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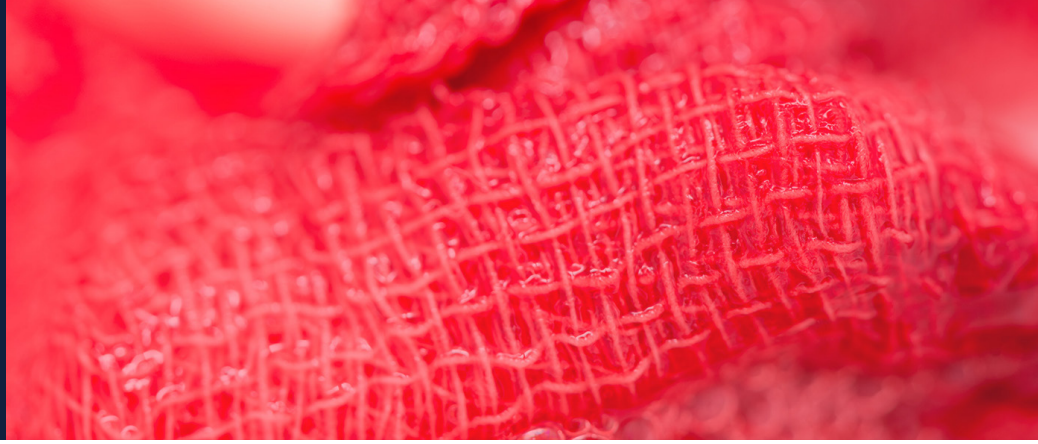
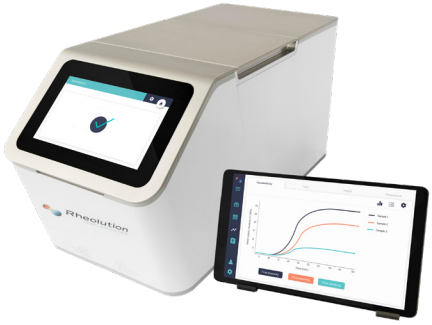
LIFE SCIENCES



Application note | ElastoSens™ Bio

Measuring the efficacy of hemostatic agents using ElastoSens™ Bio



ELASTOSENS™ BIO

BIO CHEMISTRY

BIOLOGICAL TISSUES

TEMPORAL MEASUREMENTS

SUMMARY

— The precise analysis of hemostatic agents (HA) in contact with blood are not possible with most conventional testing techniques.

— ElastoSens™ Bio successfully measured the coagulation of blood in presence of HA through the clot viscoelastic properties.

— It is shown here that increasing the concentration of HA in blood may affect the clot initiation time, clot strength and volume (swelling) depending on the mode of action (MoA) of the HA.

— ElastoSens™ Bio can be used for R&D and development of HA, QC & manufacturing and for preclinical studies.

INTRODUCTION

Hemostatic agents (HA, e.g. powders, gauzes, adhesives and sealants) have been used for decades to control bleeding. The demand for these agents is growing due to two major trends in surgical practice: the expansion of minimally invasive surgery and complex reconstructive procedures that are more limited in their capacity to obtain hemostasis [1]. Hemostatic effectiveness (i.e. time to form a clot), clot swelling and mechanical strength of the formed clots are important parameters to be evaluated for bringing potential agents to the market. However, conventional techniques for analyzing HA such as visual inspection, thromboelastrography (TEG) and rotational thromboelastometry (ROTEM) can not precisely measure clotting kinetics, swelling, and the mechanical stability of the formed clots in the presence of hemostatic agents. In this short application note, two commercially available hemostatic agents, CELOX™ and QuikClot®, have been tested using the ElastoSens™ Bio to measure the viscoelasticity and swelling of the clots as a function of time during their formation.

MATERIALS AND METHODS

CELOX™ (MedTrade Products Ltd., Crewe, UK) and QuikClot® (Z-MEDICA, LLC, Wallingford, CT, USA) were added into the ElastoSens™ Bio sample holders at different powder/blood weight dosages: 0 %, 5 % and 10 % (w/w) for CELOX™ and 5 %, 10 % and 15 % (w/w) for QuikClot®. Sample holders and hemostatic agents were pre-heated at 37 °C into the thermal chamber of the instrument. Whole sheep blood in anticoagulants

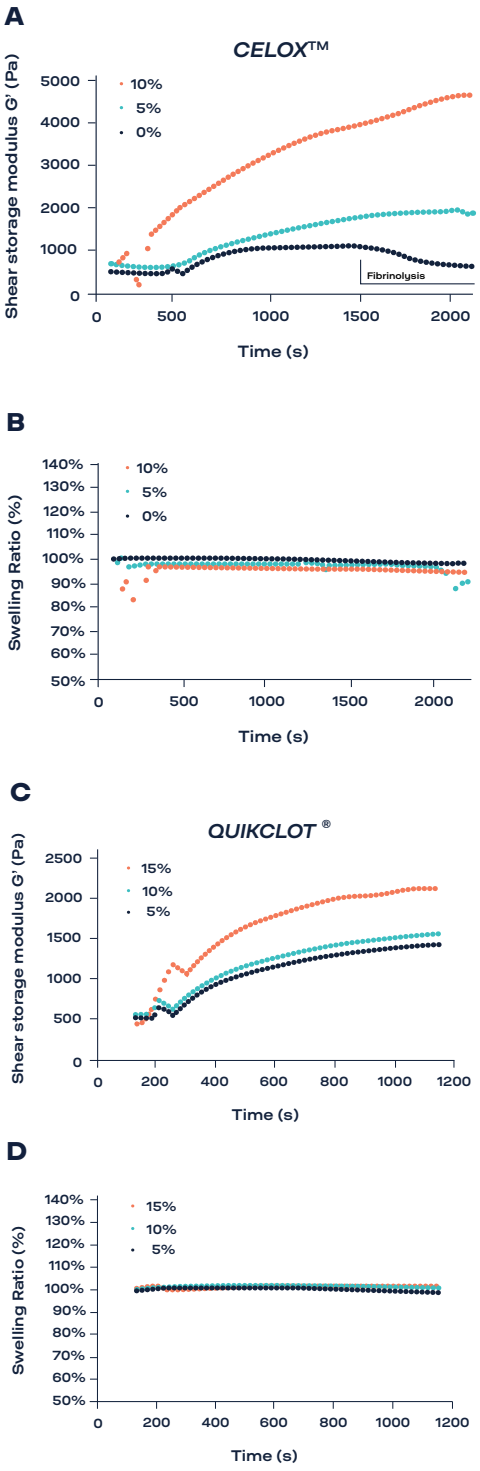


Fig. 1: Shear storage modulus (G', Pa) and swelling ratio (%) as function of time of two commercial hemostatic agents at different concentrations: CELOX™ at 0 %, 5 % and 10 % and QuikClot® at 5 %, 10 % and 15 %.

(Sodium Citrate) from Cedarlane (Burlington, ON, Canada) was heated at 37 °C in a water bath and then re-calcified by mixing with $CaCl_2$. A volume of 5 mL of re-calcified blood was then pipetted and introduced into the sample holders containing the HA and the test was initiated. The test was performed at 37 °C during 40 minutes for CELOX™ and 20 minutes for QuikClot®. The ElastoSens™ Bio was used to measure in real time the shear storage modulus (G') of the clot during its formation as well as the sample swelling ratio calculated as follows:

$$\text{Swelling ratio} = \frac{\text{Actual sample height - Initial sample}}{\text{Initial sample height}}$$

RESULTS AND DISCUSSION

Fig. 1 shows the time evolution of the shear storage modulus (A,C) and swelling ratio (B,D) of the blood with different concentrations of CELOX™ (0 %, 5 %, 10 %) and QuikClot® (5 %, 10 %, 15 %). The coagulation of re-calcified whole blood with no hemostatic agent provided a baseline (blood only control) to compare with the samples that contain hemostatic agents. The coagulation kinetics of blood with 0 % CELOX™ exhibited fibrinolysis (breaking down of fibrin network) after 1500 s. The clot initiation time for CELOX™ (A) decreased by increasing the concentration of the agent while it remained relatively stable for the QuikClot® (C) at different concentrations. The higher ratio of hemostatic agent to blood (w/w %) increased clot strength for both hemostatic agents. This ratio also affected the maximum rate of clot formation for CELOX™ but it did not seem to significantly change those of QuikClot® (Table 1). These two hemostatic agents did not yield changes in the sample height, (B,D) suggesting no significant clot swelling.

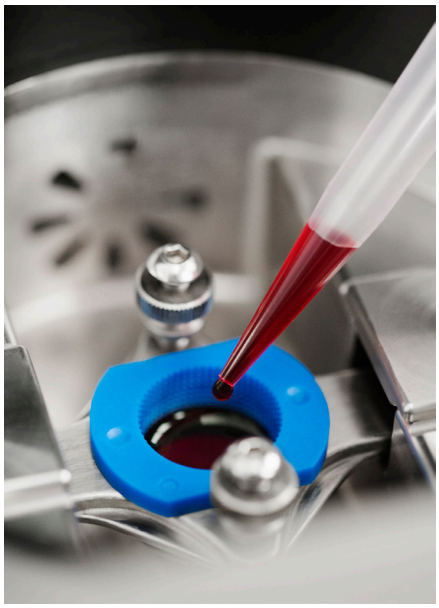
Table 1: Clot initiation time (s) and maximum rate of clot formation (Pa/s) for each HA at different concentrations.

	CELOX™			QUIKCLOT™		
Ratio of hemostatic agent to blood (w/w)	0%	5%	10%	5%	10%	15%
Clot Initiation Time (s)	442	404	255	226	210	255
Maximum rate of clot formation (Pa/s)	3.4	1.8	20.7	3.0	3.0	3.6

The differences between each HA can be related to their Mode of Action (MoA). CELOX is a chitosan-based HA that physically blocks bleeding through the formation of a cross-linked gel with the different components of blood. QuikClot® is a clay-based HA that has been suggested to act by: (1) absorbing water at the site of bleeding which can rapidly concentrate platelets and clotting factors and by (2) inducing a chemical reaction that activates the intrinsic coagulation pathway and platelets, both promoting coagulation [2-5].

CONCLUSION

Increasing the amount of HA in blood decreased the clot initiation time for CELOX™ while it remained relatively stable for QuikClot®. The higher concentration of both HA increased clot strength while no significant clot swelling was observed during the study.



PERSPECTIVES

— ElastoSens™ Bio can directly measure the evolution of viscoelasticity during clot formation with a technology that allows robust measurements and an easy interaction.

— The viscoelastic properties during clot formation can be used to understand the Mode of Action (MoA) and optimize the formulation of hemostatic agents.

ElastoSens™ Bio can be used for:

- R&D and Product Development: to get superior quantitative data to better evaluate product prototypes and accelerate research.
- QC & Manufacturing: to improve quality control processes, strengthen documented traceability, optimize costs and qualify suppliers.
- Preclinical studies: to simulate in vivo conditions to better predict clinical outcomes.

REFERENCES

[1] Wheat, J. C., & Wolf, J. S. (2009). Advances in bioadhesives, tissue sealants, and hemostatic agents. Urologic Clinics, 36(2), 265-275.

[2] Li, J., Cao, W., Lv, X. X., Jiang, L., Li, Y. J., Li, W. Z., ... & Li, X. Y. (2013). Zeolite-based hemostat QuikClot releases calcium into blood and promotes blood coagulation in vitro. Acta Pharmacologica Sinica, 34(3), 367-372.

[3] Khoshmohabat, H., Paydar, S., Kazemi, H. M., & Dalfardi, B. (2016). Overview of agents used for emergency hemostasis. Trauma monthly, 21(1).

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