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Original Research Article

FORMULATION AND CHARACTERIZATION OF NOVEL TRANSFEROSOMAL GEL SYSTEM FOR IMPROVED TOPICAL DELIVERY OF OZENOXACIN

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Abstract: The present study aimed to develop and evaluate an ozenoxacin-loaded transferosomal gel for the effective treatment of bacterial skin infections. Transferosomes were prepared using the thin-film hydration technique employing phospholipid and Tween 80 as an edge activator, followed by incorporation into a Carbopol 934 gel base. Different gel formulations were prepared by varying polymer concentration and evaluated for physicochemical characteristics, including viscosity, drug content, extrudability, and spreadability. Among the formulations studied, IGF2 demonstrated optimal properties with acceptable viscosity (3265 ± 17 cps), high drug content (99.45 ± 0.25%), good extrudability (183 ± 9 g), and satisfactory spreadability (11.36 ± 0.41 g·cm/sec). In-vitro drug release studies revealed a sustained release profile, with 89.98 ± 0.88% cumulative drug release at 12 hours. Release kinetics analysis indicated that drug release followed first-order kinetics and was primarily governed by a diffusion-controlled mechanism. Stability studies conducted under accelerated conditions for three months showed no significant changes in physical appearance, drug content, or release behavior, confirming the formulation's stability. The findings suggest that the developed ozenoxacin transferosomal gel offers a promising topical drug delivery system with enhanced drug retention, sustained release, and improved therapeutic potential for bacterial skin infections.

Keywords: Ozenoxacin, Transferosomes, Topical drug delivery, Carbopol gel, Skin infections, Controlled drug release.

INTRODUCTION

Skin and soft tissue infections (SSTIs) particularly superficial bacterial infections such as impetigo, folliculitis and localized cellulitis remain a frequent cause of outpatient visits and carry risk of complications when not treated promptly and effectively [1]. Topical antimicrobial therapy is preferred for many superficial infections because it delivers high local concentrations of drug while minimizing systemic exposure and adverse effects; however, the stratum corneum poses a formidable barrier that limits drug penetration to deeper viable epidermis and dermis where bacteria often reside, and this can reduce clinical efficacy for some agents [2].

Despite promising intrinsic antimicrobial properties, the clinical performance of topical drugs depends heavily on their ability to cross the skin barrier and deposit therapeutically effective concentrations at the site of infection. Ultra-deformable vesicular carriers commonly termed transferosomes (or transfersomes) are elastic lipid vesicles composed of phospholipids and an edge activator (surfactant) that confer high deformability and permit penetration of intact vesicles through intercellular pathways and appendageal routes.

Ozenoxacin is a novel, non-fluorinated quinolone developed for topical use that exhibits potent bactericidal activity against common Gram-positive skin pathogens, including Staphylococcus aureus (including some resistant phenotypes) and Streptococcus pyogenes [3]. Its dual targeting of bacterial DNA gyrase and topoisomerase IV produces rapid bactericidal action and a favorable microbiological profile in clinical studies of impetigo, making it an attractive candidate for topical formulations aimed at superficial bacterial skin infections [4].

Despite promising intrinsic antimicrobial properties, the clinical performance of topical drugs depends heavily on their ability to cross the skin barrier and deposit therapeutically effective concentrations at the site of infection [5]. Ultra-deformable vesicular carriers commonly termed transferosomes (or transfersomes) are elastic lipid vesicles composed of phospholipids and an edge activator (surfactant) that confer high deformability and permit penetration of intact vesicles through intercellular pathways and appendageal routes [6]. Transferosomes have repeatedly demonstrated enhanced skin permeation, improved drug deposition in deeper skin layers, and the potential to increase local bioavailability compared with conventional creams or liposomes [7].

Incorporating an antibacterial agent such as ozenoxacin into a transferosomal carrier and then formulating that carrier into a gel base combines the advantages of (a) improved skin penetration and targeted drug delivery through the use of vesicular carriers and (b) the practical benefits of a mucoadhesive/viscous topical vehicle (easy application, prolonged contact time, and controlled release) [8]. Previous studies have shown that transferosomal gels can significantly increase dermal drug deposition and therapeutic efficacy for antiviral and antibacterial drugs when compared to conventional formulations, supporting the rationale for developing an ozenoxacin transferosomal gel [9-10].

Therefore, the present study aims to formulate and characterize an ozenoxacin-loaded transferosomal gel, optimizing vesicle composition and gel matrix to maximize entrapment efficiency, vesicle deformability, stability, skin permeation, and local drug deposition with the ultimate goal of improving topical therapeutic outcomes against bacterial skin infections while maintaining a favorable safety profile. This approach leverages ozenoxacin's potent topical antibacterial activity and transferosomes' transdermal capabilities to address the clinical challenge of delivering effective drug concentrations to infected skin layers.

MATERIALS AND METHODS

Material

The materials used in the present investigation included ozenoxacin as the model antibacterial drug. Phospholipid and Tween 80 were employed for the preparation of transferosomes, while chloroform and methanol were used as organic solvents. Carbopol 934 served as the gelling agent, and propylene glycol was used as a humectant and penetration enhancer. Phosphate-buffered saline (pH 7.4) and double distilled water were used for hydration and preparation of the gel base. Sodium hydroxide was used for pH adjustment. All chemicals and reagents used were of analytical grade and were used as received without further purification.

Methods

Preparation of Ozenoxacin-loaded transferosomes

Ozenoxacin-loaded transferosomes were prepared using the thin-film hydration technique**.** Phospholipid and Tween 80 were dissolved in an organic solvent mixture consisting of chloroform and methanol (2:1 v/v, 20 mL). Ozenoxacin was then added to the organic phase, and the resulting solution was transferred to a round-bottom flask. The organic solvents were removed under reduced pressure using a rotary evaporator, resulting in the formation of a thin, uniform lipid film on the inner wall of the flask. The dried lipid film was subsequently hydrated with phosphate-buffered saline (pH 7.4, 20 mL) to obtain a coarse vesicular dispersion. This dispersion was sonicated to reduce vesicle size and achieve uniform transferosomal vesicles. The finalized ozenoxacin-loaded transferosomal formulations were stored under refrigerated conditions until further evaluation[11].

Preparation of gel base

The preparation of Ozenoxacin transferosomal gel begins with the dispersion of Carbopol 934 (0.5–1.5% w/v) into 80 ml of double distilled water under continuous stirring at 800 rpm for 1 hour to ensure uniform hydration. After complete dispersion, 10 ml of propylene glycol is added to enhance the viscosity and consistency of the gel. The total volume is then adjusted to 100 ml with distilled water. To remove entrapped air and achieve a homogeneous gel base, the mixture is sonicated using a bath sonicator for 10 minutes. The pH of the gel is adjusted to 6.8 using a suitable pH modifier such as sodium hydroxide. Finally, the transferosomal formulation containing Ozenoxacin equivalent to 1% w/w drug is incorporated into the gel base with gentle mixing to ensure uniform drug distribution [12].

Table 1: Different composition of Ozenoxacin transferosomal gel

Ingredients	IGF1	IGF2	IGF1
Ozenoxacin transfersomes eq. to. (%)	1	1	1
Carbopol 934 (%)	0.5	1.0	1.5
Propylene glycol (ml)	10	10	10
Sodium hydroxide	Qs.	Qs.	Qs.
Water (ml)	100	100	100

Characterization of Transfersomes containing gel

Measurement of Viscosity

Viscosity measurements of prepared topical Transfersomes based gel were measured by Brookfield viscometer using spindle no. 63 with the optimum speed of 10rpm; viscosity [13].

pH measurements

pH of selected optimized formulations was determined with the help of digital pH meter. Before each measurement of pH, pH meter should be calibrated with the help of buffer solution of pH 4, pH 7 and pH 9.2. After calibration, the electrode was dipped into the vesicles as long as covered by the vesicles. Then pH of selected formulation was measured and readings shown on display were noted [13].

Drug content

Accurately weighed equivalent to 100 mg of topical transfersomal gel was taken in beaker and added 20 ml of methanol. This solution was mixed thoroughly and filtered using Whatman filter paper no.1. Then 1.0 mL of filtered solution was taken in 10 mL capacity of volumetric flask and volume was made upto 10 mL with methanol. This solution was analyzed using UV-Vis. Spectroscopy[14].

Extrudability study

Extrudability was based upon the quantity of the gel extruded from collapsible tube on application of certain load. More the quantity of gel extruded shows better extrudability (Jivrani and Patel, 2014). It was determine by applying the weight on gel filled collapsible tube and recorded the weight on which gel was extruded from tube [15].

Spreadibility

Spreadibility of formulation is necessary to provide sufficient dose available to absorb from skin to get good therapeutic response. An apparatus in which a slide fixed on wooded block and upper slide has movable and one end of movable slide tied with weight pan. To determine spreadibility, placing 2-5 g of gel between two slide and gradually weight was increased by adding it on the weight pan and time required by the top plate to cover a distance of 6cm upon adding 20g of weight was noted. Good spreadibility show lesser time to spread [16].

$$Spreadibility\,(g.cm/\sec) = \frac{Weight\ tide\ to\ Upper\ Slide \times Lenth\ moved\ on\ the\ glass\ slide}{Time\ taken\ to\ slide}$$

***In vitro* drug diffusion study**

The *In-vitro* diffusion study is carried by using Franz Diffusion Cell. Egg membrane is taken as semi permeable membrane for diffusion. The Franz diffusion cell has receptor compartment with an effective volume approximately 60 mL and effective surface area of permeation 3.14sq.cms. The egg membrane is mounted between the donor and the receptor compartment. A two cm^2 size patch taken and weighed then placed on one side of membrane facing donor compartment. The receptor medium is phosphate buffer pH 7.4. The receptor compartment is surrounded by water jacket so as to maintain the temperature at 37 ± 0.5°C. Heat is provided using a thermostatic hot plate with a magnetic stirrer. The receptor fluid is stirred by Teflon coated magnetic bead which is placed in the diffusion cell. During each sampling interval, samples are withdrawn and replaced by equal volumes of fresh receptor fluid on each sampling. The samples withdrawn are analyzed spectrophotometrically [17].

Stability study

The optimized transferosomal gel formulation IGF2 was subjected to stability studies to evaluate the effect of storage conditions on its physicochemical characteristics and drug release behavior. The formulation was stored under accelerated stability conditions (40 ± 2 °C / 75 ± 5 % RH) for a period of 3 months**.** Samples were analyzed at 0, 1, 2, and 3 months for appearance, viscosity, drug content, extrudability, spreadability, and in-vitro drug release [18].

RESULTS

The present study was undertaken to develop and evaluate an ozenoxacin-loaded transferosomal gel intended for effective topical management of bacterial skin infections. Transferosomes were incorporated into a Carbopol 934 gel base to enhance skin penetration while ensuring acceptable physicochemical and application properties.

Carbopol 934 was selected as the gelling agent due to its excellent rheological behavior, skin compatibility, and widespread use in topical formulations. Varying concentrations of Carbopol (0.5–1.5% w/v) were employed to optimize viscosity, spreadability, and extrudability of the transferosomal gel formulations IGF1, IGF2, and IGF3. Propylene glycol served as a humectant and penetration enhancer, contributing to improved drug diffusion and patient acceptability. Adjustment of pH to 6.8 ensured compatibility with skin physiology and stability of the formulation.

The physicochemical evaluation revealed that all gel formulations exhibited satisfactory characteristics (Table 2). Viscosity values ranged from 3165 to 3358 cps**,** indicating that increasing Carbopol concentration led to increased gel rigidity. IGF1 showed the highest viscosity due to lower polymer flexibility, while IGF3 exhibited comparatively lower viscosity but higher extrudability.

Drug content across all formulations was within acceptable limits (96.65–99.45%), confirming uniform drug distribution and minimal drug loss during formulation. IGF2 demonstrated the highest assay value (99.45 ± 0.25%)**,** indicating optimal drug incorporation.

Extrudability and spreadability are critical parameters for topical application. IGF3 showed higher extrudability but lower spreadability, whereas IGF1 showed higher spreadability but lower extrudability. IGF2 offered a balanced profile**,** combining adequate viscosity, optimal extrudability (183 ± 9 g), and good spreadability (11.36 ± 0.41 g·cm/sec), making it the most suitable formulation for topical use.

In-vitro drug release studies of IGF2 demonstrated a sustained and controlled release pattern over 12 hours (Table 3). An initial burst release (22.25% at 0.5 h) was observed, which may be attributed to surface-associated drug and rapid hydration of the gel matrix. This was followed by a gradual release phase, reaching 89.98% cumulative drug release at 12 h**,** indicating prolonged drug availability at the application site.

The sustained release behavior can be attributed to the transferosomal vesicular structure combined with the Carbopol gel matrix, which together regulate drug diffusion.

Release kinetics analysis (Tables 4 and 5, Figure 1) showed that the drug release from IGF2 followed first-order kinetics, as evidenced by the highest correlation coefficient ($R^2 = 0.9884$). This suggests that the drug release rate was concentration-dependent.

The Higuchi model also exhibited a high correlation coefficient ($R^2 = 0.9748$), indicating that drug release was predominantly governed by diffusion mechanisms. The Korsmeyer–Peppas model showed a lower correlation ($R^2 = 0.9389$), suggesting that diffusion with minor polymer relaxation may contribute to the release mechanism. These findings confirm that IGF2 provides controlled drug release through a diffusion-dominated process.

Stability studies conducted under accelerated conditions for three months demonstrated that IGF2 remained physically and chemically stable throughout the study period (Table 6). No visible changes in appearance, homogeneity, or phase separation were observed. Only minor reductions in viscosity, drug content, extrudability, and spreadability were noted, all of which remained within acceptable limits. Drug content remained above 98%**,** indicating minimal degradation of ozenoxacin. The in-vitro drug release profile at 12 hours showed negligible variation, confirming retention of transferosomal integrity and gel structure during storage.

These results indicate that the optimized formulation possesses good shelf stability and is suitable for long-term topical application.

Among all the formulations studied, IGF2 emerged as the optimized formulation**,** demonstrating superior physicochemical properties, uniform drug content, controlled drug release, favorable release kinetics, and excellent stability. The incorporation of ozenoxacin-loaded transferosomes into a Carbopol gel matrix successfully enhanced sustained drug delivery while maintaining suitable topical characteristics. Thus, the developed ozenoxacin transferosomal gel represents a promising topical drug delivery system for the effective treatment of bacterial skin infections, potentially improving therapeutic efficacy and patient compliance.

Table 2: Characterization of gel based formulation

Formulation	Viscosity* (cps)	Assay* (%)	Extrudability* (g)	Spreadability* (g.cm/sec)
IGF1	3358±13	98.78±0.65	178±10	12.25±0.36
IGF2	3265±17	99.45±0.25	183±9	11.36±0.41
IGF3	3165±11	96.65±0.74	195±14	10.36±0.25

***Average of three determinations (n=3, ±SD)**

Table 3: *In vitro* drug release study of prepared gel formulation IGF2

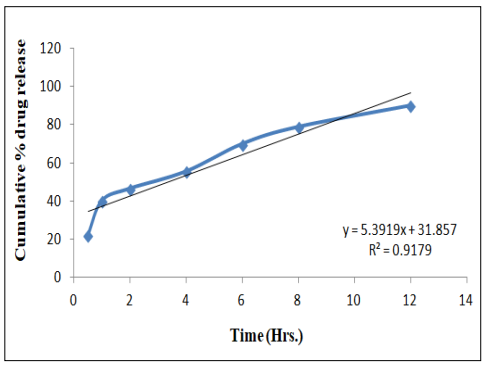
S. No.	Time (hr)	% Cumulative Drug Release
1	0.5	22.25±0.85
2	1	40.36±0.95
3	2	46.65±0.74
4	4	55.58±0.66
5	6	69.96±0.74
6	8	78.85±0.65
7	12	89.98±0.88

***Average of three determinations (n=3, ±SD)**

Table 4: *In-vitro* drug release data for optimized formulation IGF2

Time (h)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
0.5	0.707	-0.301	22.25±0.85	1.347	77.75	1.891
1	1	0	40.36±0.95	1.606	59.64	1.776
2	1.414	0.301	46.65±0.74	1.669	53.35	1.727
4	2	0.602	55.58±0.66	1.745	44.42	1.648
6	2.449	0.778	69.96±0.74	1.845	30.04	1.478
8	2.828	0.903	78.85±0.65	1.897	21.15	1.325
12	3.464	1.079	89.98±0.88	1.954	10.02	1.001

***Average of three determinations (n=3, ±SD)**



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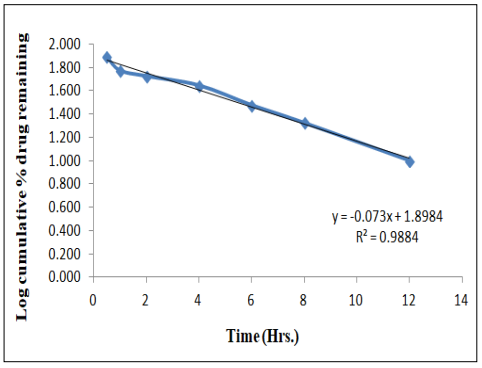

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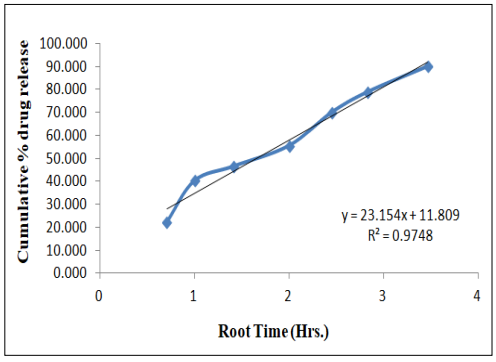
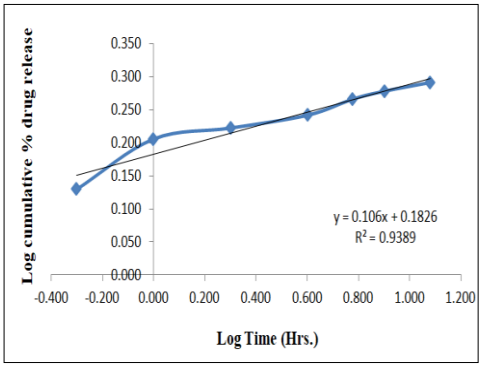


Higuchi order



Korsmeyer Peppas

Figure 1: Release kinetics study of gel based transferosomal gel formulation IGF2

Table 5: Release Kinetics of optimized gel of transferosomal gel

Formulation	Zero order	First order	Higuchi	Korsmeyer Peppas
IGF2	0.9719	0.9884	0.9748	0.9389

Table 6: Stability Study of optimized formulation IGF2

Parameter	Initial (0 month)	1 month	2 months	3 months
Appearance	Smooth, homogeneous, no phase separation	No change	No change	No change
Viscosity (cps)	3265±17	3252±18	3238±15	3215±11
Drug content (%)	99.45±0.25	99.12±12	98.86±0.36	98.35±0.63
Extrudability (g)	183±9	182±8	181±11	180±7
Spreadability (g·cm/sec)	11.36±0.41	11.28±0.85	11.20±0.74	11.12±0.36
% CDR at 12 h	89.98±0.88	89.25±0.33	88.74±0.36	88.10±0.47

***Average of three determinations (n=3, ±SD)**

CONCLUSION

The study successfully formulated and evaluated an ozenoxacin-loaded transferosomal gel for topical treatment of bacterial skin infections. The optimized formulation IGF2 showed suitable viscosity, high drug content, good spreadability, and sustained drug release up to 12 hours. Release followed first-order, diffusion-controlled kinetics, and the formulation remained stable under accelerated conditions. The transferosomal gel represents a promising and effective topical delivery system for ozenoxacin.

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