The importance of the phase behavior in determining kinetic behavior (1,2,9,10), or vice versa, has also been demonstrated. It should be noted that a combination of local adsorption phenomena and development of interfacial concentrations dependent on the relative rates of ingress or diffusion away can lead to an interfacial phase formation that is unexpected from the total concentrations of the components in the system. Thus, for example, the observation of interfacial liquid crystal formation at the oil–water interface in systems in which the total oil is less than 1% of the amount required to saturate the surfactant micelles with which the oil is in contact in initial kinetics experiments.

Both of these considerations (i.e., time scale and phase evolution) will affect the performance of a topical vehicle formulation. Humectant aspects of an applied cream, for example, will raise the water concentration at the vehicle–skin interface, thereby altering the local concentrations of the system. The effect of this will be determined by the phase behavior of the system in response to increased water and the rates at which the components diffuse into and out of the interfacial region. One possible scenario would be that for which the rate of ingress of components from the vehicle was much slower than the rate of water buildup. Here, an essentially impenetrable barrier to the passage of a hydrophobic drug could be established.

In general terms, for the rate of steady-state penetration of a drug to be attained (see Fig. 7), the effects discussed will be manifested in terms of the lag time (τ). The range of lag times encountered is from minutes to several days; thus, they are of clinical significance, and an understanding of the factors underlying them is of major importance in the design of topical systems.

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