TARGETING *STAPHYLOCOCCUS AUREUS* V8 PROTEASE AND VIRULENCE FACTORS WITH A NOVEL ACTIVE COMPLEX TO TACKLE MICROBE-INDUCED ITCH IN ATOPIC DERMATITIS

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LEARNING OBJECTIVE: To evaluate the efficacy of a new mix of active ingredients in modulating *S. aureus* virulence factors to inhibit microbe-induced itch.

TAKEAWAY MESSAGE: A new mix of active ingredients demonstrated to inhibit the expression of several *S. aureus* virulence-related genes, notably V8 protease, offering a promising approach to tackle skin microbiome-associated itch in AD.

Conflict of Interest:

V. Patra, L. Canchy, M. Brossat, C.Cheng and F. Juchaux are employees of L'Oréal.

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INTRODUCTION

Atopic dermatitis (AD) is characterized by an altered skin barrier, Th2 inflammation, **microbial dysbiosis** and neuroinflammation.

S. AUREUS: A KEY PLAYER OF MICROBIOME DYSBIOSIS IN AD

- *S. aureus* prevalence is 20x higher in patients with AD than the skin of healthy controls.
- 90% of AD lesions are colonized with *S. aureus*.

Beyond AD, *S. aureus* skin colonization is also associated with **other pruritic inflammatory skin conditions**, including **bullous pemphigoid**, **Netherton's syndrome**, and **prurigo nodularis (PN).**

Atopic dermatitis

Bullous pemphigoid

Netherton's syndrome

Prurigo Nodularis

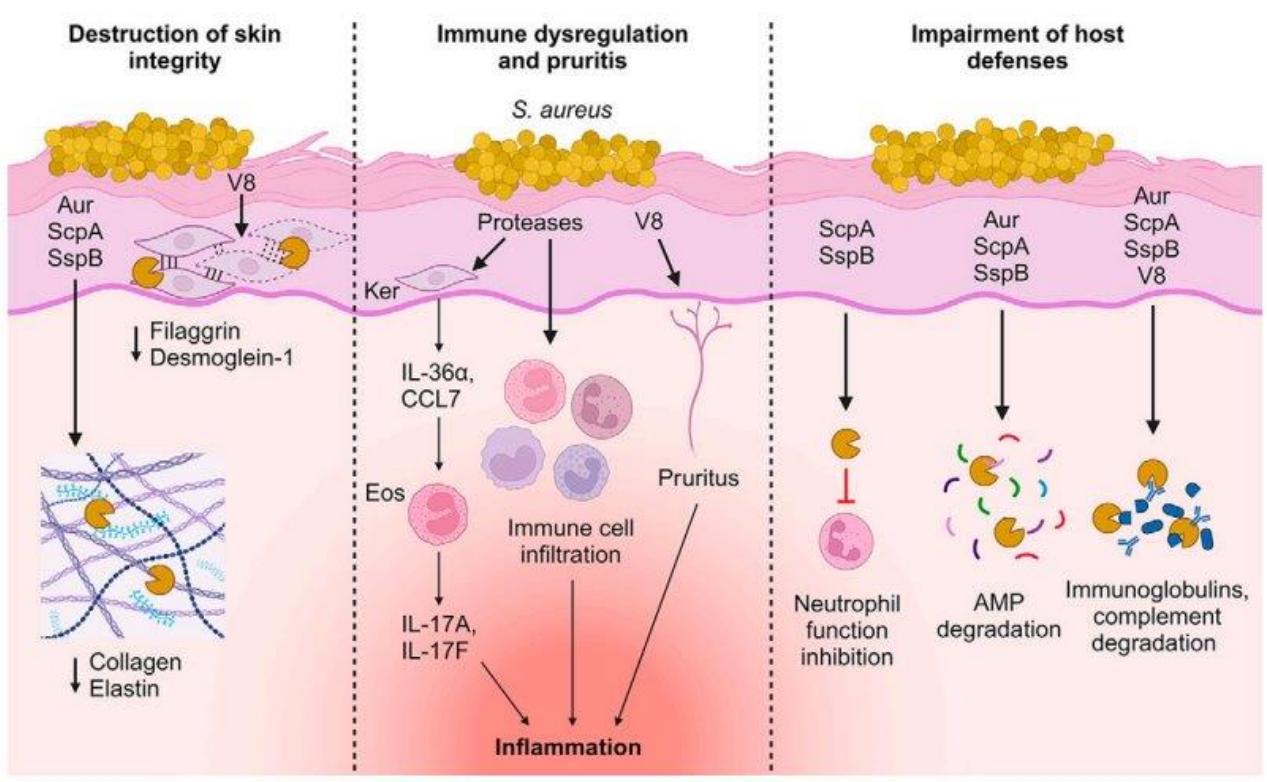
E.Ozdemir et al., (2024) Archives of Microbiology 20;206(10):410
Deng L, et al. (2023) Cell. 186(24):5375-5393.e25.
Lee HJ et al. (2025). Clin Dermatol. 27:S0738-081X(25)00090-2.

INTRODUCTION

S. AUREUS CONTRIBUTES TO AD PATHOGENESIS THROUGH EXPRESSION OF VIRULENCE FACTORS

- *S. aureus* isolates from the lesional skin of AD patients express higher levels of virulence factors.
- V8 protease is a prominent virulence factor known to cause significant skin damage by disrupting skin barrier integrity.

It has recently been demonstrated that *S. aureus* directly activates pruriceptor sensory neurons to drive itch via **V8-PAR1 pathway**.[1]



From S.Kline et al., (2024), DNA Cell Biology ;43(10):483-491

1. *Deng L, et al. (2023) Cell. 186(24):5375-5393.e25.*

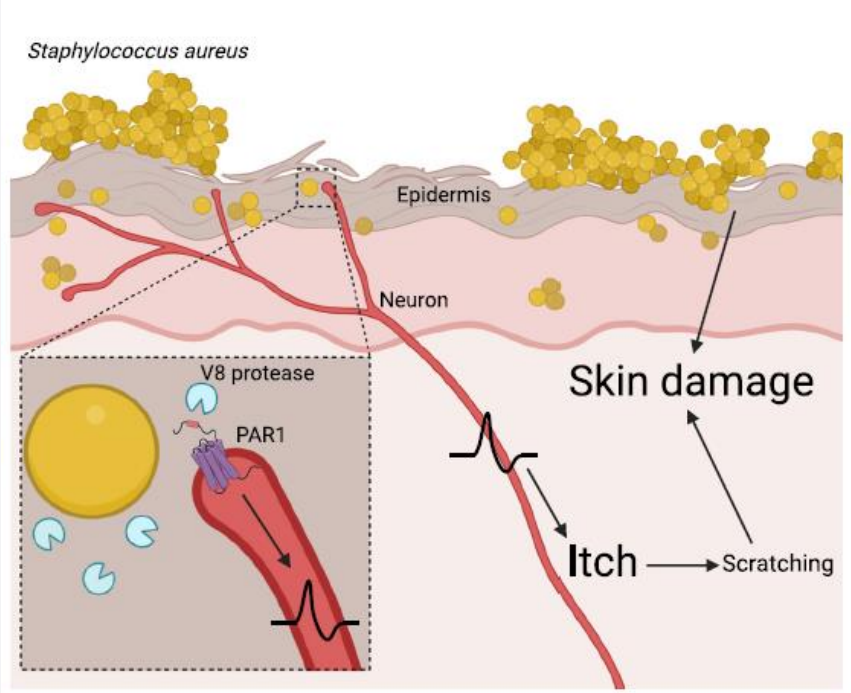
INTRODUCTION

S. AUREUS AS DRIVER OF THE ITCH-SCRATCH CYCLE IN AD

V8 protease activates sensory neurons by acting on PAR1 receptor localized at their surface, ultimately leading to **intense ITCHING and SCRATCHING**..

Deng et al. demonstrated that:

- *S. aureus* induces itch and scratch damage
- V8 protease is necessary and sufficient to induce itch during *S. aureus* exposure
- *S. aureus* V8 activates sensory neurons through PAR 1
- PAR1 deficiency of blockage ends *S. aureus*-induced itch and skin damage



Obtained from Deng, L. et al. 2023[1]

NOVEL THERAPEUTIC TARGET FOR ITCH

Deng L, et al. (2023) Cell. 186(24):5375-5393.e25.

OBJECTIVE

To evaluate the efficacy of a new mix of active ingredients in modulating *S. aureus* virulence factors to inhibit microbe-induced itch.

MATERIAL & METHODS

multi-ingredient mix
(A + B+ C)
or

Controls
(Savirin and salicylic acid)

S. Aureus
(CC1 strain)

qRT-PCR

VIRULENCE FACTORS

- Serine protease A **(SplA)**
- **V8** Protease
- Staphylococcal protein **(SpA)**
- Staphopain **(scpA)**
- Fibronectin binding protein-A **(fnbpA)**
- Iron-regulated surface determinant **(isdA)**
- Clumping factor-A **(clfA)**

1.TREATMENT

S. aureus clinical strain isolated from severe AD patient was treated with a mix of active ingredients and quorum-sensing inhibitors as controls.

2.RNA EXTRACTION

RNA was extracted at the mid-exponential phase of bacterial growth and cDNA was prepared.

3. QUANTIFICATION

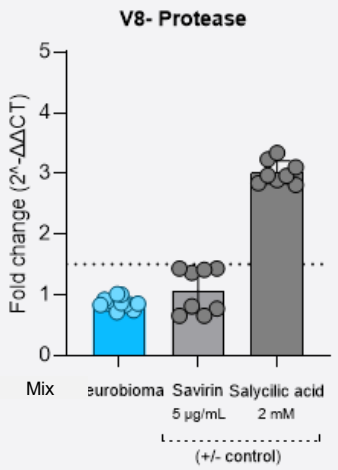
Protease and genes involved in immunomodulation by regulating cytokine expression, adhesion, and metabolic activity were quantified using qRT-PCR.

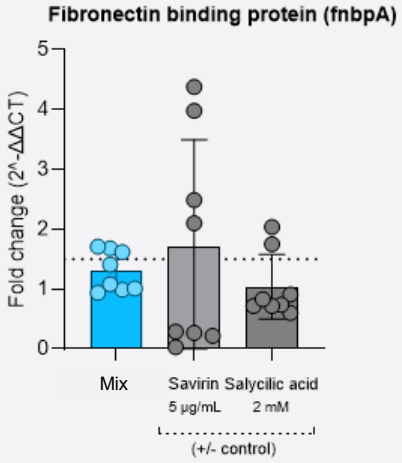
No inhibition of S.aureus at tested concentrations was previously evaluated.

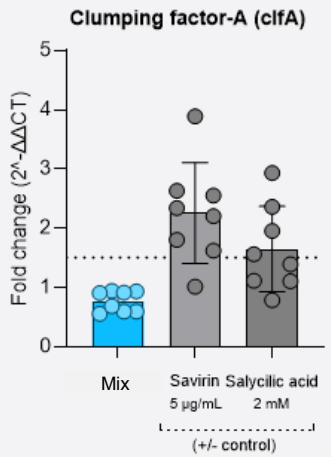
RESULTS

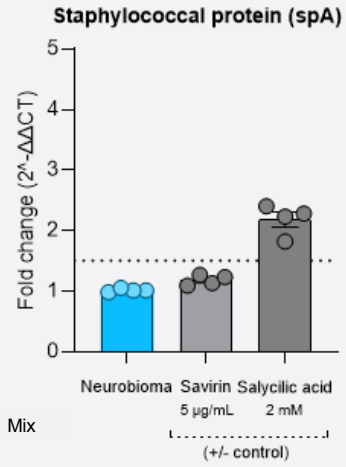
The mix of active ingredients significantly reduced the mRNA gene expression levels of several virulence factors compared to controls:

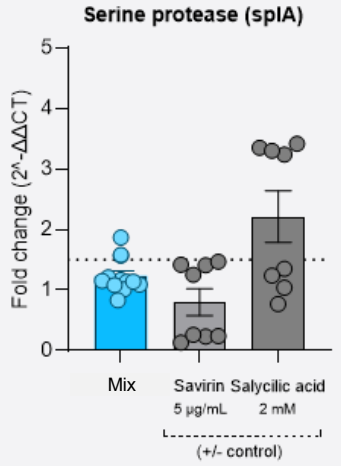
V8 protease
(p=0.002)
SplA (Serine protease A)
(p=0.021)
FnbpA (Fibronectin binding protein-A)
(p=0.026)
Clfa (Clumping factor-A)
(p=0.069)
spa (Staphylococcal protein)
(p=0.011)
IsdA (Iron-regulated surface determinant)
(p=0.045)

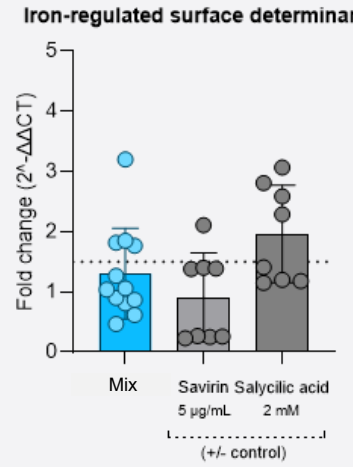












Fold change < 1.5 inhibition of gene vs control

CONCLUSION

This study demonstrates the potential of this new mix of active ingredients to inhibit the expression of several *S. aureus* virulence-related genes, notably V8 protease, offering a promising approach to tackle microbiota-associated itch in AD.

Acknowledgements

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References:

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