

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

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Are Sub-2 μ m SPP Needed for Small Molecules?

- Controversial question
 - Theory predicts efficiency advantages of smaller particles
 - SPP shown to have unusually high efficiency
 - Sub-2 μ m 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-2 μ m 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-2 μ m 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

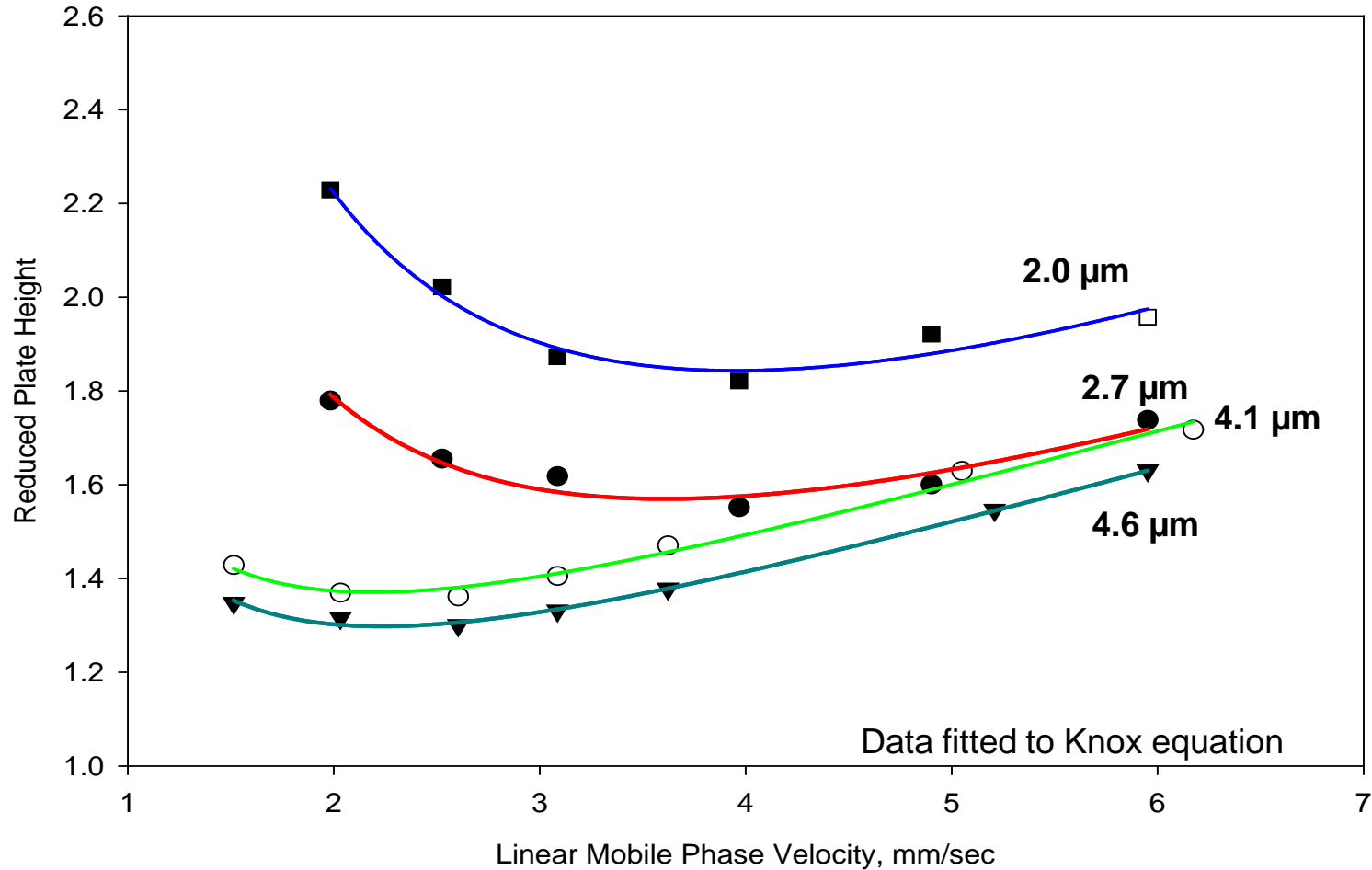
Downside of Using Sub-2 μ m Particles

- Column frits with small pores (0.2 – 0.5 μ m) required to retain particles in columns
 - More subject to plugging than 2 μ m 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-2 μ m 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 increased, indicating more homogeneity in packed beds for the larger particles.

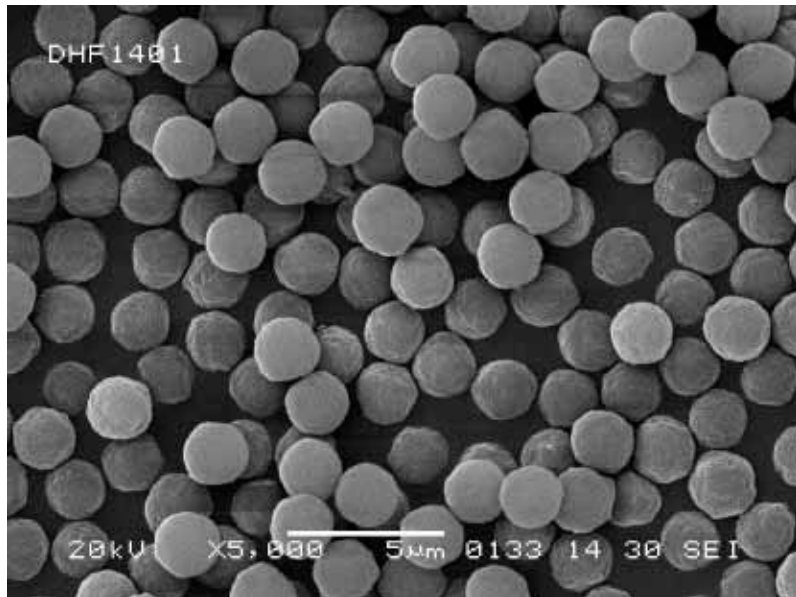
Are Sub-2 μ m SPP Needed for Small Molecules?

- 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 – 2 μ m SPP

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

2 μm HALO Particle Design



SEM image of 2 μm HALO particles

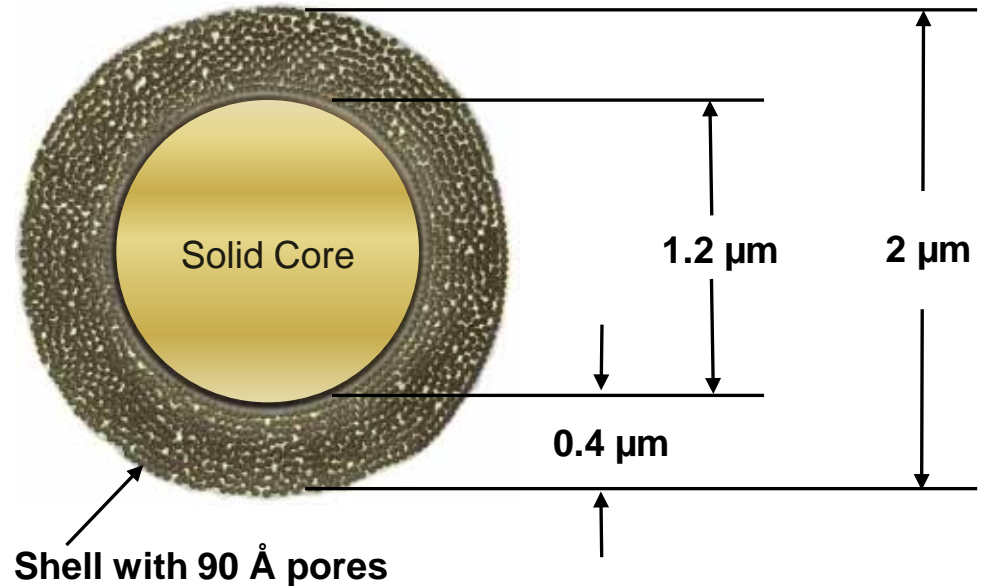
Mode – 2.006

Mean – 2.016

Median – 2.004

S.D. – 0.111 μm

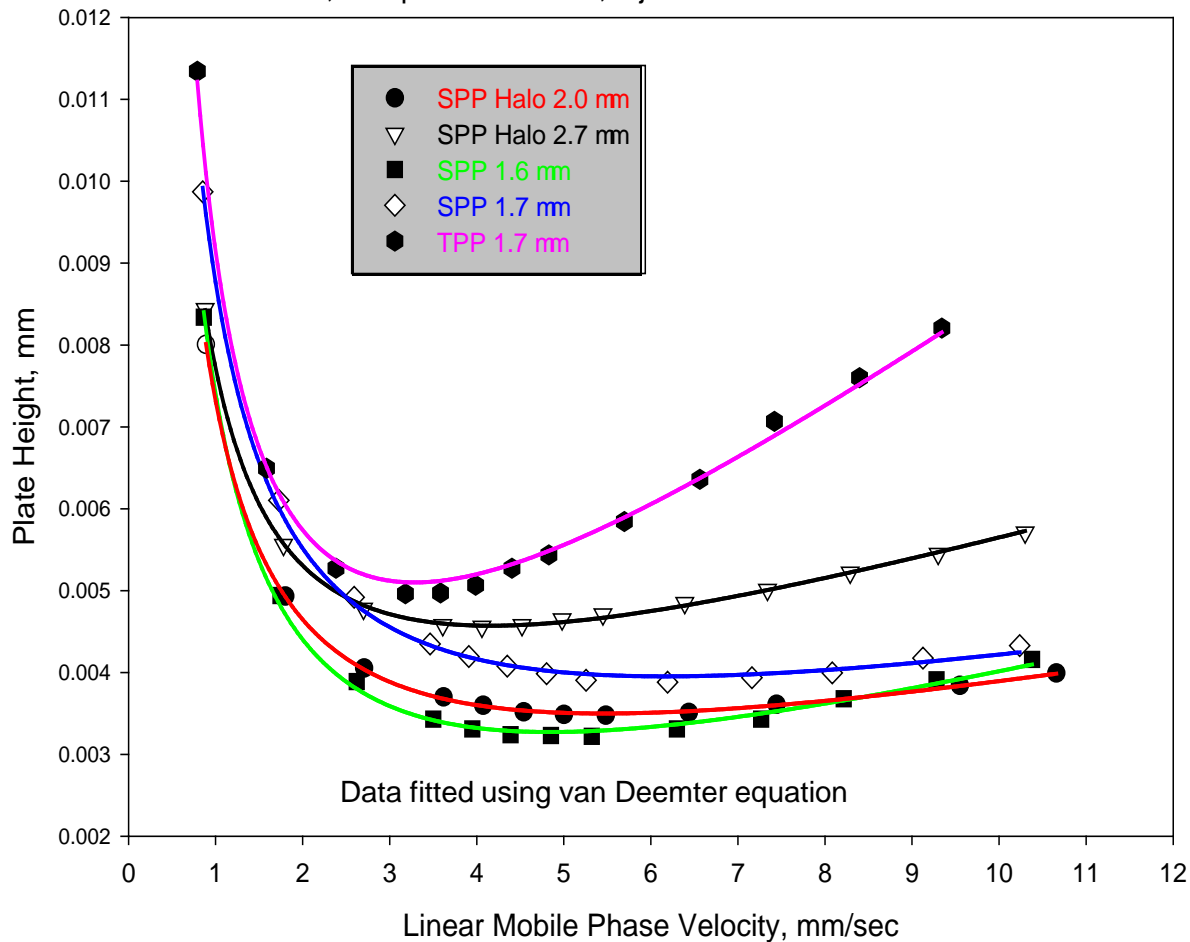
CV – 5.5%



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 °C; Injection volume: 0.2 mL



Comparing van Deemter Plots (h)

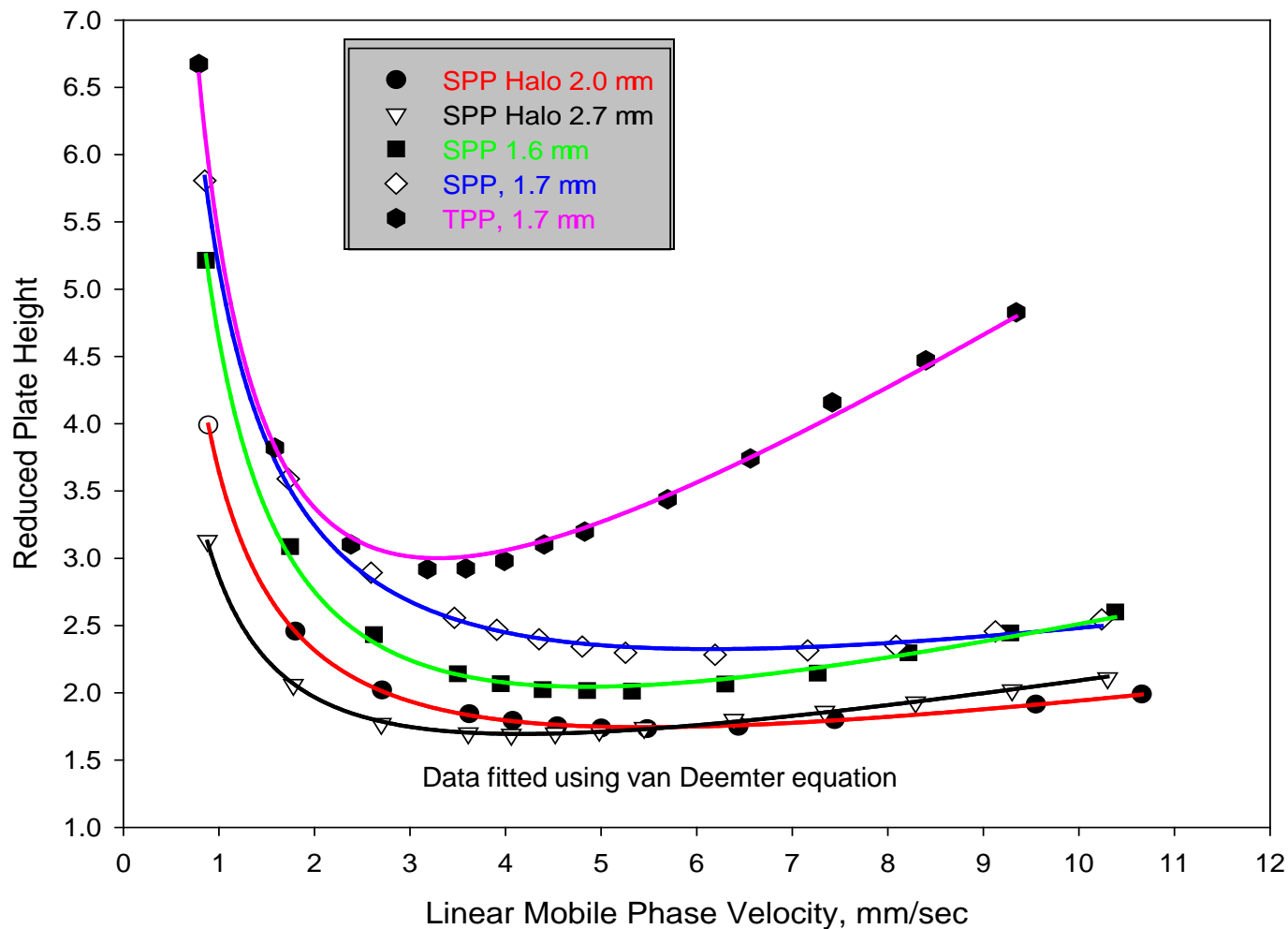
Reduced Plate Height vs. Mobile Phase Velocity Plots

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, $k = 6.2$

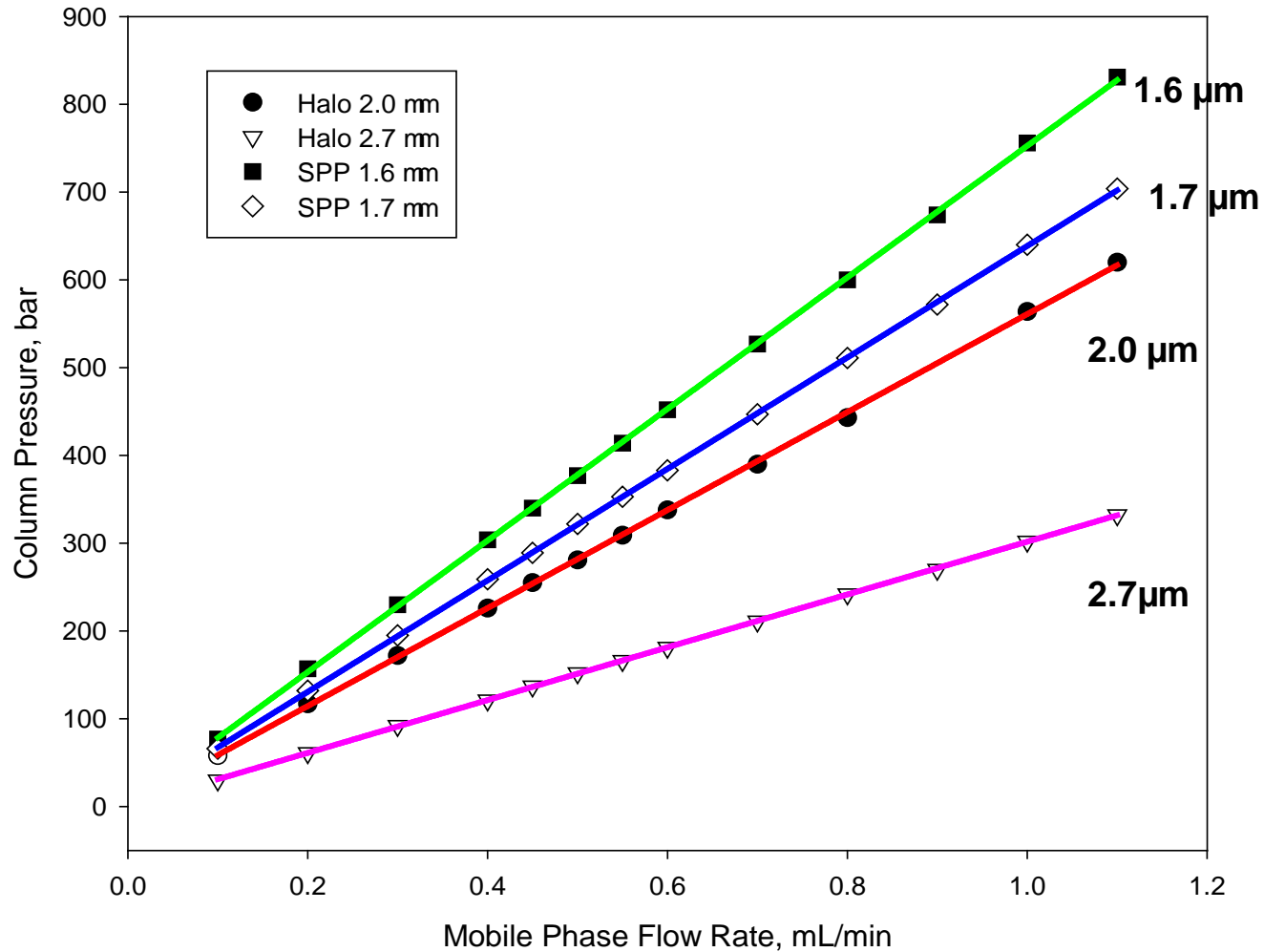
1.7 mm TPP - 48.5/51.5 ACN/water, $k=6.3$; Temperature: 35 °C; Injection volume: 0.2 mL



Pressure vs Flow

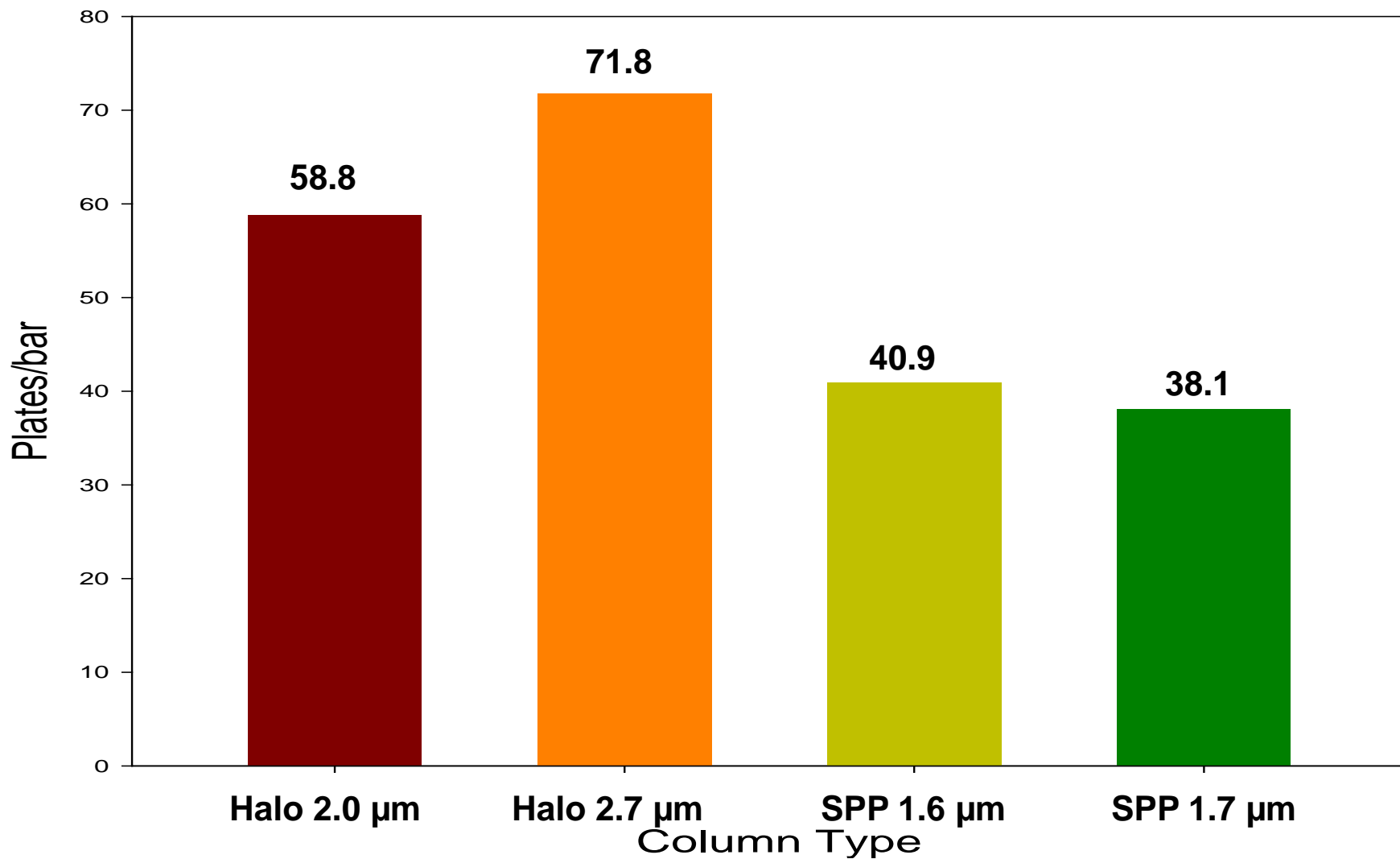
Mobile Phase/Column Pressure Plots

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 °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

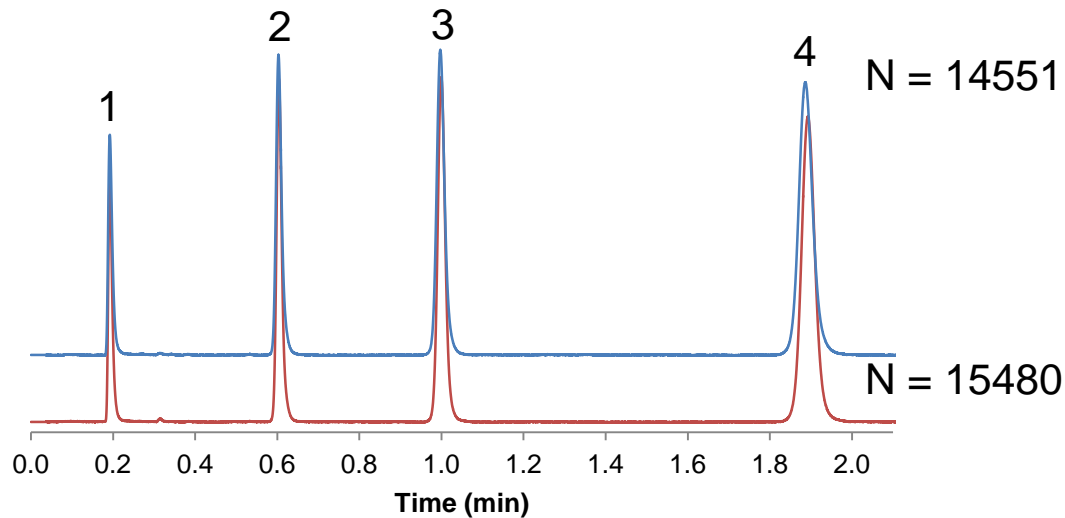


High Pressure Stability of HALO 2 C18

Columns: 2.1 x 50 mm
Instrument: Shimadzu Nexera
Injection Volume: 0.2 μ L
Detection: 254 nm
Temperature: 25 $^{\circ}$ 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 $^{\circ}\text{C}$

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 \pm 22	Before: 181 \pm 4	15570 \pm 330	
		After: 186 \pm 4	14320 \pm 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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