



Figure 1.2 Effect of thickness on cutaneous flux.

the dose-response curve. Such response is easily observed in the effect of topically applied nonsteroidal anti-inflammatory agents on guinea pigs irradiated with ultraviolet light. The blanching of the erythema can reach a maximum, after which higher concentrations provide no further benefit. Human skin is a much greater barrier and, thus, enhanced penetration is of greater value for human skin applications.

Penetration enhancers can be of great value, and formulations including enhancers should generally be prepared as an option to be evaluated in the *in vivo* system. Enhancers can be categorized conveniently in terms of the type of drug to be delivered. For polar molecules, surface active agents (5,6) are very effective enhancers. For lipophilic molecules, dimethyl sulfoxide (7,8) is the classic enhancer, but other agents such as laurocapram (Azone; 9) and polar lipids (10) are very effective. A simple model for viewing the effects of enhancers on skin is to regard the barrier as consisting of two parallel pathways. The polar pathway is thought to be hydrated protein that is quite sensitive to conformational changes induced by surfactants, heat, and the like. A marked contrast between the effects of surfactants on polar versus nonpolar molecules serves to illustrate this point (6). Enhancers for the nonpolar pathway are thought to fluidize the lipids (11). This concept is quite reasonable