Therapeutic Lantibiotic Delivery and Functionalized Antimicrobial Surfaces via Thermostable, Degradation-Resistant Nisin-Adsorbed Endospores: Engineering an Alternative to Antibiotics and Pesticides

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Antimicrobial peptides (APs) produced by a large number of microorganisms, plants, and animals hold considerable potential as broad-spectrum alternatives to traditional antibiotics, pesticides, and therapeutics. However, their clinical and industrial application is limited by their poor chemical stability, low specificity, and susceptibility to environmental degradation. This study sought to improve the stability, delivery, and application of the model AP nisin by exploiting the phenomenal physiological stability of bacterial endospores. It was hypothesized that nisin adsorbed to the glycoprotein surface matrix of B. subtilis endospores would show markedly improved chemical stability, shelf life, and resistance to protease degradation. Extensive wet lab testing including spectrophotometric BCA protein assays, broth microdilutions, and protease digests were used to characterize nisin-endospore adsorption kinetics, shelf-life, and bactericidal activity. After liquid storage for 2 weeks at 20°C, nisin-adsorbed endospores retained 80% (pH 7.0) or 40% (pH 10.0) antimicrobial activity, while free nisin lost all activity after one week. Following a 1-hour pepsin digest, nisin-adsorbed endospores retained 65% of antimicrobial activity while free nisin retained only 7%. This suggests that endospore delivery allows therapeutic proteins to be administered orally instead of intravenously and stored under non-ideal conditions using a cheap, environmentally-friendly, biocompatible carrier. Future applications to be tested include: functionalization of crops, clothing, and other surfaces to mitigate microbial growth; targeting APs to tissues and organisms, such as insects; and improved penetration of biofilms. This is the first study reporting the use of endospores to stabilize APs.