can be important if they show a tendency to, for example, adhere to surfaces, or if solutions foam. Not all surface-active drugs form micelles, because of steric hindrances. The surface activity of compounds can be determined using a variety of techniques, such as surface tension measurements using a Du Nouy tensiometer (15), Wilhelmy plate, and conductance measurements. Sigma 703 is a simple, reliable instrument for the measurement of surface and interfacial tension by Du Nouy ring or Wilhelmy plate methods (16).

7.4.6 Osmolality

A 0.9% w/v NaCl solution is iso-osmotic with blood. The commonly used unit to express osmolality is the ion, and this is defined as the weight in grams per solute, existing in a solution as molecules, ions, macromolecules, and the like, and is osmotically equivalent to the gram MW of an ideally behaving nonelectrolyte. This is an important consideration for parenteral and ophthalmic products. Extreme discomfort in the use of ophthalmic preparations is experienced when the osmolality is too high or too low. Osmolality is determined using a cryoscopic osmometer, which is calibrated with deionized water and solutions of sodium chloride of known concentrations (17). Using this technique, the sodium chloride equivalents and freezing point depressions for a large number of substances have been determined and reported.

7.5 Freeze-Dried Formulations

The stability of the solution forms intended for parenteral administration can be significantly improved by lyophilizing the solutions to dryness, without the use of heat. The solution is frozen to a very low temperature, and vacuum is applied to remove water through sublimation. The cake left is easily dispersible and thus offers a highly desirable dosage form that is reconstituted just prior to administration. Examples of lyophilized drugs include erythromycin, vancomycin, bacitracin, cyclophosphamide, cefazolin, infliximab, somatropin, trimetrexate glucuronate multivitamin injection (MVI), and doxorubicin. The Food and Drug Administration (FDA) classification for lyophilized products is as follows:

713 injection, powder, lyophilized, for liposomal suspension
705 injection, powder, lyophilized, for solution
706 injection, powder, lyophilized, for suspension
712 injection, powder, lyophilized, for suspension, extended release

Another advantage of lyophilization is that it allows the formulation without any additives; however, some are often added to increase the bulk. As a result, each drug must be formulated with a highly specific temperature and a vacuum cycle that is highly dependent on the nature of the drug, the quantity used, and the nature of the additives. The science of lyophilization is complex, and specialized training is needed