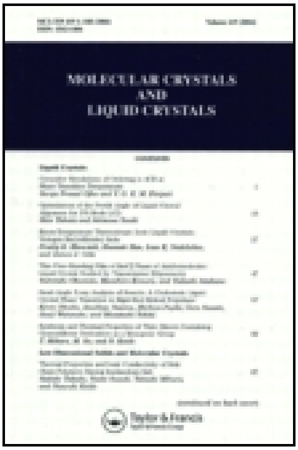

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Solubilization in Micelles and Mesophases and the Transition from Normal to Reversed Structures

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Abstract—The relationship between various kinds of solubilization and the formation of mesophases is elucidated.

In aqueous solutions of association colloids there are three processes by which mesomorphous phases form: (i) the separation of the micellar substance in mesomorphous form on reduction of the water content, (ii) the separation of the micellar substance at lower concentrations, from the c.m.c. upwards, as a result of the changes that the micelles undergo on solubilization of foreign amphiphilic and lipophilic substances, and (iii) below the c.m.c. through the formation of aggregates between the solubilizate and the molecules or ions of the association colloids. The last of these processes is typical of the solubilization of fatty acids and liquid monohydric alcohols.

In systems of sparingly soluble amphiphiles that do not give micellar aqueous solutions but take up water with swelling, mesophases often form through this " solubilization " of water, a process that is often promoted by the presence of a foreign amphiphilic or lipophilic substance.

The solubilization of lipophilic and amphiphilic substances as well as that of water can continue in the mesophases but the capacity of the various mesophase structures for incorporating these substances varies greatly. It is greatest in the lamellar mesophases, especially that with the neat phase structure. It is considerably smaller in the two-dimensional hexagonal mesophases; in the other mesophases with a particle structure the solubilization of organic substances and water or either of these substances is in most cases extremely limited—that is to say, the existence of the phases would seem to be associated with fairly definite molar or volume proportions between the water and amphiphile or between the organic components themselves.

The effect of the solubilization of a foreign organic substance on a binary system of amphiphile and water is in some systems particularly great. The regions of existence of the individual phases increase, their thermal stability changes, many of the properties of a phase may alter, and entirely new phases may form. Significant factors in this connection are whether

or not the molecules of the solubilized compound contain a hydrophilic group, the nature of the polar groups of this component and the association colloid, and the kind of interaction between these groups. Particularly far-reaching is the effect exerted by the solubilization of liquid monohydric alcohols and fatty acids, two types of amphiphiles that, even in dilute aqueous solutions below the c.m.c., lead to the formation of soluble aggregates and mesophases.

A critical examination of the experimental data on the phase equilibria and phase structures in binary and ternary systems of amphiphiles containing water shows that in binary systems of association colloids and water the presence of mesomorphous phases with a reversed particle structure has not been established with certainty, and that in binary systems of swelling amphiphiles and water, mesophases with normal particle structures appear not to have been found. On the other hand, there are both normal and reversed micellar and mesomorphous structures in a large number of ternary systems. It is primarily the above two types of amphiphile, namely liquid monohydric alcohols and fatty acids, whose solubilization in association colloid systems has proved to promote change from normal to reversed structures and vice versa.

The lamellar neat-phase structure constitutes the natural connection between the normal and reversed mesomorphous and micellar structures. Moreover, in a number of systems a direct transformation between normal and reversed micellar structures occurs in the same homogeneous solution phase.

The various stages of micellar association and mesomorphous aggregation succeed each other in a definite order, though some stages are often absent. In the binary systems of association colloid and water the reduction in the water content results in a rise in the association and aggregation. In the ternary systems the addition of the foreign amphiphile or lipophile substance increases the diversity of this series of aggregation stages, and in some systems leads to the transformation from the normal to the reversed structure. The stepwise change in the state of association and aggregation with concentration is one of the most characteristic features of the aqueous systems of amphiphilic substances.

Among the factors that are responsible for the stepwise changes and that regulate the stability of the various stages, the part played by water, the importance of the molecular structure of the amphiphilic components, and the conditions in the layers of hydrophilic groups of the aggregations of the amphiphile molecules are discussed, together with the conclusions that may be drawn from the position and the extent of the regions of existence of the homogeneous phases, and from the composition of the latter.

1. General Points on Solubilization

Solubilization, in the strict sense of the term, is the dissolving of a predominantly lipophilic substance, sparingly soluble in water, by the mediation of the micelles of an association colloid. It is considered that hydrocarbon molecules are incorporated in the hydrocarbon cores of the micelles, while amphiphilic molecules are inserted between the molecules and ions of the micelle-forming colloid, and, like these, are oriented with the hydrophilic groups

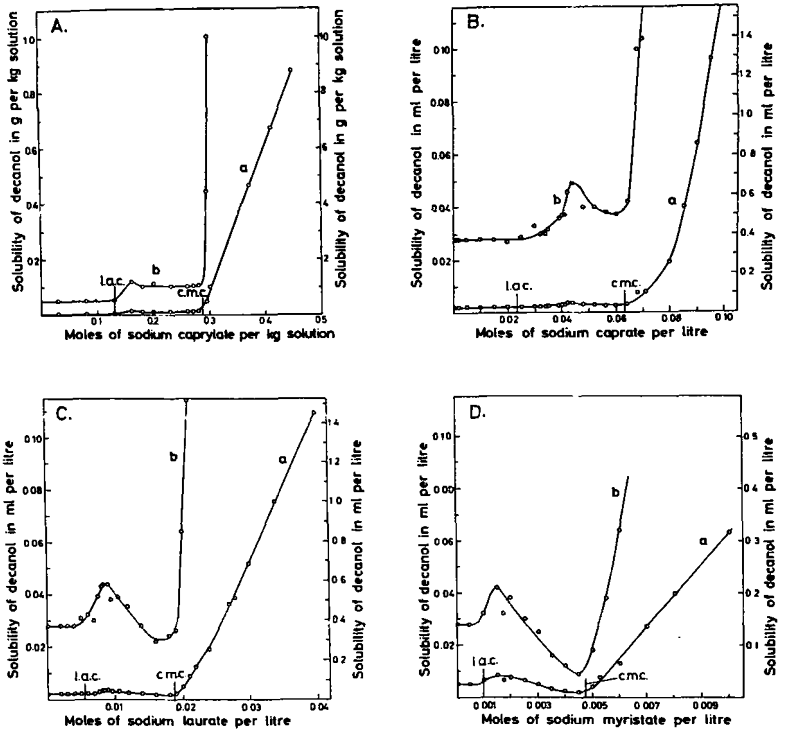


Figure 1. The solubility of decanol-1 in soap solutions.
(A) The solubility in sodium caprylate solutions at 20 °C.
(B) The solubility in sodium caprate solutions at 40 °C.
(C) The solubility in sodium laurate solutions at 40 °C.
(D) The solubility in sodium myristate solutions at 40 °C.
Curves a: Solubility around the lowered c.m.c. (scale on right);
Curves b : Solubility below the lowered c.m.c. (scale on left) (1956, 1964).

towards the surface of the micelles. This latter process, referred to as "penetration", results in an increase in the amount of the micelle-forming substance and displaces the critical concentration for micelle formation slightly towards a lower colloid concentration. In addition to these processes there sometimes occurs a solubilization phenomenon below the c.m.c. where no micelles are to be found; this is due to an interaction between the molecules of the association colloid and the amphiphilic substance that can effect an increase in the solubility far below the lowered critical concentration. About 30–40 years ago it was shown that such an interaction leads to a slight increase in the solubility of fatty acid in the soap solutions owing to the formation of soluble acid soap aggregates[4–8,11,13,15,22,32] and in the fifties it was found that in solutions of various association colloids there is a similar small increase in the solubility of the alcohols below the c.m.c. through the formation of soluble soap—alcohol aggregates.[11,13–16,22,23,25,45,46,53] (Figs. 1 and 2). Since 1927 we have systematically studied

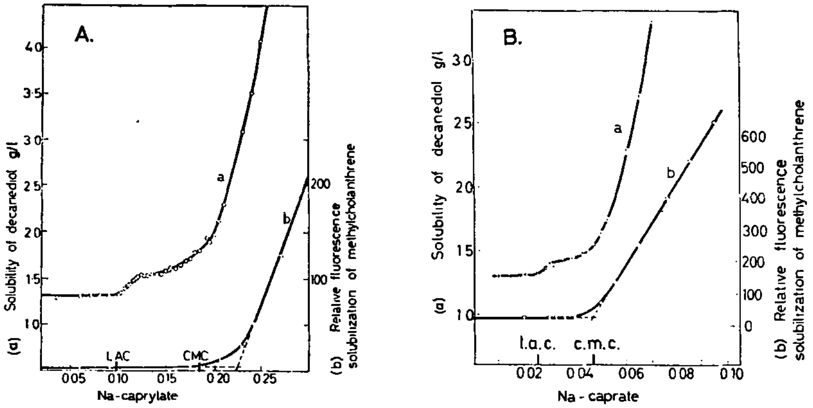


Figure 2. The solubility of decanediol-1,10 and methyl cholanthrene in soap solutions.

A. Sodium caprylate at 40 °C. B. Sodium caprate at 40 °C.

Curves a: Solubility of decanediol.

Curves b: Solubilization of methyl cholanthrene in soap solutions saturated with decanediol; the solubilization of the hydrocarbon begins at the lowered c.m.c. (1957).

these phenomena and their consequences—to begin with, the solubilization of fatty acids and later on that of alcohols and have pointed out their significance for the interpretation of the solubilization phenomena in general and the penetration processes in particular, as well as the role they play in the formation of mesomorphous phases. Until quite recently these phenomena occurring below the c.m.c. seem to have been almost overlooked by other investigators in this field.

It was evident that in this solubilization processes below the c.m.c. there is a direct or indirect interaction between the hydrophilic groups of the ionic association colloid and the fatty acid or alcohol which results in ions containing both components; but at the same time it was found that, just as the c.m.c., the lowest concentration of the colloid at which the interaction occurs was dependent on its chain length. The lowest concentration at which this increase in solubility and interaction were observed was designated the "limiting concentration" or the "limiting association concentration", l.a.c.[4–9,11,13–16,20,22,52,53] (Fig. 3). These solubility phenomena between the lowered c.m.c. and the l.a.c. constitute a stage towards the Neuberg hydrotropic phenomenon encountered in solutions of such amphiphilic substances that do not form micelles at all.[88] In many of these hydrotropic processes, too, an interaction between polar groups is probably the primary causal factor.

The maximum value of the solubilization at a given colloid concentration above the c.m.c. is dependent not only on the total amount of micellar substance in the solution but also on the type of micelles present. This is the reason why the solubilization capacity of the colloid solution does not rise linearly with the micelle content over the whole concentration range above the c.m.c.[9–16,28,29,45,48] In the case of association colloids of the paraffin-chain type the micelles in the area just above the c.m.c. are spherical, with a constant number of counter ions bound to them and likewise a constant number of water molecules bound to their hydrophilic groups.[15–18,27,30,31,51,96] In this area the solubilization of hydrocarbon increases linearly with the amount

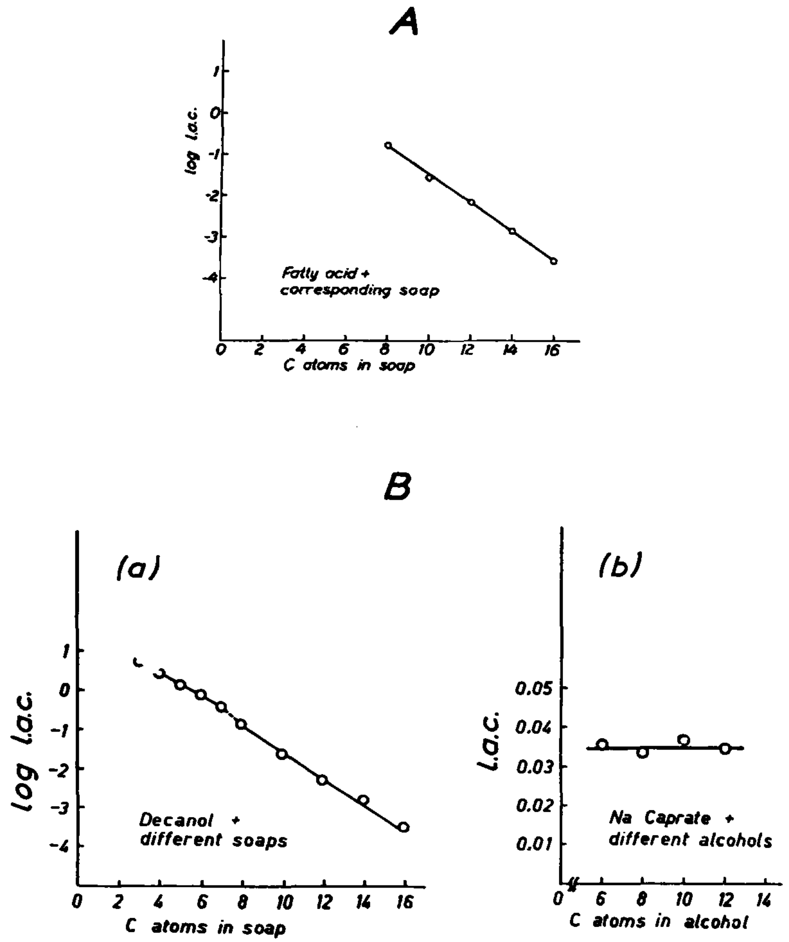


Figure 3. The dependence of the l.a.c. on the chain length.

A. The dependence of the l.a.c. of fatty acid soaps on the chain length of the soap, determined from the interaction between soap and fatty acid. (1927, 1936, 1941, 1960).

B. The l.a.c. determined from the interaction between soap and alcohol. (1951, 1956).

  (a) The dependence of the l.a.c. of fatty acid soaps on the chain length of the soap at 20 °C.

  (b) The dependence of the l.a.c. of sodium caprate on the chain length of the alcohol at 50 °C.

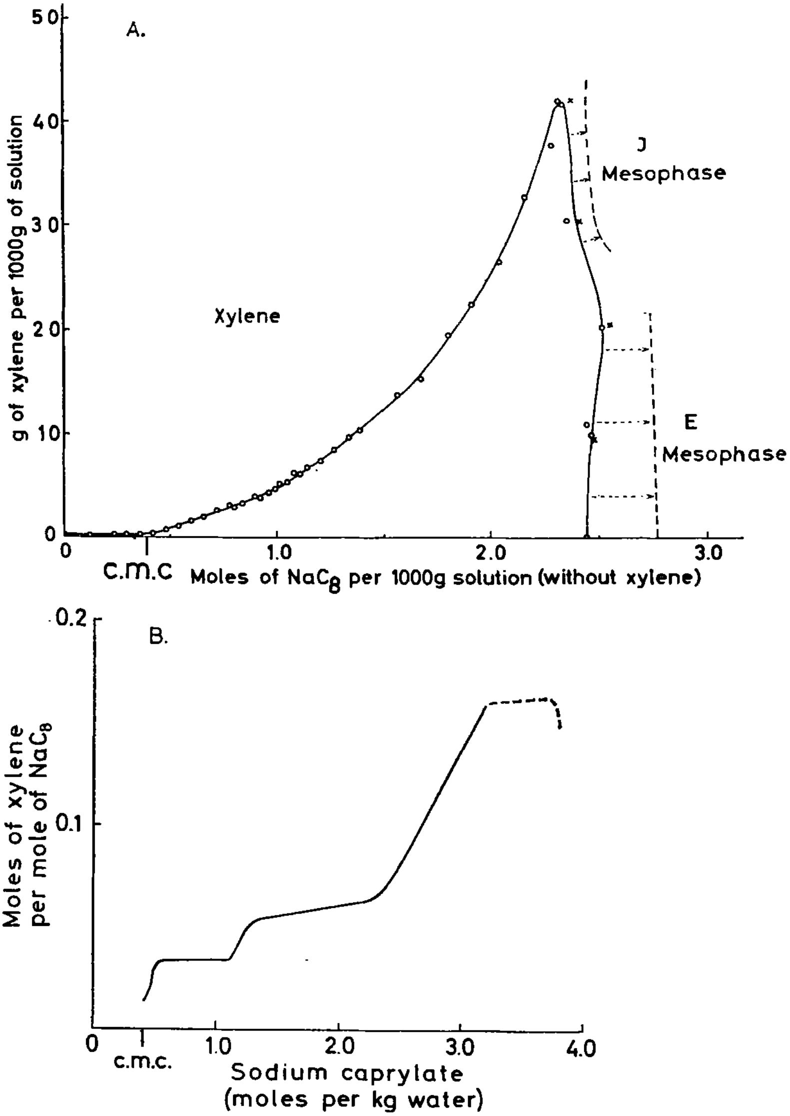


Figure 4. Solubilization of *p*-xylene in aqueous solutions of sodium caprylate at 20 °C.

A. The solubility of *p*-xylene in aqueous sodium caprylate solutions.

B. The solubilization capacity in moles of *p*-xylene per mole of micellar sodium caprylate.

of micellar substance present (Fig. 4). Then there is a change in the micellar structure, which, in solutions of ionic association colloids, is associated with an increased binding of counter ions and water, and which usually results in an increase in the capacity for solubilizing of hydrocarbons. At still higher concentrations there is a further change in the micellar structure due to the increasing crowding of hydrated spherical micelles in the solution, which results in a change in an asymmetric direction; this is often accompanied by a further rise in the solubilization capacity.[15–18, 27,30,31,51,96]

There is, however, yet another factor on which the solubilization is dependent, namely the changes that the solubilized substance produces in the surface layer of the micelles in their size and shape and in the solubility of the micellar substance. These changes can often result in the separation of the micellar substance containing solubilizate, in a more or less changed form as a mesomorphous phase, and thus termination of the solubilization in the micelles before the maximum capacity of the micellar substance to incorporate the foreign substance is fully utilized.[4–6,11,13,15,16,20, 22,24,25,45–47,53,89]

Mesomorphous substance separates from micellar solutions containing no solubilizate, when the volume fraction of hydrated micellar substance exceeds a critical value, which seems to depend on the degree of asymmetry of the micelles.[9,15–18,24,25,96] The above changes of the micelles often result in formation of a mesophase at lower concentrations.

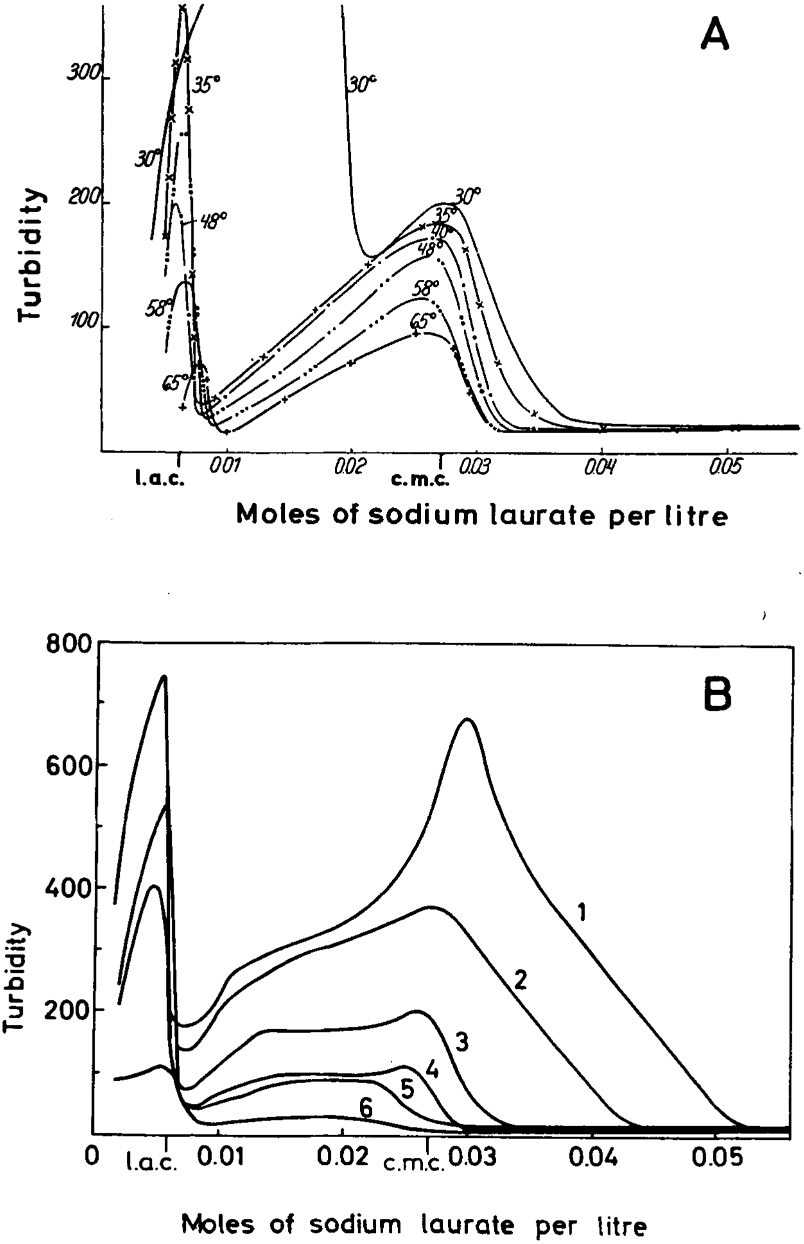
In the case of solubilization in solutions above the c.m.c. a distribution equilibrium develops between the fraction of solubilizate dissolved in the micelles and the fraction that remains dissolved in the intermicellar solution. When the intermicellar solution is saturated with the solubilizate, the excess of this separates in a more or less pure form; the maximum capacity of the micelles to dissolve the foreign substance is given by their content of solubilizate at that point.[9,11,16,24,25,45,48] When mesomorphous substance begins to form before this point is reached and before the solubilization capacity of the micellar substance is fully exploited the solubilization process continues in the mesomorphous phase.

The solubilization of a hydrocarbon usually continues over the whole concentration range until the saturation capacity of the micelles has been exhausted, the excess then separating in the almost pure state.[9,11,16,29,48] Only at concentrations where mesophase is formed already in the pure association colloid solutions do the solutions containing hydrocarbon give rise to a mesophase—in this case the mesomorphous substance contains hydrocarbon as well as the association colloid and water.

When amphiphilic compounds are solubilized the formation of mesophases often begins at quite low colloid concentrations, possibly even at the c.m.c.; then the solubilization in the solution is arrested before the maximum dissolving capacity of the micelles has been attained and the mesophase contains association colloid, water and the added amphiphile.

In systems where there is an interaction between the association colloid and the added amphiphile below the c.m.c. the formation of mesophase often begins below the c.m.c.—even at the l.a.c.[5–9,11,13,17,20,21,25,45–47,52,53,80] This is the case when the added amphiphile is of the fatty acid or liquid monohydric alcohol type (Figs. 5 and 6), (but not when it is of the alkane diol type[42]). The sodium oleate and the saturated fatty acid soaps from the caprate downwards form a liquid crystalline acid soap at 20 °C; the higher soaps do so likewise but only above a transformation temperature characteristic of each fatty acid soap (about 7–18° below the melting point of the fatty acid).[5] The alcohols from pentanol up to decanol form liquid crystalline phases at 20° from the l.a.c. upwards. Here, too, the mesophase found contains added amphiphile, besides the association colloid and water. In all these systems the solubilization of the amphiphile then continues in the mesophase.

In these systems, too, the solubility curve has a linear segment in the concentration range above the c.m.c., but the following rise in the curve is slower or is even absent, and the curve bends downwards at a lower colloid concentration, than it does in


A
Turbidity
300
200
100
30°
35°
40°
48°
58°
65°
l.a.c.
0.01
0.02
c.m.c.
0.03
0.04
0.05
Moles of sodium laurate per litre
B
800
600
400
200
0
1
2
3
4
5
6
l.a.c.
0.01
0.02
c.m.c.
0.03
0.04
0.05
Moles of sodium laurate per litre

systems where no mesomorphous substance is formed as a consequence of solubilization[16,45,46,80,89] (Fig. 7).

Above, we have considered typical association colloids—that is, amphiphiles with so high a solubility in water that micellar solutions are formed.

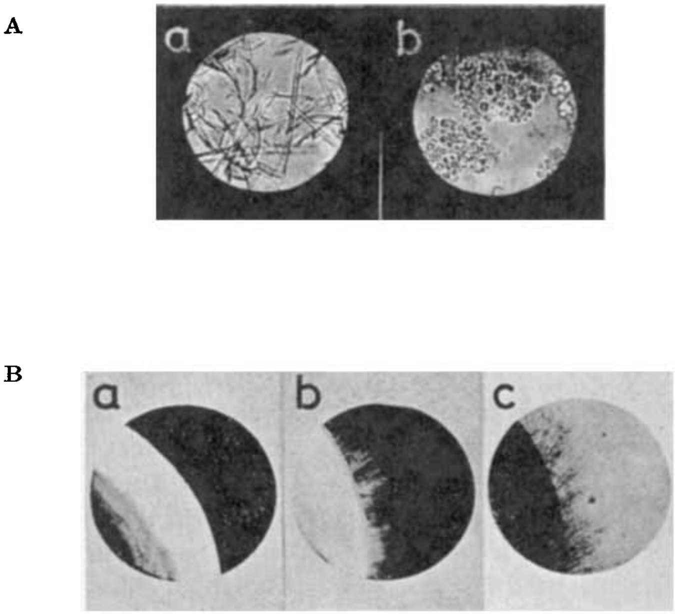
Many amphiphilic substances, however, are so sparingly soluble in water that the micellar condition is never reached; on the other hand, they swell in water—that is, they are capable of taking up quite large amounts of water by a process whereby the water molecules penetrate between the molecules of amphiphile and are bound to their hydrophilic groups—being thereby converted to a lyotropic mesomorphous form. These mesophases are, in their turn, capable of solubilizing lipophilic and amphiphilic compounds. Mixtures of two amphiphiles or of an amphiphile and a lipophile are often capable of taking up more water than the original amphiphile alone. There are also instances in which the hydrophilic/lipophilic balance of the amphiphilic substance is displaced so far in the lipophilic direction that water cannot alone penetrate between its molecules and produce a change in the mesomorphous form—but where this will become possible when the water contains a small amount of an association colloid, even at concentrations below the l.a.c. (In this manner, such sparingly soluble compounds as the solid paraffin-chain alcohols from dodecanol upwards swell to mesophases taking up water.[47])

In all these systems the water may also be considered to be

Figure 5. The formation of mesomorphous substance in sodium laurate solution as a result of the solubilization of lauric acid of decanol-1.

A. Turbidities of sodium laurate solutions containing 0.05 moles of lauric acid per 1 mole of laurate. 30–65 °C. The turbidity maximum on the left is effected by separated lauric acid, and that on the right by separated mesomorphous acid soap. (1936).

B. Turbidities of sodium laurate solutions containing 0.21, 0.157, 0.105, 0.0705, 0.0520 and 0.032 moles decanol per mole of laurate, 40 °C. The turbidity maximum on the left is effected by separated decanol, and that on the right by separated mesomorphous substance containing soap, decanol and water. (1951).



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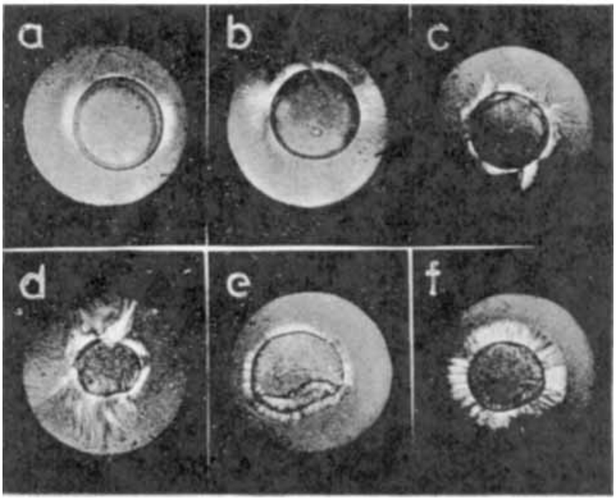

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solubilized by the amphiphile. In this process, too, micelles play an important role. For instance, there can be an amphiphile in the molten stage,[66] a liquid mixture of two amphiphiles, or of an amphiphile and a lipophile that, even in the water-free state, contains micellar aggregates[44,65,90] which take up and bind water; but there are also systems in which micelles form in mixtures of this type only with the mediation of water[18,19,34,35,44,49,50]; once formed they are capable of incorporating further, quite large, amounts of water. These micellar systems have an organic liquid as the intermicellar solution, and micelles of the reversed type, with the molecules of amphiphile oriented with their hydrophilic groups towards the centre and the hydrocarbon parts

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Figure 6. Photomicrographs showing the result of the interaction between fatty acid or alcohol and soap solutions below the c.m.c.

A. (a) Solid crystalline acid soap in 0.016 molar sodium laurate solution at 20 °C.
   (b) Liquid crystalline acid soap in 0.016 molar sodium laurate solution at 40 °C. (1936–38).

B. The first stages of the interaction between drops of decanol-1 and sodium laurate at 20 °C. (1955–56).

1. The decanol drop is seen on the left, the laurate solution on the right and the mesomorphous interaction product in the interface. (a) 0.001 m laurate solution (below the l.a.c.); dark-field condenser; (b) 0.006 m laurate solution (immediately above the l.a.c.), dark-field condenser; (c) 0.006 m laurate solution, transmitted light. 150 × .
2. Observations between crossed polaroid plates; an isotropic decanol drop surrounded by isotropic laurate solution and a layer of birefringent mesomorphous interaction product in the interface; 250 × .
   (a) Laurate concentration 0.005 m (at the l.a.c.); 2 min. from the start of the interaction.
   (b) Laurate concentration 0.005 m (at the l.a.c.); 5 min from the start of the interaction.
   (c) Laurate concentration 0.01 m (between l.a.c. and c.m.c.); 5 min from the start of the interaction.
   (d) Laurate concentration 0.02 m (between l.a.c. and c.m.c.); 2 min from the start of the interaction.
   (e) Laurate concentration 0.04 m (above the c.m.c.); 1 min from the start of the interaction.
   (f) Laurate concentration 0.04 m (above the c.m.c.); 5 min from the start of the interaction.

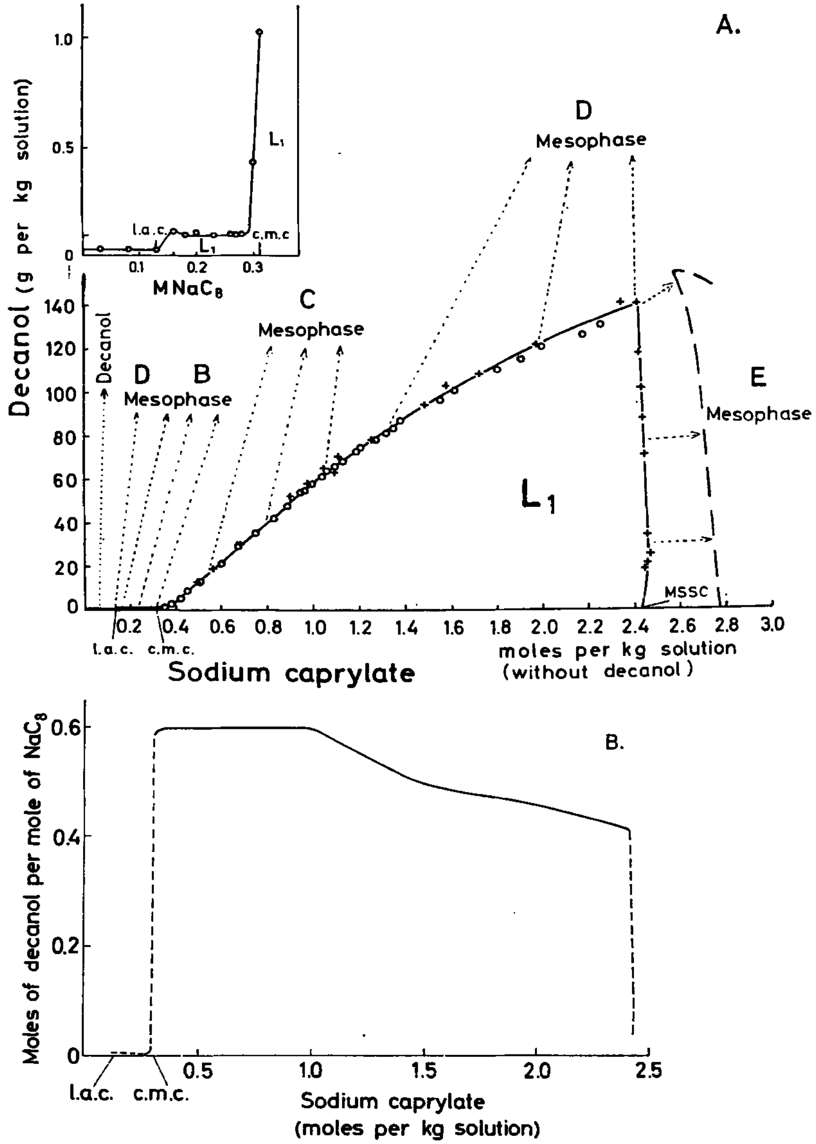

Figure 7. Solubilization of *n*-decanol in aqueous sodium caprylate solutions at 20 °C.

A. The solubility of *n*-decanol in aqueous sodium caprylate solutions.

B. The maximum amount of *n*-decanol per mole of micellar sodium caprylate dissolved in aqueous sodium caprylate solutions.

outwards; they are thus built up around a core of hydrophilic groups, usually in hydrated state, or around a water core. When the water content exceeds a certain level, or when the concentration of the other components varies, mesomorphous phases may form.

To summarize: There are two principal ways in which water-containing mesophases may form. The first way is from aqueous solutions of association colloids (i) by reducing the water content, (ii) by solubilizing lipophilic or amphiphilic compounds at concentrations above the c.m.c., and (iii) by adding certain amphiphiles to the solutions below the c.m.c. The second way is from amphiphiles in a water-free state by solubilization of water either alone or together with another amphiphilic or lipophilic component.

2. Various Lyotropic Mesophase Structures

Before proceeding to a more detailed examination of the effect of solubilization on the formation of mesophases an attempt will be made to survey the various lyotropic mesophase structures described in the literature and studied by us. The material has been collected in a table (Table 1).

The table outlines the structures and gives references to the papers where they have been described and investigated. They are divided into structures with "linear", hexagonal and cubic symmetry, and further into mesophases with lamellar and ones with particle structures. The particle structures, moreover, comprise those of normal and of reversed types; the former are composed of aggregates with a hydrocarbon core and the latter of aggregates with a water core or a core of hydrated hydrophilic groups. In the normal particle structures the amphiphile molecules are oriented with the hydrocarbon chains towards the centre and the hydrophilic groups towards the water continuum between the particles. In the reversed particle structures the amphiphile molecules are oriented with the hydrophilic groups towards the water core and the hydrocarbon chains outwards, forming a continuous hydrocarbon layer between the particles.

TABLE 1 Different Types of Lyotropic Mesomorphous Phases (the hydrocarbon parts in semiliquid state)

	Notations in the Literature	References
1. Mesophases displaying Bragg spacing ratio 1 : 1/2 : 1/3; arrangements with "linear" symmetry.		
1.1. Mesophases with lamellar structure		
D Lamellar structure with coherent double layers of amphiphilic molecules and ions separated by water layers; neat phase type	Neat phase, Phase lisse Lamellar phase; N, L.	1–3, 16, 18, 24, 26, 33, 56, 57, 63, 64, 66, 69–73, 75–77, 79–80, 83–86, 92, 93
D_s Lamellar structure with coherent single layers of amphiphilic molecules and ions separated by water layers; single layered lamellar type		37, 42
B Lamellar structure with coherent double layers of amphiphilic molecules and ions separated by water layers; mucous woven type		24, 57, 80
1.2. Mesophases with particle structure		
C Rodlike particles with hydrocarbon core in aqueous environment. Rods with predominantly quadratic cross-section in tetragonal array; normal two-dimensional tetragonal type	White phase	24, 39, 43, 57, 80
K Rodlike particles with water core in hydrocarbon environment. Rods with predominantly quadratic cross-section in tetragonal array; reversed two-dimensional tetragonal type		39, 43, 44
R Rodlike particles with hydrocarbon core in aqueous environment. Rods with rectangular cross-section in an orthorhombic array; normal two-dimensional rectangular type	Rectangular phase Phase rectangulaire	44, 64, 72, 73, 92

2. Mesophases displaying Bragg spacing ratio $1 : 1/\sqrt{3} : 1/\sqrt{4}$; arrangements with two-dimensional hexagonal symmetry (particle structures)		
E Rodlike particles with hydrocarbon core in aqueous environment. Rods with cylindrical to hexagonal cross-section in hexagonal array; middle phase type, normal two-dimensional hexagonal type	Middle phase, Phase mediane, Hexagonal phase; M, H_I	1–3, 16, 18, 24, 26, 33, 56, 57, 63, 64, 66, 69–73, 75–77, 79–80, 83–86, 92, 93
F Rodlike particles with aqueous core in hydrocarbon environment. Rods with cylindrical to hexagonal cross-section in hexagonal array; reversed two-dimensional hexagonal type	Hexagonal phase; H_{II}	18, 24, 26, 38, 44, 56, 57, 63, 73, 75–77, 79–81, 91, 92, 98
H_c Rodlike particles with complex structure in aqueous environment. Rods with cylindrical to hexagonal cross-section in hexagonal array; complex two-dimensional hexagonal type	Complex hexagonal phase Phase hexagonale complexe; H	64, 72, 73, 92
3. Mesophases displaying cubic symmetry (particle structures)	Viscous isotropic, Phase Cubique; V, C	
3.1. Isotropic mesophases with spherical to dodecahedrical particles in face-centred cubic lattice		
I_{f1} Particles with hydrocarbon core in aqueous environment; normal face-centred cubic type	Cubic phase; C_I	3, 18, 44, 58, 64, 66, 71–74, 97
I_{f2} Particles with water core in hydrocarbon environment; reversed face-centred cubic type	Cubic phase; C_{II}	58
I_{fc} Particles with complex structure; complex face-centred cubic type		44, 58
3.2. Isotropic mesophases with spherical particles in body-centred cubic lattice		
I_{b1} Particles with hydrocarbon core in aqueous environment; normal body-centred cubic type		58
I_{bc} Particles with complex structure; complex body-centred cubic type		58

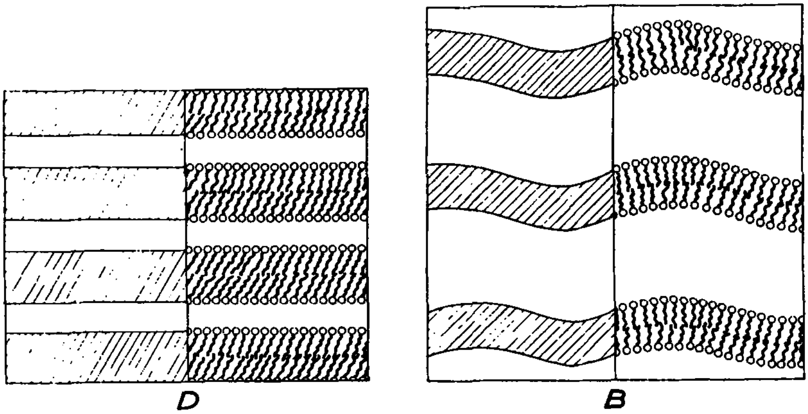

Figure 8. Schematic drawings of lamellar mesomorphous structures.

D. Coherent double layers of amphiphile molecules and ions separated by water layers. Presumed structure for the neat phase type with tilted molecules.

B. Coherent double layers of amphiphile molecules and ions separated by water layers. Presumed structure for the mucous woven type with vertical molecules.

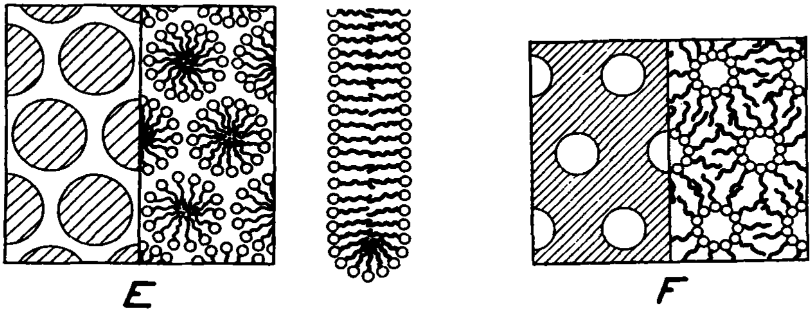

Figure 9. Schematic drawings of two-dimensional hexagonal mesomorphous structures.

E. Rod-like particles with hydrocarbon core in water environment; rods in hexagonal array. Proposed structure for the middle phase type.

F. Rod-like particles with water core in hydrocarbon environment; rods in hexagonal array. Proposed structure for the reversed two-dimensional hexagonal type.

Some of the structural models are illustrated diagrammatically in Figs. 8–11. It should be noted that while the geometry of the mesophases—that is, the mutual arrangement of the aggregates—is quite well known, we have little reliable knowledge of the arrangement of the molecules within the aggregates. However, from the fact that the hydrophilic groups are fixed in the amphiphile—water interface and, moreover, often bound to each other directly or *via* water molecules it is fairly safe to assume that the hydrocarbon chains in each phase have an average principal orientation, which varies from phase to phase, even though the hydrocarbon parts are in a semi-liquid state.[57]

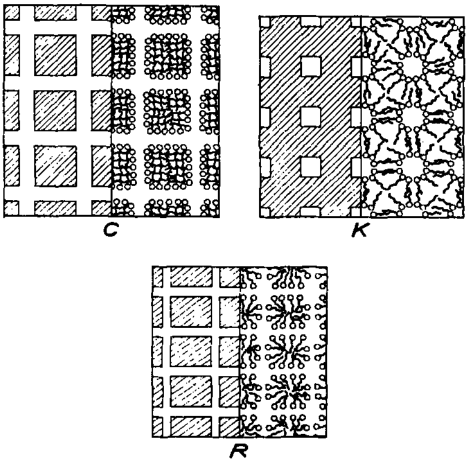

Figure 10. Schematic drawings of tetragonal and orthorhombic mesomorphous structures.

C. Rod-like particles with hydrocarbon core in aqueous environment; rods with predominantly quadratic cross-section in tetragonal array. Proposed structure for the normal two-dimensional tetragonal type.

K. Rod-like particles with water core in hydrocarbon environment; rods with predominantly quadratic cross-section in tetragonal array. Proposed structure for the reversed two-dimensional tetragonal type.

R. Rod-like particles with hydrocarbon core in aqueous environment; rods with rectangular cross-section in an orthorhombic array. Proposed structure for the normal two-dimensional rectangular type.

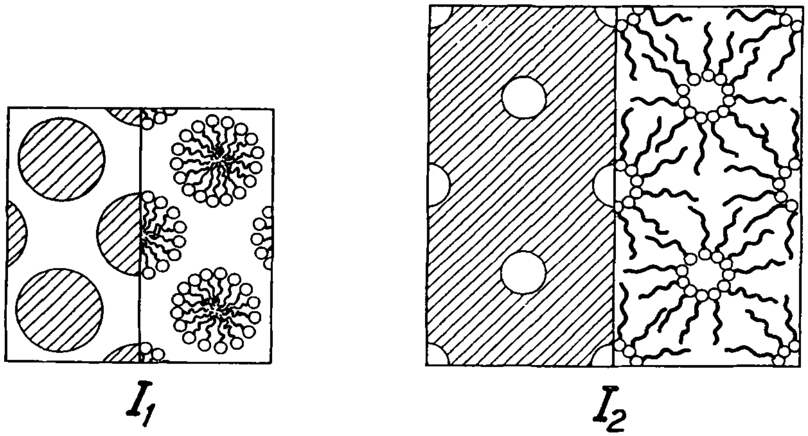

Figure 11. Schematic drawings of cubic mesomorphous structures.

I_1. Particles with hydrocarbon core in aqueous environment. Proposed structure for the normal face-centred cubic type.

I_2. Particles with water core in hydrocarbon environment. Proposed structure for the reversed face-centred cubic type.

The alphabetical notation used is largely the same as has been applied in our various experimental studies. To facilitate comparison with the results of other workers, the notation and terms (in English and French) used in their articles are also given.

3. Composition of the Systems and Occurrence of the Various Mesophases

We have reviewed what has been written in this field and examined all information about the occurrence of the various mesophase structures in systems of two, three or more components. From the large experimental material it is possible to obtain an impression of the relationship between the occurrence of the mesophases and the composition of the systems. The fundamental investigations of Luzzati and co-workers on the mesophases in *binary* systems, supplemented by the results of other workers, have shown how the mesophase type changes when the water content is decreased and the amphiphile concentration is increased. Our knowledge of the conditions in *ternary* systems is based primarily on our own systematic investigations of the effect of a solubilized foreign lipophilic or amphiphilic compound on the mesophase structure, supplemented with the results of recent work at other laboratories.

3.1. Systems with Association Colloids

A beginning will be made with systems of typical association colloids.

3.1.1. *Binary systems*

At temperatures high enough above the Krafft point for the upper limit of the region with isotropic aqueous solution to be reached, in most of the systems examined so far mesomorphous middle soap is formed as soon as this boundary is exceeded. In the direction of a lower water content this mesophase is in many systems in equilibrium with neat soap and, further, with solid crystalline colloid. In some systems, however, middle soap is in equilibrium directly with the solid colloid, but here, too, neat soap appears when the temperature is raised. In the region between middle and neat soap in some systems the Luzzati group claims to have found other mesomorphous structures—" deformed middle soap ", " rectangular ", " hexagonal complex " and " viscous isotropic " structures.[64,71–74,92] We have confirmed the formation of the rectangular and viscous isotropic structures and their existence as independent phases and have found that the latter has a normal face-centred cubic structure;[44,58] but we have so far not found the hexagonal complex structure, and in the system we have examined (potassium oleate–water 20 °C),[44] there is in the region in question a mixture of two mesophases. Nor have we observed any independent phase with deformed middle soap structure, and we infer that it may well be a deformation—within the region of the middle phase—of the cylindrical aggregates to rod-shaped ones with a hexagonal or flattened cross-section—a deformation that is due to the reduction in the water content.[44]

To judge from the experimental material as a whole; in the binary systems all structures with a higher water content than neat soap seem to be of the normal type, with aggregates having hydrocarbon cores in a water continuum. In any case no reversed particle structure has been identified with certainty between middle soap and neat soap. Nor at water contents below that of the neat soap do any reversed mesophase structures so far seem to have been observed in the binary association colloid-water systems.

3.1.2. *Ternary systems*

The experimental material is still not large enough to afford a complete picture of the ability of the various mesophases of the binary systems for solubilizing lipophilic and amphiphilic substances. However, an attempt will be made to outline our knowledge to date.

Neat soap has the greatest capacity for incorporating foreign substances; up to 40–50 per cent of some additives can be incorporated. This does not incur any change in the basic neat soap structure, but the properties often undergo considerable modification; in particular the uptake of water is greatly increased.

Middle soap, too, can incorporate fairly large amounts of foreign substances without undergoing any alteration in its basic structure (up to 27 per cent has been recorded). This is accompanied by some change in properties but no appreciable increase in the amount of water that can be taken up has been observed.

In the only system studied so far (potassium caprylate–decanol–water) the isotropic phase has proved capable of incorporating about 10 per cent of a paraffin-chain alcohol, but only so long as the water content was kept constant.[44]

The rectangular phase, too, has been examined in only one system (potassium oleate–decanol–water), and here it was practically incapable of incorporating foreign solubilizate (paraffin-chain alcohol).[44]

A more complete picture of the consequences of solubilization in systems of an association colloid and water has been obtained from the systematic study of the phase equilibria in ternary systems. The effects of some solubilizates have proved to be extremely great. These are surveyed in a number of phase diagrams that relates to the same association colloid, a fatty acid soap, namely sodium caprylate, but where the type of the foreign substance was varied.

The phase equilibria were usually determined by centrifugal separation of the various phases and subsequent analysis of the layers. The internal structure of the pure phases was examined by X-ray diffraction in the low- and wide-angle areas; they were also studied under the polarizing microscope, and their density and sometimes their rheologic properties were investigated.

In the sodium caprylate-water system at 20° the aqueous solution and the middle soap phases occur but not neat soap.

When *completely lipophilic substances* such as hydrocarbons or chlorinated hydrocarbons are added, they are solubilized in the aqueous solution, L_1, and in the middle phase, E (Fig. 12). When the amount of solubilizate is increased the structure of the mesomorphous substance undergoes a sudden change, and a viscous isotropic mesophase, I, forms—that is to say the hexagonal cylindrical structure changes to one of spheres in cubic packing.[44,58,81]

When amphiphilic compounds with *a weak hydrophilic group* (for instance a nitrile, methyl ester or aldehyde group) are added, the solubilizing capacity of the micellar aqueous solution and of the middle phase is considerably increased (Fig. 13). No cubic phase forms but when the amount of solubilizate is increased, the middle phase structure in these systems changes suddenly to a lamellar structure, D.[16,44,79,81]

When the amphiphilic compound is a liquid monohydric *alcohol* with its hydrophilic hydroxyl group, the ternary system assumes an entirely new character (Fig. 14). The lamellar neat phase, D, extends to extremely high water contents, and new mesophases and a second solution phase, L_2, appear. In the concentration region between the neat phase and the aqueous solution there appears the lamellar mesophase that we have designated mucous woven type, B, and the mesophase with a particle structure that

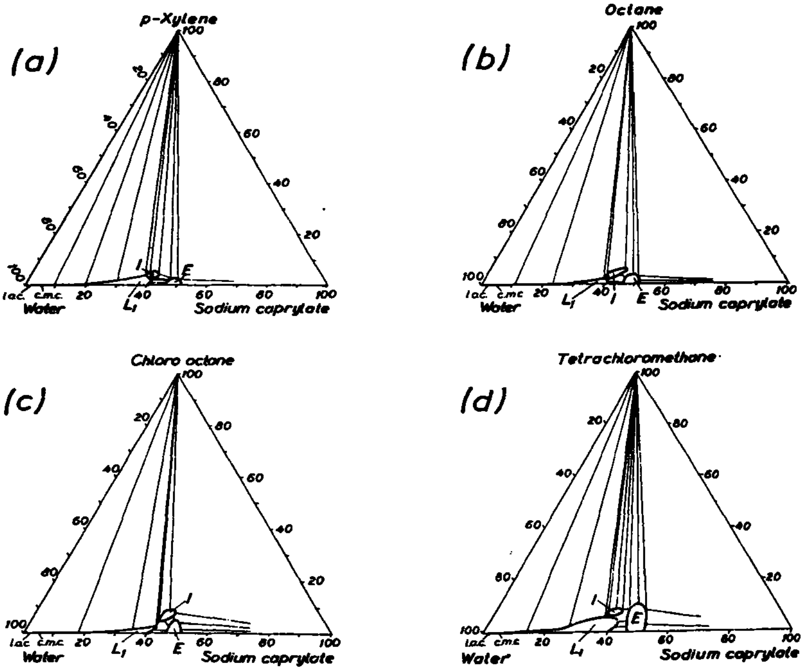

Figure 12. Phase diagrams for ternary systems containing sodium caprylate, water and a completely lipophilic substance:

(a) Sodium caprylate–*p*-xylene–water at 20 °C
(b) Sodium caprylate–octane–water at 20 °C
(c) Sodium caprylate–chloro octane–water at 20 °C
(d) Sodium caprylate–tetrachloromethane–water at 20 °C

L_1. Homogeneous isotropic aqueous solution.
E. Homogeneous mesomorphous phase displaying normal two-dimensional hexagonal structure.
I. Homogeneous viscous isotropic mesomorphous phase displaying cubic structure.

has been characterized as a normal two-dimensional tetragonal type, C, with long rib-shaped particles surrounded by water. The phase B is always in equilibrium with diluted aqueous solutions between the l.a.c. and c.m.c., and the phase C is in equilibrium with the micellar aqueous solution just above the c.m.c.[16,24,25,79–81]

(The cubic isotropic mesophase, which, in the systems containing hydrocarbon, was in equilibrium with concentrated micellar

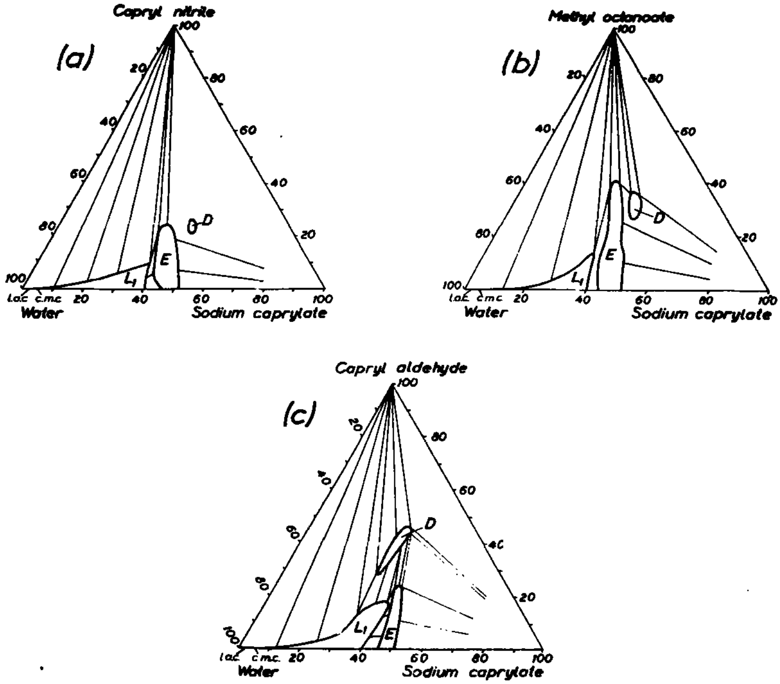

Fig. 13. Phase diagrams for ternary systems containing sodium caprylate, water and a weakly hydrophilic substance:

(a) Sodium caprylate–capryl nitril–water at 20 °C
(b) Sodium caprylate–methyl octanoate–water at 20 °C
(c) Sodium caprylate–capryl aldehyde–water at 20 °C

L_1. Homogeneous isotropic aqueous solution.
D. Homogeneous mesomorphous phase displaying lamellar structure (neat phase types).
E. Homogeneous mesomorphous phase displaying normal two-dimensional structure.

aqueous solution, occur in the alcohol systems only when the alcohol is methanol or ethanol, the high solubility of these two lower alcohols in water also affects the phase equilibria of the systems in other respects.[78])

In some alcohol systems there is also the reversed hexagonal mesophase, F, with its water cylinders in a hydrocarbon continuum. This mesophase lies between the neat phase and the other solution region, L_2, that exists in the alcohol systems.[24,38,56,57,81]

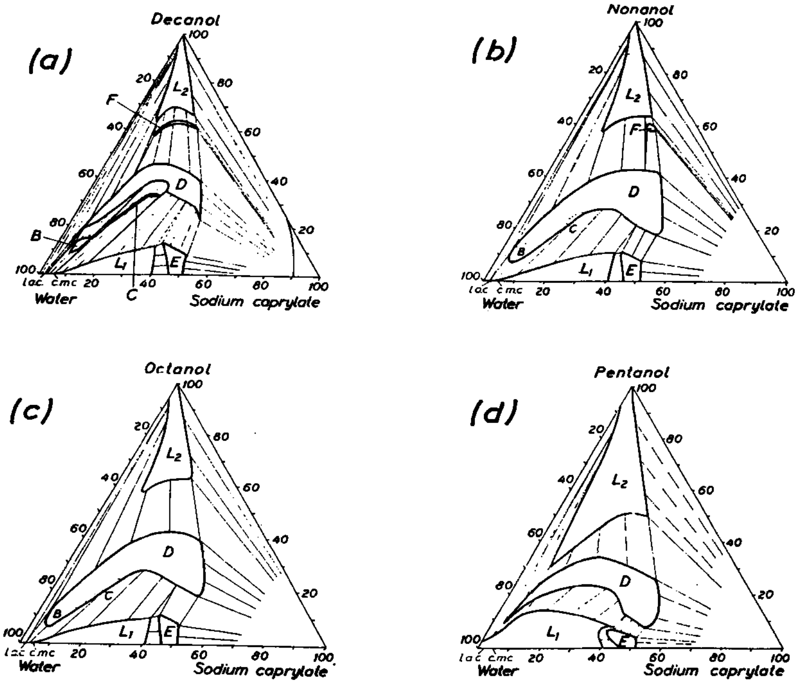

Figure 14. Phase diagrams for ternary systems containing sodium caprylate, water and an alcohol:

(a) Sodium caprylate–decanol–water at 20 °C
(b) Sodium caprylate–nonanol–water at 20 °C
(c) Sodium caprylate–octanol–water at 20 °C
(d) Sodium caprylate–pentanol–water at 20 °C

L_1. Homogeneous isotropic aqueous solution.

L_2. Homogeneous isotropic alcoholic solution.

B. Homogeneous mesomorphous phase displaying lamellar structure (mucous woven type).

C. Homogeneous mesomorphous phase displaying normal two-dimensional tetragonal structure.

D. Homogeneous mesomorphous phase displaying lamellar structure (neat phase type).

E. Homogeneous mesomorphous phase displaying normal two-dimensional hexagonal structure.

F. Homogeneous mesomorphous phase displaying reversed two-dimensional hexagonal structure.

In the solution region L_2, which extends from 100 per cent of alcohol to 20—40 per cent of soap and water, the alcohol is the solvent; the solution is micellar, the micelles being of the reversed type, with water cores surrounded by a layer of amphiphile molecules oriented with the hydrophilic groups towards the water and the hydrocarbon chains towards the intermicellar alcohol solution.[15,18,19,34,44,49,62,68]

When the solubilized foreign amphiphilic compound is a *fatty acid* with its strongly hydrophilic carboxyl group the ternary system has in many respects the same character as the alcohol systems (Fig. 15). We then have the following regions: two solution regions, L_1 and L_2; the neat phase, D, which extends in the direction of a high water content; often mesophases B and C, between the neat phase and the aqueous solution; and finally the reversed hexagonal mesophase, F, between the neat phase and the solution region L_2, where fatty acid is the solvent. In respect to the solution regions L_2, however, there are considerable differences between the fatty acid and alcohol systems.[16,76,79,81]

The fatty acid solutions form even in the absence of water owing to the fact that the soap dissolves in the water-free fatty acid to give a molecular compound, a soluble acid soap, in which the molecules are linked by hydrogen bonds between the carboxyl and carboxylate groups. This molecular compound then exists up to high water contents, the solution region L_2 thus giving off a salient down towards the water corner.[18,19,35,50,59,60]

In contrast, the alcoholic solution, L_2, does not form below a certain water content, which must suffice to surround the sodium ion of the soap with a hydration shell. No direct hydrogen bonds between the alcohol group and the carboxylate group have been found; the cohesion is apparently effected by bound water molecules.

In the fatty acid solutions, just as in the alcoholic solutions there are micelles; in both cases they form only in the presence of water and are of the reversed type. In the former they are composed of the acid soap, and the ratio of fatty acid to soap is

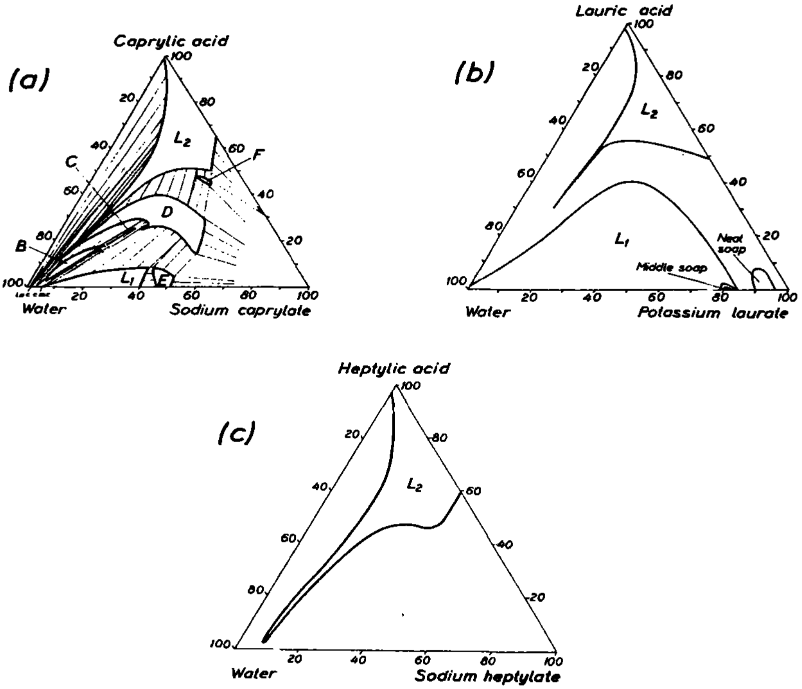

Figure 15. Phase diagrams for ternary systems containing a fatty acid soap, water and a fatty acid:

(a) Sodium caprylate–caprylic acid–water at 20 °C
(b) Potassium laurate–lauric acid–water at 175 °C (After McBain)
(c) Sodium heptylate–heptylic acid–water at 20 °C

L_1. Homogeneous isotropic aqueous solution.

L_2. Homogeneous isotropic solution in fatty acid.

B. Homogeneous mesomorphous phase displaying lamellar structure (mucous woven type).

C. Homogeneous mesomorphous phase displaying normal two-dimensional tetragonal structure.

D. Homogeneous mesomorphous phase displaying lamellar structure (neat phase type).

E. Homogeneous mesomorphous phase displaying normal two-dimensional hexagonal structure.

F. Homogeneous mesomorphous phase displaying reversed two-dimensional hexagonal structure.

therefore constant, whereas in the alcohol solutions this ratio varies within certain limits. In region L_2 of the fatty acid system there is a transition from the reversed to the normal type of micelles as the water content is increased; in the alcoholic solution, however, this is not the case.[18,19,34,35,49,50,60]

It should be noted that just these two types of amphiphiles, namely liquid monohydric alcohols and fatty acids, whose solubilization in aqueous solutions begins at the l.a.c. and, in the region between this concentration and the c.m.c., leads to the formation of water soluble aggregates, also give rise to formation of mesomorphous substance below the c.m.c. There is an obvious relationship between the formation of the aggregates in the dilute aqueous solutions below the c.m.c. and the formation of the mesophase B and the aggregates in the lower part of the salient of region L_2.

From the above investigation is thus evident that the effect of solubilization in an association colloid—water system may be extremely great, and that it is in a large measure dependent on the presence and the nature of any hydrophilic group in the molecules of the solubilizate.

To illustrate the effect of the molecular structure of the association colloid itself a number of phase diagrams are reproduced where the solubilizate is an alcohol but the type of association colloid varies.

Figure 16 shows the phase equilibria in some ternary alcohol systems containing potassium soaps of fatty acids. The main type is the same as in the sodium caprylate systems, but in one of them (the potassium oleate system) we have an example of the fact that the neat phase begins at the soap–water axis and then transverses practically the whole system in an arc. We have also (in the same or other systems) examples (1) of the limited ability of the rectangular phase to incorporate the solubilizate,(2) of a normal isotropic cubic phase that can solubilize alcohol but that exists only at a constant water content (in the potassium caprylate system), (3) of the appearance of the reversed two-dimensional tetragonal phase in a well defined region (potassium caprate

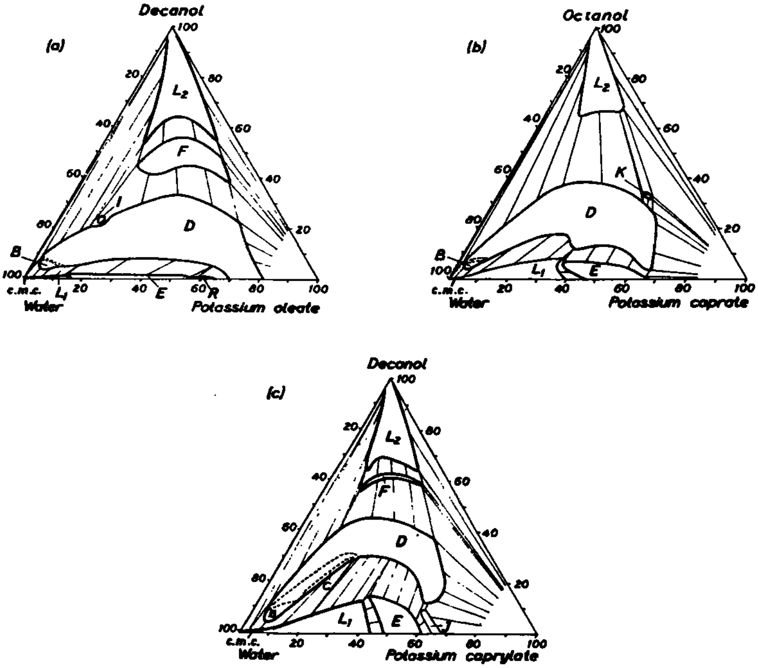

Figure 16. Phase diagrams for ternary systems containing potassium soaps, water and an alcohol:

(a) Potassium oleate–decanol–water at 20 °C
(b) Potassium caprate–octanol–water at 20 °C
(c) Potassium caprylate–decanol–water at 20 °C

L_1. Homogeneous isotropic aqueous solution.
L_2. Homogeneous isotropic alcoholic solution.
B. Homogeneous mesomorphous phase displaying lamellar structure (mucous woven type).
C. Homogeneous mesomorphous phase displaying normal two-dimensional tetragonal structure.
D. Homogeneous mesomorphous phase displaying lamellar structure (neat phase type).
E. Homogeneous mesomorphous phase displaying normal two-dimensional hexagonal structure (middle phase type).
F. Homogeneous mesomorphous phase displaying reversed two-dimensional hexagonal structure.
I. Homogeneous viscous isotropic mesomorphous phase displaying cubic structure.
K. Homogeneous mesomorphous phase displaying reversed two-dimensional tetragonal structure.

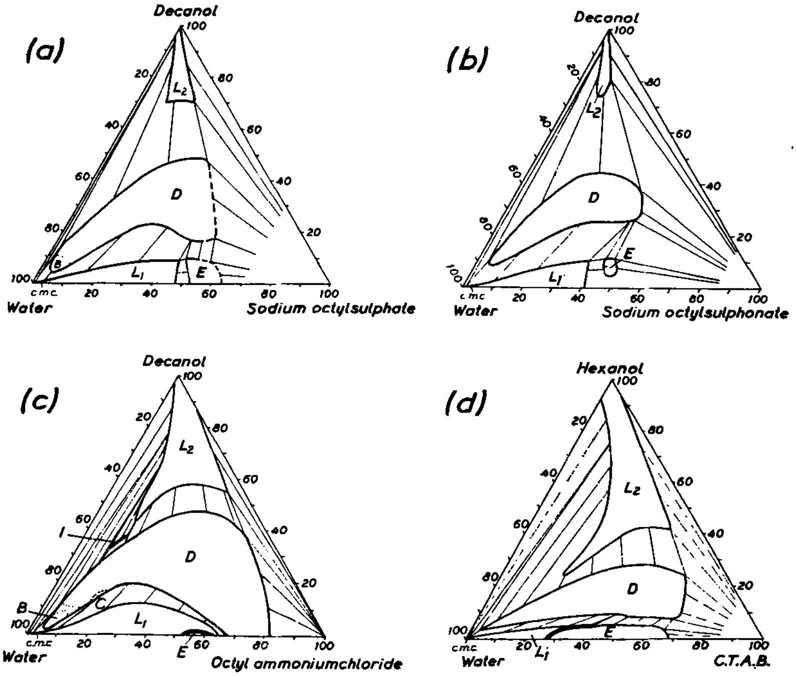

Figure 17. Phase diagrams for ternary systems containing an alkyl sulphate, alkyl sulphonate, a primary or a quaternary alkyl ammonium salt, water and an alcohol.

(a) Sodium octyl sulphate–decanol–water at 20 °C
(b) Sodium octyl sulphonate–decanol–water at 20 °C
(c) Octyl amin hydrochloride–decanol–water at 20 °C
(d) Octyl trimethylammonium bromide–hexanol–water at 25 °C

L_1. Homogeneous isotropic aqueous solution.
L_2. Homogeneous isotropic alcoholic solution.
B. Homogeneous mesomorphous phase displaying lamellar structure (mucous woven type).
D. Homogeneous mesomorphous phase displaying lamellar structure (neat phase type).
E. Homogeneous mesomorphous phase displaying normal two-dimensional hexagonal structure (middle phase type).
F. Homogeneous mesomorphous phase displaying reversed two-dimensional hexagonal structure.
I. Homogeneous viscous isotropic mesomorphous phase displaying cubic structure.

system) and, finally (4) of the appearance of a complex isotropic phase (in the potassium oleate system).[39,44,58]

Figure 17 shows the phase equilibria in the ternary alcohol systems where the fatty acid soap is replaced by an alkyl sulphate, an alkyl sulphonate or a primary or a quaternary alkyl ammonium salt. Here, too, the phase equilibria are in principle of the same type as in the sodium caprylate systems. So far as we can judge from our experience, this is the case also for the systems of these association colloids with other types of additives. All these types of ionic association colloids thus behave in the same manner irrespective of the differences between their hydrophilic groups.[44]

Finally, we have also examined ternary systems with non-ionic association colloids of the polyethylene oxide derivative type. As is seen in Fig. 18, the alcohol and fatty acid systems here belong to the same type, by virtue of the fact that in both cases there is an interaction that leads to aggregates linked by hydrogen bonds. It may be noted that in one of the systems (the lauryl deca-ethylene glycol ether–oleic acid–water system) there are, in addition to the two solution phases, L_1 and L_2, and the lamellar neat phase, D, normal and reversed two-dimensional hexagonal phases, E and F, normal and reversed isotropic phases I_1 and I_2 and a normal two-dimensional tetragonal phase, C.[16,44,58,76]

We have found it convenient to classify the phase equilibria in the ternary systems according to four main types, I–IV; these are illustrated in the Figs. 12–15. The type is determined by whether or not the molecules of the solubilized compound contain a hydrophilic group, by the character of the polar groups of this component and of the association colloid, and by the kind of interaction between these groups. There are, of course, intermediate forms between these main types, and likewise it may be expected that more complex molecular structures of the components can interfere with or preclude the formation of certain structures. Even a high melting point or a low solubility might have such an effect. This notwithstanding, a rough classification of this kind may well facilitate a general survey of this multifacetted field. The number of combinations of amphiphilic and

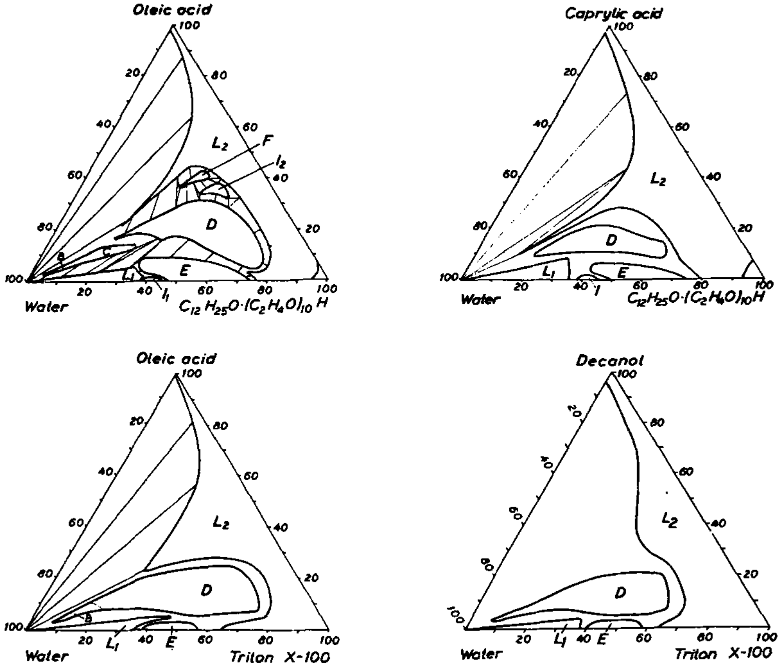

Figure 18. Phase diagrams for ternary systems containing a non-ionic association colloid, water and fatty acid or an alcohol.

(a) Lauryl deca-ethylene glycol ether–oleic acid–water at 20 °C
(b) Lauryl deca-ethylene glycol ether–caprylic acid–water at 20 °C
(c) Triton X-100–oleic acid–water at 20 °C
(d) Triton X-100–decanol–water at 20 °C

L_1. Homogeneous, isotropic aqueous solution.
L_2. Homogeneous, isotropic solution in fatty acid or alcohol.
B. Homogeneous, mesomorphous phase displaying lamellar structure (mucous woven type).
C. Homogeneous, mesomorphous phase displaying normal two-dimensional tetragonal structure.
D. Homogeneous, mesomorphous phase displaying lamellar structure (neat phase type).
E. Homogeneous, mesomorphous phase displaying normal two-dimensional hexagonal structure (middle phase type).
F. Homogeneous, mesomorphous phase displaying reversed two-dimensional hexagonal structure.
I_1. Homogeneous viscous isotropic mesomorphous phase displaying normal body-centered cubic structure.
I_2. Homogeneous viscous isotropic mesomorphous phase displaying reversed face-centered cubic structure.

lipophilic compounds that can be assigned to these four main types is already quite large.[81]

Compared with the type of the hydrophilic group, the length of the hydrocarbon chain is of little significance so long as it is not so short as to result in more or less complete solubility in water. A reduction in chain length usually leads to a smaller number of mesophases and hence a simpler phase diagram without, however, incurring any change in the actual type. An increase in the temperature has the same effect; many mesophases are extremely sensitive to temperature.

It is obvious that these four main types do not exhaust the possibilities. Major changes in molecular structure may result in the formation of further types. One example of this is provided by the bile acid salts with their many hydrophilic groups and high solubilizing capacity. They give alcohol systems that constitute a fifth main type (Fig. 19). Here we have a continuous solution region from 100 per cent of water to 100 per cent of alcohol, but no mesophases. The bile salt renders water and decanol, which are normally practically insoluble in each other, miscible in any proportions. That this property is associated with the formation of micelles has been demonstrated experimentally; the micelles

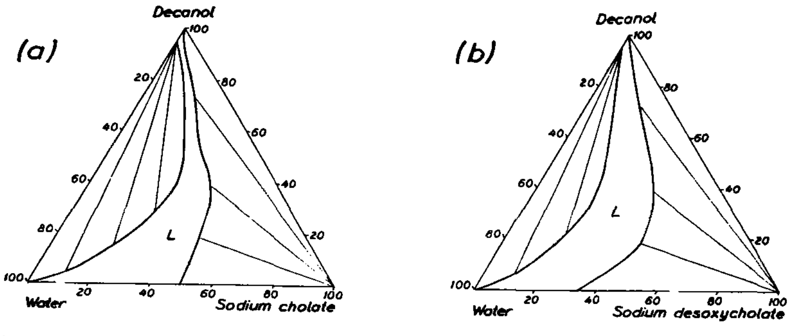

Figure 19. Phase diagrams for ternary systems containing a bile acid salt, water and decanol:
(a) Sodium cholate–decanol–water at 20 °C
(b) Sodium desoxycholate–decanol–water at 20 °C
L. Homogeneous isotropic solution.

in these systems appear to have a different structure from those in solutions of paraffin-chain colloids, but here, too, normal and reversed types have been recognized.[54,55]

From a formal standpoint similar phase diagrams are obtained in many ternary systems of paraffin-chain colloids when the temperature is raised or when the chain length of the components is shortened, and also in systems of compounds that are not known

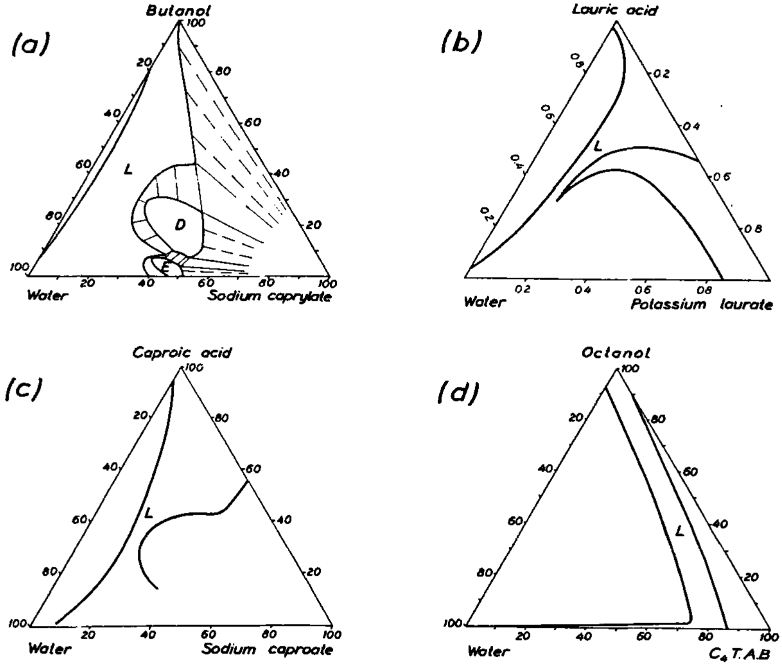

Figure 20. Phase diagrams for the ternary systems:

(a) Sodium caprylate–butanol–water at 20 °C

(b) Potassium laurate–lauric acid–water at 180 °C (After McBain)

(c) Sodium caproate–caproic acid–water at 20 °C

(d) Butyl trimethyl ammoniumbromide–octanol–water at 20 °C (After A. S. C. Lawrence).

L. Homogeneous isotropic solution.

D. Homogeneous mesomorphous phase displaying lamellar structure (neat phase type).

E. Homogeneous mesomorphous phase displaying normal two-dimensional hexagonal structure (middle phase type).

to form micelles, but that display hydrotropic properties[67,78,87] (Fig. 20). For the time being it is perhaps best to assign all these to type V. That mesophases do not occur in many of these systems is obviously due to the high solubility of the aggregates formed, or to the fact that the shape of them or the molecular structure of the components preclude the formation of the ordered states of the mesomorphous phases.

In ternary systems of association colloids so far only normal mesomorphous particle structures (normal two-dimensional hexagonal, tetragonal and rectangular phases, normal cubic phases) and also complex structures have been observed in the concentration region between the neat phase and the aqueous solution. On the other hand, no normal mesomorphous particle structures have been definitely observed in the region between neat phase and the solution region L_2, but only reversed ones (reversed two-dimensional hexagonal and tetragonal, and reversed cubic phases), and, in addition, complex particle structures.

3.2. Systems with Amphiphiles Swelling in Water

Of the amphiphiles that, though sparingly soluble in water, incorporate it, with simultaneous swelling, the type of monoglycerides is the one that has been the most thoroughly investigated. Lutton has examined 10 or so binary systems with monoglycerides, ones with saturated fatty acids, from lauric acid upwards ($C_{12}-C_{24}$), and also some with unsaturated acids,[69,70] while Larsson has extended the series downwards to monocaproin, and examined the structure of the phases in greater detail.[66]

3.2.1. *Binary systems*

Monocaproin dissolves in water in any proportions to form homogeneous, isotropic micellar solutions, where at water contents greater than about 50 per cent the micelles appear to be of a similar spherical type to those in ordinary aqueous solutions; at higher concentrations, however, there is a change to another type.[66] This lowest monoglyceride thus has properties of an association colloid.

The others, however, do not give micellar aqueous solutions. They take up water even at temperatures below the melting point, and swell to give a lamellar mesophase of the neat phase type. (The " gel " phases formed at these temperatures are disregarded in this context.[61]) The melted glycerides that, according to Larsson, have a micellar structure even in the water-free state,[66] dissolve a certain amount of water, after which neat phase forms; in some systems, however, a cubic viscous isotropic mesophase forms at a somewhat higher temperature and at still higher temperatures a mesophase of the hexagonal type.[66,69,70] There is some uncertainty as to whether the last two phases are of the normal or reversed type. Larsson claims to have evidence that the cubic phase of the monopalmitin–water system and the hexagonal phase of the monobehanin–water system are reversed mesophase structures.[66] It is open to question, however, whether this is the case also in the systems where the lamellar and cubic phases occur at the same temperature and the region of the latter appears to extend to considerably higher water contents than the former (for example, the monoolein– and monoelaidin–water systems).[69,70] The boundaries of the regions of existence of the homogeneous mesophases appear not to be entirely reliable. It would seem that the experimental data for all these systems are just as consistent with a normal structure.

In several systems the region of the neat phase in the direction towards a higher water content borders on a zone that Larsson found to be a specific structure, which he called a " dispersion "; it is described as a stable state of small spherical particles dispersed in water and is apparently regarded as a separate phase, for according to Larsson it is not neat phase.[66] The description is in many respects reminiscent of the lamellar mesophase of the mucous woven type, B, but the present authors have shown that, at least in the monocaprylin–water system at 20°, this " dispersion " is readily separated into a pure neat phase and a highly dilute aqueous solution; we therefore have a typical two-phase zone.[44] It is, moreover, no unusual phenomenon for a neat phase in two-phase zones with solutions to display a tendency for dispersion into spherical particles composed of concentric layers alternately of water and amphiphile.

Another amphiphile in which the uptake of water stops at the formation of mesomorphous phases without leading to the formation of micellar aqueous solutions is lecithin, which yields a neat phase with up to about 45 per cent of water.[94,95] According to Reiss-Husson and Luzzati the diacyl phospholipids and sphingolipids also belong to the group.[92]

The only observations of the formation of reversed mesophases in binary systems is thus that made by Larsson on two monoglycerides, namely monopalmitin and monobehenin.[66] The transformation of an amphiphile first to reversed, then to lamellar and finally to normal mesophases on addition of water seems not so far to have been observed.

Among the synthetic amphiphiles we have examples of a transition type in the groups of Aerosols. In the sodium di-2-ethylhexylsulpho–succinate–water system the water-free amphiphile at 20°C is in a two-dimensional bexagonal mesomorphous state. The uptake of water results in the transformation into an isotropic phase and a neat phase, the uptake stops at about 80 per cent of water. The two first mentioned structures probably are of the reversed type.[1,44] However, in this system an aqueous solution phase is formed with up to 1·4% Aerosol OT, this phase is reported to contain micelles of the normal type.[99]

3.2.2. *Ternary systems*

In the ternary systems of these amphiphiles with a foreign lipophilic or amphiphilic additive the conditions are essentially the same. For instance, monocaprylin with water and decanol or caprylic acids yields systems with a continuous solution region from about 4 per cent of caprylin to 100 per cent of the additive, and a neat phase with up to 45 per cent of water and 20–25 per cent of the foreign amphiphile[44] (Figs. 21a and b). In the lecithin–cholesterol–water system there is a neat phase region with up to 45 per cent of water and about 22 per cent of cholesterol[94,95] (Fig. 21c).

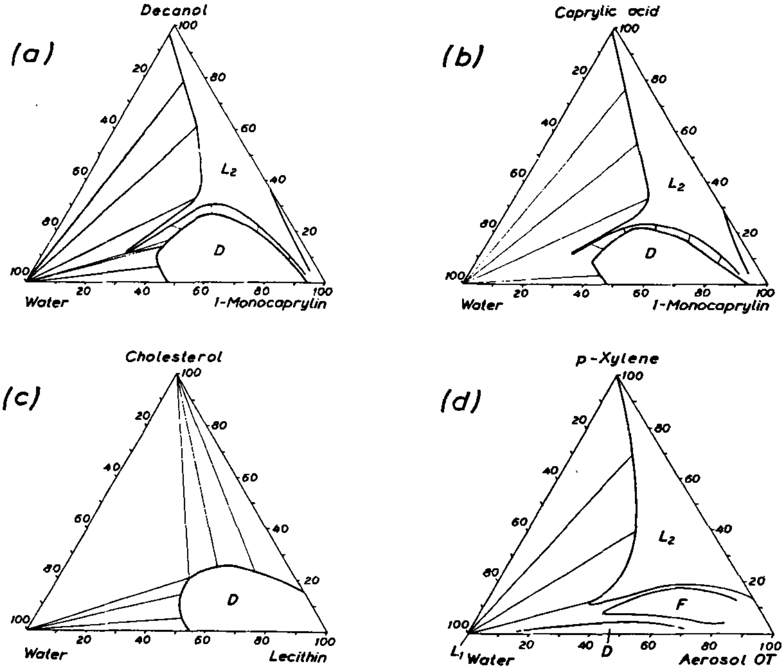

Figure 21. Phase diagrams for the ternary systems:

(a) 1-Monocaprylin–decanol–water at 20 °C

(b) 1-Monocaprylin–caprylic acid–water at 20 °C

(c) Lecithin–cholesterol–water at 20 °C (After Derivichian[94]).

(d) Aerosol OT–*p*-xylene–water at 20 °C

L_2. Homogeneous isotropic solution.

D. Homogeneous mesomorphous phase with lamellar structure (neat phase type).

With water-free hydrocarbons or chlorinated hydrocarbons the dialkyl sulphosuccinates give isotropic micellar solutions that solubilize water,[65,90], and in some concentration areas are transformed to mesomorphous phases.[44] In the Aerosol OT–xylene–water system, reversed hexagonal mesophase forms up to a fairly high water content; this is in equilibrium with lamellar neat phase in the direction of a higher water content[44] (Fig. 21d).

At constant weight ratios between the components the multicomponent system composed of cephalin, lecithin, phosphoinosotide and water was observed by Luzzati and Husson to contain two mesophases—one reversed hexagonal at low, and one lamellar at high, water contents[63,73] The same would seem to apply to systems of mitochondria lipids and water.[92]

In ternary systems these sparingly soluble amphiphiles, thus, on adding of water in many cases appear to display an initial tendency for the formation of reversed mesomorphous particle structures. Reliable observations are still too few to permit of definite conclusions, but the evidence to date points to a transition from these reversed particle mesophases to lamellar neat phase as the water content is increased.

The phase diagrams in Fig. 21 illustrate how the isotropic micellar solution formed from amphiphile and the organic additive changes to one of a reversed hexagonal or lamellar mesomorphous type. In the direction of a higher water content these are in equilibrium with a highly dilute aqueous solution that in most cases appears not to be micellar. The changes in phase equilibria resulting from the low solubility of the swelling amphiphile and the third component in water, are not so great as to preclude the assignment also of these phase equilibria to type IV. As was shown above a characteristic feature of this type is that the two organic components are miscible even in the water-free state; that this solubility in, for instance, the monocaprylin-caprylic acid system is due to a direct interaction between the hydrophilic groups has been established. In the Aerosol OT–xylene system, however, the formation of the solution is apparently due to another mechanism. It would seem justified in these cases to postulate the existence of one or perhaps several special sub-groups of type IV.

4. The Transition from Normal to Reversed Structures

From the above account it is seen that micellar and mesomorphous particle structures appear to occur on both sides of a concentration region with the lamellar structures, and that as a rule the normal and reversed particle structures are found on the sides with a higher and a lower water content, respectively. It is

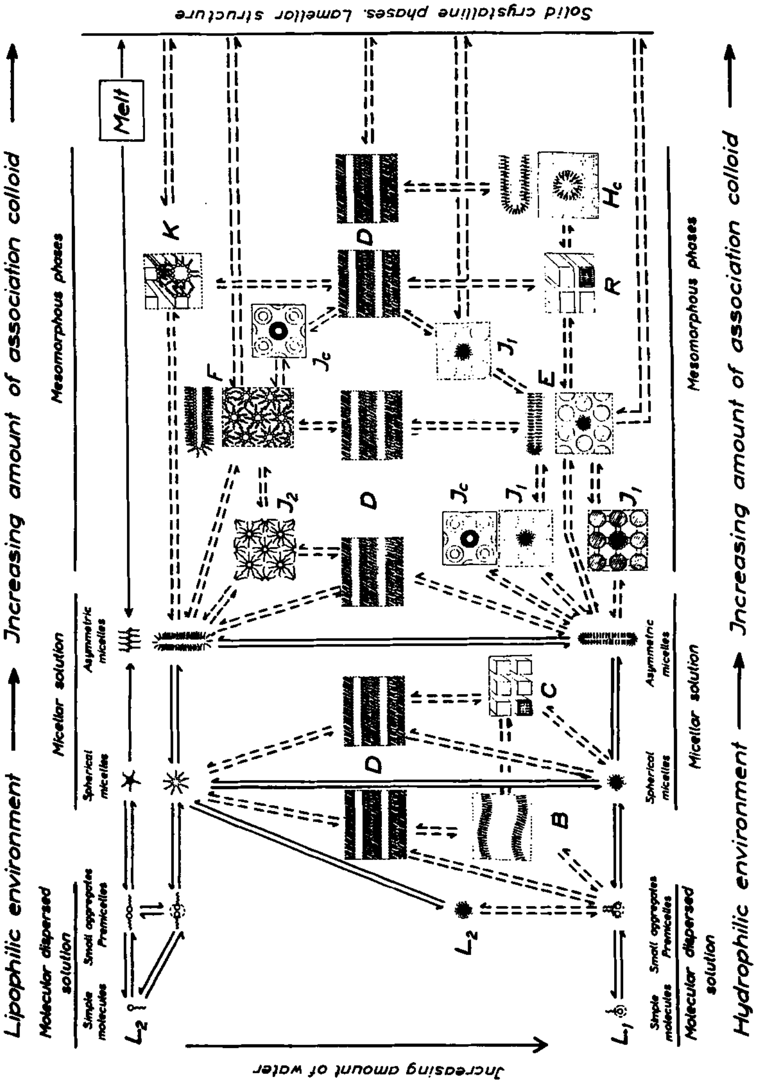

Figure 22. Survey of the transitions between different states of association and aggregation.

evident that as the concentration of the system is varied the various structures follow each other in a certain sequence. This applies not only to the binary systems—as Luzzati has shown in respect to their mesophases—but also to the ternary; in both cases, however, this is true not only for the mesophases but also for the micellar structures.

We have made an attempt in a single, highly schematic diagram to survey most of the observed and examined transitions between the various structures and phases in binary and ternary systems[18] (Fig. 22). (Winsor has recently performed a similar treatment.[100]) The micellar and mesomorphous structures are portrayed diagrammatically; the same symbol has been used for different amphiphile molecules and for mixtures of them, irrespective of differences in the nature of the hydrophilic group and the structure of the hydrocarbon part. The various mesomorphous structures are denoted by the same alphabetical notation as that used above, namely B–F, I, K, R, and the isotropic solutions by L_1 and L_2. The transformation between different association stages in homogeneous phases is indicated by continuous arrows, and the phase transformations by broken arrows.

At the bottom of the diagram, as the proportion of amphiphile is increased and the water decreased there is a succession of equilibria in an aqueous environment. From the left to right there are at first various micellar stages, followed by mesomorphous phases. In all these we have particle structures with micelles and aggregates of the normal type—that is to say, particles with a hydrocarbon core in a water continuum, and this sequence ends with a lamellar structure.

At the top of the diagram there is a fairly similar series of equilibria between particle structures in a lipophilic environment. In the uppermost row there is an indication of micelle formation in solutions of association colloids in a water-free organic liquid, but the same scheme may also illustrate any micelles in water-free melts of uniform amphiphiles. In both cases the micelles are presumably of the reversed type, with a core of hydrophilic groups. In the second line there is a series of micellar and mesomorphous particle structures that occur in the presence of small amounts of water. Here, too, the micelles and aggregates are of the reversed type—that is to say, particles with cores of hydrated hydrophilic groups or water in a hydrocarbon continuum.

From the bottom of the diagram upwards the character of the system changes gradually from strongly hydrophilic to strongly lipophilic; a succession of aggregation states is then traversed that constitutes a transformation from micellar and mesomorphous particle structures of the normal type, to lamellar structures and, further on, to mesomorphous and micellar structures of the reversed type. These transitions illustrate the effect of solubilization.

The lamellar neat phase structure, D, occupies a conspicuous place in the centre of the diagram. Experience so far indicates that a transition from a normal to a reversed *mesomorphous* structure invariably occurs *via* this layered mesophase. Most transitions from normal to reversed micellar structures occur *via* mesophases, and in many systems *via* ones with both particle and lamellar structures, but even in the systems where the former do not occur as intermediate stages the lamellar phase is always present. In addition, however, there is a direct transformation in homogeneous solution between the two *micellar* structures; such transitions are indicated in three places in the left part of the diagram; whether they pass through a layered micellar stage has not been ascertained.

Although a schematic diagram of this general type cannot portray the large volume of results that has been accumulated, it nevertheless provides an impression of the state of our knowledge in this field, today. Summarizing, one may say that in binary systems of an association colloid and water the reduction in the water content results in a rise in the association and aggregation, and that this process passes through several well defined stages. The addition of a foreign amphiphilic or lipophilic substance increases the diversity of this series of aggregation stages and often leads to a transition from the normal to the reversed structure.

The idea that the association in binary systems of association colloid and water progresses stepwise over a number of well defined stages, as has been asserted by one of the present authors since the thirties, has thus proved to be correct. Moreover it applies not only to the homogeneous solutions[5–11,13,15–18,27,28,30,32,51]; it has also proved to be valid for the ternary systems, and again not solely in homogeneous aqueous solutions containing solubilizate, where it was first demonstrated, but to a marked degree also in other parts of the system where the proportion of solubilizate is higher and where the solubilization leads to the interesting transition to reversed structures. It may thus be said that a stepwise change in the state of the association and aggregation with concentration is one of the most characteristic features of the aqueous systems of amphiphilic substances.

5. Factors Governing the Stability of the Various Structures

5.1. The Role of Water

A factor of major importance is the ratio between the amounts of water and organic substance in the system. Water serves not only as solvent or dispersion medium—constituting, as it were, the environment into which the other components and aggregates must be fitted—but participates in a more active manner in the formation of the structures. There is a direct interaction between water molecules and the hydrophilic groups of the amphiphiles, mainly *via* hydrogen bonds—and this means that a certain number of water molecules must be regarded as being bound to the aggregates of the amphiphile and thus to belong to them. In the case of ionized amphiphilic components a number of water molecules will, moreover, be oriented and bound around the ions by ion–dipole forces.

These different forms of water bonding are of particular importance in the parts of the systems having a low water content. They are directly involved in the formation of many—if not in all—reversed structures, which will not form at all below a certain minimum amount of water (the mesophases F, K, I_2 and the micelles in L_2 of the alcohol and fatty acid systems).[16,18,19,34,35,40,57,77,79]

The existence of many reversed structures would seem also to be conditional on the water not exceeding a certain amount (the above mentioned reversed structures); this appears to be related to the maximum capacity of the hydrophilic groups for binding water.[16,18,19,34,44,57]

(It is possible to calculate this maximum amount of water approximately, taking into consideration all the possibilities of hydrogen bonds between the hydrophilic groups and water molecules and a complete hydration shell of water around the ions; in the case of a fatty acid sodium soap, for instance, this would give about 5 + 6 bound water molecules, and in the case of an alcohol about 3.)

In the other mesophases, too, water binding is a factor of importance. Neat phase does not form if the water does not exceed a minimum amount, which, for systems of alkali soaps, is related to the hydration needs of the alkali ions[44] (as is the case for the reversed mesophases and micellar solutions in the same systems). In the case of neat phases, however, the maximum amount of bound water is exceeded in many systems; this is clearly manifested in the properties of the phases.[57]

In the mesophases with normal particle structures the importance of water binding is not so prominent, but even among these there are phases whose existence would seem to be dependent on all the water being bound (e.g. the normal viscous isotropic mesophase, I_1, in the potassium caprylate–decanol–water system[44]). On the other hand, two of the known mesophase types (the mucous woven type, B, and the normal two-dimensional tetragonal type, C) have so far been found only where water content was in excess of the maximum that can be bound.[57]

In systems with unbound water it is the volume ratio between unengaged or unbound water and hydrated amphiphilic substance rather than the ratio between the total volume of water and the volume of anhydric amphiphile that is of importance.[16,17,18]

5.2. Molar Structure of the Amphiphilic Components

Another factor of importance is the molecular structure of the organic components. On the basis of his experience of binary systems Luzzati emphasized the significance of the relative bulkiness of the polar groups and the paraffin moieties of the amphiphile molecule; bulky polar groups favour conformations with large surface-to-volume ratios—for example, the normal hexagonal phase at the expense of lamellar phase, and vice versa.[73,92]

The earlier experience that mixtures of various association colloids belonging to the same homologous series, or otherwise similar in type, behave as a uniform mixture in micelle formation has proved to apply also to the formation of mesophases. Even when a completely foreign amphiphile is added to the association colloid–water system the mixture behaves as a uniform mixture to the extent that the components together compose the amphiphilic parts of the micelles and the mesophases. Only in the reversed micellar solutions and mesophases (reversed hexagonal and cubic mesophases, F and I_2), where the foreign amphiphile plays the role of a solvent, is a part of it located outside the amphiphilic parts which are composed of the mixture.[18,19,38,44,49,50,57] In the lamellar and normal mesophases all the solubilizate is incorporated in the amphiphilic parts of the phases; in these, account must clearly be taken also of the distribution in the aqueous parts of the phase; but this distribution is of quantitative significance only in the case of amphiphiles that are highly soluble in water; moreover, the binding of the water to the hydrophilic groups decreases its solvent property.[18,41,42,44,56–58]

From the investigation of the ternary systems, however, it is evident that the properties of the amphiphilic mixture vary widely with its composition; the above examples show that in the case of two different amphiphiles the mixture can possess properties that the pure components do not: the solubilization of a foreign amphiphile often leads to completely new phases, or to considerable changes in the properties of a phase, even when the basic structure is permanent, or to changes in the size of the region of existence of a phase. For this reason, it is not possible to infer conditions in ternary systems from those in binary ones, nor vice versa, if only the conditions for a single composition are known.

It is, as we have seen, the nature of the hydrophilic groups that is of prime significance. As has been intimated above, this is associated with the fact that the polar groups of the foreign amphiphile are inserted between the hydrophilic groups of the association colloid and hence modify the character of the boundary layer in the amphiphile–water interface; this in turn results in changes in the water binding, leads to binding between various polar groups directly *via* hydrogen bonds or mediated by water molecules, and hence brings on a cohesion between the molecules that may necessitate a particular position of these groups in relation to each other in the boundary layer; in the case of an ionized association colloid the charge density in the interface changes, and if the process goes far enough it can result in liberation of previously bound counter ions and a change in the character of the mesophase. The area per hydrophilic group in the amphiphile–water interface is also influenced by these factors. For these reasons the molar ratio between the amphiphilic components is of significance both for the properties in various parts of a mesophase and for the occurrence and stability of the mesophases.

In the case of highly lipophilic solubilizates, which are incorporated in the hydrocarbon interior of the amphiphile aggregations, the effect on their boundary layers is far smaller; their solubilization results primarily in an increase in the volume of the hydrocarbon part. In the case of solubilizates that are only slightly hydrophilic, some of the molecules may also be situated in the interior of the aggregates and the rest inserted, with the polar groups, in the boundary layer. In the case of alcohols and fatty acids all the molecules seem to have the latter arrangement.

5.3. Regions of Existence and Composition of the Phases

While some phases may persist in spite of large variations in the molar ratio between the amphiphilic components and between these and the water, the existence of others has proved to be dependent on a relatively definite composition.

The lamellar neat phase displays the greatest tolerance of variations both in the relative amounts of the amphiphilic components and the water content. As has been pointed out above, however, a change in the composition of the amphiphile mixture can result in quite large modifications in the properties of the neat phase; these will be manifested chiefly in the capacity of the phase to take up water and the consequences of this.[18,24,26,36,44,57]

The greatest changes take place in the neat phase of the ionized association colloids. As McBain showed, in the binary systems this is of a " non-expanding type "[84,86]; that is to say, a rise in the water content is unaccompanied by any change in Bragg spacing. When amphiphiles of the alcohol or fatty acid type are solubilized in the phase, it changes first to a variably expanding and finally to a constantly expanding type.[36,44,57] In the final stage the uptake of water occurs with one-dimensional swelling, the slope of the curve $\log d$ *versus* $\log(1/v_a)$ being 1 (where d is the Bragg spacing, v_a is the volume fraction of the amphiphile). In this stage all the added water is inserted between the layers of amphiphile in the unbound stage. At the same time there is a change in the maximum capacity for water uptake, which has previously remained at the greatest amount that could be bound, but now exceeds this and rises to extremely high levels (80–90 per cent). In our opinion this is due to liberation of counter ions from the amphiphile layers, conditions thereby being created for the uptake of water through the Donnan distribution.[24,57] These changes are the result of the insertion of the alcohol or carboxyl groups of the solubilized amphiphile between the ionized groups of the association colloid, and the consequent reduction in charge density in the amphiphile–water interface; the final stage is then reached when the molar ratio between the amphiphiles exceeds a certain value (1–2 moles of solubilizate per mole of colloid), which varies slightly with the molecular structure of the amphiphiles.

Even in the binary systems the neat soap of the non-ionic amphiphiles seems to be of the constantly expanding type (with one-dimensional swelling). Their properties are not affected to the same extent by the solubilization; to judge from our experimental results so far, the uptake of water in these cases does not exceed appreciably the greatest amount that can be bound to the hydrophilic groups.[36]

The normal hexagonal mesophase structure can in some systems exist over quite large ranges of water and solubilizate. The lower limit of the water content seems to be determined by the condition that there shall be enough to provide a monomolecular layer of bound water molecules around each amphiphile aggregate.[57] In the direction of a higher water content there would seem to be no such limitation; here the existence of the phase is apparently determined by the point at which the critical volume fraction of hydrated micellar substance reaches the critical value for the formation of mesophase.[18,96] The amount of solubilizate that can be incorporated in the phase varies widely with the molecular structure of the association colloid itself, and with that of the solubilizate; the largest amounts have so far been observed for amphiphilic additives having weak hydrophilic properties. In the systems studied hitherto the region of existence of the reversed hexagonal phase has usually proved to be quite limited. Its extent would seem to be dependent on the ratio between the amphiphilic components and between them and water. The importance of the latter factor has been touched on above; it will suffice to add here that in some directions the boundary of the region of existence is determined by a lower limit for the thickness of the amphiphile layer around the water core of the cylinders.[15–18]

To judge from our experience the existence of the mesomorphous tetragonal rib structure in alkali soap–alcohol–water systems is limited to definite molar ratios between the amphhipiles—about 3 moles of alcohol to 2 moles of soap in the normal, C, and about 1 : 1 in the reversed phase, K. On the other hand, the water content can vary over a wide range in the normal type, but not in the reversed.[39,44,57] The normal rectangular rib structure, R, would also seem to exist only at quite a definite amphiphile composition (additive-free soap in the potassium oleate–decanol–water system), whereas its water content can vary.[44]

The opposite has been noticed as regards a normal isotropic mesophase of the face-centred cubic type, I_{f_1}. This exists at a limited molar ratio of water and amphiphile, whereas the amount of solubilizate in the amphiphile mixture can vary from 0 to 10 per cent (potassium caprylate–decanol–water system).[44,58] Other cubic mesophases also have limited regions of existence; this applies also to the complex isotropic structures.[44,58] It would thus seem as if all these structures occur only at fairly definite molar or volume ratios between the various amphiphiles and between these and water.

In many micellar solutions, too, the ratio between the amphiphilic components themselves and between these and water is a factor of significance. It has been shown above that in the region L_2 of the alcohol–soap and fatty acid–soap systems the water content is a significant factor for existence of the micellar solutions. In the micelles of the former the alcohol content may vary between about 1 and 4 moles per mole of soap, while in the micelles of the latter system the ratio of fatty acid to soap in the micelles appears to be constant at 2 : 1[18,19,49,50] In the micelles of the micellar aqueous solutions (L_1), on the other hand, the amount of solubilized substance in the micelles ranges from 0 to the greatest amount that will dissolve, but here it is the volume fraction of hydrated micellar amphiphile that determines the occurrence of structural modifications.[15–18,27,30,31,51]

5.4. Density of the Amphiphile Parts

Another point that must be considered is the packing density in the amphiphile parts of the mesophases as a whole and in their boundary layer.

As regards the amphiphile parts as a whole the densest packing is found in the lamellar mesophases. Approximately the same density is found in the normal tetragonal phase, while it is considerably lower in the two hexagonal mesophases.[82]

When the packing only in the boundary layer of hydrophilic groups is considered (the area per hydrophilic group, S) the relationship between the phases will be different. Here the interaction between these groups is a factor of significance, and it can result in changes in packing density with the composition of the amphiphile mixture. Such changes can occur within a single phase, but there they remain within narrow limits; in the transition from one phase to another, however, large alterations can occur. As long ago as 1962 we pointed out that the area per hydrophilic group decreased suddenly on passing from normal hexagonal to lamellar neat and to reversed hexagonal phase in a ternary alcohol system.[56] It was concluded that " the existence of various mesomorphous phases seems to be determined by the density of the packing of the end groups, which, for any particular phase, cannot deviate greatly from a certain characteristic value ". The view of the area per hydrophilic group as a quantity characteristic of a particular mesophase, and of the variation in this area as a significant factor in the transition from one mesophase to another has been confirmed by subsequent experience; but, as we have seen, the significance of other factors on which the stability of the mesophases is dependent has been recognized.

Husson and Luzzati have recently emphasized the significance of the area per hydrophilic group as a factor that governs the stability of the various mesophases, and that this, when the water content is raised, " increases or remains constant but never decreases, even in crossing phase boundaries ".[92] Even if this may be said to be the normal situation, we have examples of a decrease in the area with the amount of water in a single phase (for instance, in the neat phase of the potassium oleate–decanol–water system, where $S = 39\,\text{Å}^2$ at 28 per cent and only $26\,\text{Å}^2$ at 82 per cent of water[44]) and of a reduction in area after a transient increase at phase transitions produced by a *rise* in the water content (for instance, in the transition $D \rightarrow C \rightarrow B$ in alkali soap–alcohol–water systems, $S = 24 \rightarrow 36 \rightarrow 24\,\text{Å}^2$,[57] and in the transition $D \rightarrow I_1 \rightarrow E$ in the potassium caprylate–decanol–water system, $S = 28 \rightarrow 58 \rightarrow 40\,\text{Å}^2$)[44,58]. This occurs when a mesophase forms whose existence requires certain proportions between the components, and that under these conditions displays a special stability. These deviations from the normal imply that the area per hydrophilic group is not so important a factor in determining the stability of the mesophase as was originally supposed.

To summarize: The conditions in the boundary layer of hydrophilic groups is the critical factor. These are determined by the nature of these groups, the interaction between them, and between them and the water, and hence by the molar ratio between the various amphiphiles, on the one hand, and between the water and the amphiphiles, on the other. The volume ratio between unbound water and hydrated amphiphile, too, is an important factor.

6. Conclusions

In the water-containing systems of amphiphiles micellar and mesomorphous structures of both the normal and reversed types occur. So far, however, no *transition* from normal to reversed mesophases, or vice versa, appears to have been observed in binary amphiphile–water systems; but in ternary systems of water and two amphiphiles this transformation is common.

This transition is closely related to the variation in the water-to-amphiphile ratio in the system, the change to the reversed structure being promoted by a reduction in water content. Since, however, a certain amount of the water is bound to, or engaged by, the hydrophilic groups of the amphiphile molecules, the most significant factor here is not so much the volume of total water and the volume of anhydrous amphiphile, but rather the volume fractions of unbound water and hydrated amphiphile, or, in extreme cases, the volume fractions of hydrated hydrophilic groups and of the hydrocarbon parts. The nature of the hydrophilic groups is therefore important.

In systems of typical paraffin-chain compounds where both normal and reversed structures occur, the latter appear as a rule to be stable only so long as the greater part of the water, if not all of it, is engaged by the hydrophilic groups. On the other hand, normal structures can occur with all the water bound or with part completely free. In the latter case the structure is dependent primarily on the volume fraction of unbound water.

In systems of association colloids and water the solubilization of special types of foreign amphiphilic substances results in a transition from normal to reversed structure. This is seen, above all, in the types of amphiphiles that are solubilized in aqueous solutions already from l.a.c.—namely, liquid monohydric alcohols and fatty acids. This is due to the changes in the boundary layer of hydrophilic groups resulting from the solubilization. The interaction not only between these groups and water but also between the groups themselves is of significance in this respect. The conditions for a transformation to reversed structure would seem to be most favourable when the interaction leads to a cohesion between the groups mediated by direct hydrogen bonds or bridges of water molecules.

Analogously, the addition of a substance resembling an association colloid promotes the change from the reversed to the normal structure in systems of amphiphiles that are sparingly soluble in water but that take up water by swelling.

As a rule the transition from the normal to the reversed structure is promoted by factors that lead to a denser packing in the boundary layer, and hence to a smaller area per hydrophilic group. A bulky hydrocarbon part of the amphiphile in relation to the polar group has this effect.

A natural link between the normal and the reversed structures is the lamellar neat phase. This phase can exist under widely different conditions as regards the composition of the amphiphile mixture and the water content. This is particularly characteristic of mixtures of ionized association colloids and certain types of non-ionic amphiphiles.

The formation of the mesomorphous particle structures is, in comparison, associated with more restricted conditions of composition (for instance, the two-dimensional hexagonal E and F). Some of them (the two-dimensional tetragonal, C and K, the rectangular, R, and certain cubic mesophases, I) exist only at quite definite molar or volume ratios between the amphiphiles or between these and water, but under these conditions they appear to have a special stability.

In systems where there is a lamellar neat phase the particle structures as a rule are—or at least under suitable conditions can be—in equilibrium with this. In association colloid systems the isotropic solutions that are in equilibrium with mesophases contain micelles or other aggregates. Of the mesophases that are in direct equilibrium with these solutions the two hexagonal (E and F), the reversed tetragonal (K) and certain isotropic ones (I_{c1}) appear to be formed by a transformation of the micelles from solution to aggregates of the mesophase with no appreciable change in composition. On the other hand, the formation of the others (B, C, D) from the solutions takes place with fairly large changes in composition.

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