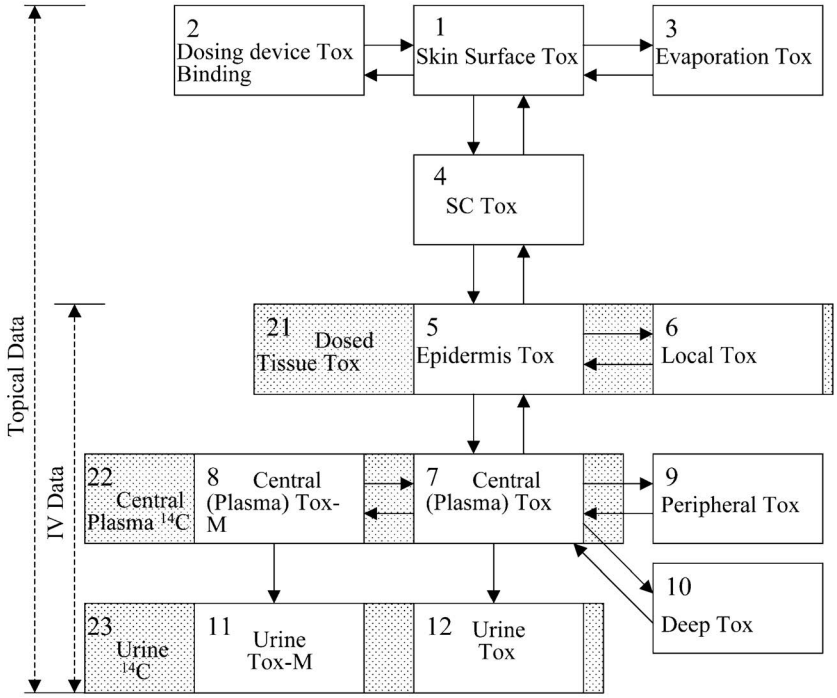

FIGURE 2.17 Dermatotoxicokinetic model for a toxic compound (Tox) and its metabolite (Tox-M). (Adapted from Reference 94.)

Hence from the observed $C_b(t)$ and $C_{iv}(t)$ and inversion of the resulting Laplace domain, expression for $\hat{j}_s(s)$ enables $J_s(t)$ to be defined. This technique is especially useful when the mathematical model for the percutaneous absorption process is not known. A comparison of the observed profile with theoretical profiles may define the underlying model for percutaneous absorption kinetics.

Examples of deconvolution analysis applied in this area include the evaluation of the absorption function from nicotine patches [96], the modeling of subcutaneous absorption kinetics [81], intramuscular absorption kinetics [129] andmodeling of a topically applied local anesthetic agent [97].

2.5.5 Penetration into Tissues Underlying the Topical Application Site

Epidermal concentrations in vivo after topical application, assuming D_e is sufficiently large to approximate a well-stirred state (i.e., compartmental representation), is defined by Equation (2.36) and at long times ($t \to \infty$) by Equation (2.29) via:

$$C_{ss} = \frac{k_p A C_v}{Cl_r + \left(k_p A / K_r\right)} \tag{2.88}$$

where Cl_r is the in vivo epidermal clearance.

A similar expression can be defined for subsequent deeper tissues using a compartment in-series model in parallel with removal to the systemic circulation and recirculation (Figure 2.18) after topical application [98]. Transport into deeper tissues could occur by either "convective" blood flow [99] or by diffusion. Nonlinear regressions of experimentally treated and contralateral tissue data with the model used simultaneous numerical integration of a series of differential equations [98, 100, 101]. The analysis showed that, whereas direct deep tissue penetration was apparent at early times, recirculation of drug from the systemic circulation accounted for tissue levels at longer times to