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Application note | ElastoSens™ Bio

Degradation and drug release of hydrogel-based drug delivery systems

ELASTOSENS™ BIO

DRUG DELIVERY

BIOLOGICAL TISSUES

TIME MEASUREMENTS

HYDROGEL FORMULATION

SUMMARY

— One of the release mechanisms of drug delivery systems based on hydrogel involves the degradation of the matrix that carries the drug.

— Conventional testing instruments are difficult to use difficult to use for evaluating the mechanical properties of hydrogel-based drug release systems during degradation.

— ElastoSens™ Bio has shown to provide precise measurements of the mechanical properties of dye-loaded gelatin/alginate composite gels.

— The temperature-dependent degradation of the gelatin beads promoted the dye release from the composite gels.

INTRODUCTION

The controlled release of drugs at precise locations within the body can prevent systemic toxicity and deliver accurate dosages to patients. Hydrogels have recently been investigated as promising drug delivery systems due to their ability to provide spatial and temporal control over the release of a number of therapeutic agents. Furthermore, the easy tunability of their physicochemical and mechanical properties allows the design of application-specific release systems [1]. One of the release mechanisms of therapeutic agents is based on the controlled degradation of the hydrogel that carries the drug. In this case, the decrease in the viscoelastic properties of the hydrogel is proportional to the amount of released drug [2]. Because conventional mechanical testing techniques are destructive, they prevent the re-testing of the same hydrogel sample for long term degradation studies. The use of these instruments requires the monitoring of multiple samples for a complete drug release study as a function of time. In addition, technical limitations of traditional instruments are usually an issue to precisely measure the soft nature of hydrogels.

In this short application note, the ElastoSens™ Bio was used to non-destructively monitor the viscoelastic properties of a degrading composite hydrogel made of dye-loaded gelatin beads and alginate. The dye was used to simulate the drug. Its release was measured along the study and correlated to the composite hydrogel viscoelasticity.

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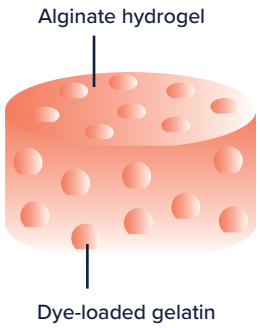

Fig. 1: Schema of the model-drug loaded gelatin beads in the alginate matrix

MATERIALS AND METHODS

Bovine gelatin (Sigma-Aldrich, MO, USA) was dissolved in deionized hot water (10 % w/w) and combined with green food dye (Club House). The dye in this study was used to simulate the therapeutic agent added in the matrix of the drug delivery system. The dye-loaded gelatin solution was dropped into ice-cold mineral oil to form gel beads and inserted in the ElastoSens™ Bio sample holders. Alginate (5 %) and $CaCl_2$ (crosslinking agent) solutions were added to form the matrix around the dye-loaded gelatin beads (Fig. 1). After gelling overnight, the gelatin beads were uniformly distributed in the alginate matrix and deionized water was added on top of each composite gel. The samples were incubated at 4 °C, room temperature, 32 °C and 37 °C for 24 hours each. At the end of incubation, images from the supernatant were analyzed by ImageJ to quantify the dye release and the viscoelasticity of the gel samples was tested in the ElastoSens™ Bio at the same temperature.

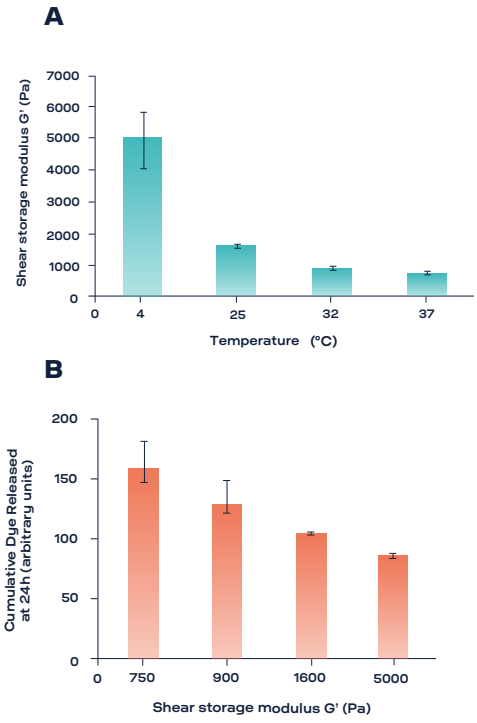

Fig. 2: Storage modulus (G') of alginate/gelatin gels at different temperatures (left) and total dye released from composite gels at 24 hours relative to average G' (right).

RESULTS AND DISCUSSION

Fig. 2 shows the effect of temperature on the shear storage modulus (G') of the composite gels (A) and the 24h-cumulative dye release as a function of the shear storage modulus of the composite gels after the incubation at each temperature (B). The samples that were maintained for 24 hours at higher temperature showed lower shear storage moduli (G'). As expected, the cumulative amount of dye released after each 24 hours increased with the softness of the composite hydrogel (Fig. 2 B) suggesting that the diffusion of the dye was faster when the carrying gels were soft. The melting of the gelatin beads promoted the release of the dye and its diffusion to the supernatant. It was observed that all samples maintained their shape integrity even at higher temperatures.

CONCLUSION

The increase in temperature led to the decrease in the storage modulus of the alginate/gelatin composite gels due to the melting of the gelatin beads. Consequently, the release of the dye was higher with the increasing in temperature.

PERSPECTIVES

- ElastoSens™ Bio is able to capture subtle mechanical changes during degradation before the sample starts to disintegrate.
- ElastoSens™ Bio can test viscoelasticity under simulated physiological conditions.
- ElastoSens™ Bio can be used to develop/formulate hydrogels, to tune their degradation profile and to test/optimize degradation mechanisms (enzymatic degradation, hydrolysis, etc.).
- Viscoelasticity measurements and degradation profiles can be correlated with the amount of drug released in order to control the release for specific therapeutic applications.

REFERENCES

[1] Li, J., & Mooney, D. J. (2016). Designing hydrogels for controlled drug delivery. Nature Reviews Materials, 1(12), 1-17.

[2] Chou, S. F., & Woodrow, K. A. (2017). Relationships between mechanical properties and drug release from electrospun fibers of PCL and PLGA blends. Journal of the mechanical behavior of biomedical materials, 65, 724-733.

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