Osmolality Testing of Viscous Formulations Using Freezing Point Depression

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Abstract

The trend towards higher concentration formulations poses various issues for the pharmaceutical industry, with an increased concentration often leading to a higher viscosity. Simultaneously, subcutaneous injections are proving more popular with both patients and healthcare providers due to their efficacy, safety, and reduced drug-delivery costs[1]. However, these trends together mean that the concentration logically increases due to the lower volumes administered.

This, in turn, impacts their osmolality measurements due to the likelihood of increased viscosity when producing higher concentration solutions. Examples of excipients incorporated into these formulations include hyaluronic acid (HA), sodium hyaluronate, and glycerols. Osmolality is a key process parameter in formulation development and product stability. However, prior to the launch of the OsmoTECH® XT Micro-osmometer, the increase in popularity of these higher concentration formulations and harder to handle components posed a challenge for freezing point osmometers.

This poster details the osmolality testing of various formulations containing sodium hyaluronate, with a range of viscosities, including semi-solid gels. The testing is part of a Quality Control (QC) check within the end user's formulation development process, making it a critical part of their work and an example of real-world application of osmolality.

Advanced Instrument's latest single sample micro-osmometer – the OsmoTECH® XT, has been developed specifically with these types of formulations in mind, and the data shown here provides evidence of the capability, precision, and accuracy of this instrument when placed in a customer laboratory.

Materials and Methods

- Osmolality was measured on an OsmoTECH® XT Single-sample Micro-osmometer with intelligent freezing technology
- Formulation components are proprietary to the customer.

OsmoTECH® XT

Results

Sample 1	
[HA] Nominal	10mg/ml
[HA] Measured	10.8mg/ml
Zero Shear Viscosity	47.1 Pa.s
Mean Osmolality	312mOsm
Standard Deviation/CV	0.69. 0.22%

Sample 2	
[HA] Nominal	15mg/ml
[HA] Measured	14.4mg/ml
Zero Shear Viscosity	261.0 Pa.s
Mean Osmolality	335mOsm
Standard Deviation/CV	1.11 0.33%

Sample 3	
[HA] Nominal	10mg/ml
[HA] Measured	10.3mg/ml
Zero Shear Viscosity	5.7 Pa.s
Mean Osmolality	288mOsm
Standard Deviation/CV	0.47 0.16%

Sample 4	
[HA] Nominal	15mg/ml
[HA] Measured	14.6mg/ml
Zero Shear Viscosity	455.5 Pa.s
Mean Osmolality	298mOsm
Standard Deviation/CV	0.50 0.17%

Sample 5	
[HA] Nominal	30mg/ml
[HA] Measured	29.4mg/ml
Zero Shear Viscosity	51.0 Pa.s
Mean Osmolality	321mOsm
Standard Deviation/CV	2.43 0.76%

Sample 6	
[HA] Nominal	22.5mg/ml
[HA] Measured	22.4mg/ml
Zero Shear Viscosity	N/A Pa.s
Mean Osmolality	281mOsm
Standard Deviation/CV	1.91 0.68%

Sample 7	
[HA] Nominal	3mg/ml
[HA] Measured	2.5mg/ml
Zero Shear Viscosity	0.17 Pa.s
Mean Osmolality	295mOsm
Standard Deviation/CV	0.75 0.25%

Figure 1 . Components and mean osmolality measurements for various formulations containing sodium hyaluronate.

Discussion

Osmolality is the measurement of solute concentration, expressed as milliosmoles per kilogram of water[2]. This measurement is critical for many reasons throughout the bioprocessing workflow, however with the ever-evolving trends within the industry, osmometers also need to be able to stay up to date. Higher concentration formulations, or formulations that may contain difficult-to-measure components, now require analytical instruments that can still precisely and accurately measure them without any issues.

As can be seen in the results section, an OsmoTECH XT user producing ophthalmic medicines based on hyaluronic acid is currently using varying formulations within their work, which also vary in aqueous nature. The osmometer is regularly used as a quality control check to minimise the risk of any potential batch deviations. The data provides evidence for the use of freezing point depression osmometry for the successful measurement of a range of sodium hyaluronate concentrations of varying viscosities.

Sample 7 represents the lowest concentration of sodium hyaluronate at 3mg/ml, with an osmolality measurement of 295mOsm, and a low coefficient of variation at 0.25%. This can then be compared to sample 5, which had the highest concentration – 30mg/ml, but with a viscosity of 51.0 Pa.s (50.83 Pa.s higher than sample 7) and a CV of 0.76% (0.51% higher CV vs. sample 7). We can then see that the relationship between concentration and viscosity is not linear, specifically shown when comparing samples 5 and 6. Whilst sample 5 contains the highest concentration, it has one of the lowest viscosities, whereas the viscosity of sample 6 (a semi-solid gel), which contains 22.5mg/ml, proved immeasurable. Nevertheless, the osmometer was capable of measuring this sample accurately and precisely, which is shown by a CV of 0.68%.

To conclude, it is clear that independent of the concentration or viscosity of the solutions, the OsmoTECH XT had the ability to maintain accurate and precise measurements and can be relied upon as a robust analytical instrument that is required within pharmaceutical laboratories today.

References

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