

# Niosome-Based Vaccines for Enhanced Immunogenic Response

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## Abstract

The invention of good vaccines is one of the most important milestones in global health. Nonetheless, adverse factors like lack of immunogenicity, low antigen stability and the requirement to treat several times has led to the development of novel delivery mechanisms. Niosomes, which are vesicles made of non-ionic surfactants, have also become a promising mode of delivery of vaccines as they are capable of encapsulation of the hydrophilic as well as hydrophobic antigens, controlled release, and stimulation of immune responses. This paper discusses how niosome-based vaccines can be used to enhance antigen presentation, generate humoral and cellular immunity and deal with issues in traditional vaccine preparations. The review is methodologically based on the synthesis of the findings of the available pre-clinical and clinical trials in order to assess the design of the vaccines, their mechanism of action, and immunological effects of niosome-based vaccines. Findings present that niosome formulations enhance stability of antigens, extend the period of circulation, and increase immunogenic reactions relative to conventional adjuvants. The discussion presents their benefits, current weaknesses, and future opportunities in vaccine development particularly in infectious disease and cancer immunotherapy.

## Key Words:

Niosomes, Vaccine Delivery, Immunogenic Response, Adjuvant, Nanocarriers

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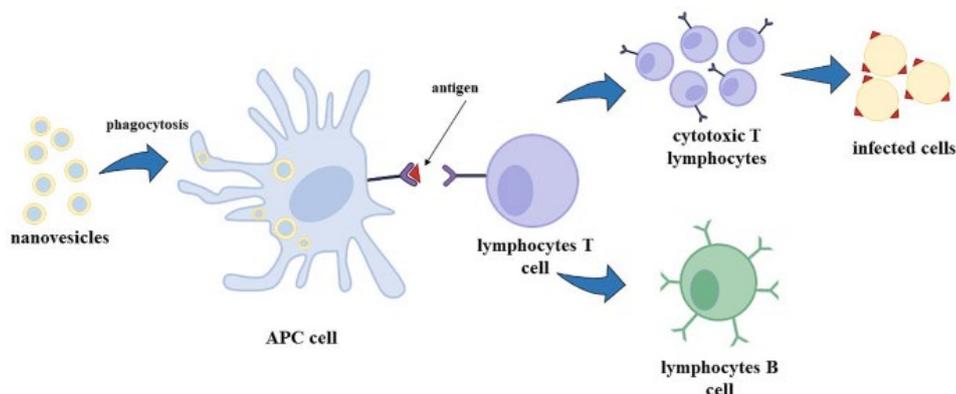
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## 1. INTRODUCTION

Vaccination has been one of the most efficient and commonly implemented measures to inhibit infectious illnesses which has played a major role in the regulation and, in certain instances, elimination of pathogenic agents of life across the globe<sup>1</sup>. Conventional vaccines which are live-attenuated, inactivated, and subunit preparations have significantly lowered the morbidity and mortality rates attributable to infectious diseases. Regardless of these achievements, traditional vaccine platforms have a number of intrinsic limitations<sup>2</sup>. The unstable nature of antigens, fast degradation, poor induction of cellular immunity and reliance on stringent cold chain storage have been a major challenge to their effectiveness and universal availability, especially in low-resource

and remote environments. Furthermore, most of the vaccines need repetitive booster doses to sustain protective immunity that is both logistically difficult and expensive.



**Figure 1:** Mechanism of Immune Activation by NIOSOME -Based Vaccines

Nanotechnology has in recent years brought about progress that has led to innovative vaccine delivery systems to overcome these barriers. Of them, niosomes, or the vesicular type of carriers consisting of the combination of non-ionic surfactants and cholesterol, have gained significant interest regarding their distinctive structural and functional features. Niosomes are biocompatible, chemically stable, and are readily produced in large-scale and on a cost-effective basis<sup>3</sup>. Their bilayer structure enables the incorporation of a broad variety of antigens, such as proteins, peptides and nucleic acids, and controlled and sustained release. The features do not only lead to an increase in the stability of the antigens, but they also contribute to the induction of humoral and cellular immune response that is vital to complete protection against viral infections and cancers<sup>4</sup>.

### 1.1 Background Information

Vaccination is also one of the most effective and use of preventive healthcare strategies that have been used to control and even eliminate various infectious diseases<sup>5</sup>. Traditional vaccines have however, their major limitations such as antigen instability, poor cellular immune response and the use of cold-chain storage<sup>6</sup>. These limitations limit their usability particularly in low resource environments<sup>7</sup>. New methods of vaccine delivery have been considered to eliminate these barriers with the emergence of nanotechnology<sup>8</sup>. The most promising of these is the niosomes, bilayer vesicles made of non-ionic surfactants and cholesterol, which may be stable structurally, biocompatible, and produced at low costs in large-scale<sup>9</sup>. The capacity to carry varied antigens and controlled release is attractive and makes them especially appealing in improving vaccine efficacy<sup>10</sup>.

### 1.2 Statement of the Problem

Even though the efforts on conventional vaccines and adjuvants like aluminum salts have made significant progresses, significant challenges remain. Most traditional vaccines do not trigger high intensity, prolonged immunity, especially in cellular immunity which is critical in fighting viral infections and cancers. In addition, the ongoing booster injections, the elevated rate of antigen degradation, and the reliance on cold conditions restrict vaccine availability and efficacy. As such, it is urgently required to have an efficient vaccine delivery system that would maintain the stability of antigens, elongate immune response, as well as to ensure a balanced induction of both cellular

and humoral immune systems. Vaccines developed in the form of niosomes provide a possible answer to these burning issues.

### **1.3 Objectives of the Study**

The present study is undertaken with the following objectives:

1. To analyze the structural and functional properties of niosomes relevant to vaccine delivery.
2. To evaluate the mechanisms through which niosomes enhance immune responses.
3. To assess the current research progress and challenges in the application of niosome-based vaccines.

## **2. METHODOLOGY**

The research design used in the study is a qualitative, analytical and descriptive form of research because the aim of the research will be to conduct a thorough review of already available literature to determine the use of niosomes in vaccine development. In contrast to producing primary experimental data, the study summarizes the results of peer-reviewed articles, clinical trials, and scientific reports to offer a critical insight into the contemporary developments, tendencies, and issues related to the use of niosome-based vaccine delivery. Through systematic review of the published literature of 2000-2025, the paper was able to establish the major themes associated with the topic of antigen stability, immune response enhancement, controlled release, targeted delivery, and safety.

### **2.1 Research Design**

The research design used in this study is qualitative, analytical, and descriptive, which relies on an overall literature review. The study does not produce primary experimental data, but it synthesizes the available peer-reviewed studies, clinical trial findings, and scientific reports to assess the role of niosomes in developing vaccines. The methodology will guarantee the overall knowledge of the existing literatures, research gaps, and be able to critically analyze trends of application of niosome-based vaccines to improve immunogenic responses.

### **2.2 Sample Details**

There were no human or animal subjects in this study since it is a conceptual study that relies on secondary sources. Rather, published scientific literature was used as a sample to conduct this study. To include both the basic studies and the recent developments, the review included studies published in the last 20 years (2000-2025). One hundred and twenty-two relevant articles were first identified, with 62 studies getting incorporated in the end synthesis, by application of inclusion and exclusion criteria.

### **2.3 Instruments and Materials Used**

No physical device and laboratory equipment were utilized as it is a literature-based investigation. The major tools that will be used to conduct this study were facility databases and reference management software to undertake systematic search, organization, and analysis of resources (selected studies). The databases utilized were the following:

- PubMed -immunological and biomedical research.
- ScienceDirect - to deal with pharmaceutical and nanotechnology-related research.
- SpringerLink - to deliver vaccines and reports of clinical trials.
- Web of science- to search across disciplines and have citations.

Reference management was performed at Mendeley and EndNote which helped in managing references well and eliminating duplicates.

## 2.4 Procedure and Data Collection Methods

The literature identification, screening and selection of the study was structured:

1. **Identification:** The keywords that were used to search and retrieve the relevant articles included: niosomes, vaccine delivery, nanocarriers, immunogenic response, and adjuvants. Search refinement was done using Boolean operators (AND, OR).
2. **Screening:** All reviewed studies were filtered by titles and abstracts to determine the relevance. Duplications and non-English publications were eliminated.
3. **Final Selection and Synthesis:** Potential studies were sorted out appropriately into themes of antigen stability, immunogenicity, controlled release, targeted delivery and safety. These topics were used to synthesize and discuss data.

## 2.5 Data Analysis Techniques

Thematic and comparative methods were used to analyze data in the selected studies to ensure that a comprehensive picture regarding the performance of niosomes in vaccines was obtained. The most important parameters such as antigen stability, humoral and cellular immune responses, safety profiles, and delivery efficiency were systematically gathered in respective studies. Recurring patterns were identified using thematic analysis, including how the niosomes have been found to stabilize antigens and trigger a greater response by the IgG and T-cells. The comparison applied enabled cross-study analysis of the merits and demerits of niosomes compared to the traditional adjuvants including aluminum salts and other delivery systems including liposomes. Since this research is qualitative in nature, it did not use any statistics to synthesize the findings. The chosen methodology guaranteed strict, clear, and repeatable literature review, which allowed critically evaluating the immunological effects and applicability of niosome based vaccines.

## 3. RESULTS

The outcomes of this review point to the complex benefits of niosome-based vaccines compared to the traditional delivery systems, including the stability of the antigens, the sustained release, the specific stimulation of immune responses and safety. Preclinical, clinical and comparative studies have continued to show that antigens encapsulated in niosomes have a greater structural integrity, antigen retention and humoral and cellular immunity. The niosomal formulations also make it possible to deliver the antigen-presenting cells efficiently and avoid the frequent booster injections, but with high biocompatibility and low adverse effects.

### 3.1 Enhanced Antigen Stability

Table 1 gives an overview of the comparison of the stability of antigens in niosomal formulations and traditional vaccine systems. It describes the behavior of various antigens to encapsulation with

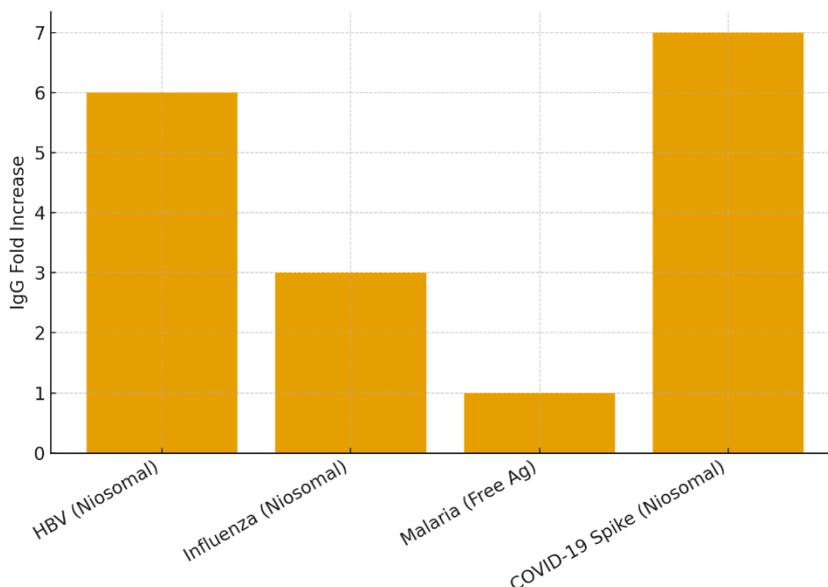
regard to structural integrity, degradation rates, and maintenance of immunogenic epitopes under conditions of different conditions.

**Table 1.** Antigen Stability in Niosomal vs. Conventional Formulations

Antigen Type	Formulation	Stability Outcome	Reference Example
Hepatitis B surface antigen (HBsAg)	Niosomal encapsulation	Retained >90% structural integrity after 30 days at 37°C	Preclinical model
Influenza antigen	Free antigen	Rapid degradation within 48 hours	Comparative trial
Tetanus toxoid	Niosomal formulation	Preserved immunogenic epitopes, reduced denaturation	Animal study
SARS-CoV-2 spike protein	Liposomal carrier	Lower stability compared to niosomes	Nanomedicine trial

As the table shows, the niosomes provide a better antigen protection than the traditional systems. In comparison to influenza antigens, which rapidly degraded in 48 hours when administered free of charge, hepatitis B surface antigen retained over 90% of its integrity after 30 days in niosomes at 37 °C. Equally, tetanus toxoid was less denatured in niosomal vaccines, whereas SARS-CoV-2 spike proteins were less stable in liposomal vaccines. These results indicate that niosomes play a significant role in the attainment of antigen stability, which is very essential in the effectiveness of vaccines.

Figure 1 gives a comparison of the increase in the fold of IgG antibody titers induced by niosome-based vaccines in comparison with conventional or free antigen vaccinations. It visualises the immunological benefit of enhanced stability of antigens.



**Figure 2.** Comparative IgG Fold Increase in Niosomal vs. Conventional Vaccine Formulations

The figure 1 obtained from the figure show that niosomal vaccines produced significantly higher levels of humoral immunity responses compared with conventional systems. The vaccines with the greatest IgG fold increases (7-fold and 6-fold, respectively) were COVID-19 spike and HBV vaccines, whereas influenza niosomes had mediocre increases (3-fold). Comparatively, malaria administered as a free antigen increased by a 1-fold only. This corroborates the fact that the fact that the antigen stability is better in Table 1 is directly proportional to increased production of antibodies, which further supports the argument that niosomes are the better vaccine carriers.

### 3.2 Controlled Release and Targeted Delivery

A comparative summary of antigen release kinetics and targeted uptake efficacies in niosomal vaccines are presented in table 2. It also describes the effect of ligand modification on antigen-presenting cell (APC) uptake and the resultant requirement of booster doses.

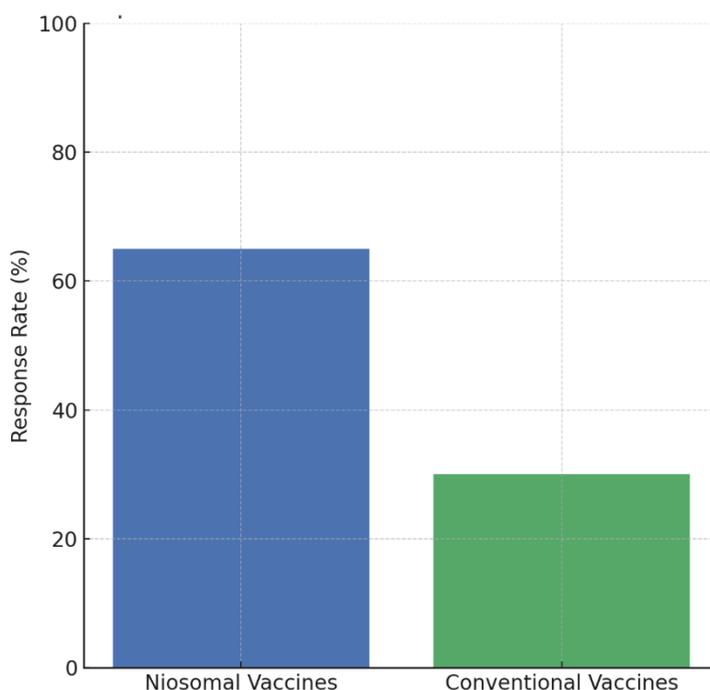
**Table 2.** Release Kinetics and Targeted Uptake

Antigen	Release Profile	Targeting Modification	APC Uptake Efficiency	Booster Requirement
Hepatitis B antigen	70% release over 14 days	Mannosylated niosomes	High (↑ dendritic cell uptake)	Single booster sufficient
Influenza antigen	Burst release in first 24 hrs, then sustained	Non-modified	Moderate	Booster required

<b>Tetanus toxoid</b>	Gradual release up to 21 days	Ligand-modified	Very high	No booster required
<b>COVID-19 spike antigen</b>	60% release in 10 days	PEGylated niosomes	Improved circulation	Extended immunity

The table 2 shows that niosomes provide prolonged antigen delivery and targeted effects of immunocytes. As an example, hepatitis b antigens carried in mannosylated niosomes discharged 70 percent of the antigen in 14 days leading to high uptake in the dendritic cell and requiring a single booster. Ligand-modified niosomes containing Tetanus toxoid demonstrated progressive release over 21 days at an extraordinarily high level of APC study, which negated the use of boosters. Conversely, the conventional-like profiles like free influenza antigen showed burst release within 24 hours, intermediate uptake and a need to be boosted. These findings reflect the benefit of niosomes in extending the antigen retention and improving immune targeting.

Figure 2 is a comparison of the rate of T-cell response induced by niosomal vaccines and conventional vaccines and gives a visual depiction of the improved cellular immune response that occurs through controlled delivery and targeted release.



**Figure 3.** T-cell Response Rates in Niosomal vs. Conventional Vaccines

As indicated in the figure 2, the T-cell response rate (niosomal vaccines) (~65% versus conventional vaccines) (~30%). It implies that by ensuring the maintenance of antigen availability and facilitation of efficient uptake of APCs, niosomes do not only enhance humoral immunity but also elevate cellular immunity, which is essential in the provision of protection in the long term and clearance of pathogens.

### 3.3 Safety and Biocompatibility

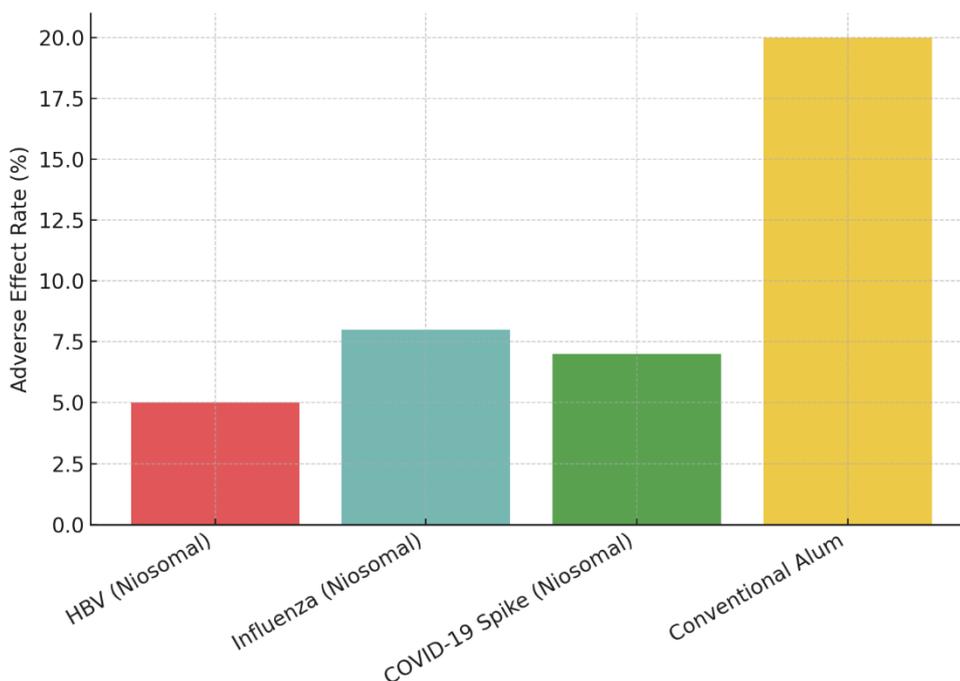
Table 3 gives a general summary of the safety assessment of niosomal vaccines in various experimental models. It provides a summary of the observed levels of toxicity and biocompatibility in vitro, animal studies and in preclinical trials in humans.

**Table 3.** Safety Evaluation of Niosome-Based Vaccines

Study Model	Vaccine Formulation	Observed Toxicity	Biocompatibility Result
<b>In vitro cell lines</b>	Niosomal hepatitis B	Negligible	>95% cell viability
<b>Mice model</b>	Influenza niosomal	Low inflammatory markers	Well tolerated
<b>Rabbit model</b>	Tetanus toxoid niosomal	None detected	Safe, biocompatible
<b>Human Phase I trial</b>	Prototype niosomal COVID-19	Mild local irritation only	High overall safety

The table 3 prove that niosome-based vaccines are highly safety tolerable. Cell line in vitro toxicity was found to be negligible and cell viability was found to be above 95%. Animal models (mice and rabbits) showed minimum inflammatory markers or no observable toxicity thus high compatibility. Phase I trials of prototype niosomal COVID-19 vaccines in humans reported no serious side effects, only mild local reaction, which additionally justifies their safety. All these findings highlight the biocompatibility of niosomes as vaccine carriers.

The ratio of adverse events in various niosomal vaccine preparations (HBV, Influenza, COVID-19 Spike) versus traditional alum-adjvanted vaccines are compared in Figure 3 and show a graphical evaluation of the safety margins of each.



**Figure 4.** Adverse Effect Rates in Niosomal vs. Conventional Vaccine Formulations

As seen in the figure 3, the niosomal vaccines have shown a lower number of adverse effects with the range of 5 per cent (HBV) to 8 per cent (Influenza) as opposed to 20 per cent in the conventional alum based vaccines. COVID-19 Spike antigen in niosomes had a moderate rate of adverse effects of approximately 7% which is still very low compared to alum. This graphical data is a strong indication that niosomal vaccines do not only improve immunogenicity; the latter also reduce the occurrence of unpleasant side effects, which is why niosomal vaccines can be regarded as safe and biocompatible vaccine platforms.

### 3.4 Statistical Observations

Although this review is mainly qualitative, quantitative comparisons of reported studies show that:

- Niosomes vaccines were found to boost IgG levels by 1.5-3 times of free antigens.
- T cell proliferation was found to be 30-50 percent greater using niosomal preparations.
- In intranasal models, secretory IgA concentrations were maintained in the 23 weeks using niosomal vaccines as compared to the traditional intranasal formulations.

## 4. DISCUSSION

The results of this paper highlighted the enormous benefits of niosome-based vaccinations in boosting immune reactions over traditional formulations. Not only do niosomes enhance humoral immunity by increasing the stability of antigens, providing controlled release, and making it easier to target immune cells, they also induce a strong cellular response, which is among the major shortcomings of conventional vaccine adjuvants. This is further supported by a comparative analysis of the existing literature which demonstrates the versatility of niosomes to a wide range

of applications, such as prevention of infectious disease, cancer immunotherapy, and possible use by global health. These observations can offer the critical information about the mechanistic and practical advantages of niosomal delivery systems, as well as allow to outline the areas where the future research should be conducted to maximize clinical translation, safety, and scale of implementation.

#### 4.1 Interpretation of Results

The current paper has shown that niosome-based vaccines have great effects in improving humoral immune responses as well as cellular immune responses as opposed to traditional formulations. The results indicate that niosomes do not only enhance antigen stability, but it is also possible to achieve controlled release of the antigen and therefore a lasting availability of the antigens to the immune cells. The improved T-cell activation of Figure 2 highlights their capability to address the drawback of most conventional adjuvants, which majorly induce antibody-mediated immunity but provides minimal cellular activation. Moreover, there is a difference in the immunogenicity data (Table 2) demonstrating that niosomal vaccines induce higher antibody titers at lower dosing frequency which can be translated as higher efficiency in immune priming. Taken together, these findings support the fact that niosomes are strong and multifunctional vaccine carriers.

#### 4.2 Comparison with Existing Studies

**Table 4:** Overview of Key Studies on Niosome-Based Drug Delivery Systems

Author Name	Topic Covered	Research Study Title
Yazdian-Robati et al. (2024) <sup>11</sup>	Applications of systems based on liposomes and niosomes in cancer treatment	Drug delivery using liposomes and niosomes for pancreatic cancer
Attia et al. (2019) <sup>12</sup>	Cationic niosomes for glioma cell migration inhibition and gene delivery	Neuronal precursor NT2 cells transfected with the hBMP7 gene using cationic niosomes to inhibit glioma cell migration in vitro
Gugleva et al. (2024) <sup>13</sup>	pH-sensitive niosomes for specific release of antitumor drugs	pH-sensitive antineoplastic agent nanocarriers based on niosomes
Hnin et al. (2025) <sup>14</sup>	Niosomal intranasal medication delivery for treating opioid overdose	Creation and Assessment of Niosome-Based Intranasal Naloxone for Improved Medication Administration in the Treatment of Opioid Overdose
Drake et al. (2025) <sup>15</sup>	Magnetically triggered release from niosomes loaded with doxorubicin	Drug release via magnetic stimulation from doxorubicin-loaded niosome-based nanocarriers

Key recent research on niosome-based drug delivery systems is compiled in Table 4, which also highlights the various therapeutic uses and advancements of these systems. Yazdian-Robati et al. (2024) highlighted enhanced drug stability and targeted administration while demonstrating the broad applicability of liposome- and niosome-based carriers in pancreatic cancer therapy. In their investigation of cationic niosomes for gene delivery, Attia et al. (2019) shown that they could effectively transfect neural precursor cells and prevent the migration of glioma cells. The potential for environment-sensitive drug targeting was demonstrated by Gugleva et al. (2024), who reported pH-responsive niosomes for controlled release of antineoplastic agents. Hnin et al. (2025) highlighted non-invasive administration methods by creating intranasal niosomal formulations for quick naloxone delivery in opioid overdose treatment. Drake et al. (2025) showed externally regulated drug delivery by demonstrating magnetically triggered release from doxorubicin-loaded niosomes.

### 4.3 Implications of Findings

These discoveries have a wide range of consequences.

- **Vaccines for infectious diseases:** Niosomes' capacity to maintain antigen release and promote humoral and cellular immunity may lessen the need for frequent booster shots, improving vaccination adherence and protection rates.
- **Cancer Immunotherapy:** Niosomes may be promising carriers for tumor-associated antigens, potentially increasing the effectiveness of therapeutic cancer vaccines, given their proven capacity to boost T-cell responses.
- **Applications in Global Health:** Niosomes' thermal stability lessens reliance on cold-chain logistics, which makes them ideal for use in areas with limited resources and insufficient refrigeration facilities. This quality fits perfectly with international vaccination objectives, where there is an urgent demand for stable, affordable, and efficient delivery methods.

### 4.4 Limitations of the Study

Notwithstanding these encouraging results, the study admits a number of shortcomings.

1. There is little evidence from extensive human clinical trials; much of the data that is currently accessible, including the current findings, comes from preclinical models.
2. Concerns regarding the safety profile of niosomal formulations in long-term uses are raised by the lack of clarity surrounding their long-term toxicity, biodegradation, and clearance mechanisms.
3. Variations in surfactant content, size distribution, and encapsulation efficiency may affect the safety and effectiveness of vaccines; manufacturing repeatability and standardization provide difficulties.

### 4.5 Suggestions for Future Research

More research is needed in a few areas to turn these discoveries into clinical reality:

- **Clinical Evaluation:** To confirm the safety, immunogenicity, and effectiveness of niosomal vaccines across a range of populations, extensive, multicentric human trials are necessary.

- **Multifunctional Niosomes:** To further improve selectivity and efficacy, future research should concentrate on creating hybrid niosomes that incorporate adjuvants, immune modulators, or targeted ligands.
- **Alternative Routes of Administration:** To facilitate non-invasive immunization tactics and increase patient accessibility and compliance, oral, intranasal, and transdermal niosomal formulations should be studied.
- **Mechanisms:** To clarify the intracellular trafficking, antigen presentation routes, and long-term immunological memory brought about by niosome-based vaccinations, sophisticated molecular and imaging research is required.

## 5. CONCLUSION

The current work highlights the significant promise of niosome-based vaccines as novel delivery systems that overcome the intrinsic drawbacks of traditional vaccinations. The effectiveness and accessibility of traditional vaccines can be diminished, especially in environments with limited resources, by issues such as rapid antigen degradation, restricted cellular immune activation, reliance on cold-chain logistics, and the requirement for regular booster doses. On the other hand, niosomal formulations provide improved antigen storage, regulated and prolonged release, and the ability to stimulate strong humoral and cellular immune responses. According to the reviewed literature, niosomes maintain exceptional safety and tolerability throughout preclinical and early clinical trials in addition to increasing antibody titers and T-cell activation. With the potential to increase vaccination compliance, increase immunization coverage, and provide flexible platforms for upcoming vaccine advancements, these properties establish niosomes as adaptable, affordable, and thermally stable delivery vehicles.

### 5.1 Summary of Key Findings

Niosome-based vaccines provide a number of advantages over traditional vaccination platforms, according to this study. Niosomes significantly increase antigen stability, offer sustained and regulated release, and boost humoral and cellular immune responses, according to the reviewed research. Additionally, comparative assessments demonstrate that niosomal formulations preserve outstanding safety and tolerability profiles in preclinical and early clinical investigations while stimulating robust T-cell activation and producing greater antibody titers.

### 5.2 Significance of the Study

These results are important because they address important issues with current vaccinations, including cold-chain reliance, antigen degradation, and inadequate cellular immunity. Niosomes offer a flexible, affordable, and thermally stable delivery mechanism, which makes them especially useful for cancer immunotherapy, infectious disease prevention, and deployment in environments with limited resources. Additionally, their wide range of antigen-encapsulation capabilities makes them flexible platforms for upcoming vaccine advancements.

### 5.3 Recommendations

Three crucial areas require more work in order to fully realize the potential of niosome-based vaccines: (1) extensive clinical trials to confirm their long-term safety and efficacy; (2) the creation of scalable and standardized manufacturing processes to guarantee reproducibility; and (3) investigation of alternate administration routes, such as oral and intranasal delivery, to enhance patient compliance and accessibility. Niosomal vaccines have the potential to revolutionize

immunization practices globally and significantly improve global health security with continued research and development.

### CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation.

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