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Poster 5

Photodynamic inactivation of methicillin-resistant *Staphylococcus aureus* using harmine-antiseptic combinations

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Abstract

Background: Antibiotic-resistant pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA), pose significant challenges in the treatment of chronic wound infections. Antibacterial photodynamic therapy (aPDT) offers a localized, resistance-independent alternative to antibiotics [1]. In aPDT, bacteria are targeted by molecules called photosensitizers (PSs) that are activated by light. Natural PSs are more eco-friendly, sustainable, cost-effective, and therefore, preferred over synthetic alternatives [2]. Harmine (HA), an alkaloid commonly found in various plants and animals, is a promising natural PS, with reported photodynamic efficacy against cancer cells [3]. **Objective:** This study explores aPDT with HA as a PS and its combined action with wound antiseptics, namely octenidine dihydrochloride (OCT), polyhexamethylene biguanide (PHMB), and hydrogen peroxide, against *S. aureus* (MJMC568-B: MRSA) to enhance antiseptic efficacy and bacterial damage while minimizing concentrations. **Methods:** The antibacterial efficacy of HA, OCT, PHMB and H_2O_2 was independently evaluated by determination of minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values using the microdilution and plating agar methods, respectively. An evaluation of the capacity of HA-antiseptics combinations to boost the antibacterial activity was conducted by a disk diffusion assay, and a checkerboard assay. The photodynamic activity of HA was assessed independently and in combination by irradiating with UV light (365 nm) using a light-emitting diode (LED) system and quantification through colony-forming unit (CFU) analysis. **Results:** Antibacterial efficacy of HA individually and in combination with antiseptics against *S. aureus* was assessed, and an increase in the antibacterial activity when combined was observed. UV-A irradiation of 19.8 J/cm^2 (5.5 mW/cm^2, 60 min) enhanced the antibacterial capacity of HA (250µg/ml), significantly reducing *S. aureus* culturability (3.85±0.39 CFU/cm^2 logarithmic reduction compared to a 0.10±0.17 CFU/cm^2 logarithmic reduction when not irradiated), highlighting its potential for aPDT applications. **Conclusions:** These findings highlight HA potential as a natural PS for aPDT and its role in enhancing antiseptic efficacy against MRSA. The combined aPDT-antiseptic approach offers a promising strategy for chronic wound management, reducing antibiotic reliance and mitigating resistance development.

Keywords: antibacterial photodynamic therapy; antiseptics; harmine

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