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European Pharmacopoeia Paracetamol Monograph: Achieving Improved Sensitivity, Resolution, and Separation for Paracetamol and All 14 Related Substances using Kinetex® 2.6 µm C18 Core-Shell Columns

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Zeshan loves to collect watches and the Back to the Future Trilogy. He has twin boys which drive him crazy! He is an Apple Fanboy for life and he likes being in the lab more than anywhere else.

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Introduction

N-(4-hydroxyphenyl) acetamide, commonly referred to as paracetamol in Europe and acetaminophen in the USA, is one of the most familiar analgesics and antipyretic therapeutics in today's drug market. As a result of its wide usage and applicability, there is significant interest in the development of fast and efficient analysis of paracetamol and related impurities. In this technical note, we have addressed identified issues with the current European Pharmacopoeia (Ph. Eur.) monograph method for the separation of paracetamol and 14 related substances. By leveraging both particle morphology and column selectivity, we were able to provide improved resolution for paracetamol and the principal degradation product, 4-aminophenol (impurity K), an impurity that can be formed by the hydrolysis of paracetamol[1]. The Ph. Eur. method requires that resolution between impurity K and paracetamol be a minimum of 5.0 to meet system suitability; resolution significantly greater was achieved here. In addition, resolution of all 14 related impurities was achieved. A UHPLC column packed with core-shell, or superficially porous, silica particles containing a C18 bonded phase, was utilized to maximize the performance of the analytical method. It should be noted that the most recent revision to the Paracetamol Ph. Eur. Method (see Pharmeuropa 28.1)[2] specifically references using a superficially porous 2.7 µm column (HALO® 2.7 µm C18 100 x 2.1 mm) in the same dimension as the Kinetex C18 2.6 µm core-shell column used here. The performance of the Kinetex 2.6 µm core-shell column was compared with the performance for the superficially porous C18 column referenced in the most recent Ph. Eur. revision for the paracetamol method. All method parameters (column dimension, injection volume, and gradient mobile phase conditions) were consistent with Ph. Eur. related substances test for paracetamol published in Supplement 9.4[3].

Experimental

Analytical reference standards for Paracetamol and Paracetamol impurity K (4-Aminophenol) were obtained from Sigma-Aldrich® (St. Louis, Missouri, USA) and evaluated with the Kinetex 2.6 µm C18 (Phenomenex, Torrance, California, USA). In addition, we compared the Kinetex results with the superficially porous HALO® 2.7 µm C18 column (Advanced Materials Technology, Inc., Wilmington, Delaware, USA) referenced by the European Pharmacopoeia. Additional paracetamol impurities (A, B, C, D, E, F, G, H, I, J, L, M, and N) were obtained from Sigma-Aldrich and TLC Pharmaceutical Standards Ltd. (Ontario, Canada).

To ensure similar and comparative results, all of the columns used in this study were individually tested using the same isocratic performance test conditions to confirm both columns were operating within expected efficiency/performance levels. The Kinetex C18 and competitor columns were both of core-shell solid support particle design with unique performance characteristics associated with this type of particle morphology. Both columns were evaluated with the use of SecurityGuard™ ULTRA guard cartridge system (2.1 mm ID with length < 5 mm) under the conditions outlined in European Pharmacopoeia 9.4 for Paracetamol related substances. The system used for this method was a Waters® ACQUITY® I-Class UPLC system equipped with a UV-VIS detection set at 254 nm (no reference wavelength was utilized). To compare effect of system dwell volume on performance of the method, an Agilent® 1260 binary HPLC system was also used with the same detector wavelength.

A mixture of analytical reference standards (15 ppm; dissolved in methanol, water (15:85 v/v)), was used to investigate and identify relative analyte retention and assess selectivity suitability, per Ph. Eur. guidelines as indicated in the Paracetamol draft monograph. The system suitability solution (Reference solution B) was prepared per European Pharmacopoeia 9.4 by dissolving 5.0 mg of Paracetamol and 5.0 mg of Impurity K in the solvent mixture (water/methanol, 15:85, v/v) in a 100-mL volumetric flask and bringing to volume; then 1 mL of this was further diluted to 100 mL with solvent mixture (prepared immediately before use). The LC conditions are listed below and were used to generate all of the chromatograms in this technical note.

LC Conditions

Column: Kinetex® 2.6 µm C18 (or HALO® 2.7 µm C18)
Dimensions: 100 x 2.1 mm
Mobile Phase: A: Phosphate buffer (prepared by dissolving 1.7 g of potassium dihydrogen phosphate and 1.8 g of dipotassium hydrogen phosphate in HPLC grade water and diluting to 1000 mL with water)
B: Methanol
Flow Rate: 1 mL/min - 2 mL/min
Gradient:

Time (min)	% B
0	5
1	5
10	10
20	10
40	34
50	34

Flow Rate: 0.3 mL/min
Column Temperture: 30 °C
Injection Volume: 5 µL
Detection: UV @ 254 nm
HPLC System: Waters® ACQUITY® I-Class UPLC (Waters Technologies Corporation, Milford, MA, USA)

The system suitability requirement pertains to the critical resolution of impurity 4-aminophenol (impurity K) and paracetamol (minimum 5.0). The analytical challenges with the separations of 4-aminophenol and paracetamol are associated with reversed phase retention challenges and the stability of 4-aminophenol. It has been observed that when 4-aminophenol is exposed to environmental heat and light it undergoes accelerated degradation.[2]

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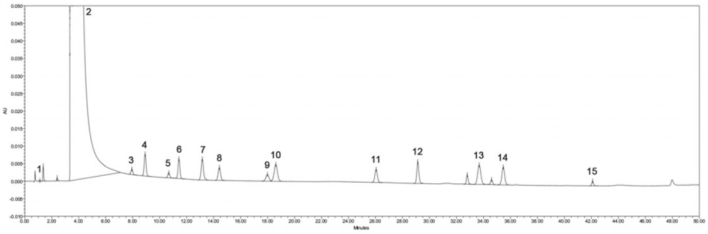
Additionally, 4-aminophenol is also the principal degradation product related to the hydrolysis of paracetamol.[1] Therefore, to demonstrate the analytical robustness of this separation we compared replicate injections of reference solution B, which had been subjected to several days exposure to laboratory environmental conditions.

After system suitability was demonstrated, (resolution >5.0 between 4-aminophenol and paracetamol), a more complex mixture containing 14 impurities (in addition to paracetamol) was used to demonstrate the complete separation of all impurities.

Results

Figure 1a shows the original EDQM (European Directorate for the Quality of Medicines) published chromatogram (also published in Pharmeuropa 28.1) for Paracetamol and 14 related impurities as obtained using the HALO® 2.7 µm C18 100 x 2.1mm column. This shows the expected elution order for paracetamol and the 14 related impurities using the conditions as published in the Ph. Eur. method for Paracetamol. **Figure 1b** shows the chromatogram obtained in our laboratory running a solution containing Paracetamol and all 14 impurities on the recommended HALO column. As noted in the chromatogram, we observed co-elution of impurities G and M and for impurities L and J, as well as an elution order reversal for impurities I and L, when compared with the EQDM published chromatogram. Two new HALO columns were tested, and both gave the same chromatogram. ***(Retention times and elution orders were confirmed by injecting the individual standards)***. The Kinetex® 2.6 µm C18 100 x 2.1mm column gave the same elution order (Figure 1c) as was obtained on the HALO column; however, baseline resolution of impurities G and M, as well as impurities L and J, were obtained, but the elution order was reversed from what was observed on the HALO column (as published in the EDQM and reproduced here as **Figure 1a**).

Figure 1a.
HALO 2.7 µm C18; 14 Impurities Plus Paracetamol, as published by EDQM (solution of paracetamol spiked with impurities at 50 ppm)[4]



1. impurity K
2. paracetamol
3. impurity A
4. impurity B
5. impurity F
6. impurity C
7. impurity D
8. impurity E
9. impurity M
10. impurity G
11. impurity H
12. impurity L
13. impurity I
14 impurity J
15. impurity N

Figure 1b.
HALO 2.7 µm C18; 14 Impurities Plus Paracetamol, as obtained using Standard Mixture with SecurityGuard™ ULTRA (solution of paracetamol with impurities at 15 ppm)

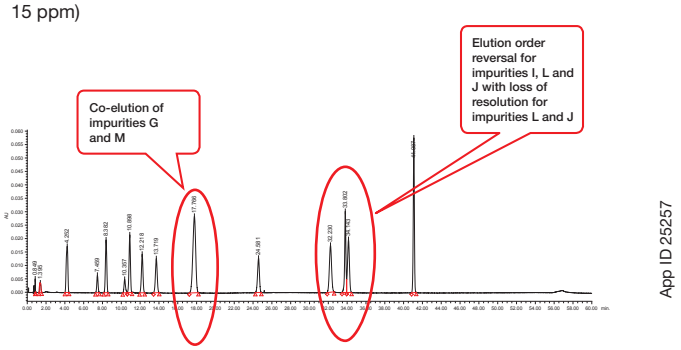


Figure 1c.
Kinetex 2.6 µm C18; 14 Impurities Plus Paracetamol, as obtained using Standard Mixture with SecurityGuard ULTRA (solution of paracetamol with impurities at 15 ppm)

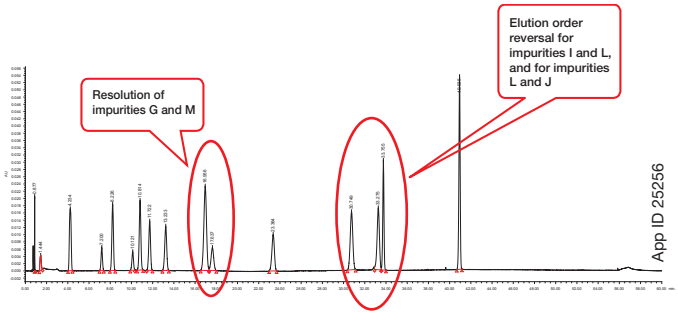


Table 1.
Kinetex 2.6 µm C18 Results Summary

		HALO w/guard	Kinetex w/guard	Kinetex w/o guard
Peak No.	Peak ID	Retention Time, min	Retention Time, min	Retention Time, min
1	Impurity K	1.40	1.44	1.42
2	Paracetamol	4.25	4.23	4.19
3	Impurity A	7.46	7.20	7.11
4	Impurity B	8.38	8.23	8.14
5	Impurity F	10.6	10.12	10.04
6	Impurity C	10.90	10.81	10.73
7	Impurity D	12.22	11.72	11.59
8	Impurity E	13.72	13.23	13.12
9	Impurity G	17.77	16.96	16.82
10	Impurity M	17.77	17.64	17.49
11	Impurity H	24.58	23.36	23.18
12	Impurity I	32.23	30.75	30.56
13	Impurity J	34.14	33.28	33.12
14	Impurity L	33.80	33.76	33.70
15	Impurity N	41.09	40.90	40.87

Co-elution of impurities G and M on HALO

Differing elution order for impurities I, J and L on Kinetex vs. HALO

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Figure 1d.
Kinetex® 2.6 µm C18; 14 Impurities Plus Paracetamol, as obtained using Standard Mixture without SecurityGuard™ ULTRA (solution of paracetamol and impurities at 15 ppm)

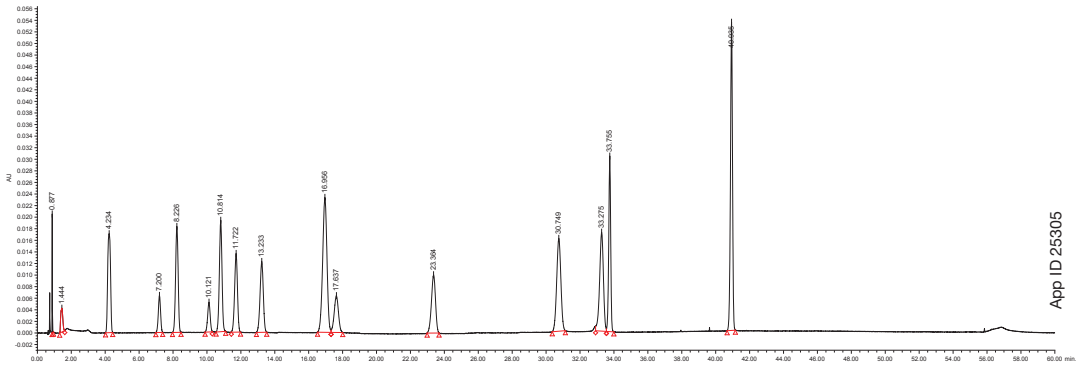

Figure 1e.
Kinetex 2.6 µm C18 100 x 2.1mm overlay with (Black) and without (Blue) SecurityGuard ULTRA

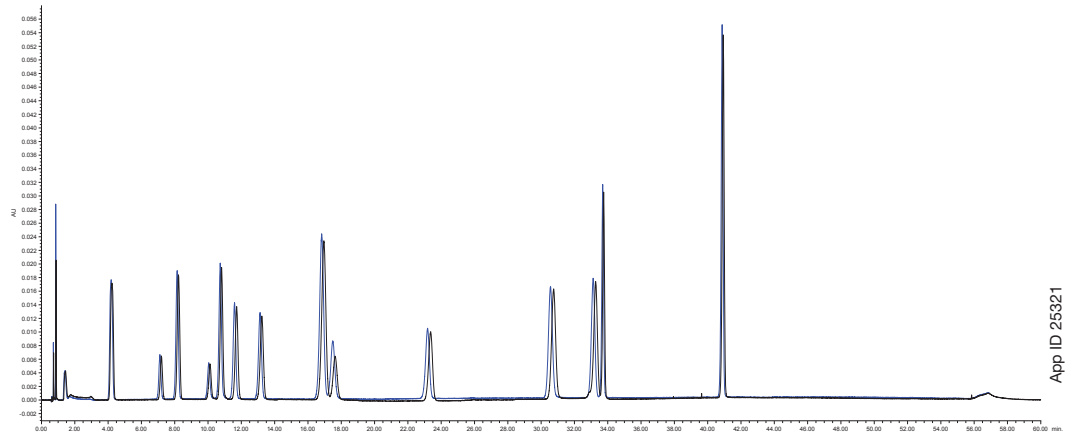

Figure 1f.
Kinetex 2.6 µm C18 100 x 2.1mm overlay with (Black) and without (Blue) SecurityGuard ULTRA – zoom in on peaks for impurity G and M to show that use of guard column does not affect selectivity

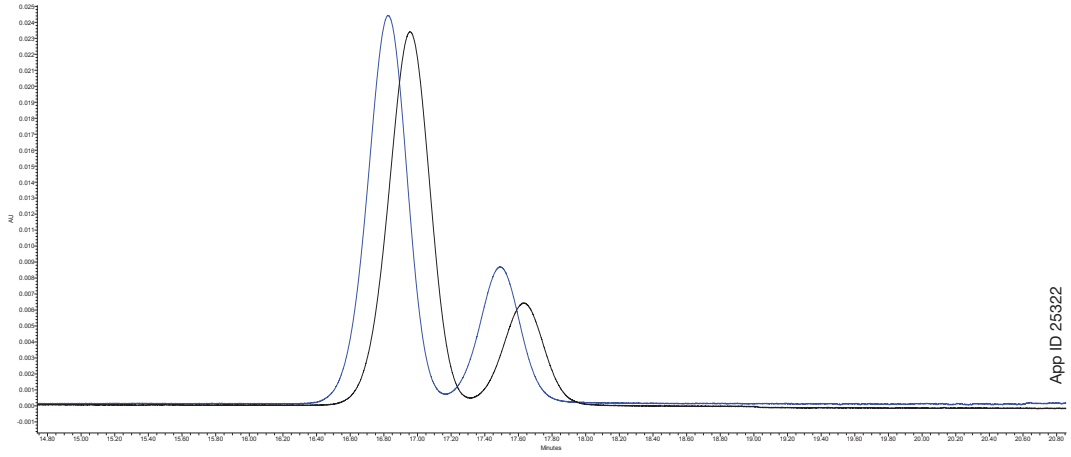

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Figure 2 demonstrates the relative selectivity and performance for system suitability using Reference solution B. The Kinetex 2.6 µm C18 column was able to provide a resolution factor between paracetamol and impurity K of 27.78 (**Table 1**), which is well above the system suitability requirement of 5.0.

LC Conditions

Column: Kinetex® 2.6 µm C18
Dimensions: 100 x 2.1 mm
Part Number: 00D-4462-AN
Mobile Phase: A: Phosphate buffer (prepared by dissolving 1.7 g of potassium dihydrogen phosphate and 1.8 g of dipotassium hydrogen phosphate in HPLC grade water and diluting to 1000 mL with water)
B: Methanol
Flow Rate: 1 mL/min - 2 mL/min
Gradient:

Time (min)	% B
0	5
1	5
10	10
20	10
40	34
50	34

Flow Rate: 0.3 mL/min
Column Temperature: 30°C
Injection Volume: 5 µL
Detection: UV @ 254 nm
HPLC System: Waters® ACQUITY® I-Class UPLC (Waters Technologies Corporation, Milford, MA, USA)

Figure 2.
Kinetex 2.6 µm C18 100 x 2.1mm, Paracetamol and 4-aminophenol (Impurity K); Reference solution B

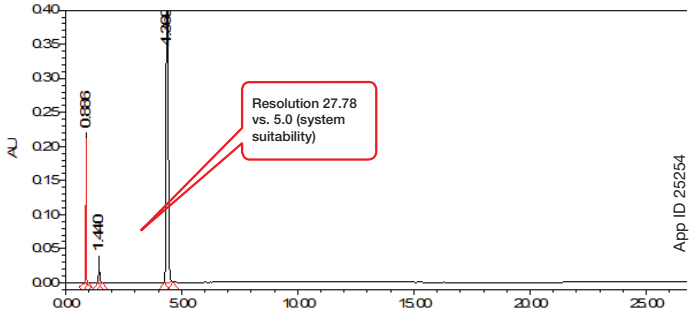

Table 1.
Kinetex 2.6 µm C18 Results Summary

Analyte	Retention Time	Area	Height	k'	Resolution (USP)
Solvent Peak	0.89	130287	212688	87.6	0.00
Impurity K	1.44	88964	30989	143.0	11.87
Paracetamol	4.39	3158799	609478	435.9	27.78

Figure 3.
Kinetex 2.6 µm C18; 5 replicate injections of a paracetamol and 4-aminophenol system suitability solution (Reference solution B) after being subjected to laboratory environmental conditions.

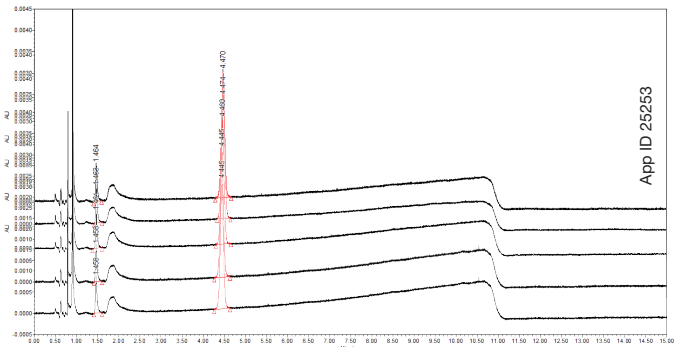

Figure 4.
HALO 2.7 µm C18; 5 replicate injections of a paracetamol and 4-aminophenol system suitability solution (Reference solution B) after being subjected to laboratory environmental conditions.

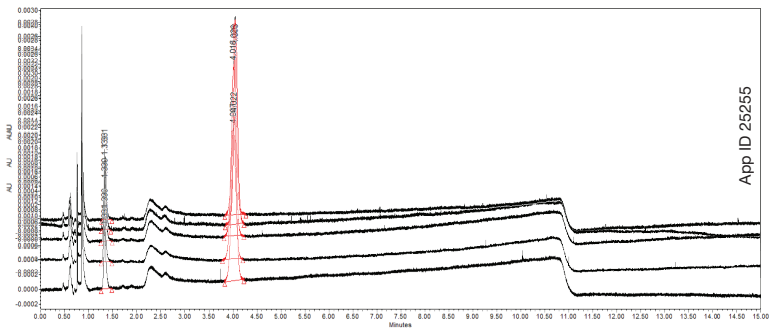

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Table 2.
Replicate Reference Solution Injection Summary

Column	4-aminophenol (impurity K) Retention Time (Mean)	Paracetamol Retention Time (Mean)	Resolution (USP)
Kinetex® C18	1.46	4.44	28.30 ± 0.58
HALO® C18	1.33	4.02	20.96 ± 2.33

Figure 5.
Kinetex C18; 14 Impurities Plus Paracetamol, Standard Mixture with SecurityGuard™ ULTRA (solution of paracetamol with impurities at 15 ppm)

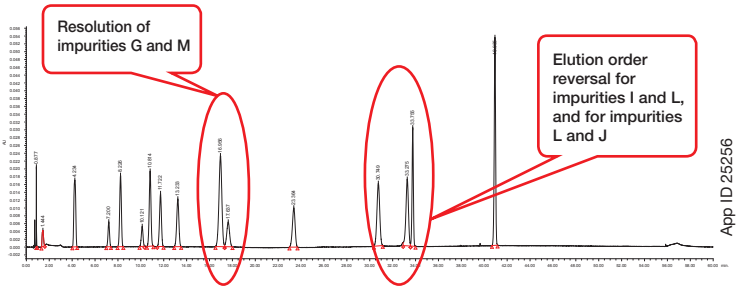

Figure 6.
HALO C18; 14 Impurities Plus Paracetamol, Standard Mixture with SecurityGuard ULTRA (solution of paracetamol with impurities at 15 ppm)

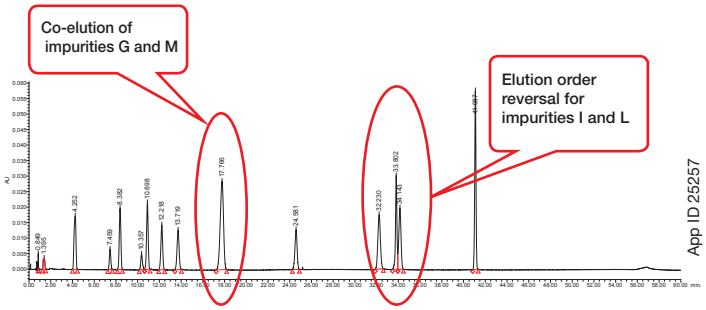

Table 3.
Kinetex C18: Results Summary for 14 Impurities

Peak No.	Peak ID	Retention Time, min	k'	USP Tailing
1	Impurity K	1.4	7.07	1.06
2	Paracetamol	4.2	22.65	0.97
3	Impurity A	7.2	39.22	0.96
4	Impurity B	8.2	44.95	0.97
5	Impurity F	10.1	55.54	0.95
6	Impurity C	10.8	59.42	0.95
7	Impurity D	11.7	64.49	0.93
8	Impurity E	13.2	72.93	0.95
9	Impurity G	17.0	93.73	0.95
10	Impurity M	17.6	97.53	
11	Impurity H	23.4	129.52	0.93
12	Impurity I	30.7	170.78	0.98
13	Impurity J	33.3	184.89	0.83
14	Impurity L	33.8	187.57	0.93
15	Impurity N	40.9	227.69	0.92

Table 4.
HALO C18: Results Summary for 14 Impurities

Peak No.	Peak ID	Retention Time, min	k'	USP Tailing
1	Impurity K	1.40	6.80	0.97
2	Paracetamol	4.25	22.75	0.85
3	Impurity A	7.46	40.67	1.00
4	Impurity B	8.38	45.83	0.97
5	Impurity F	10.36	56.86	1.26
6	Impurity C	10.90	59.88	0.93
7	Impurity D	12.22	67.26	0.96
8	Impurity E	13.72	75.64	0.98
9	Impurity G +M	17.77	98.25	0.90
10	Impurity H	24.58	136.33	0.93
11	Impurity I	32.23	179.05	0.99
12	Impurity L	33.80	187.84	
13	Impurity J	34.14	189.74	
14	Impurity N	41.09	228.54	0.95

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Effect of System Dwell Volume on Chromatorgraphic Separation

The European Pharmacopoeia monograph for paracetamol indicates that the dwell volume of the HPLC system used for the development of the method was 1.07 mL[2]. We investigated two different systems to assess the impact, if any, on the chromatographic separation. The Waters® ACQUITY® I-Class UPLC with dwell volume of ca. 100 µL and the Agilent® 1260 HPLC with dwell volume of ca. 600 - 800 µL were used to investigate the potential impact of system dwell volume on the performance of the Kinetex® and HALO® columns.

The chromatograms obtained for the HALO C18 column on the Waters ACQUITY I-Class and Agilent 1260 systems are shown in Figures 7a and 7b, respectively. As expected, the larger dwell volume associated with the Agilent 1260 binary HPLC system causes an increase in retention time for all peaks, which is far more noticeable for the later eluting peaks. For example, on the HALO column paracetamol elutes at 4.54 minutes on the Agilent system vs. 4.25 minutes on the lower dwell volume ACQUITY I-Class system; this is even more pronounced for the later eluting impurity N, which elutes at 44.33 minutes on the Agilent 1260 vs. 41.09 minutes on the ACQUITY I-Class. With the lower dwell volume system resolution between impurities L and J is slightly less than 1.5 but complete co-elution is observed with the larger dwell volume system.

The elution order remains unchanged between systems, the primary effect of the larger system dwell volume is to yield longer retention times and wider peaks, which is especially noticeable for later eluting impurities. For this, and other methods where resolution of closely eluting compounds is critical to meet system suitability requirements, it is very important to address extra-column dwell volume on your systems. In the specific case of the Agilent 1260 system here, one could reduce extra column volume by reducing the inner diameter of the connecting tubing (from injector to column, and from column to detector); in addition, a smaller volume flow cell could also be used.

Figure 7a.
HALO C18; 14 Impurities Plus Paracetamol with SecurityGuard™ ULTRA – Waters Acquity I-Class (solution of paracetamol with impurities at 15 ppm)

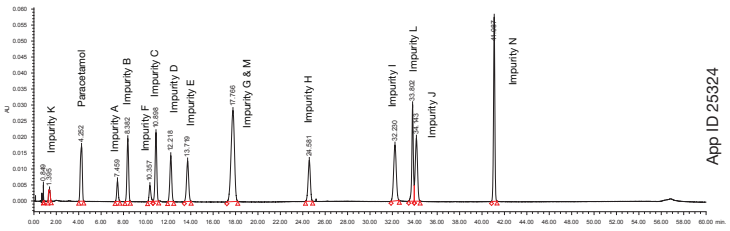
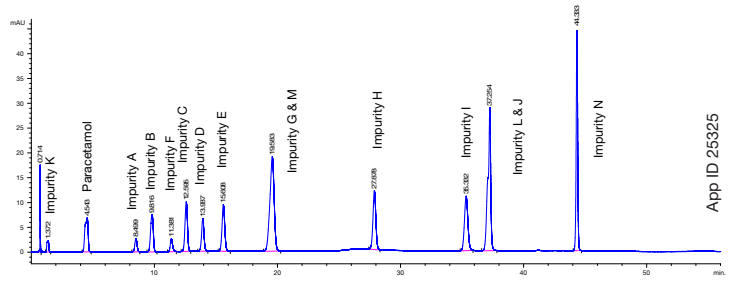


Figure 7b.
HALO C18; 14 Impurities Plus Paracetamol with SecurityGuard ULTRA – Agilent 1260 (solution of paracetamol with impurities at 15 ppm)



Observed Differences with published EDQM Chromatogram

Both Kinetex C18 and HALO C18 columns generated a different peak order for impurities I, J and L relative to the EDQM published chromatogram (**Figure 1a**). In the EDQM chromatogram impurity L (peak 12) elutes before impurity I (peak 13). On both Kinetex and HALO columns impurity I was observed to elute before impurity L, which suggests that something may be wrong with the published EDQM chromatogram. In addition, the observed elution order for impurities G and M is reversed on the Kinetex C18 column; while these two impurities were observed to co-elute on the HALO columns tested. Impurities L and J were also observed to co-elute on HALO, while on Kinetex they are resolved but with an elution order reversal relative to the published EDQM chromatogram and with impurity I eluting before both L and J, but the EDQM chromatogram shows impurity I eluting between impurities L and J (**Figure 1a**).

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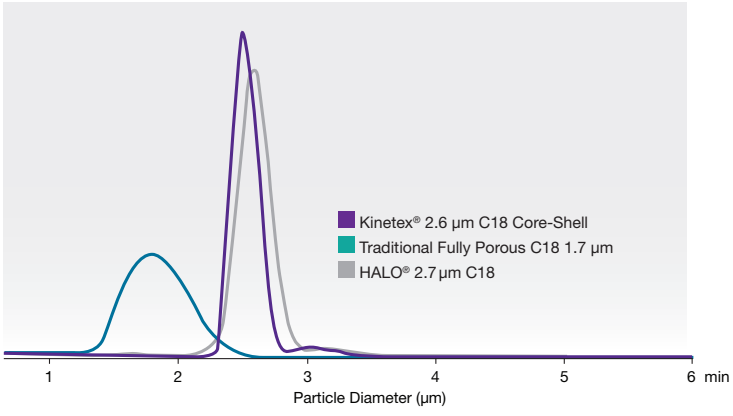
Differences in Particle Size

The manufacturing process for core-shell particles allows for a much narrower particle size distribution, reported as dp 90/10, relative to the typical particle size distribution for fully porous silica particles of similar or smaller particle diameter. This is illustrated in the figure below. Despite the narrower dp 90/10 particle size distribution for both Kinetex 2.6 µm (1.12) and HALO 2.7 µm (1.15), their particle size distribution profiles overlap significantly.

Chapter 2.2.46 (Chromatographic Separation Techniques) of the European Pharmacopoeia (9th Edition) describes the adjustments that are allowed to be made to HPLC monograph methods. Specifically, for gradient elution conditions, as is the case for the Paracetamol and related substances monograph, there is *no adjustment permitted to the particle size allowed.* This presents a bit of a problem here since the Kinetex C18 column used is packed with 2.6 µm core-shell particles, while the HALO C18 column specified in the Ph. Eur. method is packed with 2.7 µm particles. If Chapter 2.2.46 is strictly and literally interpreted, then the work represented in this technical note, which provides for chromatographic separation of all 14 related impurities for Paracetamol, would not represent an allowed adjustment. However, a close examination of the particle size distributions for the Kinetex 2.6 µm and HALO 2.7 µm particles shows that while their mean particle diameters differ by 0.1 µm, the narrow particle size distributions for each media actually overlap significantly. And both core-shell particles have demonstrably narrower particle size distribution versus a fully porous 1.7 µm particle. Therefore, one could argue that within the variability for particle diameter that is present for both core-shell particles, they are essentially the same particle diameter and such a small difference of 0.1 µm based on their commercial descriptions should not be the justification for the use, or limitation, of either of these materials. What should be a more important consideration is how these columns perform under the gradient conditions set forth in the monograph for Paracetamol and related impurities. This is an issue that will have to be addressed by Ph. Eur. and EDQM.

Figure 8.
Particle Size Distribution for Kinetex 2.6 µm and HALO 2.7 µm



Particle size (diameter) primarily impacts efficiency (N), with increases in efficiency leading to narrower peaks and in increase in resolution (R_s) or the amount of chromatographic separation (see resolution equation below).

$$R_s = \frac{\sqrt{N}}{4}\left(\frac{\alpha - 1}{\alpha}\right)\left(\frac{k}{k+1}\right)$$

The resolution equation indicates that the use of a smaller particle size will result in an increase in resolution; for example, moving from a 5 µm to 2.6 µm particle will result in efficiency improvement of about 92%, while resolution will increase by about 38%. Core-Shell particles, also known as superficially porous particles (SPP), from different manufacturers with particle diameters smaller than 3 µm differ in marketed particle size by only 0.1 to 0.2 µm. Such a small difference in particle size results in an increase in efficiency of less than 4%, and a nominally small change in resolution (<2%).

Discussion

The European Pharmacopoeia monograph for paracetamol requires system suitability for resolution between 4-aminophenol (impurity K) and paracetamol to be minimum of 5.0. Therefore, to demonstrate the analytical applicability of the Kinetex 2.6 µm C18 for this method **Figure 1** represents the separation of 4-aminophenol (impurity K) from the main API peak associated with paracetamol. The Kinetex C18 column was able to achieve a resolution value that was >>5 (**Table 1**) under the conditions specified in European Pharmacopoeia 9.4 for paracetamol related substances. Furthermore, to demonstrate the robustness of separation we compared replicate injections of the system suitability solution (reference solution b), which was a mixture of paracetamol and 4-aminophenol, after several days exposure to laboratory environmental conditions (**Figure 2**). Highly reproducible results were achieved, as indicated by the observed RSD of 0.58%). **Figure 2 – 3** are chromatographic overlays that compare the Kinetex 2.6 µm C18 to the comparable core-shell C18 column utilized in the Ph. Eur. draft revision for the paracetamol related impurities method. The Kinetex column was demonstrated a 26 % increase in resolution and lower relative standard of deviation (**Table 2**) than this comparable core-shell column.

After the demonstration that the required system suitability for resolution between impurity K and paracetamol could be easily achieved, a mixture containing all 14 known impurities for paracetamol was analyzed. The unique selectivity and particle morphology of the Kinetex 2.6 µm C18 was able to achieve separation of all 14 impurities from paracetamol (**Figure 5**). Under the Ph. Eur. conditions peak shape was satisfactory for all impurities and the API peak (**Table 3**), which should provide the desired sensitivity and allow for meeting the required reporting thresholds for all impurities, if present. In relation to the competitor comparison, the HALO C18 column was unable to fully resolve all impurity peaks. Co-elution was observed for impurities G and M (**Figure 5**). While not explicitly required, this improved separation allows for identification and quantitation of each of these impurities. In addition, there is an observed selectivity difference for impurities L and J, with the elution order reversed from what was observed on the Kinetex C18 column (**Table 4**). As for repeatability, an increase in relative standard deviation of 75% was observed with respect to resolution value between paracetamol and 4-aminophenol (impurity K) for 5 replicate injections (**Table 2**).

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Conclusion

The performance advantages of using a Kinetex 2.6 µm core-shell packed HPLC column relative to the referenced superficially porous HALO® 2.7 µm C18 column in the Ph. Eur. Monograph for paracetamol related impurities have been clearly demonstrated. The particle size, stationary phase, column dimension, and method conditions were used as documented in the European Pharmacopoeia 9.4 related substances test for Paracetamol. The Kinetex 2.6 µm C18 showed increased resolution between paracetamol and 4-aminophenol (impurity K) for system suitability (Reference solution B). In comparison to the referenced core-shell C18 column, the Kinetex C18 had an observable 75% decrease in terms of relative standard deviation for 5-replicate injections. In addition, the Kinetex column was able to fully resolve the reference standard containing 14 impurities and paracetamol with good peak shape and sensitivity for all peaks.

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References

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3. European Pharmacopoeia, Supplement 9.4, 2017, pp. 5429 – 5430.
4. EDQM Knowledge Database; Figure 0049.-1: Chromatogram for Paracetamol and Related Substances: https://extranet.edqm.eu/4DLink1/pdfs/chromatos/0049.pdf

Kinetex® Ordering Information

2.6 µm Minibore Columns (mm)				SecurityGuard ULTRA Cartridges‡
Phases	30 x 2.1	50 x 2.1	75 x 2.1	3/pk
EVO C18	00A-4725-AN	00B-4725-AN	—	AJ0-9298
Polar C18	00A-4759-AN	00B-4759-AN	—	AJ0-9532
Biphenyl	00A-4622-AN	00B-4622-AN	—	AJ0-9209
XB-C18	00A-4496-AN	00B-4496-AN	00C-4496-AN	AJ0-8782
C18	00A-4462-AN	00B-4462-AN	00C-4462-AN	AJ0-8782
C8	00A-4497-AN	00B-4497-AN	00C-4497-AN	AJ0-8784
HILIC	00A-4461-AN	00B-4461-AN	00C-4461-AN	AJ0-8786
Phenyl-Hexyl	00A-4495-AN	00B-4495-AN	00C-4495-AN	AJ0-8788
F5	00A-4723-AN	00B-4723-AN	—	AJ0-9322

for 2.1 mm ID

2.6 µm Minibore Columns (mm) (cont'd)			SecurityGuard ULTRA Cartridges‡
Phases	100 x 2.1	150 x 2.1	3/pk
EVO C18	00D-4725-AN	00F-4725-AN	AJ0-9298
Polar C18	00D-4759-AN	00F-4759-AN	AJ0-9532
Biphenyl	00D-4622-AN	00F-4622-AN	AJ0-9209
XB-C18	00D-4496-AN	00F-4496-AN	AJ0-8782
C18	00D-4462-AN	00F-4462-AN	AJ0-8782
C8	00D-4497-AN	00F-4497-AN	AJ0-8784
HILIC	00D-4461-AN	00F-4461-AN	AJ0-8786
Phenyl-Hexyl	00D-4495-AN	00F-4495-AN	AJ0-8788
F5	00D-4723-AN	00F-4723-AN	AJ0-9322

for 2.1 mm ID

‡ SecurityGuard ULTRA Cartridges require holder, Part No.: AJ0-9000

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