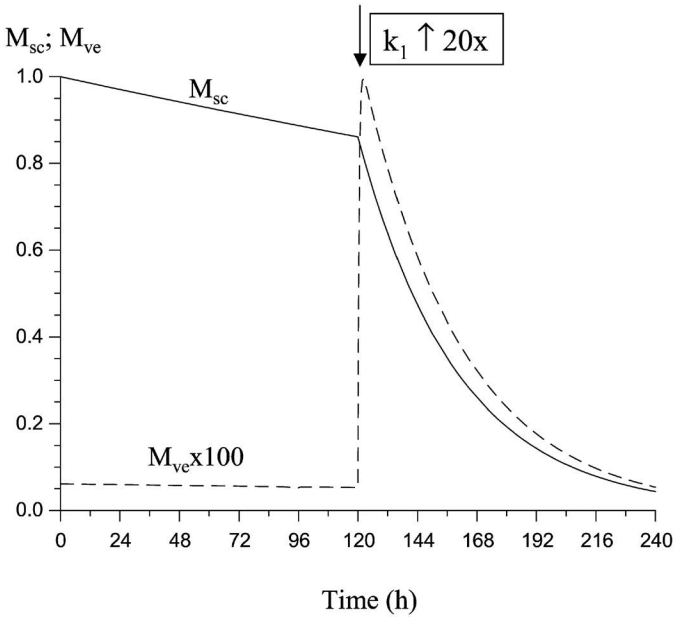

FIGURE 4.7 Amount of corticosterone remaining in the stratum corneum reservoir M_{sc} (—) and in the viable epidermis M_{ve} (x100) (– –) as a function of time based on a simple compartmental model. At 120 hours, it is assumed occlusion has increased stratum corneum diffusivity (k_1 in the compartment model shown in Figure 4.6) 20×. A lag time of 16.5 hours for hydrated epidermis (14), a stratum corneum–viable epidermis partition coefficient of about 0.5 (unpublished data) and k_3 0.3 hr^{-1} [using dermal clearance (14), and assuming a viable epidermis to stratum corneum thickness ratio of 20].

water (10). Application of an occlusive dressing leads to a reduction of transepidermal water loss and retention of water in the stratum corneum, leading to an increased hydration of various stratum corneum components and an increase in the diffusivity of corticosteroids from the stratum corneum into the viable epidermis and dermis. However, other enhancers such as urea (25) and propylene glycol (27) have also been shown to promote release of steroids from the stratum corneum.

4.8 CHANGES IN PLASMA STEROID LEVELS ASSOCIATED WITH THE CORTICOSTEROID RESERVOIR

Figure 4.8 shows that after topical application of hydrocortisone, a rebound effect in its plasma levels can be achieved when a placebo cream is applied 12 hours after the original product (27). The profiles are consistent with those predicted in Figure 4.7. One possible explanation for the data is a loss of occlusion and decrease in the stratum corneum diffusivity (k_1) between 4 and 12 hours as a result of the cream drying out or subject activity. Application of the placebo cream containing an enhancer leads to an increase in stratum corneum diffusivity and an increase in hydrocortisone release to lower tissues (Figure 4.6) and then into the blood, giving the profile observed in Figure 4.8.

4.9 ROLE OF DESQUAMATION ON STRATUM CORNEUM RESERVOIR EFFECT

In general, it has been asserted that the stratum corneum reservoir is ‘‘continuously emptied’’ by desquamation (28) and that desquamation may have a greater effect on the percutaneous penetration of more lipophilic solutes than would be indicated by the initial partitioning (29). Reddy et al. (30) have recently examined the effects of desquamation on permeation using a theoretical analysis