BIOLOGICAL PROPERTIES OF NEW CHITOSAN-FATTY ACIDS DERIVATIVES

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[Engineering of Biomaterials, 128-129, (2014), 107-108]

Introduction

Chitosan is a natural polysaccharide that is nontoxic, biodegradable, biocompatible, and has antimicrobial properties. Due to the presence of amine groups, chitosan is amenable to chemical modification, which can widen the range of potential applications.

In our previous work, we modified chitosan obtaining chitosan-fatty acid derivatives with improved physical and antimicrobial properties. The aim of this work was to investigate the blood compatibility of the chitosan-fatty acid derivatives.

Experimental

Materials and coating preparation

Chitosan-fatty acid derivatives were obtained by N-acylation of low molecular weight chitosan (CH) (ChitoClear 4300 – hqg10, Primex) with linoleic acid (LA), α-linolenic acid (ALA) (Sigma-Aldrich), and dilinoleic acid (DLA) (Croda, The Netherlands), natural hydrophobic compounds, intended to improve the physical and biological properties of chitosan. Synthesis details and characterization of antibacterial properties of the derivatives, CHLA, CHALA and CHDLA, are described elsewhere [1], [2]. Coatings were prepared by dip-coating activated polyester (copolymer of poly(ethylene terephthalate) and dilinoleic acid blocks, PET/DLA). Before coating, the surface of polyester disks was treated with argon plasma and oxygen flushing (FIG. 1, step I) to create functional groups on the surfaces. Next, disks were dipped in aqueous EDC (step II), in order to activate carboxylic groups. Carbodiimide catalyst promotes the reaction of carboxylic groups with the amine groups of chitosan in the next step (step III), the dip-coating in CH or Chitosan-FA solutions (in 1% acetic acid).

Hemocompatibility tests

The study was conducted with human whole blood (HWB), from the Regional Blood Center in Katowice, stored in citrate/phosphate/dextrose/adenine (CPDA). Flat discs (8 mm diameter) were rinsed in deionized water, dried, and sterilized with ethylene oxide, followed by contact with HWB for 24 h at 37°C. The two test groups were: negative control, HWB without contact with the test materials, and material group, samples contacted with the HWB. Hemocompatibility was evaluate by measuring:

1. free hemoglobin concentration in plasma, fHGB (g/L); measured using a spectrophotometer
2. morphological parameters of blood and red blood cell indices; measured with a hematology analyzer
3. blood cell morphology
4. the degree of hemolysis; determined by calculating the index of hemolysis (IH)

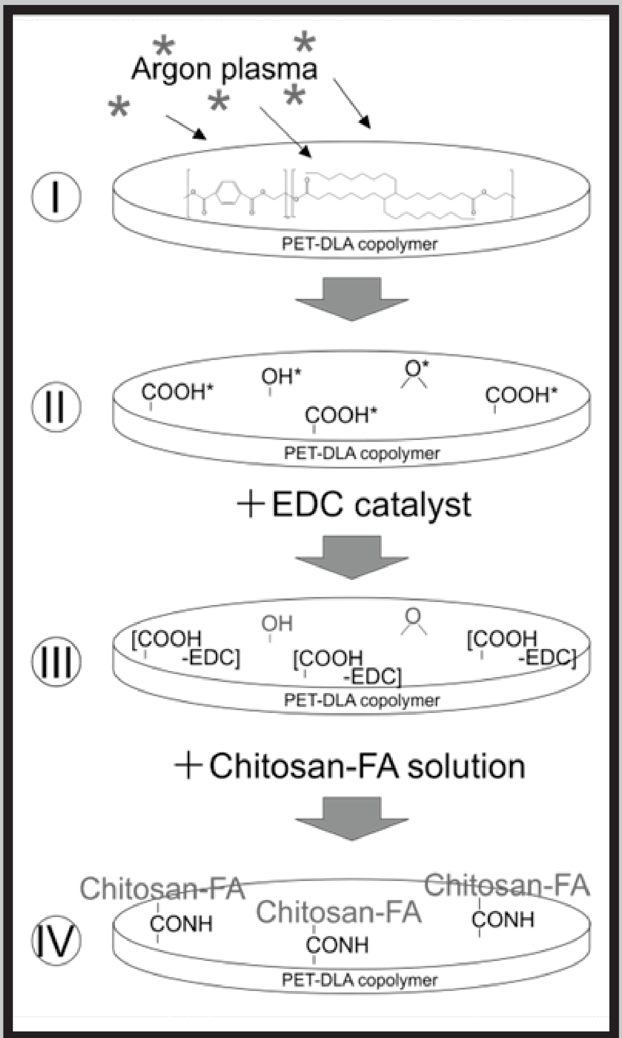

FIG. 1. Coating process.

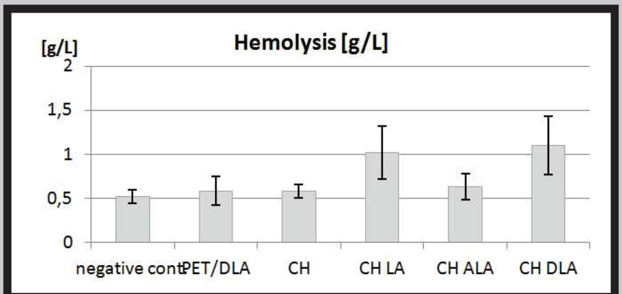

FIG. 2. Concentration of free hemoglobin released into the plasma.

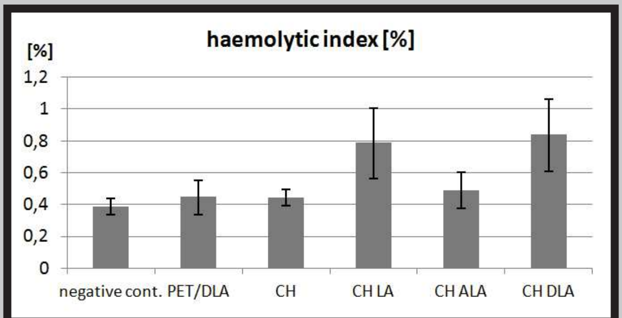

FIG. 3. The index of hemolysis for negative control, referenced materials PET/DLA and chitosan and its derivatives coating.

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Results and discussion

The free hemoglobin concentration in plasma from HWB exposed to uncoated PET/DLA samples, chitosan, and chitosan-ALA coatings was similar to that of the negative control. Samples coated with chitosan-DLA and chitosan-LA resulted in the higher concentrations of fHGB, around 1,0-1,1g / L (FIG. 2).

The Index of Hemolysis for all material is summarized in FIG. 3. The calculations were performed according to standard ASTM F 756-00. On the basis of the IH value, the degree of hemolysis was considered to be:

I. IH = 0-2% : not hemolytic,
II. IH = 2-5% : slightly hemolytic,
III. IH> 5% : hemolyzing.

Based on the above ranges of hemolysis, all of the tested materials can be classified as not hemolytic, because the IH did not exceed 2%.

Summary

In this study, we examined the hemocompatibility of chitosan-fatty acid derivative coatings on plasma-activated PET/DLA. In general, the hemocompatibility studies indicate that the tested materials are not hemolytic; however, the ALA derivative may be particularly promising for further testing.

Acknowledgements

This project has received funding from the National Science Centre grant N N507 319440 (chitosan derivative synthesis). Additionally, the project received partial financial support from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no. 286174 "UNITISS". We thank the Foundation for Cardiac Surgery Development in Zabrze for performing blood compatibility tests and dr A. Piegat and dr P. Sobolewski for useful discussions.

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OSTEOSYNTHESIS ON THE BASIS OF RESORBABLE POLYMERS IMPLANTS - SELECTED PROBLEMS

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Abstract

Use of bioresorbable materials in bone surgery opens up new possibilities in treatment of injuries and orthopaedic illnesses. Lack of necessity for implant removal surgery enables faster treatment and substantial reduction in costs of treatment. In recent years, these advantages have caused growing interest in materials of this type. It must be noted that bioresorbable materials in most cases are based on macromolecular materials – polymers which have completely different mechanical characteristics than traditional materials used in bone surgery. Bioresorbable properties give enormous possibilities but also present difficult challenges related to construction of new types of implants based on materials of this type.

Full characteristics of new materials is indispensable in construction process, especially of mechanical properties and surface properties. The latter is responsible for contact with biological environment and bioactivity is determined on the basis of hydroxyapatite precipitations amount on material surface. In case of polymer based composites, influence of phases in powder and fibre form on properties is fundamental to be proved. Addition of particle modifier into polymer matrix causes reduction in strength of polymer. This phenomenon is mostly associated with homogenic particle distribution difficult to be achieved in case of higher filler content. However biological interplay is insufficient by low filler contents. Therefore in the below presented investigations different filler contents were applied and their influence on mechanical properties was investigated to achieve compromise between mechanical properties and bioactive, antibacterial or anti-inflammatory effect of the applied particles. Acquaintance with these results allowed for elaboration of full range of material and constructive solutions for implants in bone surgery.

Biodegradable biopolymers have low mechanical properties (Young's modulus, strength, viscoelasticity). Construction process of bioresorbable implants requires to be completely changed in way of conduction. Computer simulation based investigations of stress-strain characteristics is necessary to be carried out in each stage of research. Bigger cross-sections and different shapes of implants are required to achieve suitable stiffness.

Application of bone screws made of resorbable materials requires design of these elements from the bottom up. Design of optimal shape of screw thread and point of contact between screw head and bone plate is particularly important.

9 different implants were designed within the confines of conducted research – including for tibia, humerus, radius, ulna, phalanges, clavicle, calcaneus, pelvis and metatarsus. Stress values were determined in analyzed implants. Acceptable loads were determined for individual types of plate.

Plates made of PLA can bear small loads and play role mainly as grasping and holding bone element. In most cases additional immobilization of operated bone is required in order to prevent plate or screw destruction. In case of stabilization function for resorbable materials – as many screws as possible are recommended – thanks to it, screws are less loaded and the plate-bone system is more immobilized.

[Engineering of Biomaterials, 128-129, (2014), 108]