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Bigels as a Platform for Advanced Topical Application

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Abstract

This comprehensive review examines the potential of bigels, an innovative semi-solid system that combines hydrogels and organogels, as a platform for sophisticated topical applications. Bigels possess a distinct combination of characteristics, combining the hydrophilic properties of hydrogels with the lipophilic attributes of organogels. The hydrogel portion, made up of water-loving polymers such as carbopol, hydroxypropyl methylcellulose, and alginate, offers significant water absorption capabilities and compatibility with biological fluids. Meanwhile, the organogel segment, consisting of non-polar liquids like organic solvents or oils, allows for the inclusion of lipophilic active ingredients. By taking advantage of the complementary properties of bigels, this platform can be customized to facilitate a variety of topical uses, including transdermal drug delivery, promoting wound healing, and developing cosmetic products. The bigel system can be optimized to display particular porosity, crosslinking density, and release kinetics, enabling the regulated release of active compounds. This groundbreaking platform has the ability to transform the realm of topical applications, delivering enhanced effectiveness, stability, and patient adherence. This review seeks to explore the formulation, characterization, and assessment of bigels as a flexible platform for cutting-edge topical applications, setting the stage for the creation of new, effective, and safe products.

Keywords: Bigel, Topical applications, Hydrogel, Organogel

Introduction

Gels are semi-solid systems formed of a solid and a liquid component ^[1, 2]. Hydrogels and organogels are two distinct types of gels that are categorized based on the polarity of the liquid component ^[3]. In contrast to organogels, which have apolar liquids as their continuous phase, like organic solvents or mineral or vegetable oils, hydrogels are gels whose continuous phase is frequently a polar solvent, similar to water ^[4, 5].

Hydrogel

A hydrogel is a 3D network consisting of hydrophilic polymers that has a high water or biological fluid absorption capacity ^[6]. These complexes' physicochemical compatibility with water, the competency to modify their porosity and crosslinking density, and the fact that their polymeric chains can contain hydrophilic functional groups like amino or carboxylic groups, among others, all contribute to the water absorption ^[7, 8].

Carbopol, hydroxypropyl methylcellulose, alginate, gelatin, guar gum, pectin, poloxamer 407, PVA, PVP, and sodium polyacrylate are polymers applied in the expression of hydrogels for bigels.

Organogel

Organogels are semi-solid complexes in which an organic liquid phase is immobilized by a three-dimensional network formed of self-clustered, conjugated gelator fibers ^[9]. These biphasic systems retain viscoelastic characteristics and can be opaque or transparent. They behave like solids and have elastic properties at low shear rates, but when the shear stress is high enough to make the network's physical connections break down, they turn into fluids ^[9, 10, 11].

Sorbitanmonopalmitate (Span40), sorbitanmonostearate (Span60), glyceryl fatty acid ester glyceryl monostearate, beeswax, candelilla wax, lecithin, polyethylene, fumed silica, and cetyl and stearyl alcohols are extensively used as organogelators.

Benefits of Hydrogel

- Simplicity of preparation.
- Non-oily nature.
- Good spreadability.
- Capacity to increase stratum corneum hydration.
- Cooling effect.
- Ease of removal following application.

Benefits of Organogel

- Simple to make.
- Dissolve hydrophobic drugs because of their lipophilic character.
- Make hydrophobic drugs more permeable to the stratum corneum. [12, 13, 14, 15].

Bigels are complex drug release networks that will deliver a wide range of drugs, whether small molecules or biologics, through hydrophilic and lipophilic delivery from one formulation. This methodical structure has hydrogels and organogels that could actually permit the release of drugs through the skin [16, 17].

Comparison of bigels to traditional gels and emulsions

Traditional gels and emulsions have been extensively studied and utilized due to their established roles in drug delivery systems. However, they also possess limitations, particularly concerning stability, drug release profiles, and mechanical integrity. Recent advances in gel technologies emphasize the need for enhanced systems that can overcome the limitations of traditional gels. They proposed that bigels could fulfill this requirement by offering improved stability and controlled release of therapeutic agents. The use of a hybrid system could significantly enhance transdermal drug delivery in polymer-fish oil bigels. The study revealed that bigels not only offered improved permeability but also maintained the integrity of the active ingredients better than traditional emulsions. This is particularly important for topical applications where the stability of the formulation directly impacts therapeutic effectiveness [18].

Key advantages of using bigels in topical treatments

Enhanced Drug Permeation: Bigels have been shown to act as effective permeation enhancers for transdermal drug delivery. The unique matrix structure of bigels can facilitate the movement of active ingredients through the skin barrier [19]. This characteristic is particularly beneficial for hydrophilic drugs that typically face challenges in skin permeation. The dual-phase nature of bigels allows for improved solubility and bioavailability of poorly soluble

drugs, making them ideal for various topical applications [20].

Sustained Release Profiles: The formulation of bigels allows for sustained release of drugs, which is advantageous for maintaining therapeutic levels over extended periods. The gel-like nature of bigels slows down the release of drugs compared to conventional gels and ointments [18]. This sustained release is particularly beneficial in treating chronic conditions where long-term application is necessary, thus improving patient compliance and therapeutic effectiveness.

Stability of Active Ingredients: Bigels offer enhanced stability for sensitive active ingredients. The emulsion component within bigels can protect sensitive molecules from degradation due to environmental factors like light and oxygen [21]. This stability is crucial for maintaining the efficacy of pharmaceutical products, especially those containing bioactive compounds that are often prone to degradation. Furthermore, the incorporation of antioxidants into bigel formulations can further enhance the stability and efficacy of the delivered compounds [22].

Versatility in Formulation: Bigels can be tailored to incorporate various types of active ingredients, including hydrophilic and lipophilic drugs. This versatility is advantageous for creating multifunctional topical treatments that can address multiple skin conditions simultaneously. The ability to manipulate the formulation parameters of bigels allows for the development of customized drug delivery systems tailored to specific therapeutic needs. [23].

Mechanisms of drug release from bigels: The primary method of drug release in bigels is primarily attributed to diffusion, partitioning, and swelling. Generally, drugs released from bigels provide a pattern for controlled release that lasts for a relatively long duration because the mechanism of releasing the drug from the gel matrix can be sustained over time. Temperature, pH, and ionic strength have also been shown to influence drug release rates from bigels [24, 25]. As an illustration, an increase in temperature leads to a reduction in gel viscosity, resulting in faster drug release rates.

Formulation techniques of Bigel

Step 1: Preparation of the hydrogel and the organogel separately. Typically, the creation of an organogel necessitates heating, while both hydrogel and bigel can be produced with either heating or at room temperature (RT).

Step 2: Incorporating the organogel into the hydrogel or vice versa can be done [26].

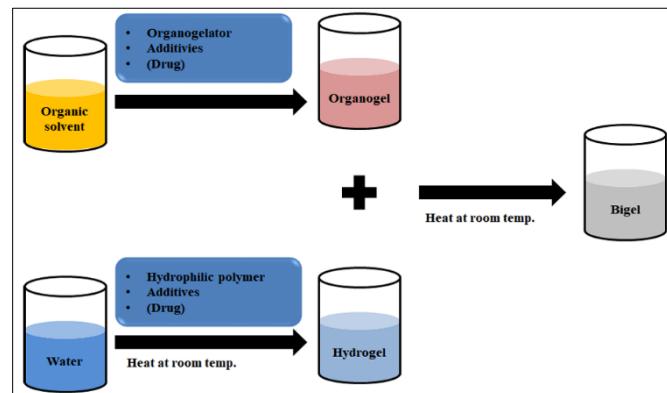


Fig 1: Development of Bigel system

The process of producing the individual gels has been described as simple. The solvent is dissolved, dispersed, or incorporated with the gelling agent and the remaining elements of each gel, similar to preservatives for the hydrogel and antioxidants for the organogel [27, 28]. Since organogels are continually created through the application of heat, the admixture of their constituent parts is generally

allowed to cool to room temperature in order to produce the actual organogel before it's combined with the hydrogel. Hydrogels produced at high temperatures may sometimes also undergo this cooling process.

Characterization of bigels

Table 1: Characterization techniques of bigels

S. No.	Characterization	Analytical techniques	Description
1	Visual Analysis	Visual assessment	assessment of color and texture
		Inversion test	to determine the formation of a "correct" bigel that can stand under its own weight, or behave as a solid under gravitational pull
2	Microstructural Analysis	Optical microscopy Phase contrast microscopy Confocal microscopy Fluorescence microscopy	to study the morphology of bigels
3	Rheological and mechanical testing	Rheology by Small-Amplitude Oscillatory Shear (SAOS) tests	to study the viscoelastic properties of gels under small deformations
		texture profile analysis (TPA)	to derive firmness, cohesiveness, adhesiveness, and spreadability
4	Other analyses	Fourier transform infrared (FTIR) spectroscopy	to identify functional groups on polymers and chemical interactions between bigel components themselves and with enclosed molecules of interest
		Storage studies	to evaluate changes in microstructural, thermal, and rheological properties over a predetermined time at a preset temperature profile
		Release profile characterization by modified Franz cells	to measure drug release, penetration and diffusion

Applications of bigels in skin

Dermatology and wound healing: Due to the fact that bigel systems are capable of delivering hydrophilic as well as lipophilic drugs from one formulation, they are highly recommended for chronic skin conditions, including psoriasis, eczema, and acne. [29, 30]. Bigels are being investigated for their use as delivery systems for corticosteroids, antifungals, and antibiotics. Thus, in this regard, bigels are allowing for localized treatment with a minimal amount of systemic absorption of therapeutic drugs. A bigel formulation with hydrocortisone and clotrimazole further indicated an enormous potential in the treatment of fungal infections when it manifested therapeutic efficacy with anti-inflammatory benefits [31, 32].

Similarly, ibuprofen-loaded bigels have been investigated for their topical anti-inflammatory and analgesic applications with promising results compared with the conventional creams and gels [33, 34].

Cosmetics form

Bigels have also proven to be useful in cosmetic formulations, serving as delivery systems for active ingredients such as antioxidants, moisturizers, or anti-aging agents. For example, a bigel formulation with vitamin C and hyaluronic acid has been shown to enhance skin hydration with considerable potential to act as an anti-wrinkle and anti-line formulation [35, 36].

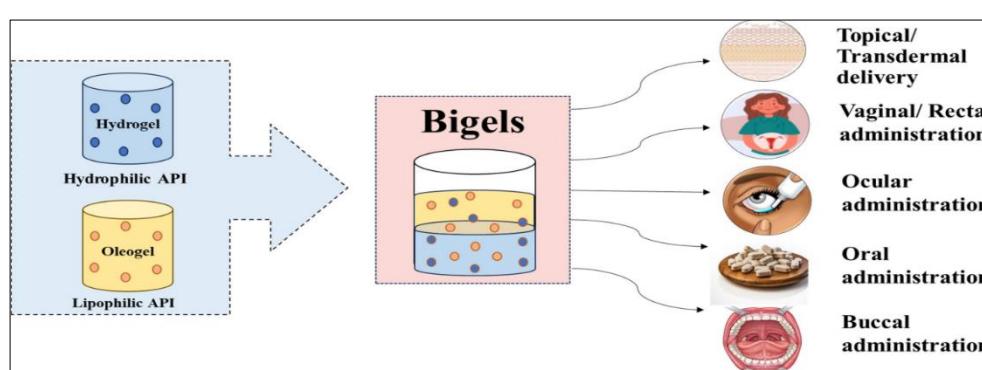


Fig 2: Applications of bigels

Safety considerations of bigels

Biocompatibility is a critical concern in the development of drug delivery systems, including bigels. Bigels must be designed to encapsulate and release drugs without degrading their efficacy or inducing toxicity. The integration of

biodegradable and biocompatible materials is paramount in enhancing the safety profile of bigels. The safety profile of bigels could be improved through the incorporation of intelligent biomaterials that enable stimuli-responsive release mechanisms. Such advancements could minimize

systemic toxicity, enhancing the therapeutic index of the delivered drugs.

Future advancements in bigel technology

Future research should focus on the optimization of bigel formulations to enhance their therapeutic efficacy and stability. Investigating the interactions between various plant oils and bigel matrices could lead to the development of more effective topical treatments. Additionally, exploring the potential of bigels in combination with other innovative drug delivery systems, such as nanocarriers, could open new avenues for advanced therapeutic applications.

Conclusion

In conclusion, bigels represent a novel and versatile platform for advanced topical applications, particularly in drug delivery and wound healing. The current literature underscores the potential benefits of bigels in enhancing therapeutic outcomes while highlighting the need for further research to address existing gaps. By continuing to explore the unique properties of bigels, researchers can pave the way for innovative solutions in dermatological and pharmaceutical applications.

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