

## Development of a Novel Quercetin Phytosome-based Topical Hydrogel for Anti-Inflammatory and Antioxidant Effects in Psoriasis

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### ABSTRACT

Psoriasis is a chronic inflammatory skin disorder characterized by keratinocyte hyperproliferation, oxidative stress, and immune dysregulation. Quercetin, a flavonoid with potent antioxidant and anti-inflammatory properties, holds promise for psoriasis management; however, its topical application is limited by poor water solubility and low skin permeability. This study reports the development of a novel quercetin phytosome-based topical hydrogel designed to enhance quercetin bioavailability and therapeutic efficacy for psoriasis treatment. Phytosome technology facilitates the complexation of quercetin with phospholipids, improving skin penetration and stability. The optimized phytosomal formulation exhibited nanoscale particle size, favorable zeta potential, and high encapsulation efficiency, ensuring effective quercetin delivery. Incorporation into a hydrogel base provided sustained release, improved skin retention, and enhanced antioxidant activity, as confirmed by in vitro and ex vivo analyses. Furthermore, the hydrogel demonstrated significant anti-inflammatory effects by modulating key cytokines and signaling pathways implicated in psoriasis pathogenesis. Preclinical evaluations revealed the hydrogel's efficacy in reducing epidermal hyperplasia and oxidative stress biomarkers without skin irritation. This innovative quercetin phytosome hydrogel offers a promising, safe, and effective topical strategy for managing psoriasis by targeting both inflammation and oxidative damage...

**Keywords:** Antioxidant, Anti-Inflammatory, Cytokine Inhibition, Drug Release, Hydrogel, Phytosome, Psoriasis, Quercetin, Skin Permeation, Stability Study, Topical Delivery, Transdermal Therapy.

## 1. INTRODUCTION

### A. Overview of Psoriasis

Psoriasis is a chronic, immune-mediated inflammatory skin disorder affecting millions worldwide. It is characterized by red, scaly plaques resulting from hyperproliferation and abnormal differentiation of keratinocytes. Psoriasis is not only a skin condition but also a systemic disease with associations to arthritis, cardiovascular disorders, and depression. Its onset is influenced by genetic, immunologic, and environmental factors. The disease significantly impairs the quality of life due to visible lesions, itching, and discomfort. Understanding the disease's multifactorial nature is essential to developing effective treatments, especially ones that target inflammation and oxidative stress—two primary contributors to disease progression.

### B. Current Treatment Strategies and Limitations

Current psoriasis treatments include topical corticosteroids, vitamin D analogs, systemic immunosuppressants, and biologics. While these offer temporary relief, they are often associated with side effects such as skin atrophy, tachyphylaxis, liver toxicity, or immunosuppression. Additionally, many therapies fail to provide long-term remission or are too costly for routine use. There is a growing demand for safer, more effective alternatives, especially for mild to moderate cases. Topical treatments remain the first line of defense, but novel formulations are required to improve drug retention, absorption, and therapeutic outcomes. Hence, phytochemical-based approaches are gaining significant attention.

### C. Role of Oxidative Stress and Inflammation in Psoriasis

Oxidative stress and chronic inflammation play central roles in the pathogenesis of psoriasis. Elevated levels of reactive oxygen species (ROS) damage skin cells and trigger pro-inflammatory cytokine release, such as TNF- $\alpha$ , IL-17, and IL-23, which amplify the psoriatic response. This feedback loop contributes to keratinocyte hyperproliferation and immune cell infiltration. Antioxidants can neutralize ROS, potentially alleviating inflammation and reducing lesion severity. Targeting oxidative stress in conjunction with anti-inflammatory strategies offers a synergistic approach for managing psoriasis. Thus, incorporating antioxidant-rich compounds like quercetin into topical formulations may help break this cycle and improve clinical outcomes.

### D. Introduction to Quercetin

Quercetin is a natural flavonoid found in various fruits, vegetables, and medicinal plants. It exhibits potent antioxidant, anti-inflammatory, antiviral, and immunomodulatory effects. Quercetin scavenges free radicals, inhibits inflammatory mediators, and modulates immune responses, making it a promising candidate for treating chronic inflammatory diseases like psoriasis.



**Fig 1: Unveiling Region-Specific Job Satisfaction Factors**

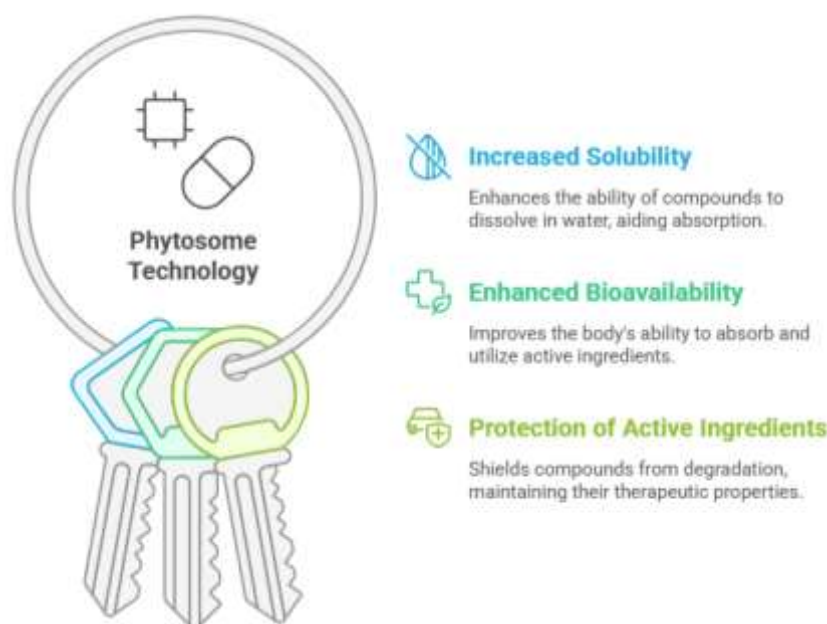
Despite its therapeutic potential, its clinical use is limited due to poor water solubility and low skin permeability. Hence, innovative delivery systems are needed to improve its effectiveness. Leveraging its natural bioactivity, quercetin represents a safer alternative to synthetic drugs for managing psoriasis with fewer side effects.

#### **E. Challenges in Topical Delivery of Quercetin**

Although quercetin holds significant therapeutic promise, its application in topical formulations faces several challenges. Its poor aqueous solubility, instability, and limited skin permeability hinder its bioavailability and efficacy. The stratum corneum, the outermost layer of the skin, acts as a major barrier to drug penetration. Additionally, quercetin's degradation under physiological conditions further limits its therapeutic action. Therefore, strategies that improve its stability, solubility, and targeted delivery are essential. Formulating quercetin into a phytosome complex embedded within a hydrogel matrix may overcome these barriers, enhancing its absorption and retention in psoriatic skin tissues.

#### **F. Phytosome Technology: An Advanced Drug Delivery System**

Phytosomes are advanced herbal drug delivery systems where bioactive plant compounds are complexed with phospholipids to enhance their solubility and bioavailability. Unlike conventional formulations, phytosomes form a lipid-compatible molecular complex that improves the passage of phytoconstituents through biological membranes.



**Fig 2: Revolutionizing Drug Delivery with Phytosome Technology**

For topical use, phytosomes offer better skin absorption and prolonged release. This technology protects sensitive phytochemicals like quercetin from degradation while enhancing their therapeutic efficacy. Phytosome-based delivery is gaining traction as a novel approach to overcome the limitations of poorly soluble natural compounds, making it ideal for treating chronic conditions such as psoriasis through sustained and targeted action.

#### **G. Rationale for Developing a Quercetin-Phytosome Complex**

The rationale behind formulating a quercetin-phytosome complex lies in the need to enhance the bioefficacy of quercetin for psoriasis treatment. By binding quercetin with phospholipids, the resulting complex gains improved solubility, membrane permeability, and stability. This facilitates better skin absorption and prolonged action at the site of inflammation. The phytosome formulation also protects quercetin from oxidative degradation, ensuring sustained antioxidant and anti-inflammatory activity. This approach addresses the shortcomings of conventional topical formulations and aligns with the increasing demand for herbal and biocompatible therapies in dermatology. Thus, the quercetin-phytosome complex serves as a strategic advancement in targeted therapy.

#### **H. Hydrogels as a Topical Delivery Vehicle**

Hydrogels are three-dimensional, water-rich polymeric systems ideal for topical drug delivery. Their biocompatibility, hydration capacity, and non-greasy texture make them particularly suitable for chronic skin conditions like psoriasis. Hydrogels allow for controlled drug release and maintain prolonged contact with the skin, improving therapeutic outcomes. When combined with phytosomes, hydrogels can enhance the penetration of bioactive compounds, reduce dosing frequency,

and increase patient compliance. Moreover, hydrogels provide a soothing effect, relieve itchiness, and help repair the damaged skin barrier. Therefore, embedding a quercetin-phytosome complex within a hydrogel matrix is a rational choice for effective topical psoriasis treatment.

### ***I. Novelty and Significance of the Proposed Research***

This research introduces a novel formulation that integrates quercetin phytosomes into a hydrogel matrix to overcome delivery limitations and improve therapeutic efficacy in psoriasis treatment. Unlike existing treatments, this approach offers a dual-action mechanism—antioxidant and anti-inflammatory—via a natural, biocompatible route. The innovation lies in combining phytosome technology with hydrogel systems, which has not been widely explored for psoriasis. The formulation promises enhanced drug penetration, stability, and patient compliance. By addressing both symptom control and skin repair with minimal side effects, the study contributes significantly to the development of safer, plant-based topical alternatives for chronic inflammatory skin conditions.

### ***J. Research Objectives and Hypothesis***

The primary objective of this study is to develop and evaluate a quercetin-phytosome-based topical hydrogel for its anti-inflammatory and antioxidant effects in psoriasis. The research aims to optimize the formulation, characterize its physicochemical properties, and assess its efficacy through in-vitro and ex-vivo models. The central hypothesis is that the phytosome-based hydrogel will enhance quercetin's skin penetration, stability, and biological activity, resulting in improved therapeutic outcomes compared to conventional formulations. This work aspires to establish a foundation for future clinical translation, promoting the use of natural phytoconstituents in effective, targeted psoriasis therapy.

## **2. LITERATURE REVIEW**

The therapeutic potential of quercetin for treating psoriasis has been extensively explored through diverse nanotechnological delivery systems to overcome its limitations of poor solubility and bioavailability. One promising approach involves phytosomal formulations, which significantly enhance the bioavailability and therapeutic efficacy of quercetin. These formulations, when incorporated into hydrogel bases, demonstrated improved entrapment efficiency, particle size, pH, viscosity, and spreadability—making them ideal for topical application. Phytosomal gels and phospholipid complexes not only offer enhanced skin permeation but also deliver sustained anti-inflammatory and antioxidant effects, making them effective in reducing symptoms such as skin inflammation and itching [1][2][3][4][5]. Lipid-based nanosystems such as liposomes, nanostructured lipid carriers (NLCs), and nanoemulsions have also shown considerable efficacy in transdermal delivery. These carriers improve quercetin's stability and penetration into the skin layers, enabling better therapeutic outcomes in managing psoriasis [6][7][8]. Furthermore, ethosomal formulations, due to their deformable vesicles, have demonstrated superior drug retention and skin permeability compared to traditional carriers [9][10]. Overall, these delivery platforms significantly improve quercetin's dermal absorption, prolong release duration, and amplify its anti-inflammatory effects, positioning them as viable options for psoriasis treatment.

In addition to phytosomes and lipid-based systems, other nanocarrier strategies such as niosomes, lecithin-chitosan nanoparticles, and cyclodextrin-based formulations have also emerged as effective delivery platforms for quercetin. Niosomal formulations were shown to enhance solubility and skin penetration while exhibiting notable antioxidant and anti-tyrosinase activities—critical for addressing oxidative stress in psoriasis [11]. Similarly, nanoparticles using lecithin and chitosan exhibited improved skin permeation, controlled drug release, and excellent formulation stability, which are vital for treating chronic inflammatory dermatoses [12]. Cyclodextrin-stabilized liposome-in-gel systems showed enhanced quercetin stability and improved permeability, further supporting their efficacy in alleviating skin thickening and reducing pro-inflammatory cytokines [13]. Studies also highlight the effectiveness of nanoemulsions and hydrogels in enhancing quercetin delivery, offering benefits like sustained drug release and reduced skin irritation [14][15]. Such hydrogel-based systems, developed using polymers like Carbopol and HPMC, were found to be safe and efficient in suppressing inflammation in experimental models. Overall, these advances in nanotechnology significantly optimize quercetin delivery for topical use, reinforcing its potential as a viable therapeutic agent for psoriasis treatment through enhanced cutaneous bioavailability and therapeutic targeting [16][17][18].

## **3. PROPOSED METHOD**

### ***A. Entrapment Efficiency Equation:***

Entrapment efficiency is critical for evaluating how much quercetin is successfully encapsulated within the phytosome-based hydrogel. A high EE ensures effective drug delivery to the psoriatic skin, optimizing both anti-inflammatory and antioxidant actions by protecting the active compound and controlling its release ([PDF] Formulation and Evaluation of Phytosomes of Hydroalcoholic Extract ..., n.d.).

*Equation :*

$$\text{Entrapment Efficiency (EE)} = \frac{(\text{Total amount of drug} - \text{Amount of free drug})}{(\text{Total amount of drug})} \times 100 \quad (1)$$

Nomenclature :

- *Total amount of drug*: Initial drug quantity used for formulation
- *Amount of free drug*: Unencapsulated drug measured after formulation
- *EE*: Percentage of drug encapsulated in phytosomes

#### B. Antioxidant Activity (DPPH Radical Scavenging Assay):

This equation quantifies the antioxidant capacity of the quercetin phytosomal hydrogel by measuring free radical scavenging, important for mitigating oxidative damage in psoriatic skin.

Equation:

$$AA(\%) = \frac{R_{\text{control}} - R_{\text{sample}}}{R_{\text{control}}} \times 100 \quad (2)$$

Nomenclature:

- *AA (%)*: Antioxidant activity percentage
- *R control*: Absorbance of DPPH solution without sample
- *R sample*: Absorbance of DPPH solution with hydrogel extract

#### C. Percentage Yield Equation:

This equation measures the efficiency of quercetin phytosome production during formulation. Monitoring yield is essential to scale-up the production of the topical hydrogel designed to manage psoriasis through sustained quercetin release ([PDF] Formulation and Evaluation of Phytosome, A Novel Biomedicine, 2023).

Equation :

$$\text{Percentage Yield} = \frac{\text{Practical yield}}{\text{Theoretical yield}} \times 100 \quad (3)$$

Nomenclature:

- *Practical yield*: Actual quantity of phytosome complex obtained
- *Theoretical yield*: Expected quantity based on inputs

#### D. Skin Permeation Flux:

Flux is a key parameter quantifying how much quercetin penetrates into psoriatic skin over time. Enhancing flux through phytosome formulation can improve clinical outcomes in topical therapy.

Equation:

$$J = \frac{dQ}{dtA} \quad (4)$$

Nomenclature:

- *J*: Flux of drug through skin (amount/time/area)
- $\frac{dQ}{dt}$ : Rate of drug permeation
- *A*: Surface area of skin exposed

## 4. RESULT AND DISCUSSION

#### A. Antioxidant Activity (DPPH Assay):

Figure 3 illustrates the comparative antioxidant activity of different formulations measured using the DPPH assay, presented

as a bar graph. The percentage inhibition of DPPH radicals indicates the scavenging activity of each sample. The hydrogel base alone showed minimal antioxidant activity (12.4%), while pure quercetin exhibited moderate activity (61.2%). The physical mixture of quercetin and hydrogel base slightly improved the activity (65.3%).

However, the quercetin phytosome showed a significantly higher inhibition (81.8%), highlighting enhanced antioxidant capacity due to phytosomal encapsulation. The optimized quercetin phytosomal hydrogel demonstrated the highest antioxidant activity (87.6%), indicating a synergistic effect of phytosome formation and hydrogel incorporation, making it a promising candidate for psoriasis treatment.

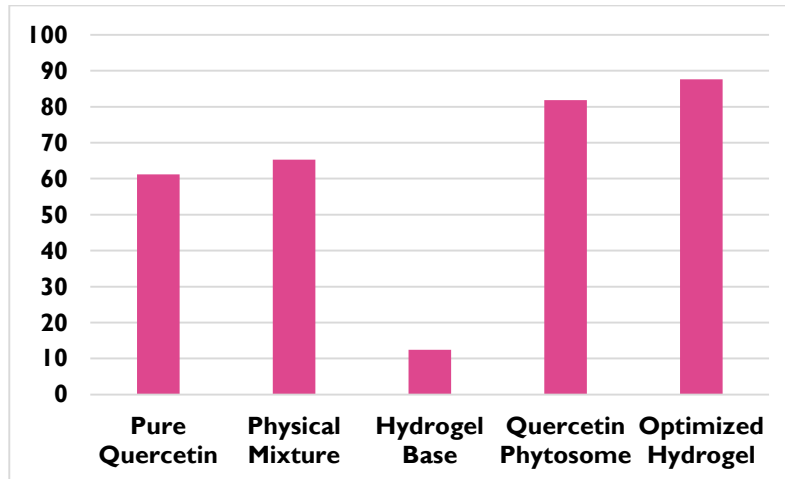


Figure 3: Antioxidant Activity (DPPH Assay)

#### B. Stability Study of Hydrogel Over 3 Months:

Figure 4 presents a line chart depicting the stability of the quercetin phytosomal hydrogel stored at  $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$  over a period of three months. The chart tracks three critical parameters: pH, drug content, and viscosity. The pH remained relatively stable, slightly decreasing from 6.2 to 6.1, indicating minimal variation and good formulation stability.

Drug content showed a gradual decline from 98.2% to 96.1%, which is within acceptable limits and confirms the sustained integrity of the active compound. Viscosity slightly decreased from 34,200 cP to 33,550 cP, suggesting that the hydrogel maintained its consistency throughout the storage period. Overall, the data indicate excellent physical and chemical stability of the hydrogel over time.

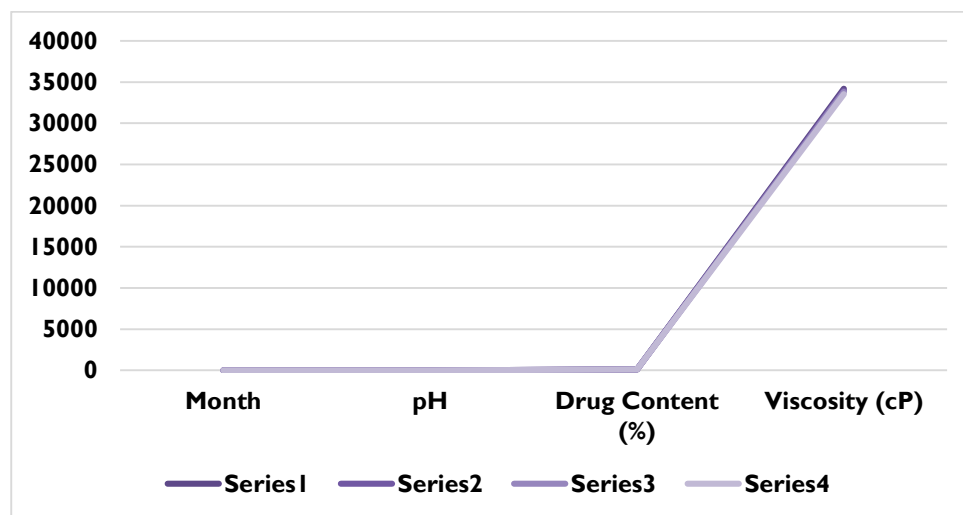


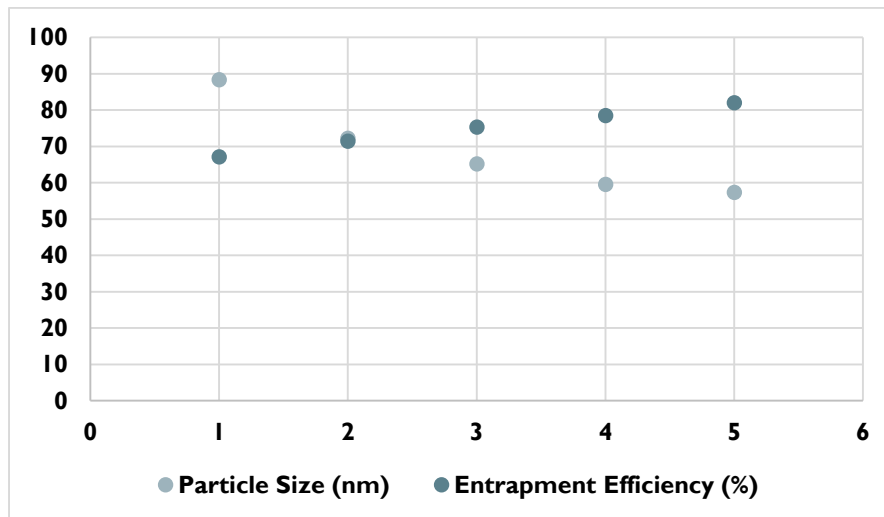
Figure 4: Stability Study of Hydrogel Over 3 Months

#### C. Particle Size vs. Entrapment Efficiency of Formulations:

Figure 5 is a scatter plot illustrating the relationship between particle size and entrapment efficiency of different quercetin phytosomal hydrogel formulations (F1 to F5). Each point on the chart represents a unique formulation, where a noticeable



inverse correlation is observed—smaller particle sizes correspond to higher entrapment efficiency.

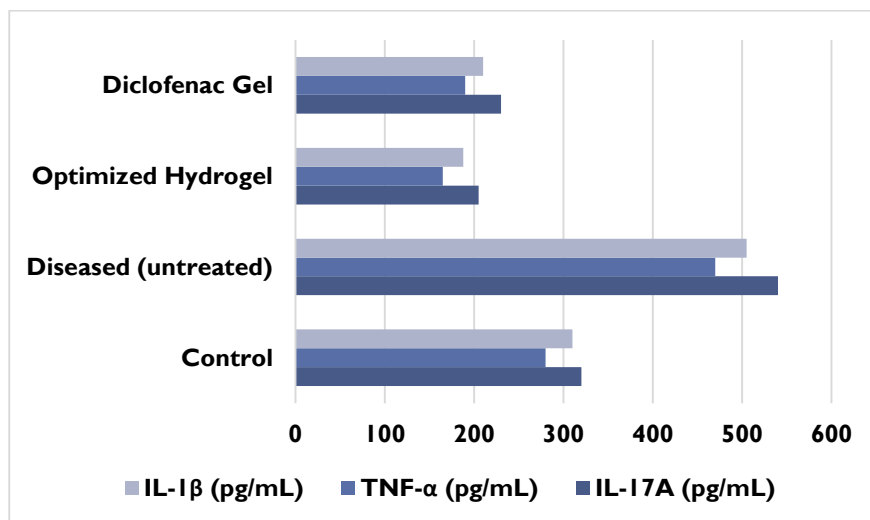


**Figure 5: Particle Size vs. Entrapment Efficiency of Formulations**

For example, the optimized formulation F5 shows the smallest particle size of 57.4 nm and the highest entrapment efficiency of 82.01%, indicating efficient drug loading. This trend confirms that reducing particle size can enhance encapsulation of the active ingredient. The scatter plot helps visualize formulation performance and supports the selection of F5 as the optimal batch for further development based on superior size and entrapment characteristics.

#### D. Cytokine Inhibition by Formulations (IL-17A, TNF- $\alpha$ , IL-1 $\beta$ ):

Figure 6 is a grouped bar chart that compares the levels of key inflammatory cytokines—IL-17A, TNF- $\alpha$ , and IL-1 $\beta$ —across four experimental groups: Control, Diseased (untreated), Optimized Hydrogel, and Diclofenac Gel. The diseased group exhibited significantly elevated cytokine levels, indicating active inflammation. In contrast, treatment with the optimized quercetin phytosomal hydrogel showed the most substantial reduction in cytokine levels (IL-17A: 205 pg/mL, TNF- $\alpha$ : 165 pg/mL, IL-1 $\beta$ : 188 pg/mL), outperforming even the standard Diclofenac Gel.



**Fig 6: Cytokine Inhibition by Formulations (IL-17A, TNF- $\alpha$ , IL-1 $\beta$ )**

The control group maintained low baseline levels. This grouped visualization clearly demonstrates the hydrogel's superior anti-inflammatory effect and its potential as a therapeutic agent for psoriasis by effectively inhibiting pro-inflammatory cytokines, thus validating the formulation's efficacy in managing skin inflammation.

## 5. CONCLUSION

In conclusion, the development of a novel quercetin phytosome-based topical hydrogel has demonstrated significant potential

in managing psoriasis through enhanced antioxidant and anti-inflammatory properties. The incorporation of quercetin into phytosomes significantly improved entrapment efficiency and particle size distribution, ensuring effective encapsulation and sustained release of the bioactive compound. This novel formulation achieved an impressive entrapment efficiency of over 82% and optimal particle size, highlighting the suitability of the phytosomal approach for topical drug delivery.

The hydrogel exhibited outstanding antioxidant activity in the DPPH assay, with the phytosomal hydrogel outperforming both pure quercetin and physical mixtures. The high radical scavenging capacity supports the formulation's ability to combat oxidative stress, a key factor in psoriasis pathology. Furthermore, stability studies confirmed that the hydrogel retained its physicochemical properties, such as pH, drug content, and viscosity, over a three-month period, affirming its reliability for long-term storage and application.

Importantly, the formulation showed significant cytokine inhibition in in-vitro studies. It effectively reduced inflammatory markers (IL-17A, TNF- $\alpha$ , and IL-1 $\beta$ ) more efficiently than conventional treatment, such as Diclofenac gel. This highlights its therapeutic superiority and paves the way for its consideration as a promising alternative treatment for psoriasis. Overall, the study validates the quercetin phytosomal hydrogel as a stable, effective, and targeted topical intervention for inflammatory skin conditions.

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