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A biodegradable and antimicrobial polymer coating for metal implants for the prevention of prosthetic joint infection

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SUMMARY

The aim of this project is to produce antibiotic-loaded poly (lactic-co-glycolic acid) (PLGA) polymer films by airbrush onto orthopaedic implants to address prosthetic joint infections (PJIs). It covered the development of an airbrush spray-coating technique, the selection and assessment of polymers and antibiotics, sample characterisation and antibacterial studies. The initial results are encouraging as the PLGA coatings exhibited a sustained drug release pattern and antibacterial ability against causative pathogens. Moreover, these PLGA coatings also possessed rapid degradation within 4 weeks which could provide favourable conditions for osseointegration. Furthermore, cytotoxicity assessment of final coatings will need to be conducted to ensure biocompatibility, as well as to determine the effect of each coating on osseointegration. Finally, the development of alternative coating techniques which are more cost-effective and suitable for large scale production might be the direction of future research.

INTRODUCTION

PJI can be defined as infections that occur in the joint prostheses and adjacent tissues after total joint replacement surgery. (Tande AJ ,2018) The consequences of PJI are debilitating. It can cause pain, seriously affecting the function of the joints, influence the quality of life or even lead to death. So far, clinical studies show that there are many different types of microorganisms, including bacteria (both Gram positive and Gram negative) and fungi, that can induce postoperative PJI. (Li, Z. L, 2018)

In terms of PJI prevention strategies, producing functional coatings on metal substrates holds considerable promise. (Franceschini, M, 2020) An ideal polymer coating should not only be able to exhibit functions such as surface adhesion prevention, bactericidal and osseointegration promotion, but also possesses desirable properties like non-toxicity, high biocompatibility and biodegradability. This project aims to produce rapidly degradable PLGA coatings which can deliver antimicrobial performance, to prevent PJI and without adversely obstructing the osteointegration process between bones and prostheses.

MATERIALS AND METHODS

Materials: poly (lactide-co-glycolic acid) (Resomer RG 502H, Mw 7000-17000), gentamicin sulphate (potency ≥ 590 μg), tetrahydrofuran (≥99.9%) Sigma-Aldrich (Poole, UK). levofloxacin (98%) Alfa Aesar. Mueller-Hinton broth (MHB), phosphate-buffered saline (PBS), soya casein digest lecithin polysorbate broth (SCDLP) were supplied by Oxoid (Basingstoke, UK). Methods: Thin polymer film-coated titanium with antibiotic loading were manufactured by airbrush spray coating technique. Then, sample

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characterisation and antibacterial assessments were also carried out.

RESULTS AND DISCUSSION

In this project, air brush spray coating technique was chosen for the coating process, the ease and simplicity of the employed method makes it applicable for coating of several materials. PLGA was dissolved in tetrahydrofuran (with heating at 70℃). The hot polymer solution was then fed into the airbrush feed cup and sprayed onto titanium samples.

Subsequently, a series of tests such as sample characterisation and drug release study were carried out to evaluate the applicability of PLGA coatings on titanium substrates. In terms of drug release study, PLGA exhibited a sustained drug release pattern as ***Fig.1.*** shows. Specifically, PLGA coatings displayed a small burst release during the first 4 hours of release amounting to 10% of total loaded levofloxacin, followed by a gradual release of 75% of its complete antibiotic content over the next 5-17 days. This drug release pattern implied PLGA coating is a very ideal antibiotic delivery system, which is capable of providing not only acute protection from early infection in the most vulnerable stage, but also constant protection to prosthetic joints for up to two weeks in both healthy and inflamed joint pH environments.

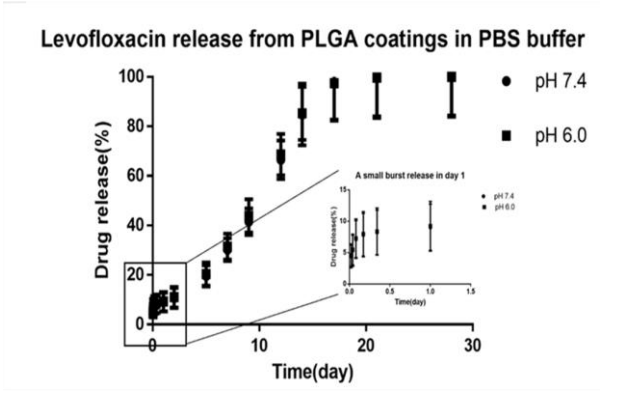

Fig.1. *Release of levofloxacin, as a percentage of total drug loading, over 30 days in PBS at pH 7.4 and 6.0 at 37℃.*

Furthermore, ***Fig.2.*** shows the results of *in vitro* bacterial adherence test of antibiotic-loaded PLGA samples against 3 most common PJI-causing pathogens. After 4h and 24h, there were no viable bacteria detected on surfaces of levofloxacin-loaded samples. In addition, gentamicin-loaded PLGA films also effectively inhibited the adhesion of *S. aureus* and *E. coli*, except for *MRSA* because of its gentamicin resistance.

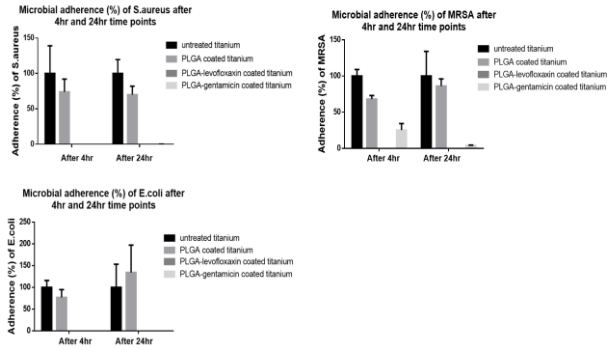

Fig.2. *The microbial adherence (%) of S.aureus, MRSA and E.coli to PLGA coated titanium, PLGA-levofloxacin coated titanium and PLGA-gentamicin coated titanium relative to the untreated titanium control, after 4 h and 24 h. Columns and error bars represent means ± SD. (n=5). * No column indicates no viable bacteria were detected*

CONCLUSIONS

Overall, the incorporation of antibiotics into PLGA produced potent antimicrobial and biodegradable coatings for titanium surfaces. Further studies, assessing cytotoxicity and osseointegration will be carried out to further investigate this approach.

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