Application Note: ANCCSCETLISIN

Analysis of Lisinopril by LC/UV Using a Core Enhanced Technology Accucore RP-MS Column

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Key Words

- Accucore RP-MS
- Fused core
- Superficially porous
- USP
- Lisinopril

Abstract

This application note demonstrates the use of the Thermo Scientific Accucore RP-MS HPLC column for the analysis of lisinopril and related substances. The method of analysis is based on the USP monograph, and was scaled down by using an in-house method transfer calculator [1].

Introduction

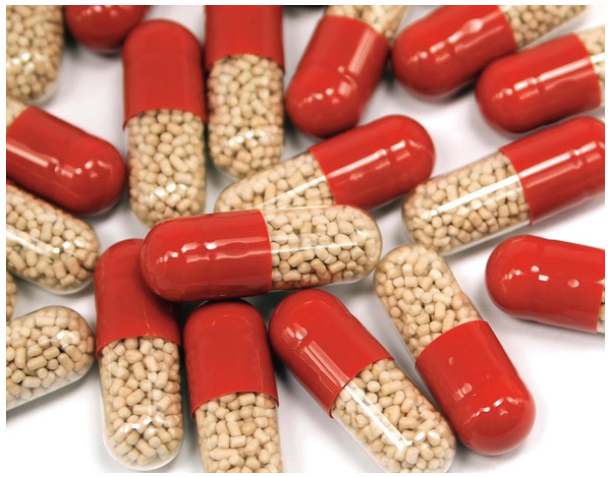
Accucore HPLC columns use Core Enhanced Technology to facilitate fast and high efficiency separations. The 2.6 µm diameter particles are not totally porous, but rather have a solid core and a porous outer layer. The optimised phase bonding creates a series of high coverage, robust phases. Accucore RP-MS uses an optimized alkyl chain length for more effective coverage of the silica surface. This coverage results in a significant reduction in secondary interactions and thus highly efficient peaks with very low tailing. The tightly controlled 2.6 µm diameter of Accucore particles results in much lower backpressures than typically seen with sub-2 µm materials.

The USP method for lisinopril specifies minimum resolution between Impurity 1 and 2- amino-4-phenylbutyric acid, between 2-amino-4-phenylbutyric acid and lisinopril, and between lisinopril and lisinopril R,S,S isomer. The maximum %RSD of the lisinopril peak area is also specified.

The implementation of Accucore RP-MS in this method allowed for the lisinopril and related substances to be analysed according to the USP monograph.

Experimental details

The lisinopril assay was run on a Thermo Scientific HPLC system. The UV detector was fitted with a 15 µL, 10mm flow cell. The column used for the analysis was a core enhanced technology Accucore RP-MS. The data was acquired and processed using Thermo Scientific ChromQuest 5.0 Software.



Sample Preparation

A sample of Lisinopril system suitability standard was weighed and diluted in mobile phase A.

Thermo Scientific Column	Part Number
Accucore RP-MS 2.6 µm 100 x 2.1 mm Measured pressure: 159 bar	17626-102130

Thermo Scientific HPLC system

Column temperature	50 °C
Injection volume	5 µL (partial loop)
Flow rate	0.4 mL/min
UV detection	210 nm (Data rate 10 Hz, rise time 0.1 s)

Mobile Phase

A: 0.026M monobasic sodium phosphate pH 3.75 with phosphoric acid

B: 80% mobile phase A / 20% acetonitrile

Gradient:

Time	A	B
0.0	97	3
15.0	70	30
30.0	70	30
35.0	97	3

Consumables	Part Number
Fisher Scientific HPLC grade water	W/0106/17
Fisher Scientific HPLC grade acetonitrile	A/0626/17
NSC Mass Spec Certified 2 mL clear vial with blue bonded PTFE silicone cap	MSCERT4000-34W
Unifilter Direct Connect Holder (3.0/2.1 mm ID)	27000

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Results

The original USP analytical conditions, based on a L1 250 x 460 mm, 5 µm column were scaled down using our method transfer calculator to accommodate for the column geometry reduction. The analysis was carried out on an Accucore RP-MS 2.6 µm 100 x 2.1 mm column. The pH was also lowered to take advantage of the increased level of deactivation of the Accupore material compared to the material originally used to develop the method. The requirements for the USP method were achieved (as demonstrated in Table 1) as the high efficiency allows the resolution limits to be exceeded. The statistical assessment is based on data from 6 replicate injections. Additionally analysis time is reduced.

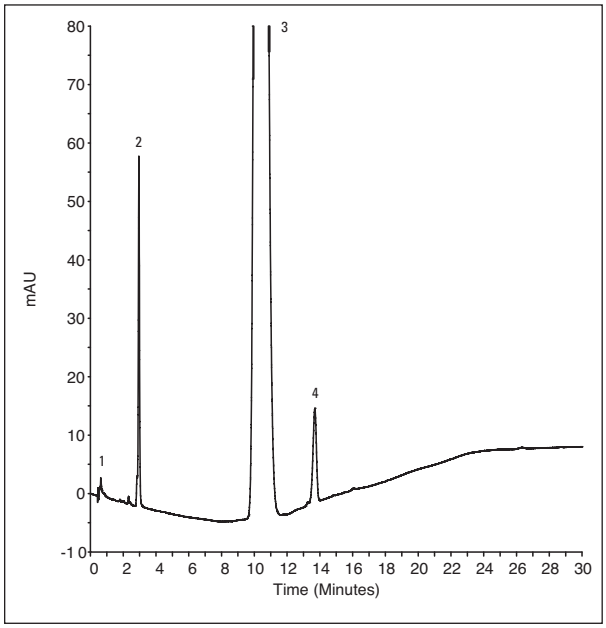

Figure 1: Chromatogram of 1000 µg/mL of Lisinopril analyzed on the Accucore RP-MS 100 x 2.1 mm, 2.6 µm column. 1. impurity 1, 2. 2-amino-4-phenylbutyric acid 3. lisinopril 4. lisinopril R,S.S isomer

	Mean	Resolution		
	Lisinopril	Peaks 1,2	Peaks 2,3	Peaks 3,4
Mean	20789225	4.68	12.74	4.72
%RSD	1.74	10.1	1.03	0.21

Table 1: Method precision (%RSD) for lisinopril and related substances (data calculated from six replicate injections)

Conclusions

The use of Accucore RP-MS column allowed to successfully scale down the USP method for the analysis of lisinopril and related substances, in order to increase sample throughput. The analytical results exceeded the specifications stated in the USP monograph. There was also excellent reproducibility between runs. Accucore RP-MS columns are therefore an excellent choice for the fast analysis of lisinopril.

References

[1] http://www.hplctransfer.com/
[2] USP Monograph for linisopril

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ANCCSCETLISIN 0611