ELSEVIER

International Journal of Pharmaceutics 137 (1996) 177–186

international journal of pharmaceutics

Sucrose esters/cosurfactant microemulsion systems for transdermal delivery: assessment of bicontinuous structures

M.A. Thevenin[a], J.L. Grossiord[b], M.C. Poelman[a,*]

[a]*Laboratoire de Dermopharmacie et Biophysique cutanée, Faculté des Sciences Pharmaceutiques et Biologiques, 4 av. de l'Observatoire, 75006 Paris, France*

[b]*Laboratoire de Physique Pharmaceutique, Faculté de Pharmacie, 5 rue J. Baptiste Clément, 92296 Chatenay-Malabry, France*

Received 13 March 1995; revised 19 February 1996; accepted 11 March 1996

Abstract

This research studies microemulsion systems containing minimal amounts of surfactant for topical use. Sucrose esters are not able to form microemulsions without a cosurfactant. Microemulsion areas were investigated for numerous systems including sucrose esters/cetearyl octanoate/alcohols/water at different surfactant/cosurfactant mass ratios, called K_m, and different HLB values. The pseudoternary isotherm diagrams were constructed by titration at 25°C. The long and unsaturated oleic chain of the surfactant improves the extent of the microemulsion zone and when K_m increases the domain becomes larger. A combination of laurates at HLB = 7 increases the water and oil solubilizing capacity. Cosurfactants affect the shape and the extent of microemulsion regions. Shorter alcohols which are expected to disorder the interfacial film gave extended microemulsion zones by destabilizing the liquid crystalline phases. Moreover, in short alcohol based diagrams, the microemulsion areas are single volume in which the percolation transition law can be applied. The electroconductive behaviour allows us to determine the percolation threshold and to identify quantitatively bicontinuous structures. These structures, owing to their very low interfacial tension, associated to their wetting properties, should be very interesting as new drug carrier systems for transdermal delivery.

Keywords: Microemulsions; Sucrose esters; Percolation; Bicontinuous structure

1. Introduction

Microemulsions are transparent fine dispersions of oil and water droplets stabilized by surfactant molecules. Microemulsions are macroscopically monophasic, isotropic and possess a flexible interfacial film which is characterized by ultralow interfacial tension values (10^{-2} mN/m) (Quemada and Langevin, 1985; Bourrel and Schechter, 1988; De Roni and Poelman, 1989). Such dispersions are easy to formulate and various structures (O/W or W/O) could be obtained, even bicontinuous.

In contrast to emulsions, they are thermodynamically stable and this stability makes them interesting as drug carrier systems for transdermal delivery. Moreover, the dispersed phase could act as a reservoir and lead to a controlled rate deliv-

---

* Corresponding author.

PII S0378-5173(96)04518-8

ery system. Due to the small size of the dispersed droplets (less than 100 nm) and their high specific surface, high percentages of surfactants are required. Skin damages then could be induced. According to Friberg, 1990, the direct contact between the microemulsion and the skin may lead to a disruption of the liquid crystalline structure of the stratum corneum layers and hence enhances penetration but increases the risk of irritation.

Drug research is very concerned in microemulsions (Ziegenmeyer and Führer, 1980; Bhargava et al., 1987; Gasco et al., 1990; Trotta et al., 1990), but safe systems should be used. A new step in microemulsion formulation should be reached with the use of mild surfactants of natural origin which could reduce skin injuries.

Recently, interest has been reported in phospholipids in isopropyl myristate microemulsions (Aboofazeli and Lawrence, 1993, 1994) but the use of sucrose esters in order to overcome the irritating potency has not yet been proposed. Compared with lecithins, sucrose esters are nonionic surfactants, approved by FAO/WHO, in Japan, the USA, the EU, as food additives owing to their high safety and excellent properties (Akoh, 1992). Such surfactants, non-toxic and biodegradable, could be helpful to formulate new microemulsion systems for cosmetic or pharmaceutical use.

The aim of this study is therefore to assess the performance of sucrose esters as surfactants to formulate microemulsions containing water and cetearyl octanoate as the oily phase and to find microemulsions containing low amounts of surfactants and cosurfactants, consistent with a pharmaceutical use.

2. Materials and methods

2.1. Materials

A homogeneous class of sucrose esters was supplied by Kagaku Foods Corporation (France). They differ in the nature of their alkyl chain and their HLB value (Table 1). The degree of purity of sucrose esters described in Table 1 is not less than 80%. Cetearyl octanoate (PCL) was supplied by Dragoco (France). Ethanol and isopropanol were purchased from Cooper (France), propanol 1 and octanol from Prolabo (France), butanol 1, hexanol 1 and heptanol 1 from Labosi (France) and pentanol 1 from Baker (Holland).

2.2. Methods

2.2.1. Influence of the surfactant

Systems containing sucrose esters, cetearyl octanoate and water were investigated first. The microemulsion zones were delimited and the influence of the surfactant chain length on the phase behaviour was studied (Table 1).

The purpose of this study is the finding of a microemulsion containing low surfactant concentrations. The different parameters which could enhance the microemulsion areas and increase the water and oil solubilizing capacity were therefore reviewed: use of a cosurfactant and influence of HLB values.

2.2.2. Role of the cosurfactant in the shape and extent of microemulsion areas: a quantitative and qualitative approach

Aliphatic alcohols were selected as cosurfactants because they constitute an homogeneous class widely used in microemulsion systems (Clausse et al., 1987a; Aboofazeli and Lawrence, 1993, 1994).

Table 1
Composition of the investigated systems: influence of the surfactant

Surfactant	HLB	Aqueous phase	Oil phase
Sucrose monolaurate	16	Distilled water	PCL
Sucrose dilaurate	5	Distilled water	PCL
Sucrose myristate	16	Distilled water	PCL
Sucrose palmitate	15	Distilled water	PCL
Sucrose stearate	7	Distilled water	PCL
Sucrose stearate	9	Distilled water	PCL
Sucrose stearate	11	Distilled water	PCL
Sucrose stearate	15	Distilled water	PCL
Sucrose oleate	15	Distilled water	PCL

Table 2
Composition of the different investigated systems: K_m ratio values studied

Surfactant	Cosurfactant	Aqueous phase	Oil phase	K_m 0.25	0.42	0.66	1	1.5	2.33
Sucrose oleate	Ethanol	Distilled water	PCL	+	+	+	+	+	+
Sucrose laurate	Ethanol	Distilled water	PCL	–	–	–	+	+	+
Sucrose dilaurate	Ethanol	Distilled water	PCL	–	–	–	+	+	+
Sucrose monolaurate	Ethanol	Distilled water	PCL	–	–	–	+	+	+

Table 3
Composition of the different mixtures investigated: cosurfactants studied

Surfactant	Cosurfactant	Aqueous phase	Oil phase	K_m
Sucrose oleate	Propanol	Distilled water	PCL	1.5
Sucrose oleate	Isopropanol	Distilled water	PCL	1.5
Sucrose oleate	Butanol	Distilled water	PCL	1.5
Sucrose oleate	Pentanol	Distilled water	PCL	1.5
Sucrose oleate	Hexanol	Distilled water	PCL	1.5
Sucrose oleate	Heptanol	Distilled water	PCL	1.5
Sucrose oleate	Octanol	Distilled water	PCL	1.5

2.2.2.1. Concentration of the cosurfactant. Ethanol was added to each system previously described. The pseudoternary phase diagrams were drawn with the top apex representing a specific surfactant to cosurfactant mass ratio called K_m (Table 2).

2.2.2.2. Nature of the cosurfactant. The effects of the alkyl chain length (n = 3–8) and of the propanol/isopropanol isomery on the interfacial film were studied (Table 3).

2.2.3. Influence of the HLB

The optimum HLB ratio mixtures of non-ionic surfactants is an important factor in increasing solubilization (Marszall, 1987). The mixture of two surfactants which have the same alkyl chain length but a quite opposite solubilizing ability towards oil and water may enhance the mutual solubilization of oil and water. Experiments were performed with sucrose monolaurate and dilaurate to achieve intermediate HLB values (5, 7, 9, 11, 13, 16) (Table 4).

2.2.4. Construction of pseudoternary phase diagrams

For a given K_m value, appropriate amounts of PCL, sucrose ester and alcohol were weighed into vials and stirred till a clear solution was obtained.

Phase diagrams were drawn by titrating 3 g of these samples with an aliquot of distilled water until the boundaries of the microemulsion zones were reached. For each K_m value, the ratios R = (lipophilic phase)/(surfactant + cosurfactant) from 1:9 to 9:1 were studied. Isotropic areas were checked through cross-polarizers. All experiments were performed twice at T = 25°C.

2.2.5. Electroconductive measurements

It has been previously demonstrated that constant correlations do exist between structure type and microemulsion electroconductive behaviour (Clausse et al., 1987a). Thus, conductimetry is a useful tool to assess microemulsion structure (Clausse et al., 1987a,b). The phase behaviour of the PCL/sucrose oleate/water/propanol system was checked by this method at K_m = 1.5 (see Table 5).

Two systems were selected which differ by their aqueous phase. The first one, containing distilled

Table 4
Composition of the investigated systems: influence of the HLB at K_m = 1, 1.5, 2.33

Surfactant	Cosurfactant	Aqueous phase	Oil phase	HLB
Sucrose mono/dilaurate	Ethanol	Distilled water	PCL	7
Sucrose mono/dilaurate	Ethanol	Distilled water	PCL	9
Sucrose mono/dilaurate	Ethanol	Distilled water	PCL	11
Sucrose mono/dilaurate	Ethanol	Distilled water	PCL	13

Table 5
Compositions of the two systems investigated for electroconductive measurements

	Surfactant	Cosurfactant	Aqueous phase	Oil phase	K_m
System 1	Sucrose oleate	Propanol	Distilled water	PCL	1.5
System 2	Sucrose oleate	Propanol	0.4 NaCl in distilled water	PCL	1.5

water, exhibits an electroconductive behaviour in spite of its non-ionic type ($\sigma_{\text{distilled water}}$ = 2.6 μs). To validate the general feature of the curve, a second system, containing 0.4% NaCl in the water phase, was chosen.

Along the experimental path investigated (R = 2:8) 30 samples were formulated which differ from each other by their water content, called the water volume fraction Φ_w. Between two consecutive mixtures Φ_w varies by 0.01.

The conductivity, σ, was recorded by means of a TACUSSEL CD 78 conductimeter at T = 24°C and at the frequencies 62.5 Hz and 250 Hz.

3. Results and discussion

3.1. Influence of the surfactant

The various sucrose esters investigated differ in their alkyl chain length, a fact which has to be considered to study the influence of this parameter on the extent and the shape of the microemulsion domain.

In spite of the large range of sucrose esters studied when used alone no microemulsion zone could be successfully found. As Aboofazeli reported for lecithins (Aboofazeli and Lawrence, 1994), we concluded that sucrose esters are not able to give isotropic solutions of water and oil without a cosurfactant under our conditions. Since the solubility of sucrose esters in the oil and water phases at room temperature was poor the use of a cosurfactant was necessary.

3.2. Role of the cosurfactant

3.2.1. Concentration of cosurfactant

In order to make sucrose ester based microemulsions pharmaceutically available, we need to use safe compounds; ethanol was then chosen as the cosurfactant.

In this part, two parameters could be assessed: (1) the qualitative effect of the surfactant at a constant K_m value on the size of the microemulsion area. Sucrose stearate and sucrose palmitate whose melting point is above 50°C could not form microemulsion systems, even in the presence of ethanol; (2) the effect of the concentration of ethanol according to K_m.

Pseudoternary diagrams (Figs. 1-4) show the evolution of the microemulsion related to K_m. From these diagrams, it is obvious that all the microemulsion zones form a single volume (called type U by Clausse). The presence of liquid crystalline areas was not detected.

Sucrose monolaurate and myristate, which possess a higher monoester content (83% and 81%, respectively), have a great affinity towards water. A micellar solubilization area appears on the left of the diagrams.

This phenomenon is greatly enhanced by ethanol which increases the effective HLB value of the system by increasing the relative affinity of

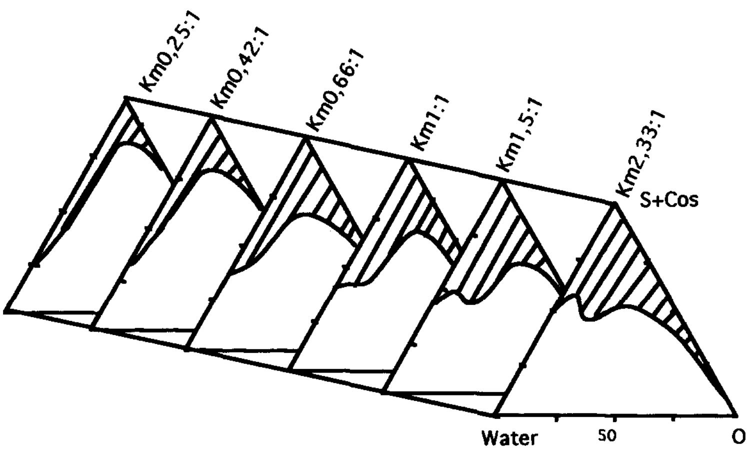

Fig. 1. Phase diagrams of the quaternary systems containing water/sucrose oleate/ethanol/PCL at different K_m values at $T = 25°C$.

non-ionics for water. With sucrose dilaurate the inverse phenomenon is observed.

For constant values of K_m (1; 1.5; 2.33), the long and unsaturated oleic chain best promotes the incorporation of large amounts of water and PCL (11% PCL, 45% water in the 40% O1570/ethanol system). This result is consistent with De Roni's work (De Roni and Poelman, 1989) which studied the same parameter with non-ionic surfactant esters of the polysorbate type. It may be explained by the great flexibility of the oleic chain, which is involved in a decrease of the interfacial tension rigidity.

Shinoda and Friberg (1975), have shown that if

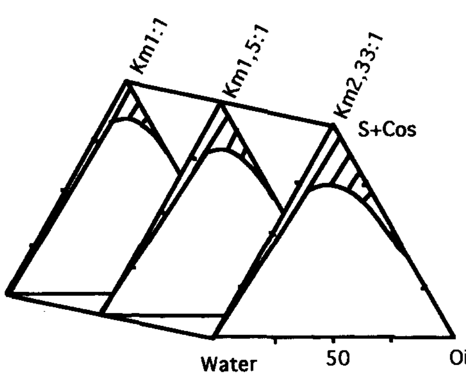

Fig. 3. Phase diagrams of the quaternary systems containing water/sucrose monolaurate/ethanol/PCL at different K_m values at $T = 25°C$.

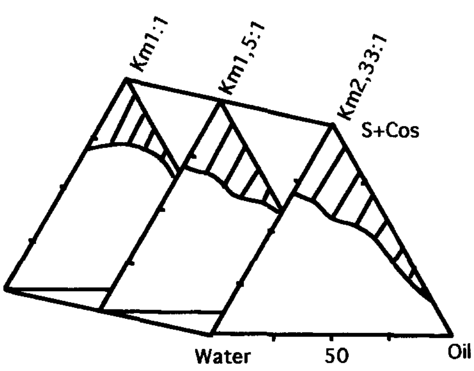

Fig. 2. Phase diagrams of the quaternary systems containing water/sucrose dilaurate/ethanol/PCL at different K_m values at $T = 25°C$.

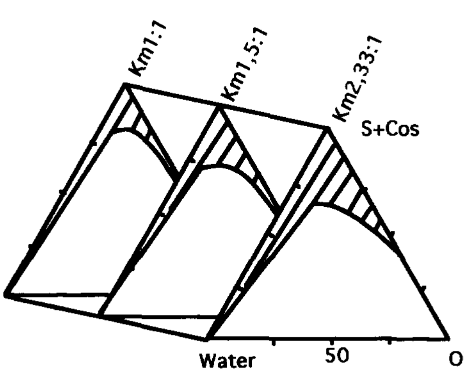

Fig. 4. Phase diagrams of the quaternary systems containing water/sucrose myristate/ethanol/PCL at different K_m values at $T = 25°C$.

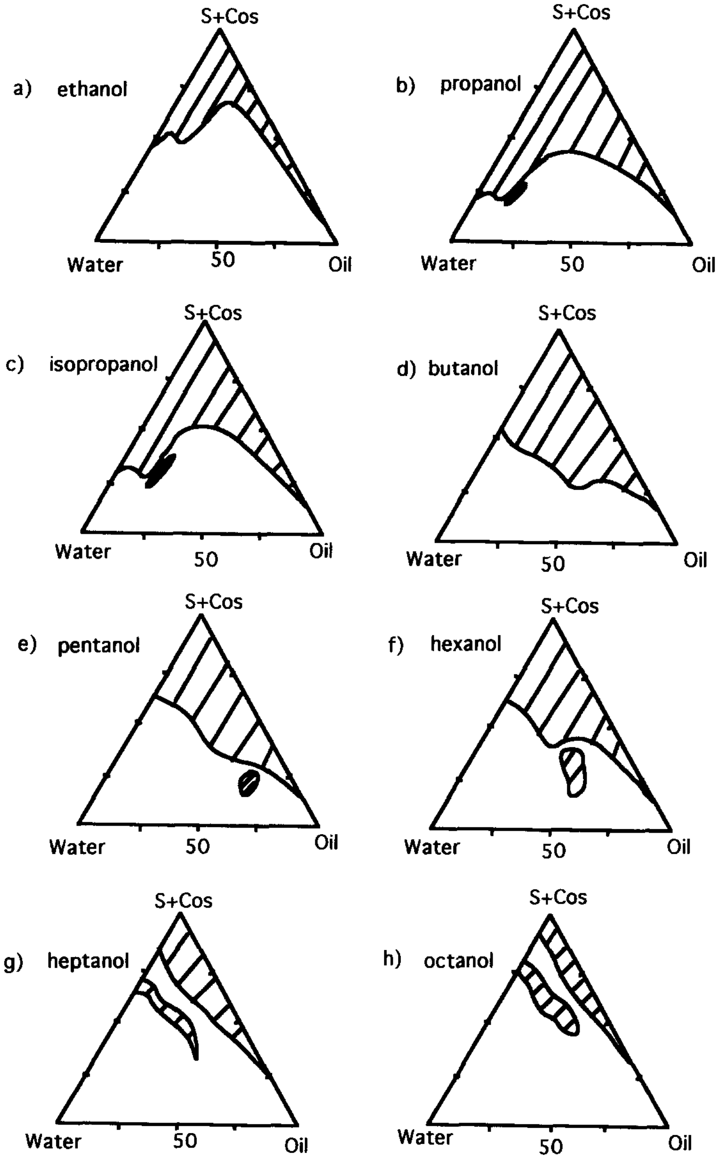

Fig. 5. Phase diagrams of the quaternary systems containing water/sucrose oleate/alcohols/PCL at K_m = 1.5 at T = 25°C.

the size of the hydrophilic and lipophilic groups of the solubilizer increases, the CMC will decrease, the aggregation number will increase and the solubilizing power will be enhanced. Our results are consistent with these authors and justify the choice of this surfactant in the following experiments.

When K_m is increasing from 0.25/1 to 2.33/1 for sucrose oleate and from 1/1 to 2.33 /1 for sucrose mono-di-laurate and myristate, the microemulsion zones become larger. This suggests that high concentrations of surfactants are necessary to enhance the extent of the microemulsion areas.

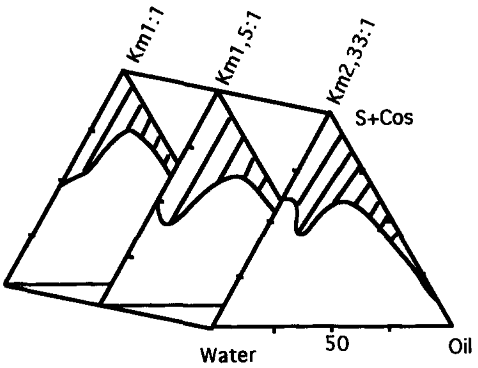

Fig. 6. Phase diagrams of the quaternary systems containing water/sucrose mono-dilaurate/ethanol/PCL at different K_m values and HLB 7 at $T = 25°C$.

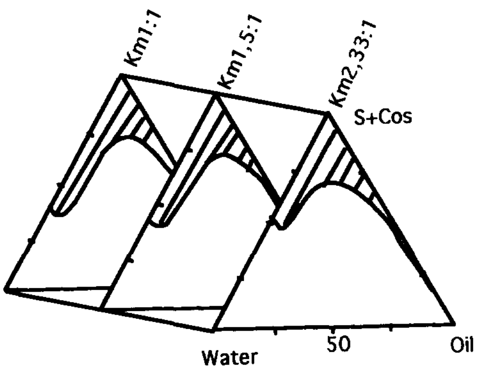

Fig. 7. Phase diagrams of the quaternary systems containing water/sucrose mono-dilaurate/ethanol/PCL at different K_m values and HLB 9 at $T = 25°C$.

It is obvious for sucrose oleate that high concentration of ethanol ($K_m = 0.25/1$), which is a polar solvent, tends to generate higher incorporation of water. This result is not surprising if one considers that ethanol addition increases the effective HLB of the surfactant (Marszall, 1987). Finally, whatever the sucrose ester used and the mass ratio K_m selected, the surfactant amount at the transition phase in the sucrose oleate system, where microemulsion with moderate amounts of surfactant could be found, is still high (43%). This result can be clearly improved by varying the type of cosurfactant or by mixing the surfactants to obtain different HLB values.

By changing the HLB of surfactants we could reach an optimum HLB at which a large solubilization of hydrocarbon and water could be obtained (Marszall, 1987; Shinoda and Lindman, 1987).

3.2.2. *Influence of the cosurfactant*

The combination of sucrose oleate and alcohols leads to the increase of mutual solubilization and to the existence of stable single phased fluid media. The results are shown in Fig. 5a–h.

The nature of the cosurfactant had a strong influence on the shape and the extent of the microemulsion zones. Alcohols with moderate molecular weights, such as pentanol or hexanol, depress the relative affinity of non-ionics for water, whereas lower alcohols have an opposite but smaller effect (Marszall, 1987).

For heptanol and octanol, the microemulsion domains were divided in two separate areas. The upper part corresponded to a W/O zone called 'L2 inverse type medium' and the lower to an O/W zone called 'L1 direct type medium'. Between these two areas, a broad range of compositions was observed, corresponding to the existence of various polyphasic media. This configuration is called 'type S' by Clausse et al., 1987a.

In the case of 1 pentanol a hybrid configuration was observed with a broad area and a smaller one

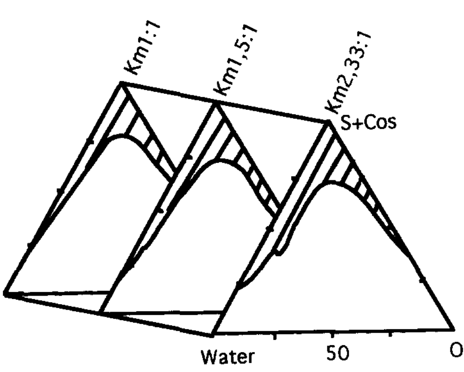

Fig. 8. Phase diagrams of the quaternary systems containing water/sucrose mono-dilaurate/ethanol/PCL at different K_m values and HLB 11 at $T = 25°C$.

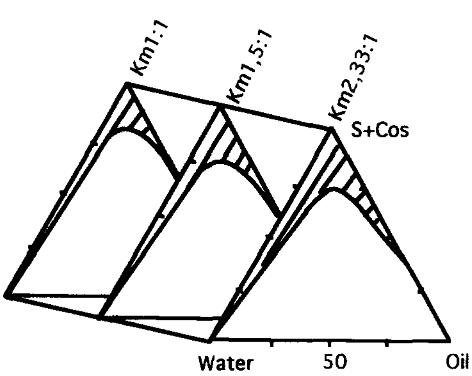

Fig. 9. Phase diagrams of the quaternary systems containing water/sucrose mono-dilaurate/ethanol/PCL at different K_m values and HLB 13 at $T = 25°C$.

included in the oily part of the diagram. With shorter alcohols (ethanol, propanol and isopropanol) the domain forms a single volume and this configuration is labelled 'type U' by Clausse et al., 1987a.

The transition from a U to an S system corresponds to five carbons in the chain length. Our results agree with the findings of Clausse et al. (1987a).

As shown by Clausse et al. (1987a) with anionic surfactants and by Aboofazeli and Lawrence (1993) with lecithins, close correlation can be seen between the microemulsion pseudoternary system configuration and the alcohol affinity towards water. The alcohols differ by their alkyl chain length, their cross-sectional areas and their solubility in water. The distribution of the alcohols between the aqueous phase, the lipophilic phase and the interface depends upon their partition coefficients (Aboofazeli and Lawrence, 1993).

Cosurfactants should be chosen for their poor affinity either with the continuous or the dispersed phase. The proper cosurfactant will migrate to the oil/water interface and form a mixed surfactant/cosurfactant film. Propanol and butanol seems to possess the best amphiphilic balance. For example, with propanol the more valuable system for our purpose contained sucrose oleate 12%, propanol 8%, PCL 9% and water 70%.

The cosurfactant causes a transitory lowering of the interfacial tension during the formation of the dispersion. A long alcohol chain increases the interfacial rigidity, and polyphasic media or liquid crystals media may occur between the L1 and L2 phases (see octanol and heptanol diagrams) (Rosano et al., 1988).

Shorter alcohols are favourable to a disordered interfacial film and the inversion phase between L2 and L1 occurs without any discontinuity in the macroscopic properties of the system.

The effect of the alcohol isomery was investigated with propanol and isopropanol. As described by Clausse for anionic surfactants (Clausse et al., 1987a), there is no significant influence of the isomery on the microemulsion domain.

3.3. Influence of the HLB

The results are reported in Figs. 6–9. When the HLB increases, the hydrophilic part of the surfactant is increasing and for a small amount of oil a continuous aqueous isotropic medium along the surfactant/water axis can be observed. For high HLB values (11, 13, 16) (Figs. 3, 8 and 9), the sucrose mono-di-laurate mixtures have a strong affinity for the water phase. In spite of relatively low HLB values (11 and 13), the micellar solubilization medium appears to be related to the presence of ethanol as a cosurfactant. At smaller HLB value (5) (Fig. 2), the phenomenon is entirely inverted.

For HLB 7 with ethanol, the equilibrium between the hydrophilic and lipophilic part of the surfactant molecule favours its location at the interface and decreases the interfacial tension. For that HLB value, the microemulsion zones are the largest. However, with the minimal cosurfactant-surfactant amount (40%), only 10% PCL can be solubilized.

3.4. Electroconductive behaviour

A strong correlation does exist between the conductivity curves of the two investigated systems. The use of the first one is therefore valid to study the microemulsion structure.

The drastic changes in conductivity around a given water volume fraction Φ_p can be attributed to a phase inversion from reverse swollen micelles (W/O) to direct micelles (O/W) (Fig. 10).

In such diagrams, we explain this transition by the emergence of bicontinuous structures which possess ultralow interfacial tension. These dynamic structures are described as water and oil pseudo-domains which rapidly exchange. These original mixtures are very promising for their wetting and substantive properties for biological membranes (Carlfors et al., 1991).

Constant correlations exist between these specific structures and the microemulsion electroconductive behaviour. This vindicates the use of electroconductimetry to localize bicontinuous media on the diagrams (Clausse et al., 1987b).

The interpretation of the curves requires the concept of percolation transition proposed by De Gennes, 1976. This concept is used for interpreting the conductivity of disordered media such as microemulsions (Laguës et al., 1978; Laguës, 1979; Laguës and Sauterey, 1980; Langevin, 1986; Safran et al., 1987). The percolation transition signifies the first emergence of an infinite cluster for a critical value of the water volume fraction Φ_p, called the percolation threshold. This state characterizes bicontinuous structures. In such systems, conductivity is governed by a universal law independent of the physical properties of the medium.

Near the percolation threshold, just before the medium becomes suddenly conducting:

$$\sigma = (\Phi_w - \Phi_p)^t$$

where σ is the conductivity (Siemens), t depends on the system dimensionality (t = 1.5–1.6 for a three-dimensional system), Φ_w is the dispersed volume fraction (= water volume fraction) and Φ_p is the dispersed volume fraction at the percolation threshold.

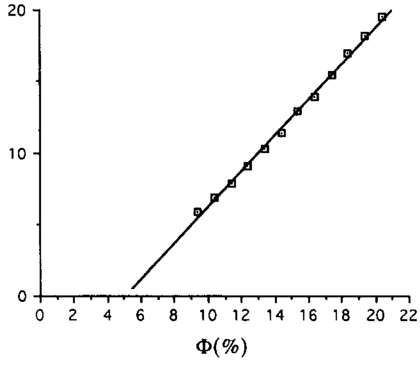

Fig. 10. Percolation threshold determination.

The σ values checked in our systems follow this law. In order to determine Φ_p and t independently, $\sigma^{1/t}$ was plotted versus Φ_w. $\sigma^{1/t}$ is linear in Φ for t = 1.5. This result is consistent with the experiment of Laguës (1979).

$$\sigma^{1/t} = -6.39 - 1.26\Phi_w$$

Our system undergoes a percolation transition and it is possible to calculate the percolation threshold which corresponds to the bicontinuous phase.

$$\Phi_p = 6.39/1.26 = 5.07\%$$

The intrinsic Φ_p value depends upon the droplet size and the interactions between them (Safran et al., 1987). The low value of the threshold is the consequence of the attractive interactions of the conductive species in the system.

4. Conclusion

This investigation demonstrates the ability of low concentrations of sucrose ester to form a microemulsion with cetearyl octanoate as the oily phase. The combination of sucrose mono-dilaurate, sucrose myristate and sucrose oleate with ethanol gives rise to extended microemulsion areas.

Microemulsions with sucrose oleate were found to contain the lower percentages of surfactant and cosurfactant. In order to optimize sucrose oleate microemulsion domains, alcohols with increasing chain length were studied and propanol gave the more interesting results.

The present study emphasizes the importance of HLB value. To optimize the microemulsion zones in the sucrose laurate/ethanol/PCL/water system, HLB 7 was found to be the proper ratio under our conditions.

Moreover, the diversity of the structures (L1, L2, bicontinuous) found in our study is of great interest for pharmaceutical technology.

Sucrose ester based microemulsions, due to their innocuity, should constitute original drug carrier systems for transdermal delivery.

References

Aboofazeli, R. and Lawrence, M.J., Investigations into formation and characterization of phospholipid microemulsions. I. Pseudoternary phase diagrams of systems containing water-lecithin-alcohol-isopropyl myristate. *Int. J. Pharm.*, 93 (1993) 161–175.

Aboofazeli, R. and Lawrence, M.J., Investigations into formation and characterization of phospholipid microemulsions. II. Pseudoternary phase diagrams of systems containing water-lecithin-isopropyl myristate and alcohol: influence of purity of lecithin. *Int. J. Pharm.*, 106 (1994) 51–61.

Akoh, C.C., Emulsification properties of polyesters and sucrose ester Blends I: carbohydrate fatty acid polyesters. *J. Am. Oil Chem. Soc.*, 69 (1992) 9–19.

Bhargava, H.N., Narurkar, A and Lieb, L.M., Using microemulsions for drug delivery. *Pharm. Technol.*, 11(3) (1987) 46–54.

Bourrel, M. and Schechter, R.S., The R ratio. In Bourrel, M., Schechter, R.S. (Eds.), *Microemulsions and related systems*, Marcel Dekker, New York, Basel, 1988, pp. 1–30.

Carlfors, J. Blute, I. and Schmidt V., Lidocaine in microemulsions. A dermal delivery system. *J. Dispers. Sci. Technol.*, 12 (1991) 467–482.

Clausse, M., Nicolas Morgantini, L., Zradba, A. and Touraud, D., Water/ionic surfactant/alkanol/hydrocarbon system: influence of certain constitution and composition parameters upon realms of existence and transport properties of microemulsion type media. In Rosano, H.L. and Clausse, M. (Eds.), *Microemulsion systems*, Marcel Dekker Inc., New York, Basel, 1987a, pp. 15–63.

Clausse, M., Nicolas Morgantini, L. and Zradba, A., Water/sodium dodecylsulfate/1 pentanol/N-dodecane microemulsions. Realms of existence and transport properties. In Rosano, H.L. and Clausse, M. (Eds.), *Microemulsion systems*, Marcel Dekker Inc., New York, Basel, 1987b, pp. 387–425.

De Gennes, P.G., La percolation: un concept unificateur. *Recherche*, 72 (1976) 919–927.

De Roni, M. and Poelman, M.C., Influence de la nature de l'agent de surface dans la formulation des microémulsions. 5th International Conference of Pharmaceutical Technology, AGPI, Paris, 1 (1989) 148–154.

Friberg, S.E., Micelles microemulsions liquid crystals and the structure of stratum corneum lipids. *J. Soc. Cosmet. Chem.*, 41 (1990) 155–171.

Gasco, M.R., Pattarino, F. and Lattanzi, F., Long-acting delivery systems for peptides: reduced plasma testosterone levels in male rats after a single injection. *Int. J. Pharm.*, 62 (1990) 119–123.

Laguës, M., Electrical conductivity of microemulsions: a case of stirred percolation. *J. Phys. Lett.*, 40 (1979) L331–L333.

Laguës, M. and Sauterey, C., Percolation transition in water in oil Microemulsions. Electrical conductivity measurements. *J. Phys. Chem.*, 84 (1980) 3503–3508.

Laguës, M., Ober, R. and Taupin, C., Study of structure and electrical conductivity in microemulsions: evidence for percolation mechanism and phase inversion. *J. Phys. Lett.*, 39 (1978) L487–L491.

Langevin, D., Microemulsions and liquid crystals. *Mol. Cryst. Liq. Cryst.*, 138 (1986) 259–305.

Marszall, L., H.L.B. of non ionic surfactants: PIT and EIP methods. In Schick M.J. (Ed.), *Non ionic surfactants: physical chemistry*, Marcel Dekker Inc., New York, Basel, 1987, pp. 493–547.

Quemada, D. and Langevin, D., Rheological modelling of microemulsions. *J. Theor. Appl. Mech.*, (1985) 201–237.

Rosano, H.L., Cavallo, J.L., Chang, D.L. and Whittam, J.H., Microemulsions: a commentary on their preparation. *J. Soc. Cosmet. Chem.*, 39 (1988) 201–209.

Safran, S.A., Grest, G.S., Bug, A.L.M. and Webma, I., Percolation in interacting systems. In Rosano, H.L. and Clausse, M. (Eds.), *Microemulsion systems*, Marcel Dekker, New York, Basel, 1987, pp. 235–245.

Shinoda, K. and Friberg, S.E., Microemulsions: colloid aspects. *Adv. Colloid Interface Sci.*, 4 (1975) 281–300.

Shinoda, K. and Lindman, B., Organized surfactant systems: microemulsions. *Langmuir*, 2, Vol. 3 (1987) 135–149.

Trotta, M., Gasco, M.R. and Pattarino, F., Diffusion of steroid hormones from O/W microemulsions:influence of the cosurfactant. *Acta Pharm. Technol.*, 36 (1990) 226–231.

Ziegenmeyer, J. and Führer, C., Mikroemulsionen als topische Arzneiform. *Acta Pharm. Technol.*, 26 (1980) 273–275.