



Figure 9-3 Potential energy curves for particle interactions in coarse suspensions. Particles in suspension are subject to van der Waals attractive and electrostatic repulsive forces. For coarse dispersions that are flocculated, weaker attractive forces occur at significant interparticle distances at the region referred to as the secondary minimum resulting in the formation of loosely aggregated particles. *Source:* From Ref. 11.

problems are caking and crystal growth. In order to understand the behavior of suspensions and methods for optimization, a basic understanding of theoretical concepts explaining these physical transformations is required. However, a detailed discussion on theory is beyond the scope of this review, and the reader is referred to appropriate texts on this subject for additional details.

The Derjaguin, Verwey, Landau, and Overbeek (DVLO) theory was originally devised to explain the stability of colloidal systems, but the principles have also been invoked to explain particle interactions in coarse dispersions such as suspensions. According to DVLO theory, the forces on particles in a dispersion are due to electrostatic repulsion and van der Waals attraction, although other forces are usually included to adequately explain interactions in dispersed systems. Potential energy curves for particle interactions are shown in Figure 9-3. The forces at particle surfaces will affect the degree of flocculation and agglomeration observed for suspensions. Thus, DVLO theory provides a framework for understanding the interactions of particles controlling physical properties of suspensions.

Referring to the composite curve in Figure 9-3, the collision of particles will be opposed if the repulsion energy is high (e.g., low electrolyte concentration in aqueous suspensions). Such a system is referred to as deflocculated. When the particles settle, the energy barrier is overcome and strong attractive forces in the potential well cause a densely packed sediment to form. Eventually, a hard cake results that is difficult to disperse using normal agitation procedures for resuspension. Such a condition is highly undesirable, as a nonuniform dispersion of particles can impact dosing reliability.

For coarse dispersions that are flocculated, the potential energy barrier is still too large to be surmounted by approaching particles. However, weaker attractive forces occur at significant interparticle distances at the region referred to as the secondary minimum in Figure 9-3. Particle interactions in this case result in the formation of loose aggregates (flocules). Flocculation can be induced in a suspension by the addition of a flocculating agent such as an electrolyte. Suspensions that are flocculated are considered pharmaceutically stable because sedimented material is readily redispersed upon normal agitation procedures.

The properties of flocculated and deflocculated suspension are compared in Table 9-6 (12,13). For flocculated suspensions, the sedimentation properties may result in a preparation that appears to contain a majority of clear vehicle upon settling. This condition is not a serious problem provided caking does not occur making the particles difficult to disperse with minor