

solid, because bioavailability of a crystalline drug suspension may vary dramatically from that of a solubilized drug. For milky white macroemulsion creams or lotions it is difficult to determine if the final product requires additional mixing time to properly disperse or solubilize the drug. However, for a microemulsion formulation, mixing until all of the solid is dissolved or solubilized, as evidenced by a clear product, provides a readily discernible endpoint for product manufacture.

The ability of microemulsion systems to solubilize poorly soluble materials is fundamental to the extensive study of these systems over the years. Because drugs frequently cannot be delivered to a therapeutic dosage because of insufficient solubility in solvents that can be ingested, injected, or applied topically; solubilization of the drug within a microemulsion may be particularly important. The alternative prodrug approach of improving solubility by molecularly changing the drug to a more soluble analogue requires toxicological studies to be completed on each analogue, which may result in unacceptable time delays or increased expense. Thus, solving problems of low solubility by using surfactants can complement prodrug approaches by satisfying solubility or solubilization demands in the short-term, while the ideal prodrug is being developed, characterized, and screened for safety.

Thermodynamic stability is important because this characteristic results in (1) a formulation the properties of which are not dependent upon process (i.e., shear rate, forced cooling, and such), and (2) a formulation that will not phase-separate, provided temperature and pressure conditions remain reasonably constant. It is useful to further consider what it means for a system to be thermodynamically stable. For a microemulsion, *thermodynamically stable* means the system is conceptually analogous to an equilibrated salt solution below saturation. As long as the system remains closed (i.e., no evaporation or chemical degradation) and the temperature and pressure remains the same, the properties of the system will remain unchanged indefinitely. However, if the temperature of the solution is decreased sufficiently to cause salt crystals to precipitate, then the single-phase solution changes to the two-phase system of solid crystals in equilibrium with saturated salt solution. Returning this system to the original temperature will reverse the phase change, and at equilibrium will result in a solution with properties and composition identical with the original salt solution. Analogously, a microemulsion once mixed (equilibrated) will not separate into its component phases provided that the temperature and pressure remain constant. If changes in storage conditions cause the microemulsion to split, it will re-form once it returns to the original conditions. Importantly the original formation or reformation of the