Roper et al. (33) tested the absorption of 2-phenoxyethanol applied in methanol through nonoccluded rat and human skin in vitro in two diffusion cell systems over 24 hours. 2-Phenoxyethanol was lost by evaporation with both nonoccluded cells, but occlusion of the static cell reduced evaporation and increased total absorption to 98.8 ± 7.0%.

El Maghraby et al. (54) investigated the transdermal delivery of progesterone from microemulsions (MEs) under occlusive and open application. This study tested an ME formulation containing oleic acid, Tween 80, propylene glycol, and water. The ME system was used neat or with ethanol (20% or 40%) as a volatile co-surfactant. Results of this study indicated that ME formulations enhanced progesterone transdermal flux compared to the saturated drug solution in 14% aqueous propylene glycol (control). Ethanol-containing ME (EME) was more effective than the ethanol-free system (EFME), with the flux increasing upon increasing the ethanol concentration in the ME (54). Occlusive application of 20% EME increased the transdermal flux by 5.7-fold compared to the control and by 2.3-fold compared to the EFM. Occlusive application of 40% EME further increased the transdermal progesterone flux, with the values being 9-fold compared to the control and 3.7-fold compared to EFME. Open application of EFME produced a minor decrease in drug flux compared to occlusive application. For EME, open application significantly reduced the flux by 26% to 28% compared to occlusive application of the same formulation, indicating the importance of occlusion on increasing the drug flux. However, the flux of EME when using open application remained significantly higher than that obtained with EFME regardless if occlusive or open application of EFME was used. This proposed the importance of supersaturation with the contribution of ethanol in the achieved skin penetration enhancement. To confirm this, the authors evaluated the transdermal delivery of progesterone from 40% ethanol in water (ETW) under occlusive and open application. The sum of fluxes obtained from ETW and EFME was lower than that obtained from EME under both application conditions. It was concluded that supersaturation played an important role in enhanced transdermal drug delivery and also occlusion. The authors introduced ME formulations containing volatile components as candidates for the formulation of sprays for dermal application (54).

Treffel et al. (28) compared permeation profiles of two molecules with different physicochemical properties under occluded vs. nonoccluded conditions in vitro over a period of 24 hours. Absorption was determined using human abdominal skin in diffusion cells under occluded and nonoccluded conditions. Occlusion increased the permeation of citropten (a lipophilic compound; partition coefficient = 2.17) 1.6 times ($p < 0.05$) greater than the nonoccluded permeation. However, the permeation of caffeine (an amphiphilic compound; partition coefficient = 0.02) did not show significant differences ($p = 0.18$) between occlusive and nonocclusive conditions. They confirmed the view, i.e., occlusion does not necessarily increase the percutaneous absorption of all chemicals (2, 4, 29).

Hafeez et al. (44) investigated the skin penetration of [14C]-formaldehyde and [14C]-salicylic acid in vitro in human skin under nonocclusion as well as under various occlusive time periods (one, four, and eight hours). The radioactivity recovery as percentage of applied dose of [14C]-salicylic acid was significantly higher under occlusion versus nonocclusion in the epidermis, dermis, and receptor fluid after 24 hours. For [14C]-formaldehyde, no significant statistical difference was observed under occlusion versus nonocclusion. The occlusion duration affected the percutaneous penetration of the lipophilic salicylic acid more than the hydrophilic formaldehyde. Further, a strong correlation between occlusion-enhanced penetration and partition coefficients of salicylic acid and formaldehyde was observed (44).

Brooks and Riviere (45) utilized an isolated perfused porcine skin flap (IPPSF) to determine the percutaneous absorption of ^{14}C-labeled phenol versus *p*-nitrophenol (PNP) at two concentrations (4 μg/cm^2 versus 40 μg/cm^2) in two vehicles (acetone versus ethanol) under occluded versus nonoccluded dosing conditions over eight hours Occlusion increased the absorption, penetration into tissues, and total recoveries of phenol when compared to nonoccluded conditions. Absorption and penetration of phenol into tissues were greater with ethanol than with acetone under nonoccluded conditions, but the opposite was observed under occluded conditions. Phenol in acetone