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REVIEW ARTICLE

Organogel as Drug Delivery System: Review

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ABSTRACT

Background: Gels are employed as a carrier medium/network for the delivery of topical medicines. Due to number of benefits gels are gaining attention day by day as a drug delivery system. Among gels Organogelare preferably active for incorporating lipophilic and hydrophilic drugs within the same gel network.
Aim: To emphasize about the basics of Organogel. Their introduction types, composition, properties, methods of preparation and advantages and applications and most importantly as topical drug delivery system.
Definition: The Organogel comes under the semi solid preparations with a definition of having two phases,one of which is organic liquid which gets immobilized by the other, that is an organogelators.
Composition: Organogel are, "mixture of lipophilic liquid and solid lipid, in which solid lipid having concentrations (<10%) can entangle bulk liquid oil by formingthreedimensionalnetwork by the physical interaction of self-assembled organogelatorsin the bulk oil"[2].
Properties: Generally Organogel are thermodynamically stable system, viscoelastic, biphasic system, no irritating, have low degree of hydration in comparison to hydrogels. Exhibit morphological and rheological properties
Method of Preparation: Solid fiber Matrix and fluid filled matrix are most common methods adopted for Organogel preparations.
Characterization: viscoelasticity, pH, Firmness, In vitro drug, release, stability, phase transition, and structural features,*Invitro* release, skin permeability were discussed along with different factors that affectOrganogel.
Applications: Organogel are used for both oral and topical delivery of number of drugs. They are used for local as well as are capable of systemic percutaneous absorption due to their lipophilic nature and penetration potentiates by the presence of penetration enhancer[3].
Keywords: Organogels, Organogelator, Solvents, Drug delivery system

INTRODUCTION

The word "gel" and jelly is devised from Latin word- "gelatin." Which means,frost/ freeze/or congeal. Thus, term, "gel" gives an idea of liquid setting to a solid or semisolid form which do not flow[4].

According to United State Pharmacopeia (USP), "a gel is a preparation in water soluble base and isconsidered as greaseless ointment".This is referred as gelator system[5].OR

"The United State Pharmacopoeia (USP) defines gels as semisolids preparations that can be either suspensions of small inorganic particles or large organic molecules interpenetrating withthe liquid". It is a biphasic system in which in-organic molecules are not soluble but are dispersed throughout the external phase(continuous phase)[3].

In the last few decades' interest in Organogel has been increased due to, discovery, development and synthesis of new molecules that cause gelling at less concentration of various organic solvents. These organogelators cause the immobilization of the liquid following their self-assembly into various networks likes rode, tubules platelets and fibers[6].

The composition of gels involve two interpenetrating systems: (a) colloidal particles which act as gelator or gallant are uniformly distributed throughout the (b)otherliquid known as solvent. The gallant may be natural, synthetic or semi synthetic and is dispersed in the solvent system which may be organic, inorganic or aqueous[7]. Gels are categorized under two classes based upon solvent nature, its affinity, physical state and type of bonding present between the gel networks. The one with reversible properties are hydrogels (polar solvent) and are bounded by hydrogen bonding or weak Vander Waals forces of attraction and the irreversible with covalent bonding are Organogel[8].

During gel formation the polymeric network expands due to swelling in order to hold the drug molecules and maintains the shape of network. Viscosity is very important parameter for gel formation. Concentration of gelling agent imparts a major role in increasing or decreasing in gel viscosity[9].

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The gels are characterized by evaluating the parameters like pH, drug content, viscosity(Brookfield viscometer), spread ability, conductivity, exturdability, skin irritation studies, in-vitro drug release, and stability studies. From the clinical indications it is proved that topical application of gel is considered to be safe and effectivefor treating differentskin related diseases. Different approaches can be used to enhance the permeability and bioavailability of topical gels for producing unique drug delivery system.The different dosage forms like emulgel, solid dispersion,hydrogel, solid lipid nanoparticles liposome and niosomes can be incorporated into the organogels[10].The gel interrelatedformulationsoffers better application and stability as compare to cream and ointment[11].

Organogel: "Organogel are bi continuous system with apolarsolvent and a gelator molecule. The organogelcan or cannot not shield water molecules arrested between the self-assembled spaces of three dimensional structure of gelator, which prevent the flow of apolar phase via surface tension[12]". An Organogel may be defined as a non-glassy thermoreversible semi-solid system composed of an organic liquid entrapped within a 3-D network[13].

The Organogel served as another type of carrier system for the delivery of small and macromolecules for oral, topical, rectal, percutaneous and ophthalmic routes.The Organogel are thermodynamically stable that is attributed to the fibrous nature due to which they remain in low energy state. Organogel exhibit sol to gel transition above room temperature which means energy is required to disrupt the gelling network of the Organogel and transforming it into sol state[14].

Additionally, the growing trend towards the use oforganogels is their thermos-reversibilityproperty. This occurs on heating above and cooling below the transition temperature. This transition temperaturechanges according to physicochemical properties of the gelling agent and the continuous phase[15].The gelator has great impact on Organogel properties. The gelling ability of gelator is related to establish a balance between solvent and the gelator being used[16]. The process of gelation is possible through the formation of a helical structure. The helix is formed by the conformational changes sterically between polymer and organic solvent. The different examples of Organogel include sorbiton

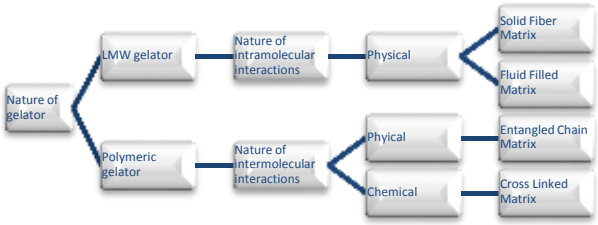
mono stearate, Lecithin, Cholesterylanthraqunone derivatives and sterol. The Organogel have been fabricated in different shapes like films, micro particles, rods, and disk depending upon the site of administration[17]. The other health benefit related to Organogel is that they are used as an alternate in foods having saturated and trans fatty acids.

Merits and DemeritsofOrganogel

Merits	Demerits
The gels are easy to prepare and handle	Not easily washable
They have good/increased mechanical strength due to presence of organogelators.	More favorable towards lipophilic drugs
Less expensive	Oily consistencyis not considered as pleasant feature for the cosmetics
Organogel can't form semisolid preparation on standing	Heat can be an issue unless lecithin can be added in the preparation(18).
Resistant to microbial contamination	When outlook for certain time organogelsnaturally shrinks & small amount ofoil syneresis out.
Thermoreversible	If impurity present gelling will not occur
Organogelshave high permeability through the skin	
Organogelsreduce the diffusion rate of drug because dug is dissolvedin polymer and transported between the chains.	Raw material (lecithin) is not accessible for large scale production(17).
Thermodynamically stable	

Classification of Organogel: The Organogel are characterized on differentbasis like organogelators type, the solvent used andthe intermolecular interaction present between them.There is a great change in the gelation properties of polymer.The parameters which effect the gelation includes: (i) The chemical structure ofgelator with less molecular weight, (ii) the polymer backbones,(iii) and linking type between gelator and the polymer[15]. The flow chat is represented below in Fig 1.

Fig.1 Schematic representation of Organogel classification (12)



Mechanism of gel formation: The Organogelare formulated by different methods. Most commonly, bycrosslinking of polymer with theorganogelators. In most of the cases, supramolecular polymers are connected either by hydrogen-bonding, van der Waals, p-stacking, and electrostatic interactions(19). They are physically intertwined by a polymerization/ curing reaction. Themonomersor theirprecursors grow into long molecular chains. The constituentswithmultiple functional groups (crosslinking points) tend to form covalent bonds resulting in formation of 3-D polymeric network. At the gel point when the polymeric network loses the mobilityitbecomes large enough toformsorganogelwith the solvents. The unreacted small molecules are trapped inside the gel network(4) as shown in fig 2(a&b).

Fig 2 (a): Gel formation mechanism by Fluid Filled method

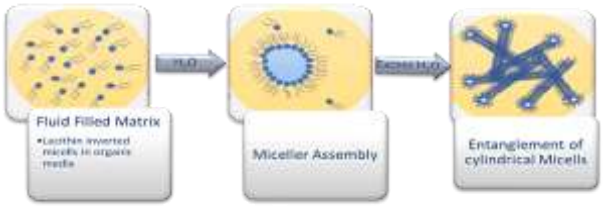
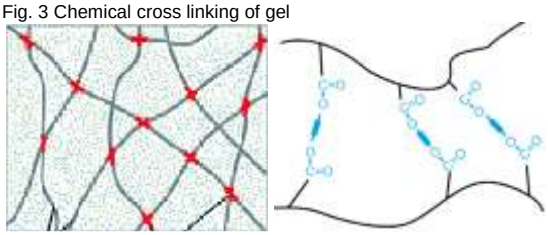


Fig 2(b): Gel formation mechanism by Solid Fiber matrix

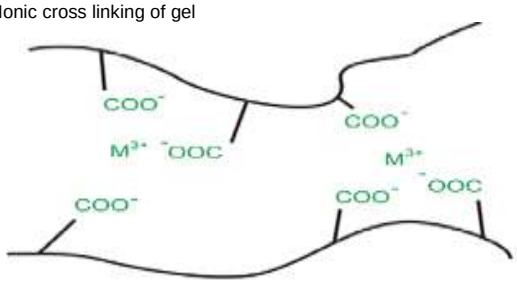
Chemical cross linking: It is reported that sometimes double or multifunctional monomerarepresent in the polymer. These polymers then cause chemical cross linking with massive molecular massmolecules as shown in Fig.3. There are some polymersthat are insoluble in solvent but when incorporated in the solvent may result in the swelling. Example is poly acrylamide gel. These gel exhibit covalent bonding and are irreversible in nature and are therefore robust and resistant to physical deformation.Examples are acrylic acid copolymers and polymeric organogel based on sodium allylsulphonate.

Fig. 3 Chemical cross linking of gel



Ionic cross linking: Cross linking occurs by the interaction of charges on polymer or other solvent molecule is called ionic cross linking. Charges attract each other and as a result of this ionic interaction gel is formed. The example of formation of gel in the presence of calcium ions is polysaccharide alginate. The gelation can also take place when pHof the solvent is changed. For example pectin forms gel when subjected to acidic pH. The cross linking by ionic interaction is shown in Fig 4.

Fig.4. Ionic cross linking of gel



Physical cross linking: The physical cross linking of the gel involves choosing the most appropriate polymer. Which dependsupon two main parameters: (i) there should be strong interaction among the chains toform a semi-permanent linkage and(ii) the gel network should have the ability to hold large amount of water[20].The physical nature of the gels is often thermo-reversible. It is noted that below critical temperature they behave as gel and above this pointbehave like sol.In some cases cross linking takes place by physical interaction that is by formation of hydrogen bonds, concentration and temperature variation, crystalline components solublization and hydrophobic interactions. Among all low molecular weight Organogel and majority of Organogel of POGs class comes under physical Organogelgels.Certain example includes, cellulose gel, dextran gels, poly (N-isopropyl acrylamide) gel[8].

Types of organogelators used in Organogel: Number of organogelators can be used for Organogelformulation. The low molecular weight organogelators are classified in two types. One forms hydrogen bond e.g. amino acid, amide, urea and carbohydrate moieties. The second one is those which do not form hydrogen bonds these are anthracene, anthraquinonoid derivatives, tropane derivatives, and steroids[21]. The hydrogen bond is responsible for gelling as in case of amide and urea where as in aromatic ring π-π stacking and hydrophobic interaction is the cause of gelling. The alkyl chains work for hydrophobic interaction and in amino acid chiral center provide the center for gelation building block[22].The n-alkanes having number of carbon 24,28,32 and 36 are the simplest type of organogelator. The most commonly used are sorbitan mono stearate, sorbitan derivatives, 12 hydroxyoctadecanoic acid, steroids and their derivatives and urea compound and carbohydrates and their derivatives. Some common gelator will be discussed here[23].

Table 1:Different types of organogelators

Organogelator types	**Application of Organogel**
Derivative Organogelators 4 -tert-Butyl-1-Aryl Cyclohexanol. Thesecome under arylcyclohexanol derivatives and are helpful in the formation of thermoreversible gels. At room temperature they are solid andexhibit less solubility in apolar solvent. Gels formed by these organogelator may be turbid or transparent depending upon apolar solvent[17]. Examples: Benzene, cyclohexane, carbon tetrachloride.	For the topical delivery
Polymeric organogelator Thesegelator have low *sol-gel*temperature and good mechanical strength. These form gels at very low concentrations[26]. Examples: The most common example of polymeric organogelatorsis L-lysine derivatives: Theseinclude (polycarbonates, polyester, polyethylene glycol, and poly (alkylene)[5].	For the prepration of organogel and for sustain release rectal formulations
Gemini gelators The gemini is a Latin word, having meaning twin. This type of organogelatorshastwo L-lysine derivatives joined by alkaline chains with different chain lengths[26]. **N-lauroyl-L-lysine ethyl ester):** These have high ability of immobilizing apolar solvents. When two N-lauroyl-L-lysine segments linked by an oxalyl amide functioned as good organogelators.	Used in topical formulations
Synthetic tripeptideorganogelator **Boc-Ala(1)-Alb(2)-ß-Ala(3)-OMe:** These are Capable of self-assembling,thermoreversible; transparent gelsin the presence of various apolar solvents, viz.,1,2-*dichlorobenzene* (DCB), monochlorobenzene and benzene.	In drug delivery and optelectronics
Low molecular weight gelator These gelatorscontain < 2%wt. in an organic liquid and fulfil two roughly defined criteria: (1) When stress is applied (below acertain limit) distortion in shape take place but this is reversible asthese gels return to their original shape whenstress is removed (2).Although they are composed of liquid and being fluid when observed under microscope, they must appear solid-like.They usually self-assemble via one-dimensional growth methods to form fibers, strands, or tapes which are frequentlycrystalline. Fatty acids and n-alkanes have ability to immobilize, only a few LMOG gels are reported to appear as thixotropic[13], at a polar solvents Concentrations*of* (< 2%)[27]. *Example*: Aminoacid-based LMW tris (bis-amido) organogelators,bile acid alkylamide derivatives,peptide-based LMOGs, tetradecylammoniumbromide, N-acyl-1,ω-amino acid compounds, 2,3-di-n-decyloxyanthracene (57), N-alkyl perfluoroalkanamides, long-chain benzoic acid hydrazides and long-chain carbomates[28].	In food industry (Alsaab, Bonam et al. 2016)

Table 2: Types of the solvents used for Organogel

Polar solvents	**Non polar solvents**
Alcohols	Benzene
Methanol,	Chlorobenzene
Ethanol,	O-dichlorobenzene
Propanol	Toluene
Isopropanol	O-xylene
Isopentanol	Dichloromethane
2-methoxyethanol.	1,1,2-trichlorotrifluoroethane
Ketones	Pentane
Acetone	Cyclopentane
Methylethyl ketone	Hexane
Methyl n-propyl ketone	Cyclohexane
Methyl isopropyl ketone	Heptane
Methyl isoamyl ketone,	Iso octane
Ethers	Dethylether
Ethylene glycol	Petroleum ether
Monobutyl ether	Pyridine
Propylene glycol	Carbon tetrachloride
Monomethyl ether	
Methyl acetate	
Ethyl acetate	
Propyl acetate	
n-butyl acetate	
Chloroform	
Acetonitrile	
Glycerol	
Dimethyl sulfoxide	
N,N-dimethyl formamide	
Tetrahydrofuran	
Pyridine	
1,4-dioxane, dimethyl acetamide	
N-methylpyrrolidone	
propylene carbonate	

Types of organogelators: Natural molecules presenting gelling properties are sugars, sugar derivatives, Vitamins, gelatin, bile salts, lipid derivatives, carbohydrate derivatives, phytosterols, peptide derivatives and waxes[24].The low molecular weight compounds, such as monoglycerides,sorbiton tri-stearate,12-hydroxystearic acid, fatty alcohols, fatty acids and polymers, such as ethyl cellulosehave also been studied as organogelators[25].

Solvents for Organogel: In the recent years solvents reported for Organogel formulation were mostly alkanes with carbon no.>5.hexane, cyclohexane, squalene, vegetable and mineral oils. Mostly used in formulations are soybean and sunflower oil. Isopropyl myristate and medium chain triglycerides considered more biocompatible[24].

Table 3: Properties of Organogel

Physicochemical Properties of Organogel	**Detail about physicochemical properties**
Viscoelasticity	Organogel tends to follow Maxwell model of viscoelasticity. they remain solid at low shear rates and begins to flow under high shear rates due to weak point of physical interaction of fiber matrix[33].
Thermoreversibility	Organogel when heated above critical temperature they start flowing. This is due to the disruption of physical interaction present between gelator molecules. On cooling the physical interactions reverts back into more stable structure[34].
Thermostability	Organogel are stable due to the self-assembly of organogelators which leads to decrease in the energy of system making Organogel more stable[35].
Non birefringence	Organogel appears dark when viewed under light microscope because they do not allow light to pass through them.This property is called non-birefringence[36].
Chirality	The presence of chiral center in low molecular weight gelator effects the growth and permanency of solid fiber matrix. This property is not present in fluid filled fibers, chirality helps in compact structure. The example is crown ether phthaloncyanine (Jha and Maurya 2013).
Opacity	Depending upon nature Lecithin Organogelistransparent and sorbitanmonostearate are opaque in nature.
Biocompatibility	Use of biocompatible components in Organogel has led to the delivery of more bioactive components to be deliver by Organogel[17].

Organogel are set by organogelators having a less molecularweight, which self-assemble in organic solvents, triggering the formation of 3-D network. There in situ biodegradable features also permit them to transport proteins,medicines, and vaccines.These Organogel have been used to develop drug depot system. These are biodegradable, non-immunogenic system can lessenthe patient discomfort by reducing the frequency of application[29].

As far as gelator is important component of Organogel, organic solvent is equally important. So at room temperature gelator remain insoluble in solvent. They dissolve on heating and form gel on cooling. So in the gelation process a balance exists between dissolute and precipitant[30].The different solvents can be used for Organogel formation[31]. Table 2 shows the type of different solvents used.The solvents show following order to form organogel: glycerol >water>formamide>ethyleneglycol. The organogel formation is sensitive to solvent structure as well as solvent physiochemical properties[32].

Method of Organogel preparation: Different methods are used for Organogel formulation these are as follows:

Fluid filled fiber mechanism

- Solid fiber method
- Mechanical homogenization and micro irradiation

Fluid filled fiber mechanism: The gelation process takes place by the addition of small amount water into apolar solvent and surfactant. Before the addition of water surfactant is mixed with the apolar solvent than water is added slowly as e.g. is lecithin[36].

Solid fiber mechanism: In this method dispersion of solid organogelators is added into the apolar solvent by hot emulsification process and solution of apolar solvent and gelator is obtained. This is allowed to cool at room temperature as a result organogelators molecules precipitates out as fibers which undergo non covalent physical interaction causing the formation of 3-Dnetworks due to assembly of organogelators molecules resulting in the development of semisolid gel by immobilization of liquid phase[37].

Fig. 5: Schematic representation of organogel formation by fluid filled mechanism.

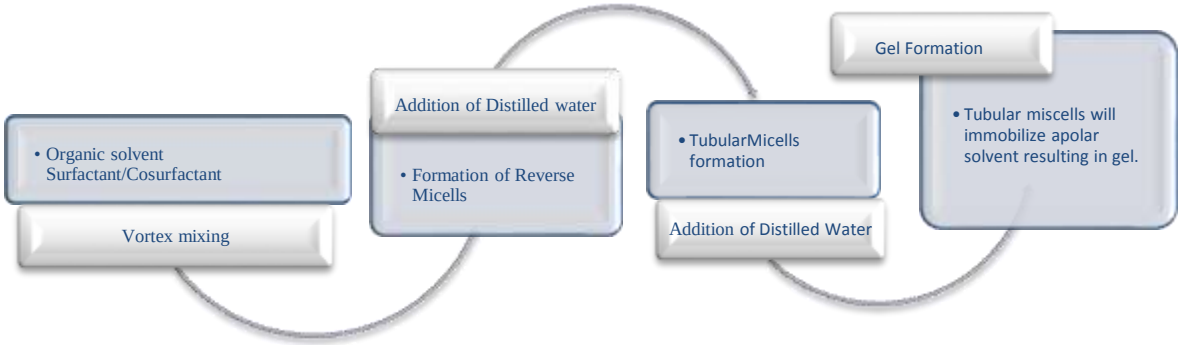
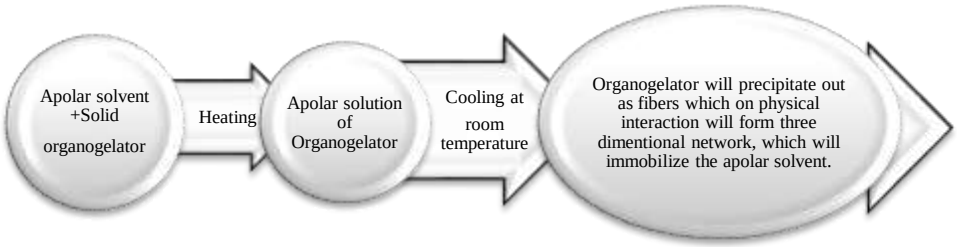


Fig.6: Schematic representation of solid fiber mechanism of Organogel formation**.**



Mechanical homogenization and micro irradiation: This innovative technique involves high speed homogenization using Ultra Turrex for 5min at 24000rpm before micro irradiation in microwave. Or way of mechanical homogenization can also be carried out by heating the solution in water bath at 80°Cand mechanical stirring at 200rpm until homogeneous and transparent dispersion is formed[38].

The other method for homogenous dispersion is by using microwave. Pour the dispersion in petri dish and expose it to micro irradiation until homogenous or transparent system is formed(39). The microwave assisted heating method is economical, efficient and require less energy for Organogel formation.

Table 4: Types of Organogel

Types of Organogel	Applications
Lecithin Organogel Extracted from various plants and animals tissue apart from Egg yolk. Experimental results indicate if lecithin contains >95% phospholipids than lecithin will not cause gellification of aplolar solvent.	Lecithin gel bears isotropic structure and are thermodynamically stable, thermoreversible (sol-gel transition 40°Cnonirritant, biocompatible,viscoelastic and transparent[40].These system are often called as living, equilibrium polymers worm like and thread like micelles[41].
Pluronic Lecithin Organogels These are Soy lecithin Organogel having isopropylmyristate and isopropylpalmitate and poloxamer 407 and water. The apolarphase consist of 22-30%v/v of water and therefore are referred as emulgel[41].	These are thermostable, biocompatible, and viscoelastic. PLO causes skin irritation.The PLO are yellow color and opaque in nature. The PLO are used for the delivery of both hydrophilic and hydrophobic drugs both for topical and transdermal applications[5].
Premium Lecithin Organogel PrLO is the second common Organogel having higher thermos-stability apart from its non-greasy nature and non-tackiness behavior. This gel does not cause skin irritation as it do not contain pluronic derivative[41]..	This PrLO is has improved skin penetration and bioavailability and is used to deliver number of drug like ibuprofen, diclofenac, progesterone and ketoprofen has been successfully used for intra dermal drug delivery.
Limonene GPI /PG/ Organogel. These gels are prepared by adding	Limonene is excellent penetration enhancer property there is used in number

appropriate quantity of PG, PGI and limonene at 120℃ on cooling it form white gel. Presence of limonene changes the rheological properties of Organogel but there is no effect on stability of gel(Alsaab, Bonam et al 2016).	of transdermal formulations for incorporation of bioactive molecules. Therefore improve the bioavailability in dermal tissues. Apart from limonene linalool, cineol and farnesol has also been incorporated in GPI/PG Organogel to increase penetration across the dermal tissues[17].
Gelatin Stabilized microemulsion based OrganogelGelatin is a protein it form gel by forming concentrated solution at 40℃ and then cooling below 35℃ Addition of gelatin in water in oil micro emulsion results in gelation of whole micellar solution and form transparent gel.	Because of ease in preparation and thermostable nature these are used for gelatin stabilized micro emulsion preparation. MBGs are used for topical /transdermal controlled delivery of hydrophobic drugs[27].
Fatty acid derived Sorbitanorganogel: This gelator is hydrophobic, non-ionicmolecule with surface active properties, it tends to immobilize various solvents like isopropyl myristate and herbal oil. These gel form solid fiber matrix when heated with apolar solvent and then cooling down to low temperature and toroidal micelles are formed. These toroidal reverse micelles form tubular structure by reorganizing themselves. Which form three dimensional networkby physical interaction occurring in them[17].	These are thermostable, thermoreversible and opaque when stored for weeks in room temperature. These gels can also be prepared by forming oil in water micro emulsion and then dissolving the gelator sat high temperature. Decreasing the temperature result in precipitation of the gelator due to the self-assembly of gelator molecules into tubular structure[34].
Sorbitan mono stearate Organogel Sorbitan mono-stearate (span60) sorbiton mono-palmitate (span40) form gel with various solvent's at low concentration[27].	They are effective for delivering hydrophilic vaccines.
EudragitOrganogel: These are formed by mixing the high concentration of Eudragit with poly hydric alcohols like glycerol, polyethylene glycol& propylene glycol	They shows high gel rigidity and stability when the concentration is low[6].
Poly (ethylene) Organogel These gels are formed when low molecular weight poly ethylene is mixed with mineral oil at temperature > 130℃and then shocked cooled.	These are used as ointment base. Gelled structure is formed by the precipitation of polyethylene molecules due to physical interaction resulting in solid fibrous structure.
L- alanine derivative Organogel N lauroyl L alanine methyl ester which gels in organic solvents like soybean and triglyceride. These system exist in gel form at room temperature[42].	These gels act as sustain release implants and are used for delivery of rivastigmine and leuprolide.

Table 5: Factors affecting organogel

Factors affecting Organogel	How they effect
Organic solvent **Polar solvents** **Non aqueous solvents** **Co solvents** Organogelators **Concentration**	The effect of polar solvent introduced into the spherical lecithin increases the cross sectional area in which the solvent is arranged. The non-aqueous solvent is not restricted as long as it replaces water of cellulose hydrogel without distorting its shape. The examples include polyethylene glycol and dimethyl ether. They influence Morphology and 3-D confirmation.They effects stability, mechanical and rheological properties[38].
Phase transition temperature (PTT)	PTT gives an insight about the microstructure present between the gels by cross linking. Narrow PTT indicate homogeneous microstructure. The PTT can be determined by DSC and hot stage microscopy which are sensitive technique for determining PTT.
Salt addition	On adding salt, it attracts water of hydration of polymer and allow formation of inter molecular secondary bond. This is known as salting out.
Temperature	The effect of temperature depends upon the polymer chemistry and mechanism of interaction with the medium. When the gel is in solution on reducing temperature gelling occurs due to reduction in degree of hydration. The gel form by chemical cross linking cannot be liquefied and diluted upon temperature change[12].
Molecular weight	Low molecular weight polymers require high concentration to meet up viscosity possibly and to set a gel.
Surfactant	Characteristics of gel can be varied depending upon the concentration and proportion of ingredients. The example is Poloxamer 407 which is polyoxyethylene and act as surfactant[43].
Physiochemical properties Charge Solubility Molecular weight/ spatial configuration	Presence of charge on polymer facilitates mucoadhesion. Poly-anions particularly polycarboxylate are preferred to poly-cations And effect mechanical and rheological properties. Mucoadhesive polymer swell on coming in contact with moisture and increase the mobility at interface of polymer this reveals more sites for bonding. It favors the entanglement and interaction after polymer and mucin have interpenetrated[44]

Table 6: Characterization of Organogel

Characterization parameters	Details for characterization parameters
Physiochemical parameters Isotropic nature and optical clarity is checked.Hydrogen bonding between the gelling networks.Molecular packing between gelling structures.	By FTIR and NMR is used. By FTIR By scanning and dynamic electron microscopy. Small angle neutron scattering[45]
Firmness of Organogel	Firmness of Organogel is checked by Texture Analyzer by using 12.3mm cylindrical probe[46].
Rheological behavior Viscoelasticity Swelling Water contents	A controlled stress rheometer will be used for measuring the rheological properties (shear viscosity and dynamic viscoelasticity) as a function of temperature[47].
pH measurement	The pH of organogel samples will be detected by using digital pH meter. The pH of the organogels was determined by dropping the bulb of the glass electrode of the pH meter into the samples. The pH of topical drug delivery preparations must falls within the range of 4.5–6.0 (skin pH), to avoid irritation to the skin[48].
Phase transition temperature PTT is used to have an insight into the micro structure that forms a gelling network.	Hot stage microscopy and dynamic scattering microscopy is used for phase transition temperature[49].
Gel kinetics Gel –sol and sol-gel transition Gel kinetics	ByTurbidity determining method By using inverted tube method[50].
In vitro drug release	By Franz diffusion cell /dialysis bag[51]
Safety and skin compatibility studies	Is checked by human or animal skin irritation testing on applying the gel[50].
Stability studies	By storing Organogel at normal and accelerated condition and noticing the syneresis of oil[52] for confirming the stability or destability of Organogel (Huri, Ng et al. 2013). By optimization through ternary phase Diagram.By using Stability Chamber
Structural features Molecular structure Hydrogen bonding	By NMR By FTIR[53]

Table 7: Therapeutic categories

Drug delivery system	Drugs used	Reference
Ocular drug delivery system	FlunarizineHCl	(54)
Topical drug delivery	Candesartan cilexetil	(38)
Topical delivery	Testosterone	(55)
	Risperidone	(56)
Oral	Acyclovir, clotrimazole	(57)
	Efavirenz	(58)
Intravaginal	voriconazole	(59)
Nasal	Ketamine	(60)
Ocular		
Buccal	Norfloxacin	(61)
Rectal	Salicylates, Procaine, and ketoprofen	(62)
Transdermal	Alfuzosin	(63)
Subcutaneous injection	Docetaxel	(14)
Subcutaneous implants	RivastigmineGranisteron	(64)
Subcutaneous	Caffine	(65)

Limitations: Despite of their convenience, Organogel also offer some limitations which need to be explored.

1. Instability is the main issue which needs to be addressed. As change in temperature and humidity may lead to phase separation, degradation, and decrease in gel opacity to this formulation.
2. They demand purity as any impurity may lead to effect the gelation.
3. Solvent contamination may lead to instability of gel network through impaired physicochemical interactions.
4. Solvent polarity also effects mainly Organogel leading to aggregation, swelling, structural instability and integrity ofOrganogel. Aggregation may lead to fibers and bundles formation in Organogel structure and change the desired structure. These aggregations may weaken the solvent and organogelators interaction weak, leading to oozing out of the fluid from organic phase.
5. Methods like micro irradiations and high speed homogenization may be adopted for large scale production.

CONCLUSION

The Organogel are most effectively used in number of drug delivery system and has been proven safe and effective. Physiochemical properties of Organogel there, viscoelasticity, thermodynamic behavior and there versatility make them unique drug delivery system. But their use in cosmetic products still need further research studies. Infuture studies regarding stability, biocompatibility studies, using biocompatible solvents needs to be under consideration. Further studies regarding degradation, elimination of byproducts and electrolyte diffusion still need to be studied in depth.

Authorship and contribution declaration: Each author of this article fulfilled following Criteria of Authorship:

1. Conception and design of or acquisition of data or analysis and interpretation of data.
2. Drafting the manuscript or revising it critically for important intellectual content.
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