Automated viscometry measurement with Junior

Introduction

Monoclonal antibodies (mAb) are an important class of therapeutic proteins used to treat a variety of diseases, including cancer and autoimmune conditions. To be effective, many mAb formulations must have high concentrations (>150 mg/mL mAb). These high mAb concentrations increase formulation viscosity, which can limit drug delivery options and complicate manufacturing. Recent publications have highlighted the utility of viscometry to predict the "developability" of protein therapeutics[1–2]; however, routine viscosity screening of drug candidates and formulations can be extremely time-consuming when using conventional manual techniques.

Unchained Labs' viscosity station automates viscosity measurements from start to finish. This microcapillary viscometer performs accurate and precise viscosity measurements of Newtonian and non-Newtonian liquids with small volume requirements (only 100 µL per sample). With this system, over 200 samples can be analyzed in a single day, with minimal hands-on time. The viscosity station can be integrated with other analytics such as turbidity, visual particle analysis and pH on the Junior or into a customized larger workflow on a Big Kahuna system configured for biologics formulation.

In this application note, we compare the viscometry results for six mAb formulations (20–200 mg/mL) measured using Unchained Labs' viscosity station and a Malvern Kinexus rheometer.

Materials and methods

Measurements using the Kinexus rotational rheometer were performed according to the manufacturer's guidelines. For each measurement, 180 µL of sample was added to the measuring plate. Viscosities were calculated from multiple shear stress and shear rates as functions of measurement time. One measurement was performed for each sample and required a total of 30 minutes – 5 minutes for manual cleaning and sample loading followed by a 25-minute measurement.

A Junior with a viscosity station was used for this study. Prior to running samples, deionized water and Brix standard solutions were used to calibrate the system for viscosities from 1–51 cP. Before each viscosity measurement the system automatically washed and dried the system. Using a disposable Rainin positive displacement pipette tip, 100 µL of sample was injected at a precise flow rate into the temperature-controlled (20 °C) capillary. Viscosities were calculated by using the shear rate and measuring the pressure response for each solution. Each measurement required approximately 6 minutes, including washing and drying.

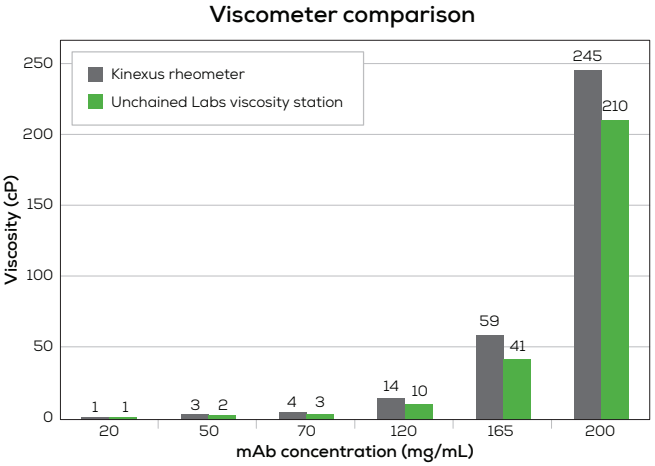

Figure 1: A comparison of the viscosity results of six mAb formulations using a Kinexus rheometer and Unchained Labs' viscosity station.

Results

Viscosity results for six drug product formulations with mAb concentrations ranging from 20–200 mg/mL are summarized in Figure 1. The same trends are observed for both the Kinexus rheometer and the viscosity station across the mAb concentrations tested. Differences in the measured viscosities between the two instruments are likely attributable to the physical and mechanistic differences of the methods. Table 1 and Table 2 summarize the data from replicate measurements at high and low shear rates, respectively.

While both systems provide comparable results, the viscosity station is faster and requires significantly less manual intervention. Each measurement required less than 6 minutes including measurement, washing and drying procedures.

The Kinexus rheometer required 30 minutes per measurement including measurement, manual washing and sample loading times. Table 3 compares the two methods for hands-on time, run time and sample volume requirements. The viscosity station not only measures viscosity faster and uses less sample than the rheometer, but also automates the entire process. Screening 40 samples takes 20 hours with the Kinexus rheometer, while the same analysis is complete in less than 4 hours with the viscosity station. When measuring 40 samples, the viscosity station is five times faster and has a 40-fold decrease in hands-on time compared to the Kinexus rheometer.

Conclusion

The viscosity station on the Junior delivers comparable results to the Malvern Kinexus

mAb (mg/mL)	High shear rate					Average results	
	Measurement (cP)	Average measurement (cP)	RSD of viscosity (%)	Shear rate (s-1)	Flow rate (µL/s)	Average measurement (cP)	RSD of measurements (%)
20	0.9	0.9	2	5436	10.0	1	2
	1.0						
	0.9						
50	1.1	1.9	4			2	10
	2.0						
	1.8						
70	2.6	2.6	2			3	4
	2.7						
	2.6						
120	10.5	9.8	7			10	6
	5.2						
	5.6						
165	43.3	42.7	2	5232	9.6	41	4
	42.5			5190	9.6		
	42.0			5365	9.9		
200	210.6	215.7	3	1087	2.0	210	4
	220.8						
	N/A			N/A	N/A		

Table 1: Viscosity results of six mAb formulations from the viscosity station using various high shear rates for measurements.

mAb (mg/mL)	Low shear rate					Average results	
	Measurement (cP)	Average measurement (cP)	RSD of viscosity (%)	Shear rate (s^{-1})	Flow rate (µL/s)	Average measurement (cP)	RSD of measurements (%)
20	1.0	1.0	1	2718	5.0	1	2
	1.0						
	1.0						
50	1.6	1.6	3			2	10
	1.6						
	1.7						
70	2.4	2.4	2	2174	4.0	3	4
	2.4						
	2.5						
120	10.8	10.3	5	1631	3.0	10	6
	10.2						
	9.8						
165	41.4	40.0	4	1359	2.5	41	4
	38.6						
	40.1						
200	203.4	203.4	N/A	652	1.2	210	4
	N/A			N/A	N/A		

Table 2: Viscosity results of six mAb formulations from the viscosity station using various low shear rates.

	Kinexus		Unchained Labs	
	Required hands-on time	Automated analysis time	Required hands-on time	Automated analysis time
Setup time	5 min	N/A	5 min	N/A
Time per sample	N/A	25 min	N/A	5.6 min
Number of samples	40		40	
Total time	3.3 hr	16.7 hr	5 min	3.7 hr

Table 3: Summarized measurement requirements for 40 samples using a Kinexus rheometer and Unchained Labs' viscosity station. Note that the Kinexus system requires scientists to return to the instrument after every measurement, whereas the Unchained Labs' system operates in a fully unattended manner.

rheometer but is five times faster, with significantly less hands-on time. With this system, a single scientist can screen 200 formulations in a day with only 25 minutes of hands-on time. Automating manual assays such as viscosity measurement, greatly improve lab productivity. Combining automated viscosity with automated pH, visual particle analysis and turbidity on the Junior or a Big Kahuna platform can really accelerate formulation development.

The viscosity station on the Junior is five times faster and has a 40-fold decrease in hands-on time compared to the Kinexus rheometer.

References

1. Lorenz T, et al. Developability Assessment of Biologics by Integrated Biologics Profiling. *American Pharmaceutical Review*. August 29, 2014.

2. Yang X, et al. Developability studies before initiation of process development. *mAbs*. 2013; 5(5):787–794.

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