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Bigel: An opportunity for topical applications

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Abstract
Bigels, which combine organogel and hydrogel, are unique solid-like formulations with enhanced qualities for usage in food, cosmetics, and medicinal applications. Bigel is superior to either individual gel and benefits from both the aqueous and oily phases. Bigels are unique because they can transport active ingredients that are both hydrophilic and lipophilic, improve stratum corneum hydration, are easily spreadable, etc. The primary objectives of this review article are to provide readers with a thorough understanding of how bigels are classified according to their morphology and synthesis process as well as to demonstrate how bigels are completely assessed by taking into account numerous characterisation methods. Information on the usage of bigels as transdermal medicine delivery devices is also highlighted heavily.

Keywords: Bigels, organogel, hydrophilic, lipophilic, stratum corneum, transdermal medication

1. Introduction
Gels are semisolid systems that normally have two parts: a liquid part that acts as a solvent (which may be polar or nonpolar) and a solid part that is known as a gelator and acts as a gelling agent. The gelling agent limits the solvent phase by forming a three-dimensional network structure and bestows semisolid characteristics [1]. Unique materials known as gels naturally combine flexibility and hardness. They are used in a variety of ways in the food, pharmaceutical, and cosmetics industries.
Gels can be divided into two groups based on the types of 3-D network architectures that gelators create: polymer gels and particle gels [2]. If the network structure is created by the aggregation of colloidal particles, the gels are referred to as particle gels rather than polymer gels, which can be created by the crosslinking of polymer molecules. Gels can also be categorised according to how polar the solvent in the liquid is. When the liquid solvent is polar, the gel is referred to as a hydrogel; however, when the solvent is non-polar, the gel is referred to as an organogel [2].
Based on the kinds of 3-D network architectures that gelators produce, gels can be separated into two groups: polymer gels and particle gels [2]. Particle gels, as opposed to polymer gels, which can be made by crosslinking polymer molecules, are referred to when the network structure is produced by the aggregation of colloidal particles. Gels can also be grouped based on how polar the liquid solvent is. The term "hydrogel" is used to describe the gel when the liquid solvent is polar; the term "organogel" is used when the solvent is non-polar. [2] Bigel is preferable to both single gels in that it combines the advantages of the aqueous and oily phases [1] the capacity to deliver both hydrophilic and lipophilic active substances; enrichment of stratum corneum hydration results in cooling and moisturising action; ease of preparation; improvement in the permeability of pharmaceuticals via the skin; capacity to control consistency and drug release rate. The instability of bigels at high temperatures prohibits these systems from becoming thermo-reversible, which is one of their other drawbacks [1].
Hydrogel systems have been widely used in the pharmaceutical business since they are so advantageous and efficient there, even though organogels have been explored since the late 1990s. Recent research have addressed additional types of gels, such as emulgels, bigels, etc., for topical delivery of drugs. An organogel is a system that resembles a solid and is made of an organic liquid trapped inside of a thermoreversible, three-dimensional network (Referred to as "Oleogels" [1] when the liquid is edible oil). The ability of organogels to immobilise solvent phase at extremely low concentrations without going above the legal limits for emulsifiers and stabilisers in meals is one of their most important qualities. The main drawback of organogels is that they are oily and sticky, which makes it challenging to remove them after applying to the skin. These systems have lower patient compliance as a result.
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In order to trap polar or aqueous phase in hydrogels, which are referred to as jelly-like systems, an adequate hydrophilic gelling agent or hydrogelator, either natural or manufactured, must first produce a three-dimensional network. Unlike organogels, which are naturally greasy, hydrogels are not, making them easier to remove from the skin after use. Additionally, hydrogels have a cooling effect, are highly spreadable, and have increased stratum corneum hydration [2, 3]. Because they can improve patient compliance, hydrogels have a high market value. The main disadvantage of hydrogels is that they have difficulty passing drugs over the stratum corneum due to reduced skin permeability and being less compatible with lipophilic medications.

Based on the distribution of both phases (organogel and hydrogel) within bigels, these systems can be categorised into three groups [2].

1. Hydrogel-in-organogel type
2. Organogel-in-hydrogel type
3. The matrix in matrix or bi-continuous

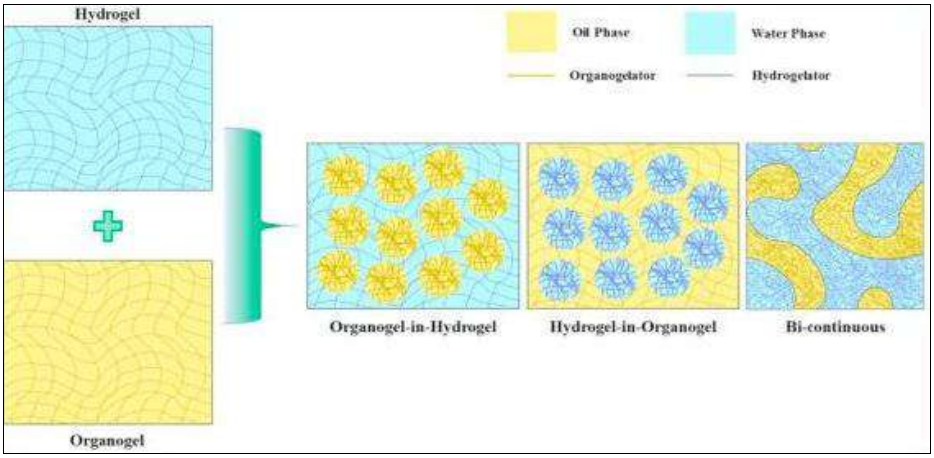

Fig 1: Formulation of Bigel

An organogel-in-hydrogel system is one that has hydrogel as a continuous phase and organogel as a dispersed phase. It's possible that this type of system has received the greatest attention in the literature. Numerous researchers have examined this type of bigel, taking into account a variety of hydrogel systems with a variety of hydrogelators/gelling agents, including gelatin-agar mixture, guar gum, xanthan gum, and acacia gum, gelatin, whey protein, pectin, starch, sodium alginate, sodium carboxymethyl cellulose, and so forth [3].

In the second form of bigel, known as the hydrogel-in-organogel system, the hydrogel phase is spread throughout the continuous matrix of the organogel. Numerous scholars explored the study of bigels created by blending hydrogels based on locust bean gum and carrageenan at different ratios with organogels based on silica and sunflower oil [2]. Confocal microscopy findings confirmed the hydrogel-in-organogel type of bigels' morphology.

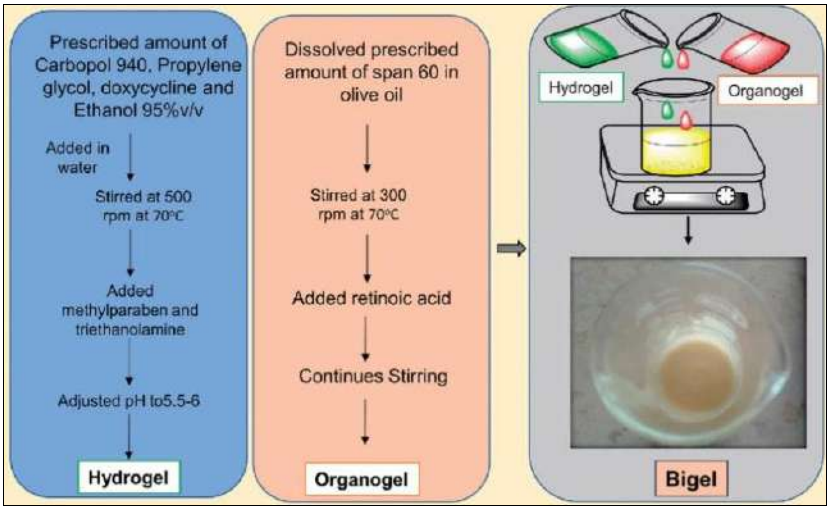

Fig 2: Preparation of Bigels.

It is difficult to discern between the continuous and scattered phases in the third type of bigel, which is conceptualised as a system with a complicated structure. According to Lupi *et al*., bigels were made using an organogel system (O/W) that contained monoglycerides of fatty acids as the organogelator and olive oil as the solvent. The outcomes showed that the highest fraction of organogel contained a complicated matrix-in-matrix structure [1].

2. Preparation of Bigel

Bigels were created by mixing the hydrogel and the organogel, which had been synthesised separately, in a

mechanical (rotor-stator) [4] homogenizer at room temperature. The features of various organogel/hydrogel ratio samples were investigated.

2.1 Materials used

Palsgaard (Denmark) generously donated glycerol mono-stearate (GMS) (90%); Difco (France) provided gelatin; Texturot (Israel) provided liquid soy lecithin; Bio-Lab Chemicals provided gycerol (99.5%); Sigma-Aldrich provided fluorescent dyes Nile red and Nile blue 133 A; and the local 134 supermarket provided canola oil [4]. The peroxide value (PV), which was calculated using glacial acetic acid, 135 chloroform, 0.1 N sodium thiosulphate solution, and potassium iodide (KI), were purchased from Bio-Lab Chemicals (Israel) (Israel). As the reagents for the 137 thiobarbuteric acid (TBA) value, tetra-ethoxy propane, thiobarbuteric acid, and dichloromethane were purchased from Merck 138 (Israel), Holland Moran (Israel), and Israel, respectively [7].

2.2 Preparation of Hydrogel

A hydrogel is an aqueous dispersion phase that contains a three-dimensional network. a natural or manmade gelling agent, such as hydrogelator, that builds a three-dimensional network to immobilise the aqueous phase Important process factors like temperature and shear speed should be modified according on how the system gels [5 6]. Physical hydrogels'reversible nature is caused by two interactions: the Van der Waals force and hydrogen bonding. Chemical hydrogels, also referred to as permanent gels, are produced by covalent bonding, which results in a cross-linked network and illustrates the schematic construction of hydrogels [5, 6].

2.3 Preparation of Organogel

Oleogel, an organogel phase, is frequently produced when either low molecular weight components or polymers trap the aqueous phase. At a temperature higher than the melting point of the organogelator, a precisely measured quantity of an organogelator-such as fatty acids, fatty alcohol, lecithin, waxes, cyclodextrins, steroids, and their derivatives—is combined with an oil phase. [7-9] The gelation will start when the temperature is decreased to room temperature (25 °C).

2.4 Preparation of Bigel

By combining hydrogel with oleogel at a high shear rate while preserving the distinctive properties of each component, bi-gel is created. The homogeneous mixture solidifies as a smooth gel at a particular temperature and shear rate. The stability of bi-gel formation is significantly influenced by the chemical composition of both phases. Finally, gel formation was examined using a schematic design of the hydrogel synthesis procedure and the tube inversion test method [10].

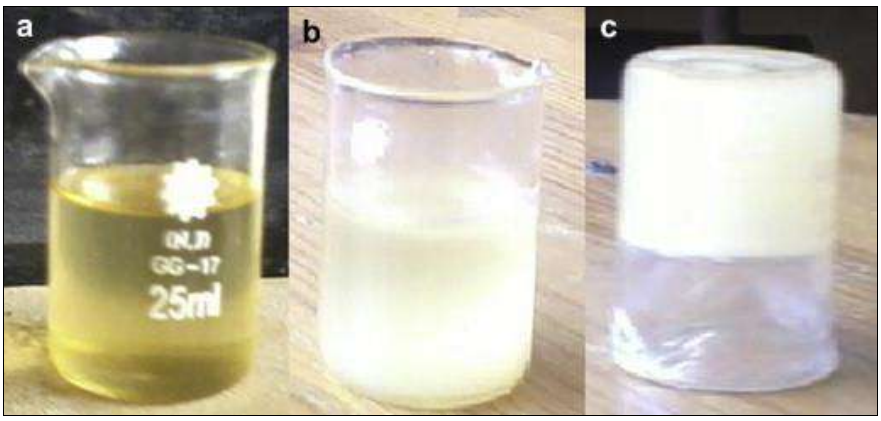

Fig 3: a) Orgenogel b) Hydrogel c) Bigel

3. Physical and chemical characteristics of Bigels

The KET content was determined after extraction. Using an Agilent HPLC system equipped with a Technologies 1200 HPLC system, a G1316A thermostat, a G1312A binary pump, and the following uses an Agilent G1379B degasser and a G1315B diode array detector in Waldbronn, Germany, samples of oleogels or bigels in ethanol at 99.9% were analysed [10, 11]. Conditions: 150, C18 mm, 5 m column, Zorbax Eclipse XDB (Agilent, Waldbronn, Germany); Mobile phase: flow rate of 1.0 mL/min for acetonitrile, methanol, and phosphate; detection at 231 nm; retention time of 4.0 min; buffer pH of 6.8 (35: 40: 25, v/v); (19); Between 5 and 150 g/mL, the standard calibration curve was more linear than average (R2 = 0.999).

3.1 PH Measurement

A glass electrode of the pH-meter Orion 3 Star was used to measure the pH. (Thermo Scientific, Waltham, MA, USA).

3.2 Size of particle analysis [11]

Under some circumstances, oleogels and bigels samples (10 g of KET) were seen. Using a camera-equipped optical microscope Motic BA 400, a 100x magnification analysis of the particle sizes was performed (Moticon, Wetzlar, Germany).

3.3 Size of Partical

A 100x optical microscope was used to examine samples of oleogels and bigels made from 10 grammes of KET, and a Motic BA 400 optical microscope with a camera was used to measure the size of the particles (Moticon, Wetzlar, Germany) [11].

3.4 Measuring viscosity and identifying rheological characteristics

An instrument of the type CPA52Z cone/plate viscometer was used to measure the viscosity (plate diameter 24 mm, Brookfield Engineering Laboratories, Middleborough, Massachusetts, USA). Method for measuring viscosity at 25

°C, 1 °C, and a 3° cone angle. The rheograms were evaluated by plotting the measured values of shear stress vs. shear rate. At a shear rate of 10, 000 s-1, the viscosity of formulations was tested (2.00-20.00 s-1) [12].

3.5Texture evaluation

The texture properties of generated formulations were examined using a Texture Analyser TA. XT Plus (Stable Micro System, Godalming, UK) for backwards extrusion measurements. After being pressed 5 mm into an oleogel/bigel sample (30 g) at a rate of 2 mm/s, a disc (35 mm in diameter) was drawn once more [11]. The software tool Texture Exponent was used to gather and process the data. The parameters firmness, compressibility, and adhesiveness were computed from the resulting force-time graphs.

3.6 Oleogels' ex vivo bioadhesive qualities

Bioadhesiveness was assessed using TA.XT. In addition, Texture Analyser was employed in conjunction with the rat skin model (Stable Micro Systems, Godalming, UK). Samples of the shaved rat skin were taken from the dorsal area and stored for no longer than 4 weeks in a freezer at -20 °C. [11, 12] On the day of the experiment, skin samples were defrosted, cut into 5 mm-diameter pieces, and thawed in physiological 0.9% NaCl saline solution at 25 °C +/- 0.5 °C for 30 minutes.

4. Advantages of Bigels

Bigels' main advantage is that it encourages better stratum corneum hydration. Bigels will also accept drugs that are both lipophilic and hydrophilic. Bigels provide controlled drug distribution. Bigels are readily spreadable and have a great moisturising effect on the skin. Bigels are simple to clean [13].

The literature has suggested many applications for the bigel system, particularly in the areas of medicine administration and aesthetics [14]. Numerous drugs, such as metronidazole, ciprofloxacin, tenofovir, and diltiazem hydrochloride, have been administered under strict control using bigel systems. Sagiri *et al*. found that bigels showed less drug release than emulsion gels. This was attributed to the internal phase's (oil phase) structuration and aggregation, which reduced medication solubility and permeability [14, 15].

Because of certain intriguing properties like high spreadability, cooling action, emollient and moisturising impact, and emollient effect, bigels have the potential for transdermal applications, notably for cosmetics [17, 18]. It was found that bigel systems have a number of highly exciting features for applications involving the delivery of medications. However, it was discovered that in bigel systems, the mechanical and drug release properties exhibited an inverse relationship. It was discovered that bigels with better mechanical properties released medications more slowly than commercial equivalents [16, 19].

5. Limitation of Bigels

The main disadvantage of bigel is destabilisation at high temperatures, which results in this bigel system's non-thermoreversibility [13].

6. Testing in Bigel

6.1 Physical-chemical analysis [20]

The pH, spreadability, colour, aroma, and appearance of the gels were evaluated at various points. A Brookfield viscometer (Model HADVIII+) was used to study the bigel's viscoelastic properties and rheology as a function of time. To determine whether the bigel could maintain structural integrity under various storage circumstances, all formulations underwent accelerated stability testing.

6.2 Microscopic examination [21]

The structural traits of the bigel formulations were investigated using optical and scanning electron microscopy techniques developed by Behera *et al*.

6.3 Studies on compatibility

The bigel formulations were scanned over 4000-400 cm1 using Fourier transform infrared (FTIR). The type of the bigel (amorphous or crystalline) and the compatibility of the drug and excipient were determined using a differential scanning calorimeter (21). In nitrogen, the experiment was carried out between 0 and 400 °C. The obtained thermograms showed any type of interaction.

6.4 Study of mucoadhesion

The mucin adsorption in the bigel formulations was examined using the Ilomuanya *et al*approach [21]. Observing the seminal fluid simulated by mucin-supernatant bigel's absorbance at 555 nm:

$$\%\text{Total mucin content adsorbed} = \frac{\text{Mucin mass} - \text{free mucin mass}}{\text{Mucin mass}} X100$$

6.5 Rate of *in vitro* drug release

A cellulose membrane containing 1 g of bigel was clamped between the donor and receiver chambers of the vertical Franz diffusion cells, providing a 1.76 cm2 useable diffusion area at 32 1 °C. The concentrations of maraviroc and tenofovir in the sample were measured using a tried-and-true high-performance liquid chromatography technique at predefined intervals, and the data were then fitted into various kinetic models [21].

6.6 Safety Evaluation

On-demand cytotoxicity: Using a method developed by Meng *et al*., [21] the MTT test was performed on HeLa cells to assess *in vitro* cytotoxicity.

Examination of electrical conductivity: As had been done earlier by Lupi *et al*. in works on analogous materials, electrical conductivity investigation was performed to examine how gels were dispersed inside the bigels structure (O/W or W/O or Bi-continuous). Actually, all samples were made with NaCl, [21] which even when it has a gel-like structure, may transmit electricity in an aqueous phase [21]. The electrical conductivity of parallel cupper plates (26 30 mm, gap 1 mm) was assessed at 100 Hz using an LCR metre (Wayne Kerr, B905A, UK).

7. Application of Bigel in Delivery System

Bigels have been hailed as viable alternatives for controlled food and drug delivery. They are especially well suited for transdermal administration because of their spreadability and cooling impact, for instance. By mixing an extra virgin olive oil-based organogel with a typical oil-in-water cosmetic emulgel made of hyperthermal water and a variety

of oils, including essential oils, Lupi *et al*. generated bigels for use in cosmetics [22]. They conducted a thorough analysis of the positioning of both phases in the bigel using a variety of approaches. The majority of the bigels reported in the literature have an organogel-in-hydrogel structure and are designed for topical administration of medications in terms of drug delivery.

The system's stages are set up in such a way that the medicine can be released in a controlled manner. Bigels have been found to contain a wide variety of drugs, [22] including antimicrobials like metronidazole, ciprofloxacin, and moxifloxacin; antiretrovirals like tenofovir and a combination of tenofovir and maraviroc; antifungals like ciclopirox olamine, and terbinafine hydrochloride; medications for treating acne like isotretinoin; immune response modifiers like imiquimod.

Despite the development of bigels for vaginal drug release, the bulk of bigels for drug delivery that can be found in the literature are for topical administration through the skin. Singh *et al*. created systems combining Carbopol hydrogel and sorbitan monostearate/sesame oil organogel to deliver drugs vaginally, primarily for the treatment of bacterial vaginosis with metronidazole. Fluorescence microscopy demonstrated an oil-in-water type of emulsiongel's microstructures, and a biocompatibility investigation discovered no noticeable variations in the survival of HaCaT cells compared to the controls. When compared to a commercial metronida- zole gel, all of the batches showed good antibacterial efficacy against Escherichia coli. Even a Fickian release mechanism was used in one batch to release the drug [22].

Bigel systems have a higher ex vivo mucoadhesion than the commercial product and comparable hydrogels and organogels. *In vitro*, the antibiotic was released over several hours by Fickian diffusion, and the antibacterial activity of these systems was on par with that of the commercial product. The bigel formulation showed the lowest drug retention in the mucosa, which would suggest a lesser risk of local cytotoxicity, and the highest initial permeability rate of all the systems studied, which would result in a quick therapeutic impact [22].

8. Conclusion

For topical drug delivery, gels have been extensively explored. Recent advances in pharmaceutical science and technology have modified classic gels, such as hydrogels and organogels, and created new semisolid systems, such as bigels. Recently, a variety of bigel formulations have been developed and altered to fulfil the requirements of various applications [23]. Bigels' ability to deliver both hydrophilic and lipophilic active agents, enrichment of stratum corneum hydration that produces a cooling and moisturising effect, water washability after application to the skin, ease of preparation, good stability, etc. are among their main advantages for controlled drug delivery [23, 24].

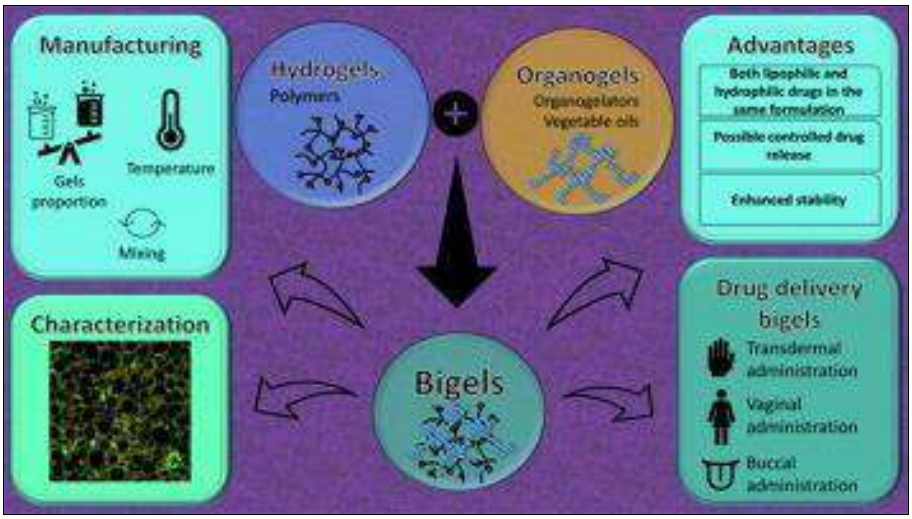

Fig 4: Overview of Bigel

Given that bigel formulations are a novel class of materials, extensive study of these systems is required before they can be applied in practical settings. A few of the factors that are essential in the synthesis of bigels by combining organogel and hydrogel are storage of bigels, mixing temperature, and the incorporation of emulsion gels rather than either organogel or hydrogel. More attention has to be paid to how these factors affect the qualities of the resulting bigel systems. Bigels with organogel-in-hydrogel type morphologies have been the focus of substantial investigation, whereas bigels with hydrogel-in-organogel and bicontinuous type morphologies have not [23].

Similar to how bigels generated by joining gel strips and colloidal bigels have not been described in the literature, bigels created by combining organogel and hydrogel have undergone substantial research studied a lot. The mechanical and rheological properties of different bigel systems, as well as their incredibly quick drug release, were thoroughly examined. The influence on a key element in pharmaceutical applications was negative. Therefore, further improvements to the current systems are required for greater mechanical and rheological performance. along with enhanced drug release properties. The utilisation of bigel formulations for transdermal, nasal, rectal, vaginal, buccal, oral, and parenteral drug delivery can also be studied.Future bigel formulations can be developed and characterised for usage in food, cosmetics, and drug delivery applications [24]. The production and study of bigel formulations for use in culinary applications in addition to medical and cosmetic ones will be made possible by future advances.

9. Reference

1. Shakeel A, Lupi FR, Gabriele D, Baldino N, De Cindio B. Bigels: A unique class of materials for drug delivery applications. Soft Materials. 2018;16(2):77-93. doi:10.1080/1539445x.2018.1424638.
2. Shakeel A, Farooq U, Gabriele D, Marangoni AG, Lupi FR. Bigels and multi-component organogels: An overview from rheological perspective. Food Hydrocolloids. 2021;111:106190. doi:10.1016/j.foodhyd.2020.106190.
3. Ibrahim MM, Hafez SA, Mahdy MM. Organogels, hydrogels and bigels as transdermal delivery systems for diltiazem hydrochloride. Asian Journal of Pharmaceutical Sciences. 2013;8(1):48-57. doi:10.1016/j.ajps.2013.07.006
4. Samui T, Goldenisky D, Rosen-Kligvasser J, Davidovich-Pinhas M. The development and characterization of novel in-situ bigel formulation. Food Hydrocolloids, 2020, 106416. doi:10.1016/j.foodhyd.2020.106416
5. Witchterle O, Lim D. Hydrophilic Gels for Biological Use. Nature. 1960;185:117-118.
6. Abdallah DJ, Weiss RG. n-Alkanes Gel n-Alkanes (and Many Other Organic Liquids). Langmuir. 2000;16(2):352-355.
7. Peppas NA, Bures P, Leobandung W, Ichikawa H. Hydrogels in pharmaceutical formulations. Eur. J. Pharm. Biopharm. 2000;50(1):27-46.
8. Placin F, Colomes M, Desvergne JP. A new example of small molecular non-hydrogen bonding gelators for organic solvents. Tetrahedron Lett. 1997;38(15):2665-2668.
9. Sahoo S, Singh VK, Biswal KU, Anis D, Rana A, Al-Zahrani UA. Development of ionic and non-ionic natural gum-based bigels: Prospects for drug delivery application. J. Appl. Polym. Sci. 2015;132(38):42561.
10. Raytthatha N, Vyas J, Shah I, Upadhyay U. Bigels: A newer system – An opportunity for topical application. Hamdan Med J. 2022;15:113-21
11. Magdalena Wr, Blewska Marta Szekalska, Anita Hafner, Katarzyna Winnicka. Oleogels And Bigels as topical drug carriers for Ketoconazole Ñ development and *in vitro* characterization; ISSN 0001-6837; ñ Drug Research, 2018;75(3):777ñ786.
12. Raytthatha N, Vyas J. Development of Bigels Containing Antifungal Agent For Vaginal Infection". International Journal of Pharmacy and Pharmaceutical Sciences. 2022 Aug, 14(10). doi:10.22159/ijpps.2022v14i10.45134.
13. Meenu Sreekumar, Mathan S, Sibi S Mathew, Shaiju S Dharan. Bigels: An Updated Review; 2020;12(10):1306-1308.
14. Shakeel A, Farooq U, Iqbal T, Yasin S, Lupi FR, Gabriele D. Key characteristics and modelling of bigels systems: A review. Materials Science and Engineering: 2018. C. doi:10.1016/j.msec.2018.12.075
15. Behera B, Sagiri SS, Pal K, Pramanik K, Rana UA, Shakir I. Polym.- Plast. Technol. Eng. 54 Bi-gel: A Novel material for transdermal drug delivery, 2015, 837-850 .
16. Sagiri SS, Singh VK, Kulanthaivel S, Banerjee I, Basak P, Battachrya M. Mech. Behav. Biomed. Mater. 43 Characterization of gelatin-agar based phase separated hydrogel, Emulgel and Bigel: A comparative study. 2015, 1-17.
17. Martín-Illana A, Cazorla-Luna R, Notario-Pérez F, Bedoya LM, Ruiz-Caro R, Veiga MD. Eur. J. Pharm. Sci. 2019;127:38-51.
18. Smart Freeze-Dried Bigels for the Prevention of the Sexual Transmission of HIV by Accelerating the Vaginal Release of Tenofovir during Intercourse ,M.M. Ibrahim, Hafez SA, Mahdy MM, Asian J. Pharm. Sci. 2013;8:48-57.
19. Sagiri SS, Singh VK, Kulanthaivel S, Banerjee I, Basak P, Battachrya M. Mech. Behav. Biomed. Mater. 43 A rheological and microstructural characterisation of bigels for cosmetic and pharmaceutical uses, 2015, 1-17.
20. Ilomuanya MO, Hameedat AT, Akang EN, Ekama SO, Silva BO, Akanmu AS. Development and evaluation of mucoadhesive bigel containing tenofovir and maraviroc for HIV prophylaxis. Future Journal of Pharmaceutical Sciences. 2020, 6(1). Doi:10.1186/s43094-020-00093-3.
21. Behera B, Singh VK, Kulanthaivel S, Bhattacharya MK, Paramanik K, Banerjee I. Physical and mechanical properties of sunflower oil and synthetic polymers based bigels for the delivery of nitroimidazole antibiotic: A therapeutic approach for controlled drug delivery. European Polym Journal. 2015;64:253-264. https://doi.org/10.1016/j.eurpolymj.2015.01.018
22. Lupi FR, Shakeel A, Greco V, Oliviero Rossi C, Baldino N, Gabriele D. A rheological and microstructural characterisation of bigels for cosmetic and pharmaceutical uses. Materials Science and Engineering: C. 2016;69:358-365. doi:10.1016/j.msec.2016.06.098
23. Andonova VY, Peneva PT, Apostolova EG, Dimcheva TD, Peychev ZL. Kassarova MI. Carbopol hydrogel/sorbitan monostearate-almond oil based organogel biphasic formulations: Preparation and characterization of the bigels. Trop. J Pharm. Res. 2017;16(7):1455-1463.
24. Gallardo V, Munoz M, Ruiz M. Formulations of hydrogels and lipogels with vitamin E. J Cosmetic Derm. 2005;4(3):187-192.