WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

REVIEW ON ORGANOGEL

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ABSTRACT

An Organogel is a class of gel composed of a liquid organic phase within a three-dimensional, crosslinked network. In the pharmaceutical field, organogels can be used for drug and vaccine delivery via different administration routes, although relatively few such formulations have investigated only a few organogels have been investigated for drug delivery despite the very large number of organogels under study. Organogels present very interesting advantages as drug delivery formulations, amongst which their ease of preparation and administration. This article will discuss the details of organogels formation and its applications in the drug delivery.

1. INTRODUCTION

Organogels are thermoreversible, viscoelastic materials formed from low-molecular-weight Organogelators. The Organogelators are a class of molecules that can undergo self-organization in particular organic solvents and/or water, often at surprisingly low concentration. The gel state has been defined in many different ways; Hermans defined the gel as a colloid disperse system that is solid-like in its mechanical properties and which consists of at least two components that extend themselves continuously throughout the whole system. Later, Flory added that a gel must have a continuous structure, for example, wellordered lamellar structures, disordered physically aggregated polymer networks, covalent polymeric networks, particulate structures. The gel is said to be a hydrogel or an Organogel depending on the nature of the liquid component. If the liquid phase is water, it is hydrogel and as an Organogel if the liquid phase is an organic solvent. In general, Organogels formation is based in the spontaneous self-assembly of individual gelator molecules into three-dimensional networks of randomly entangled fiber-like structures. This three-dimensional network holds micro domains of the liquid. In a non-flowing state mainly through surface tension. Some common examples of gelators include sterol, sorbitan monostearate, lecithin and cholesteryl anthraquinone derivates. 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. Various Organogel-based formulations have been designed for administration of the bioactive agents by different routes.

2. GEL

Gels are best fitted in all these essential criteria because of their excellent appearance, smoothness, desired consistency, fast drug release, ease of manufacturing and quality assessment and admirable stability. Recently gel formulation has been modified to yield an advance drug delivery system known as organogels. It was found that lipid-based formulation work most efficiently by improving penetration through the skin but drawback with such formulation is that they alter the hydration state to skin, cause dermatitis. On the other hand, water-based formulation able to maintain bioactive state of skin but exhibit poor penetration. Therefore, a new type of gel called organogel a promising vehicle is developed to deliver wide variety of agent through skin because of presence of both phase oil and aqueous phase and lecithin organogel deliver a bioactive agent in treatment of skin aging. 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 van der Walls interactions and hydrogen bonds, whereas chemical gels are held by covalent bonds. Depending upon the nature of the liquid component, Gels are basically classified into two types, as either organogels or hydrogels.

Types of gel:

A] Hydrogels:

Hydrogels are hydrophilic in nature and capable of absorbing large quantities of water or biological fluids, they are three-dimensional polymeric networks. Networks form by Insoluble homopolymers or copolymers, which are insoluble owing to the presence of cross-links. Chemical cross links seems to be entanglement or crystallites while the Physical cross-links include tie-points and junctions which contribute to the network formation and physical integrity. As the hydrogels having the thermodynamic compatibility when they exhibit with water, so they swell in the presence of an aqueous environment Their properties show a resemblance to natural living tissues in terms of their water content and soft texture, while the high-water content contributes to their biocompatibility. As a result, hydrogels are widely used as contact lenses, membranes for biosensors, linings for artificial hearts, materials for artificial skin, and as drug delivery devices.

B] Xero gel:

Xerogel are the solid gels with low solvent concentration. These are produced by evaporation of solvent or freeze drying, leaving the gel framework behind on contact with fresh fluid, they swell and can be reconstituted. Eg. Tragacanth ribbons, acacia tear β-cyclodextrin, dry cellulose and polystyrene.

C] Organ gel:

Organogels are thermodynamically stable, visco-elastic bi-phasic systems comprising of a gelator [any substance capable of forming gel and a nonpolar phase, with or without the presence of water molecules within the network formed by the gelator system. When compared with hydrogel they have a lower degree of hydration. Because of their non-irritating property and biocompatibility, they gained importance in the delivery of drugs over the past few years. Although organogel comprised of large number of liquid systems but it exhibits morphological and rheological properties similar to solids.

The thermodynamic and kinetic stability of these systems can be attributed to the opposing forces which are operating and are associated with the organogelator's partial solubility in the continuous phase. The Gelling matrix governs by the resulting interaction and physicochemical properties of gel components. Gels can be classified on the basis of the properties of gelators, solvents and the intermolecular interactions which converted into gels. Organogelators are mostly small molecules, while gelators in a hydrogel are polymeric in nature hence, the organogelators are well known by the name Low Molecular Weight [LMW] Organogelators. Depending upon the route of administration, organogel required the change in its formula to Administered the drugs. Solvent system in organogels are non-aqueous liquids, which is a useful topical delivery for lipophilic drug and aqueous liquids, which is useful for hydrophilic drug mentioned in various pharmacopoeias as well as for hydration of skin. Through percutaneous absorption Organogel achieved the local as well as systemic effect by the presence of a penetration enhancers: their lipophilic nature and occlusive effect are potentiated.

Structure of Organogels:

Gels are an intermediate state of the matter, containing both solid and liquid components. The solid component comprises a three-dimensional network of interconnected molecules which immobilizes the liquid continuous phase. Hydrogels have an aqueous continuous phase, and organogels have an organic solvent as the liquid continuous medium. Organogels exhibit interesting properties such as the ability to solubilize guest molecules, uses for purification and separation purposes and as transdermal delivery vehicles.

Drug Release from Organogel:

The exact mechanism of drug release varies with the organogel system used. However, in case of a majority of organogel system, drug release occurs by simple diffusion. This diffusion is controlled by the presence of three-dimension network of gelator molecules. The extent of cross-linking determines the rate of drug release. More the crosslinking [higher concentration of gelator] slower is the rate of drug release. However, in case of Eudragit-L based organogel [surface erosion] and in case of Eudragit-S based organogel [diffusion process]. In the case of transdermal and ophthalmic delivery of drug through organogels, attempts have been made to enhance the permeation of drug rather than controlling the release of drug which occurs by diffusion. when organogel are used as carrier for delivery of vaccines the percolation of interstitial fluid into three-dimensional network of the gel leads

3. FORMULATION OF ORGANOGEL

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. Entanglement of the aggregates and connections among them result in the formation of a three-dimensional network, which immobilizes and resilience to the gel. Connections among gelator are important for gel formation; in their absence, the gel state may be lost even if numerous gelator aggregates are present.

Method of Organogel Formulation:

1) Fluid-filled fiber mechanism:

2) Solid fiber mechanism:

3) Hydration Method:

4) Novel method:

4. METHOD OF FORMATION OF ORGANO GEL:

1) Fluid-filled fiber mechanism:

Non polar solvent mixed with surfactant mixture followed by formation of reverse micelles. By adding water tubular reverse micelles formed. Further addition of water 3D network formed.

2) Solid fiber mechanism:

To the organic solvent add solid organogelator. On heating at 60-70˚C hot solution of organogelator formed. After aqueous phase addition further heating proceeds which leads to formation of solid fibre entangle together to form 3D network.

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

4) Novel method:

I. Homogenisation

II. Micro irradiation

5. ORGANOGELATORS

The role of organogelators in designing organogels is evident from the above discussion. Theorganogelators may be categorized into two groups based on their capability to form hydrogen bonding. The examples of organogelators which do not form hydrogen bonds include anthracene, anthraquinone and steroid-based molecules, whereas the hydrogen-bond-forming organogelators include amino acids, amide and urea moieties and carbohydrates [10]. It would be wise to have a discussion on the different organogelators before we discuss about the different types of organogels and their applications in controlled delivery.

Types of organogels:

1. **Lecithin Organogels**: Lecithin is a phospholipid, extracted from various plants and animal tissues apart from the egg yolk. The use of lecithin for designing organogels was first described by Scartazzini and Luisi in 1988. Since then, a lot of research has been done on lecithin-based organogels. The lecithin procured from natural sources is able to form gelled structures and has been attributed to the presence of unsaturated chemistry within its structure. The synthetic lecithin and hydrogenated soy lecithin failed to develop organogels. Apart from the chemical structure, the purity of the extracted lecithin also plays an important role in the formation of organogels. Experimental results indicate that the lecithin fails to initiate the process of gellification of the apolar solvent if the lecithin contains <95% phosphatidyl content. The lecithin-based organogels have been found to be thermodynamically stable, thermoreversible (solto-gel transition temperature at 40◦C), transparent, viscoelastic, biocompatible and non-irritant. The organogels prepared using lecithin has been found to have an isotropic structure. 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. Typically, in lecithin organogels the molar ratio of water to lecithin may vary from 1 to. The formation of the organogel in the presence of lecithin may be attributed to the entanglement of fluid-fiber reverse micellar tubular structures. From the above discussion, it is clear that the lecithin-based organogels have three distinct components, viz., an apolar phase, a polar phase and a surfactant (lecithin).

2. **Pluronic Lecithin: Organogel (PLO):** PLO is a soy lecithin-based organogel which consists of isopropyl palmitate or isopropyl myristate, water and Pluronic F127 (also known as Poloxamer 407). PLO may or may not contain sorbic acid, which acts as a preservative, in both the phases. It occurs as a yellow-coloured, odourless and opaque gel which is quickly absorbed by the skin. Like lecithin organogels, PLO also consists of entangled tubular reverse-micelle structures which form temporal three-dimensional

3) **Premium Lecithin Organogels (PrLOs):** The PrLO is a second general lecithin organogel and has got higher thermostability apart from its nongreasy and non-tacky nature, which provides a cosmetically pleasing acceptability. This gel does not have a Pluronic derivative, which results in the avoidance of skin irritation and thereby local skinintolerance reactions. PrLOs are being marketed as ready-to-use intradermal bases and, hence, are also sometimes regarded PrLO premixed gels. The use of PrLO as a carrier for drug delivery has indicated that the gel helps in achieving improved bioavailability in the tissues by improving the penetration of the bioactive agents [39–41]. 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: 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. Limonene incorporated in dibutyllauroylglutamide (GP1) in propylene glycol (PG)-biocompatible organogels has been studied extensively. GP1 is an organogelators, which can be categorized as an amino-acid-type gelator. It has been proposed that the GP1 organogelators undergo extensive intermolecular hydrogen bonding amongst the amide groups present within their structure apart from the hydrophobic interactions amongst the long alkyl chains. Like any other amino-acid-type organogelator, GP1 also forms a solid-fiber based matrix. The GP1/PG organogels can be prepared by mixing the appropriate amounts of GP1, limonene and PG with subsequent incubation at 120◦C. When the mixture is cooled down, it forms a white gel. It was found that the presence of limonene within the GP1/PG organogels resulted in the alteration of the rheological properties of the organogels, although there was no significant change in the chemical stability of the organogels. Apart from limonene, various other terpene-based penetration enhancers (e.g., linalool, farnesol and cineole) have also been incorporated successfully in GP1/PG organogels. The presence of penetration enhancers within the organogels results in the improvemen of the rate permeation of the bioactive agents

6. CONCLUSION

Organogels are systems of which the existence is limited to the fine line between uncontrolled gelator aggregation and its complete solubility in the solvent. Given the strict requirements needed for formation as well as the relatively recent interest granted to these systems, many important questions still remain unanswered. For one, the precise thermodynamic and kinetic factors governing the stability of gelator fibres in the organic solvent need yet to be explored. Such knowledge could be applied to the systematic design of gelators yielding stable organogel systems. Furthermore, gel components could be chosen according to their compatibility with intended applications, such as nontoxic solvents for pharmaceutical formulations. Organogels present very interesting advantages as drug delivery formulations, amongst which their ease of preparation and administration. Some organogels are currently limited by the fast diffusion of LMW drug molecules out of the matrix and/or by water infiltration into the latter. Nevertheless, optimization of sustained drug release duration is generally thought possible by fine-tuning the organogelator structure and possibly the nature of the organic phase.

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