Pharmaceutical Dosage Forms and Drug Delivery Systems

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Accurate indications, adverse reactions, and dosage schedules for drugs are provided in this book, but it is possible they may change. The reader is urged to review the package information data of the manufacturers of the medications mentioned.

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These main features of a suspension, which depend upon the nature of the dispersed phase, the dispersion medium, and pharmaceutical adjuncts, will be discussed briefly.

Sedimentation Rate of the Particles of a Suspension

The various factors involved in the rate of velocity of settling of the particles of a suspension are embodied in the equation of Stokes' law, which is presented in the accompanying Physical Pharmacy Capsule.

Stokes' equation was derived for an ideal situation in which uniform, perfectly spherical particles in a very dilute suspension settle without effecting turbulence in their downward course, without collision of the particles of the suspensoid, and without chemical or physical attraction or affinity for the dispersion medium. Obviously, Stokes' equation does not apply precisely to the usual pharmaceutical suspension in which the suspensoid is irregularly shaped, of various particle diameters, and not spherical, in which the fall of the particles *does* result in both turbulence and collision, and also in which there may be a reasonable amount of affinity of the particles for the suspension medium. However, the basic concepts of the equation do give a valid indication of the factors that are important to the suspension of the particles and a clue to the possible adjustments that can be made to a formulation to decrease the rate of particle sedimentation.

From the equation it is apparent that the velocity of fall of a suspended particle is greater for larger particles than it is for smaller particles, all other factors remaining constant. By reducing the particle size of the dispersed phase, one can expect a slower *rate* of descent of the particles. Also, the greater the density of the particles, the greater the rate of descent, provided the density of the vehicle is not altered. Because aqueous vehicles are generally used in pharmaceutical oral suspensions, the density of the particles is generally greater than that of the vehicle, a desirable feature, for if the particles were less dense than the vehicle, they would tend to float, and floating particles would be quite difficult to distribute uniformly in the vehicle. The rate of sedimentation may be appreciably reduced by increasing the viscosity of the dispersion medium, and within limits of practicality this may be done. However, a product having too high a viscosity is not generally desirable, because it pours with difficulty and it is equally difficult to redisperse the suspensoid. Therefore, if the viscosity of a suspension is increased, it is done so only to a modest extent to avoid these difficulties.

The viscosity characteristics of a suspension may be altered not only by the vehicle used, but also by the solids content. As the proportion of solid particles is increased in a suspension, so is the viscosity. The viscosity of a pharmaceutical preparation may be determined through the use of a Brookfield Viscometer, which measures viscosity by the force required to rotate a spindle in the fluid being tested (Fig. 7–3).

For the most part, the physical stability of a pharmaceutical suspension appears to be most appropriately adjusted by an alteration in the dispersed phase rather than through great changes in the dispersion medium. In most instances, the dispersion medium is supportive to the adjusted dispersed phase. These adjustments mainly are concerned with particle size, uniformity of particle size, and separation of the particles so that they are not likely to become greatly larger or to form a solid cake on standing.

Physical Features of the Dispersed Phase of a Suspension

Probably the most important single consideration in a discussion of suspensions is the size of the drug particles. In most good pharmaceutical suspensions, the particle diameter is between 1 and 50 μm.

Particle size reduction is generally accomplished by dry-milling prior to the incorporation of the dispersed phase into the dispersion medium. One of the most rapid, convenient, and inexpensive methods of producing fine drug powders of about 10 to 50 μm size is *micropulverization*. Micropulverizers are high-speed, attrition or impact mills which are efficient in reducing powders to the size acceptable for most oral and topical suspensions. For still finer particles, under 10 μm, the process of *fluid energy* grinding, sometimes referred to as *jet-milling* or *micronizing*, is quite effective. By this process, the shearing action of high velocity compressed air streams on the particles in a confined space produces the desired ultrafine or micronized particles. The particles to be micronized are swept into violent turbulence by the sonic and supersonic velocity of the air streams. The particles are accelerated into high velocities and collide with one another, resulting in fragmentation and a decrease in the size of the particles. This