to broaden the drugs that otherwise may be unsuitable for topical or transdermal delivery (Escobar-Chavez et al., 2009). Electroporation has been reported to increase transdermal drug transport and shorten the lag time in the case of several permeants. A variety of therapeutic macromolecules, vaccines, genes, and proteins have been used as substrates for dermal and transdermal delivery.

Skin electroporation is known to increase the transdermal transport of a number of compounds that range from the low-molecular-weight (<1000 Da) therapeutic agents such as doxepin (Sameta et al., 2010), fentanyl (Vanbever et al., 1996a), piroxicam (Murthy et al., 2004), timolol (Denet and Preat, 2003), and terazosin (Sharma et al., 2000) to moderately sized drugs (<10 kDa) that include cyclosporine A (Wang and Krishnan, 1998) and human parathyroid hormone (Medi and Singh, 2003). Electroporation has been reported to enhance the transport of several drug molecules as indicated in Table 45.1.

Most importantly, electroporation is found to be a valuable technique to deliver therapeutic macromolecules like luteinizing hormone–releasing hormone (Riviere et al., 1995) and heparin (Prausnitz et al., 1995). The technique is also capable of enhancing the transdermal delivery of several compounds that range in solubilities from low (buprenorphine [Bose et al., 2001] to high (terazosin) [Sharma et al., 2000]). Electroporation has been employed to deliver drugs bearing a charge like fentanyl (anionic)[Vanbever et al., 1996a] or neutral molecules (mannitol [Vanbever et al., 1998a]). Flux enhancement for neutral and charged permeants that usually ranged in molar mass from 18 to 12,000 Da was found vary from 1 to 4 (Prausnitz, 1999).

TABLE 45.1
Application of Electroporation to Enhance the Transdermal Delivery of Drugs

Sl. No.	Therapeutic Molecule	Electrical Protocol	Skin Model	Log Enhancement Ratio	Reference
1	Alniditan	5 pulses of 200V for 500 ms.	Full-thickness abdominal skin of hairless rats	2	Jadoul et al., 1998
2	Atenolol	10 pulses of 400V for 10 ms.	Isolated human stratum corneum	2	Denet et al., 2003
3	Buprenorphine	20 pulses of 500 V for 10 ms	Full-thickness human skin	0	Bose et al., 2001
4	Domperidone	5 pulses of 250V for 700ms	Full-thickness abdominal skin of hairless rats	2	Jadoul et al., 1997
5	Fentanyl	Exponential decaying pulses 5 pulses of 150V for 300ms	Full-thickness abdominal skin of hairless rats	2	Vanbever et al., 1996a,b
6	Methotrexate	180 pulses of 150 V, 0.2 ms at 1 Hz	*In vivo* studies in mice	1	Wong et al., 2006
7	Metoprolol	5 pulses of 620 ms increased from 250 V	Abdominal hairless rat skin	3	Vanbever and Preat, 1995
8	Nalbuphine	20 pulses 300 V of 200 ms	Nude mouse skin	1	Huang et al., 2005
9	Sodium nonivamide	20 pulses 300 V of 200 ms	Nude mouse skin	1	Fang et al., 2002
10	Tetracaine HCl	400 pulses 130 V for 0.4 ms	Full-thickness rat abdominal skin	1	Hu et al., 2000
11	Terazosin hydrochloride	5 pulses of 88 V for 40 ms.	Full-thickness hairless rat skin	1	Sharma et al., 2000
12	Timolol	10 pulses of 400V for 10 ms.	Isolated human stratum corneum	1	Denet et al., 2003
13	5 Fluorouracil	20 pulses of 300V for 200ms	Nude mouse skin	2	Fang et al., 2004