



Selective condensation of bacterial chromosomes by PHMB

Experimental study

WHAT WAS INVESTIGATED?

The study investigated mechanisms of action of polyhexamethylene biguanide (PHMB) in selectively killing bacteria over host cells.

In addition to the accepted model that the antimicrobial effect of PHMB is primarily due to destruction of the microbial membrane, other aspects such as bacterial invasion and the effect on cell division was investigated.

WHAT WAS THE RESULT?

Main Result: It was shown, that PHMB entered into the cells of a range of bacterial species.

PHMB treated bacteria displayed cell division arrest and chromosome condensation.

PHMB also entered mammalian cells, but was entrapped into endosomes and excluded from nuclei.

WHAT PRODUCT REFERENCE DOES THE STUDY HAVE?

As part of the intervention package, the following products were used: polyhexamethylene biguanide (PHMB) was from Arch Chemicals (UK) and Tecrea Ltd, (UK). All other materials used are specified in the original paper.

The broad range of action of PHMB and the selective effect on bacterial chromosomes could be responsible for an antimicrobial action that makes the development of resistance unlikely.





BACKGROUND

PHMB is an antimicrobial biocide with a broad spectrum of activity. It kills bacteria, fungi, parasites and certain viruses with a high therapeutic index. Its use is widespread in clinics, private households and industry.

Despite decades of extensive use and efforts to identify acquired resistant mutants, no resistance to PHMB has yet been detected.

GOAL

The aim of the study was to decipher the mechanisms of action leading to the selective antimicrobial effect of PHMB.

DESIGN AND METHODS

In order to understand more about the bacteria-selective mode of action of PHMB, the following aspects were investigated:

- the activity of PHMB according on the bacterial cell membrane
- the ability of PHMB to enter bacteria
- the effect of PHMB on bacterial chromosomes and/or cell division
- the dependence of PHMB-mediated antibacterial effects of stress response pathways
- the suppression of antibacterial effects of PHMB by DNA ligands
- the ability of PHMB to enter mammalian cells

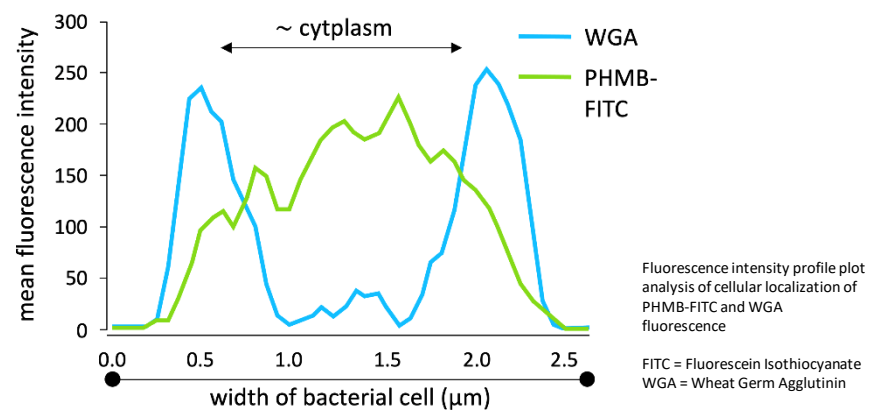
In accordance with the research question, all investigations were carried out experimentally.

RESULTS

Experimental examinations showed that

- PHMB seems not to disrupt bacterial cell membrane as the main antibacterial mechanism
- PHMB arrests cell division and condenses bacterial chromosomes
- PHMB-mediated antibacterial effects are independent of stress response pathways
- PHMB condenses bacterial chromosomes *in vitro*
- the antibacterial effects of PHMB are suppressed by a dsDNA ligand
- PHMB enters mammalian cells but is excluded from nuclei

Cellular localisation of PHMB and WGA in bacterial cells



CONCLUSION

In contrast to the accepted model of microbial membrane disruption by PHMB this observations suggests DNA binding as an alternative antimicrobial mechanism.