Combating S. aureus Resistance: Inhibiting graRS with Hesperidin and Punicalagin and Development of Natural Treatment for S. aureus Infections

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Staphylococcus aureus is a gram-positive pathogenic bacteria that causes community-onset and nosocomial infections, making it a global healthcare threat. Its ability to evade host responses and develop widespread antibiotic resistance against drugs such as methicillin and vancomycin makes it imperative to develop new treatments that can supplement currently available antimicrobials. The graRS receptor of S. aureus is a key two-component system responsible for resistance to cationic antimicrobial peptides (CAMPs) and positively charged antibiotics. The objective of the project was to identify and evaluate the efficacy of potential inhibitors in eradicating S. aureus growth by targeting the graRS system. After conducting a literature review, I analyzed the drug properties of 40 potential compounds, primarily considering stability, safety, availability, and affinity with the graRS system. Punicalagin and hesperidin proved to be the most promising compounds. To verify these results in vitro, I tested a range of concentrations of both hesperidin and punicalagin through an antibiotic disk assay and measured their efficacy in eradicating S. epidermidis, which has significant homology to S. aureus concerning the graRS receptor. Punicalagin proved to be the most effective inhibitor of S. epidermidis, showing a zone of inhibition of 706.5 mm^2 and an eradication rate of 87.5% when at 100% concentration. Furthermore, it is significantly cheaper than current treatments and has the potential to be developed as an oral supplemental medication. Based on these results, punicalagin could be immensely beneficial to combat antibiotic-resistant infections through the graRS system and warrants further study.

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