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Review Article

A Review on Hydrogels and Organogels

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ABSTRACT

Organogels and hydrogels are efficient semi-solid drug delivery devices with several uses in biological and pharmaceutical fields. The hydrophilic polymeric networks that make up hydrogels are able to absorb huge volumes of water without dissolving, which makes them extremely biocompatible and resembles genuine tissue in texture. Their sensitivity to environmental factors like light, temperature, and pH enables precise and regulated medication release. Hydrogels' high-water retention and flexibility make them ideal for application in gene therapy, wound healing, tissue engineering, and oral or rectal medication delivery. Organogels, on the other hand, are made with organic gelators and solvents such as fatty acids, lecithin, or sorbitan derivatives. In addition to being moisture-resistant and thermodynamically stable, these gels are perfect for administering hydrophilic and lipophilic medications via parenteral, transdermal, and cutaneous routes. In addition to being simple to make, organogels have outstanding penetrating qualities. Numerous approaches can be used to modify their rheological and structural characteristics, which makes them appropriate for use in topical treatments, implants, and cosmetics. Hydrogels and organogels together offer a viable platform for upcoming drug delivery innovations.

INTRODUCTION

The administration of drugs into the body is of many routes which includes Oral, sublingual, rectal, parenteral, cutaneous, and many more, these have effectively proved successful in treating illness. Topical drug delivery system when applied or administered to the specific locations on the outer surface of the body. Gels are the semi-solid

rigid systems in which movement of dispersing medium is restricted by a three-dimensional network of particles or solvated macromolecules of the dispersed phase. The word “gel” is derived from Latin. Gel is a liquid setting to a solid material that does not flow but has elasticity by some liquid characteristics. The United States Pharmacopoeia defines gel as a semi-solid system containing either suspensions made up of small

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inorganic particles or large organic molecules interpenetrated by a liquid. Gel contains a small network as separate particles. Gel is classified as a two-phase system. Both organic and inorganic molecules are employed to create a structural network of gel in two-phase system, the particle size of dispersed phase is relatively large and sometimes the gel mass is called as magma. In single-phase system, the gel consists of organic macro molecules uniformly which are circulated throughout liquid in a way where no apparent boundaries occur between the dispersed macro molecules and the liquid. Formulation considerations for pharmaceutical gels preparation are Choice of vehicle or Solvent, Inclusion of buffers, Preservatives, Antioxidants, Fragrance, Flavors or Sweetening agents (which are designed for the oral administration). [1,2]

Structure of gel

The network formed by the interlinking of the gelling substance particles is what provides the gel its firmness. The particle nature and force type are responsible for linkages, where the structure of network and properties are determined. The attraction forces are responsible for the linkage of gelling agent particles may range between strong valencies. In linear macromolecules the network is of twisted molecules and the contact point which may be relatively small and consists of several molecules of crystalline are aligned.[3]

Ideal properties of gel

- The gelling agent should be inert and safe.
- The gelling agent should not react with any other formulation contents.
- It must contain suitable or appropriate anti-microbial agent.
- The topical gel formulation must not be sticky.
- They should exhibit the mechanical properties of the solid state.

- It should have characteristics like Swelling, Syneresis, Ageing, Structure, Rheology.
- It should have optimum viscosity. [4,5]

ADVANTAGES

The gel mainly avoids first-pass metabolism which can deliver more drug selectively to a specific site of action. In comparison to other formulations, gels are easy to manufacture where gels are simple to apply on to the skin, allowing for even drug distribution and can increase a drug's bioavailability by enabling targeted delivery and controlled release. It can be a cost-effective and alternative to other dosage forms such as injectables or implants.

DISADVANTAGES

It can cause possible actions of allergic reactions as some drugs have poor permeability through skin and also by additives and gelators. Where as drugs with large particle size is not easily absorbed through skin and some may cause flocculation which results as the main factor for an unstable gel. Solvent loss may cause the formulation to dry in a gel. [6,7]

Uses

The gel formulation is widely used in cosmetic industries and food industries. It is also used as drug administration for many routes as Topical, Intranasal, Intermuscular, Parenteral in some of the cases. It is useful as delivery systems for orally administered drugs. In case of a topical gels, these are directly applied on to the Skin, Mucous membrane, or the Eye. In basis of the cosmetic industries, gels are used in Shampoo, Fragrance products, Dentifrices, Skin and Hair care formulations. [8]

Hydrogel



Hydrogels are usually referred as hydrophilic gels where the network of polymeric chains sometimes founded as colloidal gels in which dispersion phase is water. The water-swollen, cross-linked polymeric network produced by reaction of single or more monomers. It has the ability to swell and retain a significant amount of water within the structure, but it doesn't dissolve in water. These have a flexibility which is mostly similar to natural tissue. Hydrophilic functional groups linked to the polymeric backbone provide hydrogels with the capacity to absorb water, while cross-links among network chains enhance their resistance to disintegration. [9] Hydrogels can be produced using a variety of "classical" compounds. The synthesis of polymer molecules with reactive groups and their subsequent cross-linking, possibly also by reacting polymers with appropriate cross-linking agents, are examples of one-step processes such as polymerization and parallel cross-linking of multifunctional monomers, as well as multi-step processes.

Classification of hydrogel products:

The hydrogel products can be classified on different bases as detailed below: Classification based on source Hydrogels can be classified into two groups based on their natural or synthetic origins. Cross-linked skeletons can be found in homopolymers, depending on the polymerization process and type of monomer.

(a) Copolymeric hydrogels consist of two or more distinct monomer species connected in a random, block, or alternating pattern along the polymer network's chain, each containing at least one hydrophilic component.

(b) A polymer Two separate cross-linked synthetic and/or natural polymer components are arranged in a network to generate interpenetrating polymeric hydrogel (IPN), a significant class of

hydrogels. Cross-linked and non-cross-linked polymers make up the two components of semiIPN hydrogel. [10,11]

Configuration-based classification:

The following categories can be applied to hydrogels based on their chemical makeup and physical structure: Non-crystalline and amorphous.

Semicrystalline: A complex blend of crystalline and amorphous formations. Crystalline. Cross-linking type-based classification Depending on whether the cross-link junctions are chemical or physical, hydrogels can be categorized into two groups. Permanent junctions are found in chemically cross-linked networks, whereas transient junctions are found in physical networks. These junctions can be caused by ionic, hydrogen bonding, hydrophobic, or polymer chain entanglements. Arrangement according to physical characteristics. The preparation method used to polymerize the hydrogel determines whether it appears as a matrix, film, or microsphere. Groupings based on network electrical charge There are four groups of hydrogels based on their presence.

(a). Neutral (nonionic) .(b) Ionic, encompassing cationic or anionic materials. A combination of basic and acidic groups makes up an amphoteric electrolyte (ampholytic). In each structural repeating unit, zwitterionic (polybetaines) compounds have both cationic and anionic groups. Polysaccharides like starch, alginate, and agarose, as well as proteins like collagen and gelatine, are examples of natural polymers that can create hydrogel. Hydrogel-forming synthetic polymers are typically made by chemical polymerization techniques. When the external environmental conditions change, hydrogels can be engineered to respond in a controlled way by either expanding or



contracting. In reaction to a range of physical and chemical stimuli, such as temperature, light, pressure, sound, electric or magnetic fields, and solvent composition, pH, ionic strength, and molecular species, they may exhibit dramatic volume transitions. [12,13,14]

Uses

Since 1954, when Wichterle and Lim created the first synthetic hydrogels, hydrogel technologies have been used to create sanitary products. Medication delivery systems for agriculture artificial snow food additives, coal sealing, and dewatering medicines biomedical uses Regenerative medicines and tissue engineering diagnoses wound dressing, biomolecule or cell separation, barrier materials to control biological adhesions, and biosensor.

Hydrogel technical features

The following is a list of the functional characteristics of the ideal hydrogel material: maximal equilibrium swelling in saline, or the largest absorption capacity. desired rate of absorption (preferred porosity and particle size) based on the needs of the application. maximum absorbency under load (AUL). the minimal amount of residual monomer and soluble content. The least expensive. maximum stability and durability both during storage and in a swelling environment. the maximum biodegradability without the development of harmful organisms after degradation. pH-neutrality following water-induced edema. It is completely non-toxic, colorless, and odorless. stability of the photo. Rewetting capability: Depending on the application's needs (such as in sanitary or agricultural applications), the hydrogel must be able to either maintain or return the imbibed fluid.

Methods of preparation of hydro-gels

Fusion method

Cold method

Dispersion method

Semisolid dosage forms are made using one of two broad techniques, regardless of the size of the preparation scale. Two methods are used to make them: either the medicine is incorporated into the existing semi-solid basis (cold incorporation) or the liquid or liquefied components are blended at a high temperature and the solids are dispersed (fusion process). Cold incorporation is employed with heat-labile pharmaceuticals, such as plastibase, when the drug is to be added to a semi-solid base that has already been prepared or when the vehicle is heat-labile. A fusion process or a unique approach may be needed for gel preparation, depending on the gelling agent used. Because of the high heat vulnerability of this natural gum, the Tragacanth system needs to be produced at a moderate temperature. However, methyl cellulose dissolves more readily in hot water than in cold water. A special process is used to gel the Carbopol. In an acidic medium, the polymer is distributed. Gelation is caused when the dispersion is uniform and the system is neutralized with an amine, such as tri-ethanolamine, or an inorganic base (aqueous system). As a result, the polymer's acidic functional groups are ionized, attracting it into a colloidal solution where it creates the necessary structural matrix.

Advantages

The strength and elasticity of hydrogels are higher. Their considerable water content gives them a degree of flexibility that is strikingly akin to that of natural tissue. Hydrogel has excellent transparency qualities and is easily modified. In response to changes in temperature, pH, or



metabolite concentration, hydrogels can sense these changes and release their load.

Disadvantages

High cost, Low mechanical strength, Difficult to sterilize, non-adherent.

Properties

1. Swelling properties: Hydrogel may undergo rapid and reversible changes in response to a slight alteration in environmental circumstances. Changes in environmental factors like as temperature, pH, electric impulses, and the presence of enzymes or other ionic species can cause the hydrogel's physical texture to vary.

2. Mechanical characteristics: Depending on the material's intended use, the mechanical characteristics can be altered and adjusted. By raising the degree of cross linking or decreasing it through heating, a gel with greater stiffness can be produced. There are many various factors and causes that contribute to changes in mechanical characteristics, and different analyses must be conducted depending on the material.

3. Hydrogel polymers: Both synthetic and natural polymers are utilized to create hydrogels.

4. Biocompatible properties: The capacity of a material to function in a particular application with a suitable host response is known as biocompatibility.

Current Research on Hydrogels

Water purification: A water purification breakthrough may soon make it possible to produce safe, clean drinking water using only natural sunlight levels and low-cost gel technology. Engineers have created a small, affordable technology by combining gel polymer

hybrid materials. With their hydrophilic (attraction to water) and semiconducting (solar-adsorbing) characteristics, these "hydrogels"—networks of polymer chains renowned for their high-water absorbency—allow for the creation of safe, clean drinking water from any source, including contaminated supplies and the ocean.

Applications

Wound healing: Because hydrogels are cross-linked, they can retain both water and medication. Their capacity to retain water allows them to hold and cling onto wound exudates. Gels made of polyvinyl pyrrolidone or polyacrylamide with 70–95% water.

Hydrogels For the Colon: Due to the high concentration of polysaccharide enzymes in the colon area of GI, colon-specific hydrogels of polysaccharide have been specially created. Drug distribution targeted at the colon is the purpose of dextran hydrogel. Drug distribution in the GI tract: Hydrogels transport medications to particular GIT locations. When a medication loaded with colon-specific hydrogels is exposed to microflora, it exhibits tissue specificity and undergoes disintegration due to enzymatic action or temperature changes.

Rectal Delivery: Drug delivery through the rectal route is accomplished by hydrogels that have bio adhesive qualities.

Drug distribution via transdermal route: a variety of hydrogel-based drug delivery devices have been developed. To improve the penetration of goods, including as hormones and nicotine, hydrogel-based formulations are being investigated for transdermal iontophoresis.

Drug delivery in the oral cavity: Drugs are incorporated into hydrogels and delivered to the



oral cavity to treat oral disorders locally, including stomatitis, periodontal disease, fungal diseases, viral infections, and malignancies of the oral cavity.

Gene delivery: By altering the hydrogel's composition, nuclei acids can be efficiently targeted and delivered to particular cells for gene therapy. Hydrogels hold greater promise for treating a variety of inherited or acquired illnesses. In tissue engineering, macromolecules are delivered into the cytoplasm of antigen-presenting cells using hydrogels that have been micronized.

Tissue engineering: To introduce macromolecules into the cytoplasm of antigen-presenting cells, micronized hydrogels are utilized. Agarose, methylcellulose, and other naturally derived compounds are examples of natural hydrogel materials utilized in tissue engineering. The most popular application for hydrogels is in ocular medication delivery systems.^[15,16,17,18,19,20]

Organogel

Organogels are non-crystalline, thermoplastic, non-glassy solids with viscoelastic qualities. They are semi-solid preparations with limited external apolar phase mobility. Physical interactions between the structures of substances known as gelators limit the apolar phase's mobility. In Gelators include, for instance, sorbitan monostearate, lecithin, cholesterol anthraquinone derivatives, and steroids. Because of their unrestricted fibrous structure formation, which allows them to exist in low energy states, organogels are thermodynamically stable. Additionally, lecithin organogels have many amazing properties, like insensitivity to moisture, resistance to microbial contamination, undesired formation, viscoelastic activities, thermodynamic stability, and many more.^[21]

Properties

An organogel's physicochemical characteristics can be influenced by its structural characteristics. An effective characterisation technique for organogels is structural elucidation. Various spectroscopic and microscopy techniques are employed to determine the organogel's three-dimensional structure, shape, and particular interactions. Techniques for spectroscopy include magnetic resonance imaging, Fourier-transform infrared spectroscopy, and nuclear magnetic resonance, among others. Atomic force microscopy, transmission electron microscopy, scanning electron microscopy, polarized light microscopy, and other methods are examples of microscopy technique The simplest way to characterize organogel's structural characteristics is by microscopy investigation. There are a number of microscopy techniques that can be used to learn about molecular packing with the organogel network, including scanning electron microscopy, small-angle neutron scattering, and dynamic and static light scattering. Gel particle shape and microstructure organization are assessed using a transmission electron microscope. The technology of atomic force microscopy makes it possible to observe the processes of nucleation and elongation. Sites of nucleation were examined using atomic force microscopy. Techniques like nuclear magnetic resonance and Fourier-transform infrared spectroscopy make it possible for organogel to be isotopic and optically transparent. A useful method for analyzing hydrogen bonding—a weak link created by an H-molecule—as one of the main mechanisms promoting the self-assembly of organogelator molecules in organic solvents is Fourier-transform infrared spectroscopy. The nuclear magnetic resonance approach provides distinct information about different chemical interactions that take place in organogel. The purpose of the molecular



characterization investigations is to determine the physicochemical makeup of the organogel formulations. Both Fourier-transform infrared spectroscopy and X-ray diffraction are used in this investigation. A non-destructive technique is X-ray diffraction. The X-ray intensity is measured using this technique. Behavior of Rheology. Rheological characterization is highly useful in describing the physical characteristics of organogels, such as their mechanical strength, viscoelasticity, and viscosity. It is critical to distort the organogel after application to allow for simple spreading and improved medication penetration following dermal administration. The sample's strain gradually moves toward linearity after initially increasing non-linearity as the shear rate rises. [22,23,24]

Types of Organogel

Organizational Lecithin Gels (LOs): Topical use is the most common use for LOs because of their favorable physicochemical properties, which make them perfect for topical formulations. These are helpful for administering a broad range of hydrophilic and lipophilic medications via the skin. With the exception of egg yolk, lecithin is a naturally occurring component that can be separated from a variety of plant and animal sources, making it stable, safe, and biocompatible. Many bioactive substances could be transported via it. Lecithin is a phosphatidylcholine-based chemical component of the phospholipid class. If the phosphatidyl content of the lecithin is less than 95%, it has been found that it cannot gel.

PLOs (pluronic lecithin organogels): Getting large amounts of high-purity lecithin is expensive and challenging. Synthetic polymers like pluronics, which operate as stabilizers and co-surfactants, have been extensively researched in conjunction with lecithin to create lecithin micro-emulsion-based organogels because of their ease.

In 1990, a compounding pharmacy in the United States produced it for use as a topical carrier system. The main advantage of using PLs in organogels is that, at temperatures close to physiological values, they can self-assemble into micelles. The copolymer Pluronic F-127 gels when applied at concentrations of 15–30% w/v. Adding the Pluronic -F127 to the LOs creates it. Consequently, its precursor is lecithin.

Organogels of Limonene GP1/PG: A terpenoid with exceptional penetration capabilities, limonene is utilized in transdermal drug administration systems to increase the bioavailability of medications. This organogel is made by combining a proper quantity of limonene, PG (propylene glycol), and GP1 (dibutyl lauroylbutamide), an amino acid type of organogelator, and then incubating the mixture at 1200C. A white gel is formed once it has cooled to the proper temperature. Limonene's rheological behavior has been found to be somewhat influenced by its coexistence with GP1 and PG, although their chemical properties remain mostly unaffected. Because of the addition of limonene, the GP1/PG organogels typically exhibit higher gel moduli, indicating greater gel physical stability.

Gelatin-stabilized micro-emulsion-based organogels (MBG):(-) When administered topically or systemically, micro-emulsions provide good drug bioavailability. More medication is known to be delivered by micro-emulsions than by other gel systems. When gelatin is dissolved in the water microphase, the micro-emulsion system can gel, producing a gel that contains more than 80% hydrocarbon solvent. The fundamental process by which MBG is formed involves adding a gelatin-in-water solution to the parent micro-emulsion after it has been incubated in the incubation chamber at 500C. The resultant



liquid is vigorously combined and then allowed to cool to room temperature in order to create an optically transparent single phase gel.

Fatty acid-based Sorbitan organogels: The gelators of this class include Sorbitan monopalmitate (span 40) and Sorbitan monostearate (span 60). They have surfactant qualities, are hydrophobic by nature, and are non-ionic. When heated with the apolar solvent and subsequently cooled to a comparatively lower temperature, they form a solid-fiber matrix. A temperature drop creates a gel of toroidal reverse micelle, which then undergoes self-assembly to become rod-shaped tubules. The resultant gel is semisolid, white, opaque, and thermostable at room temperature. These organogels are employed to deliver hydrophilic vaccinations.

Organogel produced from L-alanine :

LAM (N-lauroyl-L-alanine methylester) gels when it comes into contact with organic solvents like soy oil and triglycerides. In comparison to other organogels, its use is not as widespread. The gel condition is maintained at room temperature. When two phases of water and an organic solvent are combined, fatty acid derivatives of L-alanine can gel the solvent-specific fraction of the mixture without gelling the aqueous portion. Because of this feature, using it in organogel is much more desirable. For a sustained release system, it can be implanted. It is currently utilized as a delivery system for medications such as leuprolide and rivastigmine. [25,26,27,28]

ADVANTAGES

Organogels are more stable than other forms of gels. Preparation is simple. Avoid the first-pass metabolism. Thermodynamically stable. Organogels are moisture insensitive. Inexpensive

due to less number of ingredients. Improved the penetration of the drug through the skin.

DISADVANTAGES

Requires an appropriate storage environment. Drugs that irritate or sensitize the skin are not suited for this method. There will be no gelling if there is an impurity present. The most expensive ingredient is lecithin, which is not widely accessible.

Organogels prepared by various methods

Fluid Filled Fiber Mechanism: Reverse micelle production occurs after a non-polar solvent and surfactant combination are combined. When water was added, reverse micelles developed. An additional water 3D network was created. **Mechanism of Solid Fiber:** Add a solid organogelator to the organic solvent. After heating to -, an organogelator hot solution was created. Further heating follows the addition of the aqueous phase, causing solid fibers to entangle together to form a three-dimensional network. [29,30]

Applications

a) Topical medication delivery systems:

these comprise the transdermal and dermal systems. As the biggest tissue in the body, the skin offers good drug bioavailability because medications intended to enter the systemic circulation through skin penetration avoid first-pass metabolism. As an apolar organic solvent, isopropyl myristate/isopropyl palmitate is present in polaxomer lecithin organogels (PLOs) and serves as a vector for the release of NSAIDs (ketoprofen, flurbiprofen, and diclofenac sodium), which are employed as analgesics. In order to administer propranolol, reverse micellar MBGs use soy lecithin, iso-octane, and water as a solvent phase.



b) Transmucosal and oral drug delivery methods:

By implanting bio-adhesive organogels, the medications can be administered as implants through the mouth cavity. The medicine can be combined with the mucoadhesive polymer after being dissolved in the organic solvent. Ibuprofen was administered using an organogel made of 12-HAS-soybean oil. The organogels can be employed as a vector for the controlled release of lipophilic medicines, according to an in-vivo investigation done on rats. Cyclosporine A is administered orally as an organogel based on sorbitan monoleate. To obtain the intended therapeutic effects, an NSAID (ibuprofen) can be added to an oral organogel.

c) Parenteral medication delivery system:

Because parenteral methods bypass first-pass metabolism and offer a faster start of action, they are the preferred method for administering medications. Leuprolide, which is used to treat prostate cancer, was delivered sustainably via an in-situ forming organogel made from L-alanine derivatives in safflower oil and administered by SC route. Over the course of 14 to 25 days, it was found that the gel gradually broke down to release the medication. Propranolol, cyclosporine A, BSA, and HA are released by the SC and intramuscular route of sorbitan monostearate (SMS) organogel formulation (7). According to a study, rats were given subcutaneous injections of safflower oil-based N-methyl pyrrolidone (NMP), which the surrounding tissues tolerated well over the course of eight weeks.[31,32,33]

CONCLUSION

Since hydrogels and organogels are flexible, biocompatible, and have controlled release, they have a lot of promise for enhancing drug delivery.

Organogels are prized for their stability and skin penetration, whereas hydrogels are favored for their water content and tissue-like qualities. Future treatments using these gel systems may be safer, more effective, and more patient-friendly with continued research and development.

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