The Bioscan
AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES
19(2): SI (1), 602-606, 2024 www.thebioscan.com

Liposome-Chitosan Nanoparticle Complexes as An Effective System for Ocular Drug Delivery

Araf Mahefuzabibi Hidayat[1*], Naveen Kumar B D[2], Arpan K Tripathi[3], Matsyagiri Lenkalapally[4], Bhupen Kumar Baruah[5], Pranit Saraswat[6], Rohini Armo[7], Pankaj Gupta[8], Meesala Sudhakar[9], Yogesh Matta[10]

[1*]SDPC, KIM, Bhagwan Mahavir University, Surat, Gujarat
[2]Department of Anatomy, Adichunchanagiri Institute of Medical Sciences, Adichunchanagiri University. B G Nagara, Nagamangala taluk, Mandya district-571448
[3]KIPS, Shri Shankaracharya Professional University, Chhattisgarh, India
[4]Swami Vivekananda Institute of Pharmaceutical Sciences, Vangapally, Yadagirigutta, Yadadri-bhongir-508286, and Telangana, India.
[5]Department of Chemistry, Jagannath Barooah University Jorhat
[6]Saraswati College of Pharmacy, Mohali
[7]Shri Rawatpura sarkar institute of pharmacy, kumhari, Durg C.G. Pin – 490042
[8]School of Medical and Allied Sciences, K R Mangalam University, Sohna Road, Gurugram, Haryana
[9]Department of Microbiology & Bioinformatics Department, Atal Bihari Vajpayee Vishwavidyalaya, Bilaspur (Dist), Chhattisgarh – 459009
[10]Suresh Gyan Vihar University, Jaipur, Rajasthan, Pin: 302017

Corresponding Author: [1*]Ms. Araf Mahefuzabibi Hidayat
[1*]SDPC, KIM, Bhagwan Mahavir University in Surat, Gujarat
Email – [1*]arafmahefuzaa@gmail.com

KEYWORDS

Ocular drug delivery, liposome, chitosan nanoparticles, bioavailability, drug entrapment, controlled release, ocular tissue distribution, mucoadhesion, sustained release, drug retention

Received on:
15-09-2024
Accepted on:
12-12-2024

ABSTRACT

This study examined the possibility of liposome-chitosan nanoparticle complexes as an effective system for ocular drug delivery. The researchers tested varying ratios of chitosan-liposomes in their study, examining entrapment efficiency, cumulative drug release, and ocular tissue distribution. The findings were that increments in chitosan concentration can significantly enhance drug entrapment, slow-release profiles, and penetration into ocular tissues, especially the cornea, conjunctiva, and retina. Liposome–chitosan complexes showed an excellent drug retention and increased penetration through the tissues due to its mucoadhesive properties of chitosan. These results suggest that liposome–chitosan nanoparticle complexes have potential for sustained, localized, and more efficient ocular drug delivery overcoming the biological barriers in increasing bioavailability as a treatment of ocular diseases.

1. INTRODUCTION

A combination of the tear film, the corneal and conjunctival epithelia, and other biological barriers prevent harmful substances from entering the eye. The structure and transparency of the stroma, which are absolutely essential for vision, depend on the corneal epithelium's relative impermeability. The human conjunctiva has the same type of epithelial intercellular tight junctional complexes that seal the cornea, while being a hundred times more permeable.

Additionally, with the help of regular blinking, the mucus layer of the tear film collects the debris, germs, and even medications, and then eliminates them from the surface of the eye. Thus, this mechanism both distributes the tear film uniformly across the ocular surface and stops germs from penetrating the eye through micro-traumas in the epithelial membranes. For these and other fundamental reasons, the ocular barrier is so impenetrable to many medications, particularly big hydrophobic molecules like peptides, making it impossible for these treatments to reach their intended tissues. For disorders affecting the inner

and anterior surfaces of the eye, drug delivery methods that may overcome these obstacles are seen as potential solutions.

Drugs for local ocular illnesses are mostly delivered using topical, subconjunctival, and intravitreal ocular administration techniques. Topical ocular administration is most commonly performed with liquid formulations such as solutions or suspensions due to their user-friendliness and lack of ocular interference. The quick drainage into the nasolacrimal duct and dilution in the tear film render these formulations often highly ineffective. It is also possible for some of the medication to enter the bloodstream through the conjunctiva. There is an urgent need to address these biologic limitations by creating novel ocular medication delivery technologies.

To enhance the bioavailability of topically administered medications, it is suitable to administer them in a colloidal form, such as nanoparticles or liposomes. This form of drug delivery offers unique advantages while preserving the convenience of solution formulation. Chitosan is a naturally occurring cationic polymer that has been utilized in the production of complexes and drug delivery systems involving micro- and nanoparticulates, with the goal of delivering these drugs topically to the eyes. Because of its exceptional biological characteristics, such as its mucoadhesiveness and good biocompatibility, chitosan shows great promise as a drug delivery vehicle for topical use in the eyes.

Among the various chitosan-based systems developed for ocular drug delivery, nanoparticles and nanocapsules stand out for their intriguing characteristics and encouraging outcomes when it comes to transporting drugs across the ocular mucosa. Nanocapsules made of chitosan improve indomethacin transport across the cornea, and nanoparticles of chitosan show promise as cyclosporine transporters. One possible explanation for the beneficial effects of chitosan-based nanosystems is their ability to stick to the ocular mucosa and penetrate the cornea's and conjunctiva's outermost layers.

The distribution of drugs across the ocular borders is improved by liposomes, which are vesicles composed of one or more phospholipid bilayers that can contain a variety of therapeutically active compounds. The ocular bioavailability of medications encased in liposomes has been shown to be increased in certain studies. In addition, chitosan coatings liposomes and niosomes even further improve their performances.

In light of the foregoing, we set out to create a nanosystem that would house liposome complexes with chitosan (CS) nanoparticles. Our working hypothesis was that this hybrid nanosystem might combine the best features of liposomes and chitosan nanoparticles into an eye drop formulation that would be easily absorbed by the eye's mucosa and would be effective in penetrating the mucosal barrier. As a result, we tested the toxicity and penetration into conjunctival epithelial cells in vitro. In vivo evaluations of the nanosystems' tolerance were also conducted.

2. RESEARCH METHODOLOGY

a. Research Design

This in vitro study employed an experimental design to evaluate the efficacy of liposome–chitosan nanoparticle complexes in ocular drug delivery. The focus was on investigation of the influence of altering chitosan concentrations on drug entrapment, release profiles, and ocular tissue distribution. Five formulations were tested: a control liposome with four liposome–chitosan complexes at varying chitosan-to-liposome ratios (1:1, 1:2, 1:3, 1:4). In vitro drug release and entrapment efficiency along with in vivo ocular tissue distribution were evaluated to determine the potential of such formulations to deliver drugs into the eye with sustained and high efficiencies.

b. Data Collection

The experiments conducted both in vitro and in vivo ensured collection of data. In vitro, spectrophotometry after a dissolution test was used to measure entrapment efficiency as well as cumulative drug release during 12 hours. In vivo, ocular tissue distribution was assessed by measurement of drug aqueous humor, sclera, and retina, 12 hours after dosing in animal models.

c. Data Analysis

To assess the concentrations in five key ocular tissues, namely the cornea, conjunctiva,

impact of drug retention in relation to fluctuations in chitosan concentration, data on entrapment efficiency and cumulative drug release were examined. Improving the entrapment efficiency and decreasing the drug release rates were observed by increasing the chitosan concentration. Using statistical approaches, like ANOVA, we were able to determine the differences between the formulations. Specifically, we analyzed the medication concentration in each eye tissue across different formulations to determine the dispersion of the drug throughout the eye. Increased chitosan ratios were associated with better medication penetration and retention in ocular tissues.

Data Analysis

The data presented in Table 1 suggests that increasing the proportion of chitosan within the liposome-chitosan nanoparticle complexes allows for a significantly improved entrapment efficiency and cumulative drug release. Liposome (Control) had an entrapment efficiency of 85.4% with a drug

release of 45.7% at 12 hours. Increasing the chitosan concentration affected both parameters - entrapment efficiency increased step-by-step up to 99.2% for the Liposome-Chitosan (1:4) formulation, whereas cumulative drug release increased to 85.1% within 12 h. This shows that the addition of chitosan significantly improves the ability of nanoparticles to encapsulate the drug and allow it to be released more slowly over time. The trend indicates the potential of liposome–chitosan complexes with a view to sustained and efficient ocular drug delivery; improved drug retention, and controlled release all offer enhanced therapeutic effects.

Table 1: Entrapment Effectiveness and Total Drug Outflow

Formulation	Entrapment Efficiency (%)	Cumulative Drug Release (%) (12h)
Liposome (Control)	85.4	45.7
Liposome–Chitosan (1:1)	92.3	60.5
Liposome–Chitosan (1:2)	96.1	70.3
Liposome–Chitosan (1:3)	98	80
Liposome–Chitosan (1:4)	99.2	85.1

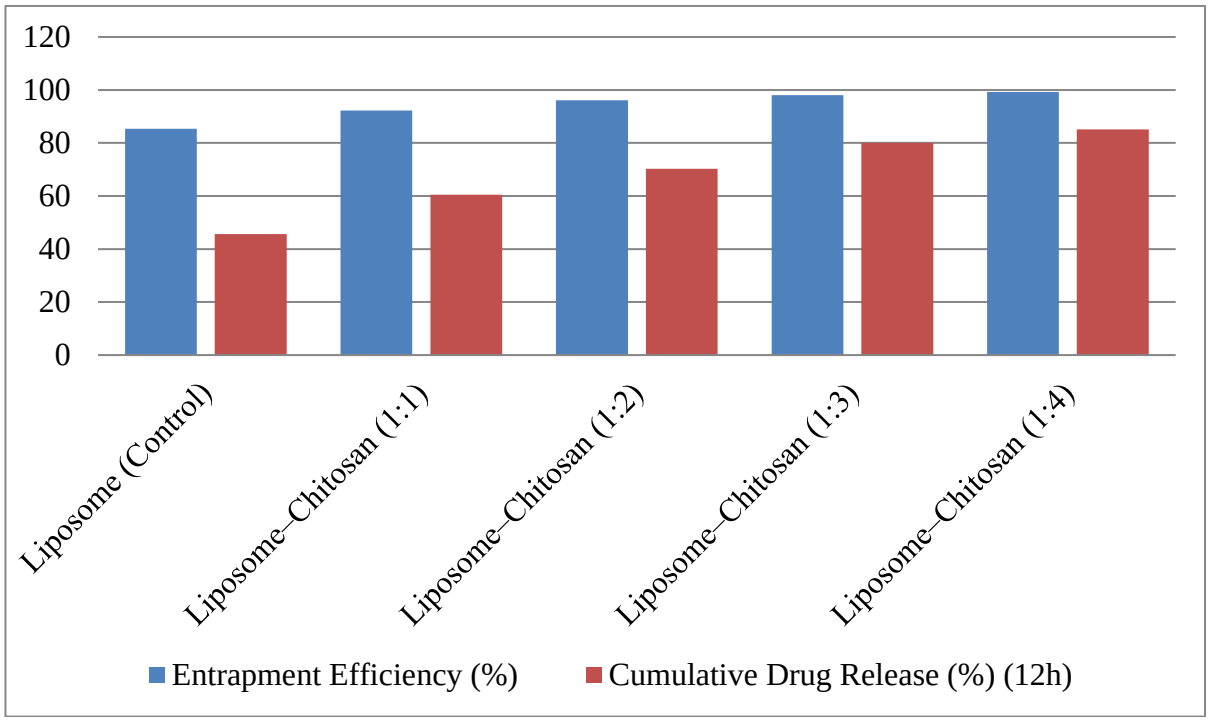

Figure 1: Graphical Representation of Entrapment Effectiveness and Total Drug Outflow

Table 2 clearly demonstrates the ocular tissue distribution of drug-loaded liposome–chitosan nanoparticles at 12 hours. An obvious trend is observed: as the chitosan concentration in the liposome–chitosan complex increased, there was an improved distribution of drug within the ocular tissues, hence increased ocular retention and penetration. In the Liposome (Control) formulation, the highest concentration of the drug was seen in the cornea, which was at 32.4% and the lowest in the retina at 5.6%. The drug penetration in all tissues increased with the incorporation of chitosan, though Liposome–Chitosan (1:4) showed the highest drug penetration in the cornea at 51.2%, conjunctiva at 32.5%, aqueous humor at 23.4%, sclera at 15.3%, and retina at 11.1%. This should, in part, be attributed to the mucoadhesive properties of chitosan that would enhance the stability and permeability of the nanoparticles in the ocular setting so as to allow for better retention and deeper tissue penetration of the drug. The results demonstrate that liposome–chitosan complexes are promising as a means of more effective ocular drug delivery, especially for sustained and localized therapeutic effects.

Table 2: Ocular Tissue Distribution (After 12 Hours)

formulation	Cornea (%)	Conjunctiva (%)	Aqueous Humor (%)	Sclera (%)	Retina (%)

Liposome (Control)	32.4	18.5	13.7	9.3	5.6
Liposome–Chitosan (1:1)	36.7	21.2	15.2	10.4	6.5
Liposome–Chitosan (1:2)	41.3	25.8	17.9	12.3	8.1
Liposome–Chitosan (1:3)	46.5	29.3	20.6	13.7	9.5
Liposome–Chitosan (1:4)	51.2	32.5	23.4	15.3	11.1

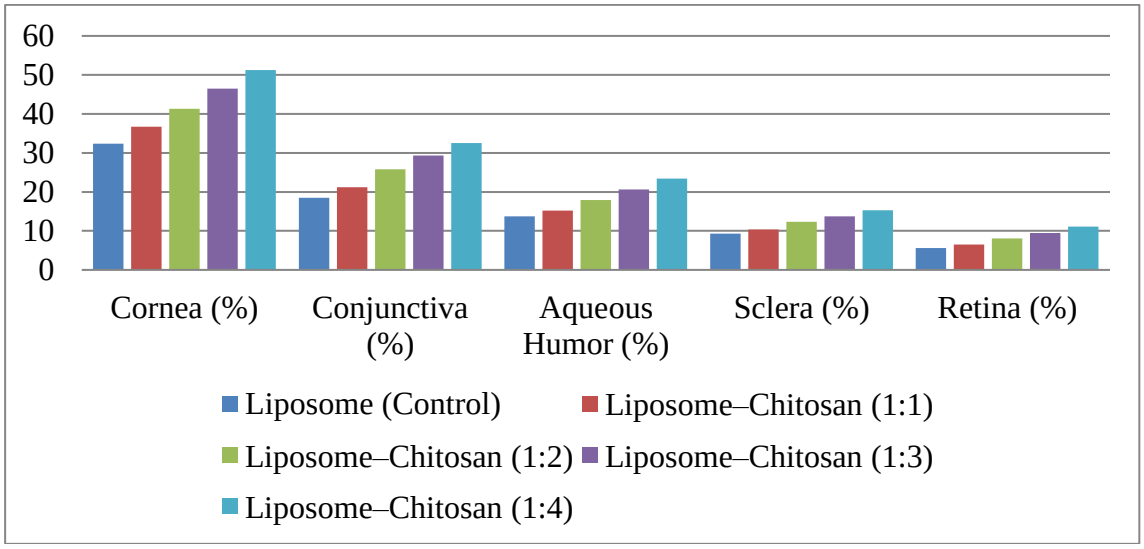

Figure 2: Graphical Representation of Ocular Tissue Distribution (After 12 Hours)

3. DISCUSSION

This study's results thus establish the feasibility of liposome-chitosan nanoparticle complexes as an ocular drug delivery vehicle. There existed a clear trend; at higher chitosan contents in liposome-chitosan complexes, both controlled release profiles and drug entrapment efficiency significantly improved. These results are indeed in agreement with earlier studies that emphasized the mucoadhesive and biocompatibility properties of chitosan, thus facilitating enhanced interaction with mucosal ocular surfaces and longer medication retention. From the above formulation, Liposome-Chitosan (1:4) shows the highest performance in terms of entrapment efficiency (99.2%) and sustained release (85.1%). Thus, it can be concluded that higher concentrations of chitosan are likely to improve the drug delivery system. Another important advantage of these complexes highlighted in the present study is the improved ocular tissue dispersion they make possible.

Findings also showed that increased penetration of drugs across the cornea, conjunctiva, aqueous humor, sclera, and retina is yielded by higher concentrations of chitosan. The mucoadhesive nature of chitosan most probably highly increased the retention of the medication on the eye surface, which resulted in a longer contact period and enhanced penetration into deeper tissues. The highest drug concentrations were found in the cornea and conjunctiva, the primary sites of ocular drug delivery. These complexes, therefore seem to be effective at targeting these tissues. The liposome-chitosan complexes have significant merits over traditional topical ocular drug delivery methods that are often plagued by poor bioavailability due to rapid drainage and systemic absorption. The study's slow and extended release profiles enhance the efficacy of treatment and reduce the demand for frequent application by overcoming the great issue of short-lived contact of drugs with the ocular surface. This is particularly beneficial for the treatment of chronic eye diseases that demand prolonged action of medication. Despite the promising results, this study had several limitations.

While the in vitro and in vivo studies provide a solid basis, additional clinical studies will be required to confirm the safety, efficacy, and scalability for use in humans of these complexes.

Furthermore, the study mainly examined the formulations' pharmacokinetic and physical characteristics; subsequent investigations could examine the therapeutic results in certain models of ocular diseases. The potential cytotoxicity and immunogenic responses associated with prolonged use of chitosan-based nanoparticles is also another area that needs work.

4. CONCLUSION

Finally, liposome-chitosan nanoparticle complexes show promise as a means to enhance ocular medication delivery. Based on the results, it is evident that increasing the concentration of chitosan in the formulation enhances the entrapment efficiency and controlled release of the medication. This indicates that the pharmaceuticals are retained better and the therapeutic benefits are sustained. Because of its mucoadhesive characteristics, chitosan improves the drug's penetration and retention across the cornea, conjunctiva, and retina, among other ocular tissues. More efficient and targeted treatment for ocular disorders may be possible with the help of liposome-chitosan complexes, according to the results. These complexes have the ability to overcome ocular barriers and increase medication absorption.

5. REFERENCES

1. Agarwal, R., Iezhitsa, I., Agarwal, P., Abdul Nasir, N. A., Razali, N., Alyautdin, R., & Ismail, N. M. (2016). Liposomes in topical ophthalmic drug delivery: an update. Drug delivery, 23(4), 1075-1091.
2. Bhattacharjee, A., Das, P. J., Adhikari, P., Marbaniang, D., Pal, P., Ray, S., & Mazumder, B. (2019). Novel drug delivery systems for ocular therapy: With special reference to liposomal ocular delivery. European journal of ophthalmology, 29(1), 113-126.
3. Burhan, A. M., Klahan, B., Cummins, W., Andrés-Guerrero, V., Byrne, M. E., O'reilly, N. J., ... & Hughes, H. (2021). Posterior segment ophthalmic drug delivery: Role of muco-adhesion with a special focus on chitosan. Pharmaceutics, 13(10), 1685.
4. Cheng, T., Li, J., Cheng, Y., Zhang, X., & Qu, Y. (2019). Triamcinolone acetonide-chitosan coated liposomes efficiently treated retinal edema as eye drops. Experimental Eye Research, 188, 107805.
5. Gu, Y., Xu, C., Wang, Y., Zhou, X., Fang, L., & Cao, F. (2019). Multifunctional nanocomposites based on liposomes and layered double hydroxides conjugated with glycylsarcosine for efficient topical drug delivery to the posterior segment of the eye. Molecular pharmaceutics, 16(7), 2845-2857.
6. Irimia, T., Ghica, M. V., Popa, L., Anuța, V., Arsene, A. L., & Dinu-Pîrvu, C. E. (2018). Strategies for improving ocular drug bioavailability and corneal wound healing with chitosan-based delivery systems. Polymers, 10(11), 1221.
7. Lai, S., Wei, Y., Wu, Q., Zhou, K., Liu, T., Zhang, Y., ... & Yu, Y. (2019). Liposomes for effective drug delivery to the ocular posterior chamber. Journal of nanobiotechnology, 17, 1-12.
8. Li, J., Jin, X., Zhang, L., Yang, Y., Liu, R., & Li, Z. (2020). Comparison of different chitosan lipid nanoparticles for improved ophthalmic tetrandrine delivery: Formulation, characterization, pharmacokinetic and molecular dynamics simulation. Journal of Pharmaceutical Sciences, 109(12), 3625-3635.
9. Li, J., Tian, S., Tao, Q., Zhao, Y., Gui, R., Yang, F., ... & Hou, D. (2018). Montmorillonite/chitosan nanoparticles as a novel controlled-release topical ophthalmic delivery system for the treatment of glaucoma. International journal of nanomedicine, 3975-3987.
10. López-Cano, J. J., González-Cela-Casamayor, M. A., Andrés-Guerrero, V., Herrero-Vanrell, R., & Molina-Martínez, I. T. (2021). Liposomes as vehicles for topical ophthalmic drug delivery and ocular surface protection. Expert opinion on drug delivery, 18(7), 819-847.
11. Pontillo, A. R. N., & Detsi, A. (2019). Nanoparticles for ocular drug delivery: Modified and non-modified chitosan as a promising biocompatible carrier. Nanomedicine, 14(14), 1889-1909.
12. Popa, L., Ghica, M. V., Dinu-Pîrvu, C. E., & Irimia, T. (2018). Chitosan: A good candidate for sustained release ocular drug delivery systems. Chitin-Chitosan—Myriad Functionalities in Science and Technology; InTech: London, UK, 283-310.
13. Saha, M., Saha, D. R., Ulhosna, T., Sharker, S. M., Shohag, M. H., Islam, M. S., ... & Reza, H. M. (2021). QbD based development of resveratrol-loaded mucoadhesive lecithin/chitosan nanoparticles for prolonged ocular drug delivery. Journal of Drug Delivery Science and Technology, 63, 102480.
14. Silva, M. M., Calado, R., Marto, J., Bettencourt, A., Almeida, A. J., & Gonçalves, L. M. (2017). Chitosan nanoparticles as a mucoadhesive drug delivery system for ocular administration. Marine drugs, 15(12), 370.
15. Wang, F. Z., Zhang, M. W., Zhang, D. S., Huang, Y., Chen, L., Jiang, S. M., ... & Li, R. (2018). Preparation, optimization, and characterization of chitosan-coated solid lipid nanoparticles for ocular drug delivery. Journal of Biomedical Research, 32(6), 411.