Rheolution
LIFE SCIENCES

Application note | ElastoSens™ Bio

ElastoSens™ Bio: A tool for hydrogel formulation

ELASTOSENS™ BIO

FORMULATION

BIO CHEMISTRY

TIME MEASUREMENTS

THERMO STIMULATION

SUMMARY

— The evaluation of hydrogel formation is conventionally performed with complex complex and destructive techniques.

— ElastoSens™ Bio has shown to be sensitive to slight changes in terms of formulation. It differentiated agar and collagen formulations through the viscoelastic properties of the forming hydrogels.

— ElastoSens™ Bio provided similar measurements compared to conventional rheometers.

INTRODUCTION

Natural polymers such as collagen, fibrin, chitosan, and agarose exhibit superior biological activity when compared to synthetic materials and so, they are often used to entirely or partially compose hydrogels. The formation of a hydrogel is governed by the development of physical or chemical bonds between the polymeric chains and depends strongly on its formulation. The formulation of a hydrogel includes the selection and dosage of the polymer, solvent and crosslinking agent (when present). These parameters constitute the first steps of optimization in order to meet the requirements of the desired application specially in terms of mechanical properties [1,2,3]. The evaluation of the gelation kinetics and the maximum elastic modulus after gelation have been conventionally performed by destructive testing techniques (e.g. rheometer, compression testers). However, these techniques are usually complex to master and present intrinsic limitations that make testing of soft hydrogels challenging, especially in the context of bioengineering and life sciences applications.

We introduce here the ElastoSens™ Bio as an easy-to-use, non-destructive and contact free testing instrument to characterize hydrogels. It includes the unique capabilities of Soft Matter Analytics to collect and analyse key data that help developing, studying and optimizing the behavior of hydrogels. In this short application note, the time evolution of viscoelastic properties during the gelation of agar and collagen solutions were measured by the ElastoSens™ Bio. A comparison between the ElastoSens™ Bio and a rotational rheometer is also presented.

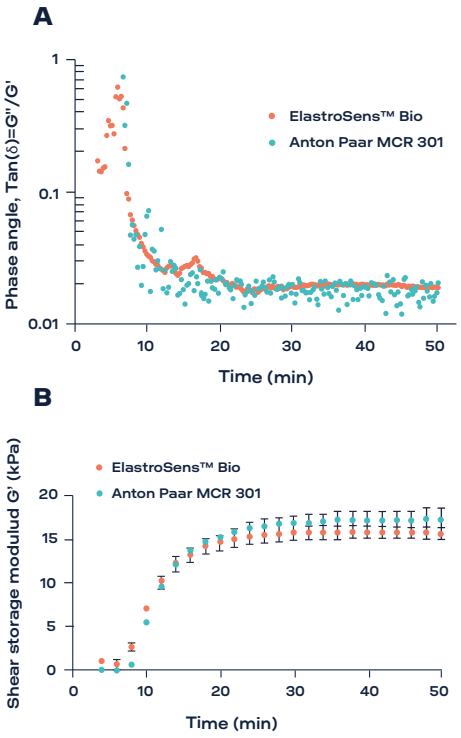

Fig. 1: Comparison of ElastoSens™ Bio and rotational rheometer measurements during the formation of agar gel: (A) comparison of the phase angle; (B) comparison of the shear storage modulus.

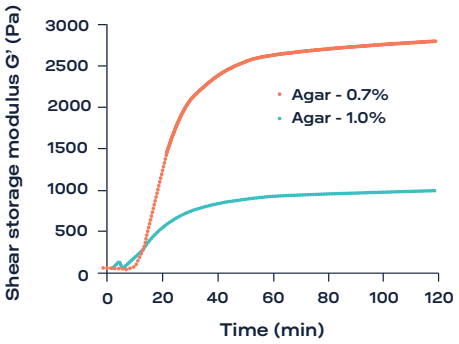

Fig. 2: Time evolution of the storage shear modulus (G') during the formation of two agar hydrogels with different concentrations (0.7 % and 1.0 %, w/w)

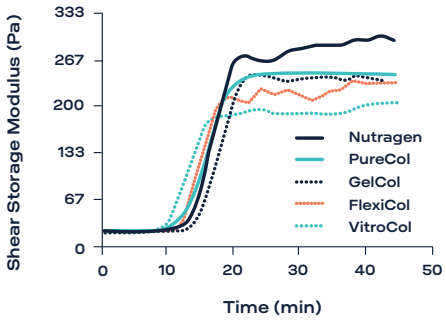

Fig. 3: Gelation kinetics of Nutragen® (6 mg/mL), PureCol® (3 mg/ml), GelCol® (3 mg/mL), FlexiCol® (3 mg/ml), and VitroCol® (3 mg/ml) at 37 °C.

MATERIALS AND METHODS

Agar powder (Sigma, St. Louis, USA) was solubilized in milli-Q water at 1.4 % (w/v) to prepare agar hydrogels. The solution was heated to 80 °C for 10 min before being used for viscoelastic measurements in ElastoSens™ Bio and a rotational rheometer. For the ElastoSens™ Bio, 2 mL of hydrogel solution was poured into the sample holders of the instrument and the test was carried out for 50 min. The hydrogel solution was also tested on a rotational rheometer (MCR 301, Anton Paar, Ostfildern-Scharnhausen, Germany) equipped with a parallel plates geometry (P25/P2). Measurements were taken at an oscillation frequency of 1 Hz and 0.1 % strain.

A similar procedure was used to prepare agar solutions at concentrations of 0.7 % and 1.0 % (w/w) for the evaluation of the concentration effect on the gel viscoelastic properties measured by the ElastoSens™ Bio. The test was conducted at 22 °C for 120 min [2].

Human (VitroCol®, 3 mg/ml), bovine (Nutragen®, 6 mg/mL; PureCol®, 3 mg/ml; and GelCol®, 3 mg/mL) and porcine (FlexiCol®, 3 mg/ml) type I collagen from Advanced Biomatrix (Carlsbad, CA, USA) were also tested on the ElastoSens™ Bio 37 C for 45 minutes.

RESULTS AND DISCUSSION

Fig. 1 shows a comparison of the 1.4 % (w/v) agar gelation kinetics measured with the ElastoSens™ Bio and the rotational rheometer. The results obtained with both methods followed the same trend and showed comparable mean values. Of note, values of phase angle obtained with the ElastoSens™ Bio showed less variability compared to those obtained with the rotational rheometer [4].

Fig. 2 shows the time evolution of the shear storage modulus (G') of two agar hydrogels prepared at different concentrations (0.7 % and 1.0 % w/w). The results support that the gelation kinetics of agar hydrogels (i.e. speed of gelification speed and maximum shear storage modulus) strongly depends on the concentration of agar. The increase by just 0.3 % (w/w) of agar in the solution led to an increase of 180 % in the G' of the gel.

Fig. 3 shows the gelation kinetics of the different types of collagen tested. All materials gelled rapidly within a relatively narrow time interval (t_{onset} = 12 ± 2 min) and consistent elasticities with shear storage modulus (G') of 285 Pa for bovine Nutragen®, 245 Pa for bovine PureCol®, 240 Pa for bovine GelCol®, 222 Pa for porcine FlexiCol®, and 194 Pa for human-derived VitroCol® (Table 1). Overall, bovine collagen gel showed the highest values of Young modulus (Young's modulus = 3xG') followed by the porcine and human collagen.

Table 1: Final shear storage modulus (G', Pa) after gelation for Nutragen®, PureCol®, GelCol®, FlexiCol® and VitroCol® at 37 °C.

	Nutragen®	PureCol®	GelCol®	FlexiCol®	VitroCol®
Shear storage modulus (Pa)	285	245	240	222	194

CONCLUSION

Measurements obtained with the ElastoSens™ Bio during the formation of agar hydrogel were similar to those obtained with a conventional rheometer. It was clear that the concentration of agar strongly influenced the gelation kinetics and the maximum storage modulus of the final gel. Collagen gelation kinetics showed sigmoidal shapes and were consistent among the different types of collagens. The bovine collagen gel showed the highest values of shear storage modulus followed by the porcine and human collagen.

PERSPECTIVES

— ElastoSens™ Bio simplifies the characterization of hydrogels during and after gelation. The instrument is easy-to-use and adapts very well for applications in life sciences.

— With the modularity of ElastoSens™ Bio, it is possible to test simultaneously multiple samples (up to five). This unique capability improves the statistical significance of measurements while it accelerates the generation of data.

— Correlating the dosages of the polymer, solvent and crosslinking agent (when present) with the gel's viscoelastic properties is made easy thanks to the Soft Matter Analytics capabilities of ElastoSens™ Bio.

— It is easy, using ElastoSens™ Bio, allows to easily expose the hydrogel to different physical or chemical conditions such as temperature, light, controlled atmosphere (inert gases) and chemical solutions.

REFERENCES

[1] Malafaya, P. B., Silva, G. A., & Reis, R. L. (2007). Natural–origin polymers as carriers and scaffolds for biomolecules and cell delivery in tissue engineering applications. Advanced drug delivery reviews, 59(4-5), 207-233.

[2] Hoffman, A. S. (2012). Hydrogels for biomedical applications. Advanced drug delivery reviews, 64, 18-23.

[3] Chai, Q., Jiao, Y., & Yu, X. (2017). Hydrogels for biomedical applications: their characteristics and the mechanisms behind them. Gels, 3(1), 6.

[4] Ceccaldi, C., Strandman, S., Hui, E., Montagnon, E., Schmitt, C., Hadj Henni, A., & Lerouge, S. (2017). Validation and application of a nondestructive and contactless method for rheological evaluation of biomaterials. Journal of Biomedical Materials Research Part B: Applied Biomaterials, 105(8), 2565-2573.

ACKNOWLEDGMENT

The study of the agar hydrogel has been performed in collaboration with Pr. S. Lerouge and Dr. C. Ceccaldi from École de technologie supérieure (ÈTS, Montreal) and with the financial support of the Natural Sciences and Engineering Research Council of Canada (NSERC Engage grant). The data of the collagen hydrogels formation have been provided by Advanced Biomatrix.