

FORMULATION AND EVALUATION OF POLYHERBAL NANOSPONGES LOADED NANOEMULGEL FOR TRANSUNGUAL DRUG DELIVERY

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ABSTRACT

The present study aimed to formulate and evaluate a polyherbal Nanosponge-loaded Nanoemulgel for transungual drug delivery. Neem extract and turmeric extract were incorporated into ethyl cellulose Nanosponges and subsequently integrated with a nanoemulsion and Carbopol/HPMC K4M gel system. Three formulations (F1–F3) were prepared by varying the herbal extract-to-polymer ratio. Nanosponges were evaluated for particle size, polydispersity index (PDI), zeta potential, entrapment efficiency and morphology, while the nanoemulsion and final Nanoemulgel were evaluated for nanoscale characteristics, physical properties, drug content, in-vitro release and stability. F2 showed the smallest Nanosponge particle size (312 ± 0.15 nm), PDI of 0.332 ± 0.07 , zeta potential of -33.6 ± 0.89 mV and highest entrapment efficiency ($78.4 \pm 0.84\%$). The optimized F2 nanoemulsion showed a droplet size of 146.8 ± 1.76 nm and PDI of 0.218 ± 0.009 . The F2 Nanosponge-loaded Nanoemulgel showed a globule size of 144.6 ± 3.8 nm, PDI 0.214 ± 0.012 , zeta potential -29.4 ± 1.0 mV, drug content $98.16 \pm 0.72\%$, pH 5.72 ± 0.02 , spreadability 6.65 ± 0.13 g·cm/sec and extrudability 0.94 ± 0.03 . The optimized formulation exhibited 99.6% cumulative release at 20 h and the Korsmeyer–Peppas model gave the highest correlation ($R^2 = 0.995$). The formulation remained smooth and homogeneous during the reported 30-day stability study. These findings indicate that the developed polyherbal Nanosponge-loaded Nanoemulgel is a promising formulation platform for further investigation as a transungual delivery system.

Keywords: Polyherbal; Nanosponges; Nanoemulgel; Transungual drug delivery; Neem; Turmeric; Nanoemulsion; Controlled release.

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1. INTRODUCTION

The nail plate is a dense, highly keratinized structure that can restrict the penetration of active pharmaceutical ingredients applied topically. Conventional topical formulations may have limited residence time and penetration across the nail barrier, creating a need for formulation strategies that improve contact, dispersion and controlled delivery at the nail site.

Nanosponges are porous nanocarriers capable of incorporating active substances and modifying their release. Nanoemulsion provide nanosized droplets and a large interfacial area, while Nanoemulgel combine nanoemulsion characteristics with the convenient application and residence properties of a semisolid gel. A Nanosponge-loaded Nanoemulgel can therefore integrate several delivery advantages within one formulation. Neem (*Azadirachta indica*) and turmeric (*Curcuma longa*) are plant-derived materials with reported pharmacological and antimicrobial relevance. Clove oil, rich in eugenol, was incorporated as the oilphase and penetration-enhancing component. The present work combined these polyherbal constituents with an ethyl

cellulose Nanosponge, nanoemulsion and Carbopol/HPMC K4M gel matrix to develop a transungual delivery system.



Figure 1: curcumin



Figure 2: Neem Extract



Figure 3: Clove Oil

2. AIM AND OBJECTIVES

To formulate and evaluate a polyherbal Nanosponge-loaded Nanoemulgel for transungual drug delivery.

The objectives were to prepare neem and turmeric extracts; perform phytochemical and Preformulation studies; prepare and optimize polyherbal Nanosponges; characterize the Nanosponges for particle size, PDI, zeta potential, entrapment efficiency and morphology; prepare Nanoemulsion; incorporate the optimized Nanosponge into a Nanoemulgel; evaluate physical properties, drug content and in-vitro release; analyse release kinetics; and assess short-term stability.

3. MATERIALS AND METHODS

Neem extract, turmeric extract, ethyl cellulose, clove oil, Tween 80, PEG 400, Carbopol, HPMC K4M, ethanol and purified water were used. F1–F3 were prepared by varying the formulation composition while maintaining 1 g each of neem and turmeric extracts.

Preformulation included curcumin estimation by UV-visible spectroscopy at the selected wavelength of 418 nm, FTIR compatibility assessment and saturation-solubility testing. The reported saturation solubility values were 18.42 mg/mL in clove oil, 25.36 mg/mL in surfactant 1 and 28.6446 mg/mL in cosurfactant 1. The co-surfactant vehicle showed the highest reported solubility and was therefore selected for formulation development.

Nanosponges were prepared using an emulsion solvent-diffusion process followed by centrifugation and drying. The optimized Nanosponge was used in the nanoemulsion and then incorporated into a Carbopol/HPMC K4M gel base to obtain the Nanosponge-loaded Nanoemulgel. The prepared formulations were characterized by standard pharmaceutical evaluation procedures reported in the project.

4. FORMULATION DESIGN

Table 1: Composition of polyherbal Nanosponge-loaded Nanoemulgel formulations

Ingredient	F1	F2	F3
Neem extract	1 g	1 g	1 g
Turmeric extract	1 g	1 g	1 g
Ethyl cellulose	4 g	2 g	1 g
Clove oil	4 g	2 g	1 g
Tween 80	4 g	2 g	1 g
PEG 400	2 g	1 g	1.5 g
Carbopol	1 g	0.5 g	0.75 g
HPMC K4M	1 g	0.5 g	0.75 g
Ethanol	5 mL	5 mL	5 mL
Purified water	q.s. to 100 g	q.s. to 100 g	q.s. to 100 g

5. RESULTS AND DISCUSSION

The three formulations showed clear differences in Nanosponge characteristics. F2 had the smallest particle size, relatively lower PDI and the highest entrapment efficiency. Its zeta potential was -33.6 ± 0.89 mV. These findings supported selection of F2 for further development.

FTIR comparison retained characteristic spectral regions of ethyl cellulose and the herbal/excipient combinations, supporting compatibility of the selected formulation components. SEM examination of F2 showed spherical to near-spherical particles with a rough and porous morphology, consistent with formation of a porous Nanosponge structure.

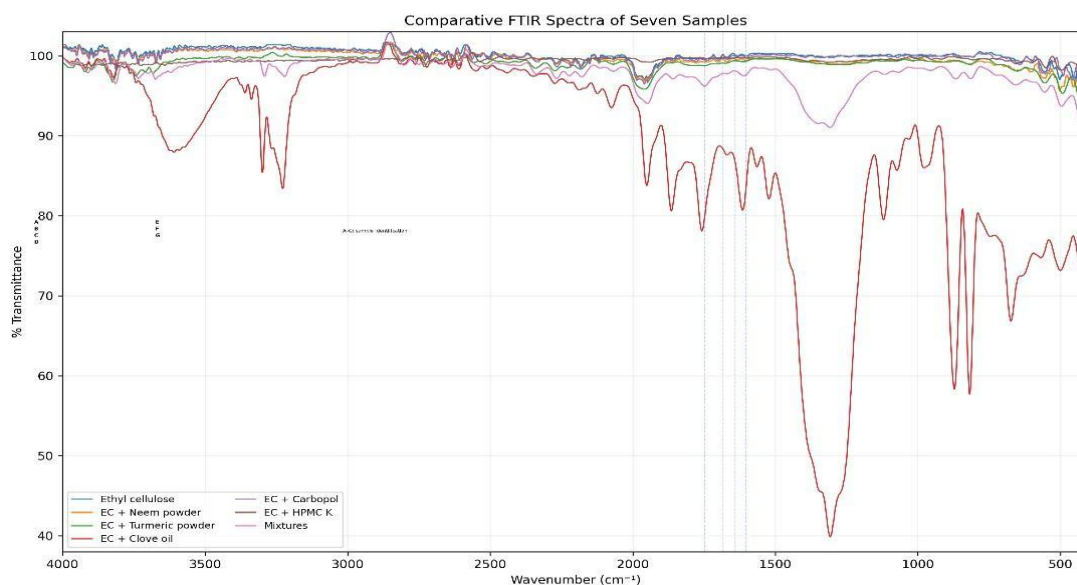


Figure 4: Comparative FTIR Spectra of Seven Samples

F2 also showed the most favourable nanoemulsion characteristics, with a droplet size of 146.8 ± 1.76 nm and PDI of 0.218 ± 0.009 . The final F2 Nanosponge-loaded Nanoemulgel was smooth and homogeneous, pale yellowish green, had a characteristic herbal odour, and showed no visible phase separation or grittiness.

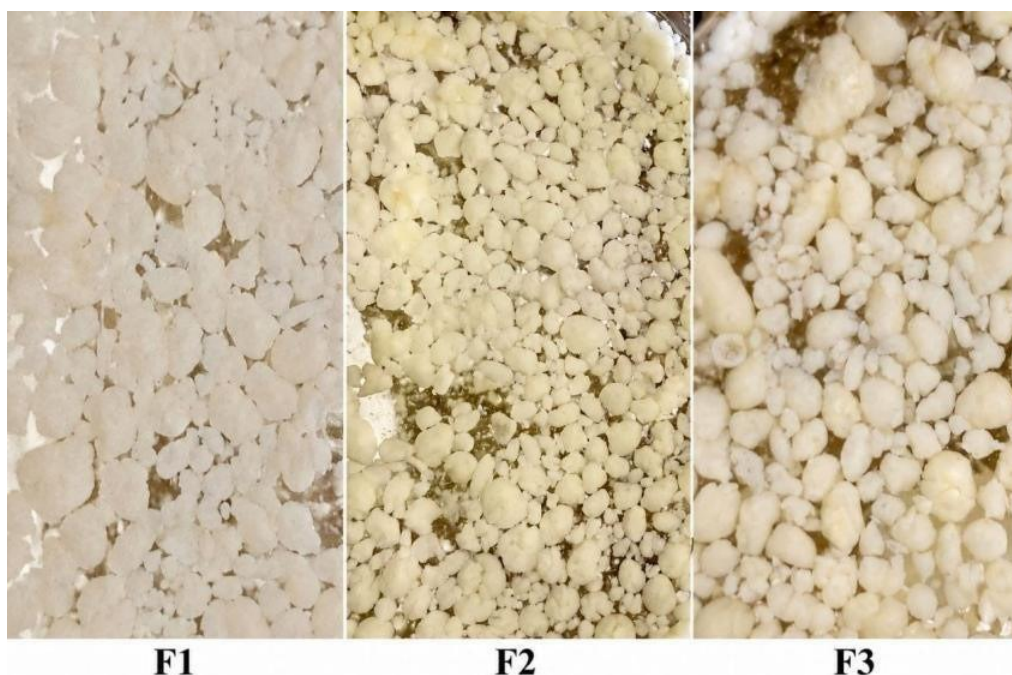


Figure 5: Image of Nanosponges (F1-F3)

SEM examination of F2 showed spherical to near-spherical particles with a rough and porous morphology, consistent with formation of a porous Nanosponge structure.

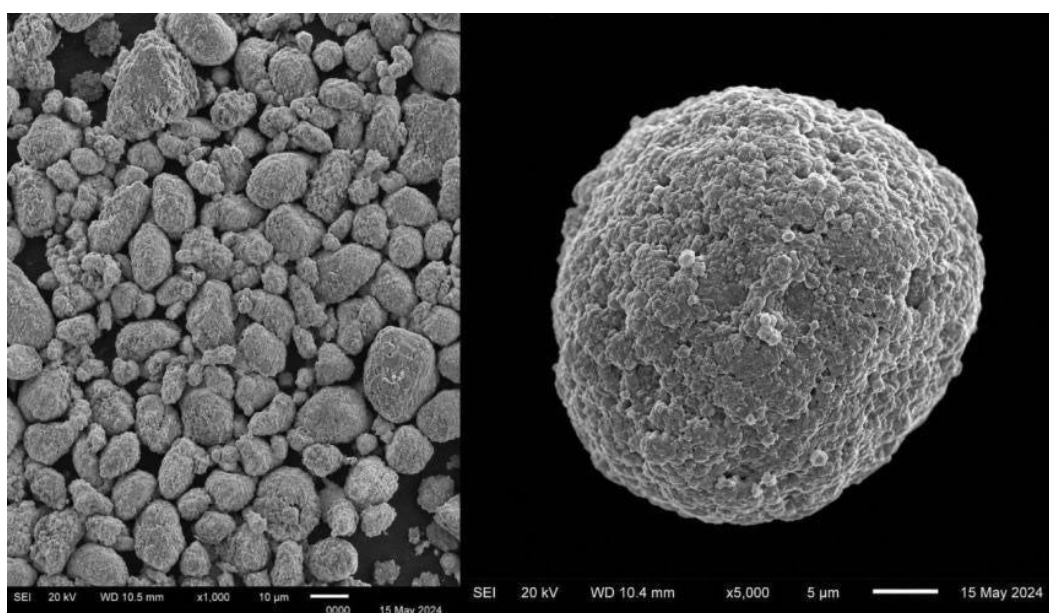


Figure 6: SEM Morphological Analysis of Formulated Nanosponges

The final formulation showed 99.6% cumulative release at 20 h. The release profile was slower and more prolonged than the initial release of F3 and was selected as optimal within the study. The highest kinetic correlation was obtained with the Korsmeyer–Peppas model ($R^2 = 0.995$), followed by Higuchi ($R^2 = 0.988$), first-order ($R^2 = 0.973$) and zero-order ($R^2 = 0.946$).

The optimized formulation remained smooth and homogeneous during the reported 30-day stability study. The pH changed from 6.2 to 6.1, viscosity from 8764 to 8420 cP, spreadability from 6.6 to 6.5 and reported drug release from 99.7% to 96.5%. These changes were comparatively small within the reported study conditions.

Table 2: Evaluation of prepared Nanosponges

Parameter	F1	F2	F3
Particle size (nm)	540 ± 0.67	312 ± 0.15	450 ± 0.26
PDI	0.543 ± 0.16	0.332 ± 0.07	0.424 ± 0.04
Zeta potential (mV)	-17.6 ± 0.34	-33.6 ± 0.89	-37.4 ± 0.86
Entrapment efficiency (%)	64.7 ± 0.72	78.4 ± 0.84	56.2 ± 0.35

Table 3: Evaluation of Nanoemulsion formulations

Parameter	F1	F2	F3
Droplet size (nm)	182.6 ± 2.14	146.8 ± 1.76	195.4 ± 2.63
PDI	0.342 ± 0.012	0.218 ± 0.009	0.376 ± 0.015

Table 4: Evaluation of Nanosponge-loaded Nanoemulgel

Parameter	F1	F2	F3
Globule size (nm)	168.4 ± 4.8	144.6 ± 3.8	157.8 ± 4.3
Viscosity (cP)	8420 ± 125	8764 ± 115	9180 ± 135
pH	5.62 ± 0.05	5.72 ± 0.02	5.68 ± 0.06
Spreadability (g·cm/sec)	6.42 ± 0.18	6.65 ± 0.13	6.51 ± 0.17
Drug content (%)	96.24 ± 0.84	98.16 ± 0.72	97.31 ± 0.65
Extrudability	0.82 ± 0.04	0.94 ± 0.03	0.87 ± 0.05
PDI	0.286 ± 0.018	0.214 ± 0.012	0.251 ± 0.016
Zeta potential (mV)	-24.6 ± 1.2	-29.4 ± 1.0	-26.8 ± 1.1
Centrifugation stability	No phase separation	No phase separation	No phase separation

Table 5: In-vitro drug release of Nanosponge-loaded Nanoemulgel

Time (h)	F1 (%)	F2 (%)	F3 (%)
0.5	12.8	10.2	13.4
1	21.4	19.8	22.7
2	34.6	32.1	36.8
4	52.8	49.7	55.4
6	67.2	54.8	69.5
8	78.4	66.9	80.1
12	—	81.9	—
18	—	91.8	—
20	—	99.6	—

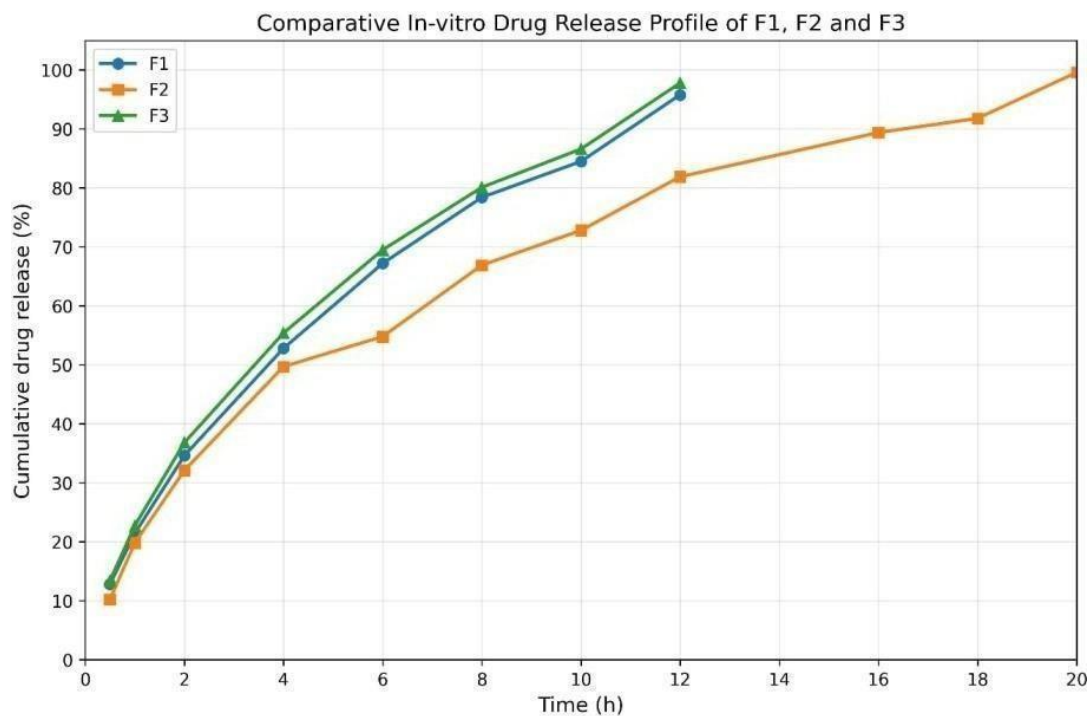


Figure 7: In-vitro Drug release of Nanosponges-loaded Nanoemulgel

Table 6: Release kinetic analysis of optimized F2

Model	R ²
Zero-order	0.946
First-order	0.973
Higuchi	0.988
Korsmeyer–Peppas	0.995

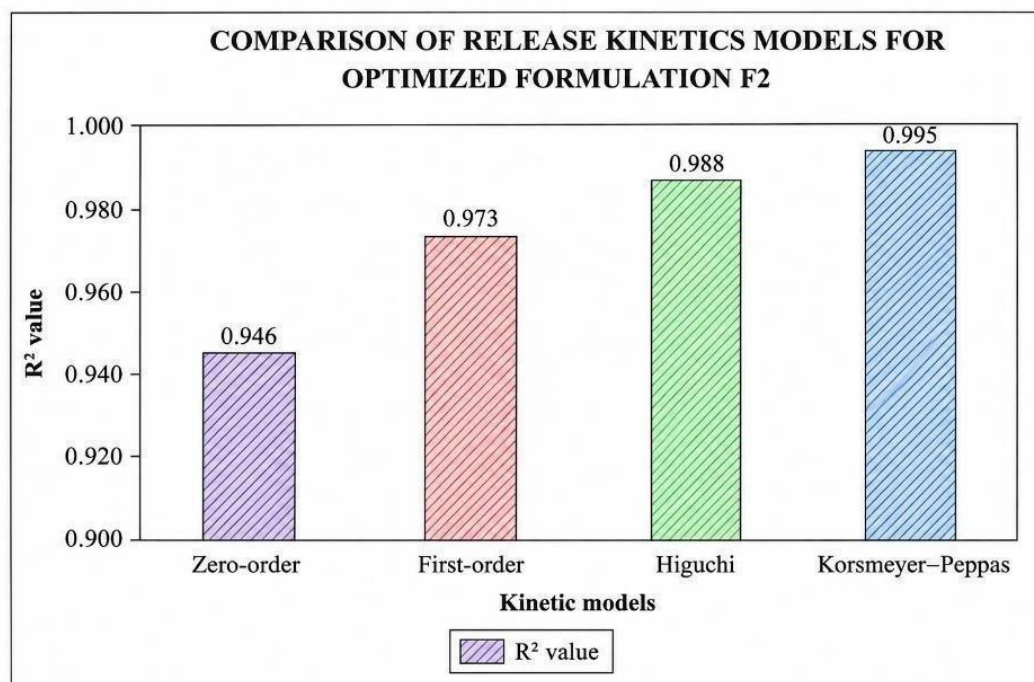


Figure 8: Release kinetics model for F2 formulation

Table 7: Stability testing of optimized F2

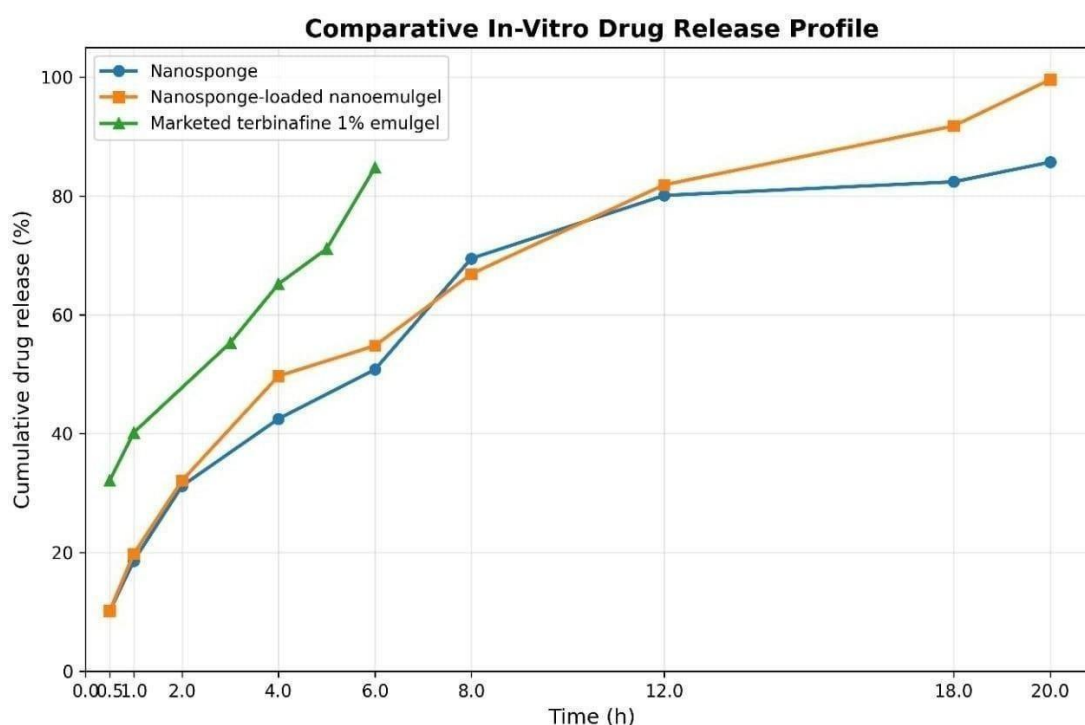
Parameter	Initial	After stability
Appearance	Smooth, homogeneous	Smooth, homogeneous
pH	6.2	6.1
Viscosity (cP)	8764	8420
Spreadability	6.6	6.5
Drug release (%)	99.7	96.5

6. COMPARATIVE RELEASE STUDY

The project compared the release profiles of Nanosponges, Nanosponge-loaded Nanoemulgel and marketed terbinafine 1% emulgel. The marketed product showed release data up to 8 h, whereas the Nanosponge and Nanosponge-loaded Nanoemulgel profiles were reported up to 20 h. Therefore, the later time values should not be interpreted as a direct 20-h comparison with the marketed product because corresponding marketed-product observations beyond 8 h were not reported.

Table 8: Comparative in-vitro drug release profile

Time (h)	Marketed terbinafine 1% (%)	Nanosponges (%)	Nanosponge-loaded Nanoemulgel (%)
0.5	32.1	10.1	10.2
1	40.2	18.6	19.8
2	55.3	31.2	32.1
4	65.2	42.5	49.7
6	71.1	50.8	54.8
8	84.8	62.5	66.9
12	—	80.1	81.9
18	—	82.4	91.8
20	—	85.7	99.6


Figure 9: Comparative In-vitro Drug Release Profile

7. CONCLUSION

A polyherbal Nanosponge-loaded Nanoemulgel was successfully developed as a candidate Transungual delivery system using neem and turmeric extracts with clove oil, ethyl cellulose and a Carbopol/HPMC K4M gel matrix. F2 was selected as the optimized formulation based on Nanosponge characteristics, entrapment efficiency, nanoemulsion properties, physicochemical evaluation and prolonged in-vitro release. The optimized formulation showed nanoscale globule size, high reported drug content, controlled release and satisfactory short-term stability. Further studies involving validated nail permeation, antifungal efficacy, skin/nail compatibility and extended stability are required before therapeutic conclusions can be made.

8. LIMITATIONS AND FUTURE SCOPE

The present work is a formulation-development and in-vitro evaluation study. Transungual permeation through human or animal nail tissue, microbiological efficacy, irritation/compatibility studies and long term stability were not established by the reported project data. Future research should therefore evaluate nail penetration and retention using validated models, confirm antifungal activity against relevant organisms, establish the relationship between formulation properties and biological performance, and perform longer-term stability studies.

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