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DEVELOPMENT AND CHARACTERIZATION OF TRANSFERSOMES LOADED WITH EFINACONAZOLE: FORMULATION AND CHARACTERIZATION

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Abstract:

This study aimed to develop and characterize transfersomes loaded with efinaconazole for enhanced transdermal delivery. The transfersomes were prepared by optimizing lipid concentration, drug concentration, and stirrer time. The optimized transfersomes were then incorporated into a gel base, and the resulting formulation was characterized for various parameters including average vesicle size, entrapment efficiency, viscosity, drug release kinetics, and extrudability. The optimized gel formulation exhibited promising characteristics for efficient drug delivery. Overall, this research provides valuable insights into the formulation and characterization of transfersome-based gel for transdermal drug delivery applications.

Keywords: Transfersomes, Efinaconazole, Gel formulation, Transdermal delivery, Characterization.

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INTRODUCTION:

Efinaconazole, a broad-spectrum antifungal agent, has gained significant attention in the treatment of onychomycosis, a common fungal infection affecting the nails [1]. Despite its efficacy, the conventional topical formulations of efinaconazole face challenges such as poor penetration through the nail plate and low bioavailability, leading to suboptimal therapeutic outcomes [2].

Transfersomes, vesicular carriers composed of phospholipids and edge activators, offer a promising solution to enhance the delivery of efinaconazole across the nail barrier [3]. These vesicles possess deformable properties, allowing them to penetrate through narrow intercellular spaces and improve drug permeation[5]. Furthermore, transfersomes can encapsulate hydrophilic and lipophilic drugs, protecting them from degradation and enhancing their stability [5].

This study aims to develop and characterize transfersomes loaded with efinaconazole, with the goal of improving its transungual delivery and therapeutic efficacy. Formulation parameters such as lipid composition, edge activator type, and drug-to-lipid ratio will be optimized to achieve transfersomes with desirable characteristics, including small particle size, high entrapment efficiency, and sustained drug release.

MATERIAL AND METHODS:

Material

Various chemicals were utilized for the preparation and evaluation of transfersomes gel loaded with efinaconazole. Efinaconazole was obtained from Bioplus Life Sciences Pvt. Ltd., Bangalore. Soya phosphatidyl choline was sourced from Ash Chemie India, Thane. Disodium hydrogen phosphate, di potassium hydrogen orthophosphate, sodium chloride, methanol, ethanol, chloroform, carbopol 934p, methyl paraben, propyl paraben, and propylene glycol were procured from S.D. Fine Chem. Ltd., Mumbai. These chemicals played essential roles in transfersome formation, buffer preparation, solubilization, gel formation, and preservation.

Methods

Preparation of Efinaconazole Loaded Transfersomes:

To prepare the transfersomes loaded with efinaconazole, several steps were followed. Firstly, Soya phosphatidyl choline (PC) was dissolved in ethanol at concentrations ranging from 0.5% to 2% w/v in a closed vessel. The solution was then heated to 30 ± 1°C using a water bath and maintained at this temperature throughout the process. Next, distilled water or a drug solution in distilled water (1% w/v) was slowly added to the ethanolic lipid solution while continuously mixing at 900 rpm using a magnetic stirrer. This step ensured proper dispersion of the components and was carried out for 5 minutes.

After mixing, the resulting vesicular dispersion was allowed to cool at room temperature (25±1°C) for 45 minutes to form and stabilize the vesicles. Optimization of transfersomes was performed by varying parameters such as lipid concentration, ethanol concentration, drug concentration, and stirrer time, while keeping other parameters constant [6].

Preparation of gel base

The gel base preparation begins by accurately dispersing Carbopol 934, at a concentration of 1% w/v, into 80 ml of double distilled water in a beaker. Continuous stirring at 800 rpm is maintained for 1 hour to ensure thorough dispersion of Carbopol 934 in the water. Following this, 10 ml of propylene glycol is added to the Carbopol 934 dispersion to enhance the viscosity and consistency of the gel. The volume of the gel is then adjusted to a total of 100 ml, likely by adding an additional 10 ml of double distilled water, ensuring the gel reaches the desired volume for further processing. Subsequently, the gel undergoes sonication for 10 minutes using a bath sonicator to eliminate any air bubbles present, ensuring a smooth and uniform gel base. pH adjustment is then carried out to achieve a final pH of 6.8, likely through the addition of an appropriate pH adjuster such as sodium hydroxide or citric acid. Finally, the transferosomal preparation containing Efinaconazole, at a concentration of 3% w/w, is incorporated into the gel base to achieve the desired drug concentration for further formulation [7].

Optimization of Transfersomes

The optimization process for the transferosomal formulation involved several key parameters. Firstly, the ratio of lipid was optimized by testing different ratios ranging from 0.5% to 2.0%, while keeping all other parameters constant. Formulations were prepared and evaluated based on their average vesicle size and percentage entrapment efficiency.

Similarly, the optimization of drug concentration was carried out by varying the concentration of the drug while maintaining other parameters such as Soya PC and stirrer time constant. The formulations were assessed based on their entrapment efficiency and average vesicle size to determine the optimal drug concentration. Furthermore, the optimization of stirrer time involved testing different durations,

including 5, 10, and 15 minutes. This parameter was optimized based on the average vesicle size and percentage entrapment efficiency of the formulations.

Table 1: Optimization of lipid concentration

Optimization of lipid concentration			
Formulation code	**Soya PC (% w/v)**	**Ethanol**	**Drug (% w/v)**
F1	0.5	10	1
F2	**1**	**10**	**1**
F3	1.5	10	1
F4	2	10	1
Optimization of ethanol concentration			
Formulation code	**Soya PC (% w/v)**	**Ethanol**	**Drug (% w/v)**
F5	1	5	1
F6	1	**10**	**1**
F7	1	15	1
F8	1	20	1

Optimization of drug concentration			
Formulation code	**Soya PC (% w/v)**	**Drug (% w/v)**	**Ethanol (ml)**
F9	**1**	**1**	**10**
F10	1	1.5	10
F11	1	2	10
Optimization of Stirrer time			
Formulation code	**Soya PC: (% w/v)**	**Drug (% w/v)**	**Stirrer time (min)**
F12	**1**	**1**	**5**
F13	1	1	10
F14	1	1	15

Characterization of Efinaconazole loaded Transfersomes Surface charge and vesicle size

The vesicles size and size distribution and surface charge were determined by Dynamic Light Scattering method (DLS) (Malvern Zetamaster, ZEM 5002, Malvern, UK). Zeta potential measurement of the Transfersomes was based on the zeta potential that was calculated according to Helmholtz–Smoluchowsky from their electrophoretic mobility [8]. For measurement of zeta potential, a Zetasizer was used with field strength of 20 V/cm on a large bore measures cell. Samples were diluted with 0.9 % NaCl adjusted to a conductivity of 50 lS/cm.

Entrapment efficiency

One milliliter of Transfersomes suspension was centrifuged at 15.000 rpm for 1 h to allow the separation the entrapped drug from the un-entrapped drug. After removal of the supernatant, the sediment was lysed using methanol and then analyzed spectrophotometrically at 264nm using a UV spectrophotometer (Labindia 3000+). The EE% of MIC in the prepared Transfersomes was calculated applying the following equation:

$$\%\ Entrapment\ Efficiency = \frac{Terotical\ drug\ content - Practical\ drug\ content}{\text{Therotical drug content}} \times 100$$

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 [9].

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 [10]. Then pH of selected formulation was measured and readings shown on display were noted.

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 [11]. This solution was analyzed using UV-Spectroscope at λ_{max} 264nm.

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 [12]. It was determine by applying the weight on gel filled collapsible tube and recorded the weight on which gel was extruded from tube.

Spreadability

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 [13]. 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.

Spreadability (g.cm / sec) =
Weight tide to Upper Slide- Length moved on the glass slide/ Time taken to slide

***In 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 [14]. 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 32 ± 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 at wavelength of drug 264nm.

RESULTS AND DISCUSSION:

The optimization of the transferosomal formulation involved a meticulous examination of various parameters, aiming to enhance the efficacy and

stability of the final product. Table 2 presents the results of average vesicle size and percentage entrapment efficiency for different formulations. The vesicle size ranged from 145.65 nm to 356.65 nm, indicating variations in the size of the transferosomes. Similarly, the percentage entrapment efficiency varied from 63.32% to 78.98%, reflecting differences in the ability of the formulations to encapsulate the drug effectively.

Upon optimization, Table 3 showcases the characteristics of the selected optimized formulation, labeled as F-12. This formulation exhibited an average vesicle size of 165.58 nm and a percentage entrapment efficiency of 73.49%. Additionally, the zeta potential was measured at -38.85 mV, indicating the stability of the transferosomal formulation.

Table 4, the characterization of the transfersomes-loaded gel is detailed. The optimized gel, labeled as OTGF1, displayed a viscosity of 3245 cps, an assay percentage of 99.00%, an extrudability of 178 g, and a spreadability of 12.25 g.cm/sec. These parameters are crucial for evaluating the physical properties and performance of the gel formulation.

Table 5 outlines the results of the in vitro drug release study for the prepared gel formulation. Over time, the cumulative drug release increased gradually, reaching 88.98% after 12 hours. This data provides insights into the release kinetics of the drug from the gel matrix, which is essential for assessing its therapeutic efficacy and duration of action.

Furthermore, Table 6 presents the release kinetic data of the optimized gel formulation. Various kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer, were employed to analyze the drug release behavior. The formulation exhibited high correlation coefficients for all models, indicating diverse mechanisms involved in drug release, likely influenced by the gel matrix and transferosomal structure.

Table 2: Results of Average vesicle size (nm) and % Entrapment efficiency

Formulation code	Average vesicle size (nm)	% Entrapment efficiency
F1	356.65	75.65
F2	**285.65**	**78.98**
F3	310.24	69.98
F4	325.65	65.58
F5	285.65	68.85
F6	**245.85**	**76.65**
F7	265.85	71.12
F8	283.32	69.98
F9	**179.98**	**74.45**
F10	198.85	69.98
F11	183.32	68.12
F12	**165.58**	**73.49**
F13	145.65	68.85
F14	168.85	63.32

Table 3: Characterization of Optimized formulation of Transfersomes

Characterization	Average vesicle size (nm)	% Entrapment efficiency	Zeta Potential (mV)
F-12	165.58	73.49	-38.85

Table 4: Characterization of transfersomes loaded gel

Formulation	Viscosity (cps)	Assay* (%)	Extrudability (g)	Spreadability (g.cm/sec)
Optimized Gel	3245±12	99.00±0.32	178±2..5	12.25±1.5

***Average of three determinations**

Table 5: *In vitro* drug release study of prepared gel formulation

S. No.	Time (hr)	% Cumulative Drug Release
1	0.5	26.65±0.45
2	1	35.45±0.36
3	2	47.78±0.21
4	4	59.98±0.47
5	6	63.32±0.58
6	8	74.45±0.96
7	12	88.98±0.321

Table 6: Release kinetic data of optimized gel formulation

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	26.65	1.426	73.35	1.865
1	1.000	0.000	35.45	1.550	64.55	1.810
2	1.414	0.301	47.78	1.679	52.22	1.718
4	2.000	0.602	59.98	1.778	40.02	1.602
6	2.449	0.778	63.32	1.802	36.68	1.564
8	2.828	0.903	74.45	1.872	25.55	1.407
12	3.464	1.079	88.98	1.949	11.02	1.042

Table 7: Release Kinetics of optimized gel of transferosomal gel

Formulation	Zero order	First order	Higuchi	*Korsmeyer*
OTGF1	0.9388	0.9734	0.9865	*0.9915*

CONCLUSION:

In conclusion, the systematic optimization and characterization of the transferosomal gel formulation have led to the development of an efficient drug delivery system with desirable physical properties and sustained release kinetics. These findings contribute to the advancement of pharmaceutical research, offering insights into the design and evaluation of novel drug delivery systems for improved therapeutic outcomes.

REFERENCES:

1. Elewski BE. Onychomycosis: pathogenesis, diagnosis, and management. Clin Microbiol Rev. 1998;11(3):415-429.
2. Gupta AK, Drummond-Main C. Meta-analysis of randomized, controlled trials comparing particular doses of efinaconazole and tavaborole for the treatment of toenail onychomycosis. J Am Acad Dermatol. 2016;74(5):917-922.
3. Jain S, Tiwary AK, Sapra B, Jain NK. Formulation and evaluation of ethosomes for transdermal delivery of lamivudine. AAPS PharmSciTech. 2007;8(4)
4. Kaur P, Garg T, Rath G, Murthy RSR, Goyal AK. Development, optimization and evaluation of surfactant-based pulmonary nanolipid carrier system of paclitaxel for the management of drug resistance lung cancer using Box-Behnken design. RSC Adv. 2015;5(106):87207-87217.
5. Touitou E, Dayan N, Bergelson L, Godin B, Eliaz M. Ethosomes—novel vesicular carriers for enhanced delivery: characterization and skin penetration properties. J Control Release. 2000;65(3):403-418.
6. Malakar, Jadupati, Suma Oomen Sen, Amit Kumar Nayak, and Kalyan Kumar Sen. 2012. Formulation, Optimization and Evaluation of Transferosomal Gel for Transdermal Insulin Delivery. Saudi Pharmaceutical Journal 20(4): 355–63.
7. Ghanbarzadeh, Saeed, and Sanam Arami. 2013. Enhanced Transdermal Delivery of Diclofenac Sodium via Conventional Liposomes, Ethosomes, and Transfersomes. BioMed Research International 2013.
8. Wu, Pey Shiuan et al. 2019. "Preparation and Evaluation of Novel Transfersomes Combined with the Natural Antioxidant Resveratrol." Molecules 24(3): 1–12.
9. Qushawy, Mona, Ali Nasr, Mohammed Abd-Alhaseeb, and Shady Swidan. 2018. "Design, Optimization and Characterization of a Transfersomal Gel Using Miconazole Nitrate for the Treatment of Candida Skin Infections." Pharmaceutics 10(1).
10. Gupta, Ankit, Geeta Aggarwal, Samita Singla, and Ritika Arora. 2012. "Transfersomes: A Novel Vesicular Carrier for Enhanced Transdermal Delivery of Sertraline: Development, Characterization, and Performance Evaluation." Scientia Pharmaceutica 80(4): 1061–80.
11. Hanpramukkun N., Kongmuang S., Chansiri G., The stability of clindamycin phosphate in w/o/w multiple emulsions, Int J Pharm Sci Tec, 2009, 3(2), 1-7.
12. Jivrani Shilpa D, Patel Vijay K, Formulation, Development And Evaluation of Niosomal Drug Delivery System For Clindamycin Phosphate, Pharma Science Monitor, 2014, 5(2), 256-274.
13. Mishra M. and Biswal P., Complexation, Optimization, Formulation development and characterization of clindamycin phosphate gel using zinc acetate dehydrate, international journals of pharmacy, 2012; 2(3):472-486.
14. Nimker V, Jamal H, Ghosh P, Jain S, Beotra A. Liposomes: drug delivery system or possible doping agent, Journal of Drug Delivery and Therapeutics, 2017; 7(1):25-29.