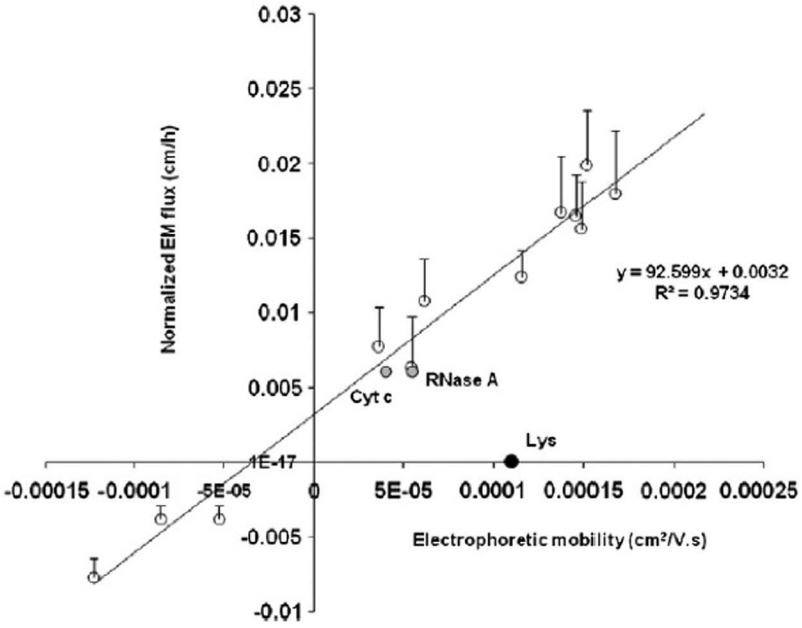

FIGURE 46.5 Correlation between normalized EM flux (J_{norm}-EM, cm/h) and electrophoretic mobility (ui, $cm^2/V{\cdot}s$) for a series of small molecules, dipeptides, Cyt c and RNase A. The flux of lysozyme (0.7 mM) is much lower than that expected based on its electrophoretic mobility (J_{norm}-EM = 92.599 ui + 0.003, r^2 = 0.97). This indicates that electrophoretic mobility alone is not sufficient to predict iontophoretic permeation. (Reproduced with permission from Dubey and Kalia 2014.)

structure of proteins can facilitate interactions with cutaneous transport pathways. As previously discussed, localized charge centers may be inconvenient even for the transport of small molecules (Santer et al. 2018).

As mentioned before, iontophoresis was clinically first used to provide a fast-burst release enabling therapeutic drug concentrations to be reached more quickly and hence reducing the time required for the onset of pharmacological action. Still, other features of iontophoresis might be even more relevant in distinguishing it from other technologies for permeation enhancement. One such aspect is the complete external control of delivery kinetics, easily achieved for delivery of molecules that have an insignificant passive permeability. In a delimited area, modulating current parameters, i.e., duration, intensity, and profile; permeated amounts; and penetration depths can be controlled. For example, this has been achieved for polypharmacotherapy with the simultaneous delivery of more than one drug (Cazares-Delgadillo et al. 2016). Another equally relevant aspect of controlling delivery kinetics is delivery efficiency. Recent studies have demonstrated that in a situation where EM was the dominant mechanism for delivery (>80%), input parameters could be controlled, achieving remarkable delivery efficiencies, an equally relevant aspect for a transdermal system that may be the decisive factor for the pharmaceutical industry (Kalaria et al. 2018). Co-iontophoresis of pramipexole (PRAM; dopamine agonist) and rasagiline (RAS; MAO-B inhibitor) achieved delivery efficiencies of ~29% and ~25%, respectively, which corresponded to thirty-eightfold and twenty-sevenfold increases over passive diffusion (Kalaria et al. 2018). Linear correlation of skin deposition and permeation with increased current densities is demonstrated in Figure 46.6. Transport and drug delivery efficiencies of both drugs are shown in Table 46.1.