A potential silver lining for antimicrobial treatments against certain bacteria

A significant amount of research has been conducted regarding the development of effective antimicrobial treatments. This appears especially true in terms of combating difficult-to-treat Gram-negative bacteria. Silver is a known antimicrobial; however, its mechanism of action remains to be elucidated. Investigating this, Jose Ruben Morones-Ramirez (Boston University, MA, USA), James Collins (Boston University) and colleagues recently demonstrated that silver interrupts various bacterial cellular processes such as metabolism and iron homeostasis. This results in a higher level of reactive oxygen species production and increased membrane permeability of Gram-negative bacteria. This “can potentiate the activity of a broad range of antibiotics against Gram-negative bacteria in different metabolic states, as well as restore antibiotic susceptibility to a resistant bacterial strain.”

The research, published in Science Translational Medicine, demonstrated in vitro and in a mouse model of urinary tract infection that the ability of silver to trigger oxidative stress could be utilized to potentiate antimicrobial activity. Furthermore, the group showed in vitro and in two mouse models of peritonitis, “Silver sensitizes Gram-negative bacteria to the Gram-positive-specific antibiotic vancomycin, thereby expanding the antibacterial spectrum of this drug.” The researchers also used combinations of silver and antibiotics in vitro to eliminate bacterial persister cells. In addition, they demonstrated that silver is capable of enhancing antimicrobial action against biofilm-producing pathogens both in vitro and in a mouse biofilm infection model.

When conducting this research, the group had to overcome a number of challenges. As Morones-Ramirez told Future Microbiology, "The first was the experimental design and systems approach to understand the mechanism of antimicrobial action of silver. In addition, a very big challenge was the design and translation of the in vitro work in vivo. We had to think about the best and most relevant infection model in mice to test our in vitro activity of silver.” The group chose to thoroughly test the effects using three different animal infection models: systemic; urinary tract infection; and a biofilm treatment in an implanted catheter. It was also necessary for the group to develop an appropriate toxicity study of silver. Therefore, they chose LD50 combined with blood chemistry studies of the treated mice, in addition to an in vitro toxicity test of silver in mammalian cells.

Taken together, the authors state, “This work shows that silver can be used to enhance the action of existing antibiotics against Gram-negative bacteria, thus strengthening the antibiotic arsenal for fighting bacterial infections.” Furthermore, Morones-Ramirez explained, “In the future, with some more research regarding the toxicity and pharmacokinetics of silver in humans, I would recommend the development of therapies where the antibiotics will be accompanied by the respective concentrations of silver, to enhance their effect in fighting infections.”


Study reveals potential new approach for tackling TB

In vitro activity of silver in a mouse model of urinary tract infection demonstrated the potential of silver to enhance antimicrobial activity against certain bacteria. Silver sensitizes Gram-negative bacteria to the Gram-positive-specific antibiotic vancomycin, thereby expanding the antibacterial spectrum of this drug. The researchers also used combinations of silver and antibiotics in vitro to eliminate bacterial persister cells. In addition, they demonstrated that silver is capable of enhancing antimicrobial action against biofilm-producing pathogens both in vitro and in a mouse biofilm infection model.

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