J Appl Biotechnol Rep. 2026 June;13(2):2052-2060

Journal of
Applied Biotechnology Reports

doi 10.30491/jabr.2025.548971.1920

Original Article

Development and Characterization of Niosomal Nanoparticles for Simultaneous Co-Delivery of Tamoxifen and Curcumin in Breast Cancer Therapy

Seyedhamidreza Emadiyanrazavi [1], Mehdi Kamali [2], Mohammad Hasan Darvishi [3], Hamidreza Javadi [3*]

[1] Department of Biomedical Engineering, Central Tehran Branch, Islamic Azad University, Tehran, Iran
[2] Department of Biotechnology, Faculty of Biological Science and Technology, Shahid Ashrafi Esfahani University, Isfahan, Iran
[3] Nanobiotechnology Research Center, New Health Technologies Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

Corresponding Author: Hamidreza Javadi, PhD, Assistant Professor, Nanobiotechnology Research Center, New Health Technologies Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran. Tel: +98-9143613493, E-mail: hjavadi53r@gmail.com

Received September 24, 2025; **Accepted** November 22, 2025; **Online Published** June 30, 2026

Abstract

Introduction: Breast cancer remains one of the most prevalent malignancies and a leading cause of cancer-related mortality worldwide. Although chemotherapeutic agents such as tamoxifen are widely employed, their therapeutic efficacy is often limited by poor bioavailability and adverse side effects. Combining tamoxifen with curcumin, a natural polyphenolic compound with well-documented anticancer potential, may enhance treatment outcomes through synergistic interactions. However, the clinical application of both agents is restricted due to issues such as low solubility and rapid degradation. To address these challenges, niosomal nanoparticles were designed and evaluated for the co-delivery of tamoxifen and curcumin.

Materials and Methods: To fabricate niosomal nanoparticles, various surfactants (Span 20, Span 60, and Span 80) in combination with cholesterol were used to optimize particle size, stability, and encapsulation efficiency. The formulations were characterized for morphology, particle size distribution, zeta potential, and drug loading capacity using dynamic light scattering (DLS) and scanning electron microscopy (SEM). Additionally, *in vitro* drug release studies were performed under physiological (pH 7.4) and acidic (pH 5) conditions to simulate the tumor microenvironment. Cytotoxicity of the formulations was assessed using MCF-7 breast cancer cells and HEK-293 normal cells via the MTT Assay.

Results: The optimized niosomal formulation demonstrated high stability, efficient dual-drug encapsulation, and a controlled release profile. Cytotoxicity studies showed that Tmx/Cur-loaded niosomes exhibited stronger inhibitory effects on MCF-7 cells compared to free drug solutions, while demonstrating low toxicity toward HEK-293 cells. The physicochemical characterization confirmed uniform particle morphology and favorable zeta potential values, supporting the stability of the prepared niosomes.

Conclusions: These findings suggest that niosomal nanoparticles provide a promising carrier system for the co-delivery of tamoxifen and curcumin in breast cancer therapy, enhancing anticancer efficacy while minimizing adverse effects associated with conventional chemotherapy.

Keywords: Niosomal Nanoparticles, Tamoxifen, Curcumin, Breast Cancer, Drug Co-Delivery, Nanotechnology

Citation: Emadiyanrazavi S, Kamali M, Darvishi MH, Javadi H. Development and Characterization of Niosomal Nanoparticles for Simultaneous Co-Delivery of Tamoxifen and Curcumin in Breast Cancer Therapy. J Appl Biotechnol Rep. 2026;13(2):2052-2060. doi:10.30491/jabr.2025.548971.1920

Introduction

Breast cancer continues to be among the most prevalent and deadly cancers globally, exhibiting high incidence and mortality rates despite improvements in early detection and therapeutic approaches.[1–3] Traditional treatments, such as chemotherapy, have been central in managing breast cancer, particularly in cases of estrogen receptor-positive tumors, where tamoxifen is frequently used.[4-6] Although tamoxifen has proven to be effective in reducing tumor growth and recurrence, its clinical outcomes can be compromised by issues such as poor bioavailability, drug resistance, and significant side effects.[5,6] Additionally, curcumin, a natural polyphenolic compound with promising anticancer properties, including anti-inflammatory, pro-apoptotic, and antioxidant effects, has shown potential in the treatment of various cancers.[7,8] However, its clinical use is restricted due to low bioavailability, limited solubility, and rapid metabolic clearance.

One promising approach for improving cancer treatment involves the combination of multiple therapeutic agents.[9,10] The combination of tamoxifen and curcumin may improve therapeutic efficacy through synergistic effects, acting on multiple molecular pathways that regulate cancer cell proliferation, apoptosis, and metastasis.[9,10] The challenge, however, lies in delivering these agents effectively to tumor sites while minimizing side effects. Nanotechnology provides a promising approach to overcome the drawbacks of traditional drug delivery systems.[11-14] Nanoparticles, particularly those formed from non-ionic surfactants, have

been widely studied for their ability to encapsulate both hydrophilic and lipophilic drugs, enhancing their solubility, stability, and bioavailability.[11,12] Among these, niosomal nanoparticles, self-assembled vesicles composed of nonionic surfactants, have attracted considerable interest because they can deliver multiple drugs in a controlled and sustained fashion. Niosomes also protect encapsulated drugs from premature degradation, enabling more targeted and efficient delivery.[15–18] In this context, niosomal nanoparticles present an excellent platform for the co-delivery of tamoxifen and curcumin in breast cancer therapy. By formulating niosomes that encapsulate both drugs, it is possible to enhance their bioavailability and facilitate their targeted release at the tumor site. This approach not only aims to improve the effectiveness of treatment but also seeks to reduce the adverse side effects commonly associated with conventional chemotherapy.

The goal of this study is to develop and characterize niosomal nanoparticles designed for the simultaneous co-delivery of tamoxifen and curcumin in breast cancer therapy. By optimizing the formulation of niosomes with various surfactant combinations, this research aims to identify a system that maximizes drug encapsulation, enhances stability, and provides controlled release of both drugs. Through the development of such a delivery system, this study contributes to the ongoing efforts to improve the efficacy and reduce the side effects of cancer treatment.

Materials and Methods

Materials

Cholesterol and the surfactants (Span 20, Span 60, and Span 80) were obtained from Sigma-Aldrich (USA). Curcumin, tamoxifen, and thymol were prepared in-house using reagents obtained from local suppliers in Iran. The PBS buffer was freshly made in the laboratory by dissolving 137 mM sodium chloride, 2.7 mM potassium chloride, 10 mM disodium phosphate, and 1.8 mM potassium dihydrogen phosphate (Sigma-Aldrich, USA) in deionized water.

Preparation of Niosomal Nanoparticles Containing Tamoxifen and Curcumin

Niosomal formulations were prepared using the thin-film hydration method. Cholesterol, surfactants, and the drugs were first dissolved in chloroform, and the solvent was then evaporated using a rotary evaporator at 60 °C for 30 minutes to produce a thin lipid film. The resulting dried film was hydrated with PBS at 60 °C for 30 minutes to form niosomal vesicles. To ensure uniform particle size and effective co-encapsulation of tamoxifen and curcumin, the dispersion was further processed by sonication for 7 minutes (Table 1).

Table 1. Formulation and Characterization of Niosomes

Drug	Formulation	Surfactant type	Lipid/Drug (Molarity Ratio)	Drug concentration (mg/ml)	Sonication time (min)	Surfactant/Cholesterol (Molarity Ratio)
Tmx/Cur	TC1	Span 20	10	1-1	7	2:1
	TC2	Span 60	10	1-1	7	2:1
	TC3	Span 80	10	1-1	7	2:1
	TC4	Span 20	20	1-1	7	2:1
	TC5	Span 60	20	1-1	7	2:1
	TC6	Span 80	20	1-1	7	2:1

Characterization of Niosomes

The physicochemical properties of the prepared niosomal formulations were evaluated using Dynamic Light Scattering (DLS). Particle size and polydispersity index (PDI) were measured to assess vesicle diameter and size distribution (Table 2). This analysis confirmed that the optimized formulation (TC6) exhibited the most favorable particle size, dispersity, and overall uniformity among the prepared formulations. To examine the morphology of the niosomes, the prepared suspension was freeze-dried for 24 hours. The dried samples were then analyzed using SEM to assess their structural characteristics.

Encapsulation Efficiency (EE) Determination

For all formulations (TC1–TC6), both tamoxifen (Tmx) and curcumin (Cur) were incorporated at an initial concentration of 1 mg/ml each, corresponding to an equal drug-to-drug ratio (1:1, w/w) and a fixed lipid-to-drug molarity ratio as indicated in Table 1. Encapsulation efficiency (EE%) for each drug was determined separately following the thin-film hydration and sonication process. Briefly, freshly prepared drug-loaded niosomes were centrifuged at 14,500 rpm for 10 min at 4 °C to separate unencapsulated drug from vesicular structures. The supernatant was carefully collected and analyzed using UV–visible spectrophotometry. Tamoxifen and curcumin measured at $\lambda_{max} \approx 275$ nm and $\lambda_{max} \approx 430$ nm, respectively.

Drug concentrations were calculated using calibration curves ($R^2 > 0.999$) prepared for each compound in phosphate -buffered saline (PBS, pH 7.4) containing 0.5% w/v sodium dodecyl sulfate (SDS) to ensure complete solubilization.

Encapsulation efficiency for each drug was calculated as follows:

$$EE\% = (WT - WF) \times 100 \,/\, WT$$

Where:
EE% = Encapsulation efficiency
WT = Total amount of drug initially added to the formulation
WF = Amount of free (unencapsulated) drug in the supernatant

In Vitro Drug Release Study

The release behavior of tamoxifen and curcumin from the niosomal formulations was examined using the dialysis technique. In brief, 2 ml of each formulation was loaded into a dialysis bag and immersed in PBS supplemented with 0.5% w/v sodium dodecyl sulfate (SDS) at pH 7.4 and 5.0. The system was maintained at 37 °C under continuous agitation. At predetermined intervals, aliquots were collected and immediately replaced with an equal volume of fresh buffer. The obtained release data were further analyzed using different kinetic models to describe and characterize the drug release mechanisms.

Stability Assessment of Niosomal Formulations

The stability of the niosomal formulations was systematically evaluated by measuring the mean particle size, polydispersity index (PDI), and encapsulation efficiency at regular intervals over a storage period of two months. Formulations were stored at both 4 °C and 25 °C to investigate the effects of temperature on their physical and chemical stability, allowing assessment of potential changes in vesicle size, homogeneity, and drug retention during prolonged storage.

Assessment of Cell Viability (MTT Assay)

The cytotoxicity of the niosomal formulations was evaluated in HEK-293 and MCF-7 cell lines using the MTT assay. Cells were seeded into 96-well plates at a density of 1×10^4 cells per well and maintained in RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin (PS) at 37 °C in a humidified 5% CO_2 incubator. Following overnight attachment, cells were exposed to different concentrations of the formulations for 72 hours. After incubation, 20 µl of MTT solution (5 mg/ml) was added to each well and incubated for 4 hours to allow formazan crystal formation. The crystals were then dissolved in 100 µl of isopropanol, and absorbance was measured at 570 nm using an ELISA plate reader (Organon Teknika Oss, Netherlands).

Statistical Analysis

All measurements are reported as mean ± standard deviation (SD). Statistical evaluations were performed using GraphPad Prism (version 8, GraphPad Software, San Diego, CA). Comparisons among groups were conducted using one-way ANOVA followed by Tukey's multiple comparison test. Differences were considered statistically significant at $p < 0.05$.

Results and Discussion

Size, Zeta Potential and Encapsulation Efficiency (EE)

As summarized in Table 1, various Tmx/Cur niosomal formulations incorporating Span surfactants were prepared at two distinct lipid-to-drug ratios. The findings (Table 2) revealed that each formulation exhibited differences in particle size and polydispersity index (PDI) depending on the molar ratio of lipid to drug and the specific surfactant employed. Among the surfactants examined, Span 80 at lipid-to-drug ratios of 10 and 20 produced the most favorable characteristics. Specifically, formulation TC6, containing both drugs, demonstrated the optimal combination of particle size, dispersity, and high encapsulation efficiency.

Table 2. Particle Size, Polydispersity Index (PDI), and Encapsulation Efficiency (EE) of Various Niosomal Formulations. Values are expressed as mean ± standard deviation (n = 3)

Formulation	Particle Size (nm) ± SD	PDI ± SD	EE% Tmx ± SD	EE% Cur ± SD
TC1	321±0.346	0.221±0.01212	90.76±1.3856	86.76±1.6166
TC2	194±1.962	0.172±0.00462	94.65±1.7893	89.50±2.3671
TC3	175±3.453	0.191±0.01616	95.78±1.5299	93.68±1.5300
TC4	367±7.273	0.232±0.02543	92.59±1.6344	90.23±1.4030
TC5	291±2.021	0.201±0.01847	96.61±1.3390	94.31±1.6859
TC6	161±1.656	0.194±0.00231	98.62±1.2702	96.76±1.2702

p-value (Particle Size): 1.60e-14; *p*-value (PDI): 0.0104; *p*-value (EE% Tmx): 2.86e-05; *p*-value (EE% Cur): 0.0091

The study also examined how factors such as surfactant type and lipid-to-drug ratio influenced the particle size, PDI, and drug encapsulation efficiency of the niosomes. Niosomes formulated with Span 20 and Span 60 at a lipid-to-drug ratio of 10 were notably smaller than those prepared at a ratio of 20. Conversely, Span 80-based niosomes were smaller when prepared at a lipid-to-drug ratio of 20 compared to a ratio of 10. This trend may be attributed to the longer hydrophobic chains in Span 80, which strengthen hydrophobic interactions among Tmx/Cur, cholesterol, and the surfactant's hydrophobic segment.[19] Furthermore, the encapsulation efficiency of both Tmx and Cur was influenced by particle size and the hydrophilic-lipophilic balance (HLB) of the surfactant, which reflects the ratio of hydrophobic to hydrophilic segments and varies with surfactant type and concentration.[19,20]

Morphological Characteristics of Optimized Niosomes

The scanning electron micrograph (Figure 1) of the optimized Tmx/Cur-loaded niosomal formulation exhibited a well-defined spherical shape with a smooth surface and uniform distribution. The mean particle diameter calculated from the micrographs was approximately 80 nm, which is consistent with the nanoscale morphology expected for

niosomal vesicles prepared by thin-film hydration followed by sonication. These morphological characteristics are comparable to those reported in recent investigations on niosomal drug-delivery systems. For instance, Ashin et al. (2024) described gemini-surfactant nanoparticles co-loaded with tamoxifen and curcumin presenting a similar spherical morphology within the 70–90 nm range. Likewise, Sardarabadi et al. (2025) observed nearly spherical vesicles of 60–100 nm for phytosomal nanocarriers prepared under analogous conditions. In line with these findings, Jana et al. (2014) and Ferreira et al. (2024) confirmed that niosomes and PLGA-based nanostructures produced by controlled hydration and mild sonication usually maintain smooth spherical contours under SEM with diameters below 100 nm after freeze-drying. The relatively smaller size observed in SEM compared to the hydrodynamic diameters obtained from DLS analysis (Table 2, 161–367 nm) can be attributed to the absence of the hydration layer and the partial collapse of vesicles during the vacuum-drying process for SEM imaging—a phenomenon broadly recognized in nanoparticle characterization studies (Abbasalipour et al. 2015 and Kim et al. 2014).

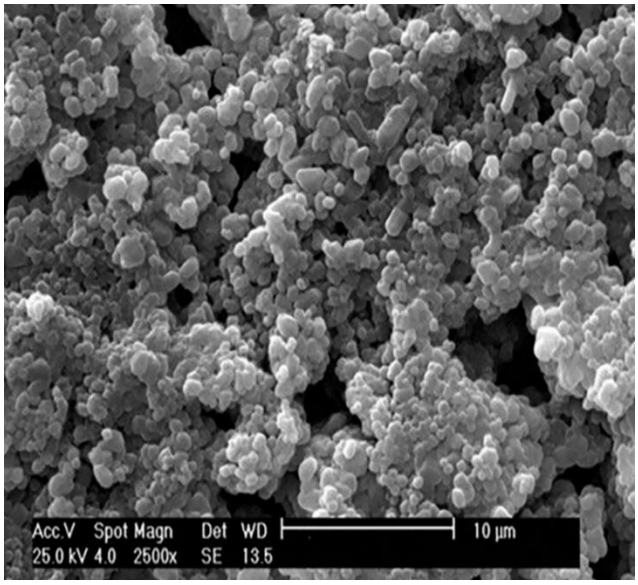
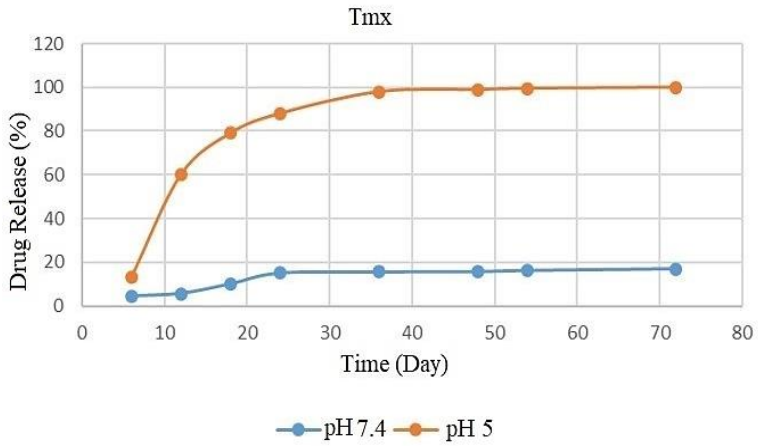


Figure 1. SEM Image Depicting the Morphological Features of the Optimized Niosomes.

Evaluation of Drug Release

The drug release profile of Tmx/Cur from the optimized niosomal formulation over 0.5–72 hours at 37 °C exhibited a biphasic cumulative release pattern, which was slower compared to the free drug formulation.[21,22] As shown in Figure 2, the release profiles at both pH 7.4 and pH 5.0 demonstrate the biphasic pattern consisting of an initial burst release followed by a sustained release phase. The release profiles were examined using various kinetic models, with the Korsmeyer-Peppas model showing the best fit, suggesting that drug release was controlled by a combination of diffusion and erosion mechanisms. The early burst release is probably due to drugs desorbing from the niosome surface, while the slower, later phase reflects diffusion through the



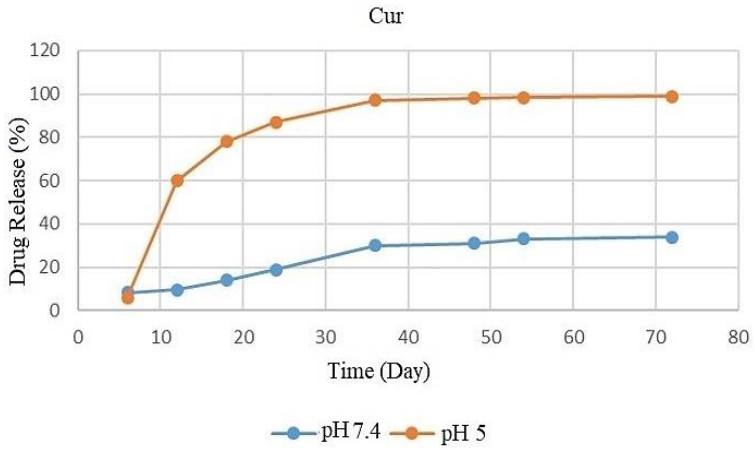
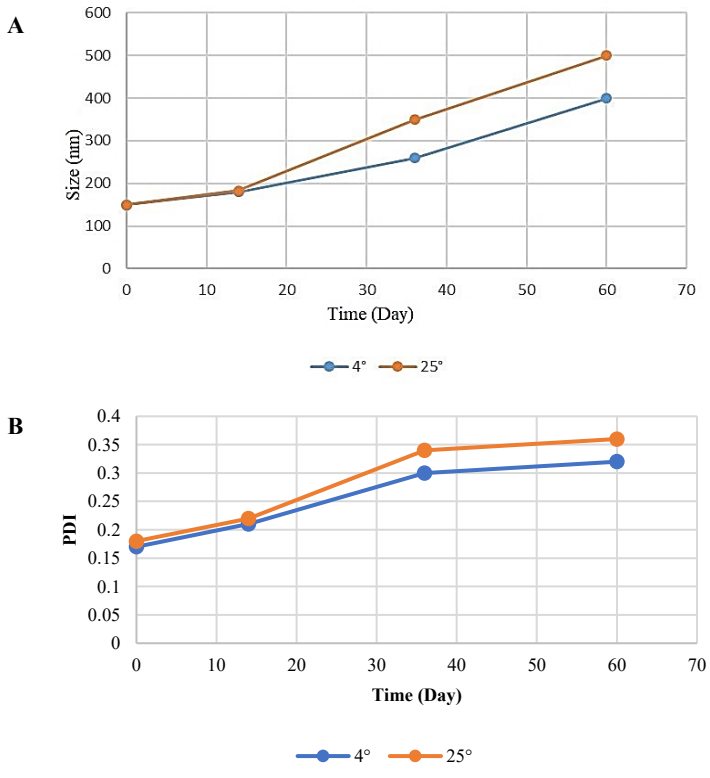


Figure 2. pH-Dependent Release of Tmx/Cur from Niosomes Measured by the Dialysis Method. Lines represent tamoxifen and curcumin release at pH 7.4 and pH 5.0.

bilayer.[23] Notably, an enhanced drug release was observed under acidic conditions,[24] attributed to swelling and partial disruption of the niosomes. Such pH-responsive release is advantageous for cancer therapy, as the extracellular environment around tumor cells is acidic compared to normal tissues. Overall, the niosomal formulation exhibited drug release controlled by both diffusion and erosion processes.[25]

Stability Study of Niosomes

As shown in the Figure 3, both the particle size and polydispersity index (PDI) of Tmx/Cur-loaded niosomes increased with higher storage temperatures and longer storage periods, whereas encapsulation efficiency (EE) decreased. Notable changes in particle size were observed on days 14, 30, and 60, while a significant rise in PDI for the TC6 formulation was detected only on day 60. For EE, marked differences were seen between the two storage temperatures, especially for curcumin on days 30 and 60. These stability results indicate that the niosomal formulation can be stored for at least two weeks with minimal changes in particle size and drug content. Samples kept at 4 °C showed slower and less pronounced alterations compared to those stored at 25 °C, likely due to reduced bilayer fluidity at the lower temperature.[26] In general, vesicle size tends to increase during storage as a consequence of fusion[27] or aggregation.[28]



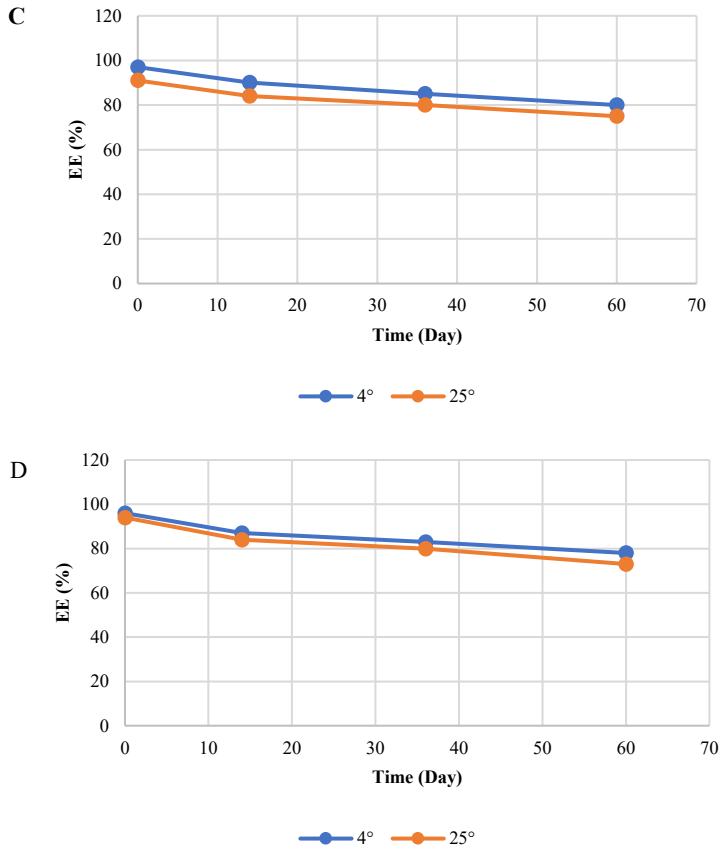


Figure 3. Influence of Storage Duration and Temperature on the Mean Particle Size (A), polydispersity index (PDI) (B), and encapsulation efficiency (EE) (C&D) of Tmx & Cur-loaded niosomal Tmx/Cur formulations.

Cytotoxicity Study

The cytotoxic behavior of free drugs and their niosomal co-formulation was evaluated on MCF-7 (breast cancer cell line) and HEK-293 (normal kidney) cell lines using the MTT assay (Figure 4). As summarized in Table 3, the co-encapsulation of tamoxifen and curcumin within niosomes markedly enhanced their cytotoxic potency against cancer cells while maintaining biocompatibility toward normal cells. The niosomal formulation exhibited the lowest IC_{50} value (20.68 µg/ml) on MCF-7 cells compared with free tamoxifen (41.98 µg/ml), free curcumin (63.12 µg/ml), and the free-drug mixture (36.16 µg/ml). This significant reduction in IC_{50} demonstrates improved anticancer efficacy due to synergistic interactions between the two drugs and their sustained intracellular release from the vesicles. In contrast, when tested on HEK-293 cells, the niosomal formulation showed a high IC_{50} (≈ 570 µg/ml), indicating low inherent cytotoxicity and suggesting selective toxicity toward malignant cells. The dual-drug niosomes therefore achieve a desirable therapeutic window, maximizing anticancer effects while minimizing adverse impacts on normal tissues. These findings are consistent with previous works reporting enhanced cytotoxicity of tamoxifen- or curcumin-loaded niosomes in cancer cell lines.[28,29]

Table 3. IC_{50} Values of Different Drug Formulations on MCF-7 Cells

Drug / Formulation	IC_{50} (µg/ml)	Notes
Tamoxifen (free)	41.98	Single drug solution
Curcumin (free)	63.12	Single drug solution
Tamoxifen + Curcumin (free mix)	36.16	1:1 (w/w) combination
Niosomal Tmx + Cur	20.68	Co-encapsulated in optimized formulation

These results are consistent with previous studies; for example, Abbasalipour et al. (2015) reported that Tmx-loaded solid lipid nanoparticles (SLNs) exhibited higher cytotoxicity in MCF-7 and MDA-MB-231 breast cancer cells compared to free Tmx.

Our findings align closely with recent 2024 review that highlight the major limitations of free curcumin including poor solubility and extremely low bioavailability and emphasize the need for nanoparticle-based delivery systems. Several recent studies have reported that curcumin, when co-treated with chemotherapeutic agents such as paclitaxel, thymoquinone, or tamoxifen, shows enhanced synergistic

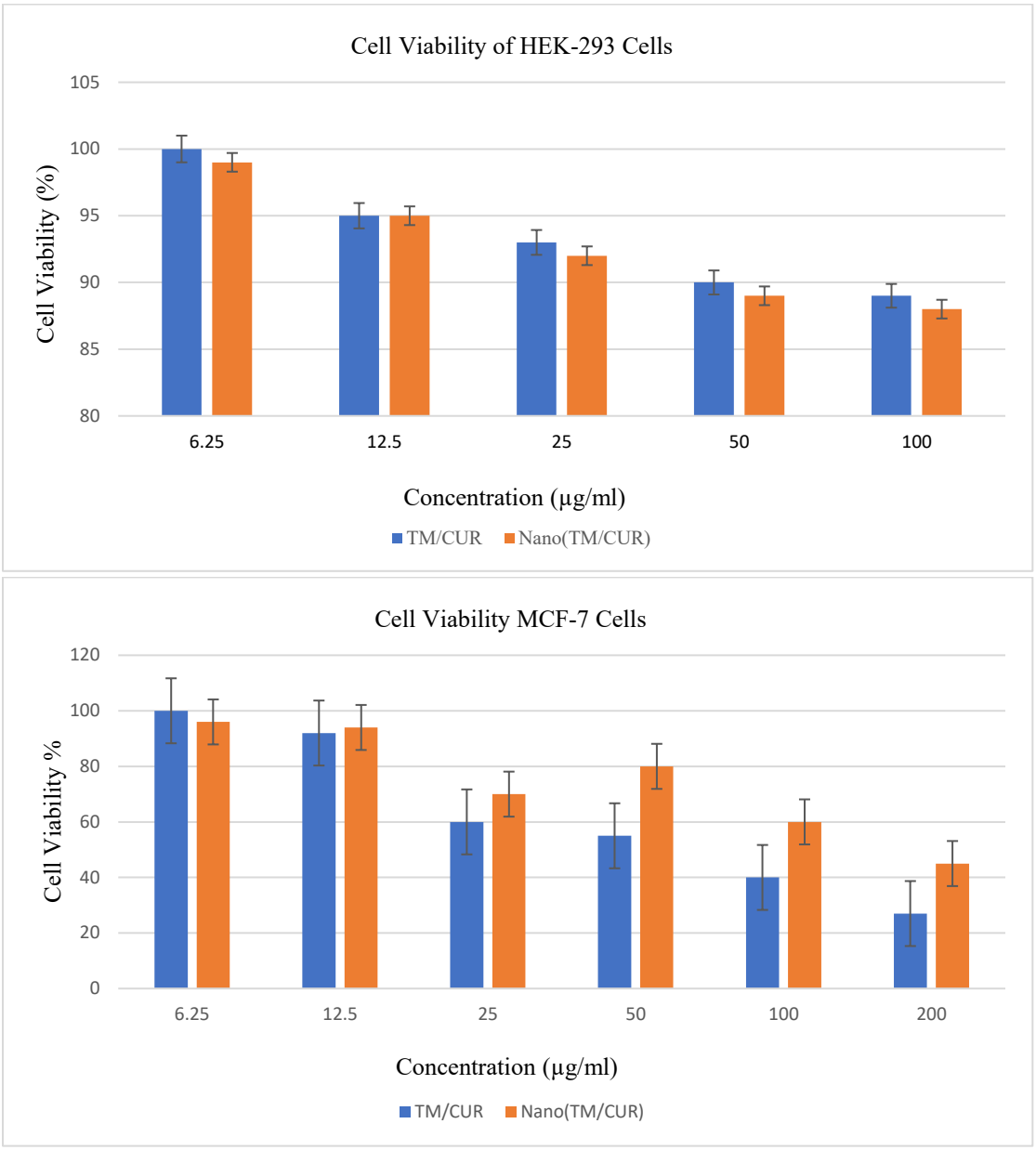


Figure 4. Impact of Different Formulations (Tmx and Cur alone, Tmx and Cur together, and nanoformulation with Tmx and Cur) on Cell Viability Assessed Using the MTT Assay. (A) Viability of HEK-293 normal cells; (B) Viability of MCF-7 breast cancer cells.

cytotoxicity and improved regulation of apoptosis and cell-cycle arrest. Consistent with these reports, our Tmx/Cur-loaded niosomal formulation demonstrated greater anticancer activity against MCF-7 cells, higher encapsulation efficiency, and a controlled release profile compared to free drugs. These similarities further support the conclusion that nano-enabled co-delivery systems represent a promising strategy for overcoming the pharmacokinetic limitations of curcumin and enhancing therapeutic outcomes in breast cancer.[30,31]

Conclusion

An optimized dual-drug niosomal formulation was successfully developed by selecting appropriate surfactants (Span 20, 60, and 80) and lipid-to-drug ratios, with Span 80 at a 10:1 molar ratio showing the best performance. The formulation exhibited controlled drug release at physiological pH and accelerated release under acidic conditions, which may enhance therapeutic efficacy in the tumor micro-environment. Cytotoxicity studies demonstrated high anticancer activity against MCF-7 cells while maintaining low toxicity toward HEK-293 cells, confirming excellent biocompatibility. Overall, these results suggest that the optimized Tmx/Cur-loaded niosomes represent a promising strategy for improving breast cancer therapy.

Authors' Contributions

All authors contributed equally to the conception, design, data collection, analysis, interpretation, and writing of this

manuscript. All authors have read and approved the final version of the paper.

Conflict of Interest Disclosures

The authors declare that they have no conflicts of interest.

Acknowledgment

We would like to thank the Research and Technology Comprehensive Laboratory (RTCL) of Baqiyatallah University of Medical Sciences for their guidance and support. The authors also appreciate the guidance and advice provided by the Clinical Research Development Unit of Baqiyatallah Hospital.

References

1. Sancho-Garnier H, Colonna M. Breast cancer epidemiology. Presse medicale (Paris, France: 1983). 2019;48(10):1076-84. doi:10.1016/j.lpm.2019.09.022
2. Winters S, Martin C, Murphy D, Shokar NK. Breast cancer epidemiology, prevention, and screening. Prog Mol Biol Transl Sci. 2017;151:1-32. doi:10.1016/bs.pmbts.2017.07.002
3. Perou CM, Sørlie T, Eisen MB, Van De Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. Nature. 2000;406(6797):747-52. doi:10.1038/35021093
4. Kim LA, Amarnani D, Gnanaguru G, Tseng WA, Vavvas DG, D'Amore PA. Tamoxifen toxicity in cultured retinal pigment epithelial cells is mediated by concurrent regulated cell death mechanisms. Invest Ophthalmol Vis Sci. 2014;55(8):4747-58. doi:10.1167/iovs.13-13662
5. Waks AG, Winer EP. Breast cancer treatment: a review. Jama. 2019;321(3):288-300. doi:10.1001/jama.2018.19323
6. Osborne CK. Tamoxifen in the treatment of breast cancer. N Engl J Med. 1998;339(22):1609-18. doi:10.1056/NEJM199811263392207
7. Ferreira T, Faustino-Rocha AI, Gaspar VM, Medeiros R, Mano JF, Oliveira PA. Contribution of non-steroidal anti-inflammatory drugs to breast cancer treatment: In vitro and in vivo studies. Vet World. 2024;17(5):1052-72. doi:10.14202/vetworld.2024.1052-1072
8. Maheshwari RK, Singh AK, Gaddipati J, Srimal RC. Multiple biological activities of curcumin: a short review. Life Sci. 2006;78(18):2081-7. doi:10.1016/j.lfs.2005.12.007
9. Ashin ZF, Sadeghi-Mohammadi S, Vaezi Z, Najafi F, AdibAmini S, Sadeghizadeh M, et al. Synergistic effect of curcumin and tamoxifen loaded in pH-responsive gemini surfactant nanoparticles on breast cancer cells. BMC Complement Med Ther. 2024;24(1):337. doi:10.1186/s12906-024-04631-x
10. Jana SK, Chakravarty B, Chaudhury K. Letrozole and curcumin loaded-PLGA nanoparticles: a therapeutic strategy for endometriosis. J Nanomed Biotherap Discov. 2014;4(123):10-4172.
11. Sebak S. Novel nanoparticles for breast cancer targeted delivery: preparation and in vitro characterization. 2009.
12. Mansoori GA, Mohazzabi P, McCormack P, Jabbari S. Nanotechnology in cancer prevention, detection and treatment: bright future lies ahead. World Rev Sci Technol Sustain Dev. 2007;4(2-3):226-57. doi:10.1504/WRSTSD.2007.013584
13. Sardarabadi H, Darvishi MH, Zohrab F, Javadi H. Nanophytomedicine: A promising practical approach in phytotherapy. Phytother Res. 2024;38(7):3607-44. doi:10.1002/ptr.8230
14. Sardarabadi H, Zarei SM, Dolati M, Darvishi MH, Tavakolizadeh M, Zohrab F, et al. Mito-phytosomal nanocarriers of purslane extract augments apoptosis in A549 cells. J Liposome Res. 2025;35(4):455-68. doi:10.1080/08982104.2025.2521718
15. Okamoto Y, Aoki A, Ueda K, Jinno H. Metabolomic analysis uncovered an association of serum phospholipid levels with estrogen-induced mammary tumors in female ACI/Seg rats. Toxicol Lett. 2018;288:65-70. doi:10.1016/j.toxlet.2018.02.017
16. Carafa M, Santucci E, Lucania G. Lidocaine-loaded non-ionic surfactant vesicles: characterization and in vitro permeation studies. Int J Pharm. 2002;231(1):21-32. doi:10.1016/S0378-5173(01)00828-6
17. Dabbagh Moghaddam F, Akbarzadeh I, Marzbankia E, Farid M, Khaledi L, Reihani AH, et al. Delivery of melittin-loaded niosomes for breast cancer treatment: an in vitro and in vivo evaluation of anti-cancer effect. Cancer Nanotechnol. 2021;12(1):14. doi:10.1186/s12645-021-00085-9
18. Salem HF, Kharshoum RM, Abo El-Ela FI, Abdellatif KR. Evaluation and optimization of pH-responsive niosomes as a carrier for efficient treatment of breast cancer. Drug Deliv Transl Res. 2018;8(3):633-44. doi:10.1007/s13346-018-0499-3
19. Rochdy Haj-Ahmad R, Ali Elkordy A, Shu Chaw C. *In vitro* characterisation of Span™ 65 niosomal formulations containing proteins. Curr Drug Deliv. 2015;12(5):628-39. doi:10.2174/1567201812666150511095432
20. Junyaprasert VB, Singhsa P, Suksiriworapong J, Chantasart D. Physicochemical properties and skin permeation of Span 60/Tween 60 niosomes of ellagic acid. Int J Pharm. 2012;423(2):303-11. doi:10.1016/j.ijpharm.2011.11.032
21. Cho KJ. Therapeutic Nanoparticles for Drug Delivery in Cancer. Korean J Otorhinolaryngol-Head Neck Surg. 2007;50(7):562-72.
22. Alemi A, Zavar Reza J, Haghiralsadat F, Zarei Jaliani H, Haghi Karamallah M, Hosseini SA, et al. Paclitaxel and curcumin coadministration in novel cationic PEGylated niosomal formulations exhibit enhanced synergistic antitumor efficacy. J Nanobiotechnol. 2018;16(1):28. doi:10.1186/s12951-018-0351-4
23. Manosroi A, Bauer KH. The entrapment of a human insulin-DEAE dextran complex in different compound liposomes. Drug Dev Ind Pharm. 1989;15(14-16):2531-46. doi:10.3109/03639048909052545
24. Rinaldi F, Del Favero E, Rondelli V, Pieretti S, Bogni A, Ponti J, Rossi F, Di Marzio L, Paolino D, Marianecci C, Carafa M. pH-sensitive niosomes: Effects on cytotoxicity and on inflammation and pain in murine models. J Enzyme Inhib Med Chem. 2017;32(1):538-46. doi:10.1080/14756366.2016.1268607
25. Sadeghi S, Ehsani P, Cohan RA, Sardari S, Akbarzadeh I, Bakhshandeh H, et al. Design and physicochemical characterization of lysozyme loaded niosomal formulations as a new controlled delivery system. Pharm Chem J. 2020;53(10):921-30. doi:10.1007/s11094-020-02100-6
26. Balasubramaniam A, Anil Kumar V, Sadasivan Pillai K. Formulation and in vivo evaluation of niosome-encapsulated daunorubicin hydrochloride. Drug Dev Ind Pharm. 2002;28(10):1181-93. doi:10.1081/DDC-120015351
27. Lawrence MJ, Chauhan S, Lawrence SM, Barlow DJ. The formation, characterization and stability of non-ionic

surfactant vesicles. STP Pharma Sciences. 1996;6(1):49-60.
28. Akbarzadeh I, Fatemizadeh M, Heidari F, MOUSAVI NN. Niosomal formulation for co-administration of hydrophobic anticancer drugs into MCF-7 cancer cells. Arch Adv Biosci. 2020;11(2):1-9.
29. Shaker DS, Shaker MA, Hanafy MS. Cellular uptake, cytotoxicity and in-vivo evaluation of Tamoxifen citrate loaded niosomes. Int J Pharm. 2015;493(1-2):285-94. doi:10.1016/j.ijpharm.2015.07.041
30. Mayo B, Penroz S, Torres K, Simyn L. Curcumin administration routes in breast cancer treatment. Int J Mol Sci. 2024;25(21):11492. doi:10.3390/ijms252111492
31. Zhu J, Li Q, Wu Z, Xu Y, Jiang R. Curcumin for treating breast cancer: A review of molecular mechanisms, combinations with anticancer drugs, and nanosystems. Pharmaceutics. 2024;16(1):79. doi:10.3390/pharmaceutics16010079