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BIGEL: A NEW APPROACH IN NOVEL DRUG DELIVERY SYSYTEM

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ABSTRACT

Topical administration is applied to deliver a drug instantaneously at the point of application, so enough drugs is depleted into the systemic circulation to cause medicinal effects. To develop an effective drug absorption through an intact skin, several topical preparations are used one of that is "Gels". Gels basically used for the purpose of topical dosage form a lot which is to deliver drug across a localized area of the skin. Gel formulation contributes for better approach concept and product stability in respect to ointment, paste and cream. Administration of topical gel drug has a limited drug delivery process anywhere in the body system through skin route, vaginal route, rectal route and ophthalmic route as darmal routes. Generally gels used in wide range as applications in food products, cosmetics products, biotechnology. Most of the gels may be designed according to their nature of the liquid phase, for example, Organic solvent containing are organogels (oleogels) and water as solvent phase called hydrogels. Recent research studies have reported many types of gels for topical drug application, like aerogel, bigel and emulgel. Topical dosage forms like Gels are evaluated with following standard parameters such as pH of formulation, homogeneity of preparation, grittiness of active drug content, extrudability and spreadability of formulation, skin irritation studies, in-vitro release and Stability studies.

INTRODUCTION

Gels are semisolid formulations which generally have two components, liquid and another solid. Where liquid phase is termed as solvent and the solid component is termed as gelling agent/ gelator/ Solidifier. Gels are 3D networked systems which have a wide range of applications in pharmaceutical field.

Gels are classified in to two classes according to the nature of 3D network structures formed by the gelators: - polymer gels and particle gels. Polymer gels are developed due to the cross-linking of the polymer molecules. Particle gels are formed by the particle aggregation of colloidal. On the basis of polarity of solvent, gels are classified in to two types/ classes: - hydrogel and organogel. When the liquid solvent is polar/ Hydro it is called hydrogel and the liquid solvent is nonpolar/ Organic it is termed as organogel. The hydrogels are 3D hydrophilic networks of homopolymeric or heteropolymeric chains and the cross-linked hydrogels have the ability to absorb huge amount of water without itself dissolving in it. Organogel is a solid like system in which organic liquid is entrapped into inside a thermo-reversibile 3D network. Preparation of Organogels is very easy and its lipophilic nature will enhance the drug permeation through the stratum corneum. Organogel is oily in nature so it is difficult to remove when it is applied to the skin. Bigels are gels formed by the combination of the two gels ie; organogel and hydrogel. Hydrogel helps in hydration of stratum corneum and organogel helps in increased penetration. Other benefits of bigels include easy washability, easy spreadability, and good contact period and bigels can overcome the disadvantages of both (Hydrogel and Organogel) gels including the limited ability to cross the lipophilic barrier and low patient compliance for hydrogels and oily residues and stickness of organogel.

Classes of bigels[6-10]

Bi-gels preparation are classified into four categories

Oleogel dispersed in hydrogel system (O/W)

This type of bi-gels contains oleogel as dispersed phase within the hydrogel as continuous phase.

Hydrogel dispered in oleo gel (W/O)

This type of bi-gels contains hydrogel as dispersed phase with in the oleogel as continuous phase.

Bicontinuous bi-gel

These bi-gel are formed when the gel formation is carried out at higher proportion of hydrogel/oleogel dispersed in lower proportion of oleogel/hydrogel phase, respectively.

Complex bi-gel
These bi-gels are prepared by adding organogel/hydrogel to an oil-in-water/water-in-oil structured emulsion.

Method of preparation of bi-gels
Preparation of hydrogel
Hydrogels are aqueous dispersion phase containing (3D) three dimensional networks. Three dimensional network formed by either natural or synthetic gelling agents such as hydrogelator to immobilize the aqueous phase.[11] Important process parameter is shear speed and temperature, should be optimized based on the gelling agent behavior of the system.[12] The physical hydrogels are reversible in nature and gellation is attributed to some interaction such as Van der Waals force and hydrogen bonding. Chemical hydrogels are also called as permanent gels which are formed through covalent bonding results in the formation of cross-linked network[13] and schematic diagram of preparation of hydrogels.

Preparation of hydrogel
Oleogels are organo phase usually made by self-assembly of either polymer or low molecular weight components to entrap the aqueous phase.[15-17] Accurately weighed quantity of organogelator such as fatty acids, fatty alcohol, and its derivatives, in predefined oil/ lipid phase at a constant homogenization condition and temperature higher than melting point of the organogelator. The gellation will be formed when the temperature is brought down to room temperature 25°C.

Preparation of hydrogel
Bigels are prepared by mixing two gels ie., organogel and hydrogel, in different proportion with continuous stirring for a particular period of time at high shear rate/rpm to get a good homogeneous system.

Characterization of the formulations
FTIR/IR spectroscopy
FTIR analysis of blank organogel and hydrogel, as well as drug loaded formulations along with its individual components, was carried out using Fourier Transformed Infrared Spectrometer. Samples were scanned in the range of 4000 to 500 cm-1.[16]

Physical evaluation
Formulations were observed visually for their colour, appearance, texture and opacity.[17]
Determination of pH
The pH of the formulations was determined using digital pH meter.

Extrudability
A definite weight of gel was filled into an ointment tube and crimped. The extrudability (cm/s) of gel was determined by measuring the length of the gel ribbon extruded from the ointment tube by applying uniform pressure over a period of 10 s.[18] The following equation was used to determine extrudability.

Extrudability = Distance travelled by the gel (cm)/10 s (1)

Spreadability
Spreadability of the formulations was determined by placing 0.1 g gel between two glass slides of equal dimensions (75 mm×25 mm×1 mm). Thereafter, known weights of 10 g, 20 g, 50 g or 100 g were loaded on the upper slide for 60 s. The initial and final spreading diameters were marked before and after placing the individual weight.[19] Finally, the % spreadability may be calculated by using the following equation.
% Spreadability = [(Di-Df)/Di] ×100 …….. (2)
Where, Di = initial spreading diameter, Df= final spreading diameter

Rheological study
The viscosity of the blank gels (organogel and bigel)were measured in Brookfield Digital Viscometer (Model LVDVI+, Brookfield Engineering Laboratories Inc, USA) with spindle no. 7 at 25 ^{0}C [20]. The apparent viscosity of organogel and bigel formulations of different compositions was measured as a function of shear rate varying from 1 to 5 rpm. Ostwald-de wale power-law model has been employed to analyze the flow behavior of organogel as well as bigel systems given as follows:
$\tau = k * \dot{\gamma}^{n}$ …….. (3)
Where the relationship between stress (τ) and shear rate ($\dot{\gamma}$) give the values for flow consistency index (k) and flow behaviour index (n). The rheological behavior may be stated as non-Newtonian pseudoplastic/shear-thinning if the values of n is<1.[21,22]

Drug content determination
Definite amount of drug-loaded gels was added to phosphate buffer (pH 5.8) which was kept undisturbed for 48 h for complete leaching of drug.[25] The drug content of formulations was determined from the calibration curve of the drug in the said buffer.

***In vitro* drug release study**
In vitro drug release study from bigels was performed through dialysis membrane in modified Franz diffusion cell.[27] Accurately weighed drug-loaded sample containing drug was placed in the donor compartment of cell and the receptor chamber containing phosphate buffer (pH 5.8) was maintained at 32±0.5 ℃ temperature. 1 ml of sample was withdrawn every hour, replaced with fresh buffer system and study was continued for 5 h.

Drug release data were subjected to mathematical modeling by using zero-order, first order, Higuchi and Korsmeyer-Peppas models.[28]

Applications
In last two decade bi-gel systems has been proposed particularly in the drug delivery system. Most of these bi-gel systems are used as a carries for the controlled drug delivery system of active ingredients for topical and transdermal application.

CONCLUSION

In recent, different bi-gel systems have been produced and modified according to the needs of different applications of drug delivery and use of food products. This present review presents the important valuable characteristics, different types of bi-gel systems and its preparation, advantages of bi-gels and its application in drug delivery and food systems.

Future prospective

Bi-gels are new approach in NDDS class of material, and therefore, extensive analysis of the system is required for commercial application. In proposed review project, detailed discussion of different important standard of evaluation parameters, such as storage of bi-gels, mixing, temperature, addition of appropriate amount of Gelling agent and organogel/hydrogel ratio, are required for the preparation of bi-gel. Bi-gel system development is going to be a most emerging trend in the cosmetic, NDDS and food applications.

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