


# Antibacterial Activity of Surfactin and Synergistic Effect with Conventional Antibiotics Against Methicillin-Resistant Staphylococcus Aureus Isolated from Patients with Diabetic Foot Ulcers [Response to Letter]

Zhaoyinqian Li <sup>1-3</sup>

<sup>1</sup>Department of Laboratory Medicine, the Affiliated Hospital of Southwest Medical University, Luzhou, People's Republic of China; <sup>2</sup>Sichuan Province Engineering Technology Research Center of Molecular Diagnosis of Clinical Diseases, Luzhou, People's Republic of China; <sup>3</sup>Molecular Diagnosis of Clinical Diseases Key Laboratory of Luzhou, Luzhou, People's Republic of China

Correspondence: Zhaoyinqian Li, Email [lizhaoyinqian@swmu.edu.cn](mailto:lizhaoyinqian@swmu.edu.cn)

## Dear editor

We are grateful to Slamet Wardoyo and Taufik Anwar for taking an interest in our previous study<sup>1</sup> and for their comments.<sup>2</sup> Surfactin has exhibited antimicrobial activity in a series of in vitro experiments against different resistance patterns of Staphylococcus aureus isolated from clinical patients with diabetic foot ulcers (DFUs). This serves as the initial step in exploring the potential of surfactin as a therapeutic agent for topical treatment of DFUs. Further evaluation of the efficacy and mechanism of surfactin needs to be conducted in animal models. If the results are positive, clinical trials can be considered. This will be a lengthy expedition of discovery.

In addition to surfactin, there are a large number of antimicrobial peptides (AMPs) that have been shown to have synergistic effects with conventional antibiotics against various types of bacteria. Many of these AMPs have been demonstrated in animal models. The mechanisms of synergy are complex and specific, but the most common one is that AMPs promote bacterial absorption of antibiotics. The main points are as follows: (1) AMPs can change the permeability of the cell membrane, allowing antibiotics to penetrate into the cell and interact with intracellular targets. (2) AMPs can interfere with the structure and function of bacterial cell membranes. (3) AMPs can target or block the activity of lipopolysaccharides on the outer membrane of Gram-negative bacteria. (4) Both AMPs and conventional antibiotics can inhibit the metabolic pathways of bacteria.<sup>3</sup> We anticipate the results of more thorough and specific research to determine the mechanism behind the synergistic effect of surfactin and conventional antibiotics.

Conventional treatment strategies for chronic wounds, such as systemic use of antibiotics and surgical debridement, tend to be costly, with long treatment durations and unsatisfactory results. AMPs could be a promising therapeutic option for infected wounds due to their broad-spectrum bactericidal effects, wound healing capabilities, anti-biofilm effects, and angiogenesis-inducing properties.<sup>4</sup> Several AMP-based wound dressings for infected wounds have been selected for clinical trials, among which pexiganan has completed Phase 3 clinical trials for the treatment of DFUs (NCT00563394 and NCT00563433). The results showed equivalent clinical improvement rates, overall microbiological eradication rates, and wound healing rates for topical pexiganan and oral ofloxacin. Additionally, no significant resistance to pexiganan was observed.<sup>5</sup>

Overall, with the rise of antimicrobial resistance, most pharmaceutical companies have ceased the development of new antibiotics and shifted their attention to developing more profitable alternatives for treating infections.<sup>6</sup> Although there are still limitations of AMPs in drug development, such as potential toxicity, susceptibility to degradation in vivo,

and expensive processes for synthesis and manufacturing, they can still provide us with several new treatment options for infections that are difficult to treat.

## Disclosure

The author reports no conflicts of interest in this communication.

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