Bigel: A Novel Drug Delivery System for Topical Application

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Abstract- A gel is a solid or perimeter system consisting of at least two passages that form a compact mass that contains and passes through a liquid. Hydrogel, emulsion gel and organogel are new gel systems that are widely known but have some disadvantages. For example, hydrogel provides hydrophilic but not sufficiently waterproof drugs and its ability to reach the stratum corneum is weaker, organogel has a slippery nature that causes stickiness and discomfort, and emulsion gel has different mechanical phases that cause uncertainty. This lack can be answered with a unique and innovative expression called bigels. The anhydrous phase is usually made of a hydrophilic polymer, while the organic phase is made of gelled vegetable oil paint due to the presence of an organogelator. The Bigel production process must take into account the possibility of a particular gelling agent, organogel/hydrogel, speed, and mixing temperature at each stage. The presence of desired properties in both hydrogels and organogels increases patient compliance and the ability to deliver lipophilic and hydrophilic drugs. Until now, testers have essentially become familiar with bigel systems for managing regulated drugs in local operations. These beagles are immersed in the search, but still have to find the fashion on demand.

Index Terms- Bigels, organogel, hydrogel, hydrophilic, lipophilic, stratum corneum, topical medication

I. INTRODUCTION

Bigels are special solid-like formulations with improved properties for use in food, cosmetics, and pharmaceutical applications. They combine organogel and hydrogel. Bigel benefits from both the oily and watery phases and is better than each separate gel. Bigels are special because they may spread quickly, enhance stratum corneum hydration, and carry active substances that are both lipophilic and hydrophilic. This review article's main goals are to give readers a comprehensive grasp of how bigels are categorized based on their morphology and synthesis process and to show how bigels are fully evaluated by taking into consideration a variety of characterisation techniques.

Gels are semisolid substances made up of two parts: a solid part known as a gelator that serves as a gelling agent and a liquid part that can be either polar or apolar and functions as a solvent. The gelator increases surface tension, which prevents solvent flow, and is typically used at concentrations less than 15% w/v. A gelling agent creates a three-dimensional (3D) network structure to entangle the solvent phase and produce semisolid characteristics. Gels are categorized according to their unique method as hydrogels, organogels, or emulgels.

A 3D network of polymeric matrices joined chemically or physically that trap liquid (water) through intermolecular space is called a hydrogel. Gels that are hydrophilic and use water as a dispersion medium are called hydrogels. As pharmaceutical forms for topical application, hydrogels offer a number of advantages, such as ease of manufacturing, non-oily appearance, great spreadability, the capacity to enhance skin barrier moisture, cooling action, and speedy removal because of their easy washability. Significant patient compliance is a result of all of this. They can, however, carry medications that are hydrophilic but not hydrophobic, and their ability to cross the epidermal barrier is diminished. Organogels are also easy to make, and because of their lipophilicity, they can dissolve hydrophobic medications and improve their absorption across the epidermal barrier. The biggest drawback of organogels is their greasy makeup, which makes it difficult to remove from the skin after application since it adheres and leaves greasy residues. This leads to a reduction in patient compliance.

Emulsion gels, sometimes referred to as emulgels, were created to solve the drug release issues with hydrogels. These are biphasic systems having a gelled continuous component that are often made up of an emulsifying component that is soluble in lipids and a water-soluble component. Emulgels combine the benefits of gels and emulsions. Emulsion hydrogels or emulsion organogels are two possible types. Because the two phases of emulgels have different structural characteristics, they have little structural stability and produce formations that are structured in both phases.

II. ADVANTAGES

• Improved capacity to wash.

• They are simple to formulate.

• Good patient compliance without sacrificing the oil's therapeutic properties.

• Because surfactants are used in smaller quantities, they are less hazardous.

• The two phases allow for the incorporation of both lipophilic and hydrophilic medicines.

• Bigels have a low barrier to skin penetration. It is therefore a superior option for transdermal medication administration.

• Bigels are a good carrier for iontophoretic drug delivery because they can control the administration of active medicinal compounds.

III. DISADVANTAGES

• In the absence of an emulsifier, phase separation happens.

• Bigels are unstable and thermo-irreversible at higher temperatures.

IV. PREPARATION OF BIGEL

Bigels were produced by combining hydrogel with organogel (which was synthesised on its own) in a rotore-stator at room temperature in a homogeniser. The characteristics of different organogel / hydrogel ratios were studied.

Preparation of Hydrogel

A hydrogel consists of a 3D network of a natural or man-made gelling agent (e.g. hydrogelator) that forms a 3D network to immobilise an aqueous phase of the dispersion phase. Important process parameters (e.g., temperature, shear speed) should be modulated depending on the way the system is gelled. Physical hydrogels are reversible due to two interactions: Van der Waals (Van der Waals force) and hydrogen bonding. Chemical hydrogels (also known as permanent gels) are formed by covalent bonds resulting in a cross-link network.

Preparation of Organogel

Oleogel is also known as organogel phase. It is often formed when low molecular weight molecules or polymers are used to trap the water phase. The organogel is formed at a temperature above the melting point by the addition of a precisely measured amount of organogelators (fatty acids, fatty alcohols, lecithins, waxes, Cyclodextrins and steroids and their derivatives). The oil phase is combined with the organogel. The gelation process will begin when the temperature drops below room temperature (25°C).

Preparation of Bigel

Bi-gel is formed by combining hydrogel and oleogel with a high shear speed while maintaining the unique characteristics of each component. The homogeneous solution solidifies as bi-gel at a specific temperature and shear speed. Stable bi-gel formation depends heavily on the chemical composition of the two phases.

V. EVALUATION OF BIGEL

V.1 PHYSICOCHEMICAL PROPERTIES

The physico-chemical properties of bigels were studied at different time intervals, including their spreadability, colour, smell and appearance.

Viscosity

The rheology of bigels over time was measured with a Brookfield Viscometer.

Spreadability

To determine the spreadability of bigels, 0.5g of bigel was placed in a 1cm diameter circle on a pre-marked glass plate. On top of the glass plate, 1 kg of mass was held for 300 s. The augmented diameter of the spreading bigel was measured using a formula.

Where, S-Spreadability = g.cm/s,

M-Weight = upper glass slide,

D-Diameter of spreading = cm,

T-Time for spread gel in section = approximately 300 s.

V.2 STABILITY STUDY

The stability of the bigel is evaluated through long-term stability studies and accelerated stability studies.

LONG TERM STABILITY STUDY

Because the bigel is made up of two semi-solid phases, the thermodynamic stability of the bigels increases many times. The bigel formulations are tested for their pH, colour and homogeneity. They are also tested for uniformity and phase separation, as well as their physical appearance.

During the long term stability study, any other signs of instability are evaluated after each freeze-thaw cycle of the thermos and at predetermined intervals (0-3, 6, 12-18, 24, or 36-months depending on the active ingredient of the bigel).

ACCELERATED STABILITY STUDY

The stability studies were performed according to ICH guidelines and lasted for 3 months. The purpose of stability studies is to obtain information on the change in the application programming interface over time as a result of environmental factors like humidity, temperature, and light.

The experiment was conducted at 25°C = 60% RH and 45°C = 75% RH. The prepared combinations were then crimped into the collapsible metal tube, and the packed bigels were stored under the different temperature and environmental factors. After the experiment the bigels were examined for percentage drug content and percentage drug release, as well as viscosity, and pH.

V.3 THERMAL PROPERTIES

The heat characteristics of formed bigels were determined by the drop-ball method using EI melting point method-931. The bigels were weighed accurately and wrapped in the pierced metal pans.

The experiment was carried out in a nitrogen environment at 40 ml/min and scanned at 5.0 °C/min in a temperature range 25–150 °C to obtain the heating and cooling characteristics of bigels using differential scanning calorimeters (DSC).

V.4 MICROSCOPY

CM, cryo scanning electron microscopy (CSEM), transmission electron microscopy (TEM) and phase contrast microscopy are some of the microscopy techniques used to determine the relative distribution of water and organic phases in bigels.

V.5 ELECTRICAL CONDUCTIVITY

The electrical properties of the bigels are measured to understand the conductivity profiles. A computer-controlled impedance analyser can be used to measure the electrical properties of bigels. The information is obtained at room temperature in a specific frequency range (for example, 0.1 Hz1 MHz). The conductivity of the formulations helps in determining the transport behaviour of the bigels under current. It also helps in understanding the microstructural structure of the bigel system. The protons in the water phase make bigels with a higher percentage of hydrogel more conductive. The insulative behaviour of water in oil bigels is very high, while the conductive behaviour of oil in water bigels is very low.

AV.6 FOURIER TRANSFORM INFRARED SPECTROSCOPY

FTIR is a widely used spectroscopic method for determining molecular interactions of hydrogels with organogels. It has been demonstrated that bigels' FTIR spectrum is affected by the hydrogel's polymer composition and bigel fraction. This method has also been used for drug-bigel interaction or compliance.

V.7 IN VITRO DRUG RELEASE

Dr. Franz's diffusion cell is used for in vitro drug release studies. The volume required for dissolution, the pH, the temperature and stirring speed are all selected. The analysis is performed over a defined time interval. Drug samples are collected at different time intervals and filtered through a 0.45mm millipore filter. The drug is analysed using Ultraviolet-visually visible spectrophotometers or high performance liquid chromatography. Many mathematical models for bigels are used to match drug release kinetics. Factors that influence drug release include (but are not limited to): initial water content; drug's content; electrostatic forces; lipid bilayers; swelling capacity; and more.

V1. APPLICATION OF BIGEL

These systems are often used as carriers for the controlled delivery of active ingredients in both topical and cross-residual applications. A wide range of drugs can be safely and effectively delivered through bigels, including antimicrobial drugs (metronidazole), antiretroviral drugs (tenofovir, tenofovir plus maraviroc), antifungal drugs (cyclopirox, olamine, terbinafine, hydrochloride), acne drugs (isotretinoin), immune response modifier drugs (imiquimod), pain relievers (paracetamol, ketoprofen), anti-inflammatory drugs (ketoprofen and ibuprofen), diethylenedioxygen (diethylamine diethylamine), calcium channel blockers (diltiazem, hydrochloride) and antioxidants (Coenzyme Naphthoquinone, vitamin E).

VII. CONCLUSION

These bigels are currently being studied in academia, but commercial and commercializable products are yet to be created. While the majority of drug loaded bigels formulated are intended for local drug delivery, various delivery methods have been proposed in the past.

Buccal bigels and vaginal bigels are two of the most promising delivery methods that could potentially expand the range of dosage forms that can be used as a drug delivery system.

VIII. REFERENCES

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. 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.

4. 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.

5. H. Alsaab, S.P. Bonam, D. Bahl, P. Chowdhury, K. Alexander, S.H. Boddu, "Organogels in drug delivery: a special emphasis on pluronic lecithin organogels," J Pharm Pharm Sci. vol. 19, 252, 2016.

6. A. Vintiloiu, J.-C. Leroux, "Organogels and their use in drug delivery — a review," J.-Control Release, vol. 125, 179–192, 2008.

7. M.M. Ibrahim, S.A. Hafez, M.M. Mahdy, "Organogels, hydrogels, and bigels as transdermal delivery systems for diltiazem hydrochloride," Asian J Pharm Sci, vol. 8 (1), 48–57, 2013.

8. C.L. Esposito, P. Kirilov, V.G. Roullin, "Organogels, promising drug delivery systems: an update of state-ofthe-art and recent applications," J Control Release, vol. 271, 1–20,2018.

9. Pandey M, Belgamwar V, Gattani S, Surana S, Tekade A. Pluronic lecithin organogel as a topical drug delivery system Drug Deliv. 2010;17:38–47.

10. Hamed R, AbuRezeq A, Tarawneh O. Development of hydrogels, oleogels, and bigels as local drug delivery systems for periodontitis Drug Dev Ind Pharm. 2018;44:1488–97.