Quercetin encapsulated in zein/chitosan nanoparticles as an antibacterial therapeutic strategy against methicillin-resistant Staphylococcus aureus strains.

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Infectious diseases caused by bacteria continue to represent a critical challenge for public health, aggravated by increasing resistance to conventional treatments. Quercetin (QUER), a broad-spectrum natural flavonoid, shows promise for the treatment of infections due to its antimicrobial, anti-inflammatory, and antioxidant properties; however, clinical limitations are associated with low solubility, chemical instability, and reduced bioavailability. Thus, encapsulation in nanoparticles has emerged as a strategic solution to overcome these limitations, and therefore, the encapsulation of QUER in zein/chitosan nanoparticles (QUER-ZNP-CH) becomes an innovative strategy, combining protection of the active molecule, controlled release, and potentiation of its therapeutic effect. Therefore, the objective of this study was to evaluate the antibacterial activity of QUER-ZNP-CH against clinical isolates of methicillin-resistant *Staphylococcus aureus* (MRSA). To achieve these objectives, QUER-ZNP-CH were prepared using the antisolvent precipitation method and subjected to physicochemical characterization by measuring particle size (Ø), polydispersity index (PDI), zeta potential (ξ), pH, and encapsulation efficiency (EE%). The clinical isolates (C047, C074, C128) used for this study are from the collection of the clinical microbiology laboratory of the Keizo Asami Institute and were genotypically characterized as containing the mecA gene. Antibacterial activity assays were performed using the broth microdilution technique following Clinical and Laboratory Standards Institute (CLSI) protocols, determining the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) against the clinical MRSA strains (ATCC 33591, C047, C074, C128). The results show that QUER-ZNP-CH presented a diameter of 320.9 nm, a PDI of 0.230, a ξ of +45.8 mV, and an %EE of 99.87%. The MIC and MBC values found for QUER were 250 µg/mL for MRSA ATCC 33591, C047, C074, and C128. The MIC determined with QUER-ZNP-CH was 31.25 µg/mL for the MRSA ATCC 33591 strain and 125 µg/mL for the clinical isolates C047, C074, and C128, and MBC >250 µg/mL in all strains analyzed. The evaluation suggests that QUER in its nanostructured form possesses bacteriostatic antibacterial activity, since there was inhibition of bacterial growth at the concentrations corresponding to the MIC, but without a bactericidal effect observed. Thus, zein/chitosan nanoparticles containing quercetin stand out as a promising nanobiotechnological approach in the control of resistant

bacteria, especially strains with an MRSA profile.

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