Electrophoresis appears to be the main underlying mechanism involved in the transport of ions across highly permeabilized skin by electroporation. In this context, the pKa value of the drug is said to determine the fraction of drug ionized at the prevalent pH and therefore the efficiency of drug transport during electroporation. Even though the transport of the neutral molecules across the skin by passive diffusion occurs during electroporation, the effect is relatively less compared to electrophoresis and passive diffusion. For instance, the transdermal transport of charged ions (protoporphyrin IX) using electrodes bearing similar charge was found to be higher than the uncharged moiety (protoporphyrin IX methyl ester) or ions bearing the opposite charge (Sen et al., 2002a). Skin, known to bear a net negative charge under physiological conditions, is found to be permselective to cations (Vanbever et al., 1998a).

The effect of the partition coefficient of the permeant in passive diffusion has been established (Barry, 2002). Theoretically, as the created new aqueous pathways or electropores are hydrophilic, the transport across the electropores is relatively more efficient for hydrophilic molecules than the lipophilic molecules.

The molecular weight of the permeant is known to influence the transdermal transport by electroporation. Generally, both electrokinetic and passive diffusion mediated transport during electroporation are inversely proportional to the molecular weight (Lombry et al., 2000). Particularly, the electrokinesis depends on the charge-to-mass ratio. The electrophoresis efficiency of a molecule decreases with a decrease in the charge-to-mass ratio. However, electroporation appears to be the only promising physical enhancement technique that has the potential to improve the permeation of therapeutic agents with a molecular mass as high as 40kDa.

The composition of the drug reservoir is generally known to affect drug delivery during electroporation. The drug transport was reported to increase nonlinearly with an increase in the drug concentration during electroporation (Denet et al., 2004). The pH shift induced by the electrodes may require the use of a buffer in the formulation of the drug reservoir. The other ions present in the drug reservoir such as the buffer ions, counterions, and the ions from the skin are known to compete with the permeant during electroporation. Hence, the key factors that need due consideration in the formulation of the drug reservoir would include selection of the appropriate pH and composition of the buffer.

45.5 ADVANTAGES AND LIMITATIONS OF ELECTROPORATION

Transdermal electroporation enables enhanced drug permeation across the skin compared to passive drug transport. The technique has a proven ability to deliver therapeutic macromolecules across the skin (Becker and Kuznetsov, 2008). Due to the dramatic increase in the skin permeability, electroporation-mediated transdermal transport is characterized by a reduced lag time. As the electrical parameters can be precisely controlled, the technique allows tailored preprogrammed drug delivery. Moreover, the technique permits rapid cessation of the drug delivery by the termination of the therapy. Besides, the technique is found to be effective on all cell types and species (Nickoloff, 1995). Above all, the technique is minimally invasive and not sensitizing and therefore considered more patient compliant (Preat and Vanbever, 2003). However, in case the electrical parameters are not optimized, the pores induced may be too large or may fail to close, causing cell damage or rupture (Weaver, 1995). The other drawback of the technique is that the material that moves in and out of the cell during electroporation is nonspecific.

45.6 APPLICATIONS OF ELECTROPORATION

The dramatic and reversible increase in the skin permeability on electroporation has been exploited to enhance the topical and transdermal drug delivery. The technique that is known to temporarily permeabilize the stratum corneum barrier to drug transport is therefore likely