HYDROGELS CROSSLINKED WITH NATURAL COMPOUNDS FOR BIOMEDICAL APPLICATIONS

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Introduction

In modern medicine there is a plenty of space for application of hydrogels, including drug carriers and tissue engineering scaffolds. There is also a wide choice of polymeric materials that can form those specific networks with high water content. Recently, special attention has been given to natural polymers, e.g. starch, cellulose, hyaluronic acid or chitosan. The latter, despite being a natural polysaccharide, is usually crosslinked using toxic compounds, like glutaraldehyde what significantly limits biomedical potential of chitosan-based hydrogels. The solution would be to find an effective crosslinker among non-toxic, natural compounds.
The aim of this study was to examine properties of the chitosan-based hydrogels crosslinked with vanillin. Blends of chitosan, poly(vinyl alcohol) and gelatin were tested along with composites modified with graphene oxide and hydroxyapatite.

Materials and Methods

Blends of chitosan (CS: Sigma-Aldrich, low molecular weight), gelatin (GEL: Avantor Performance Materials Poland S.A.) and poly(vinyl alcohol) (PVA: Avantor Performance Materials Poland S.A.) were prepared with various ratios (1:1:1, 3:1:1, 1:3:1, 1:1:3, respectively) for reference and then blends with two different weight ratios of CS:vanillin (0.5:0.3 marked as van1 and 0.5:0.4 marked as van2) were obtained as well. For composite samples, graphene oxide (GO, 1 wt%: ITME, Poland) and hydroxyapatite (HAp, 10 wt%: Chema Elektromet) were dispersed in the polymer solution using sonication. Samples were subsequently frozen in 24-well plates and freeze-dried (FIG. 1).

FIG. 1. Digital microscope image of freeze-dried 1CS_1GEL_1PVA_GO_HAp sample.

The influence of natural crosslinkers on crosslinking process was studied. Rheological properties of the solutions used to obtain the materials were examined. Mechanical properties of the blends were evaluated in a static compression test, thermal properties were studied by DSC (differential scanning calorimetry) technique. Fourier transform infrared (FTIR) spectroscopy was used to assess the structure. Surface of the samples incubated in simulated body fluid (SBF) was analyzed using a scanning electron microscope (SEM).

Results and Discussion

The rheological studies have clearly shown that the addition of vanillin increases the viscosity of the chitosan solution (FIG. 2). Moreover, FTIR results confirmed that the aldehyde group of vanillin interacts with the amino group of CS via Schiff base reaction, hence creating three dimensional hydrogel network. FTIR revealed also presence of some interactions between CS and GO. Generally, samples crosslinked with higher amount of vanillin (van2) and those with GO were more stable than their respective reference samples. It confirms not only that vanillin can act as crosslinker but suggests also that the GO plates can play similar role.

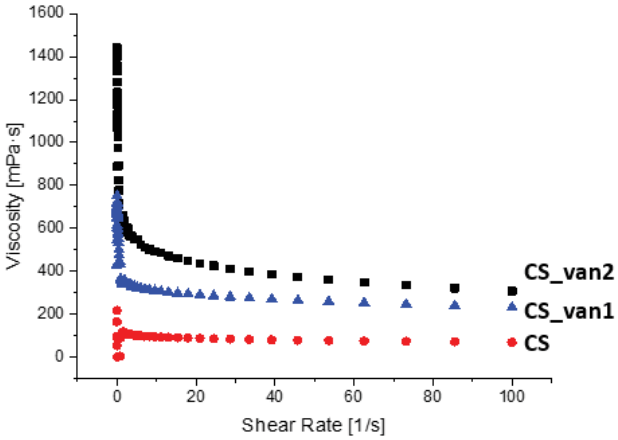

FIG. 2. Viscosity flow curve of the CS-based solution uncrosslinked and crosslinked with different amounts of vanillin.

Preliminary bioactivity assessment (SBF, 37°C) confirmed that calcium phosphates were formed on the surface of all the samples although their morphology differed (FIG. 3).

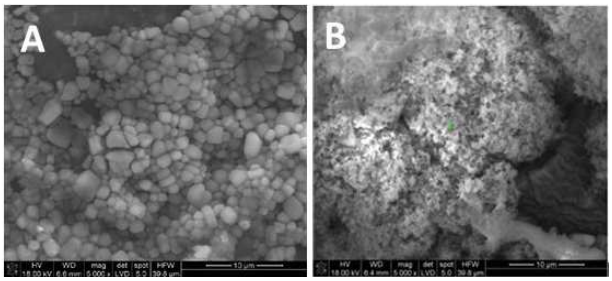

FIG. 3. SEM images of (A) 1CS_3GEL_1PVA_van2 and (B) 3CS_1GEL_1PVA_van2 ater 2 weeks of incubation in SBF.

In the end, two hydrogel systems based on 1CS:1GEL:1PVA and 3CS:1GEL:1PVA blends modified with GO and HAp. and crosslinked with vanillin (van2) were singled out for further studies as the most promising materials.

Conclusions

Vanillin can be used as a chitosan crosslinker due to the presence of aldehyde groups. Moreover, this organic compound is of natural origin and was proven to have bioactive properties. Chitosan-vanillin systems can be exploited in various biomedical applications.

Acknowledgments

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