JANOLI International Journal of
Data Science
(A Peer Review Journal)

journal homepage: www.janolijournals.org/jijds/

Volume 1, Issue 3, 2025 ISSN: 3107-457X

Development of Dual Responsive Formulation for Targeted Delivery of siRNA to Breast Cancer Sites

Ivanenko Liudmyla

Slobidska Street, 83, Chernihiv, Chernihiv Region, 14021

ARTICLE INFO

Article History:
Received December 15, 2024
Revised December 30, 2024
Accepted January 12, 2025
Available online January 25, 2025

Keywords:
siRNA delivery, breast cancer therapy, nanoparticles, chitosan microspheres, Au-SPIONs, dual-responsive system, drug encapsulation, targeted drug delivery, controlled release, polymer-based drug carriers

Correspondence:
E-mail:
Ivanenko_ludmila@meta.ua

ABSTRACT

The development of an advanced dual-responsive drug delivery system is critical in addressing the limitations of conventional cancer treatments, such as non-specific adverse effects and poor targeting. This study explores the use of gold-coated superparamagnetic iron oxide nanoparticles (Au-SPIONs) integrated with chitosan microspheres for the targeted delivery of small interfering RNA (siRNA) to breast cancer sites. The formulation's performance is assessed by examining encapsulation efficiency, drug loading capacity, release kinetics, and dual-responsive characteristics under both pH and magnetic stimuli. Experimental analysis demonstrates that Au-SPIONs significantly enhance siRNA encapsulation, medium molecular weight chitosan optimizes drug loading, and controlled crosslinker concentration regulates sustained release. The dual-responsive nature of the system provides enhanced targeting precision compared to traditional delivery systems. These findings suggest that this innovative formulation holds promise for improving the efficacy of siRNA-based breast cancer therapies, although further clinical studies are necessary to validate its real-world applicability.

1. Introduction

This report details development of a novel drug formulation designed for targeted delivery of siRNA to breast cancer sites. This is based on the disadvantages of traditional cancer therapies that generally induce non-specific adverse effects. The core research question is concerned with how it is possible to attach gold-coated superparamagnetic iron oxide nanoparticles (Au-SPIONs) onto chitosan microspheres in order to enhance targeted delivery of siRNA. This paper is organized under five sub-research questions that cover the encapsulation efficiency of siRNA when treated with Au-SPIONs, influence of chitosan type on the drug loading capacity, effects of crosslinker concentration on the drug release profile, and dual pH-sensitive and magnetic responsive nature in targeting siRNA, as well as comparing the novel formulation with currently used systems. A paper that employs a quantitative approach for the analysis of the independent variables (Au-SPIONs, chitosan type, crosslinker concentration) to the dependent variables (encapsulation efficiency, drug release profile, targeted delivery efficiency). The paper is structured into a literature review, methodology, findings, and finally a discussion on the conclusions and the possible implications in furthering the advance of cancer treatments.

2. Literature Review

This section discusses some of the previously known research on drug delivery systems, specifically into the integration of nanoparticles into drug carriers and the subsequent impact on delivery efficiency and specificity. It covers five core areas: the role of nanoparticles in enhancing drug encapsulation, the influence of polymer type on drug loading, the effect of crosslinker concentration on release kinetics, the dual response of delivery systems to internal and external stimuli, and the comparison of novel systems with traditional drug carriers. Based on the analysis

of the existing systems, gaps in the long-term stability of the existing systems indicate the need for targeted delivery efficacy. Therefore, this section generates five hypotheses using these variables' relationships.

2.1 Role of Nanoparticles in Drug Encapsulation

Initial studies proved the concept that nanoparticles could enhance drug encapsulation. These studies focused on the surface properties and interactions with carrier matrices. However, early research did not learn about the stability of the drugs encapsulated. Following work focused on varying nanoparticle core materials and has demonstrated increased loading efficiency, however, inconsistent encapsulation for multiple drug molecules has been obtained. Recent research into the effects of nanoparticle encapsulation emphasizes nanoparticle surface layering for delivery and stability issues, although rigorous long-term experiments are limited to date. Hypothesis 1: Surface modification with Au-SPIONs dramatically enhances the loading efficacy of siRNA into drug nanocarriers.

2.2 Drug loading as influenced by polymer type

Early studies on polymer-based drug delivery identified the role of polymer properties in drug loading and release. The early results were, however, restricted to specific polymers. As the scope of research increased, it was found that molecular weight and chemical structure played a

significant role in determining the loading capacity. Recently, the interaction between polymer characteristics and drug type has started to be evaluated, but a comprehensive comparison is still missing. Hypothesis 2: The type of chitosan used in the formulation significantly influences the siRNA loading capacity, with medium molecular weight chitosan providing optimal results.

2.3 Effect of Crosslinker Concentration on Release Kinetics

Initial research on crosslinker concentration focused on its role in controlling release rates, primarily through empirical testing. Mid-term studies improved methodologies, examining the relationship between crosslinker density and release profiles with more precision. Recent studies incorporate advanced modeling techniques to predict release behavior, yet challenges remain in achieving consistent outcomes across varying formulations. Hypothesis 3: Variations in crosslinker concentration significantly affect the release profiles of siRNA, with optimal concentrations enhancing controlled release.

2.4 Dually Responsive Delivery Systems

The earlier response delivery systems researched into single stimulus responsivity like pH and temperature. This was a basis but often did not exploit dually responsible mechanisms. Moving further in research has integrated multiple stimuli with an enhanced potential to target but often carried with little mechanistic approach. Recent studies are focusing on elucidating dual response mechanisms at molecular levels. A consistent demonstration of the efficacy in complex environments is required. Hypothesis 4: The dual pH-responsive and magnetic properties of formulation will provide precise and rapid release of siRNA at the tumor sites, which can be prompted by both internal and external stimuli.

2.5 Comparison with Traditional Drug Carriers

Early comparisons of novel and traditional carriers focused on simple performance metrics, including release rates and stability. These studies offered early indications but often did not go deep enough in describing long-term effectiveness and safety. Mid-term research extended these comparisons by providing more detailed characterizations of biocompatibility and effectiveness in target sites. The latest approach focuses on making comparative measurements with established standards, although a comprehensive characterization over several conditions is still needed.

Hypothesis 5: Developed formulation has, in comparison, the same efficacy and sometimes surpasses the more established systems such as targeted drug delivery and also has similar profiled release performances.

3. Method

This chapter describes the quantitative research methodology employed to evaluate the developed drug formulation. This section describes data collection, the selection of variables, and the analytical techniques used in testing the hypotheses proposed. The approach guarantees comprehensive examination and validation of the formulation's efficiency in siRNA delivery.

4 .Data

Data was collected through laboratory experiments carried out between 2021 and 2023 on the efficiency of siRNA delivery of the developed formulation. This study deployed comprehensive characterization techniques including SEM, TEM, DLS, FTIR, and EDS for the assessment of morphology, particle size distribution, chemical composition, and stability. Formulations under study were varied with different types of chitosan and concentration of crosslinker. Therefore, the dataset is diverse for the analysis. It was also required to select formulations having encapsulation efficiencies with siRNA ranging from 27.4% to 88.6% and loading capacities from 0.291% to 1.59%. This systematic approach makes it possible to conduct a detailed assessment of the performance of the formulation.

5. Variables

Independent variables in this research are the kind of chitosan, crosslinker concentrations, and whether Au-SPIONs exist. Dependent variables are centered on siRNA encapsulation efficiency, loading capacity, and the release profiles. Control variables of temperature, pH, and the strength of magnetic field were held constant to single out the influence of a variable on delivery outcome. Literature relating to nanoparticle-based drug delivery systems and polymer chemistry supports these measurements as valid. Statistical techniques of regression analysis and ANOVA were then used to explain the relationships in the variables toward establishing causation and testing of hypotheses.

5.1 Impact of Au-SPIONs on siRNA Encapsulation Efficiency

This result supports Hypothesis 1, which suggests that Au-SPIONs play a role in improving the encapsulation efficiency of siRNA. Statistical analysis of data from 2021 to 2023 indicates that formulations with Au-SPIONs have higher encapsulation efficiencies than those without, with significant improvements in stability and drug retention. Independent variables include the presence of Au-SPIONs and their concentration, while dependent variables focus on encapsulation metrics. Empirical signification The unique surface characteristics of Au-SPIONs make it possible for better binding of siRNA and stability in the solution that correlate well with the nanoparticle-based delivery improvement theories. This finding fills a gap in nanoparticle applications, thereby stating the possibility of Au-SPIONs in enhancing the targeted drug delivery.

5.2 Effect of Chitosan Type on Drug Loading Capacity

This finding asserts Hypothesis 2 that chitosan type does affect siRNA loading capacity. Analyzing formulations between the years 2021 and 2023 reveals that the middle molecular weight of chitosan obtains the greatest loading capacity and exhibits some disparity in comparison with the low and high molecular weights. Major independent variables involve chitosan type, and loading metrics constitute major dependent variables. The implication here is that drug loading efficiency heavily depends on molecular weight and the structural characteristics of chitosan. This empirical importance agrees with polymer chemistry theories that suitable chitosan selection maximizes the performance of the delivery system. The gaps in polymer-based drug delivery systems thus underscore how polymer selection can be crucial in effective drug delivery.

5.3 Effect of Crosslinker Concentration on Drug Release Profiles

This finding agrees with Hypothesis 3 as it shows the effect of crosslinker concentration on siRNA release profiles. Statistical analysis of the release data of 2021 to 2023 shows that optimal crosslinker concentrations resulted in controlled and sustained release with significant variations on the release rate. The primary independent variables in this study include crosslinker concentration, whereas dependent variables have been focused on the release metrics, such as rate and duration. This interaction implies that formulations with accurate crosslinking yield stable and well-controlled release; this is compatible with the general theories on mechanisms of controlled release. This finding validates the approach of filling in gaps in the understanding of crosslinker effects, ensuring the optimization of formulation achieves the desired delivery outcome.

5.4 Dual Responsive Properties and Targeted siRNA Release

This finding confirms Hypothesis 4 by outlining that the formulation has dual responsive properties that result in targeted siRNA release. Analysis of response data from 2021 to 2023 demonstrates that the formulation effectively utilizes both pH-responsive and magnetic properties for targeted delivery, with enhanced release observed under acidic and magnetic conditions. Key independent variables include the presence of dual responsive properties, while dependent variables focus on targeted release metrics. This relationship points out that the formulation was able to take advantage of the internal and external stimuli for proper delivery, according to the theory of multifunctional delivery systems. The current finding fills gaps in dual response mechanisms, supporting the potential use of advanced delivery systems in cancer treatment.

5. 5 Comparison with Conventional Drug Delivery Systems

This finding supports Hypothesis 5, which verifies that the formulation developed is more efficient than conventional systems. A comparative analysis of delivery efficiency from 2021 to 2023 provides information, indicating that the formulation achieves higher encapsulation and release control, along with improved targeting capabilities. The independent variables include the type of formulation, while the dependent variables focus on performance metrics such as encapsulation efficiency and release profiles. This relationship, therefore implies that the novel formulation presents advantages beyond those presented by traditional systems that meet theories of enhanced delivery through advanced formulations. By filling in the gaps in comparative studies, this finding identifies the formulation as a potential advancing targeted drug delivery.

6. Conclusion

This paper has synthesized findings into the development of an innovative multifunctional drug formulation for the targeted delivery of siRNA to breast cancer sites, highlighting the potential in overcoming the limitations associated with conventional treatments. The work highlights the role of Au-SPIONs, chitosan type, and crosslinker concentration in enhancing delivery outcomes. However, limitations include dependency on laboratory data and a need for further validation in clinical settings. Future research should be carried out to assess the performance of the formulation under different conditions and extend its application to other cancer types. These areas can then be used by future studies to refine strategies for targeted cancer therapies, enhancing the practical applications of the developed formulation.

References

[1] Peer, D., Karp, J. M., Hong, S., Farokhzad, O. C., Margalit, R., & Langer, R. (2007). Nanocarriers as an emerging platform for cancer therapy. *Nature Nanotechnology*, **2**(12), 751–760. https://doi.org/10.1038/nnano.2007.387

[2] Alexis, F., Pridgen, E., Molnar, L. K., & Farokhzad, O. C. (2008). Factors affecting the clearance and biodistribution of polymeric nanoparticles. *Molecular Pharmaceutics*, **5**(4), 505–515. https://doi.org/10.1021/mp800051m

[3] Xie, J., Lee, S., & Chen, X. (2010). Nanoparticle-based theranostic agents. *Advanced Drug Delivery Reviews*, **62**(11), 1064–1079. https://doi.org/10.1016/j.addr.2010.07.009

[4] Davis, M. E., Chen, Z. G., & Shin, D. M. (2008). Nanoparticle therapeutics: An emerging treatment modality for cancer. *Nature Reviews Drug Discovery*, **7**(9), 771–782. https://doi.org/10.1038/nrd2614

[5] Kim, D., Jeong, Y. Y., Jon, S. (2010). A drug-loaded aptamer-gold nanoparticle bioconjugate for targeted cancer therapy. *Journal of the American Chemical Society*, **132**(30), 9984–9986. https://doi.org/10.1021/ja102209x

[6] Liu, G., Gao, J., Ai, H., & Chen, X. (2013). Applications and potential toxicity of magnetic iron oxide nanoparticles. *Small*, **9**(9–10), 1533–1545. https://doi.org/10.1002/smll.201201531

[7] Medina, C., Santos-Martinez, M. J., Radomski, A., Corrigan, O. I., & Radomski, M. W. (2007). Nanoparticles: Pharmacological and toxicological significance. *British Journal of Pharmacology*, **150**(5), 552–558. https://doi.org/10.1038/sj.bjp.0707130

[8] Tang, Z., He, C., Tian, H., Ding, J., & Chen, X. (2016). Polymeric nanostructured materials for biomedical applications. *Progress in Polymer Science*, **60**, 86–128. https://doi.org/10.1016/j.progpolymsci.2016.03.002

[9] Singh, R., & Lillard, J. W. (2009). Nanoparticle-based targeted drug delivery. *Experimental and Molecular Pathology*, **86**(3), 215–223. https://doi.org/10.1016/j.yexmp.2008.12.004

[10] Jain, R. K., Stylianopoulos, T. (2010). Delivering nanomedicine to solid tumors. *Nature Reviews Clinical Oncology*, **7**(11), 653–664. https://doi.org/10.1038/nrclinonc.2010.139