Solubilization of Triglycerides by Hydrotropic Interaction: Liquid Crystalline Phases

STIG FRIBERG and **LISBETH RYDHAG**, The Swedish Institute for
Surface Chemistry, drottning Kristinas vag 45, S-114 28 Stockholm, Sweden

ABSTRACT

An investigation of the possibility of preparing aqueous solutions of triglycerides has been made by determining phase regions in systems of three and four components. The results have shown that isotropic aqueous solutions with solubilized triglyceride of up to about 15 wt % can be achieved. A primary solubilization of the triglyceride into a liquid crystalline phase of monoglyceride is followed by the addition of a hydrotrope which transforms the liquid crystalline phase into an isotropic liquid in which the triglyceride is soluble at certain component ratios.

INTRODUCTION

The term hydrotropy was introduced by Neuberg (1) in 1916 to describe the increase in solubility of poorly water soluble substances when the concentration of the added hydrotrope exceeds a range of 20 to 30 wt %. Since then a large number of investigations on the solubility-promoting power of the hydrotropic agents have been carried out. The influence of different molecular structures of the hydrotrope on the solubility concentration relationship has been thoroughly investigated (2).

Friberg and Rydhag (3) determined the phase equilibria in systems containing water, sodium xylene sulfonates and various carboxylic acids. They showed that the continuous solubility region, reaching from a solution of 25-40% hydrotrope in water, with no octanoic acid present, to increasing content of the acid (95% w/w), implied the presence of "normal" and "reversed" micelles in the same solubility area. A direct comparison with the corresponding phase diagram for sodium octanoate showed the difference of the solubilizing mechanism for liquid carboxylic acids between the hydrotrope and a conventional soap. Like the hydrotrope, soap forms normal micelles in water rich compositions and reversed micelles in carboxylic acid rich compositions. When acid is added to the water rich composition with normal soap micelles the solution will not continuously be transformed into one containing reversed micelles. Instead, one-phase regions with liquid crystalline structures are situated between the two solution areas which contain normal and reversed micelles. The addition of hydrotropes to liquid crystalline phases will transform these structures to isotropic liquids. This has been shown by Lawrence and coworkers (4) in investigations on cationic substances. Their investigation of the possibility of using this mechanism to solubilize triglycerides was of interest since these compounds cannot be solubilized by aqueous solutions of hydrotropes. The triglyceride was solubilized in a liquid crystalline phase formed by water and a monoglyceride. The addition of a hydrotrope should give an isotropic solution.

In order to avoid formation of solid crystalline compounds at room temperature the mono- and triglyceride was chosen with eight carbon atoms per chain. The results should be applicable to the corresponding oleic compounds.

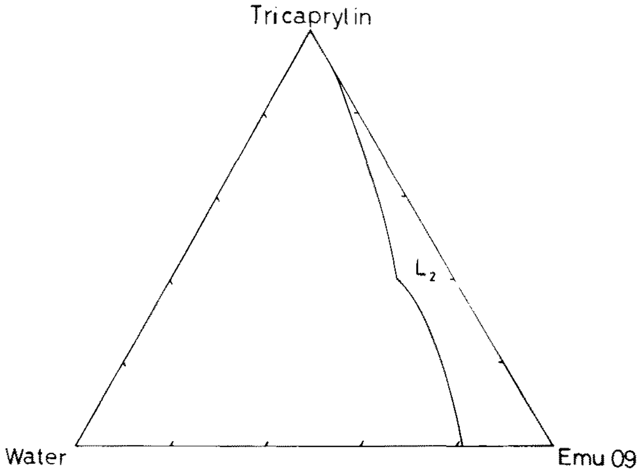

FIG. 1. The organic liquid area in the system water-nonionic emulsifier-tricaprylin. L_2 = liquid phase.

EXPERIMENTAL PROCEDURES

Materials

The sodium xylene sulfonate, a commercial product from Marchon Ltd., England, was used without purification. The monocaprylin was synthesized at the Institute of Medical Biochemistry at the University of Gothenburg, Sweden, and the tricaprylin (>99.5%) was from Eastman Distillation Products Industries. The sodium oleate, puriss. quality, was from KEBO AB, Stockholm, and the nonionic emulsifier, Emu 09, a commercial alkyl-aryl polyglycol ether, was from Berol AB, Sweden. Purified egg-lecithin (5), urea of p.a. quality from Merck, Darmstadt, and twice-distilled water were used.

Phase Equilibria

Phase equilibria were determined by visual inspection of weighed samples in a microscope with crossed polaroids,

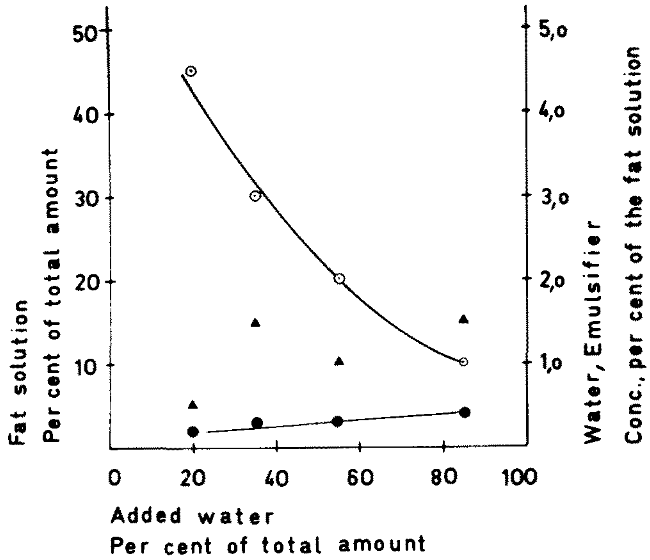

FIG. 2. Percentage tricaprylin solution which separates when water is added to a 50 wt % solution of tricaprylin in emulsifier and water and emulsifier content in the solution: —○—○— separated triglyceride solution (absc. left) —▲—▲— emulsifier concentration in the triglyceride solution; —●—●— water concentration in the triglyceride solution (absc. right).

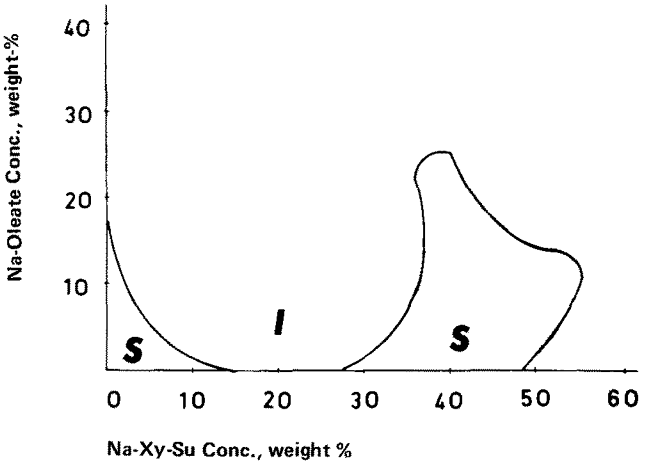

FIG. 3. Solubility of sodium xylene sulfonate in aqueous sodium oleate solutions: S, solution; I, insoluble composition.

combined with analysis of different phases in equilibrium separated by means of centrifugation. The different phases were also identified by means of their x-ray diffraction patterns (6).

RESULTS

Phase Regions

Surface Active Substances. A direct solubilization of triglycerides in a nonionic emulsifier (alkyl aryl polyethylene glycol) gave results according to Figure 1. The tricaprylin and the emulsifier are completely soluble in each other, and the combination dissolves an amount of water roughly proportional to the amount of emulsifier. Dilution of a solution of the two compounds in the ratio of 1:1 by weight gives several phases. The content of emulsifier and water in the oil-liquid phase versus the total water content is shown in Figure 2.

Sodium oleate dissolves sodium xylene sulfonate to about 25 wt % (Fig. 3). The shape of the solubility region enables the sodium xylene sulfonate to be separated by diluting with water from the solution high in soap content. The solubilization of triglyceride is, however, less than 1% in this solution.

Hydrotrope-Water-Monoglyceride. The water-sodium xylene sulfate-monocaprylin system is shown in Figure 4. The liquid solution extends in a broad region from the water-hydrotrope axis to the triangular mesomorphic phase region on the water-monocaprylin axis. The liquid crystalline phase reaches to about 45% water in a very narrow region beneath the isotropic solution. When the hydrotrope is exchanged with urea (Fig. 5) the solution will not solubilize water in excess of the liquid crystalline phase; its water content is approximately 50%.

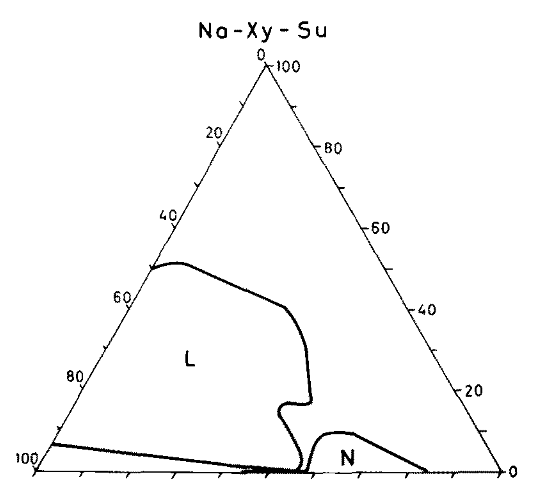

FIG. 4. The phases in the system water-monocaprylin-sodium xylene sulfonate: L, liquid phase; N, liquid crystalline phase ("neat soap").

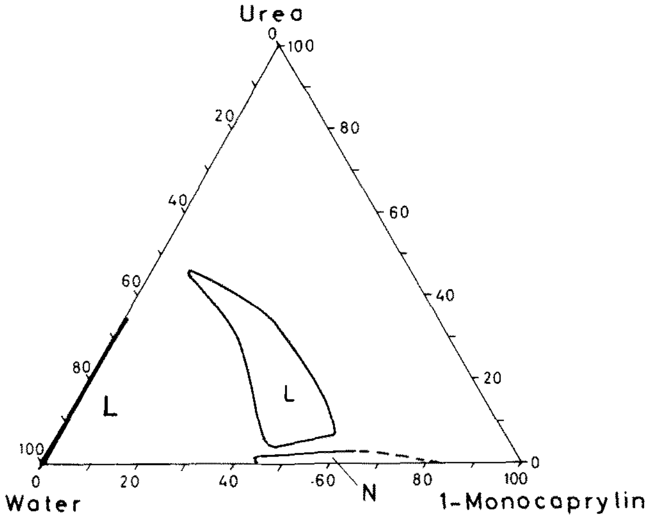

FIG. 5. The phases in the system water-urea-monocaprylin: L, isotropic solution; N, liquid crystalline phrase ("neat soap").

Using lecithin instead of the monoglyceride (Fig. 6) gives a liquid crystalline phase which is able to solubilize about 26% of the hydrotrope. The corresponding aqueous solution solubilizes the monocaprylin to a maximum of 25 wt % but only when it contains a high amount of hydrotrope, about 40 wt %.

Solubilization of Triglyceride

Tricaprylin is solubilized to less than 1% in the isotropic liquid phases in Figures 5 and 6. However, the liquid phase in Figure 4 solubilizes the tricaprylin to a maximum of about 15%, varying with the ratio of monocaprylin to hydrotrope (Fig. 7). The same figure shows the remarkable decrease of solubilizing capacity with increasing water content.

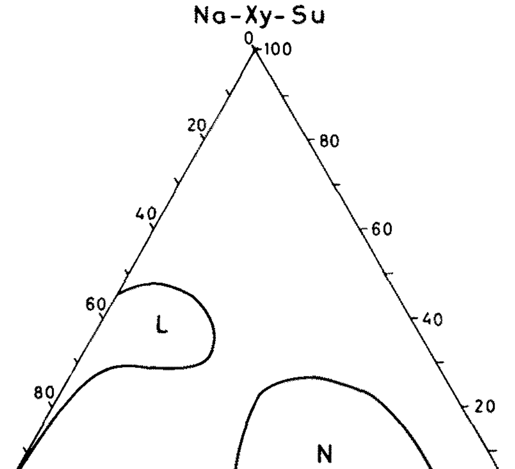

FIG. 6. The phases in the system water-lecithin-sodium xylene sulfonate: L, isotropic solution; N, liquid crystalline phase ("neat soap").

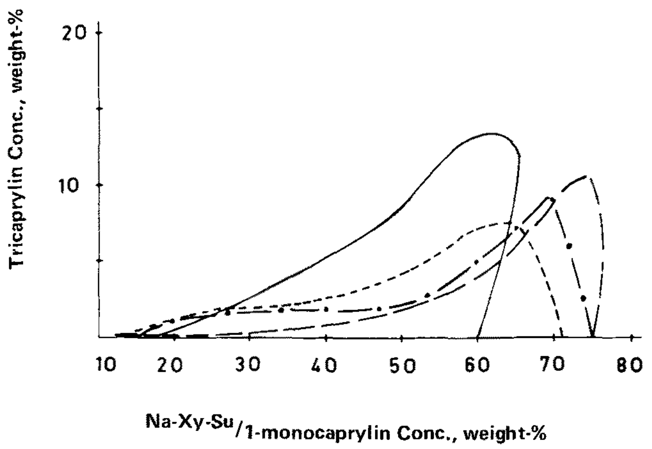

FIG. 7. Tricaprylin solubilization in aqueous solutions of sodium xylene sulfonate and monocaprylin. Ratio sodium xylene sulfonate-monocaprylin: ————, 15:85; ----, 30:70; — • — • — •, 40:60; ————, 50:50.

DISCUSSION

The results illustrate how narrow the limits for the properties of the components must be to achieve aqueous solutions of triglyceride. Aqueous solutions of an anionic surface active substance like sodium oleate will not solubilize tricaprylin in spite of the pronounced hydrophobic character of the long hydrocarbon chain. Addition of a maximal amount of the hydrotrope does not produce noticeable improvement. The nonionic emulsifier dissolves the liquid triglyceride in its pure form and these solutions solubilize water to some extent. These solutions, however, should not be considered aqueous. Dilution with water gives a spontaneous separation of the triglyceride with emulsifier and water which is left in the solution, to a magnitude of 1%. The formation of liquid crystalline phases will cause some losses of triglyceride, which will probably increase with increased chainlength of the triglyceride.

The attempts to solubilize triglycerides by means of adding a hydrotrope to a liquid crystalline structure containing the compound proved successful. The hydrophilic-hydrophobic balance of the compounds must, however, be carefully selected.

Lecithin and sodium xylene sulfonate give a combination in which the hydrotrope will not be able to transform the ordered structure of the liquid crystalline phase into an isotropic liquid. This is probably due to both the long hydrocarbon chains which, when being ordered, release more energy than the shorter chains of the monocaprylin, and to the stabilizing effect of the "zwitterions" in the polar group. Consequently, the aqueous solution will not solubilize the monoglyceride to such an extent that solubilization of the triglyceride can be made possible. The urea has too little hydrophobic character to be of value for the solubilization of the triglyceride.

The combination of sodium xylene sulfonate and monocaprylin appears to give the desired character to the solution. The addition of the hydrotrope causes a breakdown of the ordered liquid crystalline structure in the region 45-57% monocaprylin. Monocaprylin content in excess of this maximum value forms a liquid crystalline structure which can solubilize 10% of the hydrotrope. Further addition of hydrotrope results only in breakdown of parts of the mesomorphic phase and excess hydrotrope will precipitate as a crystalline compound.

The maximum solubilization of triglyceride takes place in the very region where the addition of hydrotropes causes the transformation from a liquid crystalline structure to an isotropic liquid. This effect is shown in Figure 7 (of Fig. 4); the amount of dissolved tricaprylin is reduced at about 50% water content.

Theoretically, these results make it possible to prepare aqueous solutions of triglycerides by means of hydrotropic agents. The triglyceride can be separated from the solution by dilution with water, which, however, causes the separation of a triglyceride containing some monoglyceride. The possibilities of purifying the triglyceride will be investigated in the future.

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