

Formulation and In-Vitro Evaluation of Ibuprofen Emulgel using *Zingiber officinale* Roscoe and *Nigella sativa* L. as a Natural Excipient

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ABSTRACT

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Emulgels have been developed as a potential drug delivery system for hydrophobic drugs. This study aimed to formulate an ibuprofen emulgel, utilizing Carbopol 940 as a gelling agent and ginger oil and black seed oil as penetration enhancers. An emulsion was prepared and then incorporated into a gel base. All prepared ibuprofen emulgel formulations (F0–F6) demonstrated acceptable physicochemical properties suitable for topical application. The pH values (4.1–5.8) were within the normal physiological range for skin, indicating that the emulgels are safe and non-irritating. Although increasing concentrations of ginger oil and black seed oil led to a decrease in pH values, these readings remained within the permissible range. The blank formulation (F0) exhibited the highest spreadability, while formulations containing ibuprofen and natural oils showed moderately lower values. Ginger oil formulations (F1–F3) demonstrated moderate and consistent spreadability. Black seed oil formulations (F4–F6) had slightly lower, but still acceptable, spreadability values. Viscosity tests indicated that the blank formulation had the highest viscosity. Increasing the proportion of ginger oil resulted in a rapid drop in viscosity, while black seed oil formulations maintained relatively higher viscosity values. This confirms that natural oils influence the rheology and flow properties of the gel. A skin irritation test confirmed that all formulations were non-irritating for up to 24 hours post-application. In conclusion, all screened formulations were stable, safe, and suitable for the topical delivery of ibuprofen. Variations in natural oil concentration affected viscosity and spreadability but did not compromise skin compatibility.

Keywords: Carbopol, Emulgel, Ibuprofen, Natural oils, *Nigella sativa*

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INTRODUCTION

Emulgels are a novel drug delivery system for topical application, combining the benefits of both emulsions and gels. They are particularly effective for delivering hydrophobic drugs through the skin. Emulgels are formed by incorporating a gelling agent into the aqueous phase of an emulsion during cream production, converting the emulsion into a gelled form. The careful preparation of individual emulgel components is crucial for this process. This formulation offers numerous advantages, such as thixotropic character, a non-greasy feel, ease of application and removal, improved stability, biocompatibility, excellent spreadability on the skin, and high patient acceptability [1].

Transdermal penetration of medications primarily occurs via pathways through the stratum corneum, along sweat ducts, and through sebaceous follicles. The stratum corneum is considered the primary barrier before drugs reach systemic circulation. The United States Pharmacopeia defines gels as "semi-solid systems consisting of organic or inorganic particles (dispersed phase) within a liquid (dispersion medium)." Gels are broadly classified as hydrophilic (hydrogels) or hydrophobic (organogels). However, most gels are hydrophilic and are not very effective at delivering

poorly water-soluble drugs, posing a challenge for medicinal formulators. Drug release from a typical emulgel system is governed by the properties of the emulsion droplets and the three-dimensional polymeric gel in which the emulsion is dispersed. The emulgel approach effectively incorporates hydrophobic drugs into the oil phase of an emulsion before gel incorporation [2-4].

Ibuprofen is a common nonsteroidal anti-inflammatory drug (NSAID) with analgesic, antipyretic, and anti-inflammatory properties. Introduced in 1969 as a safer alternative to aspirin, it remains one of the most widely prescribed NSAIDs globally. Its therapeutic action stems from the reversible, non-selective inhibition of both COX-1 and COX-2 cyclooxygenase enzymes, which reduces the synthesis of prostaglandins that mediate inflammation, pain, and fever. While some gastrointestinal discomfort can occur, ibuprofen generally causes fewer side effects than other NSAIDs. After oral administration, ibuprofen is rapidly absorbed, reaching peak plasma concentrations within 1–2 hours. It is extensively plasma protein bound (>98%) and has a short elimination half-life of 1–3 hours, necessitating repeated dosing to maintain steady-state concentrations. The drug distributes into inflamed tissues and synovial fluid [5-8].

Pharmacodynamically, ibuprofen inhibits the synthesis of proinflammatory prostanoids such as PGE₂ and PGL₂, resulting in reduced edema, vascular permeability, and sensitization of nociceptors. Its antipyretic property is based on an inhibition of hypothalamic prostaglandin synthesis. Thromboxane A₂ yields a temporary antiplatelet effect. Natural Excipients [9]; The selection of pharmaceutical excipients can dramatically influence the stability, release rate, and bioavailability of drugs. Growing concerns associated with the use of synthetic excipients in drug formulations have led to increasing interest in natural excipients with favorable properties [10-12].

Ginger oil (*Zingiber officinale*) contains bioactive compounds such as gingerols and shogaols, which possess reported anti-inflammatory and antioxidant properties. Various extraction methods, including advanced techniques like subcritical water extraction, have been employed to selectively recover these key compounds. Black seed oil (*Nigella sativa*) is rich in thymoquinone and other phytochemicals [13, 14]. These compounds have reported antimicrobial, anti-inflammatory, and antioxidant effects, as well as protective properties, supporting the oil's potential as a functional natural excipient [15-17].

The primary aim of this study was to formulate and evaluate a novel topical emulgel delivery system for Ibuprofen, incorporating natural oils extracted from *Zingiber officinale* (ginger) and *Nigella sativa* (black seed), and to assess their physicochemical properties, skin irritation potential, and stability. The innovation of this research lies in the strategic combination of a conventional NSAID with the synergistic anti-inflammatory and analgesic properties of two well-established medicinal plants within a single advanced topical delivery system. By employing an oil-in-water emulgel base, this formulation overcomes the limitations of both traditional creams and gels, ensuring high loading capacity for both lipophilic and hydrophilic components while improving skin permeability and sustaining drug release. The specific selection of non-ionic surfactants (Span 40 and Tween 80), humectants (propylene glycol and glycerin), and a Carbopol 940 gel base is tailored to maximize stability and minimize skin irritation. Furthermore, this study innovatively compares the effects of ginger and black seed oils side-by-side across multiple concentrations, providing valuable insight into which natural oil is most compatible and effective when co-formulated with Ibuprofen. The integrated evaluation, including comprehensive physical characterizations, rigorous skin patch testing on human volunteers, and long-term stability studies according to ICH guidelines, ensures a holistic assessment of the formulation's real-world applicability. This research demonstrates a feasible and scalable method for developing a phytopharmaceutical emulgel that offers a safer, more effective, and patient-friendly alternative for managing pain and inflammation.

Materials and Methods

Materials

Ibuprofen was kindly provided by Al-Fayhaa Company (Sama Al-Fayhaa, Iraq). Span 40 and Tween 80 were purchased from Thomas Baker, India. Stearic acid, Carbopol 940, Propyl glycol, NaOH, Benzoic acid, and Glycerine were purchased from HiMedia Laboratories, India. Ginger and black seeds were purchased from a local market in Najaf, Iraq. All other organic solvents were of analytical grade.

Extraction of Natural Oils by Soxhlet Method

The natural oils from *Zingiber officinale* (ginger) and *Nigella sativa* (black seed) were extracted using the Soxhlet extraction

procedure for exhaustive recovery of the bioactive constituents soluble in ethanol. The plant tissues were allowed to dry and powdered samples were extracted by the aforementioned extraction [18].

The technique involved thorough drying and powdering of the samples. Each sample was then successively transferred into cellulose extraction thimbles and fitted into a Soxhlet extractor. Ethanol (99.9%) was used as a solvent and placed in a round-bottom flask attached to the system. The apparatus was heated to reflux, causing the solvent to boil, evaporate, and condense. The condensed ethanol then ran through the powdered plant material, dissolving its constituents. When the absorption chamber filled to the siphon level, the solvent, now containing the extracted compounds, returned to the boiling flask. This process continued for approximately six hours [18]. The ethanolic extracts thus obtained were concentrated under reduced pressure at a temperature of 60 °C in a rotary evaporator. The concentrated extracts were cooled and preserved for formulation studies.

Formulation of Emulgel

The emulgel was prepared in three steps: (1) preparation of the oil-in-water (O/W) emulsion, (2) preparation of the gel base, and (3) continuous stirring to incorporate the emulsion into the gel base. Seven emulsion formulations (F0–F6) were developed, varying the type and concentration of natural oil in the oil phase, while the aqueous phase composition remained constant [19].

Preparation of Emulsion

Seven emulsion formulations (F0–F6) were prepared, differing only in the type and concentration of natural oil in the oil phase, while the aqueous phase composition remained constant.

Oil Phase

The oil phase primarily comprises stearic acid (1 g), Span 40 (1 g), Tween 80 (1 mL), ibuprofen (2 g), and natural oils at varying concentrations. Ginger oil was incorporated into formulations F1, F2, and F3 at concentrations of 0.5 mL, 1 mL, and 1.5 mL, respectively. Similarly, black seed oil was added to formulations F4, F5, and F6 at 0.5 mL, 1 mL, and 1.5 mL, respectively. All components of the oil phase were precisely weighed, transferred to a clean beaker, and heated with stirring at 45-50 °C on a hot plate until the mixture became clear and homogenous.

Aqueous Phase

The aqueous phase, comprising 1 mL of glycerin and 1 mL of propylene glycol, was mixed. Distilled water gradually added with gentle heating and continuous stirring. The oil phase was then slowly added to the aqueous phase with constant stirring to form an oil-in-water emulsion. The total volume was adjusted to 10 mL with distilled water.

Preparation of Gel Base

The gel base was prepared using Carbopol 940 (1.5% w/v) as the gelling agent. The required quantity of Carbopol 940 was dispersed in distilled water and stirred at 1000 rpm with a magnetic [20]. Stirrer for 1 hour to achieve a uniform dispersion. Any aggregates formed during this process were carefully broken up using a spatula. The dispersion was neutralized with a few drops of 1% NaOH solution and left at room temperature for 24 hours to allow complete swelling of the gel before use. An overview of the details of the formulation of the emulgels is shown in Table 1, while the utility of the excipients used is described in Table 2.

Table 1 Composition of Ibuprofen Emulgel Formulations (F0–F6)

Formulation	Ibuprofen	Stearic acid	Span 40	Tween 80	Ginger oil	Black seeds oil
Blank	2g	1g	1g	1ml	0	0
F1	2g	1g	1g	1ml	0.5 ml	0
F2	2g	1g	1g	1ml	1 ml	0
F3	2g	1g	1g	1ml	1.5 ml	0
F4	2g	1g	1g	1ml	0	0.5 ml
F5	2g	1g	1g	1ml	0	1 ml
F6	2g	1g	1g	1ml	0	1.5 ml

Table 2 List of Excipients and Their Functions in the Emulgel Formulation

Materials	Utility
Carbopol 940	Gelling agent
NaOH	Neutralizer
Benzoic acid	Preservative
Water	Solvent

Evaluation of the Prepared Emulgels

Physical Examination

The prepared emulgel formulations were visually inspected for color, homogeneity, clarity, and texture to assess their overall physical appearance.

pH Determination

The pH of various formulations was determined using a digital pH meter. The electrode was dipped into about 10 mL of the emulgel sample in a beaker. Electrical stability (approximately 2 minutes) was waited for and the pH was noted [21].

Viscosity Measurement

Determination of viscosity was obtained by use of a rotational viscometer with the spindle R6. A 10 mL aliquot of emulgel was placed in a beaker and the spindle lowered into the formulation. Readings were taken at 100 rpm for 10 s at 25 °C [20].

Spread Ability

Spread ability was determined using a glass plate method. A 500 mg emulgel was placed on the center of a glass plate (approximately 1 cm in diameter) and then covered with another glass plate. A weight of 500 g was placed on the upper plate until no further spreading took place and the final diameter of the spread emulgel (cm) was then measured [22, 23].

Skin Irritation Test (Patch Test)

Skin irritation potential was evaluated by patch testing in eight healthy volunteers by applying the formulated product to properly shaved skin and observing for signs of irritation (erythema or change in skin morphology) for 24 hours. The formulation was considered safe if there was no irritation; failure of the test was defined as more than two volunteers exhibiting irritation (test to be repeated in such cases).

Stability Studies

Stability testing was conducted according to ICH guidelines. The emulgel formulations were stored at different temperatures: 4 ± 2 °C, 25 ± 2 °C, and 37 ± 2 °C for a period of three months. Samples were assessed at regular intervals for any changes in appearance [24].

Statistical Analysis

Data was analyzed using Microsoft Excel software (Version 2016). Results were reported as mean $\pm$ standard deviation (SD). Statistical comparisons were performed using the t-test, and similarity was assessed using the similarity factor (f_2).

RESULTS

Evaluation of Prepared Emulgels

Based on the provided table, all formulations—from the blank F0 through F6—consistently exhibit a homogenous texture, indicating stable and uniform mixing across the entire sample set. The primary differentiator lies in their coloration, which follows a distinct gradient among the first four samples: the blank F0 is white, while F1 through F3 transition successively from pale yellow to light yellow and finally to a deeper yellow, suggesting a dose-dependent increase in a colored component. Interestingly, this trend reverts with F4, F5, and F6, all of which return to a white appearance identical to the control, implying that the factor responsible for the yellow hue in the earlier formulations is either absent or rendered colorless in these later versions. Overall, the texture remains unchanged throughout, making color the sole variable that distinguishes these otherwise physically identical preparations (Table 3).

Determination of pH

Determination of pH to confirm that the prepared emulgels fell within the safe pH spectrum of normal healthy skin (4.1–5.8) and that they were less likely to produce irritation, the pH of the emulgels was determined. The gel containing Carbopol 940 (acidic gel), which required neutralization for appropriate gel formation, was given a few drops of NaOH solution to neutralize it for the purpose of the study. All formulations gave acceptable values as per pH to topical application (Table 4).

Spreadability

The spreadability values reveal a clear distinction between the blank formulation and the modified samples, with all test formulations exhibiting reduced spread diameters compared to the control. The blank F0 demonstrates the highest spreadability at 3 cm, indicating the greatest ease of extension under applied pressure. Among the formulated samples, F1, F2, F3, and F6 all share an identical spreadability of 2 cm, suggesting that these particular modifications have a comparable and moderate effect on reducing the product's ability to spread. In contrast, F4 and F5 show the lowest spreadability at 1.5 cm, representing a more pronounced reduction in spreading capacity, which may indicate increased internal cohesion or structural resistance within these formulations. Overall, while all test samples exhibit decreased spreadability relative to the blank, the variations among them are relatively narrow-ranging only from 1.5 cm to 2 cm—with the majority clustering at the 2 cm mark, implying that the compositional changes generally exert a consistent suppressive effect on spreadability, with F4 and F5 representing the most notable deviations toward lower values (Table 5).

Table 3 Physical appearance of emulgel formulations

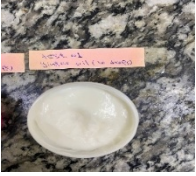
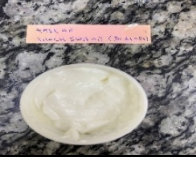
Formula	Texture	Colour	Image
F0 (blank)	Homogenous	White	
F1	Homogenous	Pale yellow	
F2	Homogenous	Light yellow	
F3	Homogenous	Yellow	
F4	Homogenous	White	
F5	Homogenous	White	
F6	Homogenous	White	

Table 4 The pH value of the different preparations.

Formula	Ph
F0 (blank)	5.81
F1	5.74
F2	5.51
F3	5.42
F4	5.35
F5	5.23
F6	5.10

Viscosity Study

All formulations-from the blank F0 through F6, were tested under identical conditions, employing a consistent paddle size of 7 and a fixed rotational speed of 100 RPM, ensuring that any observed variations in viscosity are attributable solely to compositional differences rather than instrumental parameters. The blank

formulation F0 exhibited the highest viscosity at 12,720 cP, establishing a baseline reference point.

Table 5 The spreadability value of the different preparations.

Formula	Spreadability value
F0 (blank)	3cm
F1	2cm
F2	2cm
F3	2cm
F4	1.5cm
F5	1.5cm
F6	2cm

Among the test samples, a clear decreasing trend emerges from F1 to F3, with viscosity values dropping sequentially from 11,320 cP to 11,320, then 9,640 cP, and finally reaching a low of 8,720 cP at

F3, suggesting a progressive compositional modification that reduces internal resistance to flow. However, this trend is not sustained, as F4 shows a notable rebound to 11,250 cP, followed by moderate declines through F5 (10,840 cP) and F6 (9,920 cP). Despite these fluctuations, none of the formulated samples surpass the blank's viscosity, and all values remain within a relatively close range—between 8,720 and 12,720 cP—indicating that while the modifications do influence rheological behavior, the overall impact is moderate and non-linear, with F3 representing the lowest viscosity point and F4 marking a sharp recovery toward the initial baseline (Table 4).

Table 6 The Viscosity value of the different preparations.

Formula	Paddle size	RPM	Viscosity value (CP)
F0 (blank)	7	100	12720
F1	7	100	11320
F2	7	100	9640
F3	7	100	8720
F4	7	100	11250
F5	7	100	10840
F6	7	100	9920

Skin Irritation Test

No parametric allergic symptoms like inflammation, redness, irritation occurred on skin of volunteers up to 24 h

Stability Study

Stability studies were undertaken to evaluate the changes that might take place in the emulgel formulations. For this purpose, the samples were kept at $4 \pm 2^\circ\text{C}$, $25 \pm 2^\circ\text{C}$ and $37 \pm 2^\circ\text{C}$ for three months to study the suitability of the storage temperatures for semisolid preparations.

All prepared ibuprofen emulgel formulations (F0-F6) showed acceptable physicochemical properties for a topical application. All formulations exhibited pH values within the physiological range of the skin [25, 26]. This guarantees that the drug would be safe and that Carbopol 940 was properly neutralized, but the slight reduction in pH with increasing concentration of natural oils. Spreadability values were lower in all formulations containing ibuprofen and oils than the blank, possibly due to increased viscosity; however, all values were found to be at a reasonable level for topical application. The viscosity results showed that ginger oil had a greater effect on reducing gel consistent; whereas black seed oil resulted in moderately high viscosity and better gel stability. All formulations were stable over three months and produced no redness of the skin [27-30].

Emulgel systems provide an effective strategy for delivering hydrophobic drugs such as ibuprofen, capitalizing on the advantages of both emulsions and gels, thus enhancing stability and patient compliance. Drug emulsion in a gel eliminates many shortcomings of both dosage forms. Proper selection of oils, polymers and surfactants is essential for achieving optimal stability, safety and performance. Extraction. Drying ginger and then grinding to facilitate Soxhlet extraction improved yields through better solvent penetration and increased surface area. Similarly, moderate grinding of black seeds improved oil recovery, while excessive pulverization decreased extraction efficiency [31-33].

CONCLUSION

In conclusion, all emulgel formulations demonstrated homogenous texture and acceptable pH values within the skin-

compatible range (5.10–5.81), indicating their suitability for topical application without significant irritation risk. The stability studies confirmed that the formulations remained physically stable across all tested storage temperatures (4°C , 25°C , and 37°C) over three months, with no phase separation or significant alterations observed. Furthermore, the skin irritation test confirmed the non-irritant nature of all preparations, as no volunteer exhibited inflammation, redness, or adverse reactions within 24 hours. Among the formulations, F3 exhibited the lowest viscosity (8,720 cP) while maintaining favorable spreadability (2 cm), suggesting it as a potentially optimal candidate for further development. Overall, the study successfully developed stable, safe, and cosmetically acceptable emulgel formulations with tunable rheological properties suitable for dermatological applications.

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

This in-vitro study on Ibuprofen emulgel formulated with *Zingiber officinale* and *Nigella sativa* as natural excipients was conducted in full compliance with international ethical guidelines for biomedical research. All natural materials were rigorously quality-controlled for safety and purity. The research protocol was reviewed and approved by the Research Ethics Committee of University of Alkafeel (Ethics Code: IR.ALKAFEEL.REC.1405.018). The study involves no human or animal testing, ensuring full ethical adherence throughout all experimental procedures

Consent for Publication

All authors read and approved the final manuscript for publication.

Availability of Data and Material

All the data are embedded in the manuscript.

Authors' contributions

All authors had equal role in study design, work, statistical analysis and manuscript writing.

Informed Consent

The authors declare not used any patients in this research.

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