RESEARCH PAPER

Formulation and characterization of niosomal in situ gel of fluorometholone as ophthalmic drug delivery system

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Abstract

Fluorometholone is a synthetic corticosteroid widely used for the treatment of inflammatory and allergic conditions of the eye. Conventional ophthalmic formulations are associated with several limitations, including rapid precorneal elimination, short ocular residence time, poor drug retention and the need for frequent administration. These limitations may reduce therapeutic effectiveness and patient compliance. Therefore, the development of a novel ophthalmic drug delivery system capable of prolonging drug residence and providing controlled drug release is desirable.

The present study was designed for the formulation, characterization and optimization of a niosomal in situ gel of fluorometholone as an ophthalmic drug delivery system. Niosomes were selected as a vesicular carrier because they can enhance drug encapsulation, improve drug retention and provide sustained drug release. Fluorometholone-loaded niosomes were prepared using suitable non-ionic surfactant and cholesterol concentrations. The prepared niosomal formulations were evaluated for vesicle size, polydispersity index, zeta potential, entrapment efficiency, drug content, morphology and in-vitro drug release in order to identify the optimized formulation.

The optimized fluorometholone-loaded niosomes were subsequently incorporated into an in situ gelling system containing suitable polymers. The prepared niosomal in situ gel was evaluated for appearance, clarity, pH, viscosity, gelling capacity, drug content, compatibility and in-vitro drug release. The formulation was designed to remain sufficiently fluid during administration and undergo rapid gelation after contact with the ocular environment, thereby increasing precorneal residence time and reducing rapid drainage from the eye.

The optimized niosomal in situ gel demonstrated satisfactory physicochemical characteristics and acceptable ophthalmic properties. Incorporation of fluorometholone into niosomes followed by incorporation into an in situ gel system provided improved drug retention and prolonged drug release compared with conventional ophthalmic delivery. The vesicular system facilitated drug encapsulation, while the in situ gel matrix provided sustained release and enhanced ocular residence.

Overall, the developed fluorometholone-loaded niosomal in situ gel showed considerable potential as a sustained ophthalmic drug delivery system. The combined advantages of niosomal encapsulation and in situ gel formation may minimize precorneal drug loss, prolong drug availability at the ocular site and reduce the frequency of administration. Thus, the developed formulation may provide an improved approach for the effective and convenient delivery of fluorometholone in the management of ocular inflammatory conditions.

Keywords: Fluorometholone, Niosomes, Niosomal drug delivery, In situ gel, Ophthalmic drug delivery system, Ocular drug delivery, Sustained drug release.

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Introduction

Ophthalmic drug delivery represents an important area of pharmaceutical research because the eye possesses several anatomical and physiological barriers that restrict the absorption and retention of administered drugs. Conventional ophthalmic dosage forms such as eye drops, suspensions and ointments are commonly used because of their ease of administration and patient acceptance. However, after instillation into the eye, a large proportion of the administered dose may be rapidly eliminated through blinking, tear turnover, nasolacrimal drainage and absorption through the conjunctiva. As a result, only a limited amount of drug may remain at the intended ocular site for a sufficient period. These limitations can lead to reduced therapeutic effectiveness and may necessitate frequent administration.[1]

The development of novel ocular drug delivery systems is therefore focused on increasing precorneal residence time, improving drug availability at the site of action and providing controlled or sustained drug release. Various approaches, including nanoparticles, liposomes, niosomes, microspheres, dendrimers, hydrogels and in situ gelling systems, have been investigated to overcome the limitations associated

with conventional ophthalmic preparations. Among these approaches, vesicular drug delivery systems have received considerable attention because they can encapsulate drugs within or around vesicular structures and modify their release characteristics. Such systems may improve drug retention and reduce the rapid loss of drug from the ocular surface.[2]

Niosomes are microscopic vesicular systems composed primarily of non-ionic surfactants, usually in combination with cholesterol or other membrane-stabilizing agents. They are capable of entrapping both hydrophilic and lipophilic drugs depending on their composition and structure. Niosomes offer several advantages, including improved drug encapsulation, protection of the incorporated drug, controlled drug release and the possibility of enhancing drug interaction with biological membranes. Compared with some other vesicular systems, niosomes may also provide advantages in terms of chemical stability, formulation flexibility and cost-effectiveness. These characteristics make niosomes attractive carriers for ophthalmic drug delivery.[3]

However, although niosomes can improve drug retention and release characteristics, their residence time on the ocular surface may still be affected by tear drainage and ocular movements. Incorporation of optimized niosomes into an in situ gelling system can provide an additional strategy for overcoming this limitation. An in situ gel is administered as a liquid or low-viscosity formulation and undergoes sol-to-gel transformation after administration in response to physiological conditions such as temperature, pH or ionic composition of the tear fluid. This transformation allows the formulation to remain at the ocular surface for a longer period and can provide sustained release of the incorporated drug.[4]

In situ gelling systems are particularly useful for ophthalmic administration because they combine the convenience of conventional eye drops with the prolonged residence characteristics of a gel. A formulation with suitable viscosity before administration can be easily instilled into the eye, while rapid gel formation after administration can reduce drainage and prolong contact with the corneal and conjunctival surfaces. The gel matrix can also act as a depot from which the drug or drug-loaded vesicles are gradually released. Therefore, combining niosomes with an in situ gel may provide a synergistic approach for improving ocular drug delivery.[5]

Fluorometholone is a synthetic glucocorticoid corticosteroid used topically for the treatment of inflammatory conditions of the eye. It produces anti-inflammatory effects by influencing inflammatory mediators and reducing the inflammatory response in ocular tissues. Although fluorometholone is therapeutically useful, conventional topical administration is limited by the short residence time of ophthalmic formulations on the ocular surface. Rapid removal of the formulation can limit drug availability and may require repeated administration to maintain an adequate therapeutic concentration at the site of action.[6]

The incorporation of fluorometholone into niosomes may provide several potential benefits for ophthalmic therapy. Encapsulation of the drug within vesicles can modify its release profile and potentially improve its retention at the ocular surface. The vesicles can serve as drug reservoirs, allowing gradual release of fluorometholone rather than rapid availability followed by elimination. In addition, the physicochemical characteristics of the niosomes, including vesicle size, surface charge and membrane composition, can influence drug entrapment, stability and release behaviour.[7]

Further incorporation of fluorometholone-loaded niosomes into an ophthalmic in situ gel may enhance the overall performance of the delivery system. The niosomal component can provide controlled drug encapsulation and release, whereas the in situ gel can increase ocular residence time and reduce precorneal drug loss. The combined system may therefore maintain the drug at the ocular surface for a prolonged period and provide a more sustained drug release pattern. This approach may also help to reduce the frequency of administration and improve patient convenience.[8]

The formulation and optimization of a niosomal in situ gel require careful selection and adjustment of formulation variables. The concentration and type of non-ionic surfactant, cholesterol concentration, drug-to-lipid or surfactant ratio, preparation conditions and polymer concentration can influence the characteristics of the final formulation. Important evaluation parameters include vesicle size, polydispersity index, zeta potential, entrapment efficiency, drug content, morphology, pH, viscosity, gelling capacity, clarity and in-vitro drug release. Optimization of these parameters is necessary to obtain a stable formulation with suitable ophthalmic characteristics and desirable drug-release behaviour.[9]

An ideal ophthalmic in situ gel should possess acceptable clarity, physiological pH, appropriate viscosity, rapid and adequate gelation, good drug content and satisfactory stability. It should not cause significant irritation or discomfort following administration. The formulation should also provide prolonged drug release without compromising the physical and chemical stability of the drug or vesicular carrier. Therefore, systematic characterization of the optimized formulation is

essential to establish its suitability as an ophthalmic drug delivery system.[10]

2. Methodology

Formulation and evaluation of niosomes

Accurately weighed quantity of surfactant (1: 2: 3: 4) in different molar ratio (30 µM: 60 µM: 90 µM: 120µM) and cholesterol (30 µM) fixed concentration were dissolved in chloroform and methanol (2:1v/v) solvent mixture and stirred until it gets completely dissolved. Then it was vortexed in a round bottom flask at temperature 55ºC to remove the solvent under reduced pressure in the rotary flask evaporator at 100 rpm for 30-40 minutes.

After evaporation of solvents, the surfactants and cholesterol leads to formation of thin film on the inner sides of round bottom flask (RBF). Thin film was hydrated with aqueous phase containing drug (100 mg) in 10ml of phosphate buffer pH 7.4 for 30 minutes at temperature 55ºC to obtain yellowish white dispersion of niosomes. The above white dispersion of niosomes was cooled in an ice bath and then sonicated using probe type ultrasonicator for 3 minutes at 150V. The resultant vesicles of niosomes were stored at 4ºC in a refrigerator for further studies. Plain niosomes were also prepared without using drug.[11]

Table 1 : Composition of Niosomes

Formulation Code	Drug (mg)	Surfactant	Cholesterol (µM)	Surfactant (µM)	Drug: Cholesterol: and Surfactant
F1	100	Span 20	30	30	1:1:1
F2	100			60	1:1:2
F3	100			90	1:1:3
F4	100			120	1:1:4
F5	100	Span 40	30	30	1:1:1
F6	100			60	1:1:2
F7	100			90	1:1:3
F8	100			120	1:1:4
F9	100	Span 60	30	30	1:1:1
F10	100			60	1:1:2
F11	100			90	1:1:3
F12	100			120	1:1:4

In vitro drug release studies of niosomes

In vitro drug release study of niosomal formulation was studied by membrane diffusion technique. In vitro diffusion cell was made using cellophane membrane as a semi-permeable membrane. The diffusion cell consist of a beaker , magnetic stirrer with temperature control and test tube with both ends open. One end of the test tube was closed using treated cellophane membrane as a semi-permeable membrane and the other end was kept open to introduce niosomal formulation. The diffusion medium was freshly prepared phosphate buffer saline pH 7.4 of 100 ml equilibrated at 37ºC ± 0.5ºC. The niosomal formulation 5 ml was placed inside the diffusion cell through open end of the test tube on the cellophane membrane. The diffusion medium used was freshly prepared 100 ml of phosphate buffer pH 7.4. It was placed inside the beaker in such a way that the lower surface of the cellophane membrane was made contact with the buffer. The temperature of the buffer solution was maintained at 37ºC ± 0.5ºC and stirred with magnetic stirrer throughout the study period. Aliquots (5 ml) of medium were withdrawn periodically and replaced with fresh diffusion medium of pH 7.4 buffer to maintain constant volume (sink condition). The samples were analyzed spectroscopically for concentration of drug.[12,13]

Formulation and characterization of niosomal *in-situ* Gel

In this research work, pH triggered mechanism was used to convert niosomes in to niosomal ocular in-situ gel formulation using carbopol 940 and Hydroxy propyl methyl cellulose K 15M (low and high) viscous polymers.[14]

Carbopol is an important class of ocular bio adhesiveness and it is widely used in ophthalmology to enhance precorneal retension. It is synthetic polymer composed of 62 % of carboxyl polymers with high molecular weight formed by repeating units of acrylic acid. As the concentration of carbopol increases in the vehicle, its acidic nature may cause stimulation to the eye tissues and also causes lachrymation and hence combination of polymers were used. Also in order to reduce the total polymer content of carbopol and to improve the gelling properties, a combination of polymers were used. Hydroxy propyl methyl cellulose (low & high viscous polymers) were used along with the carbopol in order to improve ocular bioavailability. However mucoadhesive polymers or stimuli sensitive polymers when used in combination with vesicular system may provide vesicles with necessary site adherence and site retension to achieve carrier and drug targeting in topical ocular therapy and endow them with the ability to mucoadhesive nature.

The optimized formulation (F9) containing 1:1 C/S ratio of span 60 and cholesterol was found to be effective and that formulation was selected as best formulation for the conversion of niosomal in-situ gel formulation. Trial formulations were carried out for developing niosomal in-situ gel using pH sensitive polymers like carbopol and HPMC K 15M (low and high viscous). Five trial formulations of the in-situ gel were prepared by dissolving various concentrations of polymers carbopol 940 and cellulose derivatives (HPMC K 15 low viscous and high viscous) in phosphate buffer pH 7.4 and they were allowed to hydrate. To this β-cyclodextrin, sodium chloride and Benzalkonium chloride were added. Niosomal dispersion of 10 ml was added to the above under constant stirring until a uniform solution was obtained. Final volume was adjusted by

using buffer. These were then filled in vials under aseptic conditions, sterilized in the autoclave at 121° C and 15 psi, for 20 minutes and were evaluated for further studies.[15,16]

Table 2: Composition of niosomal *in-situ* gel formulations

Composition	NG1	NG2	NG 3	NG4	NG5
Niosomal Dispersion (ml)	10	10	10	10	10
Carbopol 940% w/v (gm)	0.5	0.5	0.5	0.5	0.5
HPMC K 15M (Low viscous) (gm)	0.1	0.1	0.1	0.1	0.1
HPMC High viscous (gm)	0.1	0.2	0.3	0.4	0.5
Cyclodextrin (gm)	0.1	0.1	0.1	0.1	0.1
Benzalkonium chloride (gm)	0.002	0.002	0.002	0.002	0.002
Sodium chloride (gm)	0.9	0.9	0.9	0.9	0.9
Phosphate Buffer pH 7.4(ml)	100	100	100	100	100

Characterization of niosomal *in-situ gel*

pH determination

pH was measured using pH meter. The pH was noted by bringing the electrode near the surface of the formulation and allowing it to equilibrate for 1 minute and the values were measured in triplicate.[17]

Drug content analysis

Drug content of niosomal in-situ gel was determined by adding 50% n-propanol to the formulation for the lysis of vesicle. About 1ml of niosomal *in-situ* gel was then diluted to 100 ml with simulated tear fluid of pH 7.4. The drug content was estimated spectroscopically and values were measured in triplicate.[18,19]

Determination of viscosity

The viscosities of the developed niosomal in-situ gel formulations were measured by the Brookfield Viscometer DV2T model. The formulations were taken in the sampling tube and analyzed in the room temperature. The spindle 18 was connected to the viscometer in such a position and the samples were measured at 15rpm for duration of 5 minutes. Finally, obtained values were measured in units as centipoises (cP).[20]

Gelling Capacity

The determination of in vitro gelling capacity was done by visual method. Colored solutions were prepared by adding 1% amaranth dye solution in water and mixed with developed formulations of niosomal in-situ gel drug delivery system. The *in vitro* gelling capacities of prepared formulations were measured by placing 5ml of the simulated tear fluid pH 7.4 in glass tube. To this 20 µl-50 µl of colored formulation solution was added with the help of pipette. As the solution comes in contact with STF fluid 7.4, it gets converted into stiff gel. The gelling capacity of solution was evaluated on the basis of stiffness of gel formed and remains as such for a long time. Colored dye was added in the formulation in order to visualize the appearance of in situ gel formation. The in vitro gelling capacity was graded in two categories on the basis of gelation time and time period for which the formed gel remains as such.[21]

In vitro drug release of niosomal *in-situ* gel

In vitro release studies were carried out using franz diffusion cell and the temperature was adjusted to 37º C ± 5º C. Dialysis membrane was soaked overnight in STF fluid. The sample was applied on to the membrane and the membrane was placed in between donor and receptor compartment of the cell consisting of STF fluid pH 7.4. Samples were withdrawn at periodic intervals for 24 hr and replaced with fresh buffer to maintain sink condition. The drug content was analyzed using UV visible spectrophotometer using STF fluid as blank.[22,23]

Kinetic models for *in vitro* drug release data

The data obtained from in vitro drug release study of niosomal in-situ gel formulations were fitted to different kinetic models. Zero order (percentage drug release versus time), first order (logarithmic of percentage drug remaining to be released versus time), Higuchis model (percentage of drug release versus square root of time), Hixon crowell and Korsmeyer Peppas equation was used to study the drug release mechanism by analyzing (n) as the diffusion exponent.[24]

Result

Formulation of niosomes of by thin film hydration technique

Niosomes were prepared by thin film hydration technique as described in the procedure earlier. In this, formulations of niosomes were prepared by using non-ionic surfactant (Span 20, 40, 60) along with cholesterol in different ratios of (Cholesterol: Surfactant) (1:1,1:2,1:3,1:4) with the fixed concentration of cholesterol (30 µM**)** and the drug being kept constant (100mg).

Evaluation of niosomes of fluorometholone

In vitro drug release of niosomes

The in vitro release of all developed niosomal formulations were carried out by diffusion method. The studies revealed that the rate of drug release depends on the percentage of drug entrapment efficiency. Among all the twelve developed formulations, formulation (F9) i.e equi molar ratio of cholesterol and surfactant (Cholesterol /Span 60, C/S:1:1) showed maximum sustained drug release when compared with other Span series Hence, the order of drug release was found to be Span 60 > Span 40 > Span 20. From the results it was concluded that ordered state of Span 60 that decreases membrane permeability and also the presence of higher alkyl chain length of Span 60 further prolongs the release rates.

Table 3: *In vitro* release profile of niosomes

Time (h)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	8.06 ± 1.62	9.42 ± 1.57	10.88 ± 1.52	12.12 ± 1.14	8.12 ± 2.68	9.24 ± 1.66
2	15.1 ± 1.85	16.96 ± 1.76	18.76 ± 2.23	20.12 ± 1.56	12.24 ± 3.15	14.18 ± 1.18
3	20.24 ± 2.26	21.22 ± 1.54	22.18 ± 1.60	25.14 ± 1.72	17.4 ± 2.82	19.22 ± 1.59
4	25.57 ± 2.72	27.14 ± 1.62	28.64 ± 1.98	30.79 ± 1.82	23.15 ± 2.16	25.34 ± 1.07
5	30.66 ± 1.74	32.16 ± 1.95	34.12 ± 1.59	35.4 ± 1.76	27.25 ± 2.89	29.82 ± 1.84
6	34.42 ± 1.96	37.48 ± 1.23	39.64 ± 1.83	40.13 ± 1.84	32.07 ± 1.98	36.3 ± 1.76
7	38.26 ± 2.58	42.52 ± 1.45	44.6 ± 1.26	45.42 ± 1.65	36.18 ± 1.67	40.51 ± 1.58
8	42.14 ± 1.66	47.06 ± 1.62	53.72 ± 1.22	52.88 ± 1.01	41.98 ± 2.07	46.23 ± 1.89
9	46.65 ± 1.97	52.72 ± 1.58	56.18 ± 2.86	57.76 ± 1.68	45.86 ± 1.14	52.34 ± 1.15
10	50.1 ± 1.68	56.63 ± 1.44	60.14 ± 2.22	62.5 ± 1.44	50.08 ± 1.96	56.49 ± 1.84
11	54.06 ± 1.54	60.77 ± 1.40	64.16 ± 2.60	66.86 ± 1.28	54.61 ± 1.70	60.18 ± 1.29
12	60.06 ± 1.84	66.58 ± 1.58	68.48 ± 1.98	72.04 ± 1.86	58.78 ± 1.50	64.82 ± 1.17
24	86.52 ± 1.55	88.14 ± 1.66	90.22 ± 1.86	92.08 ± 1.28	84.42 ± 1.68	86.48 ± 1.94

Evaluation of optimized F9 loaded gel

Visual appearance of developed formulations were found to be milky white dispersion. Developed formulations were found to be clear and there were no particles or aggregates observed. pH of developed formulations were measured in triplicate values and they were in the range of skin pH for all developed niosomal *in-situ* gel formulations (NG1-NG5).

Drug content was measured in triplicate and they were found to be maximum in NG4. Viscosity was found to be in the range of 63.08 to 76.98 cP and suitable for instillation. As the concentration of polymer increased, viscosities of the formulations were also found to be increased. Gelation studies were measured by the immediate gelation, immediate and stiff gelation for extended period of time. Optimised formulation NF4 exhibited immediate and stiff gelation for extended period of time

Table 4: Characterization studies of niosomal *in-situ* gel

Formulation code	Visual appearance	Clarity	pH (n=3)	Drug content (n=3)	Gelation studies	Viscosity(cP)
NG1	Milky white dispersion	Clear	6.23 ± 0.24	99.67 ± 0.44	Immediate gelation	63.08
NG2			6.25 ± 0.35	99.75 ± 0.57	Immediate gelation	68.32
NG3			6.21 ± 0.74	99.63 ± 0.68	Immediate gelation	71.89
NG4			6.27 ± 0.62	99.82 ± 0.39	Immediate stiff gelation	76.98
NG5			6.19 ± 0.45	99.80 ± 0.49	Immediate stiff gelation	74.84

In vitro drug release study of niosomal *in-situ* gel

It is obvious that incorporation of niosomes in to structured vehicle resulted in a sustained release of drug. Also this is due to the presence of polymer in the preparations showed mucoadhesive properties of the gel, leading to higher viscosity of niosomal *in-situ* gel which provides an extra barrier for release of drug. Among all the gel formulations, NG4 showed slower drug release when compared with the other formulations, this may be due to the high gelling capacity of the formulation whereas other formulations showed faster release. Further the formulation NG4 showed immediate and stiff gelation for extended period of time as revealed in the gelling capacity studies. Hence based on the gelling capacity and sustained release profile, (NG4) was selected as optimized niosomal *in-situ* gel formulation and was subjected to further characterization studies.

Table 5: *In vitro* release profile of niosomal *in-situ* gel formulations

Time (h)	NG1	NG2	NG3	NG4	NG5
1	6.92 ± 0.36	5.06 ± 0.38	5.46 ± 0.23	6.34 ± 0.58	7.86 ± 0.46
2	10.86 ± 0.30	10.27 ± 0.44	11.85 ± 0.82	8.24 ± 0.63	9.26 ± 0.40
3	15.91 ± 0.46	15.94 ± 0.26	16.25 ± 0.29	12.14 ± 0.82	13.49 ± 0.58
4	20.01 ± 0.91	21.78 ± 0.21	20.94 ± 0.53	15.92 ± 0.87	16.09 ± 0.57
5	25.81 ± 0.92	26.14 ± 0.45	25.62 ± 0.79	19.68 ± 0.54	20.07 ± 0.57
6	30.87 ± 0.68	31.74 ± 0.57	30.88 ± 0.53	23.72 ± 0.48	25.23 ± 0.64
7	36.41 ± 0.72	36.65 ± 0.35	34.77 ± 0.64	27.63 ± 0.16	30.95 ± 0.48
8	40.42 ± 0.62	41.27 ± 0.21	39.92 ± 0.53	31.58 ± 0.44	35.98 ± 0.75
9	46.72 ± 0.18	46.33 ± 0.45	44.78 ± 0.62	34.92 ± 0.34	40.27 ± 0.71
10	52.92 ± 0.28	50.86 ± 0.28	49.16 ± 0.18	38.77 ± 0.30	45.98 ± 0.58
11	58.52 ± 0.34	55.65 ± 0.53	54.42 ± 0.80	42.86 ± 0.46	50.36 ± 0.56
12	63.55 ± 0.42	60.83 ± 0.59	58.18 ± 0.52	45.14 ± 0.24	55.16 ± 0.18
24	81.57 ± 0.16	79.26 ± 0.48	78.58 ± 0.86	67.71 ± 0.40	76.28 ± 0.16

Kinetics study and mechanism of drug release

The *in vitro* drug release data of all developed niosomal *in situ* gel were fitted in to various kinetic models. From the studies it was revealed that the optimized formulation NG4 obeyed first order release kinetics and followed by Hixon crowell model with and Non Fickian diffusion mechanism

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Table 6: Kinetic release studies data profile of the formulations

Kinetics Model	Parameters	NG1	NG2	NG3	NG4	NG5
Zero	R^2	0.8508	0.8388	0.8412	0.9296	0.8952
	K_0	4.353	4.254	4.134	3.403	3.839
First	R^2	0.9798	0.9894	0.9917	0.9966	0.9799
	K_1	0.070	0.068	0.065	0.048	0.057
Higuchi	R^2	0.8914	0.9091	0.9170	0.8909	0.8753
	K_H	15.188	14.903	14.491	11.725	13.265
Korsemeyer - Peppas	R^2	0.9542	0.9626	0.9689	0.9866	0.9618
	K_{KP}	9.322	9.603	9.415	6.173	7.259
	n	0.709	0.688	0.685	0.773	0.757
Hixson-Crowell	R^2	0.9816	0.9850	0.9849	0.9950	0.9812
	K_{HC}	0.021	0.020	0.019	0.015	0.017

Conclusion

Fluorometholone-loaded niosomes were successfully formulated using suitable concentrations of non-ionic surfactant and cholesterol. The prepared formulations exhibited satisfactory physical characteristics and were evaluated for important parameters such as vesicle size, polydispersity index, zeta potential, entrapment efficiency, drug content, morphology and in-vitro drug release. Optimization of the formulation variables helped in selecting a niosomal formulation with desirable vesicular characteristics, good drug entrapment and a controlled drug-release profile.

The optimized fluorometholone-loaded niosomes F9 were incorporated into an in situ gelling system using suitable gelling polymers. The developed formulation demonstrated acceptable appearance, clarity, pH, viscosity, drug content and gelling capacity, indicating its suitability for ophthalmic administration. The formulation was capable of undergoing sol-to-gel transformation after administration, which is expected to prolong the residence of the formulation on the ocular surface and reduce rapid drainage through the nasolacrimal pathway.

The in-vitro drug-release study demonstrated that incorporation of fluorometholone-loaded niosomes into the in situ gel system provided prolonged and controlled drug release compared with conventional drug delivery. The niosomes acted as drug reservoirs, while the in situ gel matrix further controlled the release of fluorometholone. This combined effect may improve the availability of the drug at the ocular site and minimize the rapid loss of drug following administration.

Overall, the developed optimized fluorometholone niosomal in situ gel NG4 showed promising characteristics as a sustained ophthalmic drug delivery system. The formulation combines the advantages of niosomal encapsulation, controlled drug release and prolonged ocular residence provided by in situ gel formation. Thus, the developed system may potentially enhance ocular drug availability, reduce precorneal drug loss and decrease the frequency of administration, thereby improving patient convenience and therapeutic effectiveness. Further in-vivo ocular tolerance, pharmacokinetic and pharmacodynamic studies would be required to establish its clinical potential.

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