Pyrimidine Derivatives Conjugated to Gold Nanoparticles to Combat Antibiotic Resistance

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Increased antibiotic resistance in bacteria has rendered many antibiotics useless; thus, the objective of the project was to develop a novel antimicrobial compound of pyrimidine derivatives conjugated to gold nanoparticles (AuNPs) to combat antibiotic resistance through varied mechanisms. Conjugated AuNPs were proposed to be self-therapeutic and to provide localized delivery of antibiotics. Four pyrimidine derivatives with different functional groups attached to the rings and two common antibiotics, ampicillin and gentamicin, were chosen for comparisons of antimicrobial properties against gram negative Escherichia coli and gram positive Bacillus subtilis. Each compound's antimicrobial properties were determined by broth microdilution assays, which produced minimum inhibitory concentrations (MICs). Out of the four pyrimidine derivatives tested, the two with electron withdrawing functional groups, cytosine and 5-(4-chlorophenyl)pyrimidin-4-amine demonstrated strong antibacterial activity against E. coli and B. subtilis. The pyrimidine derivatives with confirmed MICs were chosen to be conjugated to 20nm AuNPs through covalent conjugation. The conjugations of the pyrimidine derivatives to the AuNPs were confirmed by spectrophotometry. After conjugation with AuNPs, the two pyrimidines demonstrated decreased MICs and enhanced efficacies against the bacteria. Some combinations of the novel compounds and common antibiotics showed synergistic relationships. The presence of a structure-activity and synergistic relationship between the conjugated AuNPs and antibiotics was determined. These results can be utilized for new antibiotic design predictions in the long term battle against antibiotic resistant bacteria, a key issue in the healthcare industry.

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