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ORGANOGEL: AN IDEAL DRUG DELIVERY CARRIER

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ABSTRACT

Organogels are semi-solid systems in which a three-dimensional network of self-assembled, interlaced gelator fibers immobilizes an organic liquid phase. Despite having a mostly liquid composition, these systems exhibit a solid-like appearance and rheological behavior. They are employed as drug and vaccine delivery systems in pharmacology, with active components delivered *via* transdermal, oral, and parenteral routes. Unfortunately, the toxicity of the selected organic solvents has impeded their usage as medication delivery methods in the past. More biocompatible organogels have recently been synthesized, which has aided the development of numerous biological and pharmacological applications. This article seeks to provide a comprehensive overview of organogels, with a focus on the types, characterization, preparation, and the use of organogels as drug delivery platforms for active agent administration *via* various routes such as transdermal, oral, and parenteral is then discussed.

KEYWORDS: Organogels, Rheological, Biocompatible, Drug delivery.

INTRODUCTION

A three-dimensional network structure that has the capability of restricting the movement of a liquid phase. Gel system has various applications in various biomedical and personal care items such as toothpaste, drug delivery systems, shampoos, etc.[1] Gels are made up of two components that are the gelling agent (also known as gelator) and liquid solvent phase (either apolar or polar). It is responsible for the formation of a three-dimensional network

structure.[2] Different types of gels are there such as xerogel, hydrogel, bigel, and organogel, etc. Organogels are non-glassy, thermoplastic, non-crystalline solid having viscoelastic properties. They are semi-solid preparations having restricted movement of the external apolar phase. The apolar phase has restricted movement due to physical interactions between structures of compounds known as gelators.[3] Some of the examples of gelators are lecithin, sterol, cholesteryl anthraquinone derivatives, sorbitan monostearate, etc. Organogels are thermodynamically stable due to their unconstrained genesis of the fibrous structure by dint of which organogels can live in low energy state. Also, some of the astounding features of lecithin organogels are resistant to microbial contamination, insensitivity to moisture, unbidden formation, viscoelastic actions, thermodynamic stability, and many more. There are various advantages of organogels. Those are its easy preparation, it avoids first-pass metabolism, enhancement of drug penetration through the skin, cost-effective, insensitive to moisture, reduces frequent drug dosing. Likewise, drawbacks are also there, such as it requires proper storage conditions, impurities lead to no gelling, may irritate the skin, etc. Organogels are classified as low molecular weight gelators and polymeric gelators based on the nature of the gelator. Low molecular weight gelators are further physically classified as solid-fiber matrix and fluid-fiber matrix based on the nature of intermolecular interactions. Polymeric gelators are physically classified as entangled-chain matrix and chemically classified as a cross-linked matrix. Various methods of formation of organogels are fluid-filled fiber mechanism, hydration method, solid fiber mechanism. Novel methods include homogenization, microirradiation. Characterization of organogels includes its physicochemical properties *i.e.* optical clarity, isotopic nature optimized by Fourier-transform infrared spectroscopy, nuclear magnetic resonance spectroscopy. Gelation kinetics is set on by turbidimetry method, the inverse method.[3] Swelling of organogel is possible since gel-gel interplay is replaced by gel-solvent interplay. Safety and skin compatibility study determines very low skin irritation of organogels for which it can be topically applied for long-term applications.[4] Topical drug delivery of organogels is seen in cosmetics such as shampoo, dentifrices, etc and ophthalmic use is in ocular drug delivery due to rapid clearance of solution. Other organogels drug delivery includes oral drug delivery, rectal drug delivery, parenteral depot formulation, vaccines, gelatin gels, bioadhesives, suppositories, microbiological media, etc. The present review deals with the advantage and disadvantages, classification, types, preparation, characterization, and role of organogels in drug delivery systems.

Advantage of Organogel

i. Organogels are more stable than other forms of gels.
ii. Preparation is simple.
iii. Avoid the first-pass metabolism.
iv. Thermodynamically stable.
v. Organogels are moisture insensitive.
vi. Inexpensive due to less number of ingredients.
vii. Improved the penetration of the drug through the skin.[5,6]

Disadvantage of Organogel

i. Requires an appropriate storage environment.
ii. Drugs that irritate or sensitize the skin are not suited for this method.
iii. There will be no gelling if there is an impurity present.
iv. The most expensive ingredient is lecithin, which is not widely accessible.[5,6]

Classification of Organogel

Organogels are generally categorized based on the type of organogelator. In this study, we suggest a unique organogel categorization based on solvent applied, organogelator features, and production methods utilized, depending on the kind of intermolecular interactions (chemical, physical).[7]

Physical crosslinking

Numerous organogels are formed *via* non-covalent interactions between physical crosslinking molecules or organogelator molecules, resulting in the formation of crosslinking junction sites. Conformational alterations in the organogelator design or the inclusion of crosslinking agents induce the molecules to adhere at the atomic level.[8] These interconnections are created by rather strong physical non-covalent attractions like as □-□ stacking, solvophobic forces, weak van der Waals contacts, or even hydrogen bonding.[9] Low molecular weights organogelators are the most common type of organogelator utilized to create physical organogels. The ability of low molecular weights organogelators to self-assemble *via* non-covalent contacts allows gelation reversibility and imparts extraordinary thixotropic properties to such gels.[10]

Chemical crosslinking

Chemical organogels are generated in an organic solvent by chemical crosslinked organogelators in a swelled condition. Through covalent bonding, the 3-D network is irreversibly solidified. Temperature adjustments or simple dilution will not transform the resultant organogels into the liquid phase. Additionally, due to helical polymer analogs, they produce more strong and impervious matrices.[11] Crosslinkers like Cu(I)-catalyzed azide-alkyne compounds, which cause cycloadditions, are used to create supramolecular chemical crosslinking connections.[12] Furthermore, orthogonal couplings are induced by chemical group activations such as covalent bonding and dative, which cause gel formation.[13] Covalent crosslink junctions are divided into two groups by Fox *et al.*, i) dynamic covalent crosslink connections and ii) supramolecular connections by combining physical non-covalent and covalent crosslinks, resulting in a material with great flexibility and creep resistance.[14] Higaki *et al.*, presented a new alkoxyamine polymer-based covalent crosslinked thermodynamic system. The radical exchange reactions were followed by this kinetically based system.[15] Yang *et al.*, have designed a chemical organogel depending on crosslinker tetraethylammonium tetrafluoroborate-acetonitrile and poly (vinylidene fluoride-co-hexafluoropropylene) electrolytes that function as a potential supercapacitor device with high ionic electro-conductivity.[16]

Bigels

Bigels were initially described by Almeida *et al.*, as a combination of different polyacrylic acid hydrogels scattered in organogels forming a bi-continuous matrix.[17] Bigels can be characterized as an emollient and semi-solid formulation that generates heterogeneous colloidal systems that are categorized into three types *viz*: i) bi-continuous matrix, ii) organogel dispersed into hydrogel system (O/W), and iii) hydrogel dispersed into organogel system (W/O).[18] In reality, they were employed to regulate the distribution of both hydrophilic and lipophilic drugs; due to the synergetic effects of both gels, those systems followed Higuchi release kinetics.[19] Lupi *et al.*, produced bigel cosmetic formulations and found matrix-in-matrix bigels, which were generated by phase inversion and consisted of disorganized oil droplets scattered in a bicontinuous matrix gelled network.[20]

TYPES OF ORGANOGEL

Lecithin organogels

Organogels made of lecithin have appeared as one of the most intriguing drug carriers. A surfactant *viz* lecithin serves as a gelator molecule, a polar substance, generally water, and a nonpolar organic solvent serves as a continuous phase, makes up the organogel matrix. When a non-aqueous solution of lecithin is mixed with a minute quantity of water or some other polar solvent like ethylene glycol, formamide, or glycerol a lecithin organogel is developed. Lecithin organogels are utilized as carriers for hydrophobic and hydrophilic bioactive substances and play a significant function in the cellular metabolism and lipid matrix of cell membranes. Hydrophobic molecules dissolve in the oil phase, whereas hydrophilic drugs dissolve in water, which is subsequently mixed into an organic lecithin solution to promote gelation.[21]

Sorbitan monosterate organogels

At low concentrations, a mixture of sorbitan monopalmitate (Span 40) and sorbitan monostearate (Span 60) has been discovered to gel a variety of organic solvents. Span 60 gels were proven to be more stable than Span 40 gels and then were thoroughly researched. Organogels made of sorbitan monostearate are transparent, thermoreversible semi-solids with surfactant vesicles scattered in the organic continuous liquid phase.[21]

Organogels based on other low molecular weight gelators

The transdermal release of piroxicam from organogels made of glyceryl fatty acid ester gelators in medicinal oils has been researched by scientists. Glyceryl fatty acid ester organogels had better *in-vivo* skin penetration than standard topical formulations such as liquid paraffin, as measured by anti-inflammatory suppression of edema after therapy.[5]

Polyethylene organogels

In research involving 300 participants that began in the 1950s, polyethylene organogel patches have been demonstrated to be nonirritating and have minimal sensitizing characteristics. In a separate study, 326 participants were given spectrocin loaded polyethylene and compared to those who received spectrocin in a petroleum base alone. Two very different antibiotic ointments eradicated pyoderma and secondary infected eruptions in 3-5 days, although the polyethylene was shown to be more effective. Polyethylene was also employed in the preparation of 5-iodo-2'-deoxyuridine for the treatment of oral herpes.[22]

Supramolecular organogels

Gelators have recently been identified in molecules with a wide range of structural complexity, ranging from basic alkanes to complicated phthalocyanines. Consequently, there has been a revival of excitement in researching gels obtained from low molecular mass gelators *i.e* supramolecular gels. The goal is indeed to understand the underlying aggregate structures of gels at different length scales but to also investigate their potential for prospective technology applications. Supramolecular gels have the potential to be useful in controlled release drug delivery, gelling cryogenic fuels, and oil recovery.[22]

Eudragit organogels

Eudragit organogels are blends of Eudragit (L or S) and polyhydric alcohols such as liquid polyethylene glycol, glycerol, and propylene glycol that include high levels of Eudragit (30 or 40% w/w). Drug-loaded gels were obtained by adding the drug (ketoprofen, salicylic acid, or sodium salicylate) in propylene glycol, dumping the resultant solution into Eudragit powder (held in a mortar), and mixing with the help of a pestle for 1 minute. A spread meter and a penetrometer are used to describe spreading and gel consistency. Gel viscosities were shown to rise with increasing Eudragit concentrations and reduced with increasing drug content.[23]

Pluronic lecithin organogels

Pluronic lecithin organogels are translucent yellow gels made up of water, soy lecithin, isopropyl palmitate, and a hydrophilic polymer *i.e* Pluronic F127. The inclusion of Pluronic F127 (a hydrophilic polymer) and the larger volume of water in comparison to the oil distinguish pluronic lecithin organogels from its precursor, lecithin gels. To consolidate the formulation of gel, a hydrophilic polymer, pluronic F127 was added to the original lecithin organogel.[23]

Premium lecithin organogels

A second universal lecithin organogel is premium lecithin organogels. The use of such premium lecithin organogels as a drug delivery carrier has revealed that the gels have better thermostability, in addition to their non-tacky and non-greasy properties, aid in obtaining increased bioavailability in tissues by enhancing stability. There are no pluronic derivatives in this gel.[23]

PREPARATION OF ORGANOGEL

Organogel formulation is often accomplished by dissolving an organogelator in a hot, apolar phase, followed by a chilling process that results in gelation. Organogels are made using the following processes, which are based on their inherent nature.[24]

Chemical organogels

Crosslinked copolymeric organogels are made *via* chemical techniques including copolymerization reactions. Along with monomers, crosslinkers like N, N-methylene bisacrylamide, or polyethylene glycol diacrylate can be utilized. Under stirring at a moderate temperature (60-70°C), they form covalent connections between organogelator molecules, trapping the solvent phase.[25,26] These settings allow polymerization events to begin, resulting in the creation of gels at critical gelator concentrations (CGC). Bera *et al.*, for example, found that increasing the crosslinker content to more than 2% w/v reduced the inflammation of N-tertiary butyl acrylamide- and acrylic acid-based copolymer organogels are shown in Figure 1.[25]

Physical organogels

The heat-cool approach is most commonly used to make physical organogels.[27] Gelator molecules are dissolved in the organic solvent in this example. The liquid phase is then mechanically stirred with the help of rotor-stator homogenizers and heated to 60-80°C, even 100°C for 1,3:2,4-di-Obenzylidene-D-sorbitol organogels until a clear solution is formed.[28] The heated solution is subsequently cooled to ambient temperature, sometimes using sonication, to achieve homogenous dispersions in a couple of minutes. The physical organogels are mostly fluid-filled matrix or solid fiber matrix type and their method of preparation is shown in Figure 1.

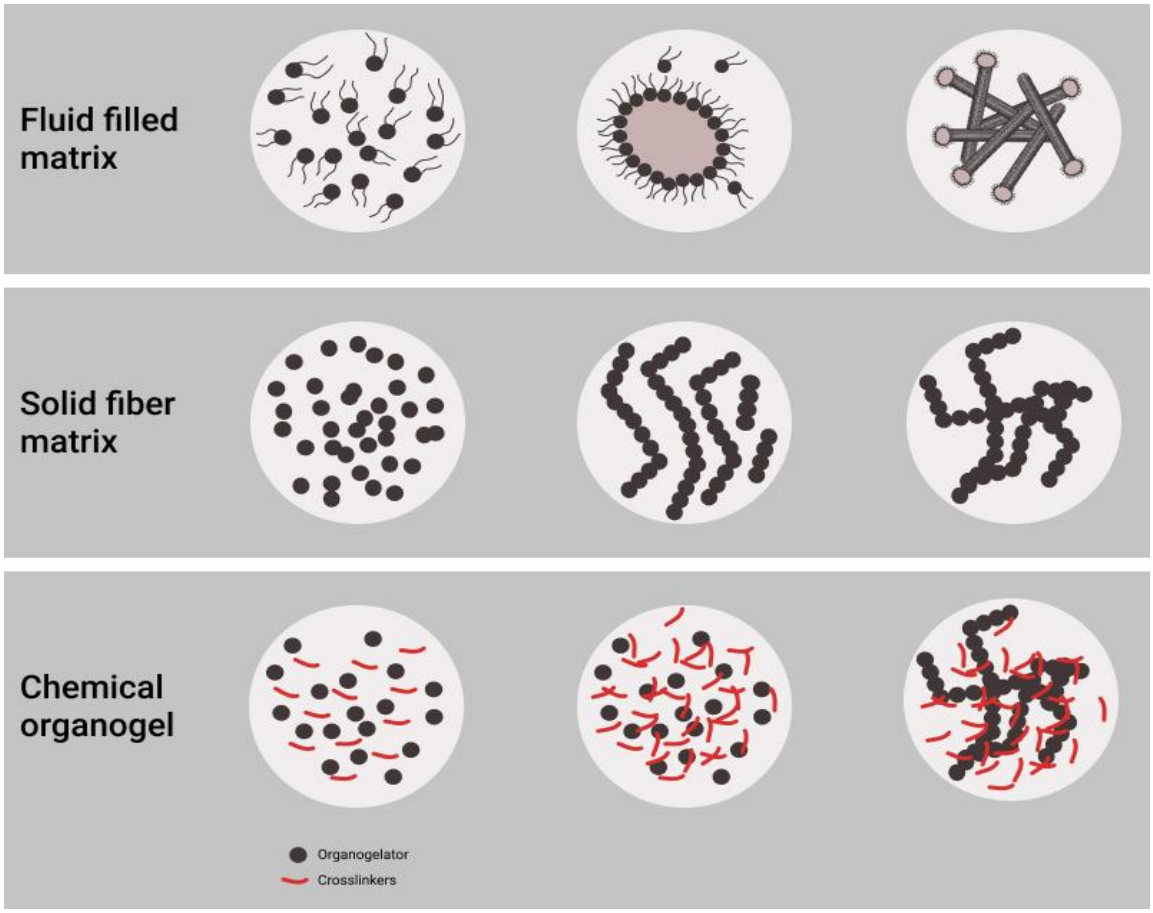

Fig. 1: Preparation methods influencing organogel structures.

Characterization of Organogel

To confirm the stability and effectiveness of organogel, characterization of organogel through various methodologies and techniques is very important.[24] Various properties such as gelator-co-gelator interactions, the gelator-polar/apolar solvent interactions, drug interactions with gel components, and the gelator assemblies may be investigated during the characterization of organogels.[29]

Physicochemical properties

Structural features can influence the physicochemical properties of the organogel. Structural elucidation is an efficient characterization methodology for organogels. Different types of spectroscopy and microscopy technique are used for the determination of the 3-D structure of the organogel, morphology, and specific interactions. Spectroscopy techniques include nuclear magnetic resonance, Fourier-transform infrared spectroscopy, and magnetic resonance imaging, etc. Microscopy techniques include transmission electron microscopy, scanning electron microscopy, atomic force microscopy, polarized light microscopy, etc.[23,24] Microscopy analysis is the simplest characterization method to analyze the structural features

of organogel. If we want to gain knowledge of molecular packing with the organogel network, then we can use various microscopy techniques such as dynamic and static light scattering, small-angle neutron scatters, scanning electron microscopy.[21] A transmission electron microscope is used to determine the microstructure organization and morphology of gel particles. Atomic force microscopy is a technique enabling to follow of elongation and nucleation processes. Atomic force microscopy investigated nucleation sites. Nuclear magnetic resonance and Fourier-transform infrared spectroscopy techniques feasible the optical clarity and isotopic nature of organogel. Fourier-transform infrared spectroscopy is a successful technique in examining the hydrogen bonding (weak bond formed by H-molecule) as one of the major driving forces in organic solvents for self-assembly of organogelator molecule.[21] The different information regarding various chemical interactions that occur in organogel is provided by the nuclear magnetic resonance technique.[29] The molecular characterization studies are done to know the physicochemical nature of the organogel formulations. This study is done by using X-ray diffraction and Fourier-transform infrared spectroscopy studies. X-ray diffraction is a non-destructive method. This method measures the X-ray intensity.[24]

The inverted vessel method: verifying the gel formation

The phases and structures formed when three or more components are mixed with the function of temperature are called ternary phase diagrams. Organogel is mainly composed of an organic solvent and a gelator. However, in some cases, organogels are capable to accommodate an additional polar phase into their structure. The minimum amount of gelator concentration required to induce gelation at room temperature is called critical gelation concentration. The gelator will fail to induce gelation and will remain present in the liquid phase if the concentration of the organogelator is less than critical gelation concentration. Similarly, if the aqueous phase concentration is beyond the upper critical limit, then gelation may not take place and results in the formation of a biphasic system. A bi-phasic system is a system where the networked form of the organogel does not have any extra water. So, this process involves stopping the formation of a gelled structure with the addition of the high amount of water and this process is known as gel solvation. The formation of gel can be determined by inversion (upside down) of the vessel/tube containing the formulation. After the inversion of the vessel/tube, if the test tube contents start flowing then it is considered as weak organogel. The flowing power of the test tube contents indicating that this formation

has failed to produce organogelation. If the test tube contents do not flow, then the formulation is considered as true organogel.[24,29]

Rheological Behaviour

To describe the physical properties of organogels *e.g.* viscoelasticity, viscosity, and mechanical strength, rheological characterization is very helpful. It is very important to deform the organogel after application sufficient shear for easy spreading and permeation enhancement of drugs after dermal application. When the shear rate increases, the strain within the sample initially increases non-linearity and progressively approaches linearity. For complete deformation of the gel, the shear rate required can be determined easily which signifies the strength and storage requirement of the gel. The study of dynamic and rheological parameters *e.g.* loss or viscous modulus (G"), shear viscosity *(η),* elastic or storage modulus (G'), and relaxation time (τ.) allow us to explain the rheological properties of organogel. The moduli are connected with the disappearing of the viscous energy and depot of elastic energy respectively. So rheological and linear viscoelastic parameters η^* and G^* can be calculated by using these parameters.[29] A gel is defined in the rheological term that it is a preparation in which the loss modulus and the storage modulus are independent of frequency and phase angle is low at all frequencies. It can be calculated by using the formula-

$$tan\delta = G" \div G'$$

Where,

tanδ is independent of frequency.

Thermal characterization

Physical organogels are heat resistant and they may remain good for more than 2 years. By using the falling ball method, differential scanning calorimetry, differential thermal analysis, and rheology, the temperature of gel to sol transition (also termed as gelation) can be studied in organogel. The falling/dropping ball method is a convenient and simple technique. The sensitivity of the falling ball method depends on the weight and size of the ball and the diameter of the tube. Different tests such as freeze/thaw cycling tests, syneresis measurements, and thermocycling tests are utilized at high or low temperatures to determine the resistance profile of the organogel samples. Syneresis is a method that is done by expulsion or extraction of the solvent molecule from the gel. This results in gel contraction. Differential scanning calorimetry is a thermoanalytical method that measures the strength of interactions. Differential scanning calorimetry also estimates the energy absorbed or released

by the gelled system. When organogels are heated by increasing temperature, the breakdown of a network of the solid-like structure of the organogel occurs. The structures are breakdown by the dissolution of the solid material and this results in an exothermic reaction. On the other hand, by decreasing the temperature or at the cooling stage, molecular packing of organogelator molecules in the network occurs.[24,29]

Biocompatibility study

Most organogels are composed of a high level of surfactant and toxic organic solvents such as n-octane, cyclohexane, kerosene, etc. They make the organogel unsuitable for human application. So, it is very important to observe the safety and irritancy of the prepared formulation for long time use. For establishing biocompatibility, hemocompatibility is commonly considered. This is done by incubating the test sample with the blood along with positive control *i.e.* 0.1 N HCl which lyses the blood cells and negative control i.e., normal saline. After incubation time, the % of hemolysis of the test sample is calculated by using the formula given below:

$$\%Hemolysis = (ODtest - ODnegative) \div (ODpositive - ODnegative) \times 100$$

If the % of hemolysis is less than or equal to 5, then the test sample is highly biocompatible if it is greater than 5 but less than or equal to 10 hemocompatible, and the test sample is not hemocompatible if it is greater than 10.[21,29]

Potential Role of Organogel In Drug Delivery System

Organogels may entrap a wide range of medicinal chemicals because of their extremely entangled fibrous nano/microstructures, making them ideal as drug delivery vehicles. Organogels must be biocompatible to be evaluated for medicinal purposes. Organogels have lately regained popularity as a result of several studies on their *in-vitro* and *in-vivo* uses at various stages of development.[7]

1. Dermal and transdermal applications

Drugs can be administered by cutaneous or dermal delivery channels into the membrane layers, as well as by percutaneous or transdermal delivery channels beyond the skin. These administration methods provide systemic effects while avoiding the first-pass metabolism. The bioavailability of a molecule provided through the skin is determined by its liposolubility, which varies depending on the delivery medium. Because of its lipophilic makeup and thickness, the stratum corneum functions as the primary barrier. Lipophilic, non-

irritating, and simple to use, they promote fast absorption. As a result, these gels have been broadly studied and produced for the topical delivery of pharmaceutical molecules in the controlling of a variety of disorders, including neuropathy, hormone-dependent cancer, and diabetes.[30,31] The list of recently developed transdermal organogel is shown in Table 1.

Lecithin: The most studied organogels for topical administration of active compounds are lecithin organogels, according to a recent study on the subject, which offered a fairly comprehensive list of explored formulations shown.[32] Because of their amphiphilic nature, lecithin organogels have several advantages for transdermal administration. First, as has been demonstrated for various model medications, lecithin and oil may readily partition with the skin and give improved penetration.[33,34] Transdermal delivery offers net advantages over oral administration in cases when a therapeutic impact is required in a localized zone near to the skin surface, primarily in terms of reduced systemic side-effects. Lecithin organogels potential benefit has been established in several labs and clinical investigations. Nastruzzi *et al.*, detected a flattening in the subcutaneous tumor. Nastruzzi *et al*., observed a decrease in subcutaneous tumor development in mice given lecithin organogels comprising an anti-tumor drug (tetra-benzamidine) transdermally.[35] The tumor continued to develop when the lecithin organogels were used away from the damaged area, indicating that the system had less systemic than local effects. Similarly, the inclusion of non-steroidal anti-inflammatory medications into lecithin organogels has piqued interest due to the possibility of administering analgesics close to the site of action, which might be beneficial in the case of rheumatism. Transdermal transport of non-steroidal anti-inflammatory medications (aceclofenac and piroxicam) from lecithin organogels was proven in conventional permeation investigations with these goals in mind. When lecithin organogels were applied to the skin for extended periods, histological tests revealed no harmful effects.[35] Acute irritation caused by the application of lecithin organogels was occasional and discrete in a study of over 150 volunteers.

Fatty acid-derived sorbitan organogels: Topical formulations made entirely of non-ionic surfactants (produced by dissolving 20% sorbitan monopalmitate organogels in liquid surfactants, such as polysorbate 20 or 80) were assessed for safety.[36] Surfactants are recognized permeation enhancers, hence the negative consequences of changes in skin structure were examined on the shaved mouse and human skin. There was no substantial surge in blood flow or epidermal irritation in either circumstance. However, there was some

epidermal thickening, indicating a strong interaction between the surfactants and stratum corneum components. Overall, volunteers found the gels to be harmless and well-tolerated after using them for five days in a row. However, no skin permeation or effectiveness trials including these organogels have been reported to our knowledge.

Organogels based on other low molecular weight gelators: Pénzes *et al.*, examined the transdermal distribution of piroxicam from glyceryl fatty acid ester gelators in medicinal oils using organogels.[37,38] Glyceryl fatty acid ester organogels had better *in-vivo* skin penetration than standard topical formulations such as liquid paraffin, as measured by anti-inflammatory suppression of edema following therapy.[38]

2. Parenteral Delivery

At the injection site, sorbitan monostearate organogels have a relatively limited half-life. This is due to the distribution of water molecules inside the gelled structure, which causes the networked structure to be disrupted as a result of the emulsification of the gel exterior.[39,40] A similar group has also conveyed the creation of a sorbitan-monostearate-based organogel that has demonstrated continuous delivery of a model antigen and radiolabelled bovine serum albumin in mice following intramuscular treatment. The results suggested that the formulation might be used as a depot.[41,42] Injectable in situ forming organogels based on L-alanine might be utilized to deliver labile macromolecular bioactive substances. These in situ forming organogels might be employed to distribute bioactive chemicals for a long time after they've been given to the body. In the presence of a hydrophilic solvent, several L-alanine derivates, such as N-stearoyl L-alanine methyl esters, can be utilized to immobilize vegetable and synthetic oil. The essence of these gels is that they are thermoreversible. The gel-to-sol transition of L-alanine-based organogels was influenced by the gelator concentration and the solvent type.[43,44] The organogel system, when injected subcutaneously in rats, releases bioactive chemicals (*e.g*. leuprolide) for 14-25 days until the gelled structure degrades.[43] The biocompatibility of the L-alanine organogels was determined by histological analysis of the injection site.[44]

3. Oral delivery

In the year 2005, the use of organogels for the oral administration of bioactive compounds was described. The authors of the study found that when cyclosporine A (a strong immunosuppressant) was given orally to beagle dogs as sorbitan monooleate, the activity of the drug-enhanced a cellulose-based organogel formulation. The creation of organogels with

soyabean oil as an apolar phase using 12-hydroxystearic acid as an organogelator. The gelled structure contained ibuprofen, a nonsteroidal anti-inflammatory medication. The release investigations revealed that when the concentration of the organogelator within the organogel increased, the rate of release of the organogels decreased. Organogels are a regulated delivery vehicle for lipophilic chemicals in rats in vivo investigations.[45,46]

4. Ophthalmic drug delivery

Lecithin-based organogels provide a possible carrier system for ocular medication delivery. Lipophilic, hydrophilic, and amphoteric bioactive substances can all be included in these gels. Because the formulations are transparent, their long-term presence in the ocular cavity does not affect vision. The medicine releases at a constant pace due to the gel's three-dimensional network structure.[47]

5. Rectal drug delivery

Organogel with Eudragit R and S has been developed for rectal medication delivery. Salicylates, procaine, and ketoprofen are the medications utilized. Furthermore, *in-vitro* testing of the drug (using the rotating disc method-JP XI) revealed that the drug followed apparent first-order kinetics following an initial burst of drug release. The fast release of drugs present on the gel surface at the time of insertion into the dissolving media is thought to be the cause of the burst effect. Rabbits were used to test these systems in vivo, and the plasma drug levels were shown to be stable. Bioavailability was shown to improve 1.55-1.75 times when 10 percent linoleic acid or oleic acid was added as an absorption enhancer.[21]

6. The delivery system for vaccines

The organogel based on microemulsions can be utilized to administer hydrophilic vaccinations. According to Florence *et al.*, these systems have several benefits, including gradual antigen release from the organogels system, which produces a depot effect, and organogels that have been engineered to include niosomes. The vaccine was discovered to be trapped in niosomes that were detected within the surfactant network in the organic medium. After *i.m* administration of these gels, a depot effect was seen.[21]

Table 1: Examples of topical and systemic cutaneous organogels preparations that have been investigated in *ex-vivo* or *in-vivo* studies.

Organogels type and therapeutic active drugs	Types of study	Comparison with commercial product/ conventional forms	Therapeutic utility
Low molecular weight organogel loaded with enrofloxacin	*Ex-vivo* on pig ear skin	Pentravan ® cream	Infectious treatment in cattle and pets
Pluronic lecithin organogel loaded with antiemethic agents	*Ex-vivo* on pig ear skin	Pentravan ®, Pentravan ® Plus, Phytobase ®, and Lipovan ®	Chemotherapy-induced nausea
Pluronic lecithin organogel loaded with mefenamic acid	*In-vivo* on albino rats	Volini ® gel	Pain and inflammation
Pluronic lecithin organogel + sorbitan organogels + bigels loaded with diltiazem hydrochloride	*In-vivo* on albino male rats	Hydroxy-propyl methyl cellulose hydrogels	Angina and hypertension
Pluronic lecithin organogel loaded with melatonin	*Ex-vivo* on human skin and porcine buccal mucosa	Ornabase ®, Montanov ® 68, NaCMC gel, and Carbopol ®940 gel	Oxidation-related pathologies
Pluronic lecithin organogel loaded with fluorescein	*Ex-vivo* on porcine skin	Lipoderm	Medical imaging
Lecithin organogels loaded with sumatriptan succinate	*In-vivo* albino mice	---	Migraines with gastric stasis
Lecithin organogels based nanoemulsion with metoprolol	*Ex-vivo* on hairless skin of male wistar rats	_	Angina and hypertension
Lecithin organogels loaded with fenretinide	*Ex-vivo* on synthetic nylon system	Conventional ointment o/w emulsion	Chemoprevention and treatment of cancers

CONCLUSION

In this review, we have recorded recent breakthroughs in organogel production, characterization, and applications. The physicochemical features of organogels play a critical role in their production and stability, as has been well documented in the literature. They have distinct properties like thermodynamic behavior, viscoelasticity, and flexibility. Simple formulation tweaks can easily tweak these features, leading to highly organized designs. Their ability to be customized as drug delivery systems is also enabled by their hybridization with other materials. In fact, these structures' properties make them great matrices for delivering an effective drug concentration over a long period, improving the likelihood of

patients adhering to their therapy regimen. Organogels are currently understudied in comparison to other gel systems, despite recent advancements, particularly in terms of biocompatibility. Innovations in the design of bio-based organogelators that can function with a larger spectrum of biocompatible solvents should be considered in the future. Organogel in situ forming matrices should benefit biomolecules such as peptides, proteins, and immunoglobulins for extremely extended releases. To further promote these new drug delivery methods, additional in-depth investigations of solvent and electrolyte diffusion, as well as matrix degradation and by-product removal, are required.

CONFLICT OF INTEREST: There are no conflicts of interests.

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