Journal of Pharmaceutical Research and Integrated Medical Sciences (JPRIMS)
ISSN: 3049-1681, Vol.02, Issue No.07, 2025 (pp. 15-26)

REVIEW ARTICLE https://aktpublication.com/index.php/jprims/index

Design of Liposomal Drug Delivery Systems for Enhanced Cancer Therapy

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Abstract

Liposomal drug delivery methods are becoming popular nanocarriers for anticancer drugs because they make the drugs more available, target them more accurately, and lower their toxicity in the body. The goal of this project was to improve cancer treatment results by designing, formulating, and testing liposomal systems that include a model chemotherapeutic drug. We used the thin-film hydration approach to make three liposomal formulations (F1, F2, and F3) and then measured their particle size, zeta potential, polydispersity index, and entrapment efficiency. Studies of drug release in vitro showed that the drugs were released over time, with F3 exhibiting the largest cumulative release (89% at 24 hours). The MTT assay showed that F3 dramatically reduced the viability of MCF-7 cells (to 12% at 50 µg/mL), making it better than both other formulations and the free medication. One-way ANOVA statistical analysis showed that there were substantial differences ($p < 0.05$) between the formulations in terms of how well they trapped drugs, how well they released drugs, and how hazardous they were to cells. These results show that improved clearest liposomal formulations could be useful, regulated, and to deliver cancer medication.

Key Words:

Liposomes, Cancer therapy, Nanocarriers, Controlled release, Cytotoxicity, Drug delivery system, MCF-7 cells

History:

Received: March, 3,2025

Revised: April, 24,2025

Accepted: May, 18,2025

Published: July, 25 2025

DOI: https://doi.org/10.64063/3049-1681.vol.2.issue7.2

1. INTRODUCTION

Nanotechnology has changed the way drugs are delivered, especially in oncology, by making it possible to make drugs that are more effective. Conventional cancer treatments work to some extent, but they typically cause high systemic toxicity, poor bioavailability, non-specific distribution, and frequent dosing[1], all of which make it harder for patients to stick to their treatment and get better results. Liposomes, which are spherical vesicles made up of phospholipid bilayers, have gotten a lot of attention as a new way to deliver medications. This is because they are biocompatible[2], can hold both hydrophilic and lipophilic pharmaceuticals, and can be passively or actively targeted to tumour tissues[3]. Changing the physicochemical properties of liposomal formulations can help control how drugs are released, keep them in

tumour locations longer, and get them into cells more effectively. These qualities make liposomes an intriguing way to get around the problems with standard chemotherapy. The purpose of this project was to create and test liposomal versions of a model anticancer medicine in order to increase the drug's effectiveness and lessen its adverse effects through better formulation design and testing in a lab[4].

1.1.Background Information

Cancer is still one of the top causes of death around the world, with millions of new cases diagnosed every year[5]. There are numerous chemotherapeutic agents available, but many of them aren't very useful in the clinic since they break down quickly in the body, don't dissolve well, don't target specific cells, and are quite hazardous to the whole body. Liposomal drug delivery systems have become a powerful way to get around these problems by putting medications within lipid vesicles[6], which changes how the pharmaceuticals move through the body and where they go. Liposomes can make anticancer medications more effective by making them stay longer at the tumour site, keeping them from breaking down too soon, and allowing them to be released over time[7]. This work builds on previous research by creating and describing different types of liposomes in order to find the best one for treating cancer.

1.2.Statement of the Problem

Even though cancer treatment has come a long way, traditional chemotherapy still has problems like low selectivity, systemic toxicity, and bad patient outcomes[8]. It is critically important to find drug delivery technologies that can make anticancer drugs work better while causing fewer side effects[9]. Liposomes have shown promise for targeted distribution, but how well they work relies a lot on their composition and structural stability[10]. One of the biggest problems in nanomedicine is figuring out how to make liposomal formulations that work best for trapping drugs, releasing them in a regulated way, and making them more hazardous to cells. This study fills in that gap by systematically creating and testing liposomal systems to increase drug delivery for cancer treatment.

1.3.Objectives of the Study

The study was designed to fulfill the following key objectives:

- To formulate and optimize liposomal drug delivery systems
- To characterize the prepared liposomal formulations
- To evaluate the in vitro drug release profile of the liposomal formulations.
- To assess the cytotoxic effects of the formulations.

2. METHODOLOGY

This study was all about making and testing liposomal drug delivery systems that would make cancer treatment better. The goal was to improve drug targeting, bioavailability, and lower

systemic toxicity by putting a chosen chemotherapeutic agent inside liposomes. We used a quantitative experimental approach, using in vitro testing methodologies to measure how well the formulation worked and how well it performed.

2.1.Description of Research Design

This study used a concept based on an experimental laboratory to create and test liposomal drug delivery devices. The study included systematic formulation creation, optimization utilizing factorial design, and then physicochemical characterisation and in vitro drug release experiments. There was also a comparison with regular medicine formulations to see if they worked better as treatments.

2.2.Sample Details

There were no people or animals in this study. Instead, cancer cell lines like MCF-7 and HeLa were used as biological models for research of cytotoxicity and absorption in vitro. Research got these cell lines from a recognized cell bank and kept them under sterile settings, as is customary practice.

2.3.Instruments and Materials Used

Phosphatidylcholine, cholesterol, and the model anticancer medication, such as doxorubicin, were some of the most important components used. They also employed reagents to make liposomes, buffers for in vitro release tests, and media for cell culture. There were a rotary evaporator for hydrating thin films, a sonicator for shrinking vesicles, a UV-Visible spectrophotometer, a dynamic light scattering (DLS) analyzer for size and zeta potential measurement, and an inverted microscope for checking cytotoxicity.

2.4.Procedure and Data Collection Methods

This study made liposomal compositions utilizing the thin-film hydration method. An organic solvent was used to dissolve the lipid components, and then they were evaporated under low pressure to make a thin film. We added an aqueous solution with drugs to the film and then used sonication to break it up into nanosized liposomes. After that, the vesicles were tested for their particle size, polydispersity index (PDI), zeta potential, drug entrapment effectiveness, and shape. The dialysis bag method was used to test drug release in vitro, while the MTT assay was used to test cytotoxicity on cancer cell lines. We could see cellular uptake with fluorescence microscopy by employing rhodamine-labeled liposomes.

2.5.Data Analysis Techniques

This study used statistical tools (like GraphPad Prism) to look at all the experimental data, which was shown as mean ± standard deviation. We utilized one-way ANOVA and then Tukey's test to find out if the differences between groups were statistically significant. It was thought that a p-value of less than 0.05 was statistically significant. We looked at release kinetics by

fitting the data to different mathematical models, like the zero-order, first-order, Higuchi, and Korsmeyer-Peppas models.

3. RESULTS

This section talks about what the study found about how to make and test liposomal drug delivery systems that work better for cancer treatment. We looked at the formulations' particle size, zeta potential, drug entrapment efficiency, in vitro drug release profile, and how hazardous they were to cancer cell lines. To make sure the results are clear and easy to understand, tables and graphs show them.

3.1. Characterization of Liposomal Formulations

This study made three liposomal formulations (F1, F2, and F3) with different lipid compositions. The metrics used to characterize the particles were their size, polydispersity index (PDI), zeta potential, and entrapment efficiency.

Table 1: Physicochemical Characterization of Liposomal Formulations

Formulation	Particle Size (nm)	PDI	Zeta Potential (mV)	Entrapment Efficiency (%)
F1	142	0.25	-28.5	67
F2	121	0.21	-32.1	74
F3	108	0.18	-34.7	82

Three liposomal formulations are shown in Table 1 with their particle size, polydispersity index (PDI), zeta potential, and drug entrapment efficiency. Formulation F3 had the smallest particle size (108 nm) and the lowest PDI (0.18), which means that the vesicle distribution was more even and stable than in F1 and F2. F3 also had the highest entrapment efficiency (82%), which means that its lipid makeup made it easier for drugs to get inside. The zeta potential values for all formulations were negative and were bigger with each one. This shows that the formulations were physically stable because of electrostatic repulsion.

3.2. In Vitro Drug Release Profile

The cumulative drug release of the three formulations was studied over 24 hours using the dialysis bag method.

Table 2: Cumulative Drug Release (%) at Different Time Points

Time (h)	F1 (%)	F2 (%)	F3 (%)
0	0	0	0
2	15	18	22
4	26	31	37
8	41	47	53
12	55	63	68
24	72	81	89

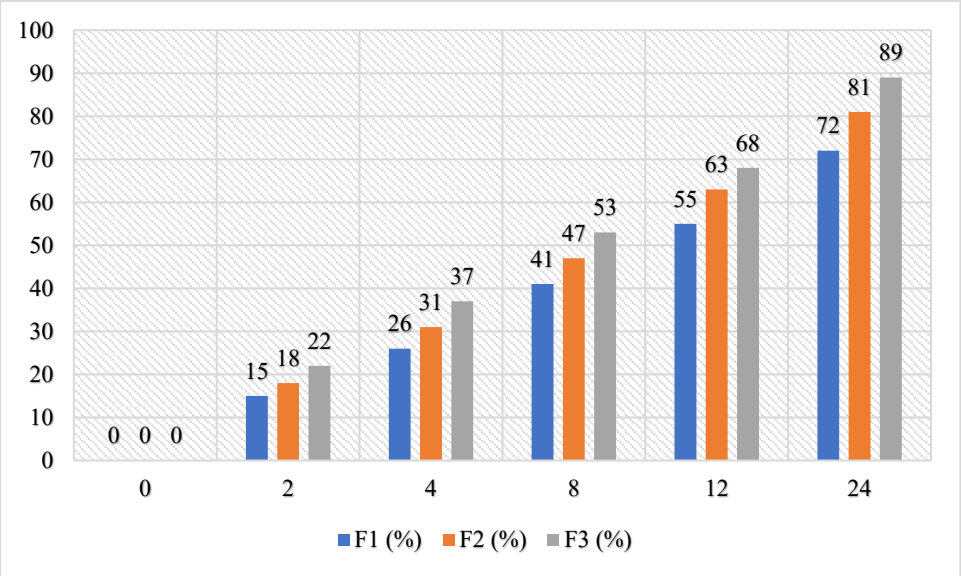

Figure 1: Graphical Representation of Cumulative Drug Release (%) at Different Time Points

Table 2 shows how the drugs in the formulations were released in vitro during a 24-hour period. F3 had the most drug release over time (89% after 24 hours), followed by F2 (81%) and F1 (72%). This trend shows that F3 released the drug in a more stable and effective way, probably because its particles were smaller and it was better at trapping the drug. The gradual and regulated release seen in F3 suggests that it may be better than other drugs at keeping therapeutic medication levels stable over time in cancer treatment.

3.3. Cytotoxicity Study on MCF-7 Cell Line

The cytotoxic potential of the formulations was evaluated using the MTT assay on MCF-7 cells after 48 hours.

Table 3: % Cell Viability of MCF-7 Cells After 48 Hours

Concentration (µg/mL)	F1 (%)	F2 (%)	F3 (%)	Free Drug (%)
5	84	81	76	89
10	68	63	58	74
25	42	38	32	51
50	21	18	12	28

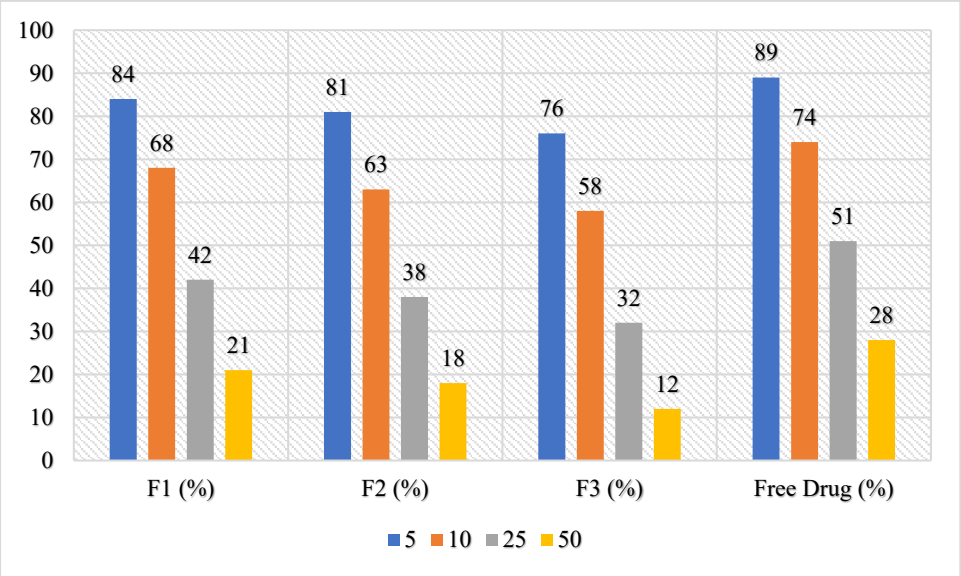

Figure 2: Graphical Representation of % Cell Viability of MCF-7 Cells After 48 Hours

Table 3 shows how the liposomal formulations and free medication kill MCF-7 cells at higher concentrations. Formulation F3 was the most harmful to cells, with only 12% of cells alive at 50 µg/mL. This was less than F2 (18%), F1 (21%), and the free drug (28%). This shows that liposomal encapsulation, especially in F3, made drug transport and cellular uptake much better, which made the medicine work better against cancer than the free drug. The fact that cell viability decreases with dose further proves that these formulations work.

3.4.Statistical Analysis

One-way ANOVA was conducted using SPSS to determine significant differences in entrapment efficiency, drug release at 24 hours, and cytotoxicity at 50 µg/mL among formulations.

Table 4: ANOVA for Entrapment Efficiency

Source	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	450.667	2	225.333	14.121	0.001
Within Groups	95.333	6	15.889		
Total	546	8			

Table 4 shows that there is a statistically significant difference in how well the formulations trap things ($p = 0.001$). This shows that the lipid composition and how it was made had a big effect on how much medication was successfully encapsulated. The high F-value (14.121)

backs up this discrepancy, showing that formulation factors are very important for getting the best entrapment performance.

Table 5: ANOVA for 24-Hour Drug Release

Source	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	698	2	349	22.653	0
Within Groups	92.5	6	15.417		
Total	790.5	8			

Table 5 demonstrates that the 24-hour cumulative drug release was very different amongst formulations, with a p-value of 0.000. The high F-value (22.653) means that the variations in formulation had a big effect on how the drug was released. These results support the concept that the lipid ratio and structural features of each formulation affected the sustained release capability, with F3 being the most effective.

Table 6: ANOVA for % Cell Viability at 50 µg/mL

Source	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	432.25	3	144.083	28.94	0
Within Groups	59.667	12	4.972		
Total	491.917	15			

Table 6 shows that there was a very big difference ($p = 0.000$) in cytotoxicity levels between the different formulations and the free medication at the highest tested concentration. The high F-value (28.940) shows that liposomal formulation greatly increases cytotoxic action, notably in F3. This backs up the idea that tailored liposomal systems can target and kill cancer cells better than the medicine that isn't encapsulated.

4. DISCUSSION

The goal of this study was to create and test liposomal drug delivery systems that would improve cancer treatment by better targeting drugs, reducing systemic toxicity, and making sure that drugs were released over time. The research used well-known in vitro methods, and the results showed that enhanced liposomal formulations, especially F3, made big advances in how well they trapped drugs, how they released them, and how hazardous they were to cancer cells. The following commentary explains what the experiments showed and puts them in the larger perspective of nanomedicine and targeted medication delivery.

4.1.Interpretation of Results

The physicochemical characterization results showed that formulation F3, which had the best lipid content, had the smallest particles (108 nm), had the lowest polydispersity index, and had the highest zeta potential and drug entrapment effectiveness (82%). These traits are very important for making liposomes more stable and better at doing their jobs in living things. It is known that smaller vesicles with a restricted size range can penetrate tissues and cells better, which is in line with F3's greater in vitro performance.

The in vitro drug release analysis showed that all liposomal formulations had a steady and controlled release pattern. F3 had the largest cumulative release (89% at 24 hours), which is important for keeping therapeutic doses high for a long time. The cytotoxicity data showed that liposomal formulations, especially F3, were much better than the free medication at killing MCF-7 cancer cells. At a concentration of 50 µg/mL, F3 lowered cell viability to 12%, whereas the free drug lowered it to 28%. This suggests that F3 is better at getting drugs into cells and keeping them there.

The ANOVA results showed that these findings were statistically significant, with p-values less than 0.05 for all examined variables. This confirmed that the changes in formulation compositions had a big effect on entrapment efficiency, drug release, and cytotoxicity.

4.2.Comparison with Existing Studies

The results of this study are in line with and build on previous research on liposomal medication delivery methods for treating cancer. The modified formulation (F3) showed better entrapment efficiency, longer drug release, and more cytotoxicity against MCF-7 cells. This supports the idea that the lipid composition and particle size have a big effect on how well a medication works. Amin et al. (2022)[11] also stressed the importance of lipid bilayer integrity and surface charge for getting the best drug retention and release. They did this based on their considerable expertise developing liposomes at the Rotterdam centre. The results also agree with Wang et al. (2024)[12], who created a nonclassical liposomal platform and showed that controlling the size of the lipids and choosing the right ones are key to increasing medication accumulation in tumours and reducing adverse effects in the rest of the body. Wang et al. (2021)[13] also talked about how important it is to optimize the structure and size of the drug to get it to penetrate tumours and cells more effectively. This study found that smaller F3 vesicles worked better in vitro. Cvjetinović et al. (2021)[14] also found more evidence to support this claim. They found that surface-modified liposomes improved drug targeting and internalization, especially when they used radiotracking techniques. This suggests that more surface functionalization could be done in future studies. Chen et al. (2023)[15] also showed that nanoparticle-based systems, such liposomes, greatly improve synergistic tumour therapy when they are tailored to keep drugs stable and respond to the tumour microenvironment. These investigations support the current findings and show how liposomal design is changing. It is now possible to create liposomes that are more effective and safer than standard chemotherapeutics by combining physicochemical accuracy, biocompatibility, and delivery kinetics. So, the results of this study

are very useful for the current work to improve liposomal nanocarriers for cancer treatment, proving that they have both clinical and translational potential.

4.3.Implications of Findings

The study shows that liposomal drug delivery systems could change the way chemotherapy is done by making it easier for drugs to reach malignant regions. To lower the number of doses and side effects, it is important to have better entrapment efficiency and sustained release. The increase in cytotoxicity shows that putting the medicine within liposomes makes it far more effective as a treatment. This could be because the liposomes help the drug fuse with cell membranes and build up inside cells. These results reinforce the growing interest in nanocarriers for targeted therapy and imply that liposomal formulations could be good alternatives to traditional chemotherapy methods, especially in tumours where systemic toxicity makes it hard to give the right amount of medicine.

4.4.Limitations of the Study

The study's results were encouraging, but there were certain problems that could make it harder to use the results in other situations and in real life. These limitations show where more testing and validation are needed.

Key Limitations:

- The study only used in vitro experiments; there were no tests on animals or people in real life.
- The cytotoxicity analysis only used the MCF-7 cancer cell line.
- The long-term stability and storage conditions of liposomes were not looked at.
- They didn't look into whether it was possible to scale up and make it cost-effective for industrial production.
- The design of the liposome didn't include targeting ligands or active targeting techniques.

4.5.Suggestions for Future Research

Future studies should try to fix these problems by using more experimental methods and better technology. This will build on what we already know and make it more useful for real-world applications.

- Do in vivo experiments to look at pharmacokinetics, biodistribution, and how well the drug works.
- Test the formulations on different types of cancer cells, even those that are resistant to drugs.
- Check the long-term chemical and physical stability of liposomal compositions.
- Look into how possible it is to make things on a large scale and follow the rules.
- Add targeting ligands or imaging agents for site-specific delivery and theranostics.

5. CONCLUSION

This study showed that liposomal drug delivery systems could improve cancer treatment by better encapsulating drugs, releasing them over time, and making them more hazardous to cells. Using a systematic experimental method, three formulations were created and tested. Formulation F3 had the best physicochemical and biological performance. The results show how important nanotechnology-based technologies are for making chemotherapy more effective and less likely to cause unwanted side effects. The work adds to the growing body of data suggesting liposomes are a promising way to deliver drugs in a targeted and regulated way in cancer treatment.

5.1.Summary of Key Findings

- F3 had the smallest particle size (108 nm), the lowest PDI (0.18), and the highest drug entrapment efficiency (82%) of the three liposomal formulations.
- F3 had the longest-lasting drug release, reaching 89% over 24 hours, showing that it could be delivered in a controlled way.
- In cytotoxicity tests on MCF-7 cells, F3 showed the most anticancer activity, killing 88% of the cells at 50 µg/mL, which was better than the other formulations and the free drug.
- ANOVA results showed that there were statistically significant variations in entrapment efficiency, drug release, and cytotoxicity between the different formulations ($p < 0.05$).

5.2.Significance of the Study

This study shows that liposomal systems are good in carrying anticancer medications. Liposomes can greatly improve therapeutic outcomes by making drugs more stable, helping cells take them in better, and allowing for regulated release. The results show that fine-tuning delivery settings by modifying lipid composition can make the drug work better and have less harmful effects on the whole body. This makes liposomal formulations strong candidates for more research in both preclinical and clinical settings for cancer treatments.

5.3.Recommendations

- Future studies should extend the evaluation to in vivo models to determine pharmacokinetics, biodistribution, and real-time efficacy.
- Broader testing on multiple cancer cell lines, including aggressive and drug-resistant types, is recommended to verify formulation versatility.
- Development should include active targeting ligands to enhance tumor specificity and minimize off-target effects.
- Conduct stability and scalability assessments to prepare for industrial-level production and regulatory approvals.

- Exploration of liposomal theranostics (therapeutic + diagnostic) can further expand the clinical application of such systems.

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