



**FIGURE 2.18** A pharmacokinetic model for local deep tissue penetration after topical application. The main symbols are  $Q$ , blood flow;  $C$ , concentration;  $V$ , volume; and  $CL$ , clearance as they relate to the various tissues and the rest of the body. (Adapted from (A) Reference 98 and (B) Reference 105.)

define deep tissue penetration of dermally applied solutes (Figure 2.18A). Roberts and Cross [102] have suggested that the half-life for elimination of a solute in such tissues is dependent not only on tissue blood flow ( $Q_p$ ) but also on the fraction unbound of solute in the tissue ( $f_{u_T}$ ) and blood ( $f_{u_B}$ ), as well as the apparent unbound volume of distribution ( $V_T$ ):

$$t_{1/2} \approx \frac{0.693 f_{u_B} V_T}{f_{u_T} Q_p} \tag{2.89}$$