Journal of Medicinal Plants and By-products (2027) 3: 211– 215

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# Formulation and Characterization of an Herbal-based Topical Organogel

Maryam H. Alaayedi[1,2]*, Ashti MH. Saeed[3], Qasim Allawi Bader[4], Zahraa Mohammed Kadhim[5], Ihab Dahham Hammoodi[6], Mustafa Ghazi Alabbassi[7,8] and Hasanain Shakir Mahmood[9,10,11]

[1] *Department of Pharmaceutics, College of Pharmacy, Ahl Al Bayt University, Kerbala, Iraq*
[2] *Department of Pharmaceutics, College of Pharmacy, University of Kerbala, Kerbala, Iraq*
[3] *Department of Pharmaceutics, College of Pharmacy, Mustansiriyiah University, Baghdad, Iraq*
[4] *Assistant professor in pharmaceutics, College of Pharmacy, Al-Zahraa University for Women, Karbala, Iraq*
[5] *Department of Pharmaceutics, College of Pharmacy, University of Kerbala, Kerbala, Iraq*
6 *Al-Esraa University, College of Pharmacy, Department of Pharmaceutics, Baghdad, Iraq*
[7] *Department of Pharmacology and Toxicology, College of Pharmacy, University of Alkafeel, Najaf, Iraq*
[8] *ARCPMS, University of Alkafeel, Najaf, Iraq*
[9] *Department of Pharmaceutics, College of Pharmacy, University of Kerbala, Kerbala, Iraq*
[10] *Department of Pharmaceutics, College of Pharmacy, University of AlKafeel, Najaf, Iraq*
[11] *ARCPMS, University of Alkafeel, Najaf, Iraq*

**Article Info**

**Article Type**
Original Article

**Article History**
Received: 16 July 2026
Accepted: 18 August 2026
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***Corresponding author**

**Maryam Alaayedi**
Department of Pharmaceutics, College of Pharmacy, Ahl Al Bayt University, Kerbala, Iraq
Department of Pharmaceutics, College of Pharmacy, University of Kerbala, Kerbala, Iraq
mariamhussein@abu.edu.iq
maryam.h@uokerbala.edu.iq

**ABSTRACT**

Bioactive ingredients like Resveratrol (RTL) and Silymarin (SLM), found in natural skincare products, are highly sought after for their anti-inflammatory, skin-protective, and antioxidant properties. However, their poor aqueous solubility limits their effective topical application. Organogels offer a solution by immobilizing and releasing lipophilic compounds within a stable, viscoelastic, semisolid delivery system. This study focused on creating, characterizing, and evaluating RTL and SLM-loaded herbal topical organogels to optimize their skin dispersion and therapeutic availability. Eight organogel formulations (F1-F8) were developed using three phases: drug, oil, and water. Key excipients included soy lecithin (SL) as a permeation enhancer, isopropyl myristate (IPM) as an emollient, and pluronic F127 as a gel stabilizer. Polyethylene glycol (PEG 400) was investigated as a co-solvent and humectant, with SL concentrations ranging from 1% to 6% w/v. The organogels were assessed for gelation temperature, viscosity, drug content uniformity, pH compatibility, and the release of natural ingredients using a dialysis bag over 6 hours. All developed organogels were homogeneous and exhibited an appealing yellow color. They demonstrated physiological skin-compatible pH values (6.1–6.7) and excellent drug content uniformity (95.13%–99.17%). Viscosities ranged from 2943 to 3963 poise, and gelation temperatures from 23°C to 36°C. An increase in SL concentration enhanced matrix viscosity and gelation temperature but also delayed drug release. Conversely, PEG 400, acting as a co-solvent, improved both drug release and solubility. The PEG-free formulation (F3) released 32% of the active ingredients within 6 hours, whereas the optimized formulation (F5), containing PEG, released 90%. Overall, the organogel system demonstrated good physiological pH compatibility, desirable viscoelastic viscosity, and an excellent drug release profile, making it a highly promising method for topical administration in cosmetics and wound healing applications.

**Keywords**: Organogel, Pluronic, Resveratrol, Silymarin, Soya Lecithin

**How to cite this paper**
Alaayedi, M., M.H. Saeed, A., Allawi Bader, Q., Mohammed Kadhum, Z., Dahham Hammoodi, I., Ghazi Alabbassi, M., Shakir Mahmmod, H. Formulation and Characterization of an Herbal-Based Topical Organogel. Journal of Medicinal Plants and By-products, 2027;16 (3): 211- 215. doi: 10.22034/jmpb.2027.373585.2236

## INTRODUCTION

In recent years, natural skin care has surged in popularity as more individuals seek safer and more environmentally friendly alternatives to conventional products. Unlike traditional skin care, which often contains harsh chemicals and synthetic compounds, natural skin care products are formulated with plant-based ingredients. The benefits of natural skin care are numerous: it is less harmful, gentler, eco-friendly, sustainable, rich in nutrients and antioxidants, and ultimately better for long-term skin health [1, 2]. Resveratrol (RTL) is a non-flavonoid polyphenol presence in many vegetables and fruits, such as peanut sprouts and grapes. Its scientific name is trans-3, 4′, 5-trihydroxystilbene [3]. Dermatologists discuss the advantages of RTL and the reasons it's an excellent antibacterial element for skin protection [4]. RTL is lipophilic, meaning it dissolves more readily in fats or oils than in water. It has very low water solubility, ranging from 0.03 to 0.05 milligrams per milliliter (mg/mL). However, RTL is significantly more soluble in organic solvents such as ethanol (up to 50 mg/mL) and dimethyl sulfoxide (DMSO) (up to 16 mg/mL). This difference in solubility arises from RTL's molecular composition, which includes both hydrophilic (water-attracting) and lipophilic (fat-attracting) components. The lipophilic components primarily dictate its overall solubility profile [5, 6]. Silymarin (SLM), a potent natural extract from the milk thistle plant, is recognized for its robust anti-inflammatory and antioxidant properties. Its powerful antioxidant capabilities are particularly beneficial for protecting skin cells. The flavonoid components of SLM, notably silybin, silydianin, and silychristin, effectively scavenge reactive oxygen species (ROS) and mitigate oxidative stress, a primary contributor to UV-induced skin damage. This mechanism involves donating electrons to free radicals, thereby neutralizing them and preventing cellular harm. Beyond its antioxidant qualities, SLM also possesses significant anti-inflammatory capabilities. Exposure to UV radiation can stimulate the production of pro-inflammatory cytokines, leading to tissue damage and skin inflammation. SLM can modulate this inflammatory response by inhibiting the creation of these molecules, for instance, by suppressing the activation of NF-κB. This action helps to reduce skin irritation and redness [7]. Researches indicate that SLM's antioxidant activity and increased DNA repair might protect skin cells from UVB-induced sunburn and DNA damage. SLM alters the signaling pathways responsible for the skin's response to damage and inflammation. Collectively, these activities help protect the skin from external pressures and enhance its natural resilience, contributing to overall skin health [8, 9]. The medications may be administered topically in several forms, including ointments, emulsions, creams, hydrogels, gels, and organogels. Organogels are a promising class of topical drug delivery systems that have garnered significant interest due to their potential to enhance therapeutic efficiency by retaining the medication payload for sustained release [10]. They are semisolid, bicontinuous systems composed of a polar solvent and gelators immobilized within the accessible gaps of a three-dimensional network structure. These systems are divided into two types: physical and chemical. Chemical organogels are formed during the gelation process via covalent crosslinks. Physical organogels, in contrast, form through non-covalent cross-linking, relying on physical interactions and the self-assembly of organogelator molecules without the need for permanent cross-linking. The viscoelastic properties of physical organogels, including those that are microemulsion-gelatin-based, monostearate limonene, pluronic lecithin, eudragit, and sorbitan, should ideally be [11]. Numerous studies have shown how well organogels work for topical medication administration for wide range of purposes [12]. Soy lecithin (SL), pluronic F127, and isopropyl myristate (IPM) are common compounds in organogel formulations. SL, a naturally occurring mixture of phosphoric acid choline esters and fatty acid diglycerides, also acts as a penetration booster. IPM is a non-oleaginous emollient with high spreading ability. Pluronic F127 stabilizes the organogel formation process and strengthens the gel network [13]. The present study will use SL, IPM, and Pluronic F127 for organogel formation and examine the impact of PEG 400 on the organogel. By delivering these natural products to the skin, RTL and SLM topical organogel may use in skincare routine for their wide range benefits.

## MATERIALS AND METHODS

### Materials

Soy lecithin, Silymarin (SLM) and Resveratrol (RTL) were purchased from Bidepharm Technology in China. Sorbic acid (SA) and PEG 400 were provided by Baoji Guokang Bio-Technology CO., Ltd., China. Isopropyl myristate (IPM) was obtained from ACMEC, a Chinese biochemical company. Potassium sorbate (PS) was purchased from Hwnan GP Chemical Co., Ltd., China, and Pluronic F127 was purchased from BASF, Germany.

### Methods

#### Preparation of Pluronic SL Organogel

RTL and SLM organogels were produced through a three-phase process: the drug phase, the aqueous phase, and the oil phase. The ingredients for the organogel formulas are detailed in Table 1. The oil phase was prepared by dissolving SL in IPM, which functioned as an emulsifying, dispersing, and stabilizing agent. This mixture was left to stand overnight to ensure complete dissolution of the SL, after which SA was added as a preservative. For the aqueous phase, PS and pluronic were solubilized in water, leading to gel formation. The resulting dispersion was then cooled to 2-4°C to ensure complete dissolution of Pluronic F127. During the drug phase preparation, RTL and SLM were dissolved in PEG 400, which served as a humectant and cosolvent. This drug solution was then incorporated into the oil phase (SL-IPM solution). Finally, the aqueous phase was gradually incorporated into the oil phase using a mechanical stirrer at 400 rpm [14].

**Table 1** The RTL and SLM organogel formulations.

| Formula code | Component (w/v%) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Natural Products Phase | | Oilly phase | | | Aqueous phase | | |
| | RTL and SLM | PEG 400 | SL | Sorbic acid | IPM | Poloxamer 407 | Potassium sorbate | Water |
| F1 | 1 of each | - | 1 | 0.3 | 30 | 30 | 0.3 | QS |
| F2 | 1 of each | - | 2 | 0.3 | 30 | 30 | 0.3 | QS |
| F3 | 1 of each | - | 3 | 0.3 | 30 | 30 | 0.3 | QS |
| F4 | 1 of each | - | 4 | 0.3 | 30 | 30 | 0.3 | QS |
| F5 | 1 of each | 4 | 3 | 0.3 | 30 | 30 | 0.3 | QS |
| F6 | 1 of each | 4 | 4 | 0.3 | 30 | 30 | 0.3 | QS |
| F7 | 1 of each | 4 | 5 | 0.3 | 30 | 30 | 0.3 | QS |
| F8 | 1 of each | 4 | 6 | 0.3 | 30 | 30 | 0.3 | QS |

QS: Sufficient Quantity

## Evaluation of RTL and SLM Organogel

### *Determination of Gelation Temperature*

A 0.25 g sample of organogel from each formulation was placed in a test tube, which was then put into a water bath at 2 °C. The temperature of the bath was increased by 5 °C every hour until it reached 50 °C. At each specified temperature, the tube was tilted 90 °, and the meniscus was assessed. The sol-gel transition was considered to occur when the contents of the tube stabilized without inclining; this temperature was recorded as the "gelation temperature." [15, 16].

### *Viscosity Measuring*

The Atago viscometer (Atago, Japan) was utilized to assess the formulation viscosity, the process of measuring was maintained at 25°C. All formulations underwent viscosity measurement tests with spindle number 6 [17].

### *pH Measurement*

All formulas were evaluated for its pH utilzing a Hanna pH meter (Hanna, India) [18].

### *Drug Content*

This study was performed by dissolving 0.5g of each formula in 50mL of ethanol and agitating the mixture for 60 minutes to ensure complete dissolution of the medication. The resulting solution was then filtered using 0.45 µm syringe filters. The filtered solutions were analyzed spectrophotometrically for RTL and SLM using a standard curve established at 306 nm and 286 nm, respectively [19-21].

### *In Vitro Release Study of the Gel*

This study utilized a type II dissolution apparatus to investigate drug release from various formulations. One gram of each formulation was placed into a 12,000-14,000 Da dialysis bag, which was then immersed in a dissolution vessel containing 200 mL of phosphate buffer (pH 6.8) maintained at 37°C. The investigation spanned 6 hours, with 3 mL samples extracted at predetermined intervals (15, 30, 45, 60, 90, 120, 180, 240, 300, and 360 minutes). To maintain sink conditions, an equivalent volume of fresh buffer was added after each sample removal. The collected samples were analyzed using a spectrophotometer at the UV lambda max for RTL and SLM [22].

## Statistical Analysis

Significance was evaluated using a one-way ANOVA, with a difference considered significance at $p<0.05$.

## RESULTS AND DISCUSSION

## Organogel Evaluation

### *Gelation Temperature*

The gelation temperature of the organogel formulas, displayed in Table 2, ranged from 23 to 36°C. It was observed that the gelation temperature increased with a higher proportion of SL, from F1 to F4. This is because an elevated SL concentration creates a thick matrix with robust linkages, requiring more energy to disrupt the structure and form the organogel.

Formulas containing PEG 400 (F5 and F6) exhibited a higher gelation temperature compared to those without PEG 400 but with the same SL percentage (F3 and F4). This rise in temperature can be attributed to the strong hydrogen bonding between PEG 400 and SL, which demands greater energy and temperature to break the SL bonds and produce the organogel [12].

### *Viscosity*

The viscosity of an organogel formulation is critical, as it directly impacts its spreadability, flow characteristics, patient adherence, and drug release. The organogel formulations tested exhibited viscosities ranging from 2943 to 3963 poise (Table 2). This viscosity test was conducted at a constant shear rate and temperature (37°C), which indicated the non-Newtonian characteristics of the gels. The viscosity of the formulation increased with higher concentrations of SL, likely due to the formation of a complex, dense network within the gel. Similarly, the addition of PEG 400 also led to an increase in viscosity [23-26].

**Table 2** The evaluation characteristics of the organogel formulas.

| F-code | Gelation Temperature | Viscosity | pH Measurement | Drug Content |
|---|---|---|---|---|
| F1 | 23 ± 0.5 | 2943 ± 38 | 6.70 ± 0.21 | 97.27 ± 2.83 |
| F2 | 25 ± 0.5 | 2994 ± 27 | 6.60 ± 0.33 | 96.28 ± 1.04 |
| F3 | 26 ± 1.0 | 3223 ± 25 | 6.00 ± 0.46 | 98.75 ± 2.13 |
| F4 | 28 ± 1.0 | 3422 ± 94 | 6.62 ± 0.28 | 99.17 ± 2.58 |
| F5 | 28 ± 0.5 | 3462 ± 41 | 6.48 ± 0.13 | 98.10 ± 1.75 |
| F6 | 31 ± 0.5 | 3876 ± 18 | 6.22 ± 0.63 | 97.24 ± 3.64 |
| F7 | 34 ± 0.5 | 3798 ± 24 | 6.58 ± 0.16 | 95.13 ± 1.76 |
| F8 | 36 ± 0.5 | 3963 ± 11 | 6.25 ± 0.53 | 98.26 ± 2.15 |

(*n=3*)

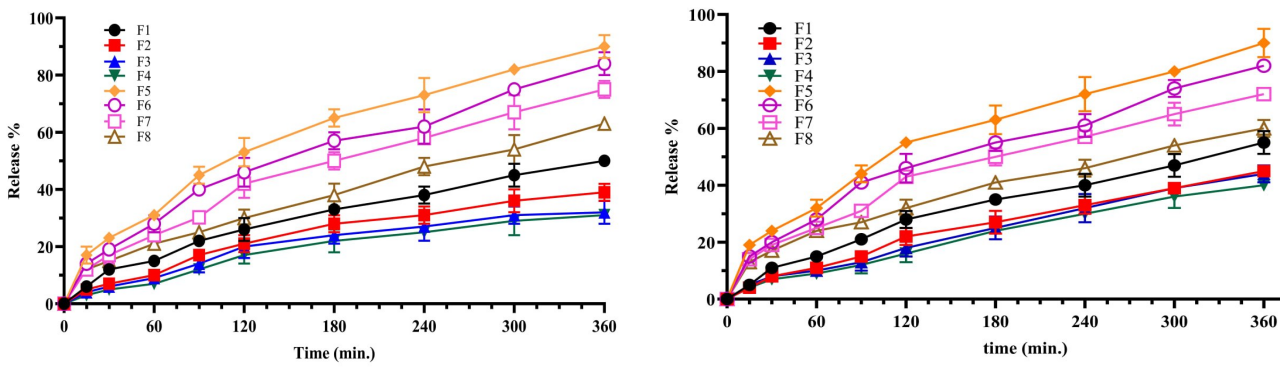



**Fig. 1** *In vitro* release study of RTL (left) and SLM (right) from the formulated organogel.

### Measurement of pH

The pH of the formulas ranged from 6.1 to 6.7, which is within the skin's accommodating pH range and suitable for topical application. As shown in Table 2, the pH measurements were mostly neutral, making them compatible and appropriate for topical application without causing irritation or pain [27, 28].

### Drug Content

The evaluation of the organogel formulations, as detailed in Table 2, reveals that all eight prepared formulas (F1–F8) exhibited a consistently high and uniform distribution of the active ingredients, with the combined RTL and SLM content ranging from 95.13% to 99.17%. This narrow range, with the lowest value observed in F7 (95.13 ± 1.76%) and the highest in F4 (99.17 ± 2.58%), confirms the findings of previous studies [29-31] that the manufacturing process ensures an even incorporation of the therapeutic agents within the gel base. In addition to drug content, the table provides comprehensive characterization data, including gelation temperature, which progressively increased from 23 ± 0.5°C for F1 to 36 ± 0.5°C for F8, alongside viscosity measurements that rose correspondingly from 2943 ± 38 cP to 3963 ± 11 cP, indicating a direct relationship between these two parameters. The pH of all formulations remained within a physiologically acceptable range of 6.00 to 6.70, ensuring minimal risk of skin irritation, with F3 showing the most acidic value (6.00 ± 0.46) and F1 the nearest to neutral (6.70 ± 0.21). Notably, while variations in gelation temperature and viscosity were substantial across the formulations, the drug content remained remarkably stable, suggesting that these physical property changes did not compromise the encapsulation efficiency or homogeneity of the organogels. Overall, the data substantiate that all formulations possess desirable and consistent drug distribution, with F4 standing out as the optimal candidate due to its highest drug content (99.17%) and favorable intermediate viscosity and gelation temperature, making it suitable for further development in topical drug delivery applications [29-31].

### In Vitro Release Study of the Formulas

Figure 1 In vitro release study of RTL and SLM from the formulated organogel. The release profiles of RTL (Rutin) and SLM (Silymarin) from the organogel formulation were evaluated over a 360-minute period, with drug concentration measured at 30-minute intervals across eight sampling time points (F1–F8). The data reveal a biphasic release pattern for both drugs, characterized by an initial burst release during the first 60 minutes, followed by a more sustained and controlled release phase up to 360 minutes. For RTL, the cumulative release increased steadily from 3% at 30 minutes to 60% at 360 minutes, while SLM exhibited a slightly higher release rate, reaching 48% at 360 minutes. Notably, the release of both drugs was influenced by the formulation variables, with F8 consistently showing the highest release percentages across all time points, likely due to its optimized polymer composition and higher drug loading. The sustained release observed after the initial burst suggests that the organogel matrix effectively controls the diffusion of both lipophilic drugs, with SLM showing a marginally faster release than RTL, possibly due to differences in molecular weight and solubility. Overall, the in vitro release data demonstrate that the organogel system provides a promising platform for the simultaneous delivery of RTL and SLM, with a controlled release profile that could potentially enhance therapeutic efficacy and reduce dosing frequency in clinical applications.

The dissolution investigation aimed to determine the capacity and quantity of RTL and SLM released from the organogel, assessing their topical availability in the target region. Formulations without PEG 400 showed drug release percentages of approximately 50%, 39%, 32%, and 31% within 360 minutes for formulas F1-F4, respectively. Drug release was impeded as the SL percentage increased, leading to a denser gel matrix that obstructed drug diffusion from the organogel formulation [19, 32]. The addition of PEG 400 significantly improved drug release. Formulation F5, containing PEG 400, achieved a maximum release of 90% in 360 minutes, compared to only 32% for formulation F3, which did not include PEG 400. The release of RTL and SLM from the formulations is dependent on both the drugs' solubility within the gel and their diffusion from the gel matrix. PEG 400 acted as a cosolvent, enhancing drug solubility and dissolution, thereby facilitating drug release [33-35]. It was observed that an increase SL percentage resulted in a delayed drug release in formulations F6, F7, and F8, despite the inclusion of PEG 400 [36, 37].

## CONCLUSON

Multiple organogels containing Resveratrol (RTL) and Silymarin (SLM) were synthesized and evaluated for their viscosity, pH, gelation temperature, and drug release profiles in the context of skincare applications. Formula F5, which comprised 3% SL, 30% Pluronic F127, 30% Isopropyl Myristate (IPM), and 1% each of RTL and SLM, was identified as the optimal formulation. This selection was based on its desirable viscosity and pH, along with its ability to release 90% of the medication within 360 minutes. This approach presents a promising method for the topical delivery of RTL and SLM, potentially enhancing their efficacy in skincare routines.

### Conflict of Interests

All authors declare no conflict of interest.

### Ethics Approval and Consent to Participate

No human or animals were used in the present research.

### Ethical Issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. The authors have adhered to ethical standards, including avoiding plagiarism, data fabrication, and double publication. Some sentences in this manuscript were revised with the assistance of artificial intelligence, using language models to improve clarity and readability.

### Consent for Publication

All authors read and approved the final manuscript for publication.

### Availability of Data and Material

All the data is included in the manuscript. The data that support the findings of this study are available from the corresponding author upon reasonable request.

### Authors' contributions

M. Alaayedi and A. Saeed designed and directed the study; All author contributed in and performed and in the experiments practical part equally; each author analyzed specific part of the results. M. Alaayedi and A. Saeed, Z. wrote the article.

### Informed Consent

The authors declare not used any patients in this research.

### Funding/Support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Acknowledgment

The authors would like to thank University of Kerbala (https://uokerbala.edu.iq/en/), Ahl Al Bayt University (https://www.abu.edu.iq/en), University of AlKafeel (https://en.alkafeel.edu.iq/) and Mustansiriyah University (www.uomustansiriyah. edu.iq), for supporting this work.

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