Organogel as a drug delivery system

Gels are defined as three-dimensional crosslinked network structures with an immobilized external solvent phase. If the immobilized solvent is an apolar liquid, the gels are referred as organogels. The methods of preparation of organogels are very simple and easy. Of late, organogels have seen an increased used as drug delivery vehicles due to patient compliance and its ability towards tailored release of the bioactive agents. The current review gives an overview on the mechanisms of organogel formation, various characterization techniques and applications of organogels in controlled delivery of bioactive agents.

Gels are quite often defined as three-dimensional networked structures, which have the ability to immobilize a liquid phase 1. Gelled systems have been used to develop various products both for daily activities and biomedical importance (e. g. drug delivery systems, toothpastes, shampoos) 2. This has been attributed to the easy handling of these products and the structuring ability of the gels. Gels are basically composed of two components, viz. a liquid phase (either polar or apolar) and a gelling agent (often regarded as gelator, which undergoes interaction to form a three-dimensional structure) 1. Based on the type of interaction an gelator is undergoing so as to form three-dimensional networks, gels may be categorized either as physical or chemical gels 3. If the interaction amongst the gelator molecules involve formation of covalent bonds, then the gelled structure is regarded as chemical gels whereas the formation of physical gels involve the physical interactions amongst the gelator molecules, i. e. no covalent bond formation is involved 4. Often, it has been found that the physical gels are thermoreversible (i. e. it appears as gel below a critical

temperature whereas it appears as sol above the critical temperature) and viscoelastic (shows solid-like behavior at lower shear rates whereas it starts to flow at higher shear rates) in nature 3, 5, for example, gelatin gels and sorbitan monooleate organogels. Depending on the polarity of liquid immobilized within the networked structures, the gels may be regarded either as hydrogel (polar solvent) or organogel (apolar solvent) 4, 6. Owing to the solid-like consistency under normal conditions, various gels have been used as a structuring agent in food and pharmaceutical industries. In the current review, attempts will be made to discuss about the probable mechanisms of organogel formation, their characterization methods and their application in the development of the controlled delivery systems.

Organogelators

It is now clear that the organogels are semisolid systems having immobilized apolar solvent as the continuous phase. The components, which have the ability to undergo interaction amongst each other so as to form a networked structure having the capability to immobilize the apolar solvent, are regarded as organogelators. The organogelators, in general, undergo self-assembly under suitable conditions to give rise to organogel. n-alkanes (where number of carbon atoms are 24, 28, 32 and 36) are the simplest form of organogelators 6. Some commonly used organogelators include 12 hydroxyoctadecanoic acid 7, sorbitan monostearate 8, steroids and their derivatives 4, bis-urea compounds and carbohydrate derivatives 9. In the current section, some commonly used organogelators will be discussed in brief.

Low Molecular Weight Organogelators

The organogelators having molecular weight < 3000 Da are categorized as low molecular weight organogelators (LMWOrs). Many LMWOrs have been found by chance 10. The formation of the gels occurs due to the interaction of fibered structures, which are developed due to the self-assembly of organogelators. These organogelator fibers may be either solid (formed due to the precipitation of the organogelator from the solution of organogelator in an apolar solvent) or fluid-filled (formed due to the entrapment of aqueous phase within the tubular reverse micelles) 11. The immobilization of the apolar solvent within the networked structures has been attributed to the surface tension acting amongst the molecules of organogelators and apolar solvent 4. The solubility profile of the LMWOrs in the apolar solvent and the presence of chiral centers in the organogelator play an important role in the formation of the organogel. The organogelators which forms solid-fiber structures generally have chiral centers whereas the organogelators which are involved in the formation of fluid-fiber structures usually lacks chiral centers within its chemical structure 12. Hydrogen bonding plays an important role in the development of organogels when peptides, sugars and bis-urea compounds are used as an organogelators whereas Vander walls force plays a dominant role when long chain alkanes are used as organogelators. When cholesterol derivatives are used as organogelators, Ï€-Ï€ interactions prevails in the organogels.

Polymeric Organogelators

The polymeric organogelators may either undergo chemical reaction or physical interaction so as to form a networked structure. The typical example of organogel includes polyethylene organogels, commonly used in the

preparation of ointment. This usually consists of low molecular weight polyethylene in mineral oil and is colorless in nature 4, 11. The other polymeric organogelators include methyl methacrylate and methacrylic acid copolymers 13 and have been used for the development of rectal suppositories.

Anthryl and Anthraquinone Derivative Organogelators

These organogelators have anthracene moieties in its structure, which helps in establishing Ï€-Ï€ interaction with apolar solvents (e. g. alcohols, ethers, ketones, cyclohexane, DMSO and halogenated molecules). The common examples of the organogelators in this category include 2, 3 Didecycloxytetracene (DDOA) and 2, 3 dihexadecycloxytetracene (DHDOT) 8, 14.

Sugar Based Organogelators

The organogelators in this category may be identidfied with the presence of Î±-glucose moiety and an aromatic moiety in its structure. The formation of the fiber- like structure may be accounted to the development of intermolecular hydrogen bonds amongst the sugar moieties with the subsequent exposure of the aromatic moieties to the apolar solvent. These compounds also have the capability to gel polar solvents. The mechanism of gelling in this case includes Ï€-Ï€ interaction amongst the sugar moieties and the polar solvent. The example of the organogelator in this category include derivatives of methyl glycosides of 4, 6-obenzylidine 15.

ALS Organogelators

The organogelators in this category have an aromatic moiety (A), which is connected with a steroidal group (S) through a linker group (L). The

mechanism of formation of a gelled structure may be attributed to the dipole-dipole interaction and Vander walls force. The example of organogelator in this category includes cholesteryl 4-(2-anthryloxy) butanoate (CAB) 16.

Gemini Organogelators

The dictionary meaning of the word Gemini is twin. The Gemini organogelators basically have two L-Lysine derivatives, which are linked to alkylene chains through amide bonds. The property of the organogelation is dependent on the length of the alkylene chains. In general, it has been found that there is a decrease in the ability of the organogelation with a subsequent increase in the chain length of alkylene chains. Bis (N-lauroyl-t-lysine ethyl ester) oxyl amide is a classical example of this category of organogelators and has the ability to immobilize a large number of apolar solvents including alcohols, ketones, cyclic ethers and acetonitrile. The other examples of Gemini organogelators are hexyl, decyl, dodecyl, 2-ethyl-1-hexyl and 3, 5, 5-trimethylhexyl derivatives of oxalyl amide 17.

Amino Acid Based Organogelators

Brosse et al. synthesized amino acid-based LMWOrs, which were able to immobilize the apolar solvents even at low concentrations (‰¤ 0. 2 wt %). The gelled structures developed using these gelators were thermostable. The group further reported that the gelation capability of these gelators varied with the change in the side groups of the amino acids 18. In a recent study, a two-component organogelation system was described. The system employed a mixture of Nepsilon-dodecyl-L-lysine esters and N-dodecyl-L-amino acids (valine, phenylalanine, alanine, glycine, L-lysine), which resulted in an

interaction amongst the amine group of the esters and the acidic group of the amino acids. The formation of the gelled structure was attributed to the entanglement of the nanofibers formed as a result of the interaction amongst the two components. A rigid gel is formed when phenylalanine derivative of N-dodecyl-L-amino acid is used whereas a thermostable gel is obtained when lysine derivative of N-dodecyl-L-amino acid is used for the gellation of dodecane. The authors concluded that the properties of the gels may be tailored by varying the composition of the ester and amino acid components 19.

Vegetable Oil Organogelators

Organic gelators (e. g. 12-hydroxystearic acid, c-oryzanol and b-sitosterol) have been found to be useful in structuring edible oils and to restrict the phase separation in the food products 20-23. Organogels developed using mixtures of c-oryzanol and b-sitosterol are transparent 21.

Mechanisms of Organogel Formation

Three mechanisms of organogel formation have been proposed till date. These mechanisms discuss about the formation of networked structure by different phenomena. The first mechanism explains the formation of networked structures with fluid-filled fibers while the second mechanism explains about the formation of networked structures with solid fibers and the third mechanism deals with the crosslinking of polymers for creating the networked structures. The process of immobilization of the apolar solvents within these networked structures was attributed to the surface active phenomena present amongst the gelators (forming the networked structures) and the apolar solvent molecules.

As per the first mechanism, organogels are formed by the entanglement of the instantaneously formed fluid-filled fibers. When surfactants are dissolved in an apolar solvent, they result in the formation of reverse micelles. The instantaneous formation of the reverse micelles help in maintaining a low interfacial tension amongst polar and apolar phases and attains a thermodynamic equilibrium. Subsequent additions of the water to the above reverse micellar solution results in the formation of tubular reverse micelles. Further addition of water results in the elongation in the tubular structure, which gets entangled, thereby forming a three-dimensional network. Most common examples of this category of organogels include lecithin organogel and pluronic lecithin organogel 8. The mechanism of formation of organogels by this method has been shown in figure 1.

The second mechanism deals with the formation of the networked structures due to the interaction amongst the solid fibers (Figure 2). This mechanism utilizes the solubility profile of the gelators in the apolar solvent for the development of organogels. The gelators used for developing the organogels are solubilized in the apolar solvent at higher temperature. Subsequently, the heated solution of the gelator in the apolar solvent is cooled down. This results in the decrease in the solubility constant of the gelator, resulting in the precipitation of the gelators which undergo self-alignment to form solid fibers. The fibers, hence formed, undergo physical interaction thereby resulting in the formation of gelled structure. Most common examples of this category of organogels include sorbitan monooleate organogels 8.

The third mechanism deals with the in situ crosslinking of the polymeric organogelators in the presence of the apolar solvent, which results in the

entrapment of the apolar solvent into the crosslinked polymeric network (Figure 3). The presence of the solvent within the polymeric structure prevents the structure from collapsing. The method of crosslinking may either be chemical or physical 11.

Characterization of Organogels

Due to the presence of self-assembled structures, the characterization of the organogels is a complex phenomenon. Certain methods have been established to study the structural, thermal and rheological properties of the organogles. Apart from this, biocompatibility studies of the organogels are also necessary to establish it utility as a product for human use. The following section will discuss about the different methods employed for the characterization of organogels.

Ternary Phase Diagrams

Typically an organogel contains a gelator and an apolar solvent. Many organogels are formulated so as to accommodate a polar solvent. The concentration of the gelator, apolar solvent and the polar solvent play an important role in the preparation of an organogel. A particular concentration of the gelator is needed before it can induce the gelation of the apolar solvent, this is regarded as the critical gelator concentration. If the concentration of the organogelator is below the critical concentration, the gelators fail to induce the organogelation and occur as a liquid phase. Similarly, there is an upper critical limit of accommodating the aqueous phase into the organogel. If the amount of the aqueous phase is above the upper critical limit, it may not allow the formation of networked structure and the system fails to induce gelation. This phenomenon of disrupting the gelled

structure with the addition of excess water is known as gel solvation. It becomes necessary to experimentally find out the different concentrations of all the three components, which have the ability to immobilize the apolar solvent. The experimental data, so obtained, are plotted in a ternary graph (figure 4). The graph divulges a lot of information including the critical gelation temperature and concentration of individual component that forms the gel.

The simplest method to determine the formation of the organogel is to conduct the inverted test-tube method and can be used to determine the compositions of the gelator, apolar solvent and aqueous phase, which can induce organogelation. In this method, the procedure for inducing the organogelation is carried out in a test-tube. After the completion of the procedure, the test-tube is inverted. If the content of the test-tube starts flowing then the system is regarded as sol, indicating that the particular composition has failed to induce organogelation (Figure 5). The system is regarded as an organogel, if the contents of the test-tube do not flow. This is the widely used method to determine the formation of organogels 24.

Structural Characterization

The structural property of the organogels can be carried out by a number of techniques. The simplest method employs the analysis of the organogels under a light microscope. Light microscopy has revealed that the sorbitan ester organogels consists of aggregated rod-like tubules within its structure. Depending upon the type of apolar phase, the sorbitan ester organogels may also contain toroidal vesicle structure as in the case when isopropyl myristate is used as an apolar phase. The presence of polysorbate 20 in the

solvent mixture can alter the microstructure of the organogels and results in the formation of star-shaped clusters. The presence of polysorbate 40, 60 and 80 results in the formation of mixed inverse micelles8.

Spectroscopic techniques, viz. nuclear magnetic resonance (NMR) and Fourier transform infra-red spectroscopy (FTIR), help in the chemical analysis of the organogels and can also reveal information on the various chemical interactions. The crystalline and non-birefringent nature of the lecithin organogels have been determined by NMR spectroscopy whereas FTIR spectroscopy have been used to determine the intermolecular interaction amongst the individual components present within the organogels. The results indicated that intermolecular hydrogen bonding plays an important role in the self-assembly of the lecithin organogelators25-26. The information about the molecular arrangement of the organogel may be obtained using scanning electron microscopy, transmission electron microscopy, dynamic & static light scattering, small angle neutron scattering and atomic force microscopy (AFM)27-30. The above mentioned techniques, allows to have an insight on the molecular arrangement even at the nanometer scale. The microscopic structure of the organogels can be viewed clearly using an AFM. AFM microscopy of the lecithin organogels indicated the presence of fibrous network throughout the organogel surface28. Figure 6 identifies the topography of novel tween-80 based organogels prepared in our laboratory.

Rheological Characterization

The rheological behavior is used to determine the physical properties of the organogels. It has been found that most organogels show plastic rheological property 31. The products showing plastic behaviour behaves as an elastic

body at lower shear rates and do not flow. As the shear rate is increased, the strain within the samples increases nonlinearly and progressively gets linearised at higher shear rates (Figure 7). The rheology of lecithin organogel has been extensively studied. It has been reported that there is a 104-106 times increase in the viscosity of the lecithin solution in apolar solvent, with the addition of trace amounts of water into it25. The rheological properties of the organogels can be tailored by altering the concentration of the organogelator and the apolar solvent for lecithin organogels. In general, with the increase in the concentration of the organogelator there is an increase in the viscosity of the organogels and has been well documented for lecithin-isopropyl myristate organogels. Apart from the concentration of the organogelator, the chemical composition of the same also plays an important role. It has been found that the lecithin organogels, which immobilized alkanes showed higher apparent viscosity. In addition to the above, the amount of water incorporated within the organogels also plays an important role in altering its rheological property32-33. The viscosity of the organogels are temperature dependent, in general with the increase in the temperature, there is a corresponding decrease in the viscosity of the physical organogels. This decrease in viscosity can be attributed to the increase in the kinetic energy amongst the fibers thereby resulting in the weakening of the interaction. If the temperature is further increased beyond the critical temperature, there is a complete disruption of the network structure and the organogels start flowing freely. Most physical organgels are thermoreversible in nature and are able to attain their high viscous state once they are cooled below the critical temperature. The lecithin and pluronic lecithin organogel are the classical examples of thermoreversible organogels 34-35.

Thermal Characterization

As mentioned in the previous section, physical organogels are thermoreversible in nature. The physical organogels are also thermostable in nature and are in a low energy state. Some of them may be stable even for 2 year36. The gel-to-sol transition temperature can be studied using a differential scanning calorimeter. During heating of the organogel, there is an endothermic peak at gel-to-sol transition. The gel-to-sol transition is basically a range of temperature marked by the initiation of the disruption of the networked structure to the complete disruption of the networked structure, when the gel starts to flow. Similarly, during cooling the system from a higher temperature to room temperature, we come across a range of temperature which corresponds to sol-to-gel transition. This is an exothermic peak and its initiation is marked by the initiation of the formation of entangled structures while its completion corresponds to the completion of the formation of the gelled structure. Depending on the composition and the property of the organogel, the gelling temperature and the melting temperature might be same or different37-38. If the organogel is isotropic in nature, the range of transition temperature should not be more than 3-5 oC39. Figure 8 shows the temperature dependence of Tween-80 based organogels developed in our laboratory. The sample showed gel-to-sol transition at 55 oC when subjected to a temperature sweep in a programmable temperature controlled water-bath.

The thermal characteristics of the organogels can also be analyzed with temperature dependent rheology and hot stage microscopy39. The temperature dependent rheology deals with subjecting the sample to a

temperature sweep with the application of shear in the linear viscoelastic region. The storage modulus and the loss modulus of the samples are determined, which reveals information on the transition temperatures. The hot stage microscopy employs a controlled heating element attached to the stage of the microscope. The samples, kept in the well-slides, are heated in a controlled manner and are continuously monitored with the microscope.

Biocompatibility Test

Most organogels developed till-date consist of toxic solvents (like cyclohexane, n-octane, kerosene) rendering them unsuitable for human applications40. Our work deals with developing and studying organogels based on generally regarded as safe (GRAS) materials11. Formulations containing 7. 5% SAM (N-stearoyl L-alanine methyl ester derivatives) in safflower oil when injected into the stratum corneum of rats, showed good biocompatibility with surrounding tissues for 8 weeks38. The in vitro nasal delivery of propanolol hydrochloride was investigated by Pisal et al. Organogel was prepared with sorbitan monostearate (SMS), isopropyl myristate and water. The investigation revealed that the surface epithelium lining and the granular cellular structure of treated nasal mucosa were intact supporting the biocompatible nature of sorbitan monostearate organogels41. Lecithin organogels are considered as most abundant biocompatible organogel for topical drug delivery system42. Various drugs such as scopolamine43 and piroxicam44 has been evaluated for both in vitro and in vivo testing of lecithin organogels. Dreher et al investigated the transdermal patch test of lecithin gels on human volunteers to find out the irritation potential of lecithin on human skin4, 45.

Organogels in Drug Delivery

Drug delivery is a process of administration of bioactive agents so as to achieve the therapeutic effect in humans. Research on the development of the various delivery systems is on the rise, which can improve the bioavailability of the bioactive agent. The sustained/ controlled delivery systems help in attaining the same due to its ability to prolong the release of the drug. Of late, the research on the use of organogels as a sustained/ controlled delivery vehicle has seen an exponential rise. This has been made possible because of the use of GRAS materials, having improved biocompatibility, in the development of organogels. In this section, attempts will be made to discuss some of the applications of organogels in controlled delivery.

Dermal and Transdermal Drug Delivery System

Skin is the largest organ of our body and provides a large surface area, which has been explored for delivering the drugs either locally or systemically. The delivery of the bioactive agents through the skin tissue has received much importance because of its non-invasive administration. Also, there is no need for the hiring a trained person as is required in invasive delivery systems. Apart from this, the bioactive agents meant to enter the systemic circulation does not undergo first pass metabolism thereby increasing the bioavailability of the bioactive agent in the systemic circulation.

The topical/ dermal delivery systems are meant to provide an increased availability of the drug at the site of application, without any significant amount of the drug gaining access to the systemic circulation. Various

organogels have shown great potential to be used in topical delivery system. Pluronic lecithin organogels (PLO) are basically soy-lecithin based organogels, which contains either isopropyl palmitate or isopropyl myristate as an apolar solvent. Additionally, these organogels contain pluronic F127, as one of the major component 46. Non-steroidal anti- inflammatory drugs (NSAID) (e. g. ketoprofen and flurbiprofen) incorporated in PLO have shown great potential in the treatment of heel pain . Piroxicam loaded organogels has been used to treat for rheumatoid arthritis. Analgesic creams containing lidocaine, ketoprofen and cyclobenzaprine have been developed successfully using PLO as base. MBGs have also been tried in topical drug delivery. The experimental results with cyclosporine-A indicated maximum concentration of the drug at the skin surface in rat models 47.

On the contrary to the dermal delivery systems, transdermal delivery systems deal with the administration of the bioactive agents to the systemic circulation by the application of the formulation on the skin surface and have been found to be patient compliant method. Apart from this, transdermal delivery systems have been considered as one of the safest route of administration 44. The permeation of the drug from the skin surface to the systemic circulation is dependent on the permeability of the skin, rate of blood flow to the administration site and the physicochemical property of the drug 48. The use of permeation enhancers (e. g. terpenes, essential oils, urea, dimethyl sulphoxides and propylene glycol) may help in the increased permeation of the drug through the skin 49. The thermoreversible nature of the organogels makes them one of the best candidates for the transdermal drug delivery. Most of the organogels are highly viscous and stable at room

temperature (25oC) which facilitates their storage and becomes less viscous and gets liquid appearance at body temperature allowing the permeation of drugs.

Lecithin organogels (LO) have been used in various pharmaceutical formulations because of its biocompatible nature. LO has the capability to immobilize a wide range of edible oils, organic solvents and various other apolar solvents of pharmaceutical use. The composition of the LO may be tailored so as to increase the permeation of the bioactive agents through the skin. For example, isopropyl palmitate (IPM) immobilized LO was able to increase the systemic bioavailability of the scopolamine and broxaterol, when administered topically 43. The presence of IPM in the LO did not initiate any skin irritation 45. IPM-based LO have shown positive results in the postoperative and emergency treatment of pain using ketorolac tromethamine, a non-steroidal anti-inflammatory drug 50. Other anti-inflammatory drugs have also been successfully incorporated within the IPM-based LO 45, 50. The improvement in the skin permeation of the bioactive agent LO is not only observed in human but also in hairless guinea pig skin 51. It has also been found that LO is also capable of improving the bioavailability of the bioactive agent in the systemic circulation by tailoring the release of the same 52. From the above discussions, it is evident that LO have the capacity to improve the patient compliance and the bioavailability of the bioactive agent as compared to the traditional oral delivery systems.

Microemulsion-based gelatin organogels (MBGs) have also shown promises as transdermal drug delivery systems 53-54. These organogels are electrically active and has shown a great potential to be used in

iontophoretic drug delivery. The antimicrobial property of the organogel is an added advantage during its shelf-life 53. The MBGs have also been used in passive transdermal drug delivery, where no electric field is being used. Various formulations using food grade oils have been successfully prepared 55.

Scientists have also explored the use of sorbitan ester organogels as a transdermal delivery vehicle. The increase in the drug concentration may increase the viscosity and the sol-gel transition of these organogels, which may be accounted to the increase in the tubular network density. Drugs (e. g. sumatriptan) incorporated within the organogel showed non-fickian release kintics indicating its potential use in reservoir-type drug delivery system 56.

Parenteral Drug Delivery System

Of late, there has been an increased interest in the development of parenteral sustained delivery system. The main advantage of this type of delivery system include the avoidance of first pass metabolism and harsh environment within the gastrointestinal tract of the bioactive agents. Organogels may play an important role in devising such a delivery system. L-alanine based organogelators (e. g. N-stearoyl l-alanine (m)ethyl esters), which can form self-assembled structures in the presence of oils, have been synthesized and characterized by Motulsky et al. as an in situ forming organogel 57-58. Hydrogen bonds and van der Waals forces have been found to play an important role in the self-assembly of the L-alanine derivatives. The subcutaneous administration of the organogels in rats indicated good biocompatibility for a period of 8 weeks. The authors concluded that the

developed organogels may be used as in situ organogel forming parenteral delivery system 57. Organogels containing tyrosine-based organogelators and safflower oil have been successfully used to deliver rivastigmine, an acetylcholinesterase inhibitor, subcutaneously in rat models. The results indicated that the developed organogels were biocompatible in nature and were able to inhibit the cholinesterase enzyme for a sustained period of time. Based on the results, it may be tried as an in situ implantable delivery system 59. Stearyl acrylate based polymeric organogels have been developed. The organogels have been found to be releasing the bioactive agents when the temperature was above 40 oC and ceased to release the bioactive agent when the temperature was brought down to 36 oC. These kinds of delivery systems may be used in thermochemotherapy combined with hyperthermia 60. Organogels developed with sorbitan monostearate as an organogelator, have been tried as depot forming system. The delivery system containing radiolabeled bovine serum albumin in the aqueous phase showed sustained delivery of the radiolabeled bovine serum albumin over a period of days when administered intra-muscularly 61.

Oral Delivery

The use of organogels in oral delivery of drugs is in the stage of infancy. Only few reports could be tracked on the application of organogels in oral delivery of bioactive agents. Bioadhesive organogels may play an important role in the delivery of the drug in the oral cavity. Poly (acrylic acid), a well-documented bioadhesive polyer, based organogels may be developed by proper mixing poly (acrylic acid), drug and organic solvent (e. g. poly ethylene glycol) in proper proportions. Poly (acrylic acid) based organogels

are mucoadhesive in nature and allows a controlled delivery of the drug for a prolonged period of time 62. Sorbitan monostearate based organogels, incorporated within hard gelatine capsules, may be used for oral delivery of bioactive agents. Drugs may be incorporated within the organogel before it is being filled within hard gelatine capsules. Murdan et al. incorporated ciclosporin A, a potent immunosuppressant, within the organogel and filled the same in hard gelatine capsules. The capsules were administered to male beagle dogs, kept on fasting. The absorption of the drug was significantly higher from organogel containing formulations as compared to hydrohillic amphiphilogel formulations and was similar to commercially available Neoral®, a microemulsion based product. The main advantage of the organogel based product over Neoral® is the ease of preparation of the organogel as compared to microemulsion 63. In a recent study, 12-hydroxystearic acid was used as an organogelator to immobilize soyabean oil. Ibuprofen, an an