

# Powdered Particle Interactions: Suspension Flocculation and Caking I

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The phenomena of caking and of flocculation in a sulfamerazine suspension system have been reported in the literature. The concept of zeta potential was used in measuring and explaining the effects obtained. Several questions have been raised with regard to this prior work, and both caking and flocculation have been examined and explained in terms of other mechanisms. Flocculation in the sulfamerazine suspension system is principally due to the chemical reaction that takes place between dioctyl sodium sulfosuccinate anions and the trivalent cations of the flocculating agent. Relatively strong bonding forces develop between the suspended particles, and flocules are formed. Caking of the sulfamerazine suspension system is seen when the particles settle to a dense sediment before bonds can be established between the closely-packed particles.

HAINES AND MARTIN have recently reported on the phenomenon of flocculation (1-3). They have shown that relationships exist between zeta potential, flocculation, and caking tendencies for the particular suspension systems under study. A careful appraisal of their work has raised several questions and has prompted this laboratory to engage in additional research on the same systems. Initially, our attention has been directed toward the sulfamerazine suspension system on which Haines and Martin worked.

Fischer (4) has said that the electrostatic charge carried by dispersed particles is an important factor in the stability of an aqueous suspension. The charge originates by ionization of the surface or by adsorption of ions from the solution. Martin (5) has said that colloidal particles, as a result of their large surface areas and great surface forces, tend to adsorb ions from the medium and become positively or negatively charged. Fischer and Martin, in their separate works, go on to refer to the distribution of other ions in the form of an ionic atmosphere surrounding the charged suspended particle. Adamson (6) has presented a graphical picture of this concept by plotting electrical potential against distance from the surface of the particle. He states that a particle surface charge may be inherent or may be due to an adsorbed desolvated layer of ions. As we move away from the particle surface, we pass through the "stern layer," which is composed of adsorbed solvated ions surrounding the particle and tightly held to its surface. Moving beyond the stern layer, we enter the "diffuse gouy layer," where a density of ionic charge has gathered in response to the underlying charges on the particle.

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If an electrical field is imposed upon a colloidal system containing electrostatically charged particles, the charged particles will tend to move toward one or the other of the poles. Where other ions are present in the suspension medium, an individual particle as it moves will carry its adsorbed ions (stern layer) and a portion of its ionic atmosphere (diffuse gouy layer) along with it. A region of shear will be created between those ions moving with the particle, and those left behind to move independent of the particle. The electrical potential at this shear layer has been defined as the zeta potential (6). Zeta potential may be measured by observing the movement of a charged particle in a known electrical field or by measuring the magnitude of the electrical potential induced by the movement of the charged particle. The proper application of the concept of zeta potential has served to explain many of the phenomena exhibited by colloidal suspensions.

Fischer (7) has described the coagulation of colloidally dispersed charged particles in terms of the following hypothetical mechanism. Uncharged particles, when brought close together, adhere because of van der Waals attractive forces. In a stable suspension, where the particles are similarly charged, electrostatic repulsive forces predominate and the particles are prevented from adhering since the electrostatic forces are of longer range than the van der Waals forces. The magnitude of the repulsion is gauged roughly by the zeta potential. If the zeta potential is sufficiently high, the charges constitute a potential barrier and the colloidal system is stable. If the zeta potential is caused to decrease, as by the addition of an electrolyte, then the particles may have sufficient kinetic energy to cross the barrier and come within range of the van der Waals attractive forces. The

particles then adhere. The zeta potential corresponding to this limit is termed the critical potential.

Abramson (8) has discussed the work of Burton, who used potassium sulfate to coagulate a copper sol. With other conditions held constant, Burton modified the zeta potential on the copper particles by the addition of electrolyte. He reported his data in terms of electrophoretic velocity of the particles *versus* time for coagulation to occur, which is directly comparable to zeta potential *versus* the time for coagulation to occur. When enough potassium sulfate had been added to reduce the electrophoretic velocity to zero (a zeta potential of zero), it took 0.04 days (just under 60 minutes) for coagulation to occur. Burton thus demonstrated that (for this system) flocculation following the neutralization of zeta potential was a slow process. The rate of coagulation was dependent on the frequency of random collisions of the copper particles in the course of their Brownian movement. This seems to correlate with Fischer's thoughts, as reviewed in the preceding paragraph. With random Brownian movement, the particles may at times have sufficient kinetic energy and be properly oriented in their motion so that they will approach close enough to one another to be held by the van der Waals forces.

Zeta potential has thus been linked with colloidal systems and with the coagulation mechanism for a colloidal system.

Haines and Martin (1-3) worked with a sulfamerazine suspension system. They used a modified Northrop-Kunitz-type electrophoresis assembly and converted their electrophoretic velocity data to zeta potential values. Their summary (2) stated that the electrophoretic velocity in a nonflocculated sulfamerazine suspension was observed in a microscope electrophoresis apparatus and was found to be high because of the predominance of a negative charge on the particle. Electrical discharge of the particle by the addition of aluminum ions, which were opposite in charge to the particle, lowered the zeta potential and brought about flocculation of the particle, thereby reducing or eliminating the tendency to cake.

The ideas of Fischer (7) as given earlier in this paper, seem to have been confirmed by the findings of Haines and Martin. An important discrepancy, from the standpoint of this laboratory, is that Fischer had been discussing colloidal systems; Haines and Martin were working with particles larger than those normally considered to be within the colloidal range. Fischer (9)

comments that the limits on colloidal particles have been variously stated, but sizes between  $1\ \mu$  and  $1\ m\mu$  encompass the usual extremes. Martin (10) gives the colloidal range as from  $10\ \text{\AA}$ . up to  $0.5\ \mu$ . The sulfamerazine particles used by Haines and Martin were in the  $2$  to  $10\text{-}\mu$  range and could be clearly seen under the microscope. Hauser (11) has said that colloidal dispersions are detectable only with the ultramicroscope, while coarse dispersions are microscopically resolvable. However, he adds that no sharp boundary exists between coarse dispersions, colloidal solutions, and true solutions. Hauser further states (12) that the principal differences between general and special types of disperse heterogeneous systems are the result of the appearance of special properties as the boundary surfaces are increased.

Among such special properties would be the van der Waals forces. Although they exist at the surface of all solid particles, they would be effective in bonding only when the solid was in an extremely fine state of subdivision, as for example in Burton's colloidal copper sol.

It is true that Kruyt (18), has referred to the theoretical existence of long-range London-van der Waals forces in connection with hydrophobic suspensions in the  $2$  to  $5\text{-}\mu$  range. However, he adds (19) that this kind of flocculation has not yet been verified experimentally. The sulfamerazine suspension under study is not a hydrophobic system, nor is it within the generally accepted colloidal range. It seems inappropriate to ascribe flocculation in such a system to the action of van der Waals forces following a neutralization of particle surface charge without experimental justification for such an assumption.

Initial work at this laboratory has shown that the flocculation of the sulfamerazine system by aluminum ions was virtually instantaneous on mixing. Burton (7) had been successful in applying zeta potential measurements to his copper sol only because the coagulation was slow to take place. The system was such that he had time to measure the zeta potential of the particles before they were lost to the coagulum. Haines and Martin were not so fortunate, and this has cast additional doubt on the use of zeta potential as a parameter for the flocculation of the sulfamerazine suspension system. They had calculated zeta potential from particle velocity data obtained in the electrophoretic cell and had assumed that cessation of particle movement was due to a neutralization of zeta potential. This does not necessarily follow, for the cessation of movement could be more aptly

explained by the flocculation phenomenon itself. Haines and Martin have indicated this to be the case, for in their discussion (2) they have said that the addition of flocculating agent caused the zeta potential to decrease, and at point B, the particles were observed in the microscope of the electrophoresis apparatus to exhibit maximum flocculation.

Two factors thus tend to negate the concept of a neutralization of zeta potential, followed by flocculation under the influence of van der Waals forces:

The particles are larger than those normally considered to be colloidal, and the effectiveness of inter-particulate van der Waals forces has not been demonstrated for suspensions of hydrophilic particles in this size range (2–10  $\mu$ ).

When sufficient aluminum ions are present, flocculation is virtually immediate on mixing.

Thus flocculation occurs before the zeta potential can be measured on the individual particles.

It seems desirable that an alternative explanation be given for the flocculation of a sulfamerazine suspension by aluminum ions. A word on the meaning of terms may be of assistance at this point. Fischer and Gans, in their chapter in Alexander (13), have defined the words "flocculation" and "deflocculation" as follows:

**Flocculation**—The formation of clusters of particles separable by a relatively weak mechanical force or by a change, as in chemical composition, at the interface between the particles and the suspending phase. Surface-active agents are often useful in reducing the extent of flocculation.

**Deflocculation**—The state of dispersion of a solid in a liquid in which each solid particle remains geometrically independent and unassociated with adjacent particles.

In an initial investigation, 2% of sulfamerazine was suspended in distilled water. A highly flocculated, bulky suspension was obtained. The uppermost curve of Fig. 1 serves to illustrate this fact. This suspension was then contrasted with a 2% suspension containing 0.010 moles per L. of aluminum chloride. There was no observable difference between the two suspensions. Both were equally flocculated according to the definition given by Fischer and Gans. It should be clearly recognized that aluminum ions have no effect on a simple sulfamerazine suspension.

Haines and Martin used dioctyl sodium sulfosuccinate (DSS)<sup>1</sup> as a wetting agent for the

sulfamerazine to reduce the hydrophobic nature of the sulfamerazine particles. This was a typical deflocculation reaction as defined above. When aluminum ions were added to such a sulfamerazine suspension system, a return to a flocculated condition was obtained. It would appear that the DSS was playing an integral part in the flocculation phenomenon, even though Haines and Martin made it a point to say (1) that the addition of the surface-active agent was found to have little or no effect on the recorded observations.

## EXPERIMENTAL

**Suspension System**—During the current studies, the suspension concentration was held at the 2% solids level. Haines and Martin had shown that higher concentrations brought on the problem of hindered settling, and lower concentrations increased the errors inherent in the reading of flocculation volumes. DSS concentrations were varied from 0.001% up to 0.25%. To prepare the suspensions, the sulfamerazine powder was weighed, transferred to a glass mortar, and triturated with the required amount of a concentrated wetting-agent solution until a smooth slurry was obtained. The slurry was then transferred, with rinsing of the mortar, to a cylindrical graduate and distilled water was added to bring the volume to the proper level. Where flocculating agents were under study, they were added in the form of a concentrated solution during the adjustment of the final volume of the suspension. The graduate was then stoppered, inverted, and agitated to insure both thorough mixing and the uniform initial suspension of the solid.

**Settling Data**—The methods used by Ward and Kammermeyer (14) were utilized in obtaining, and in some cases in reporting, the sedimentation data. It becomes necessary to qualify the above statement, for the sulfamerazine systems are not consistent in their settling characteristics. In some of the flocculation reactions, as much as 25% of the flocculated material floated to the surface of the medium rather than sedimenting as would have been expected. The total volume of flocculated material, summing the volume of both floating and sedimented floccules, was reported and used in comparing one system to another.

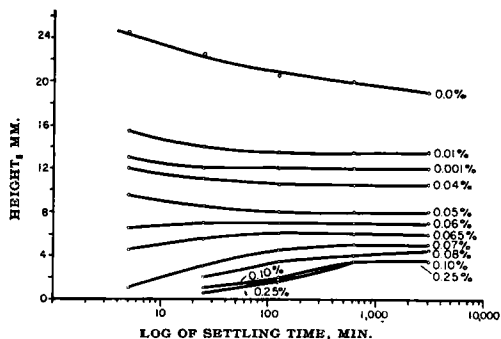


Fig. 1.—Height of sediment vs. log of settling time for 2% sulfamerazine suspended in various concentrations of dioctyl sodium sulfosuccinate solution.

<sup>1</sup> Marketed as Aerosol-OT by American Cyanamid Co., New York, N. Y.

**Equipment.**—Settling data was obtained in 100-ml. glass-stoppered cylindrical graduates. Suspension heights or flocculation volumes could be measured within  $\pm 0.5$  ml. accuracy, which was more than sufficient to point out the differences between the various suspension formulations.

**Materials.**—A commercial grade of sulfamerazine U.S.P. as supplied by Merck Sharp & Dohme was used. The suspending medium was distilled water containing the wetting agent dioctyl sodium sulfosuccinate (100%) as supplied by American Cyanamid Co. The two flocculating agents, aluminum chloride ( $\text{AlCl}_3 \cdot 6 \text{H}_2\text{O}$ ) and ferric chloride ( $\text{FeCl}_3 \cdot 6 \text{H}_2\text{O}$ ), were reagent grade chemicals as supplied by Merck & Co.

## RESULTS

Figure 1 presents the data on settling rates for 2% sulfamerazine suspensions containing various concentrations of the wetting agent. The critical micelle concentration for DSS has been given as approximately 0.07%, at 25° (5 to 15 seconds) (15).

At DSS levels above the critical micelle concentration, the sulfamerazine was held in a finely divided state and settled slowly to a dense sediment with definite caking tendencies. The sediment built up slowly at the bottom of the container and the supernatant liquid very slowly cleared to denote the completion of sedimentation. Above 0.1% DSS, changes in the wetting agent concentration gave practically no change in the settling rate curve.

Below the critical micelle concentration, the suspended sulfamerazine particles clumped and the flocculated material slowly compacted to its final volume. In this range of wetting-agent concentration, the suspension began to exhibit the hydrophobic properties of the basic sulfamerazine particle. As wetting-agent concentration decreased, increasing amounts of the solid tended to float to the surface until, in the absence of wetting agent, as much as 25% of the sulfamerazine floated to the surface.

Figure 2 illustrates the action of aluminum chloride as a flocculating agent for a 2% sulfamerazine suspension in 0.25% DSS solution. Small quantities of aluminum chloride had no apparent effect upon the suspension, other than to give the supernatant liquid a slight opalescence. The suspended particles acted just as they would at wetting-

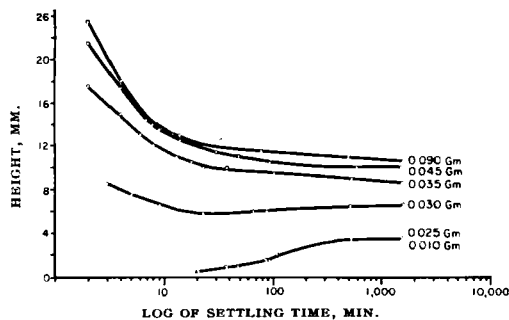


Fig. 2.—Height of sediment vs. log of settling time for 2% sulfamerazine suspended in 0.25% dioctyl sodium sulfosuccinate solution. Various amounts of aluminum chloride were added to cause flocculation.

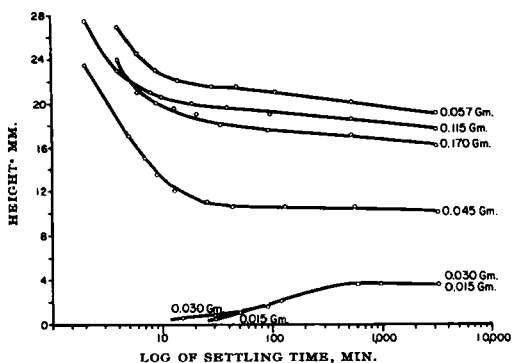


Fig. 3.—Height of sediment vs. log of settling time for 2% sulfamerazine suspended in 0.25% dioctyl sodium sulfosuccinate solution. Various amounts of ferric chloride were added to cause flocculation.

agent concentrations above the point of micelle formation.

As aluminum chloride was added in larger amounts, the sulfamerazine particles grouped as clumps or floccules, and separated from the medium both as a loose, bulky precipitate, and as a floating layer of clumped material. At these higher levels of aluminum chloride addition, the supernatant liquid was clear and colorless.

Figure 3 charts the effect of ferric ion on a sulfamerazine suspension in 0.25% DSS solution. Small additions of ferric chloride had no apparent effect upon the suspension. The supernatant liquid became slightly opalescent, but the suspension performed just as it would at wetting-agent levels above the critical micelle concentration.

At the level of 0.045 Gm. ferric chloride per 100 ml., a definite soft floc was obtained. It sedimented, leaving an opalescent solution that contained no floating particles of sulfamerazine. The floc could be easily resuspended on shaking. When 0.057 Gm. ferric chloride per 100 ml. was added, the uppermost curve on the graph was obtained. At this level, the most fluffy and voluminous floc was formed. Half of the floccules floated to the surface, while the balance slowly settled out to leave a markedly opalescent supernatant liquid.

At the higher levels of ferric chloride addition, a slightly more compacted floc was obtained. It was of interest to note that the floc took on the color of the ferric ion, while the supernatant liquid became clear and essentially colorless.

The opalescence noted in many of the above preparations indicated a possible chemical interaction between the DSS anion and the trivalent cation. When a dilute solution of aluminum chloride was added (slowly and with stirring) to an 0.25% DSS solution, an opalescence was seen. As more aluminum ion was added, a milky, colloidal suspension formed and promptly coagulated to a few floating wax-like particles. These particles were filtered off, thoroughly washed with dilute ammonium chloride solution, dried, and a weighed amount ignited to a residue of aluminum oxide. The residue was 5.00% of the original weight.<sup>2</sup> Assuming the product had been an aluminum salt of dioctyl sulfosuccinic acid, the original compound was calculated to have the formula:  $\text{Al}(\text{C}_{20}\text{H}_{37}\text{O}_7\text{S})_2 \cdot \text{Cl} \cdot x\text{H}_2\text{O}$ . The above procedure was repeated

<sup>2</sup> Analytical data by Micro-Tek Laboratories, Skokie, Ill.

using ferric chloride as the precipitating agent. A milky, orange-colored colloidal suspension was formed, from which the organic material was extracted with ether. Upon evaporation of the ether, a viscous orange-brown residue was obtained. A weighed amount of the residue was ignited to ferric oxide and the weight of the oxide proved to be 7.24% of the original weight.<sup>2</sup> Assuming the residue was a ferric salt of dioctyl sulfosuccinic acid, it was calculated to have the following empirical formula:  $\text{Fe}(\text{C}_{20}\text{H}_{37}\text{O}_7\text{S})_2\text{Cl}\cdot x\text{H}_2\text{O}$ .

Macroscopic observations on the various suspensions were correlated with microscopic studies. In those suspensions where the DSS was present in an amount above the critical micelle concentration, the sulfamerazine was present as discrete particles in a deflocculated condition. The particles were irregular, plate-like crystals of from 2 to 10  $\mu$  in size.

Where flocculating agents had been added in moderate amounts, the floccules were readily visible to the naked eye. On shaking, these relatively large flocculated masses were reduced in size, forming a finely divided suspension from which the original flocculated system was reformed within a few minutes. Microscopic observation indicated that there was some form of "adherence" between the sulfamerazine particles. The individual particles were grouped into small floccules, and these were further formed into loose, lacy masses. Higher concentrations of the flocculating agents gave floccules that were more granular in their macroscopic appearance. Microscopically, these floccules seemed to be larger in size and more compact than the flocculated masses obtained at lower levels of flocculating agent addition.

## DISCUSSION

A 2% sulfamerazine suspension system has been used to study the phenomenon of flocculation. By itself, sulfamerazine in water is seen to give a highly flocculated suspension. If a small amount of an anionic wetting agent is introduced, some wetting occurs and the degree of flocculation is reduced. The suspension is further deflocculated as the concentration of wetting agent is increased until the critical micelle concentration has been exceeded. Above this level of wetting-agent concentration, the individual sulfamerazine particles have become coated by the anions of the wetting agent and are dispersed in the form of a completely deflocculated suspension.

An 0.25% DSS solution was selected for the further experimental work. The wetting-agent concentration was thus initially above the level of critical micelle concentration. As flocculating agent (aluminum or ferric ion) was added, there was no significant change in the state of the suspension until enough flocculating agent had been added to reduce the concentration of DSS anion below the level at which it could form micelles. From this point on, gradual addition of the flocculating agent gave increasing flocculation up to the maximum value obtained. Addition of agent beyond this point seemed to produce a slightly more compacted flocculation.

From the above, we can list several factors as being involved in the flocculation of this system: (a) the wetting agent concentration, (b) the neutral-

ization or precipitation of wetting agent by the addition of flocculating agent, (c) other unknown factors, or (d) a combination of two or more of the above.

A chemical reaction has been shown to take place between aluminum or ferric ions and the dioctyl sulfosuccinate anion. If the sole effect of this reaction had been the neutralization of wetting-agent action, the flocculation curves would have coincided with those obtained by varying the amount of wetting agent in the suspension medium. This was certainly not the case with aluminum ions, and the divergence was even more marked when ferric ions were the flocculating agents. The chemical reaction thus appeared to be the most significant factor in the flocculation mechanism.

At the start of each experimental run, the sulfamerazine particles were coated with wetting-agent anions and the suspension was in a deflocculated condition. Each particle thus had a negative charge and was surrounded by its own ionic atmosphere. The general picture was that of hydrocarbon chains adsorbed to the surfaces of the particles with negative sulfonic acid radicals projecting into the surrounding medium. Aluminum ions were then added to the system, and they promptly reacted with DSS anions, whether these anions were adsorbed on particle surfaces or were available as ions in the suspension medium. Aluminum di-(dioctyl sulfosuccinate) chloride was formed as an insoluble product of the reaction. The sulfamerazine particles went into a state of flocculation which was modified by the presence of the aluminum compound.

The flocculation mechanism has been discussed, and it now remains for us to consider the phenomenon of caking in the sulfamerazine suspension system.

Haines and Martin (1) have said that when dispersed particles form into a compact mass at the bottom of the container, the suspension is said to have caked. They listed two types of structures that may be formed: the condensation or strongly bonded type, and the coagulation or weakly bonded type. Examples of both types were given. The coagulation or weakly bonded type of interaction was said to be due to the adhesion of particles by molecular interaction at points of contact between the particles. The weak bonds that are formed are due to a squeezing out of the dispersion medium at the points of contact, as in syneresis. The resulting residual layer of the dispersion medium prevents a strong molecular interaction at the points of contact. The strength of the cake which is formed depends upon the number of particles occupying a given volume. The particles may orient themselves in the sediment and, under the influence of gravity, coagulate in an arrangement of closest packing. Various clays, such as bentonite, were said to exhibit this type of sediment.

Hauser (17) has also commented on such a system. He has said that where suspended anisodimensional particles are allowed to settle of their own accord, they will tend to pack themselves in such a way that a sediment of minimum free energy results. This means that the particles will line up with their larger surfaces opposite each other. The solvated layer surrounding each particle will act somewhat like a lubricant, permitting the particles to slide over each other until they have found their proper location. With further sedimentation, the solvated

layers of the first settled particles will become distorted or deformed. Hauser goes on to say that this deformation will result in a coalescence of the solvated layers, since this would also represent a shift toward a system having a lower level of free energy. The heavier the particles, the greater the deformation of the solvated layers and thus the greater the chance for their coalescence.

Overbeek's chapter in Kruyt (19) contains the following observation: "There are, however, great differences in the sediments of stable and flocculated suspensions. The stable sediments are very closely packed because in forming the sediment the particles retain their individual freedom and roll over each other until the closest packing is reached. The flocculated sediments are more loosely built because once the sedimenting particles touch each other they adhere in the haphazard way in which they first touched and are no longer able to proceed into a more favorable position."

In the course of this study, three sulfamerazine systems were under observation:

Powered sulfamerazine in water. This suspension system was highly flocculated, and there was no caking problem.

Powdered sulfamerazine suspended in a DSS solution. This system gave a deflocculated suspension that settled to a dense sediment with definite caking tendencies.

Powdered sulfamerazine in DSS solution to which aluminum ions were added as a flocculating agent. A highly flocculated suspension with no evidence of caking was obtained.

This portion of the work has confirmed the findings of Haines and Martin (1) that a suspension in a state of fine deflocculated particles leads to rather than obviates caking. It also echoes the findings of Fischer (16) that flocculated particles settle rapidly to high volumes, while deflocculated particles settle slowly to low relative volumes. In flocculated systems, it would appear that the bonding forces between particles are relatively large, for the particles are held together in the form of loose clumps. When these clumps settle out, the particles remain distributed throughout a large volume of space. They cannot pack closely against one another and are thus unable to form into a cake.

The caking of sulfamerazine suspended in DSS solution is an example of the weakly bonded type of interaction. As originally prepared, the sulfamerazine particles are coated with DSS anions and are suspended as independent, charged particles in the medium. Since the system is not colloidal, gravity acts to pull the particles down into a sediment of low relative volume. As the particles settle, the suspension medium is squeezed out and the solvated layers surrounding each particle come into close contact with one another. Under the continuing influence of gravity, there is a coalescence of the solvated layers and a type of soft cake is formed. The cake can be returned to its original finely divided suspended state by shifting the particles enough to allow some of the suspension medium to come between them. The individual solvated layers are thus restored, and the particles can be resuspended in the deflocculated state.

Aging studies are being conducted to see if the caking reaction becomes irreversible with time.

The concept of zeta potential does not provide us with a suitable picture of the sulfamerazine suspension systems. Attention should be focused upon the strength of bonding forces and the extent to which large areas of particle surfaces come into close contact with each other. As has been said, the interparticulate bonds in the flocculated system seem stronger and are more rapidly formed than are those in the deflocculated system. When the particles flocculate, bonding strengths are such that the particles are unable to settle to a closely packed sediment. For deflocculated particles, the bonding forces seem weak and are slow to establish themselves. The particles must settle and shift until large areas of surface are in close proximity to each other before the cake is formed. The relative strength of the bonds and the extent of contact between particle surfaces are thus the determining factors in the formation of a floc, a cake, or a densely packed sediment which shows no caking tendencies.

## SUMMARY

The phenomena of caking and of flocculation in a sulfamerazine suspension system have been reported in the literature. The concept of zeta potential was used in measuring and explaining the effects obtained. Several questions have been raised with regard to this prior work, and both caking and flocculation have been examined and explained in terms of other mechanisms.

Flocculation in the sulfamerazine suspension system is principally due to the chemical reaction that takes place between dioctyl sodium sulfosuccinate anions and the trivalent cations of the flocculating agent. Relatively strong bonding forces develop between the suspended particles, and flocules are formed.

Caking of the sulfamerazine suspension system is seen when the particles settle to a dense sediment before bonds can be established between the closely packed particles.

## REFERENCES

- (1) Haines, B. S., Jr., and Martin, A. N., *THIS JOURNAL*, **50**, 228(1961).
- (2) *Ibid.*, **50**, 753(1961).
- (3) *Ibid.*, **50**, 756(1961).
- (4) Fischer, E. K., "Colloidal Dispersions," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 124.
- (5) Martin, A. N., "Physical Pharmacy," Lea and Febiger, Philadelphia, Pa., 1960, p. 538.
- (6) Adamson, A. W., "Physical Chemistry of Surfaces," Interscience Publishers, Inc., New York, N. Y., 1960, p. 184.
- (7) Fischer, E. K., *op. cit.*, p. 125.
- (8) Abramson, H. A., "Electrokinetic Phenomena and Their Application To Medicine," A. C. S. Monograph Series No. 66, Chemical Catalog Co., Inc., New York, N. Y., 1934, p. 74.
- (9) Fischer, E. K., *op. cit.*, p. 2.
- (10) Martin, A. N., *op. cit.*, p. 531.
- (11) Hauser, E. A., "Colloidal Phenomena," McGraw-Hill Book Co., Inc., New York, N. Y., 1939, p. 25.
- (12) Hauser, E. A., *op. cit.*, p. 21.
- (13) Alexander, J., "Colloid Chemistry, Theoretical and Applied," Vol. VI, Reinhold Publishing Co., New York, N. Y., 1946, pp. 286-287.
- (14) Ward, H. T., and Kammermeyer, K., *Ind. Eng. Chem.*, **32**, 622(1940).
- (15) "Aerosol Surface Active Agents," American Cyanamid Co., 1960, p. 12.
- (16) Alexander, J., *op. cit.*, p. 311.
- (17) Hauser, E. A., *op. cit.*, p. 212.
- (18) Kruyt, H. R., "Colloid Science," Elsevier, Publishing Co., Amsterdam, Netherlands, 1952, pp. 324-325.
- (19) Kruyt, H. R., *op. cit.*, p. 337.