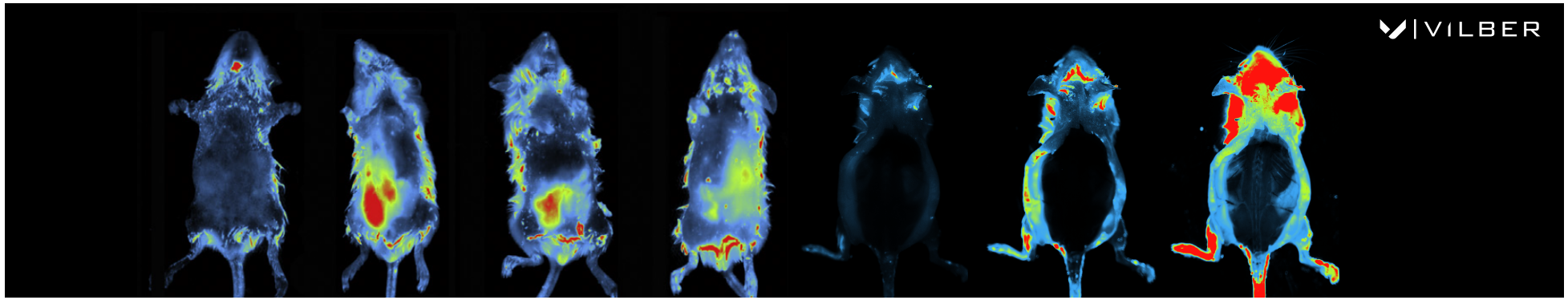

EFFICACY OF LOW MOLECULAR WEIGHT CHITOSAN-COATED SILVER NANOPARTICLES IN THE TREATMENT OF MRSA-INFECTED WOUNDS

AUTHORS

Yinbo Peng[1], Chenlu song[1], Chuanfeng Yang[1], Qige guo[1], Min Yao[1,2]
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1.Department of Burns and Plastic surgery, shanghai Ninth People's hospital, Institute of Traumatic Medicine, shanghai Jiao Tong University school of Medicine, shanghai, People's republic of china; 2.Department of Dermatology, Wellman center for Photomedicine, harvard Medical school, Massachusetts general hospital, Boston, Ma, Usa.

INTRODUCTION

Methicillin-resistant Staphylococcus aureus (MRSA) infection is the most common clinical drug-resistant infection in the burn ward. A previous study has shown that silver nanoparticles (AgNPs), widely applied as topical wound materials, have a great anti-bactericidal activity against MRSA. However, accumulated deposition of silver in the liver, spleen, and other main organs may lead to organ damage and dysfunction. Thus, protecting AgNPs antibacterial properties while reducing their absorption and toxicity in the body has become a very important challenge. Previous studies have shown that different surface stabilizers have distinct impacts on AgNP cytotoxicity. Because of its good biocompatibility and antibacterial properties, chitosan is often used as the active ingredient of topical wound materials. It has been reported that chitosan is a good stabilizer for AgNPs and promotes wound healing by AgNPs. Thus, chitosan-coated AgNPs demonstrated high efficiency in killing common bacteria and fungi. Moreover, low molecular weight chitosan (LMWC) has shown better water solubility and biological activity than a higher degree of polymerization of chitosan, suggesting that LMWC may be an ideal stabilizer of AgNPs.

OBJECTIVE

In this study, LMWC is used as a reducing agent and a stabilizer to synthesize AgNPs. Its effects have been evaluated on the antibacterial activity, biocompatibility, and body absorption of AgNPs and compared with polyvinylpyrrolidone-coated silver nanoparticles (PVP-AgNPs) and silver nanoparticles without surface stabilizer (uncoated-AgNPs) in a dorsal MRSA wound infection mouse model.

MATERIAL & METHODS

LMWC-AgNPs were synthesized by reducing silver nitrate with low molecular weight chitosan as a stabilizer and reducing agent, while PVP-AgNPs were synthesized using polyvinylpyrrolidone as a stabilizer and ethanol as a reducing agent.

Balb/c mice with 1.5×1.5 cm back full-thickness skin wounds were inoculated with 100 μL of 9×10^8 cfu/mL MRSA bacteria, and infection of mice was assessed 3 days later with Fusion Fx7 (Vilber Lourmat, France). The mice were randomly divided into groups. The infected wounds were dressed with 50 μg/g · bw of different AgNPs, bandaged with double gauze bandage, and fixed with 3 M film. In the following 2 consecutive days, Fusion Fx7 (Vilber Lourmat, France) was used to observe wound infection and healing.

RESULTS

Figure. 1 The anti-bactericidal effects of three types of AgNPs on day 3 and day 5.

The images demonstrate mice wounds inoculated with MRSA and dressed with different AgNPs. From day 3 to day 5, the amounts of bacteria in wounds on the backs of mice were determined through a chemiluminescence assay using Fusion Fx7 (Vilber Lourmat, France). Higher intensity of the red color indicates more severe infection. Scale bar = 1 cm. *In vivo* bactericidal results showed that, on day 3, the amounts of bacteria in wounds on the back of mice were similar in the three types of AgNPs treatments, which were demonstrated by the similar values of chemiluminescent MRSA in the three groups (Figure 1.D3)

Figure.2 The effects of LMWC-AgNPs, PVP-AgNPs, and uncoated-AgNPs on the control of MRSA wound infection and wound healing in mice

Images of wound infection and healing following dressing with different AgNPs on day 1, 7 and day 10 were obtained with Fusion FX7 (Vilber Lourmat, France). Acquired images clearly show that LMWC-AgNPs, PVP-AgNPs, and uncoated-AgNPs effectively control MRSA wound infection and promote wound healing without any apparent difference. Topical wound healing rate showed that, in comparison to the untreated control group, each group treated with AgNPs displayed accelerated wound healing on day 7. On day 10, most wounds healed in all the groups treated with AgNPs. Thus, the three types of AgNPs effectively controlled MRSA wound infection and promoted wound healing without apparent difference.

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CONCLUSION

Mice experiments showed that the three types of AgNPs had good anti-inflammatory effects and effective protection of wound healing in mice. Furthermore, this study suggests that LMWC-AgNPs have less risk of damage to organ functions and are effective and safer AgNPs for medical materials, which is very important for large area burn patients, who need local usage of antibacterial materials on wounds for a long time after injury. These results demonstrate the ability of the Fusion FX7 (Vilber Lourmat, France) in imaging low molecular weight chitosan-coated silver nanoparticles on dorsal MRSA wound infection *in vivo*.