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A wide-spectrum antimicrobial coating to fight multi-species biofilms in ventilator-associated pneumonia infections

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Introduction

Ventilator-associated pneumonia (VAP) is currently one of the top five most common nosocomial infections and it has been associated with prolonged hospitalization and high morbidity and mortality rates [1]. The use of an endotracheal tube (EET) constitutes the major risk factor for the development of this condition, since it is the airway access point for microorganisms. Indeed, microorganisms' migration along and within the inside of the EET results in a so-called biofilm which, combined with a network of secretions, will be ultimately leaked down to lungs [2]. Biofilm formation is a crucial step in the pathogenesis of VAP, as microbial cells within a biofilm encase themselves in a self-produced matrix of extracellular polymeric substances, conferring them protection against both antimicrobial treatments and the host immune system. Furthermore, the polymicrobial nature of biofilms formed on the surfaces of ETT has been increasingly addressed [3].

Experimental Methods

This study aimed to design a wide-spectrum antimicrobial coating to impart endotracheal tubes with the ability to prevent the adhesion and subsequent biofilm formation of several microorganisms commonly associated to VAP, without compromising the viability of lung cells. For that, ciprofloxacin (CIP) and chlorhexidine (CHX), two compounds with different action spectra, were co-immobilized on polyvinyl chloride (PVC) surfaces to obtain a dual-drug release antimicrobial coating. Immobilization was performed using a one-step polydopamine (pDA)-based approach, in which PVC substrata were simply immersed on a solution of dopamine dissolved together with CHX and/or CIP, allowing their incorporation throughout the full thickness of the pDA film.

Results and Discussion

The antimicrobial performance of modified surfaces was evaluated against 5 bacterial species (*Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Staphylococcus epidermidis*) and 1 yeast species (*Candida albicans*) as individual, dual and triple consortia. Regarding the single-species colonisation of PVC surfaces, results showed that after 24 h of exposure, co-immobilization of CHX and CIP caused a significant reduction (more than 4 Log) in the number of bacterial cells adhered to the surfaces, while being less efficient against the adhesion of *C. albicans* (0.5 Log). It is worth mentioning that the combination of CIP and CHX in the proposed coating resulted both in a synergic effect against *P. aeruginosa*, *A. baumannii* and *C. albicans* and in a facilitative effect against all tested species. Coatings were also tested against the dual adhesion of *P. aeruginosa in* consortium with all tested species. In general, results showed that the antimicrobial effect observed for each species was not compromised by the presence of any other species. Inhibition of *C. albicans* was actually more effective (approximately 2 Log reduction) when combined with *P. aeruginosa*. When the antimicrobial coating was exposed to a triple consortium comprised by *P. aeruginosa*, *S. aureus* and *C. albicans*, its antimicrobial effect against bacterial species was not compromised and it was able to inhibit the adhesion of yeast by about 1 Log. In terms of biocompatibility, the amount of CHX and CIP released from the surfaces did not compromise the growth of lung epithelial cells. Surfaces functionalization with CIP and/or CHX was confirmed by SEM, AFM and contact angle measurements.

Conclusion

In conclusion, the combination of CIP and CHX, using dopamine chemistry, results in a coating with antimicrobial activity towards a wide spectrum of microorganisms commonly associated to VAP. Therefore, this approach holds great potential to be applied in EET, proving to be important in the fight against VAP.

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