No resistance after 100 days repeated incubation of *Staphylococcus aureus* with polihexanide

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Introduction

Infection is the main cause of delayed healing in surgical, traumatic and burn wounds, and may lead to the formation of a chronic wound. Therefore, wound dressings with antiseptics are increasingly utilized in the treatment of critical colonized or infected chronic wounds. Antiseptics have a lower potency to induce bacterial resistance than antibiotics; however, concerns have been expressed regarding their overuse and the emergence of bacterial adaptation. *Staphylococcus aureus* is one of the most important pathogen of nosocomial infections and is a common complication during the treatment of chronic wounds. We have used an experimental system employing microplate-laser-nephelometry to test the adaptation capacity of *S.aureus* to polihexanide and silver nitrate, two commonly used antimicrobial agents in the treatment of infected chronic wounds.

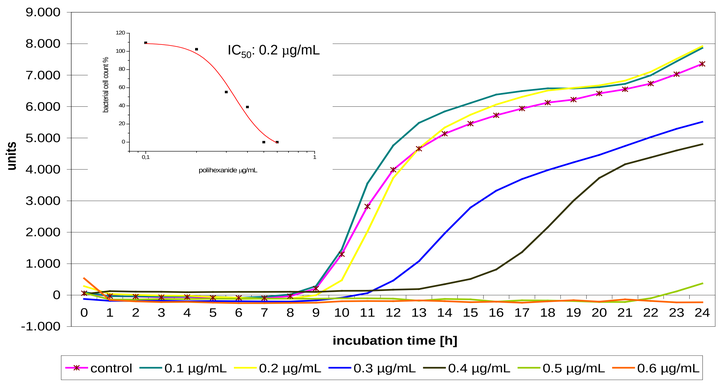

Fig. 1: Nephelometric measurement of the antibacterial activity of polihexanide against Staphylococcus aureus to determine the IC_{50}.

Material & Methods

Staphylococcus aureus was incubated with different concentrations of polihexanide (0.1 - 0.6 µg/mL) and silver nitrate (1 - 40 µg/mL). Bacterial growth was investigated by lasernephelometry (NEPHELOstar, BMG Labtech, Germany). IC_{50} concentrations (half maximal inhibitory concentration) of the antiseptics were determined. Subsequently, the microorganisms were repeatedly incubated with the respective IC_{50} concentration for 100 days. Influence of the continued treatment was determined by calculation of the current IC_{50}. Additionally, a polihexanide containing wound dressing (Suprasorb® X + PHMB) has been tested according to the JIS L 1902 for antibacterial activity using untreated and treated *S. aureus*.

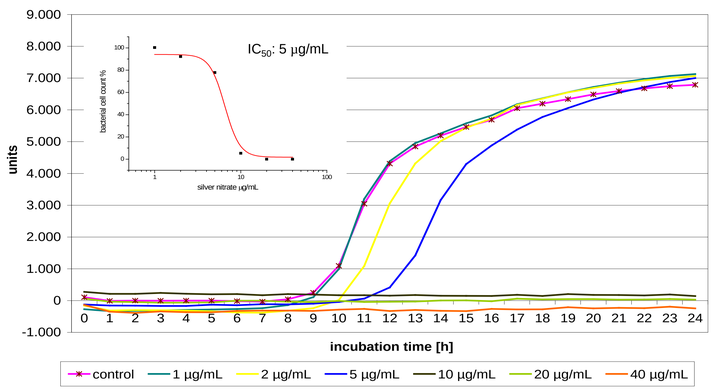

Fig. 2: Determination of the antibacterial activity of silver nitrate against Staphylococcus aureus by nephelometric measurement to calculate the IC_{50}.

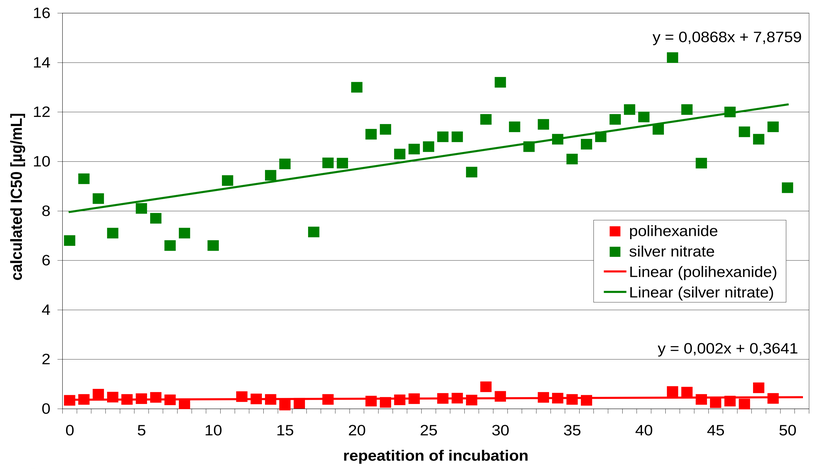

Fig. 3: Development of the IC_{50} during repeated incubation of Staphylococcus aureus with polihexanide or silver nitrate for 100 days.

Results

As figure 3 shows, the calculated IC_{50} of polihexanide increased only slightly over time (m=0.002). In contrast, a dramatic increase of the IC_{50} was observed for silver nitrate (m=0.087). Furthermore, the tests of antimicrobial activity against *Staphylococcus aureus* according to the JIS L 1902 showed a comparable reduction of treated and untreated S. aureus growth using the polihexanide containing wound dressing (fig. 4).

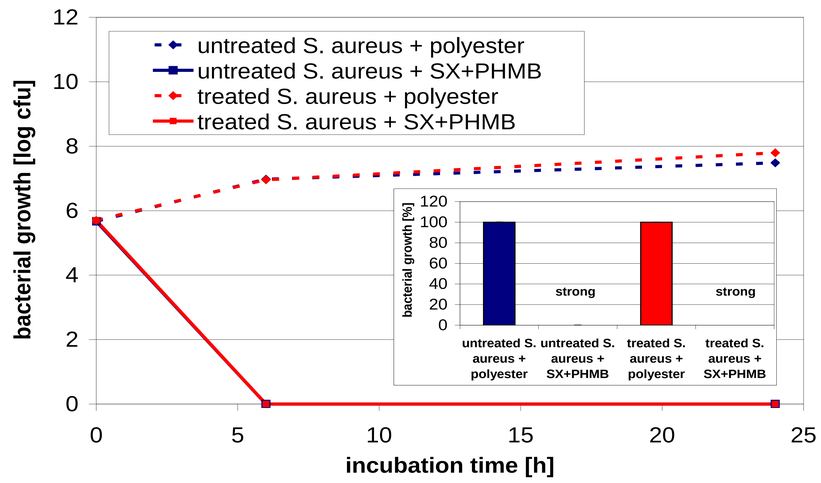

Fig. 4: Testing of the antibacterial activity of a polihexanide-containing wound dressing according to the JIS L 1902 against untreated and polihexanide adapted S. aureus (mean SE).

Conclusions

The IC_{50} for silver nitrate was found to increase with repeated treatment of S.aureus. Polihexanide on the other hand showed a much lower potency to induce adaptation in S. aureus. Furthermore, the antibacterial activity of a polihexanide-containing wound dressing against PHMB-treated and untreated S. aureus tested according to the JIS L 1902 was not altered. These results indicate that the clinically very effective silver-based products are microbicidal but should be used for short-term only in critically-contaminated or infected wounds due to a possible risk of adaptation after a longer treatment. Alternatively, polihexanide seems to be a valid option for an antimicrobial substance in wound dressings for treating chronic wounds as it possess a low risk to induce adaptation and shows a high biocompatibility

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