fluid energy grinding, sometimes referred to as *jet milling* or *micronizing*, is quite effective. By this process, the shearing action of high-velocity compressed airstreams 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 velocities of the airstreams. The particles are accelerated to high velocities and collide with one another, resulting in fragmentation. This method may be employed when the particles are intended for parenteral or ophthalmic suspensions. Particles of extremely small dimensions may also be produced by *spray drying*. A spray dryer is a cone-shaped apparatus into which a solution of a drug is sprayed and rapidly dried by a current of warm, dry air circulating in the cone. The resulting dry powder is collected. It is not possible for a pharmacist to achieve the same degree of particle size reduction with such comminuting equipment as the mortar and pestle. However, many micronized drugs are commercially available to the pharmacist in bulk, such as progesterone.

As shown by the Stokes equation, the reduction in the particle size of a suspensoid is beneficial to the stability of the suspension because the rate of sedimentation of the solid particles is reduced as the particles are decreased in size. The reduction in particle size produces slow, more uniform rates of settling. However, one should avoid reducing the particle size too much because fine particles have a tendency to form a compact cake upon settling to the bottom of the container. The result may be that the cake resists breakup with shaking and forms rigid aggregates of particles that are larger and less suspendable than the original suspensoid. The particle shape of the suspensoid can also affect caking and product stability. It has been shown that symmetrical barrel-shaped particles of calcium carbonate produced more stable suspensions than did asymmetrical needle-shaped particles of the same agent. The needle-shaped particles formed a tenacious sediment cake on standing that could not be redistributed, whereas the barrel-shaped particles did not cake upon standing (1).

To avoid formation of a cake, it is necessary to prevent agglomeration of the particles into larger crystals or into masses. One common method of preventing rigid cohesion of small particles of a suspension is intentional formation of a less rigid or loose aggregation of the particles held together by comparatively weak particle-to-particle bonds. Such an aggregation of particles is termed a *floc* or a *floccule*, with flocculated particles forming a type of lattice that resists complete settling (although flocs settle more rapidly than fine, individual particles) and thus are less prone to compaction than unflocculated particles. The flocs settle to form a higher sediment volume than unflocculated particles, the loose structure of which permits the aggregates to break up easily and distribute readily with a small amount of agitation.

There are several methods of preparing flocculated suspensions, the choice depending on the type of drug and the type of product desired. For instance, in the preparation of an oral suspension of a drug, clays such as diluted bentonite magma are commonly employed as the flocculating agent. The structure of the bentonite magma and of other clays used for this purpose also assists the suspension by helping to support the floc once formed. When clays are unsuitable as agents, as in a parenteral suspension, frequently a floc of the dispersed phase can be produced by an alteration in the pH of the preparation (generally to the region of minimum drug solubility). Electrolytes can also act as flocculating agents, apparently by reducing the electrical barrier between the particles of the suspensoid and forming a bridge so as to link them together. The carefully determined concentration of nonionic and ionic surface-active agents (surfactants) can also induce flocculation of particles in suspension and increase the sedimentation volume.

Dispersion Medium

Oftentimes, as with highly flocculated suspensions, the particles of a suspension settle too rapidly to be consistent with what might be termed a pharmaceutically elegant preparation. The rapid settling hinders accurate