Separation of Lisinopril and its Organic Impurities per USP Monograph

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Overview

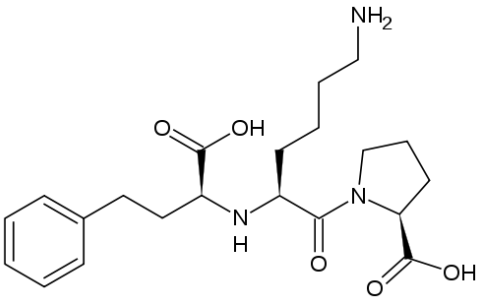
Lisinopril is an orally active angiotensin-converting enzyme (ACE) inhibitor used for the treatment of hypertension, heart failure, and acute myocardial infarction. The development of a quick and efficient analysis of Lisinopril and its related organic impurities is of interest for generic drug manufacturers. In this application note, we report the separation of Lisinopril and its related organic impurities using a Luna™ 5 µm C8(2)column and a Kinetex™ 5 µm C8 column according to the USP monograph for Lisinopril.

System suitability per USP Monograph for the Lisinopril Assay is a symmetry factor no more than (NMT) 1.7 and a percent relative standard deviation (%RSD) of NMT 0.73 % for Lisinopril. System suitability per USP Monograph for the Lisinopril Organic Impurities is a %RSD of NMT 10.0 %, and a signal-to-noise (S/N) ratio no less than 10 for Lisinopril.

The results clearly show that the system suitability criteria (Symmetry, %RSD and S/N ratio) for both assay and organic impurities per the USP monograph for Lisinopril were met with both the Luna 5 µm C8(2) and Kinetex 5 µm C8 columns. While the data demonstrates that either column would be acceptable, there are certain advantages to be gained from the use of the core-shell Kinetex C8 column, specifically shorter run times and increased sensitivity (S/N), while the Luna C8(2) column provided slightly better peak shape.

All solutions were prepared as indicated in the USP Monograph for Lisinopril. USP Lisinopril RS (Catalog No. 1368609) was purchased from USP.

Figure 1. Lisinopril



LC-UV Conditions - Assay

Column: Luna 5 µm C8(2) (00G-4249-E0)
Kinetex 5 µm C8 (00G-4608-E0)
Dimensions: 250 x 4.6 mm
Mobile Phase: Acetonitrile / Buffer (4:96, v/v)

Buffer: 2.76 g of Monobasic Sodium Phosphate was dissolved in 900 mL of water in a 1000 mL volumetric flask. Adjusted pH to 5.0 with 1N Sodium Hydroxide and diluted with water to volume.

Flow Rate: 1 mL/min (Isocratic)
Injection Volume: 20 µL
Temperature: 50 °C
Detector: UV @ 210 nm
System: Waters® ACQUITY Arc® HPLC

LC-UV Conditions - Organic Impurities

Column: Luna 5 µm C8(2) (00G-4249-E0)
Kinetex 5 µm C8 (00G-4608-E0)
Dimensions: 250 x 4.6 mm
Mobile Phase: A: Acetonitrile / Buffer (7:193, v/v)
B: Acetonitrile / Buffer (20:80, v/v)

Buffer: 3.53 g of Monobasic Sodium Phosphate Dihydrate is added to 1000 mL water and the pH is adjusted to 4.1 with Phosphoric Acid.

Gradient:

Time (min)	%B
0	0
35	40
55	40
60	0

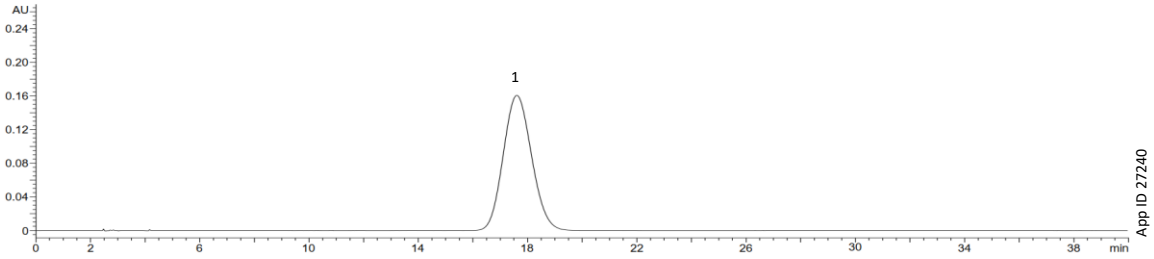
Flow Rate: 1.8 mL/min
Injection Volume: 20 µL
Temperature: 45 °C
Detector: UV @ 210 nm
System: Waters ACQUITY Arc HPLC

Table 1. Preparation of Solutions

Solution	Composition
Standard Solution – Assay	0.3 mg/mL of USP Lisinopril RS in water
Standard Solution – Organic Impurities	0.006 mg/mL of USP Lisinopril RS in Mobile Phase A
Sensitivity Solution – Organic Impurities	1.0 µg/mL of USP Lisinopril RS in Mobile Phase A from Standard Solution – Organic Impurities

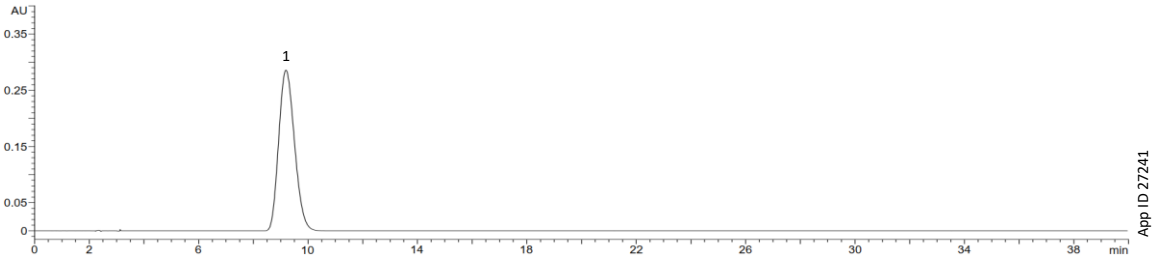
Figure 2. Standard Solution – Assay

Luna™ 5 µm C8(2) Column



Peak No.	Analyte	Retention Time (min)	Area	Area %RSD	Symmetry Factor
1	Lisinopril	17.64	11571239	0.04	1.11
N = 6 Injections					

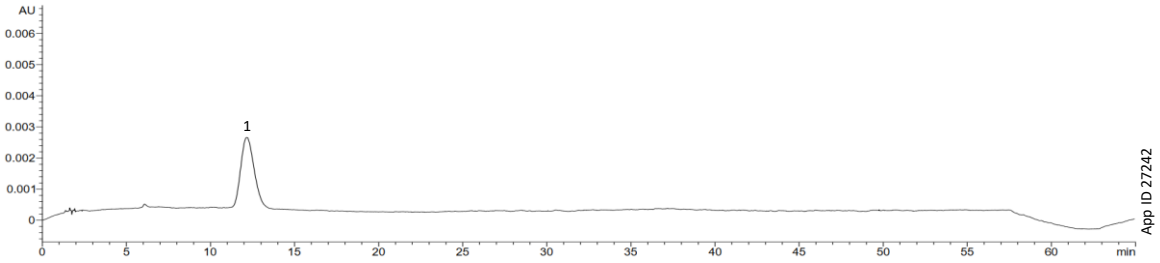
Kinetex™ 5 µm C8 Column



Peak No.	Analyte	Retention Time (min)	Area	Area %RSD	Symmetry Factor
1	Lisinopril	9.20	11393656	0.35	1.19
N = 6 Injections					

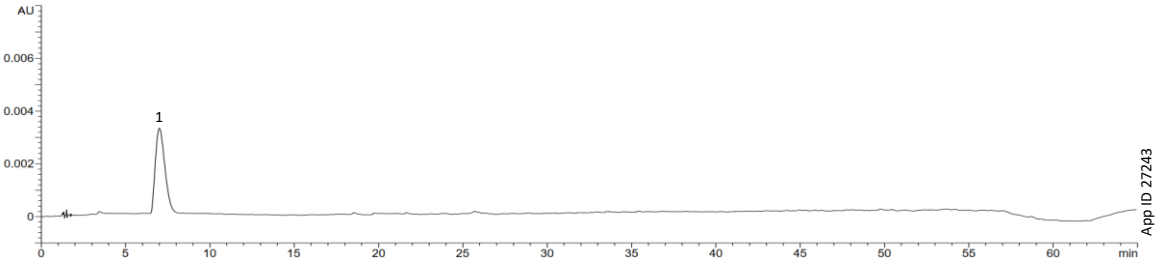
Figure 3. Standard Solution – Organic Impurities

Luna™ 5 µm C8(2) Column



Peak No.	Analyte	Retention Time (min)	Area	Area %RSD	Symmetry Factor
1	Lisinopril	12.15	127254	0.98	1.23
N = 6 Injections					

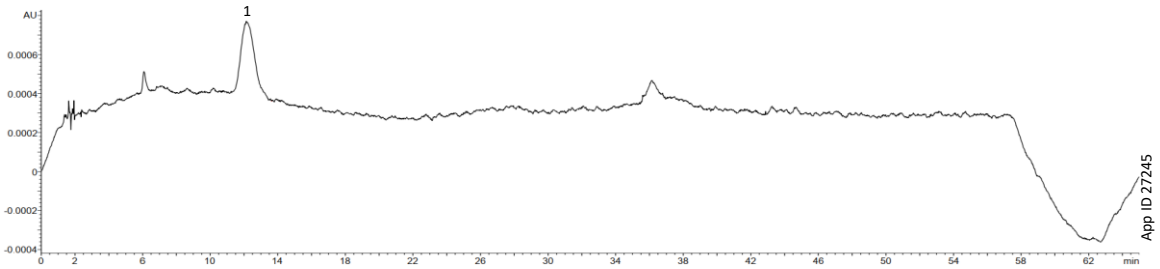
Kinetex™ 5 µm C8 Column



Peak No.	Analyte	Retention Time (min)	Area	Area %RSD	Symmetry Factor
1	Lisinopril	7.01	125862	0.73	1.38
N = 6 Injections					

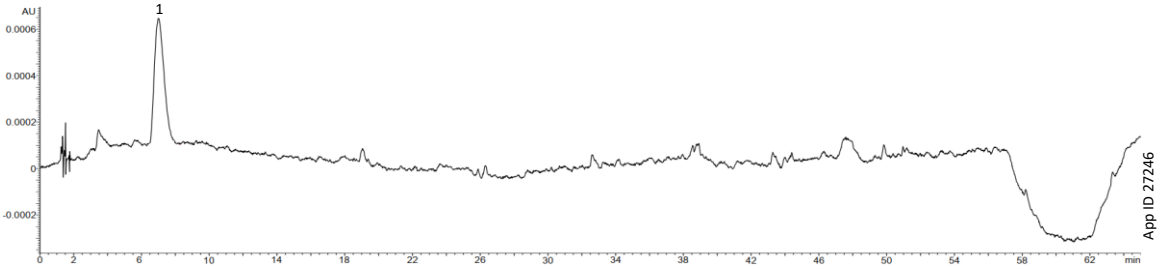
Figure 4. Sensitivity Solution – Organic Impurities

Luna™ 5 µm C8(2) Column



Peak No.	Analyte	Retention Time (min)	S/N Ratio
1	Lisinopril	12.14	35.15
N = 3 Injections			

Kinetex™ 5 µm C8 Column



Peak No.	Analyte	Retention Time (min)	S/N Ratio
1	Lisinopril	7.00	48.8
N = 3 Injections			

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