the viable epidermis may also be a determinant of stratum corneum concentrations, leading to a decrease in the loss from the stratum corneum for the more lipophilic solutes. Mimicking an increased resistance from the viable epidermis by reducing in k_3 in the present simple model leads to the amount in stratum corneum being lost at a slower rate [Equations (4.2) and (4.3)]. The use of convection diffusion equations by Reddy et al. (30) provides a more realistic representation of events. Figure 4.10, developed using such a model, shows that when chemicals diffuse slowly (i.e., long lag times—often associated with large molecules), the fraction absorbed from the stratum corneum is likely to be reduced as a result of desquamation. Increasing solute lipophilicity (i.e., increased B) will result in a greater viable epidermal resistance to transport and a reduced fraction of solute likely to be absorbed from the stratum corneum. Figure 4.10 also shows that two of the lipophilic pesticides should have a lower fraction absorbed into the body from the stratum corneum as a consequence of desquamation.

4.10 STRATUM CORNEUM RESERVOIR FOR OTHER SOLUTES

It is to be emphasized that a reservoir effect is not restricted to steroids. Benowitz et al. (31) showed that continued absorption of nicotine from the skin after decontamination is therefore evidence of the stratum corneum acting as a reservoir for nicotine (Figure 4.11). Caffeine has also been shown to have a reservoir in the stratum corneum, and this reservoir is greater for an emulsion than for acetone (32) (Figure 4.12).

Yagi et al. (33) have suggested that cationic beta-blocking drugs may accumulate in stratum corneum intercellular lipids as a consequence of binding to endogenous anionic lipids such as cholesterol-3-sulfate, palmitic acid, stearic acid, and oleic acid. As shown in Figure 4.13, caffeine and a number of sunscreen agents were retained in the stratum corneum and had not penetrated into the epidermis, dermis, or receptor fluid after 16 hours. Other solutes have a high affinity for the stratum corneum, including surfactants testosterone (35). The magnitude of epidermal binding of

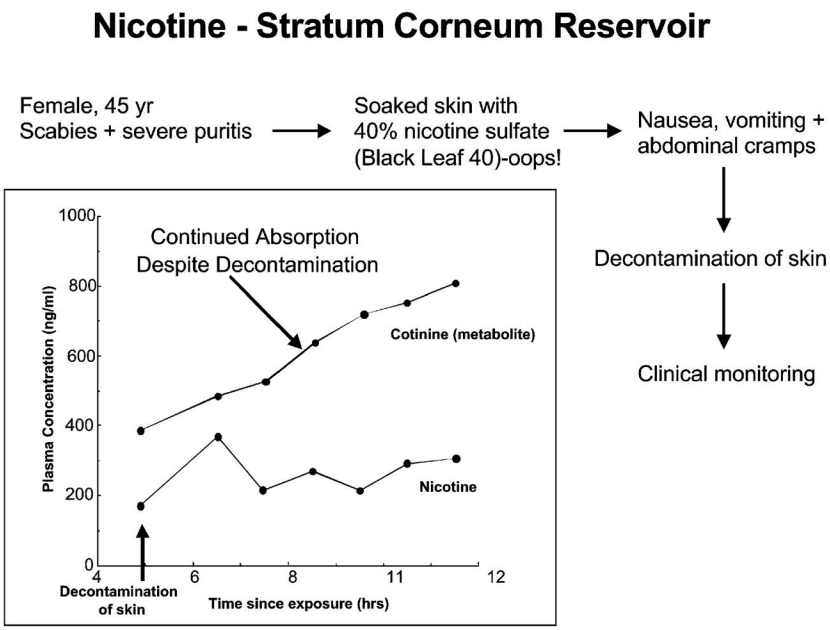

FIGURE 4.11 Evidence of a nicotine reservoir in the skin, as shown by the appearance of nicotine and its metabolite cotinine in plasma after topical decontamination. (From Reference 31.)