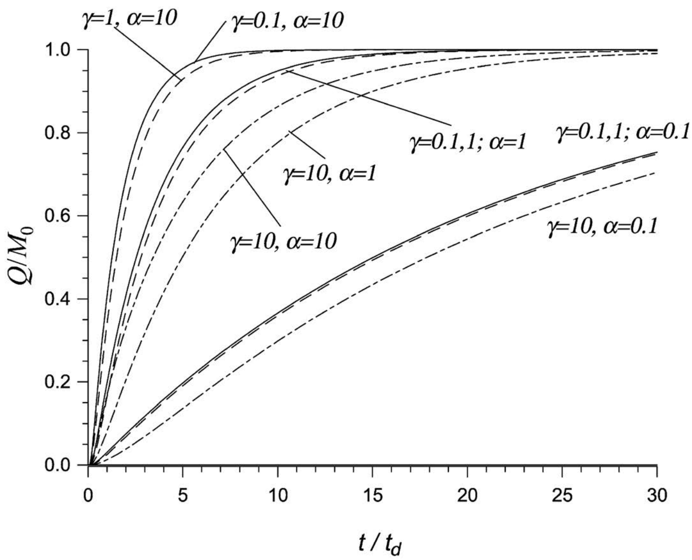

FIGURE 2.11 Cumulative amount penetrated Q normalized for amount applied M versus time normalized for diffusion time t_d for the case of both vehicle and SC limited diffusion. The two parameters varied define the relative diffusion time in vehicle relative to that in SC ($\gamma = t_{dv}/t_d$) and the interfacial barrier rate constant effect on the exit of solutes from the stratum $\alpha = k_c t_d$ [Equation (2.55)].

In the particular cases when $t_{dv} >> t_d$ and $t_d >> t_{dv}$ Equation (2.52) reduces to Equations (2.65) and (2.44), respectively.

2.1.8 In Vitro Permeability Studies with Two-Layer Diffusion Limitations in Transport

The complex cases of diffusion being a limitation in the transport through both the SC and epidermis have been considered by Hadgraft [23, 24]. He considered the case when solute exists as a reservoir in the SC. In his approach, the solute initially present in the SC diffuses from it into and through the epidermis. The case of rate-limiting removal from the epidermis (k_c) was considered.

Cleek and Bunge [25] considered a similar two phases in a series model for the amount of solute entering [Qin(t)] and determined it both as an analytical solution and simulations. This model was then extended to include solute properties as a determinant of uptake [26]. They suggested that steady-state permeability would be underestimated if not corrected for the relative permeabilities of the SC and epidermis. The result of these considerations is a steady-state Equation (2.54) similar to Equations (2.39) and (2.40):

$$Q_{in}(t) = C_{v0} k_p A \frac{1}{1+B}\left[t + t_{ds}\frac{G(1+3B)+B(1+3BG)}{3G(1+B)}\right] \tag{2.54}$$

where $k_p = K_{sv} D_{sc}/h_{sc}$, $G = t_{ds}/t_{de}$, $B = D_{sc}h_e K_e/D_e h_{sc}$, and K_{sv} is the partition coefficient between SC and the vehicle $K_{sv} = C_{sc}/C_v$.

Seko et al. [27] considered a similar model with the solute metabolism in the second phase (viable epidermis). The resulting equations for the amount exiting the epidermis for drug Q_d and metabolite Q_m are:

$$\frac{AK_{sd}C_v h_s\sqrt{st_{sd}}}{s^2 t_{sd}\left[\cosh\sqrt{st_{sd}}\,\sinh\sqrt{(s+k_m)t_{ed}} + \left(K_{sd}h_s\sqrt{st_{ed}}\,/\,K_{ed}h_e\sqrt{st_{ed}}\right)\sinh\sqrt{st_{sd}}\,\cosh\sqrt{(s+k_m)t_{ed}}\right]} \tag{2.55}$$