Primers for the adhesion of gellan gum-based hydrogels to cartilage

INTRODUCTION

A stable adhesion to the cartilage tissue is a crucial requisite for hydrogels used in the fields of cartilage substitution and regeneration. Indeed, the presence of a weak interface between the cartilage and the implanted material may lead to an early detachment, thus causing the failure of the cartilage repair or regeneration process [1]. Using an adhesive primer, namely a coating applied to the cartilage surface to promote the adhesion of materials, may overcome such an issue. Different primers (fibrin glue (FG) [2], cellulose nanofibers (CNF) [3] and catecholamines (CAT) [4]) have been proposed in the state-of-the-art. However, no studies have systematically compared their performance. This study aims at evaluating the adhesion strength between the cartilage tissue and gellan gum (GG)-based hydrogels, crosslinked using ions or, after methacrylation, through a light source.

METHODS

GG was dissolved in d-H_2O at 2 % w/v by stirring for 1 h at 37°C, while gellan gum methacrylate (GGMA) was dissolved in PBS at 2 % w/v for 1 h at 37 °C. Then, ruthenium (Ru) and sodium persulfate (SPS) were added to GGMA at a concentration of 0.2 and 2 mM, respectively.
FG was deposited evaluating different waiting times before hydrogel deposition, namely 30 s, 5 min, 15 min and, 30 min.
CNFs, dispersed in d-H_2O, were added to GG and GGMA at two concentrations (0.1 and 0.5% w/v) to form a CNF-based primer to be added before GG and GGMA. CAT-modified gelatin was dissolved in a Tris-buffered saline buffer at two concentrations (100 and 125 mg/mL). Then, the solutions were mixed with 1 mM Ru and 20 mM SPS and then crosslinked through a white LED for 30 s.
Before performing adhesion tests, GG or GGMA were cast on each primer and crosslinked for 10 min with $MgCl_2$ (1 % w/v in d-H_2O) (GG) or with the LED light (GGMA).
To evaluate the adhesion strength, two cartilage-hosting parts were used to block bovine cartilage samples and a top hydrogel-hosting part allowed pouring the primer and the hydrogel solution onto the cartilage. A traction test was performed through an Instron machine.

RESULTS

Results showed that the photo-crosslinked GGMA showed higher adhesion strength than GG in absence of primers. However, the adhesion strength of both GG and GGMA improved in the presence of FG with respect to the control. In particular, the waiting times of 5 min for GGMA (9.80 ± 3.03 kPa for GGMA) and 15 min for both the hydrogels (12.64 ± 0.87 kPa for GG and 10.99 ± 3.14 kPa for GGMA) guaranteed to match the clinical goal (10 kPa) [5]. The adhesion strength using CNFs and GG hydrogels reached a value of 12.13 ± 4.69 kPa (clinically acceptable) in the case of 0.1 % w/v CNFs, while the strength was smaller for the higher concentration of CNFs.
The adhesion strengths obtained with the CAT-based gelatin for GG increased from 6.16 ± 1.87 kPa (100 mg/mL) to 8.85 ± 2.40 kPa (125 mg/mL) and for GGMA from 2.93 ± 1.52 kPa (100 mg/mL) to 8.06 ± 1.38 kPa (125 mg/mL), without reaching the clinically accettable value.

CONCLUSIONS

We found that the use of primers can guarantee an increased adhesion of GG-based hydrogels onto the cartilage. In the case of FG primer the best condition was represented by a waiting time of 15 min between primer pouring and subsequent hydrogel deposition on the cartilage, in all cases. In the case of embedded CNFs, the fiber concentration of 0.1 % w/v considerably increased the adhesion strength of GG and GGMA hydrogels. The CAT-modified gelatin layer was less effective in promoting the adhesion between the hydrogels and the cartilage.

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