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Application note | ElastoSens™ Bio

Long term degradation analysis of chitosan hydrogel using ElastoSens™ Bio

ELASTOSENS™ BIO

HYDROGEL FORMULATION

BIOLOGICAL TISSUES

TIME MEASUREMENTS

DRUG DELIVERY

BIO CHEMISTRY

This is a short report of a study performed by Caroline Ceccaldi, Satu Strandman, Eve Hui, Emmanuel Montagnon, Cédric Schmitt, Anis Hadj Henni and Sophie Lerouge at École de technologie supérieure (ÉTS) (Montreal, Canada) entitled *Validation and Application of a Non-Destructive and Contactless Method for Rheological Evaluation of Biomaterials* and published in 2016 on the Journal of Biomedical Materials Research Part B (105B:2565–2573)

SUMMARY

— The evaluation of hydrogels degradation through their viscoelastic properties is conventionally performed with destructive techniques.

— ElastoSens™ Bio was used to test non-destructively the viscoelasticity of degrading hydrogel samples over 7 days.

— ElastoSens™ Bio has shown to provide long-term, reproducible and sensitive measurements of the degradation of chitosan hydrogels under simulated physiological conditions.

— The decrease in the shear storage modulus of chitosan hydrogels immersed with a lysozyme solution supported their degradation even without any significant change in their weight.

INTRODUCTION

Hydrogels exhibit a pronounced viscoelastic behavior similar to soft tissues. For this reason, they have been widely used in biomedical research for developing engineered tissues and novel treatments such as wound dressings and drug delivery systems. In this field, hydrogels can be composed of biodegradable natural (e.g. collagen, fibrin, chitosan) and/or synthetic polymers (e.g. PLA, PGA, PLGA). Natural materials can be degraded by naturally occurring enzymes which is an important feature for releasing a drug entrapped in the hydrogel matrix [1] or for allowing the formation of new tissues by seeded cells [2]. Therefore, the precise evaluation of this process is important for designing biomatrices with controlled degradation rates or simply for assessing whether degradation is within the desirable range for the application. In literature, degradation processes have been evaluated by the weight loss of a sample or by its mechanical properties. Since the initial stages of degradation can happen without any loss of weight,

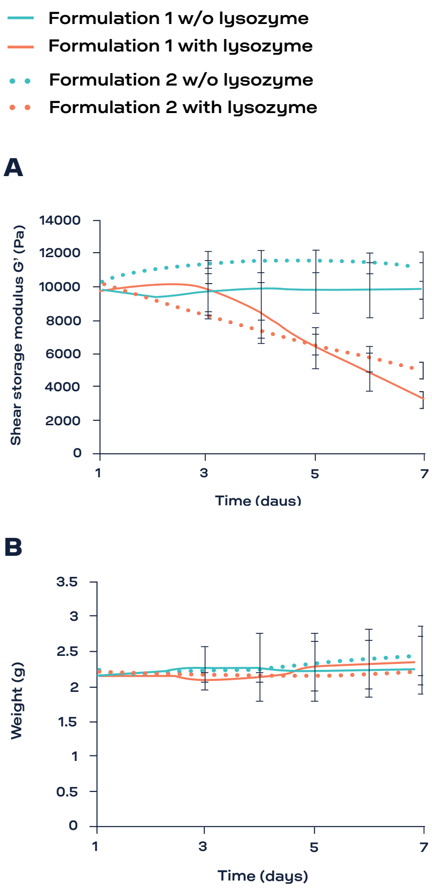

Fig. 1: Shear storage modulus (G', Pa) and weight (g) as a function of time for the two chitosan hydrogels (HDDA and LDDA) with and without the digestion solution (lysozyme).

the mechanical properties can provide more precise information of the whole degradation process. However, conventional testing technologies such as rheometers and compression mechanical testers are destructive and prevent the re-use of samples for further characterizations (multiple samples are required to study degradation over long periods of time). In this short application note, chitosan-based hydrogels were prepared and immersed with lysozyme solution for the evaluation of their degradation through their viscoelastic properties using ElastoSens™ Bio. The same sample was tested each day during a week in contact with the enzyme.

MATERIALS AND METHODS

Two different sources of chitosan: (1) HDDA MMw: Chitosan with high degree of deacetylation (DDA) and medium molecular weight (ref PSN 326–501, MarinardBiotech, Gaspe, Canada), and (2) LDDA MMw: Chitosan with low DDA and medium molecular weight (ref 448877, Sigma, St. Louis, USA) were prepared by solubilizing chitosan powder in 0.1 M hydrochloric acid (3.33 % w/v). Chitosan and gelling agents were mixed at a volume ratio of 3:2, respectively. After rapid mixing, the solution (2 mL) was poured into the ElastoSens™ Bio sample holder, which was then kept at 37 °C with PBS for 24 hours. PBS was removed and the gel was tested in the ElastoSens™ Bio to obtain their initial G' at day 1. After this time point, the samples were divided into two groups, which received either PBS (control groups) or lysozyme (human lysozyme, Sigma, 1mg/ml in PBS). The solutions were added on top of the samples inside the sample holders and they were incubated at 37 °C for 7 days. The viscoelastic tests were performed every day using the same samples during the whole study. Simultaneously, the weight of the samples was measured using an analytical balance (Mettler Toledo, model ML104, Toronto, Canada), with a readout accuracy of 0.0001 g.

RESULTS AND DISCUSSION

Fig. 1 shows the evolution of the shear storage modulus (G', Pa) as a function of time for the two chitosan hydrogels (HDDA and LDDA) with and without the digestion solution (lysozyme). The G' was stable for the samples immersed in PBS over the 7 days of the study. The progressive decrease in the G' of the hydrogels after being immersed with the lysozyme reflects their degradation. Interestingly, the weight of all samples was stable during the whole experiment. This was explained by the fact that at the initial stage of degradation by hydrolysis, these physical hydrogels can keep their cohesiveness and hydrophilicity despite the decrease in chain interactions [3].

CONCLUSIONS

The decrease in the shear storage modulus of chitosan hydrogels immersed with a lysozyme solution reflected their degradation as a function of the time even without any significant change in their weight.

PERSPECTIVES

— ElastoSens™ Bio provides relevant information to complement the standard weight test used to study degradation.

— ElastoSens™ Bio is able to capture subtle mechanical changes during degradation before the sample starts to disintegrate.

— Testing the same sample over time is now possible due to the non destructive nature of ElastoSens™ Bio.

— Viscoelasticity testing can be performed under simulated physiological and sterile conditions.

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