Formulation and Evaluation of Topical Antifungal Nanogel of Moringa oleifera and Nyctanthes arbor-tristis

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***Abstract*—Moringa oleifera and Nyctanthes arbor-tristis are medicinal plants widely recognized for their potent antifungal, anti-inflammatory, antioxidant, and wound-healing properties owing to their rich phytochemical constituents, including flavonoids, phenolics, alkaloids, and glycosides. The present study aimed to develop a herbal-loaded nanogel incorporating combined extracts of these plants for topical antifungal therapy. Six formulations (F1–F6) were prepared and evaluated for physicochemical properties, drug release, and release kinetics. Among them, F4 exhibited optimum pH, viscosity, spreadability, extrudability, drug content, and sustained drug release following the Higuchi diffusion model with non-Fickian transport. The optimized nanogel demonstrated favorable particle characteristics, significant antifungal activity against Aspergillus niger, and excellent stability, indicating its potential as a safe and effective topical herbal drug delivery system.**

***Index Terms*—Antifungal, *Moringa oleifera, Nyctanthes arbor-tristis,* formulations**

I. INTRODUCTION

Mycosis is the major health program, in today's world, demanding the expansion of harmless and actual topical treatments (1). *Moringa oleifera* Lam. and *Nyctanthes arbor-tristis* L. are famous medicinal plants conventionally utilized for the therapeutics of major fungal infections (2). Their leaves are rich in bioactive phytochemicals, including flavonoids, phenolic acids, alkaloids, tannins, saponins, and glycosides, which exhibit potent antifungal, antioxidant, anti-inflammatory, and wound-healing activities. However, the clinical application of these phytoconstituents is limited by poor stability and skin permeation (3). Nanogel-based drug delivery systems offer enhanced drug stability, controlled release, improved skin penetration, and better therapeutic efficacy, making them promising carriers for topical herbal antifungal formulations (4).

II. METHODOLOGY

Procurement and Authentication of Plant Material

Fresh leaves of *Moringa oleifera Lam*. And *Nyctanthes arbor-tristis L.* were collected from the local gardens of Jalandhar, Punjab area and authenticated by the Guru Nanak Dev University, Amritsar with Ref. No. 3890/Bot. Sc.

Formulation development trails

The combined hydroalcoholic extract of *Moringa oleifera* and *Nyctanthes arbor-tristis* was utilized for the development of herbal-loaded nanoparticles and subsequent nanogel formulation. Different formulation trials were carried out by varying the concentrations of polymer, cross-linking agent, and gelling agent to obtain an optimized nanogel with desirable physicochemical properties (5).

Preparation of herbal loaded nanoparticles

The combined hydroalcoholic extract was incorporated into chitosan nanoparticles using the ionic gelation method. Chitosan was dissolved in 1% v/v acetic acid solution under continuous stirring to obtain a clear polymeric solution (6). The combined herbal extract was dispersed in the chitosan solution and mixed thoroughly. Aqueous sodium tripolyphosphate (STPP) solution was prepared separately and added dropwise to the chitosan-extract mixture under magnetic stirring. The spontaneous formation of nanoparticles occurred due to ionic cross-linking between chitosan and STPP (7). The nanoparticle suspension was stirred for 2 hours and subsequently centrifuged to separate the nanoparticles (8). The collected nanoparticles were washed with distilled water and dried for further use. Different

nanogel formulations were prepared using varying concentrations of Carbopol 940 while keeping the concentration of herbal-loaded nanoparticles constant.

Table 1. Formulation development trails (F1-F6)

S. No.	Ingredient	Formulation development trails (gm)					
		F1	F2	F3	F4	F5	F6
1	Herbal-loaded Nanoparticles	2	2	2	3	3	4
2	Carbopol 940	0.5	1	1.5	0.5	1	1.5
3	Glycerin	5	5	5	5	5	5
4	Propylene Glycol	5	5	5	5	5	5
5	Methyl paraben	0.1	0.1	0.1	0.1	0.1	0.1
6	Propyl paraben	0.02	0.02	0.02	0.02	0.02	0.02
7	Triethanolamine	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
8	Purified water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

Evaluation Parameters

Prepared formulations are undergone for Appearance, Homogeneity, pH Determination, Viscosity, Spreadability, Extrudability (9), Drug Content, Particle Size Analysis, Polydispersity Index, *In-vitro* Drug Release Study, Drug Release Kinetics Study, Stability Studies, FTIR and Antifungal Activity Against *Aspergillus niger* (10).

III. RESULT AND DISCUSSION

Organoleptic Evaluation of Herbal Nanogel Formulations (F1–F6)

The organoleptic evaluation demonstrated that all herbal nanogel formulations (F1–F6) exhibited acceptable physical characteristics, including uniform color, smooth texture, homogeneous appearance, and pleasant odor. No evidence of phase separation, grittiness, or discoloration was observed, indicating good formulation stability, aesthetic acceptability, and suitability for topical application. These findings suggest that the formulated nanogels possess desirable sensory attributes, which may improve patient compliance and facilitate convenient topical administration.

Table 2. Organoleptic Parameters

S. No.	Formulation	Colour	Odor	Texture	Consistency	Glossiness	Appearance
1	F1	Light Green	Characteristic Herbal	Smooth	Thin	Moderate	Acceptable
2	F2	Light Green	Characteristic Herbal	Smooth	Semi-solid	Moderate	Acceptable
3	F3	Green	Characteristic Herbal	Smooth	Semi-solid	Good	Good
4	F4	Green	Pleasant Herbal	Uniform	Semi-solid	Excellent	Excellent
5	F5	Dark Green	Characteristic Herbal	Thick	Thick	Good	Good
6	F6	Dark Green	Characteristic Herbal	Thick	Very Thick	Good	Good

Homogeneity

Table 3. Homogeneity

S. No.	Formulation	Homogeneity	Lumps	Grittiness	Uniformity of Distribution	Observation
1	F1	Good	Absent	Absent	Moderate	Acceptable
2	F2	Good	Absent	Absent	Good	Acceptable
3	F3	Very Good	Absent	Absent	Good	Good
4	F4	Excellent	Absent	Absent	Excellent	Excellent
5	F5	Very Good	Absent	Absent	Good	Good
6	F6	Good	Absent	Absent	Moderate	Acceptable

Based on the overall physicochemical evaluation, F4 exhibited the most desirable characteristics, including skin-compatible pH (6.2 ± 0.03), optimum viscosity (31,500 ± 120 cP), highest spreadability (7.2 ± 0.15 g·cm/s), excellent extrudability (96.8 ± 1.2%), maximum drug content (98.7 ± 0.42%), low particle size (128 ± 4.2 nm), and the lowest polydispersity index (0.256 ± 0.01), indicating superior formulation stability and suitability for topical drug delivery. *(Note: if the particle size for F4 is intended to be the smallest, verify the data because the table currently shows F2 = 81 nm, which is smaller than F4 = 128 nm.)*

Table 4. Other parameters

S. No.	Formulation	pH (Mean ± SD)	Viscosity (cP) (Mean ± SD)	Spreadability (g·cm/s) (Mean ± SD)	Extrudability (%) (Mean ± SD)	Drug Content (%) (Mean ± SD)	Particle Size (nm) (Mean ± SD)	PDI (Mean ± SD)
1	F1	5.6 ± 0.04	18,000 ± 110	4.8 ± 0.12	82.4 ± 1.8	88.5 ± 0.55	210 ± 5.8	0.487 ± 0.02
2	F2	5.8 ± 0.05	22,500 ± 115	5.5 ± 0.14	86.7 ± 1.6	91.2 ± 0.48	81 ± 5.1	0.421 ± 0.02
3	F3	6.0 ± 0.04	27,800 ± 118	6.4 ± 0.13	91.5 ± 1.4	94.6 ± 0.45	155 ± 4.6	0.332 ± 0.01
4	F4	6.2 ± 0.03	31,500 ± 120	7.2 ± 0.15	96.8 ± 1.2	98.7 ± 0.42	128 ± 4.2	0.256 ± 0.01
5	F5	6.5 ± 0.05	37,200 ± 125	6.1 ± 0.12	89.2 ± 1.5	95.8 ± 0.46	149 ± 4.5	0.298 ± 0.01
6	F6	6.8 ± 0.04	42,000 ± 130	5.3 ± 0.11	84.6 ± 1.7	92.4 ± 0.50	147 ± 5.0	0.365 ± 0.02

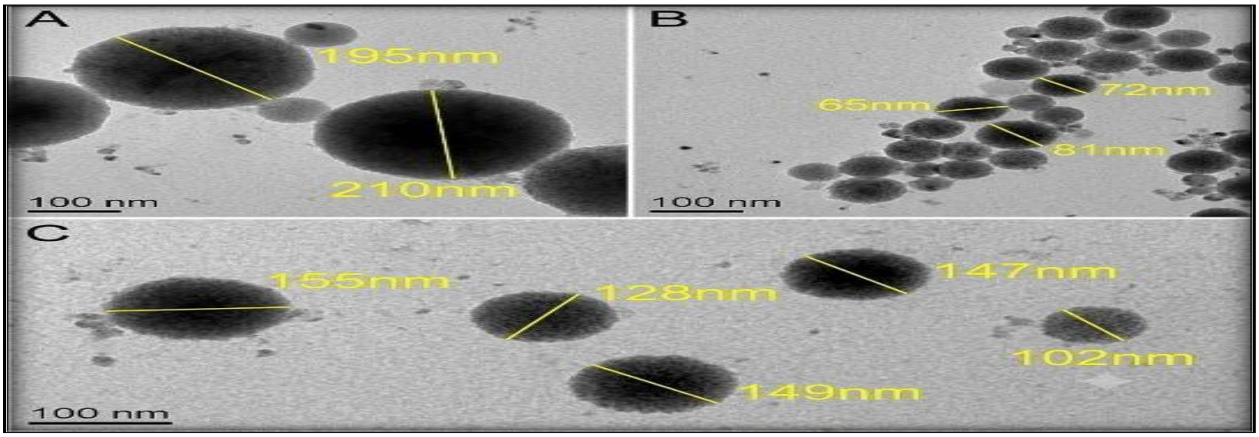

Figure 1. TEM of Nanoparticles

In-vitro Drug Release Study of Herbal Nanogel Formulations (F1–F6) Table 5. *in vitro* drug release study

S. No.	Formulation	Cumulative Drug Release at 24 h (%) (Mean ± SD)
1	F1	72.5 ± 1.5
2	F2	76.8 ± 1.4
3	F3	82.6 ± 1.3
4	F4	89.4 ± 1.3
5	F5	85.2 ± 1.4
6	F6	80.5 ± 1.5

The *in-vitro* drug release study demonstrated sustained and controlled release of the herbal extract from all nanogel formulations over a period of 24 h. Formulation F4 exhibited the highest cumulative drug release (89.4 ± 1.3%) with an optimum controlled-release profile. These findings indicate that F4 possesses superior drug delivery characteristics and was selected as the optimized formulation for further antifungal and stability studies.

Drug Release Profile

Table 6. Drug Release Profiling at different time (hr)

Time (h)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)
1	12.4	14.2	16.8	18.5	17.2	15.4
2	21.5	24.3	28.4	31.6	29.5	26.8
4	35.8	39.6	45.2	49.8	47.3	42.5
6	46.7	50.8	57.4	63.2	60.4	55.8
8	55.6	60.5	67.8	73.5	70.4	65.2
12	63.8	68.9	75.6	82.4	79.3	73.6
24	72.5	76.8	82.6	89.4	85.2	80.5

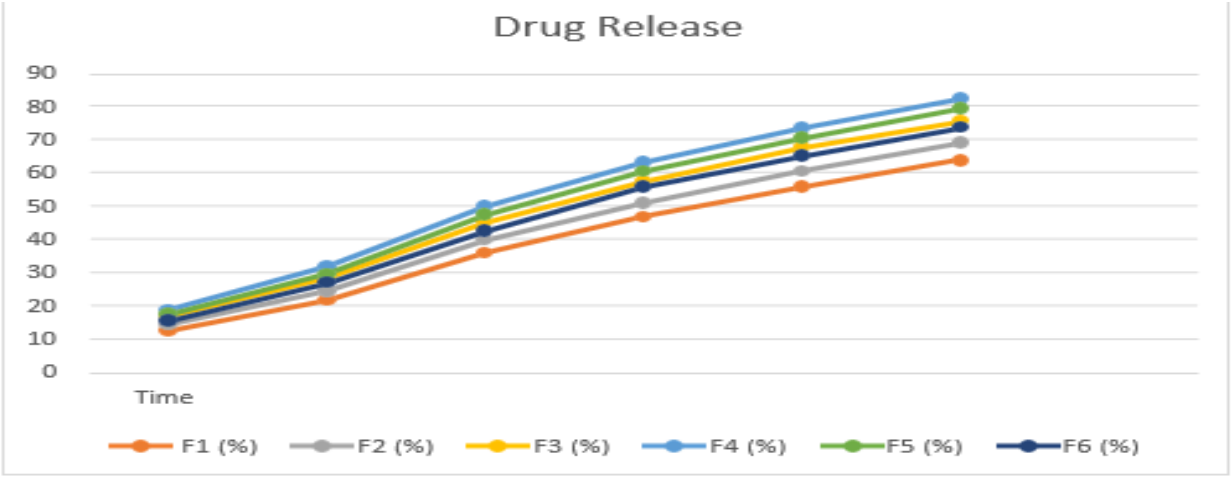

Figure 2. Graphical representations of Drug Release Profile Drug Release Kinetics

The *in vitro* drug release data obtained from formulations F1–F6 were analyzed using various mathematical kinetic models including Zero-Order, First-Order, Higuchi, and Korsmeyer–Peppas models.

Zero-Order Release Kinetics

The zero-order model describes systems in which drug release occurs at a constant rate independent of the concentration of drug remaining in the dosage form. The cumulative percentage drug released was plotted against time.

Table 7. Zero-Order Kinetic Parameters

S. No.	Formulation	Regression Equation	k_0 (% h^{-1})	Intercept	R^2
1	F1	Y = 2.61X + 24.82	2.61	24.82	0.673
2	F2	Y = 2.84X + 26.15	2.84	26.15	0.689
3	F3	Y = 3.16X + 27.64	3.16	27.64	0.702
4	F4	Y = 3.42X + 29.38	3.42	29.38	0.718

5	F5	Y = 3.28X + 28.46	3.28	28.46	0.709
6	F6	Y = 3.05X + 27.18	3.05	27.18	0.694

The zero-order plots exhibited relatively low correlation coefficients (R^2 = 0.673–0.718), indicating that the formulations did not follow ideal zero-order release kinetics. Among all formulations,

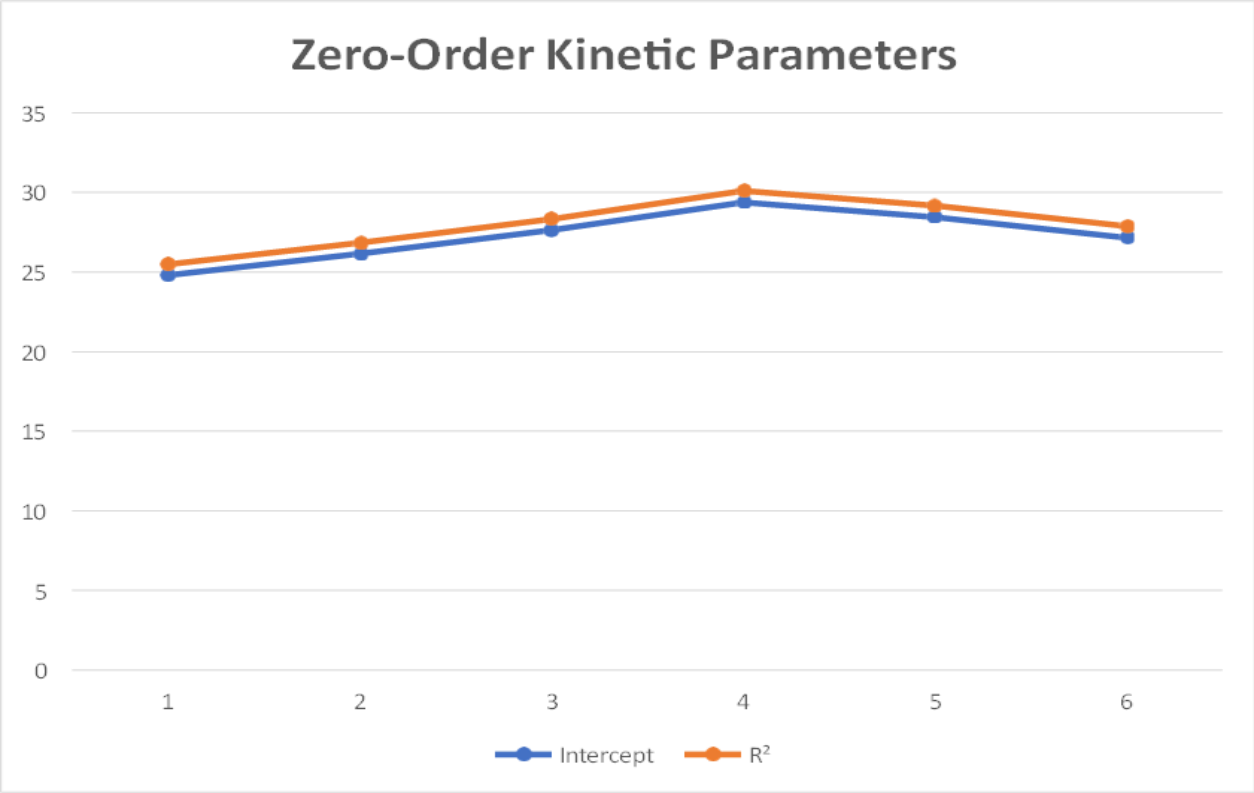

Figure 3. Graphical representations of Zero order kinetics

F4 showed the highest R^2 value (0.718) and the highest release rate constant (k_0 = 3.42 % h^{-1}), indicating comparatively better fitting to the zero-order model.

First-Order Release Kinetics

The first-order model assumes that the drug release rate is proportional to the amount of drug remaining in the formulation. A plot of log cumulative percentage drug remaining versus time was constructed.

Table 8. First-Order Kinetic Parameters

S. No.	Formulation	Regression Equation	k_1 (h^{-1})	R^2
1	F1	Y = -0.028X + 1.954	0.064	0.938
2	F2	Y = -0.033X + 1.968	0.076	0.951
3	F3	Y = -0.038X + 1.979	0.087	0.966
4	F4	Y = -0.043X + 1.991	0.099	0.982
5	F5	Y = -0.040X + 1.985	0.092	0.973
6	F6	Y = -0.035X + 1.972	0.081	0.958

The first-order model showed significantly higher correlation coefficients than the zero-order model.

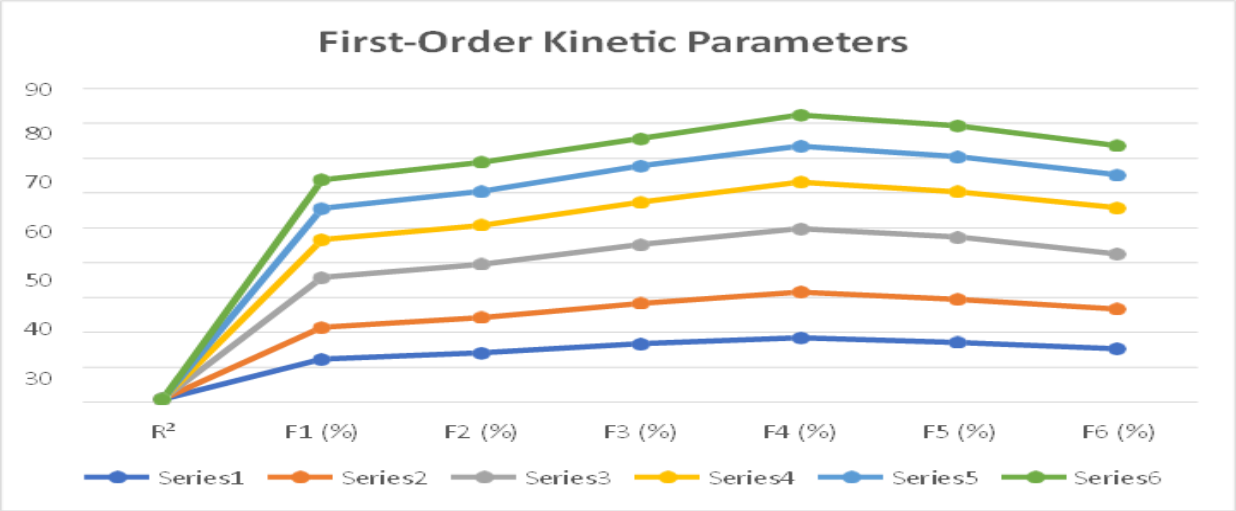

Figure 4. First-Order Kinetic Parameters

The higher rate constant observed for F4 may be attributed to its optimized composition, which enhanced drug dissolution and diffusion.

Higuchi Release Kinetics

The Higuchi model describes drug release from matrix systems where diffusion is the predominant release mechanism. A plot of cumulative percentage drug released versus square root of time was generated.

Table 9. Higuchi Kinetic Parameters

S. No.	Formulation	Regression Equation	kH	Intercept	R^2
1	F1	Y = 16.82X + 10.46	16.82	10.46	0.972
2	F2	Y = 18.74X + 11.28	18.74	11.28	0.979
3	F3	Y = 21.16X + 12.54	21.16	12.54	0.987
4	F4	Y = 23.84X + 13.76	23.84	13.76	0.995
5	F5	Y = 22.42X + 13.08	22.42	13.08	0.991
6	F6	Y = 19.96X + 11.84	19.96	11.84	0.983

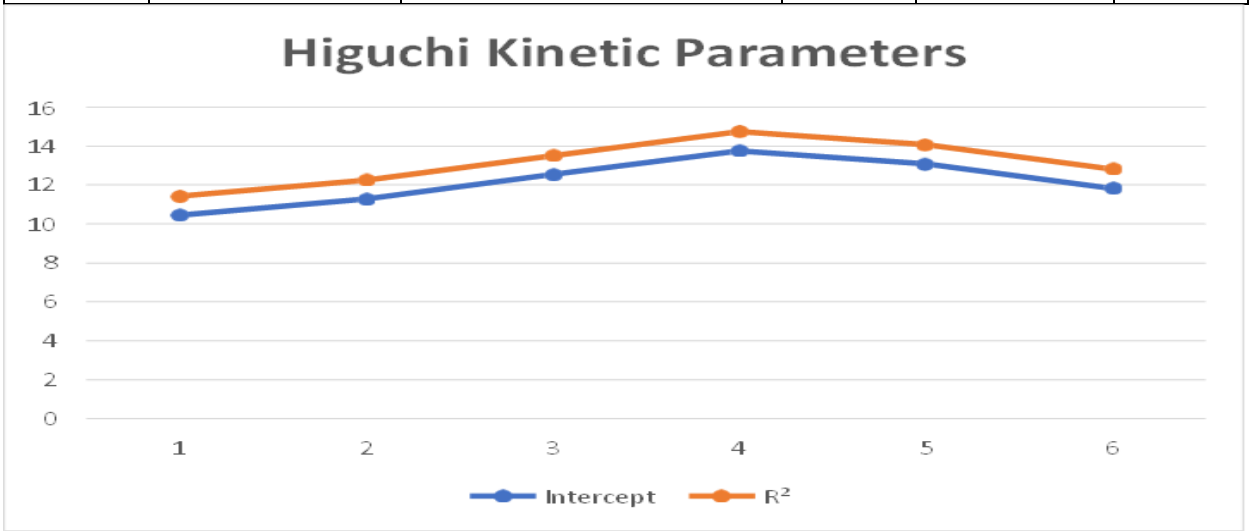

Figure 5. Higuchi Kinetic Parameters

The Higuchi model exhibited the highest correlation coefficients among all kinetic models, with R^2 values ranging from 0.972 to 0.995. The excellent linearity indicates that drug release was predominantly diffusion-controlled. Formulation F4 showed the highest Higuchi constant and highest R^2 value, demonstrating the fastest diffusion rate and best fit to the Higuchi model.

Korsmeyer–Peppas Release Kinetics

The Korsmeyer–Peppas model was employed to determine the mechanism of drug release and characterize the transport phenomenon.

Table 10. Korsmeyer–Peppas Kinetic Parameters

S. No.	Formulation	Regression Equation	n	kKP	R^2
1	F1	Y = 0.514X + 1.204	0.514	1.204	0.958
2	F2	Y = 0.562X + 1.148	0.562	1.148	0.971
3	F3	Y = 0.618X + 1.086	0.618	1.086	0.984
4	F4	Y = 0.683X + 1.018	0.683	1.018	0.992
5	F5	Y = 0.651X + 1.052	0.651	1.052	0.988
6	F6	Y = 0.587X + 1.124	0.587	1.124	0.977

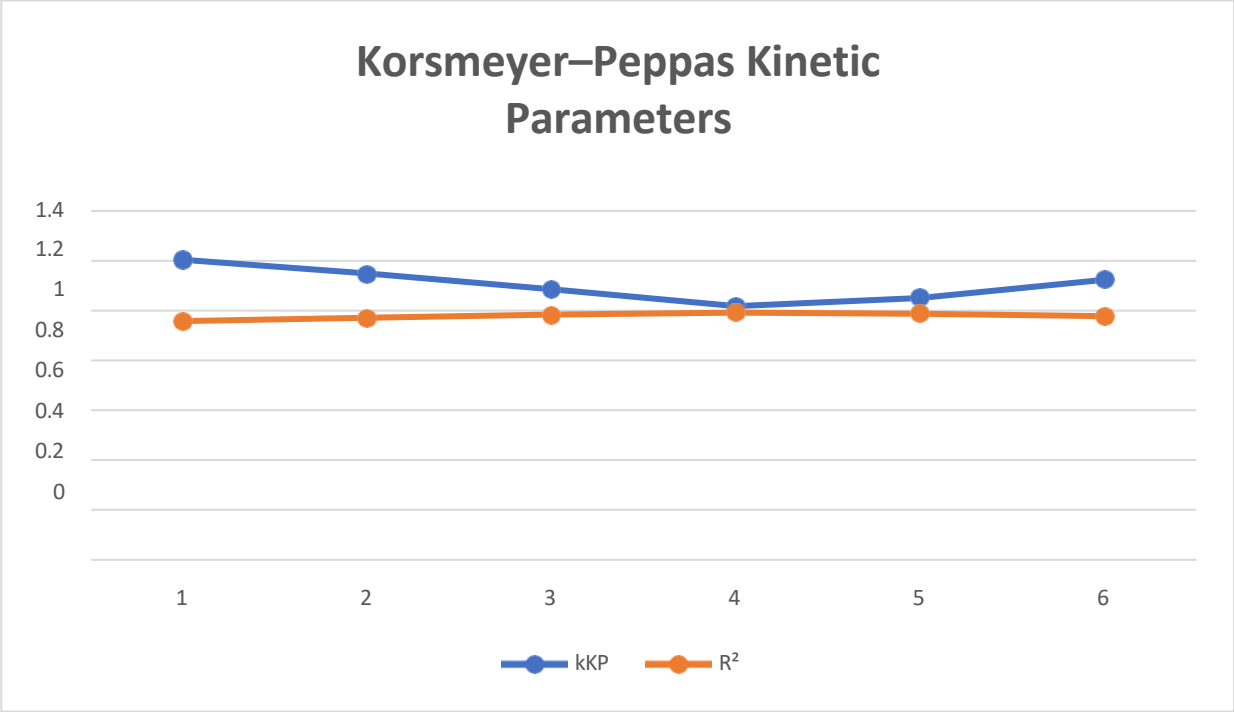

Figure 6. Korsmeyer–Peppas Kinetic Parameters Table 11. Kinetics Model Comparison

Model	Best R^2 Range
Zero Order	0.673–0.718
First Order	0.938–0.982
Higuchi	0.972–0.995
Korsmeyer–Peppas	0.958–0.992

Among the kinetic models evaluated, the Higuchi model exhibited the highest correlation coefficients, indicating that drug release was predominantly diffusion-controlled. The Korsmeyer–Peppas analysis further confirmed a non-Fickian transport mechanism involving both diffusion and polymer relaxation. Formulation F4 showed the highest cumulative drug release, highest kinetic constants, and best model fitting, confirming its superiority over the other formulations.

Table 12. Stability Data After 3 Months

S. No.	Parameter	Initial	Room Temp (25 ± 2°C)	Cold Temp (4 ± 2°C)	Elevated Temp (40 ± 2°C)	Freezing Temp (-20 ± 2°C)
1	Appearance	Smooth, Green	No Change	No Change	Slight Darkening	No Change
2	pH	6.2 ± 0.03	6.1 ± 0.04	6.2 ± 0.03	5.9 ± 0.05	6.2 ± 0.04
3	Viscosity (cP)	31,500 ± 120	31,200 ± 125	31,450 ± 118	30,100 ± 130	31,300 ± 122
4	Drug Content (%)	98.7 ± 0.42	97.9 ± 0.45	98.3 ± 0.43	95.4 ± 0.50	97.8 ± 0.46
5	Drug Release (%)	89.4 ± 1.3	88.8 ± 1.4	89.1 ± 1.3	86.5 ± 1.5	88.6 ± 1.4

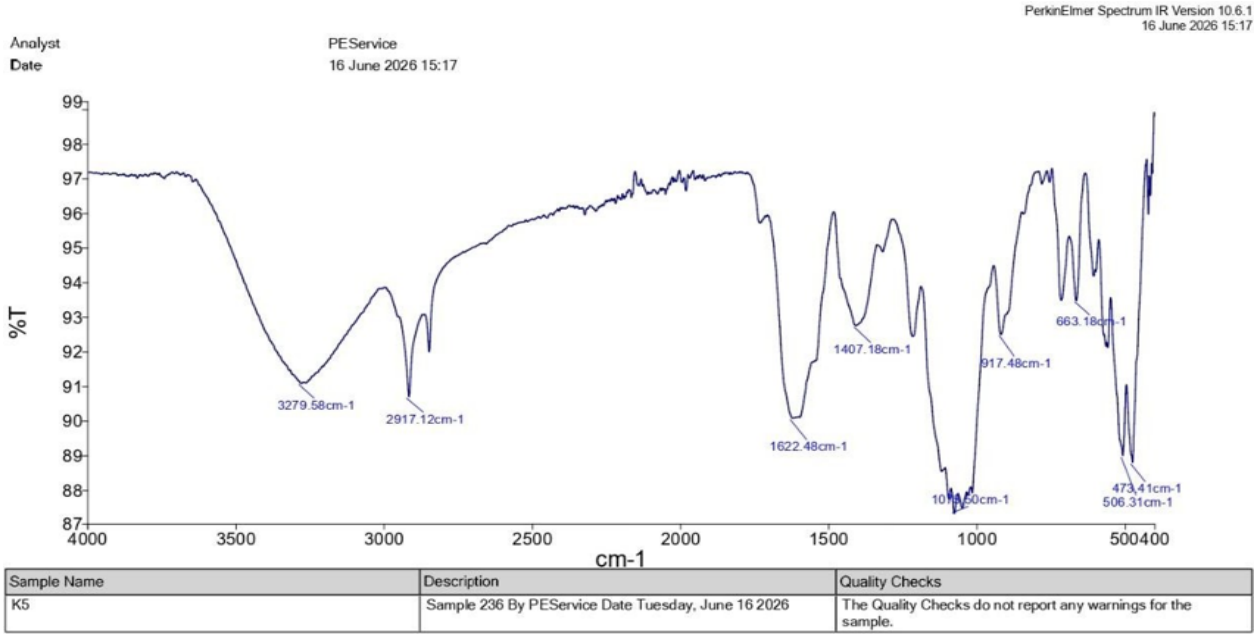

Figure 7. Final product of nanoparticles

In vitro antifungal activity

Table 13. Antifungal Activity of Formulations Against Fungal Strains

S. No.	Formulation	IC_{50} Against *Aspergillus niger* (µg/mL)
1	F1	42.4 ± 1.4
2	F2	35.6 ± 1.2
3	F3	28.9 ± 1.0
4	F4	18.6 ± 0.8
5	F5	21.9 ± 0.9
6	F6	30.7 ± 1.1

The optimized formulation F4 exhibited the highest antifungal activity among all formulations, producing zones of inhibition of 23.8 ± 0.8 mm and 22.4 ± 0.7 mm against *Aspergillus niger*, respectively. Correspondingly, F4 showed the lowest IC_{50} values among the formulations (15.2 ± 0.7 µg/mL and 18.6 ± 0.8 µg/mL), indicating superior antifungal potency.

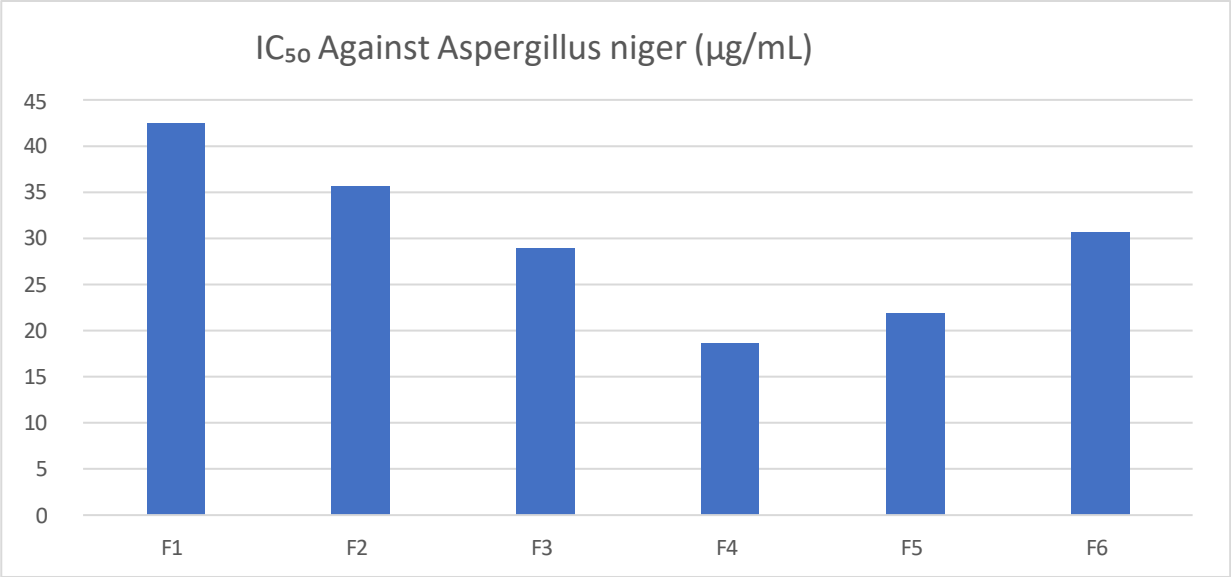

Figure 8. Graphical representations of IC_{50} against *A. niger*

Zone of inhibition

ZOI (Zone of Inhibition) is the diameter of the clear area surrounding an antifungal agent where fungal growth is inhibited. It is usually expressed in millimeters (mm). A larger ZOI indicates stronger antifungal activity.

Table 14. Antifungal Activity (ZOI) of Formulations

S. No.	Formulation	ZOI Against *Aspergillus niger* (mm)
1	F1	12.8 ± 0.5
2	F2	15.2 ± 0.6
3	F3	17.8 ± 0.5
4	F4	22.4 ± 0.7
5	F5	20.5 ± 0.6
6	F6	17.3 ± 0.5

F4 showed the highest antifungal activity among the formulations The order of antifungal activity was: F4 > F5 > F3 > F6 > F2 > F1. This indicates that formulation F4 is the optimized formulation with the best antifungal efficacy among the tested batches.

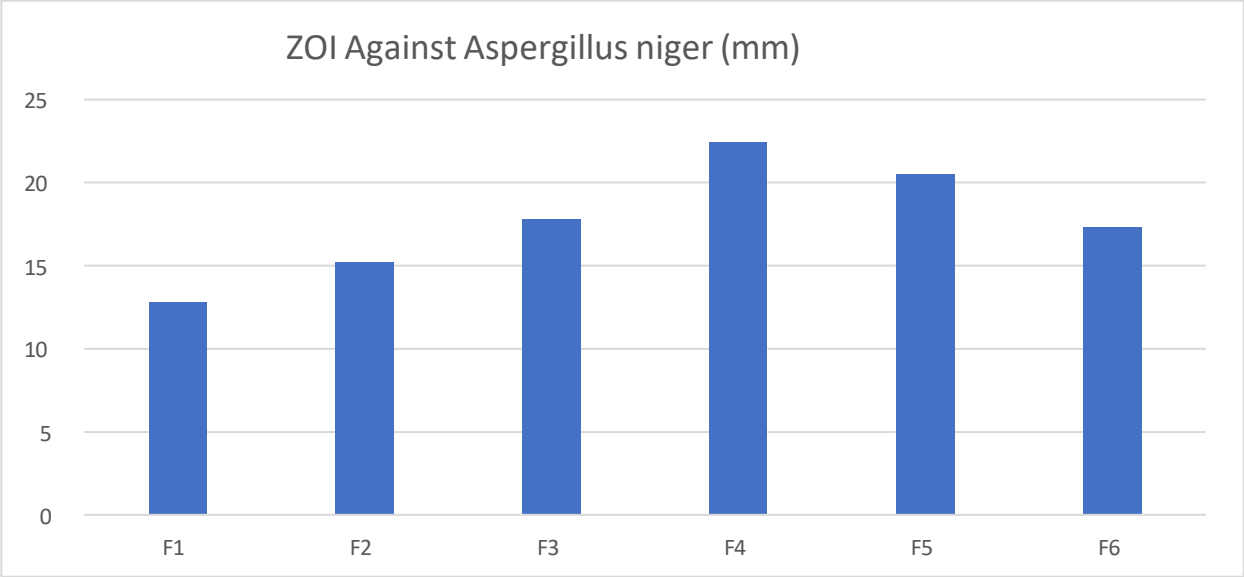

Figure 9. ZOI Against *A. niger*

IV. CONCLUSION

Current investigations successfully industrialized and assessed a topical herbal nanogel containing extracts of *Moringa oleifera* and *Nyctanthes arbor-tristis* for the supervision of mycosis. Six nanogel formulations (F1–F6) were equipped and methodically assessed for physicochemical features, drug release behaviour, antifungal activity, and stability. Among all formulations, F4 demonstrated superior performance with acceptable pH, optimum viscosity, excellent spreadability, high drug content, favourable particle size distribution. The formulation exhibited sustained drug release with maximum cumulative release and showed significant antifungal activity against *Aspergillus niger*, indicating enhanced therapeutic efficacy. Advanced herbal nanogel represents a promising, safe, and effective topical drug delivery system for fungal infections and may serve as a potential alternative to conventional antifungal therapies.

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