Design and Development of Antimicrobial Peptides

Kyung-Soo Hahm

Research Center for Proteineous Materials (RCPM), Chosun University, 375 Seosuk-Dong, Dong-Ku, Kwangju 501-759, Korea

Nature including mammals, plants, amphibians and insects produces antimicrobial compounds such as peptides as an innate host-defense mechanism of most living organisms. Using these natural antimicrobial peptides, lots of efforts have been made in order to develop novel antibiotic peptides useful for therapeutics and other purposes.

Cecropin A, Magainin 2, Melittin, PMAP-23, Pep 27 and active peptides derived from proteins such as HP (2-20) were used as model peptides for designing and developing novel synthetic antimicrobial peptides. In order to screen most active peptides, hybrid peptides including CA-MA, CA-ME, HP-MA and analogue peptides were designed and analyzed for their antibacterial, antifungal, antitumor and hemolytic activities.

Novel synthetic antimicrobial peptides were designed by investigating the structure-activity relationship (SAR) of truncated or analogue peptides utilizing CD and NMR spectra analysis.

The mechanism of these antimicrobial peptides was studied by employing fluorescence activated flow cytometry and confocal laser scanning microscopy. The action of these peptides against microbial cell membranes was further examined by investigating the change in membrane dynamics of *C. albicans* using 1,6-diphenyl-1,3,5-hexatriene (DPH) as a membrane probe and by testing the membrane disrupting activity using an artificial liposomal vesicle (PC/PS; 3:1, w/w) and by treating prepared protoplasts of *C. albicans* with the peptides.

The present data suggest that the peptides may exert its antimicrobial activity through the pore formation or detergent-like disruption of cell membranes. CD and NMR spectra analysis showed that all peptides revealed an α-helical conformation in 50% TFE and 30% SDS solution.

From these studies, novel synthetic antimicrobial peptides having potent antibiotic activity with no hemolytic activity were designed and synthesized for industrial applications.