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# ORGANOGELS: ADVANCED AND NOVEL DRUG DELIVERY SYSTEM

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**ABSTRACT**
Organogel, is a non crystalline, non-glassy thermoreversible (thermoplastic) solid material and viscoelastic system, can be regarded as a semi-solid preparation which has an immobilized external apolar phase. The apolar phase gets immobilized within spaces of the three-dimensional networked structure formed due to the physical interactions amongst the self assembled structures of compounds regarded as gelators. Often, these systems are based on self-assembly of the structurant molecules. In general, organogels are thermodynamically stable in nature and have been explored as matrices for the delivery of bioactive agents. 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. In the current manuscript, attempts have been made to understand the properties of organogels, various types of organogelators and some applications of the organogels in controlled delivery.
**KEYWORDS:** Organogels, gelators, cosmetics, controlled delivery

## INTRODUCTION

A gel may be defined as a semi-solid formulation having an external solvent phase, apolar (organogels) or polar (hydrogel), immobilized within the spaces available of a three dimensional networked structure[1]. 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[2]. Gels can also be classified according to the bonds present in the gelator network: physical gels are held by weaker physical forces of attraction such as vanderwaals interactions and hydrogen bonds, whereas chemical gels are held by covalent bonds. Hydrogels (composed of water held by a three-dimensional polymeric network) have been extensively studied as vehicles for a wide range of drugs. The organogels may be regarded as bi-continuous systems consisting of gelators and apolar solvent, which may or may not contain water-molecules entrapped within the self-assembled structures of the gelator. 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. The gelators, when used in concentration < 15 % (approx.), may undergo physical or chemical interactions so as to form self-assembled fibrous structures which get entangled with each other resulting in the formation of a three-dimensional networked structure. The three-dimensional networked structure, hence formed, prevents the flow of external apolar phase. Some common examples of gelators include sterol, sorbitan monostearate, lecithin and cholesteryl anthraquinone derivates. They have been fabricated in a variety of different shapes (e.g., rods, disks, films and microparticles) depending on the intended applications and sites of administration. In addition, some thermoresponsive gels can be administered parenterally as a liquid, which forms a gel in situ at body temperature. The thermo-reversible property of the organogels has generated much interest for the potential use of the organogels as drug delivery system. The thermodynamic stable nature of the organogels has been attributed to the spontaneous formation of fibrous structure by virtue of which the organogels reside in a low energy state. The occurrence of the gel-to-sol transition above room-temperature indicates that external energy has to be supplied to the organogels so as to disrupt the three-dimensional structure and subsequent transformation of the gelled state to the sol state. Apart from the temperature sensitivity, organogels are also sensitive to the presence of moisture which has also been explored to develop controlled delivery systems. Examples of gellable organic solvents include aliphatic and aromatic hydrocarbons, alcohols, silicone oil, dimethyl sulfoxide and vegetable oils. In contrast to hydrogels, in which the gelator is normally a polymer, most of the organogelators are relatively small molecules and they have been called low molecular weight organogelators. Various organogel-based formulations have been designed to administer of the bioactive agents by different routes administration[1].

### Advantages Of Organogels

- Organogel can't form semisolids preparation on standing.
- Organogels are moisture insensitive.
- They enhance the skin penetration and transport of the molecules.
- They are organic in character also resist microbial contamination.
- Organogel can diminish the diffusion rate of drug because the drug is dissolved in polymer & transported between chains.
- Structural integrity of organogels is maintained for longer time periods.
- Process very simple and easy to handle.
- Use of biocompatible, biodegradeable and non-immunogenic materials makes them safe for long term applications.
- Organogels provide opportunities for incorporation of wide range of substances with different physicochemical characters[3].

### Limitations Of Organogels

- Less stable to temperature.
- When a gel stands for some time, it often shrinks naturally, & some of its liquid is pressed out, known as syneresis.
- If impurity present then no gelling will occur.
- Expensive in production.
- Raw materials like lecithin are not available on large scale.
- It should be stored in a proper condition.
- When the gel is taken up of liquid with an increasing volume known as swelling[4].

### Structure Of Organogels & Mechanism Of Organogelling

The incorporation of a polar solvent, the organogelling or the gelation of the lecithin solutions in organic solvents is induced. The aggregate transformation (i.e. sphere-to-cylinder transformations) are determined by a change of a curvature for the amphipmile monolayer and this approaches developed by Israelachvili et al.[5] In particular, the effects of polar solvent introduced into spherical lecithin micelles may be associated in which the solvent with an increase in the cross-sectional area of the lecithin polar region 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.

**Gelator Self-Assembly**

A variety of gelator aggregates such as platelets, tubules, fibres, rods, worm-like chains, ribbons and fan-like structures have been reported. Aggregate thickness ranges from a fraction of a nanometre to microns. The manner in which gelator molecules self-assemble and the nature of the gelator aggregate depends to a large extent on the gelator, whose component groups dictate the forces of interactions involved in gelator self-assembly. For example, molecules of the non-ionic surfactant sorbitan monostearate are thought to assemble into bilayers, which are then organised into tubules. 12-Hydroxyoctadecanoic acid is thought to form fibrillar aggregates via extensive axial hydrogen bonding and dipolar interactions[6]. Aggregation forces between gelator molecules thus include hydrogen bonding, dipole–dipole interactions, π-stacking, electron transfer, London dispersion forces, solvophobic effects, ionic interactions and so on, depending on the chemical structures of the gelators. The manner in which the gelator molecules are packed in aggregates must not be assumed to be the same as in the neat gelator solid, and the different packing and forces of interactions in gelator aggregates and in the neat solid are often reflected in the different melting points of the two. The liquid phase of the gel plays a fundamental role in gelation and affects both macroscopic (e.g., opacity) and microscopic (e.g., aggregate size, shape, cross-sectional nature, helicity and gel network) properties of the gels. The fluid phase must provide the correct solubility/insolubility balance so that the gelator dissolves or is dispersed at high temperatures but comes out of solution (as aggregates) following cooling. Molecular shape of the solvent molecule can also have a profound effect on gelation; for example, steroidal nitroxide forms stable gels in trans-decalin and in cyclohexane but not in cis-decalin, methyl-cyclohexane and n-alkane. The higher melting point was thought to be due to the additional attractive forces provided by hydrogen bonding between 1-octanol and CAB in octanol gels. The dimensions of the container in which gelation proceeds can also have an impact on the gel network. Furman and Weiss reported that if the size of the container was smaller than the mesh size of a particular gel network, gelation was either inhibited or a different type of gel network (mesh) was formed[7].

**Types Of Organogelators**

The organogelators may be categorized into two groups based on their capability to form hydrogen bonding. The examples of organogelators the hydrogen bond forming organogelators include amino acids, amide, urea moieties and carbohydrates whereas which do not form hydrogen hydrogen bonding include anthracene, anthraquinone and steroid based molecules. The simplest organogelators are n-alkanes (C = 24, 28, 32, 36), which gel other relatively short chain n-alkanes such as hexadecane and other organic liquids. Other examples of organogelators include substituted fatty acids (e.g., 12-hydroxyoctadecanoic acid); 1,3:2,4-di-O-benzylidene-Dsorbitol (D-DBS), sorbitan monostearate, a non-ionic surfactant, steroids and their derivatives, anthryl derivatives (e.g., 2,3-bis-n-decyloxyanthracene, macrocyclic gelators (e.g., calixarenes, ALS compounds (an aromatic moiety attached to a steroidal group by a linker segment), cyclo(dipeptide)s, bisurea compounds, bisamides, bolaform amides derived from amino acids, n-alkyl perfluoroalkanamides, carbohydrate derivatives, perfluoroalkanes, which gel liquid carbon dioxide, a mixture of highly reactive methyl 2,6-diisocyanatohexanoate and alkylamines in an organic solvent, which react when mixed to form a product that gels the organic solvent, primary alkyl amines, which gel organic solvents following the uptake of $CO_2$, $NO_2$, $SO_2$ or $CS_2$, light-responsive gelators, which produce gels whose sol-to-gel transition may be switched by irradiation with UV and visible light, oxadiazole-based benzene 1,3,5- tricarboxamide, a nonfluorescent gelator, which produces highly fluoresent organogel, cobalt (II) triazole complexes, which, unlike most organogels, form gels at high temperatures and solutions at low temperatures, and fatty acid derivative of L-alanine, which selectively gels the organic solvent but not the aqueous phase when added to an oil/water mixture. Certain compounds can only gel organic solvents in the presence of other compounds, for example, aminopyrimidine and dialkylbarbituric acid gel cyclohexane when present at 1:1 molar mixtures[8]. Different types of organogelators with their property and uses are described in Table 1 .

**Table 1.** Types of organogelators with their advantages and applications[9,10]

| S.No. | Types and property of organogelators | Advantages and applications of organogelators |
|---|---|---|
| 1 | **4-tertbutyl-1-aryl cyclohexanols derivative organogelators**<br>• These gelators are solid at room temperature having low solubility in apolar solvents viz. cyclohexane, benzene and carbon tetra chloride. | 4-tertbutyl-1-aryl cyclohexanols, categorized under arylcyclohexanol derivatives, helps in designing thermo-reversible organogels. |
| 2 | **Polymer organogelators**<br>• Polymer organogelators have been found to induce organogelation even at very low concentrations and their gelling capability of these gelators may be tailored by modifying the chemical structure of the polymer backbone.<br>• Some common examples of polymeric organogelators include L-lysine derivatives apart from the conventional polymers like poly(ethylene glycol), polycarbonate, polyesters, and poly(alkaline). | • The gels developed by polymeric organogelators generally have lower gel-sol transition temperature and comparatively higher gel strength when compared with organogels developed with low-molecular weight organogelators. |
| 3 | **Gemini organogelators**<br>• The Gemini organogelators which had two L-lysine derivates connected with alkaline spacer chains, of varying chain lengths, by amide bonds. | • bis(Nε-lauroyl-L-lysine ethyl ester) oxalyl amide organogelator was able to immobilize a variety of apolar solvents.<br>• Various other oxalyl amide derivatives containing various alkyl ester groups (e.g. hexyl, decyl, dodecyl, 2-ethyl-1-hexyl and 3,5,5-trimethylhexyl) have also showed relatively good organogelation property. |
| 4 | **Boc-Ala(1)-Aib(2)-β-Ala(3)-OMe organo gelator**<br>• Boc-Ala(1)-Aib(2)-β-Ala(3)-OMe is a synthetic tripeptide which has the capability to undergo self-association so as to form thermoreversible transparent gels in the presence of various apolar solvents viz. 1, 2-dichlorobenzene (DCB), monochloro benzene and benzene. | • Formation of thermoreversible transparent gels. |
| 5 | **Low Molecular Weight (LMW) organo gelators**<br>• These gelators may produce either solid-fiber matrix or fluidfiber | |

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| | matrix depending upon the physical intermolecular inters actions.<br>• Solid-fiber matrix may be formed when a heated mixture of the organogelators in apolar solvent is cooled down below the solubility limit of the organogelators. This results in the precipitation of the organogelators as fiber-like structures which undergoes physical interaction so as to form a gelled structure. These solid fiber-like structures align themselves into bundles.<br>• fluid-fiber matrix is formed by the addition of polar solvent into a solution of amphipaths in apolar solvents. Amphipaths in apolar solvents are present as reverse micelles, which on addition of minute quantity of water forms tubular reverse micellar structures. | • Solid-fiber matrix organogels have improved mechanical properties as compared with the fluid-fiber matrix organogels. This can be attributed to the highly ordered structures present in the solid-fiber matrix organogels as compared to the simple chain entanglements in the fluidfiber matrix organogels.<br>• Apart from the above-mentioned organogels, various amphiphiles having the ability to form selfassembled structures in the presence of apolar solvents have also been tried. |

## Organogel Preparation[11]

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 selfassembly into well-defined aggregates such as tubules, rods and fibres. The physical organogels, held together by noncovalent forces, are thermoreversible; that is, following heating, the gel melts to the sol phase as the gelator aggregates dissolve in the organic liquid, whereas cooling the hot sol phase results in gelation. Mainly 3 methods are used for preparation of organogels like:

### (1) Fluid-filled fiber mechanism

Firstly surfactants and co-surfactants mixtures were dissolved in apolar solvent and formation of reverse micelles was formed. After the addition of water, tubular reverse micelles were formed. Elongated tubular reverse micelle gets entangled to form a 3-dimensional network, which immobilizes apolar solvent after the addition of water into tubular reverse micelles.

### (2) Solid fiber mechanism

Apolar solvent and solid organogelator were heated and formation of apolar solution of organogelator. After cooling to room temperature, organogeltor precipitates out as fibers which undergo physical interactions amongst each other thereby forming a 3-dimensional network structure, which immobilizes apolar solvent. To achieve a fine degree of subdivision of the particle & gelatinous character of those particles.

### (3) 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.

## Types Of Organogels

Different types of organogels are used for delivery of drugs and other pharmaceutical ingredients. Table 2 describe types, property, advantages and applications of different types of organogels.

**Table 2**. Types and property of organogels[12-15].

| S.No. | Types and property of organogels | Advantages and applications of organogels |
|---|---|---|
| 1 | **Lecithin organogels**<br>• Extracted from various plants and animal tissues apart from the egg yolk.<br>• Experimental results indicate that the lecithin fails to initiate the process of gellification of the apolar solvent if the lecithin contains < 95% phosphatidyl content.<br>• The organogels prepared using lecithin has been found to have an isotropic structure. | • The lecithin-based organogels have been found to be thermodynamically stable, thermo reversible (sol-to-gel transition temperature at 40°C), transparent, viscoelastic, biocompatible and non-irritant.<br>• The lecithin organogels help either in the solubilization or accommodation of various guest molecules within its structure. These properties of the lecithin organogels have generated great potential for the use of the same as a controlled delivery vehicle. |
| 2 | **Pluronic Lecithin Organogel (PLO)**<br>• PLO is a soy lecithin-based organogels which consists of isopropyl palmitate or isopropyl myristate, water and Pluronic F127 (also known as Poloxamer 407).<br>• The apolar phase in the PLO constitutes 22 % (v/v) and hence is often regarded as micro-emulsion-based gel. | • PLO is thermostable, viscoelastic and biocompatible in nature.<br>• PLO has also been found to produce minimal skin irritation. It has been used as a delivery vehicle for both hydrophobic and hydrophilic molecules for topical and transdermal applications. |
| 3 | **Premium lecithin organogels (PrLO)**<br>• The PrLO is a second general lecithin organogel and has got higher thermostability apart from its non-greasy and non-tacky nature, which provides a cosmetically pleasing acceptability.<br>• This gel do not have pluronic derivative, which results in the avoidance of the skin-irritation and thereby local skin-intolerance reactions. | • The use of PrLO as a carrier for drug delivery has indicated that the gel help in achieving improved bioavailability in the tissues by improving the penetration of the bioactive agents.<br>• This gel has been successfully used to accommodate various bioactive agents, *viz.* diclofenac, ibuprofen, ketoprofen and progesterone, and has been regarded as vehicle of choice for intradermal drug delivery. |
| 4 | **Limonene GP1/PG organogel**<br>• The GP1 (dibutyllauroylglutamide) / PG (propylene glycol) organogels can be prepared by mixing the appropriate amounts of GP1, limonene and PG with the subsequent incubation of the same at 120°C. When the mixture is cooled down, it forms a white gel.<br>• It was found that the presence of limonene within the GP1/PG organogels resulted in the alteration of the rheological properties of the organogels though there was no significant change in the chemical stability of the organogels. | • Limonene, a terpene, has been found to be an excellent penetration enhancer and hence has been incorporated within various transdermal formulations for the improving the penetration of the bioactive agent across the transdermal layer, thereby improving the bioavailability of the bioactive agent within the dermal tissue.<br>• Apart from limonene, various other terpene-based penetration enhancers (e.g. linalool, farnesol and cineole) have also been incorporated successfully in GP1/PG organo gels. The presence of penetration enhancers within the organogels results in the improve ment of the rate permeation of the bioactive agents. |
| 5 | **Gelatin stabilized microemulsion based organogel (MBG)**<br>• Gelatin is a protein which has been used as a structuring agent in various food preparations having excess of aqueous phase. It forms a gelled structure when a concentrated heated solution of gelatin having temperature in excess of 40°C is cooled down to a | • Microemulsions are preferred for the development of gelatin stabilized organogels because of the thermostable nature and the ease of preparation of the same. |

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| | temperature below 35°C.<br>• The addition of gelatin to the water-in-oil microemulsion results in the gellation of the whole micellar solution and the gel formed is transparent in nature. | • The MBGs have been used to device topical and/or transdermal controlled delivery vehicle for hydrophobic bioactive agents. |
| 6 | **Fatty acid derived sorbitan Organogels**<br>• These gelators are hydrophobic non-ionic molecules having surface active properties and have the ability to immobilize various solvents *viz.* isopropyl myristate, and vegetable oils.<br>• These gelators form solid-fiber matrix when the heated solution of gelator in apolar solvent is cooled down.<br>• The formation of the gel has been attributed to the formation of toroidal reverse micelles as the temperature is lowered.<br>• The toroidal reverse micelles reorganize themselves to form rod-shaped tubules which subsequently undergo physical interaction amongst each other thereby forming a three-dimensional networked structure. | • The gels developed by using these gelators are opaque, thermoreversible and thermostable at room-temperature for weeks.<br>• Organogels using fatty acid gelators may also be prepared by dissolving the gelators in a waterin- oil emulsion at a higher temperature followed by the decrease of the emulsion temperature. The decrease in the temperature results in the decrease in the solubility of the gelator with the subsequent precipitation and self-assembly of the gelators into network of tubules, which gets entangled so as to form a gelled structure. |
| 7 | **Poly (ethylene) organogels**<br>• The polyethylene organogels are colourless in nature, which are formed when the low molecular weight polyethylene is dissolved in mineral oil at a temperature >130°C and subsequently shocked cooled. | • These organogels have been extensively used as ointment bases. The formation of gelled structure may be attributed to the physical interactions of the solid-fibers formed due to the precipitation of the polyethylene molecules. |
| 8 | **Eudragit organogels**<br>• Eudragit organogels are different from the organogels they are the mixtures of Eudragit (L or S) and polyhydric alcohols such as glycerol, propylene glycol and liquid polyethylene glycol containing high concentrations of Eudragit. | • They show high gel rigidity and stability when drug concentration was low. |
| 9 | **Sorbitan Monostearate Organogels**<br>• Sorbitan monostearate (span 60) and sorbitan monopalmitate (span 40) have been found to gel a number of organic solvents at low concentrations.<br>• Prepared by heating the gelator/ liquid mixer in a water bath at 60°C and cooling of the resulting suspension. | • They are used for delivery of hydrophilic vaccines and sorbitan monostearate. |
| 10 | **L-alanine derivative organogels**<br>• Prepared from N-lauroyl-L-alanine methyl ester which gels in the organic solvents as soybean oil and triglycerides.<br>• The system exists in the gel state at room temperature. | • It could act as a sustained release implant.<br>• Used for delivery of rivastigmine and leuprolide drug. |

## Mechanism Of Drug Release

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 (the spontaneous transfer of solute from concentration regions in the solution where the concentration is lower, until there is a uniform distribution throughout) 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[16]. Fick's first law expresses the rate of diffusion of a solute, which is given by the equation.

dm/dt = - DA(dc/dx), Where dm = amount of solute diffusing, dt = time, A = Area, dc/dx = concentration gradient and D = diffusion coefficient.

## Physicochemical Property Of Organogels

In the present section, attempts will be made to discuss about the various physicochemical properties of the organogels. Table 3 describe physicochemical property of organogels .

**Table 3.** Physicochemical property of organogels[17,18,19]

| S.No | Physicochemical property | Details about Physicochemical property |
|---|---|---|
| 1 | **Viscoelaticity** | • The organogels behaves like a solid at lower shear rates and hence shows an elastic property. 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 behaviour may be best explained with the plastic flow behaviour. |
| 2 | **Non-birefringence** | • The organogels when viewed under polarized light appears as a dark matrix. This can be accounted to the isotropic nature of the organogels which does not allow the polarized light to pass through the matrix. This property of the organogels of not allowing the polarized light to pass through it's matrix is regarded as non-birefringent. |
| 3 | **Thermoreversibility** | • As the organogels are heated up above a critical temperature, the organogels loses its solid matrix- like structure and starts flowing. 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 as the heated organogels systems are subsequently cooled down, the physical interaction amongst the organogelators prevail and the organogels revert back to the more stable configuration. |
| 4 | **Thermostability** | • The organogels are inherently thermostable in nature. Then stability of the organogels may be attributed to the ability of the gelators to undergo self-assembly, under suitable conditions, so as to form organogels. As the gelators undergo self-assembly, it results in the decrease in the total free energy of the system and renders the organogels as low-energy thermostable system. |
| 5 | **Optical clarity** | • Depending on the composition of the organogels, the organogels may be transparent or opaque in nature. The lecithin organogels are transparent in nature while the sorbitan monostearate organogels are opaque in nature. |
| 6 | **Chirality effects** | • The presence of chirality in the LMW gelators has been found to affect the growth and the stability of the solid-fiber networks. Thermo reversibility of the gels formed due to the formation of the self assembled solid-fiber network has also been associated with the chirality.<br>• The presence of chiral centers within the gelators helps in the formation of a compact molecular packing, which provides a thermodynamic and kinetic stability to the organogels system. Crown ether |

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| | | phthalocyanine organogels are the excellent example of chiral organogels. |
| 7 | **Biocompatibility** | • Initially, organogels were developed using various nonbiocompatible organogels which rendered the organogels nonbiocompatible. Of late, research on organogels using various biocompatible constituents has opened up new dimensions for the use of the same in various biomedical applications. |

## Factor Affecting Organogels

Various factors related to nature of chemicals, solvents, environmental conditions and other parameters affect the preparation and stability of organogels. Table 4 describe factor affecting parameters which affect the preparation of organogel.

**Table 4.** Various parameters affect the property of organogels[20,21]

| S.No | Factors affecting parameters | Details about Factors affecting parameters |
|---|---|---|
| 1 | **Organic solvent**<br>• **Polar solvent**<br>• **Non-aqueous 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.<br>• A non-aqueous solvent is not particularly limited as long as it replaces water of the bacterial cellulose hydrogel completely without destroying its shape for example- Polyethylene glycol, dimethyl ether. |
| 2 | **Phase Transition Temperature** | • 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. |
| 3 | **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. |
| 4 | **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. |
| 5 | **Molecular weight** | • Low molecular weight polymers require a high concentration to build up viscosity and to set to gel possibly. |
| 6 | **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. |
| 7 | **Physicochemical properties**<br>• **Charge**<br>• **Solubility**<br>• **Molecular weight/ spatial configuration** | • The presence of charged groups on a polymer favours mucoadhesion. Polyanions particularly, polycarboxy lates, are preferred to polycations.<br>• Mucoadhesives swell on contact with moisture, increasing the mobility of polymer molecules at the interface and exposing more sites for bond formation.<br>• It favours change in entanglement and interaction after the polymer and mucins have interpenetrated. |

## Characterization Of Organogels

Evaluation and characterization is very important steps after the formation of organogels. Various characterization parameters are used for confirm the purity and stability of prepared organogels. Table 5 describe various characterization parameters and different techniques which are used for evaluation of these parameters.

**Table 5.** Characterization parameters and their evaluation techniques[22]

| S.No. | Characterization parameters | Techniques for Characterization parameters |
|---|---|---|
| 1 | **Physiochemical properties**<br>• The isotopic nature and optical clarity organ gel study.<br>• Establishing the hydrogen bonding as one of the major driving force for the self assembly of organogelator mole cules in organic solvent.<br>• The knowledge of molecular packing within the organogel network | • Spectroscopic techniques, namely NMR and FTIR spectroscopy.<br>• FTIR spectroscopy<br>• Scanning and transmission electron microscopies, dynamic and static light .scattering (elastic or quasielastic light scattering technique.) small angle neutron scattering {SANS}. |
| 2 | **Rheological behaviour**<br>• **Viscoelasticity**<br>• **Swelling**<br>• **Water content** | • 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.<br>• Gels can swell by absorbing liquid with an increase in volumes. Solvent penetrates the gel matrix, so that gel-gel interactions are replaced by gel solvent interaction.<br>• 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. |
| 3 | **Phase transition temperature**<br>• 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. | • Hot stage microscopy and high sensitivity differential scanning calorimetry have been reported to be useful as accurate and sensitive techniques. |
| 4 | **Gelation Kinetics**<br>• **Gel-sol and sol-Gel transitions**<br>• **Gelation kinetics** | • Inverse method<br>• Turbidimetry method |

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| **5** | **In vitro drug release** | • Franz diffusion cell |
| **6** | **Safety and skin compatibility studies** | • The irritation potential of loss has been assessed by carrying out human skin irritation study. |
| 7 | **Structural features**<br>• Molecular architecture of organogels<br>• Hydrogen bonding | <br>• NMR spectroscopy<br>• FTIR spectroscopy |

## Applications And Uses Of Organogels

Organogels are used for delivery of drugs and many pharmaceutical ingredients through various routes like oral, parenteral, topical, transdermal etc. Table 6 describe various applications and uses of organogels.

**Table 6.** Applications and uses of organogels[23-27]

| S.No. | Application and uses | Detail study of Applications and uses |
|---|---|---|
| 1 | **Topical drug delivery**<br>• **Cosmetic**<br>• **Ophthalmic**<br>• **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.<br>• Used in the cosmetic and personal care markets.<br>• Drug product like normal lachrymal turnover causes rapid clearance of solution and suspension dosage forms.<br>• 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. |
| 2 | **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.<br>• Effective delivery of antipsoriatic agents and for drugs used in eczema.<br>• Phospholipids organogel containing anti inflammatory macromolecule bromelain (15%) along with capsaicin (0.025%) has been found to be effective anti inflammatory composition. |
| 3 | **Transdermal drug delivery** | • Organogel systems have also been used as a matrix for transdermal transport of different therapeutic compounds.<br>• 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.<br>• 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. |
| 4 | **Parenteral delivery** | • L-alanine based injectable in situ forming organogels may be used for the delivery of labile macromolecular bioactive agents.<br>• Experimental results indicates that the organogels system, when injected subcutaneously in rats releases the bioactive agents (e.g. leuprolide) for a period of 14-25 days with subsequent degradation of the gelled structure. |
| 5 | **Oral delivery** | • Ibuprofen, a NSAID (non-steroidal anti-inflammatroy 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.<br>• In vivo studies in rats showed that the organogels may be used a controlled delivery vehicle for oral delivery of lipophilic compounds. |
| 6 | **Organogels in drug delivery** | • Organogels that have been studied for drug delivery include in situ forming organogels from L-alanine derivatives, Eudragit gels, lecithin gels, microemulsion-based gels (MBGs) and sorbitan monostearate gels. |
| 7 | **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. |
| 8 | **Cosmetic** | • Gels have been employed in a variety of products including shampoo, fragrance products, dentifrices and skin and hair care preparation. |
| 9 | **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. |
| 10 | **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. |
| 11 | **Microbiological media** | • Agar and gelatin gels are used as a solid media for the culture of microorganisms.<br>• 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

There has been an exponential rise in exploring the possibility of the use of organogels as a drug delivery vehicle. This has been greatly motivated due to the longer shelf life, ease of preparation and thermo-reversible nature of the organogels-based formulations. 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 few organogels that have been investigated for drug delivery have yielded interesting results, and it is hoped that some of these will make it to the market and improve drug therapy for the benefit of patients.

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