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LIPS

Title: Investigating the effect of a tryptophan- and arginine-rich antimicrobial peptide on multidrug-resistant bacteria

Abstract

Multidrug-resistant bacteria (MDR) or superbugs have developed resistance to conventional antibiotics. Antimicrobial resistance (AMR) is increasing at an alarming rate posing a significant threat to healthcare security. AMR is estimated to cause 4.95 million deaths in 2019, and it is predicted that there will be 10 million deaths by 2050, more than cancer, with a $100 trillion economic impact. The scientific community is looking for new types of antibiotics with new mechanisms of action. Antimicrobial peptides (AMPs) are promising candidates as future antibiotics. R_5W_4 is an antimicrobial peptide (AMP) in the family of antimicrobial peptides involved in host defense; it has been shown to inhibit the growth of bacteria, viruses, and fungi. Very few studies have been devoted to this peptide, to understand its mechanism of action. But the topic is still open to debate. The objective is to investigate the interactions of R_5W_4 with three model biological membranes mimicking *Escherichia coli (EC)*, *Staphylococcus aureus (SA)*, and *Bacillus cereus (BC)* membrane bilayers. UV visible, fluorescence, and infrared techniques are employed. The interaction was performed in a wide range of peptide-to-lipid weight ratios. At very low peptide concentration, R_5W_4 shows no specific interaction with the amine, carbonyl, and phosphate groups of SA and BC. However, fluorescence data indicate a blue shift of the wavelength of R5W4 in the presence of SA, and BC, not of EC. These results are confirmed by UV visible data. Taken together, IR and fluorescence data suggest that R_5W_4 inserts into the SA and BC model membranes. IR curve fitting data at very low peptide concentration reveal that R_5W_4 undergoes a lipid-induced conformational transition from helix structure to a sheet-like structure in SA and BC cells and not in EC cells. R_5W_4 may be a good antibiotic candidate against SA and EC. In the future, the antimicrobial activity of R_5W_4 will be determined by measuring its minimum inhibitory concentration (MIC) against these pathogens. To gain insights into its selectivity, its cytotoxic and hemolytic activities will also be evaluated against the human embryonic kidney cell line, HK293, and human red blood cells, respectively.