

DESIGN AND EVALUATION OF IVERMECTIN-LOADED NANO GEL FOR THE TOPICAL TREATMENT OF PARASITIC SKIN INFECTION

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Abstract- The present study describes the formulation and evaluation of an ivermectin-loaded transfersomal nanogel intended for topical drug delivery. Ivermectin was incorporated into deformable lipid vesicles using lecithin as the phospholipid and Span 80 as the edge activator, followed by incorporation of the transfersomal dispersion into a Carbopol 940 gel base. Nine formulations (F1–F9) were prepared by varying lecithin, Span 80 and Carbopol 940 concentrations while keeping ivermectin, ethanol and propylene glycol concentrations constant. Preformulation studies showed maximum ivermectin solubility in chloroform (28.64 ± 0.42 mg/mL), followed by ethanol (18.42 ± 0.36 mg/mL) and propylene glycol (12.76 ± 0.29 mg/mL), while solubility in phosphate buffer pH 7.4 was 0.021 ± 0.004 mg/mL. The partition coefficient was 61.57 ± 2.14 with $\log P$ 1.79 ± 0.02 . The prepared nanogels showed pH values of 6.72–6.83, drug

content of 96.4–99.1%, entrapment efficiency of 72.6–89.2%, and 8-h cumulative drug release of 77.8–85.6%. Formulation F5, containing 0.1% ivermectin, 1.5% lecithin, 1.0% Span 80 and 1.0% Carbopol 940, was selected as the optimized formulation based on the combined evaluation parameters. F5 showed pH 6.80 ± 0.03 , spreadability 7.54 ± 0.22 g·cm/s, viscosity $8,740 \pm 156$ cP, drug content $99.1 \pm 0.42\%$, entrapment efficiency $86.9 \pm 0.84\%$, and 81.2% drug release at 8 h. Release kinetics for F5 showed the highest correlation with the Korsmeyer–Peppas model ($R^2 = 0.995$; $n = 0.67$), indicating anomalous/non-Fickian release.

Keywords: Ivermectin; transfersomes; nanogel; Carbopol 940; Span 80; topical drug delivery; entrapment efficiency; in-vitro drug release.

1. Introduction

Ivermectin is an antiparasitic drug used in the management of several parasitic conditions. The submitted thesis focuses on developing a topical delivery system in which ivermectin is incorporated into deformable lipid vesicles (transfersomes) and subsequently dispersed in a Carbopol 940 gel matrix. Transfersomal systems are intended to improve drug incorporation and facilitate topical delivery, while the gel base provides a semisolid dosage form suitable for application to the skin. Previous studies cited in the thesis have investigated topical ivermectin formulations including microemulsions, nanocrystals and gel-based systems [5,7,8].

The present article summarizes the thesis work as a research article, including the reported formulation design, preformulation studies, physicochemical evaluation, drug entrapment, in-vitro release, release kinetics and selection of the optimized formulation.

2. Aim and Objectives

Aim: To develop and evaluate an ivermectin-loaded transfersomal nanogel for topical drug delivery.

- To study the physicochemical properties of ivermectin, including solubility, partition coefficient and FTIR compatibility.
- To prepare ivermectin-loaded transfersomes using lecithin and Span 80 by the thin-film hydration method.
- To incorporate the transfersomal dispersion into a Carbopol 940 gel base.
- To prepare and evaluate nine formulations (F1–F9) with different concentrations of lecithin, Span 80 and Carbopol 940.
- To determine pH, spreadability, viscosity, drug content, entrapment efficiency and in-vitro drug release.
- To analyze release kinetics and select the optimized formulation based on overall performance.

3. Materials and Methods [12,13]

3.1 Materials

Material	source
Ivermectin	Active drug; Sample from Axico Healthcare, Delhi
Lecithin	Phospholipid for transfersomes

Span 80	Surfactant / edge activator
Carbopol 940	Gelling agent
Ethanol	Co-solvent
Propylene glycol	Co-solvent
Triethanolamine	Neutralizing agent / pH adjustment
Chloroform	Solvent for lipid phase
Phosphate buffer pH 7.4	Hydration/receptor medium

3.2 Formulation Design ^[14,15,16]

Formulation	Ivermectin (%)	Lecithin (%)	Span 80 (%)	Ethanol (%)	Propylene glycol (%)	Carbopol 940 (%)	Water
F1	0.1	1.0	0.5	5.0	5.0	0.5	q.s. to 100 g
F2	0.1	1.5	0.5	5.0	5.0	0.5	q.s. to 100 g
F3	0.1	2.0	0.5	5.0	5.0	0.5	q.s. to 100 g
F4	0.1	1.0	1.0	5.0	5.0	1.0	q.s. to 100 g
F5	0.1	1.5	1.0	5.0	5.0	1.0	q.s. to 100 g
F6	0.1	2.0	1.0	5.0	5.0	1.0	q.s. to 100 g
F7	0.1	1.0	1.5	5.0	5.0	1.5	q.s. to 100 g
F8	0.1	1.5	1.5	5.0	5.0	1.5	q.s. to 100 g
F9	0.1	2.0	1.5	5.0	5.0	1.5	q.s. to 100 g

3.3 Preparation of Transfersomes and Nanogel

Transfersomes were prepared by the thin-film hydration technique. Ivermectin, lecithin and Span 80 were dissolved in chloroform, followed by solvent removal under reduced pressure to form a thin lipid film^[11] The film was hydrated with phosphate buffer pH 7.4 and sonicated to obtain the transfersomal dispersion. Carbopol 940 was hydrated separately and combined with ethanol and propylene glycol. The transfersomal suspension

was then incorporated into the gel base with gentle stirring, followed by neutralization with triethanolamine and adjustment to approximately pH 6.8⁽⁸⁾

The thesis methodology used a Franz diffusion cell with phosphate buffer pH 7.4 at $37 \pm 0.5^\circ\text{C}$ for 8 h for the in-vitro release study, with samples analyzed at 245 nm by UV-visible spectrophotometry^[10]

4. Results and Discussion

4.1 Preformulation Studies

Medium	Solubility (mg/mL)
Chloroform	28.64 ± 0.42
Ethanol	18.42 ± 0.36
Propylene glycol	12.76 ± 0.29
Phosphate buffer pH 7.4	0.021 ± 0.004

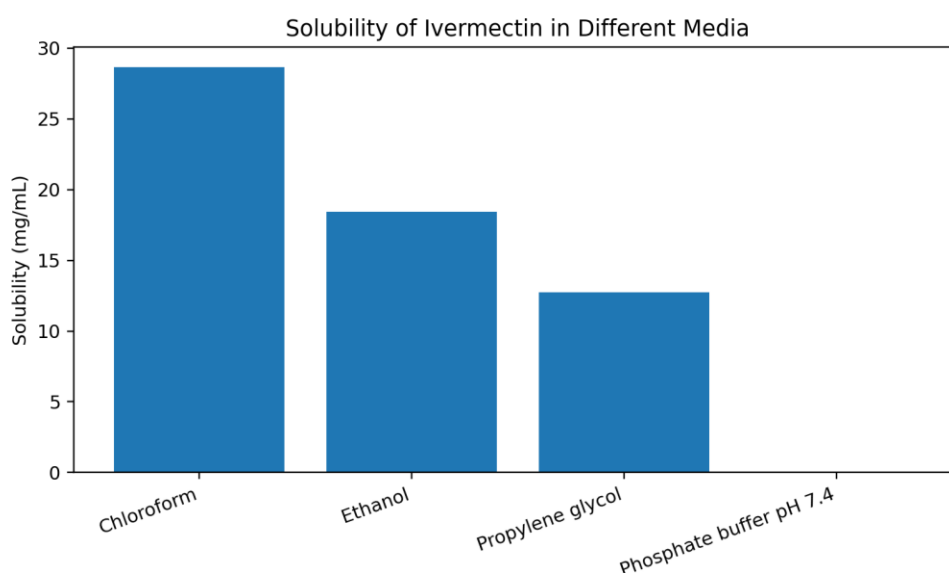


Figure 1. Solubility of ivermectin in different media.

Ivermectin showed the highest solubility in chloroform, followed by ethanol and propylene glycol, whereas its solubility in phosphate buffer pH 7.4 was very low. The thesis reported a partition coefficient of 61.57 ± 2.14 and log P of 1.79 ± 0.02 , indicating the lipophilic

character of ivermectin. FTIR findings showed retention of characteristic ivermectin peaks in the physical mixture, with no major disappearance or substantial shifting of principal bands, supporting compatibility with the selected excipients.

Table 4.2: Solubility of Ivermectin in Different Solvents

S. No.	Concentration ($\mu\text{g/mL}$)	Absorbance (at 245 nm)
1	5.0	0.1633
2	10.0	0.3220
3	15.0	0.4815
4	20.0	0.6401
5	25.0	0.7994
6	30.0	0.9579

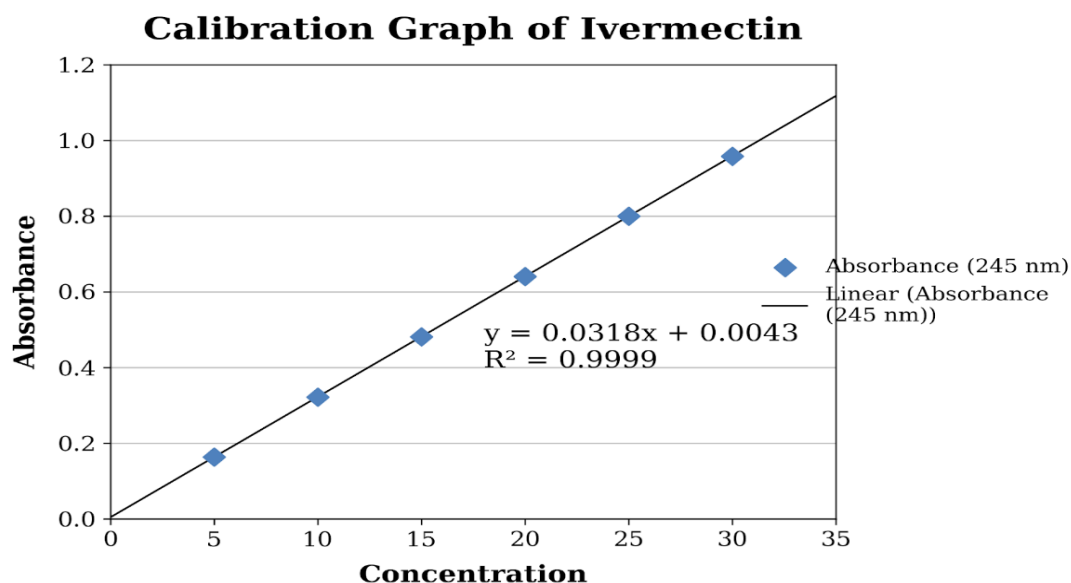


Figure 2 Calibration Curve of Ivermectin at 245 nm

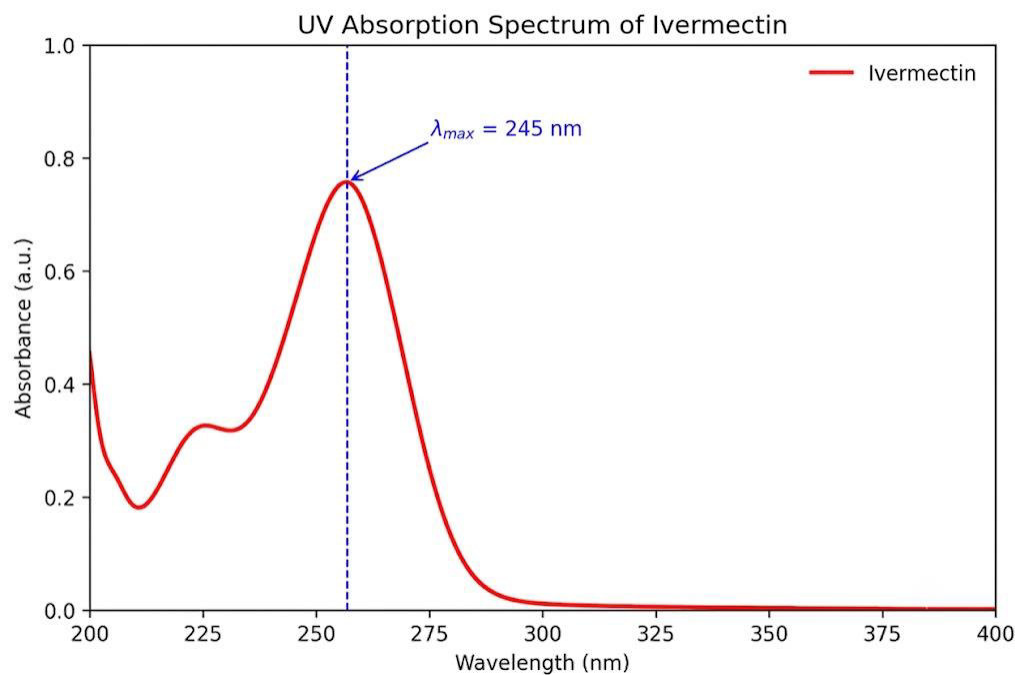


Figure3. UV Absorption Spectrum of Ivermectin ($\lambda_{max} = 245 \text{ nm}$)

The UV absorption spectrum is applied to calculate the wavelength at which maximum absorption takes place (λ_{max}). It has been identified from the spectrum that maximum absorption occurs at about 245 nm for ivermectin. The λ_{max} value of 245 nm could be due to the electronic transitions of the chromophoric moieties in ivermectin. At this wavelength, maximum UV radiation absorption takes place producing maximum absorbance. Hence, 245 nm was chosen as the analytical wavelength for the analysis of ivermectin using UV-Vis spectroscopy.

This implies that there is an increase in absorbance as the wavelength gets closer to 245 nm until it attains its peak value at this point. After the wavelength of 245 nm, the absorbance starts dropping. Selection of λ_{max} is important because measurement at the wavelength of maximum absorption provides better sensitivity and minimizes errors associated with small wavelength variations.

4.3.Partition Coefficient of Ivermectin

The partition coefficient of ivermectin was determined using the n-octanol/phosphate buffer pH 7.4 system.

Table 4.3: Partition Coefficient of Ivermectin

Parameter	Result
Concentration in n-octanol phase	8.62 ± 0.18 mg/mL
Concentration in aqueous phase	0.14 ± 0.01 mg/mL
Partition coefficient	61.57 ± 2.14
Log P	1.79 ± 0.02

Ivermectin demonstrated a substantially greater affinity for the n-octanol phase than for the aqueous phase. The calculated partition coefficient indicated that the drug possessed considerable lipophilic character.

The lipophilic nature of ivermectin is advantageous for incorporation into the lipid bilayer of transfersomes. However, excessive lipophilicity may limit aqueous dispersion and conventional topical delivery. Therefore,

incorporation into deformable phospholipid vesicles followed by dispersion in a Carbopol 940 gel was considered a suitable approach for improving topical drug delivery.

4.4.FTIR Spectral Analysis

FTIR spectroscopy was performed to identify the characteristic functional groups of ivermectin and to assess possible interactions between ivermectin and the selected excipients.

Table 4.4: Characteristic FTIR Peaks of Ivermectin

S. No	Functional group	Reported/Observed peak (cm^{-1})	Interpretation
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1	O–H stretching	3452	Hydroxyl group
2	C–H stretching	2925	Aliphatic C–H
3	C=O stretching	1734	Carbonyl group
4	C=C stretching	1648	Unsaturated group
5	C–O stretching	1162	Ether/alcohol group
6	C–O–C stretching	1080	Ether linkage

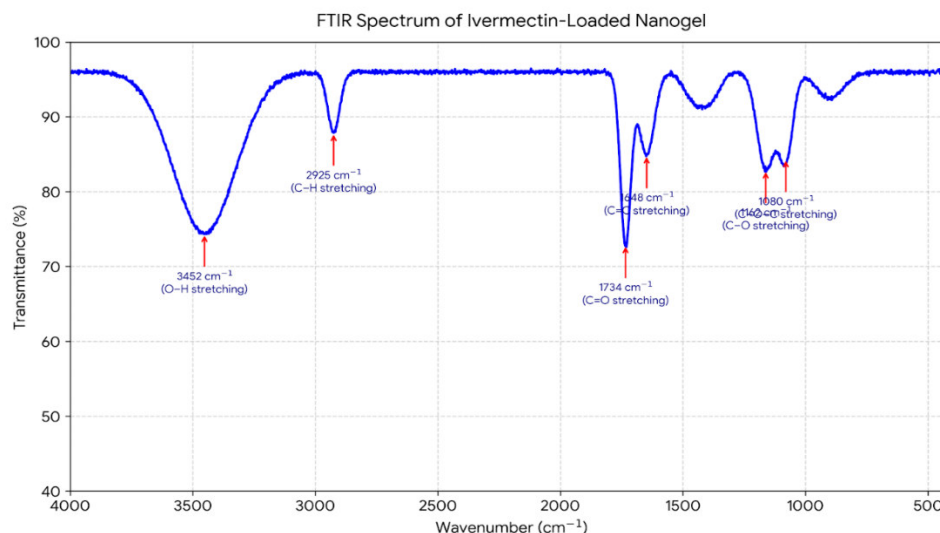


Figure .4 FTIR Spectrum of Ivermectin-Loaded Nanogel

The FTIR spectrum of pure ivermectin exhibited characteristic absorption bands corresponding to hydroxyl, aliphatic C–H, carbonyl, C=C, and C–O

functional groups. The major characteristic peaks were retained in the physical mixture containing ivermectin and the selected formulation excipients.

No major disappearance of characteristic peaks or substantial shifts in the principal absorption bands were observed. This suggested the absence of significant chemical interaction between ivermectin and the selected excipients under the formulation conditions.

The FTIR findings therefore supported the compatibility of ivermectin with lecithin, Span 80, and Carbopol 940 and indicated that the selected excipients could be used for further formulation development.

4.5 Physical Appearance, pH, Spreadability and Viscosity

Parameter	Reported range / observation
Physical appearance	White to off-white; smooth; good to excellent homogeneity; no phase separation
Ph	6.72 ± 0.05 to 6.83 ± 0.04
Spreadability	8.92 ± 0.31 to 6.18 ± 0.19 g·cm/s
Viscosity	$5,420 \pm 115$ to $13,520 \pm 205$ cP

All formulations were described as smooth and homogeneous without visible lumps or phase separation. The thesis reported that viscosity increased with increasing Carbopol 940

concentration, consistent with formation of a denser polymeric gel network. F5 had a viscosity of $8,740 \pm 156$ cP and spreadability of 7.54 ± 0.22 g·cm/s.

4.6 Drug Content

Formulation	Drug content (%)
F1	96.4 ± 0.72
F2	97.1 ± 0.64
F3	97.8 ± 0.58
F4	98.2 ± 0.61
F5	99.1 ± 0.42
F6	98.7 ± 0.47
F7	98.0 ± 0.53

F8	98.5 ± 0.49
F9	97.6 ± 0.55

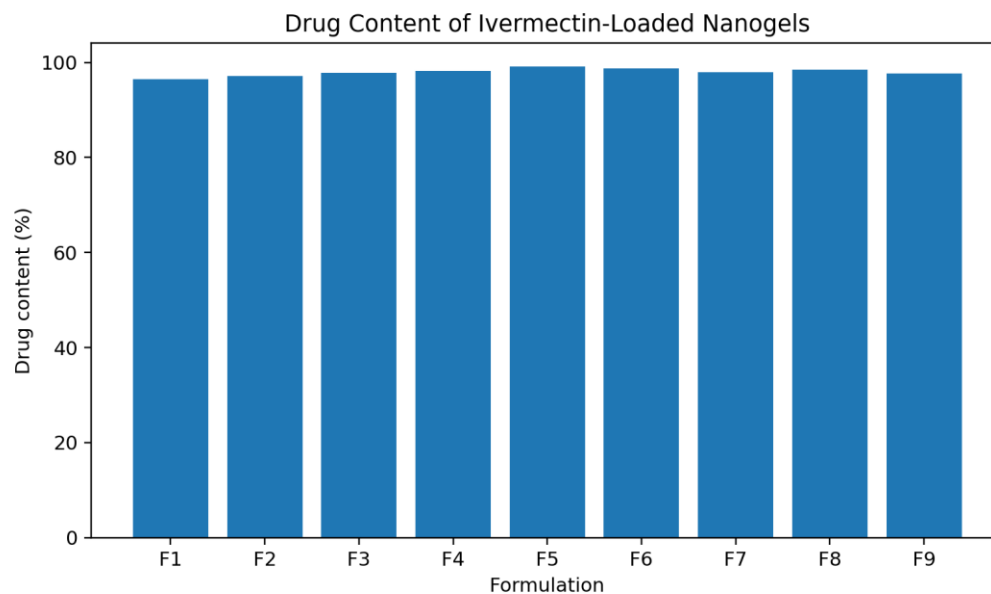


Figure 5. Drug content of ivermectin-loaded nanogel formulations F1–F9.

Drug content ranged from $96.4 \pm 0.72\%$ to $99.1 \pm 0.42\%$. F5 showed the highest reported drug

content at $99.1 \pm 0.42\%$, indicating satisfactory drug distribution within the formulation.

4.7 Entrapment Efficiency

Formulation	Lecithin (%)	Span 80 (%)	Entrapment efficiency (%)
F1	1.0	0.5	72.6 ± 1.21
F2	1.5	0.5	78.4 ± 1.08
F3	2.0	0.5	82.7 ± 0.96
F4	1.0	1.0	76.8 ± 1.15
F5	1.5	1.0	86.9 ± 0.84
F6	2.0	1.0	89.2 ± 0.79
F7	1.0	1.5	73.5 ± 1.27
F8	1.5	1.5	83.6 ± 0.91
F9	2.0	1.5	87.4 ± 0.86

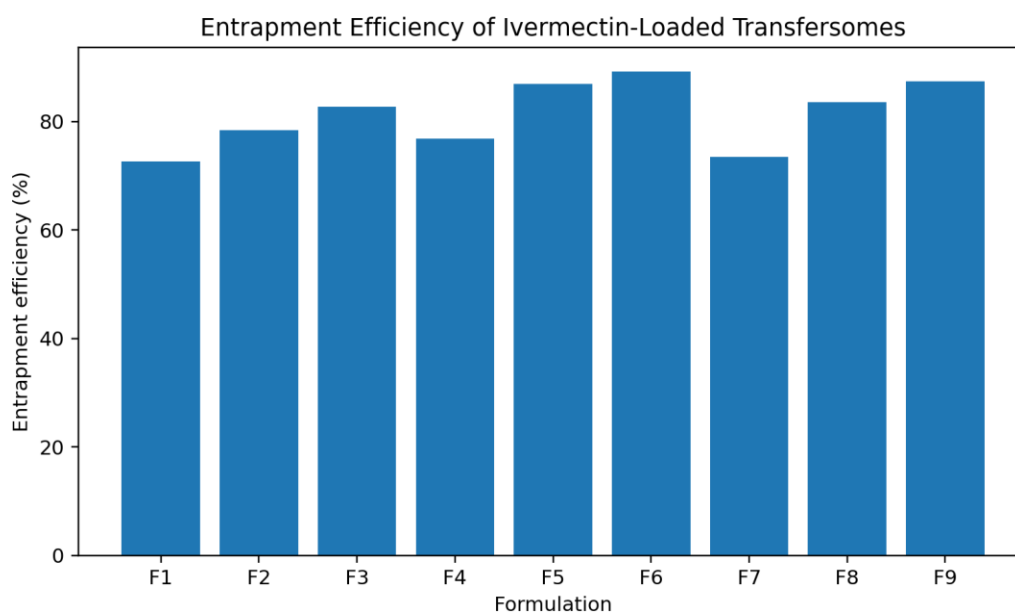


Figure 6. Entrapment efficiency of ivermectin-loaded transfersomal formulations F1–F9.

Entrapment efficiency ranged from $72.6 \pm 1.21\%$ to $89.2 \pm 0.79\%$. F6 showed the highest entrapment efficiency ($89.2 \pm 0.79\%$), while F5

showed $86.9 \pm 0.84\%$. The thesis selected F5 using the combined evaluation parameters rather than entrapment efficiency alone.

4.8 In-Vitro Drug Release

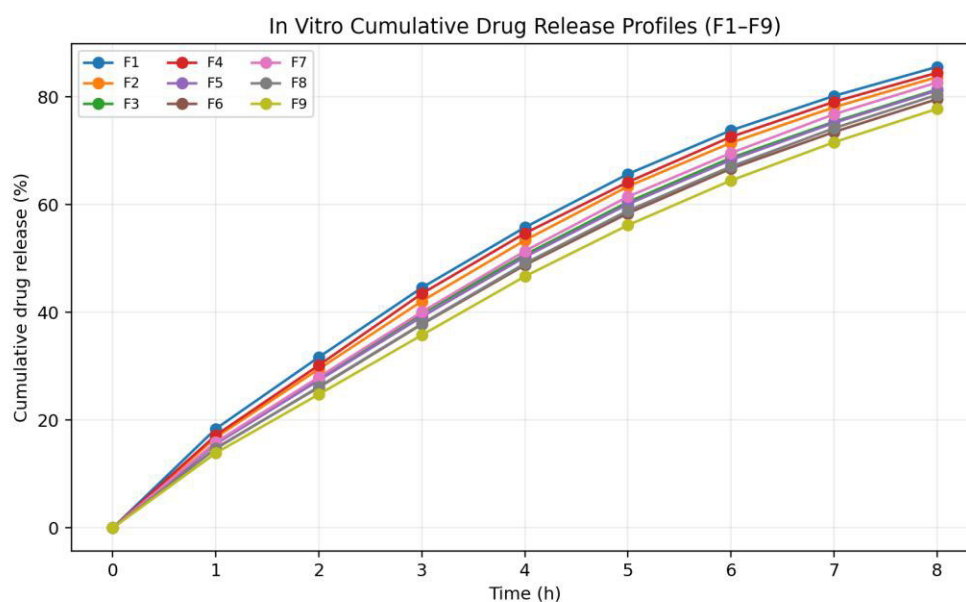


Figure 7. In-vitro cumulative drug release profiles of F1–F9 over 8 h.

Formulation	Release at 8 h (%)
F1	85.6
F2	83.7
F3	81.4
F4	84.5
F5	81.2
F6	79.6
F7	82.7
F8	80.4
F9	77.8

All formulations showed a progressive increase in cumulative drug release over time. At 8 h, release ranged from 77.8% to 85.6%. F1 showed the highest 8-h release (85.6%), while F9 showed the lowest (77.8%). F5 showed 81.2% release at 8 h. The thesis associated

slower release with higher Carbopol concentration and vesicular drug retention, while Span 80 concentration influenced the flexibility and permeability of the transfersomal membrane.

4.9 Comparative Graph: Entrapment Efficiency and 8-h Release

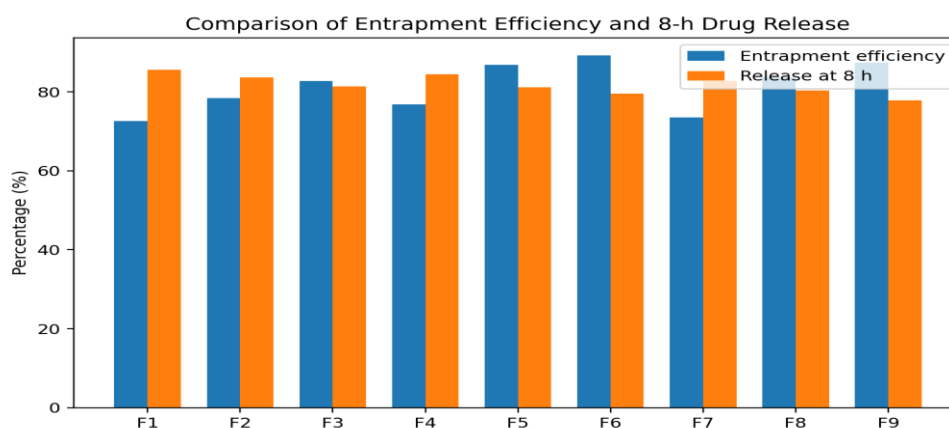


Figure 8. Comparison of entrapment efficiency and cumulative drug release at 8 h.

4.10 Release Kinetics and Optimized Formulation

Parameter	F5 result
Physical appearance	Smooth and homogeneous
Ph	6.80 ± 0.03
Spreadability	$7.54 \pm 0.22 \text{ g}\cdot\text{cm/s}$
Viscosity	$8,740 \pm 156 \text{ cP}$
Drug content	$99.1 \pm 0.42\%$
Entrapment efficiency	$86.9 \pm 0.84\%$
Drug release at 8 h	81.2%
Korsmeyer–Peppas R^2	0.995
Release exponent (n)	0.67
Major release mechanism	Anomalous/non-Fickian

F5 was selected as the optimized formulation on the basis of the combined physicochemical and drug-release characteristics. Its release exponent of 0.67 and R^2 of 0.995 under the Korsmeyer–Peppas analysis were interpreted in the thesis as anomalous/non-Fickian release involving both diffusion and polymer relaxation.

5. Discussion

The formulation study demonstrates that the composition of the transfersomal nanogel influenced drug entrapment and release. Increasing lecithin concentration was associated with increased entrapment efficiency within the tested formulation groups, while higher lipid and polymer concentrations were associated with lower release at 8 h in the

reported comparison. The optimized F5 formulation did not have the highest value for every individual parameter; instead, it provided a combined balance of drug content, entrapment efficiency, viscosity, spreadability, pH and controlled release. The thesis therefore identified F5 as the optimized formulation based on overall performance.

The findings are consistent with the formulation rationale described in the thesis and with the cited literature on topical ivermectin systems and vesicular/nanocarrier-based topical delivery [5,7,8,25,31–35]. However, the present study, as reported in the thesis, primarily provides formulation and in-vitro evaluation data; therapeutic efficacy,

long-term stability and clinical performance require further investigation.

6. Conclusion

An ivermectin-loaded transfersomal nanogel was successfully developed and evaluated using nine formulations. The formulations showed satisfactory physical appearance, pH, spreadability, viscosity and drug content, together with measurable entrapment of ivermectin and controlled in-vitro release. F5, containing 0.1% ivermectin, 1.5% lecithin, 1.0% Span 80 and 1.0% Carbopol 940, was selected as the optimized formulation. It showed $99.1 \pm 0.42\%$ drug content, $86.9 \pm 0.84\%$ entrapment efficiency and 81.2% cumulative drug release at 8 h, with Korsmeyer–Peppas R^2 of 0.995 and $n = 0.67$. These results support further investigation of the ivermectin transfersomal nanogel as a topical delivery platform, while additional ex-vivo, in-vivo, safety, stability and clinical studies remain necessary.

7. Limitations and Future Scope ^[18,19,20]

- The thesis recommends further optimization of particle size, drug entrapment, skin deposition, viscosity, spreadability and release behavior.

- Advanced characterization of vesicle structure, surface properties and drug–excipient interactions can be undertaken.
- Ex-vivo/in-vitro skin permeation and retention studies can provide information on skin deposition.
- Further in-vivo work can evaluate efficacy, pharmacokinetics, dermal safety, irritation and toxicity.
- Long-term stability, scale-up, manufacturability, packaging and regulatory considerations require investigation before translation.

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