Hybrid Molecules with Potential Activity Against Methicillin-resistance *Staphylococcus aureus*-Part III

Infectious diseases caused by Gram-positive and Gram-negative bacteria, especially drug-resistant pathogens, have led to a significantly high rate of death around the world. Methicillin-resistant *Staphylococcus aureus* (MRSA), which has been spread throughout communities since the 1990s, is one of the most common healthcare-associated multidrug-resistant organisms worldwide. Currently, over 60% of *Staphylococcus aureus* (S. aureus) isolates are MRSA, and around 2% of healthy human individuals carry MRSA. MRSA is responsible for several difficult-to-treat infections in human beings, inclusive of skin and soft tissue infections, septicemia, endocarditis, pneumonia, enteritis, meningitis, osteomyelitis and toxic shock syndrome. The high prevalence of MRSA is an important cause of morbidity and mortality in both community and healthcare settings, and challenges the limited options of effective antibiotics. Vancomycin is usually deemed as the last-resort antibiotic for the treatment of MRSA infections, but MRSA isolates with complete resistance to vancomycin have already emerged in recent years. Thus, there is an urgent demand for the development of novel anti-MRSA candidates. Hybrid molecules, obtained by the combination of structural features of two or more different active fragments, are the most popular chemical entities to develop new candidates which have the capacity to modulate multiple targets and counterbalance the side effects. It is conceivable that hybrid molecules have the potential to enhance antibacterial efficiency, overcome drug resistance, reduce side effects and improve pharmacokinetic profiles, therefore immense efforts have been made to develop hybrid molecules as novel anti-MRSA agents. Indeed, a variety of hybrid molecules such as oxazolidinone-tetrazole hybrid tedizolid and oxazolidinone-1,2,3-triazole hybrid radezolid have already been applied in clinical practice or under clinical trials for fighting against drug-resistant pathogens, including MRSA, revealing the potential of hybrid molecules as putative anti-MRSA agents. This special issue will focus on the recent development of hybrid molecules with potential activity against MRSA and demonstrates the rationale behind their design, structure-activity relationships and mechanistic studies.

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