Complex in vitro models and advanced drug delivery systems as a complementary strategy for improving drug transport across bacterial barriers and maximizing bacterial bioavailability

Mulla G. [1,2]

Kamal M.[1,2], Bali A. [1, 2], Bankar N. [1, 2] Aliyazdi S. [1, 2], Loretz B. [1]., Schneider-Daum N. [1], Lehr C.-M. [1, 2]
[1]*Helmholtz Inst. Pharm. Forschung Saarland (HIPS), Drug Delivery across Biological Barriers, Saarbrücken, Germany*
[2]*Saarland University, Pharmacy, Saarbrücken, Germany*
Organization, Address, City, Country (Calibri 10)
Glorjen.Mulla@helmholtz-hips.de

Abstract

The increasing antimicrobial resistance has dwelled the attention to hitherto almost unnoticed biological barriers such as the biofilm matrix, the bacterial cell envelope, and intracellular bacterial metabolism [1]. Overcoming these biobarriers requires thorough in vivo studies that are often difficult from a physiological, regulatory and ethical point of view. Therefore, in vitro models are needed as a test platform for advance drug delivery systems. The new paradigm is to increase bacterial bioavailability and minimize bacterial resistance [2].
A recent model of our group employs bioprinting of the bacterial biofilms on air-interface cultured lung cells as a viable strategy to obtain read outs from both the bacteria and the host [3].
Complementary, calcium peroxide nanoparticles were developed to co-deliver tobramycin as an antibiofilm strategy. The particles displayed not only increased biofilm susceptibility but also potential antimicrobial activity. In clinical settings however, tobramycin is often administered with a β-lactam antibiotic to synergistically increase the bactericidal efficiency. Nevertheless, this strategy is not sustainable as it contributes to increased antibiotic resistance. To reduce the risk, a potential strategy is to take advantage of the so-called cell-penetrating peptides that facilitate drug uptake via membrane permeabilization.
Predictive models can also be a utility in the context of delivery systems and novel anti-infective development. By coating Transwells® membranes with polymeric hydrogels or outer membrane vesicles we could simulate the drug transport across the Gram-negative cell wall. Additionally, a simple but yet effective anti-infective degradation assay was developed to evaluate the anti-infective inactivation capabilities of bacterial lysates. Such assay can be applied to a wide range of bacteria and in a timely manner, AI machine learning trained with an adequate input of data could produce meaningful read outs leading to an in silico predictive model and aid the development of novel anti-infectives.

References

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