AN INTEGRAL APPROACH FOR TAILORING OF IMPLANT-TISSUE INTERFACE: PLGA-PARYLENE C MULTIFUNCTIONAL COATING

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Introduction

The challenges of metal implant engineering are to introduce specific properties which result in optimization of the metal-implant tissue interface. Among various approaches, one of the most explored is coating metal implants with a polymer which can be additionally provided with functions essential for a long-term implantation success, namely: anti-corrosive, biocompatibility, anti-infection and therapeutic.

Extensive research worldwide is carried out on improving biocompatibility of implant surfaces in terms of osteoblasts adhesion and anti-bacterial function. Furthermore, the most common post-operation complications include prolonged inflammation and biomaterial-centered infection. For these reasons, main strategies rely on surface functionalization and/or controlled local drug release from the inserted implant, bringing a number of benefits to patients. The most significant advantages include the target tissue, which reduce the risk of side effects associated with infection as well as oral administration of high doses of medication.

The aim of the study was to develop multifunctional polymer coating based on drug+PLGA/parylene C with four essential functions. The general concept of integrated research is highlighted.

Materials and Methods

Parylene C films were prepared by CVD technique. To generate oxygen-containing functional groups and nanotopography, polymeric samples were modified using oxygen plasma with parameters which enhance its biocompatibility, remaining the bulk properties intact.

For the therapeutic layer preparation, the biodegradable D,L-lactide-co-glycolide copolymer (PLGA) (85/15) was used [1]. PLGA was dissolved in CH_2Cl_2 with ibuprofen or gentamicin and deposited on oxygen plasma modified parylene C with the use of airbrush method. The drug+PLGA/parylene C coating was then thoroughly characterized using surface-dedicated (SEM, μFTIR, LDI-MS) and biological (*in vitro* cells and microbiological tests). In order to identify drugs elution kinetics, *in vitro* drug release studies were carried out. The release data were fitted into kinetic models (first order and Korsmeyer-Peppas) [2].

Results and Discussion

The key functions of the designed coating are the anti-corrosive properties, biocompatibility, anti-infection and therapeutic (FIG. 1). Parylene C micrometric coatings provided superior increase in corrosion resistance (1×10^9 Ω cm^2) when compared with uncoated SS 316L (1×10^4 Ω cm^2) [3]. Surface modification of parylene C caused changes in its chemical composition by generation of functional groups such as –COOH, –OH as well as nanotopography. Fluorescent staining of focal contacts of MG-63 cells together with SEM observations revealed improved biocompatibility of oxygen plasma modified parylene C. The area of focal contacts (FC) was quantified for oxygen plasma treated samples and compared to unmodified parylene C, where the FC level was minor or below the detection limit. The average area of FC was 6.21±1.2 μm^2 which is comparable with the contact area created by cells in the control well of TCP (6.53±1.6 μm^2).

Generated nanotopography, effectively limited the surface area available for bacteria. SEM observations revealed, that early-stage biofilm formation on unmodified parylene C takes place after 4 h of incubation, after the same time interval, on the surface of oxygen plasma treated samples not agglomerated single bacteria cells dominated the picture.

The studies of drug+PLGA/parylene C systems revealed that the drugs molecules remain unchanged upon interaction with the PLGA matrix and the drugs distribution were homogenous. The obtained release profiles revealed that both of the investigated systems (ibuprofen- and gentamicin-loaded) are suitable for prolonged elution up to 21 days. However, they follow different kinetic models. For ibuprofen+PLGA/parylene C samples, the average drug load was 180 μg/cm^2. The drug elution was governed by dispersion and diffusion with non-Fickian transport mechanism. The antibiotic release from gentamicin+PLGA/parylene C was diffusion dominated (quasi Fickian drug migration through porous PLGA matrix), with average drug load 1.5 μg/cm^2.

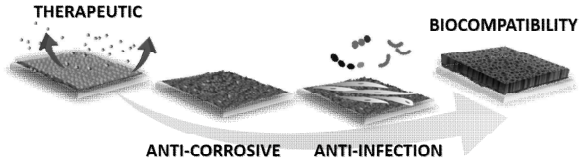

FIG. 1. The overview of the conducted research strategy based on four key functions essential for implant long-term success.

Conclusions

Oxygen insertion into the parylene C surface provides a suitable substrate for MG-63 cells attachment and spread while nanoroughness effectively limits risk of infection. Modified parylene C allows also further tuning of the coating functionality by bonding of a biodegradable drug–loaded PLGA results in prolonged in-site drug release up to targeted 21 days.

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References

[1] P. Dobrzyński, J. Kasperczyk *et al.*, Macromolecules 34 (2001) 5090-5098.
[2] P. Costa, J. Lobo, Eur. J. Pharm. Sci. 13 (2001) 123-133.
[3] M. Cieślik, S Zimowski *et al.*, Mater. Sci. Eng. C 32 (2012) 2431-2435.