

REVIEW

Emulsion stabilization by non-ionic surfactants: experiment and theory*

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QUANTIFYING THE STABILITY OF EMULSIONS

The stability of a dispersion is frequently denoted by a rate constant which is a quantitative measure of the time required for the initial concentration of particles to be reduced to some critical value.

The flocculation of hydrophobic sols has been treated in a kinetic study by Smoluchowski (1916, 1917) and a second-order reaction process was found to hold. The kinetics of coalescence of emulsion globules has been studied by van den Tempel (1953), who reported that coalescence is a first-order reaction process which occurs only between adjacent drops in an aggregate and which is independent of the number of droplets in the aggregate.

An emulsion cannot be thermodynamically stable, but it can display a high degree of permanence in the kinetic sense. Therefore, the factors determining the kinetics of degradation of emulsion systems are of great importance.

The first elaborate study of the kinetics of emulsion breakdown was made by King & Mukherjee (1939) on emulsions of olive oil and kerosene in aqueous solutions of soaps. They surmised that emulsion instability was due to the preponderance of a large interfacial area of the disperse phase and decided that a reasonable representation of the process of coalescence would be a measure of the decrease with time in the specific interfacial area S of emulsified oil.

$$S = \frac{A}{\rho V} \quad \dots \quad (22)$$

where A is the total interfacial area of emulsified oil having a volume V and density ρ . When S was plotted as a function of time, a linear relation held, which was proportional to the initial specific interfacial area S_0 , giving

$$\frac{-dS}{dt} = \frac{S_0}{k} \quad \dots \quad (23)$$

k is the rate constant which had an initial high value in the early stages of breakdown but which changed to a much lower value for the remaining life of the emulsion. Lotzkar & Maclay (1943) also measured changes in the specific interfacial area with emulsions of olive, cottonseed and mineral oils stabilized with pectin. The data were treated on the assumption that the rate of change of specific surface at any time is proportional to the specific surface at that time, or

$$\frac{-dS}{dt} = \frac{S}{k} \quad \dots \quad (24)$$

Plotting the logarithm of S against time they obtained linear relations from which values of the stability coefficient, k , were computed.

Jellinek & Anson (1950) attempted to find a suitable numerical expression which defined the stability of emulsions stabilized by α -monostearin and sodium stearate.

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They plotted several statistical quantities against time for their emulsions but the best linear plots were of specific interfacial area, and stability rate constants were determined from these. In addition, curves of the reciprocal of the number of globules per gram of disperse phase were linear with time, representing a formal agreement with the Smoluchowski theory.

The relatively simple treatment of the kinetics of emulsion breakdown by these workers has provided a plausible agreement with theory for the systems studied. It does not follow that a similar agreement would occur in other systems, particularly when materials other than surfactants are used as stabilizers. By studying these less stable systems, a greater insight into the mechanisms involved might be obtained.

Lawrence & Mills (1954) have attempted to describe the stability of their systems by incorporating into Smoluchowski's theory an expression for the mean drop volume \bar{V}_t , given by

$$\bar{V}_t = \frac{\sum_{r=1}^{\infty} N_r V_r}{\sum_{r=1}^{\infty} N_r} \quad \dots \quad \dots \quad \dots \quad \dots \quad (25)$$

(N_r is the number of aggregates of r particles and $V_r = rV_0$, the volume of the r th-sized particle composed of r primary particles each of volume V_0 .) The rate of change of the mean drop volume was expressed as

$$\bar{V}_t = V_0 + \beta\phi t \quad \dots \quad \dots \quad \dots \quad \dots \quad (26)$$

in which $\beta = 4\pi D_1 \bar{R}$. \bar{R} is the effective radius of the emulsion particles (composed of r -mer primary particles); ϕ is the phase volume fraction of disperse phase and is equal to $N_0 V_0$, the total oil emulsified in the unit volume of emulsion. Equation (26) must be modified to account for inefficiency of collisions, when the theory of "rapid" coagulation does not apply, i.e. in stabilized systems. Hence,

$$\bar{V}_t = V_0 + p\beta\phi t \quad \dots \quad \dots \quad \dots \quad \dots \quad (27)$$

Lawrence & Mills (1954) equated p to energy in an expression of the form

$$p = X \exp\left(-\frac{E}{RT}\right) \quad \dots \quad \dots \quad \dots \quad \dots \quad (28)$$

where E represents an energy barrier to effective collisions between the emulsion globules and X is the frequency of collision. p may then be evaluated from the slope of a plot of \bar{V}_t against t . In emulsions containing 1% phase volume of 3,3-ditolyl or Nujol, linear relations were obtained for both unstabilized emulsions and emulsions stabilized with 1% sodium oleate. Taking X as unity, an energy of activation, E , of 16.32 kJ mol⁻¹ was evaluated from the slope of the curve for unstabilized emulsions while a value of 27.17 kJ mol⁻¹ was found for sodium oleate stabilized emulsions. Computation of energies of activation from Jellinek & Anson's results (1950) gave comparable values.

The use of the simple Maxwell-Boltzmann factor ($\exp\{E/RT\}$) for E has been disputed by Kitchener & Mussellwhite (1968) because the "activated state" of the particles is probably a function of several physical parameters, notably the flux of particles up to the central particle. The treatment of coagulation of emulsion globules by Lawrence & Mills (1954) neglects to account for a number of factors affecting the kinetics of these systems. An attempt has been made by Kharin (1956) to account for particle size variation and the deaggregating effect of emulsion particles on the coagulation rate. The rate of disappearance of n particles of all sizes is:

$$\frac{-dn}{dt} = \beta n_1^2 \exp\left[\frac{-q_1}{kT}\right] - \alpha n_2^2 \exp\left[\frac{-q_2}{kT}\right] \quad \dots \quad \dots \quad (29)$$

The first term on the right-hand side quantifies the coagulation process where n_1 is the number of primary particles coagulating at a rate β against a potential energy barrier q_1 . The second term accounts for the deaggregation process of aggregates, n_2 , opposed by a potential energy barrier, q_2 . α is the coefficient of the dispersion process, whereas β is the coefficient of the coagulation process, equal to $4\pi D_1 R$, where the symbols have the same meaning as before. The influence of particle size is estimated from the magnitudes of q_1 and q_2 which are empirically related by $q = f(a)$. The activation energy for the coagulation process was found to be 6.28 kJ mol^{-1} for transformer oil emulsions, less than one-half the value obtained by Lawrence & Mills (1954) for their unstabilized o/w emulsions.

A new approach to the stability of emulsions has been presented by Hill & Knight (1965). They have employed a collision frequency based on a gas-kinetic model rather than the classical diffusion model to formulate a kinetic theory for the slow coagulation of emulsion systems. The assumption is made that probability of coalescence is proportional to the integral $\int(\text{area} \times \text{pressure}) \cdot dt$ for the encounter between particles with velocities distributed according to Maxwell's distribution law. The theory accounts for the average effects of coalescence over all sizes of droplets but, electrical effects and droplet deformations on collision are ignored. It has been previously stated that for stabilized emulsions the barrier to coalescence is independent of the actual size of the drops coalescing (Reerink & Overbeek, 1954; Lawrence & Mills, 1954). The change of total interfacial area, (A), with time (t) is, according to Hill & Knight,

$$\frac{1}{A} = \frac{11\beta kT}{4\alpha} t + \text{constant} \quad \dots \quad (30)$$

A plot of A^{-1} versus t should be linear, the slope β being a proportionality constant characterizing the probability of rupture of unit area of common interface under unit pressure per unit time. α is defined as the available volume of dispersed oil. The theory was tested employing results of previous workers (King & Mukherjee, 1939; Lotzkar & Maclay, 1943; Lawrence & Mills, 1954). Generally, better agreement with the new theory was found, but three of the ten plots considered could be represented equally well by Smoluchowski's theory in the form $A^{-3} = Bt + \text{constant}$. Further support of a linear relation of A^{-1} versus t for emulsions of high stability has been demonstrated by Elworthy & Florence (1967) with emulsions of anisole and chlorobenzene in aqueous cetomacrogol solutions.

The rate of coalescence of particles colliding with average violence was calculated by Hill & Knight to be 10^{-9} to 10^{-10} s^{-1} (cf. 10^{-7} s^{-1} found experimentally by Elworthy & Florence, 1967; van den Tempel, 1957), making it very unlikely that an actual coalescence would be observed in emulsions of this type. The theory is applicable to systems stabilized primarily by steric and hydrational mechanisms where electrical effects are unimportant. In some systems, however, aggregation into the secondary minimum has explained instability even when dense interfacial films are expected to be present (Prakash & Srivastava, 1967). Elastic collisions between emulsion droplets is not explained by this theory but the significance of this factor is as yet unknown.

van den Tempel (1953a,b) treated the coagulation of emulsion globules by considering the processes of flocculation and coalescence separately. Flocculation was assumed to proceed by a second-order reaction process according to the Smoluchowski theory. A convenient point in time was chosen to begin the analysis such that a "nearly stationary state" was established around each particle, i.e. the number of particles diffusing in unit time through a sphere surrounding one central particle equals the number of particles adhering to this central particle in unit time. This

state has been reached after a time $t > a^2/D$, which means that all experimental coagulation times should be large compared with a^2/D .

Measurements were made of the number of particles decreasing with time per unit volume of emulsion using an ultramicroscope which does not differentiate between single globules and aggregates. Provided the general shape of the size-frequency distribution curve does not change appreciably during coagulation, it can be shown that a 10% decrease in interfacial area is accompanied by a 27% decrease in the number of particles, making the latter a more sensitive measurement.

The total number of primary particles, n_1 at time, t , is found from

$$n = \frac{n_0}{1 + a_1 n_0 t} + \frac{a_1 n_0^2 t}{(1 + a_1 n_0 t)^2} \left[\frac{a_1 n_0}{K} + \left(1 - \frac{a_1 n_0}{K} \right) e^{-Kt} \right] \quad \dots (31)$$

where n_0 is the number of primary particles at $t = 0$, a_1 is a rate constant for flocculation equal to $8\pi D_1 R$, approximately evaluated as $10^{-11} \text{ cm}^3 \text{ s}^{-1}$ for "rapid" coagulation, and K is the rate constant for coalescence. If a_1 is large compared to K , then equation (31) may be approximated by

$$n = \frac{n_0}{Kt} \left[1 - e^{-Kt} \right] \quad \dots \dots (32)$$

Since the particle number is found to decrease nearly exponentially with time until Kt becomes large compared with unity, this supports the observations made by Lotzkar & Maclay (1943). In emulsions stabilized with macromolecules, the rate of coalescence can be very small. The exponential term of equation (32) may, therefore, be expanded in a power series, of which only the first two terms are used when $Kt \ll 1$. In this case

$$n = n_0 \left[1 - \frac{Kt}{1 + a_1 n_0 t} + \frac{Kt}{(1 + a_1 n_0 t)^2} \right] \quad \dots \dots (33)$$

A plot $1/n$ against t is linear if the emulsions are very dilute or concentrated since the rate of coagulation is unaffected by the particle concentration.

van den Tempel has rigorously tested his theory for o/w emulsions (1953, 1957). In concentrated liquid paraffin emulsions stabilized by sodium dodecyl sulphate and Aerosol OT, respectively, a plot of $\log n$ against time produced two lines corresponding to an initial "fast" rate which lasted for a few hours and a second "slow" rate which characterized the further deterioration of the emulsions. The "slow" rate could be shown to be a first order coalescence rate since flocculation had been eliminated in these systems, indicating that the coalescence of two contacting oil globules does not affect the stability at the other contact points. The initial rapid decrease in particle concentration is attributed to non-equilibrium conditions at the oil-water interface or a wide particle size distribution allowing closer packing of the particles. The time to reach equilibrium at the interface is dependent on the interfacial activity of the emulsifier. Assuming that a condensed monolayer of surfactant is necessary for stability, incomplete oil surface coverage could lead to instability in the early stages (Rowe, 1965; Neiman, Lyashenko & others, 1961).

In most studies of o/w emulsions, the emulsifier is incorporated in the continuous phase. But, for a given concentration of surfactant, the rate of adsorption at the oil-water interface will be different if the emulsifier is placed in the dispersed oil phase. If the emulsifier is soluble in both phases, then the duration of the "fast" rate of coalescence will depend on the partition coefficient of the emulsifier between the two phases and, to some extent, the orientation time of the molecules at the interface. One can never equilibrate the two phases of an emulsion before mixing because of the new interface and the finite quantities which adsorb at the interface.

The adsorption of surfactants at an interface is a rapid process. Ageing is the result of migration of surfactants between the phases. Lin & Lambrechts (1969a,b) have investigated this problem. The placing of the surfactant in the aqueous phase before emulsification produces an emulsion having rheological properties, stability and particle size distribution significantly different from emulsions of the same formulation prepared with surfactant initially in the oil phase. Therefore one factor in emulsion stability will be the possibility of changes in the location of surfactant, since this may cause undesirable changes in emulsion properties during the storage of the product. Migration of Triton X-100 through the water–iso-octane interface becomes very slow (>50 h) when a second component (Arlacel 83) is present in the oil phase.

The second or “slow” rate of coalescence of emulsions has been observed to vary with the degree of fineness or coarseness of the emulsion (Elworthy & Florence, 1969b). Thus, the mean globule size existing when the second rate comes into play is critical for the “life” of the emulsion. Plots of $\log n$ against time are shown in Fig. 8 for emulsions of anisole in aqueous cetomacrogol 1000 solutions. Slopes

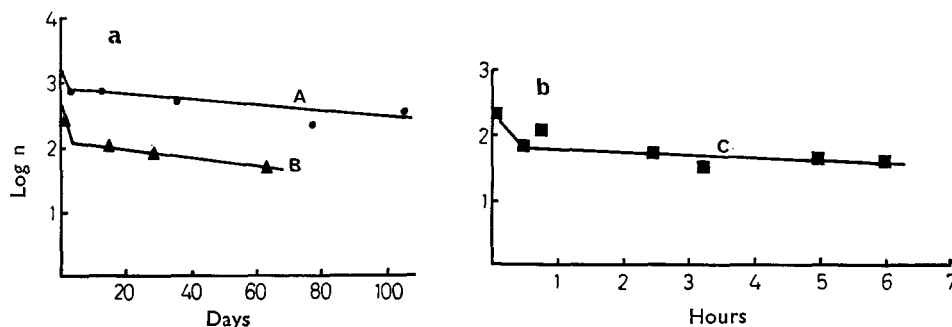


FIG. 8. Plots of $\log n$ (number of particles in arbitrary volume of emulsion, determined by the total volume of the particles sized in the initial sizing) versus time. A. Anisole $\phi = 0.56$, cetomacrogol 1000 1%. B. Anisole $\phi = 0.05$, cetomacrogol 1000 1%. C. (note time in h) Anisole $\phi = 0.20$, cetomacrogol 0.001% (CMC in water = 0.006–0.007%).

corresponding to second rate constants of the order 10^{-6} to 10^{-7} s^{-1} compare well with the values obtained by van den Tempel (1957) for ionic stabilized emulsions, suggesting that at the coalescence stage emulsion stabilization by all surfactant types has a common mechanism.

The present authors (Elworthy, Florence & Rogers, 1971b) made a detailed investigation into the effect of cetyl alcohol on the stability of $C_{16}E_6$ -stabilized chlorobenzene emulsions. Although less surface-active than the main detergent at the chlorobenzene–water interface the hexadecanol resulted in a definite increase in stability. The alcohol affected only the surface area viscosity to any great extent (and not zeta potential or interfacial tension) so it was assumed that the presence of the cetyl alcohol reduced the mobility of the emulsifier molecules so that the probability of desorption was decreased.

Prediction of particle size distribution changes in emulsions and suspensions on the basis of acceptable theories can be useful in testing the theories and serve to show how the magnitude of various forces alters the stability pattern. Recently, Suzuki, Ho & Higuchi (1969) solved the Smoluchowski flocculation rate equations for any initial particle size distribution using digital computation to obtain particle size distribution data as a function of time. It was assumed that the only rate process was the passage of the particles over an electrical barrier. The general method of analysis can be adapted to include the steric–entropic barriers which undoubtedly

exist in non-ionic-stabilized emulsions. However, until the exact role that these forces play in emulsions is elucidated, and the relevant equations to embrace all situations developed, such procedures are perhaps premature. In the cases investigated, when the electrical barrier was small any initial distribution became more polydispersed with time; when the electrical barrier was appreciable the distribution narrowed with time (Suzuki, 1969).

It is, of course, the goal to be able to predict size distributions, and hence actual stability, with a knowledge of a restricted number of experimentally accessible parameters.

DISCREPANCIES BETWEEN EXPERIMENT AND THEORY

The lack of agreement between predictions of the Smoluchowski theory employing theoretical stability ratios (W) and the observed stability of dispersions may arise from the influence of the following factors.

1. *Particle size*

The theory of Verwey & Overbeek predicts an increase in stability with an increase in particle size (Verwey & Overbeek, 1948). Studies of conventional colloids have resulted in maximum flocculation concentrations at $\log W = 0$, but recent studies of dispersions of polystyrene latex particles (Matthews & Rhodes, 1968b; Higuchi, Okada & others, 1963; Swift & Friedlander, 1964) have led to minimum values of W which are a fraction of the Smoluchowski rate for rapid coagulation when particle sizes exceed the size limit of true colloids (*ca* $0.7 \mu\text{m}$). Below about $0.5 \mu\text{m}$ in particle size, deviations from Smoluchowski theory seem to disappear.

The dependence of W on such factors as particle size, electrolyte concentration and valency has been reviewed (Verwey & Overbeek, 1948; Ottewill & Watanabe, 1960a,b,c; Somasundaran & others, 1966). The theory has also been extended to dispersions containing two particle sizes (Hogg, Healy & Fuerstenau, 1966).

2. *Polydispersity*

As emulsion systems are extremely difficult to prepare with a monodisperse particle size the influence of polydispersity on the rate of breakdown is important because most studies are made on polydisperse systems. The effect of polydispersity on the rate of coagulation of dispersions has been investigated by Müller (1926). It has been pointed out that in a dispersion consisting of equal numbers of large and small particles, the smaller particles disappear much more rapidly with time. The impression is that the smaller ones are caught by the larger ones because the collision of a small particle with a large one does not change the concentration of large particles but reduces the concentration of smaller ones. A recent study on hetero-dispersed systems has been reported by Ho & Higuchi (1968). The preferential aggregation and coalescence of small emulsion particles where moderate electrical barriers exist was determined employing equations based on the concepts of DLVO theory. It is shown that small particles may aggregate (or coalesce) with themselves or with larger particles at rates that are ten to fifty orders of magnitude faster than for particles ten times larger. These findings may explain the relatively narrow particle size distributions observed in certain aged emulsions and flocculated suspensions.

Because of the complications introduced by polydispersity, the preparation of uniformly dispersed emulsions is a desirable prerequisite for basic studies on emulsion systems, and, of course, for use for specific purposes such as parenteral emulsions. Nawab & Mason (1958) first reported an electrical dispersion method which has since been widely quoted in textbooks on emulsions as being suitable for the preparation of mono-sized emulsions with 98% by weight of the particles in the range $2.5\text{--}3.5 \mu\text{m}$

as the original authors claimed. No other papers have appeared confirming the original findings. Many experiments have been made in these laboratories in an attempt to repeat Nawab & Mason's results using identical disperse phase and non-ionic detergent, but with little success. Stirring of the continuous surfactant phase has to be so vigorous to incorporate the falling aerosol of oil that the main emulsification appears to occur by stirring and not by the electrical dispersion, hence there is little control over particle size.

Similar experience with another technique has recently been reported by Monk, Matijevic & Kerker (1969). It had been reported by Becher (1967) that a homogenization technique similar to that employed in Brown's Emulsor, produced emulsions with modal diameters in the range 1–2 μm with a very low standard deviation. Monk & co-workers (1969), repeating the work using many variations in the technique, were unable to obtain a narrow particle size distribution and the mean particle sizes determined by light-scattering of a large number of emulsions were much smaller than those quoted by Becher. It is disappointing to find these examples and frustrating to have to test the validity of the methods by trial and error. The optimistic original reports must occur through application of inadequate sizing techniques or through chance occurrences of emulsions with the size distributions quoted for them.

Dispersal of liquid systems by ultrasonics gives fine emulsions rapidly, but not with narrow size distributions. We have used the technique to disperse oils in water in the absence of emulsifier for micro-electrophoresis, and to prepare emulsions with inefficient emulsifiers. Rajagopal (1959) found that emulsions prepared in this way had a similar size distribution to those prepared by colloid mill. The difficulty with the method is the determination of the optimum sonication time, as continuation of sonication past this optimum results in a broadening of the size distribution (Söllner & Bondy, 1935, 1936; Prakash & Ghosh, 1962). Use of the method to prepare parenteral emulsions requires control to ensure that no metal particles from the probe are retained by the product.

Orthokinetic flocculation

Variations in the rates of coagulation of dispersed systems caused by systematic movements (mechanical agitation or gravitation) are referred to as "orthokinetic" flocculation, as opposed to "perikinetic" flocculation due to Brownian motion of the particles. In a fresh suspension, when the particles are small, the coagulation is perikinetic and its rate is slow. When a certain degree of aggregation has been reached, orthokinetic coagulation comes into play and aggregation is much accelerated (Overbeek, 1952).

Refinements of the coagulation theory (Collins & Kimball, 1949; Rice & Whitehead, 1967) account for incomplete adhesion of emulsion drops on collision, reversible flocculation, delayed coalescence and orthokinetic coagulation due to sedimentation.

SPECIAL CHARACTERISTICS OF EMULSION SYSTEMS

Deviations from theory result because of some special properties of emulsion systems. As the DLVO theory explains stability by describing forces preventing the close approach of the disperse particles, where instability can arise from mechanisms other than coalescence and coagulation one can expect deviation between experiment and theory. Such a mechanism of particle growth occurs in emulsions through diffusion of minute portions of oil through the continuous phase in micellar form. The more efficient the solubilizing capacity of the non-ionic stabilizer the more important will be diffusional growth of large particles in the emulsion at the expense of smaller particles. A theory pertaining to this mechanism of emulsion breakdown has been published by Higuchi & Misra (1962). For the case where

there are n_A and n_B particles of radii a_A and a_B respectively, the rate of change of the radius of B is given by:

$$\frac{da_B}{dt} = \frac{DC_\infty K}{\rho a_B^2} \left[\frac{n_A (a_B - a_A)}{n_A a_A + n_B a_B} \right] \quad \dots \quad (34)$$

where $K = (2\sigma M/\rho RT)$, σ = interfacial tension, D = molecular diffusion coefficient, C_∞ = miscibility of an infinitely large drop, ρ = density of disperse phase.

When the two initial particle radii are 0.5 and $1.0 \mu\text{m}$, degradation by diffusional processes is as shown in Fig. 9. Decrease of the diffusion rate of the oil can be achieved by increasing the viscosity of the external phase, or by addition of a third component to the dispersed phase if the additive has a sufficiently low rate of diffusion.

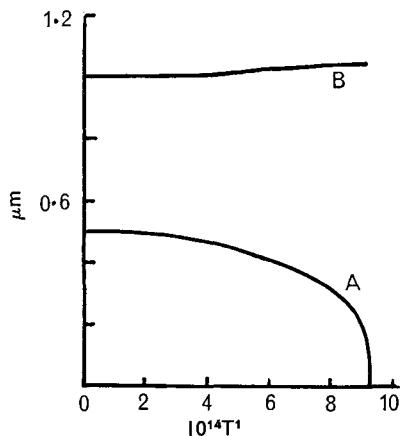


FIG. 9. The degradation of an emulsion initially composed of a mixture of $0.5 \mu\text{m}$ and $1 \mu\text{m}$ radius droplets of equal number concentration, showing the droplet diameters versus a function (T^1) of time. $T^1 = \frac{DC_\infty Kt}{\rho}$. At $T^1 = 4 \times 10^{-14}$ there is about a 10% change in a_A , after $t = 3 \times 10^7$ s (1 year), using $D = 5 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$, $\rho = 1$, even though C_∞ is only $3 \times 10^{-8} \text{ g ml}^{-1}$. From Higuchi & Misra (1962) by permission of the authors and the *Journal of Pharmaceutical Sciences*.

Deformation of the globules on collision can feasibly result in the dissipation of some of the attractive energy but, if the DLVO theory reasonably predicts the behaviour of suspensions of asymmetric particles then it is unlikely that the unknown shape of the deformed particles in an emulsion will give rise to much discrepancy. More likely to be a source of deviation is the possible dissolution of the surfactant in the disperse phase when particles come together with resultant depletion of the surface concentration of stabilizer, unless the diffusion of surfactant from the continuous phase is rapid enough to counteract this tendency. Presumably in systems with high bulk concentrations of emulsifier, replenishment of the surface is rapid; on the other hand, where the solubility of the surfactant in the oil phase is high and the total concentration is high, this inhibits diffusion of the surfactant into the oil. Therefore in both cases high concentrations of surfactant will increase stability.

Spontaneous emulsification

The formation of an emulsion, without agitation or mixing, at the interface between polar oils and aqueous non-ionic solutions has been observed (Elworthy & Florence, 1967). These so-called spontaneous emulsions are undoubtedly the result of fluctuations in the interfacial region as a result of molecular motion. It can be shown that the amplitude of a spontaneous wave in the surface region is greater

by one order of magnitude than the molecular dimensions at low values of interfacial tension, e.g. $\sigma = 1 \text{ mNm}^{-1}$ (Sheludko, 1966). In systems of chlorobenzene or anisole emulsions spontaneously formed only with the more hydrophilic emulsifiers, i.e. those, which lowered σ to 5 mNm^{-1} . Emulsions do not form spontaneously with these surfactants and non-polar oils, an observation which can perhaps be explained by the results of Fig. 2. However, Davies & Haydon (1957) find in many systems no correlation between spontaneous emulsification and interfacial tension; they discuss a number of alternative mechanisms, including disturbances caused by diffusion of surfactant from one phase to another.

The role that supramolecular layers play in stabilizing emulsions of xylene in the presence of non-ionic detergents has been investigated by Nikitina and co-workers (Nikitina, Taubman & others, 1963; Prigorodov & others, 1965).

THE HLB SYSTEM AND EMULSION STABILITY

The arbitrary numbering system devised by Griffin (1949) which is based on the hydrophilic-lipophilic balance (HLB) of the emulsifier, has been used widely in practice as a means of selecting the most effective stabilizer for a given oil. The HLB of a non-ionic detergent is defined (Griffin, 1954) as—

$$(\text{mol \% of hydrophilic group})/5$$

Polyoxyethylene glycols therefore have an HLB of 20. Briefly, each oil has a value of HLB which will provide a stable o/w emulsion; for example, for liquid paraffin it is 10–12. A single surfactant or mixture of surfactants which provides this HLB number will stabilize the liquid paraffin dispersion. Estimations of stability in order to assess the “required HLB” are carried out visually by observation of creaming of a series of emulsions prepared with a range of emulsifying agents. While this number has been invaluable for rapid choice of an emulsifier, its use still involves empirical standards. The HLB system neglects the concentration dependence of stability, as has been pointed out by Elworthy & Florence (1969c). Riegelman & Pichon (1962) have drawn attention to other drawbacks in its use; for example, while creaming is a criterion of instability in commercial formulations it is by no means the only one. It is imperative, they point out, to recognize that stability towards creaming is dependent on the rheological character of the emulsion far more than on the interfacial characteristics of the interfacial film. The influence of surfactants on the viscosity of the continuous phase is therefore of primary importance in this case. Richards & Whittet (1955) were able to obtain stable liquid paraffin-in-water emulsions with surfactant combinations having an HLB as low as 3.9. The stable emulsions were all thixotropic indicating that the surfactants were contributing to the structural viscosity of the system and thereby contributing to stability by preventing creaming.

Hadgraft (1954) also has obtained stable liquid paraffin emulsions with cetyl alcohol-cetyl polyoxyethylene ether combinations having HLB values as low as 1.9; this stability undoubtedly arises from the viscous nature of both interface and bulk phases. Recent rheological measurements on similar systems confirm this view (Talman & others, 1967).

The conclusion is that the HLB system will give a quick answer to a practical problem, but will offer little scope for basic improvements on the formulation. Vold (1969) has written “it is intriguing that HLB numbers of mixed non-ionics are additive according to the proportions of each present. One is left with the conviction that the HLB number has a rational interpretation and with a sense of frustration in not being able to show its origin conclusively”.

MICROEMULSIONS

Microemulsions or micellar emulsions are systems, usually optically clear, which can be considered to consist of oil or water laden micelles in aqueous or oily continuous media respectively. Schulman, Stoeckenius & Prince (1969) and more recently Adamson (1969) and Tosch, Jones & Adamson (1970) have contributed a large amount to the subject. Schulman emphasized that micellar emulsions are systems in true equilibrium, it being proposed that the components of the surface films in these systems produce a negative interfacial tension at the hydrocarbon water interface (Schulman & Montagu, 1961). On mixing, a spontaneous interfacial area increase occurs until zero interfacial tension is attained. In Adamson's (1969) model for micellar w/o emulsions stability is accounted for by a balance of the Laplace pressure ΔP , related to the micellar radius r and interfacial tension σ by

$$\Delta P = 2\sigma/r \quad \dots \quad (35)$$

and the osmotic pressure difference $\Delta\pi_{os}$ between the inside and outer region of the micelle which arises from the difference in ionic concentration. The osmotic pressure difference is positive hence in the presence of water an indefinite swelling of the micellar units is produced until equilibrium is reached when

$$\Delta\pi_{os} = 2\sigma/r \quad \dots \quad (36)$$

Microemulsions, prepared from benzene and water using 5 or 10% polysorbate 20-1% Span 20 blends, having dispersed phase volumes up to 0.406 had viscosities which could not be represented by any simple equation which merely related viscosity and dispersed phase volume (Matsumoto & Sherman, 1969). Particle diameters, measured by light-scattering, were in the range 54-125 nm. Viscosity depends on both particle size and the viscosity of the particles, the swollen micelles behaving not as rigid spheres although circulation within the micellar droplets is undoubtedly restricted.

Why should there be this range of particle sizes in these emulsions? If the non-ionic micellar species are essentially monodisperse as they would appear to be (Attwood, Elworthy & Kayne, 1968), then the microemulsion, if formed by growth of solubilized micelles, might also be expected to be reasonably monodisperse. However, this would not be so if formation of the emulsion is by random dispersion, although if the particles are thermodynamically stable, as is suggested, then it would seem that there should be only one equilibrium size.

INVERSION

In stable emulsion formulations, inversion can be induced by increasing the disperse phase volume, ϕ , to a round 0.7. This is a phenomenon not accounted for in stability theories. The exact value of ϕ at the inversion point depends on the surfactant present and its concentration. The viscosity of a series of chlorobenzene-in-water emulsions has been determined in this laboratory as a function of cetomacrogol 1000 concentration and ϕ . Some unpublished results are shown in Fig. 10 which indicate that the higher the concentration of cetomacrogol in the system the lower the phase volume at inversion. Becher (1958) obtained this trend with low HLB emulsifiers (e.g. sorbitan monoesters) but, in general, with polyoxyethylated compounds the inversion point increased with increasing concentration. In a recent paper, Shinoda & Saito (1969) described emulsification by a phase-inversion method, this being the preparation of a stable, finely dispersed emulsion by rapid cooling of an emulsion at its phase inversion temperature. This differs from the normal emulsification by inversion which involves alteration of phase volume, for example, by addition of water to a w/o emulsion to form an o/w type. It was concluded that the optimum HLB for stability of an emulsion cannot be obtained accurately from HLB-stability

data but that, as stability is sensitive to temperature near the phase-inversion temperature (PIT), the selection of an emulsifier according to the PIT may be more reliable.

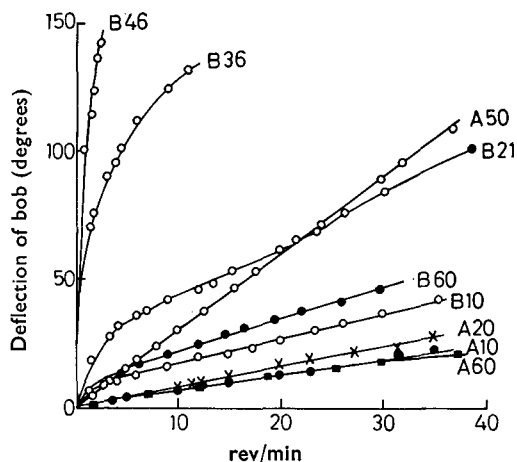


FIG. 10. Viscosity results obtained with a Couette viscometer on a series of emulsions of chlorobenzene stabilized A with 5% cetomagrogol 100 and B with 10% cetomagrogol 1000. Results are given in arbitrary units: deflection in degrees of inner bob versus rev/min of outer container. Phase volumes for both series are appended to lines as percentage oil. The diagram shows the inversion of A and B at a phase volume about 0.60 (see low viscosity of this one). B inverts before A. (Florence, A. T. & Guthrie, W., unpublished.)

Inversion of emulsion type can occur through temperature changes such as those encountered during sterilization or manufacturing procedures. Shinoda & Arai (1964) found that the more soluble a non-ionic emulsifier in a particular hydrocarbon, the lower was the phase inversion temperature of the emulsion. Hence, as Benerito & Singleton (1956) point out, emulsifiers in systems which have to withstand elevated homogenization or sterilization temperatures must be more hydrophilic than those found satisfactory at normal temperatures. However, the phase inversion temperature can be manipulated to a considerable extent by altering the composition of the oil phase. This is strikingly illustrated in Fig. 11 from the work of Arai & Shinoda (1967).

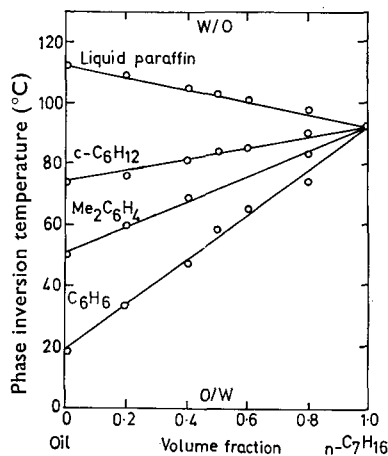


FIG. 11. The effect of the mixture of *n*-heptane with various oils on the phase inversion temperatures of emulsions stabilized with 3% w/w in water of polyoxyethylene (9.6) nonyl phenyl ether. Reproduced from Arai & Shinoda (1967) by permission of Academic Press.

Viscosity measurements have given information of the interaction forces operative between emulsion globules (Albers & Overbeek, 1959a,b; Doroszkowski & Lambourne, 1968) and the physical state of the continuous phase (Talman & others, 1967). The rheology of emulsions has been dealt with thoroughly by Sherman in two reviews (Sherman, 1964, 1968) and in one symposium volume (Sherman, 1963b) so there is no need to go into great detail here. It is sufficient to say that the apparent viscosity of an emulsion (η_{∞}) is dependent on phase volume (Fig. 10), mean particle diameter and particle size distribution (Richardson, 1953a,b), the stabilizing film and surfactant concentration. The control of the rheological properties of emulsions and creams is an important pharmaceutical problem.

Sherman (1963a) reports that multiphase globules of increasing number, size and complexity appear on increasing the concentration of sorbitan monolaurate and oil in liquid paraffin-in-oil emulsions. The multiphase globules influence η_{∞} through their effect on the globule size distribution and ϕ . At $\phi = 0.73$ and 6% surfactant concentration, inversion takes place to a w/o emulsion, the relative viscosity falling from 78.6 to 1.46 (as in Fig. 10). The resultant emulsion contains many multiple phase globules. Mulley & Marland (1970) discussed conditions in non-ionic-stabilized emulsions leading to multiple drop formation. Herbert (1965) utilized the lower viscosity of multiple emulsions to prepare parenteral mineral-oil antigen formulations. The incorporation of antigen into the aqueous phase of a w/o emulsion was proposed by Freund & Walter (1944) as an effective means of producing a prolonged antibody-response. Influenza vaccines prepared in this way, although effective (Hobson, Lane & others, 1964) have the disadvantage of high viscosity, producing problems in the syringe and *in vivo*. Herbert (1965), however, produced low-viscosity emulsions by ultrasonically redispersing w/o emulsions (containing antigen) in an aqueous phase containing a water-soluble surfactant. Samples of the multiple emulsions were stable for more than a year after storage at 56° and then at room temperature, whereas the original w/o emulsions broke down within a few months at 4°. The subcutaneous depots were diffuse and not discrete as with the viscous w/o preparation. The antibody response of mice to the multiple emulsion was superior to that of the original emulsion and the effect was well maintained. Berlin (1960) has found an inverse relation between antibody response and viscosity of w/o formulations, and there was some evidence of this trend in the system described by Herbert.

The factors affecting parenteral water-in-oil emulsions as adjuvants have been reviewed by Lazarus & Lachman (1967).

EMULSIONS AND THIN LIQUID FILMS

Because of the complexities of the real emulsion, attempts have been made to find model emulsion systems for experimental work. Latexes have been used and now that these are available commercially in monosized preparations these are very attractive systems. But, for the study of the molecular processes at work in stabilization and coalescence, foams and soap films serve as useful analogues (Sheludko, 1966, 1967). Between two emulsion globules at close approach there is left a thin film of continuous surfactant phase, the behaviour of which determines the probability of coalescence. Too often this film is neglected and the surface film of surfactant on each globule is viewed in isolation. The closest similarity to the emulsion situation is attained with aqueous soap films separating two identical oil phases (see Fig. 12), but much can be learned which has a bearing on emulsion stability from a study of soap films in air.

It is most likely that the rate of thinning of the films between the oil globules determines the coalescence probability, although thin soap films in air take minutes

to thin by a process of marginal regeneration (Mysels, Shinoda & Frankel, 1959) and vertical films of non-ionic detergents in decane thin more slowly than in air (Florence, unpublished). Undoubtedly the film between globules is under a momentary external pressure resulting from the collision of the droplets* and the suction

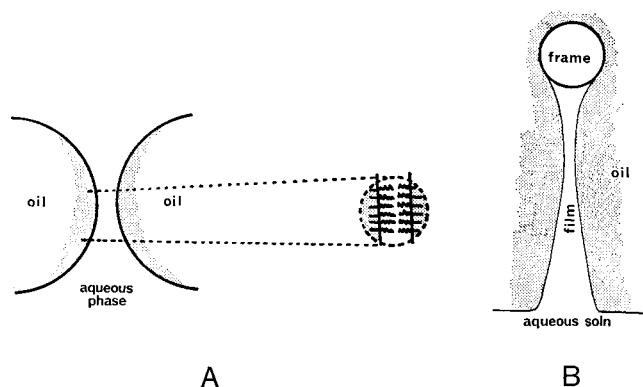


FIG. 12. A. Diagrammatic representation of the soap film between two oil globules and the arrangement of the non-ionic detergent molecules at equilibrium. B. Representation (cross section) of aqueous detergent film drawn up on a glass frame in oil for optical measurements on thickness and rates of thinning. Properties of films corresponding to w/o emulsions have been studied by Sonntag & Klare (1967).

by the Plateau borders in a film of $1 \mu\text{m}$ diameter will be much greater than in a macroscopic film. However, there is a need for the mechanisms of thinning of aqueous films in oil to be elucidated. van den Tempel (1958) measured the drainage and equilibrium thickness of the thin film between drops of liquid paraffin by an optical method and found that his thickness results agreed within experimental error with those of Derjaguin & Titjevskaja (1954) for liquid films between air bubbles (10–15 nm). van den Tempel's results appear to indicate the presence of repulsive forces other than those of electrostatic origin at distances below 125 nm.

Free aqueous films of the commercial non-ionic nonylphenyl- E_{20} (NP 20) in cyclohexane, studied by Netzel & Sonntag (1966), are thicker at equilibrium than those in air (Table 3), although at high electrolyte concentrations the thickness approaches

Table 3. *Equilibrium thicknesses of aqueous films in cyclohexane.*

Compound	Additive	Thickness (nm)	Reference
NP-20*	10^{-2} M KCl	26.0	Netzel & Sonntag (1966)
	7.5×10^{-3} M KCl	28.0	Idem
	2.5×10^{-3} M KCl	46.5	Idem
HD-15†	10^{-1} M NaCl	9.8	Duyvis (1962)
	10^{-2} M NaCl	29.1	Idem
	7×10^{-3} M NaCl	35.4	Idem
	3×10^{-3} M NaCl	55.3	Idem

* Length of molecule = 9.0 nm. Thickness of black film of OP-20 = 10.0 – 10.5 nm.

† Length of molecule = 7.8 nm. Thickness of black film in air = 11.0 nm.

that of the film in air (Duyvis, 1962). Sonntag & Netzel (1966) determined the critical thickness of aqueous non-ionic films between various oil phases. The thickness at rupture increases with increasing concentration of salt and varies with the organic

* A device for producing controlled collisions between pairs of droplets which might be useful in studies of this has been produced by Park & Crosby (1965).

phase, e.g. for octane $\delta_{\text{crit}} = 18.5$ nm, chlorobenzene 19.5 nm and for cyclohexane 21.0 nm.

It is obvious that emulsion stabilizers do not act by maintaining a thick liquid film between the globules but that they function by decreasing the probability of the rupture of the film by a factor of 10^6 – 10^8 in "stable" systems.

Sonntag, Puschel & Strobel (1967) suggested that the emulsifying power of a surfactant for a given system is characterized by the concentration of the formation of stable black films (C_{bl}). A low value of C_{bl} , such as is given by nonyl phenol polyoxyethylene oxide adducts and cetyltrimethylammonium bromide, is indicative of good stabilizing properties.

Sheludko (1966) considers it uncertain why black films appear at C_{bl} or why low-molecular weight foaming agents should not form these films. He suggests that black "spots" appear in films in air where a dense adsorption monolayer begins to form, although just which property of the monolayer is responsible is not clear.

Derjaguin, Vorpajjeua & others (1964) has postulated a theory to account for the non-contact between dispersed particles arising from an "additional force", or "disjoining pressure" exerted at right angles to the plane of the liquid film between the particles. Thus, it acts adjacent to the surface tension which exists along the plane of the interface. Equation (7) may be modified to give

$$\frac{(\Delta\mu)_{\text{E}}}{V_1} = \frac{\Delta\mu - (\Delta\mu_1)_{\text{ideal}}}{V_1} = 2 \left(\frac{d\gamma}{H} \right) = -P \quad \dots \quad (37)$$

where P is the disjoining pressure for particles at separation H , with surface free energy, γ . Equation (37), therefore, equates the disjoining pressure causing repulsion between the particles with the excess osmotic pressure in the overlapping volume. The thermodynamic view of disjoining pressure does not require the molecular origin of the forces to be specified. The main part of the disjoining pressure is due to forces of non-electrical origin, a conclusion supported by the fact that the pressure operates in the case of non-conducting liquid films and the absence of ions (Frenkel, 1955). A positive disjoining pressure is essential for stable films to exist. The unusual stability of thin liquid films in the presence of a stabilizer is due to their elasticity—which results from the dependence of their surface tension on their thickness, stretching depleting the surface layer and increasing tension [but see Sheludko (1966) for his views on role of elasticity. See also Kitchener & Cooper (1959)]. Frenkel (1955) suggests that polymolecular films must be still more effective owing to their higher elasticity. Unfortunately, in real emulsion systems polymolecular arrangements often lead to bridging of globules and hence to excessive creaming.

A possible mechanism for the spontaneous rupture of thin, free liquid films has been the subject of work by Vrij (1966), Vrij & Overbeek (1968) and Sheludko (1962). The latter proposed that instability of thin liquid films arises from spontaneous deformations on the surface which result in increased van der Waal's forces (due to closer approach of surface at some points) in spite of an increase in surface area. Vrij & Overbeek (1968) give as the critical thickness of a film of radius r , before rupture

$$\begin{aligned} h_{\text{crit}} &= 0.845 \left[\frac{A^2 r^2}{320\pi^2 f\sigma P} \right]^{\frac{1}{4}} \\ &= 0.267 (A^2 r^2 / f\sigma P)^{\frac{1}{7}} \quad \dots \quad (38) \end{aligned}$$

and the critical wavelength for rupture, Λ , as

$$\Lambda_{\text{crit}} = 2\pi \sqrt{\frac{\pi\sigma h^4}{A}} \quad \dots \quad (39)$$

If $A = 10^{-19}$ J, $\sigma = 10$ mNm $^{-1}$, and $h = 1$ μ m, Λ is 0.35 cm on a macroscopic film with a linear dimension of the order of 1 mm or 1 cm. Λ_{crit} will be reached when the thickness has decreased below 1 μ m. For a thin film existing between two emulsion droplets in a system of high phase volume when the droplet size is around 1 μ m, its thickness has to decrease below 20 nm before fluctuations can make it unstable. There appears to be no dependence of the critical thickness on the viscosity of the film (Sonntag, 1966). Experiments have not, however, shown the dependence of h_{crit} on surface tension suggested by equation (38) when σ was varied from 4 to 16 mNm $^{-1}$ (Sonntag, 1966).

Many investigators in considering mechanisms of film drainage have assumed that the interfaces of the film were immobile and that flow occurs between rigid "walls". Lee & Hodgson (1968) have dealt in more detail with other possibilities involving free movement, retarded mobility and complete immobility of the interface and have considered these conditions in relation to coalescence of liquid droplets. The three limiting conditions can represent the transition between sparsely covered surface and completely immobile surface having two surfactant components.

A theory of coalescence developed by Marrucci (1969) is probably applicable to non-ionic stabilized emulsions as it neglects electrical forces. The process of thinning is proposed to consist of two stages. The first involves an extremely rapid thinning of the film down to a quasi-equilibrium thickness, the time taken to reach this stage being negligible compared with the time of the second stage, thinning from quasi-equilibrium to rupture. The time of coalescence, governed by this second rate is an inverse function of the diffusion coefficient of the surfactant as diffusion at the border of the film controls the thinning rate. (The concentration in the film is different from that outside the film.)

CONCLUSIONS

It will probably be by further study of thin liquid films that progress will be made in our understanding of coalescence, the phenomenon that controls the ultimate stability of emulsions. The conditions and factors leading to flocculation and hence rapid creaming or sedimentation have been largely dealt with by the DLVO theory and theory of interaction of adsorbed layers. In an ideal situation theory should be able to predict size distribution at a specified emulsion age so that factors such as emulsifier concentration, emulsifier type and additive concentration can be altered to produce predictable distributions which change minimally with time. Until the theory has been developed that far, formulators will be able to predict less empirically from extant equations those factors which are likely to lead to stability and to measure more meaningful parameters in development stages of emulsion formulation. If stability can be successfully controlled then it is as pertinent to investigate the factors involved in the production of emulsions of a specified particle size distribution as it is to investigate the factors maintaining that distribution: work in both directions should succeed in reaching the degree of control most desirable in pharmaceutical systems.

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