ALGINATE-BASED HYDROGELS MODIFIED WITH GRAPHENE OXIDE AND HYDROXYAPATITE FOR CARTILAGE TISSUE REGENERATION

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Introduction

Nowadays, one of the most common problems connected with the human healthcare are cartilage tissue failures. This is related to the fact that people live longer and are more physically active. The articular cartilage is exposed mainly to strong shear and compression stresses even during basic activities such as walking. In addition it has very low self-regeneration capacity. In order to deal with this issue, new solutions of tissue engineering are proposed [1].

3D scaffold needs to meet some requirements, such as proper mechanical properties, biocompatible chemical composition, biodegradability and porosity. Good regeneration process of cartilage depends on these issues [2].

The most commonly used materials for this purpose are hydrogels. The main advantages of these materials are the structure similar to living tissue, biocompatibility, and ability to absorb a large amount of water. They can support viability of chondrocytes and synthesis of ECM [1].

Recently, alginate hydrogels became very popular for various biomedical applications. Sodium alginate (SA) is a natural polysaccharide obtained from brown algae. It consists of β-D-mannuronic acid (block M) and α-L-guluronic acid (block G) connected by glycoside bond (FIG. 1) [3].

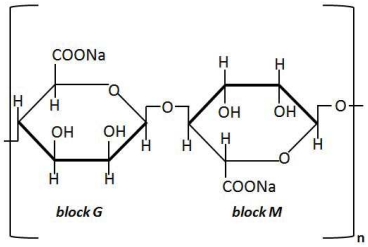

FIG. 2. The structure of sodium alginate.

In the presence of divalent cations (mainly Ca^{2+}) alginate transforms into a gel with the so-called "egg-box" structure [3].

Despite of many advantages, sodium alginate shows poor mechanical properties, strong hydrophilicity, poor thermal stability and limited bioactivity; therefore, its modification is needed [2].

In this work, sodium alginate was reinforced by graphene oxide (GO) and hydroxyapatite (HAp).

Interaction between sodium alginate and GO is possible between functional groups (such as carboxyl, hydroxyl and carbonyl) on the surface of the GO and alginate chains. Ege et al. found that that addition of GO improves the mechanical, biological and rheological properties of the polymer [4].

In case of HAp, it is desired to provide a good connection with the subchondral bone, especially with defects in the bulk of cartilage. It is the result of high biocompatibility, bioactivity and good osteoconductive properties as well as immunogenic one. Moreover, the growth of HAp surface results in advantageous changes on the biomaterial surface, what improves biological properties such as adhesion, proliferation and osteointegration [5].

Materials and Methods

Sodium alginate in the form of powder *(Acros ORGANICS)*, dehydrated calcium chloride in the form of powder *(POCH Avator Performance Materials Poland S.A.)*, graphene oxide in the form of paste *(Institute of Electronic Materials Technology)* and hydroxyapatite *(mkNano)* have been used in hydrogels preparation.

Two series of samples (one with GO and one with HAp) were prepared in the following way: (1) aqueous solution of sodium alginate (25 ml, conc. 3%) was poured into a polypropylene container; (2) GO of concentration 0,1-3% and 1-30% of HAp was dispersed into 5 ml of distilled water and added to the polymer solution; (3) aqueous solution of calcium chloride (90 ml, conc. 0,075M) was added to the polymer solution or polymer solution with additives and mixed.

The sample in the shape of ball was obtained and left for a week in order to obtain fully crosslinked hydrogel.

Properties of manufactured hydrogels such as compression strength, modulus and Poisson ratio *(using ZWICK1435 testing machine)*, chemical stability in *in vitro* conditions *(in PBS and Ringer solution)*, tribology *(using MCR302 rheometer from Anton Paar)* and bioactivity *(in SBF solution by Kokubo method)* were examined. Based on the results, the possibility of usage modified alginate hydrogels in cartilage tissue regeneration was assessed.

Results and Discussion

The obtained results show that the alginate hydrogels modified with graphene oxide nanoparticles as well as hydroxyapatite nanoparticles can be examined by various methods to confirm their regenerative potential. Mechanical and physicochemical properties were investigated to find the appropriate amount of nanoparticles in hydrogel matrix. Modification of alginate hydrogels with HAp and GO significantly affects on mechanical and tribology properties improving the possibility of usage modified hydrogels as materials for frictional surfaces. *In vitro* chemical stability tests confirmed high stability of biomaterials in PBS and Ringer solutions. Bioactivity was examined by SEM observation and EDS analysis which revealed a high content of chlorides on biomaterial surface due to curing method.

Conclusions

The observation of modified hydrogels indicated that sodium alginate hydrogels modified with GO and HAp show regenerative potential for tissue engineering.

Acknowledgments

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