in the local tissues beneath the applications. It was found that maximum bioavailability was obtained from the gel system in which just enough propylene glycol was present to completely solubilize the drug, a result totally consistent with the in vitro release studies. Similar results were obtained when fluocinonide was incorporated into various creams and ointments (54).

Along these same lines, in a study investigating the diffusion of tritiated water from a wide range of polar solvents, the absorption rate of water through human epidermis was proportional to the thermodynamic activity of water in a particular solvent (65). Barry et al. (18) correlated the thermodynamic activity of benzyl alcohol vapor with the diffusional flux of the vapor through human abdominal skin. These experiments were done in such a way that the vehicle was not in contact with the skin, thus ruling out the possibility of any direct vehicle–skin interactions. In an interesting practical application of the finite-dose method, Bronaugh et al. (60) studied the absorption of *n*-nitrosodiethanolamine through excised human skin. This compound is an impurity, believed to be a carcinogen, found in many cosmetic products. It was found that the permeability of *n*-nitrosodiethanolamine increased with an increase in the stratum corneum/vehicle partition coefficient of the agent. In another study, Turi et al. studied the permeation of diflorasone diacetate through hairless mouse skin from various vehicle formulations (59). It was observed that the permeation rate increased with the degree of solubilization up to a point, and then decreased. This observation is because, at maximum permeability, the vehicle exactly dissolves all of the drug in the formulation. Any further increase in drug solubilization results in a decrease in the partition coefficient (but no further increase in the drug's vehicle concentration). This decrease in the thermodynamic activity of the drug results in a decrease in its permeability. Sloan et al. (62,63; see Chap. 13) have compared the experimental flux of drugs through skin with theoretical predictions obtained through the use of solubility parameters. Studies of this type are significant in that they illustrate the ways in which theoretical concepts can be applied to the development of topical drug products. However, experimental conditions used in these studies generally fail to approximate the clinical situation.

C. In Vivo Studies

When all is considered, most topical products on the market have been developed using more clinical research strategies than bench-top ones. In vivo assay methods have played an important role in the development of many important topical products. Some of these studies have involved the use of animal models; however, the pres-