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Formulation and Characterization of a Capsaicin-Loaded Emulgel: A Novel Topical Approach

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A B S T R A C T :

Background: Capsaicin, a bioactive compound derived from chili peppers, exhibits potent analgesic and anti-inflammatory properties. However, its poor solubility and potential for skin irritation limit its therapeutic applications. Emulgels, combining the advantages of emulsions and gels, offer an effective delivery system for improving capsaicin's stability, bioavailability, and patient compliance. This study aims to formulate and evaluate a capsaicin emulgel for enhanced topical delivery.

Methods: Capsaicin emulgel was prepared using an oil-in-water (o/w) emulsion incorporated into a gel base. The formulation was evaluated for its physical characteristics, viscosity, pH, drug content, stability, spreadability, and antimicrobial activity. The stability study was conducted over three months under different temperature and humidity conditions, while the microbial assay assessed its inhibitory effects. A skin irritation test was also performed to ensure dermal safety.

Results: The prepared emulgel formulations exhibited homogeneity, smooth texture, and appropriate viscosity, with values ranging from 1186.41 to 2288.56 centipoise. The pH of the formulations remained between 6.0 and 6.5, ensuring compatibility with the skin. The drug content analysis confirmed uniform capsaicin distribution, and stability studies indicated no significant changes in physical appearance or chemical properties. The formulation showed good spreadability and notable antimicrobial activity, with the highest inhibition observed in formulation F6. No signs of irritation or adverse reactions were observed in the skin irritation test, confirming the formulation's biocompatibility.

Conclusion: Capsaicin emulgel demonstrated desirable physicochemical properties, stability, and therapeutic potential, making it a promising candidate for topical pain management and inflammatory skin conditions. Further clinical investigations are necessary to validate its efficacy and long-term safety in human subjects.

Keywords: Capsaicin, Emulgel, Topical Drug Delivery, Rheology, Transdermal Formulation

1. Introduction

Topical drug delivery systems offer a non-invasive approach for administering therapeutic agents directly to the affected site, enhancing local drug bioavailability while minimizing systemic side effects (Pardeike et al., 2009). Among various topical formulations, emulgels have emerged as a promising drug delivery system that combines the advantages of both emulsions and gels, leading to improved drug penetration, stability, and patient compliance (Hasan et al., 2021; Shah et al., 2023). Emulgels are particularly advantageous for delivering both hydrophilic and hydrophobic drugs, overcoming the solubility limitations associated with conventional creams, ointments, and gels (Ojha, 2019).

Capsaicin, a naturally occurring alkaloid derived from chili peppers (Capsicum species), has gained significant attention in pharmaceutical research due to its potent analgesic and anti-inflammatory properties (Basith et al., 2016; Maharjan et al., 2024). It acts by desensitizing nociceptors via transient receptor potential vanilloid 1 (TRPV1) receptor modulation, making it an effective treatment for chronic pain conditions such as osteoarthritis, neuropathic pain, and postherpetic neuralgia (Anand & Bley, 2011; Szabados et al., 2020). However, the clinical application of capsaicin is often limited by its poor water solubility, low bioavailability, and potential for causing skin irritation (Szallasi & Sheta, 2012). The development of an emulgel formulation can help overcome these limitations by providing controlled drug release, enhanced penetration, and reduced irritation upon application (Pathan & Setty, 2009).

The stability and efficacy of emulgels can be further enhanced by optimizing formulation parameters such as particle size reduction, pH modulation, and the selection of suitable emulsifiers and gelling agents (Snehal & Manish, 2013). Previous studies have demonstrated that nanosized or micronized drug particles within an emulgel matrix improve drug absorption and prolong the half-life of the formulation (da Silva et al., 2023; Vipanchi et al.,

2023). Additionally, emulgels offer better rheological properties and spreadability, ensuring uniform drug distribution over the skin surface (Khan et al., 2022).

Given the increasing interest in novel topical formulations, this study aims to develop and evaluate a capsaicin-loaded emulgel with optimized physicochemical and pharmacological properties. The study will assess the formulation's stability, viscosity, drug release profile, and skin irritation potential, following standardized evaluation protocols. The findings from this research could contribute to the advancement of capsaicin-based topical therapies, improving treatment outcomes for pain management.

2. Materials and Methods

2.1. Materials

The formulation of the capsaicin emulgel involved the use of various excipients and active ingredients. The oil phase was prepared using light liquid paraffin as the oil component, with Span 20 acting as the emulsifier. The aqueous phase consisted of purified water, in which Tween 20 was dissolved to facilitate emulsification. The gel base was formulated using a suitable polymer dispersed in purified water, with triethanolamine (TEA) used to adjust the pH to a range of 6.0 to 6.5. During the final formulation step, glycerine was incorporated into the mixture in a 1:1 ratio of gel to emulsion to enhance the consistency and spreadability of the final product.

2.2. Methods

2.2.1. Preparation of Emulgel

The preparation of the capsaicin emulgel involved three major steps: emulsion formation, gel base preparation, and incorporation of the emulsion into the gel.

Step 1: Formulation of Emulsion

The emulsion was prepared using either an oil-in-water (o/w) or water-in-oil (w/o) system. The oil phase was formulated by dissolving Span 20 in light liquid paraffin under continuous stirring until a homogeneous solution was obtained. Simultaneously, the aqueous phase was prepared by dissolving Tween 20 in purified water. Both phases were heated to the same temperature before being mixed together under continuous agitation to form a stable emulsion.

Step 2: Formulation of Gel Base

A suitable polymer was dispersed in purified water and stirred continuously at a moderate speed using a mechanical stirrer to achieve uniform dispersion. The pH of the gel base was then adjusted to 6.0–6.5 using triethanolamine (TEA) to ensure optimal gel consistency and stability.

Step 3: Incorporation of Emulsion into Gel Base

The prepared emulsion was gradually incorporated into the gel base with constant mixing. Glycerine was added during this process in a 1:1 ratio of gel to emulsion to improve the viscosity and spreadability of the formulation. The final mixture was homogenized to obtain a uniform and stable emulgel.

2.2.2. Evaluation Parameters

2.2.2.1. Physical examination

The prepared emulgel formulations were visually inspected for their color, appearance, and consistency. The formulation was assessed to ensure uniformity and absence of phase separation.

2.2.2.2. Rheological Study

The viscosity of the formulated emulgel batches was determined using a Brookfield viscometer. The viscometer assembly was connected to a thermostatically controlled water bath maintained at 25°C. The formulation was placed in a beaker covered with a thermostatic jacket, and the spindle was allowed to move freely into the emulgel. The viscosity reading was recorded to determine the flow properties of the formulation.

2.2.2.3. Skin Irritation Test

A set of eight rats were used to evaluate the skin irritation potential of the emulgel. The formulation was applied to the skin, and any undesirable changes, such as redness, inflammation, or irritation, were observed over a period of 24 hours.

2.2.2.4. Stability Studies

The stability of the emulgel was assessed by packing the formulations in aluminum collapsible tubes and storing them under different conditions for a period of three months. The samples were stored at 50°C, 25°C with 60% relative humidity, 30°C with 65% relative humidity, and 40°C with 75% relative humidity. At the end of each month, the formulations were evaluated for physical appearance, pH, rheological properties, drug content, and drug release profile according to the ICH guidelines.

2.2.2.5. pH Determination

The pH of the formulation was determined using a digital pH meter. Before measurement, the pH meter electrode was cleaned with distilled water. The electrode was then immersed in the formulation, and the pH was measured three times to ensure accuracy.

2.2.2.6. Drug Content Determination

A precisely weighed quantity of 1 gram of emulgel was dissolved in a suitable solvent and filtered to obtain a clear solution. The absorbance of the solution was determined using a UV spectrophotometer. A standard drug plot was prepared in the same solvent, and the drug content was calculated by using the equation: Drug content is equal to the product of concentration, dilution factor, volume taken, and conversion factor.

2.2.2.7. Centrifugation Studies

The stability of the emulgel was further evaluated using centrifugation. After one week of formulation, the samples were subjected to centrifugation at 3000 rpm for 30 minutes in a minicentrifuge. The formulation was assessed for any phase separation or sedimentation.

2.2.2.8. Microbiological Assay

The antimicrobial efficacy of the capsaicin emulgel was determined using the ditch plate technique. Previously prepared Sabouraud's agar plates were dried and used for the assay. A 3-gram sample of the emulgel was placed in a ditch cut into the agar plate. Freshly prepared culture loops were streaked across the agar surface at an angle from the edge of the plate. The plates were incubated at 25°C for 18–24 hours, after which fungal growth was observed. The percentage inhibition of fungal growth was calculated using the equation:

Percentage inhibition is equal to the ratio of L2 to L1 multiplied by 100, where L2 represents the inhibition zone and L1 represents the total area of microbial growth.

2.2.2.9. Dilution Test

The dilution test was conducted by adding an excess of the continuous phase to a 50- to 100-fold aqueous dilution of the emulgel. The formulation was observed for any phase separation or changes in clarity, which would indicate instability.

2.2.2.10. Spreadability Test

The spreadability of the emulgel was measured by placing a fixed quantity of 350 mg of the formulation between two glass plates. A known weight was placed on the upper plate, and the plates were allowed to rest for a fixed duration. The diameter of the emulgel spread was recorded. Spreadability was calculated using the formula:

Spreadability is equal to the product of weight tied to the upper slide and the length of the glass slide divided by the time taken to separate the slides completely.

This comprehensive methodology ensures the accurate preparation, characterization, and evaluation of capsaicin emulgel, allowing for a systematic assessment of its physicochemical and pharmacological properties.

3. Results :

3.1. Physical Examination

The prepared capsaicin emulgel formulations were visually examined for their physical attributes, including color, homogeneity, consistency, and phase separation. All formulations exhibited a smooth, homogeneous texture with a glossy appearance, indicating successful incorporation of components. The colors ranged from creamish to matte white and shiny white, with no phase separation observed in any of the formulations. These findings confirm the stability and uniformity of the prepared formulations.

3.2. Rheological Studies

The viscosity of different emulgel formulations was determined using a Brookfield viscometer at 25°C. The viscosity values varied across formulations, with F4 exhibiting the highest viscosity at 2288.56 centipoise and F3 having the lowest viscosity at 1186.41 centipoise. These variations suggest that the choice of polymer and emulsifier concentration significantly influences the rheological properties of the emulgel. The viscosity values indicate that the formulations maintain suitable consistency for effective topical application while ensuring ease of spreadability.

3.3. Skin Irritation Test

The skin irritation test conducted on human skin for 24 hours revealed no signs of inflammation, redness, or irritation, confirming the biocompatibility and safety of the emulgel formulation for topical application. The absence of adverse reactions suggests that the excipients used in the formulation did not induce any skin hypersensitivity.

3.4. Stability Studies

The stability of the emulgel formulations was assessed over a three-month period under different temperature and humidity conditions. The samples remained stable without significant changes in physical appearance, pH, viscosity, drug content, or phase separation. These results indicate that the formulations can withstand varying environmental conditions, making them suitable for commercial production and long-term storage.

3.5. pH Determination

The pH values of the formulations were measured using a digital pH meter, with readings taken six times to ensure accuracy. The average pH of all formulations ranged between 6.0 and 6.5, which falls within the ideal range for topical formulations. This pH range is compatible with skin physiology, minimizing the risk of irritation while ensuring optimal drug release.

3.6. Drug Content Determination

The drug content of the emulgel formulations was quantified using a UV spectrophotometer. The concentration of capsaicin was determined by preparing a standard drug plot and calculating the drug content using the equation: drug content is equal to the product of concentration, dilution factor, volume taken, and conversion factor. The results confirmed uniform drug distribution in all formulations, ensuring consistent therapeutic efficacy.

3.7. Centrifugation Studies

The stability of the emulgel formulations was further assessed using centrifugation at 3000 rpm for 30 minutes after a week of preparation. No phase separation or sedimentation was observed, confirming the physical stability of the formulations. This indicates that the emulsifying agents effectively stabilized the emulgel system, preventing breakdown under mechanical stress.

3.8. Microbiological Assay

The antimicrobial activity of the capsaicin emulgel was evaluated using the ditch plate technique. The highest microbial inhibition was observed in formulation F6, with a percentage inhibition of 48.48%. This suggests that the formulation exhibits notable antimicrobial properties, likely due to the bioactive nature of capsaicin, which is known for its antifungal and antibacterial effects.

3.9. Dilution Test

The dilution test was performed to assess the stability of the emulgel upon aqueous dilution. The formulations remained stable even when subjected to a 50- to 100-fold aqueous dilution, with no visible phase separation or precipitation. This indicates the robustness of the emulsifying system and its ability to maintain structural integrity upon exposure to excess aqueous medium.

3.10. Spreadability Coefficient

The spreadability of the emulgel formulations was determined by measuring the diameter of the spread emulgel when placed between two glass plates. The highest spreadability was observed in formulation F6, with a diameter of 5.7 cm, while formulation F3 exhibited the lowest spreadability at 3.9 cm. The results indicate that all formulations possess desirable spreadability characteristics, ensuring ease of application on the skin without excessive friction.

These findings collectively demonstrate the successful development of a stable, effective, and skin-compatible capsaicin emulgel formulation suitable for topical use.

4. Discussion

The present study successfully formulated and evaluated a capsaicin emulgel with desirable physicochemical properties, stability, and therapeutic potential. The physical examination confirmed the homogeneity and smooth texture of the formulations, with no phase separation, which is essential for stability and patient acceptability. These findings align with previous studies highlighting the importance of formulation consistency in ensuring the efficacy of topical preparations (Akombaetwa et al., 2023).

The viscosity of the formulations varied between 1186.41 and 2288.56 centipoise, indicating suitable rheological properties for topical application. Viscosity plays a crucial role in determining the spreadability and retention time of topical formulations, directly impacting drug absorption and patient compliance (Binder et al., 2019). The measured pH values of 6.0–6.5 were within the acceptable range for dermal applications, minimizing the risk of irritation and ensuring compatibility with the skin barrier (Lambers et al., 2006). The skin irritation test further confirmed the biocompatibility of the formulation, as no adverse effects such as redness or inflammation were observed.

The drug content analysis confirmed uniform distribution of capsaicin within the emulgel, ensuring consistent therapeutic efficacy. Stability studies demonstrated that the formulation retained its physical and chemical integrity under various environmental conditions, making it suitable for long-term storage. These findings are consistent with previous reports that emphasize the role of emulsifiers and gelling agents in maintaining the stability of emulgels (Pathan & Setty, 2009).

Furthermore, the antimicrobial assay revealed that capsaicin emulgel exhibited significant inhibitory effects on microbial growth, supporting its potential application in conditions involving secondary infections. Capsaicin has been documented for its antimicrobial and anti-inflammatory properties, which contribute to its therapeutic value in pain management and dermatological disorders (Periferakis et al., 2023).

Overall, the results indicate that capsaicin emulgel is a promising formulation for topical application, offering enhanced drug stability, spreadability, and bioavailability. Further studies involving clinical trials are necessary to validate its therapeutic efficacy and safety in human subjects.

5. Conclusion

The present study successfully developed and evaluated a capsaicin emulgel formulation with desirable physicochemical characteristics, stability, and therapeutic potential. The formulations demonstrated uniform drug content, optimal viscosity, suitable pH, and excellent spreadability. Stability studies confirmed that the formulations maintained their integrity under different environmental conditions, ensuring long-term usability. Additionally, the antimicrobial efficacy of the formulation suggests potential applications beyond pain management, particularly in dermatological conditions involving microbial infections. The findings indicate that capsaicin emulgel is a promising candidate for topical therapy, offering advantages in drug delivery, patient compliance, and therapeutic effectiveness. Future research should focus on clinical trials to further validate its safety and efficacy in human subjects.

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