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Photodynamic inactivation of methicillin-resistant *Staphylococcus aureus* on skin using a porphyrinic formulation

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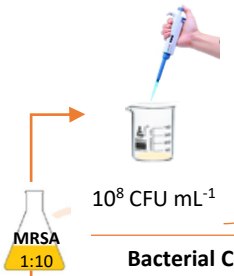
INTRODUCTION

- *Staphylococcus aureus* causes serious skin and soft-tissue infections that can progress to invasive and life-threatening pathologies;[1]
- This bacterium is capable to acquire antibiotic resistance, such as methicillin-resistant *Staphylococcus aureus* (MRSA);[2]
- Antimicrobial photodynamic therapy (aPDT) can be a promising alternative to antibiotics to treat localized infections;[3]
- This therapy requires the presence of a photosensitizer, visible light and dioxygen to produce reactive oxygen species that lead to microbial inactivation;[4,5]
- A porphyrinic formulation (FORM) based on a non-separated mixture of 5 *meso*-tetraarylporphyrins positively charged proved to be effective in aPDT of bacteria, namely *S. aureus,* and an excellent alternative to the highly efficient separated photosensitizers (PSs) since the production costs and time were reduced significantly;[6]
- aPDT effect can be also potentiated by potassium iodide (KI) that is recognized to increase the aPDT efficiency of some PSs on a broad-spectrum of microorganisms, namely trough iodine species that are extremely microbicidal;[7]
- Iodopovidone (PVP-I), indicated for wounds and skin disinfection before surgical interventions, can also provide microbicidal iodine.[8]

Objective: Evaluate the aPDT efficiency of FORM alone and combined with KI or PVP-I to treat human skin infections by MRSA[9]

METHODOLOGY



Light control (LC): PBS
LC + KI: PBS + KI at 100 mM
LC + PVP-I: PBS + PVP-I at 1%
FORM: 5.0, 1.0 and 0.5 µM
FORM + KI: FORM at 0.5 µM + KI at 100 mM
FORM + PVP-I: FORM at 0.5 µM + PVP-I at 1%
Dark control (DC): PBS + FORM at 0.5 and 5.0 µm
DC - PVP-I: PBS + PVP-I at 1%

Incubation in the dark under stirring for 10 min

60 min

In vitro

White light (400–800 nm) 25 mW cm^{-2}

Ex vivo

Bacterial Contamination

10^7 CFU mL^{-1}

Skin desinfection

Ethanol

UV - C

30 min of incubation

LC; LC+ KI; LC + PVP-I
FORM: FORM at 50 µM
FORM + KI: FORM at 50 µM + KI at 100 Mm
FORM + PVP-I: FORM at 50 µM + PVP-I at 1%

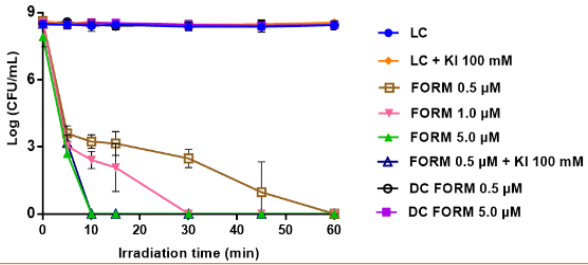
Incubation in the dark for 30 min

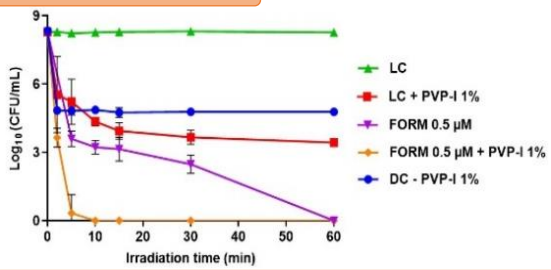
180 min (PVP-I) or 270 min (KI)

White light (400–800 nm) 60 mW cm^{-2}

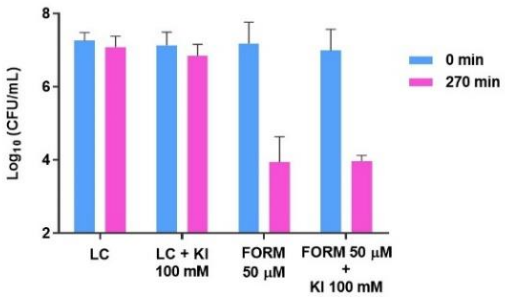
RESULTS

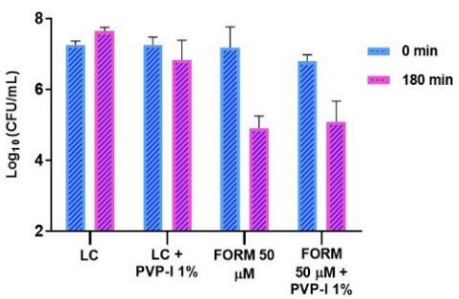
aPDT of MRSA in PBS (*in vitro* assays)





aPDT of MRSA in porcine skin artificially contaminated (*ex vivo* assays)





CONCLUSIONS

- ✓ FORM was effective to inactivate MRSA *in vitro*;
- ✓ A substantial reduction in the irradiation time was observed when FORM was combined with KI or PVP-I;
- ✓ In the *ex vivo* assays, the best achievements were obtained in the presence of FORM alone with reductions of 3.1 Log$_{10}$CFU mL^{-1};
- ✓ **aPDT using FORM can be regarded as a promising alternative to antibiotics to treat localized skin infections, including the ones caused by MRSA strains, even without potentiator agents.**

References: 1. Chaby, G *et al. Arch. Dermatol.* 2007, 143, 1297–1304; **2.** Grundmann, H *et al. Lancet.* 2006, 368, 874–885; **3.** Kharkwal, GB *et al. Lasers Surg. Med.* 2011, 43, 755–767; **4.** Huang, L *et al. Lasers Surg. Med.* 2012, 44, 490–499; **5.** Alves, E *et al. Future Med. Chem.* 2014, 6, 141–164; **6.** Marciel, L *et al. Future Med. Chem.* 2018, 10, 1821–1833; **7.** Vieira, C *et al. Front. Microbiol.* 2018, 9, 1-16. **8.** Burks, RI *Phys. Ther.* 1998, 78, 212–218. **9. Braz, M *et al. Photodiagn. Photodyn. Ther.* 2020, 30, 1–11.**

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