

# Separation of statistic MMA-MAA Copolymers using Gradient SEC

## Application Note Pharmaceutical Analysis

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Isocratic GPC/SEC is a powerful tool to separate macromolecules based on their hydrodynamic volume. In case of homopolymers GPC/SEC allows the fast, precise and easy determination of the complete molar mass distribution.

Unfortunately many modern polymeric materials are copolymers and isocratic GPC/SEC does not provide any information about the chemical composition. Here SEC-gradients or polymer HPLC is the method of choice.

### Introduction

Statistic copolymers of methyl methacrylate (MMA) and methacrylic acid (MAA) are widely used in pharmaceutical applications. Besides the molar mass distribution the chemical composition and the amount of comonomers in the copolymer is of importance. Separations by conventional gradient HPLC failed, since the polar eluents required to dissolve polymers of high acid content prevent adsorption onto the stationary phase, resulting in pronounced breakthrough peaks. The problem can be avoided applying SEC-gradients, resulting in the desired separation according to the amount of methacrylic acid. The system can be calibrated using reference materials of known composition. This allows determining the average copolymer composition as well as the compositional heterogeneity.

### System Requirements

|                  | Conditions  |
|------------------|---|
| Pump             | PSS SECcurity GPC1260 binary pump <ul style="list-style-type: none"> <li>flow rate [mL/min]: 1.0</li> <li>mobile phase: Gradient: Chloroform/DMAc</li> </ul>      |
| Injection system | PSS SECcurity GPC1260 Autosampler<br>Injection interval: 32 min   |
| Columns          | <ul style="list-style-type: none"> <li>PSS PROTEEMA precolumn (8*50 mm)</li> <li>PSS PROTEEMA, 3 <math>\mu</math>m, 100 Å (8x300 mm)</li> </ul> Temperature: 60°C |
| Calibration      | PSS MMA-MAA copolymers of different acid content (MAA: 9%, 25%, 31%, 42%, 48%wt)  |
| Loading          | Samples dissolved in DMAc <ul style="list-style-type: none"> <li>1 mg/mL, 100 <math>\mu</math>L injection volume</li> </ul>                                       |
| Detector         | <ul style="list-style-type: none"> <li>PSS SECcurity ELS1000</li> </ul> Gas flow: 1.5 SL/min<br>Nebulizer temperature: 100 °C<br>Evaporator temperature: 200 °C.  |
| Software         | PSS WinGPC UniChrom with ChromPilot and Chemical Heterogeneity module   |



## Procedure, Results & Discussion

The experimental procedure of SEC-gradients differs from conventional gradient HPLC. While in conventional HPLC the sample is dissolved in a weak eluent and injected at adsorbing conditions, the sample is dissolved in a strong mobile phase and injected at the end of the SEC-gradient. In the present application the copolymers were dissolved in DMAc.

Gradient details:

- 0-3 min: 50%DMAc
- 3-8 min: 100%DMAc
- 8-23 min: 100%CHCl<sub>3</sub>
- 23-26 min: 5%DMAc
- 26-32 min: linear increase from 5% to 50% DMAc.

Figure 1 shows the separation of 5 statistical MMA-MAA copolymers with MAA contents between 9 and 48%wt using a Chloroform/DMAc gradient from 5% to 50% DMAc. The sample components elute before the injected solvent and the different samples are clearly separated.

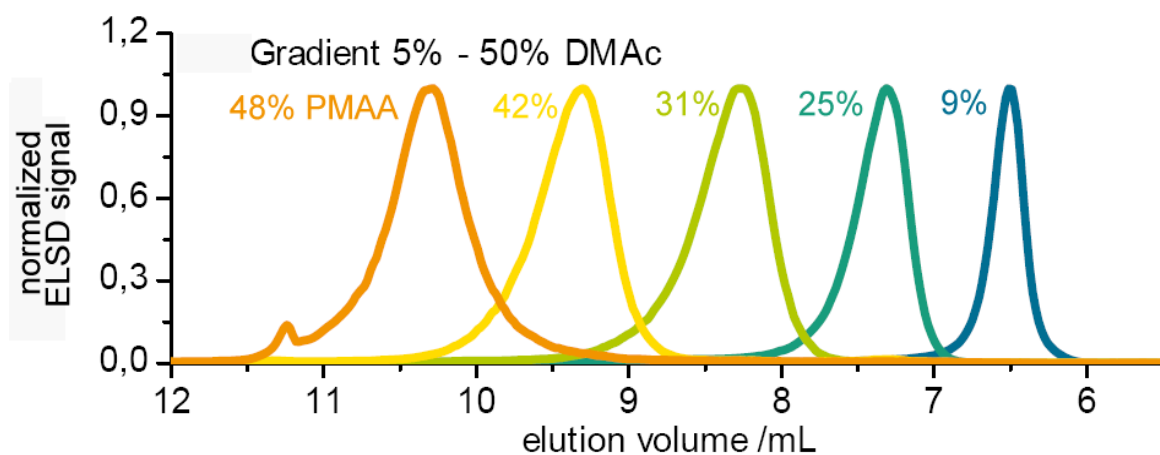


Fig. 1: Separation of 5 MMA-MAA copolymers with different PMMA content using a Chloroform - DMAc gradient on PSS PROTEEMA columns

A nearly linear dependence between MAA content and elution volume is observed. The use of this calibration curve allows the determination of the chemical composition distribution. Figure 2 shows the chemical composition distribution for the 5 samples with the PMAA content between 48% and 9%. It is observed that an increase in MAA content results in a significantly broader chemical composition distribution (CCD).

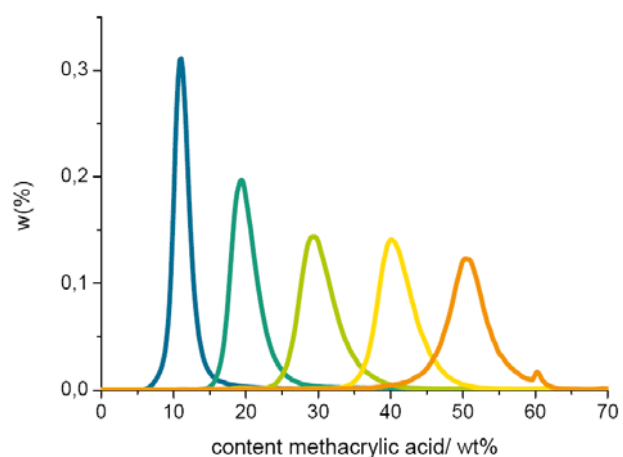


Fig. 2: Chemical composition distribution for 5 MMA-MAA copolymers. MAA content see Fig. 1