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Understanding the antibacterial mechanism of a phytochemical derived from *Urginea indica* against Methicillin-Resistant *Staphylococcus aureus*: A phytochemical perspective to impede antibiotics resistance

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ABSTRACT

Bacterial resistance to conventional antibiotics is a pressing concern in the realm of infectious disease treatment, given its rapid evolution. This underscores the urgency of identifying novel therapeutic compounds. Recent efforts have been concentrated on exploring natural sources of antibacterial compounds, with a particular focus on plant-based derivatives due to their enhanced biocompatibility. In this context, our research has led to the isolation and purification of a groundbreaking plant-based phytochemical derivative known as N-ethylacetamide. We meticulously tested its antibacterial activity against bacterial strains, *Staphylococcus aureus* and Methicillin-resistant *Staphylococcus aureus*. Remarkably, N-ethylacetamide exhibited substantial antibacterial and anti-biofilm effects within the concentration range of 5–15 μg/mL, offering promise for combating these pathogens. Our investigations revealed N-ethylacetamide's compatibility with mammalian cells, as evidenced by tests conducted on RAW 264.7 and 3 T3 fibroblast cell lines. The potential antibacterial efficacy of this purified compound was validated through *in-vitro* infection studies, and a positive immune response was observed in an *in-vivo* mice model (Balb/c). The accumulated experimental evidence underscores the potential of N-ethylacetamide as a therapeutic agent against bacterial infections. It presents the exciting possibility of addressing these challenges with minimal side effects, offering hope for a more effective and safer approach to combat bacterial diseases.

Introduction

Bacterial infections have claimed millions of lives before the widespread use of antibiotics, and they still do [1]. Today, the relative safety provided to human civilization by these amazing treatments is at risk due to the worldwide rapid emergence of antibiotic-resistant bacteria that compromise the effectiveness of traditional antibiotics [2–4]. Several reasons, such as overuse and misuse of antibiotics, as well as a lack of new drug development due to adverse economic perspectives and draconian regulatory requirements, have resulted in the escalation of the antibiotic resistance (ABR) crisis [5,6]. *Staphylococcus aureus* (*S. aureus*), one of many bacteria identified by the WHO as Priority Level-2 (High), is of special concern because of its extraordinary ability to develop antibiotic resistance, which may substantially impair the existing options for treatment [7]. One of the most common opportunistic human commensal pathogens is *S. aureus*, which is notorious for protracted morbidity with a high recurrence and death rate, in addition to its cunning ability to fool the immune system and cause countless infections in both communities and healthcare institutions [8]. Methicillin-resistant *S. aureus* (MRSA), one of the many ABR strains, is

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