

## VI. INTERACTIONS BETWEEN SKIN SURFACE LIPIDS AND TOPICAL FORMULATIONS

Research that is concerned with the interaction of topical agents and skin surface lipids can be divided into two major areas. The first is the research that is concerned with targeting sebum-rich zones of the skin (e.g., hair follicles and sebaceous glands). This is of obvious importance to acne formulations. The second is research concerned with structural changes that occur in the topical vehicle after mixing with skin surface lipid. This area is most important when formulating topical agents that will be used on lipid-rich regions of the body, such as the forehead or scalp.

The initial observation that it is possible to "target" delivery of drug substances to the hair follicle appears to have been made by investigators at Unilever (38). Their work noted that if a vehicle with low polarity (i.e., matching the polarity of sebum) and low viscosity was used, greater amounts of drug could be detected near the base of the hair follicle. Further work in our laboratories (Hatzenbuhler, unpublished results) has demonstrated that this appears true, even for drug molecules that are inherently too polar to be readily soluble in sebum. Thus, for localized delivery into the region of the hair follicle, sebum appears to present an important barrier, somewhat analogous to that of the stratum corneum barrier (although structurally totally different) across the remainder of the skin. Importantly, the much greater surface area of the stratum corneum makes this route of delivery generally dominant for the systemic delivery of topically applied drugs (39). However, this does not negate the foregoing observations for local delivery to sebum-rich regions such as the hair follicle.

The technique most widely used for the measurement of local drug distributions in tissue is autoradiography; a method that uses radiolabeled drug to measure the concentration of drug throughout thin sections (typically only a few microns thick) of the tissue. The sectioning process has been described as highly technique-dependent for any type of tissue, and it is particularly difficult for the study of skin tissue. Thus, one should carefully reproduce results before making final judgment on their validity. Classic methodology in this technique is provided in Ref. 40.

An alternative method to autoradiography, which can also be used to specifically measure the amount of drug delivered into sebum-rich regions, has been proposed by Elias (41). This technique uses different solvents to differentially extract sebum, rather than the lipids of skin surface origin. By comparing the relative amounts of drug present in extracts of skin surface lipids with extracts of