

Identifying and Quantifying Synergistic Effects of Antibiotics from *C. leucodermis* Formulated with Nanoparticles Using a Simulation-Aided Method

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Antibiotic-resistant strains of bacteria, called superbugs, require new strategies to improve infection treatment. In my previous years' research, I discovered that the Native American herb *Ceanothus leucodermis* has antibacterial properties and identified the active compounds within it as catechin derivatives. This year, motivated by research claiming that green teas containing natural nanoparticles show increased activities, I investigated if the antibacterial activity of *C. leucodermis* molecules could be enhanced by interactions with nanoparticles. I combined experimental data from diffusion assays with a Python computer program I wrote to quantify synergistic activity between antibiotics and nanoparticles. In Phase 1, I determined the optimal method for evaluating antibacterial activity of nanoparticles against *E. coli*. A well-diffusion assay was found to be the most effective method, and baseline Minimum Inhibitory Concentrations (MICs) were determined. In Phase 2, I used a laccase enzyme to conjugate *C. leucodermis* molecules to gold nanoparticles and showed that this increased the *C. leucodermis* molecules' antibacterial activity by 5 times. In Phase 3, I showed that this conjugation, rather than the mere presence of nanoparticles, was causing this synergy. I used double well-diffusion assays and my simulation to test unconjugated *C. leucodermis* molecules with nanoparticles and showed that unconjugated nanoparticles showed no added effect. This project demonstrates the antibacterial enhancement of *C. leucodermis* molecules when conjugated to nanoparticles, but not when unconjugated. It shows that reorganizing the spatial distribution of antibiotics at a molecular level can greatly increase their strength, giving a promising approach to improve existing medicines.