PHARMACEUTICAL

Blood Viscosity Analysis

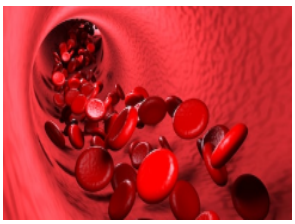
- dependence on temperature and hematocrit -

KEY BENEFITS

- FAST TEMPERATURE SCREENING
- LOW VOLUME
- QUICK & SIMPLE

Introduction

Characterization of blood viscosity in physiologically relevant conditions is fundamental to understand hemodynamics. Proper tissue perfusion occurs when blood viscosity falls within certain levels. Many parameters can influence whole blood viscosity but most notably its value is due to properties of its constituents (plasma and cells) and external paramaters like temperature. As blood flows within a wide range of vessel nature/shapes, wide shear range analysis is necessary to be representative of these conditions.



In this application note blood is tested over a wide shear range typical of circulatory system conditions. Temperature and hematocrit effect are also studied. As Fluidicam^{RHEO} uses confined microfluidic technology, blood analysis is safely conducted with no air contact and using low sample volume.

References:

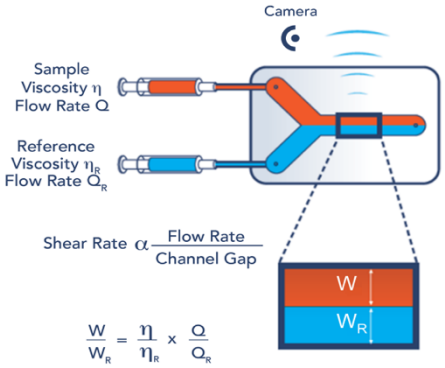
1- *Galdi, Giovanni P., Rolf Rannacher, Anne M. Robertson, and Stefan Turek. Hemodynamical Flows: Modeling, Analysis and Simulation. Oberwolfach Seminars, v. 37. Basel : [London: Birkhäuser ; Springer, distributor], 2008.*

2- *Rand, Peter W., Eleanor Lacombe, Hamilton E. Hunt, and William H. Austin. 'Viscosity of Normal Human Blood under Normothermic and Hypothermic Conditions'. Journal of Applied Physiology 19, no. 1 (January 1964): 117–22.*

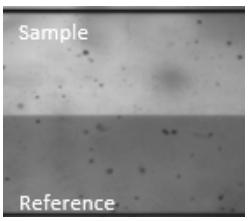
3- *Snyder, Gk. 'Influence of Temperature and Hematocrit on Blood Viscosity'. American Journal of Physiology-Legacy Content 220, no. 6 (June 1971): 1667–72.*

Reminder of the technique

Fluidicam^{RHEO} uses a co-flow microfluidic principle to measure viscosity. The sample and a reference solution are simultaneously introduced into the microfluidic channel (typically 2.2mm X 150µm) with controlled flow rates. This results in a laminar flow where the interface position between sample and reference relates the viscosity ratio and flow rates.



Images acquired during the measurement allow the software to calculate the position of the interface and directly plot an interactive flow curve.



Method

Whole defibrinated sheep blood with hematocrit (Ht=38%) and its four dilutions with Ht =34%, 25%, 18% and 8% have been used for this study. Hematocrit concentrations were obtained by diluting blood sample in sheep serum.

Using Fluidicam^{RHEO} microfluidic rheometer, samples were analyzed at four temperatures: 39°C (sheep corporal temperature)[1], 35°C, 30°C and 25°C. 150µm deep microfluidic chip allowed to measure viscosity at shear rate range from 300 to 10 000 s^{-1}.An aqueous reference solution (Formulaction, 5 mPa.s at 25°C) was used for these tests.

Typical shear rates can be expressed knowing blood flow velocity and vessel inner diameter. Table 1 below gives the estimated results for human vessel conditions [2] :

Vessel type	Mean wall shear rates [s^{-1}]
Veins	150 – 240
Femoral artery	300
Cappilaries	400 – 1600
Arteriols	8000

Table 1: Shear rates in blood vessels.

The shear rate range was selected to mimic circulatory system conditions. Five blood and one serum samples were tested to determine viscosity as a function of shear rate for different hematocrit values. The highest blood viscosity is reached for the highest Ht% and the lowest for pure serum

Results

Dependence on temperature

The viscosity of whole sheeps blood (Ht=38%) was assessed at four temperatures in order to determine the extent of viscosity variation with Temperature.

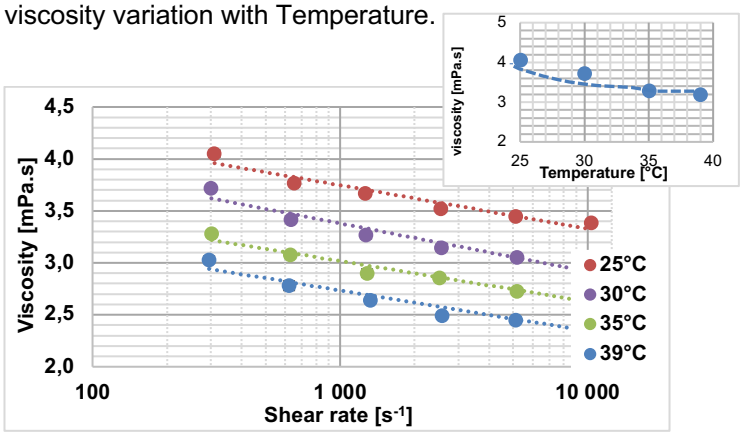


Figure 1.Visosity of sheep full blood as a function of shear rate at four different temperatures.

The shear thinning behavior of blood is observed at all conditions. As expected, viscosity decreases as the temperature rises: from 4.05 mPa.s to 3.38 mPa.s at 25°Cand 39°C respectively, for the lowest screened shear rate value.

For blood viscosity testing, the confined microfluidic provides representative data safely collected with minimum sample amount. The time to perform these tests including sampling and temperature stabilisation was **about 20 min** and volume required was **< 12 mL sample volume** for 4 flow curves.

Dependence on shear rate and hematocrit conc. at 39°C

Using a single microfluidic chip allows to cover a range of shear rates from 300 - 10 000 s^{-1} corresponding to circulatory system conditions. A single flow curve requires 3 mL sample volume and 5 min analysis time (including sampling).

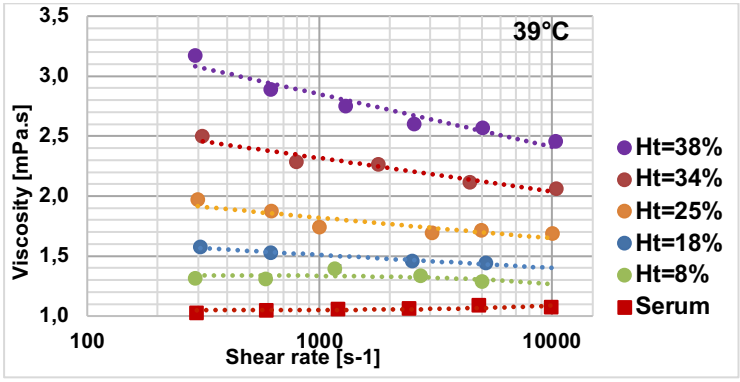


Figure 2.Viscosity as function shear rate and Ht% at 39°C.

The flow curves of the blood samples at Ht = **38%**, **34%** and **25%** show clear shear thinning behavior over the applied shear rates. Sample with **Ht = 18%** presents only slight shear thinning effect and **Ht = 8%** shows a Newtonian profile with an average viscosity value of **1.3 mPa.s**. This is consistant with the non Newtonian character being conferred by the cells present in the blood.

These results can be used to estimate the critical **Ht%**, below which blood loses its shear thining behavior, in this case it is between 8 and 18%.

In order to compare the viscosity as a function of concentration the viscosity was calculated at a single shear rate ($\dot{\gamma}$=300 s^{-1}). Figure 3 shows the results. The relationship between the viscosity and the hematocrit% can be described with the emperical equation known for human blood [2] [3]:

$$\eta_{bl} = \eta_{pl} \exp\left[K1.Ht\right]$$

η bl :Blood viscosity *η pl :Plasma visocity*
K1: constant coeff. of hematocrit *Ht: hematocrit conc.*

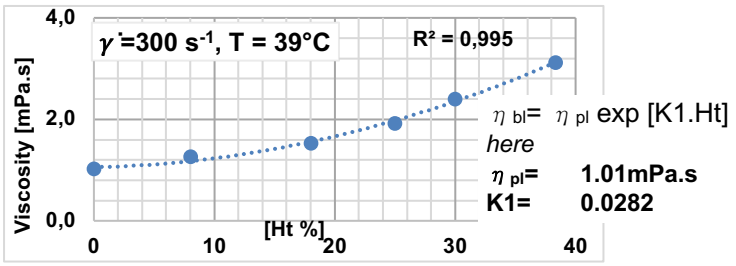


*Figure 3.Viscosity as function of Ht% at **shear rate 300 s^{-1}***

CONCLUSION

Wide shear range analysis can be used to gain insight to the complexicity of the circulatory system and characterize the blood under real conditions.Thanks to the high sensitivity of Fluidicam^{RHEO} it was possible to assess the impact of hematocrit, temperature and shear rates on blood viscosity in conditions representative of the conditions encountered in-vivo.