# Understanding the Relationship between Particle Size, Performance and Pressure

AKN0012

ACE Knowledge Note #0012

## Introduction

Chromatographers are inundated with vendor information on different particle sizes and silica platforms, which can lead to confusion as to what is the best solution for a certain problem. It is however important for the end user to understand what the benefits of these particles are, and how it affects their chromatography. There are well documented benefits to using sub 2 µm silica particles, and this Knowledge Note will look into some of these, and will look to understand the relationship between using smaller particle size and the effect on performance and column efficiency.

## Particle Size and Efficiency

Efficiency is typically spoken of in close connection with particle size. It is one of the key benefits of moving towards smaller particles, so it is therefore important to know how to compare particle sizes and what efficiency means in practice.

One method to compare the efficiency of a column is to perform a van Deemter plot, which measures height equivalent to a theoretical plate (HETP) vs linear velocity in mm/sec. The van Deemter is composed of three critical terms: eddy diffusion, diffusion coefficient and mass transfer coefficient (for more information on a van Deemter plot and its uses, see Knowledge Note KN0010). Smaller particles have smaller diffusion paths which increase mass transfer, which has the potential to reduce plate height, and therefore increase efficiency.

Plotting efficiency vs flow rate allows the chromatographer to see that each particle size has its own optimum flow rate, as seen in Figure 1. The smaller particle size has a broader optimum flow rate range at much higher flows than larger particle sizes.

Some of the key benefits for decreasing particle size include:

- **Increased column efficiency**

As shown in equation 1, efficiency is inversely proportional to particle size. This therefore means, as particle size decreases, efficiency should increase.

$$N \approx \frac{L}{2d_P} \qquad \textbf{Equation 1}$$

- **Shorter analysis time**

The smaller size particle has improved efficiencies at higher flow rates which indicate shorter analysis times are possible, without being detrimental to resolution.

- **Increased sample throughput**

With the increased flow/shorter analysis time, the sample throughput will increase, therefore potentially improving the productivity in the laboratory.

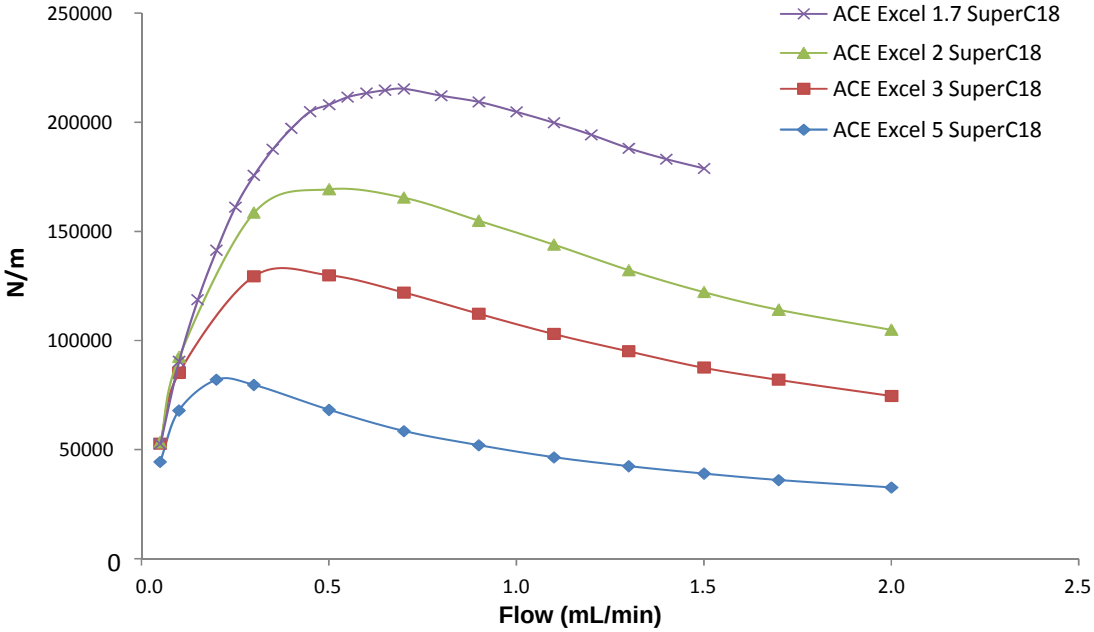



**Figure 1:** Plot of efficiency, N, against flow rate for the different ACE particle sizes.

It is important to note, however, that there is a trade off with increased back pressure when decreasing particle size, as shown in Figure 2. This should be monitored carefully in order to avoid going over the pressure rating of the LC pump and the column. The pressure drop of any particle size can be estimated using equation 2:

$$P = \frac{\eta v L}{{d_p}^2} \qquad \textbf{Equation 2}$$

Where η is the mobile phase viscosity, v is mobile phase velocity, L is column length and $d_P$ is particle size. It is important to be aware the mobile phase viscosity will change with temperature.

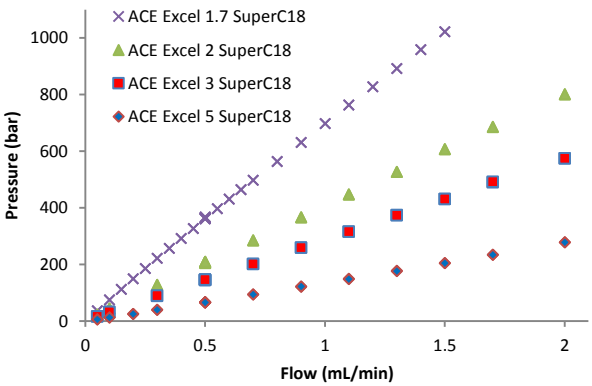
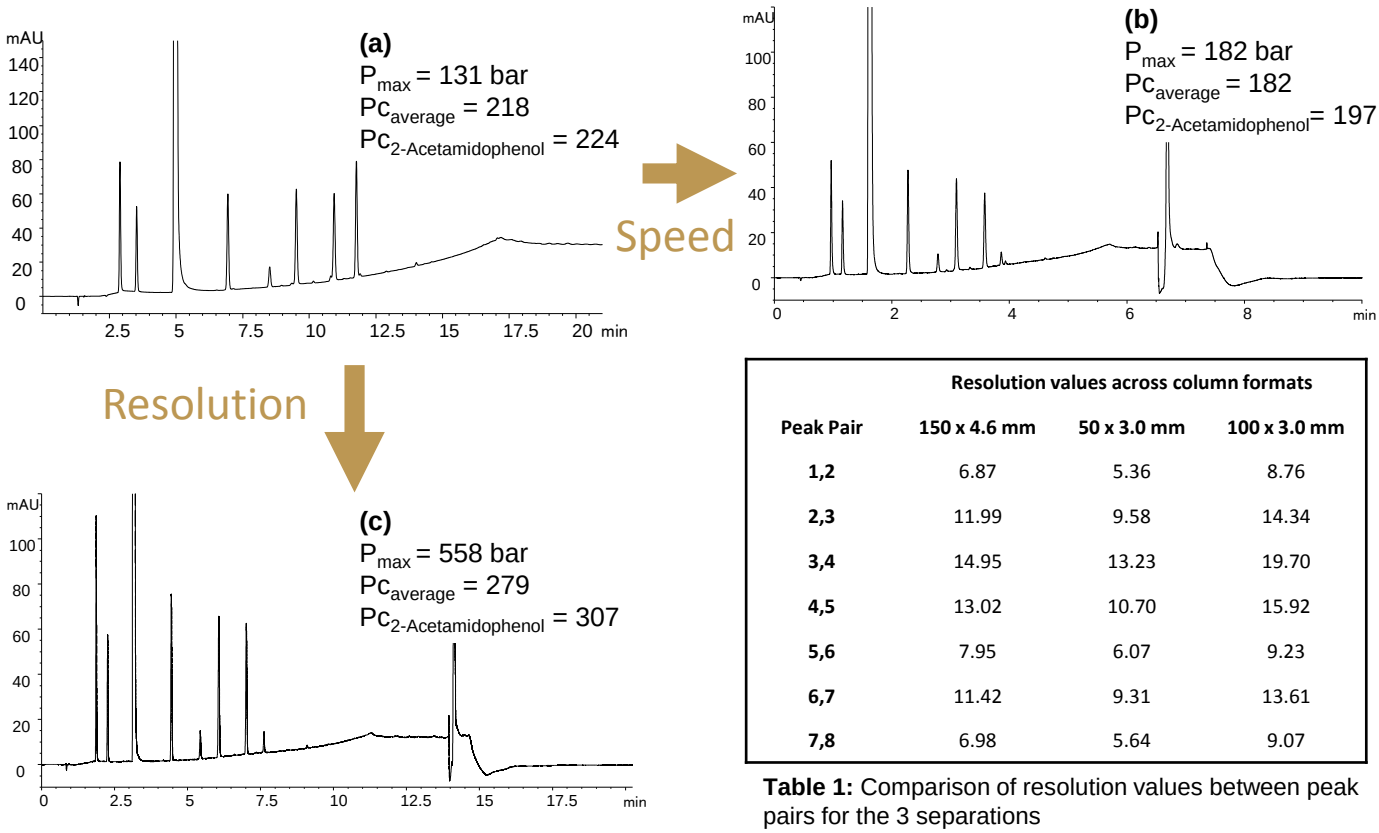



**Figure 2:** Pressure vs flow rate for different particle sizes

### How Does This Affect Chromatography?

The example shown in Figure 3 displays the benefits of 1.7 µm, for either speed or increased resolution. The paracetamol and related substances separation was originally performed on an ACE Excel 5 C18, 150 x 4.6 mm column (Figure 3a). This was translated to an ACE Excel 1.7 C18, 50 x 3.0 mm for faster analysis time (Figure 3b). As shown below, the run time has decreased by 65%, whilst approximately maintaining resolution.

The separation was also successfully translated to an ACE Excel 1.7 C18, 100 x 3.0 mm column, which increases peak capacity ($P_C$) and also increases resolution (Figure 3c) due to the increased column length. The peak capacity values are reported on the chromatograms whilst the comparative resolution data can be seen in Table 1.




| | Resolution values across column formats | | |
|---|---|---|---|
| **Peak Pair** | **150 x 4.6 mm** | **50 x 3.0 mm** | **100 x 3.0 mm** |
| **1,2** | 6.87 | 5.36 | 8.76 |
| **2,3** | 11.99 | 9.58 | 14.34 |
| **3,4** | 14.95 | 13.23 | 19.70 |
| **4,5** | 13.02 | 10.70 | 15.92 |
| **5,6** | 7.95 | 6.07 | 9.23 |
| **6,7** | 11.42 | 9.31 | 13.61 |
| **7,8** | 6.98 | 5.64 | 9.07 |

**Table 1:** Comparison of resolution values between peak pairs for the 3 separations

**Figure 3:** Paracetamol porous gradient separation: (a) ACE Excel 5 C18, 150 x 4.6 mm, 1 mL/min (b) ACE Excel 1.7 C18, 50 x 3.0 mm, 0.51 mL/min, (c) ACE Excel 1.7 C18 100 x 3.0 mm, 0.51 mL/min

The 1.7 µm particle is also extremely useful for ultra-resolution examples, as displayed in Figure 4. Ultra-resolution increases the chromatographic performance, which is necessary for difficult mixtures such as the natural product, Ginkgo Biloba. The increase in performance increases peak resolution and peak capacity, which is helpful for any complex sample.

As can be seen in Figure 5, the increased bed length increased both the sensitivity and resolution. The increased resolving power also enhanced the peak capacity, as seen in Figure 4 where more distinct peaks were observed.

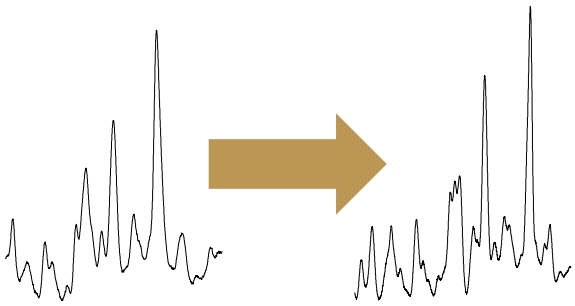


**Figure 5:** Increased sample detail.

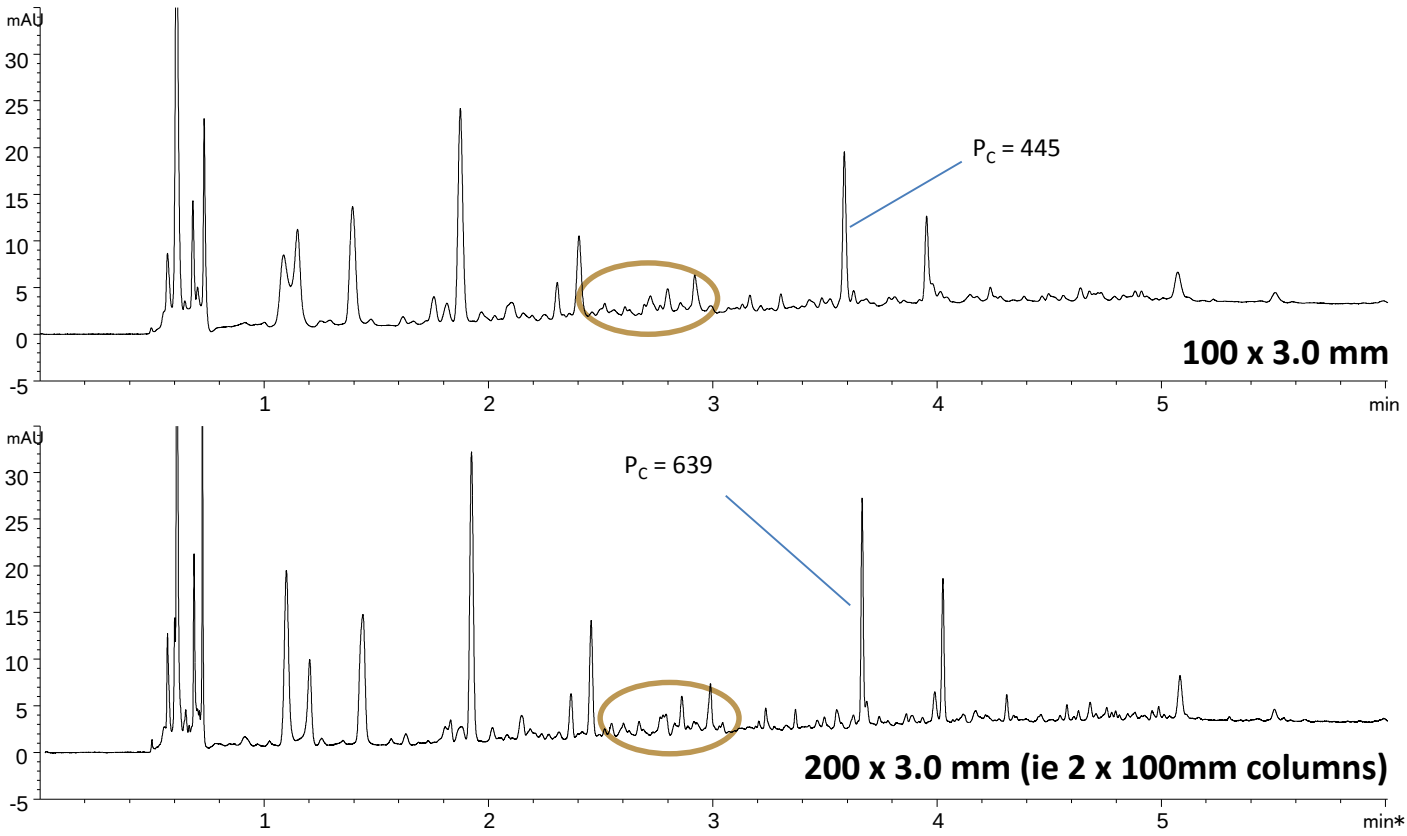



**Figure 4:** Ginkgo Biloba ultra resolution example on an ACE Excel 1.7 C18-PFP 100 x 3.0 and 200 x 3.0 mm column format.

## Conclusion

This Knowledge Note has demonstrated the benefits of using smaller particle size whilst compensating for the increase in back pressure. It has also practically demonstrated the need for smaller particle sizes for increased analysis speed, increased resolution and for ultra resolution of complex samples.