

When formulating emulsions and microemulsions, considerable effort is placed on making appropriate blends of oil and surfactant-cosurfactants to achieve a stable dispersion. With phospholipid-based liposomes that spontaneously form a stable structure, more emphasis is placed on characterizing liposome-specific properties.

Determination of vesicle size, captured volume, percent entrapment and percent incorporation have already been discussed. One other property unique to liposomes is the active ingredient *release rate* or *efflux rate*, which has important implications for the performance and stability of a formulation. It is most simply measured by monitoring the change in percent entrapment or percent incorporation of a formulation over time under a given set of conditions (temperature, other excipients, ionic strength, presence of biological fluids). Average liposome size of a formulation is an important factor in determining the release rate of small nonelectrolytes (23). However, mathematical model fitting from experimental determinations of glucose release indicates that the degree of liposome size heterogeneity (polydispersity) does not affect the release rate significantly (24).

#### D. Antimicrobial Preservatives

Topical products are usually preserved by the addition of one or more antimicrobial preservatives. Preservatives are intrinsically no different from an active ingredient, which is to say they can be entrapped in liposomes or incorporated into the bilayer or interfacial region. The end result is that microbial deterrence at a given concentration will be different from that of a similar aqueous solution without liposomes.

For instance, the commonly used parabens are inactivated by liposomes as a consequence of partitioning into the bilayer (25). The extent of inactivation will be a function of partition coefficient and the lipid concentration. Consequently, the total quantity of lipophilic preservative must be increased to achieve a satisfactory germicidal effect. If the "free" concentration ( $C_{\text{free}}$ ) required for the germicidal effect of preservative P, the formulation's liposome-water partition coefficient ( $K_p$ ) and the total lipid concentration are known, the total concentration of preservative ( $C_{\text{total}}$ ) required in the formulation can be calculated from a modification of Bean's equation (26):

$$C_{\text{total}} = C_{\text{free}} \times (\phi \times K_p + 1) / (\phi + 1) \quad [3]$$

where  $\phi \approx$  ratio of lipid to aqueous phase (w/w), and

$$K_p \approx (\text{g P/g lipid}) / (\text{g P/g aqueous phase})$$