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Capsaicin-Based Emulgel for Inflammation: Formulation, Stability, and Therapeutic Efficacy

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ABSTRACT:

Background: Inflammatory conditions such as osteoarthritis and neuropathic pain require effective and targeted therapeutic interventions. Capsaicin, a bioactive compound derived from chili peppers, exhibits potent analgesic and anti-inflammatory properties but faces challenges such as poor solubility, low bioavailability, and potential skin irritation. Emulgels, a hybrid formulation of emulsions and gels, provide an optimal delivery system for capsaicin by enhancing drug penetration, stability, and patient compliance.

Objective: This study aimed to develop and evaluate a capsaicin-loaded emulgel for topical application, assessing its physicochemical properties, stability, in vitro drug release, and anti-inflammatory efficacy.

Methods: The capsaicin emulgel was formulated using isopropyl myristate as the oil phase, Tween 80 as the emulsifier, and carbopol 934 as the gelling agent. The formulation was characterized based on physical appearance, viscosity, pH, and drug content. Stability studies were conducted under different storage conditions for three months. In vitro drug release was evaluated using a Franz diffusion cell, and anti-inflammatory efficacy was assessed using a carrageenan-induced paw edema model in Wistar rats. Skin irritation potential was also examined in albino rabbits.

Results: The formulated emulgel exhibited a smooth texture with no phase separation. The viscosity ranged from 1200 to 2300 centipoise, ensuring appropriate spreadability. The pH was found to be 6.2 ± 0.3, confirming skin compatibility. Drug content analysis indicated uniform capsaicin distribution (98.4 ± 1.2%). Stability studies confirmed the maintenance of physicochemical properties over three months. The in vitro drug release study demonstrated sustained capsaicin release, with 78% released over 12 hours. The anti-inflammatory evaluation showed significant inhibition of paw edema (65.2% at 3 hours). No signs of skin irritation were observed, indicating good biocompatibility.

Conclusion: The capsaicin emulgel demonstrated favorable physicochemical properties, sustained drug release, significant anti-inflammatory activity, and excellent skin compatibility. These findings suggest that capsaicin emulgel is a promising topical formulation for managing inflammatory conditions. Further clinical studies are recommended to validate its therapeutic efficacy in human subjects.

Keywords: Capsaicin, Emulgel, Inflammation, Topical drug delivery, Anti-inflammatory activity

1. Introduction

Inflammatory conditions, such as osteoarthritis and neuropathic pain, pose significant challenges in clinical management due to their chronic nature and limited treatment options. Topical drug delivery systems have gained prominence as non-invasive approaches for targeted therapy, enhancing local bioavailability while reducing systemic side effects (Pardeike et al., 2009). Among these, emulgels have emerged as a promising formulation, combining the benefits of emulsions and gels to improve drug penetration, stability, and patient compliance (Hasan et al., 2021; Shah et al., 2023).

Capsaicin, a bioactive alkaloid derived from chili peppers (Capsicum species), has been extensively studied for its potent analgesic and anti-inflammatory properties (Basith et al., 2016; Maharjan et al., 2024). It exerts its therapeutic effects through transient receptor potential vanilloid 1 (TRPV1) receptor modulation, leading to desensitization of nociceptive neurons (Anand & Bley, 2011; Szabados et al., 2020). This mechanism makes capsaicin an effective treatment for various chronic inflammatory conditions, including osteoarthritis, neuropathic pain, and postherpetic neuralgia. However, its clinical utility is often hindered by poor water solubility, low bioavailability, and potential for skin irritation (Szallasi & Sheta, 2012).

The development of capsaicin-loaded emulgels presents a novel strategy to overcome these limitations. Emulgels facilitate controlled drug release, enhance skin penetration, and minimize irritation, making them an ideal medium for capsaicin delivery (Pathan & Setty, 2009). Optimizing formulation parameters, such as particle size, pH, and the selection of emulsifiers and gelling agents, can further enhance the stability and efficacy of capsaicin emulgels (Snehal & Manish, 2013). Previous studies have demonstrated that incorporating nanosized or micronized drug particles in emulgels improves

drug absorption and prolongs therapeutic effects (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).

This study explores the role of capsaicin emulgel in the management of inflammatory conditions by evaluating its physicochemical properties, stability, drug release profile, and potential skin irritation effects. By optimizing the formulation and assessing its pharmacological performance, this research aims to contribute to the advancement of capsaicin-based topical therapies, offering a more effective and patient-friendly approach to 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 isopropyl myristate as the oil component, with Tween 80 acting as the emulsifier. The aqueous phase consisted of purified water, in which carbopol 934 was dispersed as a gelling agent. Glycerin was added as a humectant, and triethanolamine (TEA) was used to adjust the pH to a range of 6.0 to 6.5. Capsaicin (0.5% w/w) was incorporated as the active pharmaceutical ingredient.

2.2. Methods

2.2.1. Preparation of Capsaicin Emulgel

Capsaicin emulgel was prepared using an oil-in-water emulsion system. Capsaicin (0.5% w/w) was dissolved in a suitable oil phase consisting of isopropyl myristate and Tween 80 as an emulsifier. The aqueous phase contained carbopol 934 as a gelling agent, glycerin as a humectant, and triethanolamine to adjust the pH. The two phases were mixed under constant stirring at 2000 rpm until a homogeneous emulgel was obtained.

2.2.2. Characterization of Emulgel

The prepared formulation was evaluated for physical appearance, homogeneity, and spreadability. The viscosity was measured using a Brookfield viscometer, and pH was determined using a digital pH meter. Drug content was assessed using UV-Vis spectrophotometry at 280 nm.

2.2.3. In Vitro Drug Release Study

The drug release profile of capsaicin from the emulgel was analyzed using a Franz diffusion cell system. The receptor compartment contained phosphate-buffered saline (pH 7.4) and was maintained at 37°C. Samples were collected at predetermined intervals and analyzed using UV-Vis spectrophotometry.

2.2.4. Anti-Inflammatory Activity

The anti-inflammatory efficacy of the capsaicin emulgel was evaluated using a carrageenan-induced paw edema model in Wistar rats. Animals were divided into control, placebo, and treatment groups. Paw volume was measured at 0, 1, 3, and 6 hours post-application using a digital plethysmometer. The percentage inhibition of edema was calculated to assess anti-inflammatory efficacy.

2.2.5 Skin Irritation Test

To evaluate the safety of the formulation, a skin irritation study was conducted on albino rabbits. The emulgel was applied to a shaved dorsal skin area, and signs of erythema and edema were monitored over 72 hours.

3. Results

3.1. Physical and Rheological Properties

The capsaicin emulgel exhibited a smooth, homogeneous texture with no phase separation. The viscosity ranged between 1200 and 2300 centipoise, indicating suitable rheological properties for topical application. The pH was found to be 6.2 ± 0.3, ensuring compatibility with skin pH.

3.2. Drug Content and Stability

The drug content was determined to be 98.4 ± 1.2%, confirming uniform distribution. Stability studies revealed that the formulation maintained its physical and chemical properties for up to three months under different storage conditions (25°C, 40°C, and refrigerated conditions).

3.3. In Vitro Drug Release

The in vitro drug release study demonstrated a sustained release pattern, with approximately 78% of capsaicin released over 12 hours, indicating controlled drug release properties.

3.4. Anti-Inflammatory Activity

The carrageenan-induced paw edema test showed that capsaicin emulgel significantly reduced inflammation compared to the control and placebo groups. At the 3-hour mark, edema inhibition was 65.2%, which was comparable to standard anti-inflammatory treatments.

3.5. Skin Irritation Test

No signs of erythema or edema were observed in the treated animals, confirming the biocompatibility and safety of the formulation.

4. Discussion

The findings of this study demonstrate that the formulated capsaicin emulgel possesses desirable physicochemical properties, sustained drug release, significant anti-inflammatory activity, and excellent skin compatibility. These attributes indicate its potential as an effective topical formulation for pain and inflammation management.

The capsaicin emulgel exhibited a smooth, homogeneous texture with no signs of phase separation, confirming its stability. The viscosity range (1200–2300 cP) was appropriate for topical application, ensuring ease of spreadability and prolonged skin contact. Furthermore, the formulation's pH (6.2 ± 0.3) was close to that of normal skin, reducing the likelihood of irritation and enhancing patient compliance.

The drug content uniformity (98.4 ± 1.2%) demonstrated effective incorporation and dispersion of capsaicin in the emulgel matrix. The stability studies further confirmed that the formulation remained stable for up to three months under various storage conditions, indicating its robustness and suitability for commercial development. This stability is crucial for ensuring therapeutic efficacy over the product's shelf life.

The sustained drug release profile observed in the Franz diffusion study, with approximately 78% of capsaicin released over 12 hours, suggests that the emulgel formulation successfully controlled drug release. This controlled release is advantageous as it prolongs capsaicin's therapeutic effect, potentially reducing the need for frequent application and enhancing patient adherence to treatment.

The significant inhibition of edema (65.2% at 3 hours) in the carrageenan-induced paw edema model highlights the potent anti-inflammatory efficacy of the capsaicin emulgel. This result is comparable to standard anti-inflammatory treatments, supporting its use as a viable alternative for topical anti-inflammatory therapy. The observed efficacy may be attributed to the enhanced penetration of capsaicin through the emulgel base, leading to increased bioavailability at the site of action.

The absence of erythema or edema in skin irritation study confirms the biocompatibility and safety of the formulation. This is a crucial aspect for topical formulations, as skin irritation can limit their practical application. The use of carbopol 934 as a gelling agent and glycerin as a humectant likely contributed to the formulation's skin-friendly nature.

5. Conclusion

Overall, the results suggest that capsaicin emulgel is a promising topical formulation with excellent physicochemical stability, sustained drug release, significant anti-inflammatory activity, and good skin compatibility. Future studies should explore long-term clinical efficacy and patient-reported outcomes to further establish its therapeutic potential.

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