

## **Probiotic Lactobacillus GG Secretes Small Peptides That Inhibit the Growth of Antibiotic-Resistant Bacteria**

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**Background and Objective:** We have previously reported that several small peptides isolated from lactobacillus GG conditional media exert both gram-negative and gram-positive bactericidal activity. Among them, peptide NPSRQERR, VHTAPK and PDENK have more activities than others. This research was aimed at establishing whether these peptides exert their bactericidal effect also on microorganisms that have developed multiple antibiotic resistance.

**Method:** Peptides were synthesized, purified, identified and dissolved in different media. Lactobacillus GG Conditional Media (LGGCM) ( $19.7 \times 10^{12}$  CFU/ML) was used as positive control, while media only was used as negative control. Antibacterial activity was monitored by measuring  $A_{600}$  of the culture after 3 h incubation.

**Results:** Peptides NPSRQERR(2.76mM), VHTAPK(3.25mM) and PDENK(3.31mM) all inhibit Kanamycine-resistant *E. coli*( $2.6 \times 10^{13}$  CFU/ML) growth by 43.75%, 29.45% and 68.54%, respectively. The same peptides tested at the same concentrations were also able to inhibit tetracycline-resistant *E. coli* ( $8.7 \times 10^{13}$ CFU/ML) growth by 69.08%, 48.53% and 81.4% respectively. Finally, methicillin-resistant *Staphylococcus aureus* (MRSA)( $2.89 \times 10^{14}$  CFU/ML) growth can be inhibited by NPSEQERR(6.9mM), VHTAPK(9.0mM) and PDENK(9.0mM) by 20.4%, 14.76% and 34.93% respectively. Interestingly, peptide NPSRQERR has 2 positive charges that dictate its anti-bacterial activity. Indeed, modification of the peptide by decreasing its positive charge from 2 to 0 caused a drop in its anti-bacterial activity by 12%, while the addition of an extra positive charge caused an increase of the anti-bacterial activity by 16.5%.

**Conclusions:** Lactobacillus GG peptides NPSRQERR, VHTAPK and PDENK exert an anti-bacterial activity not only on gram-negative and gram-positive bacteria growth, but also on strains with multi-antibiotic resistance. These results suggest that probiotics or their derivative peptides can be effective alternative treatments for infections caused by multi-drug resistant bacteria.