and therefore $J(t)$ can be written as:

$$J(t) = V_{vN} C_{v0} k_p f\left(\frac{t}{t_d}\right) = V_{vN} C_{v0} k_p f(\tau)$$

where $\tau = t/t_d$, $f(\tau)$ is a function independent of V_{vN} and whose Laplace transform is $\hat{f}(s) = 1/\cosh\sqrt{s}$. It can be shown by the numerical inversion of $\hat{f}(s)$ that the maximum of the function $f(\tau)$ occurs at $\tau = 1/6$ with the value $f(\tau_{max}) = 1.850$. The maximum flux, J_{max}, and for the time of maximum flux, t_{max}, for finite-dose absorption solvent–deposited solutes are therefore described by the simple equations:

$$J_{max} = 1.85 V_{vN} C_{v0} k_p = \frac{1.85 C_{v0} D_m h_v}{h_m^2}, \quad t_{max} = \frac{t_d}{6} = \frac{h_m^2}{6 D_m} \tag{2.49}$$

Hence, the peak time corresponds to the lag time observed after application of a constant donor solution [Equation 2.12]. Scheuplein and Ross [20] provided experimental data to show that (1) J_{max} is proportional to C_{v0} for benzoic acid, (2) t_{max} for different solutes is inversely related to their D_m values, and (3) penetration was facilitated by hydrating the SC.

2.1.6 In Vitro Permeability Studies with a Finite Donor Volume and a Finite Clearance from the Epidermis into the Receptor

Another case of particular practical interest is when the donor phase is assumed to be well-stirred and finite in volume and there is limiting clearance from the epidermis to the receptor phase. Applying the boundary condition defined by Equation (2.42), together with boundary condition for $x = h_m$:

$$D_m \left.\frac{\partial C_m}{\partial x}\right|_{x=h_m} = h_m k_c C_m(h_m, t) \tag{2.50}$$

Yields for $\hat{Q}(s)$:

$$\hat{Q}(s) = \frac{M_0}{s} \frac{1}{\sqrt{s t_d}\sinh\sqrt{s t_d}\left[V_{vN} + (1/t_d k_c)\right] + \cosh\sqrt{s t_d}\left[1 + V_{vN}(s/k_c)\right]} \tag{2.51}$$

The profiles for $Q(t)$ versus t defined by Equation (2.51) for different values of k_c ($\alpha = k_c t_d$) and $V_{vN} = 1$ are shown in Figure 2.8B.

A case of finite volume of the vehicle with simultaneous rate limitations due to clearance from receptor (Cl_r), finite receptor volume (V_r), finite permeability through viable epidermis (k_p^{ve}), and finite permeability through unstirred donor layer (k_p^{d}) were analyzed by Anissimov and Roberts [18]. Equations (2.44) and (2.51) presented here for $\hat{Q}(s)$ are limiting cases of their more general solution.

2.1.7 In Vitro Skin Permeability Studies with Diffusion Limited Finite Donor and Sink Receptor Conditions

One of the first attempts at modeling percutaneous absorption with diffusion-limiting uptake from both the vehicle and the skin was made by Kakemi et al. [21]. Their one-dimensional model is shown in Figure 2.2d. Guy and Hadgraft (22) used a similar model with sink receptor conditions, as shown in Figure 2.10.