

ent discussion is limited to studies involving human subjects. The *in vivo* study of the penetration kinetics of drugs has often involved the detection of some local biological response that the drug elicits upon penetration into the skin. Examples of responses that have been utilized include vasodilation, vasoconstriction, keratinization, epidermal proliferation, and changes in blood pressure. In an early study that recognized the importance of standardizing the amount of drug placed onto the skin, Barrett et al. (52) studied the relative erythema produced by methyl nicotinate when incorporated into various vehicles. What is interesting about this study is that it involved the application of a discrete disk of vehicle of known thickness to the forearms of human volunteers, perhaps the first time that the importance of applying a standard amount (and thickness) of vehicle was recognized. Other *in vivo* techniques involve the analysis of blood or serum levels of drugs absorbed through the skin or the amounts of drugs excreted in the urine. Urinary analysis, in particular, often has been used by Feldman and Maibach to study percutaneous absorption in human subjects (66-70).

Perhaps the most well-refined of all biological assays used to develop and assess dermatological formulations are topical corticosteroid bioassays. In some instances, an inflammatory stimulus is applied to the skin, which is immediately followed by the administration of the steroid. The anti-inflammatory response is then graded. Using a method involving the application of croton oil and kerosene to induce pustules or blisters in humans, Kaidby and Kligman (71) obtained a rank order of corticosteroid activity that correlated well with the relative clinical efficacies of the drugs. Similar studies using irritants such as mustard oil and nitric acid (72), tetrahydrofurfuryl alcohol (73), and histamine (74) have been used to test corticosteroid activity. The fact that certain steroids have the ability to constrict local vasculature and turn the site of application pale has often been utilized to study both the relative potencies of steroids, as well as the ability of vehicles to deliver steroids topically. McKenzie and Stoughton (75) discovered that treating psoriasis with steroids under plastic wrap blanched the lesion as well as normal skin. This observation was used to develop a test to rank commercially available steroids in order of potency (76). This method was adopted by Sarany et al. (77) to measure the efficacy of several topical steroids from various vehicles. A method of application that had been previously employed by this group (78) was used in this study. Subsequently, Woodford and Barry (79), among others (16,26,53), have used the blanching test to compare topical steroid formulations.