Experimental study on the pH effect on polyhexanide-containing wound care products

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Introduction

Chronic wounds exhibit higher pH-values compared to acute wounds. It could be shown that the pH in chronic wounds most commonly has a range of 6.5 to 8.5 [1,2]. This alkalization is thought to be due to tissue necrosis and the presence of microorganisms. Therefore, establishing a low physiological pH might be a key factor to aid wound healing [2]. *In vitro* studies showed that wound dressings can have significant effects on the pH [3]. Moreover, the question was raised if wound pH might affect the activity and efficacy of antimicrobial agents. As chronic wounds are frequently colonized by different kinds of microorganisms, the most prominent being *Staphylococcus aureus* and *Pseudomonas aeruginosa* [2], an antimicrobial treatment is often necessary to avoid or battle wound infection. Hence, it is of interest to investigate the influence of the pH on the performance of antiseptics and antimicrobial wound dressings.

Methods

Recently, a study by Braunwarth et al. has shown that the antimicrobial effect of PHMB-containing wound dressings is pH-dependent, while silver-containing dressings possess a similar bacteriostatic effect over a pH-range of 5.5 to 9.0 [4]. These experiments were carried out using the agar-diffusion-test. Thus, the results do not only depend on the influence of the pH on the antibacterial activity but also on the diffusion capacitance of the agent tested under different pH. To further investigate the influence of the pH on the activity of antimicrobial substances and wound dressings it is advantageous to determine microbial growth using microplate-laser-nephelometry (MLN). MLN presents a valuable tool to investigate pH influence on antimicrobial activity, as it allows high-throughput-screening, incubation over a prolonged time period, and in-situ-monitoring of changes in the dose-response curves [5]. The IC_{50}, the halfmaximal inhibitory concentration, calculated from the dose-response-curves, can be used to evaluate the antimicrobial efficacy at different pH (5.0, 6.0, 7.0, 8.0, and 9.0).

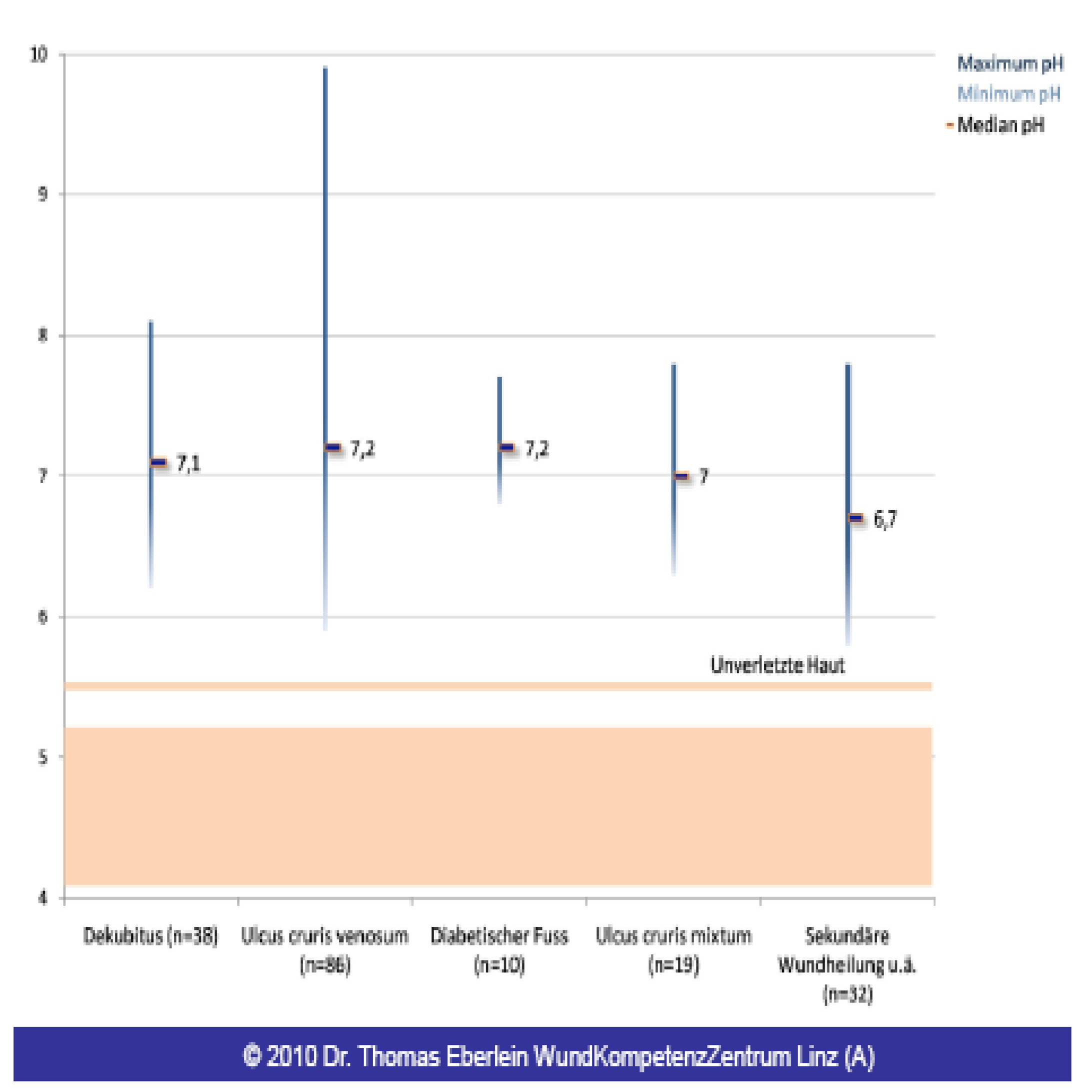

Figure 1: Chronic wounds display a shift towards higher pH values compared to acute wounds [6]. This is called the 'alkaline shift' and is thought to be due to tissue necrosis and the presence of microorganisms.

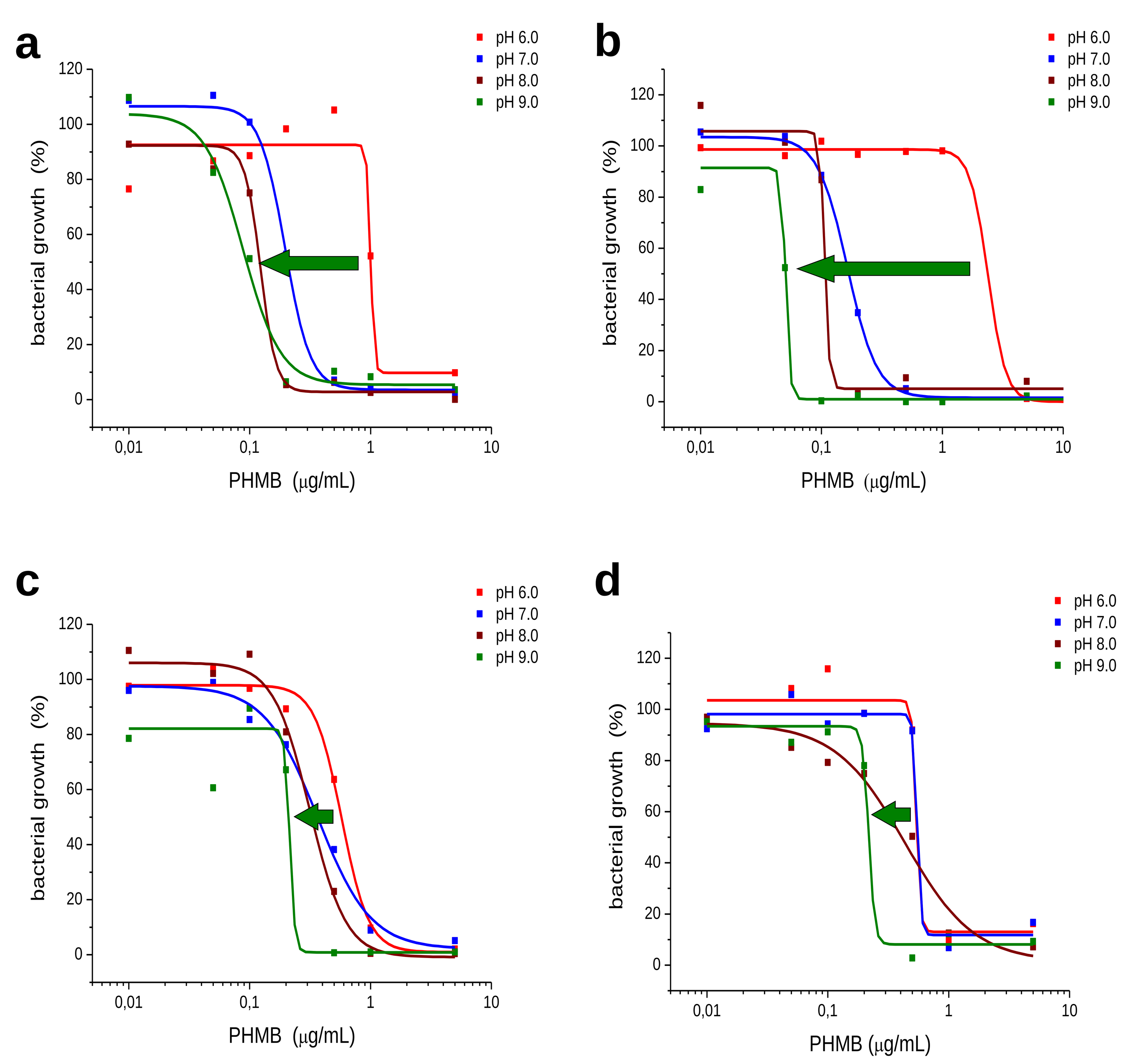

Figure 2: Effect of the pH on the dose-response-curves of *S. aureus* against Lavasept (a) and Prontosan (b) as well as for *P. aeruginosa* against Lavasept (c) and Prontosan (d). Data presented as mean. Green arrows indicate a shift towards lower IC_{50} values with increasing pH.

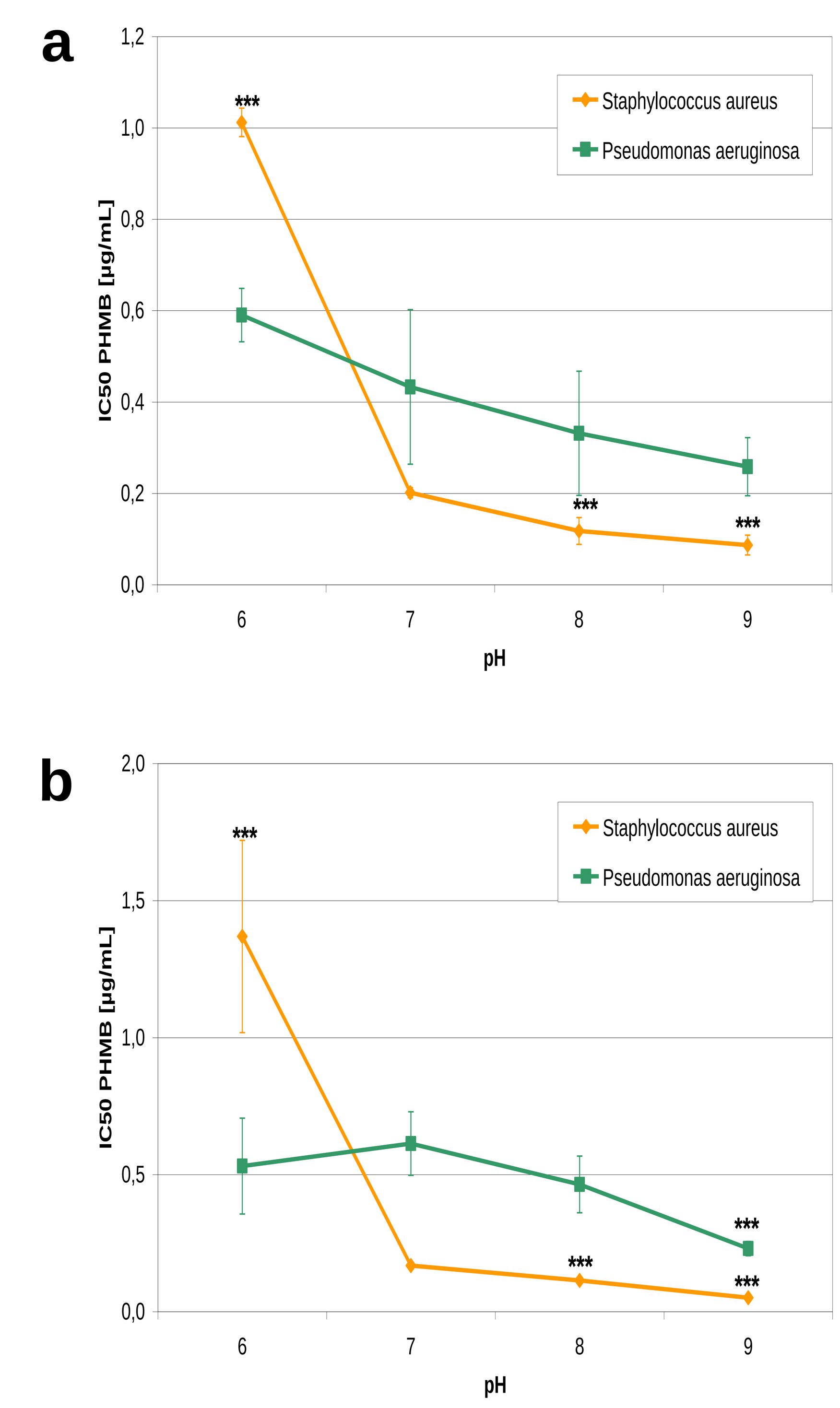

Figure 3: pH-dependency of the IC_{50} values for Lavasept (a) and Prontosan (b). Data presented as mean ± SE, n=5.

Results

Staphylococcus aureus and *Pseudomonas aeruginosa* exhibited an increasing sensitivity against polihexanide with rising pH. The increase of the efficacy of polihexanide can be explained by its polycationic nature. At physiological pH, the positively charged groups of polihexanide can bind rapidly to the negatively charged bacteria surface. This causes membrane damage and the death of the bacteria. In an alkaline solution the polycations become protonated, which leads to a higher charge density intensifying the binding to the bacterial surface. The efficacy of polihexanide was not affected regardless of which formulation was used, no significant differences between Lavasept® and Prontosan® were observed at pH 7.0 to 9.0.

Conclusion

Our results showed that the efficacy of polihexanide was not affected regardless of which formulation was used, no significant differences between the tested antimicrobials* were observed at pH 7.0 to 9.0.

References

1. Wild T, et al. Nutrition. 2010; 26 (9): 862-866
2. Dissemond J, et al. Hautarzt. 2003; 54: 959-965
3. Weindorf M, et al. ZfW. 2007; 12 (2): 1-4.
4. Braunwarth H, et al. HygMed 2011; 36-10:393-398
5. Seyfarth et al. Int J Pharmaceut 2008; 353 (4): 139–148
6. Eberlein T. DGfW congress 2010

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