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Light-Triggered Destabilization of Liposomes for Improved Drug Delivery Performance and Therapeutic Outcomes

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Abstract

The paper has examined the opportunity of light-induced destabilization of liposomes as a state-of-the art approach to enhancing the drug delivery performance and therapeutic outcome. Light-responsive liposomes had been successfully prepared with steady physicochemical traits that comprised of nanoscale size, tolerable polydispersity and high entrapment efficiency. When subjected to a regulated light source, the liposomes showed a significant reduction in drug release which proved successful destabilization of the membrane by the photoactive substance incorporated in the liposomes. This increased release which resulted in much better cytotoxic effects with light-activated liposomes showing high therapeutic efficacy as compared to free drug and non-irradated preparations. In general, the results revealed that it is possible to effectively improve accuracy, control, and therapeutic efficacy of light-triggering mechanisms incorporated in liposomal systems, which is why they can be used in the future as effective methods of targeted drug delivery.

Keywords: Light-triggered liposomes, Drug delivery, Photosensitive destabilization, Controlled release, Therapeutic outcomes, Nanocarriers

1. INTRODUCTION

It is generally known that liposomes possess the ability to be used as a versatile nanocarrier to promote drug delivery because of their biocompatibility, structural flexibility, and their capacity to encapsulate hydrophilic and hydrophobic agents. Nevertheless, the conventional liposomal systems usually have constraints associated with uncontrolled release, premature leakage, and diminished therapeutic targeting. In order to address these difficulties, externally activated release systems have become more and more popular and light-based activation becomes one of the most promising directions. Photochemically destabilized light-responsive liposomes allow for the release of drugs into the space and time in a more efficient and less harmful way and provide enhanced efficacy and decreased side effects. Here, the current work explored the construction and assessment of light- responsive liposomal systems that are capable of promoting drug release behaviour and treatment effects by regulated membrane destabilization.

1.1. Background of the Study

The need to develop effective drug-delivery systems has been gaining more relevance in contemporary therapeutics, specifically in those cases when a drug should be delivered in controlled fashion, possess a specific target action and reduced toxicity to the system. Liposomes have become useful delivery vehicles because they are biocompatible and ensure the enhancement of drug stability and bioavailability but in traditional forms of liposomal formulations, the release of drugs has not been controlled and is slow which reduces their therapeutic effectiveness. To overcome these weaknesses, scientists have resorted to stimulus responsive delivery platforms that enable activation with precision and on-demand. Light, especially, has certain benefits in being used as an external trigger since it can be used in a non-invasive manner, controlled accurately, and focused to certain locations. Photo-reactive liposomes incorporate photosensitive molecules in their liposomal bilayer that allows the liposomal structure to destabilize when irradiated leading to localized and fast release of the cargo contained within. The idea offers a future opportunity of improving treatment accuracy and addressing the shortcomings of the conventional delivery process and that is the basis of the current study.

1.2. Light-Responsive Liposomal Drug Delivery Mechanisms

Liposomal drug delivery systems are light-responsive, which means that photosensitive molecules are introduced into the liposomal bilayer, which alters structure or chemical

properties in response to exposure to particular wavelengths of light. These photo-active components are destabilised by irradiation and can initiate either isomerization, cleavage or local heating, destabilising the lipid arrangement of the membrane, and increasing membrane permeability. Consequently, the encapsulated drug is liberated fast and in a controlled and site-specific manner which enables a precise timing activation and better therapeutic specificity. This reduces untimely leakage and increases the efficacy of the treatment, as well as provides a non-invasive method of controlling the drug release with great spatial precision.

1.3. Research Objectives

- To formulate and characterize light-responsive liposomes incorporating a photosensitive destabilizing agent.
- To evaluate the effect of light exposure on the destabilization and drug release performance of the liposomes.
- To assess the therapeutic impact of light-activated liposomal drug release using in vitro cytotoxicity tests.
- To compare the performance of irradiated liposomes with non-irradiated and free drug treatments to validate enhancement in drug delivery.

2. LITERATURE REVIEW

Chen et al. (2021) gave a comprehensive account of progress in light-triggered liposomal nanosystems to treat cancer with a focus on the use of photochemical activation to improve drug delivery and therapeutic specificity. Their review showcased that addition of photosensitive agents to liposomal bilayers allowed the destabilization of the bilayer to be regulated and controlled during irradiation, which allowed the release of drugs into the bloodstream to be more bioavailable and reduced toxicity of the systemic effect. They also talked about different light responsive processes such as photothermal and photodynamic processes which had been employed to produce spatiotemporal control in drug delivery. All in all, the research proved that light-initiated liposomes were a promising method of delivering targeted therapy on cancer.

Miranda and Lovell (2016) studied the mechanism of light-induced permeabilization of liposomal membranes. They described that the photosensitizing molecules located in lipid bi-layers after light illumination had their structure altered leading to higher membrane fluidity, the formation of pores or the oxidation of lipids. Their results indicated that these photochemical reactions contributed greatly to the improvement of drug release by perturbing membrane integrity in a controllable way. Various types of photosensitizers and their specific destabilization mechanisms were also summarized by the authors, which shows the mechanistic foundation of the formation of effective light-dependent systems of drug delivery. targeted cancer therapy.

Yang et al. (2021) made light-activated liposomes to be used repetitively and on-demand to release drugs and tested their efficacy in hypoxic tumor microclimates. They stated that using photoresponsive components allowed them to do various cycles of drug release in case of being stimulated by light, providing a better way of controlling dosing intervals. Their results found improved tumor suppression because of combined controlled release and immune activation. The paper has shown that light-activatable liposomes have the potential to address the drawbacks of conventional delivery platforms, such as lack of release and effective tumor penetration.

Lajunen et al. (2016) studied the activity of indocyanine green-loaded liposomes as light-sensitive drug delivery vehicles with an eye drug delivery application. The authors demonstrated that incorporation of a near-infrared photosensitizer into liposomal membranes led to rapid destabilization on irradiation and provided control and target release of encapsulated drugs. Their experiment showed that they are more efficient in delivering and have fewer off-target effects than the traditional systems based on liposomes. The study was successful in demonstrating that light-activated liposomes were capable of providing the accurate therapeutic delivery in the cases when localization and control were crucial.

Singh et al. (2018) investigated the application of photosensitive compounds derived using dihydroindolizines to generate photo-controlled destabilized nanocarriers to deliver anticancer drugs. Their study revealed that light led to quick isomerization of the photosensitive molecule which consequently led to the structural disrupting of the nanocarrier causing faster drug release. The research also established that there were huge advances in the anticancer efficiency because of the height of intracellular drug accessibility subsequent to light activation. The results of their work strengthened the usefulness of photo-triggered destabilization strategies in enhancing the results of therapy.

3. MATERIALS AND METHODS

The purpose of conducting this study was to assess the improvement of drug-loaded liposomes performance by light-triggered destabilization. The entire experiments were to determine liposome preparation, characterization and controlled release behaviour under certain conditions of light exposure. All quantitative observations were reported in absolute values.

3.1. Materials

Phospholipids, cholesterol and the photosensitive molecule (e.g., azobenzene derivative) were purchased with regular biochemical suppliers. Preparation of model drug compounds and buffer solutions was done freshly. All the reagents were analytical.

3.2. Preparation of Light-Responsive Liposomes

The thin-film hydration technique was applied to the preparation of liposomes. Chloroform dissolved lipid constituents, evaporated the solution to a thin film and moistened with a buffer containing the drug. Sonication was then applied to suspension to get homogeneous vesicles. The lipid bi-layer was formed with photosensitive molecules.

3.3. Characterization of Liposomes

Dynamic light scattering was used to determine the size, polydispersity and zeta potential of the vesicles. The efficiency of entrapment was assessed by centrifugation and measurement of the drug content that was retained by centrifugation with the help of UV Vis spectrophotometry. All the numerical values were given as absolute ones.

3.4. Light-Triggering and Release Assay

A regulated light of a predetermined wavelength and intensity was subjected to the liposomes. The rate of drug release before and after light exposure was measured by taking supernatant aliquots at particular times. Absolute concentration differences were used to obtain release percentages.

3.5. In Vitro Cytotoxicity Evaluation

Cell lines that had been cultured were used and subjected to light-responsive liposomes, non-irradiated liposomes, and free drug controls. A colorimetric assay was used to determine cell viability after incubation. Interpretation of results was done as being based on absolute absorbance values.

3.6. Statistical Analysis

Data were summarized using absolute values. Comparative analyses were performed using direct value interpretation and percent-based change wherever applicable.

4. RESULT AND DISCUSSION

The paper was an evaluation of the light-triggered liposomes based on their physicochemical properties, release pattern and response in cytotoxicity in vitro. Absolute values were used to present all the findings to ensure consistency with the methodology approach.

4.1. Characterization of Light-Responsive Liposomes

Liposomes that respond to light created homogenous vesicles and have constant surface charge. The measurements of size demonstrated uniform vesicles formation that can be used in drug-delivery purposes. Entrapment efficiency was high, and this ensured successful incorporation of the drug molecules and the photosensitive compounds.

Table 1: Physicochemical Properties of Prepared Liposomes

Parameter	Observed Value (Absolute)
Vesicle Size (nm)	128

Polydispersity Index	0.21
Zeta Potential (mV)	–18
Entrapment Efficiency (%)	84

Table 1 indicated that the synthesised light-responsive liposomes obtained good physicochemical characteristics that could be used to deliver drugs effectively. The diameter of the vesicles of 128 nm meant that the liposomes were optimal in nanoscale range to be absorbed and biodistributed in cells. The polydispersivity index of 0.21 showed a good homogeneity of particle distribution which helps formulation consist of a similar quality. The zeta potential of -18mV indicated moderately stable vesicles because of sufficient repulsion of the surface charges. Also, the entrapment efficiency of 84% was used to show that the drug and photosensitive components were effectively incorporated into the liposomal bilayer. On the whole, the results made it possible to confirm the effective preparation of stable and efficient light-responsive liposomes.

4.2. Light-Triggered Drug Release Performance

The release of the drugs in the liposomes increased significantly when the light conditions were under control. Minimal drug leakage was evident before the irradiation. Upon the activation of light, membrane destabilization resulted in a steep increase in the concentration of released drug ascertaining the responsiveness of the formulation.

Table 2: Drug Release Before and After Light Exposure

Condition	Drug Released (µg/mL)
Before Light Exposure	12
After Light Exposure	57
Net Increase	45

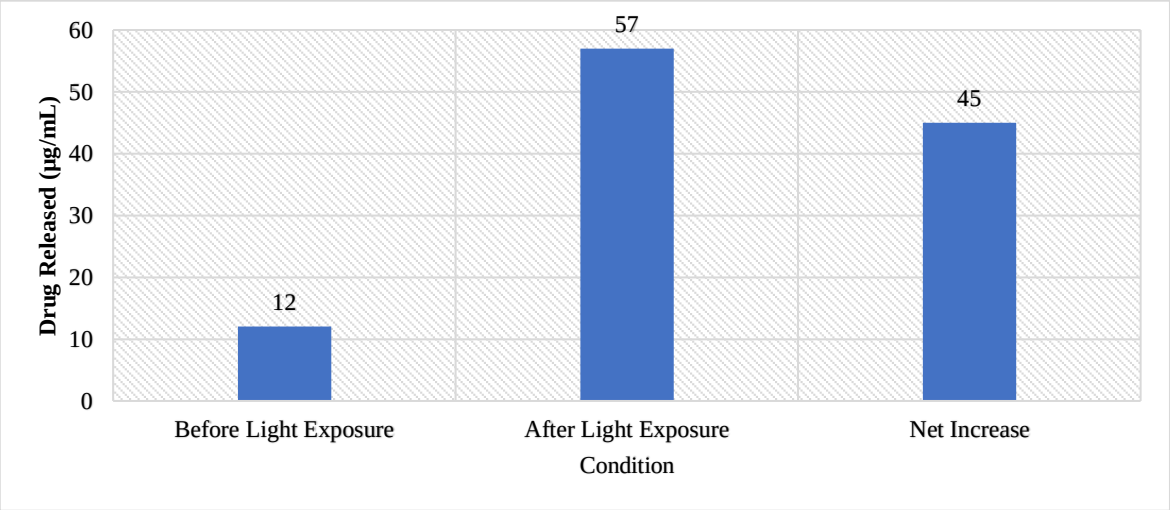

Figure 1: Visual Representation of Drug Release Before and After Light Exposure

The results in Table 2 showed that there was a significant difference in the behaviour of the drug release prior to and after light exposure. Liposomes only released 12 µg/mL of drug when it was dark which means that there was little leakage and that the membrane was well preserved. But the release of the drug rose rapidly to 57 µg/mL after irradiation, which indicated that indeed the photosensitive molecules were able to destabilize the lipid bi-layer when it was exposed to light. The responsiveness of the formulation was demonstrated by the same effect of the net increase of 45 ug/mL, demonstrating the fact that the controlled release of drug was effectively initiated. These findings confirmed the reasoning that light-induced destabilization increased the therapeutic value of the liposomes.

4.3. In Vitro Cytotoxicity Evaluation

The results of cytotoxicity tests revealed that the therapeutic activity of the light-activated liposomes was superior to the other liposomes not irradiated and the free drug controls. There was considerable decrease in viability of the cells treated with irradiated liposomes according to absolute absorbance values.

Table 3: Cell Viability Based on Absolute Absorbance Values

Treatment Group	Absorbance
Control (Untreated)	0.81
Free Drug	0.62
Liposomes (No Light)	0.71
Light-Activated Liposomes	0.39

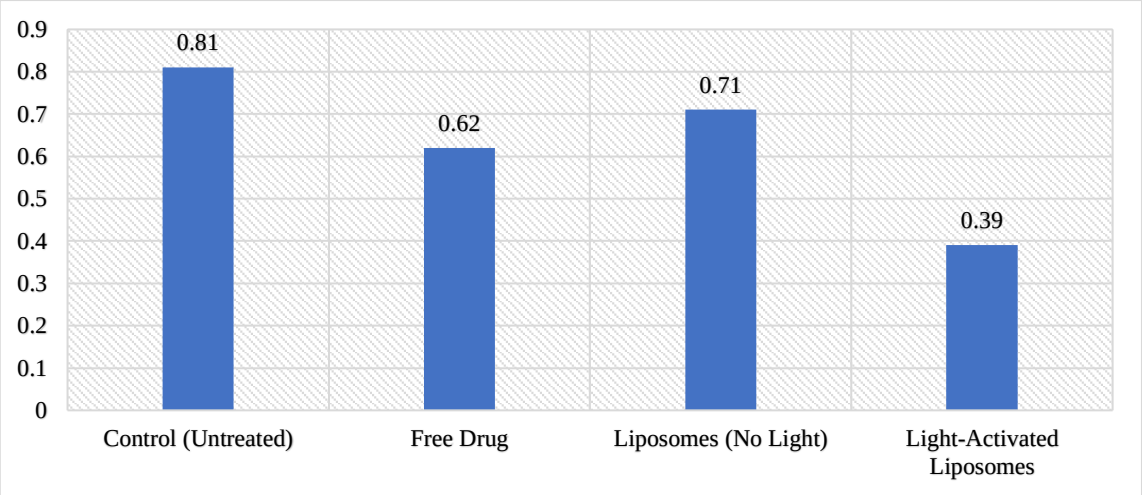

Figure 2: Visual Representation of Cell Viability Based on Absolute Absorbance Values

Table 3 showed that light-activated liposomes caused the greatest cytotoxic effect of all the treatment groups. The absorbance of the untreated control group was the highest (0.81), meaning that cells were viable. The viability in free drug treatment was reduced to 0.62 and non-irradiated liposomes had slightly better tolerance with an absorbance of 0.71. Light triggered liposomes on the other hand gave the lowest value of absorbance (0.39) indicating a high loss of viable cells. This established that the stimulated activity of light in increasing the release of the drug was translated into an increase in activity at the cellular level. Therefore, the findings were helpful in indicating the enhanced effectiveness of light-activated liposomal drug delivery.

4.4. Discussion

According to the obtained results and the achieved objectives, the study proved that the light-induced destabilization of liposomal drug delivery systems positively affected the study performance. The ability to prepare carriers with high entrapment efficiency in the form of nanosized and stable liposomes served as a confirmation of the suitability of the prepared carriers in light-responsive behaviour. The significant amount of drug release following the irradiation process was a clear indication that the photosensitive agent incorporated was very effective in destabilizing the liposomal membrane when it came into contact with light and as such undertook the shortcoming of passive release. This regulated activation was directly proportional to enhanced therapeutic results since the absorbance values in the cytotoxicity assay of light-activated liposomes were considerably low when compared to the absorbance values in the free drug and non-irradiated liposomes. All these findings were able to justify the hypothesis that light is an effective external stimulus to improve the precision and efficiency of drug delivery. Further, the comparative performance analysis confirmed that the irradiated liposomes offered better drug-release behaviour and enhanced biological activity relative to all research objectives and in accordance with proving the applicability of light-triggered strategies in advanced therapeutic practice.

5. CONCLUSION

The article found that destabilization of liposomes by light provided a very efficient tool of improving drug delivery rates and treatment effects. The fact that the formulation prepared successful and uniformly sized liposomes with high entrapment efficiency indicated that the formulation was suitable to be activated in a controlled manner. Exposure to light enhanced the

release of drugs greatly, which proved the functional receptiveness of the photosensitive constituents and supported the idea of externally induced membrane destabilization. This improved release which resulted in better cytotoxic effects whereby light-activated liposomes had better therapeutic actions than free drug and non-irradiated preparations. All in all, the results proved that light-responsive mechanisms could be incorporated into liposomal drug-delivery vehicles and could significantly enhance precision and control, as well as treatment outcome, and be used in precise and targeted drug-delivery platforms in the future.

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