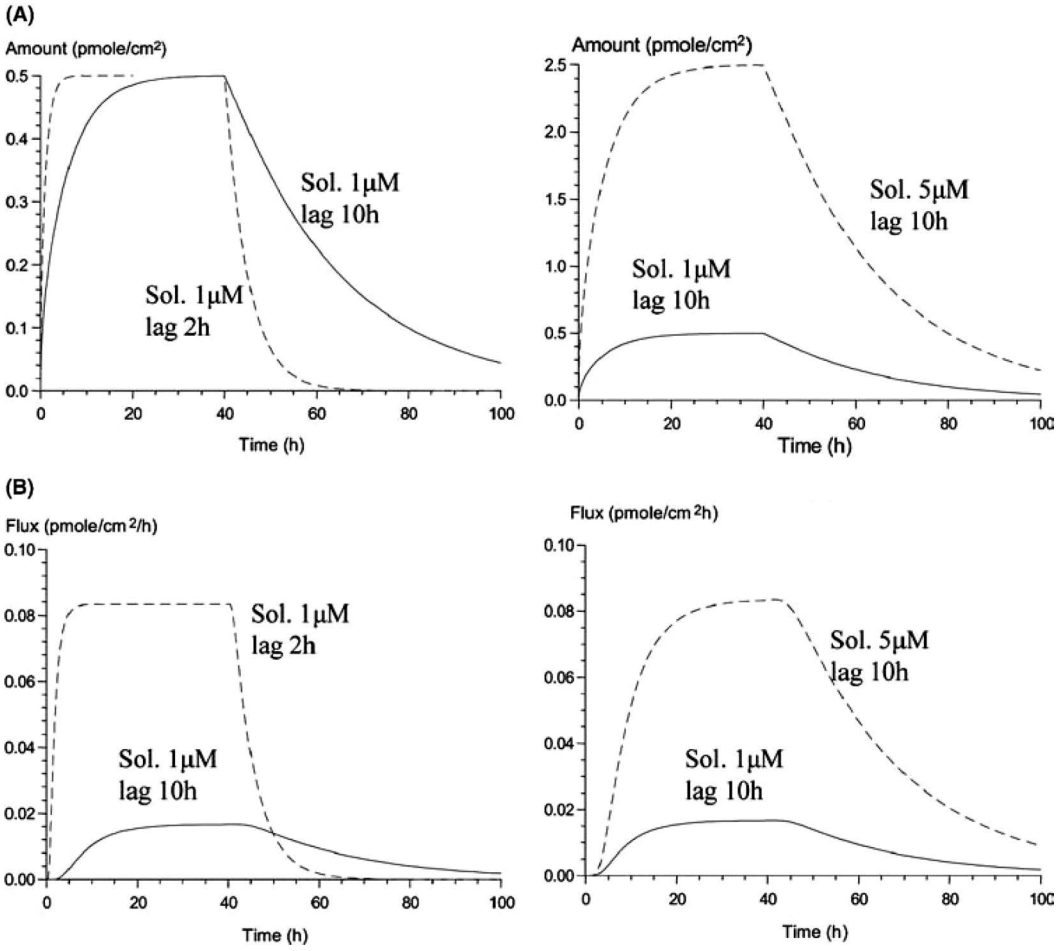

FIGURE 4.2 Amount in the stratum corneum (*a*) and flux through epidermis (*b*) based on a diffusion model for: (A) Two drugs with lag times of 2 and 10 hours and (B) two drugs with stratum corneum solubilities of 1 and 5 μM.

One could, in principle, estimate the duration of the reservoir for a given drug from the time required to reach maximal reservoir concentration (Figure 4.2) or from the epidermal lag times obtained in epidermal penetration studies. Using Equation (49) for lag time and the slowest term in Equation (23) from Roberts et al. (7), the duration time for 10% of the reservoir to remain (i.e., 90% has diffused out) is approximately 5.7 times that of the lag time. The corresponding duration time for 5% to be left remaining in the reservoir is 7.4 times the lag time. Accordingly, using a lag time for aspirin in a hydrated epidermal penetration study of about 0.6 hour (unpublished data) would suggest that 90% of the stratum corneum reservoir would be lost after about 3 to 4 hours. The actual time reported by Vickers (1) is about 240 hours, suggesting that the diffusivity in vivo is about 1/60th that for the hydrated stratum corneum in vitro. An important implication of this difference is that hydration of the stratum corneum by occlusion or other means may substantially increase diffusivity in the stratum corneum. Hydration and various penetration enhancers such as dimethylsulphfoxide have been reported to induce the steroid stratum corneum reservoir effect (1), probably as a result of their increasing drug diffusivity in the stratum corneum.