Chiral Separation of the Drug Product Sertraline Hydrochloride on Lux® Amylose-1 According to Ph. Eur. Monograph 1705

Michael McCoy[1], Emily Gish[1], Heiko Behr[2], Simon Lomas[1] and Marc Jacob[1]
[1]Phenomenex, Inc., 411 Madrid Ave., Torrance, CA 90501 USA
[2]Phenomenex, Ltd., Zeppelinstr. 5, 63741 Aschaffenburg, Germany

In this technical note, we report the enantiomeric separation between Sertraline and Impurity G (the enantiomer of Sertraline) using the Lux Amylose-1 chiral stationary phase according to the Ph. Eur. Monograph 1705. Comparison with a CHIRALPAK® AD-H® column is also provided.

Introduction

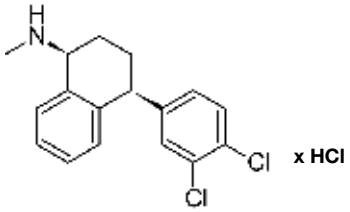
The European Pharmacopoeia (Pharmacopoea Europaea, Ph. Eur.) is a single reference work for the quality control of medicines in the signatory states of the Convention on its elaboration. The official standards published within provide a legal and scientific basis for quality control during the development, production and marketing processes. They concern the qualitative and quantitative composition and the tests to be carried out on medicines, on the raw materials used in production of medicines and on the intermediates of synthesis. All producers of medicines and/or substances for pharmaceutical use must therefore apply these quality standards in order to market their products. In the case of chiral products, such as Sertraline Hydrochloride (**Figure 1**.), a chiral HPLC method is generally used to assess chiral purity.

Sertraline (trade names Zoloft and others) is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class. It was introduced to the market by Pfizer in 1991. Sertraline is primarily prescribed for major depressive disorder in adult outpatients as well as obsessive-compulsive disorder, panic disorder, and social anxiety disorder, in both adults and children. In 2013, it was the most prescribed antidepressant and second most prescribed psychiatric medication (after alprazolam) on the U.S. retail market, with over 41 million prescriptions.

Materials and Methods

All analyses were performed using a Waters® Alliance 2695 equipped with multiple wave length UV detector 2487 (Milford, MA, USA). The Lux Amylose-1 column used for analysis was obtained from Phenomenex (Torrance, CA, USA) and the CHIRALPAK AD-H column was obtained from DAICEL® Corporation (Fort Lee, NJ, USA). All solvents were purchased from Honeywell (Morristown, NJ, USA) and Sigma-Aldrich (St. Louis, MO, USA). Ph. Eur. Standard Sertraline for system suitability CRS Cat. Code: Y0000867 was purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allée Kastner CS 30026 F - 67081 STRASBOURG (France)

Figure 1.
Sertraline Hydrochloride



Ph. Eur. Monograph 1705 for Enantiomeric Purity:

Solvent mixture: diethylamine R, hexane R, 2-propanol R (1:40:60 V/V/V).
Test solution. Dissolve 60.0 mg of the substance to be examined in the solvent mixture and dilute to 10.0 ml with the solvent mixture.
Reference solution (a). Dissolve the contents of a vial of sertraline for system suitability CRS (containing impurity G) in 1.0 ml of the solvent mixture.
Reference solution (b). Dilute 0.5 ml of the test solution to 100.0 ml with the solvent mixture.
Column:
- *size:* l = 0.25 m, Ø = 4.6 mm;
- *stationary phase:* silica gel AD for chiral separation R (5µm).

Mobile phase: mix 30 volumes of hexane R and 70 volumes of a mixture of 1 volume of diethylamine R, 25 volumes of 2-propanol R and 975 volumes of hexane R.
Flow rate: 0.4 ml/min.
Detection: spectrophotometer at 275 nm.
Injection: 20 µl.
Run time: 30 min.
Elution order: sertraline, impurity G.
System suitability:
- *resolution:* minimum 1.5 between the peaks due to sertraline and impurity G in the chromatogram obtained with reference solution (a) ;
- *signal-to-noise ratio:* minimum 10 for the peak due to sertraline in the chromatogram obtained with reference solution (b).

Limit:
- *impurity G*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.5 per cent).

Columns: Lux 5 µm Amylose-1
CHIRALPAK® 5 µm AD-H®
Dimensions: 250 x 4.6 mm
Mobile Phase: DEA/Hexane/2-propanol (according to Ph. Eur. method)
Flow Rate: 0.4 mL/min
Injection Volume: 20 µL
Temperature: 25 °C
Detection: UV @ 275 nm
Sample: Sertraline for system suitability CRS (containing impurity G)

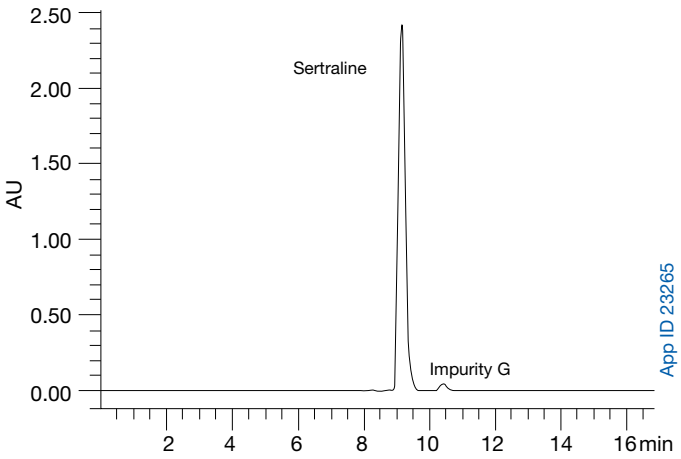
Result and Discussion:

In this technote, we report the enantiomeric separation between Sertraline (the Active Pharmaceutical Ingredient or API) depicted in **Figure 1.** and Sertraline Impurity G (the enantiomer of the API) using the new Lux Amylose-1 chiral stationary phase according to the Ph. Eur. Monograph 1705 (01/2011: corrected 7.7).

Figure 2. displays the chromatographic chiral separation between Sertraline API and enantiomeric Impurity G using a Lux Amylose-1 column. The resolution achieved between the two enantiomers is 3.26 well above the Ph. Eur. Monograph criteria of minimum 1.5 between the two peaks.

Figure 3. shows an overlay of the system suitability test run on the Lux Amylose-1 column and the competitor column CHIRALPAK AD-H. The Sertraline API retention time between the two columns is 9.15 min and 9.59 min respectively. It is important to notice that the resolution between the enantiomers is better on the new Lux Amylose-1 column with 3.26 versus 2.67 with the CHIRALPAK AD-H column.

Figure 2.
System suitability - Reference solution using Lux 5 µm Amylose-1
Resolution (Rs) of 3.26 meets system suitability criteria of minimum 1.5



* Comparative separations may not be representative of all applications.

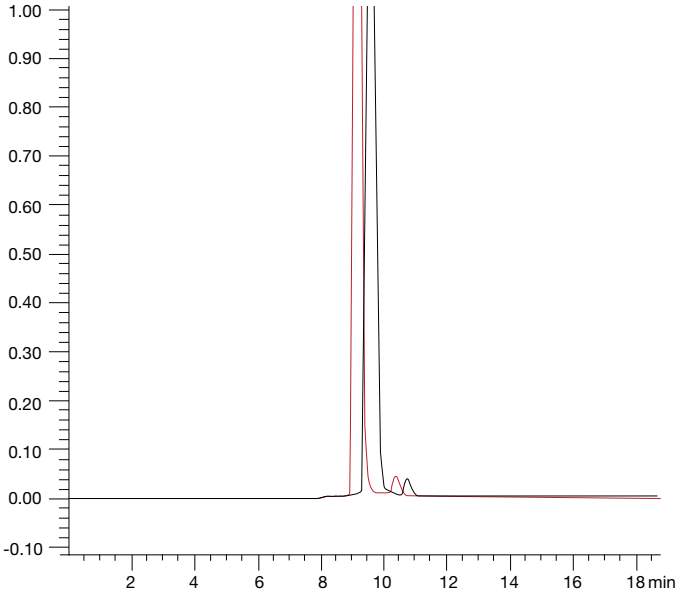
Conclusion

The results shown above demonstrate that the new Lux Amylose-1 can be successfully used to analyze Sertraline API according to Ph.Eur. Monograph 1705.

Resolution for system suitability was 3.26 which is well above the minimum of 1.5 required by the Ph.Eur. monograph method.

Superior resolution of 3.26 was obtained with Lux 5 µm Amylose-1 compared to 2.67 for a CHIRALPAK 5 µm AD-H.

Figure 3.
Overlay for Lux Amylose-1 (Red) vs CHIRALPAK AD-H (Black)



Lux 5 µm Amylose-1

Peak	Compound	Rt	Rs	Area	Area%
1	Sertraline	9.155	-	34517331	97.96
2	Impurity G	10.382	3.26	717397	2.04

CHIRALPAK 5 µm AD-H

Peak	Compound	Rt	Rs	Area	Area%
1	Sertraline	9.589	-	36251583	98.00
2	Impurity G	10.733	2.67	738344	1.99

Lux® Ordering Information

5 µm Analytical Columns (mm)					SecurityGuard™ Cartridges (mm)
Phases	**50 x 4.6**	**100 x 4.6**	**150 x 4.6**	**250 x 4.6**	**4 x 3.0***
Amylose-1	00B-4732-E0	00D-4732-E0	00F-4732-E0	00G-4732-E0	AJ0-9336
				for ID:	3.2–8.0 mm

5 µm Semi-Prep Columns (mm)		SecurityGuard Cartridges (mm)
Phases	**250 x 10.0**	**10 x 10.0‡**
Amylose-1	00G-4732-N0	AJ0-9344
	for ID:	9–16 mm

5 µm Axia™ Packed Preparative Columns (mm)					SecurityGuard Cartridges (mm)	
Phases	**150 x 21.2**	**250 x 21.2**	**250 x 30**	**250 x 50**	**15 x 21.2****	**15 x 30.0♦**
Amylose-1	00F-4732-P0-AX	00G-4732-P0-AX	00G-4732-U0-AX	00G-4732-V0-AX	AJ0-9338	AJ0-9339
				for ID:	18–29 mm	30–49 mm

* SecurityGuard Analytical Cartridges require holder, Part No. : KJ0-4282
‡ SemiPrep SecurityGuard™ Cartridges require holder, Part No.: AJ0-9281
**HPLC PREP SecurityGuard Cartridges require holder, Part No. : AJ0-8223
SFC PREP SecurityGuard Cartridges require holder, Part No. : AJ0-8617
♦ HPLC PREP SecurityGuard Cartridges require holder, Part No. : AJ0-8277
SFC PREP SecurityGuard Cartridges require holder, Part No. : AJ0-8618

guarantee

If Phenomenex products in this technical note do not provide at least an equivalent separation as compared to other products of the same phase and dimensions, return the product with comparative data within 45 days for a FULL REFUND.

APPLICATIONS

Australia
t: +61 (0)2-9428-6444
f: +61 (0)2-9428-6445
auinfo@phenomenex.com

Austria
t: +43 (0)1-319-1301
f: +43 (0)1-319-1300
anfrage@phenomenex.com

Belgium
t: +32 (0)2 503 4015 (French)
t: +32 (0)2 511 8666 (Dutch)
f: +31 (0)30-2383749
beinfo@phenomenex.com

Canada
t: +1 (800) 543-3681
f: +1 (310) 328-7768
info@phenomenex.com

China
t: +86 (0)20 2282-6668
f: +86 (0)20 2809-8130
chinainfo@phenomenex.com

Denmark
t: +45 4824 8048
f: +45 4810 6265
nordicinfo@phenomenex.com

Finland
t: +358 (0)9 4789 0063
f: +45 4810 6265
nordicinfo@phenomenex.com

France
t: +33 (0)1 30 09 21 10
f: +33 (0)1 30 09 21 11
franceinfo@phenomenex.com

Germany
t: +49 (0)6021-58830-0
f: +49 (0)6021-58830-11
anfrage@phenomenex.com

India
t: +91 (0)40-3012 2400
f: +91 (0)40-3012 2411
indiainfo@phenomenex.com

Ireland
t: +353 (0)1 247 5405
f: +44 1625-501796
eireinfo@phenomenex.com

Italy
t: +39 051 6327511
f: +39 051 6327555
italiainfo@phenomenex.com

Luxembourg
t: +31 (0)30-2418700
f: +31 (0)30-2383749
nlinfo@phenomenex.com

Mexico
t: 001-800-844-5226
f: 001-310-328-7768
tecnicomx@phenomenex.com

The Netherlands
t: +31 (0)30-2418700
f: +31 (0)30-2383749
nlinfo@phenomenex.com

New Zealand
t: +64 (0)9-4780951
f: +64 (0)9-4780952
nzinfo@phenomenex.com

Norway
t: +47 810 02 005
f: +45 4810 6265
nordicinfo@phenomenex.com

Puerto Rico
t: +1 (800) 541-HPLC
f: +1 (310) 328-7768
info@phenomenex.com

Spain
t: +34 91-413-8613
f: +34 91-413-2290
espinfo@phenomenex.com

Sweden
t: +46 (0)8 611 6950
f: +45 4810 6265
nordicinfo@phenomenex.com

United Kingdom
t: +44 (0)1625-501367
f: +44 (0)1625-501796
ukinfo@phenomenex.com

USA
t: +1 (310) 212-0555
f: +1 (310) 328-7768
info@phenomenex.com

All other countries
Corporate Office USA
t: +1 (310) 212-0555
f: +1 (310) 328-7768
info@phenomenex.com

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

TN36540915_W