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A REVIEW ARTICLE ON NOVEL DRUG DELIVERY BIGEL

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ABSTRACT

Gel are semisolid systems made up of a gelling agent and a polar liquid solvent. Gels are used in the food, pharmaceutical, and cosmetics industries. They are classified based on their structural and rheological properties. Scientists are looking for new ways to create gels with better properties. Many bigel formulations have been created and altered recently to satisfy the demands of various applications. Bigels' ability to deliver both hydrophilic and lipophilic active agents, their water washability after application to the skin, their easy preparation, good stability, and the enrichment of stratum corneum's hydration, which results in a cooling and moisturizing effect, are some of their key characteristics that make them useful for controlled drug delivery. Since bigel formulations are a new class of materials, further research into these systems is necessary before they can be used in real-world applications. When synthesizing bigels by combining organogel and hydrogel, several factors are crucial, such as bigel storage.

KEY WORDS: *Gels, Bigels, Hydrophilic, Lipophilic, Controlled Drug Delivery*

INTRODUCTION:[1]

It is possible to define gels based on two key characteristics: rheological behaviour and structural behaviours. A substance can be classified as a gel from a rheological perspective if it satisfies the following criteria:

[i] it behaves like a solid
[ii] on the analytical experiment time scale, its structure is permanent with macroscopic dimensions
[iii] it has a plateau region of storage modulus with low tanδ at an angular frequency ranging from 10-3 to 102 rad/s
[iv] it does not flow.

From a structural standpoint, gel is a system made up of molecules, particles, and chains that are partially connected to one another in a liquid medium by chemical or physical bonds; this network is what causes the system to lose its fluidity.

Gels are semisolid systems that are typically made up of two parts: a solid part that serves as a gelling agent and a liquid part that can be either polar or a polar and functions as a solvent. To produce semisolid properties, the gelling agent traps the solvent phase by creating a three-dimensional network structure. Gels are remarkable substances that possess both elasticity and rigidity by nature. They find extensive use in the food, pharmaceutical, and cosmetics industries.

Classification of Gels

Gels are classified as polymer gels (formed by crosslinked polymer molecules) and particle gels (containing colloidal particles). They are further categorized as hydrogels (with polar solvents) or organogels. Hydrogels are widely used in pharmaceuticals, while recent studies explore emulgels and bigels for topical drugs.

Organogels

Oleogels, or palatable oil organogels, are solid-like systems with a thermoreversible 3D network formed by organogelators. They efficiently immobilize organic liquids at low concentrations, ideal for enhancing drug permeation and surpassing emulsifier limits in food preparation.

Hydrogels

Hydrogels, jelly-like materials formed by hydrophilic agents, create a three-dimensional network to encapsulate water without dissolving. They are non-greasy, easily removable, offer a cooling effect, enhance skin hydration, and boast a high market value due to increased patient compliance.

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Cons of Conventional Gel
Organogels pose challenges with greasiness and stickiness, reducing patient compliance due to difficulty in skin removal. Hydrogels face limitations in delivering lipophilic medications through the stratum corneum, hampering their efficacy.

Newer Approach
Emulgels, created in the last decade, address the hurdle of dispensing hydrophobic drugs. This semisolid system combines gel and emulsion properties, with a structured continuous phase containing a dispersed liquid phase, acting like a soft particle suspension.

Bigels:[2]
Bigels, a breakthrough in multiphase formulations, address stability issues in emulgels. By structuring both internal and external phases, bigels surpass emulsions. They blend hydrogel and organogel, forming innovative materials for cosmetics and pharmaceuticals with enhanced properties.

Advantages of Bigels
Bigels combine the benefits of aqueous and oily gels, offering controlled delivery of lipophilic and hydrophilic compounds. They hydrate the stratum corneum, spread easily, are water-washable, and provide stable dispersion for 6–12 months, overcoming drawbacks of traditional gels.

Disadvantages
Bigels may also have certain disadvantages, such as the inability to be thermo-reversible due to destabilization at high temperatures.

Classification of Bigel:(22)
Depending upon the distribution of both phases (organogel and hydrogel) within bigels, these systems can be classified into three types:
1. Organogel-in-hydrogel type
2. Hydrogel-in-organogel type
3. Bi-continuous/matrix-in-matrix type

Organogel-in-Hydrogel
The organogel-in-hydrogel system comprises a dispersed organogel phase within a continuous hydrogel phase. Various hydrogelators, including gelatin, guar gum, and polyvinyl alcohol, were combined with organogels like olive oil or sorbitan monostearate for bigel formulation in different studies.

Hydrogel in organogel type
It can be defined as the system in which hydrogel phase is distributed within the continuous phase.
Second type of bigel (hydrogel-in-organogel) is the system in which hydrogel phase isdistributed within the continuous matrix of organogel. Patel et al (4). described the investigation of bigels prepared by mixing locust bean gum-carrageenan based hydrogel and sunflower oil fumed silica based organogel at several organogel-hydrogel ratios. Hydrogel-in- organogel type morphology of bigels was confirmed by the results of confocal microscopy.

Bi- continuous/ matrix in matrix type
It can be regarded as a system with complex structure in which it is difficult to identify the dispersed and continuous phase.
Third type of bigel can be regarded as a system with complex structure in which it is difficult to identify the dispersed and continuous phase. Lupi et al. (3) reported bigels made by mixinga cosmetic system (O/W) with organogels having monoglycerides of fatty acids as organogelator and olive oil as a solvent, with increasing fraction of organogel. At the maximum fraction of organogel, results revealed the presence of a complex matrix-in-matrix structure.

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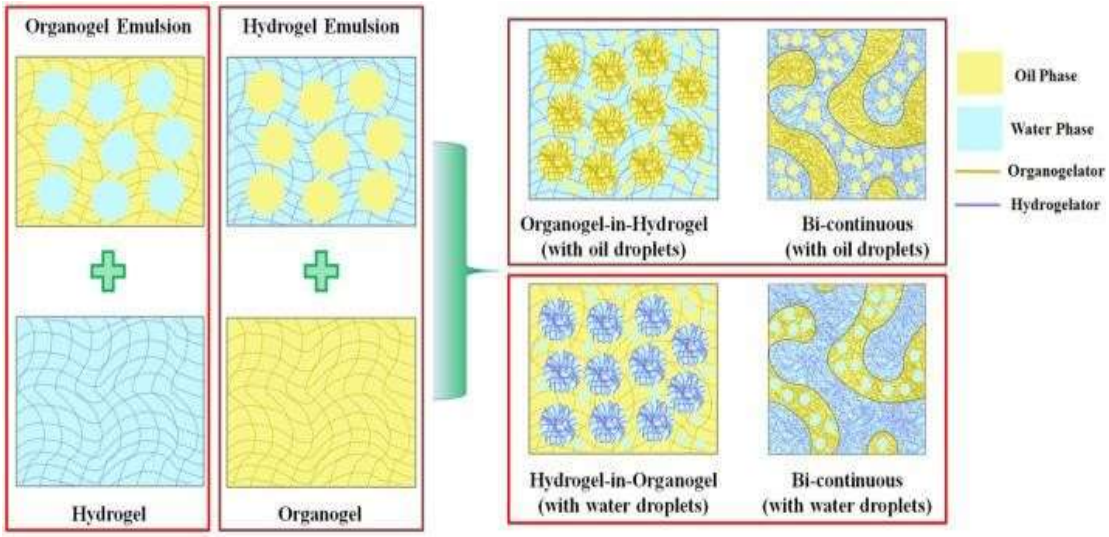

Fig 1: Types of Bigels

Method Of Preparation:[5]

The aqueous phase and the oleaginous phase are prepared separately by mixing the components at a defined speed and temperature.

Preparation of aqueous phase (Hydrogel)

Hydrogels, elastic structures with hydrophilic polymeric networks, are formed by cross-linking synthetic or natural polymers through techniques like copolymerization or radiation. Various polymerization methods create gels with monomers, initiators, and cross-linkers, while diluents control properties. Washing removes impurities post-preparation.

Preparation of Oleogel:

Oleogel, an organogel phase, is formed by self-assembly of organogelators (fatty acids, alcohols, lecithin, waxes, cyclodextrins, steroids) in a specified oil phase through homogenization at elevated temperature, solidifying at 25°C.

Preparation of Bigel

Bigel, a stable blend of hydrogel and oleogel, is prepared at high shear rates, maintaining the individual characteristics of each component. A homogenous gel forms at specific shear speed and temperature, crucially dependent on phase composition. Temperature during mixing is vital; some opt for room temperature, while others prefer higher temperatures (e.g., 50°C) for liquid phases. Thermal stability of hydrogelators is essential for the latter method. Storing individual gels before or after mixing impacts final bigel characteristics. Some create bigel systems by mixing stored gels, while others store the final bigel post-mixing. The latter method may yield a more stable system, while storing individual gels prior to mixing ensures complete gelling.

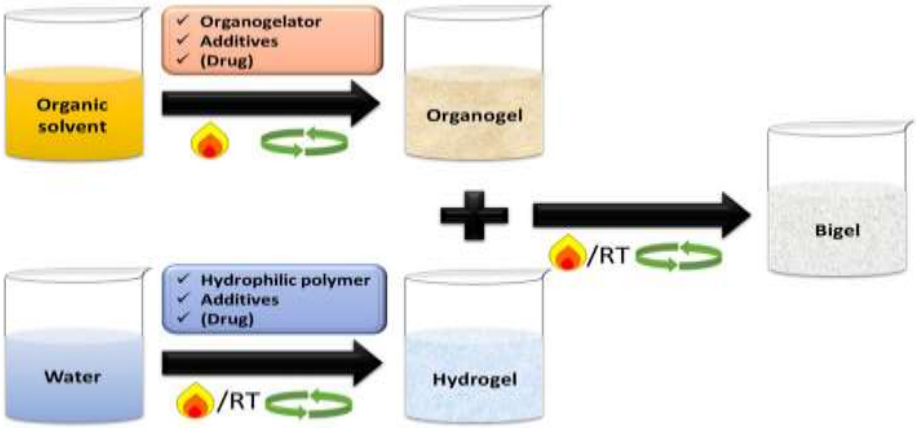

Fig 2: Bigel preparation

Characterization Techniques:[6-9]

Various techniques can be used to investigate important parameters such as the distribution of organic and aqueous phases within gels, the average droplet size of the dispersed phase, phase inversion, thermal stability, viscoelasticity, flow behaviour, antimicrobial efficiency, and drug release rate.

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Mechanical Characterization

Bigels' mechanical tests (compression, shearing, tension, bending) rely on linear motion, affected by polysaccharide branching; branched ones yield higher strength. Organogel enhances cohesiveness.

Physical Characterization

Physical characterization in pharmaceutical bigel formulations is crucial. Parameters like viscosity, shear-thinning behavior, and swelling influence drug delivery. Shear thinning enhances skin coverage, promoting transdermal absorption, ensuring efficient spreading, and minimizing gel quantity needed.

Structural Characterization

1. Microscopy
2. Fourier Transform Infrared (FTIR)
3. X-Ray Diffraction (XRD)
4. Thermal Characterization
5. Antimicrobial Testing
6. In vitro release study

Table 1:Different Bigel Systems in the literature are reported for drug delivery applications:

Oil Phase	Organogelator	Hydrogelator	Drug Incorporated
Corn oil	DIMODAN® monoglyceride	K-carrageenan	β-carotene(10)
Sweet almond oil	Span 65	Alginate	Cetavlon® (11)
Sesame oil	Sorbitan monosterate (Span 60)	Guargum	Ciprofloxacin(12)
Soyabean oil	Stearic acid	Mixture of agar and gelatin	Metronidazole (13)
Rice bran oil	Stearyl alcohol	Stearly alcohol	Ciprofloaxacin HCl (14)
Fish oil	Bees wax	Carbopol	Imiquimod (15)
Almond oil	Sorbitan monosterate (Span 60)	Carbopol	Ketoprofen (16)
Isopropyl palmitate	Mixture of soya lecithin and pluronic	Hydroxy propyl methyl cellulose	Flubiprofen (17)
TegoSoft® CT (Caprylic/capric triglycerides)	Compritol® (Liquid excipient of glycerylbehenate).	Carbopol	Ibuprofen (18)
Rice bran oil	Stearic acid	Tamarind gum	Moxifloxacin (19)
Liquid paraffin	Polyethylene	Poloxamer 407	Ciclopirox olamine and terbinafine HCl (20)
Oleogel	Polyethylene	Carbopol	NSAIDS (21)

Application of Drug Delivery

Topical drug delivery through the skin is non-invasive, requires no specialized personnel, and avoids metabolism risks. Transdermal systems, like bigels, exhibit promising drug release properties, influencing applications from medications to cosmetics and potential use in food, warranting further research.

CONCULSION

Gels have been studied extensively for topical drug delivery, and new developments in pharmaceutical science and technology have introduced new semisolid systems, like bigels, especially for topical drug delivery, in addition to modifying traditional gels, like hydrogels and organogels. Many bigel formulations have been created and altered recently to satisfy the demands of various applications. Bigels' ability to deliver both hydrophilic and lipophilic active agents, their water washability after application to the skin, their easy preparation, good stability, and the enrichment of stratum corneum's hydration, which results in a cooling and moisturising effect, are some of their key characteristics that make them useful for controlled drug delivery. Since bigel formulations are a new class of materials, further research into these systems is necessary before they can be used in real-world applications.

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When synthesising bigels by combining organogel and hydrogel, several factors are crucial, such as bige storage, mixing temperature and the use of emulsion gels in place of hydrogel or organogel.

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