



TN-1349

Separation of Valsartan and Its Chiral Impurities per USP Monograph

Michael McGinley and Bryan Tackett, PhD
Phenomenex Inc., 411 Madrid Ave., Torrance, CA 90501, USA

Introduction

Valsartan is an antihypertensive drug which selectively inhibits angiotensin receptor type II. The development of a quick and efficient analysis of Valsartan and its related chiral impurities is of interest for generic drug manufacturers. In this technical note, we report the separation of Valsartan and its related chiral impurities using a Lux 5 μ m Cellulose-1 column compared with a CHIRALCEL 5 μ m OD-H column according to the USP monograph for Valsartan, which specifies a column containing L40 (Cellulose tris(3,5-dimethylphenylcarbamate)) packing and dimensions of 250 x 4.6 mm.

System suitability per USP Monograph for Valsartan Chiral Impurities (Procedure 1) is resolution no less than (NLT) 2.0 between Valsartan Related Compound A and Valsartan, and a percent relative standard deviation (%RSD) of no more than (NMT) 5 % for Valsartan Related Compound A peak.

All solutions were prepared as indicated in the USP Monograph for Valsartan. USP Valsartan RS (Catalog No. 1708762), and USP Valsartan Related Compound RS (Catalog No. 1708773) were purchased from USP.

LC-UV Conditions

Column: CHIRALCEL® 5 μ m OD-H®
Lux™ 5 μ m Cellulose-1 (00G-4459-E0)

Dimensions: 250 x 4.6 mm

Mobile Phase: N-Hexane / 2-Propanol / Trifluoroacetic Acid
(850:150:1, v/v/v)

Flow Rate: 0.8 mL/min (Isocratic)
1.0 mL/min (Isocratic) – Lux Only

Injection Volume: 10 μ L

Temperature: 25 °C

Detector: UV @ 230 nm

LC System: Agilent® 1290 Infinity

Figure 1. Valsartan Structure.

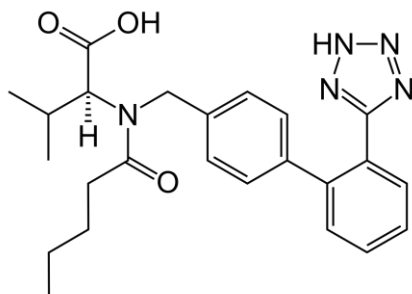


Table 1. Preparation of Solutions.

Solution	Composition
Standard Solution	0.01 mg/mL of USP Valsartan Related Compound A RS in mobile phase.
Sample Solution	1 mg/mL of USP Valsartan RS in mobile phase. Sonicate for 5 min.
System Suitability Solution	0.04 mg/mL each of USP Valsartan Related Compound A RS and USP Valsartan RS in mobile phase.



Results and Discussion

We observed greater resolution of Valsartan and Related Compound A on the Lux Cellulose-1 column when compared to the CHIRALCEL OD-H column, but there was a much longer run time on the Lux Cellulose-1 column (**Figure 2**). The flow rate was increased from 0.8 mL/min to 1.0 mL/min (25 %, an allowed adjustment according to USP Chapter <621>) to determine the impact of run time and resolution on the Lux Cellulose-1 column (**Figure 3**). The resolution decreased from 5.1 to 4.5 with the increase in flow rate, but this was still greater than the resolution on the CHIRALCEL OD-H column under the 0.8 mL/min flow rate. With the faster flow rate, the run time decreased and was closer to that of the CHIRALCEL OD-H column.

At a flow rate of 0.8 mL/min on both the CHIRALCEL OD-H column and the Lux Cellulose-1 column, there was an unknown impurity peak present at ~8.5 minutes in Standard Solution, Sample Solution (data not shown for Standard or Sample Solution), and System Suitability Solution. This unknown impurity peak elutes prior to the Valsartan Related Compound A on the Lux Cellulose-1 column, resulting in less possibility for interference with the separation between Valsartan Related Compound A and Valsartan. When the flow rate was increased to 1.0 mL/min on the Lux Cellulose-1 column, the unknown impurity peak was present at ~6.7 minutes for the same three samples. The unknown peak is not present in the mobile phase blank but was present in the diluent blank injection (data not shown).

Figure 2. System Suitability Solution – Chiral Impurities.

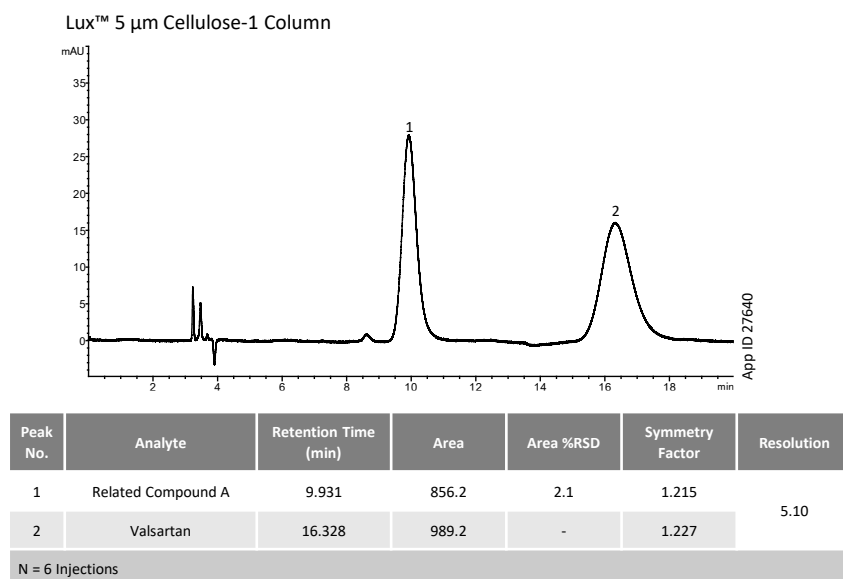
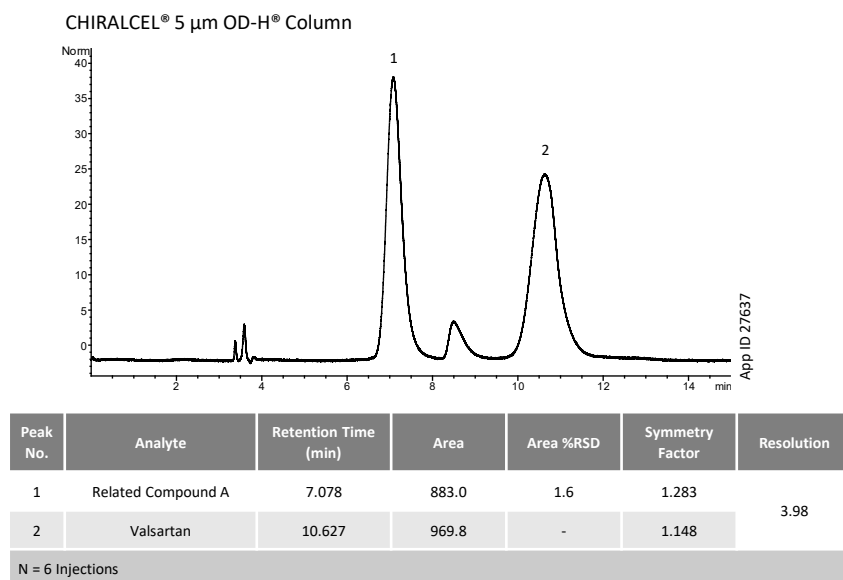
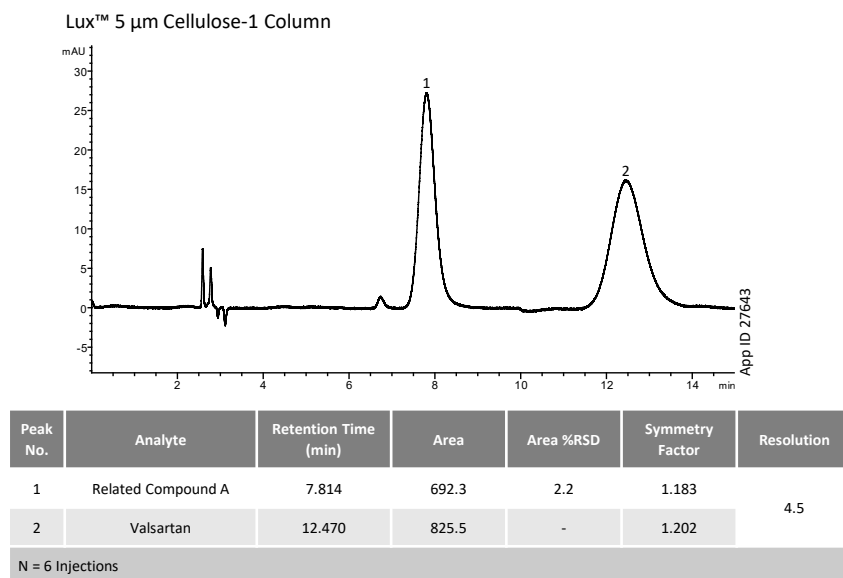


Figure 3. System Suitability Solution – Chiral Impurities; Flow Rate of 1.0 mL/min.

Conclusion

The Lux 5 µm Cellulose-1 column and the CHIRALCEL® 5 µm OD-H® column met all system suitability requirements. The Lux 5 µm Cellulose-1 column continued to meet system suitability requirements when the flow rate was increased to 1.0 mL/min. This also reduced the run time to a comparable run time to the CHIRALCEL OD-H column, but maintained a greater resolution between Valsartan and Related Compound A.

An impurity peak appeared for both columns. The diluent is a possible source of this unknown impurity peak. It should be noted that the diluent blank injection was simply mobile phase taken directly from the mobile phase bottle and pipetted into an autosampler vial. Therefore, it is also possible that the source of the unknown impurity peak is contamination in the LC system. Determination of the source of the impurity was not investigated further. However, it was noted that this unknown impurity peak eluted prior to Valsartan Related Compound A on the Lux Cellulose-1 column, thus reducing potential interference with the chiral analysis.

Lux™ Ordering Information

5 µm Minibore and Analytical Columns (mm)						SecurityGuard™ Cartridges (mm)	
Phases	50 x 2.0	50 x 4.6	100 x 4.6	150 x 4.6	250 x 4.6	4 x 2.0*	4 x 3.0*
						/10pk	/10pk
i-Amylose-1	00B-4762-B0	00B-4762-E0	00D-4762-E0	00F-4762-E0	00G-4762-E0	AJ0-8640	AJ0-8641
i-Amylose-3	—	00B-4779-E0	00D-4779-E0	00F-4779-E0	00G-4779-E0	AJ0-8651	AJ0-8650
i-Cellulose-5	—	00B-4756-E0	00D-4756-E0	00F-4756-E0	00G-4756-E0	AJ0-8631	AJ0-8632
Cellulose-1	—	00B-4459-E0	00D-4459-E0	00F-4459-E0	00G-4459-E0	AJ0-8402	AJ0-8403
Cellulose-2	00B-4457-B0	00B-4457-E0	00D-4457-E0	00F-4457-E0	00G-4457-E0	AJ0-8398	AJ0-8366
Cellulose-3	—	00B-4493-E0	00D-4493-E0	00F-4493-E0	00G-4493-E0	AJ0-8621	AJ0-8622
Cellulose-4	—	—	00D-4491-E0	00F-4491-E0	00G-4491-E0	AJ0-8626	AJ0-8627
Amylose-1	00B-4732-B0	—	00D-4732-E0	00F-4732-E0	00G-4732-E0	AJ0-9337	AJ0-9336

*SecurityGuard Analytical Cartridges require holder, Part No.: [KJ0-4282](#)

for ID: 2.0-3.0 mm

3.2-8.0 mm



Need a different column size or sample preparation format?

No problem! We have a majority of our available dimensions up on www.phenomenex.com, but if you can't find what you need right away, our super helpful Technical Specialists can guide you to the solution via our online chat portal www.phenomenex.com/Chat.

Australia

t: +61 (0)2-9428-6444
auinfo@phenomenex.com

Austria

t: +43 (0)1-319-1301
anfrage@phenomenex.com

Belgium

t: +32 (0)2 503 4015 (French)
t: +32 (0)2 511 8666 (Dutch)
beinfo@phenomenex.com

Canada

t: +1 (800) 543-3681
info@phenomenex.com

China

t: +86 400-606-8099
cninfo@phenomenex.com

Czech Republic

t: +420 272 017 077
cz-info@phenomenex.com

Denmark

t: +45 4824 8048
nordicinfo@phenomenex.com

Finland

t: +358 (0)9 4789 0063
nordicinfo@phenomenex.com

France

t: +33 (0)1 30 09 21 10
franceinfo@phenomenex.com

Germany

t: +49 (0)6021-58830-0
anfrage@phenomenex.com

Hong Kong

t: +852 6012 8162
hkinfo@phenomenex.com

India

t: +91 (0)40-3012 2400
indiainfo@phenomenex.com

Indonesia

t: +62 21 5019 9707
indoinfo@phenomenex.com

Ireland

t: +353 (0)1 247 5405
eireinfo@phenomenex.com

Italy

t: +39 051 6327511
italiainfo@phenomenex.com

Japan

t: +81 (0) 120-149-262
jpinfo@phenomenex.com

Luxembourg

t: +31 (0)30-2418700
nlinfo@phenomenex.com

Mexico

t: 01-800-844-5226
tecnicomx@phenomenex.com

The Netherlands

t: +31 (0)30-2418700
nlinfo@phenomenex.com

New Zealand

t: +64 (0)9-4780951
nzinfo@phenomenex.com

Norway

t: +47 810 02 005
nordicinfo@phenomenex.com

Poland

t: +48 22 104 21 72
pl-info@phenomenex.com

Portugal

t: +351 221 450 488
ptinfo@phenomenex.com

Singapore

t: +65 6559 4364
sginfo@phenomenex.com

Slovakia

t: +420 272 017 077
sk-info@phenomenex.com

Spain

t: +34 91-413-8613
espinfo@phenomenex.com

Sweden

t: +46 (0)8 611 6950
nordicinfo@phenomenex.com

Switzerland

t: +41 (0)61 692 20 20
swissinfo@phenomenex.com

Taiwan

t: +886 (0) 0801-49-1246
twinfo@phenomenex.com

Thailand

t: +66 (0) 2 566 0287
thaiinfo@phenomenex.com

United Kingdom

t: +44 (0)1625-501367
ukinfo@phenomenex.com

USA

t: +1 (310) 212-0555
www.phenomenex.com/chat

☎ All other countries/regions Corporate Office USA

t: +1 (310) 212-0555
www.phenomenex.com/chat

www.phenomenex.com

Phenomenex products are available worldwide. For the distributor in your country/region, contact Phenomenex USA, International Department at international@phenomenex.com

BE-HAPPY™ GUARANTEE

Your happiness is our mission. Take 45 days to try our products. If you are not happy, we'll make it right.

www.phenomenex.com/behappy

Terms and Conditions

Subject to Phenomenex Standard Terms and Conditions, which may be viewed at www.phenomenex.com/phx-terms-and-conditions-of-sale.

Trademarks

Lux, SecurityGuard, and BE-HAPPY are trademarks of Phenomenex. Agilent is a registered trademark of Agilent Technologies, Inc. CHIRALCEL and OD-H are registered trademarks of DAICEL Corporation.

Disclaimer

Comparative separations may not be representative of all applications.

Phenomenex is in now way affiliated with Agilent Technologies, Inc. or DAICEL Corporation.

SecurityGuard is patented by Phenomenex. U.S. Patent No. 6,162,362.

CAUTION: this patent only applies to the analytical-sized guard cartridge holder, and does not apply to SemiPrep, PREP, or ULTRA holders, or to any cartridges.

FOR RESEARCH USE ONLY. Not for use in clinical diagnostic procedures.

© 2023 Phenomenex, Inc. All rights reserved.

