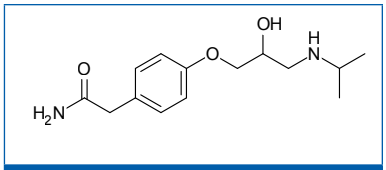
APPLICATION



Atenolol

Atenolol and Related Substances

Ph. Eur. monograph 0703

Overview

The related substances test of the Ph. Eur. Monograph 0703 outlines the separation of all relevant impurities from Atenolol. This method was studied and improvements were made to provide higher resolution (Rs) and a faster separation time within allowable adjustments.

Ph. Eur. Monograph 0703 Details	
Reference Solution (a)	Dissolve 2 mg of Atenolol for system suitability CRS* (containing Impurities B, F, G, I and J) in 1 mL mobile phase
Column	
Size	125 x 4.0 mm
Stationary Phase	End-capped octadecylsilyl silica gel for chromatography R (5 µm)
Mobile Phase	Dissolve 1.0 g of sodium octanesulphonate R and 0.4 g of tetrabutylammonium hydrogen sulfate R in 1 L of a mixture of 20 volumes of tetrahydrofuran R, 180 volumes methanol R2 and 800 volumes of 3.4 g/L solution of potassium dihydrogen phosphate R; adjust the apparent pH to 3.0 with phosphoric acid R.
Flow Rate	0.6 mL/min
Detection	Spectrophotometer @ 226 nm
Injection	10 µL
Run Time	5 times the retention time of Atenolol
Relative Retention with Reference to Atenolol (about 8 min)**	
Impurity B	about 0.3
Impurity J	about 0.7
Impurity I	about 0.8
Impurity F	about 2.0 (pair of peaks)
Impurity G	about 3.5
System Suitability	
Reference Solution (a)	Minimum resolution of 1.4 between peaks due to Impurities J and I

* Atenolol for system suitability CRS (Y0001089) was purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

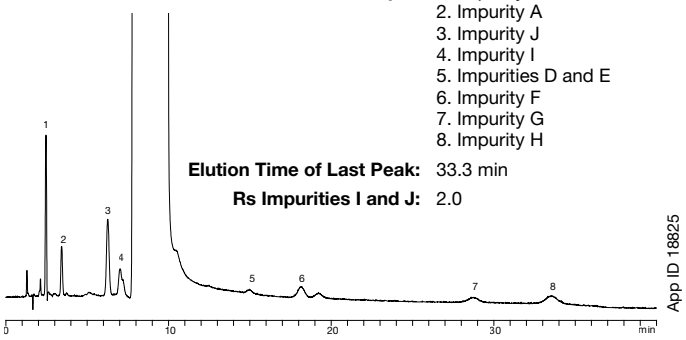
** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

Method 1

Original Method as Described in the Monograph

Column: Luna® C18(2) 5 µm Fully Porous
Dimensions: 125 x 4.0 mm
Part No.: 00E-4252-D0
Flow Rate: 0.6 mL/min
Sample:
1. Impurity B
2. Impurity A
3. Impurity J
4. Impurity I
5. Impurities D and E
6. Impurity F
7. Impurity G
8. Impurity H

Elution Time of Last Peak: 33.3 min
Rs Impurities I and J: 2.0



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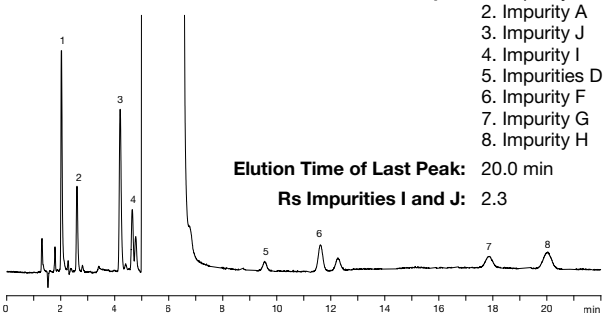
Method 2

Faster and Higher Resolution Within Allowable Adjustments

Reduce run time by >10 min

Column: Kinetex® Core-Shell C18 2.6 µm
Dimensions: 100 x 4.6 mm
Part No.: 00D-4462-E0
Flow Rate: 0.6 mL/min
Sample:
1. Impurity B
2. Impurity A
3. Impurity J
4. Impurity I
5. Impurities D and E
6. Impurity F
7. Impurity G
8. Impurity H

Elution Time of Last Peak: 20.0 min
Rs Impurities I and J: 2.3



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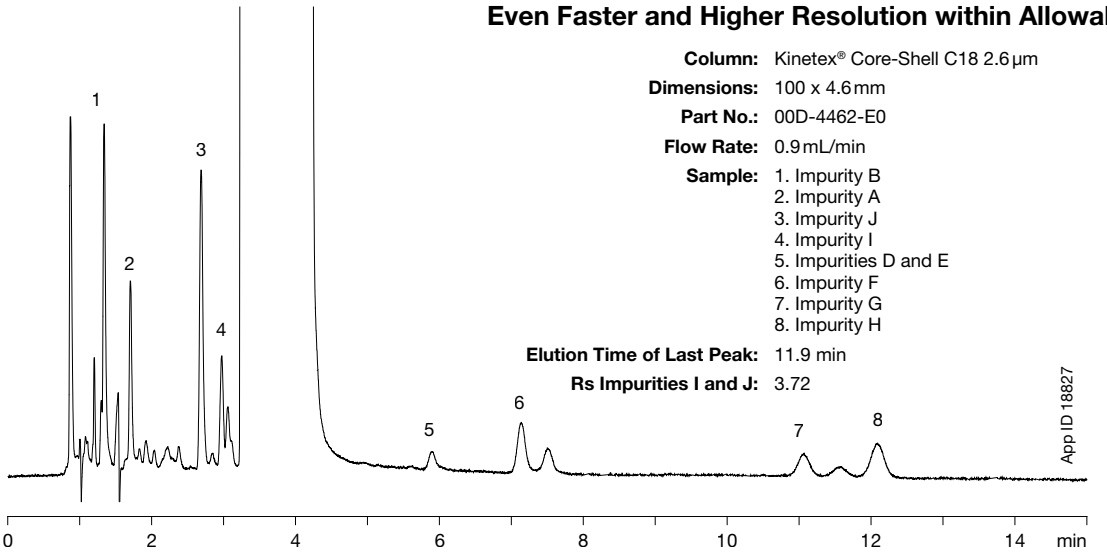
Method 3
Even Faster and Higher Resolution within Allowable Adjustments



Column: Kinetex® Core-Shell C18 2.6 µm
Dimensions: 100 x 4.6 mm
Part No.: 00D-4462-E0
Flow Rate: 0.9 mL/min
Sample:
1. Impurity B
2. Impurity A
3. Impurity J
4. Impurity I
5. Impurities D and E
6. Impurity F
7. Impurity G
8. Impurity H

Elution Time of Last Peak: 11.9 min
Rs Impurities I and J: 3.72

Adjustments for Meeting System Suitability
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2	Method 3
Mobile Phase pH	± 0.2 units	3 (as specified)	As specified	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 0703 Details Table	As specified	As specified
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 0703 Details Table	As specified	As specified
Wavelength of Detector	No deviations permitted	226 nm (as specified)	As specified	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	10 µL (as specified)	As specified	As specified
Column Temperature	± 10 °C	Ambient (as specified)	As specified	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C18 by C8)	End-capped octadecylsilyl silica gel for chromatography (as specified)	As specified	As specified
Column Length	± 70 %	125 mm (as specified)	100 mm (-20 %)	100 mm (-20 %)
Column Internal Diameter	± 25 %	4.0 mm (as specified)	4.6 mm (+15 %)	4.6 mm (+15 %)
Particle Size	-50 %	5 µm (as specified)	2.6 µm (-48 %)	2.6 µm (-48 %)
Flow Rate	± 50 %	0.6 mL/min (as specified)	As specified	0.9 mL/min (+ 50 %)

Kinetex® Ordering Information

5 µm Minibore Columns (mm)					SecurityGuard™ ULTRA Cartridges‡
Phases	30 x 2.1	50 x 2.1	100 x 2.1	150 x 2.1	3/pk
C18	00A-4601-AN	00B-4601-AN	00D-4601-AN	00F-4601-AN	AJ0-8782
					for 2.1 mm ID

5 µm MidBore™ Columns (mm)				SecurityGuard ULTRA Cartridges‡
Phases	50 x 3.0	100 x 3.0	150 x 3.0	3/pk
C18	00B-4601-Y0	00D-4601-Y0	00F-4601-Y0	AJ0-8775
				for 3.0 mm ID

5 µm Analytical Columns (mm)					SecurityGuard ULTRA Cartridges‡
Phases	50 x 4.6	100 x 4.6	150 x 4.6	250 x 4.6	3/pk
C18	00B-4601-E0	00D-4601-E0	00F-4601-E0	00G-4601-E0	AJ0-8768
					for 4.6 mm ID

5 µm Semi-Preparative Columns (mm)			SecurityGuard SemiPrep Cartridges***
Phases	150 x 10	250 x 10	3/pk
C18	00F-4601-N0	00G-4601-N0	AJ0-9278
			for 9-16 mm ID

‡SecurityGuard ULTRA Cartridges require holder, Part No.: AJ0-9000

***SemiPrep SecurityGuard Cartridges require holder, Part No.: AJ0-9281

Luna® Ordering Information

5 µm Microbore and Minibore Columns (mm)								SecurityGuard™ Cartridges (mm)
Phases	50 x 1.0	150 x 1.0	250 x 1.0	30 x 2.0	50 x 2.0	150 x 2.0	250 x 2.0	4 x 2.0*
								/10pk
C18(2)	00B-4252-A0	00F-4252-A0	00G-4252-A0	00A-4252-B0	00B-4252-B0	00F-4252-B0	00G-4252-B0	AJ0-4286
								for ID: 2.0-3.0 mm

5 µm MidBore and Analytical Columns (mm)								SecurityGuard™ Cartridges (mm)	
Phases	30 x 3.0	50 x 3.0	150 x 3.0	250 x 3.0	30 x 4.6	50 x 4.6	75 x 4.6	4 x 2.0*	4 x 3.0*
								/10pk	/10pk
C18(2)	00A-4252-Y0	00B-4252-Y0	00F-4252-Y0	00G-4252-Y0	00A-4252-E0	00B-4252-E0	00C-4252-E0	AJ0-4286	AJ0-4287
								for ID: 2.0-3.0 mm	3.2-8.0 mm

5 µm Analytical and Semi-Prep Columns (mm)					SecurityGuard™ Cartridges (mm)	
Phases	100 x 4.6	150 x 4.6	250 x 4.6	250 x 10	4 x 3.0*	10 x 10‡
					/10pk	/3pk
C18(2)	00D-4252-E0	00F-4252-E0	00G-4252-E0	00G-4252-N0	AJ0-4287	AJ0-7221
					for ID: 3.2-8.0 mm	9-16 mm

*SecurityGuard™ Analytical Cartridges require holder, Part No.: KJ0-4282
‡SemiPrep SecurityGuard Cartridges require holder, Part No.: AJ0-9281

guarantee

If Phenomenex products in this technical note do not provide at least an equivalent separation as compared to a competing product of the same particle size, similiar phase and dimensions, return the product 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: +86 400-606-8099
f: +86 (0)22 2532-1033
phen@agela.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: 01-800-844-5226
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

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