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Conductivity Studies of Suspension Systems in Different States of Aggregation

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Abstract □ The electrical conductivity effects of dispersed, coagulated, and flocculated systems were investigated using sulfamerazine powder, an insoluble, hydrophobic drug to prepare the suspension systems. For the dispersed systems, a peak in conductivity was observed at a drug concentration between 5 and 15%. The critical coagulating concentration was defined as the concentration of drug at which a maximum in specific conductance was observed. At this concentration, a maximum number of charged particles were in the system. Coagulated suspensions showed higher conductance values than the dispersed systems at equivalent concentrations; however, the critical coagulating concentration value appeared to be the same. For flocculated suspensions there was an increase in conductance with drug concentration with no perceptible peak conductance value.

Keyphrases □ Conductivity—use in studies of suspension systems in different states of aggregation □ Aggregation states—electrical conductivity effects on dispersed, coagulated, and flocculated systems □ Suspension systems—electrical conductivity effects on dispersed, coagulated, and flocculated systems

As defined in the United States Pharmacopeia (1), suspensions are preparations of finely divided, undissolved drugs in liquid vehicles. Insoluble particles dispersed in a liquid medium have large specific surface areas which render the suspension system thermodynamically unstable. The particles tend to settle and form aggregates which have a reduced surface area and, thus, a decreased surface free energy. This results in a system of greater thermodynamic stability. Two types of aggregation are identified: coagulation and flocculation. Unfortunately, these terms are used frequently in the literature in a way that confuses the nature of the systems being described (2).

Here, a dispersed system in water is described as consisting of primary particles acting as independent entities in the bulk water polar medium. The settling process, in general, is relatively slow with each particle settling separately.

In a coagulated system the aggregated particles, including adsorbed surface films, are in surface contact with each other and each aggregate of particles (coagula) acts as a unit. The particles are held together by film–film bonds. The interstitial water is structured and exhibits nonpolar behavior. Coagulated suspensions tend to form caked systems which can be difficult, if not impossible, to redisperse.

In a flocculated system the aggregated particles are held together by one of several mechanisms: adsorption bridging, chemical bridging, or long-range Van der Waals forces (secondary minimums). The particles settle out as a "floc," a loosely packed aggregate having a network-like structure. A hard cake does not form and the sediment is readily redispersed to the original suspension form. The water medium is bulk polar water.

The classification of these systems was first reported by Ecanow *et al.* (3) and has since been referred to by others (4). The properties of dispersed, coagulated, and flocculated systems have been compared in terms of caking (5), sedimentation rate (6), rheology (3), gas adsorption (7), and filtration rates (8). In the present study, the electrical conductivity effects of these systems were investigated. Sulfamerazine powder, a hydrophobic drug, was used to prepare the suspensions, and docusate sodium (I), an anionic surfactant, rendered the drug particles hydrophilic in the formation of the dispersed and the coagulated systems. Compound I and aluminum chloride were used to form the flocculated systems (9) of sulfamerazine particles.

EXPERIMENTAL

Materials—Sulfamerazine[1] was USP grade and ranged in particle size from 5 to 20 μm. Docusate sodium[2] USP was employed as the surfactant, and aluminum chloride[3] NF served as the flocculating agent. All other chemicals were reagent grade and were used without further treatment.

[1] Sigma Chemical Co., Lot 103C 2660.
[2] Aerosol OT, Fisher Scientific Co., Lot 732561.
[3] Mallinckrodt Chemical Works, Lot WLJD.

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Table I—Specific Conductance Values for Dispersed and Aggregated Suspension Systems

Suspension Concentration, %(w/v)	Conductance, mmho		
	Dispersed System	Coagulated System	Flocculated System
2	0.28 ± 0.018[a]	0.34 ± 0.013	1.19 ± 0.103
5	0.49 ± 0.078	0.68 ± 0.010	2.59 ± 0.370
10	0.62 ± 0.016	0.82 ± 0.013	4.10 ± 0.346
15	0.55 ± 0.038	0.63 ± 0.015	5.40 ± 0.535
20	0.49 ± 0.075	0.58 ± 0.015	6.30 ± 0.770
25	0.40 ± 0.061	0.55 ± 0.006	7.50 ± 0.577
30	0.36 ± 0.052	0.52 ± 0.015	8.25 ± 0.500
35	0.31 ± 0.017	0.37 ± 0.014	9.00 ± 0.000

[a] Mean value based on at least four determinations ± *SD*.

Apparatus—A conductivity apparatus[4] designed for testing suspension systems was used to measure the specific conductances of the suspension systems.

Suspension Systems—Sulfamerazine dispersed suspensions and coagulated systems contained 2, 5, 10, 15, 20, 25, 30, 35% (w/v) sulfamerazine. In each system the concentration of I was one-tenth the sulfamerazine content.

In the flocculated systems the concentrations of sulfamerazine and I were the same as in the previous systems, but, in addition, the concentration of aluminum chloride in each system was equal to 5% that of the sulfamerazine content.

The suspensions were prepared by weighing out the calculated amount of sulfamerazine powder and transferring the powder to a glass mortar. The appropriate volume of a 5% solution of I was added to the mortar and the mixture was triturated until a smooth slurry was formed. The slurry was then transferred to a 100-ml graduated cylinder with additional rinsings of the mortar using distilled water. Sufficient water was added to bring the volume to the 100-ml mark. For the preparation of the flocculated suspensions, the same procedure was followed except that the appropriate volume of a 20% aluminum chloride solution was added to the cylinder prior to filling to the mark with distilled water. The cylinder was then capped with a glass stopper, inverted, and agitated sufficiently to ensure both thorough mixing and the formation of a uniform initial suspension of the powder.

The conductance of the initial suspensions (dispersed systems) was measured immediately by immersing the conductivity cell into each suspension system. The systems were then allowed to settle for 48 ± 2 hr before additional conductivity data were obtained. During the settling period, aggregation took place resulting in the formation of a coagulated system. Before the conductance reading was taken, the cylinder containing the coagulated system was agitated sufficiently to ensure dispersion of the coagula. The conductivity of the dispersed system was then measured immediately. The flocculated systems were treated in the same manner as the coagulated systems. Conductivity readings were measured after thoroughly agitating the system to ensure redispersion of the flocules.

RESULTS AND DISCUSSION

Conductance data for all of the suspension systems are shown in Table I. The data for dispersed systems were analyzed statistically by the Student t test. The t value was 4.131 corresponding to a p value of < 0.005, indicating that conductance is dependent on concentration. Analysis of the data for the coagulated systems by the Student t test produced a t value of 4.102, which corresponds to a p value <0.005. The t value obtained for the flocculated suspensions by comparing concentration with the mean conductance value was 2.837, which corresponded to a p value <0.01.

It was the purpose of this study to observe the electrical conductivity properties associated with different states of suspension aggregation and to note the effect of variable concentration of an insoluble drug on the electrical conductivity of each suspension system. Specific conductance, rather than equivalent conductance, was determined since it is a measure of conductance capacity of all ions present in a unit volume of solution and thus, varies with concentration.

[4] Solu Bridge Soil Tester, Beckman Instruments, Inc., Model RD-B15, Ser. 21034.

The system can be described as follows: The sulfamerazine powder is in the paracolloid particle size range (5–20 μm). Compound I, an anionic surfactant, acts by coating the insoluble drug particles and converting them to hydrophilic particles (9). Therefore, each particle has a negative charge and is surrounded by its own ionic atmosphere. Closely associated with the hydrophilic particles are water molecules from the suspension medium. Sodium ions of I balance the negatively charged particles. Compound I molecules are present in the system as individual ionic species and as micelles, since the critical micelle concentration for I is about 0.07% at 25°. This concentration was exceeded in all suspensions prepared in this study.

It is evident that, for the dispersed suspension system, the conductivity increases with drug concentration at low concentrations of drug. This is expected because the number of charged particles in the system has increased. However, at some concentration between 5 and 15%, a peak in conductance is reached after which the conductance values decrease with increasing drug concentration. This may be explained by the fact that after a peak value is reached, the charged particles begin to aggregate by forming associated particles, or coagula, which results in fewer, but larger, charged species. Because the actual number of charged particles is decreased, the specific conductance will be lower. The concentration of drug in a dispersed or coagulated system at which the specific conductance is a maximum is the critical coagulating concentration. At this concentration there is a maximum number of charged particles in the system which accounts for the maximum in specific conductance.

The coagulated suspensions behaved similarly to that of the dispersed systems. The conductance values for the coagulated systems were consistently higher than the corresponding dispersed systems (Table I). Since the coagulated suspensions consist of fewer and larger charged particles, it would be expected that the specific conductance would be lower than in the dispersed systems (as noted previously in connection with the effect of drug concentration on the conductivity in the dispersed systems). One possible explanation of this behavior is that because the water in the film–film bonds of the coagula is highly structured (nonpolar) (10), electrolytes are squeezed out of the films, thus increasing the concentration of charged species in the polar aqueous medium of the supernate. This, in effect, produces higher conductance values for the coagulated systems.

The data for the flocculated systems show an almost direct linear relationship between conductance and drug concentration. This is in contradistinction to that observed for the dispersed and coagulated systems. In a separate study, a similar relationship was observed with only aluminum chloride and I (the sulfamerazine was excluded). Apparently, the aggregation state of the suspended particles does not affect the conductance of the flocculated system. In this system each suspended drug particle behaves independently. The precise nature of aluminum ion participation in the flocculation process was reported previously (9) and first identified as a chemical bridging reaction.

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