4.5 STRATUM CORNEUM RESERVOIR AND EPIDERMAL FLUX

Epidermal flux (J_{sc}) is defined by the product of the concentration of available drug in the stratum corneum and the diffusivity of a drug in the stratum corneum. Accordingly, percutaneous absorption may be related to the extent of reservoir function. At any given time, the amount of drug in the stratum corneum will be defined by the diffusivity into and affinity for the stratum corneum, as discussed earlier. Dupuis and co-workers (16) in 1984 first showed that the amount of different drugs absorbed in the body of a hairless rat could be correlated with the amounts found in the skin after topical application. This work was then confirmed in man (17) and extended to show that the relationship existed irrespective of anatomical site (18) or type of vehicle used (19).

4.6 STRATUM CORNEUM RESERVOIR AND SUBSTANTIVITY

Substantivity is a measure of the binding of solutes to sites in the stratum corneum, as evident by a resistance to be washed off or removed. Sunscreen substantivity has been defined as resistance to removal by water. The European Cosmetic, Toiletry, and Perfumery Association (COLIPA) has defined a water resistance retention for sunscreens (%WRR) in terms of the sun protection factors prior to (SPF_{dry}) and after water immersion (SPF_{wet}) (20):

$$\mathrm{WRR}(\%) = \frac{\mathrm{SPF}_{\mathrm{wet}} - 1}{\mathrm{SPF}_{\mathrm{dry}} - 1} \times 100 \tag{4.1}$$

Stokes and Diffey (20) showed that moisturizing products and sunscreens making no claims about water resistance were readily washed off. Waterproof lotions had the greatest retention of sunscreen (>80% after two applications), followed by water-resistant sunscreens (>60% after two applications). Wester et al. (21) showed that the retention of DDT and benzo[a]pyrene in skin after application in vitro for 25 minutes followed by a soap and water wash was 16.7% and 5.1%, respectively, after acetone application and 0.25% and 0.14%, respectively, after application in soil. Billhimer et al. (22) showed that the amount of 3,4,4'-trichlorocarbanilide remaining on the skin 24 hours after a final soap wash was sufficient to effectively inhibit the growth of *Staphylococcus aureus* added to the skin for 5 hours. A remnant antibacterial effect has been shown for a number of antiseptic products. The substantivity of hair dyes has recently been reviewed (23). Bucks (24) examined the long-term substantivity of hydrocortisone, estradiol, and five phenolic solutes following a one-day and a one-week wash using 10 stratum corneum tape strips after application of radiolabeled solutes to the ventral forearms of healthy male volunteers. He reported retention levels of 0% to 5% of the applied solutes after a week and suggested that the least lipophilic and most poorly penetrating chemicals had the higher substantivity.

4.7 MODELING THE VASOCONSTRICTOR EFFECT ASSOCIATED WITH THE CORTICOSTEROID RESERVOIR

Recently, Clarys et al. (25) carried out a study, which elaborates on the initial work of Vickers. They showed that blanching on reocclusion depended on the time of the reocclusion after the original application, the concentration of steroid, and whether an enhancer was used (Figure 4.5). The extent to which a reservoir is evident after such an application will be dependent on a number of factors (Figure 4.4). First, the reservoir of steroid in the skin achieved after topical application will be depleted (emptied) at a given rate. As Clarys et al. (25) point out, the amount of steroid remaining in the skin after low concentrations of halocinonide (0.005% and 0.05%) is not sufficient to exert a dermal vasoconstrictive effect when the site was reoccluded between 34 and 106 hours after the initial application. However, with 0.2%, a reservoir effect was demonstrated on reocclusion for at least 106 hours. Second, if the enhancement increased more than provided by reocclusion alone,