Effect of Ultrasound on Particle Size of Suspensions of Polyethylene Spheres

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The effect of ultrasound energy on the particle size of polyethylene spheres in aqueous suspension, with and without additives such as surfactants and deflocculating agents, and using variable times of exposure to ultrasound, were studied. Particle size was determined microscopically and expressed as the mean diameter of the particles. It was found that ultrasonic waves, at a frequency of 100 kc., caused a significant reduction in particle size only if surfactants were present. It was also observed that surfactants having high HLB values were the most efficient of all additives. Increasing time of exposure to the ultrasound waves brought about a continued reduction of particle diameter up to 2 hr., but that after this time the particle size stabilized, and further exposure produced no significant decrease in the mean diameter of the polyethylene spheres.

In recent years, ultrasonic energy has been shown to cause particle size reduction in emulsions (1–4) and suspensions (5–9).

There are conflicting reports on the influence of the total time of exposure to the ultrasonic waves, however. Some authors stated that an optimum period was needed and that continued exposure could even cause an increase in particle size in emulsions (2, 3). Others found that after an optimum exposure time there is little or no change in particle size of emulsions (4). A similar observation has been made with suspensions (6). Another paper reports that the particle size reduction continued as the time of exposure was lengthened (8). It is very possible that the conflicting results of these studies might have been due to differences in the intensity and frequency of ultrasound that was used or to variance in the crystalline structure of the compounds used in the suspensions.

It was the aim of this investigation to correlate, if possible, the time of exposure to ultrasound to the degree of size reduction of suspension particles in a highly reproducible suspension under closely controlled experimental conditions; a second objective was to evaluate the effect of various concentrations of surfactants and deflocculants on the exposed suspensions. The third objective was to determine if the concentration of suspension particles is important.

A generator producing sound waves at a frequency of 100 kc. was selected. It was felt that higher frequencies could cause some side reactions to occur which might introduce other variables, and very high plate power is required to produce cavitation at higher frequencies.

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EXPERIMENTAL

Equipment and Materials.—The apparatus used to supply ultrasonic power for all experiments consisted of a 100-kc. generator,[1] and a bath equipped with a barium titanate transducer. A round copper coil, attached to a circulating constant-temperature bath, was inserted in the transducer bath in order to keep the temperature constant at 25 ± 1° during the investigation.

The instrument selected for the determination of the particle size of the suspensions was a Spencer microscope with an AO Spencer micrometer.[2]

A microfine polyethylene resin,[3] was selected to prepare the experimental suspensions. This substance offers several characteristics to commend it for this use: (*a*) the polyethylene is hydrophobic and cavitation occurs more easily at hydrophobic surfaces; (*b*) the particles are spherical and, therefore, easy to count; (*c*) there are two size ranges available, 3–20 μ diameter (Microthene 500) and 8–30 μ (Microthene 510); and (*d*) the material is inexpensive.

Procedure.—An 0.5% suspension of Microthene 500 or 510 was used as the basic suspension. Additives were used in varying concentrations at different times to study their effect. These included the surfactants polysorbate 20[4] and sodium lauryl sulfate, and the deflocculating agents Darvan,[5] Daxad,[5] and Marasperse.[6] The suspension to be exposed was placed in a 125-ml. flask, and this was immersed in the transducer bath so that the level of the suspension was always below the level of water in the transducer bath. Temperature was kept constant at 25°, and the generator plate voltage was kept at 1000 v. After varying intervals of time, representative samples of the suspension were withdrawn from the flask, particle sizes were determined microscopically by measuring the diameters of 200 particles for each sample, and the mean diameter was calculated for each sample. Later the concentration of Microthene 500 and Microthene 510 was varied from 0.5 to 4%. Poly-

[1] McKenna model 100 generator, McKenna Laboratories, Santa Monica, Calif.
[2] American Optical Co., Buffalo, N. Y.
[3] Marketed as Microthene by the U. S. Industrial Chemical Co., New York, N. Y.
[4] Marketed as Tween 20 by the Atlas Chemical Co., Wilmington, Del.
[5] Dewey and Almy Chemical Co., Cambridge, Mass.
[6] Marathon Chemical Corp., Division of American Can Co., Neenah, Wis.

sorbate 20 was added to all of these suspensions in a concentration of 0.1%.

RESULTS

The mean particle sizes of Microthene 500 and 510 suspensions containing varying concentrations of polysorbate 20 and sodium lauryl sulfate are shown in Tables I–IV. It is apparent that the addition of these agents facilitated a substantial reduction in particle size after 2 hr. exposure time, but that, usually, a plateau was reached at that time, and longer exposure caused little or no further reduction in the mean particle diameter.

It is also apparent that a 0.05 to 0.1% concentration of surfactant is satisfactory, and that higher concentrations do not increase the effectiveness of the ultrasound.

A study of the effect of the HLB (10) of surfactants was made by using mixtures of sorbitans[7] and polysorbates. The results are shown in Table V. It appears that there is little difference in effect on particle size reduction if the HLB of the surfactant mixture is greater than 10, but that as the HLB is reduced below that point, the effect of ultrasound is reduced.

There is no significant difference in the magnitude of the decrease between Microthene 500 and Microthene 510 if the decrease in particle size is computed on the basis of percentage of change of mean particle diameter.

Particle size reduction of Microthene suspensions in the presence of deflocculants such as Marasperse, Darvan, and Daxad was negligible, and practically the same as when no additive at all was used. These agents are charged particles which are adsorbed on the surface of the suspended particles preventing flocculation by electrical repulsion without appreciably affecting surface tension. Table VI, which shows the effect of ultrasound in a Microthene suspension in the presence of Darvan, is typical.

The effect of increasing the concentration of the suspended phase is shown in Tables VII and VIII. It is apparent that the effect of ultrasound in reducing particle size becomes less marked as the concentration of the suspended phase increases.

TABLE I.—EFFECT OF ULTRASOUND ENERGY ON PARTICLE SIZE OF MICROTHENE 500 WITH VARYING CONCENTRATIONS OF POLYSORBATE 20[a]

Polysorbate 20, %	Time of Exposure, min. 0	60	120	180	240
None	5.5	5.3	5.2	5.2	5.1
0.05	5.4	4.7	4.6	4.6	4.6
0.1	5.4	4.8	4.3	4.3	4.3
0.2	5.2	5.1	4.7	4.4	4.4

[a] All mean diameters are given in microns.

TABLE II.—EFFECT OF ULTRASOUND ENERGY ON PARTICLE SIZE OF MICROTHENE 500 WITH VARYING CONCENTRATIONS OF SODIUM LAURYL SULFATE[a]

Sodium Lauryl Sulfate, %	Time of Exposure, min. 0	60	120	180	240
None	5.4	5.3	5.1	5.2	5.2
0.05	5.4	4.9	4.6	4.5	4.5
0.1	5.5	5.1	4.4	4.4	4.4
0.2	5.4	5.1	4.5	4.2	4.3
0.3	5.4	5.2	4.3	4.3	4.3

[a] All mean diameters are given in microns.

TABLE III.—EFFECT OF ULTRASOUND ENERGY ON PARTICLE SIZE OF MICROTHENE 510 WITH VARYING CONCENTRATIONS OF POLYSORBATE 20[a]

Polysorbate 20, %	Time of Exposure, min. 0	60	120	180	240
None	9.8	9.6	9.3	9.3	9.2
0.05	9.75	9.2	8.5	8.5	8.4
0.1	9.8	9.2	8.3	8.2	8.2
0.2	9.7	9.4	9.3	8.6	8.6

[a] All mean diameters are given in microns.

TABLE IV.—EFFECT OF ULTRASOUND ENERGY ON PARTICLE SIZE OF MICROTHENE 510 WITH VARYING CONCENTRATIONS OF SODIUM LAURYL SULFATE[a]

Sodium Lauryl Sulfate, %	Time of Exposure, min. 0	60	120	180	240
None	9.8	9.5	9.3	9.2	9.3
0.05	9.7	9.0	8.4	7.9	7.8
0.1	9.8	9.2	8.2	8.0	8.0
0.2	9.7	9.1	8.3	7.9	7.9

[a] All mean diameters are given in microns.

DISCUSSION

In all of the experiments in which there was a substantial reduction in particle size of the suspended material, a plateau was noticed after an exposure time of about 2 to 2.5 hr., after which time no further significant reduction in size occurred. These results parallel the results reported by Singiser and Beal (4) for a liquid–liquid system although this study is concerned with a solid–liquid system. No reasonable explanation for this effect can be obtained from the data available, but it was seen consistently.

Substantial reduction in mean particle diameter occurred only in the presence of surfactants. This result can be explained partially from the character of the suspensions obtained. When surfactants having high HLB values were present, the particles were readily dispersed, and, therefore, the individual particles were completely surrounded by liquid; in the absence of surfactants the particles tended to remain clumped together and, therefore, not surrounded by liquid. Since the ultrasound waves and cavitation shock waves are transmitted to the particles through the liquid medium, a much reduced effect would be expected in the poorer suspensions.

It was observed that the deflocculating agents used did not lessen flocculation of the Microthene particles to a significant degree. The very small

[7] Marketed as Spans by the Atlas Chemical Co., Wilmington, Del.

TABLE V.—EFFECT OF HLB OF SURFACTANTS ON THE PARTICLE SIZE OF MICROTHENE 510 (0.5% SUSPENSION)[a]

Additives, %			Time of Exposure, min.				
Polysorbate 20	Sorbitan Monolaurate	HLB	0	30	60	90	120
75	25	14.6	10.0	9.6	8.8	8.3	8.2
50	50	12.6	9.9	9.4	8.9	8.2	8.3
50	50	10.8	9.8	9.6	8.9	8.5	8.5
20	80	10.0	10.0	9.4	8.9	8.3	8.4
10	90	9.5	10.0	9.7	9.2	8.8	8.8
5	95	9.1	10.0	9.8	9.6	9.6	9.5
0	100	8.6	9.9	9.7	9.6	9.6	9.6

[a] 0.05% total surfactant was used in all cases. All particle sizes are in microns.

TABLE VI.—EFFECT OF ULTRASOUND ENERGY ON PARTICLE SIZE OF MICROTHENE 500 WITH VARYING CONCENTRATIONS OF DARVAN[a]

Darvan, %	Time of Exposure, min.				
	0	60	120	180	240
None	5.5	5.5	5.3	5.3	5.3
0.05	5.5	5.5	5.2	5.2	5.2
0.1	5.6	5.5	5.2	5.3	5.1
0.2	5.5	5.3	5.0	5.1	5.1
0.3	5.6	5.2	4.9	5.0	5.0

[a] All mean diameters are given in microns.

TABLE VII.—EFFECT OF INCREASING CONCENTRATION OF MICROTHENE 500 IN SUSPENSIONS

Microthene 500, % in Suspensions[a]	Particle Size, μ	
	Before Exposure	After 2 hr. Exposure
0.5	5.6	4.5
1.0	5.6	4.4
1.5	5.7	4.6
2.0	5.6	4.8
2.5	5.5	4.8
3.0	5.7	5.0
3.5	5.5	5.1
4.0	5.7	5.3

[a] All suspensions contained 0.1% polysorbate 20.

TABLE VIII.—EFFECT OF INCREASING CONCENTRATION OF MICROTHENE 510 IN SUSPENSIONS

Microthene 510, % in Suspensions[a]	Particle Size, μ	
	Before Exposure	After 2 hr. Exposure
0.5	10.1	8.1
1.0	9.9	8.2
1.5	9.8	7.9
2.0	9.9	8.5
2.5	9.7	8.3
3.0	9.9	8.6
3.5	10.0	9.1
4.0	9.8	8.8

[a] All suspensions contained 0.1% polysorbate 20.

size reduction in these suspensions could be explained on the same basis as above, *i.e.*, the ultrasound waves and cavitation shock was not transmitted to the individual particles.

The effect of increasing the concentration of the suspended phase was quite predictable. In addition to the possibility of a greater degree of flocculation as more particles were present, it was noted that higher concentrations appeared to have a damping effect on cavitation by the ultrasound waves as evidenced by decreased agitation in the flask.

SUMMARY AND CONCLUSIONS

1. The purpose of this investigation was to study the effect of ultrasonic energy on the particle size of certain highly reproducible suspensions. It was observed that ultrasound waves had some reducing effect in all cases.

2. The effect of the time of exposure to ultrasonic energy appeared to be that the size changed significantly up to a period of 2 hr. and that after that a plateau was reached.

3. The use of deflocculating agents did not cause any significant change in the reduction of the particle size.

4. It was also noted, from this study, that a minimum concentration of a surfactant was necessary to obtain maximum effect on particle size reduction but that addition of surfactant above this concentration produced no noticeable change.

5. The HLB of the surfactant also has an effect on the reduction in the particle size. Surfactants with high HLB were found to be most effective, and if the HLB was less than 10, practically no effect was observed.

6. As the concentration of the suspended phase was increased, the change in particle size of suspension became less marked.

7. In view of the results of this study, it can be concluded that ultrasonic energy might be a useful tool for the reduction of particle size of certain pharmaceutical suspensions to make them more stable.

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