

Intralipid is approved for parenteral nutrition and is generally well tolerated upon intravenous administration (Li et al., 1998). Thus, large numbers of new drug candidates can be investigated without the need for intensive and time-consuming formulation development. In terms of reaching high dosing concentrations by prevention of precipitation of coadministered lipophilic nonionizable compounds, these vehicles are often superior to the formulation approaches such as pH adjustment, cosolvent, and micelles.

The formation of microemulsions usually involves a combination of oil, water, surfactant, and cosurfactant. The tendency toward a w/o (water-in-oil) or an o/w (oil-in-water) microemulsion is dependent on the properties of the oil and the surfactant, cosurfactant, the water-to-oil ratio, and the temperature. Nonionic surfactants are conveniently classified on an empirical scale known as hydrophilic–lipophilic balance (HLB), which (in practice) ranges from 1 to 20. In general, w/o microemulsions are formed using surfactants that have an HLB in the range of about 3–6 while o/w microemulsions are formed using surfactants that have an HLB value in the range of about 8–18. The role of the cosurfactant, usually a short-chain alcohol, is to increase the interfacial fluidity by penetrating into the surfactant film and consequently creating a disordered film owing to the void spaces among surfactant molecules (Leung and Shah, 1989). However, the use of cosurfactant in microemulsions is not mandatory. For maximum solubilization, it is desirable to have most of the surfactant at the interface between the oil and water, rather than dissolved in the oil or water phases. Increasing the interfacial area should also increase solubilization. The spontaneous formation of an emulsion upon drug release in the GIT presents the drug in a dissolved form, and the small droplet size provides a large interfacial surface area for drug absorption. For selecting a suitable self-emulsifying microemulsion vehicle, it is important to assess (1) the drug solubility in various components, (2) the area of self-emulsifying region in the phase diagram, and (3) droplet size distribution following self-emulsification (Kommuru et al., 2001). Self-emulsifying formulations have been assessed by simple dispersion tests in aqueous media coupled with particle size measurements to define the resulting dispersion. More recently, however, it has been suggested that additional assessment of the impact of lipid digestion on the solubilization capacity of a lipid-based formulation is required to more accurately explain the *in vivo* performance of lipid-based formulations (Dahan and Hoffman, 2006).

Microemulsion formulation process starts with the construction of pseudoternary phase diagram. The microemulsion phase was identified as the area in the phase diagram where clear and transparent formulations are obtained on the basis of visual inspection of many samples. One common approach to construct a ternary phase diagram considers two components as a single one, for example, the oil and surfactant or surfactant and cosurfactant. For the preparation of the drug-containing microemulsion, the following procedure was employed: the desired amount of the drug was first weighed out and then dissolved in the appropriate amount of oil phase. The oil phase containing the drug was subsequently added to the right amounts of the surfactant and cosurfactant mixture (Constantinides and Scalart, 1997).

Lipid emulsions have a significant impact on the pharmacokinetic profile of coadministered compounds. Depending on the time for the emulsion to circulate the system, the affinity of the drug to the oil phase, and the particle size of the oil droplets, intravenous emulsions are likely to affect the pharmacokinetics of the incorporated drug. In addition to the factors mentioned earlier, emulsion formulations for oral administration are also likely to affect the pharmacokinetics of the drug by the digestion of oil components *in vivo*. Cuine et al. (2007) reported that drug solubilization was markedly affected by lipase-mediated digestion, and a reduction in lipid (and an increase in surfactant) content resulted in increased drug precipitation. Consistent with these data, the bioavailability of Danazol decreased significantly when the lipid content in the formulations was reduced.