from concentration/distance profiles. A glass cylinder containing a hydrocortisone–liquid crystal solution was brought into contact with a cylinder of plain liquid crystal. Diffusion was allowed to proceed for several days, and the cylinders were then separated. The liquid crystal was pressed from the cylinders, scraped off, and weighed. Each liquid crystal segment was assayed for hydrocortisone, and the data obtained was used to calculate the diffusion coefficient. The following equation was employed in the calculations:

$$D = \frac{x^2}{4t}\left[\frac{1}{\text{erf}^{-1}\left[1 - \frac{2C}{C_0}\right]}\right]^2 \qquad [26]$$

where x is the distance along the diffusion axis, t is time, C is the concentration of drug at x, and C_0 is the initial concentration of drug in the gel.

IV. DIFFUSION STUDIES INVOLVING SKIN

A. In Vitro Studies

A frequently employed technique to test the relative permeability of topical drugs involves the in vitro use of excised skin mounted in diffusion chambers. Historically, the method used most often is one in which skin is mounted as a barrier between two stirred, fluid-filled chambers. The donor chamber is filled with a drug solution with samples withdrawn from the receptor as a function of time. Typically, a steady-state or quasi–steady-state condition arises in this diffusional situation, because generally there is an inappreciable alteration of the concentration differential existing between donor and receiver chambers over the course of the experiment. This method has been used frequently to systematically study mechanisms of skin permeability (49–52). Poulsen et al. utilized infinite dosing in the development of several topical formulations (25,26,53). One must continually remember, however, that this type of diffusion cell experiment has little in common with the delivery of drugs from topical applications and is used to get mass transfer coefficients for membranes.

To more adequately depict true clinical situations, so-called finite-dose diffusion cells have been used (54,55–57). A membrane, typically skin, is mounted vertically in the diffusion cell, a small amount of formulation is applied to the membrane, and samples are withdrawn from a stirred receiver compartment beneath the membrane (skin) as a function of time. An advantage of this method is