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Review Article

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ORGANOGEL: A VIABLE ALTERNATIVE FOR EXISTING CARRIER SYSTEM

Stuti Gupta*[1], Ravindra Pal Singh[2], Ananya Sarkar[1], Hiten Panchal[1] and Deepak Pandey[1]

[1]School of Pharmaceutical Sciences, Jaipur National University, Jaipur, Rajasthan, India.
[2]School of Pharmacy, Suresh Gyan Vihar University, Jaipur, Rajasthan, India.

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ABSTRACT

A **gel** come from the Latin term *gelu*-freezing, cold, ice or *gelatos*-frozen, immobile is a solid, jelly-like material that can have properties ranging from soft and weak to hard and tough. Gels are defined as a substantially dilute cross-linked system, which exhibits no flow when in the steady-state. By weight, gels are mostly liquid, yet they behave like solids due to a three-dimensional cross-linked network within the liquid.

An **organogel** is a non crystalline, non-glassy thermoreversible (thermoplastic) solid material composed of a liquid organic phase entrapped in a three-dimensionally cross-linked network. The liquid can be, for example, an organic solvent, mineral oil, or vegetable oil. The solubility and particle dimensions of the structurant are important characteristics for the elastic properties and firmness of the organogel. Often, these systems are based on self-assembly of the structurant molecules. Organogels have potential for use in a number of applications, such as in pharmaceuticals, cosmetics, art conservation, and food. An example of formation of an undesired thermoreversible network is the occurrence of wax crystallization in petroleum.

Keywords: Organogel, gel, semisolid, lecithin.

INTRODUCTION

Gels: A gel is a solid semi-solid system of at least two constituents, consisting of a condensed mass enclosing and interpenetrated by a liquid. When the coherent matrix is rich in liquid, the product is often called as jelly.

The United States pharmacopoeia defines gel as **"semisolid, being other suspension of small inorganic particle or large inorganic molecules interpenetrated with liquid".** This is a true phase system, as an inorganic particle is not soluble but merely dispersed throughout the continuous phase.[1]

CLASSIFICATION OF GELS

1. On the basis of phase system

- Two phase system: The gel mass may consist of floccules of small particles rather than large molecules. The gel structure in these systems is not always stable. Such gels may be thixotropic, forming semisolid on standing and become liquid on agitation. e.g. aluminium hydroxide gel, bentonite magma.
- Single phase system

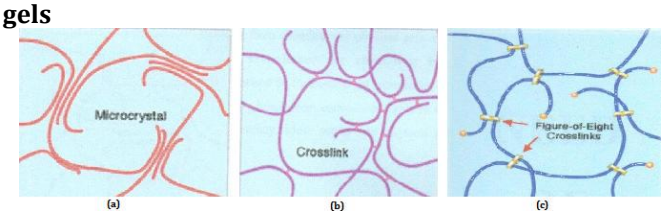
2. On the basis of Chemical Nature

- Inorganic gel
- Organic gel

3. On the basis of structural arrangement

- Physical gels: unstable at high temperatures or in solvents.
- Chemical gels: not tough due to uneven structure.
- Slide-ring gels: these gels are differ from physical and chemical gels in that the polymer chains are neither covalently cross linked nor attractively interacted; rather they are interlocked by figure- of- eight cross links.[2,3] (Figure **1**)

Figure 1. a) Physical gel, b) Chemical gel, c) Slide-ring gels



NEED OF ORGANOGELS

The organogel do not form semisolids on standing. Because an organogel may consists of macromolecules existing as twisted matted strands. The units are of bound together by strong types of Vanderwaal forces so as to form crystalline amorphous regions throughout the entire system.[4,5]

The organogels have lower hydrations, the drug dissolving polymer and is transported between the chains. Cross linking increases hydrophobicity of gels & diminishes the diffusion rate of drug.[6]

Advantages:

- Organogel can't form semisolids preparation on standing.
- Organogel can diminish the diffusion rate 0f drug. Because the drug is dissolved in polymer & transported between chains.

Disadvantages:

- When a gel stands for some time, it often shrinks naturally, & some of its liquid is pressed out, known as syneresis.

***Corresponding Author:**
Stuti Gupta
Department of pharmaceutics, School of pharmaceutical sciences, Jaipur National University, Jaipur-302025, Rajasthan, India.
Contact no: +91-9351410921, Email: stutipharmabird@gmail.com

- When the gel is taken up of liquid with an increasing volume known as swelling.

ORGANOGEL STRUCTURE & MECHANISM OF ORGANOGELLING

The organogelling or the gelation of the lecithin solutions in organic solvents is induced as a result of the incorporation of a polar solvent. Approaches developed by Israelachvili et al, the aggregate transformation (i.e. sphere-to-cylinder transformations) are determined by a change of a curvature for the amphipmile monolayer.[7]

In particular, the effects of polar solvent introduced into spherical lecithin micelles may be associated with an increase in the cross-sectional area of the lecithin polar region in which the solvent is arranged. The shape of the hydrated molecules is close to a cylinder. This shape leads to packing constraints in the spherical micelles that are diminished through the transition into the cylindrical ones with a smaller curvature.[8]

MECHANISM OF DRUG RELEASE[9]

A drug may be regarded as a random network permeated by pores that are filled with a liquid component; substances that are soluble in the liquid component will tend to permeate through the gel by diffusion in solution through the space in the network. The rate of diffusion of substances through gels by this means will therefore be affected by those factors that normally affect simple diffusion in solution and by additional factors that are associated with the presence of the gel network.[10,11,12]

Diffusion in Solution: This process may be defined as the spontaneous transfer of solute from concentration regions in the solution where the concentration is lower, until there is a uniform distribution throughout. Fick's first law expresses the rate of diffusion of a solute, which is given by the equation.[6]

$$\frac{dm}{dt} = -DA\frac{dc}{dx}$$

Where dm = amount of solute diffusing
dt = time
A = Area
dc/dx = concentration gradient
D = diffusion coefficient

METHOD OF PREPARATION[13]

Flocculation of lyophilic colloids by salt or precipitating liquid, evaporation of certain colloidal solution such as collodion, again chemical reactions with that lead to a change in shape of lyophilic molecule colloid by denaturation of molecule of the albumin on heating involves some uncoiling of the protein molecule and a gel, swelling of a dry (xerogel) when placed in contact with a suitable liquid ex- starch granules added to the water.[14-17]

Precipitation method: To achieve a fine degree of subdivision of the particle & gelatinous character of those particles.

Hydration method: gel may be prepared by directly hydrating the inorganic chemical, which produces dispersed phase of the dispersion. In addition of water vehicle, other agents as propylene glycol, propyl gallate and hydroxyl propyl cellulose may be used to enhance gel formation.

EXAMPLE OF GEL

1. Lecithin gels
2. Phospholipids organogels

Formulation 1

Triglyceryl distearate Glycerol phase

Glycerol	2%
Dipropylene glycol	47%
Ascorbic acid	18%
Glycerol phase	5%
Oily phase	
Apricot kernel oil	27%
Tocopheryl acetate	1%

Formulation 2

Glycerol phase	
Hydrogenated lecithin	2%
Glycerol	36%
Dipropylene glycol	14%
Ascorbic acid	10%
Oily phase	
Apricot kernel oil	27%
Tocopherol acetate	1%
Plant DNA gel in water	10%

GEL FORMING COMPOUND

A. Natural polymer
- Alginate
- Carrageenan
- Tragacanth
- Pectin
- Xanthan gum
- Gellan gum
- Guar gum
- Other gum
- Chitosan

B. Acrylic polymers
- Carbomer-934

C. Cellulose derivatives-
- Carboxy methyl cellulose
- Methyl cellulose
- Other cellulose

D. Colloidally Dispersed solid
- Microcrystalline silica
- Clays
- Microcrystalline cellulose

FACTOR AFFECTING ORGANOGELS

Organic solvent[18]:
- *Polar solvent:* The effect of polar solvent introduces into spherical lecithin micelles may be associated with an increase in cross-sectional area of the lecithin polar region, in which the solvent is arranged.
- *Non-aqueous solvent:* A non-aqueous solvent is not particularly limited as long as it replaces water of the bacterial cellulose hydrogel completely without destroying its shape. Ex-Polyethylene glycol, Dimethyl ether.

Phase Transition Temperature[19]: It gives an insight into nature of microstructures that form the gelling cross linked network. For ex- a narrow PTT range is indicative of homogenous microstructures within the gel. For determination of PTT hot stage microscopy and high sensitivity differential scanning calorimetry is accurate and sensitive techniques.

Salt addition: Salt may attract part of water of hydration of the polymer allowing more formation inter molecular secondary bond, this is known as salting out.[20]

Temperature: The effect of temperature depends on the chemistry of the polymer and its mechanism of interaction with the medium. If the temperature is reduced once the

gel is in the solution, degree of hydration is reduced and gelation occurs. Gel resulting from the chemical cross linking often cannot be liquefied by dilution or temperature changes.[3]

Molecular weight: Low molecular weight polymers require a high concentration to build up viscosity and to set to gel possibly.

Surfactants: Gel characteristics can be varied by adjusting the proportion and concentration of the ingredients. Poloxamer 407 is a polyoxyethylene that function as a surfactant.

Physicochemical properties[21]

Charge: the presence of charged groups on a polymer favors mucoadhesion. Polyanions particularly polycarboxylates, are preferred to polycations.

Solubility: mucoadhesives swell on contact with moisture, increasing the mobility of polymer molecules at the interface and exposing more sites for bond formation.

Molecular weight/ spatial configuration: It favors change in entanglement and interaction after the polymer and mucin have interpenetrated.

CHARACTERIZATION OF GELS

Physiochemical properties: Physiochemical properties of the organ gel are due to its structural features. An efficient characterization methodology for any organ gel system begins with its structural elucidation. The isotopic nature and optical clarity organ gel study is feasible by various spectroscopic techniques, namely NMR and FTIR spectroscopy. FTIR spectroscopy has been found to be successful in establishing the hydrogen bonding as one of the major driving force for the self assembly of organogelator molecules in organic solvent. The knowledge of molecular packing within the organogel network has been obtained using scanning and transmission electron microscopies, dynamic and static light scattering (elastic or quasielastic light scattering technique.) small angle neutron scattering {SANS}.

Rheological behaviour[22]**:** The critical parameter such as spreadability, adhesiveness, cohesiveness and gel consistency need to be modified:

Viscoelasticity: Organogels have been studied extensively for their rheological attributes and have been determined to be viscoelastic in nature. Scartazzini and Luisi performed the dynamic shear viscosity prepared using different types of organ gel solvent (eg. linear and cyclic alkenes, amines). The higher values obtained using linear alkenes were related to the higher state of structural organization organogels. Similarly, Schurtenberger E T found that increasing the gelator concentration leads to an increase in the viscosity and in turn the gel strength.

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

Water content: Water content of organ gel system is critical, as the water loss by evaporation can lead to consequent decrease in viscosity thus affecting the gel stability. Near infra red spectroscopy studies on lecithin/IPP/water organogel system by measuring the water absorption in the NIR region (1800-2200nm). In this region, water shows a strong absorption peaks at 918nm due to H-O-H stretching overtones, which are easily detectable and quantifiable.

1. **Phase transition temperature:** The phase behavior of organogel varies on changing temperature condition. The phase transition temperature (PTT) (i.e. sol to gel or gel to sol) gives an insight into the nature of micro structure that form gelling cross linked network. For the determination, hot stage microscopy and high sensitivity differential scanning calorimetry have been reported to be useful as accurate and sensitive techniques. PTT also reveals the micro structural homogeneity of the prepared organogel system. For example, a narrow PTT range (i.e. 3) is indicative of homogenous microstructures within the gel.

APPLICATION & USES[23]

Topical drug delivery: 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.[24-26]

i) *Cosmetic:* well used in the cosmetic and personal care markets.
ii) *Ophthalmic:* Drug product like normal lachrymal turnover causes rapid clearance of solution and suspension dosage forms.
iii) *Ointments:* It is of various advantages like good tolerability, formation of a protective film over the cornea, protection from conjuctival adhesion.

Methazolamide ineffective as an ophthalmic solution has been incorporated into carbomer and poloxamer gels for treatment of Glaucoma.

Topical Delivery of therapeutic substance incorporated in lecithin organogels

Organogel Formulation	Major findings
Lecithin (200mM)IPP gel of broxaterol and scopolamine	Transdermal delivery of compounds.
Soybean lecithin/IPP gels containing 10% to 20% short chain esters such as ethyl acetate or propyl acetate	Transdermal delivery of aromatic tetra-amidines for anti cancer activity
IPP lecithin gel of diclofenac and indomethancin	Enhanced efficacy of NSAIDs administered through topical route
Nicardipine lecithin –iso propyl myristate organogel	Enhanced skin permeation across guinea pig and human skin.
Methimazole in lecithin organogel	Significant percutaneous absorption of methimazole

Dermal drug delivery: The muscle relaxants administered in lecithin –Isopropyl myristate organogel is shown to provide immediate relief of pain resulting from bruxism (tooth grinding) and tooth clenching. A United States Patent granted to Crandall, describes the PLO formulation for effective delivery of antipsoriatic agents and for drugs used in eczema. The patented formulation is composed of lecithin (containing = 95% phosphatidylcholine). Organogel have also been found to be an excellent matrix for the delivery of macromolecule with a molecular weight of 33000 Daltons. Phospholipids organogel containing anti inflammatory macromolecule bromelain (15%) along with capsaicin (0.025%) has been found to be effective anti inflammatory composition. Direct application of this Phospholipids organogel at the site of inflammation has been found to be useful in treating a variety of inflammatory indications.

Transdermal drug delivery

Organogel systems have also been used as a matrix for transdermal transport of different therapeutic

compounds. Willimann and luisi were first to study organogel as matrix system for transdermal transport of drugs. The author investigated the transdermal delivery scopolamine(an active drug against motion sickness) and broxaterol(a bronchodilator agent) employing lechitin gel composed of 200mM of lecithin in a biocompatible solvent IPP, in 2 separate studies. The solubility of various drugs such as nifedipine, clonidine, scopolamine. And broxaterol was noted to be increase in lecithin –IPP solution compared with drug solubility in IPP alone, suggesting the solubility enhancing properties of the organogels. Ciribassi et al have reported the systemic absorption of fluoxetine hydrochloride through the skin using phospholipid organogel as a topical vehicle. In another study, Nicardipine, a calcium channel blocker, because of its low dose, short half live and extensive first pass metabolism, has been incorporated in the system in order to achieve systemic absorption through topical route. Thus, with the inflow of several research reports on the varied fundamental aspects organogel along with some promising results on the front drug delivery, these systems can be seen as potential tools in the field of topical drug delivery applications.

Bioadhesives

Bioadhesives of pharmaceutical interest are mucoadhesives this implies that the substrate for adhesion is the mucus itself. Many of the alternate routes of administration (buccal, ophthalmic, nasal, vaginal, etc) lend themselves bioadhesives because of the presence of mucosal tissue.[27]

Cosmetic

Gels have been employed in a variety of products including shampoo, fragrance products, dentifrices and skin and hair care preparation.

Dosage forms

Glycogelatin gels are frequently used as a basis for medicated pastilles. They are used in the formulation of some suppositories e.g. Glycerin suppositories BP 1968.

Gelatins gels

They are employed in the preparation of hard and soft capsules that may be used to mask the unpleasant tastes of solids and liquids.

Microbiological media

Agar and gelatin gels are used as a solid media for the culture of microorganisms. The diffusion of antibiotics, antiseptics, vitamins and enzymes through the culture media is used in the microbiological assays of these materials. Such diffusion produces zones of either retarded or enhanced growth on seeded agar plates depending on the activity of the diffusing substance.

CONCLUSION

Organogel have emerged as one of the most potential carrier system. In contrast to other lipid based system such as vesicular system (liposome and noisome), organ gel system may prove to have edge in terms of efficacy, stability and most important technological feasibility. Moreover, the topical delivery of new biotech- generated proteinaceous molecules in the protective non polar micro environment of these systems may help to protect these sensitive micromolecules from degradation during transport to the desired site.

The organogel may prove to be highly promising systems in realizing the drug delivery objectives while scientist are desperately trying for more viable alternatives i.e. existing carrier systems.

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