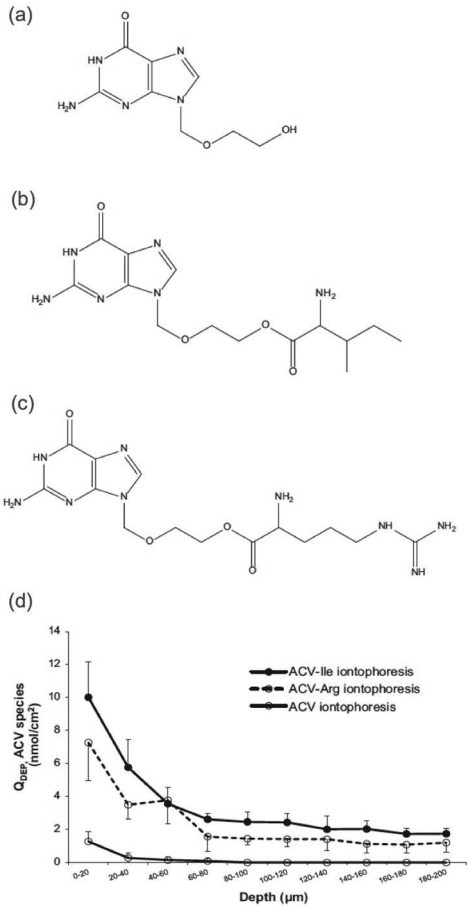

FIGURE 46.3 Chemical structure of (a) ACV, (b) ACV-Ile, and (c) ACVArg. (d) represents cutaneous biodistribution of ACV and ACV-X following iontophoresis of ACV, ACV-Arg, or ACVIle (5 mM) in 10 mM MES buffer (pH 5.5) at 0.25 mA/cm^2 for five minutes as a function of position to a depth of 200 µm. (Mean ± SD; $n = 5$). (Adapted and reproduced with permission from Chen et al. 2016b.)

the propensity of interaction with negative charges in the tissue and hindered electromigration (Figure 46.4). Indeed, the dipole moment, which indicates the localization of the positive charge in TA-Lys, was almost double that of TA-Ala (84 and 40, respectively), and the highest degree of melanin binding was confirmed for TA-Lys (Santer et al. 2018).

46.2.4.4 Nanoencapsulation

Attempts to further increase iontophoretic drug delivery by incorporating drugs in charged nanoparticles have obtained contradictory results (Malinovskaja-Gomez et al. 2016, 2017; Takeuchi et al. 2017). Nanoparticles with average diameters of approximately 100 nm have much larger hydrodynamic sizes than most of the proteins iontophoresed until now (e.g., cytochrome c has a molecular weight of 12.4 kDa and a Stokes radius of 1.7 nm [La Verde et al. 2017]). Such nanoparticles would also be larger than transient "nano-pores" created under the influence of the electric field, which has estimated ~20 nm of pore radii (Aguilella et al. 1994). As would be expected considering such dimensions, no improvement in drug delivery has been