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A REVIEW ON ORGANOGELS: LIPID BASED CARRIER SYSTEMS

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ABSTRACT

Organogel is a viscoelastic carrier system, can be regarded as a semi-solid preparation which has an immobilized external organic (apolar) phase. Organogels have evolved as one of the potential carrier system for topical delivery. When compared to other lipid based carrier systems, these prove to be better in terms of efficacy, feasibility and shelf life. Organogelator such as n-alkanes, fatty acids are used for preparation of organogels. Organogel is a non crystalline, non-glassy, thermoplastic solid material composed of a liquid organic phase entrapped in a three-dimensionally cross-linked network. Organogel consists of both hydrophobic and hydrophilic components; both hydrophobic and hydrophilic drugs can be incorporated. Characterization of organogels contains Rheological Behaviour, Physiochemical properties, Optical Clarity and In vitro drug release.

Keywords: Organogel, Viscoelastic , Organogelator, Characterization.

INTRODUCTION

Gels are defined as semi-solid preparations having both solid and liquid components within its structure. The solid component forms a networked structure, which results in the immobilization of the liquid component. Immobilization of liquid component within the networked structure of the solid component has been attributed to the interfacial tension amongst the solid and liquid components. [1] The gel is said to be a hydrogel or an organogel depending on the nature of the liquid component water in hydrogels and an organic solvent in organogels. Out of the topical applications available, gels are obtaining more popularity because of the ease of application and better absorption through the skin layers. [2]

TYPES OF GELS: [3]

1) Organogels:

An organogel is a non-crystalline, non-glassy thermoplastic solid material composed of a liquid organic phase entrapped in a three-dimensionally cross-linked network. The liquid can be an organic solvent, mineral oil, or vegetable oil.

2) Hydrogels / Aquagel:

Hydrogel is a network of polymer chains that are hydrophilic, sometimes found as a colloidal gel in which water is the dispersion medium. Hydrogels are highly absorbent (they can contain over 99.9% water) natural or synthetic polymers. Hydrogels also possess a degree of flexibility very similar to natural tissue, due to their significant water content.

3) Xerogels:

A xerogel is a solid formed from a gel by drying with unhindered shrinkage. Xerogels usually retain high porosity (15-50%) and enormous surface area (150–900 m^2/g), along with very small pore size (1-10 nm).

ADVANTAGES OF ORGANOGELS: [4]

1. Ease of preparation.
2. They are organic in character and also resist microbial contamination.
3. Cost reduction due to less number of ingredients.
4. Longer shelf life.
5. Thermodynamically stable.
6. Both hydrophobic and hydrophilic drugs can be incorporated.
7. Organic solvents could be of natural origin eg: sunflower oil, mustard oil, etc

LIMITATIONS OF ORGANOGELS: [4, 5]

1. Should be stored in a proper condition.
2. The organogel has greasy property.
3. Less stable to temperature.
4. When a gel stands for some time, it often shrinks naturally and some of its liquid is pressed out, known as syneresis.

5. If impurity present then no gelling will occur.
6. Row material like lecithin is not available on large scale.

ORGANOGELATORS: [6]

1. n-alkanes such as hexadecane and other organic liquids
2. Fatty acids (e.g. 12-hydroxyoctadecanoic acid)
3. Sorbitan monostearate
4. Non- ionic surfactant
5. Steroids and their derivatives
6. Anthryl derivatives (e.g. 2, 3-bis-n-decyloxyanthracene).
7. Macrocyclic gelators (e.g. calixarenes).
8. Cyclo(dipeptide).

METHOD OF PREPARATION:

Most organogels are prepared by heating a mixture of the gelator and the liquid component to form an organic solution/dispersion, followed by cooling of the latter, which sets into a gel. Heating allows dissolution of the gelator in the liquid. Following cooling, the solubility of the gelator in the liquid phase decreases, and gelator solvent interactions are reduced, which results in the gelator molecules 'coming out' of solution. Gelator gelator interactions lead to gelator self-assembly into well-defined aggregates such as tubules, rods and fibres. [7]

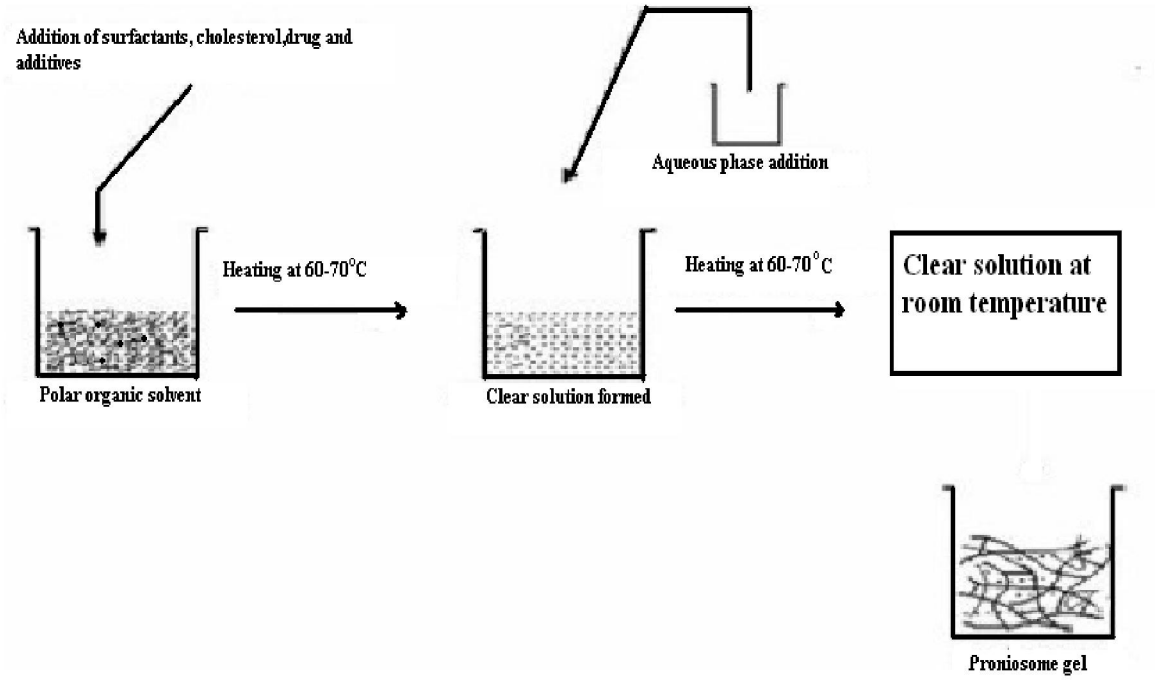

Fig: Method of Preparation of organogels

Mainly three methods are used for preparation of organogels which are;

1) Fluid-Filled Fiber Mechanism:

Firstly surfactants and co-surfactants mixture where dissolved in apolar solvent and reverse micelles where formed. After the addition of water, tubular reveres micelles where formed. Elongated tubular reverse micelles gat entrapped to form a 3 dimensional network, which immobilize apolar solvent after the addition of water into tubular reverse micelles.

2) Solid Fiber Mechanism:

Apolar solvent and solid organogelater where heated and formation of apolar solution of organogelater. After cooling to room temperature, organogelator precipitate out as fiber which undergoes physical interaction amongst each other there by forming the 3 dimensional network structures, which immobilize apolar solvent.

3) Hydration Method:

Gel may be prepared by directly hydrating the inorganic chemicals, which produce dispersed phase of dispersion. In addition of water vehicle, other agents like propylene glycole, propyl gallate and hydroxyl propyl cellulose may be used to enhance gel formation. [8]

TYPES OF ORGANOGELS:

1) Lecithin organogels
2) Sorbitan monostearate organogels
3) In situ formation of an organogel of l-alanine derivative
4) Eudragit organogels
5) Microemulsion-based gels

1) Lecithin Organogels:

Lecithin or phosphatidylcholine is the most abundant phospholipid in biological systems and is typically purified from soy beans and egg yolk. From a drug delivery standpoint, lecithin organogels (LO) are very interesting systems, owing to their biocompatibility, their amphiphilic nature, facilitating dissolution of various drug classes, as well as their permeation enhancement properties.[9] Lecithin Organogels (LO) are thermodynamically stable, clear, viscoelastic, biocompatible and isotropic gels composed of phospholipids appropriate organic solvent and a polar solvent. LOs are jelly-like phases consist of a 3-dimensional network of entangled reverse cylindrical (polymer-like) micelles which immobilizes the continuous or macroscopic external organic phase, thus turning a liquid into a gel. [10]

2) Sorbitan Monostearate Organogels:

Sorbitan monostearate (Span 60) and sorbitan monopalmitate (Span 40) have been found to gel a number of organic solvents at low concentrations. They are prepared by heating the gelator/liquid mixture in a water bath at 60°C (which results in dispersion of the gelator in the liquid medium) and cooling of the resulting suspension, following which the latter sets to an opaque, white, semisolid gel. [11]

3) In Situ Formation of an Organogel of L-Alanine Derivative:

N-lauroyl-L-alanine methyl ester (LAM) was found to gel the pharmaceutically acceptable organic solvents, soybean oil and medium-chain triglycerides. Normally, the system exists in the gel state at room temperature. However, the addition of ethanol to a gelator/solvent solution inhibits gelation because the ethanol disrupts the formation of hydrogen bonds (essential for gelator self-assembly into aggregates) between the gelator molecules. This means that a solution of LAM in an organic solvent can remain in the sol phase at room temperature when some ethanol is added to the mixture. When such a sol phase (20% LAM + 14% ethanol in soybean oil) was placed in phosphate buffered saline at 37°C it turned into a opaque gel within 2 min as the hydrophilic ethanol diffused away into the aqueous buffer, and as gelator-gelator hydrogen bonds were formed.[12]

4) Eudragit Organogels:

Eudragit organogels are different from the organogels as they are really mixtures of Eudragit (L or S) and polyhydric alcohols, such as glycerol, propylene glycol and liquid polyethylene glycol, containing high concentrations (30 or 40% w/w) of Eudragit. Drug containing gels were prepared by dissolving the drug (salicylic acid, sodium salicylate, procaine or ketoprofen) in propylene glycol, pouring the resulting solution into Eudragit powder, and immediately mixing with a pestle for 1 min. Gel viscosity was found to increase with increasing concentrations of Eudragit and to decrease with increasing drug content. [13]

5) Microemulsion-Based Gels:

In microemulsion-based gels (MBGs) the gelator, gelatin, is a hydrophilic polymer, which gels water. MBGs were initially prepared by dissolving solid gelatin in a hot W/O microemulsion followed by cooling. In MBGs the gelatin would dissolve in the water droplets of the w/o microemulsion and that cooling of the system would result in gelation of the water droplets which would lead to clouding of the system and possibly phase separation. [14]

CHARACTERIZATION OF ORGANOGELS:

1) Physiochemical Properties: [15]

Physiochemical properties of the organogel are due to its structural features. An efficient characterization methodology for any organogel system begins with its structural elucidation. The isotopic nature and optical clarity organogel study is feasible by various spectroscopic techniques, namely NMR and FTIR spectroscopy.

2) Rheological Behaviour:

Swelling:

Gels can swell by absorbing liquid with an increase in volumes. Solvent penetrates the gel matrix, so that gel-gel interaction is replaced by gel solvent interaction. Limited swelling is usually the result of some degree of cross linking gel matrix that prevents total dissolution. [16]

Viscoelaticity:

Viscoelasticity is associated with the materials having both viscous and elastic properties. The organogels seems to follow Maxwell model of viscoelasticity. Organogels are the three-dimensional structures which are formed due to the physical interactions amongst the gelator molecules. The organogels behaves like a solid at lower shear rates and hence shows an elastic property. [17] As the shear stress is increased, the physical interacting points amongst the fiber structures start getting weakened until the shear stress is high enough to disrupt the interactions amongst the fiber structures, when the organogels starts flowing. This behavior may be best explained with the plastic flow behavior. [18]

Water content:

Near infra red spectroscopy study on lecithin organogel system by measuring the water absorption in the NIR region (1800-2200nm). In this region water has strong absorption peaks at 918nm due to H-O-H stretching overtone, which are easily detectable and quantified. [19]

3) Optical Clarity:

Depending on the composition of the organogels, the organogels may be transparent or opaque in nature. [20] The lecithin organogels are transparent in nature while the sorbitan monostearate organogels are opaque in nature. [21]

4) Thermo Reversibility:

Organogels are heated up above a critical temperature, they loses its solid matrix like structure and starts flowing.[22] This has been attributed to the disruption in the physical interactions amongst the gelator molecules due to the increase in the thermal energy within the organogels. But on cooling, the physical interaction amongst the organogelators prevails and the organogels revert back to the more stable configuration. [23]

5) In Vitro Drug Release:

The permeation apparatus designed as described by Chowder teal. Al. was employed to study the relese profile of druge from semisolid formulation. The buffer 6.4 used as receptor fluid. The relese of drug from gel through various membranes was determined using Franz diffusion cell. [24]

6) Safety and Skin Compatibility Study:

The irritations potential has been assured by carrying out human skin irritation study.

APPLICATIONS: [25]

1) Topical drug delivery
2) Parenteral delivery
3) Oral delivery

1) Topical drug delivery: [26]

- Cosmetics
- Ophthalmic
- Ointments

Therapeutic compounds of different chemical and physicochemical background such as muscle relaxants, steroids hormones, analgesics, antiemetic, and cardio vascular agents have been incorporated in the organogel with some encouraging results. [27]

2) Parenteral Delivery:

Intramuscular administration of the v/w/o gel yielded the longlasting depot effect (48 h). This can be readily explained by the combined barriers to diffusion present in this formulation (niosomes and gel matrix). Controlled release of contraceptive steroids levonorgestrel and ethinyl estradiol was achieved by Gao et al. from subcutaneously-injected biodegradable organogel formulations prepared from glyceryl ester fatty acids in derivatized vegetable oil.[28]

Subcutaneously injected in situ forming organogels prepared from L-alanine derivatives in safflower oil were used in the long-term delivery of leuprolide, a luteinizing hormone releasing hormone agonist used in prostate cancer.[29]

3) Oral Delivery:

Cyclosporine A (a potent immunosuppressant) showed improved activity when it was delivered orally to beagle dogs as sorbitan monoleatebased organogel formulation. [30] Ibuprofen, a NSAID (non-steroidal anti-inflammatory drug), was incorporated within the gelled structure. The release studies indicated that with the increase in the organogelator concentration within the organogel, there was a subsequent decrease in the release rate of the organogels. In vivo studies in rats showed that the organogels may be used a controlled delivery vehicle for oral delivery of lipophilic compounds. [31]

CONCLUSION

Organogels have emerged as one of the most potential lipid based carrier system for topical drug delivery. When compared to other lipid based carrier systems, these prove to be better in terms of efficacy, feasibility and shelf life. Produces sustained and controlled level of drug in plasma thus reduces the chance of over or under dosing. Since it consists of both hydrophobic and hydrophilic components, both hydrophobic and hydrophilic drugs can be incorporated.

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