from the skin, which increases the hydration of the stratum corneum, and the corneocytes become less compact while the inter-corneocyte gaps become wider. These changes increase the stratum corneum permeability, which can promote drug penetration (51). SLNs and NLCs differ in the extent of occlusion which they provide, i.e., SLNs have a higher occlusion property at similar lipid concentrations (49, 52).

Dermal and transdermal drug delivery systems have a high level of interest; in practice, skin is not readily breached in the therapeutic level because of barrier resistance. Various approaches have been employed to enhance absorption. Occlusion, perhaps due to its simplicity and convenience, has been extensively adopted to increase absorption. This chapter focuses on the effect of occlusion on percutaneous absorption and summarizes related details. Table 14.1 summarizes the brief data of the effect of occlusion on percutaneous absorption.

14.2 PERCUTANEOUS ABSORPTION IN VITRO

Gummer and Maibach (30) examined the penetration of methanol and ethanol through excised, full-thickness, guinea pig skin in vitro at varying volumes and under a variety of occlusive conditions over a period of 19 hours. Neither compound showed an increase in penetration with increasing dose volume. But occlusion significantly enhanced ($p < 0.01$) penetration of both when compared to non-occluded skin. The nature of the occlusive material significantly influenced the penetrated amounts of both compounds, as well as the profiles of the amount penetrating per hour.

Hotchkiss et al. (31) evaluated absorption of model compounds nicotinic acid, phenol, and benzoic acid and the herbicide triclopyr butoxyethyl ester (triclopyr BEE) with in vitro flow-through diffusion cells using rat and human skin. After application, the skin surface was either nonoccluded or covered with Teflon caps as an occlusion device. The absorption of each compound across the skin and into the receptor fluid at 72 hours was calculated. Occlusion significantly ($p < 0.05$) enhanced absorption of the model compounds, but varied with the compound and the skin (rat or human) used. They observed the effect of vehicle and occlusion on the in vitro percutaneous absorption of [methylene-^{14}C]-benzyl acetate (1.7 to 16.6 mg/cm^2) in diffusion cells using full-thickness skin from male Fischer 344 rats (32). When benzyl acetate in ethanol was applied to the skin and occluded with Parafilm, the extent of absorption at 48 hours was not significantly different from nonoccluded skin, but at 6 hours, as the ethanol content of the application mixture was increased, the absorption of benzyl acetate through occluded skin was enhanced proportionally ($r = 0.99$). With phenylethanol as a vehicle, the extent of the benzyl acetate absorption through occluded skin at 48 hours was significantly ($p < 0.05$) enhanced compared with nonoccluded skin, but this did not correlate with the proportion of phenylethanol in the application mixture. With dimethyl sulfoxide as a vehicle, the extent of benzyl acetate absorption through occluded skin at 48 hours was enhanced ($p < 0.05$) compared with nonoccluded skin; when dimethyl sulfoxide content of the application mixture was increased, the absorption of benzyl acetate was enhanced proportionally. The researchers concluded that occlusion often significantly enhanced absorption, but the effect varied with time and vehicle.

Cross and Roberts (53) confirmed that the occlusion effect on drug penetration through the skin strongly depends on the vehicle used. They evaluated in vitro human epidermal penetration of a mixture of paraben ester preservatives from a commercially available test ointment and two commonly employed solvent vehicles (acetone and ethanol), together with the effect of occlusion. Parabens were applied in finite doses and occlusion was achieved by the placement of a piece of high-density polyethylene over the application site immediately after dosing (53). There was a significant difference in the epidermal flux of paraben esters from each of the vehicles following occlusion. Increases of drug flux were observed for acetone and ethanol vehicles, while a decrease was seen following occlusive application of the ointment formulation. This decrease in flux appeared to be a result of a significant decrease in the epidermal partitioning of the esters following occlusion of the ointment, while the increased flux of parabens from solvents resulted from an increase in the epidermal diffusivity of parabens following occlusion of the solvent vehicles (53).