The use of cosolvents improves the solubility as a result of the polarity of the cosolvent mixture being closer to the drug than it is in water:

$$\log S_m = f \log S_c + (1 - f) \log S_w \tag{7.9}$$

where S_m is the solubility of the compound in the solvent mix, S_w is the solubility in water, S_c is the solubility of the compound in pure cosolvent, f is the volume fraction of the cosolvent, and σ is the slope of the plot of $\log(S_m/S_w)$ versus f. There is a definite correlation between the s value and indices of the cosolvent polarity, such as the dielectric constant, solubility parameter, surface tension, interfacial tension, and octanol–water partition coefficient. The aprotic cosolvents give a much higher degree of solubility than the amphiprotic cosolvents. This means that if a cosolvent can donate a hydrogen bond, it might be an important factor in determining whether it is a good cosolvent. Use of cosolvents with polar drugs can reduce the solubility.

On formulating parenteral dosage forms, the use of cosolvents to prevent precipitation can be hampered by the quantity of the allowed cosolvents in the formulation for toxicity and hemolysis considerations. Other considerations such as dilution prior to administration and the rate of administration (dilution factor) should also be simulated using in vitro techniques. Although cosolvents can increase the solubility of compounds, on certain occasions, they can have a detrimental effect on their stability. One point that is often overlooked when considering cosolvents is their influence on buffers or salts. As these are conjugate acid–base systems, it is not surprising that by introducing solvents into the solution, a shift in the pK_a of the buffer or salt can result. These effects are important in formulation terms, as many injectable formulations that contain cosolvents also contain a buffer to control the pH.

7.4 Emulsion Formulations

For drugs with poor water solubility, emulsion formulation, such as oil-in-water (O/W), where the drug has good partitioning in the oil phase chosen, often offers an excellent choice. The particle size of the emulsion and its stability (physical and chemical) then become significant factors, as larger globule sizes may lead to phlebitis. To achieve smaller particle size, the technique of microfluidization is often used, among other available homogenization methods. The phospholipids added stabilize emulsions through surface charge changes and provide a good mechanical barrier.

The particle size of an emulsion is governed by the method used. Figure 7.7 shows the various particle sizes achieved by using different methods.

The particle size is measured using PCS (10), a technique for measuring particle size distributions. When fine particles are suspended in a fluid, they are constantly in random motion as a result of collisions with the molecules of the fluid. This is known as “Brownian motion” and was first observed in the 1820s. When the suspension is irradiated by a beam of laser light, some of the light is scattered by the particles. Very fine particles exhibit wavelength smaller than that of light (typically 500–700 nm), and as they move relative to the light beam, the phase of the light scattered from each particle will vary. The intensity of the scattered light, measured at some fixed point, is the sum of the light scattered from all the individual particles, formed by constructive