

PHYSICAL PHARMACY CAPSULE 14.2 CONT.

If a different dispersion medium, such as glycerin, is used in place of water, a further decrease in settling will result. Glycerin has a density of 1.25 g/mL and a viscosity of 400 cP. The larger particle size powder (2.5 μm) will settle at this rate:

$$\frac{(2.5 \times 10^{-6})^2 (1.3 - 1.25)(980)}{18 \times 4} = 4.25 \times 10^{-10} \text{ cm / s}$$

The smaller particle size (0.25 μm) powder will now settle at this rate:

$$\frac{(2.5 \times 10^{-5})^2 (1.3 - 1.25)(980)}{18 \times 4} = 4.25 \times 10^{-10} \text{ cm / s}$$

A summary of these results is shown in the following table:

| CONDITION | RATE OF SETTLING (CM/S) |
|---------------------------------------|-------------------------|
| 2.5 μm powder in water | 1.02×10^{-4} |
| 0.25 μm powder in water | 1.02×10^{-6} |
| 2.5 μm powder in glycerin | 4.25×10^{-8} |
| 0.25 μm powder in glycerin | 4.25×10^{-10} |

As is evident from this table, a change in dispersion medium results in the greatest change in the rate of settling of particles. Particle size reduction also can contribute significantly to suspension stability. These factors are important in the formulation of physically stable suspensions.

The Stokes equation was derived for an ideal situation in which uniform, perfectly spherical particles in a very dilute suspension settle without producing turbulence, without colliding with other particles of the suspensoid, and without chemical or physical attraction or affinity for the dispersion medium. Obviously, the Stokes equation does not apply precisely to the usual pharmaceutical suspension in which the suspensoid is irregularly shaped and of various particle diameters, in which the fall of the particles *does* result in both turbulence and collision, and also in which the particles may have some affinity for the suspension medium. However, the basic concepts of the equation do give a valid indication of the factors that are important to suspension of the particles and a clue to the possible adjustments that can be made to a formulation to decrease the rate of 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. Reducing the particle size of the dispersed phase produces 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 used in pharmaceutical oral suspensions, the density of the particles is generally greater than that of the vehicle, a desirable feature. 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