APPLICATIONS

Chiral Separation of the Drug Product Tamsulosin Hydrochloride on a Lux® Amylose-1 Column According to Ph. Eur. Monograph 2131

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

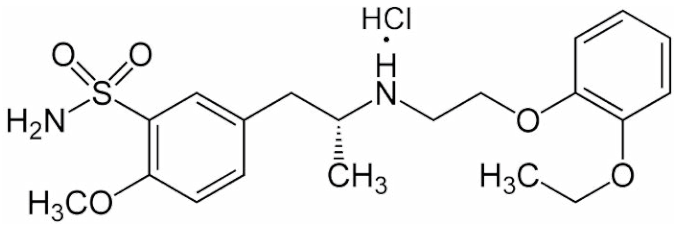
In this technical note, we report the enantiomeric separation between Tamsulosin and Impurity G (the enantiomer of Tamsulosin) using the Lux Amylose-1 chiral stationary phase according to the Ph. Eur. Monograph 2131. Comparison with a CHIRALPAK® AD-H® column is also provided.

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 Tamsulosin (**Figure 1**.), a chiral HPLC method is generally used to assess chiral purity.

Tamsulosin is an α_{1A}adrenergic receptor antagonist used in the symptomatic treatment of benign prostatic hyperplasia. Tamsulosin was developed by Yamanouchi Pharmaceuticals (now part of Astellas Pharma) and was first marketed in 1996 under the trade name Flomax, and also under the name Omnic. Tamsulosin is used in the treatment of difficult urination, a common symptom of enlarged prostate. Tamsulosin, and other medications in the class called alpha blockers, work by relaxing bladder neck muscles and muscle fibers in the prostate itself and make it easier to urinate. The U.S. patent for Flomax expired in October 2009. The U.S. Food and Drug Administration (FDA) approved generic Flomax in March 2010.

Figure 1.
Tamsulosin Hydrochloride



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 Tamsulosin racemate CRS for system suitability Cat. Code Y0000653 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).

Ph. Eur. Monograph 2131 for Enantiomeric Purity

Test solution. Dissolve 50.0 mg of the substance to be examined in methanol R and dilute to 25.0 mL with the solvent.

Reference solution (a). Dilute 1.0 mL of the test solution to 100.0 mL with methanol R. Dilute 2.0 mL of this solution to 10.0 mL with methanol R.

Reference solution (b). Dissolve 5.0 mg of tamsulosin racemate CRS in methanol R and dilute to 25.0 mL with the same solvent. Dilute 2.0 mL of this solution to 10.0 mL with methanol R.

Column:
- *size: l = 0.25 m, Ø = 4.6 mm*
- *stationary phase: silica gel AD for chiral separation R*
- *temperature: 40°C*

Mobile phase: diethylamine R, methanol R, anhydrous ethanol R, hexane R (1:150:200:650 V/V/V/V)

Flow rate: 0.5 mL/min

Detection: spectrophotometer at 225 nm

Injection: 10 µL

Relative retention with reference to Tamsulosin (retention time = about 14 min): impurity G = about 0.8

System suitability: reference solution (b):
- *resolution: minimum 2 between the peaks due to impurity and Tamsulosin.*

Limit:
- *impurity G: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent).*

Result and Discussion

In this technote, we report the enantiomeric separation between Tamsulosin (the Active Pharmaceutical Ingredient or API) depicted in **Figure 1** and Tamsulosin Impurity G (the enantiomer of the API) using the new Lux® Amylose-1 chiral stationary phase according to the Ph. Eur. Monograph 2131 (01/2008: corrected 6.5).

Figure 2. shows the chromatographic chiral separation between Tamsulosin API and enantiomeric Impurity G using the Lux Amylose-1 column. The resolution achieved between the two enantiomers is 6.77, well above the Ph. Eur. Monograph minimum criteria of 2 between the two peaks. In **Figure 3**. a chromatogram for the system suitability test run on CHIRALPAK® AD-H® column is shown. The Tamsulosin API retention time between the two columns is 13.532 min and 13.453 min respectively. It is important to note that the resolution between the enantiomers is better on the Lux Amylose-1 column, 6.77 versus 5.84 with the CHIRALPAK AD-H column (**Table 1**.).

Table 1.
Comparison between Lux Amylose-1 and CHIRALPAK 5 µm AD-H for reference solution (b)

Lux 5 µm Amylose-1

Compound	RT	Rs	Area	% Area
Impurity G	10.337		2,286,807	49.6
Tamsulosin	13.532	6.77	2,327,696	50.4

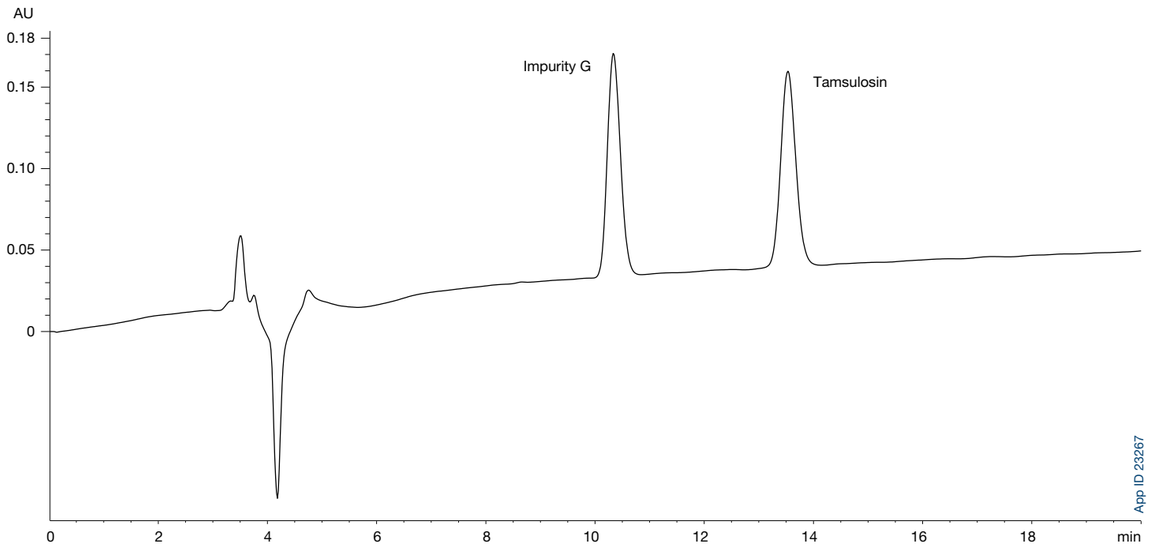
CHIRALPAK 5 µm AD-H

Compound	RT	Rs	Area	% Area
Impurity G	10.671		2,453,166	49.4
Tamsulosin	13.453	5.84	2,510,767	50.6

HPLC Conditions for both columns:

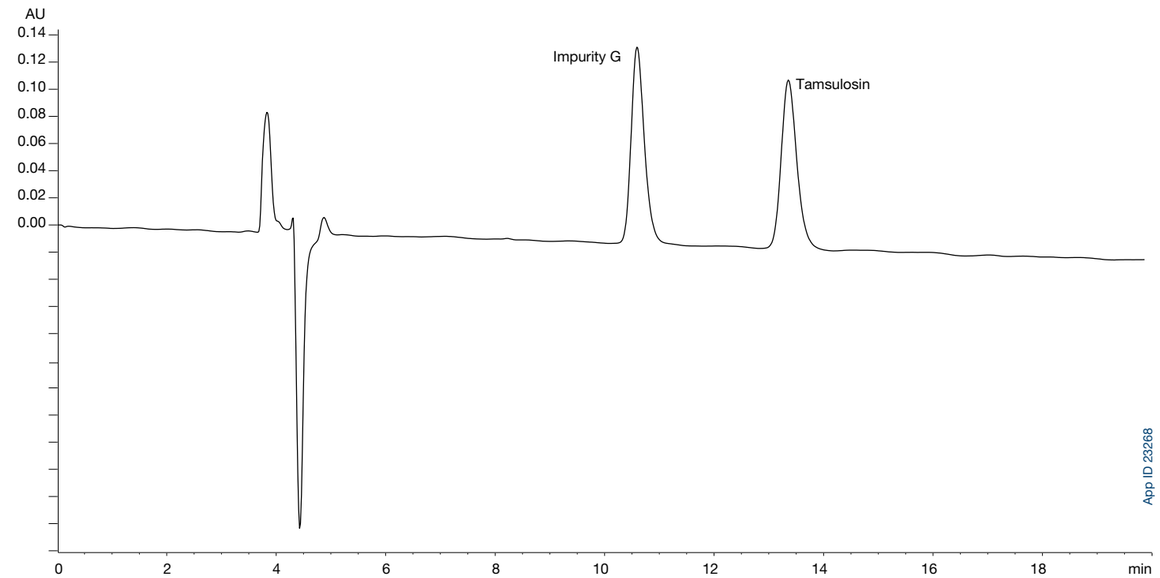
Column: Lux 5 µm Amylose-1
CHIRALPAK 5 µm AD-H
Dimensions: 250 x 4.6 mm
Mobile Phase: According to Ph. Eur. method
Flow Rate: 0.5 mL/min
Detection: UV @ 225 nm
Temperature: 40 °C
Injection Volume: 10 µL
Sample: Tamsulosin racemate CRS (containing impurity G)

Figure 2.
System suitability - Reference solution (b) using **Lux 5µm Amylose-1**
Resolution (Rs) of 6.77 meets system suitability criteria of minimum 2.



Comparative separations may not be representative of all applications.

Figure 3.
System suitability - Reference solution (b) using **CHIRALPAK® 5µm AD-H®**
Resolution (Rs) of 5.84 meets system suitability criteria of minimum 2.



Conclusion

The results shown above demonstrate that the new Lux® Amylose-1 column can be successfully used to analyze Tamsulosin API according to Ph. Eur. Monograph 2131. Resolution for system suitability was 6.77 which is well above the minimum of 2 required by the Ph. Eur. monograph method. Additionally, resolution was superior with the Lux 5 µm Amylose-1 (6.77) compared to a 5 µm CHIRALPAK AD-H. (5.84)

Comparative separations may not be representative of all applications.

APPLICATIONS

Lux® Amylose-1 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*
Amylose-1	00B-4732-B0	00B-4732-E0	00D-4732-E0	00F-4732-E0	00G-4732-E0	AJ0-9337	AJ0-9336
					for ID:	2.0–3.0 mm	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 Lux analytical columns (less than or equal to 4.6 mm ID) do not provide at least an equivalent or better separation as compared to a competing column of the same particle size, similar phase and dimensions, return the column with comparative data within 45 days for a FULL REFUND.

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

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