P0382

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TARGETING SAERS TO DISARM *S. AUREUS* : AN INNOVATIVE EMOLLIENT WITH *AQUAPHILUS DOLOMIAE* EXTRACT-G1 AND DEXTRAN SODIUM SULFATE VALIDATED IN A RECONSTRUCTED HUMAN EPIDERMIS MODEL

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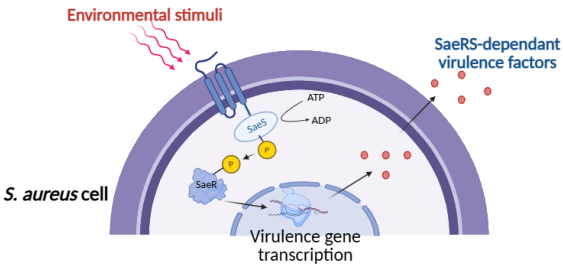
INTRODUCTION

Staphylococcus aureus is a pivotal contributor to the pathogenesis of atopic dermatitis (AD), primarily through the secretion of virulence factors that compromise the integrity of the skin barrier and modulate immune responses. Upon skin colonizing, *S. aureus* transitions from a commensal organism to a pathogen entity, producing virulence factors that exacerbate AD. The regulation of virulence in the bacterium is governed by a sophisticated network of two-component system (TCS) signal transduction pathways, which enable the bacteria to activate virulence programs in response to host defense mechanisms. Targeting these TCSs pathways offers an innovative approach for the discovery of antivirulence approaches.



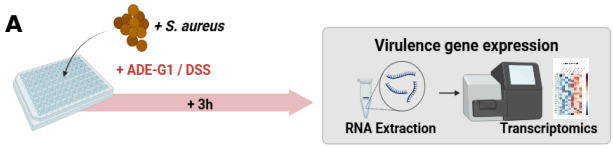
REGULATORY ROLE OF THE SAERS SYSTEM IN MODULATING VIRULENCE GENE EXPRESSION IN *S. AUREUS*

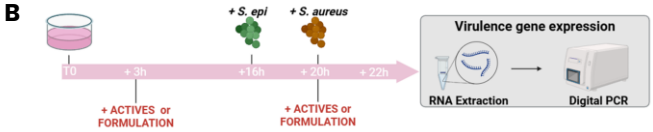
The SaeRS two-component system is a key regulator of virulence in *S. aureus*. It consists of the sensor kinase SaeS and the response regulator SaeR, which activate multiple virulence genes transcription in response to environmental stimuli. This system allows the bacteria to rapidly adapt to host defenses during infection,

Here, we present a study demonstrating that the combination of *Aquaphilus dolomiae* extract-G1 (ADE-G1) and dextran sodium sulfate (DSS) can lower *S. aureus* virulence by targeting SaeRS system, both in an *in-tubo* assay (Calvez et al, 2024) and in a more relevant RHE model co-colonized with *Staphylococcus* species.

METHODOLOGY

Previously, i*n-tubo* assay (A) was first performed on planktonic *S. aureus* cells to assess the ability of selected actives to inhibit the SaeRS regulatory system. Transcriptomic analysis was carried out to quantify changes in *saeR and saeS* expression following exposure to ADE-G1 + DSS.
Subsequently, an experimental model based on Reconstituted Human Epidermis (RHE) co-colonized with *Staphylococcus* strains (B). Digital PCR (dPCR) analysis was then performed to investigate the effects of topical formulas and actives on *saeR* expression in this more physiologically relevant context.





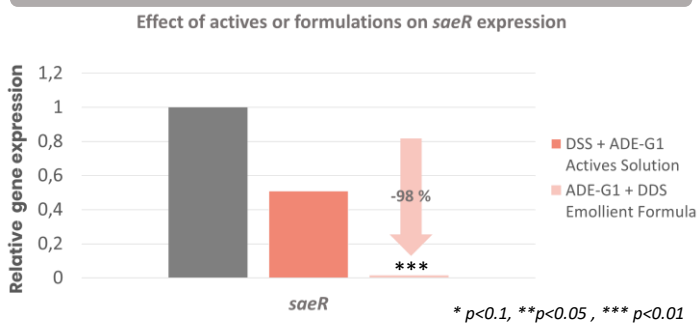
RESULTS

IN-TUBO S. AUREUS EXPERIMENT

** p<0.1, **p<0.05 , *** p<0.01*

The *in-tubo* study using transcriptomic analysis, revealed that the combination of DSS and ADE-G1 significantly reduced the expression of the *saeR* and *saeS* genes by 30% in a planktonic culture of *S. aureus*.

IN-VITRO RHE MODEL CO-COLONIZED WITH S.AUREUS AND S.EPI



** p<0.1, **p<0.05 , *** p<0.01*

The formulation demonstrated a markedly superior effect compared to the active components alone, achieving a 98 % reduction in *saeR* expression, suggesting enhanced bioavailability of the actives following formulation.

CONCLUSIONS

The novel emollient containing DSS and ADE-G1 effectively inhibits *saeR*, one of the key genes of the SaeRS virulence regulator in *S. aureus*. These new insights, provided by a RHE model study, confirm the association DSS and ADE-G1 as a promising anti-virulent approach for reducing *S.aureus* pathogenicity and thus decreasing its competitivity inside the microbiota. Further evaluation, as presented in poster **P0383**, highlights the potential of this approach for preventing AD flare-ups by focusing not only on the expression of virulence genes governed by SaeRS but also on the effect of the active ingredients on rebalancing *Staphylococcus* populations.