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## Bactericidal effect of bovine lactoferricin by D-amino acid substitution against *Escherichia coli* and *Staphylococcus aureus*

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*Escherichia coli* strains are major food-borne pathogens that often cause outbreaks of diarrheal diseases and extra intestinal infections in both animals and humans, also including meningitis, pneumonia, and urinary tract infection in human. Another important resistant bacterial strain *Staphylococcus aureus* is leading cause of infection at numerous sites in the body (including skin, soft tissue, blood and lungs) in both humans and animals. Since antibiotics have the adverse effects in the treatment of pathogen infection, discovery and development of new antimicrobial agents is urgently needed. Lactoferricins have shown a broad-spectrum of antimicrobial activity. In our previous study, Lfcin5 (C3A, R4F, Q7A, M10W, G14A), a new derivative of bovine lactoferricin (LfcinB) 17-33 showed higher activity and lower hemolytic activity than the parent peptide LfcinB17-33. Further experiments aimed to optimize the antimicrobial activity and stability of Lfcin5 via D-amino acid substitution. The minimum inhibitory concentrations (MICs) of D-Lfcin5 against *E. coli* and *S. aureus* were 4 μg/ml, respectively with an 8-fold and 16-fold reduction compared to the parent peptide Lfcin5. In addition, D-Lfcin5 had high stability over a wide pH range of 2.0–10.0 and high thermal stability from 20 to 80 , and remarkable resistance to pepsin and trypsin. To evaluate the protective effect of D-Lfcin5 in the mice model of pathogen infection, the mice were injected with Lfcin5/D-Lfcin5 (5 and 7.5 mg/kg) at 24h prior to challenge with a lethal dose of *E. coli* CVCC1515 and *S. aureus* CVCC546, respectively. The survival rates of mice administered D-Lfcin5 were 37.5%–100%, respectively, which was higher than that of Lfcin5 at the same doses (12.5%–37.5%). The survival rate of mice treated with 5 mg/kg D-Lfcin5 at 24h and 8h before pathogen infection was 100%, whereas the survival rates of mice treated with Lfcin5 were 33.3% and 66.7%, respectively.

### Recent Publications

1. Wang X, Wang X M, Teng D, Mao R Y, Hao Y, et al. (2018) Increased intracellular activity of MP1102 and NZ2114 against *Staphylococcus aureus in vitro* and in vivo. Scientific Reports 8(1):4204.
2. Li Z Z, Wang X, Teng D, Mao R Y, Hao Y, et al. (2018) Improved antibacterial activity of a marine peptide-N2 against intracellular *Salmonella typhimurium* by conjugating with cell-penetrating peptides-bLFcin(6)/Tat(11). European Journal of Medicinal Chemistry 145:263–272.
3. Hao Y, Yang N, Teng D, Wang X M, Mao R Y, et al. (2017) A review of the design and modification of lactoferricins and their derivatives. BioMetals 2:1–11.
4. Hao Y, Yang N, Wang X M, Teng D, Mao R Y, et al. (2017) Killing of *Staphylococcus aureus* and *Salmonella enteritidis* and neutralization of lipopolysaccharide by 17-residue bovine lactoferricins: improved activity of Trp/Ala-containing molecules. Scientific Reports 7:44278.
5. Wang X, Wang X M, Hao Y, Teng D and Wang J H (2017) Research and development on lactoferrin and its derivatives in China from 2011–2015. Biochemistry and Cell Biology 95:162–170.

### Biography

Hao Ya received her Master's Degree from Anhui Agricultural University in 2013. Now she is the Research Assistant of innovative team of alternatives to antibiotics, Gene Engineering Laboratory, Feed Research Institute, Chinese Academy of Agricultural Sciences, and has participated in two national natural science funds and was a Winner of Beijing S&T Award, 1st class (2017). She is mainly engaged in the research of antimicrobial peptide for feed use, and is responsible for studying of the molecular design, modification and antibacterial mechanism of bovine lactoferricin peptides (LfcinBs). Also, she has been trying to establish an enzyme-linked immunosorbent assay method for antimicrobial peptides.

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