SOLUBILIZATION OF NONPOLAR GASES BY PHARMACEUTICAL SUSPENSION SYSTEMS

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Differences in anesthetic gas absorption in dispersed, coagulated, and flocculated systems were determined. Gas solubilization was measured by gas chromatography with a modified tonometer as an absorption chamber. Uptake of two nonpolar anesthetic vapors, halothane and trichloroethylene, by aqueous sulfamerazine-dioctyl sodium sulfosuccinate-aluminum chloride systems was observed. The coagulated systems showed greater absorption than did flocculated structures. Surfactant concentration was also important in determining the amount of gas solubilized.

The flow and settling properties of suspension systems have been shown experimentally to be primarily functions of the aggregating structure present within the fluid media (1, 2). Sulfamerazine suspension systems can adsorb and concentrate the surface-active molecules (surfactant) at the particle-liquid interphase by an adsorption mechanism at the particle surface. These particle aggregates are formed by the direct effect of surface-active molecules or by a process mediated by them. It is significant that, in sulfamerazine suspensions, the aggregate-suspension type is a function of surface-active molecules present in solution (3).

Suspended particles with adsorbed quantities of surfactant join in various aggregations which are structurally dependent on the concentration of adsorbed surfactant acting either as a micellular film or as individual bridging molecules at the surface of the particles (2, 4). These aggregated structures are referred to as coagules and floccules, respectively. The converse to an aggregated state, the dispersed state, is due to surfactant molecule charge repulsion or to the adsorption of ionic solution constituents (adsorbed to the surfactant or particle surface) (2, 4). The relationship of aggregating structures (dispersed, coagulated, and flocculated) to that of surfactant content has been demonstrated experimentally (3, 4, 5).

In dispersion, the initial adsorption of ionic surfactant causes a mutual repulsion of suspended particle surfaces and results in a state characterized by the presence of individual non-aggregating particles (3, 6). The individual particles sediment as independent units, closely approximating Stokes' equation.

With increase in concentration of surfactant molecules more of these molecules are adsorbed upon the surface of the suspended particle until a continuous film of molecules covers its entire surface (3, 6). The films of adjacent particles adhere to each other and, as a result of film-to-film binding, the particle clusters known as coagules are formed. The exterior surface area of the cluster is significantly less than the sum of the surface areas of individual particles which form the coagulate. Coagules are relatively nonporous structures which, when closely packed, lead to formation of a caked suspension (2, 6).

Floccules, having open network structures (2, 6), can result from aggregation of surface-charged particles, due to adsorbed ionic surfactant which reacts chemically with an added flocculating agent or exhibits adsorption bridging of a nonionic surfactant. The particles then become cross-linked by means of the resulting chemical or physical bridges.

The chemical bridge can form when an ionic surfactant and an ionic flocculant are combined. An ion pair can result when a reactive oppositely charged flocculating ion is added to the adsorbed ionic surfactant-particle system (3). Physical bridging can occur with nonionic surface-active substances, especially if the surface-active molecule is macromolecular. In the case of physical bridging, the surface molecules are adsorbed to two or more particles simultaneously (3).

This flocculation mechanism has been shown to be responsible for aggregation of various sulfamerazine suspensions (3). Flocs cules occupy relatively large volumes; a large amount of the fluid medium is trapped between the bridging molecules and the particles.

MATERIALS AND METHODS

Air-free, non-polar anesthetic vapor samples of halothane and trichloroethylene (equivalent to 25 ml at standard temperature and pressure) were studied for gas uptake in dispersed, flocculated, and coagulated systems consisting of sulfamerazine, dioctyl sodium sulfosuccinate (Aerosol OT®), and aluminum chloride. The formula used to convert liquid forms of halothane and trichloroethylene to the desired vapor volume has been described in a previous report (6).

Gas solubilization at room temperature was determined and followed by gas chromatography. The absorption chamber was a modified tonometer constructed of glass and fitted with rubber stoppers to permit obtaining of non-polar gas samples (6). A WCLID 1670 model gas chromatograph equipped with dual hydrogen flame ionization detectors was utilized to follow the course of gas uptake. The stainless steel ¼-inch x 6-ft columns used for analysis of gas uptake were packed with 25% silicone gum rubber SE-30 on Anakrom (70/80 mesh). Operating temperatures used for the gas chromatograph are listed in Table 1.

TABLE 1. *Gas chromatography operating temperatures.*

Gas	Temperature (C) at Ports		
	Injection	Column	Internal detector
Trichloroethylene	180	152	156
Halothane	165	125	130

The dispersed, coagulated, and flocculated systems were each prepared with 2% (w/v) sulfamerazine concentrations and a dioctyl sodium sulfosuccinate (Aerosol OT®) solution at 0.1% or 0.5% (w/v) concentration. Aluminum chloride was used as the flocculating agent in preparation of the flocculated systems. This was added in the form of a concentrated solution (10%, w/v) during adjustment of the suspension volume to produce a final concentration of 0.25% (w/v).

The tonometer gas concentration (microliters per milliliter) in the vapor phase above the liquid sample versus the time (minutes) the nonpolar gas was present in the closed system was plotted to follow graphically the uptake. Sample volumes of 100μl were removed for analysis at approximately 1-min intervals for a period of 20 min, the time which was found to be adequate for observation of uptake of a significant quantity of gas. The method of measuring the amount of anesthetic gas remaining in the tonometer was by both peak height and curve area, and was validated by comparison with freshly prepared standards. The graphs show a decrease in gas concentration in the vapor phase and, thereby, the amount of gas absorbed by the suspension system.

RESULTS AND DISCUSSION

The distinctive structural characteristics of the sulfamerazine suspensions have been reported previously (1, 2, 3), and they have also been identified in the present study, by both their sedimentation rates and microscopic appearance. The gas-absorbing ability of each system differed. The two aggregated systems, coagulated and flocculated, could be distinguished by the evident differences in gas uptake, as illustrated in Figures 1 and 2. In contrast, a 2% solution of Aerosol OT alone absorbs no more than 5% in 20 minutes (6).

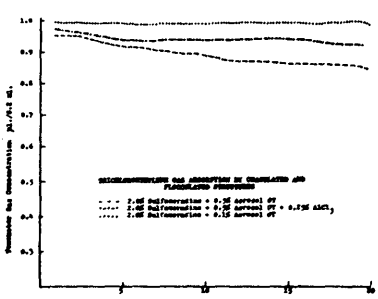

FIGURE 1. Trichloroethylene gas absorption. Coagulated system at 20 min measurement, $t = 8.35$, $p<0.001$; flocculated system at 20 min measurement, $t = 13.92$, $p<0.001$.

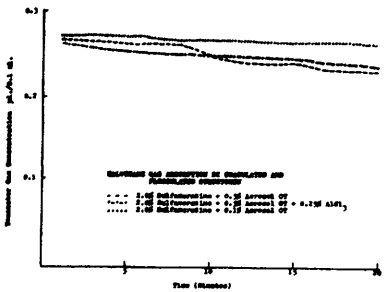

FIGURE 2. Halothane gas absorption. Coagulated system at 20 min measurement, $t = 8.77$, $p<0.001$; flocculated system at 20 min measurement, $t = 6.71$, $p<0.001$.

The dispersed system (2.0% sulfamerazine + 0.1% Aerosol OT), as shown in both curves, absorbed essentially no halothane or trichloroethylene, while the coagulated structure (2.0% sulfamerazine + 0.5% Aerosol OT) absorbed the largest quantity. In the studies of halothane uptake, the flocculated structure (2.0% sulfamerazine + 0.5% Aerosol OT + 0.25% $AlCl_3$) initially absorbed more gas than did the coagulated structure. However, after approximately 11 min, the coagulated structure began to absorb the gas more rapidly, and at the end of the 20-min period there was a greater total absorption. The trichloroethylene absorption was consistently greater by the coagulated system. The flocculated system again showed a larger amount of absorption at the outset, but the absorption rate gradually leveled off during the latter part of the observation period.

The film of surfactant in the coagule-structured system is, presumably, a micellar molecular aggregate which absorbs the nonpolar anesthetic gases. The floccule may entrap some of the gas because of its open structure with minimal surfactant; however, it cannot solubilize a quantity of gas equivalent to that absorbed by the coagule, with its closely packed structure in a matrix of micellar surfactant.

The concept of solubilization is frequently applied to pharmaceutical systems. Gas absorption of the type studied can be explained by similar solubilization mechanisms. Gas uptake could be applied as a means of detecting coagulated or flocculated structures.

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