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"Preparation And Evaluation of Fluconazole-Loded Ethosomal Gel by Thin Film Hydration and Mechanical Dispersion Methods"

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ABSTRACT: Topical delivery of antifungal agents is limited by the barrier function of the stratum corneum. Ethosomes, composed principally of phospholipids, ethanol and water, offer a deformable vesicular platform intended to improve cutaneous drug delivery. This study compared two preparation approaches, mechanical dispersion and thin-film hydration, for fluconazole-loaded ethosomes and incorporated the optimized vesicles into Carbopol 934 gel. Ethosomes were prepared using soya lecithin and ethanol. Mechanical dispersion was optimized by varying phospholipid and ethanol concentration, stirring, sonication and drug concentration; thin-film hydration by varying hydration medium, temperature and time. Formulations were characterized for particle size, polydispersity index (PDI), zeta potential, drug content and entrapment efficiency. Optimized suspensions were incorporated into Carbopol 934 gel and evaluated for pH, viscosity, spreadability and in-vitro release, with kinetic modelling. Stability was assessed for one month at 30 ± 2 °C/65 ± 5% RH. The optimized mechanical-dispersion formulation (F5) showed particle size 179.6 nm, PDI 0.184, zeta potential −39.4 mV, drug content 89.0% and entrapment efficiency 85.6%. The optimized thin-film-hydration formulation (F6) showed 110.5 nm, PDI 0.429, −41.7 mV, 99.5% and 93.0%, respectively. At 12 h, cumulative release was 79.05% (mechanical dispersion) and 87.27% (thin-film hydration) from suspensions, and 67.68% and 80.94% from the corresponding gels. The thin-film-hydration gel best fitted the Higuchi model (R^2 = 0.9920; Korsmeyer–Peppas n = 0.446). Changes after one month were minor. Under the conditions studied, thin-film hydration produced smaller vesicles, higher drug content and entrapment efficiency, and greater in-vitro release than mechanical dispersion. The Carbopol 934 gels showed measurable viscosity, spreadability and sustained release. Ex-vivo permeation, antifungal efficacy, dermal safety and longer-term stability studies are required before clinical conclusions can be drawn.

KEYWORDS: Fluconazole; ethosomes; topical drug delivery; thin-film hydration; Carbopol 934 gel.

I. INTRODUCTION

Superficial and cutaneous fungal infections remain an important therapeutic problem, particularly in warm and humid environments. The skin is both the target tissue for many topical antifungal treatments and a highly effective barrier to drug transport. The stratum corneum is the principal permeability barrier and its lipid-rich organization can restrict the entry of many therapeutic molecules.[1–3]

Topical administration can provide drug directly at the affected site and may reduce exposure associated with systemic administration. However, conventional topical dosage forms may provide limited and variable drug deposition because of the barrier properties of the stratum corneum. The stratum corneum acts as a rate-limiting barrier, which provides the rationale for advanced carriers for topical antifungal delivery.[4]

Ethosomes are soft, deformable phospholipid vesicles containing a relatively high concentration of ethanol. Their proposed delivery advantage arises from the combined effects of ethanol-induced modification of stratum-corneum lipid organization and the flexibility of the vesicle membrane. Reviews of ethosomal delivery describe these systems as promising carriers for dermal and transdermal delivery because they can improve drug deposition and permeation compared with conventional vesicular systems.[5–8]

Fluconazole is a triazole antifungal agent with established antifungal activity. Its use in topical delivery provides an appropriate model for investigating vesicular systems intended to improve local drug delivery. Previous research has

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investigated topical fluconazole delivery using emulsion-based systems, demonstrating the relevance of formulation design to skin penetration and retention[9,10].

Although ethosomal systems have been widely studied, preparation variables can substantially affect vesicle size, size distribution, surface charge and drug entrapment. Thin-film hydration provides a controlled route involving formation of a dried lipid film followed by hydration, whereas mechanical dispersion forms the vesicular dispersion through direct mixing and mechanical energy. The present work therefore addresses a formulation-development question: how do these two approaches perform under the selected experimental conditions when applied to fluconazole-loaded ethosomes?[11]

The objective of the present study was to develop and comparatively evaluate fluconazole-loaded ethosomal suspensions prepared by mechanical dispersion and thin-film hydration, identify optimized formulations from each approach, incorporate the optimized vesicles into Carbopol 934 gels, and compare their physicochemical properties, in-vitro release behaviour, release kinetics and short-term stability.

II. MATERIALS AND METHODS

A. Materials

The materials used in the present study included fluconazole as the active pharmaceutical ingredient, procured from Micro Labs Pvt. Ltd. Soya lecithin, used as the phospholipid for ethosome preparation, and chloroform were obtained from Sisco Research Laboratories Pvt. Ltd., Mumbai. Ethanol, which served as a permeation enhancer and co-solvent, was procured from Avantor Performance Materials India Ltd. Carbopol 934, used as the gelling polymer, was purchased from S.D. Fine Chem Pvt. Ltd., while triethanolamine (SDFCL) was used as a neutralizing agent to adjust the pH and achieve the desired gel consistency.

B. Preformulation and analytical characterization

Fluconazole was identified by FTIR after KBr pellet preparation. The FTIR spectrum showed characteristic bands at 3111.29, 2918.45, 1705.13, 1512.24, 1352.15 and 1296.21 cm−1. The drug showed absorption maxima at 210 and 260 nm in phosphate buffer pH 7.4; 210 nm was selected for quantitative analysis because it produced the higher-intensity signal and linearity over 10–100 µg/mL. The reported calibration curve had $R^2 = 0.9958$ and slope = 0.0107.[12,13]

Drug–excipient compatibility was assessed by FTIR using fluconazole, soya lecithin and ethanol. The characteristic drug peaks were retained in the physical mixture without major spectral changes, supporting compatibility under the tested conditions.

C. Preparation of fluconazole-loaded ethosomes by mechanical dispersion

Soya lecithin was dispersed in ethanol, followed by incorporation of fluconazole with continuous stirring. Distilled water was added gradually under mechanical stirring to promote vesicle formation, followed by sonication to reduce vesicle size and improve dispersion uniformity. The optimization matrix varied phospholipid concentration (1.0–2.0 g), ethanol volume (10–20 mL), stirring speed (500–900 rpm), stirring time, sonication time and drug concentration. The formulation ultimately selected as F5 contained 0.5 g fluconazole, 1.5 g soya lecithin, 20 mL ethanol and 30 mL water, with 700 rpm stirring and 5 min sonication.[5]

D. Preparation by thin-film hydration

Fluconazole and soya lecithin were dissolved in an organic phase containing chloroform. The solvent was removed under reduced pressure to form a thin lipid film. The dried film was hydrated with aEthanol and water and subsequently sonicated. The optimization variables included aqueous hydration medium, hydration temperature and hydration time. The final optimized formulation, F6, used 0.5 g fluconazole, 1.5 g soya lecithin, 15 mL ethanol, 20 mL water and 15 mL chloroform, with hydration at the selected temperature and 60 min hydration time according to the formulation matrix[14]. The two preparation routes are summarized in Fig. 1.

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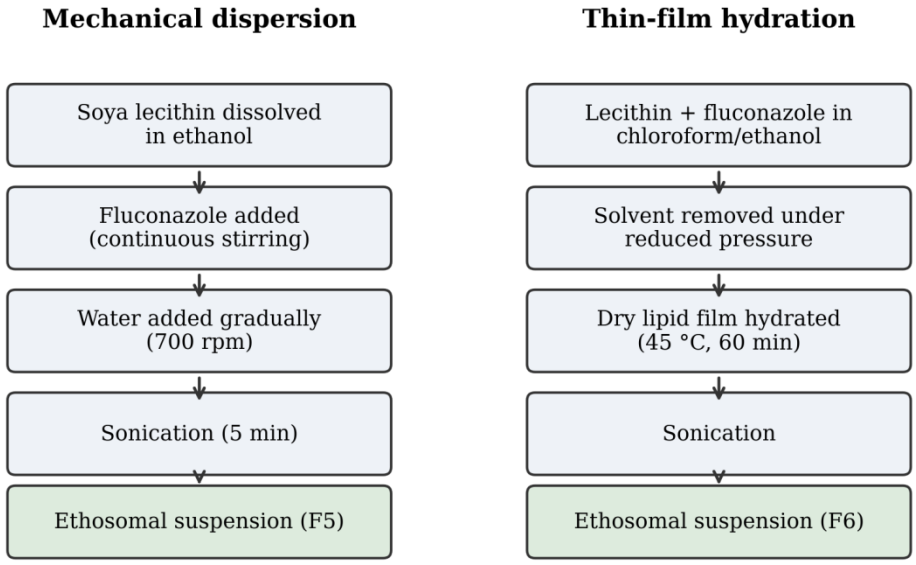

Fig. 1. Schematic of the preparation of fluconazole-loaded ethosomes by mechanical dispersion and thin-film hydration, followed by incorporation into Carbopol 934 gel.

E. Vesicle characterization

Particle size and PDI were determined by dynamic light scattering. Zeta potential was measured as an indicator of surface charge and dispersion stability. Entrapment efficiency was determined after separation of unentrapped drug, and drug content was calculated from the measured drug concentration relative to the theoretical amount.[15]

F. Preparation and evaluation of ethosomal gel

Optimized ethosomal suspensions were incorporated directly into a Carbopol 934 gel system. For 30 mL of optimized ethosomal suspension, 0.6 g Carbopol 934 (2% w/v) was gradually dispersed, followed by overnight hydration. Approximately 2–3 drops of triethanolamine were subsequently added to facilitate neutralization and gel formation.[16] The gel was evaluated for appearance, pH, viscosity and spreadability.

The measured viscosity values were 3144 cP for the mechanical-dispersion gel and 3418 cP for the thin-film-hydration gel. Spreadability was 8.23 mm² and 9.71 mm², respectively, while the reported gel pH was 5.75.

G. In-vitro drug release and kinetic analysis

In-vitro release was performed using the bag diffusion method in phosphate buffer pH 7.4 at 37 ± 0.5 °C with continuous stirring. Samples were withdrawn at predetermined intervals and replaced with fresh medium to maintain sink conditions.[17,18] Release data were fitted to zero-order, first-order, Higuchi and Korsmeyer–Peppas models. The Korsmeyer–Peppas exponent (n) was used to interpret the release mechanism.

H. Stability study

The optimized mechanical-dispersion and thin-film-hydration formulations were stored for one month at 30 ± 2 °C/65 ± 5% RH. Changes in appearance, pH, viscosity, spreadability, particle size, PDI, zeta potential, drug content, entrapment efficiency and drug release were monitored.[19]

III. RESULTS

A. Drug identification and compatibility

The FTIR spectrum of fluconazole was consistent with the characteristic functional groups recorded in the study. The physical mixture with soya lecithin and ethanol retained the principal fluconazole bands, with no major changes indicating an overt chemical incompatibility under the tested conditions.

The analytical method showed linearity over 10–100 µg/mL at 210 nm, with $R^2 = 0.9958$. This supported the use of the calibration relationship for quantitative analysis in the formulation studies.

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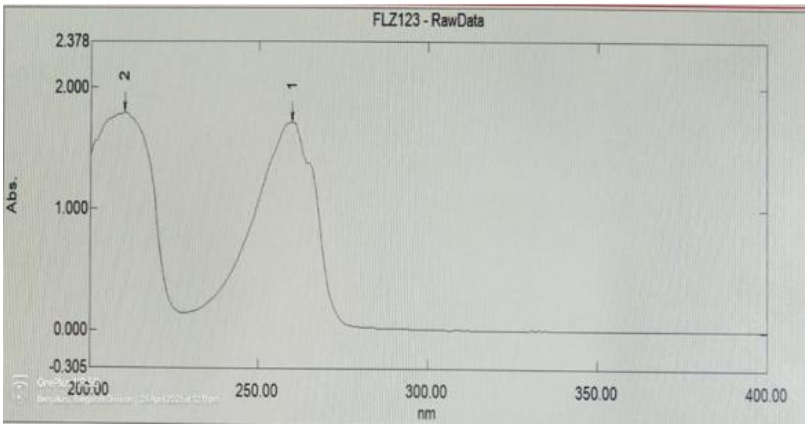

Figure 2: λmax of Fluconazole

Table 1: Concentration and Absorbance of Fluconazole in PBS pH 7.4 (210 nm)

Concentration (µg/ml)	Absorbance (Mean ± SD) (n=3)
10	0.171 ± 0.0025
20	0.336 ± 0.0030
30	0.431 ± 0.0030
40	0.548 ± 0.003
50	0.628 ± 0.0036
60	0.762 ± 0.0035
70	0.857 ± 0.0035
80	0.953 ± 0.0035
90	1.052 ± 0.0035

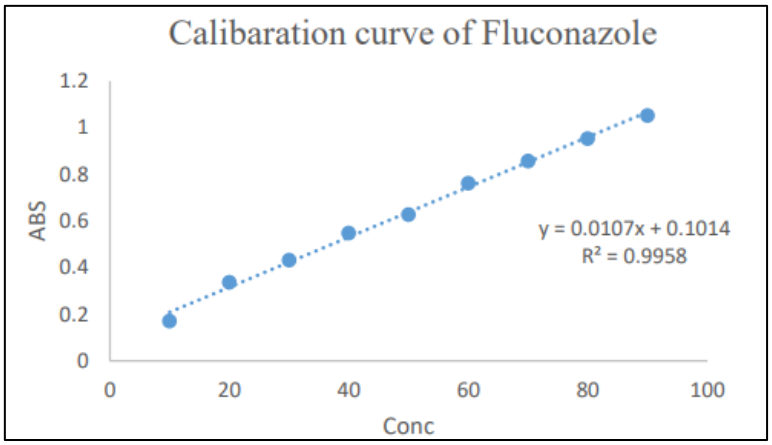

Figure 3: Calibration Curve of Fluconazole in PBS pH 7.4 (210 nm)

International Journal of Pharmaceutical research and Applications
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B. Optimization of mechanical-dispersion ethosomes

Table 2. Characterization of mechanical-dispersion ethosome formulations (F1–F13). EE, entrapment efficiency; PDI, polydispersity index

Formulation	Particle size (nm)	Zeta (mV)	PDI	Drug content (%)	EE (%)
F1	198.3	−33.0	0.116	56.0	70.0
F2	208.5	−35.0	0.015	79.0	83.0
F3	930.0	−39.0	0.213	71.0	78.0
F4	1283.4	−38.7	0.125	51.0	45.4
F5 (optimized)	179.6	−39.4	0.184	89.0	85.6
F6	2289.5	−39.8	0.217	70.8	72.6
F7	1292.0	−39.5	0.185	83.9	86.3
F8	352.6	−38.9	0.675	63.0	76.5
F9	166.6	−39.8	0.815	78.0	65.3
F10	1019.8	−38.5	0.985	47.0	80.1
F11	158.3	−39.6	0.167	84.0	79.8
F12	1008.0	−37.8	1.103	10.66	15.0
F13	1296.0	−38.5	1.245	81.0	88.0

The mechanical-dispersion optimization (Table 2) demonstrated marked sensitivity to formulation and process variables. F5, containing 1.5 g phospholipid and 20 mL ethanol, produced 179.6 nm vesicles with PDI 0.184, zeta potential −39.4 mV, 89.0% drug content and 85.6% entrapment efficiency. Several formulations (F3, F4, F6, F7, F10, F12 and F13) produced vesicles larger than 1000 nm, indicating that the influence of the process variables was formulation-specific rather than a simple monotonic effect.

C. Optimization of thin-film-hydration ethosomes

Table 3. Characterization of thin-film-hydration ethosomes formulations during optimization

Formulation	Particle size (nm)	Zeta (mV)	PDI	Drug content (%)	EE (%)
F1 – water	214.0	−39.0	0.563	98.3	92.5
F2 – PBS	426.0	−37.8	0.450	57.4	65.0
F3 – 30 °C	950.4	−38.2	0.709	80.1	73.0
F1 – 40 °C	214.0	−39.0	0.563	98.3	92.0
F4 – 45 °C	131.0	−40.0	0.361	92.0	92.1
F5 – 30 min	1277.3	−34.6	0.959	65.3	70.0
F4 – 45 min	131.0	−40.0	0.316	97.5	92.1
F6 – 60 min (optimized)	110.5	−41.7	0.429	99.5	93.0

The thin-film-hydration series (Table 3) showed a progressive improvement under the selected optimization sequence. Water-based hydration outperformed phosphate-buffer hydration in the recorded experiment, with F1 showing smaller size and higher drug content/entrapment than F2. Increasing hydration temperature to 45 °C and hydration time to 60 min further improved the recorded vesicle characteristics. F6 was selected as the optimized formulation, with 110.5 nm particle size, PDI 0.429, zeta potential −41.7 mV, drug content 99.5% and entrapment efficiency 93.0%.

International Journal of Pharmaceutical research and Applications
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D. Comparative evaluation of optimized formulations

Table 4. Comparison of the optimized mechanical-dispersion (F5) and thin-film-hydration (F6) formulations

Parameter	Mechanical dispersion (F5)	Thin-film hydration (F6)
Particle size (nm)	179.6	110.5
PDI	0.184	0.429
Zeta potential (mV)	−39.4	−41.7
Drug content (%)	89.0	99.5
Entrapment efficiency (%)	85.6	93.0

As shown in Table 4, under the conditions of this study, thin-film hydration produced a smaller mean particle size and higher drug content and entrapment efficiency than mechanical dispersion. The more negative zeta potential also indicated a strongly charged vesicle surface in the optimized thin-film-hydration formulation. The PDI of 0.429 was higher than that of F5 (0.184), so the comparison should not be described as uniformly superior across every measured parameter. Rather, the main advantages observed for F6 were particle size, drug content and entrapment efficiency. The main parameters are compared graphically in Fig. 2.

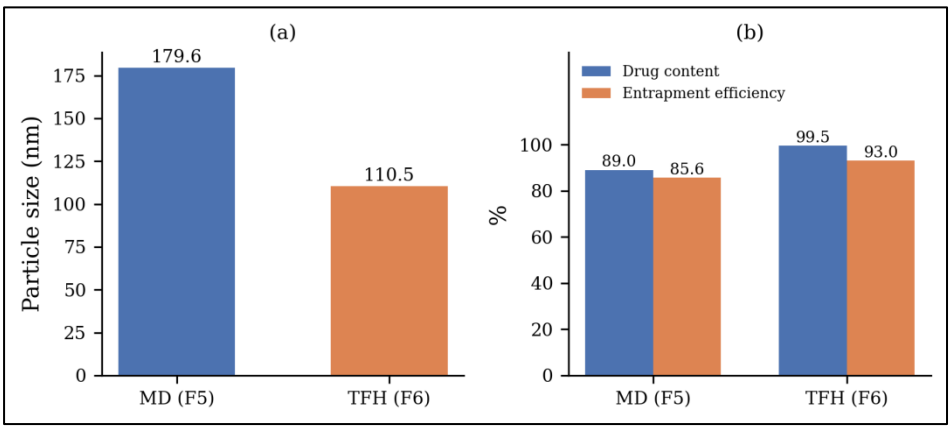

Fig. 4. Comparison of the optimized mechanical-dispersion (MD, F5) and thin-film-hydration (TFH, F6) formulations: (a) particle size; (b) drug content and entrapment efficiency.

E. In-vitro drug release

Table 5. Cumulative in-vitro drug release (%) over 12 h. MS, mechanical-dispersion suspension; TS, thin-film-hydration suspension; MG, mechanical-dispersion gel; TG, thin-film-hydration gel; MR, marketed gel

Time (h)	MS (%)	TS (%)	MG (%)	TG (%)	MR (%)
0	0.00	0.00	0.00	0.00	0.00
0.5	22.30	25.11	16.97	18.12	18.61
1	28.15	35.14	22.20	28.09	22.26
2	33.67	48.65	25.72	39.10	29.07
4	40.43	57.77	35.94	49.44	37.82
6	42.23	63.18	39.41	55.40	50.11
8	45.61	68.36	43.42	66.95	61.05
10	65.77	79.17	54.18	74.37	73.82
12	79.05	87.27	67.68	80.94	87.93

The release profiles of the mechanical-dispersion suspension (MS), thin-film-hydration suspension (TS), mechanical-dispersion gel (MG), thin-film-hydration gel (TG) and marketed gel (MR) showed progressive drug liberation over 12 h (Table 5, Fig. 3). The thin-film-hydration suspension released 87.27% at 12 h compared with 79.05% for the mechanical-dispersion suspension. For the gels, the thin-film-hydration gel released 80.94%, whereas the mechanical-dispersion gel released 67.68%. The marketed gel showed 87.93% release at 12 h.

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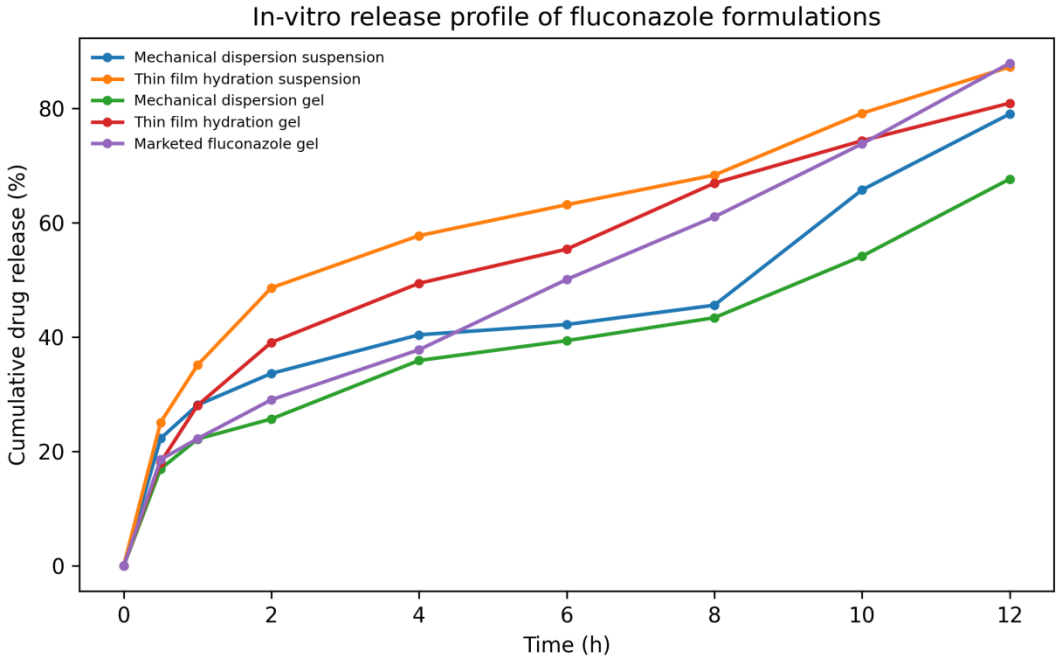

Fig. 5. In-vitro release profiles of fluconazole formulations (MS, TS, MG, TG and MR as defined in Table 5).

F. Release kinetics

Table 6. Release kinetic modelling of the fluconazole formulations

Formulation	Best-fit model	R^2	Korsmeyer–Peppas n
MS	Zero-order	0.9386	0.342
TS	Higuchi	0.9779	0.363
MG	Zero-order	0.9434	0.395
TG	Higuchi	0.9920	0.446
MR	Zero-order	0.9974	0.483

As shown in Table 6, the thin-film-hydration suspension showed the highest correlation with the Higuchi model (R^2 = 0.9779), while the thin-film-hydration gel showed a still stronger Higuchi fit (R^2 = 0.9920). The Korsmeyer–Peppas n values for MS, TS, MG and TG were 0.342, 0.363, 0.395 and 0.446, respectively, supporting predominantly Fickian diffusion within the interpretation framework used. The marketed gel showed zero-order best fit (R^2 = 0.9974) with n = 0.483.

G. Gel evaluation

Table 7 summarizes the physicochemical properties of the ethosomal gels.

Table 7. Evaluation of the ethosomal gels

Parameter	Mechanical-dispersion gel	Thin-film-hydration gel
pH	5.75*	5.79*
Viscosity (cP)	3144	3418
Spreadability (mm^2)	8.23	9.71

International Journal of Pharmaceutical research and Applications
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H. One-month stability

Table 8. One-month stability data at 30 ± 2 °C/65 ± 5% RH. TFH, thin-film hydration

Parameter	Mechanical initial	Mechanical 1 month	TFH initial	TFH 1 month
Particle size (nm)	179.6	183.2	110.5	114.3
Zeta potential (mV)	−39.4	−39.0	−41.7	−41.2
PDI	0.184	0.185	0.429	0.435
Entrapment efficiency (%)	85.6	84.80	93.0	92.40
Drug content (%)	89.0	87.05	99.55	99.10

Only minor changes were recorded after one month (Table 8). For mechanical dispersion, particle size increased from 179.6 to 183.2 nm and entrapment efficiency decreased from 85.6% to 84.80%. For thin-film hydration, particle size increased from 110.5 to 114.3 nm and entrapment efficiency decreased from 93.0% to 92.40%. PDI and zeta potential changed only slightly.

IV. DISCUSSION[19–23]

The central finding of this comparative formulation study is that preparation method materially affected the physicochemical performance of fluconazole-loaded ethosomes. Mechanical dispersion generated a reproducible nanosized vesicular system, but the optimized thin-film-hydration formulation achieved a smaller mean size and greater drug content and entrapment efficiency. This is consistent with the general principle that the sequence of lipid-film formation and controlled hydration can influence vesicle organization and drug distribution.

The mechanical-dispersion optimization illustrates the importance of balancing mechanical energy and formulation composition. In the study, F5 provided a combination of 179.6 nm size, PDI 0.184, −39.4 mV zeta potential, 89% drug content and 85.6% entrapment efficiency. Changes in particle size and entrapment are attributed to lipid concentration, ethanol concentration, stirring and sonication, with excessive mechanical stress or changes in vesicle structure potentially affecting drug retention.

Ethanol is a key component of ethosomal systems because it can increase lipid fluidity and alter the organization of the stratum corneum. Literature reviews describe the combined ethanol and vesicle effects as a major rationale for ethosomal skin delivery. The present formulation used ethanol both as a component of the vesicular system and, in the preparation design, as a co-solvent/permeation-enhancing component.

For thin-film hydration, F6 showed 110.5 nm size and 93% entrapment efficiency. The smaller size may increase the effective surface area available for drug release and may contribute to the greater release observed for TS compared with MS. The release results support this formulation-level association, although the current study did not directly measure skin deposition or permeation. Therefore, it would be inappropriate to conclude from the in-vitro release experiment alone that F6 necessarily provides superior in-vivo skin penetration.

The PDI comparison deserves careful interpretation. F5 had a lower PDI (0.184) than F6 (0.429), meaning that F5 showed the narrower size distribution among the two optimized formulations. Consequently, thin-film hydration cannot be described as superior in every vesicle-quality parameter: the evidence supports superiority in mean particle size, drug content, entrapment efficiency and in-vitro release, while mechanical dispersion showed the lower PDI.

The release study further differentiated the two approaches. TS reached 87.27% at 12 h, compared with 79.05% for MS. When incorporated into the gel, release decreased to 80.94% for TG and 67.68% for MG, consistent with the additional diffusional resistance introduced by the polymeric matrix. The marketed product released 87.93% at 12 h. These findings demonstrate that formulation architecture—not simply the identity of the active ingredient—substantially influences release behaviour.

The kinetic analysis indicates that the optimized thin-film-hydration gel was best described by the Higuchi model ($R^2 = 0.9920$), with a Korsmeyer–Peppas n value of 0.446. This supports a predominantly diffusion-associated release process under the experimental conditions. However, model fitting should be treated as descriptive rather than definitive evidence of mechanism, particularly when the release study is based on a single in-vitro system

International Journal of Pharmaceutical research and Applications
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and no independent diffusion coefficient or membrane-transport experiment was performed.

The gel characteristics were also suitable for continued formulation investigation. Viscosity values of 3144 and 3418 cP indicate semisolid systems capable of remaining at the application site while permitting spreadability. The thin-film-hydration gel showed greater spreadability in the present dataset. The pH value of 5.75 is within an acidic-to-near-neutral range commonly relevant to topical products, but tolerability should ultimately be established experimentally rather than inferred from pH alone.

The one-month stability data are encouraging but preliminary. Both optimized formulations exhibited only small changes in particle size, PDI, zeta potential, drug content and entrapment efficiency. The study nevertheless covered only one month and one storage condition. These findings therefore represent short-term stability evidence rather than definitive shelf-life evidence.

V. CONCLUSION

Fluconazole-loaded ethosomal suspensions were successfully prepared using mechanical dispersion and thin-film hydration, and optimized formulations from both approaches were incorporated into Carbopol 934 gels. Under the experimental conditions reported, thin-film hydration produced smaller vesicles (110.5 nm), higher drug content (99.5%) and higher entrapment efficiency (93.0%) than mechanical dispersion (179.6 nm, 89.0% and 85.6%, respectively), although the mechanical-dispersion formulation showed a lower PDI. The thin-film-hydration suspension and gel also exhibited greater cumulative drug release at 12 h. The optimized thin-film-hydration gel demonstrated 3418 cP viscosity, 9.71 mm^2 spreadability and Higuchi-dominant release behaviour with R^2 = 0.9920. One-month stability testing showed only minor changes. Overall, the findings support thin-film hydration as the more productive preparation approach within this experimental design, while additional permeation, microbiological, safety and longer-term stability studies are needed to establish the formulation's therapeutic and translational potential.

REFERENCE:

[1]. Touitou E, Dayan N, Bergelson L, Godin B, Eliaz M. Ethosomes — novel vesicular carriers for enhanced delivery: characterization and skin penetration properties. Journal of Controlled Release. 2000 Apr;65(3):403–18. doi:10.1016/S0168-3659(99)00222-9

[2]. Touitou E, Godin B, Weiss C. Enhanced delivery of drugs into and across the skin by ethosomal carriers. Drug Dev Res. 2000 Jul;50(3–4):406–15. doi:10.1002/1098-2299(200007/08)50:3/4<406::AID-DDR23>3.0.CO;2-M

[3]. Verma P, Pathak K. Therapeutic and cosmeceutical potential of ethosomes: An overview. J Adv Pharm Technol Res. 2010;1(3):274. doi:10.4103/0110-5558.72415

[4]. Pandey V, Golhani D, Shukla R. Ethosomes: versatile vesicular carriers for efficient transdermal delivery of therapeutic agents. Drug Delivery. 2015 Nov 17;22(8):988–1002. doi:10.3109/10717544.2014.889777

[5]. Das SK, Chakraborty S, Roy C, Rajabalaya R, Mohaimin AW, Khanam J, et al. Ethosomes as Novel Vesicular Carrier: An Overview of the Principle, Preparation and its Applications. CDD. 2018 Jun 27;15(6):795–817. doi:10.2174/1567201815666180116091604

[6]. Akhtar N, Varma A, Pathak K. Ethosomes as Vesicles for Effective Transdermal Delivery: From Bench to Clinical Implementation. CCP. 2016 Sep 20;11(3):168–90. doi:10.2174/1574884711666160813231352

[7]. Mbah CC, Builders PF, Attama AA. Nanovesicular carriers as alternative drug delivery systems: ethosomes in focus. Expert Opinion on Drug Delivery. 2014 Jan;11(1):45–59. doi:10.1517/17425247.2013.860130

[8]. Nainwal N, Jawla S, Singh R, Saharan VA. Transdermal applications of ethosomes – a detailed review. Journal of Liposome Research. 2019 Apr 3;29(2):103–13. doi:10.1080/08982104.2018.1517160

[9]. Godin B, Touitou E. Mechanism of bacitracin permeation enhancement through the skin and cellular membranes from an ethosomal carrier. Journal of Controlled Release. 2004 Feb;94(2–3):365–79. doi:10.1016/j.jconrel.2003.10.014

[10]. Touitou E, Godin B, Dayan N, Weiss C, Piliponsky A, Levi-Schaffer F. Intracellular delivery mediated by an ethosomal carrier. Biomaterials. 2001 Nov;22(22):3053–9. doi:10.1016/S0142-9612(01)00052-7

[11]. Dayan N, Touitou E. Carriers for skin delivery of trihexyphenidyl HCl: ethosomes

vs. liposomes. Biomaterials. 2000 Sep;21(18):1879–85. doi:10.1016/S0142-9612(00)00063-6

[12]. Elsayed MMA, Abdallah OY, Naggar VF, Khalafallah NM. Lipid vesicles for skin delivery of drugs: Reviewing three decades of research. International Journal of Pharmaceutics. 2007 Mar;332(1–2):1–16. doi:10.1016/j.ijpharm.2006.12.005

[13]. Bouwstra JA, Honeywell-Nguyen PL. Skin structure and mode of action of vesicles. Advanced Drug Delivery Reviews. 2002 Nov;54:S41–55. doi:10.1016/S0169-409X(02)00114-X

[14]. Dayan N, Touitou E. Carriers for skin delivery of trihexyphenidyl HCl: ethosomes vs. liposomes. Biomaterials. 2000 Sep;21(18):1879–85. doi:10.1016/S0142-9612(00)00063-6

[15]. Verma S, Utreja P. Transethosomes of Econazole Nitrate for Transdermal Delivery: Development, In-vitro Characterization, and Ex-vivo Assessment. PNT. 2018 Dec 18;6(3):171–9. doi:10.2174/2211738506666180813122102

[16]. Ayub AC, Gomes ADM, Lima MVC, Vianna-Soares CD, Ferreira LAM. Topical Delivery of Fluconazole: In Vitro Skin Penetration and Permeation Using Emulsions as Dosage Forms. Drug Development and Industrial Pharmacy. 2007 Jan;33(3):273–80. doi:10.1080/03639040600829989

[17]. Verma P, Pathak K. Nanosized ethanolic vesicles loaded with econazole nitrate for the treatment of deep fungal infections through topical gel formulation. Nanomedicine: Nanotechnology, Biology and Medicine. 2012 May;8(4):489–96. doi:10.1016/j.nano.2011.07.004

[18]. Maheshwari RGS, Tekade RK, Sharma PA, Darwhekar G, Tyagi A, Patel RP, et al. Ethosomes and ultradeformable liposomes for transdermal delivery of clotrimazole: A comparative assessment. Saudi Pharmaceutical Journal. 2012 Apr;20(2):161–70. doi:10.1016/j.jsps.2011.10.001

[19]. Abdel-Rahman S, Newland. Update on terbinafine with a focus on dermatophytoses. CCID. 2009 Apr;49. doi:10.2147/CCID.S3690

[20]. Song CK, Balakrishnan P, Shim CK, Chung SJ, Chong S, Kim DD. A novel vesicular carrier, transethosome, for enhanced skin delivery of voriconazole: Characterization and in vitro/in vivo evaluation. Colloids and Surfaces B: Biointerfaces. 2012 Apr;92:299–304. doi:10.1016/j.colsurfb.2011.12.004

[21]. Verma S, Utreja P. Vesicular nanocarrier based treatment of skin fungal infections: Potential and emerging trends in nanoscale pharmacotherapy. Asian Journal of Pharmaceutical Sciences. 2019 Mar;14(2):117–29. doi:10.1016/j.ajps.2018.05.007

[22]. Tanrıverdi ST, Özer Ö. Novel topical formulations of Terbinafine-HCl for treatment of onychomycosis. European Journal of Pharmaceutical Sciences. 2013 Mar;48(4–5):628–36. doi:10.1016/j.ejps.2012.12.014

[23]. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. International Journal of Pharmaceutics. 1983 May;15(1):25–35. doi:10.1016/0378-5173(83)90064-9