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Opinion

Methicillin Resistant *Staphylococcus aureus* and Antibiotic Resistance

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Antibiotic resistance in important nosocomial infectious pathogens has become the health concern for the world population today. Infact, the widespread use of antibiotic drugs is one of the reasons for this resistance phenomenon and Methicillin Resistant *Staphylococcus aureus* (MRSA) or oxacillin-resistant *Staphylococcus aureus* (ORSA) is one the most common bacterium causing multi drug resistance infections with significant morbidity and mortality. Although, the rates of MRSA infections have been stabilised in certain developed countries, still continue to increase rapidly in many developing regions [1]. Generally, methicillin resistant *Staphylococcus aureus* (MRSA) is resistant to many of the β-lactam antibiotics mainly due to the presence of a 78-kDa cell wall synthesizing enzyme known as penicillin-binding protein (PBP2a), which is basically expressed when the organism acquires the mecA gene set [2]. The PBPs are a group of membrane-bound enzymes, which is revealed to consist of three broad domains namely (a) transmembrane anchor (b) non-penicillin-binding domain and (c) C-terminal transpeptidase domain. Interestingly, the crystal structures of both methicillin susceptible and resistant PBP2a have provided the molecular details describing the mechanism of β–lactam resistance achieved by PBP2a [2]. However, the transpeptidase domain catalyzes the specific cross-links between the peptide side chains of neighbouring glycan strands. It proteolytically removes D-Ala at the C-terminal end of the pentapeptide enabling the formation of a new amide bond between the amino group of the cross bridge and the carbonyl group of D-Ala at position 4, thereby synthesises the cell wall [3]. Thus, it was targeted and despite the broad-spectrum resistance to β-lactams, some newer fifth generation cephalosporins including Ceftaroline and Ceftobiprole have been reported to be successful and effective against MRSA [4,5]. However, the resistance to ceftaroline has already been observed at a low frequency among MRSA [6]. Hence, considering their limitations [7], alternate method of using plant derived compounds (phytochemicals) which posses the capability to act as an inhibitor and stimulate the similar conformational change in PBP2a like Cephalosporin derivatives has now gained importance. Thus, "combination therapy" or "synergistic therapy" against resistant microorganism has opened a new chapter [8,9] and accordingly, medicinally valued flavonoid "Quercetin" in combination with antibiotics are in the forerun and my laboratory has geared up research in this direction [10-14].

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