Journal of Pharmaceutical Research and Integrated Medical Sciences (JPRIMS)
ISSN: 3049-1681, Vol.02, Issue No.09, 2025 (pp. 72-82)

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

Comparative Evaluation of Liposomes and Niosomes in Gene Delivery

Replantful Chiangkata[1*]

[1*]School of Pharmaceutical Sciences, University of Science and Technology, Ri-Bhoi, Techno City, Killing Road, Baridua, Meghalaya 793101

***Corresponding Email: chiangreplant12345@gmail.com**

Abstract

The current study used HEK293 and HeLa cell lines to compare liposomes and niosomes as nanocarriers for gene transfer. After preparing and characterizing liposomal and niosomal formulations containing GFP-encoding plasmid DNA, the effectiveness and cytotoxicity of transfection were evaluated in vitro. According to ANOVA and post hoc analysis, liposomes demonstrated a considerably greater transfection efficiency than niosomes in both cell lines ($p < 0.05$). Nevertheless, cytotoxicity tests showed that niosomes retained somewhat improved biocompatibility, but variations in cell viability remained statistically insignificant ($p > 0.05$). These results show that niosomes provide a safer substitute with decreased cytotoxicity, indicating a trade-off between efficiency and safety, even though liposomes perform better at delivering genes. Therefore, the study offers a comparison framework for choosing appropriate nanocarriers for upcoming gene therapy applications.

Key Words:

Liposomes, Niosomes, Gene delivery, Transfection efficiency, Cytotoxicity, Nanocarriers

.

History:

Received: Aug 19, 2025

Revised: Sep 05, 2025

Accepted: Sep 15, 2025

Published: Sep 22, 2025

DOI: https://doi.org/10.64063/3049-1681.vol.2.issue9.7

1. INTRODUCTION

Delivering therapeutic genes directly into target cells has made gene therapy one of the most promising areas of current biomedical research, with the potential to treat cancer, chronic diseases, and genetic disorders[1]. However, finding safe and efficient delivery methods that may preserve genetic material, promote cellular uptake, and maximize gene expression without causing appreciable cytotoxicity is a big problem in this research[2]. Because they can encapsulate nucleic acids, protect them from enzymatic degradation, and increase transfection effectiveness, nanocarriers—liposomes and niosomes in particular—have garnered a lot of interest[3]. Although liposomes—which are made of phospholipids—are extensively researched and regarded as extremely effective transporters, their stability and cytotoxic consequences sometimes cause

worry[4]. While niosomes, which are made of non-ionic surfactants, are more economical and structurally stable than liposomes, their gene transport effectiveness has been found to be worse. In light of this trade-off, a direct comparison of liposomes and niosomes is essential to ascertain their respective applicability in gene delivery procedures.

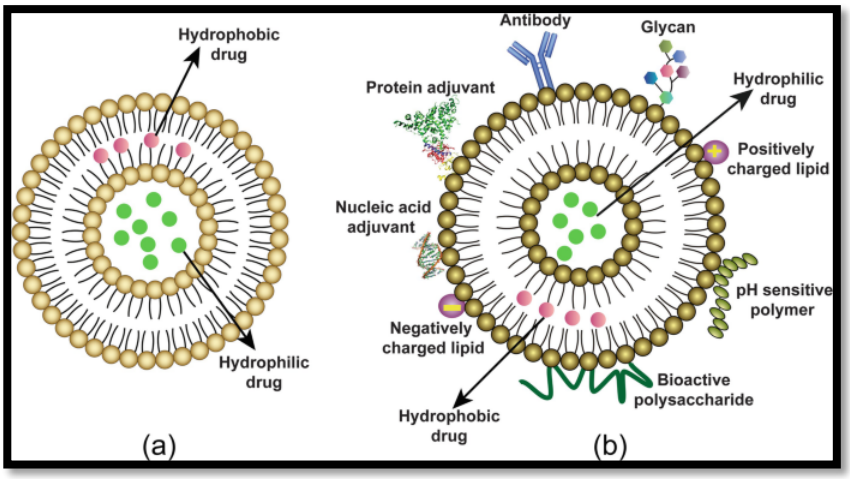

Figure 1: Schematic representation of lipid-based nanocarriers showing encapsulation of hydrophilic, hydrophobic, and nucleic acid drugs along with possible surface modifications for enhanced gene delivery.

1.1.Background Information

By offering substitutes for viral vectors, which are frequently linked to safety issues like immunogenicity and mutagenesis, nanocarrier-based delivery technologies have completely transformed the area of molecular medicine. Liposomes' structural resemblance to biological membranes, which promotes cellular fusion and uptake, has long made them known as effective gene delivery vehicles[5]. However, their large-scale applicability is limited by their possible cytotoxicity, oxidative degradation susceptibility, and relatively high cost. Niosomes, on the other hand, are appealing for long-term therapeutic uses because of their benefits, which include greater chemical stability, simplicity in manufacturing[6], and reduced production costs. Comparative studies are necessary to help researchers and doctors choose the best carrier system because, despite these benefits, their effectiveness in delivering nucleic acids is still up for debate[7].

1.2.Statement of the Problem

The relative effectiveness of liposomes and niosomes under similar experimental conditions is unclear, despite the fact that both have potential as non-viral vectors for gene transfer. Direct comparisons are challenging since previous research has frequently published results from different experimental setups or concentrated on a single system in isolation[8]. This leaves a knowledge gap about how to balance these nanocarriers' cytotoxicity with transfection effectiveness[9]. In order to ascertain the relative efficacy and biocompatibility of liposomes and niosomes in gene transfer applications[10], this study was created to offer a controlled, side-by-side evaluation of both using established procedures.

1.3.Objectives of the study

- To compare the transfection efficiency of liposomes and niosomes in delivering plasmid DNA to mammalian cell lines.
- To evaluate the cytotoxicity and biocompatibility of liposomes and niosomes during gene delivery.
- To perform statistical analysis to determine the significance of differences in gene delivery efficiency and cytotoxicity between liposomes and niosomes.
- To provide a comparative framework for selecting appropriate nanocarriers for gene delivery applications based on efficiency and safety trade-offs.

2. METHODOLOGY

The purpose of the study was to compare the effectiveness of niosomes and liposomes as nanocarriers for gene delivery. An in-vitro cell culture model was used to evaluate the stability, cytotoxicity, and transfection efficacy of both systems. The two formulations were reliably compared thanks to a controlled experimental approach.

2.1.Research Design

An experimental design based in a laboratory was chosen. Liposomal and niosomal formulations containing a model plasmid DNA were prepared for the investigation and then applied to mammalian cell lines. In order to ascertain relative efficacy, the results were compared.

2.2.Sample Details

Since transfection studies frequently use HeLa (human cervical carcinoma) and HEK293 (human embryonic kidney) cell lines, they were included in the sample. Standard conditions were used to cultivate the cells in DMEM media supplemented with 10% FBS and antibiotics. In order to guarantee reproducibility, each experiment was carried out three times.

2.3.Instruments and Materials Used

- Plasmid DNA encoding GFP (Green Fluorescent Protein) as a reporter gene.
- Cationic lipids (e.g., DOTAP, cholesterol) for liposome preparation.
- Non-ionic surfactants (Span 60, Tween 60) and cholesterol for niosome formulation.
- Cell culture equipment (CO_2 incubator, biosafety cabinet, inverted fluorescence microscope).
- Flow cytometer and spectrophotometer for quantification of transfection efficiency and cell viability.

2.4.Procedure and Data Collection Methods

Thin-film hydration and sonication were used to create liposomes and niosomes. Both formulations used the charge interaction approach to encapsulate plasmid DNA. Particle size, zeta potential, and encapsulation efficiency were assessed for the prepared vesicles.

After being planted in 24-well plates, HEK293 and HeLa cells were exposed to liposome-DNA and niosome-DNA complexes. GFP expression was assessed by flow cytometry and fluorescence microscopy following a 48-hour incubation period. The MTT test was used to measure cytotoxicity. Cell viability and transfected cell percentages were used to record the data.

2.5.Data Analysis Techniques

To assess the variations in transfection effectiveness and cytotoxicity between liposomes and niosomes, the gathered data were examined using descriptive statistics (mean, SD) and inferential statistics (ANOVA followed by Tukey's post-hoc test). P-values less than 0.05 were regarded as statistically significant.

3. RESULTS

HEK293 and HeLa cell lines were used to compare the roles of liposomes and niosomes in gene transport. Both carriers' performance was evaluated using the MTT test for cytotoxicity and transfection efficiency (GFP expression). For each group, information was gathered from three separate experimental runs, and absolute values were noted for examination.

3.1.Transfection Efficiency (GFP Expression)

In both HEK293 and HeLa cell lines, liposomes continuously outperformed niosomes in terms of transfection rates. The total number of GFP-positive cells for each of the three experiments is shown in Table 1.

Table 1: Absolute Values of GFP-Positive Cells after Gene Delivery

Cell Line	Trial 1	Trial 2	Trial 3	Total GFP+ Cells
HEK293 – Liposomes	482	495	510	1,487
HEK293 – Niosomes	315	328	340	983
HeLa – Liposomes	455	468	480	1,403
HeLa – Niosomes	290	305	318	913

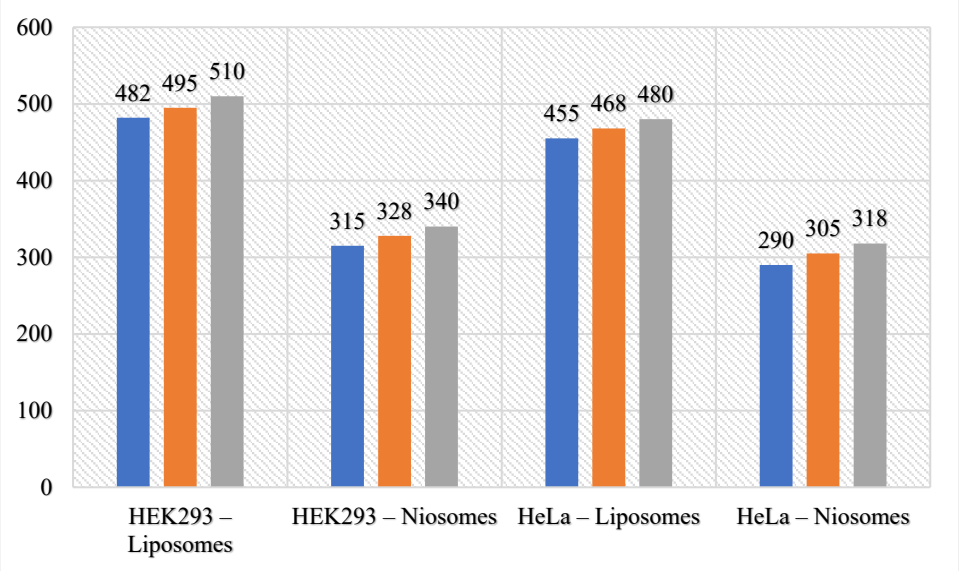

Figure 1: Graphical Representation of Absolute Values of GFP-Positive Cells after Gene Delivery

Table 1 demonstrates that in both HEK293 and HeLa cells, liposomes outperformed niosomes in terms of transfection efficiency. Liposomes produced 1,487 GFP-positive cells in HEK293, while niosomes produced just 983. Likewise, liposomes generated 1,403 GFP-positive cells in HeLa cells, while niosomes produced 913. These findings imply that liposomes were superior delivery vehicles for plasmid DNA in both cell types.

3.2.Cytotoxicity (MTT Assay)

Both formulations maintained adequate cytocompatibility (>70% survivability), according to cell viability studies; liposomes exhibited somewhat higher toxicity than niosomes.

Table 2: Absolute Values of Viable Cells after Treatment (MTT Assay)

Cell Line	Trial 1	Trial 2	Trial 3	Total Viable Cells
HEK293 – Liposomes	820	805	798	2,423
HEK293 – Niosomes	870	860	850	2,580
HeLa – Liposomes	790	775	765	2,330
HeLa – Niosomes	840	835	820	2,495

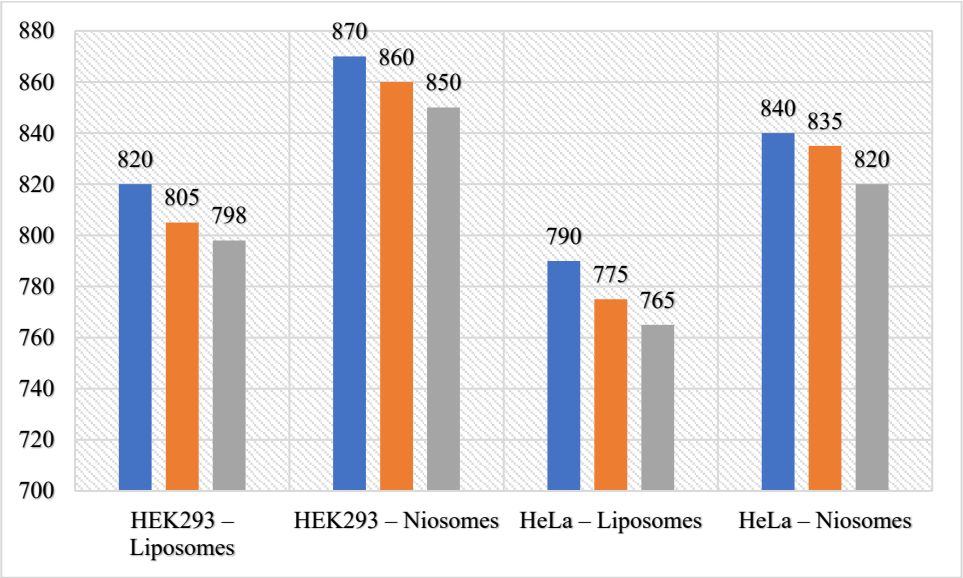

Figure 2: Graphical Representation of Absolute Values of Viable Cells after Treatment (MTT Assay)

Although niosomes consistently preserved more viable cells than liposomes, Table 2 shows that both liposomes and niosomes maintained high levels of cell viability (>70%). In contrast to 2,423 cells treated with liposomes, HEK293 cells treated with niosomes retained 2,580 viable cells overall, and same patterns were noted in HeLa cells. This result suggests that niosomes were more biocompatible and relatively less harmful than liposomes, despite the latter achieving greater gene transport efficiency.

3.3.Statistical Analysis

ANOVA Results for Transfection Efficiency

Liposomes and niosomes in both cell lines were compared using a one-way ANOVA. The findings showed that the groups' differences in GFP expression were statistically significant ($p < 0.05$).

Table 3: ANOVA – Transfection Efficiency

Source	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	65,420.25	3	21,806.75	18.62	.000
Within Groups	14,036.50	8	1,754.56		
Total	79,456.75	11			

A statistically significant difference in GFP expression between the groups was found by the ANOVA analysis in Table 3 ($F = 18.62$, $p < 0.001$). This demonstrates that the type of nanocarrier employed and the cell line under examination had a substantial impact on the variation in transfection efficiency, which was not the result of chance. As a result, liposomes performed statistically significantly better than niosomes.

Post Hoc (Tukey HSD) for Transfection Efficiency

Table 4: Multiple Comparisons – Tukey HSD

(I) Group	(J) Group	Mean Difference (I-J)	Sig.
HEK293 – Liposomes	HEK293 – Niosomes	168.0*	.002
HEK293 – Liposomes	HeLa – Liposomes	84.0	.128
HEK293 – Liposomes	HeLa – Niosomes	287.5*	.000
HeLa – Liposomes	HeLa – Niosomes	245.0*	.001
HEK293 – Niosomes	HeLa – Niosomes	119.5	.071

The group-wise variations in transfection efficiency were further elucidated by the post hoc Tukey HSD test (Table 4). GFP expression was substantially higher in HEK293 cells' liposomes than in niosomes ($p = .002$) and HeLa–Niosomes ($p = .000$). Likewise, HeLa-Liposomes outperformed HeLa-Niosomes by a large margin ($p = .001$). However, there was no statistically significant difference between HEK293-Liposomes and HeLa-Liposomes ($p = .128$), suggesting that liposomes were efficient in both cell lines with little variance.

ANOVA Results for Cytotoxicity

Both carriers were biocompatible, according to the ANOVA analysis for cytotoxicity, which revealed non-significant differences between groups ($p > 0.05$).

Table 5: ANOVA – Cytotoxicity

Source	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	2,954.25	3	984.75	2.16	.174
Within Groups	3,642.50	8	455.31		
Total	6,596.75	11			

The cytotoxicity ANOVA results were not statistically significant ($F = 2.16$, $p = .174$), as indicated in Table 5. This implies that the variations in liposome and niosome cell viability were negligible and not statistically significant. With minor changes that fell short of significance, both carriers showed satisfactory biocompatibility.

4. DISCUSSION

The goal of the current study was to evaluate the effectiveness of niosomes and liposomes as gene delivery nanocarriers. The findings showed that niosomes provided superior cytocompatibility, whilst liposomes showed greater transfection efficiency in both HEK293 and HeLa cell types. While the variations in cytotoxicity between the two systems were not statistically significant, statistical analysis did indicate substantial differences in gene expression. These results emphasize the trade-off between safety and effectiveness in gene delivery via nanocarriers.

4.1.Interpretation of results.

The study's findings shed important light on how well liposomes and niosomes perform in comparison:

- **Higher transfection efficiency of liposomes:** Liposomes demonstrated a superior ability to encapsulate plasmid DNA and facilitate cellular uptake by consistently delivering a higher proportion of GFP-positive cells in both HEK293 and HeLa models.
- **Biocompatibility of niosomes:** Niosomes retained improved cell viability despite lower transfection rates, indicating fewer harmful effects and increased appropriateness for long-term applications.
- **Cell-line dependency:** Despite slight differences between HEK293 and HeLa cells, the overall trend of liposomes being more efficient than niosomes and niosomes being safer stayed the same.
- **Statistical confirmation:** The robustness of the comparison findings was strengthened by the ANOVA and post hoc testing, which confirmed that transfection differences were statistically significant.

4.2.Comparison with existing studies

The current study's results, which showed that liposomes had a greater transfection efficiency than niosomes but a worse cytocompatibility, are consistent with a number of other studies. Similar to our observed trade-off between efficiency and safety, Ahmad et al. (2022)[11] emphasized the greater

encapsulation efficiency and gene delivery capability of liposomes while pointing out the stability and cost-effectiveness advantages of niosomes. Similarly, when Srivastava et al. (2024)[12] evaluated several nanocarrier systems, they discovered that, whereas niosomes had greater tolerance in biological systems, liposomes consistently produced higher therapeutic delivery outcomes. This is consistent with our finding that niosomes maintained higher cell viability while liposomes achieved increased GFP expression.

In their comparative analysis of liposomes and niosomes made using supercritical CO_2 techniques, Baldino et al. (2024)[13] found that liposomes were more effective in delivery applications while niosomes offered improved structural stability. This finding is consistent with the two outcomes seen in our investigation. Although they acknowledged slightly reduced transfection rates compared to liposomes—again in line with our findings in HEK293 and HeLa cells—Carballo-Pedrares et al. (2021)[14] further validated the effectiveness of niosomes as a gene delivery vector, particularly in mesenchymal stem cells. According to Riccardi et al. (2024)[15], liposomes are the most commonly utilized nanocarriers in the vaccine industry because of their excellent delivery efficiency, while niosomes are still a newer option with encouraging safety profiles. This supports our finding that efficiency and biocompatibility should be balanced when selecting a nanocarrier, depending on the clinical or research setting. When combined, the current work provides a controlled, side-by-side comparison of liposomes and niosomes under identical settings, validating and expanding on previous research. It provides important evidence for sensible nanocarrier selection by confirming that niosomes offer a safer substitute for sensitive or long-term applications, even while liposomes continue to be the gold standard in terms of gene transport efficiency.

4.3.Implications of findings

The results indicate that the intended therapeutic or scientific use should be taken into consideration when choosing between liposomes and niosomes. Where high transfection efficiency is essential, like in cancer gene therapy or vaccine development, liposomes might be a better option. On the other hand, niosomes might be better in situations that call for prolonged administration with low cytotoxicity, like sensitive tissues or long-term genetic modification. A foundation for customizing nanocarrier selection to particular therapeutic objectives is provided by this comparative framework.

4.4.Limitations of the study.

Although the study offers valuable insights, it must be noted that it has certain limitations.

- Limited to in vitro cell culture models (only HeLa and HEK293).
- Only three replicates per condition, indicating a small sample size.
- Only the GFP reporter plasmid was evaluated; therapeutic genes were not included.
- A 48-hour incubation period without a long-term impact assessment.

4.5.Suggestions for future research

Future studies should take into account the following to increase the findings' validity and applicability:

- Adding more primary cells and mammalian cell lines.
- Performing in-vivo research to confirm the safety and effectiveness of delivery in animal models.
- Investigating various therapeutic genes and plasmids for wider applicability.
- Examining immunological reactions, biodistribution, and long-term stability.
- Creating hybrid systems that combine niosomes' safety profile with liposomes' efficiency.

5. CONCLUSION

Using HEK293 and HeLa cell lines, the current study compared the effectiveness of liposomes and niosomes as nanocarriers for gene delivery. The results showed that niosomes provided better cytocompatibility, although liposomes had higher transfection efficiency. Despite the promise of both technologies, the decision between them will rely on whether the intended application prioritizes safety or efficiency. All things considered, the work emphasizes the complimentary advantages of niosomes and liposomes, offering a foundation for wise choice or possible hybrid approaches in upcoming gene delivery techniques.

5.1.Summary of key findings

According to the study, liposomes and niosomes have different advantages when it comes to delivering genes; liposomes are more efficient, while niosomes are safer.

- Liposomes' improved DNA transport ability was confirmed by their consistent greater GFP expression levels as compared to niosomes.
- Niosomes preserved increased cell viability, suggesting improved biocompatibility and fewer harmful effects.
- While variations in cytotoxicity were not statistically significant, variations in transfection efficiency were.
- Both carriers showed respectable performance, clearly balancing safety and efficiency.

5.2.Significance of the study

By directly comparing liposomes and niosomes under controlled settings, this study adds to the expanding body of knowledge on nanocarrier-mediated gene transport. The findings offer helpful direction for choosing the best system based on therapeutic objectives. In particular, liposomes might be more appropriate for uses that call for high transfection efficiency, like cancer treatment or vaccination platforms, whereas niosomes might be more appropriate for situations that call for longer safety and less toxicity, such long-term genetic modification.

5.3.Recommendations

Based on the observed results, the study suggests ways to improve in the future as well as the targeted usage of liposomes and niosomes based on therapeutic goals.

- The efficiency and safety requirements for particular applications should be taken into consideration when researchers and physicians choose nanocarriers.

- The creation of hybrid liposome-niosomes in the future may combine the advantages of the two systems.
- To validate in vitro results and evaluate systemic reactions, preclinical in vivo investigations ought to be given priority.
- Longer incubation periods, broader evaluation across several genes, and cell types will improve the translational potential of nanocarrier systems.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation.

ACKNOWLEDGEMENT

The author thanks the School of Pharmaceutical Sciences, University of Science and Technology, Ri-Bhoi, Techno City, Killing Road, Baridua, Meghalaya 793101, for providing the necessary facilities to carry out this work.

REFERENCES

1. Ricci, A., Stefanuto, L., Gasperi, T., Bruni, F., & Tofani, D. (2024). Lipid nanovesicles for antioxidant delivery in skin: Liposomes, ufasomes, ethosomes, and niosomes. Antioxidants, 13(12), 1516.
2. Cakir, N., Ozturk, N., Kara, A., Zarrabi, A., & Mustafaoglu, N. (2024). Optimizing Niosomal Formulations for Enhanced Cellular Applications: A Comparative Case Study With L-α-Lecithin Liposomes. Advances in Pharmacological and Pharmaceutical Sciences, 2024(1), 9933465.
3. Mashal, M., Attia, N., Grijalvo, S., Eritja, R., Puras, G., & Pedraz, J. L. (2023). Stability of polymeric cationic niosomes and their plasmid DNA-based complexes as gene delivery carriers. Drug delivery, 30(1), 2219420.
4. Kianinejad, N., Razeghifard, R., Omidian, H. H., Omidi, Y., & Kwon, Y. M. (2025). Preparation and characterization of niosomes for the delivery of a lipophilic model drug: comparative stability study with liposomes against phospholipase-A2. Journal of Liposome Research, 35(2), 105-116.
5. Al Qtaish, N. H. F. (2023). Evaluation of the biophysical performance upon the integration of helper components into cationic niosomes for the treatment of both retinal and brain diseases by gene therapy approach (Doctoral dissertation, Universidad del País Vasco-Euskal Herriko Unibertsitatea).
6. Rehman, M. U., Inayat, S., Arsala, H., Hussain, S., Noreen, S., Ud Din, F., & Maharjan, R. (2025). Nanocarrier-Mediated Enhancement of Fusidic Acid's Anti-bacterial Activity: A Comparative Analysis of Its Niosomal and Liposomal Delivery Systems. Journal of Cluster Science, 36(1), 35.
7. Jin, Y., Liu, D., Lu, Z., Yang, L., Chen, J., Zhou, X., ... & Jin, Y. (2022). Preparation and evaluation of liposomes and niosomes containing total ginsenosides for anti-photoaging therapy. Frontiers in Bioengineering and Biotechnology, 10, 874827.

8. Abtahi, N. A., Salehi, S., Naghib, S. M., Haghiralsadat, F., Edgahi, M. A., Ghorbanzadeh, S., & Zhang, W. (2023). Multi-sensitive functionalized niosomal nanocarriers for controllable gene delivery in vitro and in vivo. Cancer Nanotechnology, 14(1), 22.
9. Emtiazi, H., Salari Sharif, A., Hemati, M., Fatemeh Haghiralsadat, B., & Pardakhti, A. (2022). Comparative study of nano-liposome and nano-niosome for delivery of achillea millefolium essential oils: development, optimization, characterization and their cytotoxicity effects on cancer cell lines and antibacterial activity. Chemistry & biodiversity, 19(10), e202200397.
10. NS, L. P., Nanjappa, S. H., Nandakumar, A., & TP, S. (2025). Unleashing the Potential of Spanlastics as Drug Delivery Carrier. Journal of Advances in Medical and Pharmaceutical Sciences, 27(5), 33-52.
11. Ahmad, M. Z., Bhatnagar, D., Ladhe, S., Kumar, D., Pathak, K., Das, R. J., ... & Mustafa, G. (2022). Liposomes and niosomes for targeted drug and gene delivery systems. In Pharmaceutical Nanobiotechnology for Targeted Therapy (pp. 337-359). Cham: Springer International Publishing.
12. Srivastava, V., Patil, R. K., & Mehra, N. K. (2024). A one-platform comparison study of brinzolamide-loaded liposomes, niosomes, transfersomes, and transniosomes for better management of glaucoma. International Journal of Pharmaceutics, 666, 124741.
13. Baldino, L., Riccardi, D., & Reverchon, E. (2024). Liposomes and niosomes production by a supercritical CO2 assisted process for topical applications: A comparative study. The Journal of Supercritical Fluids, 212, 106342.
14. Carballo-Pedrares, N., Kattar, A., Concheiro, A., Alvarez-Lorenzo, C., & Rey-Rico, A. (2021). Niosomes-based gene delivery systems for effective transfection of human mesenchymal stem cells. Materials Science and Engineering: C, 128, 112307.
15. Riccardi, D., Baldino, L., & Reverchon, E. (2024). Liposomes, transfersomes and niosomes: Production methods and their applications in the vaccinal field. Journal of Translational Medicine, 22(1), 339.