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Specific lysis of methicillin susceptible and resistant *Staphylococcus aureus* by the endolysin Staphefekt SA.100™

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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 *in vitro* activity against methicillin susceptible (MSSA) and resistant (MRSA) *S. aureus* of the endolysin Staphefekt SA.100™. Furthermore, the *in vivo* effect on *S. aureus* skin carriage is described in a case series of rosacea and eczema.

Methods

The activity of Staphefekt SA.100™ was evaluated against 28 clinical strains of MSSA and 8 strains of MRSA, and four control strains (*S. epidermidis, S. hominis, S. haemolyticus* and *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 Staphefekt SA.100™ (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 Staphefekt SA.100™ 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 Staphefekt SA.100™ on lesional skin carriage of *S. aureus*.

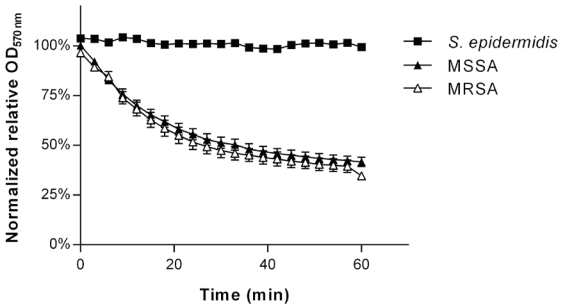

Figure 1. Specific lysis of MSSA and MRSA by Staphefekt™ The mean lytic effect of 30 micrograms/ml Staphefekt on twenty eight strains of MSSA, eight strains of MRSA and one strain of *S. epidermidis* was calculated by normalizing the absolute OD to the matching controls (0 micrograms/ml). A similar reduction in OD was found with MSSA and MRSA, while no significant reduction was found with *S. epidermidis*. (mean +/- SEM)

Results

A dose dependent reduction in OD was observed with all *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 *S. aureus* carriers. After the local application of Staphefekt SA.100™, *S. aureus* was eradicated from the lesion, while other skin inhabitants remained present.

Conclusion

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

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