

15.4.3 Remarks on Holins

The small number of studies on the antibacterial activity of holins suggest that they have potential against many pathogenic bacteria, including multidrug-resistant bacteria. The antibacterial properties seem to be related with their characteristic transmembrane domains and hydrophobicity, but further studies need to be carried out to understand their mode of action, especially to understand how these proteins that exert their natural action on biological membranes interact with the cell wall of Gram-positive bacteria that possess peptidoglycan as their external layer.

Activity improvement was shown to be a possible approach that can increase the range of sensitive bacteria, but holin unspecificity can be a drawback to their use as antimicrobials, limiting their application to surface disinfection or foodstuff sterilization. In cases where specificity is required, new strategies have to be designed and can include their fusion with other proteins that specifically bind to the target bacteria. This seems a promising approach since fusions have been shown not to affect the holin activity (White et al. 2011). Proteins with potential to confer specificity to holins include the CBDs of endolysins or phage recognition binding proteins, both from phage origin.

The potential of holins as antimicrobials has been impaired by their hydrophobic, insoluble, and toxic nature making difficult their cloning and expression in high yields that are required for their study. Consequently, exploring all their potential as antimicrobials will depend on the technological advances to solve these issues.

15.5 Final Considerations

The current and serious global crisis of antimicrobial resistance has been caused by incorrect use and abuse of antibiotics leading the humankind to a post-antibiotic era where small injuries or infections may result in death. This is demonstrated by the common appearance of bacterial strains showing resistance to most or even all existing classes of antibiotics, a fact already warned by the WHO.

Driven by this crisis and the difficulty in discovering new antibiotics, research on alternatives has increased considerably, particularly on bacteriophage proteins with antimicrobial activity (mainly endolysins) and their possible applications. Research on this field has undergone a significant acceleration in the last decade. The potential of phage enzymes is so obvious that a recent review on possible alternatives to antibiotics (Czaplewski et al. 2016) pointed phage endolysins as the therapeutics with the greatest potential considering their high clinical impact and high technical feasibility. But the use of phage lytic proteins is not limited to medicine; their antimicrobial potential has also been