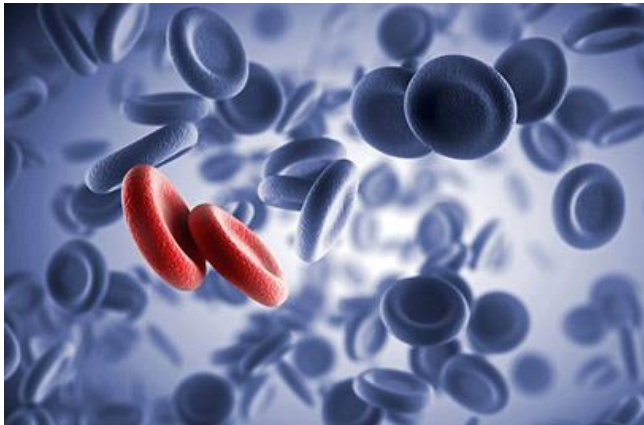


Viscosity Measurement of Whole Blood

Relevant for: Medical Research, Blood Analysis, Clinical Laboratories

Increased blood viscosity is correlated with all known risk factors for cardiovascular diseases including high blood pressure, cholesterol, diabetes, and side-effects of smoking. Lovis 2000 M/ME Microviscometer allows for comprehensive blood viscosity measurement. Low sample volume, a built-in software compliant to GMP and 21 CFR part 11, as well as optionally available pharma qualification packages round off the advantages.



1 Introduction

The viscosity of blood is a direct measure of the ability of blood to flow through arteries and veins. It determines how much friction the blood causes against the vessels, how hard the heart has to work to pump the blood through the body, and how much oxygen is delivered to organs and tissue.

Blood viscosity is correlated with all known risk factors for cardiovascular diseases. Elevated blood viscosity is a strong independent predictor of cardiovascular events.

While serum or plasma viscosity measurements play an important role in the clinical management of patients prone to hyper-viscosity syndrome, these tests do not account for hematocrit, blood cell deformability or factors increasing RBC (red blood cell) aggregation.

Whole blood is a non-Newtonian liquid. Its viscosity changes with the applied shear stress. The blood viscosity rises and falls from one extreme to the other with every cardiac cycle, comparable to blood pressure. Therefore, a meaningful blood viscosity test requires more than one measurement:

systolic blood viscosity (high shear rate), which is affected by hematocrit, and plasma viscosity and diastolic viscosity (low shear rate), which is affected by several factors like stickiness of platelets, immune complexes that increase the aggregation of RBCs, triglycerides, cholesterol, and many more. Find detailed information on blood viscosity in the following sub section.

1.1 Background reading on blood viscosity

1.1.1 Hematocrit

A higher percentage of red blood cells (RBCs) results in thicker blood. The hematocrit accounts for about 50 % of the difference between normal and high blood viscosity.

1.1.2 Erythrocyte deformability ("thickness of blood")

Erythrocyte deformability refers to the ability of the RBCs to elongate at "high shear" and to bend and fold themselves in order to make their way through the narrow passageways of the capillaries. RBC deformability is correlated with blood viscosity, meaning that the more deformable the RBCs are, the less viscous the blood is. Young RBCs are more deformable than older RBCs. Erythrocyte deformability is, after hematocrit, the second most important determinant of blood viscosity.

1.1.3 Plasma Viscosity

Plasma viscosity refers to the thickness of the fluid portion of blood. Plasma viscosity is highly affected by hydration and by plasma proteins (e.g. immunoglobulin and fibrinogen). Studies have shown that dehydration significantly increases the blood viscosity.

1.1.4 Erythrocyte aggregation ("stickiness" of blood)

Erythrocyte aggregation reflects the tendency of RBCs to be attracted to each other and to stick together. Several factors can increase sedimentation and aggregation. Blood viscosity is directly correlated with both, RBC aggregation and plasma viscosity.

1.1.5 Clinical Implications of altered blood viscosity

Blood flows through the vessels in a laminar flow – blood forms layers that slide easily over each other. The faster the blood flows in the center layers, the slower it moves in the outer layers near the walls of the vessels.

Highly viscous blood does not slide as smoothly as less viscous blood, leading to turbulences that can damage delicate parts of the blood vessels. Turbulence is also generated at curves and bifurcations in blood vessels, particularly in the large vessels nearest the heart, which are subject to great changes in pressure with each heartbeat.

The consequences of hyper-viscous blood are primarily damage to the blood vessels, overwork of the heart and decreased delivery of oxygen to the tissues. A growing number of studies point to the role of blood viscosity in cardiovascular diseases – blood viscosity is an important predictor of cardiovascular events in the adult population.

2 Sample preparation

- A blood sample of 9 mL was taken from one person by Anton Paar's company physician.
- The sample was stabilized with EDTA to avoid coagulation.
- 6 mL of sample were put into the refrigerator overnight. Viscosity measurements were performed the next day.
- 3 mL of sample were used to measure the hematocrit value by the company physician.

3 Instrument

3.1 DMA™ M Density Meter plus Lovis 2000 ME

The Lovis 2000 M/ME Microviscometer measures the rolling time of a ball inside an inclined capillary. The integrated software automatically calculates kinematic and dynamic viscosity (provided the sample density is known). For simultaneous density measurement, combination of a Lovis 2000 ME module with a DMA™ M density meter is recommended.



Figure 1: DMA™ plus Lovis 2000 ME Microviscometer Module

Variable inclination angles allow for measurements at different shear rates. Temperature control via Peltier elements is extremely fast and highly accurate. Capillaries with only 100 µL filling volume suit the limited sample quantity.

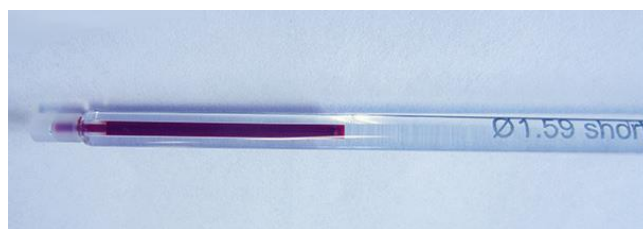


Figure 2: Low-volume capillary (100 µL) filled with blood

3.2 Measuring settings

- Separate filling of DMA™ measuring cell and Lovis. Filling volume of density cell: approximately 1 mL
- Capillary Lovis 1.59 short: filling volume 100 µL
- Before measurement, the capillary was adjusted with a certified water standard at 37 °C over an angle range from 20° to 70°.
- Temperature settings for multiple viscosity measurement and angle scan:
 - Measuring temperature: 37 °C
 - Temperature equilibration time: 20 s

Lovis specific settings:

- Measurement cycles: 3 (per determination)
- Measuring angle for multiple viscosity measurements: 60°
- Angle scan: 70° to 30°, 10° increment
- Set Variation Coefficient: 0.3 %

Tip: Use a microliter syringe with a hollow needle attached for precise filling of the low-volume capillary.

Recommended cleaning liquids:

1st step – deionized water

2nd step – ethanol (for fast drying)

For intensive sterilization, the capillary can be put into an autoclave. The outside of the instrument can be disinfected by wiping with ethanol.

4 Results

- Hematocrit: 41.3 %
(not determined with DMA™ + Lovis)
- Density at 37 °C: 1.04737 g/cm³

4.1 Multiple viscosity measurements

Dynamic Viscosity [mPa.s]	Variation Coefficient [%]	Shear Rate [s ⁻¹]
2.716	0.23	222.2
2.675	0.10	225.6
2.659	0.07	227.0
2.661	0.21	226.8
2.661	0.14	226.7
2.661	0.14	226.7
2.664	0.29	226.5
2.651	0.27	227.6
2.660	0.03	226.8
2.659	0.14	226.9

Table 1: 10 viscosity determinations at 37 °C and 60° angle

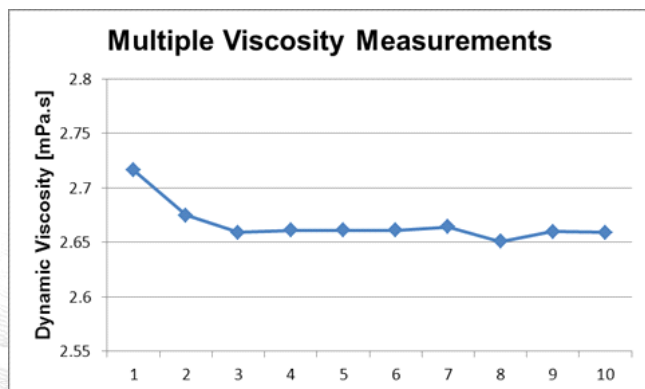


Figure 3: 10 viscosity determinations at 37 °C and 60° angle

4.2 Angle scan (shear rate scan)

Measuring Angle [°]	Shear Rate [s ⁻¹]	Dyn. Viscosity [mPa.s]	Variation Coefficient [%]
70	263.1	2.4652	0.17
60	238.0	2.5359	0.04
50	205.9	2.5974	0.19
40	165.9	2.7066	0.25
30*	117.9*	2.9648*	0.53*

Table 2: Lovis angle scan at 37 °C

* At this low shear rate the blood sample starts to separate into two phases.

5 Conclusion

The Lovis 2000 M/ME Microviscometer is perfectly suited for testing whole blood sample:

- Due to the small capillary size, only little sample volume (100 µL) is required. The density cell requires approximately 1 mL of sample.
- The closed system avoids contamination. There are only three wetted parts – the inner surface of the glass capillary, the steel ball and the plug. The plug and the ball are disposables, so the only part to clean is the glass capillary.
- The built-in Peltier elements provide high-precision temperature control.
- The Lovis 2000 M/ME software includes several measurement modes, such as time scan and angle scan, which allow users to gain a maximum of information from one single blood sample.
- Lovis and DMA™ are compliant with 21 CFR Part 11. Additionally, Pharma Qualification Packages can be offered.

6 References

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2. Robert Rosencranz, BSEE, IE, ME and Steven A. Bogen, MD, PhD, "Clinical Laboratory Measurement of Serum, Plasma and Blood Viscosity", American Society for Clinical Pathology, 2006

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