Pharmaceutical Emulsions and Suspensions

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2
Formulation Concepts for the Emulsion Maker

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I. INTRODUCTION AND DEFINITIONS

This chapter and the following one deal with the formulation and the properties of emulsions, i.e., dispersions of drops of some liquid in another immiscible one, which exhibit more or less stability depending on the application (1-2). The stability against drop coalescence is provided by the presence of a small amount of a third component, so-called emulsifier, which is in general a surface-active-agent or surfactant, that adsorbs at the drop interface and produces some interdrop repulsion according to a variety of static and dynamic phenomena (3).

The word *emulsion* is found in both *microemulsion* and *macroemulsion* (as well as the recently introduced terms *miniemulsion* and *nanoemulsion*), so that some confusion arises from this labeling. Macroemulsions (or simply emulsions) are liquid-in-liquid dispersions, with drop size ranging typically from 1 to 100 μm (that can be extended in special cases down to 0.5 μm or up to 500 μm). In this range, the drops are in general large enough to settle under gravity influence. Emulsions are thermodynamically unstable systems because their decay does result in a decrease in free energy. However, the kinetic mechanisms involved in emulsion breaking can be so slow that the corresponding emulsion may be considered as (meta)stable as far as the application is concerned. In what follows, the emulsion properties, with exception to stability, will be considered to remain constant during the time scale required for the experiment or for the practical application to be carried out.

Surfactant molecules contain both a polar and an apolar group. Hence, they won't be completely at ease either in an aqueous phase or in an organic phase, since one of their groups would not get the right match with the solvent, be it aqueous or organic. For such a reason, surfactant molecules exhibit a very peculiar behavior, which is inherent to their structure. First, they tend to adsorb at interfaces, where they can fulfill their dual affinity with the hydrophilic group located in the aqueous phase and the hydrophobic one in oil or air. Second, they reduce the mismatch with the solvent through a very specific kind of aggregation process known as micellization (4-6).

Micelles are colloidal aggregates that form above some concentration, the so-called critical micelle concentration (CMC), according to the pattern shown in Fig. 1. In a normal micellar aggregate (left) the surfactant hydrophilic groups are in contact with the aqueous solvent, while the hydrophobic "tails" are located in the micelle core away from the aqueous environment - a favorable situation from an energetic point of view. Inverse micelles (right) are similar in structure but this time the solvent is an oil phase and the surfactant hydrophilic groups are located inside (3).

The micellar aggregation is favorable but it is opposed by molecular random agitation. Thus, a certain micellar size is attained as the best dynamic compromise between the two effects.
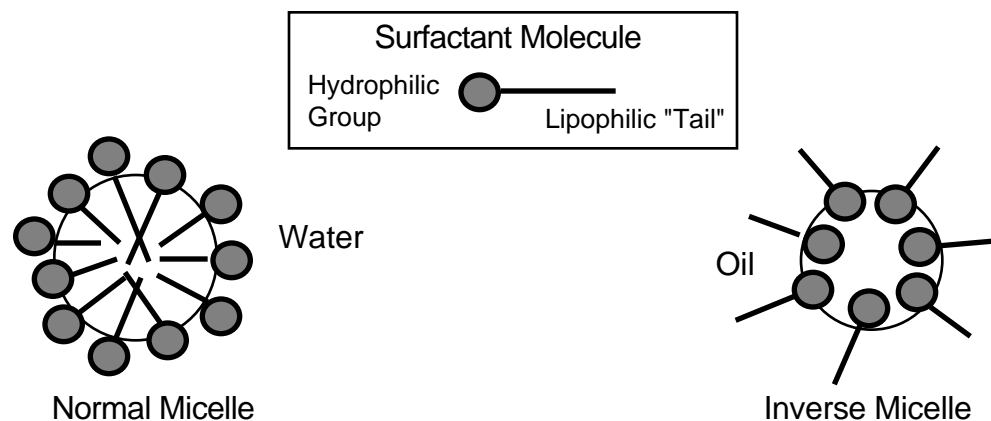
Figure 1 Micellar type aggregates

It is worth remarking that since micelles exchange surfactant molecules with the bulk phase at a very fast rate, the shape is spherical only in average. Accordingly, micelles size and shape can change very quickly to satisfy new physicochemical conditions, as those produced by a variation in formulation or temperature.

The core of a micelle is an exclusion region where substances that are incompatible with the solvent can enter spontaneously in a process called *solubilization* (4, 7). Because of solubilization, micelles become swollen and they may attain a size of a small droplet, i. e., 1000 Å or 0.1 μm. If the surfactant concentration increases well above the CMC, many micelles are formed. If another phase is present, e.g., oil if the solvent is water, and provided that the physicochemical formulation is appropriate, the micelles would solubilize large amounts of this phase and become swollen until they start interacting in a phenomenon called percolation. Such packed swollen micelle structures that could solubilize large amounts of both oil and water have been called microemulsions because they were first thought to be extremely small droplet emulsions (8-11). Actually this is a misnomer for at least two reasons. First, a microemulsion is before all a single-phase system, which is thermodynamically stable. Second, many microemulsions cannot be considered as dispersions of very small droplets, but rather as percolated or bicontinuous structures (12) in which there is no internal nor external phase, and no possibility of dilution as in normal emulsions.

Conversely miniemulsions (13) are macroemulsions, i. e., two-phase systems in which the drop size has been made extremely small by some tricky process (not only by stirring); miniemulsion drop size is actually of the same order of magnitude than the microemulsion structure, which is why they have been called nanoemulsions as well (14). However and contrarily to microemulsions, they are not thermodynamically stable and they can be diluted with their external phase. Because of their extremely small drop size miniemulsions are often transparent and viscous, and have been called also gel emulsions (15-17).

There are several types of emulsions depending on how the oil and water phases are located in the dispersed system. Note that in all cases the terms oil and water are used in a broad sense, i. e., the less polar and more polar of the two immiscible phases.

Figure 2 indicates the different types of emulsions. Simple emulsions are labeled as oil-in-water (O/W) when they exhibit oil drops dispersed in an aqueous phase, or water-in-oil (W/O) if the opposite occurs, while multiple or double emulsions are symbolized either by $W_1/O/W_2$ or $O_1/W/O_2$. W_1 (respectively O_1) and W_2 (respectively O_2) indicate the most internal phase and the most external one. Note that phases with subscript 1 and 2 may be identical or different. If they are not the same a likely difference in chemical potential may drive a mass transfer process, a phenomenon that is advantageously harnessed for controlled-release applications. Biemulsions are emulsions containing two different internal phase droplets, either of the same nature (but different size) or of different nature (whatever the size). The first kind of biemulsion is used to control some property, as, for example, emulsion viscosity, whereas the second may be used to produce controlled chemical reaction or mass transfer between the two internal phases.
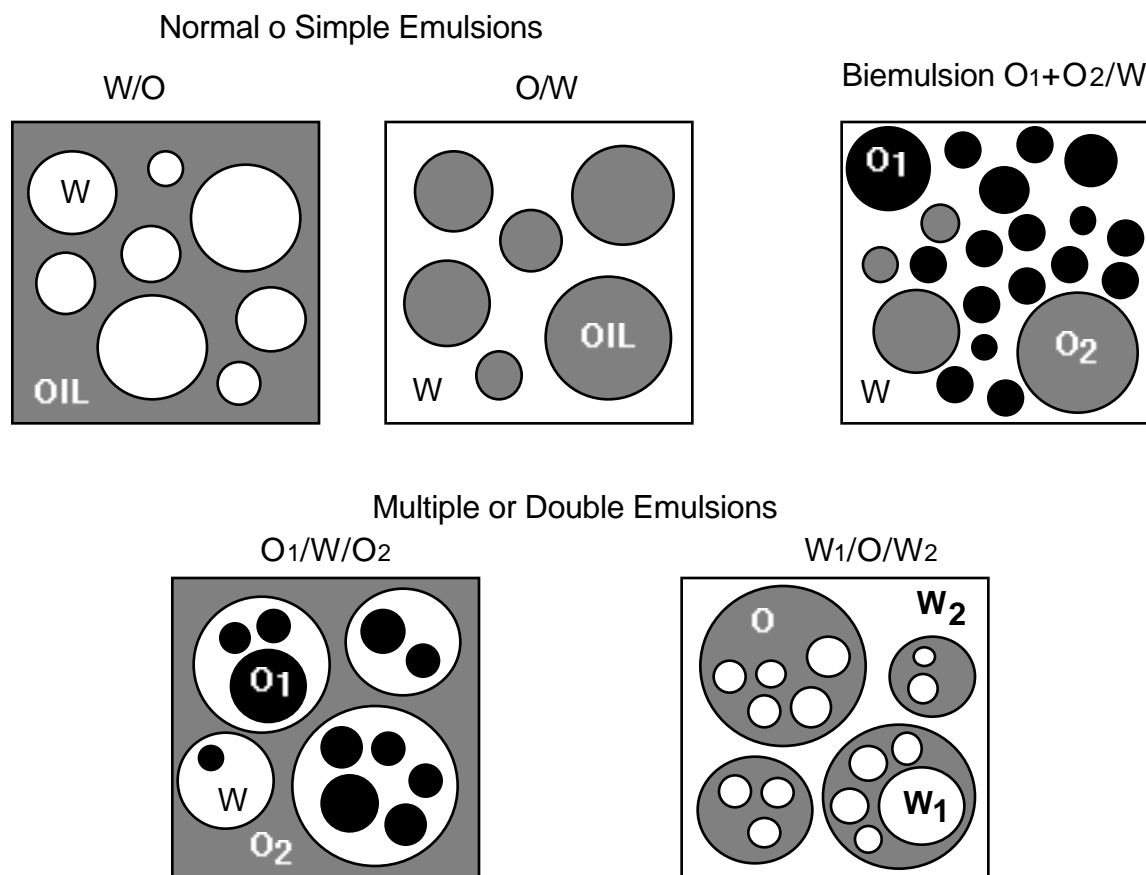
Normal o Simple Emulsions

W/O   O/W   Biemulsion O_1+O_2/W

Multiple or Double Emulsions

$O_1/W/O_2$ $W_1/O/W_2$

Figure 2   Different Types of Macroemulsions

II. EMULSION MAKING - IMPORTANCE OF FORMULATION

In a broad sense, the making of an emulsified system involves several choices and activities, that may be classified in three categories according to the type of variables that are dealt with. The two first elections, concerning what to put into the emulsion and how much of it, are the subjets of this chapter. The third one, which addresses the question of how to make the emulsion, will be discussed in the next and several other chapters of this book.

The first choice to be made is the nature of the substances that will make the emulsion, will be the oil and aqueous phases, as well as the emulsifier. In most cases, none of them will be a pure substance but rather a mixture, sometimes a very complex one. For instance, the aqueous phase generally contains different kinds of electrolytes in variable concentration.

Naturally occurring oil phases, either hydrocarbons or glyceride esters, contain scores of chemical species. Commercial surfactants are rarely pure substances. Either for economic limitations or chemical synthesis reasons, they are often mixtures. In certain cases a surfactant mixture is purposely made to attain some intermediate property or to produce some synergetic effect.

These so-called *field* or *formulation variables* are, with temperature and pressure, the intensive physicochemical variables that define the thermodynamic equilibrium conditions of the system through the equality of chemical potentials. The typical expression of the chemical potential of a surfactant molecule in solution (either in oil or water) can be written as:

$$\mu = \mu^\circ + RT \ln a \qquad\qquad\qquad\qquad [1]$$

where "a" is the activity (or the concentration if an ideal solution behavior is assumed, as, for instance, below the CMC), and μ° is the standard chemical potential in some reference state. This standard chemical potential depends on the nature of both the solute and the solvent, as well as on temperature and pressure.

In the simplest practical case they are four variables: three formulation variables that define the surfactant, oil, and water nature, in addition to temperature, since the effect of pressure is generally neglected in liquid systems for the sake of simplicity. In a typical commercial application, as many as ten formulation variables may be involved. It is worth noting that such a high number of degrees of freedom is a challenge to any systematic study. For instance, if only 5 alternatives are to be picked out for each of the 10 formulation variables, this means that 100,000 different cases would have to be surveyed - an appalling number for any practical situation.

This is why in many instances the selection of formulation variables has been so far a matter of expertise or experience. Fortunately, the practical understanding of the concept of physico-chemical formulation and its effects on phase behavior and other system properties, has improved

considerably in the past decade and a comprehensive approach is now available. This will be discussed in the following sections.

The second choice deals with the so called *composition variables*, which define the relative amounts of the different substances involved in the system. In a surfactant-oil-water (SOW) ternary system, two independent composition variables are sufficient, since the third one is the complement to 100%. Most often, the surfactant concentration (or proportion) and the water–to-oil ratio (WOR) are the selected independent variables.

In many practical instances there are many more than three components, but the basic ternary (SOW) accounts for most of the system mass or volume, and minor additives such as alcohol or electrolyte, may be neglected in the overall composition inventory, although they can completely change the phase behavior. It means that the representation of the composition effect can be carried out on a two-dimensional graph like a triangular ternary diagram, while taking the other composition variables as external conditions (i. e., not represented in the diagram), like temperature and pressure.

If for some reason there are two surfactants or a surfactant and a co-surfactant, that are to be treated as independent components, a quaternary representation is required, as for instance in a tridimensional tetrahedron diagram. Although such a three-dimensional diagram is not going to be handled as straightforwardly as a ternary diagram, currently available tools like 3D software may provide the means to cope with the third dimension.

The last category involves several choices dealing with the *emulsification protocol* that can range from straightforward to whimsical, depending on the degree of nonequilibrium features that are introduced.

For instance, some emulsions are attained by simply stirring a biphasic system in a more or less violent fashion during a certain time. A variety of emulsifying devices are available from slow-motion ribbon mixers for very viscous materials, to highly turbulent stirrers as colloid mills or high pressure homogenizors. It is often very difficult to precisely describe what exactly happens in this type of device, particularly because most of the research on two-phase stirring and mixing deals with oil/water systems in absence of surfactants, i. e., dispersions rather than emulsions (18-19). Nevertheless, when only fluid mechanical variables are involved, it seems that the process can be repeated and is relatively easy to master and manipulate.

Other emulsification protocols are based upon a transient phenomenon, in which a dominant role is played by an unsteady mechanism, e. g., mass transfer through interface, which is not easy to ascertain nor to control. Often, the nonequilibrium is driven by a continuously programmed change in a single variable such as temperature, amount or type of surfactant, water-to-oil ratio, etc., so that a phase behavior frontier is crossed and some event such as an emulsion inversion is triggered.

In such a case a precise recipe has to be closely followed to avoid divergence from the sought-after result.

The making of an emulsion involves many nonequilibrium features, at least from the mechanical point of view. Actually the product of the interfacial tension by the produced surface area   A, which is the interfacial energy, is always much smaller than the mechanical energy put into the system by the stirring device. A significant characteristic is the way and the efficiency in which the energy is provided to the drop so that breaking is favored over coalescence. This has to do not only with the device, but with formulation and eventual transient events.

In effect, the two phases and the interface can be in physico-chemical equilibrium or not prior to emulsification. If the SOW system is preequilibrated there will be no mass transfer nor chemical potential driving force, only adsorption on newly created surface. If not, mass transfer through interface could produce spontaneous emulsification and other unusual phenomena, both during the emulsification and during the decay.

After emulsification is carried out, the emulsion is generally handled or stored for some length of time, which is long compared to the duration of emulsification. The changes during this period are related to emulsion stability, that deals with how the emulsion decay or breaking takes place. This involves many different mechanisms to be discussed later on. For now it is enough to point out that the direction of change is indicated by the free energy decrease produced by drop coalescence, since a   G =   A decrease implies a reduction in surface area. It is worth remarking, however, that this decay can be delayed for so long, that it would not happen in practice. When the emulsion is poured in a vessel and left to rest, or when it is pumped into a pipeline or carried in a tank, it is submitted to a variety of decay conditions. Emulsion decay, either slow or fast, involves different steps, such as settling and thin-film drainage. The first depends upon physical variables, while the second one is commanded by the phenomenology of two approaching interfaces, involving various phenomena, all transient in nature.

The role of the surfactant, as the essential ingredient in the formation and persistence of an emulsion, is associated with several nonequilibrium processes. When the drops are formed by effect of mechanical shearing the presence of surfactant reduces the interfacial tension, so that breaking is favored. On the other hand, the adsorption of surfactant onto the freshly produced interface results in a repulsion that prevents the immediate coalescence of neighboring droplets. Thus, the surfactant plays a role in both the breaking and coalescence steps, i. e., the dynamic balance that determine the drop size.

After all these comments on the presence of several transient events and unsteady state phenomena involved in many instances of the emulsion life, how can it be useful to scrutinize the effect of physicochemical formulation on phase behavior, which is an equilibrium concept? The answer is because it is helpful to understand the equilibrium-related situation to substantiate the nonequilibrium phenomenology, that would otherwise be impossible to interpret because it involves

changes that are kinetically slow, mechanistically complex and often result in metastable configurations. As recently stated by Laughlin in his recent book (20) *"an independent determination of the equilibrium phase behavior is essential if one is to diagnose correctly the kinetics and colloidal phenomena that exist. Doing so is of considerable value industrially, because diagnosing problems correctly is the key to addressing them efficiently".*

It is found that whenever a SOW system is at physicochemical equilibrium prior to emulsification, things become much easier to forecast. As a matter of fact, if an isotropic turbulent stirring is applied for emulsification, a preequilibrated SOW system (PES) would lead to predictable emulsion type and properties, according to the phenomenology to be described in the next chapter.

If tricky programming is carried out for some nonequilibrium purposes, things are not so easy to foresee, but the PES phenomenology could be helpful whether the changes are slow so that quasi-equilibrium is reached, or conversely, very rapid so that a memory feature generates to a metastable state by quenching any possible change.

Before going into the topic of formulation, it is worth remembering some basic concepts about phase equilibria. Since emulsions are two phase systems, their physicochemical formulation should be such that there are two phases in equilibrium, which are in due time stirred to make it a dispersion. Thus, formulation is to be studied according to its influence on the phase behavior of the SOW system, with emphasis in the cases where two (or more) phases coexist in equilibrium. The well known phase rule can be stated as:

$$P = C + 2 - F \qquad\qquad [2]$$

where P is the number of phases at equilibrium, C the number of components and F the degrees of freedom, i. e., the number of system variables that must be specified to define the state of the system (see for instance Ref. 20).

In the case of a ternary, the number of components is C = 3, and the field variables are up to four: two chemical potentials (linked with two independent composition variables), and temperature and pressure.

Single phase behavior (P = 1) results in F = 4; temperature and pressure, as well as two composition variables must be fixed to define the state of the system. Thus the single-phase region would take over a bidimensional zone in the ternary diagram.

When P = 2, and at a fixed temperature and pressure, then F = 3, and only one composition variable is free to be selected, at constant temperature and pressure. This means that the two phase equilibrium occurs along a unidimensional line, i. e., the binodal boundary.

Three phase occurrence (P = 3) requires the system to be invariant at fixed temperature and pressure. In other words, there is no degree of freedom in composition, and the three phases occur at fixed (composition) points in the diagram.

According to the above discussion, the ternary SOW systems are expected to exhibit up to three-phase behavior at equilibrium. Note that this statement implies that temperature and pressure, as well as nature of the three components be fixed.

SOW systems are special cases among ternary systems because the surfactant is compatible with both other (otherwise incompatible) components. In effect, surfactants are amphiphilic substances with a strong affinity towards both oil and water. Consequently, many surfactants are both completely miscible both in water thanks to their hydrophilic group, and in oil thanks to their lipophilic group. This situation may be taken as general, since it is often true only at low surfactant concentration, up to a few times the CMC. However, when the surfactant concentration is higher than a few percentage points, mesophases of the liquid crystal type often occur, although they might be destroyed by raising the temperature or by introducing a disorder factor such as a cosurfactant.

The SOW ternary is characterized by the fact that it has only one miscibility gap that takes place when oil and water are mixed. The surfactant may be viewed as an additive that reduces this miscibility gap. These concepts will be made clear in the following section.

III. FORMULATION INFLUENCE ON PHASE BEHAVIOR

A. Phase Separation and Phase Diagrams

The thermodynamic potential that is used to analyze the phase behavior of multicomponent systems at constant temperature and pressure is the Gibbs free energy G. A spontaneous change will take place any time it is associated with a reduction in free energy (G < 0).

To make things as simple as possible, let us start with the case of a binary mixture containing components 1 and 2. Its composition depends on a single independent variable which is identified as some fraction of component 1, i.e., X_1. In this case the variation of its free energy versus composition variable (X_1) readily indicates whether the mixture would be miscible in all proportions or would exhibit a miscibility gap, i. e., a region in which two phases would separate as in the case of oil and water (see Fig. 3).

The left diagram case indicates the typical aspect of the G graph for a completely miscible binary. The minimum indicates that the mixing results in a decrease of free energy, probably because of the associated disorder and entropy increase.
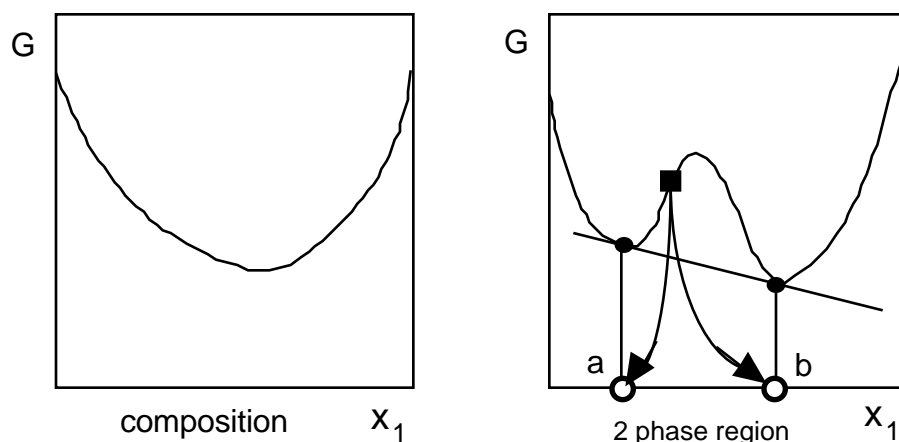
Figure 3 Shapes of free energy variation versus composition for a binary system

In the other case that is illustrated in the right diagram, the free energy curve exhibits two minima. Actually the two minima are not required for what follows, only the fact that there is an inflexion point so that a common tangent can be drawn through two points. In the middle zone, the free energy of the single phase system (square dot) is higher than the free energy of the split phases located at the points of contact of the common tangent (black dots). Hence, when the composition of the system is located between "a" and "b", then the system spontaneously separates into two phases, that are represented by composition "a" and "b" (white dots).

The system is thus biphasic in the a-b zone (called a miscibility gap), while it is monophasic elsewhere. In the two-phase region there is an equilibrium between phase "a" that contains component 2 saturated with 1, and phase "b" that contains mainly 1 saturated with 2. The relative amount of a and b are readily calculated according to the level rule.

A similar situation occurs with ternary systems, but this time a three-dimensional representation (with two independent variables) is required, and the free energy is a surface depending upon two independent variables (called X_1 and X_2). As predicted by the phase rule, the free energy surface may exhibit up to three phases, so that the tangent plane at this surface may contact it in one, two or three points, depending on the case.

Figure 4 is a tridimensional diagram in which the free energy G is plotted (vertically) against two independent composition variables X_1 and X_2, that are arranged to produce a equilateral triangular diagram at the bottom. Figure 4 indicates the case in which the tangent plane touches the surface in three points (black dots).

The composition of the phases represented by each of these black dots is indicated as a white dot on the bottom triangular phase diagram. Any monophasic system whose composition lies inside the triangle made by these three points has a representative point on the G surface that is
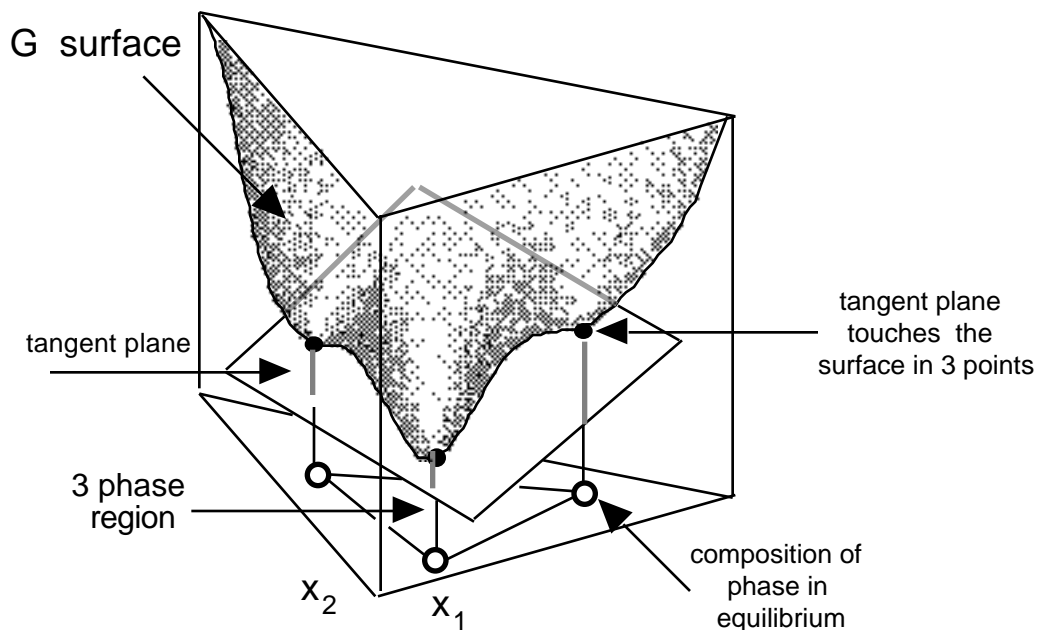
G surface

tangent plane

3 phase
region

tangent plane
touches the
surface in 3 points

composition of
phase in
equilibrium

x_2 x_1

Figure 4   Shape of free energy surface versus composition for a ternary system

above the tangent plane, and thus a split into three phases (represented by the white dots which have a fixed position because of the invariance of the system) results in a free energy decrease and thus takes place spontaneously. The phase behavior analysis is generally carried out in the bottom bidimensional phase diagram for the sake of simplicity.

The SOW ternary system may be essentially viewed as a nonmiscible OW binary, which is made more and more compatible by adding a surfactant. This is essentially similar to the way the temperature effect, as a miscibility enhancing factor, is studied on a binary diagram.

Figure 5 shows a series of binary diagrams that illustrate the variation of the free energy G vs. water-oil composition at increasing surfactant content. In absence of surfactant (bottom graph), there is a large miscibility gap, that ranges essentially from pure water to pure oil, with two extremely narrow miscible regions at both extremes, that correspond to the mutual solubilities of oil in water and water in oil.

The second diagram from bottom (same figure) characterizes a system that contains a small amount of surfactant. The black dot represents the same overall composition on the binary OW (plus S) graph and ternary SOW triangular phase diagram. The line that connects the two minima on the G curve is the same (tie) line that passes through the black dot on the ternary diagram and ends at the frontier of the two phase region (called binodal frontier). The compositions of the two phases in equilibrium are registered at the two extremes of this tie line on both diagrams. The ternary representation provides additional data on the surfactant partitioning through the tie line slope.
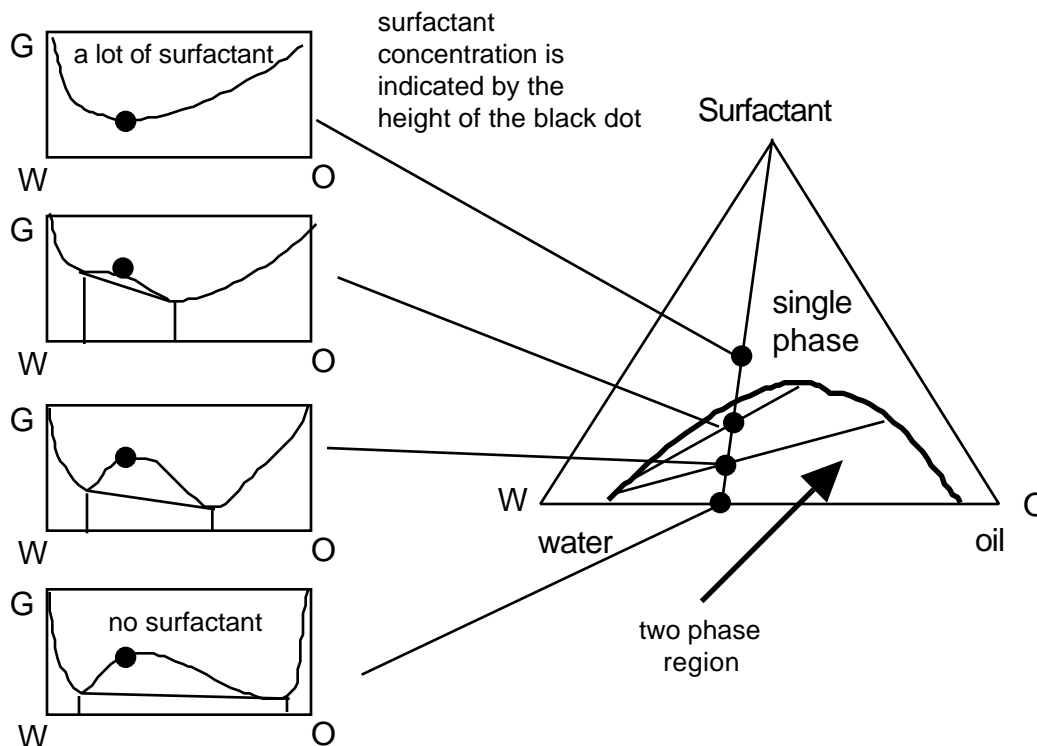
Figure 5   Shape of free energy curves versus composition for a W/O binary to which different amounts of surfactant are added, and equivalent ternary diagram

In the next graph a narrower two-phase region indicates that the miscibility gap is shrinking. At some point (between the third and fourth G graphs) there is no longer a tangent common to two points, and a single phase is attained at all compositions.

If the two contact points merge together, the crossing of the binodal frontier takes place at a critical point.

When more and more surfactant is added, the miscibility gap shrinks and the compositions of the phases in equilibrium are shifted. In Fig. 5 case, the aqueous phase composition remains essentially the same, while the oil phase composition is displaced from right to left. The only way an oil phase can contain more water is to solubilize it inside its (inverse) micelles. The right extreme of the tie line on the ternary diagram also moves not only to the left (because the oil phase is solubilizing water) but also vertically, an indication that the oil phase is taking up most of the surfactant. Such an oil phase that contains a lot of surfactant and that has solubilized a lot of water is probably a microemulsion or a liquid crystal, since no consolute phase would exist in these conditions. This is a particular case predicted in Winsor's analysis half a century ago.

B. Winsor Phase Behavior Diagrams

In a series of papers (21) and a review book (22), Winsor reported the relationship between the phase behavior of amphiphile-oil-water and the nature of the different components of a ternary

system, i. e., what we now call the formulation variables. By studying various ternary systems, he surveyed and rationalized the phase behavior situations into three typical cases of amphiphile-oil-water ternary system. In what follows the amphiphile is generally a pure surfactant, although it may also be a mixture of surfactant and co-surfactant (alcohol) with similar affinities for the oil and water phases.

Figure 6 indicates the three different phase behavior diagrams according to Winsor's classification. All three diagram types display a widely spread single phase region from the A vertex down, which extends on both sides down to the W and O vertices. In practice the single-phase region does not always extend down to both the oil and water, but this is the case for a "exemplary" amphiphile that ought to be miscible in all proportions with both water and oil. In real cases this region may include mesophase zones, that can however be "made liquid" by increasing temperature or disorder (e. g., by adding alcohol).

The unique miscibility gap is located near the OW side, where there is a polyphasic region in the three diagram cases. This region width tends to shrink as more and more amphiphile is added, as a confirmation of the capability of the amphiphile to diminish the miscibility gap. It may be said that the diagram type essentially relies upon the configuration of its polyphasic region.

In Type I diagram the polyphasic region phase behavior has been labeled 2, since it becomes visible as a two-phase separation with an amphiphile rich aqueous phase being lower phase, from which the lower bar.
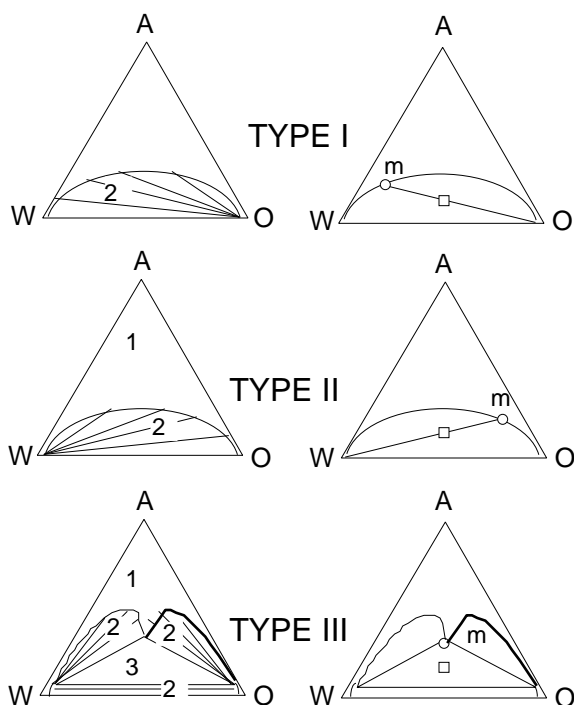

Figure 6   Winsor's three ternary diagram types

As its surfactant content increases and the solubilized oil amount augments, the amphiphile-rich aqueous phase may contain S_1 type normal micelles, extremely swollen micelles, an O/W microemulsion, then a percolated microemulsion in which the oil islands touch one another to end up forming some kind of bicontinuous structure. This surfactant-rich phase is located at the boundary of the single phase region in equilibrium with almost pure oil, as indicated by the tie line slope. Note that in this type I diagram, the critical point where the tie line becomes tangent to the binodal boundary is located on the extreme right of the binodal frontier.

Winsor's Type II diagram and phase behavior, which is noted $\bar{2}$ for a similar reason as exposed previously, embodies the opposite situation, in which the polyphasic equilibrium consists of an inverse micellar oil solution S_2, that eventually solubilizes enough water to become a W/O microemulsion with separated or percolated water droplets or a bicontinuous one, in equilibrium with an essentially pure aqueous phase. In this case the tie line slope is slanted the other way and the critical point is located at the extreme left of the binodal curve.

In between type I and II cases, an intermediate diagram with a biphasic zone with horizontal tie lines could be expected. Such an occurrence does happen with some amphiphiles like alcohols, but not generally for surfactants, in which case a type III diagram and phase behavior is exhibited instead (23). Though it looks much more complex than the two previous ones, type III diagram is no exception and can be found in many systems. The polyphasic region possesses a three-phase zone surrounded by three two-phase zones according to Schreinemaker rule of alternation (20, 24).

Systems whose composition is located inside the three-phase triangle split into an amphiphile rich phase (m) which is in the center of the diagram at the boundary of the single phase region, and two excess phases, which are essentially pure aqueous phase and pure oil. The amphiphile-rich phase which is found to be a bicontinuous microemulsion, has been called the middle-phase because it appears in between the oil and water phase in a test tube. Since the middle phase is at equilibrium with both excess phases, it cannot be diluted either by water or oil, and it is thus neither water- nor oil-continuous.

The two biphasic regions located above the three phase triangle are quite like type I (right) and type II (left) biphasic cases. However, in both cases the point representing the amphiphile-rich phase is very near the center of the diagram, a fact that reveals that this phase would contain similar amounts of oil and water. For instance, a system whose representative point is inside the left lobe would separate into an amphiphile-rich phase that contains almost as much water than oil, and an excess water phase that is essentially pure water. The amphiphile-rich phase is thus to be considered as the oil phase which has solubilized a lot of water, up to the point that such an oil phase could actually contain more water than oil. The composition of such a phase is similar to the middle phase one, i. e., a bicontinuous microemulsion.

Since oil and water are not miscible with each other, there is necessarily a biphasic region near the OW side of the ternary diagram, so-called bottom biphasic region, which is a thin strip of very small extension in most diagrams. Experimental evidence indicates that the bottom tie-line of the three-phase triangle is located at a height that corresponds to the CMC, so that no aggregation structure is found in the excess phases, a situation that precludes the existence of any solubilization.

Winsor reported that the single phase region that appears in all types of diagrams could also exhibit liquid crystalline phases of different structure (lamellar, hexagonal, cubic) containing both oil and water in-between the surfactant bilayers. This circumstance appears above the multiphase region, i. e., at high amphiphile concentration. As in the case of a single liquid phase microemulsion it does not bring any specific information about the type of diagram and is thus of no help as far as the type of diagram is concerned.

C. Phase Behavior Diagram Transition - Winsor's R

Experimental evidence gathered by Winsor and scores of other researchers afterwards have shown that as a field variable (one of the formulation variables or temperature) is changed as in Fig. 7, the phase behavior diagram exhibits a continuous transition from type I to type II passing through type III, or vice versa, depending on the selected scan variable (11, 22, 25-27).
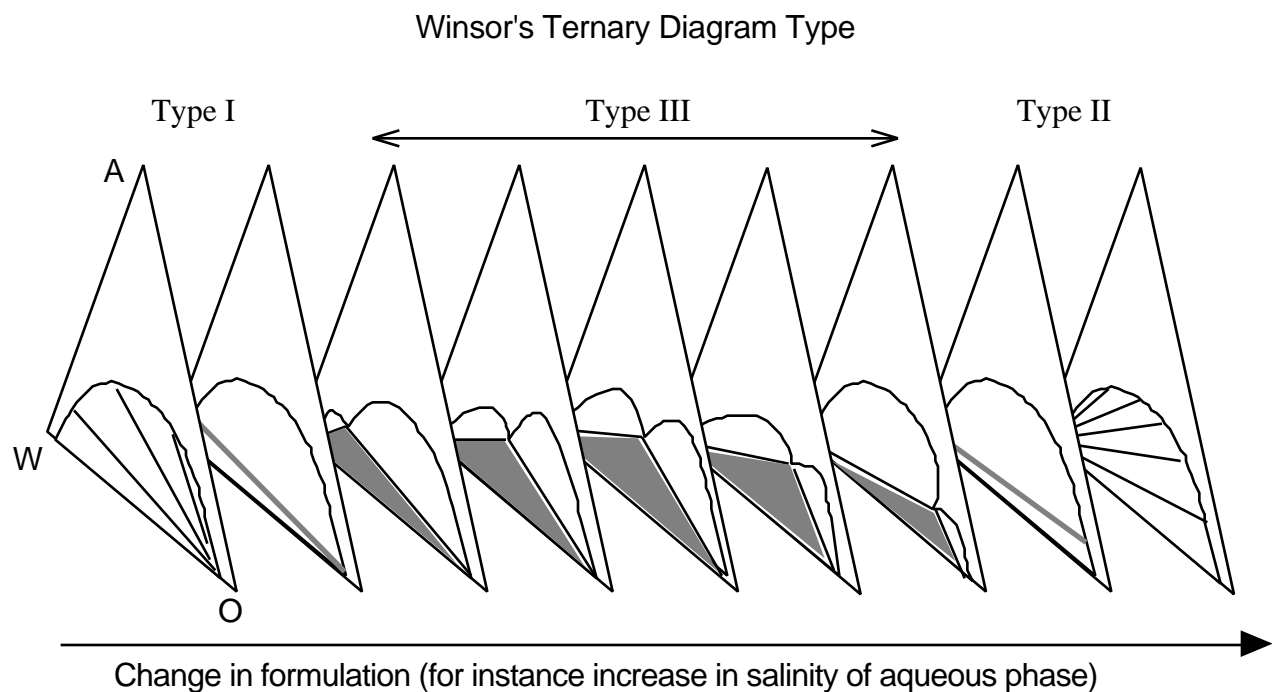
Winsor's Ternary Diagram Type

Figure 7   How Winsor's ternary diagram evolves when one formulation variable is changed

The point that represents the microemulsion middle phase in central type III diagram moves from one side of the diagram to the other as indicated in Fig. 7. It is seen that at both extremes of type III diagram occurrence, the three-phase tie triangle collapses when an upper lobe and bottom tie lines merge together (penultimate diagram on each side) (28-29).

Thanks to the experimental data he gathered on different systems, Winsor was able to associate the phase behavior to the physicochemical situation at interface. He proposed an pedagogical approach to interpret the results which would make use of the ratio of the interactions energies at interface.

Figure 8 represents the molecular population near the interfacial limit between the oil (O) and water (W) phases, where C represents the amphiphile or amphiphile mixture layer. The A's represent the molecular interaction energies per unit area. In Winsor notation:

$$A_{CW} = A_{HCW} + A_{LCW} \qquad\qquad\qquad\qquad [3]$$

where A_{CW} represents the interaction between the amphiphile and the aqueous phase, A_{HCW} the interaction between the hydrophilic group of the amphiphile and the water, and A_{LCW} the interaction between the lipophilic group and the water, which is by the way probably much smaller than A_{HCW}. For a similar reason the interaction between the hydrophilic group of the surfactant and the oil A_{HCO} is probably much smaller than the interaction of the lipophilic group and oil noted as A_{LCO}.

According to Winsor, A_{CO} and A_{CW} promote miscibility, while A_{OO}, A_{CC} and A_{WW} promote the segregation of the components in different phases or in regions of higher local concentration of these components. The cosolubilizing effect of the amphiphile C will be greater, the higher both A_{CO} and A_{CW}.
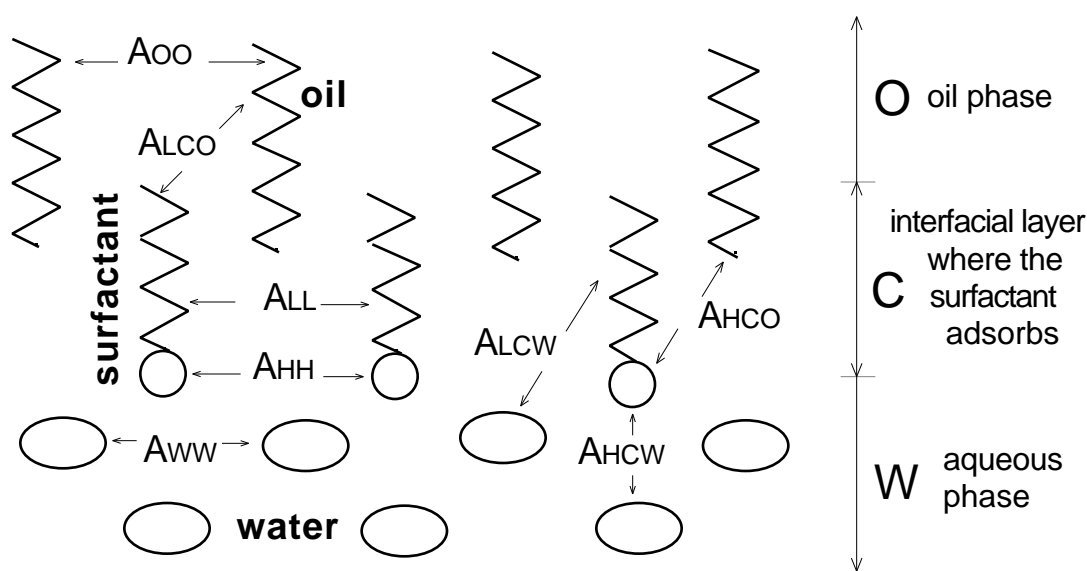

Figure 8   Molecular Interactions in the interfacial region according to Winsor notation

It was postulated by Winsor that the ratio of A_{CO} to A_{CW} would provide a rationale to determine the curvature of the C layer, which is directly linked with the phase behavior situation. The original R ratio was written as A_{CO}/A_{CW}, and it was suggested later that a better R ratio would be

$$R = \frac{A_{CO} - A_{OO} - A_{LL}}{A_{CW} - A_{WW} - A_{HH}} \tag{4}$$

because it takes into account all the neat differences in interactions between the SOW mixed system and the separated component case.

For a given O-W component pair the C region would become concave towards W whenever the interactions between the amphiphile and the O phase are larger than the interaction of the amphiphile and the W phase or conversely (see Figure 9). This is essentially equivalent to the so-called oriented wedge model (30-31) but with each amphiphile molecule associated with a certain amount of both O and W molecules, so that the resulting wedge units determine the bending when they are placed aside in the micellar or microemulsion structure.

Then, if R < 1 the interfacial layer has more interaction with the water phase and the interfacial layer would exhibit a concavity towards oil, i. e., it would form normal micelles. This situation corresponds to Winsor type I diagram occurrence. If there is enough surfactant, say a few percentage points, and if the micelles are solubilizing enough oil phase in their core, then this aqueous phase is a microemulsion above the 2 biphasic region. The tie line slope in the 2 biphasic region indicates that the surfactant-rich phase is the aqueous phase, in accordance with the fact that the surfactant has more interactions with that phase since R < 1.

If R > 1 the opposite occurs. Micellar systems are of the inverse type, and if there is enough surfactant to produce a microemulsion it will be the type encountered in Winsor type II diagram above the biphasic region.

According to this model, the R = 1 case would be associated with a zero curvature C layer, that could be satisfied by a lamellar liquid crystal structure with alternating O and W flat layers, or a zero curvature surface of the Schwartz type or as a transient and fluctuating combination of micelles and inverse micelles (see Figure 10).
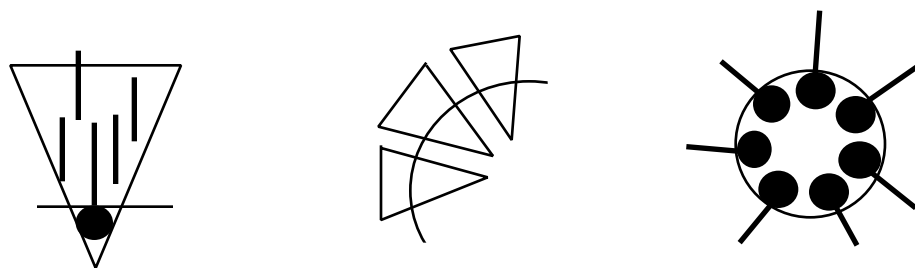

Figure 9 Wedge theory model for micellar and interface curvature

It is now well accepted that middle phase microemulsions, which are in equilibrium with both oil and water excess phases (as in type III diagrams), exhibit some zero average curvature bicontinuous structures (12, 32-33) that are not far away from a fluctuating mixture of swollen normal and inverse micelles predicted by Winsor. This fluctuating model makes sense because micellar structures are not rigid. Actually, the micelle spherical shape is only an average, and the rate of exchange of surfactant molecules between the micelles' palissade region and the bulk phases is very fast, with relaxation times in the microsecond range.

By changing systematically one formulation variable (or temperature) at the time, a diagram transition type I (R < 1)   type III (R = 1)   type II (R > 1) or inversely takes place.
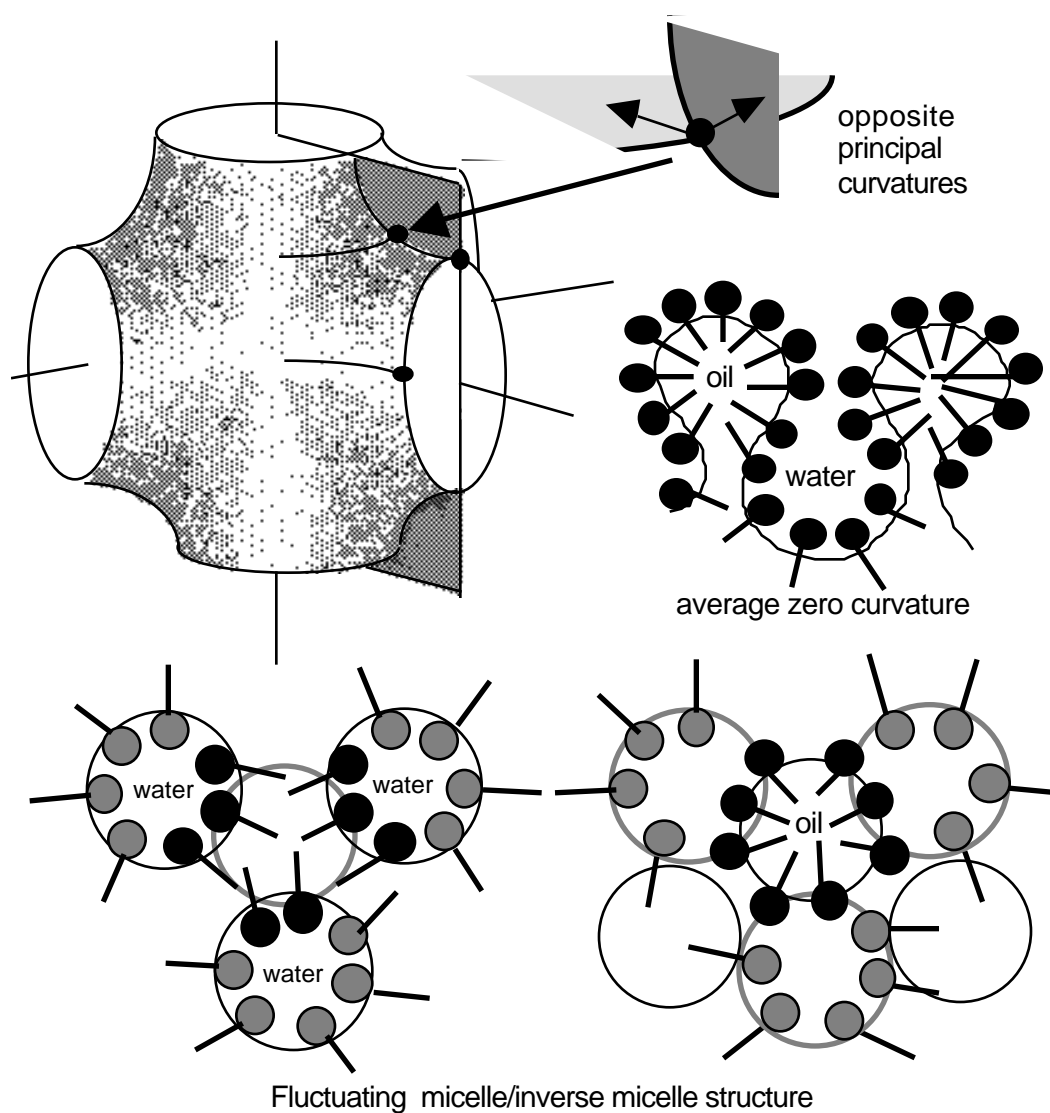

Figure 10   Schwartz Surface of zero Curvature and other models for Bicontinuous Microemulsion

Winsor was able to corroborate the effect of each physicochemical formulation variable and temperature, and to correlate it to change in R value, as indicated in Table 1.

The first three effects are readily explained by the change in R numerator and denominator. As the surfactant lipophilic "tail" gets longer, the interaction with the oil phase A_{CO} is increased. In a similar way, a longer polyethylene oxide chain (hydrophilic group) of a nonionic surfactant results in an increase of the interaction with water A_{CW}.

The third effect is much more important with ionic surfactant systems than with nonionic ones, since it is linked with the shield effect produced by electrolyte ions with respect to the ionic group-water A_{CW} interaction.

The forth case is related to the fact that with most anionic surfactants, alkaline metal salts are more dissociated than their bivalent cation counterparts. Thus, the calcium or magnesium salts are less hydrophilic. This is also true for nonionic surfactants, although to a much lesser degree.

The effect of the oil chain length (alkane carbon number, ACN) is more complex to understand, since it modifies both A_{CO} and A_{OO} interactions with opposite effects. However, it is possible to solve this stalemate by remarking that London-style interactions may be taken as proportional to the number of methylene groups in each interacting molecules (34). Thus:

$$A_{CO} = \quad SACN \ ACN \ and \ A_{OO} = \quad ACN^2 \qquad [5]$$

where SACN is the number of carbon atoms in the surfactant alkyl group. As oil ACN increases the second interaction increases faster (as the square) than the first one.

Table 1   Effect of formulation variables on Winsor R ratio

When this variable is increased	Effect on interaction energies	and R
Amphiphile hydrophobe chain length	A_{CO} increases	increases
Ethylene oxide polyether chain length (nonionic surfactant)	A_{CW} increases	decreases
Aqueous phase salinity	A_{CW} decreases	increases
Aqueous phase electrolyte valence (Na+ Ca++)	A_{CW} decreases	increases
Oil phase length (alkane hydrocarbon) increases	A_{CO} increases	
	A_{OO} increases more	
	A_{CO}-A_{OO} decreases	decreases
Temperature increases (nonionic surfactant)	A_{CW} decreases	increases
Temperature increases (ionic surfactant)	A_{CW} increases	decreases

As a consequence the A_{CO}-A_{OO} summation decreases (provided that ACN is large enough). In other words, a higher ACN oil exhibit a lower neat interaction energy with the C layer because of its more favorable self association energy.

Nonionic surfactants of the polyethoxylated type, exhibit a temperature dependency which is illustrated by the so-called cloud point phenomenon. As a matter of fact, the hydrophilicity of the polyether chain depends upon a directional interaction between each -O- atom and surrounding water molecules. As temperature increases this interaction becomes looser because of the amplified randomness of the molecular motion. Hence, the hydrophilic character decreases and finally vanishes, as well as the A_{CW} interaction.

With ionic surfactants, an increase in temperature tends to slightly increase the A_{CW} interaction, in accordance with the increase in solubility exhibited by most ionic species, and an opposite effect is attained, although of much lesser magnitude.

This is in agreement with the overall effect that is corroborated by experimental data. It is worth noting, however, that the actual temperature effect is probably much more complex to ascertain in Winsor's R ratio framework. In effect, temperature is likely to change not only A_{CW}, but many or all other interactions as well, a situation that complicates the interpretation of experimental data. Moreover, the temperature range that can be studied without too much experimental trouble is not very extended, since it matches the liquid state of water. This is why a change in temperature is not the easiest to handle or to interpret experimental variation in order to produce a change in R value. As a matter of fact, the electrolyte concentration (salinity) and ethylene oxide number (EON) have been often preferred by experimentalists as scanning variables, for ionic and nonionic systems, since their effect is easier to manipulate, predict and interpret.

The main lesson behind Winsor's pioneer work, is that it reveals that there are essentially three phase diagram elementary cases, although the number of formulation variables (including temperature and pressure) can be much higher than three. Winsor's R ratio allows to bring together the effect of all formulation variables into a single one, i. e., the R ratio value, that commands the phase behavior of the SOW system. Consequently, the effects of the different formulation variables and temperature are competitive, and a certain R value may be attained in different ways - a favorable feature as far as practical formulation work is concerned.

It can be said that Winsor's R ratio has the best pedagogical value of all formulation concepts because it is simple to understand and at the same time it allows quite good qualitative predictions. If it were amenable to numerical calculations there would be no need for alternate formulation concepts. This is not the case, however, because the molecular interactions A_{XX} cannot be calculated with sufficient accuracy yet. The R ratio would thus be the choice understanding framework to carry out qualitative inferences and to predicts trends.

However a quantitative instrument would be required when it comes down to serious formulation business.

D. Other Concepts Related to Formulation

The three cases of phase behavior related to Winsor R ratio have been disclosed through a different approach by other researchers. The oldest one is Bancroft's rule of thumb, i. e., the emulsion external phase is the one in which the surfactant preferentially partitions (35-36). Since it is obvious that the surfactant preferentially partitions into the phase for which it exhibits a greater affinity, a rather hydrophilic amphiphilic layer (R < 1) would produce O/W emulsions and vice versa, a result which is essentially the one resulting from the oriented wedge theory applied to an emulsion droplet. Although the wedge theory could be useful in interpreting the interactions whenever the colloid size is ten or twenty times larger than the molecular size, i. e., in a micelle or up to a miniemulsion 200-Å drop, it is obvious that at a 10-μm drop interface the surfactant molecule cannot "feel the curvature". Nevertheless, the oriented wedge model has been recently brought back to life, when it was shown that the monolayer bending energy is related to the free energy of a transition state that affects coalecence rate and thus decides the emulsion type (37).

In presence of a solvent, e. g., water, it is known that mesophase can be lamellar (zero curvature), hexagonal or cubic (20). In presence of both oil and water, both phases may penetrate in between the surfactant bilayers, and liquid crystals of the curved type could occur with the water or the oil toward concavity. In between, i. e., for the R = 1 case, a zero curvature, that may be attained either with a lamellar structure of the LC type, or a bicontinuous microemulsion with monkey saddle zero curvature geometry everywhere, is expected.

 Thus the curvature may be considered as a state variable that can describe the situation of the system as Winsor's R ratio (38). The problem is that the substitution of the R ration by the curvature does not produce any awesome advance in practice, because curvature cannot be calculated directly in a quantitative way from the system formulation, but through computations that are probably too complex for the practitioner (39).

An interesting feature is however that there is a natural or spontaneous curvature that indicates the preferred state of the interfacial layer, which is not necessarily the actual state. The preferred curvature could be the one related to R concept, i. e., physicochemical formulation effects, while the actual one would result from the emulsification process. The difference between the two is some kind of bending energy frustration, which by the way could be related with the concept of stability of the interfacial structure, and of the resulting emulsion.

This could be linked with a model that connects the emulsion type with the relative coalescence rates of O/W and W/O emulsions (40).

IV. EMPIRICAL APPROACH TO FORMULATION QUANTIFICATION

While it is extremely important to develop fundamental concepts to understand and interpret the observed phenomena, it is tantamount important for the practitioner to have at hand effective tools to culminate his research path in a pragmatic solution to his problem. It has been said that even a simple formulation problem may exhibit many degrees of freedom, often too many for a systematic study to be carried out. The fundamental concepts enable the practitioner to know the expected trend and the direction in which he should start looking. They do not give him much information on the equivalence of different variables as far as the effect is concerned, critical information when economic matters or toxicity problems are dealt with. They do not give him any information either, on the magnitude of the change he should apply to attain his purpose. Accordingly, the expertise or previous experience is the most quoted value. This experience is often translated into a rule of thumb or other intuitive or in house "guesstimating" method.

In the following paragraph review, it is seen that several alternate practical methods are paving the way to a full quantification of the formulation effect.

A. Hydrophile-Lipophile Balance HLB

The first approach consisted in simplifying the problem by considering only one or two of the formulation variables, assuming that the selected variables were the most important for the particular problem, and/or that the other formulation variables were either constant or had a negligible effect.

This was the stance taken in the first empirical yardstick, i. e., Griffin Hydrophile-Lipophile Balance or HLB introduced at the end of the 1940's (41-42). The HLB is a parameter characteristic of the surfactant and the required HLB (or HLB_{req}) is an attribute of the oil phase, which is determined as the HLB of the surfactant that provided the best match with a given oil to produce the maximum stability of an emulsion along a surfactant HLB scan.

All surfactants are assigned a HLB number according to a procedure that was first arbitrary, e. g., for oleic acid HLB = 1 and for potassium oleate HLB = 20, and was then deduced from consistency tests, particularly by comparing several kinds of properties. Table 2 indicates the HLB

number of several well known commercial surfactants. For polyethoxylated nonioic surfactants (with no other hydrophilic group) the HLB may be estimated by the following formula (43):

$$HLB = \frac{100}{5} \ \frac{\text{weight ofpolyethylene oxide chain}}{\text{total molecular weight}} \qquad [6]$$

As an essential feature of the HLB scale, it was assumed that the HLB of a surfactant mixture could be calculated from a linear average mixing rule based on weight composition. Thus intermediate HLB could be attained simply by mixing two or more surfactants by using the relationship:

$$HLB\text{mixture} = \sum_{i=1}^{n} X_i HLB_i \qquad [7]$$

For anionic surfactants, Lin (44) proposed the empirical equations also listed in table 2 as a first approximation. These relations indicate that the HLB varies in a linear fashion with the lipophilic "tail" length.

This follows the earlier sugested group contribution splitting proposed by Davies (40) to calculate HLB as an algebraic summation using group contributions as follows:

$$HLB = 7 + \sum (\text{hydrophilic group numbers})$$
$$+ \, n \, (g\text{roup number per C atom in tail}) \qquad [8]$$

where n is the number of carbon atoms in the "tail". The group number values are also listed in table 2. It is worth remarking that the "neutral" or balanced HLB is 7 instead of 10 in other calculations. Note also that the ethylene oxide group is hydrophilic (positive value) while the propylene oxide group is slightly lipophilic (negative), although less than a single carbon group (methyl or methylene). This group contribution feature is easy to handle and attractive for the practitioner who does not want to get into too much physicochemical trouble. However the calculated values are not ganranteed to match other calculations better than ± 3 HLB units, a large inaccuracy that indicates that the decimal digits listed in the table could be rounded with no grief.

The physical or physicochemical signification of the HLB scale could be ascertained by associating the HLB value with some surfactant properties, e. g., water dispersibility. Surfactants with HLB < 8 are not dispersible in oil, while those with HLB > 12 are fully soluble in water. Intermediate HLB surfactants are more or less dispersible depending upon other factors. Scores of papers have related HLB to other surfactant properties, as reported in an exhaustive computer screening prepared by Becher (2).

The HLB scale essentially pretends to indicate that while HLB is <10, =10 or >10, then the conditions attained for Winsor's R < 1, =1 or >1 are met.

Table 2 HLB number values from different sources

Surfactant type	Griffin's (42) HLB Number
Sorbitan trioleate/tristearate (85:65)	1.8 - 2.1
Glycerol monostearate	3.8
Sorbitan monooleate (80)	4.3
Sorbitan monostearate (60)	4.7
Diethylenglycol monostearate /monooleate	4.3 - 4.7
Diethylenglycol monolarate	6.1
Sorbitan monopalmitate (40)	6.7
Tetraethylenglycol monostearate /monooleate	7.7
Sorbitan monolaurate (20)	8.6
Polyoxyethylene Nonylphenol (5EO)	10.0
Polyoxyethylene (5 EO) sorbitan monooleate (81)	10.0
Polyoxyethylene (20 EO) sorbitan trioleate (81)	11.0
Polyoxyethylene (7EO) Tridecanol	12.1
Polyoxyethylene (5 EO) sorbitan monolaurate (21)	13.3
Polyoxyethylene (20 EO) sorbitan monooleate (80)	15.0
Polyoxyethylen (20 EO) sorbitan monolaurate (20)	16.7

Anionic surfactants (44)	HLB relationship.
$RnOSO_3Na$	HLB = 47.5 - 0.475 n
RnCOOK	HLB = 28.1 - 0.475 n
RnCOONa	HLB = 26.1 - 0.475 n
$RnSO_3Na$	HLB = 18.0 - 0.475 n

Groups	(Davies' HLB Group numbers) (40)		
$-OSO_3$ Na	+ 38.7	-COO Na	+ 19.1
-COOK	+ 21.1	-N tertiary amine	+ 9.4
Ester (sorbitan ring)	+ 6.8	Ester (free)	+ 2.4
-COOH	+ 2.1	-O-	+ 1.3
-OH (free)	+ 1.9	-OH (sorbitan ring)	+ 0.5
$-CH_2-CH_2-O-$ (EO group)	+ 0.33	$-CH(CH_3)-CH_2-O-$ (PO group)	-.015
$-CH_3$, $-CH_2-$, =CH-	- 0.475		

Of course Winsor R takes into account not only the surfactant type but also several other variables such as the oil and aqueous phase nature, as well as temperature, while HLB number does not. This means that the HLB number could exhibit discrepancies whenever systems with different oil and aqueous phases are compared.

In order to improve the HLB number's practical interest, a second parameter was introduced to describe the oil phase nature, the so-called required HLB or HLB_{req}, so that a better description of the physicochemical environment would be attained. The oil HLB_{req} is the HLB of the surfactant that results in the most stable emulsion. In order to estimate the oil $HLB_{req,}$ a HLB scan for emulsion stability has to be carried out. This is done by preparing several systems with the same oil and aqueous phases but different HLB surfactants or surfactant mixtures so that a whole HLB scan is carried out, say from definitely lipophilic (HLB = 2 - 4) to definitely hydrophilic (HLB >14).

In many cases and in whatever way the stability is measured, two maxima appear on such a plot as in Fig. 11, one at low HLB (for W/O emulsions) and another one at high HLB (for O/W emulsions). There is thus an oil HLB_{req} for O/W emulsions and another one for W/O emulsions.

This experimental protocol proposed by Griffin is, however, tedious and it lacks accuracy, for several reasons. While the maximum at low HLB is essentially at the same position for most HLB scans, so that HLB_{req} for W/O is about 5-6 for most oil phases, the maximum at high HLB is often difficult to pinpoint with accuracy because the O/W emulsion stability does not change very much with HLB. On the other hand, the stability curve and thus minima position are not strictly dependent upon the HLB scale but are found to change when the surfactant type is changed.

Although the HLB number is still used nowadays because it is based on extremely simple arithmetic, it should be stressed that it gives an approximate information only, and that it cannot take
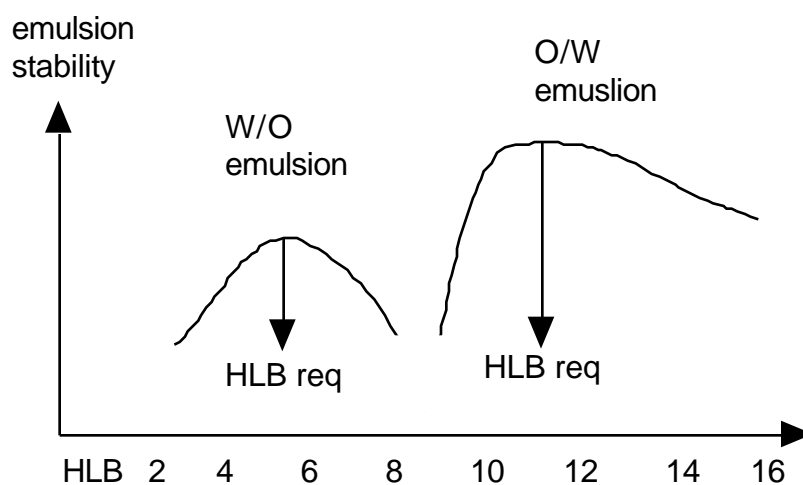

Figure 11   Determination of oil phase HLB req for W/O and O/W emulsions

into account formulation effects that are known to be relevant as the nature and structure of both the hydrophilic and lipophilic groups, the aqueous phase salinity, or the presence of an alcohol, or the influence of the temperature, since none of these variables appear in the HLB rationale. On the other hand, it may be advantageously used as a yardstick to compare surfactants to one another, particularly of the same family, and provided they are going to be used in the same physico-chemical environment (oil, brine, temperature, etc).

Since the previous relationships indicate that the HLB number would steadily increase as the hydrophilic group increases in size, it is no wonder that HLB numbers can be correlated with many properties that depend on the relative hydrophilicity (2, 45-47).

B. Phase Inversion Temperature PIT

The second intent to numerically characterize the formulation concept was the so-called Phase Inversion Temperature (PIT), originally introduced by K. Shinoda in 1964 as the temperature at which a polyethoxylated nonionic surfactant switched its dominant affinity from the aqueous phase to the oil phase to produce a change in emulsion type. This was both easy to determine experimentally and simple to understand as far as the related phenomenology was concerned (48-50).

The PIT (with water and a given oil phase, i. e., hexadecane) was first correlated with the cloud point, i. e., the temperature at which a surfactant phase separates from a low concentration, e.g., 3%, surfactant solution (48). It is worth noting that the cloud point indicates a property of the surfactant, somehow the HLB, while the PIT takes into account the interaction with both the aqueous and oil phase. Early experimental evidence indicated that the PIT increased as the nonionic surfactant polyethylene chain length increased, increased as the hydrocarbon oil chain length increased, and decreased as the salt concentration increased in the aqueous phase. Since the PIT is the physicochemical situation in which Winsor $R = 1$, and since an increase in temperature tends to reduce the A_{CW} interaction, the interpretation of the previously mentioned trends is straightforward when the numerator and denominator of Winsor R are equated.

$$A_{CO}\text{-}A_{OO}\text{-}A_{LL} = A_{CW}\text{-}A_{WW}\text{-}A_{HH} \tag{9}$$

An increase in polyether chain length compels A_{CW} to increase, and an increase in temperature is required to decrease it, so that the equation still holds. When the hydrocarbon chain length increases, the $A_{CO}\text{-}A_{OO}$ term tends to decrease as discussed previously, and an increase in temperature is required to decrease A_{CW} in the same amount and keep the equality. Finally when electrolyte are added the A_{CW} term decreases, and a decrease of temperature is required to turn it

back to its previous value. The PIT was thus an equivalent to Winsor approach, but for the first time a formulation concept had a numerical attainable value, that could be related with the SOW system.

Recent work on the partitioning of ethoxylated alkylphenol surfactants (51) has shown that the energy of transfer of a surfactant molecule from water to oil $\Delta G_{w \to o}$ can be written as

$$\Delta G_{w \to o} = \Delta G^*(alkylphenol_{w \to o}) + EON \times \Delta G^*(EO\ group_{w \to o}) \qquad [10]$$

It is found that the ΔG for the transfer of an EO group from water to heptane decreases from 0.6 to 0.4 cal. as temperature increases from 25 to 50°C. It means that it is easier to transfer an EO group from water to oil at higher temperature. Oil phase nature also seems to be quite important in this energetic barrier. Recent evidence indicates that with aromatic oil phases, the $\Delta G^*(EO\ group_{w \to o})$ may be much smaller than with aliphatic oils, may be zero with pure benzene. This corroborates the trends found on the PIT some forty years ago.

It is worth noting that the PIT of a surfactant mixture can be calculated according to a linear mixing rule, where the X's are the mole fractions.

$$PIT_{mixture} = \sum_{i=1}^{n} X_i\ PIT_i \qquad [11]$$

This is an odd formula at first sight since temperatures generally do not add up, but it turns out to be easy to embrace when it is understood that the PIT is not a temperature, but a numerical indicator of the dual affinity of the surfactant for its physicochemical environment, i. e., an energy term that is usually summed up as in the thermodynamics first law.

Although it is now obvious that a tentative approach for assimilating or adapting the PIT as the experimental measurement of Winsor's R, would have evolved into a quite general and practical formulation concept, Shinoda's first goal was rather to relate it to HLB (52), which was at this time the quite widely accepted reference, in spite of its drawbacks. As a consequence, the PIT did not evolve into the generalized formulation concept it could have been for any practitioner in the mid-1960's, and was only used by scholars working with nonionic surfactants who could sense its underlying significance.

Because of its basic phenomenon, the PIT is however limited to ethoxylated nonionic surfactant systems, and its experimentally attainable range (that fits the liquid water state at atmospheric pressure) is sometimes rather narrow, particularly in dealing with highly ethoxylated detergents and emulsifiers.

Nevertheless, it is important to stress again that the PIT procedure was the first method making use of the technique of unidimensional formulation scan, in which a physico-chemical

formulation variable (temperature) is changed continuously with all other formulation variables held constant, until a very clear-cut situation arises that can be detected experimentally.

At the light of the current formulation state of the art, it can be said that the PIT was a clever and precursory technique. Today the PIT can be viewed as the optimum temperature in the multivariant SAD (Surfactant Affinity Difference) concept to be discussed later on.

C. Cohesive Energy Ratio

In a tentative approach to attain a formulation concept with both the theoretical content of Winsor's R and the down-the-bench numerical data feature of the HLB, Beerbower and collaborators introduced the cohesive energy ratio (CER) approach in 1971 (53-54). From the conceptual point of view it was very similar to Winsor interaction energies ratio, but this time it was the ratio between the adhesion energy of the surfactant "layer" with the oil phase, and the adhesion energy of the surfactant "layer" to the water phase. It must be recalled that the cohesion energy between molecules of a pure component system is calculated as:

$$2 = \frac{H_{vap}}{v_L} \tag{12}$$

where H_{vap} is the enthalpy of vaporization per mole, and v_L the molar volume in the liquid state, both measurable quantities. is the solubility parameter, a direct measurement of the intermolecular cohesion forces. When a mixed system is considered, the adhesion force between the two kinds of molecules is calculated according to the London's geometric mean relationship.

$$\text{if} \quad 2_{AA} = \frac{H_{A.vap}}{v_{A.L}} \quad \text{and} \quad 2_{BB} = \frac{H_{B.vap}}{v_{B.L}} \tag{13}$$

$$\text{then} \quad 2_{AB} = \quad_{AA}\quad_{BB} \tag{14}$$

Solubility parameters have been measured and tabulated for hundreds of substances, and they are often used in relation with the regular solution model to estimate the activity coefficient in a mixture and the eventual separation into two phases (55).The adhesion between the surfactant and the oil phase was estimated by calculating a 2_{AB} term where A represented the oil phase and B stood for the lipophilic part of the surfactant that was assumed to be similar to that of a hydrocarbon with the same chain length. This assumption happened to be perfectly reasonable and satisfactory. Unfortunately, the corresponding adhesion energy on the water side of the interface was not easily calculated, in particular because of the lack of experimental data for the hydrophilic group of some surfactants, since an hydrophilic group cannot be analyzed separately from the rest

of the molecule. It also seems that the theoretical basis of the regular solution theory was not strong enough to handle the extreme incompatibility between oil and water.

Due to these drawbacks, the final numerical value of the cohesive energy ratio was as inaccurate as the HLB number and even worse in some cases, and it had to be dropped.

D. Empirical Correlations for Optimum Formulation

The formulation concept was one of the aims of a large-scale research effort to develop enhanced oil recovery methods after the 1973 oil embargo. The goal was to inject a surfactant solution in the oil reservoir in order to overwhelm the capillary forces that trap the almost 75% of the original oil in place remaining in the reservoir after waterflooding.

It was soon found that the best conditions to attain an ultralow interfacial tension coincides with Winsor type III physicochemical situation in which a bicontinuous microemulsion is in equilibrium with both oil and water excess phases. Such a case was called optimum formulation since it was associated with the successful mobilization of petroleum (56-57). The adjective optimum is still used to describe the R =1 case, no matter whether it corresponds or not to the best case in the studied application. Since there are many ways to attain R = 1, particularly in real systems with many components, one of the goals was to find out a numerical relationship that conveys the fact that R = 1.

The experimental technique used to find an optimum formulation, known as unidimensional scan, goes on as follows. Series of surfactant-oil-water systems are prepared in test tubes, all with identical composition, and with the same formulation with the exception of the scanned variable, that is in general the aqueous phase salinity for ionic systems, and the average number of ethylene oxide groups per molecule (EON) if the systems contain an ethoxylated nonionic surfactant mixture.

The fixed composition is typically selected so that the representative point is in the polyphasic region of a ternary diagram; in this case Winsor-type and thus R value can be deduced from the phase behavior observation. It is found that 1-3% surfactant and equal proportions of oil and water is a fairly good choice in most systems. In ionic systems a very few percentage of an alcohol is often added to avoid the formation of mesophases. If the formulation should not be altered by the alcohol a good choice is *sec*-butanol.

In these conditions it is obvious that from one test tube to the next the only difference is the value of the scanned variable. The test tubes are closed with a screw cap or sealed, and are left to equilibrate at constant temperature until there is no apparent change, often no more than two or three days in practice. Then the phase behavior is deduced from a visual observation of the transition expected in a scan.
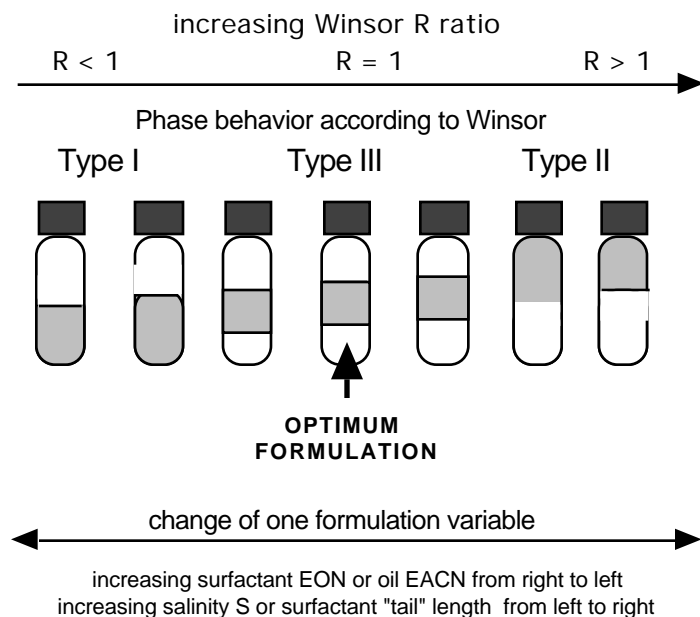
increasing Winsor R ratio

R < 1   R = 1   R > 1

Phase behavior according to Winsor

Type I   Type III   Type II

**OPTIMUM
FORMULATION**

change of one formulation variable

increasing surfactant EON or oil EACN from right to left
increasing salinity S or surfactant "tail" length from left to right

Figure 12   Aspect of test tube series in a unidimensional formulation scan at constant composition

The optimum formulation of the scan is the value of the variable that corresponds to the center of the three-phase behavior range as indicated in Fig. 12. If the three-phase range is quite spread, an additional measurement could be required to pinpoint the optimum formulation, such as the solubilization or interfacial tension, as will be discussed later.

The quantification of formulation effects requires a method to find the equivalence between two changes in the physicochemical situation. The most used experimental technique has been the bidimensional scan, which is based on a double variation of competing effects, i. e., two counteracting changes as illustrated in Fig. 13.

Starting at an optimum formulation (where R=1), a first formulation variable X_1 is changed by an amount X_1, that results in a change in one of the interaction energy, and the resulting change in the R ratio value. For instance, suppose that X_1 is the salinity of the aqueous phase.
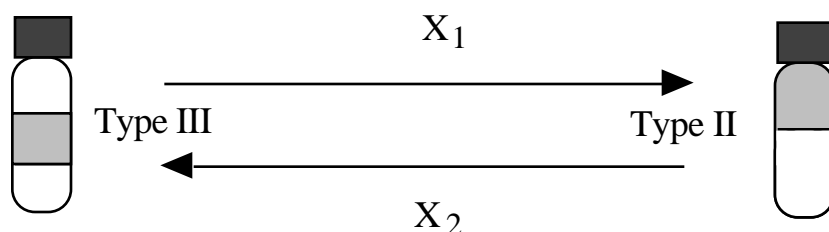
$$X_1$$

Type III   Type II

$$X_2$$

Figure 13 Double formulation change to produce compensating effects

The increase in salinity X_1 produces a decrease in A_{CW}, which means that the R ratio will increase from R = 1 to some R > 1 value, and that the phase behavior will exhibit a type III   type II change as indicated in Fig. 13.

Let us now select a second formulation variable X_2 and let us change it in the direction where the change in R would be opposite to the previous one, i. e., a decrease in R, until a type II   type III transition is attained again, as well as R = 1. For instance, an increase in the oil phase EACN will produce a reduction of the A_{CO}-A_{OO} term in the numerator of R. Such an increase X_2 is pursued until R goes back to 1, as evidenced by the return to a type III three-phase behavior situation.

At this point it can be said that the two formulation changes X_1 and X_2 have produced exactly opposite effects on R, and are thus equivalent from the physicochemical point of view, but with opposite effects.

For instance, it is found that for an alkylbenzene sulfonate-alkane-NaCl brine system an increase in ACN of four units is compensated by an increase in salinity measured by an increase of 0.64 of the natural logarithm of the salinity, whatever the other variables, as seen in Fig. 14.

This means that a relationship such as

$$\ln S = K \quad ACN \qquad\qquad \text{where } K = 0.16 \qquad\qquad\qquad [15]$$

can be integrated as $\qquad\qquad LnS - K\,ACN = C \qquad\qquad\qquad\qquad [16]$
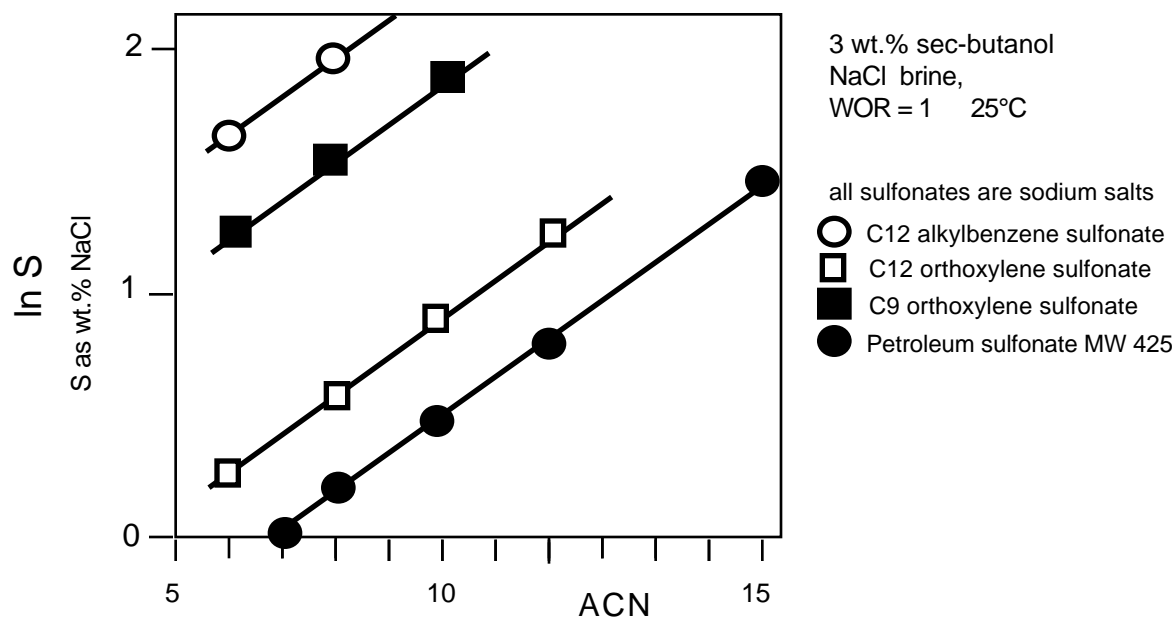

Figure 14   Relation between aqueous phase salinity (as a natural logarithm) and oil phase Alkane Carbon Number so that optimum formulation is attained.

where C does not depend on salinity nor oil EACN, but on other formulation variables and temperature.

This technique of double change with compensating effects allows to quantify the respective influence of the different formulation variables, and it has been widely used in performing a large amount of experimental work to quantify Winsor concept. Extensive experimental work showed that a three-phase system of the type III phase behavior was attained whenever a certain empirical relationship, so-called correlation for optimum formulation was satisfied. For anionic surfactants the correlation has been expressed as (11, 58) :

$$\ln S - K \, ACN - f(A) + \sigma - a_T \, \Delta T = 0 \qquad\qquad [17]$$

Later on it was showed that the same correlation was valid as well for cationic surfactant systems with slightly different values of the parameters (59). For nonionic surfactants a similar correlation was found (60-62)

$$\alpha - EON + b \, S - k \, ACN - \phi(A) + c_T \, \Delta T = 0 \qquad\qquad [18]$$

In these expressions, S is the salinity, and lnS is the neperian logarithm of the salinity expressed in wt% NaCl with respect to the aqueous phase, ACN or Alkane Carbon Number is a characteristic parameter of the oil phase, f(A) and ϕ(A) are functions of the alcohol type and concentration, σ and α are parameters characteristic of the surfactant structure, and EON is the average number of ethylene oxide group per molecule of nonionic surfactant. ΔT is the temperature deviation measured from a certain reference (25 ˚C), b, k, K, a_T and c_T are empirical constants that depend on the type of system.

K is 0.16 for alkylbenzene sulfonates, about 0.10 for alkyl sulfate and fatty acid sodium soaps, 0.17 for *n*-alkyl ammonium salts at low pH, and 0.19 for quaternary *n*-alkyl trimethyl ammonium salts, while k is found to be 0.16 for nonionic systems. The coefficient of the salinity effect for nonionic surfactants is small, i. e., 0.13 and 0.10 (in EON unit per wt% salt in aqueous phase) respectively for sodium and calcium chloride.

Not many investigations have been dedicated to the salinity effect when the electrolyte is not sodium chloride, may be because the effect is more complex, not amenable to a simple expression in particular with divalent cations and ionic surfactants. However some trends are available in applied publications (27, 63). Worth noting is a systematic study of the effect of the electrolyte anion on the equivalent salinity of different sodium salts, that showed that the correlation is followed for all sodium salts and that the effective or equivalent molar salinity only depends on the valency of the anion (64).

The nonionic surfactant characteristic is split into its ethylene oxide number (EON), i. e., the average number of ethylene oxide group per molecule, and the hydrophobe contribution α. Only scarce data are available for α, which has a value near 6.6 and 6.3, respectively for the branched

nonyl and octyl phenol species, and 4.4 for the linear tridecanol base group. Much more data is available for ionic surfactants, particularly anionic ones, under the form of σ/K which is characteristic of the contribution of the surfactant :

$$\sigma/K = \sigma_O/K + 2.25 \ SACN \qquad\qquad [19]$$

where σ_O is characteristic of the hydrophilic group and SACN is the surfactant alkyl carbon number, i. e., the number of carbon atoms located in its single long hydrophobic tail. The data that are gathered in Table 3 fit a normal synthetic surfactant isomer mixture (58, 65, 66).

Note that the correlation may be written as:

$$\sigma/\xi = ACN + \frac{- \ln S + f(A) + a_T \ \Delta T}{K} \qquad\qquad [20]$$

From the above relation, it is obvious that σ/K is the oil ACN for attaining an optimum formulation when the numerator of the right-hand fraction is equal to zero, a situation that happens at unit salinity (S =1 and ln S = 0), no alcohol so that f(A)=0, and ambient temperature ($\Delta T=0$).

For such a reason σ/ξ was labeled as EPACNUS, an acronym for extrapolated preferred ACN at unit salinity (58).

It can be seen from the table that the introduction of two methyl groups in ortho of the main alkyl on the benzene ring results in an increase in σ/K of 5 units, which is equivalent to the addition of two carbon atoms. The variation from alkanesulfonate to alkylbenzene sulfonate is about 18 units, i. e., the benzene group is contributing the equivalent of about 8 carbon atoms rather than 6. This discrepancy of 2 units may be attributed, according to the previous discussion, to the fact that the alkanesulfonate is probably much more linear in average than the alkylgroup of the alkyl-benzene sulfonate.

Table 3 Hydrophilic group contribution to the surfactant characteristic parameter

Surfactant family	σ_O/K value	
Alkyl sulfate Na salt	- 55	± 3
Fatty acid Na soap	- 48	± 5
Alkane sulfonate Na salt	-48	± 3
Alkyl trimethyl ammonium salt (Br⁻ or Cl⁻)	- 45	± 2
n-Alkyl ammonium salt (Br⁻ or Cl⁻) at pH 3	-32	± 3
Alkyl benzene sulfonate Na Salt	- 30	± 1
Alkyl ortho xylene sulfonate Na salt	-25	± 2

The characteristic parameter of ionic surfactant mixture can be readily calculated from a linear mixing rule on its /K so that (65, 67):

$$\text{/K mixture} = \sum_{i=1}^{n} X_i \, (\text{/K})_i \qquad\qquad [21]$$

Let us now come back to the correlation and turn the attention to the effect of the oil phase nature. If the oil phase is not an alkane, its equivalent ACN, i. e., the ACN of the alkane that exhibits the same behavior, is used instead (11, 68). Since the EACN of an oil mixture can be deduced from its composition by a linear mixing rule based on a molar fraction, it has been possible to measure the EACN of many oils.

The lower the EACN of an oil, the higher its polarity. For instance EACN is zero for benzene, and it is equal to the number of carbon atoms in the alkyl group of alkylbenzenes. Alkyl cyclohexanes have an EACN that is equal to the number of carbon atoms in their alkyl group augmented by 3. In other words the saturated cyclohexane structure accounts for three units in the EACN, while the aromatic benzene ring does not count.

The ester polar group cuts the lipophilic contribution quite a lot, about 12 EACN units, since ethyl oleate is found to exhibit an EACN = 6, as well as oleic acid based triglyceride oils such as Soja oil (69, 70). The EACN of pinene (double cycle terpene) and limonene (single cycle) essential oils are found at about 7 and 8.5 respectively (71).

The EACN of chorinated solvents was recently reported as well in relation to soil remediation methods by microemulsion cleaning (72-74).

The alcohol functions f(A) and (A) depend both on the type and concentration of the added alcohol as reported in the two correlation papers (58, 61) that are the only ones to give a numerical dependency. Very few other papers report some data on alcohol effect both as a co-surfactant (23, 75), and as an additive that tends to reduce the interfacial rigidity (76). In Fig. 15, the concentration is expressed in gram per deciliter (gpdl) with respect to the whole system, very close to wt% vol. unit. Both expressions are very much alike but different in numerical value, so that the following discussion applies for all systems.

Water soluble alcohols present a slightly positive function, i. e., their addition increases the hydrophilicity of the surfactant/alcohol amphiphile, but very little indeed. As a consequence isopropanol effect in the correlation is negative, i. e., the same than decreasing salinity. *sec*-butanol and *ter*-pentanol have practically no formulation effect since their functions are essentially nil whatever the concentration. These are the alcohols that are the more interface seeking ones, and their main effect is to dilute the surfactant adsorption density without changing the formulation.
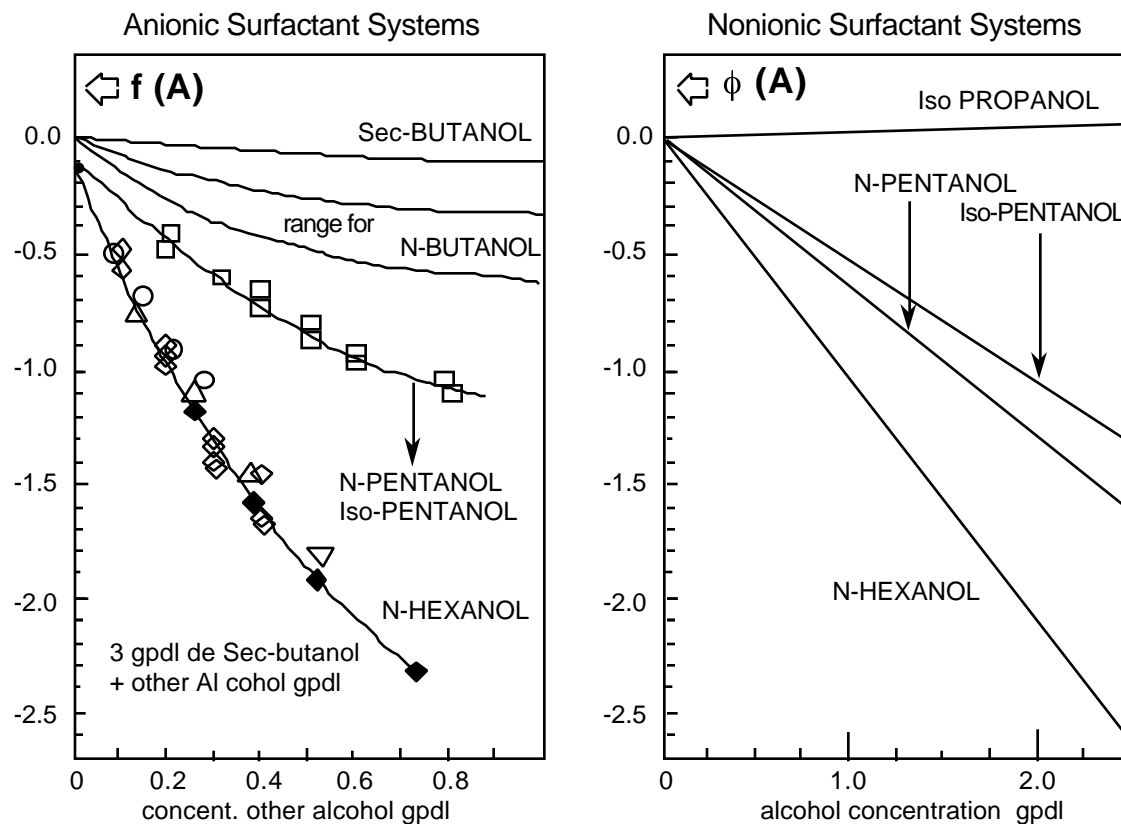
Anionic Surfactant Systems

Nonionic Surfactant Systems

Figure 15   Effect of alcohols on optimum formulation as f(A) and f(A) (adapted from ref. 58)

On the contrary, water insoluble alcohols produce an increasingly negative function as the alcohol concentration increases, and the more lipophilic the alcohol is, the more negative the function is, with an almost linear variation. These functions are independent of the system starting with pentanol and above, which is a nice feature, since it is much easier to handle the alcohol this way than through a fourth component in a phase diagram. Thus they produce a positive contribution in the correlation, as an increase in salinity.

N-butanol and *sec*-pentanol are intermediate affinity alcohol that are more or less water-soluble depending on the nature of the oil phase in equilibrium. For them the alcohol function is found to depend on the oil-water system. In any case the function does not follow a straight line variation as in other cases but tends toward an asymptote located between -0.5 and -1.0 depending of the system.

More information can be found in the original articles or in a review book on the subject (11). Relations conceptually similar to [17] and [18], sometimes more accurate but limited to the effect of the temperature or other one or two variables were proposed by several investigators (57, 63, 77-81). The temperature effect (58-59, 82-83) is mentioned in correlation [Eqs. (17) aned (18)] as a linearized approximation over the narrow interval of experimental range, and may be considered as a trustworthy estimate for ionic surfactants, whereas is it rather approximate for nonionic ones.

The direction and intensity of change are indicated by the coefficient signs and values. The temperature coefficient a_T is 0.01 °C^{-1} for anionic systems (58), and about twice as much for cationic ones (59). However, these numbers are not very precise since the temperature effect on ionic systems is rather small and difficult to estimate with accuracy. In any case the sign before the coefficient is negative, which means that an increase in temperature is equivalent to a reduction in salinity.

On the contrary, the temperature coefficient for nonionic surfactant c_T is positive and much larger, typically 0.06, although it has been reported to change with the surfactant average EON, typically increasing from 0.04 to 0.08 when EON increases from 3 to 10 (84). The inaccuracy comes from the fact that most nonionic systems produce a three-phase behavior range that extends over a large zone of temperature, in which the optimum temperature must be selected (61, 85). Because of the positive sign before the coefficient in the correlation, an increase in temperature would be equivalent to an increase in salinity or a decrease in EON.

The correlation for optimum formulation may be written with the temperature term on the left side, such a

$$T - T_{ref} = \frac{EON - \quad - b\,S + k\,EACN + \quad (A)}{c_T} \qquad [22]$$

In this relation, T is the temperature at optimum formulation where R = 1, i. e., the PIT according to Shinoda's premise, an expression that deserves the latter label HLB-temperature. This relationship is very close to the one deduced by some researchers (78) who used the surfactant HLB instead EON- , to arrive to a similar result as far as the combined effects of temperature, salinity, and oil ACN is concerned. The above formula indicates how the PIT increases with the number of ethylene oxide group in the surfactant molecule, increases with oil chain length and decreases with electrolyte concentration and surfactant "tail" length (proportionally to). It also predicts a variation with the alcohol type and concentration - a decrease with lipophilic species.

It is seen that the above relationship implies that the linear mixing rule on EON or EACN, would compel a linear mixing rule on optimum temperature, which is an a posteriori justification of the PIT mixing rule.

E. Surfactant Affinity Difference SAD: Generalized Formulation Concept

The correlations are the numerical translations of the R = 1 concept in Winsor terminology. The correlations are linear forms of all the formulation variables with no crossed term, so that the different variable effects are independent, which might seem to be too much of a coincidence. A few

years after the correlations were empirically found, it was showed that they are actually a numerical expression proportional to the "surfactant affinity difference" (SAD), i. e., the difference between the negative of the standard chemical potential of the surfactant in the oil phase and the corresponding term for the water phase, in a three-phase optimum system (38, 86-87)

$$SAD = - \mu°_O - (- \mu°_W) = \mu°_W - \mu°_O \qquad [23]$$

Now, it is clear that SAD is a form of the generalized formulation parameter, hopefully expressed in terms of measurable and manipulable variables. Again, it is worth noting that the correlations do not contain any cross term, and are, on the contrary, linear forms of independent terms.

$$\frac{SAD}{RT} = \ln S - K \, ACN - f(A) + \quad - a_T \quad T \qquad [24]$$

$$\frac{SAD}{RT} = \quad - EON + b \, S - k \, ACN - \quad (A) + \, c_T \quad T \qquad [25]$$

Each term can be viewed as an energetic contribution to the overall interaction balance, which is expressed as an algebraic sum instead of a ratio as in Winsor R. The positive contributions (including the alcohol functions for lipophilic alcohol) tend to produce the transition in one way (from R <1 to R >1) while the negative terms do it the other way.

Whenever SAD is respectively negative, zero, or positive, R is respectively inferior, equal or superior to 1. An optimum formulation can be thus taken as a reference state, that can be accurately pinpointed by experiment.

On the other hand, an off-optimum formulation can be defined as a deviation from optimum formulation by its SAD value. Thus, it is possible to compare systems in a same physicochemical state (same deviation from optimum formulation) although they have no single formulation variable with a common value. This concept has been used successfully to correlate and predict the influence of the formulation on the properties of macroemulsified systems in many applications (88-94).

Aside Shinoda and collaborators who introduced the PIT, other investigators have presented similar conceptual approaches that are worth mentioning, although they did not achieve the detailed numerical quantification of the SAD expression.

Krugliakov (95-97) proposed a concept called hydrophile-lipophile Ratio (HLR), which is the ratio of the energy of adsorption of the surfactant molecule from the water phase to its energy of adsorption from the oil phase. The HLR is a good alternative, but it suffers from the same drawback that Winsor R ratio does, i.e., it is difficult to evaluate numerically and it is a ratio of energy terms instead of an algebraic difference.

The early proposal by Davies (40) to use the partition coefficient of the surfactant between the oil and water phase as a formulation parameter was retaken by Marquez and collaborators (98) as a way to measure the free energy of transfer from water to oil, a successful technique to deal with complex fractionating surfactant mixtures (99). The free energy of transfer of a molecule of surfactant from water to oil is:

$$G_{(w)} = RT \ln (C_W/C_O) \qquad [26]$$

where the C_W and C_O are the surfactant concentrations in water and oil respectively. This time the partitioning was measured between the excess phases of a three-phase Winsor type III system at optimum formulation, and there were plenty of degrees of freedom available to estimate the change of partitioning with the different formulation variables. Marquez data (51) showed that the partition coefficient of a surfactant specie is an excellent yardstick of the concept of generalized formulation. In the assumption that the activity coefficients are unity, which is legitimated by the low surfactant concentration found in the excess phases of Winsor type III systems, then the equilibrium between the water and oil phases can be written in terms of the chemical potentials of the surfactant:

$$\mu_W = \mu_O = \mu^*_W + RT \ln C_W/C_{W.ref} = \mu^*_O + RT \ln C_O/C_{O.ref} \qquad [27]$$

where the standard chemical potentials are indicated with an asterisk, while the concentration references bear the subscript ref. If the partition coefficient is defined as $K = C_W/C_O$, then

$$RT \ln K + constant = \mu^*_O - \mu^*_W = G_{(w\ o)} = - SAD \qquad [28]$$

Thus RT ln K and SAD should exhibit similar (and opposite) variations with respect to the formulation variables. By measuring the partition coefficient with different systems exhibiting a variety of oils, surfactant characteristics, alcohol content, brine salinity, and temperature, Marquez was able to correlate the term RT ln K with the formulation variables in a linear relationship very similar to the correlations. For instance, it was found that (98) :

$$RT \ln K(EON, SACN) = \qquad [29]$$
$$EON \times \mu^*(EO\ group) + SACN \times \mu^*(CH_2\ group) + \mu^*(other\ factors)$$

where $\mu^*(EO\ group) = 0.62$ cal. by transferred EO group from the aqueous phase to the oil phase, and $\mu^*(CH_2\ group) = -0.06$ cal. by transferred CH_2 group from the aqueous phase to the oil phase.

In the past 10 years several studies on the effect of different oils, different electrolytes, and other surfactants, have brought additional data for using the numerical correlations to help the

practitioner to make use of the SAD approach as a generalized formulation yardstick (27, 64, 72, 74, 80, 83, 100-105).

There is not yet a comprehensive treatise to gather these data and to explain how to handle it beyond the book of Bourrel and Schechter (11), but only some attempts like this chapter and other reviews with different approaches in recent books (106-107). Accordingly, the formulator should start from the basics that are explained here, and find his way to his own case, keeping in mind that a similar SAD value does mean a similar physicochemical environment. The correlations will provide both the direction of change to follow and the equivalence between the different possible changes, a valuable feature when cost and toxicity constraints are present.

The previous section dealt with formulation variables, i. e., those that are able to change the type of diagram according to Winsor rationale. In order to study the formulation effect, a specific composition was selected (typically 1-3% surfactant and equal amounts of oil and water) which lies inside the polyphasic region so that the diagram type could be deduced from the observed phase behavior at this point. This is satisfactory only if the diagram is of the Winsor type, that is in presence of an ideal ternary behavior. In other cases, particularly in presence of a dual amphiphile like a mixture of surfactant and alcohol, it is necessary to analyze the whole diagram, and to locate the different phase behavior regions as a function of the composition.

V. EXPERIMENTAL METHODS APPLIED TO REAL CASES

A. Some Experimentsl Diagram Cases

In many truly ternary diagrams where the Winsor phase behavior regions are found, additional regions where different types of mesophases, specially liquid crystals of various types depending on the formulation and the relative amount of the components, are present. Often these mesophase regions would tend to disappear as temperature is increased, although it could be at the expense of a change in formulation, particularly with nonionic surfactants.

In many instances the SOW ideal ternary case is not sufficient to describe the behavior of an actual system. It has been noted that the addition of alcohol, as a disordering agent, is often required to avoid viscous or solid like mesophases, particularly to produce microemulsions with ionic surfactant systems (108). According to the correlations for optimum formulation, the alcohol effect can also be that of a co-surfactant that modifies the overall balance of affinity through the f(A) and   (A) terms. The use of two surfactants is also often recommended to attain a better emulsion stability, a statement which should not be taken for granted in all cases, although it could prove correct in some cases. Hence, it is often necessary to carry out a study of a system whose

amphiphile is composed of two substances, two surfactants or a surfactant and an alcohol, which exhibit different degrees of hydrophilicity and thus cannot be included in a single pseudocomponent.

Quaternary systems, for instance surfactant-alcohol-oil-water (SAOW) are analyzed in a quaternary diagram made in a regular tetrahedron as indicated in Fig. 16. The brute force method that consists in selecting hundreds of composition points in the diagram (located at some grid) and in analyzing the phase behavior in all these points is of course too tedious to be carried out.

The typical way to handle this problem is to use pseudoternary cuts, i. e., plane cuts through the tetrahedron. Since the two amphiphiles are often the principal source of unknown asymmetry, the usual tactic is to make a cut as indicated in Fig. 16, which is a triangle passing through the oil and water vertices, as well as one point of the surfactant-alcohol side located by the ratio of surfactant to alcohol. All the points located in the gray triangle (Fig. 16 right) will contain a same ratio S/A, which is called a pseudocomponent.

The phase behavior is then studied in the S/A-O-W pseudo-ternary diagram (Fig. 16 left), according to usual techniques, which may be grid scanning or others whenever some extra information is available to guide the selection of the trial points.

When the S/A pseudocomponent point is moved along the SA side, the shaded triangle sweeps the whole tetrahedron volume. A systematic way to map the phase behavior in the tetrahedron is thus to map it in several bidimensional cuts made at S/A constant. Let us further discuss this point on a first example, in which the amphiphile contains a rather hydrophilic surfactant (octylphenol with 7.5 EO groups in average) and a lipophilic alcohol (*n*-pentanol)

Figure 17, upper left is a tetrahedron representation of a quaternary diagram containing an hydrophilic surfactant and a quite lipophilic alcohol (109). The other diagrams in Figure 17 are different cuts at constant S/A ranging from a very hydrophilic mixture (85 % surfactant and 15% alcohol) to a rather lipophilic one (50 % surfactant and alcohol) in which the lipophilic characte r of
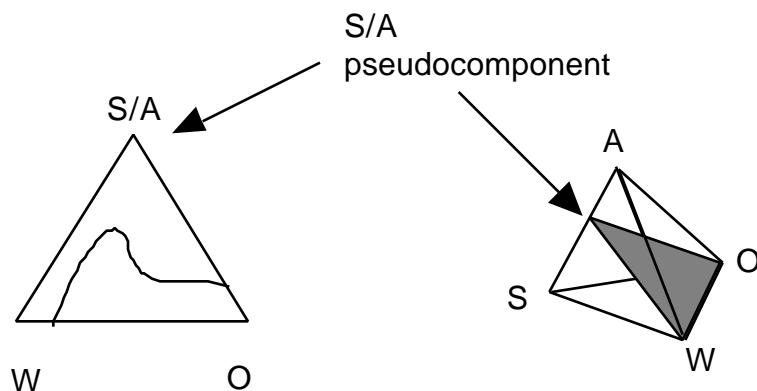

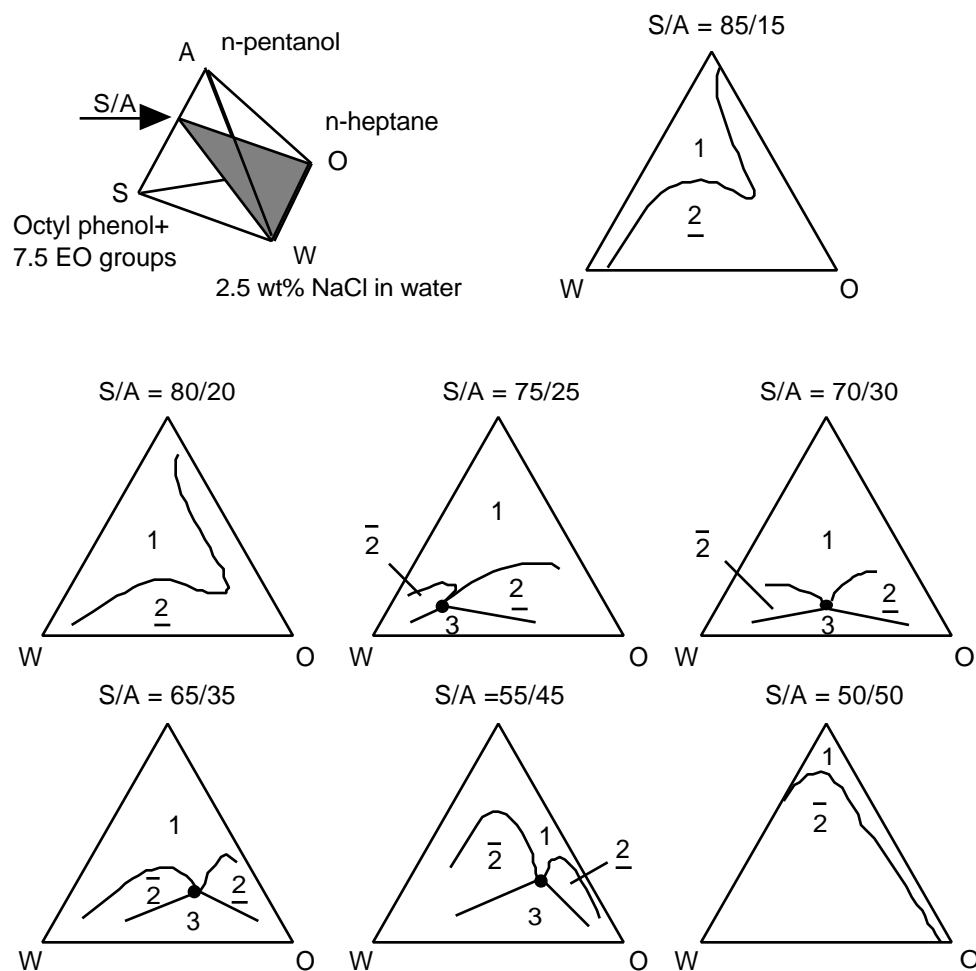**Figure 16**   Quaternary diagram and pseudoternaty cut

Figure 17 Quaternary diagram and different pseudo ternary cuts at S/A constant (adapted from reference 109)

the alcohol prevails. It is worth noting that the proportions are expressed in weight percentage, so that 50% alcohol represents a composition with a large excess of alcohol on a molar basis.

As the S/A ratio decreases a sequence of phase behavior takes place, so that the amphiphilic mixture becomes more and more lipophilic since the content of the more lipophilic component increases. The first diagram at S/A = 85/15 shows that the amphiphilic mixture is completely miscible with water but not with the oil phase, which is essentially the case for the surfactant alone.

It is essentially a Winsor type I diagram with this modification near the (S+A)-O side. At S/A=80/20 the situation is basically unchanged, although the single phase region has augmented in size, i. e., the miscibility gap has diminished.

From S/A=75/25 to 55/45 the diagram exhibits a three-phase behavior region which is not very different from Winsor type III diagram, with the middle phase composition moving from left to right, i.e., taking up more and more oil phase.

It is worth noting that the tie lines are not fully indicated in the pseudoternary diagrams, because they are not actually laying in the plane of the cut. In effect, the amphiphile mixture content of the phases in equilibrium does not match the S/A ratio because of the so-called preferential partitioning. For instance in a two-phase split, the oil phase would contain more alcohol that indicated by the S/A ratio, while the aqueous phase would contain more surfactant than indicated by the S/A ratio. Since the binodal curve is determined by trial and error by diluting a single phase system located just above the polyphasic region with an O+W mixture, the middle phase microemulsion (black dot) is in general extremely near the plane of cut if not exactly in it (110). Between S/A=55/45 and S/A=50/50, the phase behavior changes to mostly lipophilic, and the Winsor type II region invades the whole diagram. In this case the surfactant is not hydrophilic enough to compensate for the alcohol effect. It is also probable that such a high amount of alcohol results in a consolute system in which most of the alcohol is miscible in the oil phase at equilibrium with an almost pure water phase. Note that a nonionic surfactant of the alkylphenol type with even 7.5 EO groups in average, is certainly at least ten times more soluble in a mixture of heptane and pentanol than in water (98).

The changes of the S/A ratio result in a transition not unlike the one seen in a formulation change R < 1   R = 1   R > 1. This is due to the fact that an increase in alcohol content in the amphiphilic mixture is essentially equivalent to an increase in lipophilicity in this combined amphiphile. The change of S/A, i. e., a composition change, is thus also a formulation change, just like the one in oil nature or in salinity could produce. The same sequence of Winsor diagrams when the surfactant/alcohol ratio is swept, has been found for different systems (78, 111- 115). The three-phase volume body in a quaternary diagram has a very peculiar shape that has been studied both from the experimental and thermodynamic point of view (116-117).

Not all the cases are so simple. For instance let us examine a case in which there is a very hydrophilic surfactant and a slightly lipophilic alcohol. Figure 18 indicates the phase behavior of such a case, with a pseudoternary cut at a S/A near unity. The phase behavior which is represented in Fig. 18, right is hypothetical and even simplified with respect to real cases, but it is reasonably representative of a system containing sodium dodecyl sulfate and *n*-butanol. In this system, the excessive hydrophilicity of the dodecyl sulfate is compensated by factors that are known to reduce the interaction of the surfactant for the aqueous phase (a high-salinity brine), and to favor its interaction for the oil phase (short alkane or aromatic oil) (118-119). It is seen that the polyphasic region map found in such a cut does not match any one of Winsor diagrams. However, the different phase behaviors do, and there are regions in which one phase (a microemulsion), two phase (Winsor type I or II) , and even three phase behavior are exhibited.
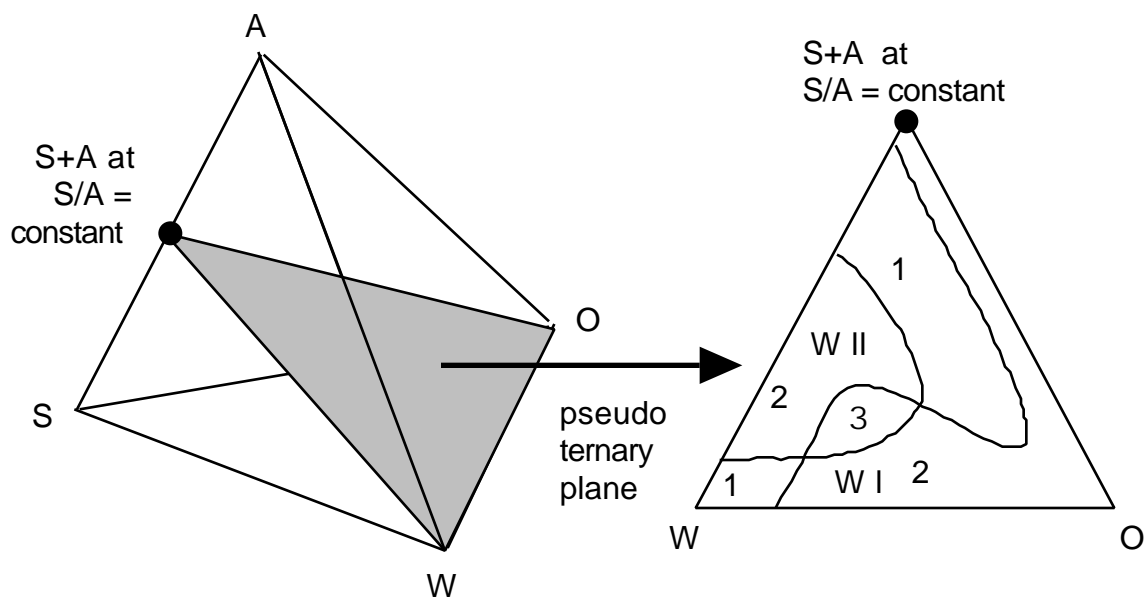
Figure 18   Hypothetical non Winsor Type diagram in a ternary cut, in a quaternary like dodecylsulfate, high salinity brine, aromatic oil and n-butanol.

The present phase behavior is typical of the case in which the surfactant is very hydrophilic while the alcohol is only slightly lipophilic. In the present case it is obvious that a change in total amphiphile concentration, i.e., a vertical displacement on the left side of the diagram, would produce a type I   type III   type II transition. This is because the increase in S+A really produces a change due to the increase in alcohol effect, whereas the surfactant effect is roughly independent of its concentration. This is because it is very hydrophilic from the start but then does not change anymore, while the alcohol is water soluble at low concentration, reaching its saturation in water and becoming more and more oil-soluble with a resulting lipophilic effect. This behavior of intermediate alcohols such as *n*-butanol has been typified to be difficult to handle since it changes from one system to another.

This is a typical case with an alcohol that is slightly water-soluble, but much less than the surfactant. On the right part of the diagram (more oil than water) there is quite an extended W/O type microemulsion region.

In the previous case the phase behavior transition was produced by a change in the ratio S/A, i .e., in the amphiphilic mixture hydrophilicity. In the present one the phase behavior change is mainly due to the total concentration of amphiphile mixture, that drives a considerable hydrophilicity variation. These are two cases of quaternary systems in which a composition change produces a phase behavior change typical of the formulation effect in Winsor's diagrams. Such a

coupling of formulation and composition is not an exception, but rather a rule when the amphiphile is composed of various substances. Many other diagrams exhibit a lot of similarities with these two cases (102, 111, 120).

B. Solubilization-Related Phase Diagrams

The coupling of the two kinds of variables has been advantageously examined in the so-called solubilization vs. formulation diagrams that have been used by several industry researchers, particularly Bourrel and co-workers (63, 121-125). Such diagrams are concerned with a very practical problem, i. e., the amount of surfactant and alcohol that is required to reach the binodal curve frontier with the single-phase microemulsion region, since this is obviously related to the cost of co-solubilizing oil and water.

Figure 19 indicates the way to construct such plots. In each diagram (see upper left diagram) an amphiphile concentration scan allows to detect the height of the polyphasic region. This is done by adding surfactant and alcohol (S+A) at a fixed S/A ratio to a W+O system (generally at unit water-to-oil ratio for the sake of simplicity) until a monophasic region appears. turbidity appears.
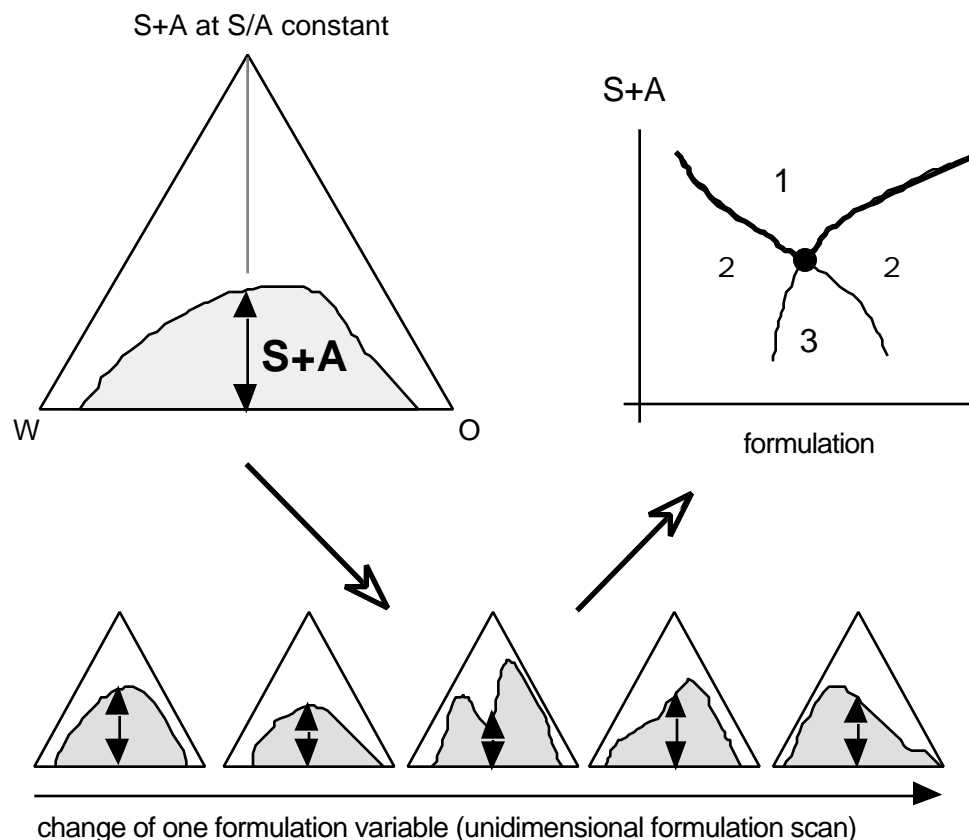

Figure 19 How to construct a S+A vs. formulation plot

In reality the contrary is easier to do, i. e., a single phase SAOW system containing the S/A fixed ratio as well as equal amounts of oil and water is diluted with equal aliquots of oil and water until a turbidity appears.

The procedure is repeated with different diagrams along a unidimensional formulation scan, and the S+A data are recorded. Then they are plotted as S+A composition to reach the single phase vs. formulation. As a matter of fact, the whole phase behavior is reported, i. e., the frontier between two- and three-phase behavior as well. The typical S+A vs. formulation plot is indicated in Fig. 19 (above right) where it is seen that the S+A amount passes through a minimum just at optimum formulation for three-phase behavior. In effect, below the lowest point of the curve (black dot) occurs a three-phase region, not a biphasic one. Note that at this formulation, the required amount of surfactant+alcohol to cosolubilize equal amounts of oil and water undergoes a minimum. It is said that the microemulsion solubilization, which is the amount of oil or water that is solubilized per gram of amphiphile (the inverse of the plotted data) passes through a maximum - a now well recognized property of optimum formulation.

Extensive studies to separate the effects of the different formulation variables on solubilization were carried out by Bourrel and collaborators in the past decade (11, 121-125). The first diagram to be dealt with is a formulation scan with a perfect ternary that strictly follows Winsor phase behavior. This may be, for instance, reasonably represented by a system containing an alkylbenzene sulfonate and *sec*-butanol amphiphile mixture, an alkane, and NaCl brine, in which the relation surfactant/alcohol is kept constant.

Figure 20 shows the general aspect of such a diagram in which the phase transition frontier looks like a lowercase Greek gamma. Note that if rotated 90° as done in studies that use temperature instead of formulation as the field variable, it looks like a fish (126).
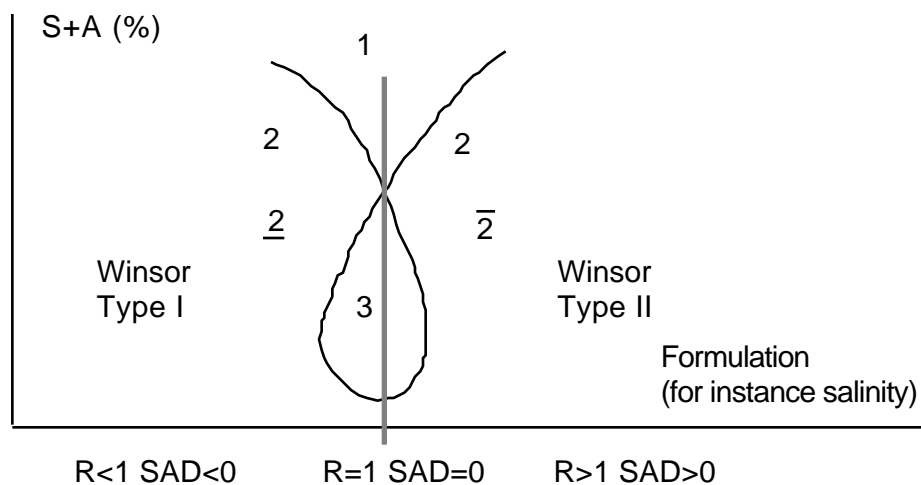

Figure 20   Normal S+A versus formulation phase behavior diagram with the total S+A concentration.

Coming back to Fig. 20, it is seen that the maximum solubilization is attained at the minimum of the single phase region, i. e., at the crossing from one-phase to three-phase regions, which is the exact position of the middle phase microemulsion that contains equal amounts of oil and water.

The optimum formulation corresponds to the center line of the single- and three-phase regions that here is a vertical (dashed) line passing through the crossing point. It is indicated as SAD = 0 or R = 1 on the abscissa axis.

In the second so-called twisted diagram illustrated in Fig. 21, the gamma shape is not in the vertical direction, but this time it is inclined. At each S+A level, the optimum formulation is also the center line of the single- and three-phase regions since it represents the value of the formulation variable for which the center of the three- or single-phase range is attained. In other words, it may be said that with this type of diagram the optimum formulation (dashed line) changes.

Note that if a vertical path is drawn from bottom to top (arrow in Fig. 21) along an increasing amount of S+A, the phase behavior changes from Winsor type I to type III and to type II, and finally to a single phase, as was the case in the S/A = 1 ternary cut through a quaternary diagram with sodium dodecyl sulfate and butanol seen in a previous section (Fig. 18). It is worth remarking that what seemed an extremely complex phase behavior is simply the consequence of the twisting of the diagram. This twisting is due to the fact that the surfactant and the alcohol do not exhibit the same hydrophilicity; thus one of them dominate. Here the lipophilic amphiphile dominates because at high S+A the formulation (salinity) is lower; thus everything occurs as if the amphiphile were less hydrophilic according to the relation between the salinity and the surfactant characteristic parameter discussed in the previous section. The opposite has been also found to occur with hydrophilic alcohols (63).
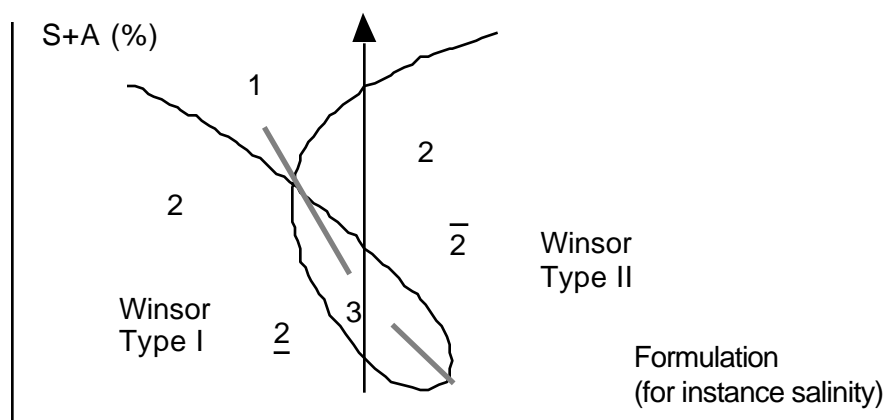

Figure 21 Twisted S+A versus formulation phase behavior diagram

C. Formulation in Practice

It has been shown that the generalized formulation corresponds to the departure from an optimum formulation, and this is the way it is found useful when correlating the emulsion properties. It is thus important to find out an experimental method to know the formulation state of a given system.

If the system contains a single phase, it is sufficient to dilute it with oil and water to fall in the polyphasic region, and if the system exhibits three phases, it is at or very near optimum formulation, so that these cases do not result in any interpretation problem. In most cases, however, the system would exhibit two phases at equilibrium and the determination of the phase behavior type of paramount importance.   According to all reviewed concepts, the partitioning of the surfactant preferentially into the water (respectively oil) phase indicates a Winsor type I (respectively type II) phase behavior. In many cases the phase that contains surfactant in amount above the CMC can be detected by the light diffusion known as Tyndall effect, which turns it bluish or slightly opaque. However, if the micelles are small enough the phase is completely transparent to visible light, and it is recommended to check the light scattering with a low-power laser (something like a laser pointer is sufficient). Whenever there are some micelles, the laser beam path through the phase will turn visible.

On the other hand the aspect of the surfactant-rich phase may serve as a tell-tale information about the formulation departure from optimum. It has been seen that near optimum formulation the solubilization is high, i. e., a lot of oil and water are enclosed in the surfactant structures, whatever they are. The enclosure is like a surfactant layer, and the amount of surfactant is thus proportional to the surface area of the structure. On the other side, the solubilized phases are inside the structure islands and their amount is thus proportional to the structure unit volume. If it is assumed that the structure is composed of spherical or pseudo-spherical units of radius R, the surface area is $4\pi R^2$ while the volume is $4/3\ \pi R^3$, so that the volume per unit surface is proportional to R. In other words, a high solubilization should be associated to large structural units, which are likely to produce a lot of light scattering. This is corroborated by experience, and it may be said that the micellar phase or microemulsion tends to become more opaque whenever optimum formulation is approached from both sides. A turbid microemulsion phase is thus a good hint that the system is very near optimum formulation.

Once the system is found to be one of the basic Winsor types, it is important to know how near or how far from optimum formulation it is located. With the exception of the light scattering discussed in the previous paragraph, there is no other way but to carry a formulation scan to find out how far the optimum formulation is.

If the system is found to be of Winsor type I, then the affinity of the surfactant toward the aqueous phase dominates and some formulation changes have to be accomplished to produce a shift toward a lesser hydrophilic interaction or a larger lipophilic interaction, until optimum formulation is reached.

With an ionic system, such displacement results from an increase in salinity of the aqueous phase, a reduction of the oil EACN either by using a shorter alkane or by adding polar or aromatic components, the addition of some lipophilic alcohol starting with *n*-pentanol up to a few vol. %, less with hexanol or higher alcohols. Finally the surfactant may be mixed with a less hydrophilic surfactant of the same family (e. g., with a longer tail). If the system contains nonionic surfactants an increase in temperature would decrease the hydrophilic interaction quite rapidly while the electrolyte effect would be almost negligible, with the exception of polyvalent cation salts.

If the system is of Winsor type II, an increase in hydrophilic interaction, or a reduction in lipophilic interaction is required to approach optimum formulation. This may be done by increasing the oil EACN, particularly by reducing its polar or aromatic content, by reducing the salinity of the aqueous phase, particularly if divalent ions are presents and/or if the system contains ionic surfactants, by reducing the lipophilic alcohol concentration and/or chain length, by reducing the temperature if the system contains nonionic surfactants. Again the surfactant can be mixed, this time with a more hydrophilic member of the same family.

It is worth remarking that the temperature is not used for ionic systems, while the salinity is mainly used to alter ionic ones.

In all experimental cases, the optimum formulation can be detected by any of the phenomena that happen there, such as (a) three-phase behavior, (b) single-phase behavior in-between two biphasic behaviors at high surfactant concentration, (c) interfacial tension minimum, which is particularly suitable when a very small amount of surfactant is present so that no microemulsion is formed, (d) change in preferred partitioning, (e) several emulsion properties such as emulsion inversion and minimum stability that will be discussed in detail in the next chapter.

Once the change or combination of several changes has shifted the formulation to optimum, some accounting is required to measure the distance from optimum. The "intensity" of each change is calculated according to the correlation expression, and in cases of various concurrent changes, they are summed up. Since both correlations contain the term ACN with a coefficient which is nearly the same, a comparison in terms of deviation in ACN unit is preferred. Moreover, ACN units are also used to estimate EPACNUS, the ionic surfactant characteristic parameter.

If the actual formulation change was not due to a variation in oil ACN or EACN, the equivalent change in ACN units is readily found by applying the correlation. For instance a ACN = + 10 units is equivalent to a fivefold decrease in salinity so that lnS = - 0.16 x 10 = - 1.6, a change in surfactant EPACNUS = /K = - 10, which is equivalent to remove 4.4 carbon atoms from the ionic surfactant "tail", or to increase EON = + 1.6 ethylene oxide group in the polyether

chain. It also corresponds to an increase of about 160 °C for ionic surfactants and a   T change from - 20 to - 40°C (decrease) for nonionic systems, or to the removal of a lipophilic alcohol effect f(A) or   (A) = - 1.6 equivalent to about 1.5 (respectively 2.5) % of *n*-pentanol or 0.4 (respectively 1.4) % *n*-hexanol, for ionic (respectively nonionic) systems.

The point is now to evaluate how many ACN units is a small or a large deviation from optimum formulation. But first, it is worth finding out the accuracy of the numerical calculations that are carried out. If the formula to calculate the HLB of a nonionic surfactant is applied to ethoxylated nonylphenols containing five and six ethylene oxide groups symbolized as NP5 and NP6, it turns out that

$$HLB_{(NP5)} = \frac{100}{5} \frac{5 \times 44}{5 \times 44 + 220} = 10.0$$

while

$$HLB_{(NP6)} = \frac{100}{5} \frac{6 \times 44}{6 \times 44 + 220} = 10.9$$

Thus, near HLB = 10, a change of one unit in HLB is roughly equivalent to a change in one EO group in the polyether chain, which is roughly equivalent to a change in 6-7 ACN units according to the previous paragraph.

The accuracy of the detection of the position of the optimum formulation is roughly about half an ACN unit or a 10% change in relative salinity in good conditions and one ACN unit as routine. This is equivalent to about 0.2 units of HLB, a fairly good accuracy compared with the ± 2 units uncertainty generally associated to HLB.

Experience indicates that the amount of change that can be viewed as significant, as far as a modification in emulsion property is concerned, is of about 1 ACN unit near optimum formulation and 2 ACN units at some distance from it. It will be seen that the change from a very stable O/W emulsion to an unstable one, can occur typically over a 8-10-ACN units change in formulation, and a complete shift from the maximum instability of a O/W emulsion to the maximum stability of the W/O (see figure 11) could be from 20 to 40 ACN units depending on the system.

As a rule of thumb it can be said that a 1- or 2-ACN unit change is the minimum to try to get some variation, while a 10-ACN-unit change could produce a complete alteration of the situation and properties. As a matter of fact the phenomenology associated with the vicinity of the optimum formulation is noticed at about ± 5 ACN units.

This chapter was dedicated to set up the formulation and composition variables framework which is going to be used extensively in the next chapter to describe the relationship between the formulation and the emulsion properties.

ACKNOWLEDGMENTS

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