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The Synergistic Antibacterial Activity of Nisin and Lactoferrin Hydrolysates against *Staphylococcus aureus*

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Extended Abstract

Staphylococcus aureus, a facultative Gram-positive coccus, is one of the most common causes of foodborne illness. It is also a critical human pathogen, which causes life-threatening systemic infections such as pneumonia, septicemia, endocarditis, and osteomyelitis (Pan et al., 2002). The abuse of antibiotics has resulted in frequent occurrence of the antibiotics resistant strains. Combining use of two or more of antibacterial agents has been found effective in reducing the occurrence of resistant bacteria (Ejim et al., 2011). Nisin, a 34-residue-long antimicrobial peptide, is the prototype lantibiotic and has been approved by the US Food and Drug Administration (FDA) for use in food products. Nisin is bactericidal against many Gram-positive bacteria by a dual-cidal mechanism: the inhibition of peptidoglycan biosynthesis and membrane pore formation. Lactoferrin (LF), an 80 kDa iron-binding glycoprotein contributing to protect the infant from infectious disease, possesses antimicrobial activity against a large panel of microorganisms by iron sequestration, which deprives the microorganism of this nutrient, thus creating a bacteriostatic effect (Gonzalez-Chavez et al., 2009). Lactoferricin (Lfcin) derived from pepsin-catalyzed LF hydrolysate has been demonstrated a different antimicrobial mechanism from its parent molecule: altering membrane permeability of target cell and allowing the passage of small ions, and resulting in the loss of both the transmembrane electrochemical and pH gradients (Gifford et al., 2005 Murdock, et al., 2010). This research was intended to evaluate the antibacterial activity of nisin co-applied with lactoferrin hydrolysates (LfH), for their potentially synergistic effect and a broad-spectrum antimicrobial activity. The results showed that the optimal antibacterial activity of pepsin-hydrolyzed-lactoferrin could be obtained at 300 minutes. The minimum inhibitory concentration (MIC) of nisin against *Escherichia coli* BCRC 10675, *S. aureus* BCRC10451, *S. aureus* BCRC10780 (SA 780), and methicillin-resistant *S. aureus* 16 (MRSA 16) were > 640, 5, 5, and 5 IU/mL, respectively; the MIC of LfH were 400, 800, > 6400, and > 6400 μg/mL, respectively. The MIC for combination use of nisin / LfH were 5/200, 1.25/100, 1.25/800, and 1.25/800 (IU/mL)/(μg/mL), respectively, where their fractional inhibitory concentration (FIC) were determined: < 0.51, 0.38, < 0.37, <0.37, respectively, all representing synergistic effect. According to the morphological changes of the tested strains observed in scanning electron microscope (SEM), nisin and LfH showed different antibacterial behaviour; besides, combination use of both agents demonstrated a complete lysis of target cells.

Keywords: *Staphylococcus aureus*, synergistic, nisin, lactoferrin hydrolysate, antibacterial activity, antibacterial mechanism

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