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Pusat Asasi

NanoRelief Gel: An Advanced Celecoxib Nanoemulgel for Effective Pain and Inflammation Relief

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ABSTRACT

Celecoxib (CXB) is a medication for the treatment of relieving pain and reducing inflammation in osteoarthritis and rheumatoid arthritis. It has low bioavailability when administered orally due to its lipophilic nature and low water solubility. Transdermal administration can allow targeted drug delivery without first-pass metabolism. However, it is difficult to get through the outermost layer of the skin due to the nature of the stratum corneum. To solve this issue, nanoemulsion (NE) serves as a vehicle for the delivery of various active pharmaceutical ingredients and has attracted great attention in the drug delivery field. One of our approaches is to modify NE into a new dosage form, which is nanoemulgel (NEG) for improved skin permeability. NanoRelief Gel is a topical gel that contains CXB as the active component. The gel's particle size of 149.07±1.42 nm demonstrates great permeability and therapeutic effects, with a narrow size distribution of 0.21±0.01 and good stability with the zeta potential value of -33.07±2.87 mV. NanoRelief gel provides effective alternative to traditional oral pain relief medications and can be site-specific, further enhancing its effectiveness. It has strong commercial potential value for arthritis patients due to its safety and effectiveness.

Keywords: Celecoxib; Fractionated medium chain triglycerides (FMCTs) oils; Nanoemulsion gel; Transdermal delivery; Pain and inflammation relief

INTRODUCTION

Celecoxib (CXB) is a nonsteroidal anti-inflammatory drug that belongs to Biopharmaceutics Classification System (BCS) Class II and has a low water solubility (4 mg/ml) due to its lipophilic properties. This restricts its oral use because of its inability to enter the gastrointestinal tract, resulting in poor bioavailability and inadequate absorption [1]. Transdermal delivery of CXB through the skin, on the other hand, provides advantages over oral delivery since it avoids hepatic first-pass metabolism and can be managed directly to specific sites of action, reducing the amount of drugs used and potential side effects [2].

The main problem for transdermal delivery is getting through the skin's outermost layer, which is challenging due to the stratum corneum's nature. According to research, nanosized topical formulations known as nanoemulsions (NE) with particle size ranging from 20 to 200 nm can improve drug permeability by disrupting the skin's lipid matrix [3]. However, because of its low viscosity, NE has a shorter contact time with the skin. To overcome this issue, gelling agents are combined with NE to form the NEG system, which has additional transdermal

applications and dual control releases. NEG also enhances colloidal stability and viscosity, resulting in improved treatment and therapeutic outcomes [4].

It has been suggested that NEG as an excellent carrier system for the delivery of lipophilic drugs [5]. Hence, the NanoRelief Gel was formulated as a solution to deliver lipophilic drugs like CXB to treat inflamed skin and pain in osteoarthritis and rheumatoid arthritis. The gel uses oil-in-water (O/W) NE systems and xanthan gum (XG) as a gelling agent, which is known to be a promising delivery system for lipophilic drugs. The components of the NE system, including fractionated medium chain triglycerides (FMCTs) oils namely medium chain triglycerides (MCTs) and palm kernel olein (PKOlein) oils and non-ionic surfactants, can effectively enhance drug permeation safely through the skin [6]. The gel's high viscosity, spreadability, thixotropic behavior, and easy removal make it an excellent transdermal drug delivery option [7].

INNOVATION DEVELOPMENT

NanoRelief Gel was formulated in three steps were involved as shown in Figure 1. First, a mixture of MCTs and PKOlein was used as the oil phase, and 1% of CXB was added to it. Then, mixed surfactants (Smix) of Tween 80 (T80) and Tween 85 (T85) in ratio 1:2 were added to the oil phase at room temperature. Deionized water was slowly added to this mixture in a dropwise manner, and it was homogenized for 30 minutes. Mixed oil phase and Smix of T80 and T85 were selected due to their high solubilizing potential for CXB as reported in our previous work [8]. Second, XG was added to deionized water to make a hydrogel base. Third, the hydrogel and NE system were mixed separately and then combined in a 1:1 ratio to form the final product, NanoRelief Gel, as shown in Figure 2.

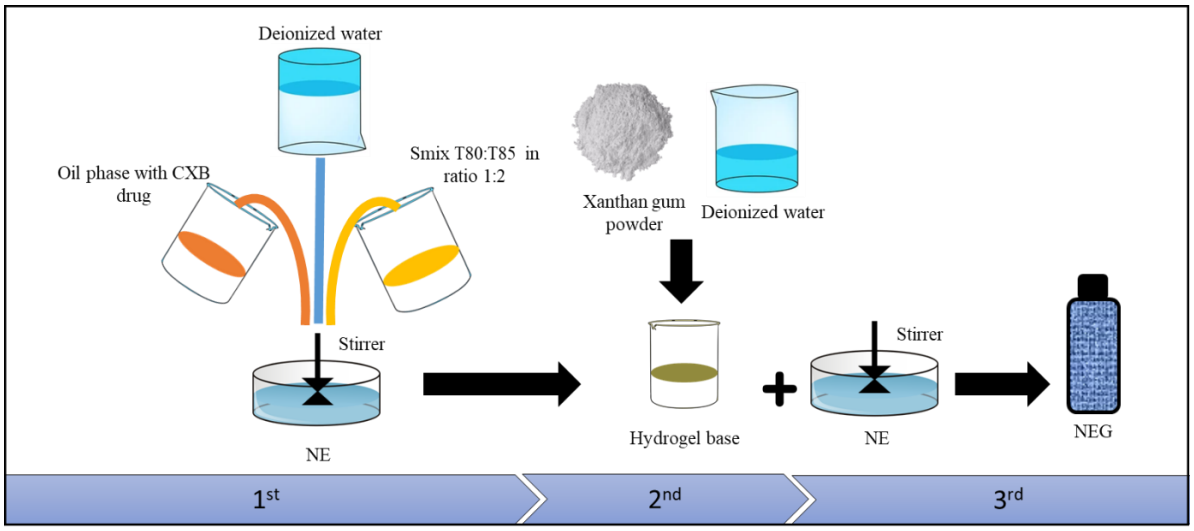

Figure 1: Innovation development of NanoRelief Gel.

Figure 2: Innovation prototype of NanoRelief Gel.

The particle size, polydispersity index (PDI), and zeta potential of both NanoRelief Gel and NE were then analysed (Figure 3). Results showed that both had a particle size of less than 200 nm (149.07±1.42 nm and 154.37±0.12 nm respectively) allows an effective penetration of the active ingredient CXB into the skin [9]. The PDI for both was less than 1.0 (0.21 and 0.22 respectively), indicating consistent and reliable product performance [10]. The zeta potential for both was less than -20 mV (-33.07±2.87 mV and -23.67±1.68 mV respectively), indicating that it is highly stabilized particles and an improved shelf life for the product (Figure 4).

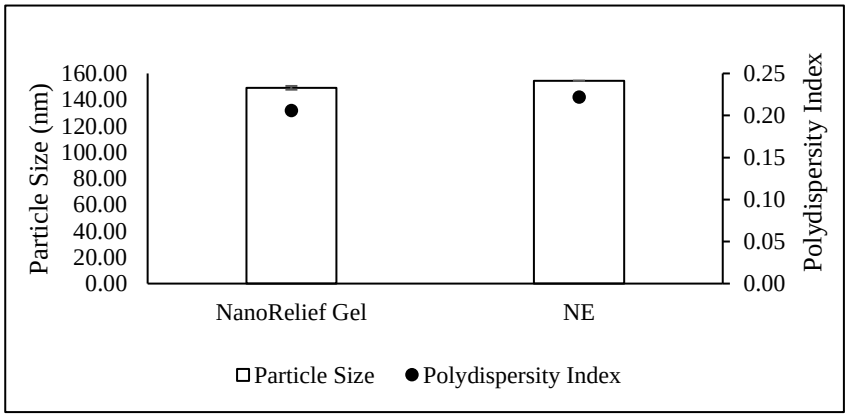

Figure 3: The particle size and polydispersity index (PDI) values between NanoRelief Gel and NE (n=3).

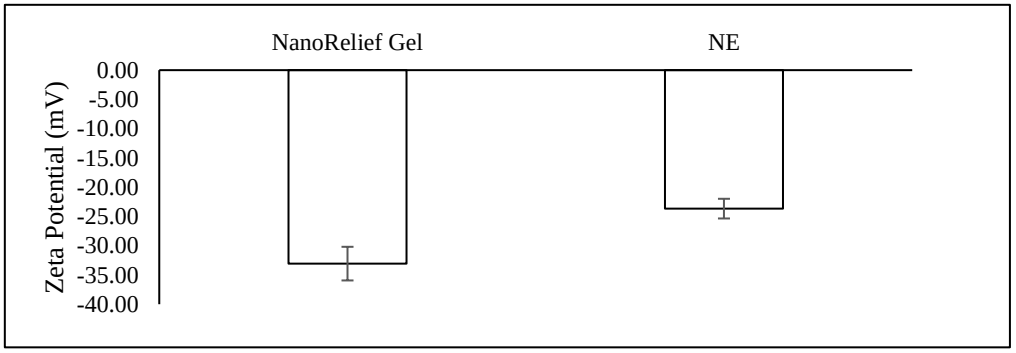

Figure 4: The zeta potential value between NanoRelief Gel and NE (n=3).

COMMERCIAL POTENTIAL

NanoRelief Gel is an innovative product that addresses the issues raised by conventional drug delivery systems. The stratum corneum layer of the skin forms a highly effective barrier, making transdermal drug delivery difficult and limiting the therapeutic potential of many topical formulations on the market. However, NanoRelief Gel can overcome this barrier due to its unique features, such as its small droplet size, which allows for better skin penetration. The gelling agent in the gel controls drug release, lowering the frequency of administration and the risk of overdose. NanoRelief Gel, unlike typical NE, is appropriate for transdermal delivery due to its improved viscosity and stability, allowing it to be retained on the skin surface for extended periods, sustaining drug release and improving drug absorption through the skin.

NanoRelief Gel contributes to new knowledge and technology by introducing an improved drug delivery system that combines the benefits of NE and hydrogel systems to improve drug stability, bioavailability, and therapeutic efficacy of CXB. This technology has revealed new insights into the role of NEG and the skin barrier in drug delivery without the need for chemical penetration enhancers, making it a safe and effective option.

NanoRelief Gel also offers a more environmentally sustainable product such as reducing the need for frequent dosing such as syringes, needles, and other medical waste, making it a viable choice for users seeking effective and safe transdermal drug administration. Also, it provides an alternative to parenteral drug delivery, which can be invasive and uncomfortable for patients. This could improve patient compliance and quality of life.

The O/W NE formulation's nanosized droplets improve therapeutic efficacy and reduce adverse effects by increasing the drug's surface area, which improves penetration and permeation through the skin. Instead of dangerous chemical penetration enhancers, NanoRelief Gel used harmless skin penetration enhancers such as FMCT oils and non-ionic surfactants. This makes NanoRelief Gel safer and more user-friendly solution for patients, particularly those with sensitive skin or chemical allergies. Thus, NanoRelief Gel offers several benefits that make it a promising solution for users in need of effective and safe transdermal drug delivery.

In terms of market needs, the global market for osteoarthritis treatments alone is expected to reach over $8.7 billion by 2027 [11]. This shows there is a growing demand for effective pain relief and anti-inflammatory treatments for osteoarthritis and rheumatoid arthritis patients. Thus, NanoRelief gel is well-positioned to address this market need, providing a safe and effective alternative to traditional oral pain relief medications that can have harmful side effects. As a result, there is a high market potential for this product as there is a growing demand for alternative routes of drug delivery that are safe, effective, and convenient.

CONCLUSION

In conclusion, the development of the NanoRelief Gel for transdermal drug delivery, offers a promising solution to the challenges of delivering drugs through the skin. Further studies could be conducted to evaluate the safety and toxicity of the NanoRelief Gel.

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