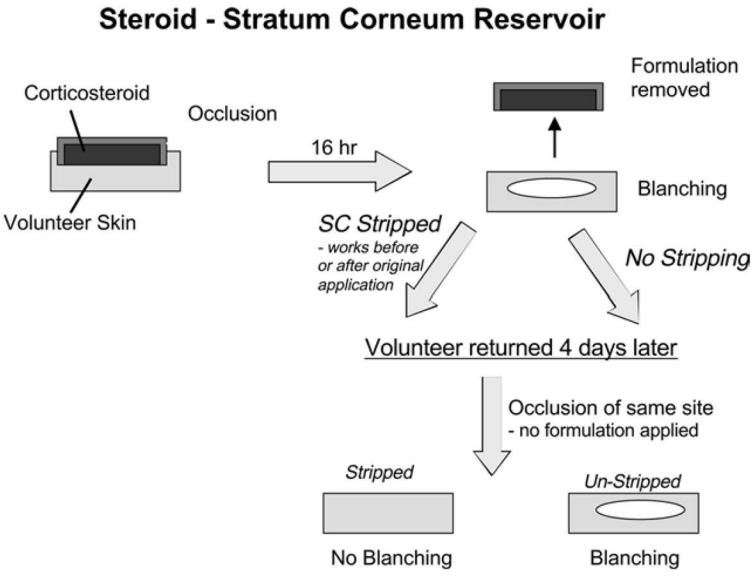

FIGURE 4.1 The reservoir effect as demonstrated by Vickers (6) in 1963.

with concentration distance profiles when a diffusion model is used to characterize the penetration process (7). The presence of a corticosteroid depot has been confirmed in a number of later papers (8, 9). Vickers (1) further observed that the duration of the reservoir depended on the nature of the drug, the vehicle used, the temperature of the skin, and the relative humidity to which the skin is exposed.

4.4 MODELING THE FORMATION AND DURATION OF THE STRATUM CORNEUM CORTICOSTEROID RESERVOIR

We propose that in a simplistic representation, the stratum corneum reservoir is defined by three independent variables: (1) the diffusivity of the drug in the stratum corneum, (2) the amount of drug in the stratum corneum, and (3) clearance of drug from the epidermis.

4.4.1 Diffusivity

The diffusivity of solutes in the stratum corneum determines the time to reach steady state or to desorb from the stratum corneum. When diffusivity is very slow, sufficient drug will not be taken up into the stratum corneum to be recognized as establishing a reservoir. Vickers (1) recognized that occlusion (via an increased humidity and temperature) was necessary to promote a reservoir effect. Occlusion leads to an increased hydration of the skin and a promotion of diffusivity (10). Further, as shown in Figure 4.2, if the duration of the application is too short relative to the diffusion time of the drug, a reservoir may not be evident. Vickers (1) suggested that, for steroids, ‘‘an occlusion of 8 hr resulted in (if any) a short-lived reservoir that was often not reproducible.’’ The increase in the stratum corneum reservoir for sodium fusidate, with increases with both temperature and increase in relative humidity, is consistent with these variables also increasing the percentage of sodium fusidate that had penetrated through the epidermis over 24 hours (1). The duration of the reservoir is also related to the nature of the drug, as shown in Figure 4.3. The duration of the reservoir for aspirin < fusidic acid < fluocinolone acetonide (1). Barry and Woodford (11) have suggested that a corticosteroid reservoir in the skin lasts for 8 to 14 days.