The safety profile of PHMB. An Alternative Antimicrobial

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Introduction and Methods

Topical antimicrobials are fast becoming a preference in managing wound infection, because of the known bacterial resistance problems associated with the long term use of antibiotics. Topical antimicrobial agents differ from antibiotics in that they are able to target the bacterial cells and therefore lower the risk of resistance[1,2]. PHMB (polyhexamethylene biguanide) is one topical option which has a proven broad spectrum antimicrobial activity.

This poster outlines the toxicity profile of this substance through biocompatibility end point testing in accordance with ISO10993-1, literature reviews and *in vitro* testing.

Literature Review and Discussion

PHMB has two posited modes of action:

1. Disruption of bacterial membranes preventing growth and multiplication of the bacteria.
2. Disruption of bacterial chromosomes which are not protected by nuclei (unlike human cells) resulting in cell death. This mechanism suggests that the compound could be selective to bacteria as the nuclei in mammalian/human cells offer protection to the genetic material.

The NOAEL (no-observed-adverse-effect-level) is a very high at 200mg/kg/bodyweight/day, and in a study of chronic intake of 100mg/kg/bodyweight/day over two years no adverse reactions were seen, demonstrating high tolerance for the compound[3].

The biocompatibility index of PHMB has been seen to outperform PVP iodine, chlorhexidine and triclosan against *E.coli* and *S.aureus*[5]. This index is calculated using antimicrobial efficacy vs. cytotoxicity. This shows that PHMB was more damaging to bacteria than to fibroblasts in comparison with the other antimicrobials suggesting a good efficacy to safety ratio.

Kramer et al[3] showed no evidence of mutagenicity or carcinogenicity in either *in vivo* or *in vitro* testing, further corroborating the safety of the compound.

Willenegger[4] determined with detectability of 10ppm that no uptake of the compound could be proven by skin or wounds suggesting that the body does not actively absorb the compound.

References:

1. Drosou A. Antiseptics on wounds: an area of controversy. Medscape Wounds 2003;15. Available from: www.medscape.com/viewarticle/456300_1 (Accessed Sept 28th 2022)
2. Leaper DJ, Schultz G, Carville K, et al. Extending the TIME concept: what have we learned in the past 10 years? Int Wound J 2012;9 Suppl 2:1–19.
3. Hübner NO, Kramer A. Skin Pharmacol Physiol 2010;23(suppl 1):17–27;
4. Willenegger, H. Lokale Antiseptika in der Chirurgie-Wiedergeburt und Weiterentwicklung.Unfallchirurgie 20, 94–110 (1994).
5. Müller and Kramer Journal of Antimicrobial Chemotherapy (2008) 61, 1281–1287
6. Internal report: P3774R Silicone PHMB Biological Evaluation Report

Biological Testing Results[6]

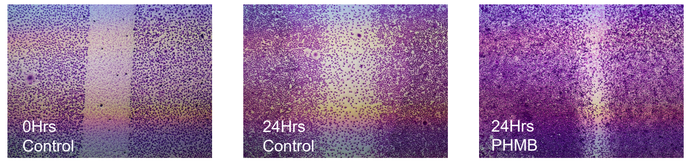
Cytotoxicity (potential to cause cell death)	Sub-Acute & Sub-Chronic Toxicity (Toxicity profile)	30 day Subcutaneous Implantation (Toxicity within the body)
NON-CYTOTOXIC	NO BIOREACTIVITY	NO EVIDENCE OF TOXICITY

In Vitro Testing Scratch Assay

An *in vitro* scratch assay was performed in accordance with the guidelines stated in ISO 10993-5, Biological Evaluation of Medical Devices, Part 5: Tests for *in vitro* Cytotoxicity.

L929 mouse fibroblast cells were used to create confluent cell layers and a scratch applied to simulate a break in wound integrity. Samples were treated with the test product and left for 24hrs.

Microscopy was used to image the cells which demonstrates the fibroblast cells exposed to extracts of PHMB Silicone Foam were able to close the scratch wound.



Conclusion

A review of available data demonstrates that PHMB devices are safe to use in wound care over a prolonged contact duration with no known resistance, and have a safe toxicological profile. This is because the suggested mode of action means PHMB may be ‘selective’ to bacterial cells and unable to affect, and therefore unlikely to harm, mammalian cells (human cells). PHMB is able to disrupt the bacteria cells which are causing the infection and kill the organism, therefore allowing the wound to progress.

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