

Liquid Crystalline Phases in Aerosol Formation II: Influence of Liquid Crystalline Phases on Foam Stability

G. JEDERSTRÖM*, L. RYDHAG, and S. FRIBERG[▲]

Abstract □ Aerosol foam stability was determined by visual observation of time-dependent change in foams of different propellant compositions. Compositions that contained both a liquid crystalline phase and a liquid phase gave rise to foams with pronounced stability compared with those where only a liquid phase was present.

Keyphrases □ Aerosol foams—effect of liquid crystalline phases on foam stability □ Foam stability, aerosols—effect of liquid crystalline phases □ Propellant compositions—effect of liquid crystalline phases on foam stability

The stability of thin films is of importance for foam stability and the stability of emulsions against coagulation from the flocculated state. Extensive research has been undertaken in order to understand the reasons for the stability of such films. Generally, the Derjaguin, Landau, Verwey, and Overbeek (DLVO) theory (1, 2) has been applied to the phenomena (3, 4), giving four factors (3): (a) the Laplace capillary suction pressure, (b) the electrical double-layer repulsion, (c) the long-range Van der Waals pressure, and (d) "steric hindrance" of close-packed monolayers.

The last factor is not based on theory but is "vaguely described as the resistance from close-packed monolayers to lateral flow" (3).

The DLVO theory is obviously insufficient for an explanation of emulsion stability against coagulation when the continuous phase is nonpolar; the stability of water/oil emulsions shows no dependence on the surface potential (5).

The importance of chemical associations of different emulsifiers was observed early (6, 7), and recently attempts have been made (8) to relate the stability of aerosol foams to the formation of "molecular complexes." This hypothesis was criticized (9); it was demonstrated that molecular complexes formed by

Table I—Initial Composition of Samples

Series	Sample Number	C ₈ OOH, wt. %	C ₂ F ₄ Cl ₂ , wt. %	Water, wt. %	C ₈ NH ₂ , wt. %
B (Fig. 2a)	1	0	29.69	23.40	46.85
	2	10.30	31.51	19.38	38.77
	3	18.18	31.51	16.76	33.52
	4	26.06	35.15	12.92	25.85
	5	41.20	31.51	9.08	18.17
	6	49.69	28.48	7.26	14.53
C (Fig. 2b)	1	0	32.11	18.73	49.13
	2	7.87	32.72	16.39	42.99
	3	26.66	30.30	11.87	31.14
	4	37.57	30.90	8.69	22.81
	5	47.87	28.48	6.52	17.10
	6	56.35	33.33	2.84	7.45
D (Fig. 2c)	1	0	27.27	14.39	58.32
	2	11.51	28.48	11.87	48.12
	3	19.39	27.87	10.43	42.28
	4	29.69	29.09	8.15	33.05
	5	40.60	32.72	5.27	21.38

the emulsifiers bore no relation to emulsion stability. The importance lies in the presence of liquid crystalline phases (10, 11) in which the emulsifiers, water, and the oil phase are all associated into an ordered structure.

The importance of the association into liquid crystalline phases for foam stability was also demonstrated recently (12). Stable foams actually may be prepared from hydrocarbons when small amounts of water are present, associated into a liquid crystalline phase with the surfactants (13). The importance of liquid crystalline phases for the stability of foams from aqueous solutions (14) and also for the rate of thinning of thin films (15) has been shown independently.

Since the technical and pharmaceutical importance of these facts is obvious, an investigation into the application of these mechanisms to aerosol foam formulations was conducted. The phase equilibria of the propellant compositions were published earlier (16) (Fig. 1).

EXPERIMENTAL

Materials—The water was twice distilled. 1-Aminooctane¹ (C₈NH₂) (purity by GLC >99%), octanoic acid² (C₈OOH), and a propellant³ were used.

Foam Stability—The acid, amine, and water were weighed into glass containers which were sealed and cooled to -20°. The liquid crystalline phase involved in the experiments does not solidify at temperatures above -28°, so no crystallization problems occurred. At that temperature (-20°), the propellant (C₂F₄Cl₂) was added and the pressurized packaging, the aerosol, was formed as the temperature slowly rose to 20°. The container⁴ was shaken before spraying to obtain as homogeneous conditions as possible between phases

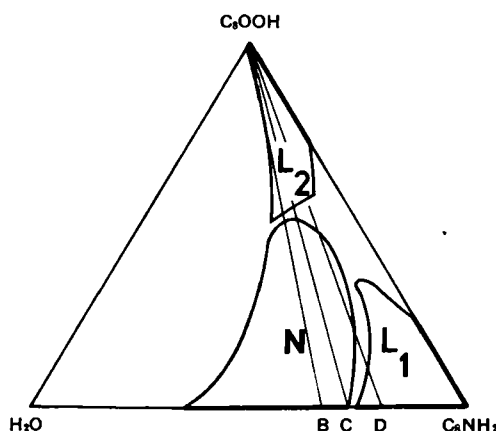


Figure 1—Phase regions in the water (H₂O)—octylamine (C₈NH₂)—octanoic acid (C₈OOH) system. The lines ending at B, C, and D denote series used in the aerosol experiments. L₁ and L₂ = liquid isotropic phases. N = liquid crystalline, lamellar, "neat" phase.

¹ Fluka puriss.

² Eastman Kodak p.a.

³ Cryoflurane, Frigen 114, Hoechst.

⁴ Valve, English precision; cup, LL till plate conical; stem, 0.50 cm. (0.20 in.) × 2; housing, 2.03 cm. (0.80 in.) PF with 0.50 cm. (0.20 in.) VPT, fitted with diptube; and actuator, J.S. 0.40 cm. (0.16 in.) stepped.

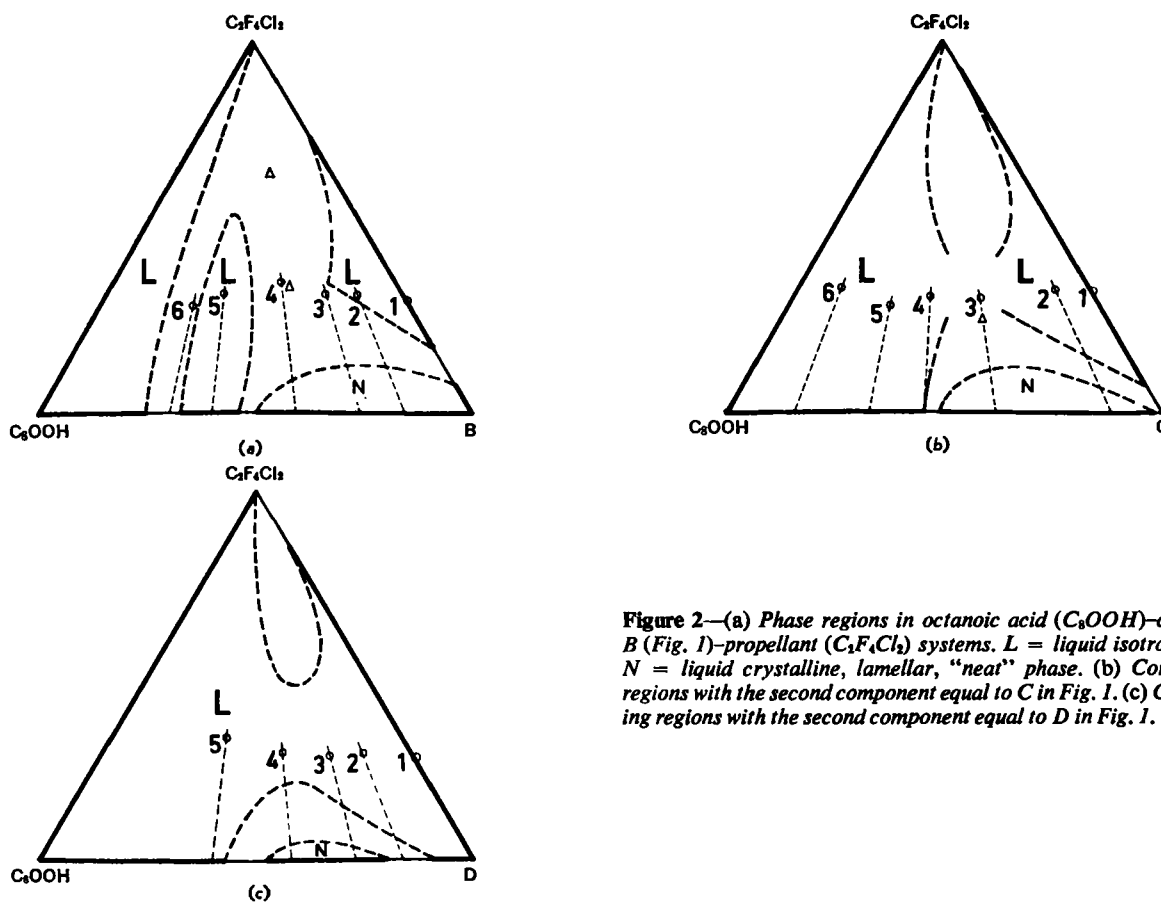


Figure 2—(a) Phase regions in octanoic acid (C_8OOH)—composition B (Fig. 1)—propellant ($C_2F_4Cl_2$) systems. L = liquid isotropic phases. N = liquid crystalline, lamellar, "neat" phase. (b) Corresponding regions with the second component equal to C in Fig. 1. (c) Corresponding regions with the second component equal to D in Fig. 1.

in the aerosol. The aerosol foams were extended into conical test tubes to facilitate the determination of drainage rates. The samples were photographed, and the foam height was measured on the photographs as a function of time.

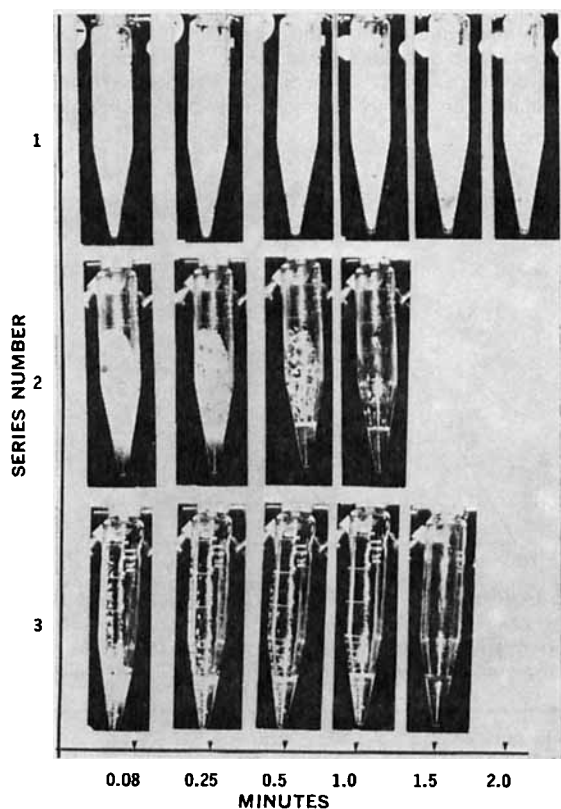


Figure 3—Photographs showing the foam height as function of time.

RESULTS

Phase Equilibria—The phase regions when the propellant is added to compositions C_8OOH -B, C_8OOH -C, and C_8OOH -D in Fig. 1 are given in Fig. 2, where the actual compositions prior to foam extrusion are marked on the diagram (Table I). The phase regions and their determining factors were described previously (16).

Foam Stability—Figure 3 demonstrates the general features of the photographs obtained. There usually was a pronounced difference between stable and unstable foams; the height of the former was reduced to less than half the initial value in less than 10 sec. while the corresponding time for the latter was several minutes. The foam in Series 1 showed no change over 2 min. while the others completely collapsed in 10 sec.

Diagrams of foam height *versus* time on a linear scale (Fig. 4) consequently show two groups of curves; one group for stable foams and one group at zero height for unstable foams. A logarithmic time scale was used to compare fast and slow foam height decay in identical diagrams.

Figure 5 shows the foam height for Samples 1–6 marked in Fig. 2a. The four samples containing a liquid crystal in the aerosol prior to addition of the propellant gave rise to stable foams. The foams from the two samples in which there were no liquid crystals were unstable, with half-lives of less than 10 sec.

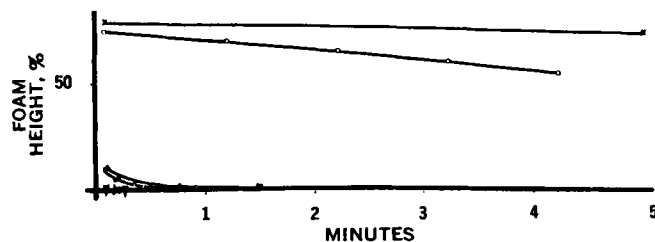


Figure 4—Foam height versus time in a linear scale (compositions according to Fig. 2b). Key (Series): Δ , 1; \circ , 2; \times , 3; \square , 4; ∇ , 5; and \star , 6.

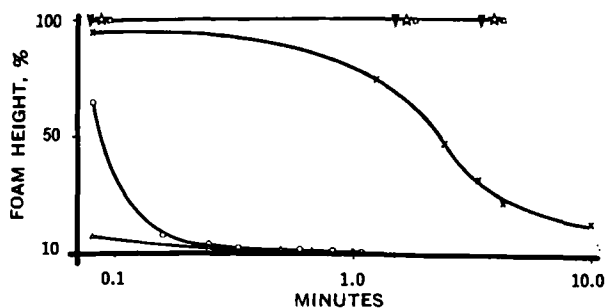


Figure 5—Foam height versus logarithm of time (compositions according to Fig. 2a). Key (Series): X, 1; ☆, 2; ▼, 3; □, 4; ○, 5; and △, 6.

The second series in Fig. 2b contained six samples. Of the three with liquid crystals present in the aerosol composition (16) (exclusive of propellant), the one without acid gave rise to unstable foams and the other two to stable foams (Fig. 6). All samples containing no liquid crystals produced unstable foams. The samples in Series D showed the same general pattern; the foams from the two samples containing a liquid crystalline phase, prior to addition of propellant, were more stable than any of the other samples (Fig. 7). Sample 3 was not extremely stable, with a half-life of about 20 sec., but the difference from the samples with no liquid crystalline phase was distinct; all of the latter had half-lives of less than 5 sec.

DISCUSSION

The results were analyzed with regard to both the practical subject of reliable compositions for foam aerosol packings and the theory of stability of thin films.

Composition Method—In all cases, foams from samples originally containing only liquid phases gave completely unstable foams. The samples that contained a liquid crystalline phase prior to addition of the propellant gave rise to extremely stable foams with two exceptions. These two samples both had original compositions close to the phase limit and, furthermore, no liquid crystalline phase could be found in the collapsed foam. This probably was due to the fact that the phase diagrams in Figs. 1 and 2 were obtained under equilibrium, while the system was not in equilibrium when foamed. Original compositions close to the phase limit could well be expected to change their composition to outside the phase region during the foaming process.

It is also necessary that parts of the propellant should be incorporated into the liquid crystalline phase. Such a condition automatically implies stability only for compositions a few percent inside the liquid propellant region.

In themselves, these results indicated a simple method for the reliable evaluation of foam stabilizers for aerosol foams. Essentially, the composition prior to addition of propellant should contain a liquid crystalline phase and this phase should be able to include some of the propellant. This method will help avoid problems associated with impurities in the emulsifier which are encountered in practice. Variations in impurity level may well change the limits of the liquid crystal region, causing an unstable foam. This problem can be avoided by using initial compositions that are centrally positioned in the liquid crystalline region, where composi-

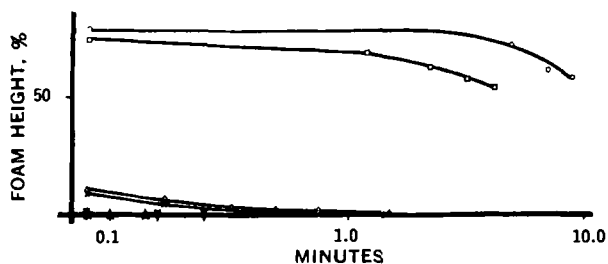


Figure 6—Foam height versus logarithm of time (compositions according to Fig. 2b). Key (Series): △, 1; □, 2; ○, 3; X, 4; ▼, 5; and ☆, 6.

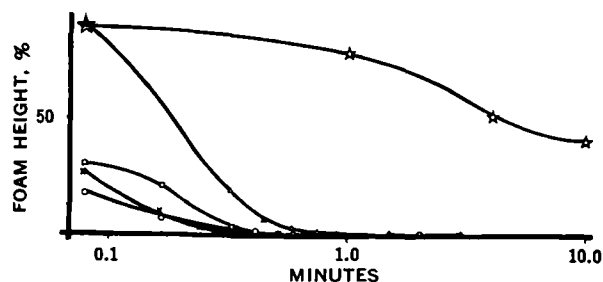


Figure 7—Foam height versus logarithm of time (compositions according to Fig. 2c). Key (Series): ○, 1; □, 2; △, 3; ☆, 4; and X, 5.

tions would be expected to show optimal resistance to changes in the properties of the emulsifiers due to variations in composition.

Stability of Thin Films—A thin film is never in the state of lowest free energy. The reason why it is stable is the presence of one or several minima in the potential energy versus thickness function. These energy minima may sometimes be extremely shallow. The presence of an energy minimum implies a small rise of the free energy in the system for small changes in its dimensions.

The final bursting of a thin film in equilibrium takes place due to small disturbances of it. In case these small changes in dimensions are not sufficiently self-damping, bursting takes place. An increase in energy when the film is disturbed may be related to the surface free energy, γ , and to the potential energy, V , which depends on the thickness of the film. According to Vrij (17), the change in free energy:

$$\Delta G = \iint \left\{ \frac{1}{2} \gamma \sum_{ij=1}^2 \left(\frac{\partial z_i}{\partial x_j} \right)^2 + \frac{1}{2} d^2 V / dh^2 \sum_{i=1}^2 z_i^2 \right\} \prod_{j=1}^2 dx \quad (\text{Eq. 1})$$

where z denotes vertical changes in the upper ($i = 1$) or lower ($i = 2$) plane of the horizontal film. The indexes j indicate the two Cartesian horizontal coordinates in these planes.

In hydrocarbons or even polar organic solvents, the surface energy is low and has a minor importance; the first term in Eq. 1 is of little importance. This is one reason why foams from hydrocarbons have not been taken into account (3) when the stability of thin films was treated. The present results, which show the importance of the presence of a liquid crystalline phase, may help explain the stability of thin films in hydrocarbons by focusing attention on the connection between the characteristic structure of liquid crystals and the second term in Eq. 1.

The lyotropic liquid crystalline phases are mainly lamellar or form a hexagonal array of cylinders. The reason why foams from hydrocarbons are stable when two-phase systems, solution-liquid crystalline phase, are formed is probably to be found in the fact that the structure of the thin film consists of a central part of liquid crystalline structure surrounded by layers of a nonpolar liquid. In such a structure, the surface energy of the system has no importance whatsoever for the stability. The hydrocarbon surface of the film has low surface energy which does not change with the geometric dimensions.

Changing the geometrical dimensions of the film will, on the other hand, require considerable energy additions due to the fact that the liquid crystalline phase spontaneously forms ordered structures. If z_1 and z_2 have the same size in Eq. 1, the alteration in the geometry is bending of the film. The change is resisted by viscous forces only. These are of a different magnitude from those found in a solution, but intuitively the influence of changes of this kind is of less importance than those encountered when z_1 and z_2 have different signs. That implies a thinning of the film, which means that the layers or cylinders constituting the liquid crystal must be moved on top of each other. Such a mechanism includes either a transport of amphiphilic molecules through the lipid layer part of the liquid crystalline phase or a simultaneous motion of a high number of molecules. Both of these mechanisms require a high free energy and have small probability in a liquid crystalline phase compared to conditions in a liquid phase.

The investigations will be continued on systems of mixed emulsifiers.

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* Present address: Pharmacia Co, Box 604, S-751 25 Uppsala 1, Sweden.

▲ To whom inquiries should be directed.

Aggregations of Certain Nucleosides in Aqueous Solutions from Osmometric Measurements: Theory

HANNA N. BORAZAN

Abstract □ Two models, the mononuclear and multinuclear, are proposed for self-aggregating systems such as dilute aqueous solutions of 2'-deoxyadenosine, 2'-deoxyguanosine, uridine, cytidine, and thymidine, which are characterized by two linear slopes in plots of their osmolal *versus* total molal concentrations. Their first slopes indicate a monomeric behavior and a formation of critical micelle-like concentrations. By correlating the results of both models on a semiempirical basis, theoretical curves were generated that agree with previous experimental work. Equilibrium constants, osmotic coefficients, and concentrations of various associated forms can be calculated.

Keyphrases □ Nucleosides in aqueous solution, self-aggregation—osmometric measurements, theoretical curves compared to experimental data, calculation of equilibrium constants, osmotic coefficients, and species concentrations □ Osmometric measurements—self-aggregation of nucleosides in aqueous solution, theoretical curves compared to experimental data □ Aggregation of nucleosides in aqueous solution—osmometric measurements, theoretical curves compared to experimental data

The thermoelectric osmometer developed by Goyan and Johnson (1, 2) has been improved and used to study dilute aqueous solutions of caffeine and other substances of pharmaceutical interest (3). The measured osmotic property plotted against molal concentration resulted in two linear slopes for many substances. The point of break was sharp whenever it occurred and was regarded as evidence of a critical micelle concentration (CMC). The molal concentration where this break occurs is a critical concentration in that it is a property of a substance. It evidently has been overlooked by other

workers, probably because of the difficulty of exploring the concentration range between 0.01 and 0.10 *M*. Later, Borazan (4) and Borazan and Goyan (5) extended past work (6, 7) into this region of concentration and included other compounds. The characteristic break between linear slopes was found for very dilute solutions of 2'-deoxyadenosine, 2'-deoxyguanosine, uridine, cytidine, and thymidine.

This paper presents some theoretical considerations in an effort to explain experimental results reported previously (3-5). An attempt is also made to recalculate equilibrium constants that might hold over a wider range of concentration than those given previously (8, 9).

THEORY

An attempt is made to explain the two intersecting linear slopes determined experimentally, when plotting a colligative property *versus* molal concentration (3-5), by using a simple mathematical model:

$$nA = A_n \quad (\text{Eq. 1a})$$

$$K = (A_n)/(A)^n \quad (\text{Eq. 1b})$$

The osmolal, *o*, and total molal, *m*, concentrations are given by the equations:

$$o = (A_n) + (A) \quad (\text{Eq. 2})$$

$$m = n(A_n) + (A) \quad (\text{Eq. 3})$$

In Eqs. 1-3, *A* represents the monomer and *A_n* represents the associated form. Parentheses indicate molal concentration. By