Membrane biosynthesis gene disruption in methicillin- resistant Staphylococcus aureus (MRSA) as potential mechanism for reducing antibiotic resistance

ABSTRACT

The aim of this study was to evaluate the effectiveness of the membrane biosynthesis gene disruption in MRSA (methicillin resistant Staphylococcus aureus) using sea cucumber extract (SBE). The disruption of membrane biosynthesis gene also known as multiple peptide resistance gene (mprF), would impair the lysylation of cell membrane phosphatiglycerol and thus reduce antibiotic resistance in MRSA. The membrane permeability assay was done to determine the degree of homology of the SBE treated RNA and the resulting translated protein in MRSA. Bacterial cell permeabilization test was performed to confirm the permeabilization effect of SBE on bacterial cell membranes of the MRSA treatments. The effectiveness of SBE on mprF gene disruption was further confirmed using fluorescence microscopy, modified disc diffusion assay, minimal inhibitory concentration and checkerboard method. Up to 35 % of nucleotide changes at RNA level were detected in methicillin-susceptible S. aureus (MSSA) isolates and less than 10 % in MRSA isolates when treated with SBE, each resulted in alterations in the post-translation protein sequence. The fluorescence assay showed the uptake of fluorescence dye by the bacteria cells treated with SBE, indicating rupturing of the bacterial cell MSSA and MRSA membrane barriers. The in-combination treatments between SBE and classical antibiotics against MRSA resulted in improved inhibitory activities. This study illustrated that the use of SBE caused mprF gene disruption to increase MRSA susceptibility towards AMP substances and classical antibiotics. Thus, disruption of mprF gene can be potential means for reducing antibiotic resistant in MRSA.

Keyword: Antibiotic resistance; Membrane biosynthesis; Membrane permeability; Methicillin-resistant Staphylococcus aureus; Multiple peptide resistance genes (mprF) gene; Staphylococcus aureus