In this study, the phospholipid used was a hydrogenated soy phospholipid, identified as 30% phosphatidylcholine and 70% phosphatidylethanolamine. The preparation was not characterized and identified as liposomes. Other investigators have used freeze-fracture, x-ray diffraction, and phosphorus nuclear magnetic resonance (NMR) techniques to characterize similar lipid mixtures as in a transition phase between the bilayer (lamellar) phase of pure phosphatidylcholine and nonbilayer (reversed hexagonal phase) of pure phosphatidylethanolamine preparations (55). Nishihata's study is unique in that lecithin (phosphatidylcholine) was not the major lipid species, which raises interesting questions about the role of lipid composition and nonbilayer phases in promoting percutaneous absorption.

Phospholipid effects on percutaneous absorption have also been studied in organic solvent vehicles in which liposomes are not present. Kato et al. (56) studied the effects of 1% lecithin (w/v) in propylene glycol on the in vitro percutaneous absorption of bunazosin, theophylline, or isosorbide dinitrate across excised hairless mouse skin. The addition of lecithin increased the amount of drug penetrating in vitro at 24 hr, for all drugs, with the greatest effect for bunazosin (55-fold). Lecithin, at concentrations used in this study, did not change bunazosin solubility in propylene glycol.

The in vivo penetration of bunazosin (about 23 mg/g solvent) dissolved in propylene glycol with 3% lecithin was compared with bunazosin–propylene glycol alone applied to rabbits. In vivo penetration was undetectable in the drug–solvent vehicle, but the addition of 3% lecithin was able to effect significant plasma levels during the 24 hr of observation. Because the formulations used were all saturated solutions of drug (similar thermodynamic activity) and because lecithin did not change bunazosin saturation, the authors propose that the mechanism of lecithin action is by changing the permeability barrier of the skin. This is plausible, but, since the chemical purity of the lecithin was not characterized, it is impossible to separate the action of phosphatidylcholine from that of its degradation products, free fatty acids, and lysophosphatides. These known penetration enhancers would indeed be expected to change the permeability barrier of the skin.

D. Conclusions

The results of many studies may be summarized by the general observations that

1. Liposome binding to some topical surfaces can be mediated by electrostatic interactions.