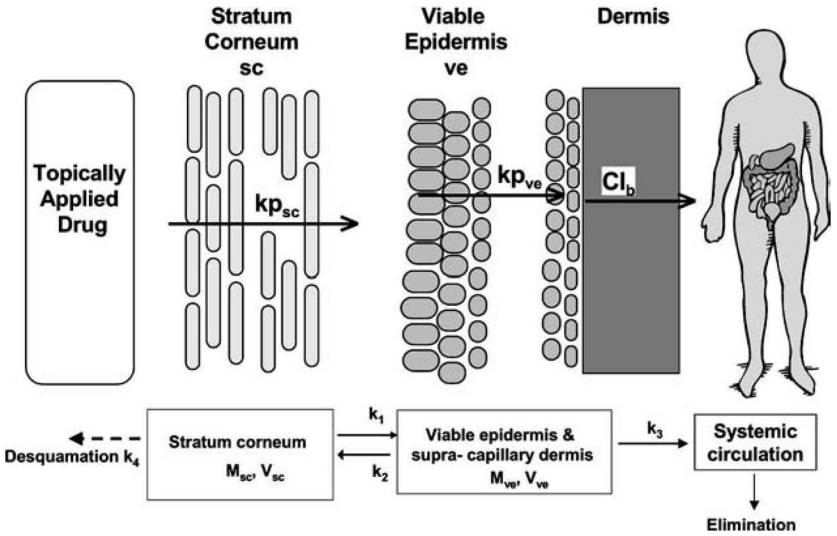


**FIGURE 4.6** One-compartmental model representations of stratum corneum and viable avascular tissues used to examine the stratum corneum reservoir effect.

The model differential equations are as follows:

$$\frac{dM_{sc}}{dt} = k_2 M_{ve} - k_1 M_{sc}, \frac{dM_{ve}}{dt} = k_1 M_{sc} - (k_2 + k_3) M_{ve} \tag{4.2}$$

where $M_{ve}$ is the amount in the viable tissue and $M_{sc}$ is the amount of solute in the stratum corneum. Sink conditions are defined by $k_3 >> k_2, k_1$; for this special case $M_{ve}$ is relatively small, and we apply an approximation of $M_{ve}$ 0 and $dM_{ve}/dt$ 0 in Equation (4.2) to give:

$$M_{ve} \approx M_{sc} \frac{k_1}{k_2 + k_3} \tag{4.3}$$

Equation (4.2) defines the amount of solute in the viable tissue, as well as the concentration $C_{ve}$, since $C_{ve} = M_{ve}/V_{ve}$. It is evident from Equation (4.3) that an increase in stratum corneum permeability, as evident by an increase in $k_1$ from, for instance, reocclusion, will increase $M_{ve}$ and therefore, in the case of steroids, the extent of vasoconstriction. The more $k_1$ is increased, the greater $M_{ve}$ is. It should also be noted that the amount remaining in the stratum corneum is expressed in this case as:

$$M_{sc} \approx M_r \exp(-k_1 t) \tag{4.4}$$

where $M_r$ is the amount of drug in the stratum corneum reservoir after loading. Hence, an increase in the stratum corneum permeability rate constant $k_1$ will deplete the amount in the reservoir $M_{sc}$ more rapidly. Also, Equation (4.4) states that the amount in the reservoir $M_{sc}$ is depleting at a rate defined by a rate constant $k_1$ so that at a sufficient time and in the absence of no further application, the reservoir will be sufficiently depleted so that it no longer exists. Figure 4.7 shows an illustration of these concepts for corticosterone. It is evident that a twentyfold increase in diffusivity as a consequence of occlusion greatly accelerates steroid loss from the stratum corneum reservoir and increases the viable epidermal concentration with the consequential effect of likely vasoconstriction.

In general, the reservoir effect will be observed when a stratum corneum permeability enhancer is applied and causes an increase in the release of the solute from the stratum corneum. In the case of corticosteroids, the most commonly applied enhancer used to demonstrate the reservoir effect is