# Formation of liquid crystal and other non-fluid phases in emulsions containing non-ionic surfactants

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The relation between the phase distribution of components and the nature and properties of dispersions formed in a four-component system containing dodecane, water and two homogeneous non-ionic surfactants has been investigated by phase-rule techniques. Phase equilibrium diagrams for the four ternary systems were investigated and the phase boundaries for the various regions formed in these systems were defined by synthetic and analytical methods. In some of the ternary diagrams a narrow three-phase region occurs where 'gel' or liquid crystal as well as two isotropic liquid phases are present. Dispersions containing the gel phase were very stable. The four-component system has not been fully investigated due to the presence of extensive liquid crystal phases and three-phase regions. However, some distribution data for the quaternary system was obtained. In the presence of sufficient amounts of the short chain non-ionic surfactant  $C_{10}H_{21}(O.CH_2.CH_2)_3OH$ , a three-liquid phase region occurs where multiple drops readily form.

Although emulsions are usually treated as twoliquid phase dispersions there is a growing body of evidence that a third phase is commonly present and some results show that the stability and other nroperties of emulsions are entirely controlled by this phase, which usually takes the form of a gel or is liquid crystalline (see Marland & Mulley, 1971 and refs cited). Even in the systems belonging to the two-phase class, the disperse phase may not be a simple liquid but a phase in the liquid crystal state. For most members of the ionic and non-ionic classes of synthetic surfactants used in pharmacy, the concentration range of the emulsifying agent forming simple liquid-liquid dispersions is often extremely limited (below 1%), and this is probably also true of many surfactants used in other fields. **Further** phase-rule studies on model systems are required to delineate the relation between component composition, the number and nature of the phases present and the surfactant distribution, because this information is essential to an understanding of the factors controlling emulsion type and stability.

In the present paper two non-ionic surfactants  $C_{10}E_6$  and  $C_{10}E_3$  (see Mulley, 1967 for an explanation of the nomenclature) have been investigated in dodecane-water dispersions. This mixture of low molecular weight emulsifying agents approaches

<sup>•</sup> Present address: Department of Pharmaceutics, Faculty of Pharmacy, University of Khartoum, Sudan. <sup>†</sup> Correspondence. quite closely in properties those which might be used in practice in medicinal and other emulsions but which are themselves too complicated for initial studies. The results may be expected to demonstrate the principle phenomena involved and extend the earlier exploratory studies.

## MATERIALS AND METHODS

# Materials

n-Dodecane (BDH Ltd), 99% by g.l.c. The two surfactants were 3,6,9-trioxanonadecan-1-ol (C10H21- $[O-CH_2-CH_2]_3OH)$  or  $C_{10}E_3$  (Mulley, 1967), and 3,6,9,12,15,18-hexaoxacosan-1-ol,  $(C_{10}H_{21}[O-CH_{2} CH_2-CH_2]_6OH$ ) or  $C_{10}E_6$ . Pure samples were prepared by the two-stage Williamson's method (Mulley, 1967). The physical data obtained for  $C_{10}E_3$  and  $C_{10}E_6$  were (b.p. 132–135°/1 mm, f.p.  $6.8^{\circ}$ ,  $n_{\rm D}^{25}$  1.4453 and b.p. 200–204°/1 mm, f.p. 17.4°,  $n_{D}^{25}$  1.4521) respectively. These results are in good agreement with values reported in the literature for the same compounds (Mulley, 1960; Gingras & Bayley, 1957). The compounds were also assessed by infrared spectroscopy and g.l.c. The results indicated that the two surfactants were at least 99% pure which makes them satisfactory for the present investigation.

# Phase-rule measurements

Phase equilibria diagrams for the binary and ternary systems were investigated at  $25^{\circ}$  by either synthetic or analytical methods or a combination

of these (Marland & Mulley, 1971). The concentrations of the two surfactants and dodecane in each phase were measured by g.l.c. (a Pye series 104 Model 64 chromatographic instrument had temperature programming and a flame ionization detector; column: stainless steel 5 ft  $\times$  3/16 inch i.d.; packing: 20% SE52 on 45/60 mesh acidwashed Chromosorb W; oven temperature: 220-325° at 16° min<sup>-1</sup>; nitrogen and hydrogen flow rates: 30 ml min<sup>-1</sup>. The injector detector port: 400°). The method used for analysis was the 'absolute method'. A series of standard solutions of the compound being analysed were prepared in isopropanol and compared with a test solution of one of the phases in isopropanol. As the detector response/concentration ratio was not linear, dilution of the test and standard were made so that their peak heights were approximately similar. Sample sizes ranged from  $1-10\,\mu$ l depending on the concentration of component to be detected. Retention times of 2,  $7\frac{1}{2}$  and  $14\frac{1}{2}$  min were recorded for dodecane, C10E3 and C10E6 respectively. The water content was measured by difference.

#### RESULTS

The terms 1L, 2L, 1L + LC, 2L + LC, 1L + G, 2L + G, and 3L represent one-liquid, two-liquid, one-liquid plus liquid crystal, two-liquid plus liquid crystal, one-liquid plus gel, two-liquid plus gel, and three-liquid phases respectively. The phase changes were determined visually on the following criteria. Single isotropic phases (1L) were clear, of low viscosity, and showed no birefringence. Gel phases were clear, of high viscosity, and showed no birefringence. Single liquid crystal phases (LC) were almost clear, of high viscosity, and showed birefringence. Systems containing two or three isotropic phases were turbid or milky, of low viscosity, and showed no birefringence. Composition data for all systems are given in % w/w of  $C_{10}E_6$ ,  $C_{10}E_3$ , water and dodecane in that order. Broken lines indicate that the boundary at this particular region of the diagram was not accurately known. In the figures, circles mark points determined by the synthetic method or tie-line points calculated from composition data by the method of similar triangles; crosses define tie-line data obtained by analysis.

#### Binary systems

The system  $C_{10}E_6 + water$ . The two components were miscible at 25° in all proportions except the range from 45 to 60.6% of  $C_{10}E_6$  where its solu-

bility was limited by the formation of liquid crystal. In the systems  $C_{10}E_6 + C_{10}E_3$ ,  $C_{10}E_6 + dodecane$ , and  $C_{10}E_3 + dodecane$ , the components were completely miscible at 25°. The solubility of dodecane in water has been reported as  $8.9 \times 10^{-10}$ mol fraction at 25° (Franks, 1966).

The system  $C_{10}E_3$  + water. Results illustrating the effect of temperature on phase equilibria in this system are shown in Fig. 1. At temperatures up to



FIG. 1. Phase diagram of the system  $C_{10}E_3$ -water. Ordinate: Temperature (°C). Abscissa: %  $C_{10}E_3$  in water.

30° the aqueous phases contained only about 0.1%  $C_{10}E_3$  while at higher temperatures (point c) the solubility increased to 24.1%. However, when the temperature further increased above the curve MK, the surfactant became again almost insoluble and at the solubility limit an isotropic liquid phase was formed, not liquid crystal.

#### Ternary systems

The system  $C_{10}E_6$ -water-dodecane. Figs 2 and 3 represent the phase diagrams for this system. There are seventeen regions; one-phase (four), MJT(G), E'HKVD(LC), ALBE(1L), DVXYQNC-(1L); two-phase (nine), ALNC(2L), XWY(2L), LBMJ(1L + G), MTQN(1L + G), BEE'H (1L + LC), DD'V(1L + LC), HKJT(LC + G); KVWQ-(1L + LC), VX(1L + LC); three-phase (four), LMN(2L + G), BHJ(L + LC + G), KTQ(LC + G + L), WXV(LC + 2L). The two-liquid phase



FIG. 2. Phase diagram of the system  $C_{10}E_6$ -water-dodecane at 25°. Dod: Dodecane.



Fig. 3. The dodecane-rich corner of the system  $C_{10}E_6$ -water-dodecane at 25°. Dod: Dodecane.

region ALNC in the base of the figures is confined to a remarkably narrow area with less than 1% of the surfactant being present at the higher proportions of dodecane. The heterogeneous regions at higher surfactant concentrations involve mainly quilibria between the extensive liquid crystal region and a liquid phase which is almost pure dodecane, but at lower ratios of surfactant to water the tieline data shows equilibria between an aqueous phase containing most of the surfactant and a remarkable gel-like phase occurring at high dodecane concentrations. The compositions at which this phase forms are best shown in Fig. 3. The gel has unusual properties and does not behave as a

phase in all respects. It is difficult to isolate from and equilibrate with other phases and the equilibria seem to be sensitive to the pressures involved even in centrifuges exerting moderate forces on the systems. The results in which the gel phase was not involved gave readily reproducible data providing adequate precautions were taken to ensure that equilibrium between the phases had been achieved. The results obtained when the gel phase was present depended in some degree on the conditions under which the system was prepared. These conditions have been specified as far as possible in the following account, but the results are somewhat unsatisfactory because of the experimental difficulties. The gel region MJT has been defined mainly by analytical data in other heterogeneous areas. Mixtures of the components within its area did not readily equilibrate.

When first prepared the system was obviously mainly dodecane with a small volume of another liquid phase which was not clear and which was probably water containing most of the surfactant. After several days and with vigorous shaking between periods of equilibration at 25°, the gel phase began to form and eventually the whole of the liquid phases were absorbed into the gel. Liquid phases could not then be separated by centrifugation. The gel phase was isotropic in polarized light as a bulk phase and also when examined microscopically. It was rigid, and did not form a liquid meniscus. When removed from a sealed container it could be cut into smaller pieces but within a few seconds of exposure to air it melted or otherwise released an isotropic liquid which is presumably mainly dodecane.

The three-phase region (2L + G) is drawn in the figures from the most reliable data obtained in the triangular region LMN. Centrifugation of mixtures in this region gave two isotropic liquid phases and a clear, rigid, gel-like material occupying the intermediate position in the centrifuge tube. The lower aqueous phase on analysis defined point L, the upper organic phase gave point N while the middle gel phase fixed point M (Fig. 3). However it is noteworthy that mixtures having compositions slightly above or below the triangular region LMN, separated, unexpectedly, into two liquids plus gel. When examined in polarized light the gel material did not exhibit birefringence, unlike the liquid crystal phase which appeared in region E'HKVD. In all systems containing high concentration of dodecane (over 90%) equilibration was a problem. The mixtures did not form readily and prolonged

agitation was necessary. On the other hand systems containing about the same concentrations of dode. cane and lower amounts of surfactant (region ALNC) were unstable and separated immediately into two liquids. Equilibration for seven days and continuous shaking did not produce any change and the formation of the isotropic gel phase could not be induced. All the upper organic liquid phases in the C10E6-water-dodecane system change little in composition, being almost entirely dodecane and consequently cannot be shown as individual points in Fig. 2. Points representing compositions of these phases were plotted in Fig. 3. It was found by the synthetic method that when the concentration of C10E6 was 4% only 0.38% of the water was dissolved in dodecane. Consequently, in plotting these points it was assumed that the amount of water was proportional to the concentration of the surfactant found in each upper organic phase. The directions of the tie-lines in Fig. 2 where both ends cannot be shown in the figure, were drawn by calculating the positions of the solid points shown in the figure by means of similar triangles using the composition of one of the phases and either the initial composition of the system or the analytical result for the second phase.

The system  $C_{10}E_3$  + water + dodecane. The results for this system are shown in Fig. 4. There are two two-liquid phase regions, DMEF and MGN. A narrow triangular region LMN where two liquid phases and liquid crystals are in equilibrium occurs, and there is a liquid crystalline phase surrounded by a region where liquid crystal is in equilibrium with an isotropic liquid phase.

The system  $C_{10}E_6 + C_{10}E_3 + water$ . Fig. 5 shows the phase diagram for this system. There are two liquid crystalline phases surrounded by regions where liquid crystal is in equilibrium with an isotropic liquid phase. Points A and C represent the solubility of  $C_{10}E_3$  in water and water in  $C_{10}E_3$ respectively. The remaining part of the diagram consists of an isotropic liquid (1L).

The system  $C_{10}E_6 - C_{10}E_3 - dodecane$ . At 25° the three components were miscible in all proportions.

# The quaternary system

One three-liquid phase region only was investigated (Table 1). This is related to a similar region reported earlier (Marland & Mulley, 1971). The compositions involved were near the face of the tetrahedron representing the four component system and contained about equal quantities of water and dodecane



FIG. 4. Phase diagram of the system  $C_{10}E_3$ -water-dodecane at 25°. Dod: Dodecane.



FIG. 5. Phase diagram of the system  $C_{10}E_6-C_{10}E_3$ -water at 25°.

and 1 to 2.5% of  $C_{10}E_6$ . In the two-phase, threecomponent systems in the face of the tetrahedron, the surfactant partitions mainly into the aqueous phase. Additions of 3 to 7.2% of  $C_{10}E_3$  produced four-component systems with three liquid phases in equilibrium. As shown by the results in Table 1,  $C_{10}E_6$  is removed from the aqueous phase in the presence of  $C_{10}E_3$  and the two emulsifying agents concentrate in a middle phase containing substantial amounts of water and dodecane. The dodecane-rich phase contains small amounts of the surfactants. Formation of complex multiple-drop dispersions were observed in this region before phases were isolated for analysis.

Initial composition			Upper phase			Middle phase			Lower phase		
A	B	D	A	B	D	A	B	D	A	B	D
2·2	5·5	46·5	0·34	2·1	96·0	3.6	7·2	23·7	0.01	0.016	
2·5	4·8	49·1	0·27	1·8	97·3	3.6	6·8	21·4	0.013	0.014	
2·0	4·7	44·2	0·30	1·6	98·1	3.1	7·1	28·3	0.014	0.02	
1·8	3·9	47·4	0·29	1·6	96·5	3.1	6·3	21·3	0.01	0.012	
2·2	7·2	44·8	0·43	1·9	97·0	3.3	9·8	42·4	0.01	0.013	
1·3	3·5	49·3	0·22	2·0	97·3	3.3	8·6	37·3	0.013	0.01	
1·3	4·3	49·6	0·24	2·2	96·9	4.0	11·1	36·6	0.016	0.02	
1·0	3·0	48·6	0·21	2·1	96·0	2.8	8·1	24·5	0.01	0.016	

Table 1. *Tie-line data in the three-liquid region at 25°*. A— $(C_{10}E_6)$ , B— $(C_{10}E_3)$ , D—(dodecane). The water compositions may be obtained by difference.

(--) The amount of dodecane in the aqueous phase was too little to detect (less than 0.001 %).

#### DISCUSSION

The phase diagram for the binary  $C_{10}E_3$  - water system (Fig. 1) is similar to the diagrams of Mulley (1961) for Brij 30 and that of Winfield (1968) for the  $C_{12}E_3$  - water system. The increase in the solubility of the surfactant from virtually nothing to a much higher value with rise in temperature is unexpected. Similar temperature effects on some non-ionic surfactants were reported by Elworthy & Macfarlane (1964) and Elworthy & McDonald (1964). Although the water hydrogen bonded to ether oxygens will decrease with rise in temperature, the water trapped in the polyoxyethylene mesh may increase (Nakagawa, 1967). Such an interpretation might, partly, explain the increase in the solubility observed in the present system.

The famous 'emulsion' of Pickering (1907) in which 99% by volume of 'lighting oil' was emulsified by 1% by volume of aqueous potassium oleate, is related to certain regions of the  $C_{10}E_6$  - water dodecane system. The gel phase encountered at high dodecane concentrations in the latter system (Fig. 3) has properties which are similar in many respects to those of Pickering's 99% oil 'emulsion'. In the present system, however, the gel is almost transparent and not opaque as in Pickering's systems. Although Pickering claimed his system to be an oil-in-water emulsion it has been argued that these systems are not emulsions at all, but a paste of oil and solid soap, that is, a continuous oil phase thickened by a mass of hydrated soap crystallites (Lawrence, 1937).

In the present system the surfactant is of the non-ionic type with a lower melting point and is a liquid at room temperature and therefore Lawrence's interpretation is excluded. It would seem possible that the gel has a structure similar to that suggested by Luzzati, Mustacchi & Skoulios (1958) for the

viscous isotropic phase (Cubic I) found in certain binary soap systems, and also reported by Fontell Mandell & Ekwall (1968). These reports describe such phases in both ionic and non-ionic ternary systems. According to Luzzati & others (1958) the structure is formed by spherical micelles packed in a cubic face-centred network with the micelles containing the hydrocarbon chains in an environment in which water is continuous. The gel in the present system occurs at very high concentrations of dodecane and consequently the volume fraction of the sphere-forming substance would be greater than 0.74, that is, the maximum volume fraction which can be filled by the densest packing of uniform spheres; this, however, does not absolutely exclude such a structure if it is assumed that the spheres may tend to be distorted. This structure might explain the rigidity and stability of the gel when kept in a sealed container. It seems that the amount of water present in the gel is crucial to its structure; on exposure to air the gel melted, presumably due to loss of moisture. Another possibility is that the gel might not be a single phase, but simply a mixture of phases, that is, a fine dispersion of oil-in-wateremulsion type, with a very high ratio of oil to water. This again is only possible if the droplets are nonuniform in size, distorted in shape or both. However, it might be expected that such systems, with a very high proportion of internal phase, would be extremely unstable.

This is not the case in the present system where the gel is extremely stable. Furthermore, if it is assumed that the rigidity of the gel is only due to the high concentration of droplets, then a point will be reached where further addition of dodecane to the 'concentrated emulsion' would result in the latter being inverted into water-in-oil emulsion, and this should be accompanied by a sharp drop in viscosity. This is exactly the case in the two-liquid region (ALNC). But when mixtures s and t (Fig. 3) were made, each separated into a rigid gel and an upper liquid phase which was mainly dodecane. The analytical results, although not completely reliable (the technique needs to differentiate between phases containing 96 and 99.9% of dodecane and between low surfactant concentrations), showed that the gel has its own composition region. Nevertheless, the gel has unusual properties and does not behave as a phase in all respects and therefore it must be emphasized that: (a) the interpretation of the nature of the gel phase is speculative and that equilibrium is a problem, (b) that the gel might be an intermediate state of matter between a true phase and a fine dispersion of one phase in another, (c) that observations are dependent on the conditions under which the system has been prepared.

The dispersions formed in the extensive liquid plus gel area (region LBJM) were very stable compared with the normal liquid-liquid emulsions found in the narrow two-liquid region ALNC (Fig. 2). The gel phase in this region was observed only after centrifugation. For example, when mixtures a, b and c (region LBJM) were first made they did not appear to be very different from the dispersions formed in the two-liquid region ALNC or the triangular region LMN. Microscopy revealed the presence of 'droplets' dispersed in a continuous water phase, and thus it might be concluded that this is a dispersion of oil-in-water type. An objection to this conclusion is the fact that a rigid gel-like material, rather than an organic liquid phase was produced on centrifugation. The gel phase is in equilibrium with an aqueous phase which contained most of the surfactant, possibly in the form of Hartley micelles.

In the triangular region LMN, the gel phase is in equilibrium with an aqueous phase and another liquid phase which is mainly dodecane and containing the least amount of the surfactant, presumably molecularly dispersed. Mixtures having compositions slightly outside the triangular region also separated into three phases, a phenomenon which is apparently in contradiction with the phaserule. However, this discrepancy is thought to be due to the displacement of the equilibrium caused by the centrifugation process. Similar difficulties were reported by Mandell & Ekwall (1968). The two-liquid phase regions ALNC in the base of the diagrams (Figs 2 and 3) consists of two isotropic phases, one mainly aqueous and the other of almost pure dodecane. The surfactant dissolves almost

entirely in the aqueous phase but complex changes in its partition occur in a manner related to that reported by Marland & Mulley (1972), but exhibiting also a number of differences. Full results of the distribution data and an interpretation in terms of micelle formation will be reported in another paper. The tie-line data in the two-liquid binodal WXY (Fig. 2) indicate that one of the organic phases is mainly dodecane, and what surfactant it contains is possibly molecularly dispersed. The other organic phase (at q' or r') probably contains micelles of the inverse, Hartley type, but it is difficult to explain why these organic solutions are not miscible with each other if this is true. There seems to be an affinity between the dissolved water and the nonionic surfactant which leads to the separation of the second organic solution containing virtually all the water and  $C_{10}E_6$ .

There remain the phases separating in the threephase region VWX. The organic phase at W should again be molecularly dispersed. But the other organic phase at X is possibly of the inverse water sphere type already mentioned. The anisotropic phase at V seems to be linked to the extensive liquid crystal region of the diagram. This liquid crystal region corresponds to that found at  $25^{\circ}$  in the binary system, and according to Clunie, Corkill & others (1967) the liquid crystal is analogous to 'middle' soap and has a two-dimensional hexagonal structure.

The tie-line results in the  $C_{10}E_3$  - water - dodecane system (Fig. 4) show that almost all the  $C_{10}E_3$  is dissolved in the organic phase. This solution can then solubilize large amounts of water to give a fairly extensive area, which is an isotropic organic solution. A comparison of Figs 2 and 4 reflects the different hydrophilic/lypophilic balance of the two  $C_{10}$  non-ionic compounds studied. The compound with only three ethylene oxide units per molecule has a lower water solubility (0.1%) and therefore no solubilization is shown in the 1L region, the binodal curve DEF cutting the water-dodecane axis at their mutual solubilities at 25°. Friberg, Mandell & Fontell (1969) studied the water - nonyphenol diethylene glycolether - p-xylene system at  $20^{\circ}$ , and their diagram shows many similarities to the present system. However, two regions of liquid crystal were reported in their diagram. The mesophase F has a two-dimensional hexagonal structure made of long rod-shaped aggregates consisting of an aqueous core surrounded by surfactant molecules, that is, the inverse of the structure proposed by Luzzati & others (1958) for the middle soap. The extensive

liquid crystal D, according to these authors, has a lamellar structure and occurs in a similar concentration region as the liquid crystal found in the  $C_{10}E_3$ system, but in the latter the liquid crystal region extends to extremely low concentration of the surfactant. In the three-phase region LMN (Fig. 4) the liquid crystal is in equilibrium with two isotropic liquid phases. The aqueous phase (L) is virtually water, and because of the lack of solubilization in this phase it is reasonable to assume that the surfactant is molecularly dispersed. The solution structure in the other isotropic phase at M is possibly of the inverse spherical micelle, but judging from the amount of water solubilized, the micelles must be very much swollen. This is perhaps why small fluctuations in temperature cause cloudiness in this solution. The occurrence of a liquid crystal phase in the region LMN of the ternary system  $C_{10}E_3$  - water - dodecane caused an increase in the viscosity and stability of the emulsions formed in that region, compared with the extremely unstable o/w dispersions formed in the two-liquid region of the system.

In the four-component system the surfactant is almost completely removed from the aqueous phase into a third intermediate isotropic phase when sufficient  $C_{10}E_3$  is added to the dodecane, and there is a three-liquid phase region where multiple-drop dispersions readily form. Three-liquid phases have been reported in non-ionic surface-active systems containing three (Nakagawa & Tori, 1960; Mulley & Metcalf, 1964) or four components (Marland & Mulley, 1971) and their possible structures have been discussed. Although multiple emulsions have been reported by several workers (Seifriz, 1925; Parke, 1934; Clayton, 1943; Pavlushenko & Yanishevski, 1959; Davis, 1976), none of these attributed the phenomenon to the presence of three-liquid phases. The present results confirm that this could be responsible for some of the reported cases of multiple emulsion globules. This observation is of interest since multiple dispersions may have advantages over other medicinal dosage forms and may therefore become of some medical significance (Davis, 1976). Treatment of multiple emulsions as two-phase dispersions could be misleading in the development of an understanding of their properties (Mulley & Marland, 1970). For example, some forms of coalescence are excluded if the multiple drops consist of three immiscible phases.

In conclusion this work demonstrates that even in simple systems containing low molecular weight surfactants in low concentration more than two phases can readily form, one or more of which has a highly organized structure which plays a vital role in the nature and properties of dispersions of the phases present. The results also suggest that if longer alkyl chains surfactants are used, as is frequently the case with practical emulsions, the dispersions produced will be more complex than in two-phase emulsions, and regions containing liquid crystal or gel phases will be even more extensive than in the present system. The high stability of the 'oil' (gel)-in-water dispersions in the region LBJM is particularly thought provoking. since macroscopic and microscopic examination indicates a liquid-liquid dispersion. Disperse phases with some form of organized structure may commonly occur in emulsion systems and greatly influence coalescence, even in cases where the phases appear to be isotropic.

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