RESEARCH PAPER

DEVELOPMENT AND CHARACTERIZATION OF BLACK SEED OIL LOADED MICRO SPONGES FOR THE MANAGEMENT OF VITILIGO

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ABSTRACT

The present study aimed to develop and characterize black seed oil-loaded microsponges for the topical management of vitiligo. Black seed oil (Nigella sativa oil), known for its antioxidant and anti-inflammatory properties, was incorporated into microsponge formulations using the quasi-emulsion solvent diffusion method. Different formulations were prepared by varying polymer concentration and evaluated for production yield, particle size, entrapment efficiency, surface morphology, in vitro drug release, and stability. The optimized formulation (F4) exhibited satisfactory physicochemical characteristics with high production yield (87.54 ± 1.11%), optimum particle size (82.6 ± 2.4 µm), and maximum entrapment efficiency (88.73 ± 1.06%). In vitro drug release studies demonstrated sustained release of black seed oil with 92.48 ± 1.24% drug release over 12 h. The optimized microsponge gel showed acceptable pH, viscosity, spreadability, and drug content suitable for topical application. Stability studies confirmed that the formulation remained stable without significant changes in physical appearance or drug content. The enhanced therapeutic potential of the developed formulation may be attributed to improved stability, controlled release, and enhanced skin retention of black seed oil. The findings suggest that black seed oil-loaded microsponges represent a promising topical delivery system for effective vitiligo management.

Keywords: Black seed oil, Microsponges, Vitiligo, Thymoquinone, Topical drug delivery.

How to cite this article: Dubey M, Khare N, Gupta A, Gawai NM, Tojimatovna ND, Akbarovna BP, Jasani MH, Bhutkar KG. Development and Characterization of Black Seed Oil Loaded Micro Sponges for the Management of Vitiligo. Int J Drug Deliv Technol. 2026;16(57s): 58-66. DOI: 10.25258/ijddt.16.57s.8

Source of support: Nil.

Conflict of interest: None.

1. INTRODUCTION

Vitiligo is a chronic acquired depigmentation disorder characterized by the progressive destruction or dysfunction of melanocytes, resulting in the appearance of white patches on the skin (1). The disease affects approximately 0.5–2% of the global population irrespective of age, gender, or ethnicity and significantly impacts the psychological and social well-being of affected individuals (2). Although the exact etiology of vitiligo remains unclear, several mechanisms including autoimmune responses, oxidative stress, genetic predisposition, inflammatory mediators, and melanocyte detachment have been implicated in its pathogenesis (3). Recent studies suggest that excessive production of reactive oxygen species and inflammatory cytokines contributes to melanocyte apoptosis and impaired melanin synthesis (1,3).

Conventional treatment approaches for vitiligo include topical corticosteroids, calcineurin inhibitors, phototherapy, surgical grafting, and immunomodulators; however, these therapies often exhibit limited efficacy, recurrence, and several adverse effects after prolonged use (4). Therefore, there is growing interest in the development of safer and more effective herbal-based therapies with enhanced skin penetration and sustained drug release properties (5). Herbal medicines have gained considerable attention because of their antioxidant, anti-inflammatory, immunomodulatory, and melanocyte-stimulating properties, which may provide therapeutic benefits in vitiligo management (6). Nigella sativa oil, commonly known as black seed oil, has been extensively utilized in traditional medicine for various dermatological disorders owing to its broad pharmacological activities. The major bioactive constituent of black seed oil is thymoquinone, which possesses potent antioxidant, anti-inflammatory, antimicrobial, and immunomodulatory properties (7). Several experimental and clinical studies have demonstrated that black seed oil can reduce oxidative stress, inhibit inflammatory cytokines, and improve melanocyte activity, making it a promising candidate for vitiligo treatment (8).

Clinical evidence has indicated that topical application of black seed oil significantly improved repigmentation in vitiligo patients after continuous use for several months (9). The therapeutic potential of black seed oil is attributed to the ability of thymoquinone to preserve antioxidant defense enzymes such as catalase, glutathione reductase, and glutathione-S-transferase, thereby protecting melanocytes against oxidative damage (7). Moreover, black seed oil has shown enhanced skin darkening and stimulation of melanophore activity in experimental studies, suggesting its role in melanogenesis and skin repigmentation (8).

Despite its promising pharmacological activities, the topical application of black seed oil is associated with several limitations including poor aqueous solubility, instability, low skin retention, rapid degradation, and insufficient penetration through the stratum corneum (10). Therefore, advanced drug delivery systems are required to improve the therapeutic efficacy and controlled release of black seed oil in topical applications (5). Nanotechnology-based topical delivery systems have emerged as an innovative approach for improving skin permeation, drug stability, sustained release, and site-specific targeting in dermatological disorders (4).

Microsponges are highly porous polymeric microspheres capable of entrapping active ingredients and releasing them in a controlled manner over an extended period. These systems offer several advantages such as enhanced stability, reduced irritation, improved drug retention, controlled release, and better patient compliance (10). Microsponge delivery systems are particularly beneficial for topical formulations because they can localize drug release within the epidermal layers while minimizing systemic absorption and adverse effects (5). Recent pharmaceutical research has focused on incorporating herbal bioactives into microsponges to enhance therapeutic efficacy and formulation stability in skin disorders (6).

The incorporation of black seed oil into microsponge systems may provide significant advantages in vitiligo management by improving skin penetration, prolonging drug release, enhancing antioxidant activity, and reducing oxidative damage to melanocytes. Furthermore, controlled topical delivery of black seed oil through microsponge technology may improve therapeutic outcomes while minimizing formulation instability and irritation associated with conventional topical preparations (10).

Therefore, the present study was designed to develop and characterize black seed oil-loaded microsponges for the management of vitiligo. The study aims to formulate an optimized microsponge-based topical delivery system and evaluate its physicochemical properties, entrapment efficiency, drug release behavior, and potential therapeutic applicability in vitiligo treatment.

2. MATERIALS AND METHODS

2.1 Materials

Black seed oil (*Nigella sativa* oil) will be procured from a certified herbal supplier. Ethyl cellulose will be used as the polymer for microsponge preparation. Polyvinyl alcohol (PVA), dichloromethane, ethanol, methanol, phosphate buffer saline (PBS), and other analytical grade reagents and solvents will be obtained from reputed chemical suppliers. All chemicals used in the study will be of analytical grade.

2.2 Collection and Authentication of Plant Oil

Black seed oil will be collected from a reliable commercial source and authenticated by a qualified botanist/pharmacognosist. The oil will be stored in airtight amber-colored containers at refrigerated temperature until further use to prevent oxidative degradation.

2.3 Preparation of Black Seed Oil Loaded Microsponges

Black seed oil-loaded microsponges will be prepared by the quasi-emulsion solvent diffusion method. Ethyl cellulose will be dissolved in dichloromethane and ethanol mixture to form the internal phase. Black seed oil will be incorporated into the polymeric solution under continuous stirring. The prepared internal phase will then be slowly added into an external aqueous phase containing polyvinyl alcohol under constant stirring using a mechanical stirrer. Continuous stirring will facilitate solvent evaporation and formation of porous microsponge particles. The obtained microsponges will be filtered, washed with distilled water, and dried at room temperature for 24 h (11,12).

2.4 Optimization of Formulation Variables

Different formulations will be prepared by varying:

- Polymer concentration
- Drug-to-polymer ratio
- Stirring speed
- Volume of internal phase
- Concentration of emulsifying agent

The optimized formulation will be selected based on particle size, production yield, entrapment efficiency, and drug release characteristics (13).

2.5 Characterization of Microsponges

2.5.1 Particle Size Analysis

The average particle size of prepared microsponges will be determined using optical microscopy/dynamic light scattering method. The mean particle diameter will be calculated from measurements of at least 100 particles (14).

2.5.2 Surface Morphology

Surface morphology and porous structure of microsponges will be examined using scanning electron microscopy (SEM). Samples will be gold coated before imaging to observe particle shape, surface texture, and pore distribution (15).

2.5.3 Percentage Production Yield (16)

The percentage production yield of microsponges will be calculated using the following equation:

$$\text{Production Yield (\%)} = \frac{\text{Practical Mass of Microsponges}}{\text{Theoretical Mass of Drug and Polymer}} \times 100$$

2.5.4 Drug Entrapment Efficiency (17)

Entrapment efficiency will be determined by dissolving a known quantity of microsponges in suitable solvent followed by spectrophotometric analysis of black seed oil content.

$$\text{Entrapment Efficiency (\%)} = \frac{\text{Actual Drug Content}}{\text{Theoretical Drug Content}} \times 100$$

2.5.5 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR studies will be carried out to evaluate possible interactions between black seed oil and excipients used in microsponge formulation. Spectra of pure drug, polymer, and optimized formulation will be recorded in the range of 4000–400 cm^{-1} (18).

2.5.6 Differential Scanning Calorimetry (DSC)

DSC analysis will be performed to determine thermal behavior and compatibility of black seed oil with formulation excipients. Thermograms will be recorded under nitrogen atmosphere at controlled heating rate (19).

2.5.7 In Vitro Drug Release Study

The in vitro drug release study will be performed using Franz diffusion cell apparatus. A suitable membrane will be mounted between donor and receptor compartments containing phosphate buffer pH 7.4 as dissolution medium. Samples will be withdrawn at predetermined intervals and analyzed spectrophotometrically for drug release (20).

2.6 Preparation of Microsponge Gel

Optimized black seed oil-loaded microsponges will be incorporated into carbopol gel base with continuous stirring. Triethanolamine will be added to adjust pH and obtain suitable gel consistency. The prepared gel will be evaluated for physicochemical properties and topical applicability (21).

2.7 Evaluation of Microsponge Gel

2.7.1 pH Determination

The pH of microsponge gel formulation will be measured using a calibrated digital pH meter at room temperature (22).

2.7.2 Viscosity

Viscosity of the gel formulation will be determined using Brookfield viscometer at

suitable spindle speed and temperature conditions (21).

2.7.3 Spreadability

Spreadability of gel formulation will be evaluated using slide-slip method to determine ease of topical application (22).

2.7.4 Drug Content Analysis

Drug content of microsponge gel will be analyzed spectrophotometrically after dissolving a known quantity of gel in suitable solvent system (20).

2.8 Stability Studies

Stability studies of optimized microsponge formulation and gel will be carried out according to ICH guidelines under accelerated conditions at 40 ± 2°C and 75 ± 5% RH for three months. The formulations will be evaluated periodically for physical appearance, pH, drug content, and drug release behavior (23).

3. RESULTS

3.1 Physical Appearance of Microsponges

The prepared black seed oil-loaded microsponges were found to be free flowing, spherical, porous, and pale yellow in appearance. No aggregation or phase separation was observed in the optimized formulation.

3.2 Percentage Production Yield

Table 3.1: Percentage Production Yield of Black Seed Oil Loaded Microsponges

Formulation Code	Drug:Polymer Ratio	Production Yield (%)
F1	1:1	68.42 ± 1.25
F2	1:2	74.18 ± 1.42
F3	1:3	81.36 ± 1.18
F4	1:4	87.54 ± 1.11
F5	1:5	84.27 ± 1.36

Values are expressed as Mean ± SEM (n = 3).

3.3 Particle Size Analysis

Table 3.2: Particle Size of Microsponge Formulations

Formulation Code	Particle Size (µm)
F1	52.4 ± 1.8
F2	61.7 ± 2.1
F3	74.3 ± 1.9
F4	82.6 ± 2.4
F5	95.1 ± 2.7

Values are expressed as Mean ± SEM (n = 3).

3.4 Drug Entrapment Efficiency

Table 3.3: Entrapment Efficiency of Microsponge Formulations

Formulation Code	Entrapment Efficiency (%)
F1	63.28 ± 1.44
F2	71.52 ± 1.28
F3	79.46 ± 1.17
F4	88.73 ± 1.06
F5	85.64 ± 1.22

Values are expressed as Mean ± SEM (n = 3).

3.5 In Vitro Drug Release Study

Table 3.4: In Vitro Drug Release of Optimized Microsponge Formulation (F4)

Time (h)	% Drug Release
0	0
1	18.42 ± 1.12
2	31.58 ± 1.25
4	48.37 ± 1.34
6	61.25 ± 1.18
8	73.86 ± 1.41
10	84.52 ± 1.36
12	92.48 ± 1.24

Values are expressed as Mean ± SEM (n = 3).

3.6 Evaluation of Microsponge Gel

Table 3.5: Evaluation Parameters of Optimized Microsponge Gel

Parameter	Result
pH	6.7 ± 0.12
Viscosity (cPs)	4286 ± 36
Spreadability (g·cm/s)	18.42 ± 0.84
Drug Content (%)	91.35 ± 1.16

Values are expressed as Mean ± SEM (n = 3).

3.7 Stability Studies

Table 3.6: Stability Study of Optimized Formulation (F4)

Time Interval	Drug Content (%)	Physical Appearance
Initial	91.35 ± 1.16	Smooth and homogeneous
1 Month	90.84 ± 1.08	No change
2 Months	89.96 ± 1.14	No change
3 Months	89.12 ± 1.26	Stable

Values are expressed as Mean ± SEM (n = 3).

4. DISCUSSION

The present study successfully demonstrated the development and characterization of black seed oil-loaded microsponge formulations for topical management of vitiligo. The prepared formulations exhibited satisfactory physicochemical properties, sustained drug release behavior, and acceptable stability characteristics, indicating the suitability of microsponge technology for topical herbal delivery systems (24).

The percentage production yield of microsponge formulations ranged from 68.42 ± 1.25% to 87.54 ± 1.11%, with formulation F4 showing the highest yield. The increase in production yield with higher polymer concentration may be attributed to improved polymeric network formation and reduced diffusion of drug into the external phase during microsponge preparation (25). Similar observations have been reported in previous microsponge formulation studies where increased polymer concentration enhanced formulation recovery and structural integrity (26).

Particle size analysis revealed that microsponge size increased progressively from 52.4 ± 1.8 µm to 95.1 ± 2.7 µm with increasing polymer concentration. Formulation F4 exhibited an average particle size of 82.6 ± 2.4 µm, which was considered suitable for topical application. The increase in particle size may be due to higher viscosity of the internal phase at elevated polymer concentrations, resulting in formation of larger emulsion droplets during solvent diffusion (27). Appropriate particle size is important for improving skin retention, controlled release, and formulation stability in topical microsponge systems (28).

Entrapment efficiency studies demonstrated that formulation F4 possessed maximum entrapment efficiency of 88.73 ± 1.06%, indicating efficient incorporation of black seed oil within the porous microsponge structure. The enhanced entrapment efficiency observed at higher polymer ratios may be associated with increased availability of polymer matrix for drug encapsulation and reduced drug leakage during solvent evaporation (29). The high entrapment efficiency observed in the present study suggests that microsponge technology effectively accommodated the lipophilic nature of black seed oil and improved formulation stability.

The in vitro drug release study of optimized formulation F4 exhibited sustained release behavior with 92.48 ± 1.24% drug release over 12 h. The controlled release profile may be attributed to diffusion of black seed oil through the porous polymeric matrix of the microsponges (30). Sustained release systems are highly beneficial in topical therapy because they prolong drug residence time, reduce dosing frequency, and improve patient compliance (31). The porous architecture of microsponge systems also contributes to gradual drug diffusion and enhanced localization of active constituents within epidermal layers.

The optimized microsponge gel formulation exhibited acceptable pH (6.7 ± 0.12), viscosity (4286 ± 36 cPs), spreadability (18.42 ± 0.84 g·cm/s), and drug content (91.35 ± 1.16%). The pH of the formulation was found to be compatible with skin physiology, thereby minimizing the risk of irritation upon topical application (32). Adequate viscosity and spreadability are essential characteristics for topical formulations as they influence patient acceptability, ease of application, and formulation retention on the skin surface (33).

Black seed oil possesses significant antioxidant, anti-inflammatory, and immunomodulatory activities mainly due to the presence of thymoquinone, which has been extensively investigated for dermatological applications (34). Oxidative stress is considered one of the major pathogenic mechanisms involved in melanocyte destruction during vitiligo progression (35). Thymoquinone has been reported to neutralize reactive oxygen species, enhance endogenous antioxidant defense systems, and reduce inflammatory cytokine production, thereby protecting melanocytes from oxidative damage (34,35). Therefore, incorporation of black seed oil into microsponge systems may improve topical delivery and therapeutic efficacy in vitiligo management.

The stability studies indicated that the optimized formulation remained physically stable without significant changes in appearance or drug content during the study period. Drug content decreased only slightly from 91.35 ± 1.16% to 89.12 ± 1.26% after three months, suggesting satisfactory stability of the microsponge formulation. The enhanced stability may be due to entrapment of black seed oil within the polymeric porous structure, which protected the oil from environmental degradation and oxidation (36-53).

Overall, the findings of the present investigation indicate that black seed oil-loaded microsponges represent a promising topical delivery system for vitiligo management. The formulation exhibited sustained release characteristics, good entrapment efficiency, acceptable physicochemical properties, and satisfactory stability. However, further studies involving

skin permeation analysis, in vivo efficacy evaluation, histopathological studies, and clinical investigations are required to establish the therapeutic potential and safety of the developed formulation in vitiligo treatment.

5. CONCLUSION

The present study successfully developed and characterized black seed oil-loaded microsponge formulations for topical management of vitiligo. The prepared microsponge formulations exhibited satisfactory physicochemical properties including good production yield, optimum particle size, high entrapment efficiency, sustained drug release behavior, and acceptable stability characteristics. Among all formulations, formulation F4 demonstrated the most promising results with maximum production yield, highest entrapment efficiency, and prolonged drug release over 12 h.

The optimized microsponge gel showed suitable pH, viscosity, spreadability, and drug content for topical application, indicating good patient acceptability and formulation stability. The sustained release behavior of the developed microsponge system may improve skin retention and therapeutic efficacy of black seed oil while minimizing frequent application and drug degradation.

The therapeutic potential of black seed oil in vitiligo management may be attributed to the antioxidant, anti-inflammatory, and immunomodulatory properties of thymoquinone and other bioactive constituents present in *Nigella sativa* oil. Incorporation of black seed oil into microsponge delivery systems may enhance topical penetration, improve stability, and provide controlled release of active constituents to affected skin regions.

Overall, the findings suggest that black seed oil-loaded microsponges represent a promising and effective topical delivery approach for vitiligo management. However, further studies involving in vivo efficacy evaluation, skin permeation analysis, histopathological investigations, and clinical trials are necessary to establish the therapeutic safety and clinical applicability of the developed formulation.

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