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RESEARCH ARTICLE

Enhanced Therapeutic Potential of Paclitaxel-Loaded Niosomes on Ovarian Cancer Cell Line

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Abstract

Background: Paclitaxel is a widely used chemotherapeutic agent for ovarian cancer treatment; however, its clinical application is limited by poor solubility and severe side effects. Niosomes, non-ionic surfactant vesicles, have emerged as a promising nanocarrier for targeted drug delivery. This study investigates the enhanced therapeutic potential of paclitaxel-loaded niosomes in ovarian cancer cell line. **Methods:** Paclitaxel-loaded niosomes were prepared using the thin-film hydration method and characterized for size, zeta potential, and polydispersity index (PDI). The morphology of the niosomes was evaluated by scanning electron microscopy (SEM). Cytotoxicity of paclitaxel-loaded niosomes was assessed using the MTT assay on ovarian cancer cell line (A2780S) after 24 and 48 hours of incubation. The results were compared with free paclitaxel to evaluate the effect of the niosomal formulation on drug efficacy. **Results:** The paclitaxel-loaded niosomes exhibited a mean size of approximately 285 nm, a PDI of 0.44, and a negative zeta potential of -21 mV. SEM images confirmed the spherical morphology of the niosomes. The MTT assay results showed a significant increase in cytotoxicity in the niosomal formulation compared to free paclitaxel at both 24 and 48 hours ($p < 0.05$, $p < 0.01$), indicating enhanced therapeutic efficacy. **Conclusion:** Paclitaxel-loaded niosomes demonstrate improved drug delivery and enhanced cytotoxicity in ovarian cancer cell lines. The results suggest that niosomal paclitaxel could be a promising strategy for improving the therapeutic potential of paclitaxel in ovarian cancer treatment. Further in vivo studies are warranted to confirm these findings and explore the clinical applicability of niosomal formulations.

Keywords: Paclitaxel- Niosomes- Ovarian Cancer Cell Line

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Introduction

Therapeutic methods for addressing physical and mental problems have made significant progress with the advancement of technology [1-13]. Technological advancements have significantly transformed the landscape of healthcare, particularly through the integration of artificial intelligence (AI), blockchain, and data-driven decision-making models. These innovations enhance efficiency in medical supply chains by improving transparency, security, and operational effectiveness, ultimately leading to better healthcare outcomes [14]. Additionally, AI and deep learning have played a crucial role in deciphering immune system complexities, allowing for more precise immunotherapy applications, particularly in the treatment of autoimmune diseases [15]. Furthermore, emerging research suggests that existing pharmaceuticals, such as metformin, could have neuroprotective effects, as seen in mitigating microstructural changes in the white matter of Alzheimer's patients [16]. The growing intersection of AI and healthcare also extends to the study of disease pathogenesis, where computational models are enhancing our understanding of T cell specificity and immune responses, paving the way for improved diagnostic and therapeutic approaches [17]. As these technologies continue to evolve, their integration into

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clinical practice will not only optimize treatment strategies but also foster innovations that advance global healthcare accessibility and effectiveness [18]. With the advancement of technology, newer and more serious problems are clearly emerging [19]. Various diseases have threatened human life and can emerge as pandemics [20]. Many diseases only harm individuals' physical bodies, but many others affect their mental and emotional well-being [21, 22]. Cancer is a complex disease that is increasing day by day [23]. Ovarian cancer remains one of the most aggressive and challenging gynecological malignancies, ranking as the fifth leading cause of cancer-related deaths among women worldwide [24]. Despite advances in diagnostic techniques and the development of treatment strategies, the overall prognosis for ovarian cancer patients is still poor, primarily due to late-stage diagnosis, resistance to chemotherapy, and the severe side effects associated with conventional treatment regimens [25-27]. Standard chemotherapy, typically involving agents such as paclitaxel and cisplatin, remains the cornerstone of treatment; however, the clinical effectiveness of these drugs is often compromised by several inherent challenges [28, 29]. Paclitaxel, a potent chemotherapeutic agent, is widely used in the treatment of ovarian cancer due to its ability to inhibit cancer cell division by stabilizing microtubules [30]. Despite its proven efficacy, paclitaxel suffers from significant drawbacks, including poor aqueous solubility, low bioavailability, and rapid systemic clearance, which contribute to its limited therapeutic window and the high incidence of severe side effects, such as neurotoxicity, myelosuppression, and cardiotoxicity [31, 32]. These limitations highlight the need for novel drug delivery systems that can improve the pharmacokinetic profile of paclitaxel, enhance its therapeutic index, and reduce the associated toxicity [33]. In recent years, nanotechnology has emerged as a promising approach to overcome the limitations of traditional drug delivery systems [34]. Among various nanocarriers, niosomes non-ionic surfactant-based vesicles have attracted significant attention due to their unique properties [35]. Niosomes are biocompatible, stable, and capable of encapsulating both hydrophilic and hydrophobic drugs, making them ideal candidates for delivering paclitaxel [36, 37]. Their ability to improve the solubility and bioavailability of paclitaxel, prolong its circulation time in the bloodstream, and target drug release to cancer cells offers a compelling strategy to enhance treatment efficacy while minimizing systemic toxicity [38, 39]. The formulation of paclitaxel-loaded niosomes has the potential to significantly improve the delivery and therapeutic action of paclitaxel in ovarian cancer treatment [40]. Niosomes can not only serve as an effective carrier for paclitaxel but also offer controlled drug release, which may reduce the frequency and severity of adverse effects [41]. Furthermore, their size, surface charge, and composition can be tailored to optimize their interaction with cancer cells, providing a more targeted and effective treatment strategy [42, 43]. This study aims to explore the therapeutic potential of paclitaxel-loaded niosomes in ovarian cancer treatment. Specifically, we investigate the physicochemical properties of the niosomal formulation, including particle size, zeta potential, and morphology, as well as its cytotoxicity against ovarian cancer cell lines (A2780S). Using the MTT assay, we will evaluate the effectiveness of paclitaxel-loaded niosomes at different time intervals (24 and 48 hours) and compare the results to free paclitaxel. We hypothesize that encapsulating paclitaxel in niosomes will enhance its cytotoxicity, improve its therapeutic efficacy, and reduce its side effects. Through this research, we aim to provide a deeper understanding of the potential benefits of paclitaxel-loaded niosomes as a novel therapeutic strategy for ovarian cancer. The findings from this study could pave the way for the clinical application of niosomal drug delivery systems, potentially transforming the treatment landscape for ovarian cancer patients by improving outcomes and reducing treatment-related toxicity.

Materials and Methods

Materials

All necessary reagents, including Paclitaxel, Span 40, Cholesterol, Polyethylene Glycol 3350, RPMI 1640 culture medium, Ethanol, Isopropanol, and Diethyl Ether, were meticulously acquired from the Sigma Corporation to ensure the highest quality standards for the experiments. Additionally, the A2780S ovarian cancer cell line utilized in this study was generously supplied by the Cell Bank affiliated with the Iranian Pasteur Institute, guaranteeing a reliable and consistent source of cellular material for our research purposes."

Preparation of nanoparticles

Initially, a precise combination of 80 milligrams of Span 40, 30 milligrams of Cholesterol, and 25 milligrams of Polyethylene Glycol 3350 (a molar ratio of about 25:10:1) was prepared in a solvent system consisting of 40 milliliters of Diethyl Ether, ensuring proper dissolution of the components. To this mixture, two separate aliquots of Ethanol (96%), each containing 14 milligrams of Paclitaxel, were gradually introduced over time, with each addition carefully monitored to ensure uniform dispersion of the drug. Once all components were thoroughly mixed, the solution was subjected to a gentle agitation process for a duration of one hour at 37°C, maintaining a consistent speed of 300 rotations per minute to promote complete solubilization and homogenization of the ingredients. Once fully dissolved, the resulting solution was slowly poured into 14 ml of phosphate buffer (pH 7.2) that was preheated to 70°C and continuously stirred. Due to the temperature difference between the two phases, the ether quickly evaporated, leading to the formation of niosomes. To ensure the homogeneity and proper encapsulation of the active ingredient, the mixture was subsequently processed using a sonicator at room temperature for five minutes, providing sufficient energy to produce uniform vesicles.

Determination of size of nanoniosomes

To determine the mean diameter of nanoniosomes, a formulation was prepared using a 1:50 nanoniosome-to-PBS ratio at pH 7.2. Nanoparticle concentration was

measured by absorbance at 633 nm, while size and surface charge were analyzed with a Malvern Nano ZS3600 zetasizer. Morphology was examined using a Philips XL30 SEM. For SEM analysis, 200 µL nanoparticle suspensions were centrifuged at 13,000 RPM for 30 minutes at 4°C to obtain pellets. These pellets were resuspended in 200 µL of 15 mg/mL sucrose as a cryoprotectant, lyophilized, coated with a thin gold layer, and then imaged with the SEM.

MTT test

The cytotoxicity of the Paclitaxel formulation was evaluated using the MTT assay and compared to the standard drug. A2780S cells were seeded in a 96-well plate and cultured for 24 hours before being treated with varying concentrations of either the drug formulation or free drug for 24 and 48 hours. After treatment, MTT solution was added and incubated for one hour, then replaced with isopropanol to dissolve the formazan crystals. Absorbance was measured at 540 nm using an ELISA reader. Cytotoxicity (%) was calculated as:

Cytotoxicity (%) = [1 - (Absorbance of treated cells / Absorbance of control)] × 100

Cell viability was determined as 100 minus the cytotoxicity percentage. The IC_{50} value was calculated using the Pharm program.

Statistical analysis

The data were statistically analyzed using SPSS version 11, and all phases of toxicity were evaluated with Pharm software.

Results

Characterization of nanoparticles

Paclitaxel-loaded niosomes were characterized to determine their physicochemical properties. The formulations exhibited a mean particle size of 285 nm and a polydispersity index (PDI) of 0.440, indicating a moderately broad size distribution. The zeta potential was measured at -21 mV, suggesting sufficient colloidal stability (Table 1). Additionally, scanning electron microscopy (SEM) images confirmed the spherical morphology of the niosomes, demonstrating uniform and consistent structural characteristics (Figure 1).

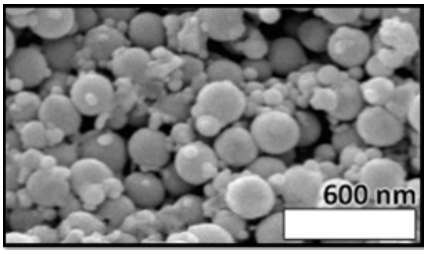

Figure 1. Scanning Electron Microscopy (SEM) of Nanoparticles.

Table 1. Characterization of Nanoparticles

Parameter	Value	Unit
Mean Particle Size	285±14	nm
Polydispersity Index (PDI)	0.44±0.9	-
Zeta Potential	-21±1.8	mV

In vitro cytotoxicity assay

The cytotoxicity of paclitaxel-loaded niosomes was evaluated in comparison to conventional paclitaxel using A2780S ovarian cancer cells. Cells were incubated with equivalent doses of either the niosomal formulation or the free drug for 24 and 48 hours at 37°C. Figure 2 illustrates the dose-response curves for both formulations, highlighting the lower IC_{50} values achieved by the niosomal paclitaxel at each incubation period. Specifically, the IC_{50} for the niosomal formulation decreased from 100 µM at 24 hours to 65 µM at 48 hours, whereas the free paclitaxel maintained higher IC_{50} values of 140 µM and 130 µM at the respective time points. These results demonstrate that encapsulating paclitaxel within niosomes significantly enhances its cytotoxicity against A2780S cells, potentially due to improved cellular uptake and sustained drug release. The increased efficacy of the niosomal formulation over conventional paclitaxel underscores its potential as a more effective therapeutic strategy for ovarian cancer treatment (Table 2).

Discussion

The use of niosomes as drug carriers in cancer treatment represents an innovative advancement in nanotechnology. These non-ionic surfactant-based vesicles can encapsulate both hydrophilic and lipophilic drugs, enhancing treatment efficacy by improving targeting precision while reducing side effects. For example, a study by Nowroozi et al. (2018) demonstrated that theranostic niosomes containing doxorubicin and Ag2S quantum dots, when directly injected into tumors, significantly increased drug accumulation in the tumor and inhibited tumor growth by 71.7%. This method highlighted the high efficacy of direct intratumoral injection in breast cancer models [44]. Additionally, Akbarzadeh et al. (2021) developed niosomes loaded with curcumin for breast cancer treatment. These niosomes significantly increased cell death and apoptosis in MDA-MB231 and SKBR3 cancer cell lines, effectively delivering hydrophobic drugs to target cells while minimizing side effects. This innovative formulation highlights the potential of niosomes in enhancing the efficacy of cancer therapies [45]. Due to their high stability and ability to target specific cells, niosomes are recognized as a powerful tool in delivering anticancer drugs, offering significant improvements to current treatments. This study investigates the improved therapeutic efficacy of paclitaxel-loaded niosomes in an ovarian cancer cell line (A2780S), highlighting the potential benefits of niosome encapsulation in enhancing drug delivery and cytotoxic effects. The results demonstrate that the niosomal formulation of paclitaxel significantly reduces IC_{50} values at both 24 and 48 hours when compared to the free drug, indicating enhanced cytotoxicity against ovarian cancer cells. This improvement in drug efficacy suggests that niosomes enhance drug solubility, stability, and cellular

Table 2. Cytotoxicity of Paclitaxel Formulations on A2780S Cells

Treatment	IC_{50} (μM), 24 Hours incubation	IC_{50} (μM), 48 Hours incubation
Conventional Paclitaxel	140±11.1 μM	130±5.5 μM
Paclitaxel-Loaded Niosomes	100±8.7 μM	65±10.0 μM

*Values represent the mean ± standard deviation of three independent experiments. $p < 0.05$ vs. conventional paclitaxel at 24 hours, $p < 0.01$ vs. conventional paclitaxel at 48 hours.

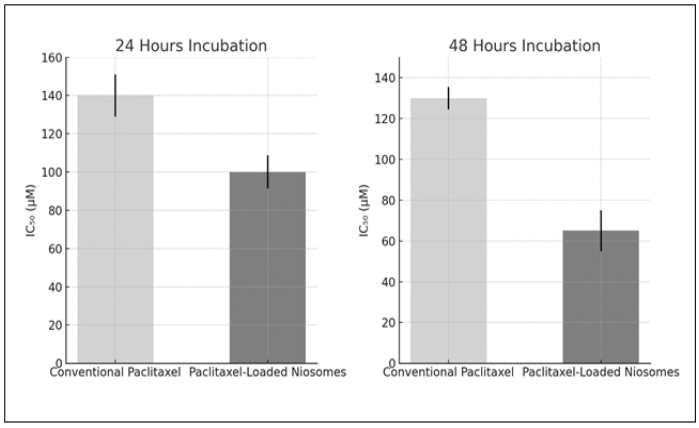

Figure 2. Comparative Cytotoxicity of Paclitaxel-loaded Niosomes and Conventional Paclitaxel on A2780S Cells after 24 and 48 hours of Incubation. Error bars represent standard deviations. Significant differences are indicated with asterisks ($p < 0.05$, $p < 0.01$).

uptake, allowing for more efficient drug delivery directly to cancer cells [46, 47]. Consequently, niosomes may reduce the required dosage of paclitaxel, potentially lowering systemic toxicity. The niosomes' mean size of 285 nm and negative zeta potential indicate good stability and suitability for biological interactions, while the moderately broad PDI suggests a relatively uniform size distribution, essential for consistent drug delivery and bioavailability [48-51]. The spherical morphology observed in SEM further supports the effective encapsulation and expected cellular uptake behaviors. This study positions niosomes as a promising nanocarrier for paclitaxel, particularly due to their ability to address the drug's poor water solubility and severe side effects. By enhancing drug delivery and therapeutic outcomes, niosomes may reduce the limitations of traditional formulations that often require higher doses, increasing the risk of adverse side effects. Although this study provides essential insights, further research, particularly in vivo studies, is needed to assess the pharmacokinetics, biodistribution, and long-term safety of niosomal paclitaxel. Moreover, understanding the molecular mechanisms underlying the enhanced drug uptake and efficacy of niosomes could provide a deeper understanding of their therapeutic potential. Ultimately, the promising findings from this study suggest that niosomal paclitaxel could offer a safer and more effective alternative for ovarian cancer treatment, with future clinical trials critical to validating these results and establishing niosomal paclitaxel as a standard treatment option.

In conclusion, Humanity, through technological advancements, has consistently contributed to combating a wide range of diseases [52-62]. For example, the use of paper-based sensors for detecting cancer markers offers rapid, cost-effective, and accurate diagnostic methods that could play a crucial role in enhancing health outcomes and treatment efficacy [63]. Cancer is a complex, multifactorial disease characterized by the uncontrolled proliferation of malignant cells that can invade healthy tissues and disrupt the normal function of various organs [64-69]. Recent studies employing advanced analytical techniques such as hybrid metaheuristic machine learning for obesity risk prediction [70], finite mixture modeling for investigating health risk behavior disparities [71], and cardiac marker evaluation as predictors of mortality in methanol toxicity [72] underscore the critical role of data-driven approaches in enhancing our understanding of complex health determinants and improving public health outcomes. This study underscores the potential of niosomal encapsulation to significantly enhance the therapeutic efficacy of paclitaxel, presenting a viable advancement in the treatment of ovarian cancer. The improved delivery and increased cytotoxicity observed in vitro lay a strong foundation for further development and clinical investigation of niosomal drug delivery systems.

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Data availability

Not applicable as we used information from previously published articles.

Approved by any scientific Body

Not applicable as the manuscript is not a part of any student thesis or study.

Ethical issue and approval

Not applicable as we used information from previously

published articles.

Consent for publication

All authors have given consent for publication.

Conflict of interest

The authors declare no potential conflict of interest.

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