Are Sub-2 µm Superficially Porous Particles Needed for Small Molecules?

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Are Sub-2µm SPP Needed for Small Molecules?

- Controversial question
  - Theory predicts efficiency advantages of smaller particles
  - SPP shown to have unusually high efficiency
  - Sub-2µm SPP already available
  - General consensus is “Yes”
  - Previous studies within AMT showed practical limitations

- This presentation
  - Authors’ opinions on topic; no equations
  - Large molecule separations not discussed

Upside of Using Sub-2µm Particles

- Smaller particles allow faster separations
  - High efficiency in short columns
  - Improved productivity
  - Short run times = less solvent usage
  - Sharper peaks for more sensitivity
- High number of theoretical plates possible in longer columns
  - Improved peak capacity for complex mixtures
- Keeping up with state-of-the-art technology

Downside of Using Sub-2µm Particles

- Specially designed (expensive) instruments required for optimum use
  - 400 – 600 bar often insufficient for optimum flow
  - Low-dispersion design required to minimize extra-column effects for highest efficiency
    - Small ID tubing and flow cells significantly add to operational pressure
  - Maintenance is expensive and often not user-friendly

Downside of Using Sub-2µm Particles

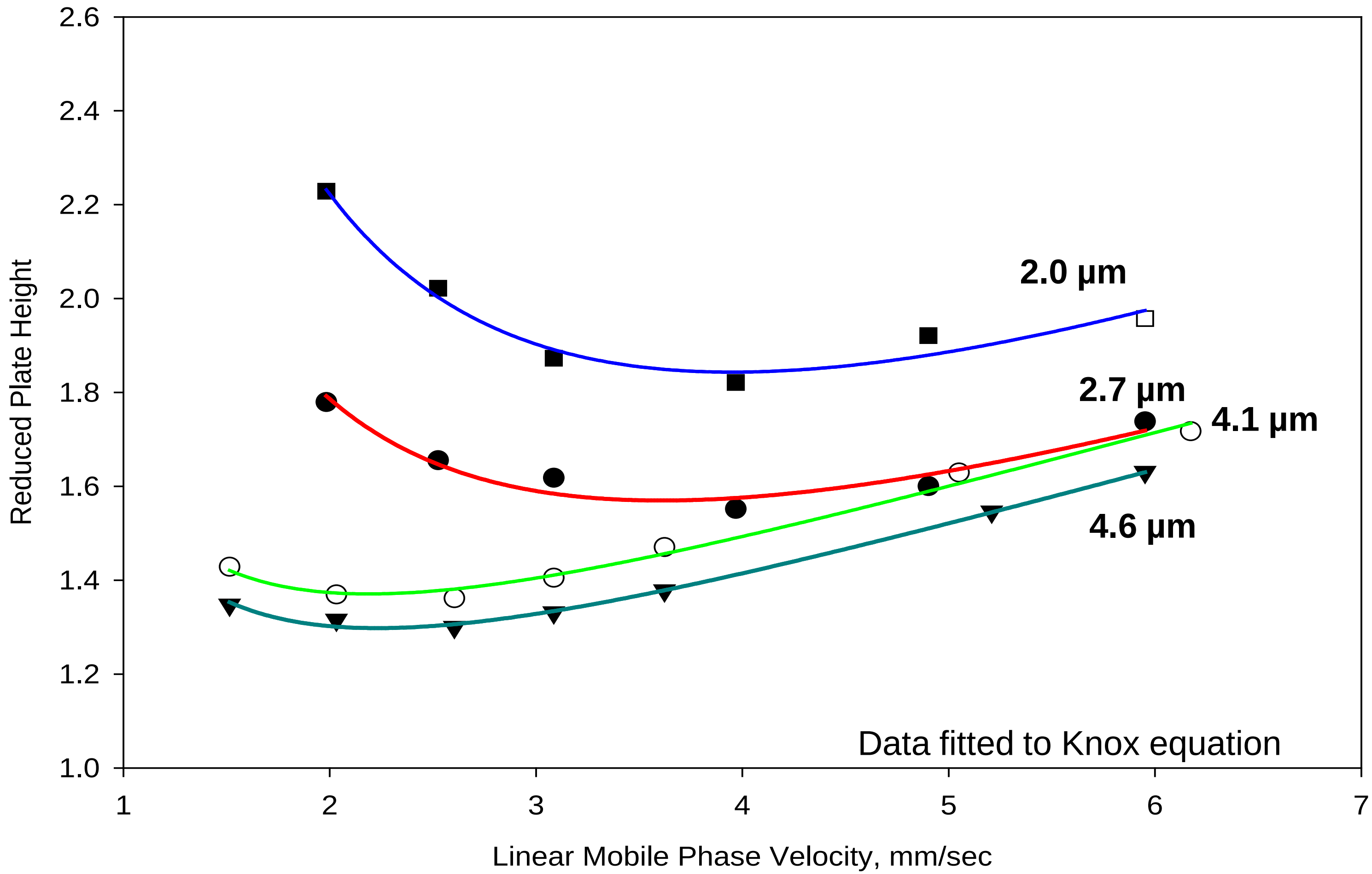
- Column frits with small pores (0.2 – 0.5µm) required to retain particles in columns
  - More subject to plugging than 2µm frits
  - Additional efforts needed to avoid particulate fouling (filter samples and mobile phases)

- Frictional heating of columns
  - More pronounced as d_p is reduced
  - Can result in band-broadening and changes in retention
  - ≤ 3 mm i.d. columns required to minimize frictional heating effects

Downside of Using Sub-2μm Particles

- **High pressure can cause changes in retention and selectivity vs low pressure separations**
  - **Problematic to convert separations made with small particles to columns of larger particles suited for routine analyses**
- **Columns may not exhibit expected efficiency or stability**
  - **Small particles harder to pack into homogeneous beds for highest efficiency**

Effect of Particle Size on h vs v Plots



Reduced Plate Heights ($h = H/d_p$) get smaller as the particle size is <u>increased</u>, indicating more homogeneity in packed beds for the larger particles.

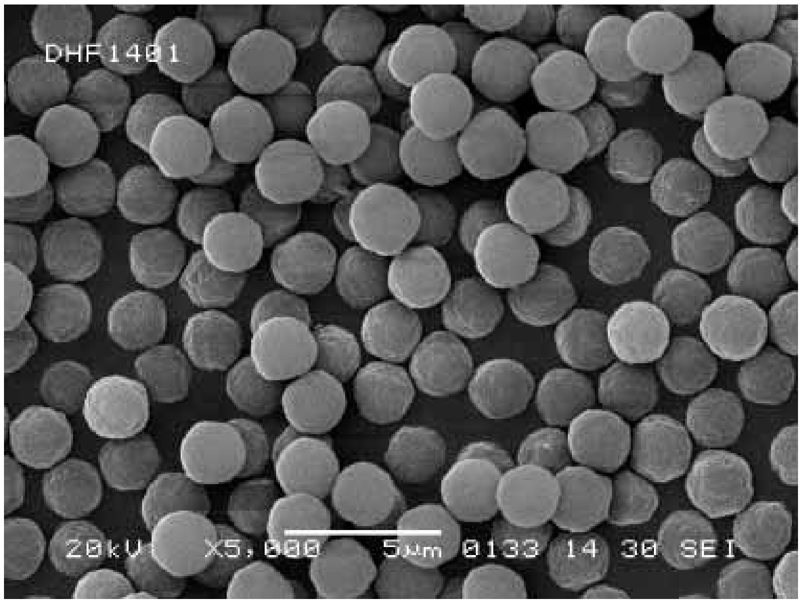
Are Sub-2μm SPP Needed for Small Molecules?

- **Our conclusion: useful but not necessary**
  - **Upsides not sufficient to overcome the Downsides for most small molecule applications**
  - **Small molecules do not require shorter diffusion paths of small particle size SPP for adequate mass transfer**
  - **A compromise alternative is suggested**

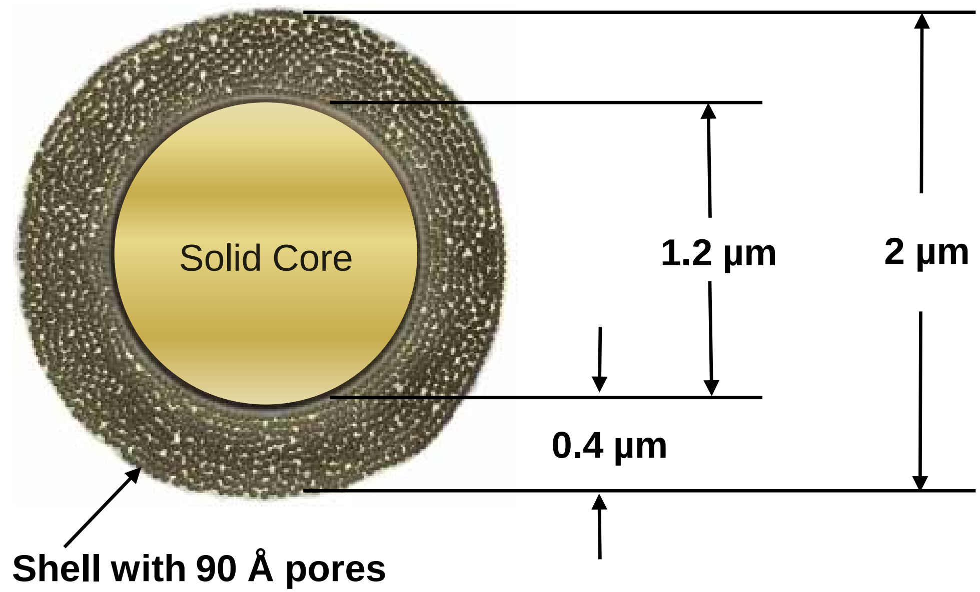
An Alternative – 2µm SPP

- Retains most of advantages of sub-2µm
  - Higher efficiencies than sub-3µm SPP
- Minimizes disadvantages of sub-2µm
  - Lower pressure requirements

2 µm HALO Particle Design



SEM image of 2 µm HALO particles

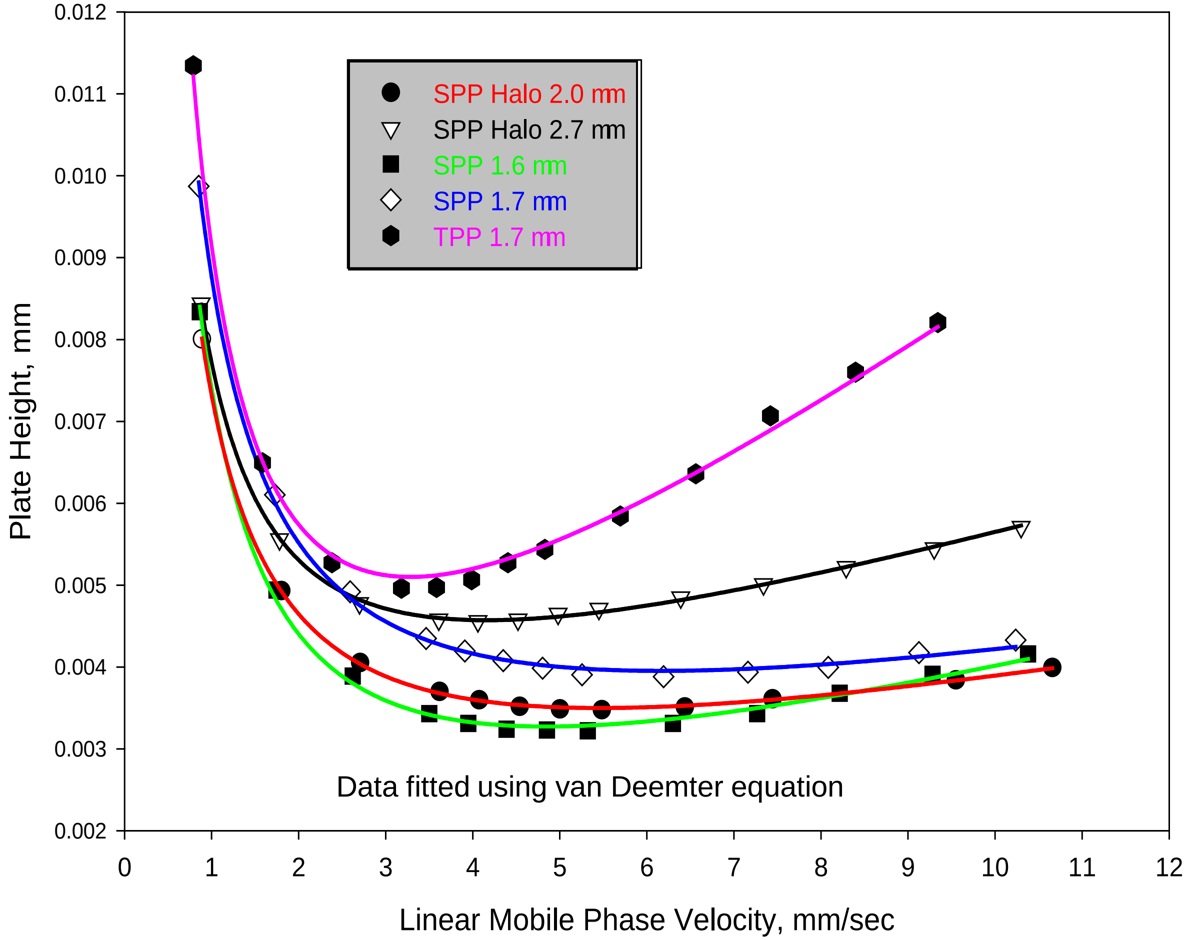


Mode – 2.006
Mean – 2.016
Median – 2.004
S.D. – 0.111um
CV – 5.5%

Comparing van Deemter Plots (H)

Plate Height vs. Mobile Phase Velocity Plots

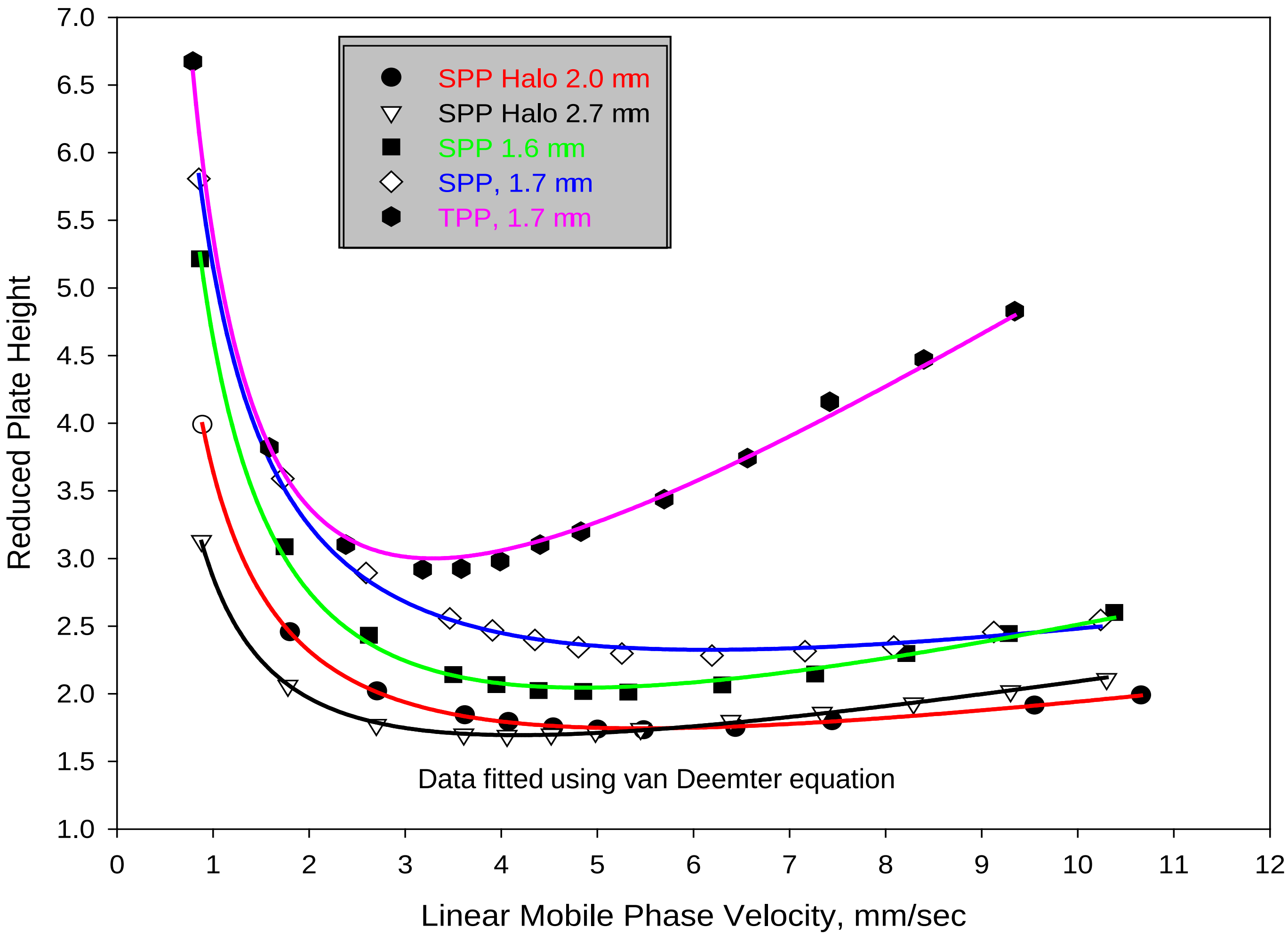
Columns: 50 x 2.1 mm; Instrument: Shimadzu Nexera; Solute: naphthalene
Mobile phase: Halo - 50/50 ACN/water, k=6.3; 1.6 mm SPP - 48.5/51.5 ACN/water, k=6.3;
1.7 mm SPP - 47/53 ACN/water, k=6.2; 1.7mm TPP - 48.5/51,5 ACN/water, k=6.3
; Temperature: 35 ^{o}C; Injection volume: 0.2 mL



Comparing van Deemter Plots (h)

Reduced Plate Height vs. Mobile Phase Velocity Plots

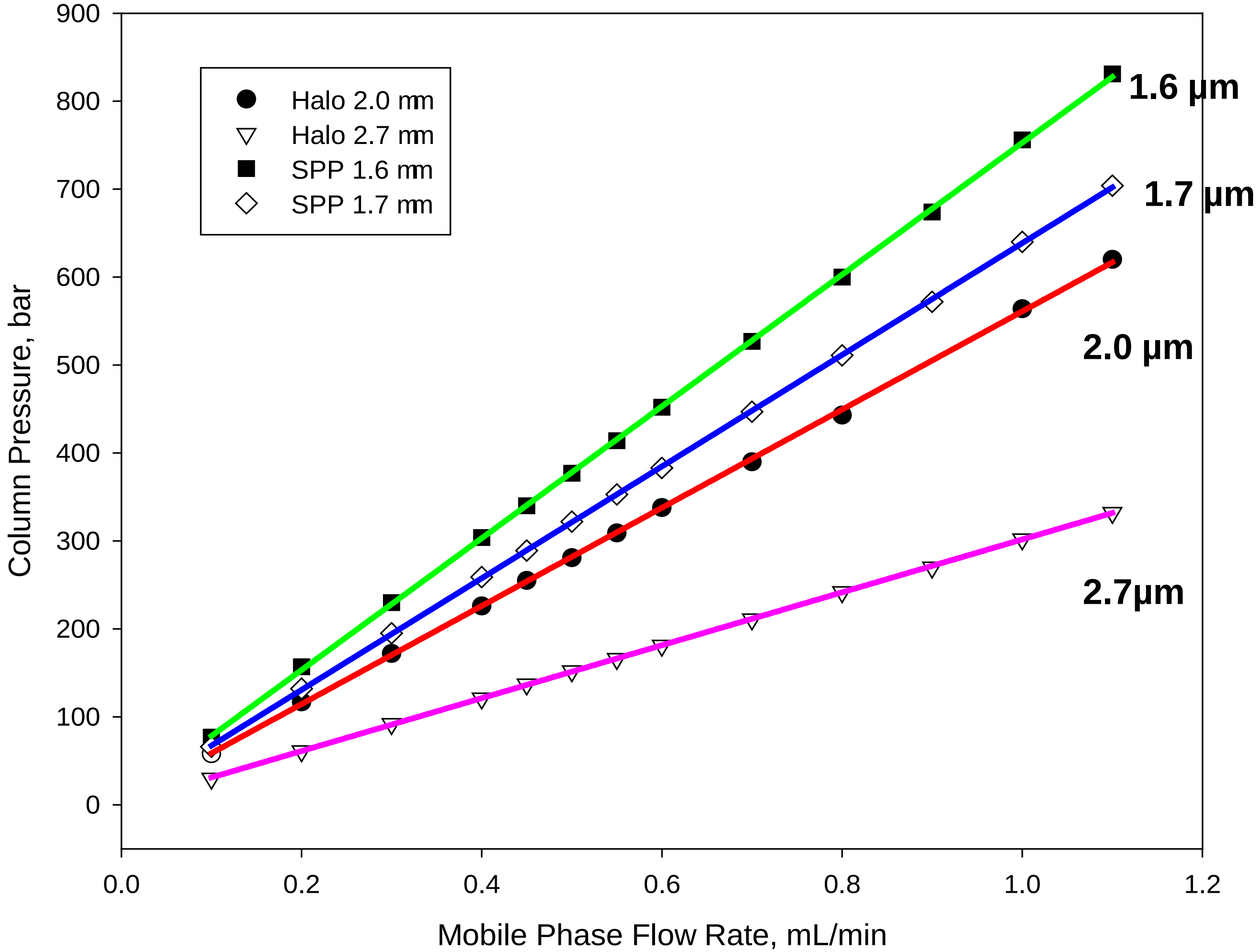
Columns: 50 x 2.1 mm; Instrument: Shimadzu Nexera; Solute: naphthalene
Mobile phase: Halo - 50/50 ACN/water, k = 6.3;
1.6 mm SPP - 48.5/51.5 ACN/water, k = 6.3; 1.7 mm SPP - 47/53 ACN/water, k = 6.2
1.7 mm TPP - 48.5/51.5 ACN/water, k=6.3; Temperature: 35 °C; Injection volume: 0.2 mL



Pressure vs Flow

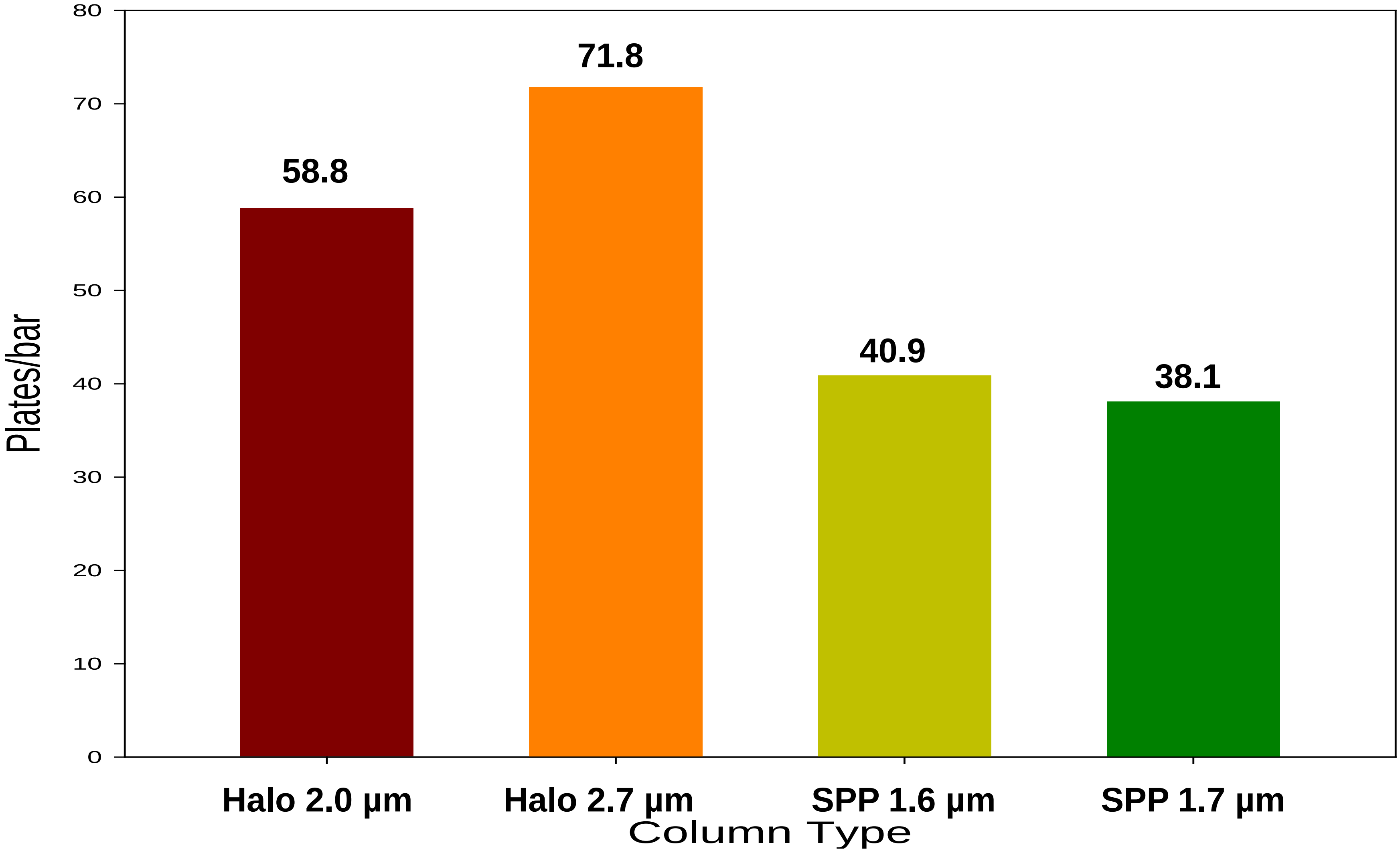
Mobile Phase/Column Pressure Plots

Columns: 50 x 2.1 mm, C18: Instrument: Shimadzu Nexera; Solute: naphthalene
Mobile phase: Halo, 50/50 ACN/water, k=6.3; SPP 1.6 mm, 48.5/51.5 ACN/water, k=6.3
SPP 1.7 mm, 47/53 ACN/water, k=6.2; Temperature: 35 ^{o}C; Injection volume: 0.2 mL



Plates per Bar

Columns: 50 x 0.21 mm C18; Instrument: Shimadzu Nexera; Solute: naphthalene
Mobile phase: 50/50 - 47/53 ACN/water; Flow rate: 0.5 mL/min; Temperature: 35 °C

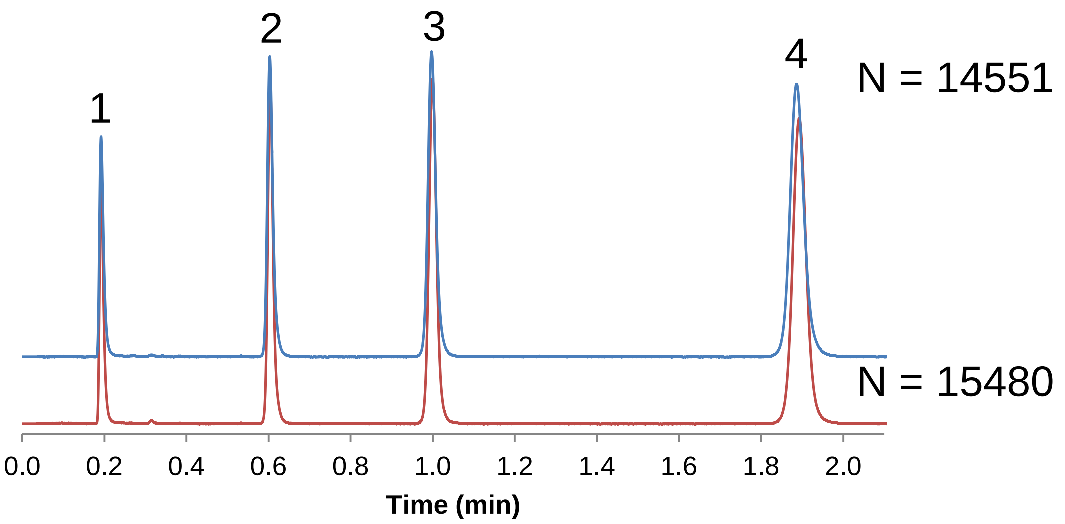


High Pressure Stability of HALO 2 C18

Columns: 2.1 x 50 mm
Instrument: Shimadzu Nexera
Injection Volume: 0.2 µL
Detection: 254 nm
Temperature: 25 °C

Mobile Phase A: water
Mobile Phase B: acetonitrile
Ratio A:B: 15/85
Flow rate: 0.5 mL/min

Peak Identities:
1. Uracil
2. Pyrene
3. Decanophenone
4. Dodecanophenone



Column performance is maintained after injections at high pressure (950 bar)
Red trace = before high pressure
Blue trace = after high pressure

Column Stability Test

Columns: 50 x 2.1 mm, Halo 2.0 µm C18; Flow rate: 2.50 mL/min; Temperature: 25 ºC
Solute: naphthalene**;** Mobile phase: 85% ACN/15% water
One sigma results

Columns	Average Injection Pressure, bar	Average Test Pressure, bar	Average Plate Number	Average % Plate Number Loss
6 - Halo 2.0 µm	980 ± 22	Before: 181 ± 4	15570 ± 330	
		After: 186 ± 4	14320 ± 550	8%

Conclusions

- Sub-2 µm SPP useful for R&D but less practical for most routine small molecule applications
- Larger SPP are less problematic for daily operation
- Columns of 2-µm SPP appear to be a good compromise of speed and efficiency with superior advantages for small molecule applications

Acknowledgements

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