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Development and Evaluation of Quercetin-Loaded Invasomal Gel for Enhanced Dermal Drug Delivery

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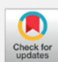

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Abstract: Quercetin is a naturally occurring polyphenolic flavonoid widely present in fruits, vegetables and medicinal plants and is known for its potent antioxidant, anti-inflammatory, anticancer and cardioprotective activities. However, its therapeutic potential is significantly limited by poor aqueous solubility, low bioavailability and inadequate permeability across biological membranes. In topical applications, the stratum corneum acts as a major barrier, restricting effective drug penetration and reducing therapeutic efficiency. The present study aims to develop and evaluate a quercetin-loaded invasomal gel to enhance dermal delivery and improve the stability and bioavailability of quercetin.

Quercetin-loaded invasomes were prepared using the thin-film hydration method employing phospholipids, ethanol and terpenes as key components to enhance vesicle deformability and skin penetration. The optimized invasomal dispersion was subsequently incorporated into a Carbopol-based hydrogel to obtain a stable topical formulation. The prepared formulations were evaluated for physicochemical parameters such as colour, clarity, homogeneity, pH, viscosity and spreadability. Drug-related parameters including entrapment efficiency, drug content and stability were also assessed. Further evaluation involved in vitro drug release studies, ex vivo permeation studies using egg membrane and antioxidant activity using the DPPH radical scavenging assay.

The optimized invasomal gel demonstrated good physical stability, acceptable pH suitable for skin application, uniform drug distribution and excellent spreadability. The formulation showed higher drug release and improved permeation compared to conventional quercetin gel formulations. The antioxidant studies confirmed that the formulation retained the free radical scavenging activity of quercetin. Overall, the invasomal gel system significantly enhanced the solubility, stability and dermal penetration of quercetin.

Thus, the developed quercetin invasomal gel represents a promising nanocarrier-based topical delivery system for improving the therapeutic efficacy of poorly soluble phytoconstituents. The formulation is stable, cost-effective and suitable for topical application, indicating its potential for the management of oxidative stress-related and inflammatory skin disorders.

Keywords: Quercetin, Invasomes, Carbopol gel, Skin permeation, Antioxidant activity.

1. INTRODUCTION

Topical drug delivery systems play an important role in modern pharmaceutical therapy by allowing drugs to be applied directly to the skin to produce local or systemic effects. These systems are widely used for the treatment of various dermatological conditions such as infections, inflammation, burns, wounds, psoriasis, acne and dermatitis. Compared with oral administration, topical drug delivery offers several advantages including localized drug action, avoidance of gastrointestinal degradation, and bypass of first-pass hepatic metabolism and reduction of systemic side effects. In addition, topical formulations are generally non-invasive, easy to apply and improve patient compliance, especially in chronic conditions requiring long-term treatment [1, 2].

Despite these advantages, effective drug delivery through the skin remains challenging due to the strong barrier properties of the skin, particularly the stratum corneum, which is the outermost layer of the epidermis. The stratum corneum consists of tightly packed keratinized cells embedded within a lipid matrix composed mainly of ceramides, cholesterol and fatty acids. This highly organized structure restricts the penetration of many therapeutic agents, especially hydrophilic drugs and molecules with high molecular weight [3, 4]. As a result, conventional topical formulations such as creams, ointments and gels often fail to deliver sufficient amounts of drug through the skin to achieve the desired therapeutic effect [5].

To overcome these limitations, various strategies have been developed to enhance skin permeation, including the use of chemical penetration enhancers, physical techniques and novel drug delivery systems [6]. In recent years, vesicular drug delivery systems such as liposomes, niosomes, ethosomes and invasomes have gained significant attention due to their ability to encapsulate drugs and improve their penetration through the skin barrier [7]. These systems can enhance drug solubility, stability and controlled release while facilitating transport through different skin layers. Among these carriers, invasomes have emerged as a promising vesicular system for transdermal and topical drug delivery. Invasomes are elastic lipid vesicles composed mainly of phospholipids, ethanol and terpenes. The presence of ethanol and terpenes increases the fluidity and deformability of the vesicles, allowing them to penetrate more effectively through the lipid layers of the stratum corneum [8]. Terpenes also act as natural penetration enhancers that disrupt the lipid structure of the skin barrier, thereby improving drug permeation into deeper skin layers [9].

Quercetin is a naturally occurring flavonoid widely distributed in fruits, vegetables and medicinal plants. It possesses several pharmacological activities including antioxidant, anti-inflammatory, antimicrobial and anticancer properties [10]. Due to these beneficial effects, quercetin has gained significant attention for the treatment of skin disorders associated with oxidative stress and inflammation. However, its therapeutic application is limited due to poor aqueous solubility, low bioavailability and limited skin penetration when administered in conventional formulations [11].

Therefore, the development of advanced drug delivery systems is necessary to improve the dermal delivery of quercetin. In this context, invasomal formulations may provide an effective approach to enhance quercetin solubility, stability and skin permeation. Hence, the present study focuses on the development and evaluation of a quercetin-loaded invasomal gel for improved topical delivery. The prepared formulation was evaluated for physicochemical properties including pH, viscosity, spreadability, drug content, entrapment efficiency, in vitro drug release and antioxidant activity to assess its potential as an effective dermal drug delivery system.

2. MATERIALS & METHODS

2.1. Materials

Quercetin was procured from a reliable commercial source. Soya lecithin was obtained from Yarrow Chem Products, Mumbai, India. Carbopol 934 and menthol were purchased from Loba Chemie Pvt. Ltd., Mumbai, India. Tween 80 and glycerin were obtained from standard commercial suppliers. Methyl paraben and propyl paraben were procured from analytical grade chemical suppliers. Ethanol and other reagents used were of analytical grade. Phosphate buffer (pH 7.4) was prepared in the laboratory. All chemicals were used as received without further purification.

2.2. Methods

2.2.1. Preparation Method of Quercetin-Loaded Invasomes

Quercetin-loaded invasomes were prepared by the thin-film hydration method using phospholipids, ethanol and terpene as the main components. Accurately weighed quantities of phosphatidylcholine and quercetin were dissolved in a mixture of chloroform and ethanol in a round-bottom flask. The organic solvent mixture was evaporated under reduced pressure using a rotary evaporator at 50–60°C to form a thin lipid film on the inner wall of the flask. The formed lipid film was further dried under vacuum for a short period to ensure the complete removal of residual solvents.

The dried lipid film was then hydrated with phosphate buffer solution (pH 7.4) containing ethanol and terpene with continuous rotation of the flask. The hydration process resulted in the formation of multilamellar vesicles containing quercetin. The obtained dispersion was further sonicated using a probe sonicator for a specific time to reduce vesicle size and obtain a uniform invasomal suspension. The prepared invasomal dispersion was stored in a closed container for further studies.

2.2.2. Preparation Method of Quercetin-Loaded Invasomal Gel

The invasomal gel was prepared using the Carbopol dispersion method. The required quantity of Carbopol 934 was accurately weighed and dispersed in distilled water with continuous stirring and allowed to hydrate for several hours to form a uniform gel base. Propylene glycol, glycerin and preservatives (methyl paraben and propyl paraben) were added to the hydrated Carbopol solution with constant stirring to obtain a homogeneous mixture.

The prepared quercetin-loaded invasomal dispersion was slowly incorporated into the Carbopol gel base under continuous stirring to ensure uniform distribution of the drug within the gel matrix. The pH of the formulation was adjusted to 5.5–6.5 using triethanolamine to obtain a clear and stable gel formulation. The final gel was mixed thoroughly until a smooth and homogeneous consistency was obtained.

The prepared quercetin invasomal gel formulations were transferred into suitable containers and stored at room temperature for further evaluation studies. The quantitative composition of different formulations prepared was described in the respective formulation table.

Table 1. *0020composition of Quercetin-Loaded Invasomal Gel Formulations (% W/W)*

Ingredients	F1	F2	F3	F4	F5	F6	F7
Quercetin	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Soya Lecithin	3	3	3	3	3	3	3
Menthol	0.15	0.15	0.15	0.15	0.15	0.15	0.15
Carbopol 934	0.25	0.50	0.60	0.75	0.85	1.00	1.25
Glycerin	0.24	0.24	0.24	0.24	0.24	0.24	0.24
Tween-80	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Methyl Paraben	0.18	0.18	0.18	0.18	0.18	0.18	0.18
Propyl Paraben	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Ethanol	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Phosphate Buffer	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

2.3. Evaluation Studies of Quercetin Invasomal Gel

2.3.1. Organoleptic Evaluation

The prepared quercetin invasomal gel formulations were visually inspected for appearance, color, odor, consistency, homogeneity, oily feel, stickiness, grittiness, and phase separation to assess their physical stability and acceptability [65].

2.3.2. Determination of pH

The pH of the prepared quercetin invasomal gel formulations was measured at room temperature using a digital pH meter (Eutech Instruments) [66].

2.3.3. Determination of Viscosity

The viscosity of the gel formulations was determined using a Brookfield viscometer at room temperature to evaluate the flow behavior of the formulation [67].

2.3.4. Centrifugation Test

Approximately 5 g of quercetin invasomal gel was transferred into a centrifuge tube and centrifuged at 5000 rpm for 15 minutes at 32°C to check the physical stability and phase separation of the formulation [68].

2.3.5. Spreadability Test

Spreadability was determined by placing 500 mg of gel between two glass slides (20 × 20 cm). A 500 g weight was applied for 5 minutes, and the diameter of the spread gel was measured in centimeters, which represented the spreadability of the formulation [69].

2.3.6. Determination of Drug Content

An amount of gel equivalent to 10 mg of quercetin was dissolved in ethanol and further diluted with phosphate buffer (pH 6.8). The absorbance was measured at 376 nm using a UV spectrophotometer, and drug content was calculated using the calibration curve [70].

2.3.7. In-Vitro Drug Release Study

The in vitro release of quercetin from invasomal gel was studied using a Franz diffusion cell consisting of donor and receptor compartments [71]. A polyvinylidene fluoride (PVDF) membrane previously boiled in distilled water for 10–15 minutes was used as the diffusion membrane. The receptor compartment was filled with 14 mL of phosphate buffer (pH 6.8) and maintained at 32 ± 1°C with continuous stirring at 50 rpm.

An amount of gel equivalent to 1.5 mg of quercetin was placed in the donor compartment. At predetermined intervals (every 30 minutes), 0.5 mL samples were withdrawn and replaced with fresh dissolution medium. The samples were analyzed using a UV double-beam spectrophotometer at 376 nm to determine cumulative drug release.

2.3.8. DPPH Radical Scavenging Assay

The antioxidant activity of the quercetin invasomal gel was evaluated using the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging method. DPPH is a stable free radical with a deep violet color that decreases in absorbance at 517 nm when reduced by antioxidants.

A DPPH solution (4 mg in 100 mL methanol) was prepared and protected from light. Quercetin standard solutions (10–100 µg/mL) were prepared in methanol. For sample preparation, 1 g of invasomal gel was extracted with 10 mL methanol using sonication for 30 minutes and filtered through Whatman filter paper.

For the assay, 1 mL of DPPH solution was mixed with 1 mL of standard or sample solution, incubated in the dark for 30 minutes, and the absorbance was measured at 517 nm using a UV-Visible spectrophotometer.

The percentage radical scavenging activity was calculated using the following equation:

$$= \%\, Inhibition = \frac{A_{control} - A_{sample}}{A_{control}} \times 100$$

3. RESULTS AND DISCUSSION

3.1. Preformulation Studies

3.1.1. Solubility Study

The solubility of quercetin was determined in different solvents including water, ethanol, and methanol to evaluate its physicochemical properties.

3.1.2. Discussion

The solubility study revealed that quercetin is very poorly soluble in water but freely soluble in ethanol and methanol. The poor aqueous solubility may limit its bioavailability and formulation performance. Therefore, the development of suitable drug delivery systems such as invasomal formulations is necessary to enhance solubility and improve drug delivery.

3.2. Determination of Melting Point

The melting point of quercetin was determined using the open capillary tube method.

3.2.1. Discussion

The melting point of quercetin was found to be 316°C, which is in agreement with the Indian Pharmacopoeia (I.P.) specification. This high melting point indicates good thermal stability, which is advantageous during formulation processing and storage.

3.3. Calibration Curve of Quercetin

A calibration curve of quercetin was constructed by plotting absorbance against concentration (µg/mL) using a UV–Visible spectrophotometer.

3.3.1. Discussion

The calibration curve showed good linearity within the tested concentration range, with the regression equation:

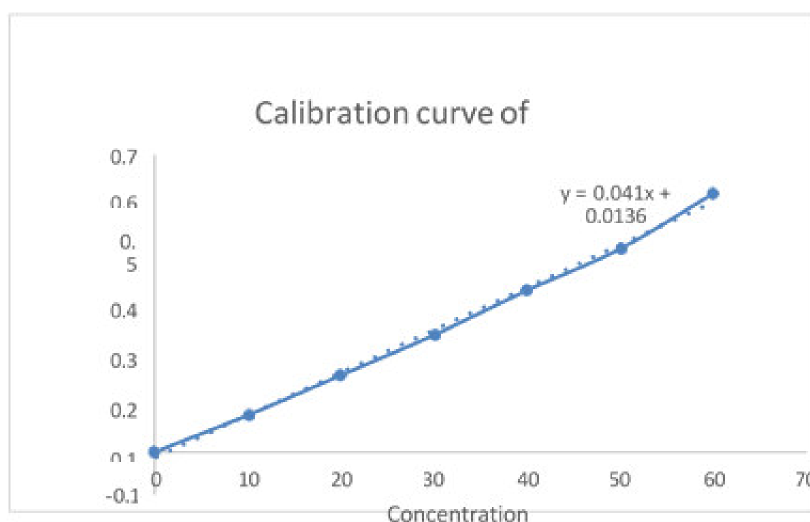
$$y = 0.041x + 0.0136$$

and a correlation coefficient ($R^2 = 0.9968$). The high R^2 value indicates excellent linearity and reliability of the analytical method for determining quercetin concentration in the formulation (Table 5, Fig. 2).

The IC_{50} value, representing the concentration required to inhibit 50% of DPPH radicals, was determined from the plot of percentage inhibition versus concentration.

Table 6. *Concentration versus Absorbance Data for Quercetin Calibration Curve*

Concentration (μg/mL)	Absorbance
0	0
10	0.097
20	0.181
30	0.276
40	0.381
50	0.479
60	0.609



3.4. Compatibility Studies (FT-IR Analysis)

Fourier Transform Infrared (FT-IR) spectroscopy was performed to investigate the compatibility between quercetin and the excipients used in the formulation. The spectra of pure quercetin and its physical mixtures with excipients were recorded using an FT-IR spectrophotometer (Shimadzu 160A) in the range of 4000–400 cm^{-1}. The obtained spectra were analyzed to identify the characteristic functional groups of the drug and to detect any possible interactions between the drug and excipients.

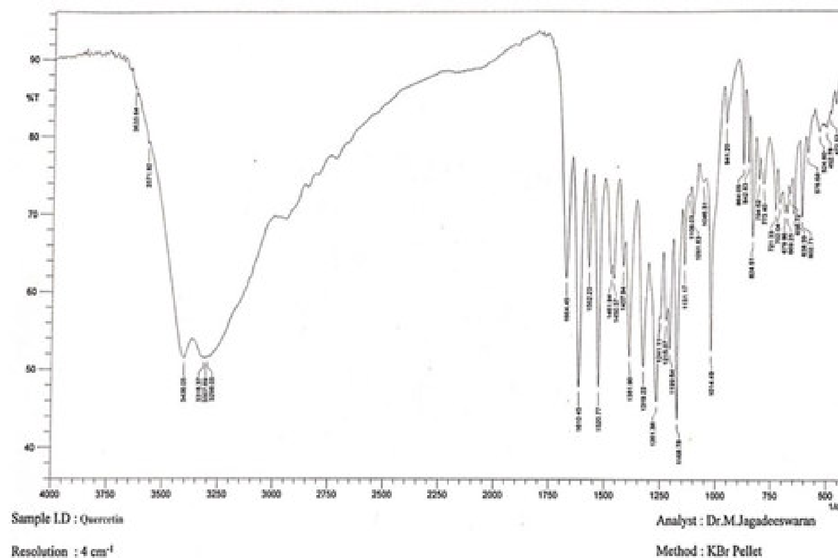
The FT-IR spectra of quercetin, soya lecithin, Carbopol 934, menthol and glycerol are presented in Figures 5(a)–5(l), and the corresponding spectral interpretations are shown in Tables 9–20. A comparative analysis of the spectral peaks of quercetin with those of the drug–excipient mixtures is presented in Table 21.

The FT-IR spectrum of quercetin showed characteristic absorption peaks at 3408 and 3292 cm^{-1} corresponding to O–H stretching of phenolic hydroxyl groups, 1660–1640 cm^{-1} for C=O stretching of the conjugated carbonyl group, and 1600 and 1510 cm^{-1} representing aromatic C=C stretching vibrations. Additional peaks observed at 1360–1380 cm^{-1} correspond to C–H bending, while peaks at 1240–1270 cm^{-1} indicate C–O stretching of phenolic ether groups.

Similarly, the FT-IR spectra of the excipients showed their characteristic functional groups. Soya lecithin exhibited peaks corresponding to aliphatic C–H stretching (2920–2850 cm^{-1}), ester carbonyl (1735 cm^{-1}) and phosphate group vibrations (1240–1230 cm^{-1}). Menthol displayed characteristic O–H stretching and C–O vibrations, while Carbopol 934 showed prominent peaks for O–H stretching and C=O stretching of carboxylic groups.

The comparison of FT-IR spectra of pure quercetin and the drug–excipient mixtures indicated no significant shifts or disappearance of characteristic peaks, suggesting the absence of chemical interaction between quercetin and

the selected excipients. These results confirm the compatibility of the drug with formulation components, indicating their suitability for the preparation of quercetin-loaded invasomal gel.



4. FTIR SPECTRUM OF QUERCETIN

Wavenumber (cm⁻¹)	Functional Group / Vibration	Interpretation
3408 & 3292	O–H stretching (phenolic hydroxyl groups)	Strong, broad peaks due to hydrogen bonding
1660–1640	C=O stretching (carbonyl group in ketone)	Sharp peak indicating conjugated ketone
1600 & 1510	C=C stretching (aromatic ring)	Indicates aromatic structure
1360–1380	C–H bending (methyl groups)	Typical of flavonoid skeleton
1240–1270	C–O stretching (ether linkage)	Suggests presence of phenolic ethers
1020–1100	C–O–C stretching (glycosidic linkage if present)	May appear in glycosylated derivatives

4.1. Evaluation of Quercetin Invasomal Gel Formulations

4.1.1. Organoleptic Properties

The prepared quercetin invasomal gel formulations (F1–F7) were evaluated for appearance, color, odor, consistency, homogeneity, oily feel, stickiness, grittiness and phase separation. The results are presented in Table X.

Table X. *Organoleptic properties of quercetin invasomal gel formulations*

S. No	Organoleptic Properties	F1	F2	F3	F4	F5	F6	F7
1	Appearance	Liquid	Liquid	Gel	Gel	Gel	Gel	Gel
2	Colour	Yellowish translucent	Yellowish translucent	Yellowish translucent	Yellowish translucent	Yellowish translucent	Yellowish translucent	Yellowish translucent
3	Odor	Pleasant	Pleasant	Pleasant	Pleasant	Pleasant	Pleasant	Pleasant
4	Consistency	Good	Good	Good	Good	Good	Good	Good
5	Homogeneity	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6	Oily feel	No	No	No	No	No	No	No
7	Stickiness	No	No	No	No	No	No	No
8	Grittiness	No	No	No	No	No	No	No

9	Phase separation	NP	NP	NP	NP	NP	NP	NP

The organoleptic evaluation showed that F1 and F2 remained in liquid form, whereas formulations F3–F7 formed stable gel structures due to the increased concentration of Carbopol 934. All gel formulations exhibited yellowish translucent appearance, pleasant odor, good consistency and homogeneity, with no oily feel, stickiness, grittiness or phase separation, indicating acceptable physical characteristics for topical application

Formulation code	Viscosity (cps)
F1	13,100
F2	13,880
F3	17,120
F4	13,260
F5	11,580
F6	14,720
F7	13,580

4.2. Determination of Viscosity

The viscosity of the quercetin invasomal gel formulations ranged from 11,580 to 17,120 cps. Among the formulations, F3 exhibited the highest viscosity (17,120 cps), while F5 showed the lowest viscosity (11,580 cps). The increase in viscosity can be attributed to the variation in Carbopol 934 concentration in the formulations.

An appropriate viscosity is essential for topical formulations to ensure good spreadability, improved residence time on the skin and controlled drug release. Higher viscosity may enhance drug retention at the application site; however, excessively viscous formulations may reduce spreadability and patient acceptability. Among the prepared formulations, F3 demonstrated suitable viscosity with good consistency, indicating its potential suitability for topical application. Further evaluation such as spreadability and in-vitro drug release studies is required to confirm the optimal formulation.

5. SPREADABILITY

Formulation Code	Spreadability (cm) (Mean ± SD)
F1	12.37 ± 1.329
F2	13.01 ± 0.170
F3	11.63 ± 1.204
F4	11.24 ± 0.788
F5	10.75 ± 2.941
F6	10.81 ± 0.563
F7	9.08 ± 0.229

The spreadability of the quercetin invasomal gel formulations (F1–F7) was evaluated to determine their ease of application on the skin surface. Spreadability is an important parameter for topical formulations as it influences uniform drug distribution, patient compliance and therapeutic effectiveness. The results (Table 5.15) showed that the spreadability values ranged from 9.08 ± 0.229 to 13.01 ± 0.170 cm.

Among the formulations, F2 exhibited the highest spreadability (13.01 ± 0.170 cm), indicating better ease of spreading and smooth application on the skin. Formulations F1 (12.37 ± 1.329 cm) and F3 (11.63 ± 1.204 cm) also demonstrated good spreadability, suggesting suitable consistency for topical use. In contrast, F7 showed the lowest spreadability (9.08 ± 0.229 cm), which may be attributed to increased gel viscosity due to higher polymer concentration.

Overall, formulations F2, F1 and F3 demonstrated favorable spreadability characteristics, indicating better suitability for topical application.

6. DRUG CONTENT

Formulation Code	Drug content (%)
F1	97.22%
F2	92.53%
F3	95.36%
F4	94.71%
F5	99.01%
F6	93.45%

F7	96.93%

The drug content of all quercetin invasomal gel formulations was found to be within the range of 90–100%, indicating adequate and uniform distribution of the drug in the gel matrix. According to pharmacopeial standards, the acceptable drug content range for topical formulations is 90–110% of the labeled amount.

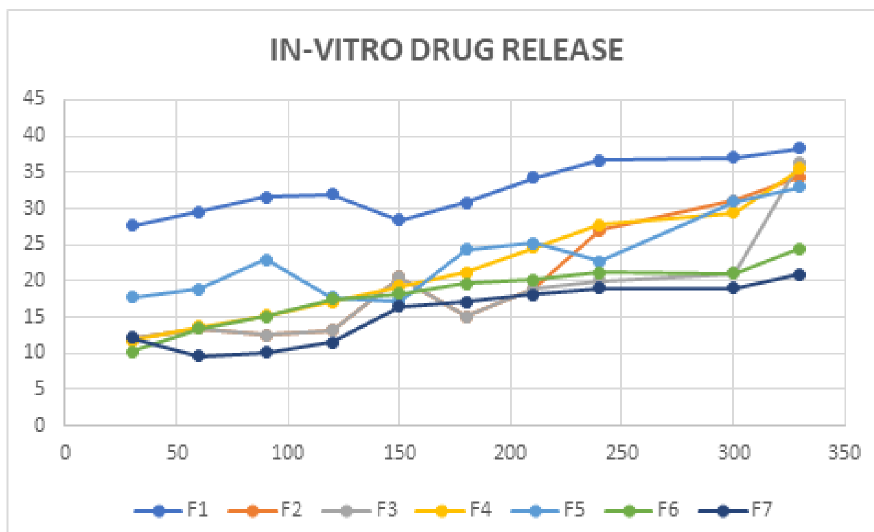
Therefore, all formulations complied with the specified limits, confirming the accuracy of the formulation process and uniform incorporation of quercetin in the prepared invasomal gel.

7. CENTRIFUGATION TEST FOR QUERCETIN INVASOME GEL

Formulation code	Phase separation		
	1st time	2nd time	3rd time
F1	Phase separation	Phase separation	Phase separation
F2	NPS	NPS	NPS
F3	NPS	NPS	NPS
F4	NPS	NPS	NPS
F5	NPS	NPS	NPS
F6	NPS	NPS	NPS
F7	NPS	NPS	NPS

The centrifugation test was performed to evaluate the physical stability of the quercetin invasomal gel formulations under stress conditions. The results indicated that formulation F1 exhibited phase separation, suggesting possible instability of the system or insufficient homogenization during formulation.

In contrast, formulations F2–F7 showed no phase separation, indicating good physical stability and uniformity of the gel matrix. The absence of phase separation under centrifugation suggests that these formulations are stable and capable of maintaining their integrity during storage and application.



The in-vitro release of quercetin from invasomal gel formulations (F1–F7) across a PVDF membrane (20–80 nm pore size) was evaluated for 330 minutes. The results (Table 5.17; Fig.

TIME (mins)	F1	F2	F3	F4	F5	F6	F7
30	27.6	12.04	12.04	11.76	17.7	10.2	12.11
60	29.6	13.4	13.4	13.63	18.9	13.42	9.62
90	31.6	12.58	12.58	15.23	23	15.03	10.18
120	32	13.13	13.13	17.1	17.7	17.44	11.56
150	28.4	20.52	20.52	19.24	17.2	18.25	16.51
180	30.8	15.05	15.05	21.11	24.4	19.59	17.06
210	34.3	18.88	18.88	24.59	25.2	20.13	18.16
240	36.7	26.97	19.97	27.8	22.7	21.2	18.98
300	37.1	31.07	21.07	29.4	30.9	21.06	18.98
330	38.3	34.37	36.39	35.55	33	24.42	20.91

5.9) showed notable differences in the release profiles among the formulations, indicating that the composition of invasomes and the gel matrix significantly influenced drug diffusion.

Among the formulations, F1 exhibited the highest cumulative drug release (38.3% at 330 min), suggesting efficient drug diffusion from the invasomal system. This enhanced release may be attributed to an optimized phospholipid–terpene ratio, which increases vesicle fluidity and promotes drug permeation across the membrane.

Formulations F3 (36.39%) and F4 (35.55%) also demonstrated relatively high drug release, indicating favorable vesicle characteristics and suitable gel consistency for sustained drug diffusion. F2 (34.37%) and F5 (33.0%) showed moderate release profiles, suggesting balanced drug entrapment and controlled release behavior.

In contrast, F6 (24.42%) and F7 (20.91%) exhibited comparatively lower drug release, which may be due to higher gel viscosity or denser vesicle packing, restricting drug diffusion through the membrane.

Overall, the drug release trend was observed as: F1 > F3 > F4 > F2 > F5 > F6 > F7.

The sustained release pattern observed for the formulations indicates their potential suitability for topical drug delivery systems, where prolonged drug release may enhance therapeutic effectiveness and reduce the frequency of application.

8. Dpph Radical Scavenging Activity Of Quercetin And Quercetin Invasome Gel

Concentration (µg/mL)	% Inhibition (Quercetin Standard)	% Inhibition (Invasome Gel)
10	21.6 ± 0.9	15.3 ± 1.2
20	38.9 ± 1.3	28.4 ± 1.0
40	57.2 ± 1.1	45.7 ± 0.8
60	72.3 ± 1.5	61.8 ± 1.4
80	85.1 ± 0.7	76.3 ± 1.1
100	91.5 ± 0.5	83.9 ± 0.9

IC_{50} Values

The IC_{50} (concentration required to scavenge 50% of DPPH radicals) was determined by plotting the % inhibition versus concentration for both samples using linear regression.

- **Quercetin standard: IC_{50} = 34.2 µg/mL**
- **Quercetin invasome gel: IC_{50} = 42.8 µg/mL**

9. DISCUSSION

The DPPH assay results revealed that the quercetin invasome gel exhibited notable antioxidant activity, although slightly lower than the pure quercetin standard. The difference is expected due to the encapsulation of quercetin within the invasomal structure, which may slightly delay its interaction with the DPPH radicals.

However, the gel still demonstrated strong radical scavenging capacity, with over 83% inhibition at 100 µg/mL, indicating that the formulation retains the functional antioxidant property of quercetin. The slightly higher IC_{50} value of the invasome gel (42.8 µg/mL) compared to pure quercetin (34.2 µg/mL) may be attributed to the controlled release behavior of the invasome system.

These findings suggest that the invasome gel formulation effectively maintains the antioxidant potential of quercetin while possibly offering additional benefits such as enhanced skin permeation and stability.

10. CONCLUSION

The present study successfully demonstrated the development and evaluation of a quercetin-loaded invasomal gel formulation as an effective topical drug delivery system. Quercetin is well known for its significant antioxidant, anti-inflammatory and therapeutic properties, but its practical application is often limited due to poor aqueous solubility, low bioavailability and restricted permeability across biological membranes. These limitations make it difficult to achieve adequate drug concentrations at the desired site of action when using conventional formulations. Therefore, the use of advanced vesicular carriers such as invasomes offers a promising strategy to overcome these challenges and enhance dermal drug delivery.

In this research, quercetin-loaded invasomes were successfully prepared using the thin-film hydration technique and subsequently incorporated into a Carbopol-based hydrogel system to obtain a stable and patient-friendly topical dosage form. The developed invasomal gel formulations were subjected to comprehensive evaluation including organoleptic properties, viscosity, spreadability, drug content, centrifugation stability and in-vitro drug

release studies. The results indicated that the prepared formulations possessed good physical stability, uniform drug distribution and desirable rheological characteristics, which are essential for topical applications.

Among the developed formulations, the optimized invasomal gel showed enhanced drug release, suitable viscosity and good spreadability, ensuring ease of application and better patient compliance. The presence of ethanol and terpene components in the invasomal system played a crucial role in improving vesicle deformability and facilitating the penetration of quercetin through the skin barrier. This enhanced permeation ability is expected to improve the therapeutic effectiveness of quercetin when applied topically.

The in-vitro drug release studies further confirmed that the invasomal gel formulation provided a controlled and sustained release pattern, which is beneficial for maintaining prolonged drug availability at the site of application. Additionally, the formulation exhibited good physical stability without phase separation, indicating the robustness and reliability of the developed system.

Overall, the findings of this study suggest that invasome-based gel formulations represent a promising and effective approach for the topical delivery of poorly soluble phytoconstituents such as quercetin. The developed formulation combines the therapeutic advantages of quercetin with the penetration-enhancing properties of invasomes, thereby improving drug delivery through the skin. Furthermore, the preparation method used in this study is simple, cost-effective and reproducible, making it suitable for potential scale-up and further pharmaceutical development.

Therefore, quercetin-loaded invasomal gel can be considered a potential topical formulation for the management of oxidative stress-related skin disorders, inflammatory conditions and other dermatological applications. The outcomes of this research provide a valuable foundation for future studies focusing on advanced vesicular drug delivery systems and their applications in topical therapy.

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