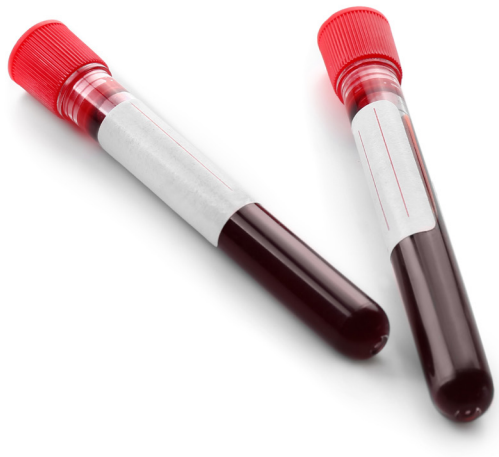
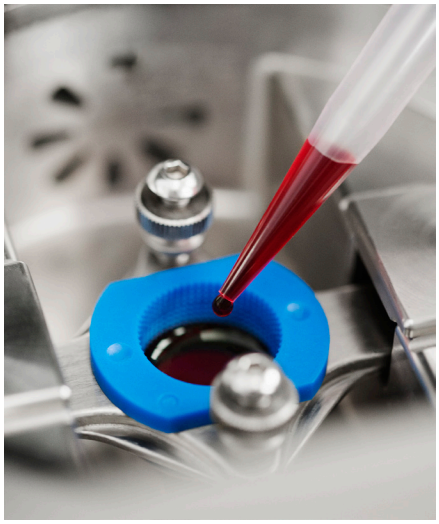
Rheolution
LIFE SCIENCES



Application note | ElastoSens™ Bio

Blood coagulation analysis using ElastoSens™ Bio



ELASTOSENS™ BIO

BLOOD

TIME MEASUREMENTS

BIOLOGICAL MATERIALS

BIO CHEMISTRY

This is a short report of a study performed by Shiva Naseri, Newsha Koushki, Ehsan Rezabeigi, Allen Ehrlicher and Showan N. Nazhat at McGill University (Montreal, Canada) which title is A nondestructive contactless technique to assess the viscoelasticity of blood clots in real-time (published in 2020 in the Journal of the Mechanical Behavior of Biomedical Materials, 110, 103921).

SUMMARY

— The measurement of the absolute blood viscoelastic properties during coagulation is not possible with most conventional techniques.

— ElastoSens™ Bio has shown to provide repeatable and sensitive measurements to test blood coagulation through the viscoelastic properties of the forming clot.

— The concentration of $CaCl_2$ in blood affects the initialization of coagulation (showing a non-linear behavior). The stiffness of the developed clot is proportional to the concentration of $CaCl_2$.

— ElastoSens™ Bio's measurements were similar to those obtained with a rotational rheometer. The ElastoSens™ Bio's data showed a better correlation to $CaCl_2$ concentration compared to TEG.

INTRODUCTION

The viscoelastic properties of coagulating blood can be correlated with several diseases and genetic conditions that affect the natural blood coagulation process including bleeding disorders, hemophilia, rare factor deficiencies, von Willebrand disease and platelet function disorders. Therefore, the evaluation of blood clot properties can be valuable for the study, diagnosis and eventually treatment of these diseases. Conventional and more recent techniques used to assess blood coagulation such as thromboelastography (TEG), rotational thromboelastometry (ROTEM) and magnetomotive optical coherence elastography do not directly measure the absolute viscoelasticity of the clot. Furthermore, they normally offer a destructive testing which prevents complementary characterization of the clots and/or the monitoring of the dynamic changes during blood coagulation. Other issues related to these techniques also include low sensitivity and repeatability. In this short application note, ElastoSens™ Bio was used for monitoring the shear storage modulus (G') of whole blood during coagulation induced by different concentrations of $CaCl_2$ [1]. In addition, similar tests were performed using TEG and rheometer for comparison.

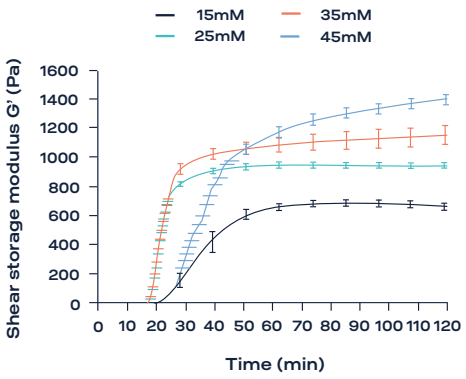


Fig. 1: Shear storage modulus G' time evolution during coagulation of bovine whole blood after recalcification with 15, 25, 35 and 45 mM $CaCl_2$ (Error bars: Standard deviation: SD, n = 3).

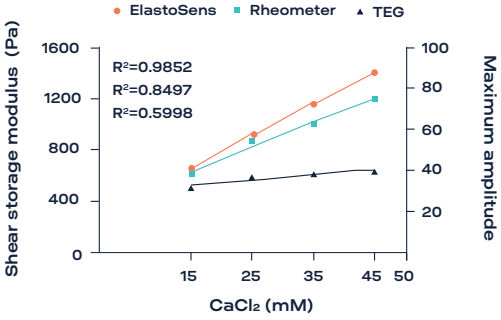


Fig. 2: The correlation between the shear storage modulus (Pa) and $CaCl_2$ concentration (mM) measured by ElastoSens™ Bio and Rheometer (left y-axis). TEG results show the correlation of the maximum amplitude with $CaCl_2$ concentration (right y-axis).

MATERIALS AND METHODS

Citrated bovine blood (Cedarlane, ON, Canada) was pre-warmed at 37 °C and recalcified with 0.5 mL of $CaCl_2$ (Sigma-Aldrich) at different concentrations (15, 25, 35, and 45 mM). After 10 gentle vial inversions, the mixture (4 mL of citrated blood + 0.5 mL of $CaCl_2$) was immediately loaded into the ElastoSens™ Bio sample holders which were previously heated and placed in the chamber of the instrument. The test was performed at 37 °C for 120 minutes. In the case of the rheometer (MCR 302 Anton Paar, Austria), 0.65 mL of recalcified blood was loaded between its parallel plates. Measurements were performed under a constant oscillation frequency of 1.5 Hz and an amplitude of 0.1 % at 37 °C for 120 minutes. For the TEG (Haemoscope Corporation, USA), measurements were conducted according to the manufacturer's specifications in native mode at 37 °C for 40 min.

RESULTS AND DISCUSSION

Fig. 1 shows the shear storage modulus (G') evolution of blood samples as a function of time after the addition of $CaCl_2$ at different concentrations. The increase of the $CaCl_2$ concentration from 15 mM to 25 mM led to a shorter reaction time (the time at which G' begins increasing). However, a further increase from 35 mM to 45 mM resulted in longer reaction time. The final G' values increased with increasing calcium concentration (Fig. 2) showing the formation of stiffer clots. This trend was consistent with the results obtained with the Rheometer and TEG. The relation between the $CaCl_2$ concentration and blood coagulation obtained with the ElastoSens™ Bio and the rheometer were closer when compared with those from the TEG. This is explained by the fact that the two first techniques directly measure the elastic modulus while TEG measures an indirect parameter (typically rotational displacement) that correlates with viscoelasticity [2,3].

CONCLUSION

The increasing concentration of $CaCl_2$ from 15 mM to 35 mM reduced the clotting time while a further increase (to 45 mM) led to a longer reaction time. The higher concentration of $CaCl_2$ resulted in higher clot stiffness. The relation between $CaCl_2$ concentration and the clot final storage moduli measured by the ElastoSens™ Bio was close to those measured by the rheometer. In turn, this information was correlated to the results obtained by TEG (the conventional instrument used in clinics).

PERSPECTIVES

ElastoSens™ Bio can directly measure the evolution of viscoelasticity during clot formation. It provides robust measurements and an easy-to-use platform. The instrument can be used for:

— R&D: providing superior quantitative data to better investigate blood coagulation.

— Preclinical studies: to study the effect of medication on blood coagulation.

REFERENCES

[1] Naseri, S., Koushki, N., Rezabeigi, E., Ehrlicher, A., & Nazhat, S. N. (2020). A non-destructive contactless technique to assess the viscoelasticity of blood clots in real-time. Journal of the Mechanical Behavior of Biomedical Materials, 110, 103921

[2] Evans, P. A., Hawkins, K., Lawrence, M., Williams, R. L., Barrow, M. S., Thirumalai, N., & Williams, P. R. (2008). Rheometry and associated techniques for blood coagulation studies. Medical engineering & physics, 30(6), 671-679.

[3] Whiting, D., & DiNardo, J. A. (2014). TEG and ROTEM: technology and clinical applications. American journal of hematology, 89(2), 228-232.

Rheolution LIFE SCIENCES

Contact us today to start your Soft Matter Analytics™ journey

+1 514 270-2090
www.rheolution.com
info@rheolution.com

Rheolution Inc.
5333 Casgrain Ave., Suite #601
Montreal, QC, H2T 1X3, Canada