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BIGELS: THE FUTURE OF COSMETICS DELIVERY

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ABSTRACT
Bigels are systems that are often created by combining hydrogel with organogel. An organogelator is present in the organic phase, which contains a gelled vegetable oil, while a hydrophilic biopolymer often forms the aqueous phase. The amount of organogel added to the hydrogel was increased to create model bigels, and microstructural analysis showed that all of the samples under investigation exhibited an organogel-in-hydrogel behavior—although at the maximum organogel concentration, a more complicated structure appeared to emerge. There have also been reports of certain novel gels, like bigels and emulgels. The stratum corneum is kept hydrated by these formulations' high-water content in their structure. The bigel's hydrogel aids in the correct hydration of the stratum corneum, and the organogel's.

KEYWORDS: Bigels, Hydrogel, Organogel, Organogelator.

INTRODUCTION
Gels are semisolid systems made up of two components: a liquid phase and a solid compound that combine to produce a three-dimensional network that traps the liquid phase. Typically, the gelator is employed at concentrations less than 15% w/v, which raises surface tension and obstructs solvent movement. Gels are divided into two categories based on the polarity of the liquid components: hydrogels and organogels. In contrast to organogels (also known as oleogels), which are gels with a continuous phase made of a polar liquid such as mineral or vegetable oils or organic solvents, hydrogels are gels with a continuous phase made of water, which is typically the polar solvent utilized. There have also been reports of certain novel gels, like bigels and emulgels. These formulations' compositions contain a good quantity of water.

Gels are categorized into two types based on the nature of the 3D network structures created by the gelator: polymer gels and particle gels. Polymer gels are generated by the crosslinking of polymer molecules. Particle gels are created when colloidal particles aggregate. Gels are categorized into two categories based on the polarity of the solvent: hydrogels and organic gels. When the liquid solvent is polar, it is referred to as a hydrogel, and when it is nonpolar, it is known as an organogel. Hydrogels are 3D hydrophilic networks composed of homopolymeric or heteropolymeric chains, and cross-linked hydrogels can absorb large amounts of water without dissolving in it. Organogel is a solid-like structure in which organic liquid is confined.

Bigels have been identified as a promising possibility for controlled drug delivery. Some of their features, such as superior spreading ability and cooling impact, make them ideal for transdermal administration. Nanosystem-based bigels have also been created for drug delivery. The drug's shape altered the rheological qualities of the bigels. Although the majority of drug delivery bigels in the literature are for topical application through the skin, bigels for vaginal medication release have also been created. In recent years, drug delivery bigels have been designed for buccal administration.

DEFINITION: Bigels are systems that usually result from mixing a hydrogel and an organogel: the aqueous phase is commonly formed by a hydrophilic biopolymer, whereas the organic phase comprises a gelled vegetable oil because of the presence of an organogelator.

IDEAL PROPERTIES
- Bigels have high stability which means they can hold their shape without breakingdown easily.
- They have good drug release properties, making them suitable for controlled releaseapplications.
- They have high loading capacity, allowing them to encapsulate a large amount of activeingredients.
- They offer enhanced stability which means they can protect the drug from degradation and maintain its

effectiveness.
- They provide controlled release capabilities, allowing for a more precise and sustained drug delivery.
- It has excellent biocompatibility, which means they are well tolerated by the body andhave minimal side effects.
- They can also be easily formulated into different shapes and sizes, allowing for versatileapplications.

ADVANTAGES
- Bigel drug delivery system encourages better stratum corneum hydration and controlleddrug distribution.
- Bigels will also accept drugs that are both lipophilic and hydrophilic.
- Bigels are readily spreadable and have a great moisturizing effect on the skin and are simple to clean.
- Bigels have high spread ability, cooling action, emollient and moisturizing impact, and emollient effect.
- Bigels gives good moisturizing effect to the skin
- Bigels provide good spread ability and wash ability
- Good patient compliance without compromising the beneficial effects of the oil.
- They are easy to formulate.
- They are less toxic due to usage of less amount of surfactants
- Bigels can easily penetrate through the skin. Hence it is a better choice for transdermaldrug delivery.
- Bigels are having the capability to regulate the delivery of active pharmaceuticalsubstances.

DISADVANTAGES
- Bigels are thermo-irreversible and unstable at higher temperatures.
- Phase separation occurs if an emulsifier is absent.
- Their production may be more challenging and time consuming due to complexity oftheir formulation.
- Stability of bigels can be affected by temperature changes, which may require special storage conditions.
- Scale-up of bigel production for commercial purposes can be a bit more challengingcompared to other drug delivery system.

APPLICATION OF BIGELS
- Texture Modification: Bigels contribute to texture enhancement, providing a smooth and luxurious feel upon application.
- Stability Improvement: They enhance the stability of cosmetic formulations, preventing separation or degradation of active ingredients over time.
- Moisturization: Bigels can be designed to deliver long-lasting moisture, addressing dryness and improving skin hydration.
- Customizable Formulations: Their versatile nature allows for the creation of customized formulations, catering to specific skin types or desired effects.
- Improved Delivery of Actives: Bigels facilitate the effective delivery of active ingredients, ensuring better absorption and efficacy on the skin.
- Enhanced Product Performance: Cosmetic products incorporating Bigel technology often exhibit improved overall performance, from application to wear.
- Multifunctional Products: Bigels enable the formulation of multifunctional products, combining various cosmetic benefits in a single application.
- Extended Shelf Life: The stability provided by Bigels can extend the shelf life of cosmetic products, enhancing their longevity and usability.
- Consumer Appeal: With their ability to enhance sensory aspects and product performance, Bigels contribute to consumer satisfaction and loyalty in the competitivecosmetics market.
- Drug Formulations: Bigels are used to create novel drug formulations, enabling controlled release and improved bioavailability of pharmaceutical compounds.
- Topical Medications: Bigels can be employed in the development of topical medications, providing sustained release of drugs for enhanced therapeutic effects in dermatological applications.
- Transdermal Drug Delivery, Oral Drug Delivery, Targeted Drug DeliveryTopical drug delivery
  Biocompatible Carriers: Bigels serve as biocompatible carriers for drug delivery, protecting sensitive pharmaceutical compounds and improving their stability during storage and transport.

TYPES OF BIGELS
- Organogel-in-hydrogel (O/H): An organogel-in-hydrogel system is one that has hydrogel as a continuous phase and organogel as a dispersed phase.
- Hydrogel-in-organogel (H/O): Hydrogel-organogel system, the hydrogel phase is spread throughout the continuous matrix of the organogel. The study of bigels created by blending hydrogels with organogel forms hydrogel in organogel
- Complex bigel: Complex bigels are prepared by adding organogel/hydrogel to an oil- in-water/water-in-oil structured emulsion.
- Bicontinuous bigel: This bigel is formulated when the gel formation is carried out at ahigher proportion of hydrogel/oleogel dispersed in a lower proportion of oleo gel/hydrogel phase.

PREPARATION

The preparation of bigel involves three steps as they consist of two individual gels inmaking, the steps are
- Preparation of organogel
- Preparation of hydrogel
- Mixing of hydrogel and organogel to form bigel.

Bigels are made by first preparing the hydrogel and the organogel separately and then mixing them together. This second phase can be completed by integrating the organogel into the hydrogel, or vice versa. Overall, two

variations of this procedure may be distinguished: one in which the individual gels are created and stored separately before mixing, and another in which the gels are mixed and the already formed bigel is allowed to set. Bigel is formed by mixing hydrogel with organogel. It is the most crucial phase in the creation of bigel. Bigel was prepared using an optimized formulation of organogel and hydrogel. The needed amount of optimized hydrogel and organogel was taken and combined in the specified ratio. The process

Hydrogel preparation

The preparation of hydrogels involves the crosslinking of polymer chains to create a three- dimensional network that can absorb and retain water. Here is a general overview of the steps:

1. Selection of Polymers: Choose water-soluble polymers such as polyvinyl alcohol(PVA), polyethylene glycol (PEG), or natural polymers like agarose or alginate.
2. Crosslinking Agents: Use crosslinking agents to form the 3D network. Common crosslinkers include glutaraldehyde, genipin, or chemical initiators for free-radical polymerization.
3. Polymer Dissolution: Dissolve the selected polymer in a suitable solvent or water to form ahomogeneous solution.
4. Crosslinking: Introduce the crosslinking agent into the polymer solution and initiate the crosslinking reaction. This can involve chemical reactions, exposure to UV light, or other methods depending on the chosen polymers and cross linkers.
5. Gel Formation: As crosslinking progresses, the polymer chains link together, forming a gel. Control the reaction conditions to achieve the desired gel properties.
6. Removal of Unreacted Components: Wash or extract any unreacted polymer or cross linker to purify the hydrogel.
7. Hydration and Swelling: Allow the hydrogel to hydrate fully in water, facilitating swelling and ensuring it can absorb and retain water effectively.
8. Adjusting Properties: Fine-tune the properties of the hydrogel by adjusting factors such as polymer concentration, cross linker concentration, and reaction time.
9. Forming Hydrogel Shapes: Shape the hydrogel as needed, either by moulding it directly or cutting it into specific shapes.

Various technologies involved in hydrogel formation are

- **Bulk polymerisation**

Bulk polymerization involves a monomer and an initiator as the main components, without a solvent. The polymerization conforms to the fixed shape of the reactionvessel when solidification occurs.

- **Free radical polymerisation**

Free radical polymerization is a widely used method for creating polymers from ionic monomers. Free radical polymerization proceeds through a chain reaction mechanism consisting of initiation, propagation, chain transfer, and termination as the elementary steps.

- **Solution polymerization**

Solution polymerization uses solvent in the reactor to enhance heat transfer. At the beginningof the process, the initiator and the solvent are added into the reactor. Initiator will initiate the polymerization process by decomposition to form primary free radicals.

- **Suspension polymerization**

In suspension polymerization, all reactions are carried out in relatively large droplets or in polymer particles stabilized by a small amount of water-soluble gum. It is particularly useful in the production of polymers Water as the continuous phase facilitates agitation and promotes heat transfer. The viscosity of the suspension remains relatively constant with monomer conversion and thus forms hydrogel beads.

Organogel preparation

The preparation of an organogel involves a few general steps

1. Selection of Components:Choose an organic liquid (often a solvent or oil) and a gelator's. The gelator is a molecule that self-assembles to form a gel network.
2. Dissolution:Dissolve the gelator in the selected organic liquid. Heating or stirring may be required to ensure complete dissolution.
3. Cooling or Aging:Allow the solution to cool or age. During this process, the gelator molecules self-assemble to form a three-dimensional network that immobilizes the organic liquid, turning it into a gel.

Mixing of hydrogel and organogel to form bigel

Bigels are made by first preparing the hydrogel and the organogel separately and then mixing them together. This second phase can be completed by integrating the organogel into the hydrogel, or vice versa. Overall, two variations of this procedure may be distinguished: one in which the individual gels are created and stored separately before mixing, and another in which the gels are mixed and the already formed bigel is allowed to set. Bigel is formed by mixing hydrogel with organogel. It is the most crucial phase in the creation of bigel. Bigel was prepared using an optimized formulation of organogel and hydrogel. The needed amount of optimized hydrogel and organogel was taken and combined in the specified ratio. The process.

IN-VITRO EVALUATION

Peltier plate immersion cell method

To study the mechanical properties of a formed bigel material, the sample had to be pre- moulded or cut into a disk with a smooth and uniform surface. The parallel plategeometry is the preferred geometry for this measurement. Also, an appropriate normal force must be applied to the sample during the test to ensure that the

sample is in full contact with the geometry with no slippage. The amount of normal force that is needed is highly dependent on both the flatness and the strength of the bigel. If the normal force is too low, the sample will slip during the test. If the normal force is too high, it may damage the bigel structure.

Rheological and Mechanical Testing

The rheological and mechanical properties of bigels are commonly used to evaluate thequality and utility of the produced bigels, since these parameters directly impact thecommercial applicability of the products. The flow behaviour and viscosity of the bigels are significantly affected by organo/hydrogelators molecular weight, concentration, and structure.

Small-Amplitude Oscillatory Shear (SAOS) tests

SAOS used to study the viscoelastic properties of bigels under small deformations. They allowus to gain insights into the type, strength and number of interactions of bigel structure. Strain sweep test would be utilized to determine the linear viscoelastic region, whichallows for the identification of the extent of deformation of the bigel structure. Stress sweep test would allow for the determination of the yield stress associated with the bigel structure The response of the bigel to a constant stress provides information on the viscoelastic behaviour of the bigel undermoderate deformations.

Texture profile analysis (TPA)

The bigel textural properties, such as firmness, cohesiveness, adhesiveness, and spread ability,have been derived from TPA.

Microstructural Analysis

They explore the internal structure of bigels at the micro scale, revealing information about their emulsion and gel components. Microstructural analyses are frequently carried out to studythe morphology of bigels. Microscopy is a simple characterization technique encompassing several modes with distinct suitability for analysing different bigel types. Confocal laser scanning, phase contrast, optical including fluorescence and polarized light, transmission electron, and scanning electron microscopy have been used for this purpose. All microscopy techniques provide insights into the microstructure of the bigel and the arrangement of the phases. However, unique microscopy techniques could be selected to gain additional information about the materials. For example, micro-spectroscopy techniques such as Raman microscopy could provide spatial chemical mapping of the material without staining the samples, potentially lending insights into the distribution of active agents in the bigel.

Preliminary Characterization

The tube inversion technique is the confirmation test for checking whether the bigel is formed or not. This is the most certainly used gelation technique that involves turning a test tube or vial with a sample present in it and checking whether it flows under its weight. A good bigel is formed if the sample does not flow. The stability of bigels is determined by leaching of the internal phase of the system after 1 h at room temperature using filter paper. They also quantified the oil leakage after the compression of the bigels and after soaking in water for 1h at 37 °C. Once the bigel is formed numerous properties such as homogeneity, smoothness, pH, and colour have been evaluated. It is commonly described as a milky white system, a feature that has been attributed to the dispersion of the light from the interface of both phases of the system. They are opaque and generally have a smooth texture. Bigels have a Ph between 5 to 7 thus assuring physiological tolerance and safe application to the skin. Bigels for vaginal useare usually having pH in the range of 4.0 and 4.9.

Microscopical Studies

The microscopic techniques are used to study the stability of the formulations. Bigels are observed under optical microscopy, phase contrast optical microscopy is also used. This microscopic study allowed a higher particle size to be attributed to batches containing a higher proportion of the organogel. Fluorescence microscopy is also used to study bigel formulation. This microscopy is used to confirm the formation of organogel-in-hydrogel structures and thedetermination of droplet size is also done and 3D digital microscopy. The surface microstructure of dried and freeze-dried bigels has been studied with field emission SEM.

Fourier Transform Infrared Spectroscopy

To determine molecular interactions Fourier transform infrared spectroscopy (FTIR) is a spectroscopic technique that has been widely used. The hydrogel and organogel mixture are concluded that no chemical interactions occurred in the bigels formation. FTIR enabled us to determine the importance of hydrogen bonding in the structure of bigels. Both the amount of the gel and the concentration of the polymer in the hydrogel affect the FTIR spectrum of the bigels. The compatibility studies between the drug and the bigel have also been studied by using this spectroscopic technique.

IN-VIVO EVALUATION

ANIMAL STUDY

Male Wister rats weighing 240-270gms were taken and randomly divided into three test groups of nine animals each. One group was used as control which received oral drug suspension andthe other two groups. One test group received prepared bigel applied topically while in the other test groups plain bigel of drug was applied topically. The animal in the control group wasfasted overnight and administered with 7.2mg/kg of drug suspension in distilled water. The rats in test groups were anesthetized and hair from the abdominal area was removed using an electrical clipper and drug-loaded bigel was applied. Serial blood sampling (0.5ml) was done. Plasma was separated by centrifugation at 3000 rpm, 4oC, for 15 min and 4ml methanolwas added to 200 µl plasma samples for

deprotienation and extraction of the drug. The mixturewas then vortexed for 2 min, followed by centrifugation for 5 min at 3,200 rpm. The organic layer was separated and filtered using a 0.2- µm membrane syringe filter. About 20 µl of the filtrate was injected into the HPLC for estimation of drug concentration.

SKIN PERMEATION STUDIES

Excised human abdominal skin as the standard for in vivo studies was used. The fatty tissue attached to the epidermis was removed, carefully washed with water, and stored in the refrigerator. From the stored skin, circular samples with a diameter of 25 mm were punched out with the help of a plunger and hammer. The epidermis was thoroughly washed with waterand allowed to hydrate for 1 h. This determine how much drug is released or permeated throughthe skin to reach the dermis and potentially the systemic circulation.

TAPE STRIPPING METHOD

The tape stripping method was employed to determine the amount of drug present in the uppermost layer of the skin stratum corneum to treat the superficial infection of the skin. After24 h, the skin was removed from the Franz diffusion cell. The skin surface was washed 10 times with a cotton swab to remove the extra amount of gel present on the skin's surface. The skin was then placed on a flat surface and fixed with the help of pins at the corners of the skin so that the stratum corneum faced upward. Modified Scotch Magic Tape was used to remove the stratum corneum from the skin completely. A tape strip was applied on the skin, and after application, a roller was rolled with a uniform force above it in two opposite directions, and the tape strip was removed with the help of forceps. The same procedure was repeated 12 timesto ensure complete removal of stratum corneum.

SKIN IRRITATION TEST

For skin irritation study, Guinea pigs were used. The animals were maintained on the standardanimal feed and had free access to water. The animals were kept under standard conditions.

Hair was shaved from the back. 5 ml of each sample was withdrawn periodically at 1,2,3,4,5,6,7 and 8h and each sample was replaced with an equal volume of fresh dissolution medium. Thenanalysed the samples for drug content by using phosphate buffer as guinea pigs and an area of 4 cm was marked blank on both the sides, one side served as control while the other side was test. The bigel was applied (500 mg/ guinea pig) twice a day for 7 days and the site was observed for any sensitivity and the reaction if any.

FREEZE-THAW THERMO CYCLING METHOD

Three-month stability studies performed at 30°C ± 2°C/65 ± 5% RH without any significant variations in organoleptic characteristics, drug content or PH. Bigels were tested by the accelerated stability through the freeze–thaw thermo cycling method, and evaluated visual andorganoleptic changes and the stability of drug-loaded bigels by drug release and antimicrobial efficiency tests. The condition for intermediate stability study is 30 ± 2 °C/65 ± 5% RH for 6 months, looking for physical changes, such as phase separation in the bigels, and again for druginstability through drug release and antimicrobial studies The systems containing a higher amount of the organogel were considered more stable, which was attributed to the structure of the organogelator, and the drug and antimicrobial efficacy remained stable in all cases.

CONCLUSION

The concept of bigels is relatively new, and research in this area has been largely conducted over the past 10 years. The study of the components of bigels (hydrogels and organogel) and some of their combinations, such as emulsions, as dosage forms in themselves is already well advanced, which facilitates the preparation and characterization of bigels. Research in the field of cosmetics has also served as useful tools for the manufacture of drug delivery bigels. Although most of the drug-release bigels developed is intended for administration through the skin, other routes of administration have already been suggested. Although some bigels characteristics, such as their microstructure and mechanical properties are widely investigated, there is still a long way to go in this field. Some of their most promising features, namely the possibility of including drugs in both the aqueous and oily phases of the same formulation have recently begin to be exploited in the preparation of bigels for drug delivery.

In recent years, various bigel systems have been produced particularly in drug delivery. Most of these bigel systems are used as a carrier for controlled drug delivery of active ingredients for topical application. Bigels have good spread ability and no pieces of evidence of phase separation. Bigel is also having high stability and its preparation is very easy. We can use hydrophilic as well as a lipophilic drugs in the bigel formulation. The unique structure of bigelsallows for controlled release and prolonged action, enhancing the performance of cosmetic products. They offer benefits like improved stability, enhanced penetration, and extended release, making them a promising technology in the beauty industry. Since then bigels has become a leading name in the beauty world trusted by millions of people world-wide for their skin care needs.

REFERENCE

1. Araceli Martín-Illana A, Fernando Notario-Pérez A, Raúl Cazorla-Luna A, Roberto Ruiz-Caro A, Maria C. Bonferoni B, Aitana Tamayo C, María D. Veiga-Bigels As Drug Delivery Systems: From Their Components To Their Applications, April, 2022; 27(4): 1008-1026.
2. H. Alsaab, S.P. Bonam, D. Bahl, P. Chowdhury, K. Alexander, S.H. Boddu - Organogelsin drug delivery: a special emphasis on pluronic lecithin organogels J

Pharm Pharm Sci., 2016; 19(2): 252.
3. M.M. Ibrahim, S.A. Hafez, M.M. Mahdy- Organogels, hydrogels and bigels as transdermal delivery systems for diltiazem hydrochloride Asian J Pharm Sci., 2013; 8(1): 48-57.
4. Alyssa Francavilla, Maria G. Corradini-Bigels as Delivery Systems: Potential Uses and Applicability in Food, 9(8): 648.
5. Martín-Illana, A.; Notario-Pérez, F.; Cazorla-Luna, R.; Ruiz-Caro, R.; Bonferoni,M.C.; Tamayo, A.; Veiga, M.D.- Bigels as Drug Delivery Systems: From Their Componentsto Their Applications. Drug Discov. Today, 2022; 27: 1008–1026.
6. Lupi, F.R.; Shakeel, A.; Greco, V.; Oliviero Rossi, C.; Baldino, N.; Gabriele, D.- A Rheological and Microstructural Characterisation of Bigels for Cosmetic and Pharmaceutical Uses. Mate. Sci. Eng. C., 2016; 69: 358–365.
7. Meenu Sreekumar, Mathan S, Sibi S Mathew, Shaiju S Dharan. Bigels: An Updated Review, 2020; 12(10): 1306-1308
8. Raytthatha N, Vyas J, Shah I, Upadhyay U. Bigels: A newer system – An opportunity for topical application. Hamdan Med J., 2022; 15: 113-21.
9. Singh V, Banerjee I, Agarwal T, Pramanik K, Bhattacharya MK, Pal K. Guar gum and sesame oil based novel bigels for controlled drug delivery. Colloid Surf B Biointerfaces, 2014; 123: 582-92.
10. M. Ivaskiene, A. Mazurkeviciute, K. Ramanauskiene, M. Ivaskiene, A. Grigonis, V. Briedis, "Topical Antifungal bigels: Formulation, characterization and evaluation," Acta Pharm, vol., 2018; 68(2): 223–233.