The Effect of Silica Particle Purity and Morphology on Flash Chromatography Performance

David Kennedy, J. Preston, **Zeshan Aqeel**, and Rola El Abaji
Phenomenex, Inc., 411 Madrid Ave., Torrance, CA 90501 USA

Introduction

Flash chromatography is an essential purification tool for both chemical synthesis and natural products. The technique has developed a reputation for being fast (Flash!) and cheap, but also for being crude. In other words, users don't expect good chromatography in flash applications and often settle for sub-optimum performance. This has given rise to the erroneous belief that "all flash columns are the same" and you should just go for the cheapest product.

Flash chromatography may not operate at the same level of performance as high performance liquid chromatography (HPLC), but it does operate on the same physical principles. In this Technical Poster we will demonstrate that silica particle shape, size and purity are just as important in Flash as they are in HPLC. In both cases, thoughtful management of these parameters can significantly improve chromatographic performance.

The Impact of Ultra-Pure Silica

The ordinary, commercial grade silica used in most Flash columns contains impurities (such as heavy metals) which create areas of high surface activity that can distort the interaction of adsorbed solutes with the bulk silica surface. This is manifested in peak shifting, broadening and tailing, particularly for basic and acidic compounds. Claricep™ CS Flash columns are made with ultra-pure silica which results in much less abnormal surface activity. This produces chromatograms with much sharper peaks.

The difference between Claricep CS media and ordinary Flash media can be seen in **Figures 1** and **2.** Claricep CS results in more symmetric peak shapes for both a basic and an acidic compound.

FIGURE 1.

Aniline Peak Shape Symmetry and Retention Test

Flash Conditions:

Column: Claricep Irregular Silica CS (40-60 µm, 60 Å, 40 g)
Brand I: Flash Irregular Silica (40 g)
Mobile Phase: Dichloromethane/ Methanol (99:1)
Flow Rate: 20 mL/min
Detector: UV @ 254 nm
Temperature: Ambient
Retention Time: CLARICEP CS: 4.090 min
Brand I: 4.373 min
Sample: Aniline

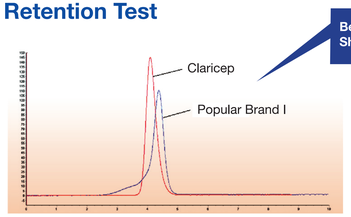


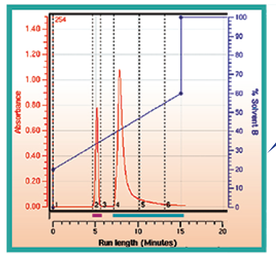
FIGURE 2.

Comparison of Claricep CS vs. Popular Brand I

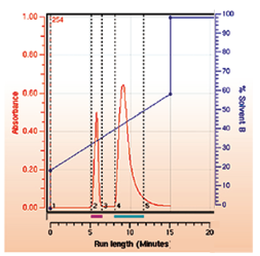
Flash Conditions:

Column: Claricep Irregular Silica CS (40-60 µm, 60 Å, 40 g)
Brand I: Flash Irregular Silica Column (40 g)
Mobile Phase: Hexane/Ethylacetate (gradient)
Detector: UV @ 254 nm
Temperature: Ambient
Sample: Phenyl acetone,4-aminobenzoic acid

CLARICEP CS 40 g



Popular Brand I 40 g



Specially Deactivated Silica

Additional improvements can be made by using Claricep CM which employs silica that is further purified with a proprietary acid washing process which results in even lower surface activity. In **Figure 3**, Claricep CM is compared to unmodified silica for use in purifying a catechol sample. Again, improved peak shape and resolution are the result.

FIGURE 3.

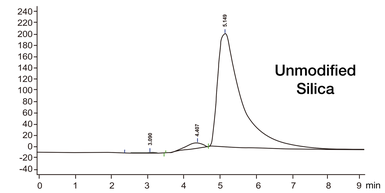
Comparison of Peak Shape with CM Deactivated vs. Unmodified Silica

HPLC Conditions:

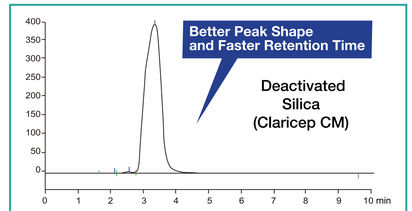
Dimensions: 4.6 x 150 mm
Mobile Phase: Dichloromethane/Methanol (98:2)
Flow Rate: 1.8 mL/min
Injection Volume: 5 µL
Temperature: 30 °C
Detector: UV @ 254 nm
Sample: Catechol 100 µg/mL

HPLC TEST:

Unmodified and Deactivated Silica were packed into individual stainless steel columns (4.6 x 150 mm) and then evaluated on a HPLC System



Comparative separations may not be representative of all applications.



Spherical Silica

Even further performance advances can be made by using a spherical silica rather than standard irregular silica. As is well known in the HPLC world, regular, similar-sized particles can be packed in a column much more uniformly which reduces eddy flow currents and lateral diffusion. The result is greater peak symmetry and baseline resolution than is possible with irregular silica particles.

This is demonstrated in **Figure 4** where a methacrylic acid ester is purified on Claricep 20-35 µm spherical and compared with purification on 20 µm spherical silica. As can be seen, the application of Claricep 20 µm spherical results in a much improved chromatogram.

Purification of Sample with Methacrylic Acid Ester Target Compound

Sample Information:
The sample is colorless liquid, with about 60 % target compound by weight. Dissolve 0.2 mL of sample into 1.5 mL ethanol under ultrasonic.

Flash Conditions:

Column A: Claricep Spherical Silica (20-35 µm, 100 Å, 12 g, 2 columns in tandem)
Column B: Claricep Spherical Silica (20 µm, 100 Å, 12 g, 2 columns in tandem)
Mobile Phase: A: Hexane B: Ethanol
Gradient:

Time (min)	B %
0	5
20	55

Flow Rate: 12 mL/min
Detector: UV @ 254/220 nm
Sample Loading 0.2 mL

Structure:

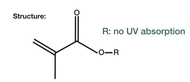
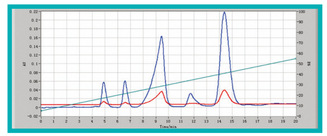
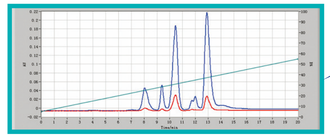


FIGURE 4.

Comparison of Claricep Spherical Silica 20-35 µm vs. Claricep Spherical Silica 20 µm



Column A: Claricep 20-35 µm



Column B: Claricep 20 µm

Claricep Flash silica 20 µm is a better choice for complex sample polarity. It provides higher resolution and better purification performance.

Conclusion

Initially, it may appear to be advantageous to use the least expensive Flash column that works to perform a routine purification. However, with difficult purifications, it can be more economical to use a higher performing Flash column. The value of obtaining a higher purity product while expending less time and effort, far exceeds the small amount of money saved by using a sub-optimal column. This example demonstrates the improved column efficiency that is achieved when the chromatographic media has a more narrow particle size distribution, even when both columns use particles of similar diameter.

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