Controlled Delivery of Multiple Antimicrobial Agents by Janus-type Dressings for Combating Wound Biofilms

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Introduction

Biofilms pose a great challenge for wound management. Herein, this study describes a near-infrared (NIR) light responsive microneedle patch for on-demand release of antimicrobial peptide for treatment of wound biofilms. IR780 iodide as a photothermal conversion agent and molecularly engineered peptide W379 as an antimicrobial agent are loaded in dissolvable poly(vinylpyrrolidone) (PVP) microneedle patches followed by coating with a phase change material 1-tetradecanol (TD). After placing in an aqueous solution or biofilm containing wounds ex vivo and in vivo, upon exposure to NIR light, the incorporated IR780 induces light-to-heat conversion, causing the melting of TD. This leads to the dissolution of PVP microneedles, enabling the release of loaded W379 peptide from the microneedles into surrounding regions (e.g., solution, biofilm, wound bed). Compared with traditional microneedle patches, NIR light responsive microneedle patches can program the release of antimicrobial peptide and show high antibacterial efficacy in vitro. Meanwhile, this work indicates that NIR light responsive TD-coated, W379-loaded PVP microneedle patches show excellent antibiofilm activities ex vivo and in vivo. Additionally, this microneedle system could be a promising platform for delivering other antimicrobial agents.

Methods

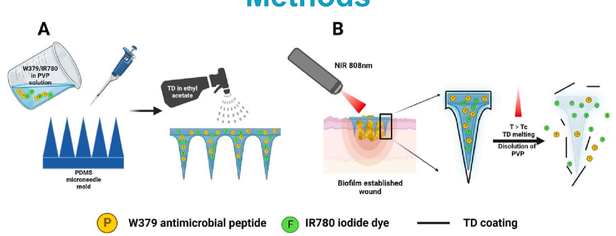

Fig. 1. Schematic illustrating 1-tetradecanol (TD)-coated, IR780 iodide dye and W379 peptide co-loaded PVP microneedle patches for treatment of biofilms in chronic wounds.

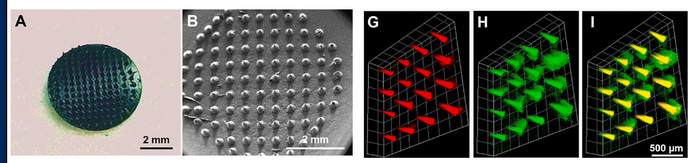

Fig. 2. Morphology of TD-coated, IR780 iodide dye and W379 peptide co loaded PVP microneedle patches. (A): Photograph showing a TD-coated, IR780 iodide dye and W379 peptide co-loaded PVP microneedle patch. (G)-(I): Fluorescent images of an FITC-TD coated, IR780 iodide dye and W379 peptide co-loaded PVP microneedle patch. (G) IR780 iodide dye and W379 peptide co-loaded PVP microneedle in red. (H): FITC-TD coating in green. (I): merged (G) and (H).

NIR light controlled release properties and antibacterial effects in vitro

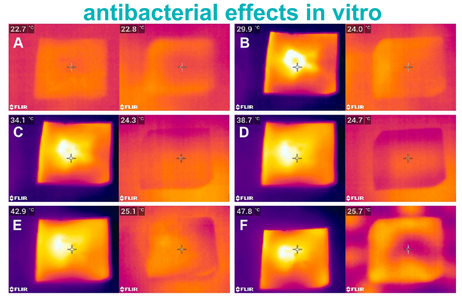

Fig. 3. TD-coated, IR780 iodide dye and W379 peptide co-loaded PVP microneedle patches are thermally responsive to NIR irradiation. (A)-(F): Thermal infrared camera photographs of microneedle patches with (left) and without (right) containing 0.4 wt% IR780 iodide dye upon continuous exposure to 0.4 W/cm2 NIR irradiation for 180 s. (G): Temperature-time curves of microneedle patches incorporated with different amounts of IR780 in microneedles.

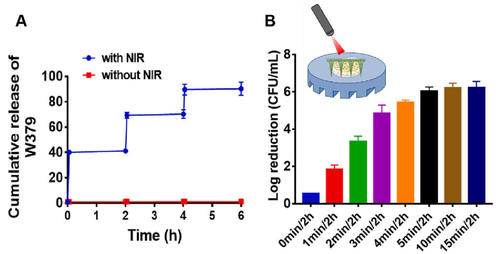

Fig. 4. NIR light controlled release of W379 antimicrobial peptide from microneedle patches and their antimicrobial activity in vitro. (A): Release profiles of W379 peptide from microneedle patches with and without NIR irradiation. (B): In vitro ntibacterial activities of microneedle patches with NIR irradiation for different periods of time and incubation for 2 h.

In vitro cytotoxicity test

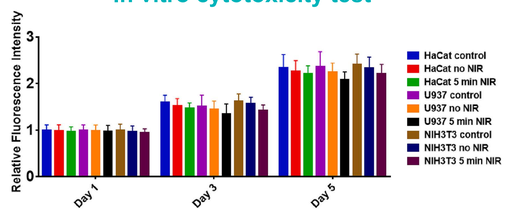

Fig. 5. In vitro cytotoxicity of TD-coated, IR780 iodide dye and W379 peptide co-loaded PVP microneedle patches with and without NIR irradiation for 5 min

Efficacy of microneedle patches against biofilms ex vivopeptides

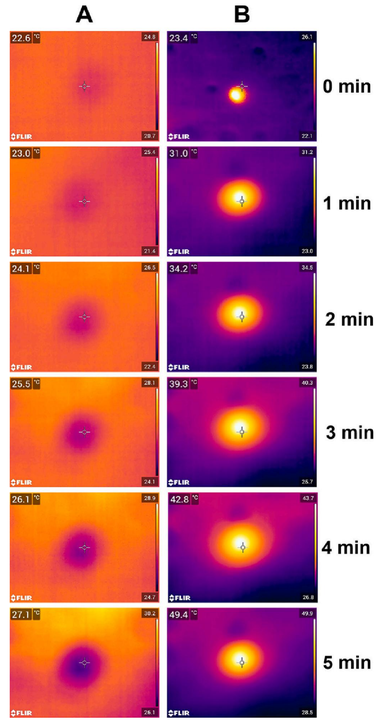

Fig. 6. Thermal infrared camera photographs of TD-coated, W379 peptide loaded PVP microneedle patches without (A) and with (B) containing IR780 iodide dye placed on partial-thickness biofilm containing wounds created on human skin explants upon continuous irradiation of 0.4 W/cm2 NIR light for 5 mins.

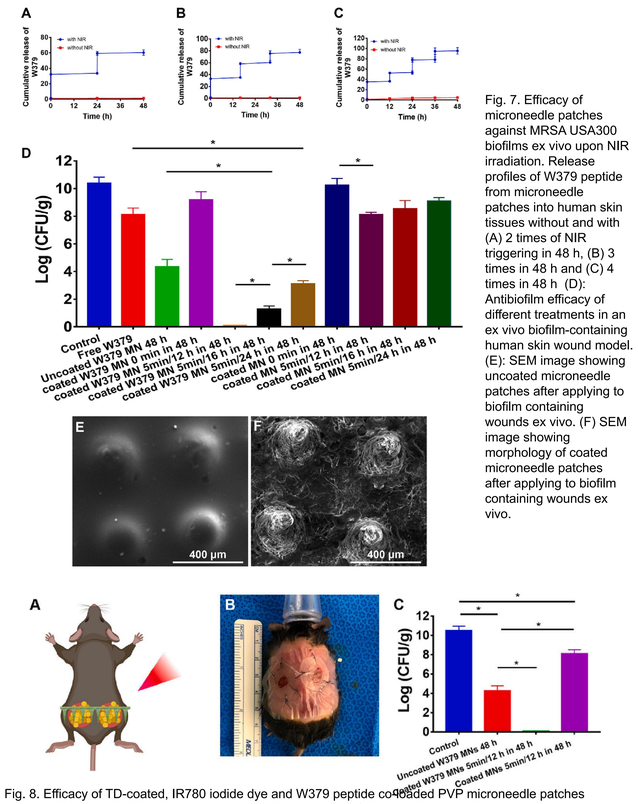

Fig. 7. Efficacy of microneedle patches against MRSA USA300 biofilms ex vivo upon NIR irradiation. Release profiles of W379 peptide from microneedle patches into human skin tissues without and with (A) 2 times of NIR triggering in 48 h, (B) 3 times in 48 h and (C) 4 times in 48 h (D): Antibiofilm efficacy of different treatments in an ex vivo biofilm-containing human skin wound model. (E): SEM image showing uncoated microneedle patches after applying to biofilm containing wounds ex vivo. (F) SEM image showing morphology of coated microneedle patches after applying to biofilm containing wounds ex vivo.

Fig. 8. Efficacy of TD-coated, IR780 iodide dye and W379 peptide co-loaded PVP microneedle patches against MRSA USA300 biofilms in vivo upon NIR irradiation. (A): Schematic illustrating the in vivo experiment. (B): Photograph showing wounds were created and fixed with splints, and MRSA was inoculated for 48 h. (C): Antibiofilm efficacy of different treatments. *p < 0.05

Conclusions

1. We have demonstrated the fabrication of TD-coated, W379 and IR780 co-loaded PVP microneedle patches through the molding and spray coating.
2. Under the NIR irradiation, the TD coating melted, promoting the release of encapsulated W379 from PVP microneedles. The TD-coated, W379 and IR780 co-loaded PVP micro needle patches showed an intermittent release profile corresponding to the NIR light on/off cycle.
3. The prepared microneedle patches displayed an excellent photothermal responsive antibacterial effect without significant cytotoxicity in vitro.
4. These patches showed high efficacy in combating wound biofilms ex vivo and in vivo.

References

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(2)Lakshmaiah Narayana J, Mishra B, Lushnikova T, et al. Proceedings of the National Academy of Sciences, 2020, 117(32): 19446-19454.

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