GPC/SEC analysis of hydroxyethyl cellulose used in pharmaceutical products

Application Note

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Introduction

Suspension and viscosity-increasing polymer excipients such as hydroxyethyl cellulose are used to uniformly disperse other ingredients throughout a formulation, and maintain their suspension so that actives do not precipitate or settle under gravity. This is particularly valuable for liquid formulations, during and after manufacture.

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Hydroxyethyl cellulose in organic eluent

Hydroxyethyl cellulose (HEC) is widely used by the cosmetic and pharmaceutical industries, for example, as a carrier gel for microbiocides. It is a nonionic polymer with many useful properties as a thickening agent, stabilizer, emulsifier or dipersant, and it easily dissolves in hot and cold water.

HECs can be analyzed by aqueous GPC but very often they are soluble in polar organic solvents, such as dimethyl formamide (DMF). PLgel 5 µm MIXED-C columns are well suited to the analysis of these celluloses. LiBr modifier is added to minimize sample aggregation as some of these materials are ionic (Figure 1). PEO/PEG standards are used as calibrants; polystyrene is soluble in DMF, but some adsorption is apparent. Table 1 shows the dispersity and molecular weight averages of three samples of hydroxyethyl cellulose.

Table 1. *Molecular weight averages and dispersity of three hydroxyethyl celluloses*

Sample	Molecular weight average			Polydispersity (Mw/Mn)
	Mn	Mw	Mp	
A	27,000	140,000	80,000	5.2
B	30,000	159,000	102,000	5.2
C	39,000	345,000	190,000	8.9

Columns: PLgel 5 µm MIXED-C, 7.5 x 300 mm (Part No. PL1110-6500)
Eluent: DMF + 0.1% LiBr
Flow Rate: 1.0 mL/min
Temp: 50 °C
Detector: RI

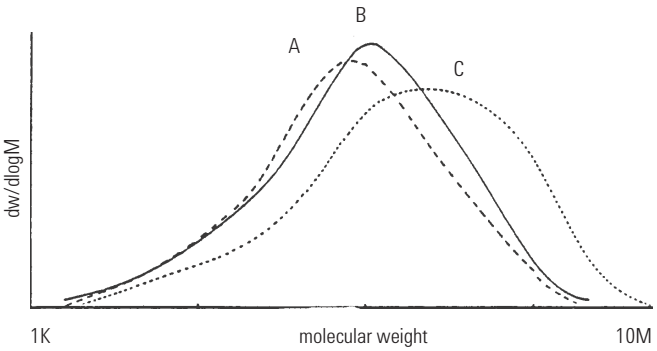

Figure 1. *Analysis of three samples of hydroxyethyl cellulose using Agilent PLgel 5 µm MIXED-C columns*

These three materials were quite different in molecular weight, indicating potential performance differences in end-use.

Hydroxyethyl cellulose in aqueous eluent

Three samples of hydroxyethyl cellulose were analyzed by size exclusion chromatography using PL aquagel-OH columns. The calculated molecular weight averages were compared with manufacturers' quoted viscosity values. Calibration was done using pullulan polysaccharide standards, also from Agilent. Figure 2 shows the raw-data chromatograms for a mixture of hydroxyethyl celluloses. A good correlation between viscosity and molecular weight averages was obtained, as can be seen in Table 2.

Table 2. *Molecular weight averages and viscosity ranges of three hydroxyethyl celloloses*

Sample	Molecular weight average			Viscosity range (cps)
	Mn	Mw	Mz	
A	60,300	179,000	139,000	75 to 112
B	413,000	849,000	1,552,000	250 to 324
C	914,000	2,016,000	3,422,000	1,500 to 2,500

Columns: PL aquagel-OH 60 8 µm, 7.5 x 300 mm (Part No. PL1149-6860)
PL aquagel-OH 40 8 µm, 7.5 x 300 mm (Part No. PL1149-6840)
Eluent: 0.05 M NaH_2PO_4 + 0.25 M NaCl at pH 7
Flow Rate: 1.0 mL/min
Temp: 50 °C
Detector: RI

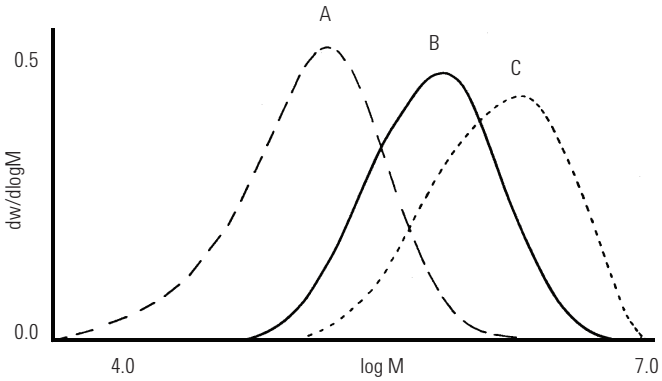

Figure 2. *Raw-data chromatograms for a mixture of hydroxyethyl celluloses on Agilent PL aquagel-OH columns*

Modified hydroxyethyl cellulose

Modifying the hydrophobicity of HEC alters the molecular weight, and such changes can be assessed by size exclusion chromatography with PL aquagel-OH 40 and PL aquagel-OH 60 8 µm columns from Agilent.

In this case, two different PL aquagel-OH columns were connected in series to cover a molecular weight range from 10^4 to 10^7. Column calibration was achieved using Agilent pullulan standards.

Figure 3 shows overlaid molecular weight distributions of a sample of HEC before and after modification to its hydrophobicity. Sample A is HEC. Sample B is Sample A after hydrophobic modification.

Samples: Hydroxyethyl cellulose before and after modification
Columns: PL aquagel-OH 60 8 µm, 7.5 x 300 mm (Part No. PL1149-6860)
PL aquagel-OH 40 8 µm, 7.5 x 300 mm (Part No. PL1149-6840)
Eluent: 0.05 M NaH_2PO_4 + 0.25 M NaCl at pH 7
Flow Rate: 1.0 mL/min
Temp: 50 °C
Detector: RI

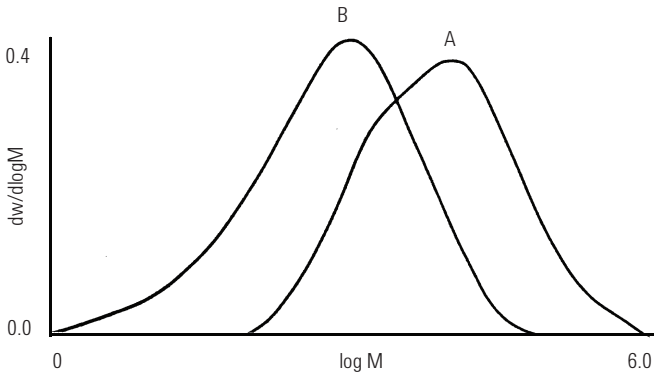

Figure 3. *Overlaid molecular weight distributions of a sample of hydroxyethyl cellulose before and after modification*

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