that, in principle, the amounts of formulated drug applied can reasonably reflect the usage situation. In addition, the cell can be left open to the ambient conditions of the laboratory for the formulation to undergo the same compositional changes as occur clinically. Another advantage to the finite dose method is that phenomena of topical drug delivery, such as skin penetration enhancement, can be realistically evaluated.

To test the usefulness of the finite-dose diffusion cell, Franz (54,55) studied the in vitro diffusion of various compounds from thin solid deposits through human skin. Data obtained were compared with previously obtained in vivo data. Good agreement was reported between the two sets of data. Mollgaard and Hoelgaard, with the use of finite-dose diffusion cells, investigated the diffusion of estradiol from 21 different vehicles through excised human abdominal skin (58). It was concluded that, for the vehicles chosen, drug permeability was most influenced by the direct vehicle effect on the barrier. The degree to which the thermodynamic activity of the drug in the vehicle influenced the course of events was relatively minimal. One questionable aspect of this work was that the baseline diffusion rate of estradiol through the skin was measured from a solid drug deposit, a great departure from the situation in which the drug is in solution in the vehicle. This certainly affects the quantitative interpretations of the studies.

Finite-dose diffusion cells have often been used incorrectly to assess drug delivery, in that formulations have been applied so thickly that diffusion occurs from an infinite slab, changing the whole kinetics of the drug transport process. This basic flaw is evident in several studies (59,60–63).

B. Role of Thermodynamic Activity in Topical Drug Delivery

Important conceptual work concerning the role of topical vehicles in the delivery of drugs through the skin was pioneered by Poulsen, Ostrenga, and others (25,26,53,64). These studies focused on the role of the drug's thermodynamic activity in the overall diffusional flux through the skin. The first of these studies dealt with the effect that the drug's thermodynamic activity has on its release rate from the vehicle (24). The work was based on T. Higuchi's theoretical supposition that the steady-state diffusion of a drug dissolved in a vehicle through the skin can be represented by

$$\frac{dM_t}{dt} = A\,K\,Cv\left[\frac{D_{sc}}{h_{sc}}\right] \qquad [27]$$

and