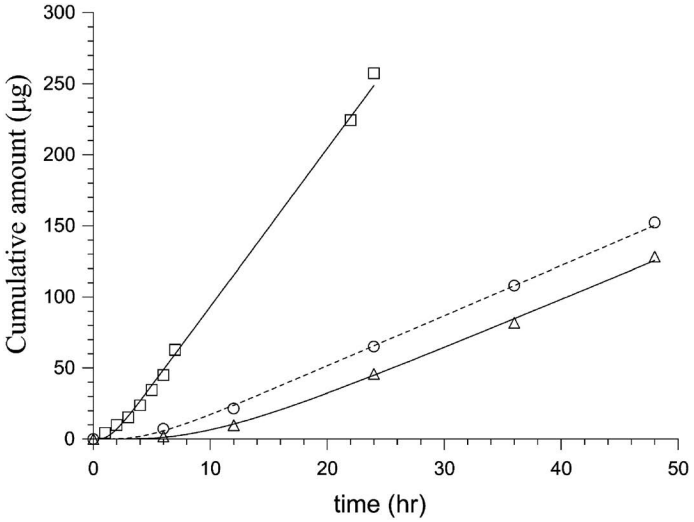


**FIGURE 2.4** Nonlinear regressions of cumulative amount penetrating human epidermis with time using Equation (2.13) and a weighting of $1/y_{obs}$. Data correspond to triethanolamine salicylate [□, $t_d$ = 9.8 hr, $J_{ss}$ = 11.1 µg/hr, diclofenac skin 1 (○, $t_d$ = 32.7 hr, $J_{ss}$ = 3.5 µg/hr) and diclofenac skin 2 (Δ, $t_d$ = 68.0 hr, $J_{ss}$ = 3.8 mg/hr)].

Figure 2.3 (curve 3) also shows the amount of solute taken up by the SC with time. These profiles are of interest for those solutes that may be targeted for retention in this tissue, e.g., sunscreens, or that may be sequestered in this tissue, e.g., steroids. The time domain and Laplace domain solutions for the amount of solute $M(t)$ taken up into an assumed homogeneous SC with time are:

$$M(t) = M_\infty \left\{ 1 - \frac{8}{\pi^2} \sum_{n=0}^{\infty} \frac{1}{(2n+1)^2} \exp\left[ -\frac{t}{t_d} \pi^2 (2n+1)^2 \right] \right\} \tag{2.14}$$

$$\hat{M}(s) = M_\infty \frac{2}{s} \frac{\cosh \sqrt{st_d} - 1}{\sqrt{st_d} \sinh \sqrt{st_d}} \tag{2.15}$$

where $M_\infty$ is the amount of solute in the skin at steady state and is given when a linear concentration gradient is assumed.

The summation of $Q(t)$ and $M(t)$ yields the expression for the amount, which leaves the vehicle $Q_{in}(t)$ (the profile shown in Figure 2.3, curve 4):

$$Q_{in}(t) = K_m A C_v h_m \left[ \frac{t}{t_d} + \frac{1}{3} - \frac{2}{\pi^2} \sum_{n=1}^{\infty} \frac{1}{\pi^2} \exp\left( -\frac{t}{t_d} \pi^2 n^2 \right) \right] \tag{2.16}$$

When $t \to \infty$, Equation (2.16) reduces to:

$$Q_{in}(t) = K_m A C_v h_m \left( \frac{t}{t_d} + \frac{1}{3} \right) = k_p A C_v \left( t + \frac{t_d}{3} \right) = k_p A C_v \left( t + \text{neglag} \right) \tag{2.17}$$

Hence, the linear portion of $Q_{in}(t)$ vs. $t$ has a slope of $k_p AC_v$ and intercepts on the negative side of the time axis at a point of neglag = $t_d/3 = h_m^2/3D_m$ (Figure 2.3, curve 5).