In addition, Table 20.1 includes examples of natural AMPs that may exert an anti-biofilm activity.

Although numerous studies claim the potent anti-biofilm activity of natural AMPs, even in the case of biophimes formed by multiresistant pathogens, there are some limitations to their future clinical use, such as high production costs, high toxicity to mammalian cells, immunomodulatory effects undesirable, and rapid degradation by proteases (Fjell et al. 2011; Strempel et al. 2015). Therefore, efforts are required for the development of synthetic AMP anti-biofilm with improved properties (Strempel et al. 2015).

20.3.1.1 Synthetic Anti-Biofilm Peptides

Synthetic anti-biofilm peptides can be defined as molecules developed through *in cerebro* rational design methods, for example, physicochemical methods and methods based on a model sequence, or by computer-assisted design methods – evolutionary methods and *de novo* methods – (Diller et al. 2015) that have a broad spectrum of activity and are indicated as a favorable alternative to conventional antimicrobials for the treatment of biofilm infections (Jorge et al. 2012; Fuente-Núñez et al. 2016; Pletzer and Hancock 2016).

Synthetic AMPs are peptides that resemble natural AMPs in relation to the structure, such as reduced size, presence of cationic amino acids, and a high proportion of hydrophobic residues, but they differ in origin and activity (Hancock and Sahl 2006; Fuente-Núñez et al. 2012). As for the activity, the synthetic AMPs may present anti-biofilm action at concentrations that do not affect planktonic growth, or they may be able to fight only biofilms, thus demonstrating a selective activity (Fuente-Núñez et al. 2012, 2014b).

Another relevant approach involving this type of peptide has been the combination of these molecules with conventional antimicrobials. Given that, synthetic AMPs may enhance the antimicrobial action to prevent biofilm formation and also eradicate mature biofilms (Reffuveille et al. 2014; Fuente-Núñez et al. 2015; Ribeiro et al. 2015). In addition, this approach may decrease the effective concentration of the active molecules and broaden their action spectrum, minimizing the possible toxic side effects and selective pressure in the development of resistance often exercised by monotherapy (Fuente-Núñez et al. 2016; Walkenhorst 2016). Table 20.2 contains synthetic peptides with anti-biofilm activity.

20.3.1.2 Mechanism of Action

Different mechanisms of anti-biofilm activity have been proposed to the AMPs (natural or synthetic) (Batoni et al. 2016b). These molecules are capable of combating biofilms at different stages of formation and maintenance (Figure 20.1) (Segev-Zarko et al. 2015).

Among them, AMPs can prevent biofilm formation by (i) preventing biofilm maturation, targeting the first colonizers on the surface; (ii) inhibiting the