To overcome the barrier properties of the stratum corneum, attempts have been made to enhance skin permeation using chemical penetration enhancers (Shivakumar and Murthy, 2010). The chemical skin penetration enhancers are known to primarily act by increasing the solubility of the permeant in the stratum corneum or by disrupting the lipid domain of the skin. Considering the limitations of skin penetration enhancers in enhancing the permeation of therapeutic macromolecules, physical enhancement techniques such as sonophoresis, iontophoresis, and electroporation have been explored (Prausnitz, 1999). Sonophoresis enhances the transport of drug molecules through the skin under the influence of ultrasound. Transient cavitation is thought to be the principal mechanism of low-frequency ultrasound that would induce extensive disruption of stratum corneum lipids to enhance drug permeation through the skin. Generally, the enhancement in drug transport was known to increase with the decrease in ultrasound frequency (Meidan and Michniak, 2010). However, the application of ultrasound was known to only reduce the lag time without significantly increasing the drug delivery through the skin (Cullander and Guy, 1992).

Iontophoresis is an electrically mediated technique that promotes the transport of charged ions through the skin under the applied voltage or constant current by electrorepulsion and electro-osmosis (Pliquett and Weaver, 1996). The principal mechanism of iontophoresis is electrorepulsion that involves the enhancement of the permeation of ions through the skin by an electrode bearing the same polarity. Moreover, iontophoresis was found to induce electro-osmosis by promoting bulk transport of solvent along with the ions. Studies in the past indicate that iontophoresis involves electrically mediated transport that happens through aqueous pore pathways withoutalteration in the stratum corneum structure (Dinh et al., 1993). The technique has been explored to enhance the transdermal permeation of several charged permeants, including peptides and oligonucleotides, which otherwise need to be delivered only via the invasive parenteral route (Banga et al., 1999). However, iontophoresis was found to be more efficacious in enhancing the transport of low-molecular-weight ions compared to charged therapeutic macromolecules (Prausnitz, 1999). The technique has been successfully used in clinics for the last couple of decades in dermatology and dentistry for the delivery of several hydrophilic low-molecular-weight therapeutic agents.

45.2 ELECTROPORATION

Electroporation was initially used in molecular biology as a tool for gene transfection in which brief electrical pulses were used to create pores in the cell membranes that would promote the entry of DNA or other macromolecules (Treco and Selden, 1995). The technique was found to be a viable physical strategy to enhance the permeability of human skin that is composed of multilayer intercellular lipids analogous to the cell membrane (Figure 45.1). The technique has been

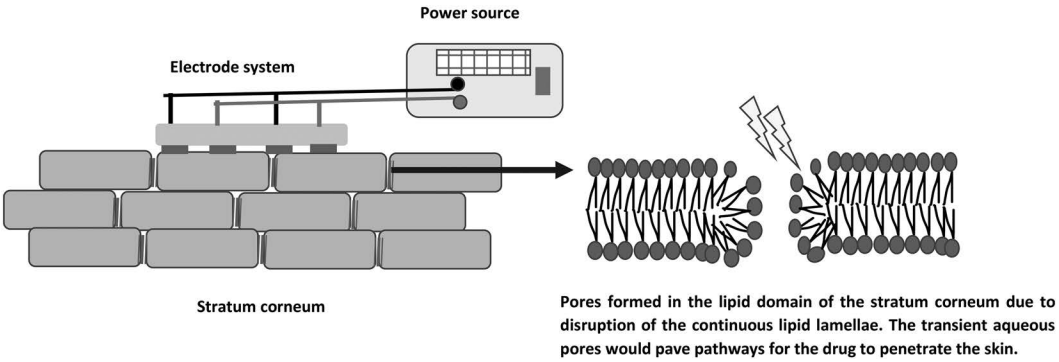

FIGURE 45.1 Illustration of skin electroporation. The skin electrodes are connected to the power source for application of the electrical pulses. The electrical pulses applied on the stratum corneum would lead to formation of pores in the intercellular lipid domains.