



Application of Peptide Compounds as Anti-Bacterial Agent versus Bacteria

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ABSTRACT

Today, in order to extend shelf life, consumers ask for formulating food with natural preservatives instead of chemical preservatives due to their no harm affections on human. Nisin is peptide produced by Lactic acid bacteria during fermentation with anti-bacterial effects. Nisin has superior properties in comparison with chemical preservatives such as being non-toxic, natural, appropriate stability versus acid and heating. This article reviews Nisin functionality on gram positive bacteria and the mechanism of its action on cell.

Keywords: Nisin, Plasma membrane, Positive Gram

INTRODUCTION

Antibacterial peptides refer to those peptides with different numbers of amino acids and limitation of 100. Regarding the type, origin, size, and structure and activation way. They act against microorganisms vary from bacteria to viruses and etc. Aps categorizes in 4 groups β -sheet, α -helical, loop and extended peptides. Since APs mostly are rich in basic amino acid such as arginine they have a net positive charge. Perhaps may say that first time APs extracted from a basillus strain by which mice were protected against a kind of cocci infectious (1-6). During time, other antibacterial peptides discovered with affection on gram positive and negative bacteria even fungi (2, 7-14). The target organs in which APs are findable varies from type to type, for example frog skin is the source for many of them (3, 15-21).

There are several affections introduced for APs such as direct involvement in immunity, on inflammatory when infections (however antibiotic suffers from the lack of this kind property (4, 5, 22, 23) and so forth (6, 24-27). As we mentioned before α -helix, B-sheet, loop and extended are 4 discovered structures for APs (7, 28-32). In fact mostly aps belongs to one of 4 types, but some belongs to a group with no similarity to mention ones even their active form is when interact with cell walls (8, 33-37). They also may reconform in case of reaction with DNA (9, 38-41).

While APs have the possibility of protecting against pathogens, their use is still a controversial issue due to some toxicity to human (10, 42-46), affection on environment, no competitively/selectively versus some serotypes (11, 47-52). Mostly enzymatic activities are not critical property in classifying APs and they categorize based on the targeted microorganisms for each one.

Antiviral peptides may act in 3 ways including disrupting of envelopes, blocking of receptors, preventing of viral particle entrance in host's cells (12, 52-55). For viral case, APs may not have the ability of competition with glycoproteins in regards with bonding to the cell receptors. An example of antiviral peptides which is extracted from cell rabbits is NP-1 which prohibits HSV-2 (13, 56-58). Antibacterial peptides are the most studied type of APs which cause to change in integrity of the lipid bilayer structure as hydrophobic region (14, 58). In some cases of killing unsuitable microorganism, APs interfere the mechanism of some important pathways (15, 59-61). For example, Drosocin with its 18-20 amino acids with a site for their intracellular interactions. Nisin and Vancomycin prevent synthesizing of cell membrane.

In case of fungi, APs act differently via increasing permeability of plasma membrane (16, 62) or disrupting the cell wall through creation of direct pores in it (17, 63). Due to the presence of different structural types of antifungal peptides, it can not concluded that there is significant correlation between the type of antifungal structure and targeted microorganism even in case of positive and negative charge amino acids in their structures (18, 64-67).

Perhaps may say that magainin is the first antiparasitic peptide to destroy *Paramecium Caudatum* (19, 68). Cathelicidin is another peptide with ability of destroying *Caernohabditis* parasite, Other type of killing mechanism can involve direct destroying of cell membrane (20).

Control of microorganism is one of the most important issues of food preservation so that removing of pathogens commonly is targeted through most researches. Estimated that 6.5-30 million people infect by Food pathogens every year which damage 2.9-6.7 billion USD. Among them %25-55 of costs are due to gram positive bacteria. Regarding the possible resistance versus preservatives, and their incidence in nations, reminds necessity of resistant serotypes detection and inhibiting methods. Preservatives define as substances use in cosmetic, drug and food stuffs in order to protect them against bacteria, yeast, molds and extend their shelf life. Both chemical and natural preservatives are using, but the natural ones are more asked recently due to consumers' changing concepts about chemical preservatives because of being toxic or cancer creating properties. Natural preservatives come from microbes, animals and plants. A group of anti-microbial peptides produced by bacteria named bactericide like Nisin, pediocin etc with anti-bacterial activity used as preservative in foodstuffs. Nisin is one of the bactericide with anti-bacterial activity on gram positive bacteria. Nisin is polypeptide composed of 34 amino acids produced by LAB which introduced by Rogers first time in 1928 as a substance inhibiting *Lactobacillus bulgaricus* growth in industrial cheese. WHO announced Nisin as a preservative in 1969. Some Nisin properties include non-toxicity and good potential of storing, decomposable by digesting enzymes and no change in food flavors. Nisin creates holes in cytoplasmic membrane which causes to destruct cytoplasmic membrane and prevent vital ions gradient through membrane, leakage of ATP and amino acids. Nisin also prevents germination of spores and less affection on gram negative bacteria, molds and viruses. Nisin along with chemical naturals causes to reduce required preservative, sterilization temperature, reduction of thermal processing time, reduction of nutrient loss, and extending shelf life. Today's, Nisin applied in cured meat, alcoholic beverages, milk, cheese and so forth in more than 50 countries. Lactic acid bacteria's bacteriocins inhibit growth of pathogens and food spoiling bacteria.

Nisin which is one the conventional antibiotics is a peptide antibiotic (E 234) (21, 22) which produces by *Lactococcus lactis* and activates versus a wide range of gram positive bacteria (23). Nisin is a heat and acid resistance bacteriocine with anti-bacterial affection on gram positive bacteria including *Listeria Monocytogenes*, *Staph aureus*, and prevent germination of *Clostridium* and *Bacillus* spores as well. Nisin's C terminal connects to cytoplasmic membrane of germinating cells and create holes which allow outflow of Potassium ions, ATP and amino acids (21). Commonly, Nisin is much more active in less pHs while temperature affections on its functionality is controversial (24). Nisin also effects on gram negative bacteria but less than gram positive ones and usually effective in combination of complex agents. Nisin is active in nano molar concentration with no toxic affections on human. Nisin interferes in Synthesizing of Cell wall. Bacteria membrane of *B. subtilis* partially perforates with no immediate death even vital activities of cell continues for 30 min after addition of Nisin. Gradually lengthening of bacteria causes to continuous of inhibitory cover and quick dividing causes to shortening cell. Abnormal morphology close to dividing zone depicts initial place of Nisin affection. Morphological changes are one of the proteins covering of string cells (Mbl) and Min system is dividing inhibitory. Nisin biosynthesis includes modifications after synthesis of peptide substrate translation by ribosome which contains of unusual amino acids such as Lanthionin, dehydroalanin, dehydrobutyrin (23).

Nisin is positive charged peptide able to connect negative charged plasma membrane through electrostatic reaction. The mechanism of anti-bacterial activity of Nisin includes penetration ability to cytoplasmic membrane and interference to bacteria cell wall biosynthesis. Nisin targets lipid II substrate of cell wall & pyrophosphate endcaprynyl, then penetrability of membrane is created after Nisin-lipid II complex forming. This reaction leads to create holes which lose electrostatic potential of membrane along with prevention of vital solution gradients (23). Shal et al studied inhibitory affection of Peptidoglycan during anti-microbial action of lanthionin in natural environment (25). Peptidoglycan is a dynamic system at which attaching of new peptidoglycan biosynthesis and decomposition through autolysis intensely as complementary of each other (23). The last stage of bacteria cell wall biosynthesis creates in out layer of membrane where biosynthesis interference is as the target of several cell wall inhibitory antibiotics.

CONCLUSION

Nisin causes to leak cytoplasmic content resulting in reduction of cross-section of bacteria. Forming of septum continues in presence of Nisin however many anomalies may observe. Cytokines occurs 30 min after adding Nisin which is in contrast with conventional concepts death cell occurring after addition of antibiotic. The main location of Nisin inhibitory is dividing area where peptidoglycan quickly forms. Nisin penetrates to plasma membrane, increases cell division and forms small cells, additionally setting out cell cover forming. Since Nisin lonely unable to prevent the growth of all microorganism and effects just on gram positive bacteria, it must be used with other preservatives.

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