

Effect of Inorganic Additives on Solutions of Nonionic Surfactants V: Emulsion Stability

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Received June 14, 1982 from the School of Pharmacy, Temple University, Philadelphia, PA 19140.

Accepted for publication October 7, 1982.

Abstract □ Electrolytes often break emulsions to which they were added as active ingredients, adjuvants, or impurities. The stability of oil-in-water emulsions containing octoxynol 9 NF as the emulsifier and various added electrolytes was investigated by measuring droplet size, turbidity, and oil separation on storage at various temperatures and in a centrifugal field at 25°. Electrolytes were added to hexadecane emulsions after emulsification (direct addition); alternatively, hexadecane was emulsified in octoxynol 9–electrolyte mixtures (reverse addition). Xylene emulsions were prepared by direct addition only. Hexadecane emulsions containing 0.10% octoxynol 9 were considerably more stable than xylene emulsions containing 0.60% because the surfactant is practically insoluble in hexadecane, but miscible in all proportions with xylene. An emulsifier soluble in the disperse phase as well as the continuous phase evidently forms less stable interfacial films. The electrolytes investigated were sulfuric and hydrochloric acids, magnesium nitrate, and aluminum nitrate, which salt octoxynol 9 in by complexation between its ether groups and their cations; sodium thiocyanate, which salts the surfactant in by destructuring water; and sodium chloride and sodium sulfate, which salt octoxynol 9 out. The addition of these electrolytes at concentrations up to 2 or 3 *m* to hexadecane emulsions produced fast and extensive creaming, little or no flocculation, no coalescence, and only minor changes in droplet size or turbidity on storage at room temperature. The extent of coalescence during centrifugation was actually reduced by the additives. Such stability is unusual. Droplet size and turbidity depended mainly on octoxynol 9 concentration. The greatest decrease in the former and increase in the latter occurred when the concentration was increased from 0.10 to ~0.4%. All emulsions became slightly coarser on storage at 25°. Stability at 50° was impaired by aluminum nitrate and magnesium nitrate and to a lesser extent by sodium sulfate and sodium chloride. Reverse-addition emulsions differentiated better between the electrolytes than direct-addition emulsions. Electrolytes salting octoxynol 9 in, especially by complexation, generally produced the finest and most stable emulsions. Similarly, xylene emulsions were destabilized more by the electrolytes which salted the emulsifier out than by those salting it in. Centrifugation of hexadecane emulsions at 7800×*g* compressed the creamed emulsion layer into a plug of clear, transparent, isotropic gel from which coalesced hexadecane separated slowly on further centrifugation. These semisolid gels contained the hexadecane as discrete, uncoalesced droplets because, on immersion in water or octoxynol 9 solutions with or without electrolytes, they turned opaque, liquefied, and redispersed spontaneously into emulsions of nearly the same average droplet size as the original emulsions.

Keyphrases □ Hexadecane—emulsions with octoxynol 9, stability, effect of added electrolytes □ Xylene—emulsions with octoxynol 9, stability, effect of added electrolytes □ Stability—of hexadecane and xylene emulsions with octoxynol 9, effect of added electrolytes □ Emulsions—hexadecane with octoxynol 9, xylene with octoxynol 9, stability, effect of added electrolytes

The principal effect of electrolytes on aqueous solutions of polyoxyethylated nonionic surfactants consists of salting in or salting out, depending on whether the electrolyte increases or decreases the solubility of the surfactants, raising or lowering their cloud points. Electrolytes in the first category contain either cations capable of forming complexes with the ether groups of the polyoxyethylated moiety of the nonionic surfactants, or large and polarizable anions that break the hydrogen-bonded structure of water. All di- and trivalent cations, plus the hydronium and lithium cation, form complexes with model ethers and

increase the solubility of polyoxyethylated surfactants by complexation (1, 2). Only salts of sodium, potassium, ammonium, tetramethylammonium, and cesium tend to salt out the surfactants (1–4) because these cations do not form complexes with the ether oxygen atoms.

Large anions that break the structure of water include iodide, thiocyanate (4, 5), and perchlorate (2) as well as the guanidinium cation (6). Depolymerization of water increases the hydration of the ether linkages of the surfactants through hydrogen bonding by disrupting the hydrogen bonds among the water molecules (1, 2). The salt effects of the anions are in agreement with the Hofmeister or lyotropic series (4).

Salts are frequently incorporated into emulsions for a variety of purposes or occur as impurities. The objective of the present work was to investigate how salting-in and salting-out electrolytes affect the stability of oil-in-water emulsions prepared with a nonionic polyoxyethylated emulsifier. The main variables to be investigated were surfactant concentration, nature and concentration of the electrolytes, temperature, and order of addition. The range of electrolyte concentrations was extended to the high values at which the surfactant is extensively salted in or out.

The surfactant, octoxynol 9, was selected because it is a monograph in the National Formulary and because its interactions with electrolytes have been investigated extensively with regard to cloud point (1–3, 5), micelle formation, and surface properties (7). Moreover, it is used commercially as an emulsifying and suspending agent and as a detergent for hard surfaces and skin.

EXPERIMENTAL

Materials—The surfactant, octoxynol 9 NF¹, is a branched octylphenol with an average of 9–10 ethylene oxide units. It is a viscous, anhydrous liquid with a hydrophilic–lipophilic balance (HLB) of 13.4 and a critical micelle concentration of 0.16 g/liter at 25°.

The oils used were hexadecane² and xylene³. The electrolytes were ACS reagent grade. The water was double distilled. Electrolyte concentrations are expressed as molality (*m*); the concentrations of oil and octoxynol 9 are expressed as percent (w/w) based on the weight of the water present in the solutions and emulsions as 100%. Thus, a 5.00% octoxynol 9 solution or emulsion contains 5.00 g of octoxynol 9 in 100 g of water.

Emulsification—In the direct-addition procedure, the electrolytes were added in the final stage. Preliminary coarse emulsions containing 50% oil were made in 100-g batches, as illustrated for a hexadecane emulsion with a 0.10% octoxynol 9 content: 1.40 g of a 5.00% octoxynol 9 solution, 65.29 g of water, and 33.31 g of hexadecane were added in this order to a tall-form 200-ml beaker. The octoxynol 9 solution was at least 2 days old to ensure full hydration. The mixture was stirred for 20 min at 30-V input with a mixer equipped with two counter-rotating propel-

¹ Triton X-100, Rohm & Haas Co., Philadelphia, Pa.

² Practical grade, Eastman Organic Chemicals.

³ Purified, J. T. Baker Chemicals.

Table I—Effect of Octoxynol 9 Concentration, Storage Temperature, and Emulsion Age on Mean Droplet Size and Specific Turbidity of Hexadecane–Water Emulsions

Emulsion No.	Octoxynol 9 Concentration, % (w/w)	Storage Temperature, °	Emulsion Age, days	D_a^a , μm	D_{vs}^b , μm	$\frac{\tau/C^c}{10^{-3}} \left(\frac{\text{g of diluted emulsion}}{\text{g of hexadecane}} \right)$
<u>Direct Addition</u>						
1	0.10	25	0	3.29	5.28	8.05
2	0.10	25	9	3.47	5.26	8.01
3	0.10	25	30	—	—	7.81
4	0.10	25	64	3.49	5.50	7.73
5	0.10	37	22	3.65	5.17	—
6	0.15	25	4	2.26	3.55	13.8
7	0.20	25	1–2	1.96	2.97	15.0
8	0.20	25	7	2.13	3.41	14.6
9	0.20	25	46	2.52	3.57	14.8
10	0.20	50	8	2.26	3.53	14.8
11	0.30	25	6	1.31	2.53	16.2
12	1.0	25	0	0.93	2.21	18.0
<u>Reverse Addition</u>						
13	0.10	25	1	1.71	3.77	14.9
14	0.10	25	11	2.01	3.42	14.4
15	0.10	25	22	2.40	4.33	14.1
16	0.10	25	57	—	—	13.5

^a Arithmetic mean diameter. ^b Mean volume–surface diameter defined by Eq. 1. ^c Specific turbidity, derived from Eq. 2.

lers⁴. The stirring conditions were selected because higher speeds and/or longer agitation caused foaming while lower speeds produced coarser droplets. The emulsion was further comminuted by passing it three times through a stainless steel hand-operated homogenizer⁵, applying maximum tension to the spring. The second and third pass did not substantially reduce the mean droplet size, but improved the reproducibility.

The finished emulsion was prepared by mixing weighed amounts of a 5.00% aqueous octoxynol 9 solution, water, aqueous electrolyte solution, and homogenized emulsion to give the desired composition. The surfactant concentration was the same, for instance, 0.10%, in the preliminary and the finished emulsion. The oil content was 25% for most finished hexadecane and all finished xylene emulsions. Most hexadecane emulsions contained 0.10 or 0.20% octoxynol 9. Since the xylene emulsions were intrinsically less stable, their octoxynol 9 content was 0.60%. The preliminary coarse xylene emulsions made with the counter-rotating mixer contained, therefore, 8.37 g of a 5.00% octoxynol 9 solution, 58.43 g of water, and 33.20 g of xylene.

The reverse-addition procedure was used for hexadecane emulsions only. The order of mixing of the ingredients was as follows: 5.00% octoxynol 9 solution, water, and aqueous electrolyte solution to give a solution containing 0.10% octoxynol 9 and the desired electrolyte molality. This solution was stored at room temperature for at least 2 days prior to the addition of hexadecane and emulsification. The preliminary coarse emulsion was made in 100-g batches containing 25% hexadecane by stirring for 20 min at 30-V input with the counter-rotating mixer. The emulsification was completed by three passes through the hand-operated homogenizer.

Storage—To characterize the emulsions, various measurements were made on aliquots withdrawn at regular intervals. During the period of investigation, most emulsion samples were stored at $25 \pm 0.5^\circ$. A few were stored at $50 \pm 1^\circ$.

Visual Observation of Coalescence—Some xylene emulsions were so unstable that they separated visible amounts of clear oil at room temperature. For quantitative comparison, 55-g emulsion samples were stored in milk-test Babcock bottles; the volume of xylene separated after various storage times at 25° was calculated from its height in the neck.

Higher coalescence rates at elevated temperatures were measured for xylene or hexadecane emulsions by weighing 20- to 23-g emulsion samples into stoppered 25-ml graduated cylinders, immersing the cylinders into constant-temperature baths, and recording the volume of clear oil separated as a function of time. All emulsions used for measuring coalescence rates at elevated temperatures or in a centrifuge at room temperature, which contained 25% hexadecane or xylene, were prepared by direct addition.

Droplet Size Measurements—The method used for microscopic measurements of droplet size is described in a separate publication (8). Prior to the measurements, the emulsions were diluted ~600-fold, using either an octoxynol 9 solution of the same concentration as the emulsion, which was thickened with polyvinyl alcohol, or a warm gelatin solution, which gelled on cooling.

Turbidity Measurements—Emulsions containing 25% hexadecane were opaque. Transmittance was measured as a function of hexadecane concentration after diluting the emulsions to varying degrees. Dilutions, which usually ranged from 200- to 2000-fold, were made with octoxynol 9 solutions having the same surfactant concentration as the emulsions. Emulsions were diluted immediately before measuring their transmittance.

Transmittance measurements were made with a double-beam spectrophotometer⁶ and 1-mm quartz cells. Even though the emulsions were "white," their transmittance varied with the wavelength. Unless otherwise specified, the wavelength used was 475 nm.

Centrifugation—The stability of hexadecane emulsions was studied by centrifugation at 25° and 10,000 rpm or 7800 \times the acceleration of gravity (g) for 65 min, using a thermostated centrifuge⁷. The glass tubes used had a capacity of 12 ml and an inside diameter of 12.5 mm. They were filled with an amount of emulsion containing 1.80 g of hexadecane, which ranged from 9 to 11 g.

Centrifugation separated the emulsions into four layers, which were (from bottom to top) a clear aqueous solution, a white opaque viscous layer of creamed emulsion a few millimeters thick, a clear gel layer with a thickness of up to 18 mm, and a layer of clear hexadecane a few millimeters thick. The tubes were stoppered and stored in a vertical position at 25° . On standing, the gel reverted gradually and almost completely to a white opaque cream over a 15-hr period, separating small amounts of clear hexadecane. The creamed emulsion layer continued to bleed additional small amounts of clear hexadecane for a few hours after the disappearance of the gel. When the oil separation was essentially complete, the clear hexadecane was aspirated quantitatively and weighed. Storage times after emulsification were, therefore, 17–24 hr for emulsions with 0.10% octoxynol 9 and 48 hr for emulsions with 0.20%. Results are expressed as percent hexadecane separated, based on the 1.80 g present in the emulsion samples placed in the centrifuge tubes.

Xylene emulsions, being less stable, were centrifuged at speeds of only 4000–5000 rpm for only 15–30 min to distinguish the effects of different additives. Even though only small amounts of clear gel formed, the centrifuged emulsions were stored for 24 hr at 25° prior to separating and weighing the coalesced xylene.

⁵ Emulsion homogenizer, Arthur H. Thomas Co., Philadelphia, Pa.

⁶ Coleman Model 124.

⁷ Beckman Model J-21 preparative centrifuge, equipped with a fixed-angle rotor Type JA-20.

RESULTS

Droplet Size from Microscopic Measurements—Droplet sizes were measured in incremental intervals of 1 μm . The data were used to determine the droplet size distributions. The average droplet sizes were represented by the arithmetic mean diameter, D_a , and the mean volume-surface diameter, D_{vs} :

$$D_{vs} = \frac{\sum N_i D_i^3}{\sum N_i D_i^2} \quad (\text{Eq. 1})$$

where D_i is the diameter equal to the midpoint of the i th size interval and N_i the number of droplets in that interval.

The mean volume-surface diameter is inversely related to the specific surface area of the emulsion sample. For a given sample, it is larger than the arithmetic mean diameter because each droplet contributes to the latter only in proportion to the first power of its diameter. The mean volume-surface diameter is influenced to a greater extent by larger droplets and, hence, reflects more effectively increases in droplet size than the arithmetic mean diameter (9).

Table I lists the effects of various experimental variables on the mean droplet size of hexadecane emulsions in the absence of additives. The most influential variable was octoxynol 9 concentration. When it was increased from 0.10 to 0.30%, the D_a and D_{vs} values of freshly prepared emulsions decreased by 61 and 53%, respectively. Another approximately threefold increase in concentration, from 0.30 to 1.0% octoxynol 9, reduced the mean diameters by only 29 and 13%, respectively. Plots of average droplet size versus octoxynol 9 concentration level off at $\sim 0.4\%$ (Fig. 1).

Aging of the emulsions at room temperature or at 37° or 50° produced minor, but consistent, increases in droplet size (compare emulsions 1-5 and 7-10). The reverse-addition procedure resulted in smaller droplet sizes than direct addition. This fact is to be expected because, during the preliminary emulsification and the homogenization, the ratio of octoxynol 9 to hexadecane was twice as large in the reverse-addition procedure. Moreover, in the reverse addition, as opposed to direct addition, the entire volume of the emulsion was subjected to homogenization. Furthermore, all emulsions, regardless of the volume fraction of oil, were quite fluid: their relative viscosities were only ~ 2 . Therefore, the shear stress during homogenization of the direct-addition emulsion, which at that point had twice the hexadecane concentration as the reverse-addition emulsion, was not substantially greater. A few hexadecane-water emulsions prepared by direct addition but containing 10% hexadecane had mean diameters comparable with standard 25% hexadecane emulsions prepared under identical conditions.

The purpose of this investigation was to compare the effect of various salting-in and salting-out electrolytes on emulsion stability. Therefore, electrolytes were employed at concentrations corresponding to comparable salting-in and salting-out efficiencies. When their solubilities permitted, the effect of salting-out electrolytes was compared at concentrations at which they lowered the cloud point of octoxynol 9 by 35° in the absence of hexadecane, *i.e.*, from 65° to 30°. Such a concentration is 0.40 m for sodium sulfate and 2.20 m for sodium chloride.

The effect of salting-in electrolytes was investigated mainly at concentrations at which they raised the cloud point of octoxynol 9 by 30° in the absence of hexadecane. These concentrations are 3.0 m for sulfuric and hydrochloric acids and 1.80 m for sodium thiocyanate (1). The corresponding magnesium nitrate concentration, 4.25 m , is too close to the solubility limit, so this salt was studied at 2.00 m . Higher and lower concentrations for all electrolytes were also investigated.

The effect of electrolytes is described first for emulsions stored at 25°. Comparison of the average diameters in Tables I and II illustrates two surprising facts. All hexadecane emulsions were remarkably stable towards electrolytes, even at 1-3 m concentrations. Neither salting-in nor salting-out electrolytes produced major changes in droplet size.

Since most emulsions became slightly but consistently coarser on aging, the average diameters were compared for emulsions of approximately the same age. When examining the effect of additives, emulsions were always compared at equal octoxynol 9 concentrations since this was the most important factor affecting droplet size.

For a few emulsions prepared by direct addition, electrolytes actually produced smaller droplets than blank emulsions without additives. For instance, emulsions 17-20 with added electrolytes have smaller D_a and D_{vs} values than emulsion 1 (blank). For most emulsions, the changes in droplet size produced by various additives were minor. The following emulsions have nearly identical values for D_a and D_{vs} , respectively: 6 (blank) and 23 and 24; 7 (blank) and 36, 39, 41, 44, 52, and 59; 8 (blank) and 27, 29, 34, 37, 45, 50, and 55; and 11 (blank) and 62 and 63.

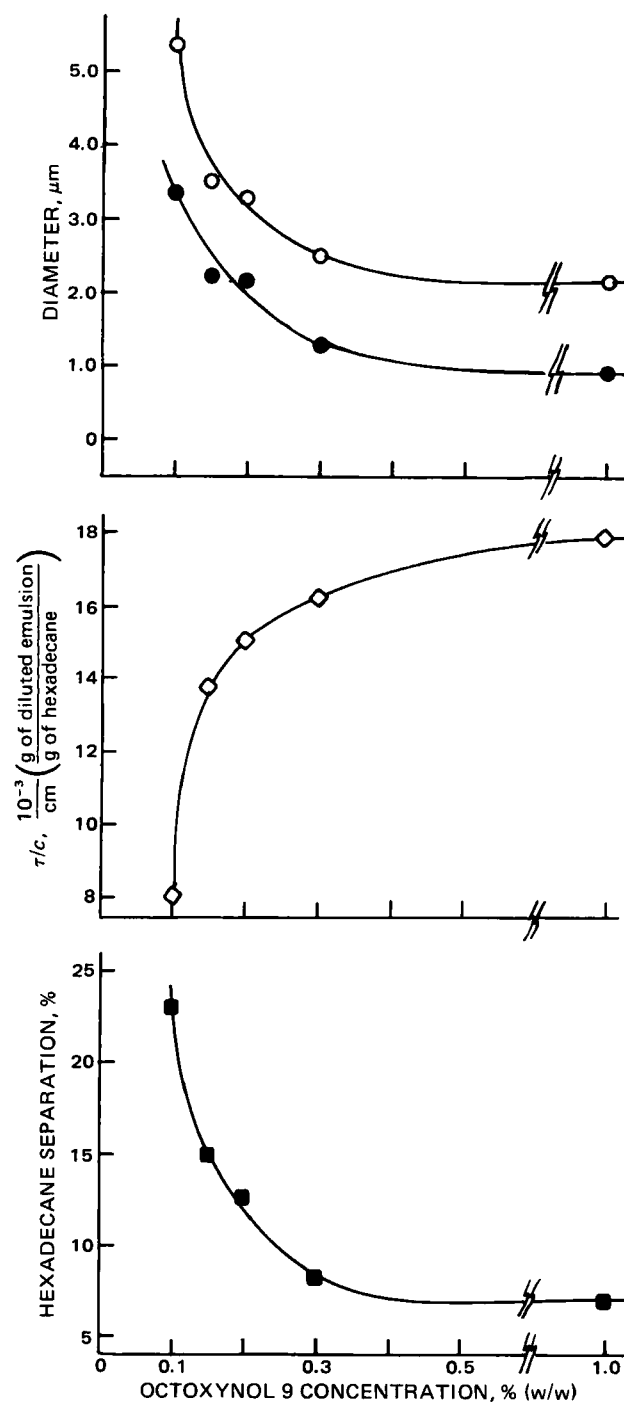


Figure 1—Effect of octoxynol 9 concentration on mean volume-surface diameter, D_{vs} , arithmetic mean diameter, D_a , specific turbidity, τ/C , and hexadecane separation in the centrifuge. Key: (O) D_{vs} ; (●) D_a ; (◇) τ/C ; (■) hexadecane separation.

Where additives were investigated at several concentrations, no consistent trend of either increasing or decreasing average droplet sizes with increasing additive concentration are noticeable. This observation holds for the salting-in additives hydrochloric acid (compare emulsions 26, 28, 30, 33, and 36; 27, 29, 31, 34, and 37; and 32, 35, and 38), aluminum nitrate (compare emulsion 39 with 41 and 40 with 43), and magnesium nitrate (compare emulsion 44 with 47 and 46 with 48) as well as for the salting-out additives sodium chloride (compare emulsions 49, 52, and 54; also 51, 53, and 56) and sodium sulfate (compare emulsion 57 with 59).

The difference between the effect of salting-in and salting-out electrolytes on droplet size are clear-cut only in the case of emulsions prepared by reverse addition. Emulsions containing the salting-in complexing electrolytes sulfuric acid and magnesium nitrate had about the

Table II—Effect of Additives on Droplet Size and Specific Turbidity of Hexadecane–Water Emulsions Stored at 25°

Emulsion No.	Octoxynol 9 Concentration, % (w/w)	Additive	Additive Concentration, m	Emulsion Age, days	D_a^a , μm	D_{vs}^b , μm	$\frac{\tau/C^c}{10^{-3} \left(\frac{\text{g of diluted emulsion}}{\text{g of hexadecane}} \right)}$
<u>Direct Addition</u>							
17	0.10	H ₂ SO ₄	3.00	0	2.51	4.52	6.89
18		NaSCN	1.50	0	2.74	5.27	7.72
19		NaCl	2.20	0	2.54	4.97	—
20		Na ₂ SO ₄	0.40	0	2.64	4.67	7.77
21				56	—	—	6.53
22				167	3.16	5.06	—
23	0.15	H ₂ SO ₄	3.00	4	2.36	3.68	13.8
24		Na ₂ SO ₄	0.40	4	2.30	3.66	13.8
25	0.20	H ₂ SO ₄	3.00	5	1.97	4.05	14.7
26		HCl	0.10	2	2.44	3.60	15.8
27				9	2.06	3.31	15.3
28			0.50	2	2.62	3.75	16.3
29				9	2.12	3.68	16.3
30			1.00	1	1.51	3.52	15.4
31				9	1.52	3.49	15.3
32				50	2.30	3.94	—
33			2.00	1	1.51	3.21	15.7
34				9	2.40	3.60	15.4
35				50	2.69	4.15	—
36			3.00	1	2.03	3.33	14.7
37				9	2.26	3.44	14.6
38				46	2.31	3.50	14.0
39		Al(NO ₃) ₃	0.50	1	1.94	2.98	16.0
40				48	2.42	3.54	15.6
41			1.40	1	1.90	2.89	14.9
42				9	2.02	2.95	14.8
43				46	2.41	3.15	14.6
44		Mg(NO ₃) ₂	0.50	1	2.05	3.25	14.9
45				9	2.22	3.27	14.9
46				46	2.26	3.35	—
47			2.00	1	1.88	3.09	15.5
48				48	2.37	3.65	15.5
49		NaCl	0.50	1	1.68	2.89	15.7
50				9	2.14	3.46	15.2
51				50	2.74	3.76	—
52			1.20	1	1.94	3.54	15.6
53				48	2.60	3.68	—
54			2.20	1	1.65	2.99	15.5
55				9	2.26	3.71	—
56				50	2.75	4.01	—
57	0.20	Na ₂ SO ₄	0.20	2	2.24	3.45	16.1
58				9	2.39	3.46	16.2
59			0.40	1	1.89	3.19	15.7
60				5	1.91	3.18	15.5
61				48	2.45	3.67	14.2
62	0.30	H ₂ SO ₄	3.00	6	1.35	2.58	16.6
63		Na ₂ SO ₄	0.40	6	1.67	2.88	16.4
64	1.00	H ₂ SO ₄	3.00	3	1.88	2.72	17.9
65				17	2.09	3.16	17.4
66		Na ₂ SO ₄	0.40	3	2.33	2.98	17.7
67				17	2.41	3.09	—
<u>Reverse Addition</u>							
68	0.10	H ₂ SO ₄	3.00	1	1.67	4.14	7.9
69		Mg(NO ₃) ₂	2.00	1	1.74	3.79	11.2
70				11	1.97	4.30	10.6
71			3.00	1	1.88	2.98	13.6
72		NaSCN	1.50	1	1.91	4.03	11.7
73				11	2.19	5.11	11.0
74		NaCl	2.20	1	2.37	4.08	9.9
75				11	2.86	4.31	9.1
76		Na ₂ SO ₄	0.40	1	2.55	5.16	8.5
77				11	2.61	5.33	7.4
78				63	—	—	6.4

^a Arithmetic mean diameter. ^b Mean volume–surface diameter defined by Eq. 1. ^c Specific turbidity, derived from Eq. 2.

same D_a and D_{vs} values, respectively, as emulsions without additives [compare emulsion 13 (blank) with 68, 69, and 71; and 14 (blank) with 70].

The two salting-out electrolytes sodium chloride and sodium sulfate produced coarser emulsions by reverse addition than the blanks [compare emulsions 13 (blank) with 74 and 76; and 14 (blank) with 75 and 77]. Sodium thiocyanate, which salts in octoxynol 9 by destructuring water, had an intermediate effect on droplet size (compare emulsions 13 with 72 and 14 with 73).

Emulsions stored above room temperature were gently inverted nearly once a day to redisperse the creamed layer throughout the entire volume. Mean droplet diameters are listed in Table III. As was observed for emulsions prepared by direct addition stored at 25°, both salting-in and salting-out additives produced only minor changes in droplet size [compare emulsions 2 and 4 (blanks) with 79 and 80; also 10 (blank) with 81–95]. Storage at 50° for 22 days (not listed in Table III) resulted in only slightly larger droplet sizes than storage for 7–9 days, with D_a increasing, on the average, 14% and D_{vs} 8%.

Table III—Effect of Additives on Droplet Size and Specific Turbidity of Hexadecane–Water Emulsions Prepared by Direct Addition and Stored at Elevated Temperatures

Emulsion No.	Octoxynol 9 Concentration, % (w/w) ^a	Additive	Additive Concentration, <i>m</i>	Emulsion Age, days	<i>D</i> _a ^b , μm	<i>D</i> _{vs} ^c , μm	10 ⁻³ $\frac{\tau/C^d}{\text{cm}} \left(\frac{\text{g of diluted emulsion}}{\text{g of hexadecane}} \right)$
79	0.10 (37°)	H ₂ SO ₄	3.00	22	3.45	5.62	—
80	0.20 (50°)	Na ₂ SO ₄	0.40	22	4.56	6.00	—
81		HCl	0.10	9	1.83	2.82	15.7
82			0.50	9	2.20	3.17	16.1
83			1.00	7	1.95	2.96	15.9
84			2.00	7	1.98	3.22	16.0
85		3.00	7	2.34	3.59	14.8	
86	Al(NO ₃) ₃	0.50	7	1.84	2.79	16.1	
87		1.40	7	2.12	3.20	14.7	
88		0.50	7	2.36	3.17	14.8	
89	Mg(NO ₃) ₂	2.00	7	2.13	3.52	15.9	
90		0.20	9	2.58	3.52	15.9	
91	Na ₂ SO ₄	0.40	7	2.35	3.27	15.7	
92				42	—	—	12.7
93	NaCl	0.50	7	2.40	3.55	15.5	
94		1.20	7	2.18	3.36	15.6	
95		2.20	7	2.13	3.34	14.7	

^a Storage temperature in parentheses. ^b Arithmetic mean diameter. ^c Mean volume–surface diameter defined by Eq. 1. ^d Specific turbidity, derived from Eq. 2.

However, prolonged storage at 50° led to partial coalescence for all emulsions containing 0.20% octoxynol 9, ranging from <5% of the amount of emulsified hexadecane for emulsions without additives and those containing hydrochloric acid or sodium thiocyanate to 25–50% for emulsions containing aluminum nitrate within 250 days (see below).

Most xylene emulsions containing 0.60% octoxynol 9 underwent detectable coalescence within a few days at room temperature, separating at least traces of clear xylene. Moreover, they coalesced considerably on dilution with water. Therefore, xylene emulsions were not characterized by microscopic droplet size measurements.

Turbidity—To include any submicroscopic droplets that may have been present, microscopic droplet size measurements were supplemented by turbidity determinations. Turbidity, τ , is the inverse of the light path length, *L*, that reduces the intensity of a beam of light to 1/*e* of its original value by scattering or absorption (10):

$$\tau = \frac{\ln(I_0/I_t)}{L} \quad (\text{Eq. 2})$$

The light intensities *I*₀ and *I*_t refer to the incident and transmitted beams, respectively. The turbidities of hexadecane–water emulsions were thus calculated from the measured transmittance values by dividing the natural logarithm of the reciprocal of the transmittance by the path length, which was 0.1 cm.

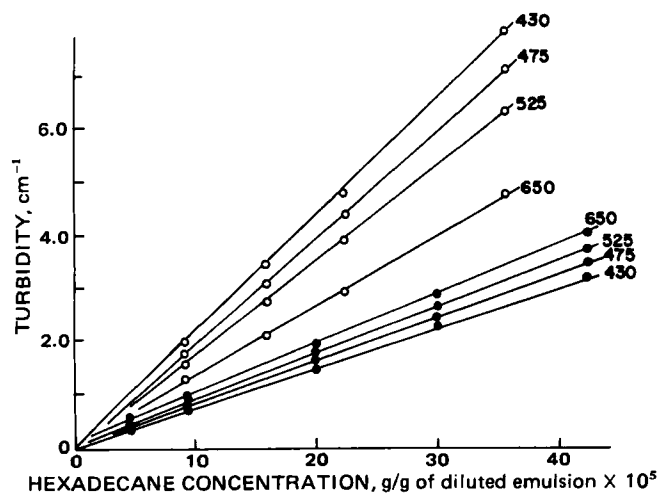


Figure 2—Turbidity, defined by Eq. 2, of diluted hexadecane–water emulsions versus hexadecane concentration at four wavelengths. Numbers on lines designate wavelengths in nanometers. Key: (●) 0.10% octoxynol 9; (O) 1.00% octoxynol 9.

Plots of turbidity versus hexadecane concentration, *C*, expressed as g of hexadecane/g of diluted emulsion, were straight lines going through the origin. Their slopes equal the specific turbidity, τ/C , expressed in units of (1/cm) (g of diluted emulsion/g of hexadecane). The specific turbidity is, thus, formally analogous to absorptivity, the difference being that the former includes light scattering and absorption whereas the latter, which refers to solutions, involves light absorption only (11).

Specific turbidities were generally calculated from transmittance values at five concentrations by linear regression as the slope of the straight line passing through the origin. Standard deviations of the slope (12) usually ranged from 0.4 to 3%.

At constant oil concentration, smaller droplet sizes result in more opaque emulsions. The specific turbidity is inversely proportional to the mean volume–surface droplet diameter (11, 13, 14) and can be used to assess the effect of additives on the latter.

Figure 2 contains plots of turbidity measured at four wavelengths versus hexadecane concentration for two 2-month-old emulsions without additives which were diluted immediately before the transmittance determinations. The upper set of curves represents an emulsion with 1.00% octoxynol 9 (*D*_{vs} = 2.21 μm) and the lower set represents an emulsion with 0.10% octoxynol 9 (*D*_{vs} = 5.28 μm). The slopes of the two sets of curves, representing specific turbidity, have the opposite wavelength dependence. The coarser emulsion scattered red light (650 nm) more strongly than violet (430 nm); the specific turbidities increased from violet to blue (475 nm) to green (525 nm) to red. The finer emulsion scattered violet light more strongly than red; the specific turbidities increased from red to green to blue to violet light.

Such a reversal of the wavelength dependence of turbidity is not uncommon. Plots of the total scattering coefficient (*K*) or of extinction versus the droplet size parameter ($\alpha = \pi nD/\lambda$) are sinusoidal (11, 13, 14). In that expression, *n* is the refractive index of the continuous phase and λ is the wavelength of the light. Hence, for some droplet size ranges, light scattering and turbidity increase as the wavelength increases (a descending branch of the *K*– α plot). For others, *K* increases with decreasing λ (an ascending branch).

The reason for selecting blue as the wavelength for subsequent transmittance measurements was that the ratio of the specific turbidities of the two additive-free emulsions containing 1.00 and 0.10% octoxynol 9, respectively, obtained with blue light approaches most closely the inverse ratio of their mean volume–surface diameters. The inverse *D*_{vs} ratio is 5.28/2.21 = 2.39. The specific turbidity ratios are 1.38, 1.96, 2.37, and 2.84 for red, green, blue, and violet light, respectively. The theoretical inverse *D*_{vs}– τ/C relationship in the range of droplet sizes encountered in the present work is, thus, most closely obeyed for turbidities measured with the blue light ($\lambda = 475$ nm).

It was not possible to measure the transmittance of xylene emulsions. Dilution with an octoxynol 9 solution having the same concentration as the emulsion, namely, 0.60%, reduced the size and number of droplets through micellar solubilization. This octoxynol 9 concentration exceeded the critical micelle concentration almost 40-fold and xylene, as opposed

Table IV—Effect of Additives on the Coalescence of Oil–Water Emulsions Prepared by Direct Addition

Additive	Additive Concentration, <i>m</i>	Time to Separate Listed Fraction of Oil Present											
		Xylene ^a										Hexadecane ^b	
		25° ^c		40° ^c		45° ^c		50° ^c		98° ^c			
		25% ^d	50% ^d	25%	50%	25%	50%	25%	50%	25% ^d	50%		
—	—	^e		^{f, g}									
NaCl	1.20	24 day	—	4.4 min	5.9 min	11.5 day ^f	14 day			104 min	7.9 hr		
	2.20	4 hr	12 hr	3.8 min	4.0 min	1.2 min	1.6 min	1.1 min	1.5 min	14.1 min	18.0 min		
Na ₂ SO ₄	0.20	17 day	—	4.5 min	5.0 min	2.0 min	2.2 min	1.6 min	1.8 min				
	0.40	23 hr	10 day							1.8 min	2.2 min		
HCl	1.00	^e		15.0 min	22.8 min	4.9 min	7.5 min	2.7 min	3.2 min				
	3.00	^e						3.1 min	3.6 min	103 min	3.6 hr		
Mg(NO ₃) ₂	2.00	^e		18 hr	3 day	57 min	4.0 hr	10.3 min	39.2 min	5.4 min	6.5 min		
Al(NO ₃) ₃	1.20	^e				11 min	55 min	5.6 min	7.7 min	4.9 min	8.2 min		
NaSCN	1.50	^e		62 day ^f	77 day	6.3 hr	25 hr	8.0 min	15.3 min	104 min	5.7 hr		

^a Emulsions contained 0.60% octoxynol 9. ^b Emulsions contained 0.20% octoxynol 9. ^c Storage temperature. ^d Volume of oil separated as clear supernatant under the influence of gravity, expressed as percent of the 25% oil present in emulsion. ^e No oil separation in 24–26 days. ^f Approximately 5% of the oil separated in 17–19 hr. ^g Less than 10% of the oil separated in 80 days.

to hexadecane, is solubilized extensively. Dilution of the xylene emulsions with water resulted in coalescence.

The conclusions derived from the turbidity measurements are similar to those from droplet size determinations, although the inverse proportionality between τ/C and D_{vs} was not always exactly obeyed. The exceptions were caused by changes in droplet size distribution, possibly involving submicroscopic droplets.

The most important factor determining specific turbidity was octoxynol 9 concentration. The major increase in τ/C with increasing surfactant concentration took place at <0.4% (Table I, Fig. 1). Aging produced small, but consistent, decreases in τ/C .

The addition of salting-in and salting-out electrolytes alike produced only minor changes in specific turbidity for emulsions prepared by direct addition. Major differences were observed for emulsions prepared by reverse addition, where emulsions without additives had the highest τ/C values. These values were considerably higher than the τ/C values of direct-addition emulsions without additives having the same 0.10% octoxynol 9 level; they were practically identical with those of direct-addition emulsions containing 0.20% octoxynol 9 (compare emulsion 13 with 1 and 7, and 14 with 2 and 8 in Table I). The near equality of the specific turbidities of the direct-addition blank emulsions containing 0.20% octoxynol 9 and the reverse-addition blank emulsions containing 0.10% octoxynol 9 is ascribed to the fact that both types had the same ratio of octoxynol 9 to hexadecane during the preliminary emulsification and homogenization.

Among the emulsions prepared by reverse addition, those without additives had the highest specific turbidities. Emulsions with sodium thiocyanate and magnesium nitrate (emulsions 69, 71, and 72) had intermediate values, while the remaining additives produced lower specific turbidities that were still larger than those of the corresponding emulsions prepared by direct addition.

Coalescence on Storage—Hexadecane emulsions prepared by direct addition containing 0.20% octoxynol 9 and all additives at the levels listed in Tables III–V were completely stable on storage for 8 months at 25°. Despite extensive creaming, resulting in the separation of concentrated emulsion layers above practically clear aqueous phases, no coalesced hexadecane could be detected. Gentle inversion of the containers readily redispersed the creamed layers, reconstituting intact and uniform emulsions.

Hexadecane emulsions stored at 50° separated cream layers that were viscous. In some samples, coalesced oil became evident after 42 days and more oil separated during the following 80–90 days. During an additional 120–130 days at 50°, the amount of coalesced oil increased only slightly except for emulsions containing aluminum nitrate, which already underwent extensive coalescence during the first 126-day period and which separated substantially more oil subsequently.

The emulsions are ranked below in order of increasing stability. Percentages in parentheses following the formula of the additive represent approximate volumes of coalesced hexadecane, expressed as percent of the total volume of hexadecane in the sample, observed after 126 ± 5 or 250 ± 5 days storage at 50°. When two percentages are listed, the first refers to hexadecane separated after 126 days, the second to separation after 250 days; single percentage values indicate that coalescence did not increase noticeably between 126 and 250 days. Absence of percentage values indicates that, while some hexadecane did coalesce in 126 and 250 days, it amounted to <5%. The ranking on storage at 50° is: 1.40 *m*

Al(NO₃)₃ (30%, 50%) < 0.50 *m* Al(NO₃)₃ (20%, 25%) < 2.00 *m* Mg(NO₃)₂ (15%) < 0.50 *m* Mg(NO₃)₂ (12%) = 0.50 *m* NaCl (12%) < 0.40 *m* Na₂SO₄ (10%) < 0.20 *m* Na₂SO₄ (8%) < 1.20 *m* NaCl (<5%, 10%) < 2.20 *m* NaCl = blank = 0.10, 0.50, 1.00, 2.00, and 3.00 *m* HCl = 1.50 *m* NaSCN.

Hexadecane emulsions immersed in boiling water were unstable (Table IV). Those without additives, with hydrochloric acid, and with sodium thiocyanate coalesced more slowly than those containing sodium sulfate, aluminum nitrate, magnesium nitrate, and sodium chloride.

Xylene emulsions, despite their higher octoxynol 9 content, had considerably shorter shelf lives than hexadecane emulsions at comparable temperatures. The latter were more stable at 98° than the former at 50°. All four salting-in electrolytes investigated (hydrochloric acid, sodium thiocyanate, magnesium nitrate, and aluminum nitrate) destabilized the xylene emulsions only moderately compared with the blank while both salting-out electrolytes (sodium chloride and sodium sulfate) accelerated their coalescence considerably (Table IV).

Centrifugation Studies—The highest centrifugal speed that the glass tubes could withstand was 10,000 rpm or 7800*g*. At that speed, 65 min provided optimum discrimination between the variables. Shorter periods, 30 or 45 min, separated smaller amounts of coalesced hexadecane and increased the coefficients of variation. Centrifugation periods of 2 or 4 hr increased the amounts of coalesced hexadecane without enhancing the differences between additives.

The separation of hexadecane did not follow zero-, first-, or second-order kinetics (15) nor the Vold–Mittal empirical equation (16). Therefore, the data presented in Table V are merely the amounts of hexadecane coalesced after 65 min centrifugation, expressed as percent of the total weight of hexadecane in the tube.

When the amount of emulsion containing 25% hexadecane (based on the weight of water) was increased from 7 to 8.5 and to 10 g in preliminary experiments, the percent coalesced hexadecane separated after 65 min centrifugation remained constant for blank emulsions and for emulsions containing each of the various additives. Despite this observation, the measurements presented in Table V were standardized by weighing into each centrifuge tube an amount of emulsion containing 1.80 g of hexadecane.

The driving force that promotes creaming of the emulsions, compression of most of the oil phase into a clear gel layer, and coalescence and separation of oil is directly proportional to the difference in density between the continuous aqueous phase and the oil droplets (10). Hence, at comparable acceleration, the centrifugal force is considerably greater when the aqueous phase is a concentrated and dense electrolyte solution than when no electrolytes were added to the water. To compensate for the increased buoyancy of the oil droplets in dense electrolyte solutions, the percent hexadecane separated (5th column of Table V) was multiplied by the factor $(d_{\text{water}} - d_{\text{cetane}})/(d_{\text{salt}} - d_{\text{cetane}})$, where d_{water} , d_{cetane} , and d_{salt} represent the 25° densities of water, of hexadecane (0.771), and of the aqueous electrolyte solutions, respectively. Neglecting the effect of octoxynol 9 on the densities changed the factor by <1%. The corrected hexadecane separation (last column of Table V) shows the intrinsic effects of electrolytes on emulsion stability. This correction generally magnified the trends produced by the various electrolytes shown in the 5th column.

Higher octoxynol 9 concentrations reduced the oil separation because they produced finer emulsions. At comparable octoxynol 9 concentrations, emulsions containing sodium sulfate separated somewhat less

Table V—Effect of Additives and of Octoxynol 9 Concentration on Coalescence of Hexadecane–Water Emulsions in a Centrifugal Field

Octoxynol 9 Concentration, %	Additive	Additive Concentration, <i>m</i>	Emulsion Age, days ^a	Hexadecane Separation, % ^b	<i>N</i> ^c	Corrected Hexadecane Separation, % ^d		Octoxynol 9 Concentration, %	Additive	Additive Concentration, <i>m</i>	Emulsion Age, days ^a	Hexadecane Separation, % ^b	<i>N</i> ^c	Corrected Hexadecane Separation, % ^d		
						Hexadecane Separation, % ^d	Hexadecane Separation, % ^d									
Direct Addition																
0.10	—	—	0	23.1 ± 1.6	16	23.1		0.20	NaCl	0.50	8	8.5 ± 0.4	8	7.8		
			30	24.3	2	24.3	43				10.9 ± 0.5	4	10.0			
			153	24.3	2	24.3	8*				8.7 ± 0.3	4				
		Na ₂ SO ₄	0.005	0	19.3 ± 0.9	6	19.2				43*	11.8 ± 0.5	4			
			0.10	0	20.6 ± 1.6	8	18.8				8	9.1 ± 0.5	8	7.5		
			0.20	0	22.4 ± 1.0	8	20.2				43	10.4 ± 0.9	4	8.6		
			0.40	0	19.2 ± 0.8	8	15.8				8*	10.5 ± 0.7	4			
				68	19.8	2	16.3				43*	13.0 ± 0.5	4			
			118	20.7	2	17.0	8				9.1 ± 0.4	8	6.8			
			153	55.6	2	45.7	43				10.6 ± 0.1	4	7.8			
		NaCl	0.010	0	23.6	2	23.6				8*	18.0 ± 1.0	4			
			0.50	0	14.1	2	13.0				43*	20.1 ± 1.1	4			
			1.50	0	14.1	2	11.2				HCl	0.50	7	6.0 ± 0.4	8	5.8
			1.75	0	16.3	2	12.6					7*	6.9 ± 0.5	4		
			133	17.1	2	13.2					1.00	7	4.3	2	4.0	
			2.20	0	19.9	2	14.6				43	5.5 ± 0.3	12	5.1		
			2.95	0	26.2	2	17.8				43*	7.6 ± 0.5	8			
		H ₂ SO ₄	0.001	0	23.2	2	23.2				8	2.5 ± 0.3	4	2.2		
			0.01	0	19.6	2	19.5				43	4.6 ± 0.3	4	4.0		
			0.10	0	15.7 ± 1.0	6	15.2				8*	5.6 ± 0.4	4			
	1.00		0	12.1 ± 0.9	4	9.6	43*	8.9 ± 0.5	4							
	2.00		0	9.0 ± 0.4	4	6.0	Mg(NO ₃) ₂	0.50	43	9.1 ± 0.8	4	7.4				
		3.00	0	7.3 ± 0.4	7	4.3	43*	10.1 ± 0.6	4							
		5.00	0	4.5	2	2.2	2.00	6	3.6	2	2.0					
0.10	HCl	0.002	0	20.7	2	20.7	43	3.8 ± 0.2	4	2.1						
		0.01	0	16.9 ± 0.2	4	16.8	43*	4.6 ± 0.4	4							
		1.00	0	15.6 ± 0.5	4	14.4	Al(NO ₃) ₃	0.50	6	2.9 ± 0.3	3	2.2				
		2.00	0	15.4 ± 0.4	4	13.4	43	3.3 ± 0.3	8	2.5						
		3.00	0	15.8 ± 0.8	8	13.0	43*	9.2 ± 0.6	4							
			4.00	0	14.7	2	11.5	1.40	7	3.9	2	2.1				
			6.00	0	13.8	2	9.9	43	5.2 ± 0.4	4	2.8					
		Mg(NO ₃) ₂	0.05	0	13.0	2	12.7	43*	10.1 ± 0.7	4						
			0.10	0	11.1	2	10.5	0.30	—	—	3	8.2 ± 0.5	3	8.2		
			1.50	0	2.7	2	1.6	Reverse Addition								
			2.00	0	5.2 ± 0.2	4	2.8	0.10	—	—	0	16.0 ± 0.9	4	16.0		
		NaSCN	0.01	0	26.5 ± 0.7	4	26.4				11	17.4 ± 1.1	3	17.4		
			0.50	0	13.2 ± 0.9	6	12.1	Na ₂ SO ₄	0.40	0	29.8	2	24.5			
			1.50	0	14.1 ± 0.6	12	11.2		11	33.0	2	27.1				
	0.15	—	—	3	15.0	2	15.0				63	40.1	2	33.0		
0.20	—	—	1–2	12.7 ± 0.8	10	12.7					0	25.0 ± 1.2	4	18.4		
			7–8	13.0 ± 1.0	8	13.0	NaCl	2.20	27	35.9 ± 1.3	3	26.4				
			43	16.1 ± 1.1	4	16.1			63	37.8 ± 1.0	3	27.8				
			7–8*	15.4 ± 0.7	4	15.4			0	30.0 ± 1.4	4	17.5				
			43*	17.7 ± 0.8	4	17.7	H ₂ SO ₄	3.00	0	21.1 ± 0.6	3	11.4				
		Na ₂ SO ₄	0.20	1	9.9 ± 0.7	4	8.9	Mg(NO ₃) ₂	2.00	0	34.3 ± 2.6	3	18.6			
	7			9.3 ± 0.6	4	8.4			11	38.0 ± 1.8	3	20.6				
	7*			9.8 ± 0.7	4				24	32.6 ± 2.3	3	15.1				
	8			7.9 ± 0.5	4	6.5	NaSCN	1.50	0	13.3 ± 1.1	4	10.6				
	43			8.8 ± 0.5	4	7.2			11	14.2 ± 1.2	3	11.3				
			8*	12.4 ± 0.5	4					62	18.5 ± 1.3	3	14.7			
			43*	29.5 ± 0.6	4											

^a Stored at 25° unless marked by asterisk, indicating storage at 50°. ^b Weight of coalesced hexadecane, expressed as percent of the 1.80 g of hexadecane present per tube, ± SD. ^c Number of measurements. ^d See text for density correction.

hexadecane than emulsions without additives. The extent of hexadecane separation first decreased somewhat and then increased with progressively higher concentrations of sodium chloride at the 0.10% octoxynol 9 level. At the 0.20% level, no significant changes in hexadecane separation were observed beyond 0.50 *m* NaCl.

The salting-in electrolytes lowered the hexadecane separation significantly compared with emulsions without electrolytes of comparable octoxynol 9 concentration, especially those electrolytes which form complexes with octoxynol 9, namely, sulfuric and hydrochloric acids and magnesium and aluminum nitrates. Higher concentrations of these electrolytes resulted in considerably lower hexadecane separation. Only a few percent hexadecane was separated at the highest concentrations of these electrolytes (Table V): 5.00 *m* H₂SO₄, 2.00 *m* HCl only with 0.20% octoxynol 9, 1.50 or 2.00 *m* Mg(NO₃)₂, and 0.50 or 1.40 *m* Al(NO₃)₃ almost

completely prevented coalescence of hexadecane at 7800×*g*. Sodium thiocyanate, which salts in octoxynol 9 by destructuring water, reduced coalescence only slightly.

Aging the emulsions at 25° prior to centrifugation caused small but significant increases in hexadecane separation. Aging at 50° generally produced more extensive separation.

Emulsions without added electrolytes prepared by direct addition separated more hexadecane on centrifugation than emulsions of comparable octoxynol content prepared by reverse addition, in keeping with their smaller droplet size. The presence of all electrolytes except sodium thiocyanate increased the separation of hexadecane during the centrifugation of emulsions prepared by reverse addition when compared with the corresponding emulsions without additives. The salting-out electrolytes sodium chloride and sodium sulfate increased the hexadecane

Table VI—Low-Speed Centrifugation of Xylene–Water Emulsions

Additive	Additive Concentration, <i>m</i>	Xylene Separated, % ^a	<i>N</i> ^b	Corrected Xylene Separation, % ^d
—	—	0.8 ± 0.2	4	0.8
Na ₂ SO ₄	0.20	19 ± 3	4	17
	0.40 ^c	71 ± 3	4	58
NaCl	2.20 ^c	80	2	59
	2.00	3.2 ± 0.8	4	2.8
HCl	3.00	4.8 ± 0.7	4	4.0
	2.00	0.05	2	0.03
Mg(NO ₃) ₂	2.00	0.3	2	0.2
Al(NO ₃) ₃	1.40	0.3	2	0.2
NaSCN	1.50	7.6	2	6.0

^a Weight of coalesced xylene, expressed as percent of the 1.80 g of xylene present per tube, ± SD. ^b Number of measurements. ^c Appreciable separation before centrifugation. ^d See text for density correction.

separation somewhat more for reverse-addition emulsions than for those prepared by direct addition. The major difference between the two types of emulsions occurred with the salting-in complexing electrolytes sulfuric acid and magnesium nitrate, which slightly increased the oil separation during centrifugation of the reverse-addition emulsions while strongly reducing the oil separation of the direct-addition emulsions.

The xylene emulsions employed in the low-speed centrifugation studies of Table VI contained 0.60% octoxynol 9 and were prepared by direct addition. After aging for 30 min at 25°, emulsion quantities containing 1.80 g of xylene were centrifuged for 30 min at 5000 rpm or 1960×*g*. Centrifugation of emulsions containing salting-in complexing electrolytes (hydrochloric acid, magnesium nitrate, and aluminum nitrate) produced a slight amount of clear gel, while the bulk of the emulsified droplets collected in an opaque creamed layer. The other emulsions produced no clear gel at all. Despite this observation, all centrifuged emulsions were stored for 24 hr at 25° prior to removing and weighing the coalesced xylene.

The differences between the effects of the various types of electrolytes during the centrifugation of xylene emulsions were pronounced. Sodium sulfate and sodium chloride, the salting-out electrolytes, caused extensive coalescence. Of the electrolytes which salt the surfactant in by complexation, magnesium nitrate and aluminum nitrate reduced the xylene coalescence even further than the already small extent observed for emulsions without additives, while hydrochloric acid increased it somewhat. Sodium thiocyanate, which salts octoxynol in by destructuring water, caused more extensive coalescence, but still considerably less than the salting-out electrolytes.

Freeze-Thaw Cycles—This technique was not well suited for studying the stability of emulsions containing high concentrations of electrolytes because they creamed rapidly before freezing and because the electrolytes lowered the freezing point of the aqueous phase considerably. Reproducible results were difficult to obtain even when agitating the emulsions while freezing them in a dry ice–acetone mixture. After one freeze–thaw cycle, thawed hexadecane emulsions containing only 0.10% octoxynol 9 were more opaque than emulsions also containing 0.40 *m* Na₂SO₄ or 3.00 *m* H₂SO₄, but the differences between the latter two were only minor. No significant amounts of coalesced hexadecane were observed in any of the thawed emulsions.

DISCUSSION

Shelf Stability—Emulsion stability can be defined in terms of three phenomena: creaming or clearing; flocculation or aggregation; and demulsification, coalescence, or breaking (17). Because of the high density of many of the aqueous electrolyte solutions employed, most emulsions used in this study creamed rapidly. The droplets in the concentrated cream layer preserved their identity, however, and gentle agitation redispersed them throughout the aqueous phase with no change in their size distribution.

Flocculation, another possible measure of instability, was moderate even in the presence of high electrolyte concentrations. By contrast, emulsions stabilized with ionic surfactants are prone to extensive flocculation even at comparatively low electrolyte concentrations, which may lead to coalescence. Instability, as used here, refers to the irreversible coalescence of small droplets into larger drops, resulting eventually in the separation of a clear layer of oil.

Nature of Oil Phase—Hexadecane emulsions prepared by direct

addition with high concentrations of salting-in as well as salting-out electrolytes were unusually stable. The differences between the effects of the two types of electrolytes were only minor. Hexadecane emulsions prepared by reverse addition showed some discrimination between electrolytes. Salting-in electrolytes operating through complexation with the ether groups of octoxynol 9 generally increased the emulsion stability, salting-out electrolytes decreased it, while sodium thiocyanate, which salts octoxynol 9 in by destructuring water, was intermediate.

Xylene emulsions prepared by direct addition were considerably less stable than hexadecane emulsions even at a sixfold higher octoxynol 9 level. The electrolyte effects were more pronounced, but qualitatively similar to those observed with reverse-addition hexadecane emulsions.

The large difference in the stability of xylene and hexadecane emulsions based on octoxynol 9 is ascribed to the difference in solubility of the surfactant in the two hydrocarbons. Xylene and octoxynol 9 are miscible in all proportions. The solubility of octoxynol 9 in hexadecane at 25°, determined spectrophotometrically at 277 nm, was ~1.4% (w/v). This value is an upper limit because of the polydispersity of the surfactant and the likelihood that the species with the lowest degree of ethoxylation, *i.e.*, with the highest concentration of the absorbing phenyl group, have the highest solubility in hexadecane and were preferentially extracted from the bulk octoxynol 9.

The fact that octoxynol 9 is miscible in all proportions with the disperse phase as well as the continuous phase of xylene–water emulsions evidently reduced the stability of the interfacial octoxynol 9 films compared with those in hexadecane–water emulsions, where the surfactant is only slightly soluble in the disperse phase. This cause of emulsion instability is unusual because few surfactants are freely soluble in both water and oils.

In the case of xylene–water emulsions, salting-out electrolytes tend to displace octoxynol 9, including the octoxynol 9 forming the interfacial film surrounding the droplets, into the xylene phase. Thereby, these electrolytes were effective in breaking the emulsions. In the case of hexadecane–water emulsions, salting-out electrolytes can displace octoxynol 9 only as far as the hexadecane–water interface, thereby possibly increasing the thickness of the interfacial film. Such a stabilizing effect is probably offset, at least in part, by reduced hydration of the polyoxyethylene moiety of the adsorbed octoxynol 9 film, compressing that film and reducing its effectiveness as a barrier against coalescence. These considerations do not account for the effect of salting-in electrolytes on emulsion stability.

Stabilization Mechanisms and Salt Effects—Nonionic surfactants stabilize aqueous dispersions primarily by steric interactions (18) between the polyoxyethylene moieties of adsorbed surfactant molecules. Electrostatic repulsion plays, at best, a minor role even in the absence of electrolytes (19, 20). At the high and swamping electrolyte concentrations employed in this study, electrostatic forces are unlikely to make any contribution to emulsion stability. Therefore, surface, interfacial, and bulk properties of aqueous solutions of nonionic surfactants containing various electrolytes are examined below for an explanation of the differences between salting-in and salting-out electrolytes, which were especially noticeable in xylene emulsions and in hexadecane emulsions prepared by reverse addition.

The surface areas of polyoxyethylated surfactant molecules adsorbed at air–water or oil–water interfaces depend mainly on the cross-sectional areas of their randomly coiled polyoxyethylene moieties, which are immersed in the aqueous phase (21). Effects of electrolytes on the surface properties of octoxynol 9 and other nonionic surfactants were relatively small (22). In plots of surface tension *versus* the logarithm of concentration, the negative slopes in the region of saturation adsorption were rendered somewhat steeper by the addition of electrolytes at concentrations up to 3 *m*, corresponding to moderate reductions in the surface area per adsorbed surfactant molecule (7). The monolayers of adsorbed surfactant became more closely packed. Salting-in electrolytes produced somewhat larger decreases in surface area than salting-out electrolytes. The largest decreases, observed with cadmium nitrate and sulfuric acid, were 30% (7).

Salting-in electrolytes increased or decreased the plateau surface tensions above the critical micelle concentration by a few dyne/cm at most, and their effectiveness was unrelated to their capacity to raise cloud points (7). Sodium nitrate in concentrations up to 0.1 *M*, calcium nitrate up to 0.01 *M*, and aluminum nitrate up to 10⁻⁴ *M* produced only minor changes in the interfacial tension of the system chlorobenzene–water containing 1% or 10% of the homogeneous nonionic surfactant hexaoxyethylene glycol monohexadecyl ether (HLB = 10.4) (23).

These observations, which refer to monolayers of surfactants, do not adequately explain the differences between the effects of salting-in and

salting-out electrolytes on emulsion stability. On the other hand, an effect similar to the salt-induced contraction of the polyoxyethylene coils of octoxynol 9 molecules forming interfacial films was observed in bulk with aqueous solutions of high molecular weight polyethylene oxides. Their intrinsic viscosity was reduced by cloud-point-depressing electrolytes, indicating a contraction of their hydrodynamic volume⁸ (24). Weaker cloud-point depressants produced smaller reductions in intrinsic viscosity (24), while salting-in electrolytes actually increased the intrinsic viscosity⁸.

Another approach to interpreting the effects of electrolytes is in terms of steric stabilization. Steric stabilization of emulsions requires that the free energy change of the overlap interaction between the polyoxyethylene moieties of the surfactant molecules adsorbed on two approaching droplets be positive. The resulting repulsion may overcome the attraction due to London-van der Waals forces (18). The steric repulsion caused by interpenetration of the adsorbed surfactant layers can be ascribed to an entropic (volume restriction) effect due to a decrease in the conformational entropy of the polyoxyethylene chains and/or to a heat of mixing or osmotic effect (18).

It has been suggested that the increase in the heat of hydration and of mixing caused by salts such as sodium thiocyanate, which salt in nonionic surfactants by destructuring water, results in an increase in the enthalpic contribution to the steric barrier against coalescence (25). Electrolytes which salt in octoxynol 9 by complex formation between their cations and the ether groups are likely to cause an increase in the excess osmotic pressure arising from the overlap of the polyoxyethylene layers of two approaching droplets. An equivalent concept is that these electrolytes increase the positive value of the second virial coefficient of aqueous polyoxyethylene solutions, thereby increasing the repulsion between the polyoxyethylene layers surrounding the droplets (*cf.* Eq. 57 of Ref. 18).

The difference in the effects of salting-in and salting-out electrolytes on the stability of hexadecane emulsions prepared by direct and reverse addition indicates that the interfacial octoxynol 9 films were profoundly affected by the order of addition. This behavior, while not unusual in systems that are intrinsically unstable, is not readily explained by steric stabilization. If the interfacial octoxynol 9 film consisted of multilayers, the observed effects could be ascribed to the formation of a liquid crystalline phase at the hexadecane-water interface (26).

In this connection, it is of interest to estimate the thickness of the layer of octoxynol 9 adsorbed at the surface of the hexadecane droplets. The limiting cross-sectional area per octoxynol 9 molecule adsorbed at the iso-octane-water interface is obtained from the bottom curve of Fig. 8 of Ref. 27, which is a plot of the interfacial tension, $\gamma_{O/W}$, versus the molar concentration, C_2 , of octoxynol 9. The plot is linear from $10^{-5} M$ to the critical micelle concentration, indicating that saturation adsorption prevailed over that concentration range. The equation of the linear portion, obtained by regression analysis from the data points on the graph, is:

$$\gamma_{O/W} = -31.52 - 4.857 \ln C_2 \quad (\text{Eq. 3})$$

Using the value of the slope, $d \gamma_{O/W}/d \ln C_2 = -4.857$ in the Gibbs adsorption equation results in an area of 84.7 \AA^2 per molecule of adsorbed octoxynol 9 at saturation adsorption, *i.e.*, in a close-packed monolayer.

The standard hexadecane emulsions contained 25 g of hexadecane per 100 g of water. Those with 0.10% octoxynol 9 had $D_{vs} = 5.28 \times 10^{-4} \text{ cm}$, which corresponds to an interfacial area of $367,000 \text{ cm}^2$. Assuming that all surfactant molecules in excess of the critical micelle concentration (0.016%) are adsorbed at the oil-water interface, 100 g of a 0.10% octoxynol 9 solution contains 0.084 g of surfactant available for adsorption. This amount covers $686,000 \text{ cm}^2$, *i.e.*, enough for $1.87 \times$ a monolayer, or nearly a bilayer of close-packed octoxynol 9 molecules.

The curves in Fig. 1 tend to level off at $\sim 0.4\%$ octoxynol 9, corresponding to $D_{vs} = 2.28 \text{ \mu m}$. At that point, the amount of octoxynol 9 present exceeds that needed to cover the emulsion droplets with a close-packed monolayer by a factor of 3.7. This value is approximate because the area per octoxynol 9 molecule in an adsorbed multilayer is unlikely to be the same as that in a monolayer. The surfactant films surrounding the droplets, having a thickness of ~ 4 molecules, could well form a liquid crystalline interphase which, though birefringent, is too thin to be visible under the microscope between crossed polarizer and analyzer.

Centrifugal Stability—The first stage in the centrifugation of common oil-water emulsions is the separation of an opaque creamed layer containing all of the oil droplets from a lower clear aqueous layer. Emulsions containing high electrolyte concentrations cream even on standing.

In high centrifugal fields, such as the $7800 \times g$ used here, the spherical oil droplets are probably pressed so close together in the cream layer that they become distorted into polyhedra similar to foams. The centrifugal force then squeezes liquid from the flattened aqueous lamellae separating the oil droplets, which drains through Plateau borders. Coalescence occurs on rupture of the interfacial octoxynol 9 films, resulting in the separation of a clear oil layer (28, 29).

In the course of centrifugation of the hexadecane emulsions, the opaque white cream layer changed within minutes almost completely into a new phase, namely, a transparent gel layer, which propagated from the bottom to the top. Coalescence of hexadecane droplets, resulting in the formation of a clear oil supernatant, occurred slowly from this transparent gel plug.

Despite extensive studies of ultracentrifugation of emulsions by Vold's group (15), Garrett (30), and Rehfeld (31), only brief mention is made (30) of a "translucent cream" above the opaque cream layer. The transparent gel observed in the present work apparently was not detected previously because it is as clear as the coalesced oil and, since it consists of almost pure oil, has almost the same refractive index. The boundary between gel and coalesced hexadecane is faint and becomes evident only to the touch, on separating the layers. Thus, it took a preparative rather than an analytical ultracentrifuge to detect the clear gel.

This gel, unlike the viscous opaque cream layers compacted by centrifugation, had a substantial yield value. Its plastic viscosity was low. Even though the gel consisted mainly of hexadecane, water was the continuous phase. When the centrifuge tubes containing hexadecane emulsions were stored after centrifugation, the clear gel plugs reverted to opaque cream layers as the aqueous phase diffused into them from below.

When pieces of gel were immersed in aqueous solutions, they slowly disintegrated to fluid emulsions. The hexadecane droplets preserved their identity and remained intact in these gels, as shown by the following set of experiments. Gels were prepared by centrifuging standard hexadecane emulsions containing 0.20% octoxynol 9 and either no electrolyte, or 2.00 *m* HCl, or 0.40 *m* Na_2SO_4 . When these gels were redispersed in aqueous media of the same composition as those of the original emulsions, the mean volume-surface diameters of the reconstituted emulsions were 3.66 \mu m for the blank, 3.38 \mu m in 2.00 *m* HCl, and 4.75 \mu m in 0.40 *m* Na_2SO_4 . These diameters are only 23, 5, and 49% larger, respectively, than the D_{vs} values of the original emulsions (Table II).

The gels were transparent and isotropic; they showed no birefringence when examined between crossed polarizer and analyzer. The individual oil droplets could not be distinguished under the microscope. These facts indicate that the thickness of the aqueous lamellae separating the distorted hexadecane droplets in the gels was considerably smaller than the wavelength of light. Thus, light passing through the clear gels underwent little or no refraction.

The chief driving force for the penetration of water or of aqueous solutions of octoxynol 9 and electrolytes into the gel plugs, transforming them back into cream layers and eventually redispersing them into dilute emulsions, is probably the osmotic or enthalpic component responsible for the steric stabilization of emulsions. Centrifugation of the cream layers squeezed the aqueous lamellae between distorted, polyhedral oil droplets down to a thickness of a few nanometers, causing compression or interpenetration of the polyoxyethylene moieties of the octoxynol 9 molecules adsorbed on adjacent droplets. The aqueous lamellae thus contained a high concentration of polyoxyethylene chains, *i.e.*, they were hypertonic compared with the bulk aqueous phase. Elastic retractive forces tending to expand the compressed polyoxyethylene chains and interfacial tension tending to restore the spherical droplet shape probably contributed somewhat to the penetration of aqueous media into the gel plugs.

In connection with the osmotic effect, it is significant that gels made from emulsions containing 0.20% octoxynol 9 plus 2.00 *m* HCl were somewhat more stable than gels formed from emulsions containing octoxynol 9 only, whereas gels from emulsions containing 0.20% octoxynol 9 plus 0.40 *m* Na_2SO_4 were less stable, separating some hexadecane on standing. The former gels probably had somewhat thicker lamellae than gels prepared from emulsions without electrolytes due to the presence of hydrochloric acid molecules bound to the ether groups of octoxynol 9 forming an oxonium compound. The latter gels probably had thinner aqueous lamellae owing to the salting-out effect of sodium sulfate.

The observation that stability measurements by centrifugation and

⁸ Hans Schott, unpublished data.

by the other methods were not in complete agreement is ascribed to the complex sequence of steps occurring during the former. The correlation between long-term shelf stability of emulsions and their resistance to high-speed centrifugation was not sufficiently good to make the latter a reliable technique for predicting the former (32, 33).

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ACKNOWLEDGMENTS

Support by the National Institutes of Health under Grant GM 27802 is gratefully acknowledged.

X-ray Structural Studies and Physicochemical Properties of Cimetidine Polymorphism

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Received April 2, 1982, from the Osaka College of Pharmacy, 2-10-65 Kawai, Matsubara-City, Osaka 580, Japan.

Accepted for publication October 7, 1982.

Abstract □ Four crystalline forms of cimetidine, three anhydrous (forms A, B, and D) and a monohydrate (form C), obtained by slow evaporation of aqueous solutions of varying concentrations were characterized by IR spectroscopy, X-ray powder patterns, dissolution rates in deionized water, and thermal analyses. Among the three anhydrous forms of cimetidine, form A was thermodynamically more stable than the others. The structural conversion of form C into form A on dehydration was confirmed by IR spectroscopy and X-ray powder patterns. The structures of forms C and D were determined using X-ray diffraction. Form D was of spirally curled conformation; it was linked in a head-to-tail arrangement with the neighboring molecules via intermolecular hydrogen bonds between the imidazole nitrogen and guanidine nitrogen atoms. Form C was characterized by its folded conformation due to the weak stacking interaction between the imidazole and guanidine moieties; there was stabilization by double hydrogen bond formation with neighboring molecules and via water molecules of crystallization. The dissolution rate constant

in deionized water for form C was ~1.29, 1.70, and 1.90 times greater than those measured for forms A, D, and B, respectively. There was a similar relationship among the four forms with respect to the rates of inhibition of stress ulceration. Regarding the molecular conformations of the crystalline forms and the rates of inhibition of stress ulceration, the *gauche* orientation of the guanidine group relative to the imidazole ring would be the conformation necessary for effective binding to the histamine H₂-receptor. The compactly folded conformation of form C appears to be optimal for binding to the active site of the receptor and for clinical efficacy.

Keyphrases □ Cimetidine—polymorphic crystalline forms, X-ray structural studies, physicochemical properties □ Polymorphism—cimetidine crystals, X-ray structural studies, physicochemical properties □ Structure—polymorphic crystalline forms of cimetidine, X-ray studies, physicochemical properties

Cimetidine, *N*'-cyano-*N*-methyl-*N*'-[2-[(5-methyl-1*H*-imidazol-4-yl)methyl]thio]ethyl]guanidine, a specific competitive histamine H₂-receptor antagonist, inhibits the secretion of histamine-stimulated gastric acid. Because of

its minimal side effects, it is widely used in the treatment of human peptic ulcers (1). Cimetidine has different crystalline forms (polymorphism) when crystallized under various conditions (2, 3). Since the bioavailability of