where

$$\beta = \frac{Rh}{h_v} \qquad [11]$$

$$\alpha_n \text{ is a root of } \alpha \tan \alpha = \beta \qquad [12]$$

$$\tau = \frac{6D}{h^2} t \qquad [13]$$

$$J_s = \frac{D\,C(0, 0)}{h}$$

and h_v is the thickness of the vehicle. The dimensionless parameter, τ, is used for a general solution in terms of number of lag times. Thus, a graph of flux versus τ can be used for any diffusion coefficient and membrane thickness.

A plot of the ratio J/J_s versus τ is given in Figure 2 for several values of β. For $\beta < 0.1$ the flux is near the steady-state value for many lag times. For $\beta \simeq 1$, however, the maximum flux is only 60% of the steady-state value, and it decays rapidly after two lag times. For example, consider the application of 5 mg/cm^2 of cream containing 20% oil and 1% salicylic acid. After evaporation one is left with an oil film about 10 μm thick (corresponding to 1 mg/cm^2). Here, $R \simeq 1$, and β is unity if we use $h \simeq 10$ μm. For a molecule like salicylic acid that penetrates well (short lag time), one cannot reach steady-state flux, nor maintain it, without a thicker film or a solvent in which salicylic is more soluble (e.g., polyethylene glycol).

This type of behavior is observed in vivo (monitoring urinary excretion) for benzoic acid penetration from a lipophilic matrix (3). The mathematical description of the in vivo situation is similar to that described here, but it is more involved because of the addition of whole-body pharmacokinetics (4).

A simple in vitro test to determine the effect of film thickness is useful before conducting an in vivo study so that one can know the film thickness required to obtain steady state. Evaporation and penetration of the vehicle components that are not extremely volatile will complicate the analysis but will serve to keep the concentration higher and, thus, maintain the flux more in a plateau region, although the decay rate will be faster when the reservoir is depleted.

D. Penetration Enhancers

The performance of a topical dosage form is linked to the flux of drug across the skin, unless one has reached beyond the plateau on