permeation are problematic (Huovinen 2001). Many other antibiotic–antibiotic combinations are used in empirical therapy in the clinic including those of tigecycline + gentamicin, tigecycline + colistin, and carbapenem + colistin (Falagas et al. 2014).

18.5 Antibiotic–Adjuvant Combination Approach

Arguably the most successful therapeutic strategy of the twenty-first century, the antibiotic–adjuvant approach has resulted in several drug entities in the market. The paradigm entails the use of bioactive adjuvants that augment the antibiotic efficacy of a primary antibiotic against drug-resistant pathogens. The adjuvant may possess weak to no antibacterial activity on its own but is able to either impede antibiotic resistance mechanisms or potentiate antibiotic action. An adjuvant may be an efflux pump inhibitor to prevent extrusion of drugs, a membrane permeabilizer to increase the number of molecules that penetrate the membrane, or an enzyme inhibitor to prevent degradation of drugs before reaching their targets. Moreover, inhibition of the intrinsic repair pathway of cells by preventing biofilm formation or by assisting in *in vivo* clearance of an infection by the host besides may also be useful to design adjuvants (Mansour et al. 2014; Brown 2015; Gill et al. 2015; Hancock et al. 2016; Wright 2016).

18.6 β-Lactam and β-Lactamase Inhibitor Combination

Augmentin® is a clinically used broad-spectrum antibiotic combination of amoxicillin and clavulanic acid (White et al. 2004). Clavulanic acid is a β-lactamase inhibitor that acts in synchrony with the β-lactam amoxicillin to prevent bacterial growth. These β-lactamase inhibitors, such as clavulanic acid, block the function of β-lactamases or β-lactam-hydrolyzing enzymes by forming an irreversible bond with the enzyme's functional/reactive site. Clavulanic acid by itself possesses poor intrinsic activity against pathogens, but it efficiently inhibits widespread β-lactamases such as many types of the extended-spectrum β-lactamase (ESBL) family (Drawz and Bonomo 2010). Inhibition of ESBLs is especially important as this group of β-lactamases is promiscuous and is able to hydrolyze penicillins, cephalosporins (first, second, and third generations), and monobactams (such as aztreonam) (Gniadkowski 2001; Paterson and Bonomo 2005). Augmentin was first introduced in 1981 by GlaxoSmithKline and continues its clinical usefulness even today (Ball 2007; Geddes et al. 2007). Unfortunately, their use is compromised by the global spread of bacterial