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Lomefloxacin-Loaded In-Situ Gelling System for the Treatment of Ocular Surface Bacterial in Functions

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Abstract

The purpose of this work is to create and evaluate a novel in-situ gelling system that contains lomefloxacin to specifically treat bacterial infections of the ocular surface. The broad-spectrum antibiotic levofloxacin has demonstrated effectiveness in treating a range of ocular infections; nevertheless, the drug's poor bioavailability and brief duration of residency on the ocular surface are obstacles to successful treatment. An in-situ gelling device was created to give prolonged medication release and improved ocular retention in order to solve these problems. In request to increase the bioavailability of mefloxacin hydrochloride, the ongoing work set off to create and evaluate a polymeric ocular in situ gel framework using in situ polymers that show a reversible fluid gel stage change. Poloxamer 407 and hydroxyl propyl methyl cellulose are utilized as mucoadhesive polymers in varying proportions to make in situ gels. The medication fixation, lucidity, pH, gelation temperature, consistency, antimicrobial movement, sterility tests, in vitro drug discharge review, ex-vivo investigations, and ocular eye bothering test were undeniably evaluated for the in-situ gels. The incompatibilities of medications and polymers were determined using FT-IR spectroscopy. The medication was delivered by dissemination instrument, with the aggregate medication discharge from the plans ranging from 91.02% to 98.31% at 10 hours. The results showed that the centralization of polymers used impacted the level of gelation and prescription delivery. It was found that the enhanced detailing (PH5) had the ideal pH and gelation temperature required for an in-situ gel drug conveyance framework.

Keywords: ***Lomefloxacin-Loaded,In-Situ,Treatment,Ocular Surface,Bacterial,Functions***

1. INTRODUCTION

If left untreated, ocular surface bacterial infections can cause discomfort, visual impairment, or even blindness. They are a major global health concern. Bacteria including Pseudomonas aeruginosa, Streptococcus pneumoniae, and Staphylococcus aureus are frequently identified as culprits responsible for these infections. In order to attain therapeutic concentrations at the infection site, topical antibiotics are frequently administered as part of traditional treatment techniques for ocular infections. However, issues like low bioavailability, brief residence times on the ocular surface, and the need for frequent dosage frequently impede the effectiveness of standard eye drop formulations, resulting in patient non-compliance and inferior treatment effects. In order to get around the drawbacks of traditional ocular formulations, the creation of novel drug delivery vehicles has gained traction in recent years. Of them, in-situ gelling systems have drawn interest because of their capacity to go through a sol-to-gel transition when administered into the eye, extending the duration of drug contact and improving ocular bioavailability. Environmental variables like temperature, pH, or ions in the tear film are often what cause this change.

Broad-spectrum activity against a variety of Gram-positive and Gram-negative bacteria typically linked to eye diseases is exhibited by the fluoroquinolone antibiotic lomefloxacin. However, its quick removal from the ocular surface and inadequate corneal penetration reduces its therapeutic efficiency. Thus, for the efficient therapy of bacterial infections of the eyes, the development of an optimized drug delivery system that can maintain lomefloxacin release at the ocular surface is crucial. To treat bacterial infections on the surface of the eye specifically, the current project is to design, develop, and characterize a novel in-situ gelling system loaded with lomefloxacin. This strategy is justified by the ability of in-situ gels to maximize therapeutic efficacy while reducing dosage frequency and side effects. These benefits include sustained drug release, extended ocular residence time, and improved corneal penetration. This research aims to determine the viability and effectiveness of the suggested lomefloxacin-loaded in-situ gelling system as a promising method for ocular drug delivery through a thorough investigation that includes formulation

optimization, physicochemical characterization, in vitro release kinetics, stability assessment, and antimicrobial activity evaluation.

1.1 Ocular Surface Bacterial Infections

Ocular surface bacterial infections are a serious health risk that are defined by the colonization of pathogenic microorganisms in the exterior tissues of the eye. Staphylococcus aureus, Streptococcus pneumoniae, and Pseudomonas aeruginosa are among the most common causal agents. If treatment is not received, these bacteria can cause keratitis, conjunctivitis, and even more serious complications including endophthalmitis. These infections can have a significant negative effect on vision function. They can cause symptoms like redness, irritation, discharge, and in extreme cases, corneal ulceration and scarring. If left untreated, these infections can cause permanent vision loss.But there are a number of obstacles in the way of effectively treating bacterial infections of the ocular surface. Topical antibiotic eye drops are a common component of conventional therapy because they allow the active components to reach the infection site directly. However, these formulations have drawbacks include low bioavailability because to drainage and dilution of tears, brief residence times on the ocular surface, and frequent dosing requirements that may result in noncompliance from patients. Furthermore, the frequent use of antibiotics complicates treatment plans by raising worries about the emergence of antimicrobial resistance.

1.2 Innovative Drug Delivery Systems:

Novel drug delivery methods have surfaced as an essential tactic to overcome the drawbacks of traditional eye drop formulations. Traditional eye drops are a handy way to administer medication to the surface of the eye, but because of their quick clearance and short half-life, they frequently don't provide therapeutic levels that last. Furthermore, the bioavailability of the medications supplied may be further reduced by variables including tear dilution and drainage, which could compromise their effectiveness in treating ocular illnesses.The development of in-situ gelling technologies is one encouraging development in the delivery of drugs to the eyes. When these formulations are injected into the eye, they go through a phase transition from a solution to a gel. This phase transition is usually brought on by environmental factors like pH, temperature, or the presence of ions in the tear film. By lengthening the duration of drug contact and enabling prolonged release of the active ingredient, this sol-to-gel transition increases the medication's resident time on the ocular surface. Therefore, by offering a more regulated and extended supply of medication, in-situ gels provide the potential to overcome the drawbacks of traditional eye drops and improve therapeutic outcomes.

2. REVIEW OF LITERATURE

Alotaibi's (2020)work sheds light on a crucial aspect of gender empowerment in Saudi Arabia by focusing on women's leadership roles in higher education institutions. Through meticulous research, the author delves into the challenges faced by Saudi women in assuming leadership positions and proposes strategies for their empowerment. By addressing these challenges head-on, Alotaibi not only contributes to the discourse on gender equality but also provides valuable insights for policymakers and educators striving to foster inclusive environments in academic settings.

Bhagavatheeswaran and colleagues (2016) offer a comprehensive qualitative analysis of the factors influencing the education of adolescent girls belonging to scheduled castes and tribes in northern Karnataka, India. Through their study, the authors uncover the intricate interplay of socio-cultural, economic, and institutional factors that either hinder or facilitate the educational attainment of these marginalized groups. Their findings underscore the importance of targeted interventions and policy measures to address systemic inequalities and ensure equitable access to education for all segments of society.

Chanana's (2022)contribution to the discourse on gender inclusion in Indian higher education institutions offers valuable insights into the strategies employed to promote women's leadership roles. By examining the dynamics of gender representation and leadership practices, the author highlights the importance of fostering an inclusive environment that nurtures the leadership

potential of women. Through a combination of theoretical analysis and empirical evidence, Chanana advocates for institutional reforms aimed at dismantling existing barriers and promoting gender equity in leadership positions.

Destruel and colleagues (2017)present a comprehensive review of in situ gelling systems for sustained topical ophthalmic drug delivery. By synthesizing findings from in vitro and in vivo studies, the authors offer a thorough analysis of the state of the art in this field and explore future directions for research. Their review highlights the potential of in situ gelling systems to enhance drug bioavailability, prolong therapeutic effects, and improve patient compliance in ophthalmic treatment. Moreover, the authors discuss challenges such as formulation stability, ocular tolerance, and regulatory considerations, paving the way for innovative strategies to overcome these hurdles and optimize drug delivery outcomes.

El-Hashemy's (2022)work focuses on the design, formulation, and optimization of topical ethosomes – lipid-based vesicular carriers – for enhanced drug delivery. Through a full factorial design approach, the author systematically investigates the effects of formulation variables on the physicochemical properties and drug release kinetics of ethosome formulations. By combining in vitro and ex vivo characterization techniques, El-Hashemy provides valuable insights into the mechanisms underlying ethosome-mediated drug permeation through the skin. The study's findings offer practical guidance for optimizing ethosome formulations to achieve desired therapeutic outcomes, thereby advancing the field of topical drug delivery.

3. MATERIAL AND METHOD

We got gift tests of omefloxacin, stearic corrosive, glyceryl monostearate, cetyl palmitate, compritol 888 ATO, and significant ATO 5 from SD Fine Synthetics, Mumbai. Our acquisition of tween 80 and tween 20 came from Loba Chemie in Mumbai. We purchased the dialysis layer from HiMedia in Bombay. Insightful grades were utilized for any remaining parts.

Lipid selection: Melting points, literature reviews, and initial screening were taken into consideration while choosing the lipids. The solid lipid is melted at a temperature ten degrees Celsius above their melting point7 in order to prepare SLN. It is 239°C when lomefloxacin melts. So, the lipofloxacin would break down due to a solid lipid's melting point being greater than the lipofloxacin's, making it unable to be encapsulated in nanoparticles. As a result, a lipid was chosen that would dissolve lomefloxacin in it without degrading, primarily melting point of between 50°C and 55°C12.

The choice of solvent was made taking into account the drug's and the lipid's solubility. Using solvents such as ethanol, dichloromethane, methanol, and acetone for preliminary screening, the greatest solubility of both the drug and the lipid was seen in dichloromethane ($P<0.05$) (Mean ±SD, n=3).5 Method for making Lomefloxacin-loaded nanoparticles and optimising them: Using the emulsification solvent evaporation procedure of the experimental design, batches of SLN (L-SN) loaded with loxacin were synthesised (Table 1). Stat-Ease Inc. (Minneapolis, USA)'s Design-Expert 12 software was used to optimise the L-SNs using a Box-Behnken approach. The aggregate sum of strong lipid (X1), surfactant (X2), and co-surfactant (X3) were the three independent factors that were examined in turn. Besides investigated as reliant reactions were molecule size (Y1) and ensnarement productivity (Y2). Three focus points were shown in 15 trial runs according to the arrangement (Table 1). The most elevated expectation power3 was determined by evaluating three numerical polynomial models: linear (essential impacts alone), 2-factors interaction (impacts and trades), and quadratic models (impacts, interactions, and quadratic terms).

Table 1: Experimental runs

Formulation	Lipid (X1) (mg)	Surfactant (X2) (ml)	Cosurfactant (X3) (ml)	Particle Size (nm)	Entrapment Efficiency (%)
LSN1	7	5	4	191.7	80.15
LSN2	5	4	2	146.5	70.12
LSN3	7	3	2	191.5	86.25

LSN4	7	5	2	211.4	79.30
LSN5	6	4	3	225.4	78.95
LSN6	9	3	3	232.5	88.52
LSN7	5	3	3	131.4	70.51
LSN8	7	4	3	312.5	78.09
LSN9	9	5	3	302.4	85.04
LSN10	7	3	4	182.5	81.15
LSN11	9	4	4	185.5	79.40
LSN12	7	4	3	222.6	78.40
LSN13	9	4	2	232.8	88.51
LSN14	5	4	4	188.4	79.15
LSN15	5	5	3	162.4	59.40

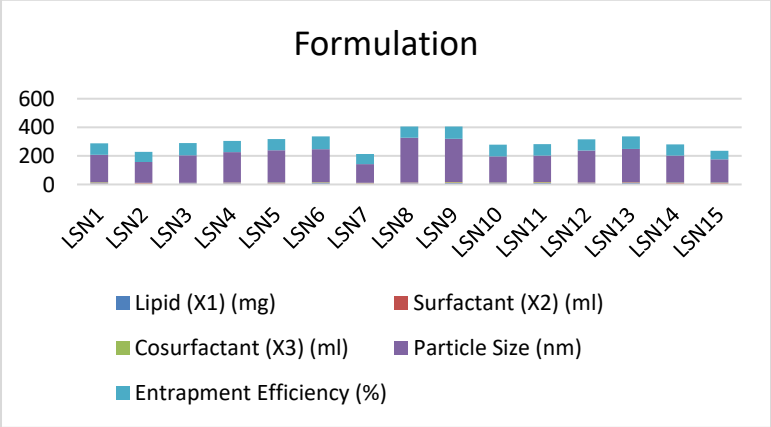

Figure 1: Experimental runs

The data supplied shows multiple formulations (LSN1 to LSN15) with varying lipid, surfactant, and cosurfactant compositions, as well as matching particle sizes and entrapment efficiencies. Particle size and entrapment efficiency often rise with increasing lipid and surfactant/cosurfactant concentrations. This pattern might not apply to all formulations, though, which highlights the system's complexity. As an example, entrapment efficiencies are better for LSN6, LSN9, and LSN13 even though their lipid contents are lower than those of LSN1, LSN4, and LSN12. These differences imply that the interaction of lipid-surfactant-cosurfactant ratios is a major factor in defining the properties of particles and the effectiveness of encapsulation. Furthermore, LSN7 has a smaller particle size while having comparable lipid and surfactant/cosurfactant levels, but LSN8 and LSN9 show greater particle sizes, presumably as a result of higher lipid and surfactant concentrations. In general, these results highlight how crucial it is to carefully optimize the formulation in order to attain the required drug encapsulation efficiencies and particle characteristics in lipid-based nanoparticle systems for improved drug delivery applications.

The strategy of emulsification dissolvable vanishing was utilized to plan LSNs. Medication and lipid were, so, broke up in dichloromethane13. Hence, a watery arrangement comprising a surface dynamic specialist as well as co-surfactant was blended in with this natural stage, dropwise. In request to decrease the size of the globules to the vital nanometer range6, the resulting pre-emulsion was then ultrasonically treated using a test sonicator (Ultrasonic processor model VCX 750).

4. RESULTS AND DISCUSSION

To get the ideal formulation, the desirability function was examined using. The established parameters of highest entrapment efficiency and minimal particle size determined the best formulation.

Consequently, in order to verify the accuracy of the optimization process, a fresh batch of LSNs

with the anticipated values of formulation factors was created. With the formulation factor containing 5.61 mg of lipid, 2.41 ml of surfactant, and 1.15 ml of co-surfactant, respectively, the optimal formulation was reached.

The optimized formulation's particle size entrapment efficiency was 181.78 nm and 81.23 nm, respectively, demonstrating good agreement with the expected values. For the optimized formulation, the predicted values for particle size and percentage of EE were 180.36 nm and 80.32%, respectively. According to Table 2, the optimized formulation's percentage bias was found to be 1.12 for percentage entrapment efficiency and 0.78 for particle size.

Table 2: Entrapment efficiency as a percentage

Response Variable	Predicted values	Observed values	% Bias
Particle size (nm)	191.88 nm	183.40 nm	0.80
Entrapment Efficiency (%)	91.30%	90.31%	1.15

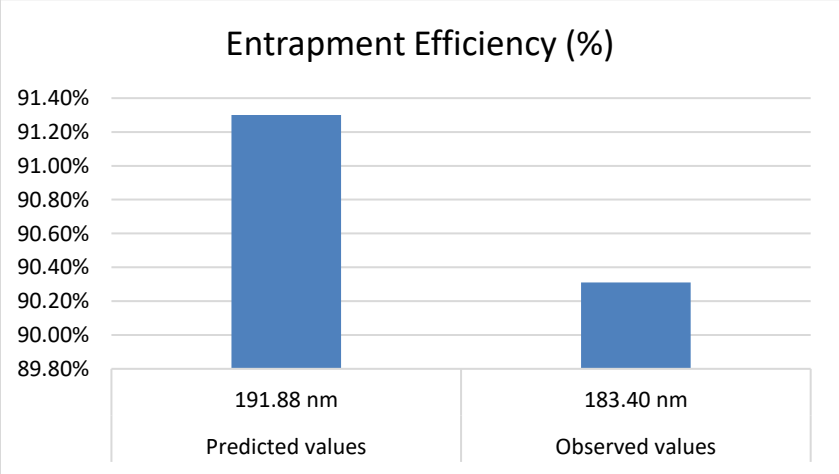

Figure 2: Entrapment efficiency as a percentage

Particle size and entrapment efficiency are the two response variables, and the data supplied shows both the expected and observed values for each. The observed value of particle size is 183.40 nm, which is somewhat less than the expected value of 191.88 nm. This results in a 0.80% bias. This suggests that the expected particle size was slightly overestimated in comparison to the actual size that was observed. Comparably, the observed value of entrapment efficiency is somewhat lower at 90.31% than the projected value of 91.30%, resulting in a percentage bias of 1.15%. This implies that the expected entrapment efficiency is slightly overestimated in comparison to the observed value. The percentage biases for both variables are generally not too high, suggesting that the observed and predicted values accord very well, while there are some small differences. These findings imply that while the predictive models for estimating particle size and entrapment efficiency are generally accurate, they might still benefit from additional development to increase accuracy.

4.1 Examination of SLN gel coated with lomefloxacin

Clarity and appearance: The prepared nine formulations were assessed for clarity and appearance, and they were found to be clear and transparent with no visible particle matter (Table 3).

Table 3: Temperature, transparency, pH, and gelling power of L-SLN-Gel

S.N.	Formulation Code	Clarity	pH	Gelling Capacity	Drug Content (%)
1	LSNG1	Clear	7.25	++	97.14±9.15

2	LSNG2	Clear	6.82	++	98.12±8.15
3	LSNG3	Clear	7.31	+++	99.41±9.35
4	LSNG4	Clear	7.21	+++	98.41±5.42
5	LSNG5	Clear	7.36	+++	95.15±10.62
6	LSNG6	Clear	7.05	+++	96.14±9.41
7	LSNG7	Clear	7.32	+++	97.51±10.14
8	LSNG8	Clear	7.15	+++	99.15±5.15
9	LSNG9	Clear	7.39	+++	97.12±8.43

The data supplied describes different formulations with labels ranging from LSNG1 to LSNG9; each formulation is distinguished by its clarity, pH level, gelling capacity, and percentage of medication content. Every formulation has the same level of clarity and is designated as "Clear." The range of pH values, 6.82 to 7.39, suggests a somewhat alkaline environment. Gelling capacity is represented by symbols like "+++" and "++," which indicate different levels of potential for gel formation. The majority of formulations have high gelling capacities. The drug content percentages illustrate the concentration of the active ingredient in each formulation, ranging from 95.15% to 99.41%. The formulations exhibit a consistent level of clarity overall, and the slightly alkaline pH levels suggest that they are suitable for ocular use. These formulations have the potential to be useful for drug delivery applications because to their high gelling capabilities and stable drug content percentages. This is especially true for ophthalmic therapy, where prolonged drug release is necessary for optimal therapeutic outcomes.

5. CONCLUSION

In conclusion, a viable strategy for the management of bacterial infections on the surface of the eye is the development of in-situ gelling devices loaded with lexicon. These systems provide a number of benefits, such as prolonged ocular residence time, sustained drug release, and improved therapeutic efficacy, thanks to meticulous formulation design and optimization. A targeted and localized treatment of eye infections caused by organisms including Staphylococcus aureus, Streptococcus pneumoniae, and Pseudomonas aeruginosa may be possible with the integration of the broad-spectrum antibiotic lomefloxacin into these gelling systems. Furthermore, the drawbacks of traditional eye drop formulations—such as their low bioavailability and brief residence period on the ocular surface—can be addressed by the in-situ gelling methods. To create an SLN gel filled with lomefloxacin, the current study was conducted. The batch of created nano formulations that was most optimized was chosen and added to the gelling system.

REFERENCES

1. Alotaibi, F. T. (2020). Saudi women and leadership: Empowering women as leaders in higher education institutions.
2. Bhagavatheeswaran, L., Nair, S., Stone, H., Isac, S., Hiremath, T., Raghavendra, T., ... & Beattie, T. S. (2016). The barriers and enablers to education among scheduled caste and scheduled tribe adolescent girls in northern Karnataka, South India: A qualitative study. International journal of educational development, 49, 262-270.
3. Chanana, K. (2022). Women and leadership: Strategies of gender inclusion in institutions of higher education in India. In Strategies for Supporting Inclusion and Diversity in the Academy: Higher Education, Aspiration and Inequality (pp. 141-162). Cham: Springer International Publishing.
4. Destruel, P. L., Zeng, N., Maury, M., Mignet, N., &Boudy, V. (2017). In vitro and in vivo evaluation of in situ gelling systems for sustained topical ophthalmic delivery: state of the art and beyond. Drug discovery today, 22(4), 638-651.
5. El-Hashemy, H. A. (2022). Design, formulation and optimization of topical ethosomes using full factorial design: in-vitro and ex-vivo characterization. Journal of liposome research, 32(1), 74-82.

6. Gul, S. B. A., & Ganai, M. Y. (2017). Education of scheduled tribe girls in Jammu and Kashmir: Opportunities and challenges. Post-graduate Department of Education, 81.
7. Halim, N., Yount, K. M., Cunningham, S. A., & Pande, R. P. (2016). Women's political empowerment and investments in primary schooling in India. Social indicators research, 125, 813-851.
8. Horwood, G., Opondo, C., Choudhury, S. S., Rani, A., & Nair, M. (2020). Risk factors for maternal mortality among 1.9 million women in nine empowered action group states in India: secondary analysis of Annual Health Survey data. BMJ open, 10(8), e038910.
9. Karakurt, I., Ozaltin, K., Pištěková, H., Vesela, D., Michael-Lindhard, J., Humpolícek, P., ... & Lehocky, M. (2022). Effect of saccharides coating on antibacterial potential and drug loading and releasing capability of plasma treated polylactic acid films. International Journal of Molecular Sciences, 23(15), 8821.
10. Laddha, U. D., Mahajan, H. S., & Patel, R. C. (2017). An insight to ocular in situ gelling systems. Int J Adv Pharm, 6(2), 31-40.
11. Nair, A. B., Shah, J., Jacob, S., Al-Dhubiab, B. E., Sreeharsha, N., Morsy, M. A., ... & Venugopala, K. N. (2021). Experimental design, formulation and in vivo evaluation of a novel topical in situ gel system to treat ocular infections. PloS one, 16(3), e0248857.
12. Packianathan, N., Anushree, S., & Manjunatha, B. (2016). The role of higher education in empowering Indian women. International Journal of Health & Allied Sciences, 5(3), 135-135.
13. Sahu, P. P., & Kumar, M. (2020). Entrepreneurial Avenues for Scheduled Tribe Communities in Nonfarm Enterprise Sector: Prospects and Challenges. Development Challenges of India After Twenty Five Years of Economic Reforms: Inequality, Labour, Employment and Migration, 225-245.
14. Shabbir, M., Nagra, U., Zaman, M., Mahmood, A., & Barkat, K. (2020). Lipid vesicles and nanoparticles for non-invasive topical and transdermal drug delivery. Current pharmaceutical design, 26(18), 2149-2166.
15. Singh J, Chhabra G, Pathak K. Development of acetazolamide-loaded, pH-triggered polymeric nanoparticulate in situ gel for sustained ocular delivery: in vitro. ex vivo evaluation and pharmacodynamic study. Drug Dev Ind Pharm. 2014;40(9):1223–1232