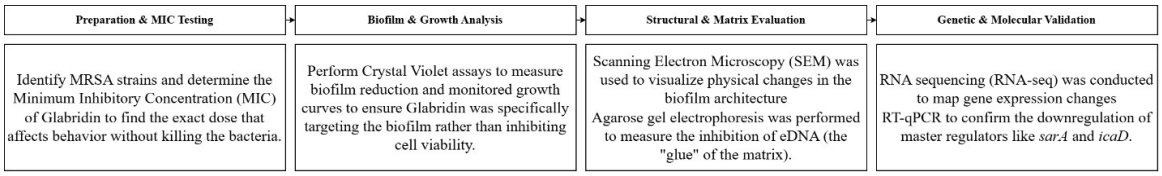
Transcriptomic Analysis of the Effect of Glabridin on Biofilm Formation in Staphylococcus Aureus

A. INTRODUCTION

Staphylococcus aureus, particularly methicillin-resistant strains (MRSA), remains a major global health threat due to its ability to form robust biofilms that protect bacteria from antibiotics and the host immune system. These biofilms contribute significantly to chronic infections and the rapid spread of multi-drug resistance, rendering many conventional treatments ineffective. Glabridin (Glb), a natural flavonoid extracted from licorice/akar manis (*Glycyrrhiza glabra*), has emerged as a promising antimicrobial candidate with known antiviral and antibacterial properties. However, the precise molecular mechanisms by which it disrupts *S. aureus* biofilms remain largely unexplored. This study aims to evaluate the antibiofilm efficacy of Glabridin and elucidate its underlying regulatory pathways, offering a potential novel strategy to combat the escalating challenge of bacterial resistance.

B. METHODS



C. RESULTS

1. **Non-Toxic Biofilm Inhibition**

   Glabridin effectively inhibits the formation of *S. aureus* biofilms at sub-inhibitory concentrations (1/2, 1/4, and 1/8 MIC) without killing the bacteria or affecting their normal growth rate.

2. **Structural Disruption**

   Scanning Electron Microscopy (SEM) images show that Glabridin disrupts the physical architecture of the biofilm, leading to a significant reduction in bacterial adhesion and a thinner, more scattered biofilm layer.

3. **eDNA Reduction**

   The treatment significantly suppresses the secretion of extracellular DNA (eDNA), which is a vital "glue" that holds the biofilm matrix together.

4. **Transcriptomic Impact**

   RNA-seq analysis identified 184 differentially expressed genes (DEGs), showing that Glabridin triggers a broad genetic response in the bacteria.

5. **Downregulation of Key Regulators**

   Glabridin downregulates critical global regulatory genes, specifically *sarA*, which is essential for biofilm development.

6. **Inhibition of Matrix & Virulence Genes**

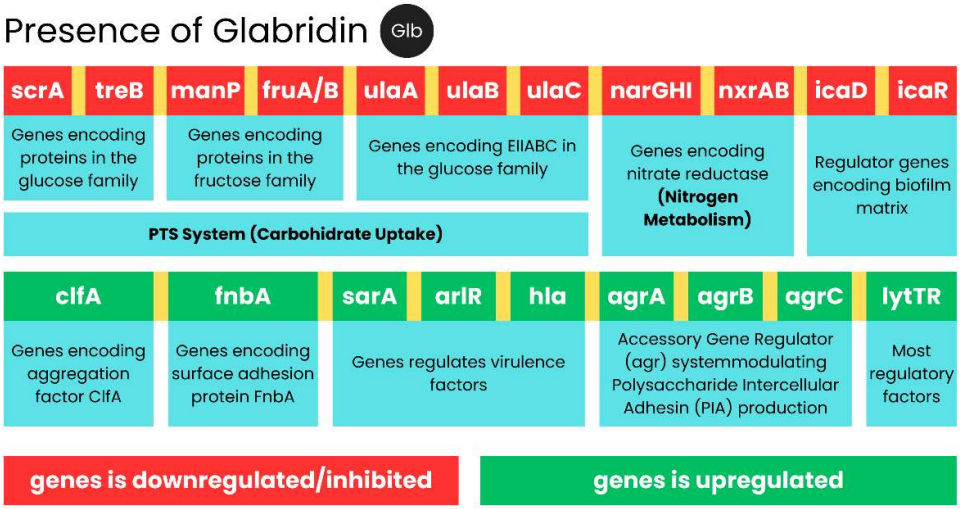
   There is a marked decrease in the expression of genes responsible for biofilm synthesis (*icaD*) and those related to bacterial virulence (*hla*), which reduces the bacteria's ability to cause infection.

7. **Metabolic Modulation**

The results indicate that Glabridin influences metabolic pathways, including the phosphotransferase system (PTS) and galactose metabolism, further hindering the bacteria's capacity to form a stable biofilm environment.

D. DISCUSSION

Glabridin acts as a highly effective antibiofilm agent without imposing selective pressure that leads to antibiotic resistance, as its mechanism does not directly kill the bacterial cells. The researchers explain that the reduction in biofilm formation is fundamentally driven by the inhibition of eDNA secretion and the downregulation of global control systems, specifically the *sarA* gene and the *icaD* operon. These findings indicate that Glabridin disrupts bacterial communication and metabolic pathways (such as the PTS system), ultimately weakening the virulence of *S. aureus* and highlighting the potential of this natural compound as a novel strategy for treating recalcitrant chronic infections.



E. CONCLUSION

Glabridin is a potent natural antibiofilm agent that disrupts *S. aureus* integrity and adhesion by inhibiting eDNA secretion without affecting cell viability. Transcriptomic analysis shows its efficacy stems from downregulating master regulators like *sarA* and key functional genes (*icaD*, *hla*), while modulating essential metabolic pathways. These findings suggest Glabridin is a promising anti-virulence candidate for combating persistent infections and global antimicrobial resistance.

F. REFERENCE

Ma, Y., Mao, Y., Kang, X., Zhang, B., Wang, J., Wang, G., & Wang, G. (2024). Transcriptomic analysis of the effect of glabridin on biofilm formation in Staphylococcus aureus. Foodborne Pathogens and Disease, 22(7), 489–497. https://doi.org/10.1089/fpd.2024.0038