Relative Stabilizing Effects of Several High Molecular Weight Polymers on the Stability of a 2 Percent Hexadecane in Water Emulsion

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The stability characteristics of a 2 percent hexadecane in water emulsion containing 0.09 percent dioctyl sodium sulfosuccinate (AOT) were investigated. Size distribution analyses of the emulsified hexadecane particles within the diameter range of 1–25μ were made over an extended time. The volume concentrations of the emulsified oil in this diameter range were calculated. The mass median, the number median, the volume surface, and the arithmetic mean diameters were also calculated. The data obtained established that the changes in particle-size distribution observed were largely the result of coalescence. This system was then employed as a standard to evaluate the effectiveness of methylcellulose, 25 cps., polyvinylpyrrolidone, polyvinyl alcohol, and polyoxyethylene glycol 6000 in retarding the degree and rate of coalescence of this emulsion. It is suggested that strongly hydrated films at the oil-water interface form effective barriers to coalescence.

THE STABILITY of emulsions is a complex phenomenon in which the electrical forces (1, 2) and the film-film interaction forces play an important role (3). The latter force is important especially in the case of emulsions stabilized with nonionic surfactants.

One important group of nonionic surfactants includes certain high molecular weight polymeric substances. King and Mukherjee (4) reported that these agents produced a coarser but more stable emulsion than those stabilized with soaps. Jellinek (5) found that emulsions stabilized with hydrophilic colloidal substances underwent rapid initial changes. The rate of change observed in these systems decreased after a period of time. In another study methylcellulose was found to stabilize latex particles against coagulation with electrolytes by forming a protective film around the particles. The stabilizing effect of methylcellulose increased as its concentration was raised (6).

One of the most widely used methods for studying the stability of emulsions is size-distribution analysis. Usually size analysis data are presented as number count, number percent, and volume or weight percent distributions. Reliance on one parameter may be misleading, since calculations based on volume or weight percents tend to show the importance of small numbers of large globules, while number counts or distributions will minimize the presence of a few large globules which are important in emulsion stability. Thus, the combination of the number-size distributions and weight-size distributions serves to give a better understanding of the nature of changes which occur in emulsions (7).

Deaggregation in hexadecane in water emulsion systems containing various concentrations of dioctyl sodium sulfosuccinate has been reported by Higuchi *et al.* (8) and by Mourad and Lemberger (3, 9). However, none of these studies involved an investigation of coalescence of larger globules. The purpose of this study was to critically examine the coalescence in a 2% hexadecane in water emulsion containing 0.09% dioctyl sodium sulfosuccinate as a basis for further study of the influence of high molecular weight polymers on the stability of the system. Methylcellulose, polyvinylpyrrolidone, polyvinyl alcohol, and polyoxyethylene glycol 6000 were selected for examination as additives.

EXPERIMENTAL

Materials—The hexadecane used for the preparation of the emulsions was purified by redistillation under reduced pressure. Dioctyl sodium sulfosuccinate[1] (AOT) was further purified by the fractional precipitation method (10) from methanol and a water–methanol solvent mixture. The fraction selected for use was that capable of solubilizing 40–50 molecules of water. Water used was doubly distilled from permanganate in a glass apparatus. The poly-

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[1] Aerosol OT, 100% pure, American Cyanamid Co., New York, N. Y.

mers used were methylcellulose 25,[2] polyvinylpyrrolidone, polyvinyl alcohol, and polyoxyethylene glycol 6000.[3]

Instruments—The instrument used for the size-distribution analyses was the Coulter counter, model B.[4] The model B has the advantage of counting particles between two different size limits, thus simplifying the reduction of the raw data. The size analyses were conducted by using a 100-μ aperture tube which had been calibrated with a monodisperse latex system at all the instrument settings used in this study.

The samples were tumbled at a constant temperature in a water bath fitted with a rotating mechanism.

Procedure—The emulsions were prepared by the high-voltage electrical dispersion method described by Nawab and Mason (11) and used previously in these laboratories (3, 8, 9) with a slight modification. A second syringe with needle was mounted above the apparatus such that the oil discharged into the water from the lower syringe was continuously replaced with oil from the top syringe thus maintaining a constant pressure head. Six kilovolts were applied to a 25-gauge needle whose tip was evenly cut perpendicular to its axis. The stock emulsion contained 40% v/v of hexadecane and 1.8% AOT. It was placed in a polyethylene bottle and was aged for 1 week in a rotating wheel-type constant-temperature bath at 30° prior to dilution.

Preparation of 2% Methylcellulose Solution—Methylcellulose powder was added to boiling water ($^1/_3$ of the volume of the needed solution) and stirred to wet the powder completely. The remainder of water was added (cooled at 5°) with stirring. The solution was then stored in a refrigerator for 8 days prior to its use.

Preparation of Polyvinyl Alcohol—The PVA in powder form was added with stirring to cold water (20° or less) until a smooth slurry was obtained. This slurry was heated at 75–80° until complete solution was obtained.

Preparation of Polyvinylpyrrolidone and Polyoxyethylene Glycol 6000—Solutions of polyvinylpyrrolidone and polyoxyethylene glycol 6000 were prepared by dissolving the powders in cold water with stirring.

All the above solutions were filtered with suction through a sintered-glass funnel. Microscopic examinations of these solutions indicated that they were free of particulate matter that might be confused with oil globules.

Preparation of the 2% Hexadecane in Water Emulsions—For a given experiment the stock emulsion was diluted 1–20 by volume in order to obtain a 2% hexadecane emulsion containing 0.09% AOT. Sufficient quantities of concentrated aqueous solutions of the polymeric solutions were added to the system during the dilution of the stock emulsion to give the desired final concentrations of these substances in the emulsion. The concentration of the various additives was set at 0.25, 0.5, 1.00, and 2.00% w/v. The samples containing the various concentrations were placed in 15-ml. glass vials and tumbled gently in the constant-temperature bath at 30°. All emulsions studied were prepared by dilution of the same stock emulsion for each experimental run.

For particle-size analysis exactly 0.5 ml. of the emulsion was diluted to 25 ml. with 0.09% sodium chloride injection solution.[5] Four milliliters of this dilution was further diluted to 100 ml. with more of the sodium chloride solution. This suspension of oil globules was then analyzed for its size distribution using the particle counter fitted with a 100-μ aperture tube. The diluted emulsion samples were analyzed for oil globules within the range of 1–25 μ. Each emulsion system studied was run in triplicate determinations.

Size-distribution data were recorded and processed for the calculation of the different diameter values and determination of the volume of oil in each sample. The volume of the oil particles per given sample volume of the emulsion was referred to as V. The raw data obtained from the size-analysis measurements were processed with the aid of an IBM 1604 computer.

RESULTS AND DISCUSSION

The raw counts obtained by the particle counter were processed to obtain the number and the weight percent distributions. A plot of these weight percents *versus* the particle diameters produced weight-size distribution curves. The number percent distribution curves were obtained by plotting the number percents *versus* the particle diameters. The arithmetic mean diameter, $d_{me.}$, and the volume surface diameter, $d_{vs.}$, were calculated from the data. The mass median and the number median diameters were easily obtained from the plots of weight and number percents against the particle diameters, respectively.

Tables I and II show typical weight and number distribution data, respectively, for the 2% hexadecane in water emulsion stabilized with 0.09% dioctyl sodium sulfosuccinate. Table I also includes values for the mass median (d_m), the number median (d_n), the arithmetic mean, and the volume surface diameters. The total volume of the oil counted (V) and the polydispersity ratio d_m/d_n were also recorded in Table I. Size-distribution analyses and the other parameters were recorded as the average of three samples/run. Graphical representations of Tables I and II are shown in Figs. 1 and 2, respectively.

It is apparent from Figs. 1 and 2 that the size distributions within the size range selected for analysis changed with time. Specifically, it is seen that the larger particles disappeared from the system. Since the large particles constitute a larger percentage of the population on a weight basis than on a number basis, one would expect the size distributions of Fig. 1 to be affected to a greater extent over the time of observation.

The comparative change in size distributions based on weight and number percents can be illustrated even more clearly with the differential plots given in Figs. 3 and 4. The larger particles (>6 μ) are disappearing and, as a result, the smaller particles constitute an increasing fraction of the total population of the aged systems.

An approximate index to the behavior of this system upon aging is provided by the mass median

[2] Methocel 25, Dow Chemical Co., Midland, Mich.
[3] Carbowax 6000, Union Carbide and Carbon Corp., New York, N. Y.
[4] Coulter Electronics, Inc., Hialeah, Fla.
[5] Abbott Laboratories, Chicago, Il

TABLE I—TYPICAL DATA OBTAINED FROM WEIGHT PERCENT DISTRIBUTION ANALYSES OF A 2% HEXADECANE IN WATER EMULSION STABILIZED WITH 0.09% AOT

du	1 day	4 days	7 days	11 days	16 days	42 days	94 days	224 days
24.88	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
19.78	4.04	0.30	0.00	0.00	0.00	0.00	0.00	0.00
15.67	12.27	2.30	1.32	0.83	0.69	0.40	0.70	0.64
12.43	24.64	7.20	3.42	1.70	1.21	1.13	1.01	1.03
9.87	38.02	18.78	9.04	4.93	3.22	1.41	1.29	1.25
7.83	52.19	31.66	18.85	11.56	7.50	2.67	1.48	1.43
6.21	64.73	45.81	32.13	22.63	16.69	5.95	2.13	1.64
4.92	75.15	61.30	49.06	38.88	32.06	15.89	6.29	2.06
3.92	84.98	75.35	66.65	59.48	52.98	34.94	20.57	3.26
3.11	91.86	86.69	82.48	78.34	74.43	60.98	47.93	12.15
2.46	95.83	94.20	93.09	91.56	89.66	84.10	77.63	41.88
1.95	98.49	98.24	98.30	97.87	96.96	95.88	94.99	77.16
1.65	99.48	99.50	99.59	99.43	99.21	99.01	98.97	92.54
1.43	99.90	99.95	99.93	99.90	99.85	99.91	99.82	98.66
1.14	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
				Calculated Values				
d_m	8.00	6.70	5.60	4.70	4.10	3.35	3.05	2.30
d_n	2.47	2.62	2.71	2.67	2.58	2.48	2.40	1.95
d_m/d_n	3.23	2.53	2.06	1.80	1.59	1.35	1.26	1.18
$d_{me.}$	2.76	2.72	2.69	2.60	2.49	2.36	2.26	1.83
$d_{vs.}$	5.63	4.53	3.94	3.60	3.33	2.92	1.65	1.05
Volume $\times 10^{-53}$	4.65	4.41	3.75	3.54	2.70	1.86	1.67	1:31

diameter and number median diameter of the particles as read from the appropriate plots. The volume surface diameter calculated from the raw data is also indicative of the behavior of the system. The ratio between the mass median and number median diameters, d_m/d_n, termed the polydispersity by Rowe (12) is also useful as a criterion of emulsion stability. As this ratio approaches unity, the emulsion system is approaching the monodisperse state.

The disappearance of the larger particles could be accounted for either by coalescence or by deaggregation. Significant deaggregation seems the less likely explanation, however, because in this case, one would expect to see a much more pronounced increase in the frequency of the small particles on a number percent basis than actually occurs. This conclusion seems further justified by the marked decrease in cumulative volume of particles counted in the sample taken as the emulsion aged (Table I).

Influence of Additives—The arithmetic mean diameters, volume-surface diameters, the mass median diameters, the number median diameters, and the polydispersity ratios for emulsion systems containing various concentrations of polymeric substances were obtained over a period of aging. These parameters are given in Tables III, IV, V, and VI for methylcellulose, polyvinyl alcohol, polyoxyethylene glycol 6000, and polyvinylpyrrolidone containing systems, respectively. Since each system was prepared from a separately prepared standard emulsion the values for each of these emulsions are also given in the tables. From the data presented it can be seen that all standard systems demonstrated essentially the same behavior.

Examination of Tables III and IV reveals that addition of either methylcellulose or polyvinyl alcohol resulted in a stabilizing effect. Perhaps of most significance is the observation that d_m did not decrease as markedly over the aging period while d_n tended to remain constant or actually to increase slightly in value. Thus, the polydispersity tended to stabilize indicating that the particle-size distribution of the emulsified hexadecane remained essentially the same. This is also confirmed in Figs. 5 and 6 which show the weight percent size distributions of the emulsions containing 2% methylcellulose and

TABLE II—TYPICAL DATA OBTAINED FROM NUMBER PERCENT DISTRIBUTION ANALYSES OF A 2% HEXADECANE IN WATER EMULSION STABILIZED WITH 0.09% AOT

du	1 day	4 days	7 days	11 days	16 days	42 days	94 days	224 days
24.88	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
19.78	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00
15.67	0.16	0.02	0.01	0.01	0.00	0.00	0.00	0.00
12.43	0.55	0.15	0.05	0.01	0.01	0.01	0.00	0.00
9.86	1.40	0.57	0.25	0.11	0.06	0.01	0.01	0.00
7.83	3.12	1.71	0.94	0.50	0.27	0.05	0.13	0.01
6.21	6.23	4.13	2.80	1.80	1.19	0.30	0.52	0.01
4.92	11.68	9.44	7.36	5.61	4.26	1.48	0.66	0.04
3.92	20.83	19.04	17.46	15.24	12.64	7.57	4.02	0.44
3.12	34.45	34.65	35.27	33.14	29.79	23.16	17.18	2.24
2.47	49.91	55.23	58.96	57.96	54.17	50.78	45.61	15.87
1.95	70.97	77.44	82.43	81.60	77.53	78.41	78.80	48.16
1.65	85.54	90.77	91.04	92.37	92.55	93.09	93.56	74.52
1.44	95.79	98.45	98.26	98.90	98.30	98.54	98.02	91.23
1.14	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00

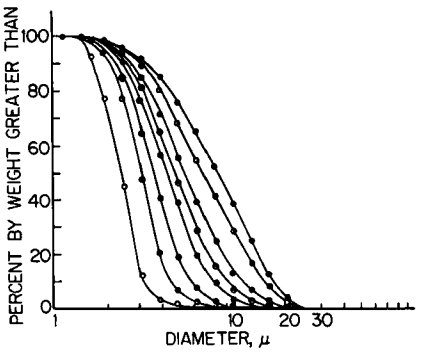

Fig. 1—Typical weight percent–particle-size distribution curves for a 2% hexadecane emulsion containing 0.09% AOT. Key: ◐, 1 day; ◑, 4 days; ●, 7 days; ◓, 11 days; ◒, 16 days; ⊕, 42 days; ⊙, 129 days; ○, 224 days.

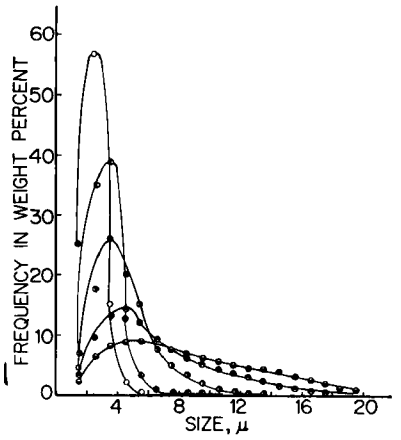

Fig. 3—A plot of frequency in weight percent against size for a 2% N hexadecane emulsion containing 0.09% AOT. Key: ◒, 1 day; ◓, 4 days; ◑, 17 days; ◐, 94 days; ○, 224 days.

2% polyvinyl alcohol over the period of observation. The stabilizing effect of different concentrations of these additives is also indicated by the $d_{vs.}$ values obtained. The volume-surface diameter decreased markedly with time of aging in the standard system, whereas the $d_{vs.}$ tended toward a constant value as the concentration of additive was increased. That these additives not only stabilized the size distribution but also reduced coalescence rates is demonstrated in Figs. 7 and 8. In these figures the reciprocal of the volume of hexadecane in the sample analyzed is plotted as a function of time. The manner of plotting is analogous to that of Smoluchowski (13, 14). It is seen that coalescence occurs rapidly initially in the standard emulsions probably due to the formation of droplets larger than 25 μ in diameter from the larger droplets initially present. Since the sample included particles to a maximum of 25 μ in diameter, the total volume of the emulsified hexadecane particles larger than this would be lost to observation. Increasing concentrations of methylcellulose 25 and polyvinyl alcohol progressively reduced the rate of coalescence and at the maximum concentration used in these studies, the total volume of internal phase remained constant. This observation coupled with the size-distribution analyses data indicate that, principally, the larger globules seem to be stabilized against coalescence to form particles larger than 25 μ.

A similar family of plots for emulsions containing polyvinylpyrrolidone and polyoxyethylene glycol 6000 are given in Figs. 9–12. As one would expect from the data given in the tables of these systems, there is no evidence of stabilization. Neither the polydispersity ratios nor the volume-surface diameters obtained differed significantly from those obtained with the standard emulsion. The weight percent size distributions of the systems containing 2% of these additives are seen to change during the aging period in the same manner as the control emulsions. The plots of $1/V$ against time give families of roughly parallel lines showing that the rate of coalescence in these systems is identical to that of the control emulsions.

The polymeric substances used in this study possess surface-active properties. They reduce surface tension of water and have the ability to be adsorbed at the interfaces (6, 15–17). The mode of the orien-

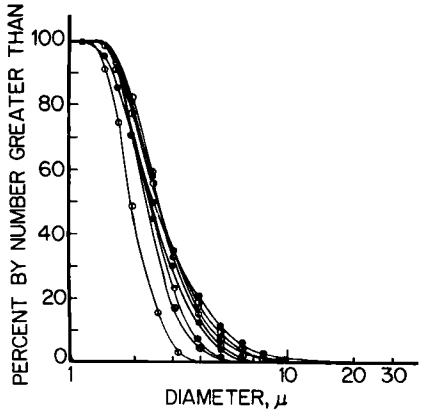

Fig. 2—Typical number percent–particle-size distribution curves for a 2% hexadecane emulsion containing 0.09% AOT. Key: ●, 1 day; ◑, 4 days; ◐, 7 days; ⊙, 11 days; ◒, 16 days; ◓, 42 days; ⊕, 94 days; ⓓ, 224 days.

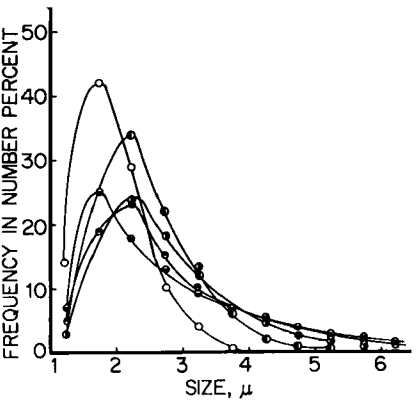

Fig. 4—A plot of frequency in number percent against size for a 2% N hexadecane emulsion containing 0.09% AOT. Key: ◒, 1 day; ◓, 4 days; ◑, 17 days; ◐, 94 days; ○, 224 days.

TABLE III—VARIOUS VALUES CALCULATED FOR THE STANDARD SYSTEM CONTAINING METHYLCELLULOSE

	1 day	4 days	7 days	11 days	16 days	42 days	94 days	224 days
Standard, μ								
$d_{me.}$	2.76	2.72	2.69	2.60	2.49	2.36	2.25	1.83
$d_{vs.}$	5.63	4.53	3.94	3.60	3.33	2.92	2.65	2.05
d_m	8.00	6.70	5.60	4.70	4.10	3.35	3.05	2.30
d_n	2.47	2.62	2.71	2.67	2.58	2.48	2.40	1.94
d_m/d_n	3.23	2.53	2.06	1.80	1.59	1.35	1.26	1.18
Standard + 0.25% methylcellulose, μ								
$d_{me.}$	2.79	2.72	2.62	2.71	2.65	2.65	2.50	2.14
$d_{vs.}$	5.57	4.74	4.24	4.09	3.84	3.48	3.11	2.77
d_m	8.00	6.40	5.45	5.05	4.80	4.00	3.60	2.90
d_n	2.56	2.58	2.60	2.69	2.67	2.74	2.63	2.24
d_m/d_n	3.13	2.51	2.08	1.87	1.79	1.46	1.36	1.29
Standard + 0.50% methylcellulose, μ								
$d_{me.}$	2.69	2.71	2.51	2.58	2.51	2.49	2.43	2.33
$d_{vs.}$	5.57	5.22	4.84	4.69	4.61	4.43	3.99	3.76
d_m	8.15	7.20	6.60	6.05	5.80	5.30	4.70	4.40
d_n	2.42	2.48	2.31	2.44	2.36	2.36	2.36	2.26
d_m/d_n	3.38	2.89	2.86	2.47	2.45	2.24	1.99	1.95
Standard + 1.00% methylcellulose, μ								
$d_{me.}$	2.59	2.59	2.49		2.39	2.48	2.53	2.51
$d_{vs.}$	5.68	5.31	5.04		4.92	4.61	4.23	3.64
d_m	8.60	7.60	7.30	no data	7.00	6.25	5.70	4.70
d_n	2.31	2.34	2.15		2.13	2.27	2.39	2.54
d_m/d_n	3.72	3.24	3.38		3.04	2.74	2.38	1.84
Standard + 2.00% methylcellulose, μ								
$d_{me.}$	2.64	2.65	2.46		2.41	2.54	2.55	2.52
$d_{vs.}$	5.74	5.55	5.28		5.16	4.47	4.76	4.57
d_m	8.10	8.05	7.70	no data	7.40	6.60	6.40	6.00
d_n	2.34	2.36	2.17		2.08	2.27	2.32	2.34
d_m/d_n	3.68	3.40	3.51		3.56	2.90	2.78	2.56

TABLE IV—VARIOUS VALUES CALCULATED FOR THE STANDARD SYSTEM CONTAINING POLYVINYL ALCOHOL (PVA)

	1 day	3 days	6 days	10 days	16 days	42 days	129 days	212 days
Standard, μ								
$d_{me.}$	2.45	2.43	2.42	2.44	2.33	2.25	2.00	1.85
$d_{vs.}$	4.62	4.33	4.08	3.75	3.40	2.89	2.40	2.13
d_m	6.40	5.80	5.30	4.80	4.30	3.40	2.75	2.40
d_n	2.25	2.29	2.31	2.40	2.32	2.33	2.09	1.94
d_m/d_n	2.84	2.53	2.28	2.00	1.85	1.45	1.32	1.23
Standard + 0.25% PVA, μ								
$d_{me.}$	2.33	2.37	2.39	2.42	2.45	2.51	2.42	2.40
$d_{vs.}$	4.51	4.43	4.35	4.13	3.83	3.48	3.01	2.82
d_m	6.40	6.00	5.80	5.42	5.00	4.25	3.55	3.30
d_n	2.10	2.16	2.21	2.28	2.15	2.53	2.57	2.45
d_m/d_n	3.03	2.76	2.62	2.36	2.32	1.67	1.38	1.34
Standard + 0.50% PVA, μ								
$d_{me.}$	2.33	2.35	2.38	2.43	2.43	2.57	2.61	2.48
$d_{vs.}$	4.64	4.55	4.46	4.20	4.03	3.65	3.27	3.06
d_m	6.40	6.25	6.08	5.55	5.30	4.55	3.90	3.60
d_n	2.00	2.24	2.16	2.29	2.31	2.60	2.76	2.64
d_m/d_n	3.19	2.78	2.80	2.42	2.29	1.75	1.41	1.37
Standard + 1.00% PVA, μ								
$d_{me.}$	2.22	2.37	2.34	2.34	2.34	2.49	2.72	2.60
$d_{vs.}$	4.66	4.63	4.68	4.60	4.55	4.27	3.97	4.12
d_m	6.70	6.50	6.40	6.30	6.15	5.60	5.00	4.70
d_n	1.95	2.17	2.09	2.08	2.09	2.32	2.75	2.53
d_m/d_n	3.42	2.98	3.05	3.02	2.94	2.41	1.82	1.85
Standard + 2.00% PVA, μ								
$d_{me.}$	2.28	2.29	2.28	2.36	2.31	2.37	2.66	2.53
$d_{vs.}$	4.81	4.70	4.78	4.75	4.60	4.61	4.42	4.38
d_m	6.90	6.80	6.85	6.80	6.65	6.40	6.15	5.65
d_n	1.99	2.00	1.98	2.10	1.95	2.12	2.53	2.38
d_m/d_n	3.45	3.39	3.45	3.23	3.39	3.01	2.43	2.36

TABLE V—VARIOUS VALUES CALCULATED FOR THE STANDARD SYSTEM CONTAINING POLYOXYETHYLENE GLYCOL 6000

	1 day	3 days	6 days	9 days	15 days	33 days	129 days	212 days
Standard, μ								
$d_{me.}$	2.51	2.39	2.38	2.41	2.43	2.29	2.00	1.76
$d_{vs.}$	4.66	4.38	4.14	3.97	3.65	3.22	2.39	2.00
d_m	6.40	6.00	5.55	5.20	4.70	4.10	2.75	2.25
d_n	2.33	2.20	2.25	2.33	2.42	2.34	2.12	1.87
d_m/d_n	2.74	2.62	2.46	2.22	1.94	1.75	1.30	1.20
Standard + 0.25% polyoxyethylene glycol 6000, μ								
$d_{me.}$	2.48	2.32	2.39	2.34	2.40	2.21	1.78	1.63
$d_{vs.}$	4.70	4.28	4.13	3.93	3.59	3.20	2.13	1.87
d_m	6.20	5.60	5.38	5.00	4.50	3.90	2.35	2.05
d_n	2.31	2.15	2.25	2.27	2.38	2.25	1.86	1.70
d_m/d_n	2.68	2.50	2.38	2.19	1.95	1.73	1.26	1.20
Standard + 0.5% polyoxyethylene glycol 6000, μ								
$d_{me.}$	2.42	2.38	2.42	2.36	2.42	2.23	1.83	1.66
$d_{vs.}$	4.37	4.28	4.00	3.77	3.53	2.99	2.11	1.86
d_m	6.00	5.60	5.20	4.90	4.40	3.70	2.30	2.00
d_n	2.27	2.30	2.31	2.27	2.40	2.19	1.93	1.77
d_m/d_n	2.70	2.68	2.26	2.17	1.83	1.68	1.19	1.13
Standard + 1.00% polyoxyethylene glycol 6000, μ								
$d_{me.}$	2.45	2.36	2.37	2.34	2.38	2.31	1.98	1.86
$d_{vs.}$	4.75	4.29	4.00	3.73	3.54	3.18	2.40	2.19
d_m	6.00	5.65	5.20	4.80	4.50	3.80	2.70	2.36
d_n	2.25	2.19	2.26	2.24	2.37	2.31	2.09	2.00
d_m/d_n	2.68	2.64	2.40	2.14	1.90	1.64	1.28	1.18
Standard + 2.00% polyoxyethylene glycol 6000, μ								
$d_{me.}$	2.34	2.39	2.36	2.36	2.43	2.33	1.90	1.68
$d_{vs.}$	4.39	4.29	3.98	3.84	3.52	3.22	2.24	1.90
d_m	6.00	5.60	5.25	4.90	4.50	3.90	2.45	2.00
d_n	2.18	2.24	2.24	2.28	2.42	2.30	2.02	1.75
d_m/d_n	2.74	2.58	2.34	2.14	1.86	1.69	1.22	1.14

TABLE VI—VARIOUS VALUES CALCULATED FOR THE STANDARD SYSTEM CONTAINING POLYVINYLPYRROLIDONE (PVP)

	1 day	4 days	7 days	12 days	21 days	43 days	80 days	140 days
Standard, μ								
$d_{me.}$	2.52	2.55	2.57	2.59	2.54	2.57	2.53	2.37
$d_{vs.}$	4.69	4.33	4.98	3.92	3.66	3.45	3.26	3.04
d_m	6.20	5.60	5.10	4.80	4.50	4.15	3.90	3.40
d_n	2.43	2.49	2.56	2.61	2.58	2.66	2.65	2.48
d_m/d_n	2.54	2.28	1.99	1.83	1.74	1.56	1.46	1.37
Standard + 0.25% PVP, μ								
$d_{me.}$	2.46	2.34	2.43	2.42	2.35	2.29	2.23	2.11
$d_{vs.}$	4.51	3.96	3.74	3.56	3.42	3.19	3.00	2.88
d_m	6.00	5.00	4.70	4.40	4.20	3.75	3.50	3.20
d_n	2.37	2.39	2.40	2.35	2.33	2.30	2.18	
d_m/d_n	2.52	2.09	1.96	1.82	1.78	1.61	1.52	1.46
Standard + 0.50% PVP, μ								
$d_{me.}$	2.44	2.48	2.50	2.52	2.37	2.40	2.32	2.19
$d_{vs.}$	4.46	4.09	3.89	3.71	3.32	3.27	3.04	2.76
d_m	5.90	5.05	4.75	4.50	4.05	3.80	3.60	3.30
d_n	2.38	2.44	2.47	2.53	2.39	2.46	2.39	2.16
d_m/d_n	2.48	2.06	1.92	1.78	1.68	1.54	1.49	1.50
Standard + 1.00% PVP, μ								
$d_{me.}$	2.38	2.47	2.49	2.51	2.47	2.44	2.38	2.30
$d_{vs.}$	4.42	3.99	3.83	3.68	3.42	3.30	3.04	2.64
d_m	5.80	5.00	4.80	4.50	4.30	3.90	3.60	3.20
d_n	2.41	2.43	2.47	2.52	2.50	2.50	2.42	2.30
d_m/d_n	2.41	2.05	1.94	1.78	1.71	1.56	1.49	1.38
Standard + 2.00% PVP, μ								
$d_{me.}$	2.49	2.50	2.52	2.53	2.50	2.50	2.40	2.27
$d_{vs.}$	4.48	4.06	3.88	3.77	3.59	3.42	3.07	2.79
d_m	5.80	5.00	4.80	4.60	4.40	4.20	3.70	3.20
d_n	2.43	2.47	2.50	2.53	2.53	2.57	2.51	2.39
d_m/d_n	2.38	2.03	1.91	1.81	1.73	1.63	1.47	1.34

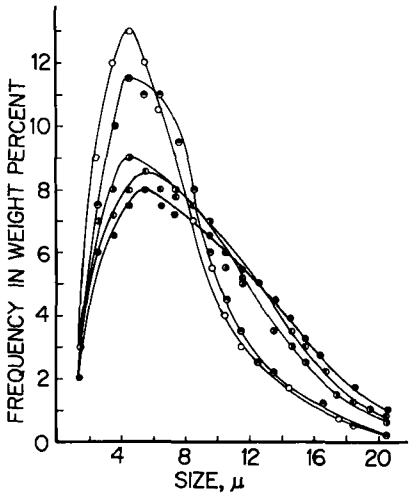

Fig. 5—A plot of frequency in weight percent against size for the system containing 2.0% methylcellulose as an additional stabilizer. Key: ●, 1 day; ◐, 4 days; ◑, 17 days; ◓, 94 days; ○, 227 days.

tation of these substances might be responsible for the differences in their stabilizing effect on the emulsions under study. Since the concentration of AOT in the system (0.09%) is below the critical micelle concentration, it can also be assumed that the monolayer surrounding the oil particles will be of the expanded type. If enough substance is adsorbed at the interface, the expanded monomolecular film may change to a more condensed film which, in turn, may protect the globules against coalescence. It, therefore, could well be that the stabilizing effect of methylcellulose and polyvinyl alcohol was a result of their adsorption and orientation at the interface in such a manner as to ensure the transformation of the expanded AOT film to a more condensed, stronger monomolecular layer. The degree of this transformation appears to be dependent upon the concentration of the additive as had been reported by Saunders (6). He found that the stabilization of latex particles by methylcellulose was dependent upon the concentration of the latter substance. He also reported that latex particles were stable when enough methyl-

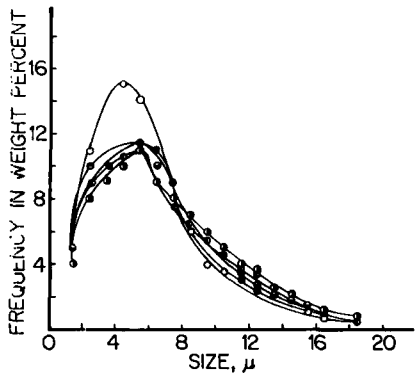

Fig. 6—A plot of frequency in weight percent against size for the system containing 2.00% polyvinyl alcohol as an additional stabilizer. Key: ◑, 1 day; ◐, 3 days; ◓, 16 days; ◒, 129 days; ○, 224 days.

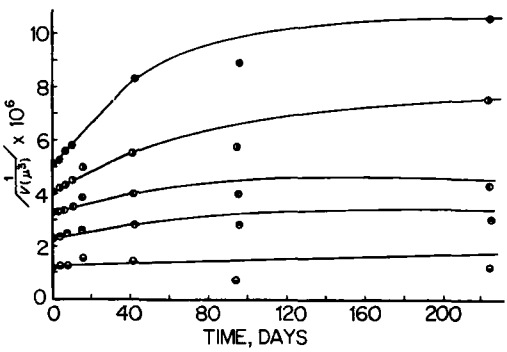

Fig. 7—A plot of the reciprocal of the volume of emulsified particles/50 ml. of emulsion (V) against time for systems containing methylcellulose as an additional stabilizer. Key: ●, standard (+3); ◑, 0.25% (+2); ◐, 0.50% (+1); ◒, 1.00%; ◓, 2.0% (−1). (Values in parentheses indicate a factor added to value of 1/V for plotting purposes only.)

cellulose was added to ensure a condensed monolayer around the particles.

Methylcellulose and polyvinyl alcohol possess hydroxyl groups in their structures. These hydroxyl groups are strongly hydrophilic because of their tendency toward hydrogen bonding with the water molecules in the external phase. Thus, upon adsorption at the interface, the methylcellulose and the polyvinyl alcohol orient themselves in such a way that a hydrated film is formed around the oil globules which tends to protect them against coalescence.

The stabilizing effect of such hydrated films was observed by Van den Temple (18) in his work with paraffin in water emulsions. He described the oil particles as being separated by a water film which might be the result of hydration or solvation of the original film.

On the other hand, polyoxyethylene glycol 6000 and polyvinylpyrrolidone showed no stabilizing effect on the emulsion under study, although one can as-

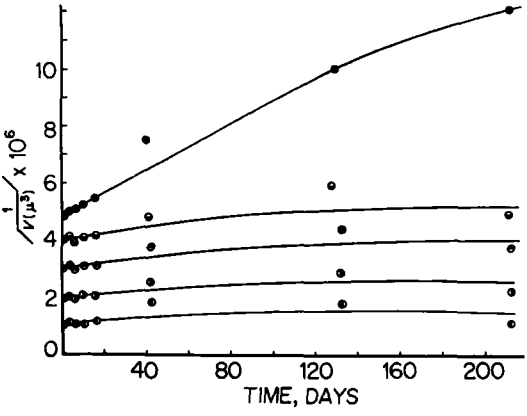

Fig. 8—A plot of the reciprocal of the volume of emulsified particles/50 ml. of emulsion (V) against time for systems containing polyvinyl alcohol as additional stabilizer. Key: ●, standard (+3); ◓, 0.25% (+2); ◒, 0.50% (+1); ◑, 1.00%; ◐, 2.00% (−1). (Values in parentheses indicate a factor added to value of 1/V for plotting purposes only.)

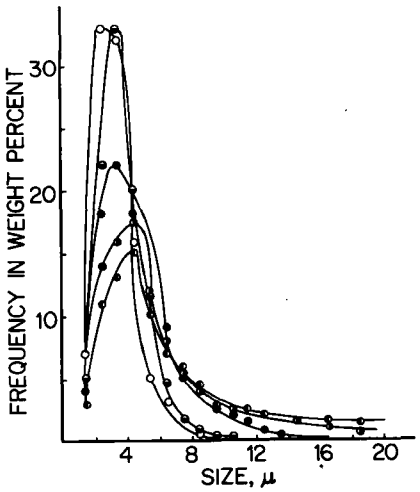

Fig. 9—A plot of frequency in weight percent against size for the system containing 2.00% polyvinylpyrrolidone as an additional stabilizer. Key: ◐, 1 day; ◑, 4 days; ●, 21 days; ◒, 80 days; ○, 140 days.

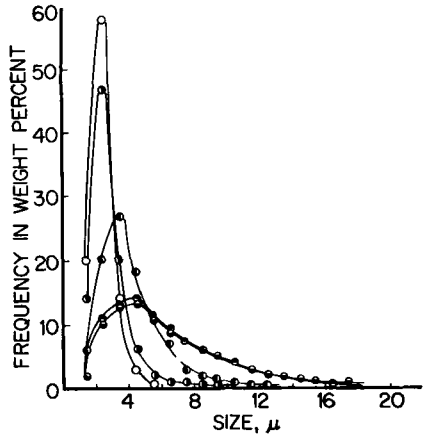

Fig. 10—A plot of frequency in weight percent against size for the system containing 2.00% polyoxyethylene glycol 6000 as an additional stabilizer. Key: ◒, 1 day; ◓, 3 days; ◐, 33 days; ◑, 129 days; ○, 212 days.

sume that water molecules could be attracted to at least some of the ether oxygen atoms by hydrogen bonds. The hydrophilic nature of the polyoxyethylene glycol or polyvinylpyrrolidone may not be sufficient to induce orientation of the molecu'e at the interface in such a definitive manner as with methylcellulose or polyvinyl alcohol.

Eley (17) described the molecule of polyoxyethylene glycol adsorbed at the interface as lying approximately flat in the water surface. He also added that molecules will not be expected to pack well when lying flat in a surface. Thus, it seems reasonable to assume that the polyoxyethylene glycol films formed around the oil globules were not oriented in such a manner as to produce strongly hydrated films. The same may be true for polyvinylpyrrolidone, but further studies are needed to investigate the mode of adsorption of these polymeric substances at the interface before more definitive statements can be made.

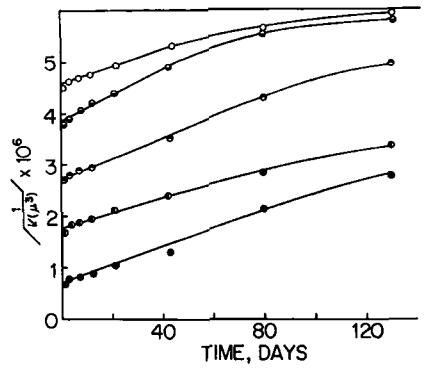

Fig. 11—A plot of the reciprocal of the volume of emulsified particles/50 ml. of emulsion (V) against time for systems containing polyvinylpyrrolidone as an additional stabilizer. ○, standard (+3); ◒, 0.25% (+2); ◓, 0.50% (+1); ◐, 1.00%; ●, 2.00% (−1). (Values in parentheses indicate a factor added to value of 1/V for plotting purposes only.)

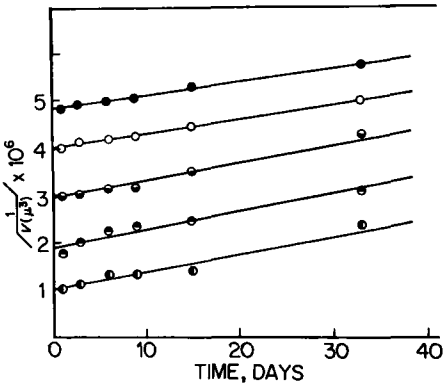

Fig. 12—A plot of the reciprocal of the volume of emulsified particles/50 ml. of emulsion (V) against time for systems containing polyoxyethylene glycol 6000 as an additional stabilizer. Key: ●, standard (+3); ○, 0.25% (+2); ◒, 0.50% (+1); ◓, 1.00%; ◐, 2.00% (−1). (Values in parentheses indicate a factor added to value of 1/V for plotting purposes only.)

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Keyphrases

Emulsion stabilization—polymers
Hexadecane-water emulsion—high mol. wt. polymers, stabilization
Particle-size distribution—emulsions
Polymers, effect—emulsion particle size
Stability, emulsions—aging, polymer effect

Evaluation of Physical and Pharmaceutical Factors Involved in Drug Release and Availability from Chloramphenicol Capsules

By A. J. AGUIAR, L. M. WHEELER, S. FUSARI, and J. E. ZELMER

The importance of physical and pharmaceutical factors involved in chloramphenicol release and availability from four commercial lots of chloramphenicol was evaluated. The study was carried out in three parts: (*a*) deaggregation or dispersion determinations, (*b*) dissolution studies, and (*c*) *in vitro* gut permeation using an everted sac technique. A correlation between drug release as reflected by the deaggregation and dissolution rates and chloramphenicol plasma levels in humans is demonstrated. In this specific instance the results of the study demonstrate that, although the products tested contain analytically the same quantity of chloramphenicol, the rate of release of the antibiotic, and hence its availability from the capsules differs significantly. The commonly accepted scheme which defines drug absorption from dosage forms is modified to include the deaggregation rate.

THE IMPORTANCE of physical properties of drugs in relation to their pharmacological availability and activity has been demonstrated and emphasized repeatedly in the past. Until recently, proportionally little attention was paid to studies related to drug release from pharmaceutical dosage forms. For example, there has been a vast amount of research done to evaluate dissolution rates of drugs from tablets where the geometry of the dissolving surface is kept constant during the dissolution process. However, most tablets and capsules of drugs used in clinical therapy are intended to disintegrate in the gastrointestinal environment after oral administration.

If the tablets or capsules disintegrate, the surface area and the geometry of the dissolving surface will change continuously with time. The dissolution rate which is dependent on the surface area will also change. Therefore, studies in which the dispersion (or deaggregation) as well as the dissolution rates are measured are of greater value in assessing the optimum formula for a capsule or tablet of a drug than simple dissolution measurements. The studies would also allow a closer correlation of drug availability from the dosage forms with plasma levels or other pharmacological criteria of drug efficacy.

The present work is an evaluation of the availability of chloramphenicol from four commercial lots of chloramphenicol capsules. Specifically the study is an attempt to relate pharmaceutical and physical factors with the differences in plasma levels observed when the four capsules were tested in adult human volunteers. The human absorption studies are reported elsewhere (1, 2).

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EXPERIMENTAL

The capsules tested were four commercial lots of chloramphenicol capsules produced by different manufacturers and were purchased from a local