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ORGANOGELS IN TOPICAL DRUG DELIVERY SYSTEM: A SYSTEMATIC REVIEW

Dr. Mariya Saifee[1] and Pratiksha Pramod Gosavi*[2]

YB Chavan College of Pharmacy, Aurangabad, 431001.

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***Corresponding Author**
Pratiksha Pramod Gosavi
YB Chavan College of Pharmacy, Aurangabad, 431001.

ABSTRACT

In topical drug delivery system, the gel has gained increasing attention due to the ease of fabrication methods, provides local and systemic effect, greater drug loading capacity, ability to penetrate into deeper skin layers, easy to apply, minimum side effects etc. Organogels are gels formulated with organic liquid phases, which are distinguished from hydrogels infiltrated with water/aqueous solutions in a three-dimensional network. In this review fundamental understandings of organogels, their basic composition, different types of organogelators, factors affecting organogel, gelation mechanisms, types of organogels fabrication methods, various bioactive agents that can be incorporated inorganic gels, evaluation parameters and applications in drug delivery and recent advancements are summarized. Finally, the remaining challenges and prospects of organogel are addressed.

KEYWORDS: Topical drug delivery, organogels, Hydrogels.

INTRODUCTION

Topical drug delivery system is a way to deliver medication that is applied on to a particular part of the body typically on the skin. Topical drug delivery is an interesting option because it is convenient and safe. This offers several potential advantages over conventional routes like avoidance of first pass metabolism, minimizing undesirable side effects, and most significantly it provides patient compliance as the drug delivery is painless. Topical gels are semisolid dosage forms in which a liquid phase is constrained within three-dimensional polymeric metrics derived from natural or semi synthetic sources. Gels are defined as semi-solid system in which liquid solvent phase immobilised within a 3D network structure formed by the gelator molecules by physical or chemical manner. Depending upon the nature of the dispersed solvent phases gels can be typically classified into hydrogels and organogels.

Hydrogels are the type of gel formulations with water-based solvents as a continuous phase and are capable of absorbing large quantity of water or biological fluids. Hydrogels have distinctive nature and characteristics such as water affinity, dispersibility as colloids, soft texture, high hydration ability, flexibility, and biocompatibility. Organogels are distinguished from other gels by adopting organic filling liquids. They exhibit a series of unique properties and functionalities such as topical delivery for hydrophobic and hydrophilic drugs.[1] Organogels are vehicle base for the drug delivery through the dermal and transdermal route. Organogels are class of gel composed of liquid organic phase within a three-dimensional crosslinked network. They can be applied and act either locally or systemically, and can penetrate into stratum corneum, the skin permeation barrier. In the pharmaceutical field, organogels can be used for drug and vaccine delivery via different administration routes by using different types of organogelators. Thus, current review focus on the various aspects of the organogels and organogelators, their mechanism and the applications in drug delivery.

Basic composition of organogels

Organogels basically consists of organic solvents and low molecular weight or polymeric organogelators or surfactants. Common organic solvents such as ethanol, butanol, polyethylene glycol, propylene glycol, hydroxy ethyl lactate, vegetable oils, groundnut oil, olive oil soybean oil, sunflower oil, mineral oil, soybean oil, olive oil, linseed oil, canola oil can be used as an organic solvent for formulation of organogels. Organogelators the network is composed of either low molecular weight organogelators (LMOGs) or polymeric organogelators (POGs). Low molecular weight organogelators such as N, N dimethylurea derivatives[2] sugar or sugar derivatives[3], phytosterol[4], carbohydrate derivative[5], vitamin derivative[6], peptide derivative[7], lipid derivatives[8,9], bile salts or waxes[10-16], alanine derivatives[17], glyceryl fatty acid esters derivatives[18], amino acid, steroid[19], are commonly used. there is physical interaction between gelator and organic solvent which may be either solid fibre matrix or fluid fibre matrix.

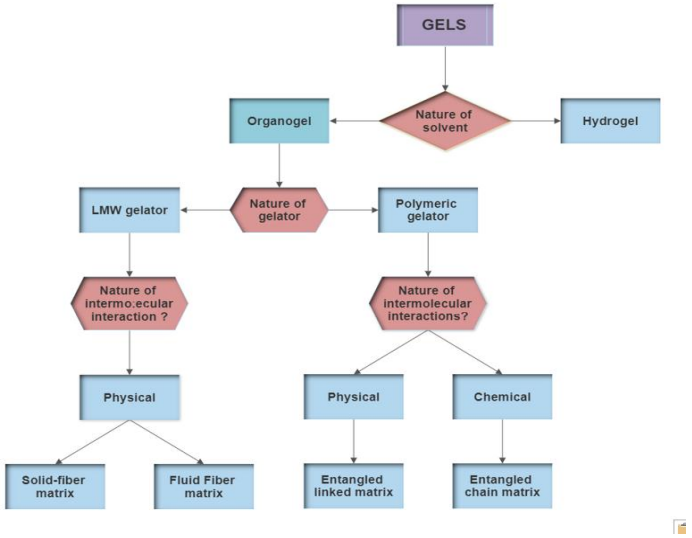


Figure 1: Types of organogels and organogelators.

Polymeric organic gelatos forms 3d network of organogels by self-assemblies. These are versatile in nature and have ability to form good gelling and in many organic solvents at low concentration various types of POGs are such as polyethylene and its Co-polymers[20], Poly (methyl methacrylate)[21], poly(myth acrylic acid Co-methyl methacrylate)[22] Poly (acrylic acid) Co-polymers[23], sodium allyl sulfonate and sodium ally sulphonate co-polymers[24], N-tertiary butyl acrylamide-acrylic acid co-polymers[25], Poly (dimethyl siloxane), poly(ethylene glycol) poly(propylene glycol), L-alanine derivatives, ethyl oleate glycerol, 2 -pyrrolidone, canola oil soybean oil silicone oil These can interact by both physical and chemical by forming cross linked matrix and entangled chain matrix respectively. The type of organogelators is selected based upon the properties of gelator, solvents and nature of drug to be incorporated in the organogel.

Table 1: Examples of organogels with diverse compositions and application.

Sr no.	Class of gelator	Organogelators	Interaction mechanism	Organic solvent	Application
1	LMOGs	12 hydroxy stearic acid	Hydrogen bonding	Canola oil/ soybean oi/l mineral oil	Drug delivery[26]
2	LMOGs	Lecithin	Hydrogen bonding	Isooctane	Drug delivery[27]
3	LMOGs	Pluronic F- 127 and lecithin	Hydrogen bonding	Isopropyl palmitate/ myristate// ethyl alcohol dimethyl sulfoxide	Drug delivery[28]
4	LMOGs	Cellulose acetate	Not available	Propylene glycol /polyethylene glycol 200, glycerol/ dimethyl isosorbide/ isopropyl palmitate	Drug delivery[29]

5	LMOGs	N-sterol L-alanine methyl ester	Vander walls interaction and hydrogen bonding	Safflower oil	Drug delivery[30]
6	LMOGs	Surbiton monostearate	Hydrogen bonding	Vegetable oils system oil groundnut oil olive oil soybean oil sunflower oil	Drug delivery[31]
7	LMOGs	Mono glycerides and polyethyleneimine	Not available	Soybean oil	Drug delivery[32]
8	POGs	Polyurethane	Hydrogen bonding hydrophobic interaction	1,3- propanediol	Drug delivery[33]
9	POGs	Protein	Protein ligand bind and solvent exchange	Ethylene glycol	In sensors[34]
10	POGs	Poly methyl siloxane	Hydrogen bonding	Silicone oil	Antifouling agent[35]
11	POGs	Acrylic copolymer		Propylene glycol	Drug delivery[36]

3. Gelation mechanism in organogels

Mainly four types of gelation mechanisms exist in organogel which includes fluid-filled matrix organogel, gelation mechanism of physical organogels from POGS, gelation mechanism of monomer molecules via chemical gelation along with cross linker and chemical gelation of polymer with crosslinker or curing agent in organic solvent.

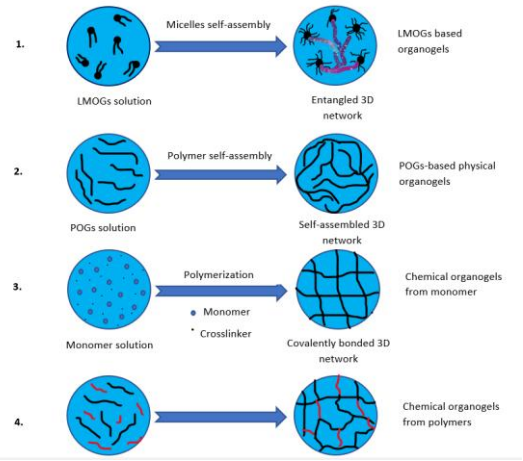


Figure-2 Gelation mechanisms of organogel.

Fluid matrix organogels formed by dynamic exchange of organ is a later molecule with the liquid leads to the formation of aggregations the tips micelles which are self-assembled to form organogels. Polymeric organic gelatos are dissolved in organic solvent to form POGs solution in which polymers are self-assembled and forms 3D networks which leads to the formation of POGs based physical organogels. Monomers dissolved in organic solvent via

polymerization and cross linkers forms covalently bonded 3D networks leads to the formation of chemical organogels from monomers. Cross linkers or curing agents are used along with polymers which leads to form chemical oregano gels from polymers by joining the chains by covalently bonded 3D network. The organogels formed by the chemical intermolecular interactions are generally very robust and irreversible in nonspecific environments.

4. Skin permeation mechanism of organogels

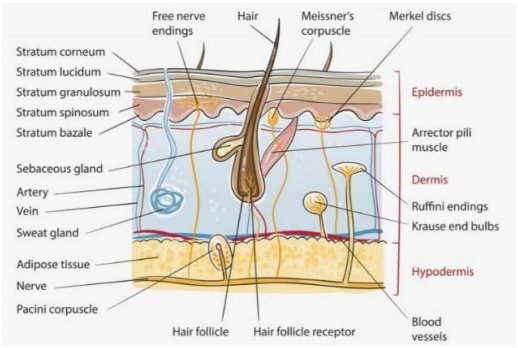


Figure-3 Structure of skin.

Skin plays important role in topical drug delivery system as primary barrier to transdermal or topical drug delivery system is skins outermost layer called stratum corneum which is 10 to 20 micrometres thick underneath this layer is epidermis, dermis and hypodermis. Organic gel permeates through the skin by meaning 2 mechanisms.

1. Percutaneous absorption

Organogels penetrates through skin which is rate determining step. stratum corneum provides greatest resistance to penetration hence permeation enhancers are used which alters the skin as barrier, finally diffusion through stratum corneum to epidermis then dermis and lastly into blood circulation occurs.

Steps involved are[37]

1. Sorption by stratum corneum
2. Penetration through epidermis
3. Uptake of the drug by the capillary network in the dermal layer

2. Permeation

It includes trans appendageal route -Permeation through sweat gland and hair follicles and trans-epidermal route in which molecule passes through stratum corneum by either intracellular pathway or transcellular pathway.

Types of organogels

They are classified in two types based upon the cross linking involved and type of organogelators used in the formation of organogel.

- **Based on the cross linking**

Physical Organogel

Chemical Organogel

- **Based on the type of organogelators**

Lecithin organogels

Pleuronic lecithin organogels

Premium lecithin organogel

Limonene-GP1/PG organogel

Gelatin stabilized micro-emulsion based organogel

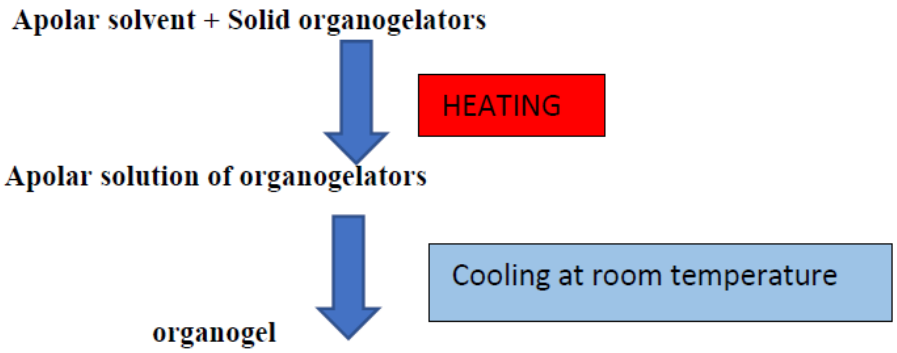
Fatty acid derived sorbitan organogeld

1. **Based on cross linking**

1. **Physical organogels**

Non covalent crosslinking is involved which occurs by heating followed by cooling process. It consist of 3 phases.[38]

1. Dissolution of the gelator molecule.
2. Mechanical stirring and heating.
3. Cooling at room temperature.



mainly low molecular weight organogelators are used forming solid matrix or fluid matrix organogels. In solid matrix organogels solid aggregates and self-assembled by physical intermolecular interactions and formation of gel state is established they are assembled into

rod or tube-like fibres with certain length to width ratio. in fluid matrix addition of polar solvents result in the specific organization of surfactant molecules and due to increased surface tension organic solvent molecules are trapped into a network of gelator molecules, generally required at high concentration for sufficient viscosity and gelling capacity. But POGs are required lower concentration than LMOGs. LMGOs often introduced into gelation systems to trigger interactions for gelation.[39,40]

2. Chemical organogels

Covalent crosslinking is involved. firstly, gelators are dissolved into a polar solvent to form monomer solution, crosslinker are added thus monomer growth into longer molecular chains by polymerization process. Cross linker converts the organogels into swollen state. In general, the swelling ability of gels is inversely proportional to the cross-linking concentration. As polymerization process of monomer solution is complicated process formulation of chemical organogels from reactive polymers by covalent cross linking is done which is relatively simple process.

2. Based on the type of organogelators

1. Lecithin organogel: Lecithin feels yellow brownish fatty substance occurring in animal and plant tissue amphiphilic in nature used as organogelators. Lecithin organogels are made up of lecithin and organic solvent. They possess thermo-dynamic stability, chemically inert, viscous-elastic, biocompatible in nature.

2. Pluronic lecithin organogel: it is microemulsion based gel that has been effectively used by to deliver hydrophilic and lipophilic drugs topically and transdermal across the stratum corneum. These are lecithin based organogels are broadly used as a medium for enhancing permeability though the skin for many drugs.

3. Premium lecithin organogel: These are also known as second generation lecithin Organogel. They have more thermodynamic stability, have non-oily and non-sticky property, due to this they are widely use cosmetically.

4. Limonene GP1/PG Organogel: It is a hydrocarbon, used as outstanding penetration enhancer, classical mean for improving transdermal drug delivery it can be used transdermal patch due to its good skin compatibility. They are long-acting formulation and can be used for delivery of drug at sustained percutaneous rate. it is use in organogel containing gelator GP1 and propylene glycol (PG).

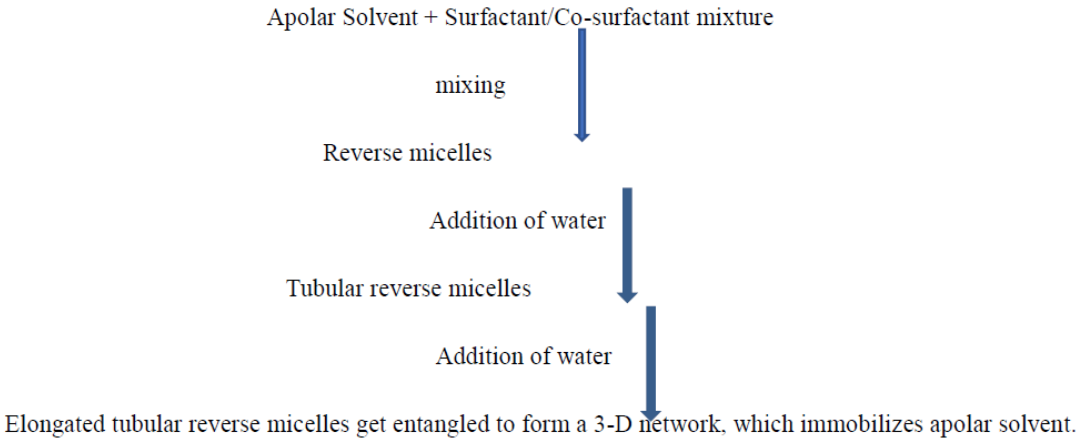
5. Gelatine-Stabilized Micro-Emulsion-Based Organogel: MBG gelatine can be use as protein for several food as structural agent. Formulations containing excess of aqueous phase.

6. Fatty-Acid-Derived Sorbian organogels: Sorbitan monostearate and sorbitan mono palmitate based organogel which are an Ester of sorbitan and stearic acid and food additive respectively. They are lipophilic non-ionic molecule with surface-active property, which can immobilize several solvents, like, isopropyl myristate and vegetable oils. A solid-fiber matrix is formed by gelators in apolar solvent, when cool down from its transition temperature. The configuration of gel has been achieved by reverse micelle's formation as, the temperature is decreased. The gels formed from using these gelators are cloudy in appearance, thermo-reversible and are thermo-stable at room-temperature for several days.

7. Polyethylene organogels: These are colourless, odourless preparations. These formulations are produced by maintaining the temperature of mineral oil at >130◦C and adding low molecular weight polyethylene into it, this blend kept until it cools down. Polyethylene organogels are commonly implemented for the preparations of base in different formulation of ointments. The reason behind the gelation or formation gelled network is an account of solid-fibers interaction with polyethylene.

Method of preparation

1. Fluid Filled Fiber Mechanism[41]



2. Solid Fiber Mechanism

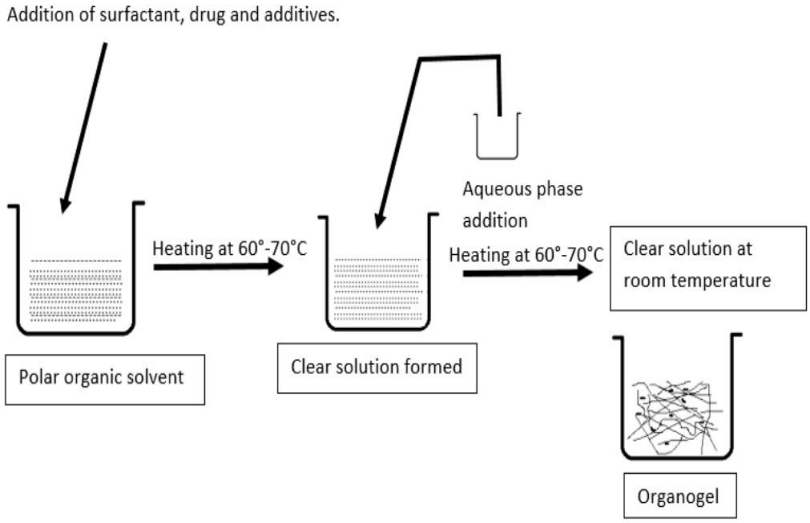


Figure No. 4 – Solid Fiber Mechanism.[41]

3. Hydration method: In this method Gel are prepared by directly hydrating the inorganic chemical resulting in dispersion. Introduction of water vehicle and other agents which can enhance gel formation.

4. Novel method

1 Homogenisation

2 Micro-irradiations

Factors affecting organogels[37]

Table 2: Factors and its effect on organogel.

Sr. no.	factor	Effect of factor
1	Organic solvent • Polar solvent •Non-aqueous solvent	The solvent interaction plays a key role in mediating organic gel formation and eventually determines the properties of the gel have the concentration of drug and organogelators that dissolve in a solvent depends on the solubility of particular drug and gelater in the organic solvent.
2	Phase Transition Temperature	Narrow PTT range can show a homogenous microstructure within the gel. It can give a vision of nature of microstructures that form gelling cross-linked network.
3	Salt addition	Salt out occurs when the part of water of hydration attracts the polymer which allow more formation of inter molecular secondary bonds.
4	Temperature	Its effect depends on the polymer mechanism of interaction and its chemistry with solvent.

5	Molecular weight	High concentration of Low molecular weight polymers is needed for the viscosity and to set gel as required.
6	Surfactants	Gel characteristics can be improved by varying the ratio and concentration of the ingredients used.

Table 3: Various bioactive agents that can be incorporated in organogels.[42]

Bioactive agents	Mechanism
Vitamin C, coenzyme Q 10 ferulic acid green tea.	Free radical scavenging and inhibition of lipid peroxidation
Hydroquinone and its derivatives	Inhibits production of melanin
Lactic acid	Hydration of stratum corneum and prevention of skin damage
Para amino- benzoic acid derivatives	UV filters
Vitamin A	Reduce collagen breakdown by inhibiting the metalloproteinases
Vitamin B N-acetyl glucosamine, metals (zinc, copper, selenium)	Anti-inflammatory action Link with protein super oxide dismutase and melatonin and act as antioxidants
cinnamates	UV filters
Soybean derivatives	Inhibits protease activated receptors
silymarin	Free radical scavenging and inhibition of lipid peroxidation
Malik acid, citric acid, mixed fruit acid, triple fruit acid and sugar cane extract.	Production of melanin is inhibited.
salicylates retinoids benzophenone octocrylene, ensulizole, butyl methoxy di benzoyl and meradimate	UV filters

Many drug such as paliperidone as parenteral thermo-sensitive organogels for schizophrenia therapy[43], haloperidol as transdermal delivery for schizophrenia[44], Propolis organogel as a novel topical delivery system for treating wounds[45], Nifedipine in Pluronic Lecithin Organogel topically to treat Raynaud's phenomenon and progressive diabetic foot ulcers[46], organogels containing hyaluronan microparticles for topical delivery of caffeine[47] Development of amphotericin b Based organogels against mucocutaneous fungal infections[48], luliconazole organogel for treatment against pathogenic fungi[49], olive oil (OO) based organogels using sorbitan monostearate (SMS) and sorbitan monopalmitate (SMP) as organogelators for controlled drug delivery of Metronidazole[50], Development and Characterization of Imatinib Mesylate Loaded Pluronic Lecithin Organogel for antifungal activity[51], Strongly fluorescent organogels and self-assembled nanostructures from pyrene coupled coumarin derivatives which finds application in cell imaging[52], silver sulphadiazine loaded egg oil organogel for improving its therapeutic efficacy in burn wounds[53], an

organogel system containing ascorbic acid microparticles produced with propolis by-product for antioxidant and radicle scavenging activity[54] Zidovudine for Transdermal drug delivery as antiviral therapy[55] Novel Organogel System Capable of Enhancing Skin Penetration Characteristics of Acyclovir[56], Ondansetron, dexamethasone loaded Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital,[57] *N*-palmitoyl L-alanine-based Organogels as Sustained Implants of Granisetron and Evaluation of their Antiemetic Effect[58], in vitro nasal delivery of propranolol hydrochloride by using organogels as a carrier[59] and Transdermal Delivery of Sumatriptan by using Sorbitan Ester Organogels[60] are successfully incorporated.

Advantages of organogels[61]

- Ease of preparation.
- Cost reduction due to a smaller number of ingredients.
- Longer shelf life.
- Thermodynamically stable.
- Since it consists of both hydrophobic and hydrophilic components, both hydrophobic and hydrophilic drugs can be incorporated.
- Organic solvents could be of natural origin, e.g.: sunflower oil, mustard oil, etc.
- Various bioactive agents can be incorporated.
- Suitable for topical drug delivery.
- Elegant non greasy formulation.
- Excellent adherence property to application site.
- Used for both local and systemic effect.

Evaluation parameters of organogels

After formulation and development there is need to evaluate the physical properties of organogels, for testing their efficacy, safety, potency. Various evaluation parameters include physical appearance, viscosity determination, water content, drug content, pH measurement, particle size, Zeta potential, extrudability studies, in vitro drug release studies and finally stability studies.

Applications of Organogels

In the literature many applications of organogels are reported which includes various types of drugs and bioactive agents' incorporation in organogels to achieve specific effects. Various

applications of organogels are strongly dependent on their properties. physical organogels have intermolecular non covalent interactions such as hydrogen bonding, pie stacking, Vander Val forces, electrostatic, coordination interactions or even solvophobic forces that are their primary mechanism for gelation which give rise to a transient and weak polymer network therefore these are less stable with low mechanical strength but relatively poor stability declares a good fit of possible biodegradability and rheological properties of drug delivery and processing applications. Chemical organogels are most stable and has better mechanical properties due to the strong covalently crosslink network and possess various applications. organogels are promising drug delivery systems for delivering various types of drugs such as formulation of eucalyptol and thymol organogel for GIT, oral and hepatic disorder[62], applications of organogel in drug delivery and their uses such as anti-icing, anti-fouling, drop manipulation, food delivery are mentioned.[63] There is successful formulation of olive oil based organogels for the topical application of fluconazole and other antifungals[64], conventional organogels and microemulsion lidocaine based organogels were formulated for exploring its therapeutic effect[65], formulation for non-invasive delivery of tenoxicam across the skin was successfully developed[66], indomethacin Pluronic lecithin loaded organogel showed a significant oedema inhibition as compared with oral indomethacin formulation[67], organogels in skin aging treatment and other skin disorders was used successfully[68], novel antimicrobial drug delivery system based on organogel was developed for limonene[69], various antimicrobial drugs was successfully incorporated in organogels, metronidazole loaded organogel showed almost similar antimicrobial activity against *Escheria coli* when compared to the commercially available metrogyl gel[70], Pluronic lecithin organogels of propolis to improve its availability and antimicrobial activity[71], roxithromycin loaded nano particles for follicular targeting in organogels was developed[72], and evaluated the suitability of lecithin organogels containing aceclofenac for topical application and compare in vitro and in vivo effects with conventionally used hydrogels.[73]

Also, 12 hydroxy stearic acid based organogel demonstrated as in situ forming implants for the controlled delivery of hydrophilic acyclovir and lipophilic clotrimazole.[74] The successful case of organogel based nano emulsion for the oral delivery of curcumin has established the approach to enhance bioavailability of pharmaceutical molecules using organic gels oral formulations.[75] formulation and evaluation stable ketoconazole organogel preparation to increase the solubility of ketoconazole and release the drug for prolonged period of time.[76] Dai et al. Reported an in situ organogel using soybean oil, stearic acid, and N-methyl-2-

pyrrolidinone to deliver poorly water soluble flunarizine hydrochloride for treatment of brain diseases by intraocular administration.[77] organogels are used in the food industries -the strategy of using edible organogels in the food processing is the current promising practice.[78,79]

Along with these existing applications many recent advances are done in formulation of organogels, various types of bioactive agents are incorporated in organogels by using different types of organogel for drug delivery. Various other applications in other fields help are also been explored such as parenteral in situ forming systems by loading pharmaceutical molecules that could be found by gelling in vivo.[80] food processing, replacement of trans and saturated fats for example organogel formed with monoglycerides and high oleic sunflower oil where also investigated to replace the commercial margarine in muffins[81] 1,3 propanediol loaded organogel showed bactericidal activity by 80%[82] some permeation enhancers were reported to incorporated within organogels such as urea, terpenes, essential oils[83], organogels prepared with soya lecithin, vegetable oil showed effective cutaneous drug delivery therapy[84], oleic acid lanolin and poloxamer mixture enhanced the topical administration of the lidocaine[85], dermal delivery of various bioactive agents such as vitamin c[86], aceclofenac[87,88], calcineurin inhibitors[89], epigenin[90], glycolic acid[91], aromatic tetra amidines[92], trazodone as psychopharmaceuticals[93] by using lecithin organogels was successfully done. Aryl cyclohexanol derivatives as Topical formulations[94] Polymeric organogelators such as Polycarbonate, polyesters, poly(ethylene glycol) and poly(alkylene) Used in the preparation of organogels and sustained release formulations for rectal administration.[95] Gemini gelators such as N-lauryl-L-lysine ethyl ester are used as Topical formulations.[94] Synthetic tripeptide are used in Drug delivery, optoelectronics, sensors.[96] Low molecular weight gelators such as Fatty acids and n-alkanes have High ability to immobilize apolar solvents at small concentrations (< 2%) which finds many applications in Food industry[97] anti-inflammatory effect of ricinolic acid poloxamer gel system was improved for transdermal therapy[98], A transdermal formulation of methadone in PLO gel became available through compounding pharmacies[99] Connor and Haine, describes the transdermal delivery to the eye with a therapeutically effective amount of progestogen, a testosterone, in treating dry eye[100] and furthermore organogels are gaining attraction with respect to the development of nutraceuticals delivery based on the self-assembly mechanisms of the molecules present in them.[101,102] In summary organogels finds potential application in drug delivery as well as in other areas such as sensors, they find application of conductive

materials and flexible energy storage devices but are not fully explored yet. Overall organogels finds various applications in various fields which needs to be further explored.

Summary and outlook

This review focuses on the various aspects of organogels, their basic composition, different types of organogelators, mechanism of organ gelation, mechanism of skin permeation, fabrication methods and their applications. Together with drug delivery organogels are widely explored for practical applications as anti- icing anti-fouling coatings. their various characteristics such as biocompatibility, biodegradability and versatility of organogelators and solvents allow organogels hybridising and stabilization with bioactive agents in the microporous structured matrix and possess desired thermodynamic behaviour and rheological properties to customising their potential as drug delivery and cosmetic system. According to recent studies edible artificial organogels structured with vegetable oil have been developed in food processing field for the fat replacement.

Despite the great progress of organogels challenges still remain compared to the hydrogels. organogel suffer from an obvious drawback deriving from the organic solvents, the major component high priced organic solvents lead to in evitable high cost in organogel manufacturing, the durability of organic phase inside network and the stability of the liquid layer require further considerations especially for the application in the relatively harsh conditions or strictly controlled domain. organogels still face serious drawbacks for example in case of food processing the stability of organogels directly determines the shelf time of final food product, in case of acting as interfacial material their interface interactions are deemed to be weak leading to the inefficiency and high usage cost, their low mechanical strength restricts them from diverse applications. In addition, biomedical effect of organic solvents in organogels on the environment and human demands further evaluation before practical employment especially in the field of drug delivery, food delivery and cosmetics formulations.

In the future organogels are expected to explored fully for their various unique properties, their applications and self-healing mechanisms. Stimuli responsiveness of organogels can be used for long term utilization will lead to formulation of novel organogels with novel formulation strategies. Furthermore, types of bioactive agents as well as drug can be incorporated within organogels for their intended effect successfully.

REFERENCES

1. Zeng L, Lin X, Li P, Liu FQ, Guo H, Li WH. Recent advances of organogels: From fabrications and functions to applications. Progress in Organic Coatings, 2021 Oct 1; 159: 106417.
2. George M, Tan G, John VT, Weiss RG. Urea and Thiourea Derivatives as Low Molecular-Mass Organogelators. Chemistry–A European Journal, 2005 May 20; 11(11): 3243-54.
3. Cui J, Zheng Y, Shen Z, Wan X. Alkoxy tail length dependence of gelation ability and supramolecular chirality of sugar-appended organogelators. Langmuir, 2010 Oct 5; 26(19): 15508-15.
4. Murdan S, Gregoriadis G, Florence AT. Inverse toroidal vesicles: precursors of tubules in sorbitan monostearate organogels. International Journal of pharmaceutics, 1999 Jun 10; 183(1): 47-9.
5. Robinson RC. Plastibase, a hydrocarbon gel ointment base. Bulletin of the School of Medicine (Baltimore, Md.), 1955 Jul; 40(3): 86-9.
6. Bajaj AK, Gupta SC, Chatterjee AK. Plastibase: a new base for patch testing of metal antigens. International journal of dermatology, 1990; 29(1).
7. Kawata M, Suzuki T, Kim NS, Ito T, Kurita A, Miyagoe Y, Goto S. Preparation and evaluation of Eudragit gels. II: In vitro release of salicylic acid, sodium salicylate, and ketoprofen from Eudragit L and S organogels. Journal of pharmaceutical sciences, 1991 Nov 1; 80(11): 1072-4.
8. Jones MC, Tewari P, Blei C, Hales K, Pochan DJ, Leroux JC. Self-assembled nanocages for hydrophilic guest molecules. Journal of the American Chemical Society, 2006 Nov 15; 128(45): 14599-605.
9. Grace DA, Rogers JA, Skeith KE, Anderson KE. Topical diclofenac versus placebo: a double blind, randomized clinical trial in patients with osteoarthritis of the knee. The Journal of rheumatology, 1999 Dec; 26(12): 2659-63.
10. Mahler P, Mahler F, Duruz H, Ramazzina M, Liguori V, Mautone G. Double-blind, randomized, controlled study on the efficacy and safety of a novel diclofenac epolamine gel formulated with lecithin for the treatment of sprains, strains and contusions. Drugs under experimental and clinical research, 2003 Jan 1; 29(1): 45-52.
11. Spacca G, Cacchio A, Forgacs A, Monteforte P, Rovetta G. Analgesic efficacy of a lecithin-vehiculated diclofenac epolamine gel in shoulder periarthritis and lateral

epicondylitis: a placebo-controlled, multicenter, randomized, double-blind clinical trial. Drugs under experimental and clinical research, 2005 Jan 1; 31(4): 147-54.

12. Agrawal GP, Juneja M, Agrawal S, Jain SK, Pancholi SS. Preparation and characterization of reverse micelle based organogels of piroxicam. Die Pharmazie-An International Journal of Pharmaceutical Sciences, 2004 Mar 1; 59(3): 191-3.
13. Nastruzzi C, Gambari R. Antitumor activity of (trans) dermally delivered aromatic tetra-amidines. Journal of controlled release, 1994 Feb 1; 29(1-2): 53-62.
14. Bhatnagar S, Vyas SP. Organogel-based system for transdermal delivery of propranolol. Journal of microencapsulation, 1994 Jan 1; 11(4): 431-8.
15. Aboofazeli R, Zia H, Needham TE. Transdermal delivery of nicardipine: an approach to in vitro permeation enhancement. Drug Delivery, 2002 Jan 1; 9(4): 239-47.
16. Shaikh IM, Jadhav KR, Gide PS, Kadam VJ, Pisal SS. Topical delivery of aceclofenac from lecithin organogels: preformulation study. Current Drug Delivery, 2006 Oct 1; 3(4): 417-27.
17. Dreher F, Walde P, Walther P, Wehrli E. Interaction of a lecithin microemulsion gel with human stratum corneum and its effect on transdermal transport. Journal of controlled release, 1997 Mar 17; 45(2): 131-40.
18. Lim PF, Liu XY, Kang L, Ho PC, Chan YW, Chan SY. Limonene GP1/PG organogel as a vehicle in transdermal delivery of haloperidol. International journal of pharmaceutics, 2006 Mar 27; 311(1-2): 157-64.
19. Pénzes T, Blazso G, Aigner Z, Falkay G, Erős I. Topical absorption of piroxicam from organogels—in vitro and in vivo correlations. International journal of pharmaceutics, 2005 Jul 14; 298(1): 47-54.
20. Suzuki M, Owa S, Shirai H, Hanabusa K. New Poly (propylene glycol)-and Poly (ethylene glycol)-Based Polymer Gelators with l-Lysine. Macromolecular rapid communications, 2005 May 19; 26(10): 803-7.
21. Goto S, Kawata M, Suzuki T, Kim NS, Ito C. Preparation and evaluation of Eudragit gels. I: Eudragit organogels containing drugs as rectal sustained-release preparations. Journal of pharmaceutical sciences, 1991 Oct 1; 80(10): 958-61.
22. Bialik-Wąs K, Pielichowski K, Zielina M. Acrylic hydrogels containing MET-loaded poly (acrylic acid-co-methyl methacrylate) micro-and nanoparticles. Journal of Polymer Research, 2015 Jan; 22(1): 1-2.

23. abiri K, Azizi A, Zohuriaan-Mehr MJ, Marandi GB, Bouhendi H. Poly (acrylic acid–sodium styrene sulfonate) organogels: preparation, characterization, and alcohol superabsorbency. Journal of Applied Polymer Science, 2011 Mar 5; 119(5): 2759-69.
24. Kabiri K, Azizi A, Zohuriaan-Mehr MJ, Marandi GB, Bouhendi H. Alcohophilic gels: Polymeric organogels composing carboxylic and sulfonic acid groups. Journal of Applied Polymer Science, 2011 Jun 15; 120(6): 3350-6.
25. Bera R, Dey A, Chakrabarty D. Studies on Gelling Characteristics of N-Tertiary Butyl Acrylamide–Acrylic Acid Copolymer. Advances in polymer technology, 2014 Jun; 33(2).
26. Stortz TA, Zetzl AK, Barbut S, Cattaruzza A, Marangoni AG. Edible oleogels in food products to help maximize health benefits and improve nutritional profiles. Lipid Technology, 2012 Jul; 24(7): 151-4.
27. Upadhyay KK, Tiwari C, Khopade AJ, Bohidar HB, Jain SK. Sorbitan ester organogels for transdermal delivery of sumatriptan. Drug development and industrial pharmacy, 2007 Jan 1; 33(6): 617-25.
28. Richards H, Thomas CP, Bowen JL, Heard CM. In-vitro transcutaneous delivery of ketoprofen and polyunsaturated fatty acids from a pluronic lecithin organogel vehicle containing fish oil. Journal of pharmacy and pharmacology, 2006 Jul; 58(7): 903-8.
29. Dey A, Chakraborty M, Dey S, Nandy P. Implementations of Green synthesized Nanoparticles from Biomedical to Construction Industry: An approach of sustainability. International J. of Biomed Research, 2021; 1(1).
30. Bastiat G, Plourde F, Motulsky A, Furtos A, Dumont Y, Quirion R, Fuhrmann G, Leroux JC. Tyrosine-based rivastigmine-loaded organogels in the treatment of Alzheimer's disease. Biomaterials, 2010 Aug 1; 31(23): 6031-8.
31. Singh VK, Pramanik K, Ray SS, Pal K. Development and characterization of sorbitan monostearate and sesame oil-based organogels for topical delivery of antimicrobials. Aaps Pharmscitech, 2015 Apr; 16(2): 293-305.
32. Dai M, Bai L, Zhang H, Ma Q, Luo R, Lei F, Fei Q, He N. A novel flunarizine hydrochloride-loaded organogel for intraocular drug delivery in situ: Design, physicochemical characteristics and inspection. International Journal of Pharmaceutics, 2020 Feb 25; 576: 119027.
33. Liu DE, Chen Q, Long YB, Ma J, Gao H. A thermo-responsive polyurethane organogel for norfloxacin delivery. Polymer Chemistry, 2018; 9(2): 228-35.

34. Smith NL, Coukouma AE, Wilson DC, Ho B, Gray V, Asher SA. Stimuli-responsive pure protein organogel sensors and biocatalytic materials. ACS applied materials & interfaces, 2019 Dec 10; 12(1): 238-49.
35. Yao X, Wu S, Chen L, Ju J, Gu Z, Liu M, Wang J, Jiang L. Self-Replenishable Anti-Waxing Organogel Materials. Angewandte Chemie International Edition., 2015 Jul 27; 54(31): 8975-9.
36. Dey A, Chakraborty M, Dey S, Nandy P. Implementations of Green synthesized Nanoparticles from Biomedical to Construction Industry: An approach of sustainability. International J. of Biomed Research, 2021; 1(1).
37. Khan F, Maurya R, Ramteke S. ORGANOGEL CONTROLLED RELEASE FORMULATION: A NOVEL APPROACH.
38. Esposito CL, Kirilov P, Roullin VG. Organogels, promising drug delivery systems: An update of state-of-the-art and recent applications. Journal of controlled release, 2018 Feb 10; 271: 1-20.
39. Yang Y, Huang Q, Niu L, Wang D, Yan C, She Y, Zheng Z. Waterproof, ultrahigh areal-capacitance, wearable supercapacitor fabrics. Advanced Materials, 2017 May; 29(19): 1606679.
40. Tasaki-Handa Y, Abe Y, Ooi K. Fabrication of a monolithic cryogel from the cyclohexane organogel of a coordination polymer based on a phosphoester. RSC advances, 2016; 6(75): 71404-8.
41. Bhattacharya C, Kumar N, Sagiri SS, Pal K, Ray SS. Development of span 80–tween 80 based fluid-filled organogels as a matrix for drug delivery. Journal of pharmacy & bioallied sciences, 2012 Apr; 4(2): 155.
42. Raut S, Bhadoriya SS, Uplanchiwar V, Mishra V, Gahane A, Jain SK. Lecithin organogel: A unique micellar system for the delivery of bioactive agents in the treatment of skin aging. Acta Pharmaceutica Sinica B., 2012 Feb 10; 2(1): 8-15.
43. Wang D, Zhao J, Liu X, Sun F, Zhou Y, Teng L, Li Y. Parenteral thermo-sensitive organogel for schizophrenia therapy, in vitro and in vivo evaluation. European Journal of Pharmaceutical Sciences, 2014 Aug 18; 60: 40-8.
44. Lim PF, Liu XY, Kang L, Ho PC, Chan YW, Chan SY. Limonene GP1/PG organogel as a vehicle in transdermal delivery of haloperidol. International journal of pharmaceutics, 2006 Mar 27; 311(1-2): 157-64.

45. Balata G, El Nahas HM, Radwan S. Propolis organogel as a novel topical delivery system for treating wounds. Drug delivery, 2014 Feb 1; 21(1): 55-61.
46. Allen Jr LV. Nifedipine 160 mg/mL in Pluronic Lecithin Organogel. US Pharm., 2011; 36(12): 39-40.
47. Simsolo EE, Eroğlu İ, Tanrıverdi ST, Özer Ö. Formulation and evaluation of organogels containing hyaluronan microparticles for topical delivery of caffeine. AAPS Pharm Sci Tech., 2018 Apr; 19(3): 1367-76.
48. Gopalan K, Jose J. Development of amphotericin b Based organogels against mucocutaneous fungal infections. Brazilian Journal of Pharmaceutical Sciences, 2020 Sep 18; 56.
49. Sharma AK, Naruka PS, Soni SL, Sarangdewot YS, Khandelwal M, Aman S. Formulation, Development and Evaluation of Luliconazoe Organogel. International Journal of Current Pharmaceutical Review and Research, 12(1).
50. Shah DK, Sagiri SS, Behera B, Pal K, Pramanik K. Development of olive oil based organogels using sorbitan monopalmitate and sorbitan monostearate: A comparative study. Journal of applied polymer science, 2013 Jul 15; 129(2): 793-805.
51. Binita K. *Development and Characterization of Imatinib Mesylate Loaded Pluronic Lecithin Organogel* (Doctoral dissertation, PSG College of Pharmacy, Coimbatore).
52. Lalitha K, Nagarajan S. Strongly fluorescent organogels and self-assembled nanostructures from pyrene coupled coumarin derivatives: application in cell imaging. Journal of Materials Chemistry B., 2015; 3(28): 5690-701.
53. Thakur K, Mahajan A, Sharma G, Singh B, Raza K, Chhibber S, Katare OP. Implementation of Quality by Design (QbD) approach in development of silver sulphadiazine loaded egg oil organogel: An improved dermatokinetic profile and therapeutic efficacy in burn wounds. International Journal of Pharmaceutics, 2020 Feb 25; 576: 118977.
54. de Francisco LM, Pinto D, Rosseto HC, de Toledo LD, Dos Santos RS, Costa PJ, Oliveira MB, Sarmento B, Rodrigues F, Bruschi ML. Design and characterization of an organogel system containing ascorbic acid microparticles produced with propolis by-product. Pharmaceutical Development and Technology, 2020 Jan 2; 25(1): 54-67.
55. Raut S, Suruse PB, Shivhare UD, Bhusari KP. Development and evaluation of non-ionic surfactant based organogels for transdermal delivery of zidovudine. International Journal of Comprehensive Pharmacy, 2010; 3(7): 1-7.

56. Lee SK, Lee JH, Choi YW. A Novel Organogel System Capable of Enhancing Skin Penetration Characteristics of Acyclovir. Journal of Pharmaceutical Investigation, 2006; 36(6): 401-3.
57. Bourdon F, Lecoeur M, Leconte L, Ultré V, Kouach M, Odou P, Vaccher C, Foulon C. Evaluation of Pentravan®, Pentravan® Plus, Phytobase®, Lipovan® and Pluronic Lecithin Organogel for the transdermal administration of antiemetic drugs to treat chemotherapy-induced nausea and vomiting at the hospital. International journal of pharmaceutics, 2016 Dec 30; 515(1-2): 774-87.
58. El-Nassan HB, ElMeshad AN, Wadie W, Sayed RH. Synthesis, Characterization and Biocompatibility of N-palmitoyl L-alanine-based Organogels as Sustained Implants of Granisetron and Evaluation of their Antiemetic Effect. Pharmaceutical Research, 2018 Aug; 35(8): 1-7.
59. Pisal S, Shelke V, Mahadik K, Kadam S. Effect of organogel components on in vitro nasal delivery of propranolol hydrochloride. Aaps Pharmscitech, 2004 Dec; 5(4): 92-100.
60. Agrawal V, Gupta V, Ramteke S, Trivedi P. Preparation and evaluation of tubular micelles of pluronic lecithin organogel for transdermal delivery of sumatriptan. Aaps PharmSciTech., 2010 Dec; 11(4): 1718-25.
61. Sreedevi T, Ramya D, Vedha H. An emerging era in topical delivery: Organogels. Int. J. Drug Dev. Res., 2012; 4(2): 35-40.
62. Singh G, Khan MW, Patel A. Formulation and Biological Implication of Eucalyptus Globulus and Trachspermum ammi Organogel for Topical Delivery. Reviews in Pharmacy and Pharmaceutical Sciences, 2022 Jan 3; 1(1): 1-4.
63. Esposito CL, Kirilov P, Roullin VG. Organogels, promising drug delivery systems: An update of state-of-the-art and recent applications. Journal of controlled release, 2018 Feb 10; 271: 1-20.
64. MMA F. Olive oil based organogels for effective topical delivery of fluconazole: in-vitro antifungal study.
65. Hamed R, Farhan A, Abu-Huwaij R, Mahmoud NN, Kamal A. Lidocaine microemulsion-laden organogels as lipid-based systems for topical delivery. Journal of Pharmaceutical Innovation, 2020 Dec; 15(4): 521-34.
66. Yassin TM, Saleh KI, Sarhan H, Osman SK. Formulation and Evaluation of Sorbitanmonostearate Organogel as a Topical Delivery System for Tenoxicam.

67. Mohammed AM, Faisal W, Saleh KI, Osman SK. Self-assembling organogels based on pluronic and lecithin for sustained release of etodolac: In Vitro and in vivo correlation. Current Drug Delivery, 2017 Nov 1; 14(7): 926-34.
68. Mehta C, Bhatt G, Kothiyal P. A Review on organogel for skin aging. Indian Journal of Pharmaceutical and Biological Research, 2016 Jul 1; 4(3): 28.
69. Zahi MR, Liang H, Yuan Q. Improving the antimicrobial activity of D-limonene using a novel organogel-based nanoemulsion. Food Control, 2015 Apr 1; 50: 554-9.
70. Singh VK, Anis A, Banerjee I, Pramanik K, Bhattacharya MK, Pal K. Preparation and characterization of novel carbopol based bigels for topical delivery of metronidazole for the treatment of bacterial vaginosis. Materials Science and Engineering: C., 2014 Nov 1; 44: 151-8.
71. Balata G, El Nahas HM, Radwan S. Propolis organogel as a novel topical delivery system for treating wounds. Drug delivery, 2014 Feb 1; 21(1): 55-61.
72. Główka E, Wosicka-Frąckowiak H, Hyla K, Stefanowska J, Jastrzębska K, Klapiszewski Ł, Jesionowski T, Cal K. Polymeric nanoparticles-embedded organogel for roxithromycin delivery to hair follicles. European Journal of Pharmaceutics and Biopharmaceutics, 2014 Sep 1; 88(1): 75-84.
73. Shaikh I, Jadhav SL, Jadhav KR, Kadam VJ, Pisal SS. Aceclofenac organogels: in vitro and in vivo characterization. Current drug delivery, 2009 Jan 1; 6(1): 1-7.
74. Esposito CL, Tardif V, Sarrazin M, Kirilov P, Roullin VG. Preparation and characterization of 12-HSA-based organogels as injectable implants for the controlled delivery of hydrophilic and lipophilic therapeutic agents. Materials Science and Engineering: C., 2020 Sep 1; 114: 110999.
75. Yu H, Huang Q. Improving the oral bioavailability of curcumin using novel organogel-based nano emulsions. Journal of agricultural and food chemistry, 2012 May 30; 60(21): 5373-9.
76. Patil MP, Shinde GP, Kshirsagar SJ, Parakh DR. Development and characterization of ketoconazole loaded organogel for topical drug delivery. Inventi Rapid NDDS., 2015; 3: 1-0.
77. Dai M, Bai L, Zhang H, Ma Q, Luo R, Lei F, Fei Q, He N. A novel flunarizine hydrochloride-loaded organogel for intraocular drug delivery in situ: Design, physicochemical characteristics and inspection. International Journal of Pharmaceutics, 2020 Feb 25; 576: 119027.

78. Pehlivanoğlu H, Demirci M, Toker OS, Konar N, Karasu S, Sagdic O. Oleogels, a promising structured oil for decreasing saturated fatty acid concentrations: Production and food-based applications. Critical reviews in food science and nutrition, 2018 May 24; 58(8): 1330-41.
79. Hwang HS, Singh M, Winkler-Moser JK, Bakota EL, Liu SX. Preparation of margarines from organogels of sunflower wax and vegetable oils. Journal of food science, 2014 Oct; 79(10): C1926-32.
80. Hu Y, Xu L, Zhou C, Wu H, Gao W. Intratumoral injectable in situ-forming low-molecular-weight organogels against subcutaneous tumor. Nanomedicine: Nanotechnology, Biology and Medicine, 2016; 2(12): 517.
81. Giacomozzi AS, Carrín ME, Palla CA. Muffins elaborated with optimized monoglycerides oleogels: From solid fat replacer obtention to product quality evaluation. Journal of food science, 2018 Jun; 83(6): 1505-15.
82. Liu DE, Chen Q, Long YB, Ma J, Gao H. A thermo-responsive polyurethane organogel for norfloxacin delivery. Polymer Chemistry, 2018; 9(2): 228-35.
83. Wang K, Jia Q, Han F, Liu H, Li S. Self-assembled L-alanine derivative organogel as in situ drug delivery implant: characterization, biodegradability, and biocompatibility. Drug development and industrial pharmacy, 2010 Dec 1; 36(12): 1511-21.
84. Park H, Yang S, Kang JY, Park MH. On-demand drug delivery system using micro-organogels with gold nanorods. ACS Medicinal Chemistry Letters, 2016 Dec 8; 7(12): 1087-91.
85. A.A. Vigato, S.M. Querobino, N.C. de Faria, A.C.P. de Freitas, G.R. Leonardi, E. de Paula, C.M.S. Cereda, G.R. Tófoli, D.R. de Araujo, Synthesis and characterization of nanostructured lipid-poloxamer organogels for enhanced skin local anesthesia, Eur. J. Pharm. Sci., 2019; 128: 270–278.
86. Vintiloiu A, Leroux JC. Organogels and their use in drug delivery—a review. Journal of controlled release, 2008 Feb 11; 125(3): 179-92.
87. Kumar R, Katare OP. Lecithin organogels as a potential phospholipid-structured system for topical drug delivery: a review. Aaps Pharmscitech, 2005 Jun; 6(2): E298-310.
88. Dreher F, Walde P, Luisi PL, Elsner P. Human skin irritation studies of a lecithin microemulsion gel and of lecithin liposomes. Skin Pharmacology and Physiology, 1996; 9(2): 124-9.

89. Garg BJ, Saraswat A, Bhatia A, Katare OP. Topical treatment in vitiligo and the potential uses of new drug delivery systems. Indian Journal of dermatology, venereology and Leprology, 2010 May 1; 76: 231.
90. Crandall WT, inventor. Method for topical treatment of scars with protein kinase C inhibitors. United States patent US 6, 306, 383. 2001 Oct 23.
91. Sand BJ, Babich M, Haghighi AZ, inventors; Nuviance Inc, assignee. Transdermal drug delivery compositions and topical compositions for application on the skin. United States patent application US 12/281,768. 2009 Feb 26.
92. Gupta S, Singh RP, Sarkar A, Panchal H, Pandey D. Organogel: a viable alternative for existing carrier system. Int J Compr Pharm., 2011; 2: 1-5.
93. Murdock RW, Williams CD, inventors; Pharmaceutical Applications Associates LLC, assignee. Method and composition for transdermal administration of pharmacologic agents. United States patent US 6,290,986. 2001 Sep 18.
94. Bertrand H, Kyriazis M, Reeves KD, Lyftogt J, Rabago D. Topical mannitol reduces capsaicin-induced pain: results of a pilot-level, double-blind, randomized controlled trial. PM&R., 2015 Nov 1; 7(11): 1111-7.
95. Goto S, Kawata M, Suzuki T, Kim NS, Ito C. Preparation and evaluation of Eudragit gels. I: Eudragit organogels containing drugs as rectal sustained-release preparations. Journal of pharmaceutical sciences, 1991 Oct 1; 80(10): 958-61.
96. Adams DJ. Dipeptide and tripeptide conjugates as low-molecular-weight hydrogelators. Macromolecular bioscience, 2011 Feb 11; 11(2): 160-73.
97. Toro-Vazquez JF, Morales-Rueda JA, Dibildox-Alvarado E, Charó-Alonso M, Alonzo-Macias M, González-Chávez MM. Thermal and textural properties of organogels developed by candelilla wax in safflower oil. Journal of the American Oil Chemists' Society, 2007 Nov; 84(11): 989-1000.
98. Alsaab H, Bonam SP, Bahl D, Chowdhury P, Alexander K, Boddu SH. Organogels in drug delivery: a special emphasis on pluronic lecithin organogels. Journal of Pharmacy & Pharmaceutical Sciences, 2016 Jul 12; 19(2): 252-73.
99. Ghosh TK, Bagherian A. Development of a transdermal patch of methadone: in vitro evaluation across hairless mouse and human cadaver skin. Pharmaceutical development and technology, 1996 Jan 1; 1(3): 285-91.
100. Connor CG, Haine C, inventors; Southern College Of Optometry, assignee. Treatment for dry eye using testosterone and progestagen. 2008 Jun 12.

101. Pehlivanoğlu H, Demirci M, Toker OS, Konar N, Karasu S, Sagdic O. Oleogels, a promising structured oil for decreasing saturated fatty acid concentrations: Production and food-based applications. Critical reviews in food science and nutrition, 2018 May 24; 58(8): 1330-41.
102. Martins AJ, Vicente AA, Cunha RL, Cerqueira MA. Edible oleogels: An opportunity for fat replacement in foods. Food & function, 2018; 9(2): 758-73.