), 400. DOI: 10.3390/pharmaceutics16030400
46. Mishra, M.; Gupta, A. D.; Dadhich, R.; Ahmad, M. N.; Dasgupta, A.; Chopra, S.; Kapoor, S. Mycobacterial lipid-derived immunomodulatory drug-liposome conjugate eradicates endosome-localized mycobacteria. *Journal of Controlled Release* **2023**, 360, 578-590. DOI: 10.1016/j.jconrel.2023.07.013
47. Zhou, H.; Pan, H.; Raza, F.; Zafar, H.; Ge, Y.; Wang, N.; Zheng, R.; Zhang, D.; Yang, Y. Thermosensitive drug-loaded liposomes for photothermal and chemotherapeutic treatment of colon cancer. *Material Advances* **2024**, 5, 2456-2469. DOI: 10.1039/D3MA01060K
48. Allahou, L. W.; Madani, S. Y.; Seifalian, A. Investigating the Application of Liposomes as Drug Delivery Systems for the Diagnosis and Treatment of Cancer. *International Journal of Biomaterials* **2021**, 2021 (1), 1-16. DOI: 10.1155/2021/3041969
49. Pawar, H. R.; Bhosale, S. S.; Derle, N. D. Use of liposomes in cancer therapy: a review. *International Journal of Pharmaceutical Sciences and Research* **2012**, 3 (10), 3585-3590. DOI: 10.13040/IJPSR.0975-8232.3(10).3585-90
50. El-Hamid, E. S. A.; Gamal-Eldeen, A. M.; Eldeen, A. M. S. Liposome-coated nano doxorubicin induces apoptosis on oral squamous cell carcinoma CAL-27 cells. *Archives of Oral Biology* **2019**, 103, 47–54. DOI: 10.1016/j.archoralbio.2019.05.011
51. Balazs, D. A.; Godbey, W. T. Liposomes for Use in Gene Delivery. *Journal of Drug Delivery* **2010**, 326497, 1-12. DOI: 10.1155/2011/326497
52. Mahato, R. I.; Smith, L. C.; Rolland, A. Pharmaceutical Perspectives of Nonviral Gene Therapy. *Advances in Genetics (Volume 41)*; Hall, J. C.; Dunlap, J. C.; Friedmann, T.; Giannelli, F., Eds.; Academic Press, 1999, pp 95-156. DOI: 10.1016/S0065-2660(08)60152-2
53. Baru, M.; Axelrod, J. H., Nur, I. Liposome-encapsulated DNA-mediated gene transfer and synthesis of human factor IX in mice. *Gene* **1995**, 161 (2), 143-150. DOI: 10.1016/0378-1119(95)00281-A
54. Bagasra, O.; Amjad, M.; Mukhtar, M. Liposomes in Gene Therapy. *Gene Therapy Principles and Applications*; Blankenstein, T. Ed.; Birkhäuser Basel, 2003, pp 61-71. DOI: 10.1007/978-3-0348-7011-5_5
55. What is shRNA and how do you use it? *horizon* https://horizondiscovery.com/en/applications/rnai/shrna-applications (accessed 2025-04-30).
56. Raja, I.; Tennyson, J. Small RNA – regulator of biotic stress and pathogenesis in food crops. *Plant small RNA in Food* Crops; Guleria, P., Kumar, V., Mo, B., Eds.; Academic Press, 2023, pp 223-269. DOI: 10.1016/B978-0-323-91722-3.00010-5
57. Wang, C.; Pan, C.; Yong, H.; Wang, F.; Bo, T.; Zhao, Y.; Ma, B.; He, W.; Li, M. Emerging non-viral vectors for gene delivery. *Journal of Nanobiotechnology* **2023**, 21 (272), 1-18. DOI: 10.1186/s12951-023-02044-5
58. Nsairat, H.; Alshaer, W.; Odeh, F.; Esawi, E.; Khater, D.; Al Bawab, A.; El-Tanani, M.; Awidi, A.; Mubarak, M. S.; Recent advances in using liposomes for delivery of nucleic acid-based therapeutics. *OpenNano* **2023**, 11, 100132. DOI: 10.1016/j.onano.2023.100132
59. Yildiz, S. N.; Entezari, M.; Paskeh, M. D. A.; Mirzaei, S.; Kalbasi, A.; Zabolian, A.; Hashemi, F.; Hushmandi, K.; Hashemi, M.; Raei, M.; Goharrizi, M. A. S. B.; Aref, A. R.; Zarrabi, A.; Ren, J.; Orive, G.; Rabiee, N.; Ertas, Y. N. Nanoliposomes as nonviral vectors in cancer gene therapy. *MedComm* **2024**, 5 (7), e583. DOI: 10.1002/mco2.583
60. Blau, R.; Krivitsky, A.; Epshtein, Y.; Satchi-Fainaro, R. Are nanotheranostics and nanodiagnostics-guided drug delivery stepping stones towards precision medicine? *Drug Resistance Updates* **2016**, 27, 39-58. DOI: 10.1016/j.drup.2016.06.003
61. Huang, X.; El-Sayed, M. A. Plasmonic photo-thermal therapy (PPTT). *Alexandria Journal of Medicine* **2011**, 47 (1), 1-9. DOI: 10.1016/j.ajme.2011.01.001
62. Doughty, A. C. V.; Hoover, A. R.; Layton, E.; Murray, C. K.; Howard, E. W.; Chen, W. R. Nanomaterial Applications in Photothermal Therapy for Cancer. *Materials* **2019**, 12 (5), 779. DOI: 10.3390/ma12050779
63. Rengan, A. K.; Bukhari, A. B.; Pradhan, A.; Malhotra, R.; Banerjee, R.; Srivastava, R.; De, A. In Vivo Analysis of Biodegradable Liposome Gold Nanoparticles as Efficient Agents for Photothermal Therapy of Cancer. *Nano Letters* **2015**, 15 (2), 842-848. DOI: 10.1021/nl5045378
64. Rengan, A. K.; Jagtap, M.; De, A.; Banerjee, R.; Srivastava, R. Multifunctional gold coated thermo-sensitive liposomes for multimodal imaging and photo-thermal therapy of breast cancer cells. *Nanoscale* **2014**, 6, 916-923. DOI: 10.1039/C3NR04448C
65. Beniwal, N.; Verma, A.; Putta, C. L.; Rengan, A. K. Recent Trends in Bio-nanomaterials and Non-invasive Combinatorial Approaches of Photothermal Therapy against Cancer. *Nanotheranostics* **2024**, 8 (2), 219-238. DOI: 10.7150/ntno.91356
66. Liao, W. T.; Chang, D. M.; Lin, M. X.; Lee, J. W.; Tung, Y. C.; Hsiao, J. K. Indocyanine-Green-Loaded Liposomes for Photodynamic and Photothermal Therapies: Inducing Apoptosis and Ferroptosis in Cancer Cells with Implications beyond Oral Cancer. *Pharmaceutics* **2024**, 16 (2), 224. DOI: 10.3390/pharmaceutics16020224
67. Repeat of 33 Zhou, H.; Pan, H.; Raza, F.; Zafar, H.; Ge, Y.; Wang, N.; Zheng, R.; Zhang, D.; Yang, Y. Thttps://pubs.rsc.org/en/content/articlehtml/2024/ma/d3ma01060k
68. Immunotherapy; American Cancer Society. https://www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html (accessed 2025-04-30)
69. Lee, G.; Choi, Y.; Hong, J.; Kim, J.; Chae, J.; Ahn, S.; Ha, H.; Jeong, E.; Lee, H. Y.; Choi, J. All-Rounder Liposomes in Cancer Immunotherapy: Strategies and Design Applications of Engineered

Liposomal Nanomaterial. *BioChip Journal* **2024**, 18, 211-232. DOI: 10.1007/s13206-024-00147-1
70. T cell. *National Cancer Institute*, National Institutes of Health. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/t-cell (accessed 2025-04-30)
71. Van der Walle, C. F.; Godbert, S.; Saito, G.; Azhari, Z.; Formulation Considerations for Autologous T Cell Drug Products. *Pharmaceutics* **2021**, 13 (8), 1317. DOI: 10.3390/pharmaceutics13081317
72. T-cell Transfer Therapy. *National Cancer Institute*, National Institutes of Health https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/t-cell-transfer-therapy (accessed 2025-04-30)
73. Dahotre, S. N.; Romanov, A. M.; Su, F. Y.; Kwong, G. A. Synthetic Antigen-Presenting Cells for Adoptive T Cell Therapy. *Advanced Therapeutics* **2021**, 4 (8). DOI: 10.1002/adtp.202100034
74. Wang, S.; Chen, Y.; Guo, J.; Huang, Q. Liposomes for Tumor Targeted Therapy: A Review. *International Journal of Molecular Sciences* **2023**, 24(3), 2643. DOI: 10.3390/ijms24032643
75. Antoniou, A. I.; Giofre, S.; Seneci, P.; Passarella, D.; Pellegrino, S. Stimulus-responsive liposomes for biomedical application. *Drug Discovery Today* **2021**, 26 (8), 1794-1824. DOI: 10.1016/j.drudis.2021.05.010
76. Inglut, C. T.; Sorrin, A. J.; Kuruppu, T.; Vig, S.; Cicalo, J.; Ahmad, H.; Huang, H. C. Immunological and Toxicological Considerations for the Design of Liposomes. *Nanomaterials* **2020**, 10 (2), 190-213. DOI: 10.3390/nano10020190
77. Matalqah, S.; Lafi, Z.; Mhaidat, Q.; Asha, N.; Asha, S. Y. Applications of machine learning in liposomal formulation and development. *Pharmaceutical Development and Technology* **2025**, 30 (1), 126-136. DOI: 10.1080/10837450.2024.2448777
78. Eugster, R.; Orsi, M.; Buttitta, G.; Serafini, N.; Tiboni, M; Casettari, L.; Reymond, J. L.; Aleandri, S.; Luciani, P. Leveraging machine learning to streamline the development of liposomal drug delivery systems. *Journal of Controlled Release* **2024**, 376, 1025-1038. DOI: 10.1016/j.jconrel.2024.10.065
79. Hoseini, B.; Jaafari, M. R.; Golabpour, A.; Zahra, R.; Maryam, K.; Eslami, S. Machine Learning-Driven Advancements in Liposomal Formulations for Targeted Drug Delivery: A Narrative Literature Review. *Current Drug Delivery* **2024**, ASAP Article. DOI: 10.2174/0115672018302321240620072039

Author

Nandini Sipani is a senior at the Sancta Maria International School in Hyderabad, India. She is passionate about the world of biotechnology and bioengineering and wants to pursue a career in this field, making a difference in the world. In her free time, Nandini writes short stories and plays the violin.

DOI: 10.36838/v8i1.70