# Novel Sorbitan Monostearate Organogels

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**Abstract** □ Sorbitan monostearate, a hydrophobic nonionic surfactant, gels a number of organic solvents such as hexadecane, isopropyl myristate, and a range of vegetable oils. Gelation is achieved by dissolving/dispersing the organogelator in hot solvent to produce an organic solution/dispersion, which, on cooling sets to the gel state. Cooling the solution/dispersion causes a decrease in the solvent–gelator affinities, such that at the gelation temperature, the surfactant molecules self-assemble into toroidal inverse vesicles. Further cooling results in the conversion of the toroids into rod-shaped tubules. Once formed, the tubules associate with others, and a three-dimensional network is formed which immobilizes the solvent. An organogel is thus formed. Sorbitan monostearate gels are opaque, thermoreversible semisolids, and they are stable at room temperature for weeks. The gels are affected by the presence of additives such as the hydrophilic surfactant, polysorbate 20, which improves gel stability and alters the gel microstructure from a network of individual tubules to star-shaped "clusters" of tubules in the liquid continuous phase. Another solid monoester in the sorbitan ester family, sorbitan monopalmitate, also gels organic solvents to give opaque, thermoreversible semisolids. Like sorbitan monostearate gels, the microstructure of the palmitate gels comprise an interconnected network of rodlike tubules. Unlike the stearate gels, however, the addition of small amounts of a polysorbate monoester causes a large increase in tubular length instead of the "clustering effect" seen in stearate gels. The sorbitan stearate and palmitate organogels may have potential applications as delivery vehicles for drugs and antigens.

## Introduction

Gels are an intermediate state of matter, containing both solid and liquid components. The solid component comprises a three-dimensional network of interconnected molecules or aggregates which immobilizes the liquid continuous phase. Hydrogels have an aqueous continuous phase, and organogels have an organic solvent as the liquid continuous medium. Gels may also be classified based on the nature of the bonds involved in the three-dimensional solid network—chemical gels arise when strong covalent bonds hold the network together, and physical gels when hydrogen bonds and electrostatic and van der Waals interactions maintain the gel network.[1]

Interest in the physical organogel field has increased, with the discovery and synthesis of a number of substances able to gel organic solvents. Examples of such organogelators) include 12-*d*-hydroxyoctadecanoic acid (12-HOA),[2] D-homosteroidal nitroxide (SNO),[3] calixarenes,[4] 1,3:2,4-di-*O*-benzylidene-D-sorbitol (D-DBS),[5] ALS compounds (an Aromatic moiety attached by a Linker segment to a Steroidal group),[6] lecithin,[7] bis(2-ethylhexyl) sodium sulfosuccinate (AOT),[8] gelatin,[9] 2,3-bis-*n*-decyloxyanthracene (DDOA),[10] and some azobenzene cholesterol derivatives.[11] These organogels exhibit interesting properties such as acute temperature/moisture sensitivities,[12,8] the ability to solubilize guest molecules[12] and to act as templates[13] and nonaqueous media for synthesis,[14–19] uses for purification and separation purposes,[20] as transdermal delivery vehicles,[21] and as carriers for liquid crystals.[22] Some of these potential applications are discussed in a review by Hinze et al.[12]

We have previously reported the gelation of certain organic solvents, e.g. *n*-alkanes, cyclohexane, vegetable oils, isopropyl myristate by the nonionic surfactant, sorbitan monostearate (Span 60).[23–25] Gelation is achieved by dissolving/dispersing the gelator in the solvent at 60 °C and then cooling the resulting solution/suspension, which conseqently gels as thermoreversible organic systems that are opaque and semisolid with a smooth, silky "feel". Microscopical examination reveals a network of tubular aggregates in the liquid disperse phase. Since these aggregates were large enough to be visualized by a light microscope, we followed their formation and the establishment of a gel network as a hot suspension was cooled to the gel state, using hot-stage light microscopy. X-ray diffraction measurements have provided further information on the microstructure of the gels, and we report here the possible arrangement of the gelator molecules in the gel network. Other members of the sorbitan ester family were also studied as were the effects of additives with the aim of finding the structural features responsible for gelation.

## Materials and Methods

Sorbitan monostearate was purchased from Sigma (UK) and used as received. Like most sorbitan esters, sorbitan monostearate is a mixture of sorbitan esters, with the stearate and palmitate esters predominating. Other sorbitan esters (sorbitan monolaurate, sorbitan monopalmitate, sorbitan monooleate, and sorbitan tristearate) were also purchased from Sigma (UK). Like sorbitan monostearate, these sorbitan esters are mixtures, their fatty acid compositions being as follows: sorbitan monolaurate, lauric acid ~50%, and the balance primarily myristic, palmitic, and linolenic acids; sorbitan monopalmitate, palmitic acid ~90%, and the balance primarily stearic acid; sorbitan monooleate, oleic acid ~75%, and the balance primarily linoleic, linolenic, and palmitic acids; sorbitan tristearate, stearic acid ~50%, and the balance palmitic acid. The polysorbates (polysorbates 20, 40, 60, 65, 80, and 85) were purchased from Fluka (UK). The organic solvents were all of analytical grade. Hexadecane, *cis*-decalin, *trans*-decalin, isopropyl myristate, ethyl oleate, ethyl formate, squalene, and the vegetable oils (cottonseed oil, soybean oil, sesame oil, corn oil, and olive oil) were bought from Fluka (UK); hexane and cyclohexane were purchased from Rathburn (UK); octane, isooctane, decane, dodecane, tetradecane, and octadecane were obtained from Sigma (UK); benzene and toluene were from BDH (UK). All the reagents were used as received, except for hexadecane, isopropyl myristate, and the vegetable oils, which were dried in a vacuum oven

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(Gallenkamp, UK) at room-temperature overnight to ensure the absence of any moisture which might affect gelation.

**Gel Preparation**—Sorbitan monostearate (10% w/v) was dispersed/dissolved in the organic solvent at 60 °C. The resulting dispersion/solution was then allowed to cool by standing at room temperature. An opaque, semisolid gel was obtained. To obtain gels containing polysorbate additives, sorbitan monostearate (10% w/v) and the polysorbate (2% w/v) were weighed into a vial, and the organic solvent was added. The mixture was heated in a water-bath at 60 °C and then allowed to cool and set to a gel at room temperature.

**Light Microscopy**—A light microscope (Nikon Microphot-FXA, Japan) was used, with attached camera (Nikon FX-35DX, Japan) or a high-speed camera (Microscope Service & Sales, UK) and a hot-stage (Linkam TC93, UK). A video recorder was also used to record the events in selected experiments.

**Differential Scanning Calorimetry (DSC)**—A Perkin-Elmer DSC7 (UK) differential scanning calorimeter was used to determine gelation temperatures. Samples were weighed into aluminum pans using a Perkin-Elmer AD-4 autobalance and the pans then sealed nonhermetically. The samples were heated at a rate of 10 °C/min from 20 °C to 70 °C. The melting point was taken as the temperature corresponding to the melting endotherm. The equipment was calibrated using indium, and low temperatures were maintained using liquid nitrogen.

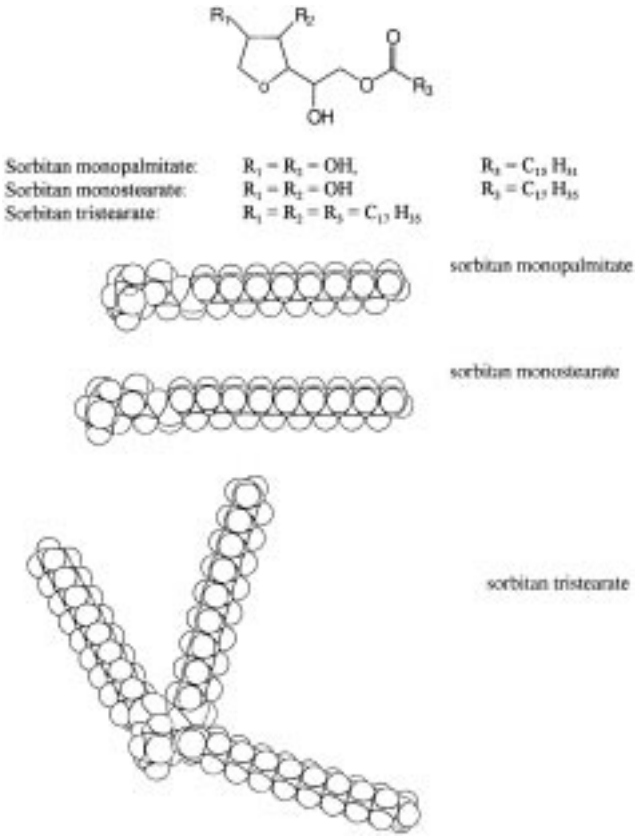
**X-ray Diffraction Studies**—X-ray data on the gel sample was collected on a Siemens D500 diffractometer (in the Department of Crystallography, Birkbeck College) equipped with a copper tube and a quartz primary-beam monochromator giving a wavelength ($\lambda$) = 1.54056 Å. The X-ray tube was run at 45 kV and 30 mA. The sample was mounted in a flat-plate specimen holder and flattened with a glass microscope slide. The sample was spun about an axis normal to its flat-plate surface. Diffraction patterns were measured using a scintillation detector. The data were obtained for the $2\theta$ range 1−35° in steps of 0.05° at 10 s per point.

## Results and Discussion

**Sorbitan Monostearate Gels**—Sorbitan monostearate is a small (MW = 431), monoalkyl, lipophilic (HLB 4.7), nonionic surfactant (Scheme 1). A waxy solid with a grainy texture, it disperses in hexadecane (at 10% w/v) on heating at 60 °C to give a slightly turbid suspension. On cooling, the latter suspension sets to an opaque, white, semisolid gel with a smooth texture. Cooling the suspension results in reduced affinities between the solvent and the surfactant, and this appears to cause surfactant self-assembly into aggregates. The aggregates join with one another to form a three-dimensional network which captures the solvent. The latter is thus immobilized and a gel is formed, as the bulk viscosity is increased by the network.

*Solvents Gelled by Sorbitan Monostearate*—The solvent has a prime role in gel formation. It must provide the correct solubility/insolubility balance toward the gelator so that the latter is dissolved or dispersed at high temperatures and is sufficiently insoluble when the organic solution/suspension is cooled such that the gelator molecules self-assemble into aggregates or otherwise associate. We tested a number of solvents by incubating the gelator (10% w/v) in the solvent at 60 °C for 0.5 h and then cooling by standing at room temperature. Sorbitan monostearate gels alkanes (C > 5), e.g., hexane, cyclohexane, octane, decane, *cis*- and *trans*-decalins, dodecane, tetradecane, hexadecane, octadecane, the alkene squalene, vegetable oils, e.g., corn oil, sesame seed oil, olive oil, cottonseed oil, and the long-chain synthetic esters, isopropyl myristate, ethyl oleate, and ethyl myristate.

The ungellable solvents include the more polar alkanols, ethanol, 2-propanol, and butanol, and chloroform and dichloromethane, which dissolve sorbitan monostearate (10% w/v) on heating, but which allow the sorbitan ester to precipitate on cooling. Benzene and toluene proved to be too good solvents in which the surfactants do not gel.




**Scheme 1**—Structures and Space-Filling Models of Some Sorbitan Ester Surfactants

*Gelation Temperature*—The gelation temperature of a hexadecane gel containing 10% w/v sorbitan monostearate was found to be 41−44 °C by differential scanning calorimetry. This relatively broad gelation temperature range is typical of physical organogels, involving the rupture of the junctions between aggregates and dissolution of the surfactant aggregates as the temperature rises, causing a corresponding increase in the surfactant solubility in the solvent. The melting point of the solid sorbitan monostearate is 51 °C. A melting point of the neat gelator higher than that of the gel seems to be a universal property of organogels. The organogel is thermoreversible, i.e., it melts on heating to the sol phase which can once again be gelled upon cooling. Heating and cooling cycles can be repeated a number of times without any appreciable change in gel properties.

*Gelling Concentration*—Sorbitan monostearate gels hexadecane at concentrations as low as 1% w/v (0.02 M). At this concentration, 170 solvent molecules are immobilized by each surfactant molecule. At lower concentrations, e.g., 0.2% w/v, a white fibrous gel mass is formed within the hexadecane solvent. The fibrous mass within the solvent becomes denser with increasing surfactant concentration until all the hexadecane is gelled. An increase in surfactant concentration was expected to cause a gradual increase in the viscosity of the bulk sample due to an isotropic dispersion of the increasing number of aggregates in the solvent until gelation occurred at the critical gelling concentration. It seems however, that aggregate−aggregate interactions are stronger than solvent−aggregate affinities, resulting in a preferential ordered flocculation of aggregates to form a three-dimensional network within the solvent. The surfactant network, anisotropically dispersed in the solvent, is then able to gel only that part of the solvent, and a fibrous gel mesh is observed within the

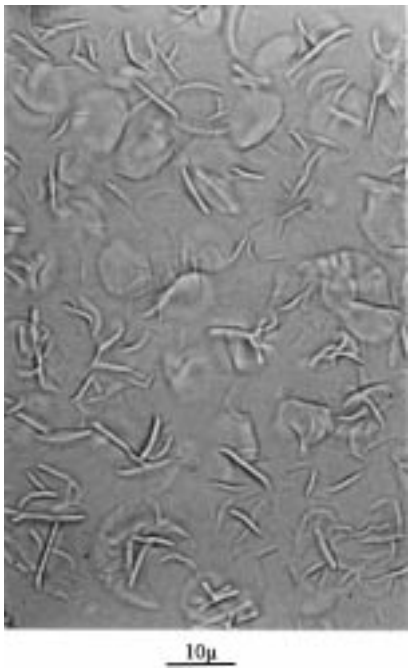



**Figure 1**—Organogel microstructure: tubular aggregates formed by the self-assembly of sorbitan monostearate molecules in hexadecane solvent.

excess solvent. The excess solvent is defined here as the fluid not gelled by the surfactant network.

This partial gelation within the excess solvent was most strikingly apparent in hexadecane. Other solvents such as isopropyl myristate, decane, corn oil, and squalene showed the anticipated isotropic dispersion of surfactant aggregates and a gradual increase in viscosity with increasing surfactant concentration until all the solvent was gelled. This difference in the gelation phenomenon with insufficient amounts of gelator, reflects the importance of the solvent, which influences the attractive forces between the gelator aggregate structures. In hexadecane, aggregate–aggregate interactions are maximized so that the aggregates join to form a meshwork which immobilizes part of the solvent. In other solvents, e.g., isopropyl myristate, the aggregate–aggregate interactions required for entanglement and formation of a three-dimensional network seem to be less favored, probably because of stronger solvent–aggregate attractions. The latter promote an isotropic dispersion of gelator aggregates in the solvent and consequently a progressive increase in the sample viscosity is observed upon increasing the sorbitan monostearate concentration until the critical gelling concentration is reached.

*Gel Microstructure*—Light microscopy of the organogels has revealed the surfactant aggregates to be rodlike tubules (Figure 1). The aggregates associate with others through contact points and a three-dimensional network is established which immobilizes the solvent. Figure 2 shows examples of gel networks in different solvents. The three-dimensional network acts as the gel skeleton. The importance of the contact points between tubules is seen when small amounts of ethanol are added to a gel sample. The contact points are disrupted with a consequent loss of the gel state even though tubules are still present.

*Events Occurring at Gelation*—In an attempt to understand the formation of tubular aggregates, the gelation process was followed microscopically as a hot suspension of sorbitan monostearate in isopropyl myristate was slowly cooled using a hot-stage. As the suspension cools and the solvent–surfactant affinities decrease, doughnut shaped, membrane-bound, inverse toroidal vesicular structures are seen to form as the sorbitan monostearate surfactant

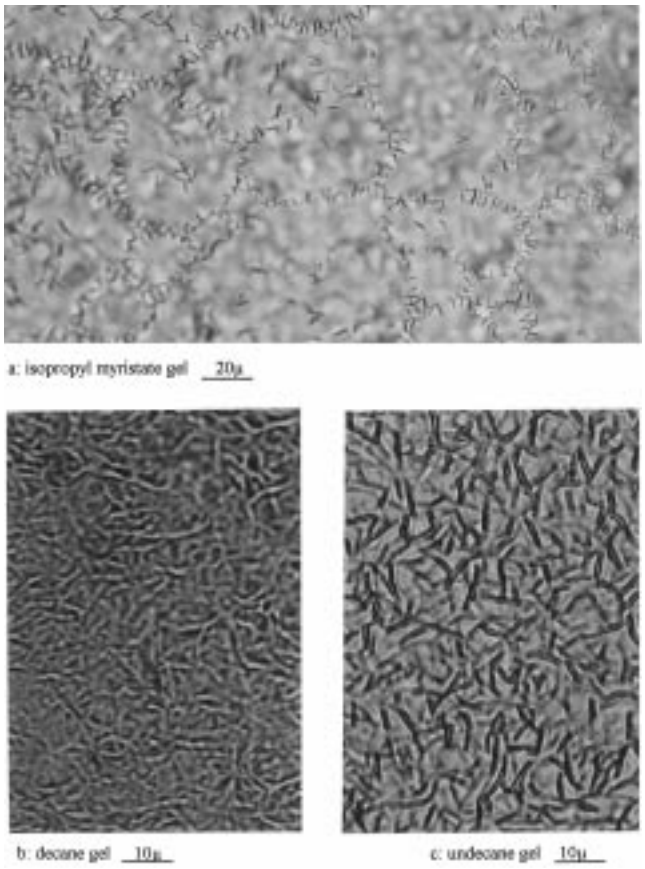



**Figure 2**—Examples of gel networks in different solvents.

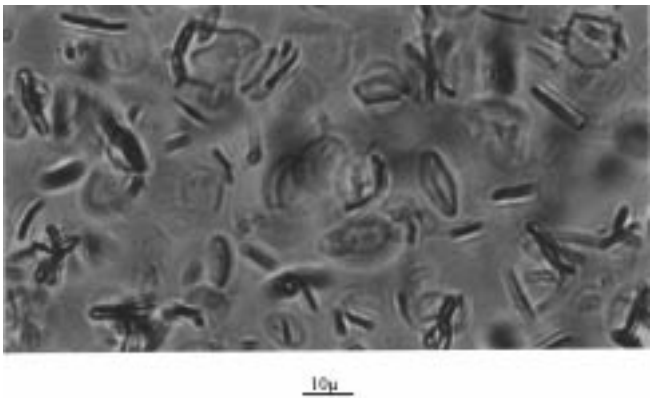



**Figure 3**—A photomicrograph of an isopropyl myristate formulation at the transition temperature between sol and gel phases. A number of toroidal vesicular structures can be seen.

molecules self-assemble. These toroidal vesicles (Figure 3) are in constant motion about their axis. Using a high-speed camera, one of the toroidal vesicles was photographed in quick succession as it rotated about its axis (Figure 4), and the toroidal rather than spherical shape of the vesicle was confirmed.

The toroids are short-lived structures, existing only at the gelation temperature (44–41 °C). Further cooling results in their conversion into tubules. The mechanism of such a change is not understood at present. The toroid might contract into a more tubular shape or it might split into one or more cylindrical segments, giving rise to the tubules seen in Figure 1. The latter structures are believed to be tubular and not toroidal vesicles lying perpendicular to the plane of the micrograph as the probability that all the toroidal vesicles would lie at such an angle is rather small.

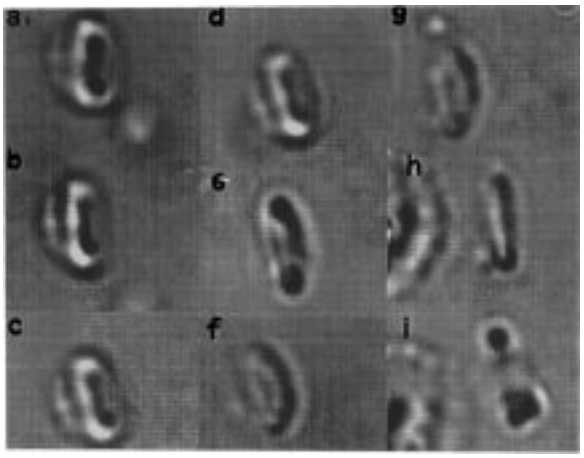



**Figure 4**—One of the inverse toroidal vesicular structures seen in Figure 3 was photographed in rapid succession as it rotated about its axis.

Formation of the surfactant aggregates is followed by random association between the aggregates and the establishment of junction points. The sequential pictures in Figure 5 obtained from a video recording of gelation demonstrates the migration of one aggregate to join another. From the sequential stills, the aggregate–aggregate interaction seems to be an active process, probably due to relatively strong forces of attraction between the surfactant assemblies and an overall negative energy change. Extensive joining of individual tubules finally creates a three-dimensional network which acts as the skeleton, "holds" the solvent, and forms the gel. Such flocculation of the surfactant aggregates and the obvious attractive forces among them (most clearly seen in Figures 2a and 5) suggest the existence of long-range forces of attraction in the system and provides another example of how large structures "seem to recognize each other's presence at rather great distances" as suggested by Adamson.[26] Further work is required to be done to more fully understand the energetics of gel formation.

*Ultrastructure of Tubules and the Possible Molecular Organization of Surfactant Molecules*—The toroids most probably consist of bilayers of surfactant molecules, in a fashion similar to other well-known vesicles—liposomes and niosomes. The difference lies in their toroidal shape and the inverted nature of the bilayers. Preferential self-assembly of surfactant molecules into toroidal vesicles may be due to the reduced membrane curvature required in toroids. Figure 6 shows a diagrammatic representation of such a toroidal vesicle consisting of surfactant bilayers. Assuming this surfactant organization is retained upon gelation, the tubules present in the gel would also consist of concentric sheets of bilayers (Figure 6). A bilayer organization of surfactant molecules in the tubules is suggested by X-ray diffraction measurements on a sorbitan monostearate/hexadecane gel, which show peaks corresponding to distances 5.9 and 0.4 nm. These distances relate to the bilayer thickness and the distance between two adjacent surfactant tails, respectively, as shown in Figure 6. These values agree with the corresponding to theoretical calculated distances (using Quanta and CHARMm software), which are 5.91 and 0.46 nm, respectively, assuming close packing of the surfactant molecules in the bilayers. Such an arrangement of the amphiphiles ensures the solvophobic headgroups are shielded from the organic solvent.

*Gel Stability*—The two markers of gel stability normally used are gelation temperature and gel lifetime. Gelation temperature usually increases with gelator concentration and is dependent on the solvent. The gel lifetime is the

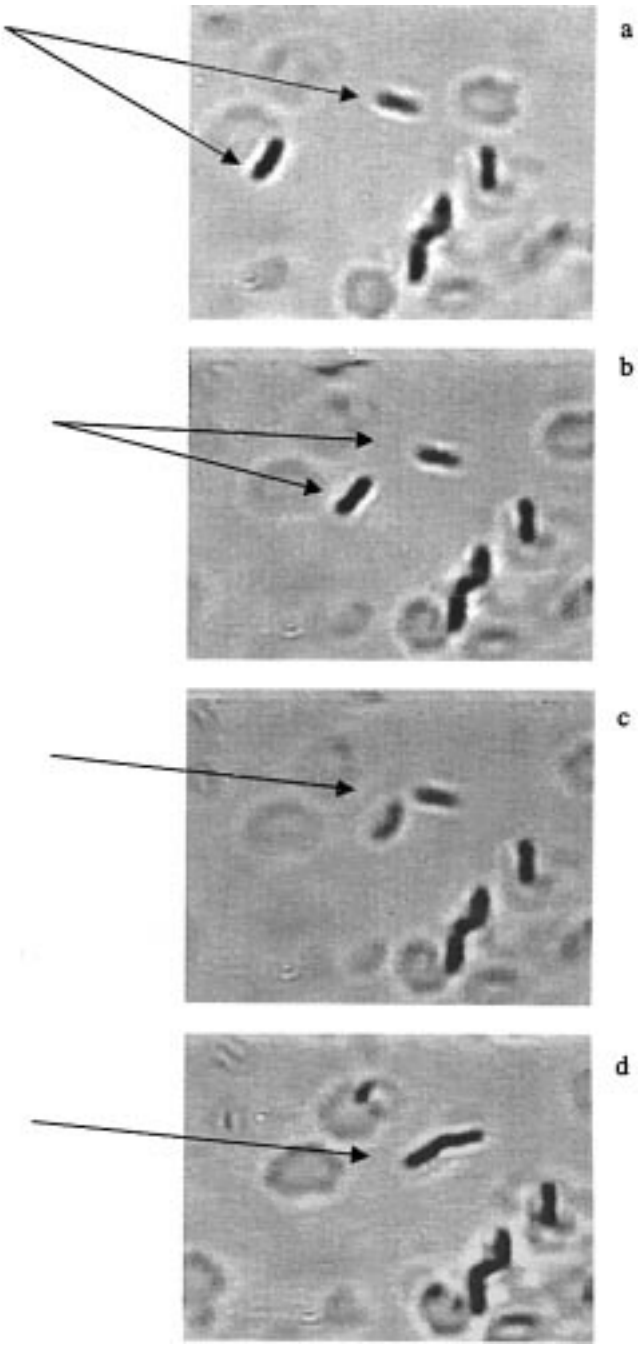



**Figure 5**—Sequential micrographs (a–d) show the migration of one surfactant aggregate to join another in the formation of the three-dimensional network.

length of time a gel remains intact when stored in sealed vessels at room temperature, without syneresis (the separation of the solid and liquid components). Like gelation temperature, the gel lifetime depends on gelator concentration and the solvent. A hexadecane gel containing 10% w/v sorbitan monostearate remains intact for a few weeks before syneresis occurs. Hexadecane gels also have a longer lifetime compared to isopropyl myristate and vegetable oil gels.

Gel stability was found to be drastically altered when small amounts of a second nonionic surfactant, polysorbate 20, was included in the formulation.

**The Influence of Polysorbate Additives on Sorbitan Monostearate Gels**—Small amounts of polysorbate 20 (Tween 20), a hydrophilic nonionic surfactant (HLB 16.7), was included in a sorbitan monostearate/hexadecane organogel when the latter was used as the continuous

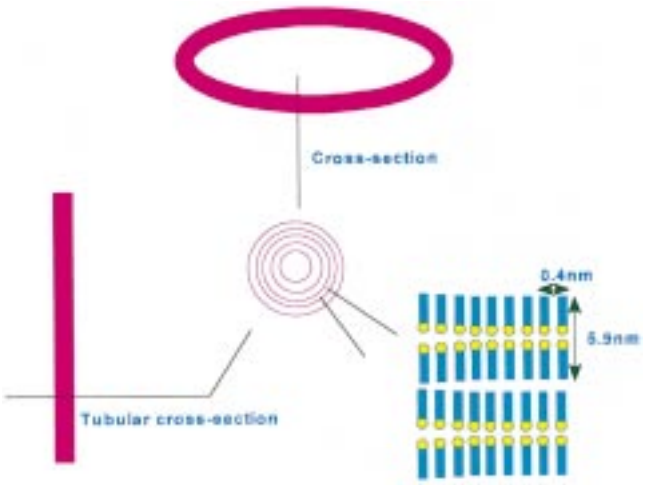



**Figure 6**—Diagrammatic representations of a surfactant tubule, its precursor, an inverse toroidal vesicle and the aggregates' cross-section. A segment of the cross-section has been magnified to show the suggested surfactant organization, i.e., inverse bilayers.

external oil phase in the formation of multiple emulsions.[24] It was anticipated that the addition of the hydrophilic polysorbate 20 would stabilize the emulsion due to the formation of mixed surfactant films at the w/o interface. This was indeed realized. Addition of polysorbate 20 also had interesting effects on the gel lifetime and stability.

Polysorbate 20 seems to enhance the solubility of sorbitan monostearate in hexadecane, such that a sorbitan monostearate/polysorbate 20/hexadecane system is a clear, transparent solution at 60 °C (compared to a slightly turbid suspension in the absence of polysorbate 20). The enhanced solubility is probably mediated via the formation of mixed inverse micelles of the two surfactants in the hexadecane solvent at high temperatures.

The transparent mixed surfactant solution cools to a semisolid, opaque gel which is similar in appearance to the gel without polysorbate 20. The gel lifetime and stability is, however, drastically improved. Hexadecane gels spiked with polysorbate 20 were found to be stable for months (compared to weeks in the absence of polysorbate 20) at room temperature without syneresis. Penetrometer studies also showed a slight increase in gel consistency upon the addition of polysorbate 20 (unpublished results). Such an enhanced gel stability seems to be a direct result of the enhanced solubility in the system described above. Inclusion of polysorbate 20 in hexadecane gel moves the solubility toward the optimum level required for stable gel formation.

This solubility-enhancing effect of polysorbate 20, is, however, not universal: solubility was enhanced in some solvents, but it was reduced in others. An enhanced solubility is always followed by improvement in gel lifetime and stability. Polysorbate 20 reduces the solubility of sorbitan monostearate in the shorter chain alkanes (C < 14) with consequent deterioration of the gels, as evidenced by syneresis. Polysorbate 20 has no effect in tetradecane. The solubility of sorbitan monostearate is increased in longer chain hydrocarbons, e.g., hexadecane, octadecane, and squalene, with a consequent enhancement of the gel formed. The long chain esters, ethyl oleate, isopropyl myristate, and ethyl myristate, and the vegetable oils also show an enhancement of the gel upon the addition of polysorbate 20. Table 1 recapitulates these findings. The key feature seems to be the size of the solvent molecule: a relatively large size or a long hydrocarbon chain seems to be required for polysorbate 20 to exert a beneficial effect on solubility and gelation. It is unclear at present why this should be so.

**Table 1—The Effects of Polysorbate 20 on the Solubility of Sorbitan Monostearate in Hot Solvents (60 °C) and on the Resulting Gels**

| solvent | effects of polysorbate 20 on the solubility of sorbitan monostearate | effect of polysorbate 20 on gel lifetime and stability: enhancement (↑) or deterioration (↓) |
|---|---|---|
| hexane | ↓ | ↓ |
| cyclohexane | ↓ | ↓ |
| octane | ↓ | ↓ |
| isooctane | ↓ | ↓ |
| *cis*-decalin | ↓ | ↓ |
| *trans*-decalin | ↓ | ↓ |
| decane | ↓ | ↓ |
| dodecane | ↓ | ↓ |
| tetradecane | no effect | no effect |
| hexadecane | ↑ | ↑ |
| octadecane | ↑ | ↑ |
| squalene | ↑ | ↑ |
| ethyl oleate | no effect | ↑ |
| isopropyl myristate | no effect | ↑ |
| ethyl myristate | no effect | ↑ |
| cottonseed oil | no effect | ↑ |
| soybean oil | no effect | ↑ |
| sesame oil | no effect | ↑ |
| corn oil | no effect | ↑ |
| olive oil | no effect | ↑ |

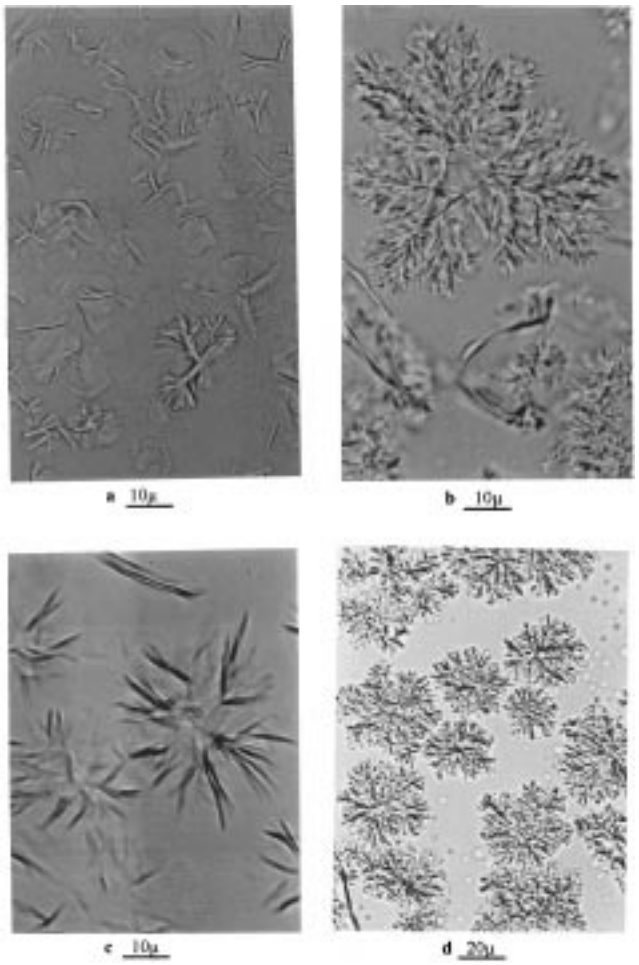



**Figure 7**—Microstructures of sorbitan monostearate gels: (a) absence of polysorbate surfactant, (b) + polysorbate 20, (c) + polysorbate 60, and (d) + polysorbate 80.

Gel microstructure is affected by the inclusion of polysorbate 20. Gels spiked with the hydrophilic surfactant comprise star-shaped "clusters" of surfactant tubules in the

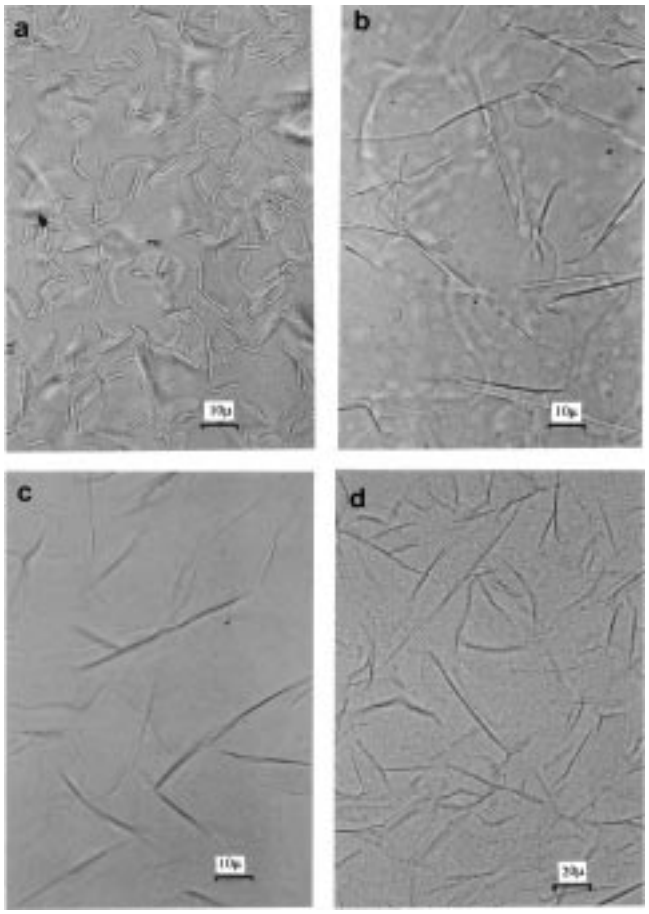



**Figure 8**—Microstructures of sorbitan monopalmitate gels: (a) absence of polysorbate surfactant, (b) + polysorbate 20, (c) + polysorbate 60, and (d) + polysorbate 80.

organic medium (Figure 7). On cooling a hot solution, these "clusters" were found to grow as an entity, rather like the opening of a clenched fist. The polysorbate 20 molecules are thought to become incorporated into the inverted surfactant bilayers and thus into the tubular aggregates.

The other polysorbates tested, polysorbate 40, 60, and 80 showed similar effects to polysorbate 20 in hexadecane gels. The solubility of sorbitan monostearate in hexadecane was enhanced, presumably due to the formation of mixed inverse micelles and the resulting more stable gels resulted from star-shaped clusters of surfactant tubules (Figure 7). The triesters, polysorbates 65 and 85, do not affect the solubility of sorbitan monostearate in hexadecane. It is possible that their large size and shape do not allow mixed micelle formation, and thus the solubility of the gelator is not enhanced.

**The Gelling Abilities of Other Sorbitan Esters**—To determine the key properties of sorbitan monostearate as an organogelator, other members of the sorbitan ester family which are in the solid state at room temperature, namely, sorbitan monopalmitate (Span 40) and sorbitan tristearate (Span 65), were investigated for any gelling ability. Sorbitan monopalmitate was found to gel hexadecane. The thermoreversible gel obtained is similar in appearance to sorbitan monostearate gel described, i.e., it is opaque, semisolid, with a smooth silky "feel" and the microstructure comprises rodlike tubular aggregates (Figure 8a). When gelation was followed using hot-stage microscopy, the surfactant tubules were found to be formed from toroidal vesicular precursors as described above for sorbitan monostearate.

Sorbitan tristearate does not gel hexadecane, but crystallizes out on cooling the hexadecane. The conical shape of the triester (Scheme 1) is not conducive to the formation of bilayers and thus tubule formation. Reports on vesicle formation by sorbitan tristearate in aqueous media could not be found in the literature. On the other hand, the cylindrical shape (Scheme 1) of the sorbitan monoesters (monostearate and monopalmitate) seems to allow molecular packing in bilayers such that the surfactant molecules can assemble into tubular aggregates responsible for gelation.

Sorbitan monopalmitate gels are less stable than the stearate gels at 10% w/v gelator concentration. Gelation temperature is lower, and syneresis occurs at a faster rate. As in the case of monostearate gels, the addition of polysorbate monoesters (polysorbates 20, 40, 60, and 80) increases the solubility of sorbitan monopalmitate in hexadecane, presumably via the formation of mixed inverse micelles, with consequent enhanced gel stability. The effects on the microstructures of the palmitate gels were, however, very different: the tubular length was drastically increased when the gels were spiked with polysorbates (Figure 8). These long tubules were formed from large toroidal vesicular precursors generated at the gelation temperature. Why the polysorbates have such widely different effects on the two sorbitan esters which only differ in their hydrocarbon chains by a $C_2H_4$ group remains to be solved.

## References and Notes

1. Hermans, P. H. Reversible Systems. In *Colloid Science*; Kruyt, H. R., Ed.; Elsevier: Amsterdam, 1969; Vol II, pp 483−651.
2. Terech, P. 12-d-hydroxyoctadecanoic acid organogels − a small angle neutron scattering study. *J. Phys. II* **1992**, *2*, 2181−2195.
3. Terech, P. Structure of nonionic rodlike surfactant aggregates in apolar solvents − study of the influence of the nature of the solvent in steroid hydrocarbon organogels. *J. Phys.* **1989**, *50*, 1967−1982.
4. Aoki, M.; Nakashima, K.; Kawabata, H.; Tsutsui, S.; Shinkai, S. Molecular design and characterisations of new calixarene-based gelators of organic fluids. *J. Chem. Soc., Perkin Trans. 2* **1993**, 347−354.
5. Yamasaki, S.; Tsutsumi, H. The dependence of the polarity of solvents on 1,3/2,4-di-o-benzylidene-d-sorbitol gel. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 123−127.
6. Lin, Y.; Kachar, B.; Weiss, R. G. Novel family of gelators of organic fluids and the structure of their gels. *J. Am. Chem. Soc.* **1989**, *111*, 5542−5551.
7. Scartazzini, R.; Luisi, P. L. Organogels from lecithins. *J. Phys. Chem.* **1988**, *92*, 829−833.
8. Xu, X. D.; Ayyagari, M.; Tata, M.; John, V. T.; McPherson, G. L. Formation of novel organogels by the addition of phenols to AOT micelles in isooctane. *J. Phys. Chem.* **1993**, *97*, 11350−11353.
9. Haering, G.; Luisi, P. L. Hydrocarbon gels from water-in-oil microemulsions. *J. Phys. Chem.* **1986**, *90*, 5892−5895.
10. Terech, P.; Bouas-Laurent, H.; Desvergne, J. P. Small molecular luminescent gelling agent 2,3-bis-*n*-decyloxyanthracene: rheological and structural study. *J. Colloid Interface Sci.* **1995**, *174*, 258−263.
11. Murata, K.; Aoki, M.; Suzuki, T.; Harada, T.; Kawabata, H.; Komori, T.; Ohseto, F.; Ueda, K.; Shinkai, S. Thermal and light control of the sol−gel phase transition in cholesterol-based organic gels. Novel helical aggregation modes as detected by circular dichroism and electron microscopic observation. *J. Am. Chem. Soc.* **1994**, *116*, 6664−6676.
12. Hinze, W. L.; Uemasu, I.; Dai, F.; Braun, J. M. Analytical and related applications of organogels. *Curr. Opin. Colloid Interface Sci.* **1996**, *1*, 502−513.
13. Petit, C.; Pileni, M. P. Synthesis of cadmium sulfide in situ in reverse micelles and in hydrocarbon gels. *J. Phys. Chem.* **1988**, *92*, 2282−2286.
14. Backlund, S.; Eriksson, F.; Hedstrom, G.; Laine, A.; Rantala, M. Lipase-catalyzed enantioselective esterifications using different microemulsion-based gels. *Colloid Polym. Sci.* **1996**, *274*, 540−547.

15. De Jesus, P. C.; Rezende, M. C.; Nascimento, M. G. Enzymatic resolution of alcohols via lipases immobilised in microemulsion-based gels. *Tetrahedron: Asymmetry* **1995**, *6*, 63−66.
16. Jenta, T. R. J.; Batts, G.; Rees, G. D.; Robinson, B. H. Biocatalysis using gelatin microemulsion-based organogels containing immobilized chromobacterium viscosum lipase. *Biotechnol. Bioeng.* **1997**, *53*, 121−131.
17. Nascimento, M. G.; Rezende, M. C.; Vecchia, R. D.; de Jesus, P. C.; Aguiar, L. M. Enzyme-catalysed esterifications in microemulsion-based organo gels. *Tetrahedron Lett.* **1992**, *33*, 5891−5894.
18. Scartazzini, R.; Luisi, P. L. Reactivity of lipase in an optically transparent lecithin-gel matrix. *Biocatalysis* **1990**, *3*, 377−380.
19. Stamatis, H.; Xenakis, A.; Provelegiou, M.; Kolisis, F. N. Esterification reactions catalyzed by lipases in microemulsions -the role of enzyme localization in relation to its selectivity. *Biotech. Bioeng.* **1993**, *42*, 103−110.
20. Crecchio, C.; Ruggiero, P.; Pizzigallo, M. D. R. Polyphenoloxidases immobilised in organic gels: properties and applications in the detoxification of aromatic compounds. *Biotechnol. Bioeng.* **1995**, *48*, 585−591.
21. Willimann, H.; Walde, P.; Luisi, P. L.; Gazzaniga, A.; Stroppolo, F. Lecithin organogel as matrix for transdermal transport of drugs. *J. Pharm. Sci.* **1992**, *81*, 871−874.
22. Seeboth, A.; Wustneck, R.; Kragel, J. Gel dispersed liquid-crystals. *Colloid Polym. Sci.* **1994**, *272*, 1151−1156.
23. Yoshioka, T.; Florence, A. T. Vesicle (niosome)-in-water-in-oil (v/w/o) emulsions: an in vitro study. *Int. J Pharm.* **1994**, *108*, 117−123.
24. Murdan, S.; Gregoriadis, G.; Florence, A. T. Nonionic surfactant based organogels incorporating niosomes. *STP Pharma Sci.* **1996**, 44−48.
25. Murdan, S. Nonionic surfactant based organogels: properties and potential as immunoadjuvants, 1998, Ph.D. Thesis, School of Pharmacy, University of London.
26. Adamson, A. W. The gentle force of entropy. *Science* **1998**, *280*, 655−657.

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