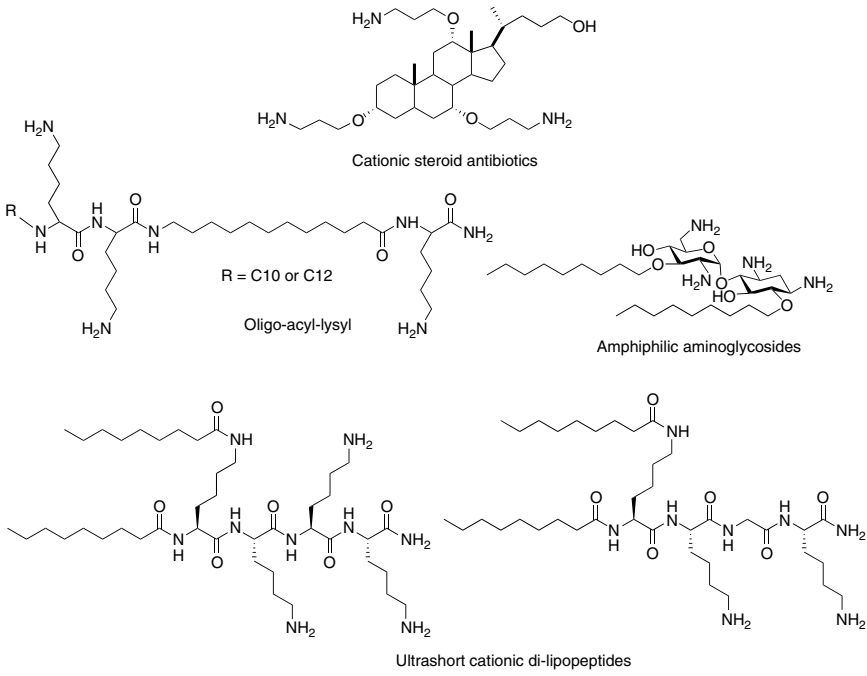

Figure 18.2 Structure of non-polymyxin-based outer membrane permeabilizers.

EPIs (Watkins et al. 2003). Some polybasic aminoglycosides can also induce ototoxicity (Lanvers-Kaminsky et al. 2017). In this case, reducing the number of amino functions can reduce nephro- and ototoxicity (Coleman et al. 2016a).

18.10 Repurposing of Hydrophobic Antibiotics with High Molecular Weight by Enhancing Outer Membrane Permeability Using Polybasic Adjuvants

Antibiotics are taken up into bacterial cells by entropy-driven diffusion across the membranes (passive transport) or by porin-mediated, energy-dependent transport (active transport). GNB possess two cellular membranes with orthogonal penetrating properties. The negatively charged lipopolysaccharide (LPS) core, stabilized by cross-linking to bivalent metal cations on the outer leaflet of the OM, forms an effective impermeable barrier for most hydrophobic agents (Silhavy et al. 2010). Compounds that are able to traverse the OM typically do so slowly, through narrow β-barrel proteins (porins) that are lined with charged amino acids (Denyer and Maillard 2002). Once inside the