Specific lysis of methicillin susceptible and resistant \textit{Staphylococcus aureus} by the endolysin \textit{Staphefekt SA.100\textsuperscript{TM}}

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Objectives
New strategies in the treatment of infections are warranted, as antibiotic resistance is emerging. Endolysins originating from bacteriophages combine two characteristics essential for such new strategies: powerful killing of bacteria and limited likelihood of emerging resistance. We describe the \textit{in vitro} activity against methicillin susceptible (MSSA) and resistant (MRSA) \textit{S. aureus} of the endolysin \textit{Staphefekt SA.100\textsuperscript{TM}}. Furthermore, the \textit{in vivo} effect on \textit{S. aureus} skin carriage is described in a case series of rosacea and eczema.

Methods
The activity of \textit{Staphefekt SA.100\textsuperscript{TM}} was evaluated against 28 clinical strains of MSSA and 8 strains of MRSA, and four control strains (\textit{S. epidermidis, S. hominis, S. haemolyticus} and \textit{S. lugdunensis}). Specificity of the activity and dose responsiveness was determined in a lysis assay, incubating $10^6$ cfu/ml in phosphate buffered saline (PBS) with a concentration range of \textit{Staphefekt SA.100\textsuperscript{TM}} (0-120 microgram/ml) and measuring optical density (OD) during one hour. The bactericidal activity was measured by counting the drop in cfu/ml six hours after incubating $10^6$ cfu/ml with 0 and 30 microgram/ml \textit{Staphefekt SA.100\textsuperscript{TM}} in PBS. Minimal inhibitory concentrations (MIC) were determined in tryptic soy broth (TSB) with a starting concentration of $10^6$ cfu/ml. After 24 hours of incubation, growth was visually determined.

Skin cultures were taken in seven patients with rosacea and two patients with eczema to study the effect of \textit{Staphefekt SA.100\textsuperscript{TM}} on lesional skin carriage of \textit{S. aureus}.

Results
A dose dependent reduction in OD was observed with all \textit{S. aureus} strains. The mean reduction in OD did not differ between MSSA and MRSA (58+/−11.6% vs. 65+/−4.1% with 30 microgram/ml, mean +/- SD, p>0.05; figure 1). Only 1-15% reduction was observed with the four control strains. A similar 100-fold reduction of viable bacteria was seen with both MSSA and MRSA (0.8+/−0.7% vs. 0.6+/−0.5%; p>0.05). MIC’s did not differ for MSSA and MRSA, with a median MIC of 64 microgram/ml.

Three of seven rosacea patients and two of two eczema patients were lesional \textit{S. aureus} carriers. After the local application of \textit{Staphefekt SA.100\textsuperscript{TM}}, \textit{S. aureus} was eradicated from the lesion, while other skin inhabitants remained present.

Conclusion
The \textit{in vitro} data show that lysis of \textit{S. aureus} by \textit{Staphefekt SA.100\textsuperscript{TM}} is dose dependent, specific and efficient. MSSA and MRSA are equally susceptible to the endolysin, and \textit{Staphefekt SA.100\textsuperscript{TM}} is equally effective in killing both methicillin susceptible and resistant strains. The case series furthermore provides evidence of the \textit{in vivo} applicability of \textit{Staphefekt SA.100\textsuperscript{TM}} to specifically eradicate \textit{S. aureus} without disturbing the normal skin flora. These results support further clinical studies in a placebo controlled setting on the effect of \textit{Staphefekt SA.100\textsuperscript{TM}} on \textit{S. aureus} related skin diseases.

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