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REVIEW ARTICLE

ORGANOGELS IN DRUG DELIVERY

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ABSTRACT

Organogels are semi-solid systems, in which an organic liquid phase is immobilized by a three-dimensional network composed of self assembled, intertwined gelator fibers. The apolar phase gets immobilized within spaces of the three-dimensional networked structure formed due to the physical interactions amongst the self assembled structures of compounds regarded as gelators. In general, organogels are thermodynamically stable in nature and have been explored as matrices for the delivery of bioactive agents. In the last decade, interest in physical organogels has grown rapidly with the discovery and synthesis of a very large number of diverse molecules, which can gel organic solvents at low concentrations. In the current manuscript, attempts have been made to understand the properties of organogels, various types of organogelators and some applications of the organogels in controlled delivery.

KEYWORDS: Organogels, Organogelators, Gelation, Properties, Appliations

INTRODUCTION:

A simple definition of the term 'gel' is a soft, solid or solid-like material, which contains both solid and liquid components, where the solid component (the gelator) is present as a mesh/network of aggregates, which immobilizes the liquid component [1]. A gel is a semi-solid material composed of low concentrations (< 15%) of gelator molecules that, in the presence of an appropriate solvent, self-assemble via physical or chemical interactions into an extensive mesh network preventing solvent flow as a result of surface tension. Gels have been eloquently described as being the result of "crystallization gone awry" [2]. The gel is said to be a hydrogel or an organogel depending on the nature of the liquid component. If the liquid phase is water, it is hydrogel and as an organogel if the liquid phase is an organic solvent [3]. In general, organogels formation is based in the spontaneous self-assembly of individual gelator molecules into three-dimensional networks of randomly entangled fiber-like structures. This three-dimensional network holds micro domains of the liquid in a non-flowing state mainly through surface tension [4]. Some common examples of gelators include sterol, sorbitan monostearate, lecithin and cholesteryl anthraquinone derivates. The thermo-reversible property of the organogels has generated much interest for the potential use of the organogels as drug delivery system. The thermodynamic stable nature of the organogels has been attributed to the spontaneous formation of fibrous structure by virtue of which the organogels reside in a low energy state [5]. The occurrence of the gel-to-sol transition above room-temperature indicates that external energy has to be supplied to the organogels so as to disrupt the three-dimensional structure and subsequent transformation of the gelled state to the sol state. Apart from the temperature sensitivity, organogels are also sensitive to the presence of moisture which has also been explored to develop controlled delivery systems [6]. Various organogel-based formulations have been designed for administration of the bioactive agents by different routes.

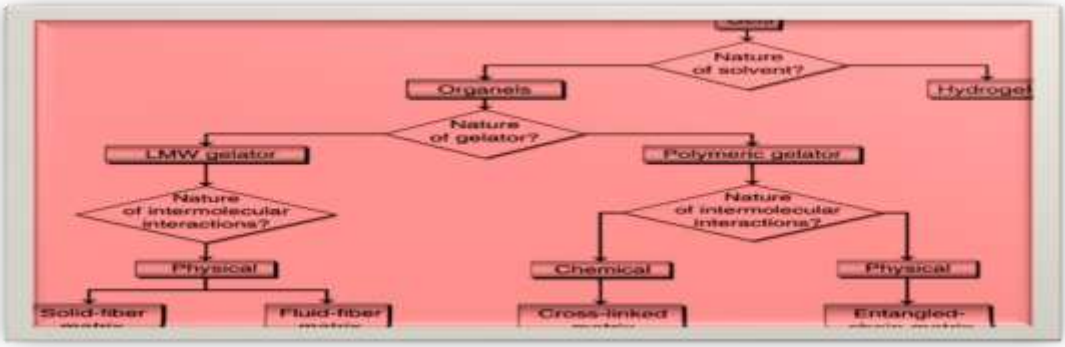

Figure1: Organogel Classification

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PROPERTIES:

1. **Viscoelasticity**: The organogels seems to follow Maxwell model of Viscoelasticity and behave like a solid on low shear rates and starts flowing on high shear rates due to weakening of physical interacting point of fiber matrix [7, 8].
2. **Non-Birefringence**: The organogels when viewed under polarized light appears as a dark matrix. This can be accounted to the isotropic nature of the organogels. Organogels do not allow polarized light to pass through its matrix. This property of organogel is termed as Non-Birefringence [9, 10]
3. **Thermoreversibility**: When organogels are heated above a critical temperature it lose its solid matrix and start flowing and settel back again on cooling. This has been attributed to the disruption in the physical interactions amongst the gelator molecules due to the thermal energy within the organogels [11, 12].
4. **Thermostability**: Organogels are thermostable in nature. The stability of the organogels may be attributed to the ability of the gelators to undergo self-assembly, under suitable conditions, so as to form organogels. As the gelators undergo self-assembly, it results in the decrease of the total free energy of the system and renders the organogels as low-energy thermostable system [13].
5. **Opacity**: Depending on the composition of the organogels, the organogels may be transparent or opaque in nature. The lecithin organogels are transparent in nature while the sorbitan monostearate organogels are opaque in nature [14, 15].
6. **Chirality effects**- The presence of chirality in the Low Molecular Weight gelators have been found to affect the growth and the stability of the solid-fiber networks. In general, it has been found that a good solid-fiber gelator has a chiral center whereas chirality does not have any effect on fluid-fiber gelators. The presence of chiral centers within the gelators helps in the formation of a compact molecular packing, which provides a thermodynamic and kinetic stability to the organogels system. Crown ether phthalocyanine organogels are the excellent example of chiral organogels [16, 17].
7. **Biocompatibility**: Now a days research on organogels using various biocompatible constituents has opened up new dimensions for the use of the same in various biomedical applications. They are found to be biocompatible in nature [18].

TYPES OF ORGANOGELS:

Lecithin organogels: Lecithin organogels have emerged as one of the most potential carrier systems. The organogel matrix mainly consists of a surfactant (lecithin) as gelator molecules, a nonpolar organic solvent as external or continuous phase, and a polar agent, usually water. A lecithin organogel is formed when small amounts of water or other polar substances, such as glycerol, ethylene glycol or formamide, are added to a non-aqueous solution of lecithin. The transfer into jelly-like state has been demonstrated only for nonaqueous solutions of naturally occurring unsaturated lecithins [19, 20]. The latter are mainly separated from soy bean and egg yolk. Lecithin is a trivial name for 1, 2-diacyl-sn-3-phosphocholine. It belongs to a biologically essential class of substances termed phosphoglycerides or phospholipids. The latter form the lipid matrix of biological membranes and also play a key role in the cellular metabolism [21]. Lecithin organogels have been used as carriers for hydrophilic and hydrophobic drug molecules. Hydrophobic drugs are dissolved in the oil phase (lecithin + organic solvent) whereas hydrophilic molecules are dissolved in water, which is then added to an organic solution of lecithin to induce gelation. As a biocompatible surfactant, it is widely used in everyday life including human and animal food, medicine, cosmetics, and manifold industrial applications [22, 23]. Synthetic lecithins containing residues of saturated fatty acids failed to form organogel. The gelling formation was also not observed with hydrogenated soybean lecithin. These studies indicate the importance of lecithin in the naturally occurring form, which contains unsaturated fatty acids [24, 25].

Sorbitan monosterate organogels: Sorbitan monostearate (Span 60) and sorbitan monopalmitate (Span 40) have been found to gel a number of organic solvents at low concentrations. Span 60 gels were found to be more stable than Span 40 gels and were investigated in greater depth. The thermoreversible gels are prepared by heating the gelator/liquid mixture in a water bath at 60°C (which results in dispersion of the gelator in the liquid medium) and cooling of the resulting suspension, following which the latter sets to an opaque, white, semisolid gel. Cooling results in reduced affinities between the solvent and the gelator molecules, which self-assemble into tubules. X-ray diffraction and freeze-fracture studies indicate that sorbitan monostearate molecules are arranged in inverted bilayers within the tubules. Sorbitan monostearate organogels are opaque, thermoreversible semi-solids whose microstructure consists of surfactant tubules dispersed in the organic continuous phase. Inverse toroidal vesicles are the precursors of the surfactant tubules. The gelation process was observed as an isotropic sol phase of sorbitan monostearate in isopropyl myristate was cooled using hot-stage light microscopy. At the gelation temperature, inverse toroidal vesicular structures were seen to grow in the organic phase. These toroids are thought to be analogous to other well-known vesicles,

liposomes and niosomes, except for their toroidal (rather than spherical) shape and their inverse nature. They are rather short-lived structures: on further cooling of the sol phase, tubules form in the organic medium: it is speculated that the toroids elongate into tubular shapes or split into rod-shaped segments [26-28].

Micro/Nano-emulsion based organogels: Microemulsions are dispersions of at least two immiscible liquids. They are thermodynamically unstable systems that are stabilized kinetically [29]. Microemulsion appears to have the ability of deliver larger amount of topically applied agents into the mucosa than the traditional gel & creams. Microemulsions are defined as thermodynamically stable transparent, single optically isotropic liquid system of water, oil and surfactants frequently in combination with suitable cosurfactants. Microemulsions are known to enhance the bioavailability of drugs via topical and systemic routes. The use of a microemulsion gel as vehicle may enhance transdermal penetration by various mechanism, many molecules or solubilised in microemulsion in addition microemulsion induce a change in the thermodynamic activity of the drug they contain, modifying their partition coefficient and thus favour penetration of the stratum corneum. Furthermore, their component surfactant reduces the functional barrier of stratum corneum [30-32]. Nanoemulsions are thermodynamically stable transparent (translucent) dispersions of oil and water stabilized by an interfacial film of surfactant and cosurfactant molecules having a droplet size of less than 100 nm [33].

Organogels based on other low molecular weight gelators: Scientists have investigated the transdermal delivery of piroxicam from organogels composed of glyceryl fatty acid ester gelators in pharmaceutical oils. The in vivo skin penetration of the drug, evaluated by measuring the anti-inflammatory inhibition of oedema after treatment, was found to be superior for glyceryl fatty acid ester organogels as compared to traditional topical formulations such as liquid paraffin [34, 35].

Use of a long-chain glutamate based gelator has demonstrated by scientists (N-lauroyl-L-glutamic acid di-n-butylamide) at concentrations of 2–10% to gel isostearyl alcohol and propylene glycol, yielding translucent and opaque gels, respectively. In vitro permeation studies on human skin using haloperidol, an anti-psychotic drug, showed facilitated permeation upon incorporation of 5% limonene, a known permeation enhancer [36, 37].

Poly (ethylene) organogels: Very few polymeric organogels have been geared towards pharmaceutical applications. The only two such systems have been widely tested for drug delivery applications are poly (ethylene) and P (MAA-co- MMA) organogels. In a study dating back to the 1950s and involving 300 patients, PO patches were shown to be non-irritating and have low sensitizing properties [38]. In a related investigation, 326 patients were treated with spectrocin-containing PO and compared with patients treated with spectrocin in petrolatum base alone. Both antibiotic ointments cleared pyoderma and secondarily infected eruptions in 3–5 days, but it was found that the PO provided a faster, more efficient release. Poly (ethylene) was also used in the formulation of 5-iodo-2'-deoxyuridine for the treatment of oral herpes simplex lesions. A 10% drug-loaded formulation showed a resolution of herpetic lesions in 3-days after treatment initiation, compared to 1–2 weeks in untreated control patients [39].

Supramolecular organogels: Although a low molecular mass gelator was discovered in the early nineteenth century, the supramolecular nature of these materials was poorly understood and they were largely neglected until the late 20th century. In the recent past, molecules of a great structural diversity, for instance from the simplest alkanes to the complex phthalocyanines, have been discovered to be gelators. Recently immense interest has been generated in studying gels derived from low molecular mass gelators (supramolecular, or simply molecular gels). The motivation for this is not only to understand the fundamental aggregate structures in the gels at different length scales, but also to explore their potential for futuristic technological applications. Gels have been made sensitive to external stimuli like light and chemical entities by incorporating a spectroscopically active or a receptor unit as part of the gelator molecule. This makes them suitable for applications such as sensing and actuating. The diversity of gel structural architectures has allowed them to be utilized as templates to prepare novel inorganic superstructures for possible applications in catalysis and separation. Gels derived from liquid crystals (anisotropy gels) that can act as dynamically functional materials have been prepared, for example, for (re-writable) information recording. Supramolecular gels can be important in controlled release applications, in oil recovery, for gelling cryogenic fuels etc. They can also serve as media for a range of applications. This tutorial review highlights some of the instructive work done by various groups to develop smart and functional gels, and covers a wide spectrum of scientific interest ranging from medicine to materials science [40, 41].

Eudragit organogels: Eudragit organogels are really mixtures of Eudragit (L or S) and polyhydric alcohols, such as glycerol, propylene glycol and liquid polyethylene glycol, containing high concentrations (30 or 40% w/w) of Eudragit. Drug-containing gels were prepared by dissolving

the drug (salicylic acid, sodium salicylate, procain or ketoprofen) in propylene glycol, pouring the resulting solution into Eudragit powder (contained in a mortar), and immediately mixing with a pestle for 1min [42, 43]. Gel consistency and spreading is described using a penetrometer and a spreadmeter [44]. Gel viscosities were found to increase with increasing concentrations of Eudragit and to decrease with increasing drug content. The inclusion of the drug procaine was also found to reduce gel rigidity, which was thought to be due to the influence of the drug molecules on the intermolecular forces (e.g., hydrogen bonds) between Eudragit and propylene glycol. The authors suggested that drug content in Eudragit organogels be kept low (e.g., 1.25% w/w) to maintain gel rigidity and stability. The release of model drugs salicylic acid, sodium salicylate and ketoprofen from Eudragit L and S organogels was investigated *in vitro* by the rotation disk method. Interestingly, the mechanism of salicylic acid release from Eudragit L and S organogels into a phosphate buffer were totally different. Release was due to surface erosion of the Eudragit L organogel but to diffusion through the Eudragit S gel matrix. Drug release from Eudragit S organogel thus increased with increasing temperature and agitation rate of the release medium [45].

***In situ* forming organogel of L-alanine derivative:** *N*-lauroyl-L-alanine methyl ester (LAM) was found to gel the pharmaceutically acceptable organic solvents, soybean oil and medium-chain triglycerides [46]. Normally the system exists in the gel state at room temperature. However, the addition of ethanol to a gelator/solvent solution inhibits gelation because the ethanol disrupts the formation of hydrogen bonds (essential for gelator self-assembly into aggregates) between the gelator molecules. This means that a solution of LAM in an organic solvent can remain in the sol phase at room temperature when some ethanol is added to the mixture. When such a sol phase (20% LAM + 14% ethanol in soybean oil) was placed in phosphate buffered saline at 37°C it turned into a opaque gel within 2 min as the hydrophilic ethanol diffused away into the aqueous buffer, and as gelator–gelator hydrogen bonds were formed. Thus, theoretically, such a LAM/ethanol/soybean oil solution could form gels *in situ* following its subcutaneous injection, due to ethanol diffusion away from the formulation, into the surrounding tissues; *in situ* gel formation in rats was indeed investigated. The main advantage of *in situ* forming gels is their
injectability at room temperature. Once a drug-containing gel is formed *in situ*, it could act as a sustained-release implant [47].

Pluronic lecithin organogels: Pluronic lecithin organogels are opaque, yellow gel, PLO is composed of isopropyl palmitate, soy lecithin, water and the hydrophilic polymer, Pluronic F127. The difference between PLO and its precursor, lecithin gels, is the presence of Pluronic F127 (a hydrophilic polymer that gels water) and the greater amount of water compared with the oil. Thus, PLO is not really an organogel but it may be thought of as an 'organogel' due to its name. PLO was developed by a compounding pharmacist in the US in the early 1990s as a topical vehicle [48]. Pluronic F127 was added to the original lecithin organogel in order to stabilize the gel formulation. The gel's physicochemical properties have not been investigated. However, collaborations between local physicians, their patients and the inventor pharmacist led to the incorporation of many different drugs, such as nonsteroidal anti-inflammatories, haloperidol, prochlorperazine and secretin for patient use and to anecdotal evidence of its efficacy as a transdermal drug delivery vehicle. Many more drugs have since been incorporated within PLO [49]. PLOs are mainly used as a topical or transdermal drug carrier, for example, for hormones [50, 51]. PLOs have also been investigated/proposed as a vehicle to the oral cavity and mucosa [52].

Table 1: Organogel formulations and their applications in drug delivery

Sr. No.	Organogelator used in formulation	Route of administration	Study conducted	Model drugs
1	Lecithin	Transdermal	Clinical trials *In vivo* skin permeation and efficacy *In vitro* skin permeation *2In vitro* release	Diclofenac [55, 56]. Piroxicam [57]. Tetrabenzamidine [58]. Scopolamine and boxaterol [59]. Propranolol [60]. nicardipine [61]. Aceclofenac [62]. Indomethacin and diclofenac [63].

2	Glyceryl fatty acid esters	Transdermal	*In vivo* efficacy	Levonorgestrel and ethinyl Estradiol [64].
3	N-lauroyl-l-glutamic acid di-n-butylamide	Transdermal	*In vitro* release	Haloperidol [65, 66].
4	Poly(ethylene)	Transdermal	*In vitro* release	Spectrocin [67].
5	Sorbitan monostearate (SMS) or molaureate	Nasal, Oral, Subcutaneous and Intramuscular	*In vitro* release *In vitro* release *In vivo* efficacy	Propranolol [68]. Cyclosporin A [69]. Bovine serum Albumin and haemagglutin [70, 71].
6	N-stearoyl l-alanine methyl or ethyl ester	Subcutaneous	*In vitro/in vivo* release *In vitro/in vivo* release and efficacy	Rivastigmine [72]. Leuprolide [73].
7	Poly (methacrylic acid-co-methylmethacrylate). Poly (methacrylic acid-co-methylmethacrylate). and crosslinked poly (acrylic acid	Buccal, Rectal	*In vivo* efficacy *In vivo* efficacy	Salicylic acid Bovine serum Albumin [74].

ADVANTAGES:

Template vehicle: Organogels provide opportunities for incorporation of wide range of substances with diverse physicochemical characters viz: chemical nature, solubility, molecular weight, and size etc [75].

Process Benefits: Spontaneity of organogel formation by virtue of self-assembled super molecular arrangement of surfactant molecule makes the process very simple and easy to handle.

Structural/Physical Stability: The organogel do not form semisolids on standing because an organogel consists of macromolecules existing as twisted matted strands. The units are of bound together by strong types of Vanderwaal forces so as to form crystalline amorphous regions throughout the entire system. Being thermodynamically stable, the structural integrity of organogels is maintained for longer time periods [76].

Chemical Stability: Organogels are moisture in senstive and being organic also resists microbial contamination. Since it consists of both hydrophobic and hydrophilic components, both hydrophobic and hydrophilic drugs can be incorporated [77].

Topical Delivery Potential: Being well balanced in hydrophilic and lipophilic character, they can efficiently partition with the skin and therefore enhance the skin penetration and transport of the molecules. Organic solvents could be of natural origin, e.g.: sunflower oil, mustard oil, etc which have been already studied. Drug delivery into the skin layers (cutaneous or dermal delivery) and beyond (percutaneous or transdermal delivery) is advantageous because it provides a non-invasive, convenient mode of administration, allowing the circumvention of first pass degradation of the active ingredient, an important aspect for highly liver-metabolized molecules [78].

Safety: Use of biocompatible, biodegradable and non-immunogenic materials makes them safe for long term applications [45].

ORGANOGELS WITH SPECIAL CHARACTERISTICS:

Switchable Fluorescent Organogels and Mesomorphic Superstructure Based on Naphthalene Derivatives: Bisurea-functionalized naphthalene organogelators via cooperative hydrogen bonding and *л-л* stacking interaction were designed and synthesized. The gelators showed excellent gelling capability in various solvents and performed switchable fluorescence in the gel state. The fluorescent emission of these compounds strongly depends on the aggregation of the fluorophore and is very sensitive to the temperature and chemical stimuli. A stronger and red-shifted emission was found in the gel state compared with the original solution. The gel-sol transition of the systems, as well as the fluorescent emission, is reversibly controlled by a change of the temperature or upon alternative addition of fluoride anions and protons. The influence of fluoride anions on the fluorescence and gel-sol processes is a result of the dissociation of intermolecular hydrogen bonds by bonding of fluoride anions with urea groups of the gelator. The obtained sol is turned to the gel

state again upon addition of trifluoroacetic acid. Furthermore, polaring optical microscopy and small-angle X-ray scattering indicated that the gelator exhibited the liquid crystalline property and displayed the column phase. In conclusion, we present an effective approach to fluorescent organogel systems, which are sensitive to temperature, fluoride anions, and protons [79].

Improved mechanical strength and electrical conductivity of organogels containing carbon nanotubes: These are organogel/carbon nanotube composites using 12-hydroxystearic acid (HSA) as the gelator molecule, multi-wall carbon nanotubes as the nanofillers, and 1, 2-dichlorobenzene as the organic solvent. Significant improvements in the mechanical and electrical properties of the organogels are achieved by incorporating pristine or carboxylated carbon nanotubes. For example, the linear viscoelastic regime of the HSA organogel, an indicator of the strength of the gel, extends by a factor of four with the incorporation of 0.2 wt% of the carboxylated nanotubes. Also, the carbon nanotubes (specially the pristine tubes) improve the electrical conductivity of the organogels, e.g. six orders of magnitude enhancement in electrical conductivity with 0.2 wt% of pristine tubes. Differential scanning calorimetry experiments indicate that the nanotubes do not affect the thermoreversibility of the organogels. These organogel composites could be useful in most applications where the organogels or xerogels find their uses. In addition, freeze drying or supercritical drying the organogel composites will lead to highly porous, threedimensionally- interconnected aerogels, which may find broad applications including fillers for multifunctional polymer nanocomposites, electrode materials for lithium batteries and supercapacitors and catalyst supports for fuel cells [80].

Self-assembly and semiconductivity of an oligothiophene supergelator: A bis(trialkoxybenzamide)-functionalized quaterthiophene derivative was synthesized and its self-assembly properties in solution were studied. In non-polar solvents such as cyclohexane, this quaterthiophene π-system formed fibril aggregates with an H-type molecular arrangement due to synergistic effect of hydrogen bonding and π-stacking. The self-assembled fibres were found to gelate numerous organic solvents of diverse polarity. The charge transport ability of such elongated fibres of quaterthiophene π-system was explored by the pulse radiolysis time resolved microwave conductivity (PR-TRMC) technique and moderate mobility values were obtained. Furthermore, initial Atomic Force Microscopy (AFM) and UV-vis spectroscopic studies of a mixture of our electron-rich quaterthiophene derivative with the electron acceptor [6, 6]-phenyl-C61-butyric acid methyl ester (PCBM) revealed a nanoscale segregated assembly of the individual building blocks in the blend.

Our studies revealed the versatile and very effective gelation ability of the present system compared to the previously reported oligothiophene gelators. The critical gelation concentrations in numerous solvents are remarkably low and in few cases even in the range of supergelators. The impact of facile self-assembly of newly developed oligothiophene building block on its material properties is reflected in promising charge transport characteristics [81].

Rheometry of an androstanol steroid derivative paramagnetic organogel: Comparison between the behavior of two different gelators using rheological and neutron scattering methods has been made. The flow properties of a steroid-made paramagnetic organogel in cyclohexane were presented. The original gelator D-homosteroidal nitroxide in steroid-made paramagnetic organogel (STNO) is important in the class of organogels as being one of the most documented and as such is a good candidate for comparisons with another reference system, the 12-hydroxy stearic acid (HSA) gel. The linear viscoelastic regime of deformations of STNO gels is identified and analyzed in the context of self-assembled fibrillar networks. Rheological and neutron scattering experiments show that the kinetics of gel formation exhibits long equilibration times corresponding to the elaboration of entangled fibrillar aggregates. Comparison of the linear elasticities between STNO and HSA gels demonstrates that HSA gels are much stiffer. Contributions from the cross-sectional sizes, the mesh size of the networks, the solubility concentrations, and the Young's modulus of the materials are discussed. Non-linear flow properties are also compared using thixotropic loops. They indicate that the transduction of the chirality from the molecular to the supramolecular stages is more efficient with STNO gels having strong chiral junction zones. Simplified scattering and optical protocols are proposed to facilitate comparisons between different organogels [82].

Enzymatically Derived Sugar-Containing Self-Assembled Organogels with Nanostructured Morphologies: Researchers examined the synthesis of sugar-based diesters by using the lipase B from Candida Antarctica (CALB). Transesterification reactions were performed in acetone that contained either vinyl stearate or vinyl butyrate as highly or moderately hydrophobic ester donors, respectively, and with several common disaccharides including sucrose, maltose, lactose, and trehalose. Interestingly, only the reactions with trehalose,

a symmetrical disaccharide with an a-1, 1 glycosidic bond, resulted in gel formation during the course of the transesterification reactions (Table 1, gelators 2 and 5), thereby confirming the importance of monomer structure in gel assembly. Trehalose-6, 6'-distearate and trehalose- 6, 6'-dibutyrate were obtained as the sole products from the respective enzymatic reactions in yields of >50%. Hence, CALB was highly regiospecific in its acylation of trehalose. The purified dieters were tested in a wide range of solvents for their gelation ability. The trehalose distearate was insoluble in water and soluble in chloroform and 1, 4-dioxane, whereas trehalose 6, 6'- dibutyrate was insoluble in cyclohexane and olive oil and soluble in water. Gels were formed in all other solvents tested. As a result of these studies, they generated a series of additional diesters with chain lengths of C2 to C14 (1, 3, 4, and 6) and assessed their gelation capacity in several key solvents, ranging from the hydrophilic acetonitrile to the hydrophobic p-xylene. The minimum gelator concentration (cmin) required to induce gelation is strongly dependent on the acyl chain length. In most of the cases, a shorter chain length promotes gelation at lower gelator concentration, with the exception of gelation in acetonitrile and isopropanol. These results sharply contrast with typical sugar-based amphiphilic organogels, which require long-chain alkyl or aryl moieties to induce gelation. Surprisingly, the trehalose-6,6'-diacetate was capable of inducing gelation at a cmin of 0.04% (w/v; 0.84 mm) in ethyl acetate and nearly this low in methyl methacrylate. This represents, to our knowledge, the lowest cmin value reported for a sugar ester gelator. For ethyl acetate, the cmin represents over 12000 solvent molecules being associated per molecule of trehalose-6, 6'-diacetate. This can be translated into a swelling of the weight of the gelator approximately 2500- fold [83].

Preparation and gas sensing properties of novel CdS-supramolecular organogel hybrid films: A novel CdS-supramolecular organogel hybrid film with unusual morphology has been fabricated by exposing a supramolecular organogel film containing $Cd(Ac)_2$ in an H_2S atmosphere at room temperature. The organogel film was prepared by spin-coating a low-molecular weight organic gelator (LMOG) gel of dmethyl sulfoxide onto a glass plate substrate. Amines are a family of compounds, and have become intense pollutants due to their extensive uses in the preparation of fertilizers, pharmaceuticals, surfactants, biological buffers and colorants, etc. Furthermore, volatile amines can be found in agricultural areas, and they are taken as indicators of decayed food, as in the case of fish products, and thereby accurate and fast detection of amines is of great importance. It is well known that CdS films and particles have been widely used in gas-sensing. XRD, SEM, EDS, TG-DTA, UV–vis, PL (photoluminescence) spectroscopy and PL lifetime measurements were employed to characterize the film. Ellis and coworkers have embarked on the area for years, and found that CdS or CdSe in single crystal state can be used as a 'luminescent litmus test' to sense the presence of a variety of Lewis acids and bases. The photoluminescence (PL) was found to increase when CdS or CdSe was exposed to Lewis bases and decrease when exposed to Lewis acids. The increase or decrease in the PL response appears to reflect adsorbate-induced changes in the semiconductor's depletion width, and can be modelled by a dead-layer model. It is to be noted that the depletion width is the thickness of the near-surface electric field, which is produced by the equilibrium of the semiconductor Fermi level with surface states. The electrical conductivity and photoconductivity of CdS have been used for the detection of SO_2 and CO, respectively. In addition, NH_3 can also be determined by monitoring the PL emission of a powdered CdS Different from fluorescence sensors based upon organic fluorophores, the gas-sensing properties of CdS are highly dependent upon its morphological and microstructural features, such as particle size, size distribution, shape and density etc. Recently, considerable efforts have been devoted to the development of film sensors. This is because film sensors are, generally speaking, reusable, and easily made into devices [84].

Macroporous Polyisobutylene Gels: A Novel Tough Organogel with Superfast Responsivity: Design of gels with a good mechanical performance together with a fast response rate is crucially important in many existing and potential application areas of soft materials. However, polymeric gels that are highly swollen in a liquid are normally very brittle. This feature of gels originates from their very low resistance to crack propagation due to the lack of an efficient energy dissipation mechanism in the gel network. Macroporous gels were prepared by solution crosslinking of butyl rubber (PIB) in frozen benzene solutions using sulfur monochloride (S_2Cl_2) as a crosslinking agent. The effect of different preparation conditions, including the crosslinker concentration and the gel preparation temperature, on the gel properties was investigated. S_2Cl_2 was found to be an efficient crosslinking agent even at very low reaction temperatures up to -22 °C and at crosslinker ratios down to about 0.9 mol S_2Cl_2/mol internal vinyl group on PIB. The gels prepared from frozen solutions of PIB contain about 97% organic liquid, and they are very tough; they can be compressed up to about 100% strain without any crack development, during which the total liquid inside the gel is removed. Further, the compressed gel immediately swells in contact with good

solvents to recover its original shape. The low-temperature gels have a porous structure with irregular large pores of 101-102 μm in diameter, separated by pore walls of about 10 μm in width with a high polymer concentration, which provide structural support to the material. The gels also exhibit completely reversible swelling-deswelling cycles in toluene and methanol, respectively, i.e., they return to their original shape and original mass after a short reswelling period. The results suggest that both phase separation of PIB chains at low temperatures and the presence of frozen benzene templates are responsible for the porosity formation in PIB gels. We described the preparation of a novel tough organogel with superfast responsive properties. The gels were prepared from frozen solutions of butyl rubber in benzene using sulfur monochloride (S_2Cl_2) as a crosslinking agent. Effects of the crosslinker concentration and gel preparation temperature on the properties of PIB gels were investigated. S_2Cl_2 was found to be an efficient crosslinking agent even at very low reaction temperatures up to -22 °C and at crosslinker ratios down to about 0.9 mol S_2Cl_2/mol internal vinyl group on PIB. The gels prepared from frozen solutions of PIB contained about 97% organic liquid and they were very tough; they can be compressed up to about 100% strain without any crack development. The compressed gel immediately swells in contact with good solvents to recover its original shape. The low-temperature gels have a porous structure with irregular large pores of 101-102 μm in diameter, separated by pore walls of about 10 μm in width with a high polymer concentration, which provide structural support to the material [85].

CONCLUSION:

In the last 10 years there has been an explosive growth in research on organogels and on publications related to organogels. Most of the latter report the discovery and/or synthesis of new organogelators, investigations into the chemical groups necessary for the molecule to be an organogelator, the properties of their gels including the gel microstructures, and the manner in which the gelator molecules could be arranged in the gelator aggregates. Research into the applications of these gels is still in its infancy despite great excitement about their potential industrial uses. As far as drug delivery is concerned, the absence of an aqueous phase is beneficial as the non-aqueous medium is less likely to support microbial growth. The non-aqueous medium of organogels also indicates their potential suitability as carriers for oil-soluble drugs, whereas their soft, semisolid consistencies point to their use as vehicles for application to the skin. However, only a few organogels have been investigated for drug delivery, mainly due to the fact that the components of most organogels are not pharmaceutically acceptable. Thus, before the organogels can be studied as a drug carrier, they must be reformulated using pharmaceutically acceptable components. Drug incorporation into the gels is known to alter the gel properties; such as viscosity, and, in some cases, drug incorporation even destroys the gel. Care must be taken, therefore, when drugs are dissolved or suspended in organogels and the drug-containing formulations must be thoroughly characterized. Currently, literature on the influence of drug incorporation on the physicochemical properties of organogels is limited.

Lecithin gels have received more attention as transdermal drug delivery vehicles, presumably due to the presence of lecithin: a known skin permeation enhancer. The promise shown by lecithin gels as a transdermal delivery vehicle has resulted in its adoption and adaptation into PLO (which is not an organogel despite the terminology). PLO is currently the vehicle of choice of US compounding pharmacists and veterinarians for the delivery of drugs by the topical route, despite the lack of any hard, scientific evidence of PLO efficacy as a transdermal drug carrier. Apart from the topical/transdermal route, organogels have been investigated for oral, rectal and parenteral applications. Sorbitan monostearate organogels and amphiphilogels have shown promise as parenteral vaccine adjuvants and as oral vehicles for poorly water-soluble drugs, respectively. Given

that many drugs suffer from poor water solubility, which often leads to low bioavailability, the ability of sorbitan monostearate amphiphilogels to solubilise such drugs to increase bioavailability should be investigated further. The potential of amphiphilogels to enhance the transdermal delivery of small drug molecules has not yet been investigated.

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