

Intrinsic Viscosity Measurements of Hyaluronic Acid: High-Throughput, Automated, Integrated and Compliant



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Polymer Insights: Hyaluronic acid (HA) is a glycosaminoglycan polymer found in connective tissues. Composed of glucuronic acid and N-acetylglucosamine units, it holds up to 1000 times its weight in water, crucial for tissue hydration and elasticity. With low immunogenicity and biocompatibility, HA is widely employed in diverse applications, from tissue engineering to cosmetic procedures, as a versatile biomolecule enhancing hydration and tissue integrity.

Experiment Protocol

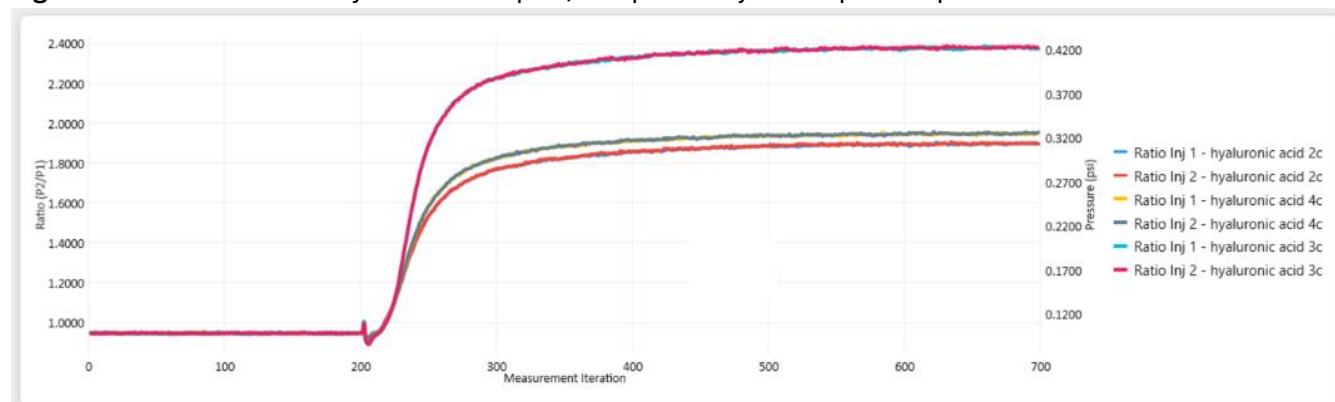
Overview: Hyaluronic Acid samples from 3 manufacturers were dissolved in water at 40°C for 90 minutes. After dissolution each sample IV was measured twice. Details are listed in Table 1 (below).

Preparation workflow: Sample mass was recorded in the HaikuFlow software using a connected XS105 balance. Vials were placed in the sample preparation block with individually stirred positions after a PTFE stir bar and cap were added. No further user intervention was required. Dissolution solvent volume was calculated by the software and added to samples by the integrated syringe dosing pump. After a preset dissolution timer expired, samples were loaded and analyzed automatically.

Table 1: Sample Preparation, Dissolution and Temperature Settings Details

Application			Dissolution			Temperature (°C)		
Sample ID	Polymer	Solvent	Conc. (g/dL)	Time (minutes)	Stir Speed (RPM)	Heater Block	Inline H/X	Visc Oven
hyaluronic acid 2c	HA	water	0.024	90	200	50	30	30
hyaluronic acid 3c	HA	water	0.027	90	200	50	30	30
hyaluronic acid 4c	HA	water	0.020	90	200	50	30	30

Figure 1: P2/P1 Ratio Overlay of 3 HA Samples, 2 Replicate Injections per Sample



Experiment Results

Hyaluronic acid samples are generally expected to be high molecular weight (MW). With MW ranges from under 500,000 g/mol up to some HA samples reported at over 1,800,000 g/mol, extremely high IV values are expected. The IV results for these commercially available HA samples match those expectations. Detailed Results are shown in Table 2 (below).

Table 2: Experimental Results

Sample Details			Viscosity Results				Repeatability
Sample ID	Conc. (g/dL)	Analysis Time	RV1	RV2	IV1	IV2	% RSD (IV)
hyaluronic acid 2c	0.024	4:23:33	2.008	2.010	29.054	29.086	0.055
hyaluronic acid 3c	0.027	4:28:42	2.515	2.517	34.803	34.836	0.048
hyaluronic acid 4c	0.020	4:33:50	2.055	2.057	36.023	36.057	0.047

Discussion

For high MW samples, ensuring dissolution without degradation is critical to proper IV measurement.

The extremely low deviation between samples shows that the samples were completely dissolved and were not undergoing degradation. The range of IV values conformed to the expected MW ranges provided by the manufacturers, whose product designations are withheld for the sake of NDA compliance.

Increasing IV values from injection 1 to injection 2 indicates incomplete dissolution, whereas decreasing IV values from injection 1 to injection 2 indicates degradation is occurring.

Each replicate injection was completed in around 2.5 minutes, giving a total analysis time of approximately 5 minutes for each sample. Matching these ultra-fast analysis times to the interval between sample preparation time ensures that results are not influenced by the position in the sample queue.

A Focus on Integration and Compliance: Haiku Leads the Market in Medical Polymers QC

Documenting compliance for 21CFR part11 has not been available in IV instrument software until today.

Your HaikuFlow software for instrument control, data acquisition and reporting ensures the highest degree of security available where data integrity and compliance are concerned. Some of these features include:

HaikuFlow Feature	Relevance for 21CFR Part 11
Secure SQLite database structure	Prevents external tampering with results
Multi-level user access controls	Shows only features appropriate to user's authority
Changelogs for settings and methods	Records changes made to methods and settings
Direct LIMS / ERP connectivity	Prevents human error in transferring data to LIMS



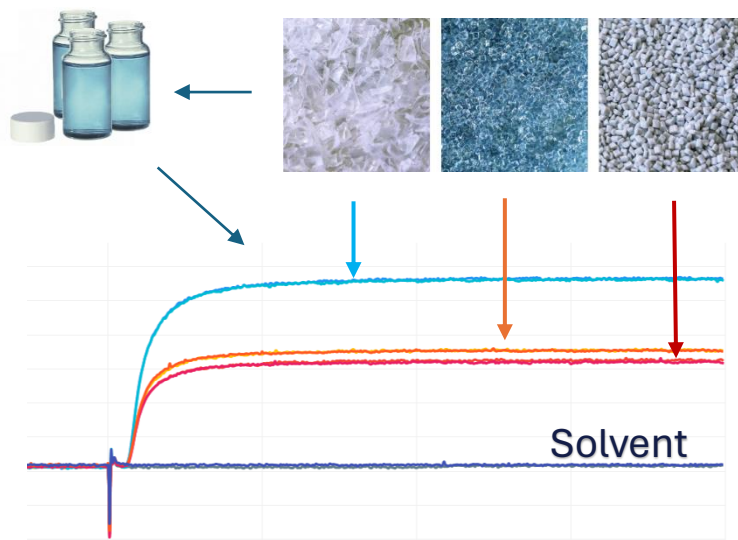
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The Model 575 Intrinsic Viscometer
Generation 2

The Most Rapid and Reliable Measurement of Molecular Weight and Intrinsic Viscosity

Fully Automated Sample Preparation and IV Analysis
According to ISO 1628 and ASTM D5225



Workflow Step	Critical Advantages
Sample Mass Determination	Guided Workflow with connected Analytical Balance
Solvent Dispensing	Fully Automated; no user interaction with solvents
Dissolution	24 Individually Stirred Autosampler Positions
Sample Analysis	Begins automatically after dissolution
Criterion	Specification
Viscosity Measurement Type	Dual Differential, Relative Viscosity, Forced Flow
IV Measurement Resolution	0.005 dL/g
Measurement Precision	Better than 0.2% RSD RV @ 0.800 dL/g
Shear rates	200-500 s ⁻¹ (typical, depending on application)
Sample Analysis Time	4-6 minutes per sample, includes duplicate injection
Solvent Compatibility	Organic, Aqueous, Acids, Halogenated
Temperature Range (Dissolution)	30°C to 160°C
Temperature Range (Analysis)	10°C to 160°C
Total Solvent Per Sample (prep + analysis + wash)	25mL
Integration, Compliance, Connection	LIMS/ERP, 21CFR part11, USB 2.0 / Windows 10

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