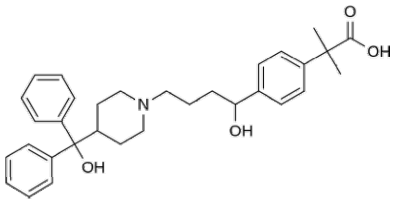
Fexofenadine and Related Substances (USP)



Fexofenadine

Fexofenadine is an antihistamine pharmaceutical drug used in the treatment of allergy symptoms, such as hay fever, nasal congestion, and urticaria. Common trade names are: Allegra, Fexidine, Telfast, Fastofen, Tilfur, Vifas, Telfexo, Allerfexo.

The current USP monograph method for Fexofenadine and related substances specifies the use of a 250x4.6 mm column with L11 (Phenyl) packing as stationary phase, which is identical to conditions in the assay method also. No particle size mentioned wherefore the ratio must be calculated using the largest particle size consigned in the USP definition of the column.

System suitability requirements specify a chromatographic resolution not less than (NLT) 10 between fexofenadine and fexofenadine related compound A; a peak tailing factor of not more than (NMT) 2.0.

The following pages illustrate that the acceptance criteras are being met for Fexofenadine assay and its related substances methods by following the current USP monograph and using identical matched column. Using a 250x4.6 mm Purospher® STAR Phenyl (5 µm) column you can comply with the requirements for Fexofenadine assay and its related substances analysis.

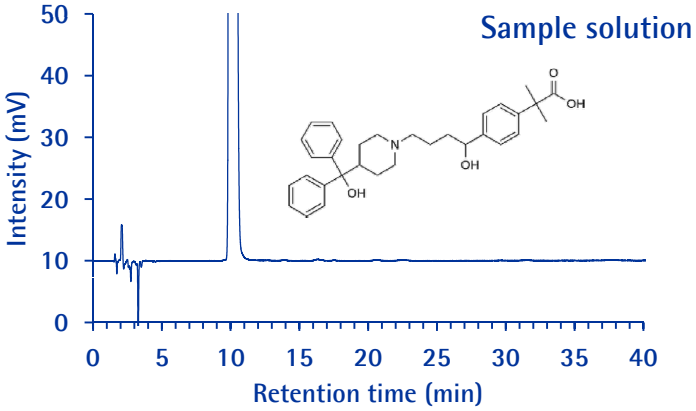
To address the current trend of monograph modernization, and improving the method in terms of selectivity, speed and sensitivity, we also scaled this method to a 100x2.1 mm UHPLC column; Purospher® STAR Phenyl (2 µm). The acceptance critera are met for the for Fexofenadine monograph. This is however, a non-allowed scaling and would require a complete revalidation of the new method for approval.

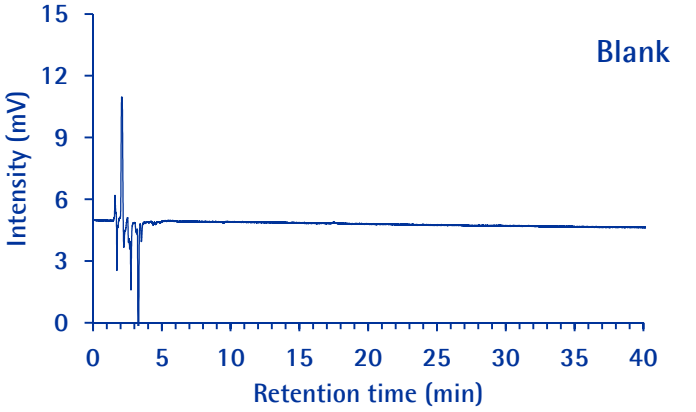
Fexofenadine and Related Substances (USP)

Purospher® STAR Phenyl – HPLC

Chromatographic Conditions

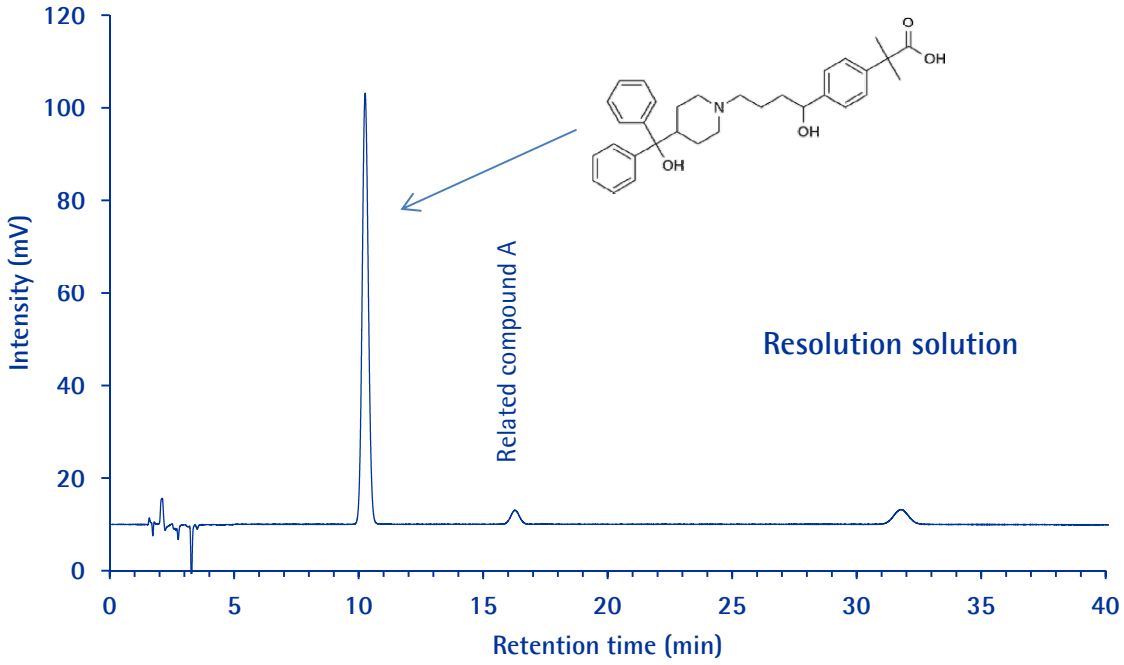
Column:	Purospher® STAR Phenyl (5µm) Hibar® RT 250x4.6 HPLC column	1.51918.0001
Injection:	20 µL	
Detection:	UV 220 nm	
Cell:	10 µL	
Flow Rate:	1.5 mL/min	
Mobile Phase:	Buffer: 6.64 g/L of monobasic sodium phosphate and 0.84 g/L of sodium perchlorate in water. Adjust with phosphoric acid to a pH of 2.0. Mix acetonitrile and buffer 7:13 (v/v). Add 3 mL/L of triethylamine.	
Temperature:	25°C	
Diluent:	Acetonitrile and Buffer 1:1 (v/v)	
SST Solution:	0.06 mg/mL of Fexofenadine Hydrochloride RS and 0.005 mg/mL of Fexofenadine Related Compound A in Mobile phase	
Sample Solution:	1.0 mg/mL of Fexofenadine Hydrochloride in Diluent	
Pressure Drop:	164 Bar (2378psi)	





Fexofenadine and Related Substances (USP)

Purospher® STAR Phenyl – HPLC



Suitability requirement: NLT 10 in resolution
NMT 2.0 in Tailing factor

Chromatographic Data :

No.	Compound	Retention Time (min)	Resolution	Tailing Factor
1	Fexofenadine	10.3		1.1
2	Related compound A	16.3	10.9	1.0

Recommended chemicals and reagents

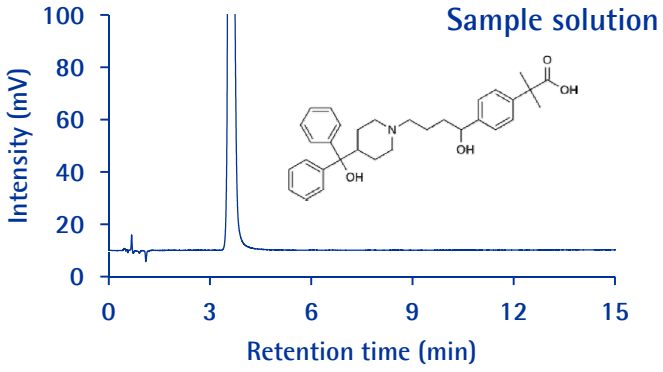
	Name of the chemical	Article Number
1	Sodium dihydrogen phosphate dihydrate for analysis EMSURE® Reag. Ph Eur	1.06342
2	Sodium perchlorate monohydrate for analysis EMSURE®	1.06564
3	ortho-Phosphoric acid 85% for analysis EMSURE® ACS,ISO,Reag. Ph Eur	1.00573
4	Acetonitrile gradient grade for liquid chromatography LiChrosolv® Reag. Ph Eur	1.00030

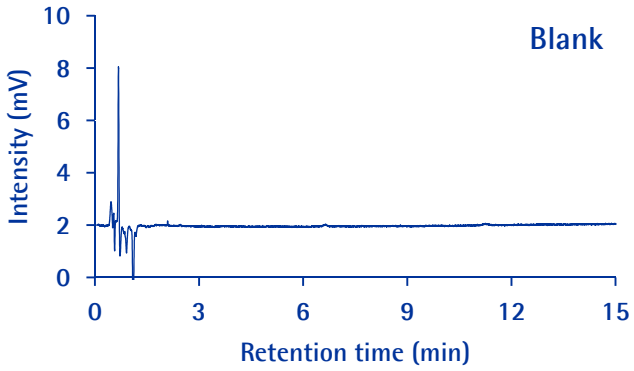
Fexofenadine and Related Substances (USP)

Purospher® STAR Phenyl – UHPLC

Chromatographic Conditions

Column:	Purospher® STAR Phenyl.(2 µm) Hibar® HR 100x2.1 mm	1.51014.0001
Injection:	2 µL	
Detection:	UV 220 nm	
Cell:	2.5 µL	
Flow Rate:	0.4 mL/min	
Mobile Phase:	6.64 g/L of monobasic sodium phosphate and 0.84 g/L of sodium perchlorate in water. Adjust with phosphoric acid to a pH of 2.0. Mix Acetonitrile and buffer 7:13 (v/v). Add 3 mL/L of triethylamine.	
Temperature:	25°C	
Diluent:	Acetonitrile and Buffer 1:1 (v/v)	
SST Solution:	0.06 mg/mL of Fexofenadine Hydrochloride RS and 0.005 mg/mL of Fexofenadine Related Compound A in mobile phase	
Sample Solution:	1.0 mg/mL of Fexofenadine Hydrochloride in Diluent	
Pressure Drop:	388 Bar (5626psi)	





Scaling 250x4.6 to 100x2.1

Column volume reduction: 12X
(and thereby injection volume also)

Flow rate reduction: 12X
(to maintain same retention time)

Flow rate reduction: 4.8 X
(to maintain same linear velocity)

Injection volume should be:20/12= 1.67
but we used 2 µL (more practical)

Flow rate should either be 0.115 or 0.315 mL/min. **We used 0.4 mL/min to optimize analysis time and still comply with system suitability criterias**

Flowrate per USP 37 change guidelines

$F2=1.5 \times (2.1^2 x5)/(4.6^{2'}2) = 0.78$ mL/min

This would be completely impractical and backpressure would be beyond tolerance of column and system.

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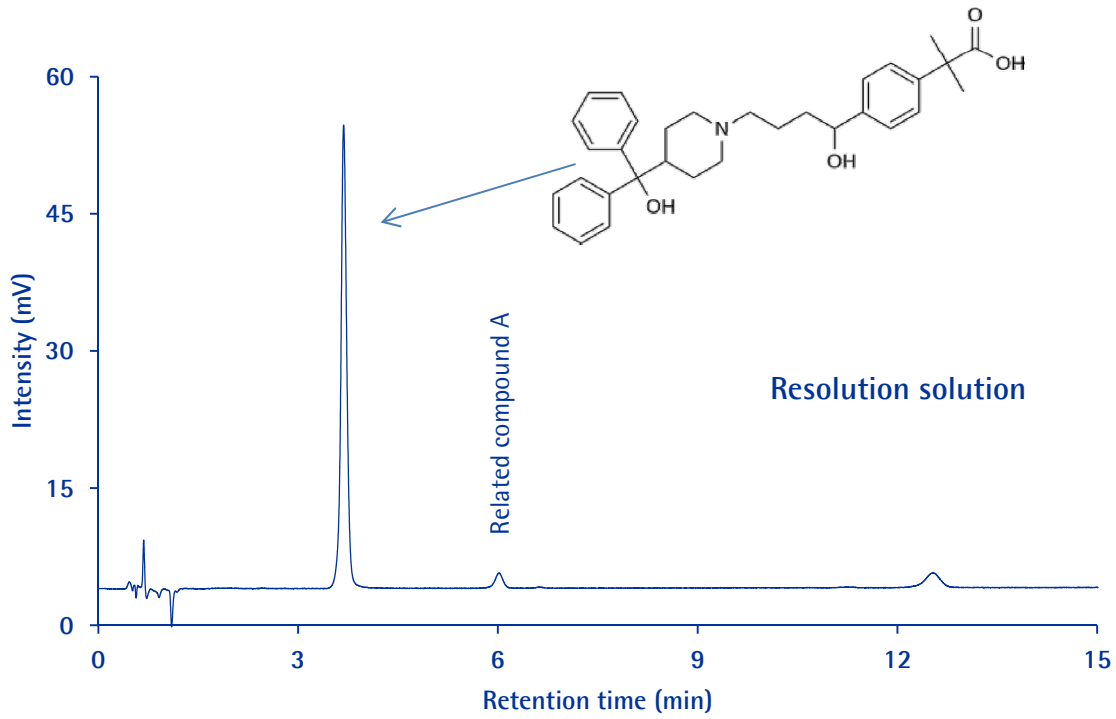
Purospher® STAR Phenyl – UHPLC



Suitability requirement: NLT 10 in resolution
NMT 2.0 in Tailing factor

Chromatographic Data :

No.	Compound	Retention Time (min)	Resolution	Tailing Factor
1	Fexofenadine	3.7		1.0
2	Related compound A	6.0	12.7	1.0

Recommended chemicals and reagents

	Name of the chemical	Article Number
1	Sodium dihydrogen phosphate dihydrate for analysis EMSURE® Reag. Ph Eur	1.06342
2	Sodium perchlorate monohydrate for analysis EMSURE®	1.06564
3	ortho-Phosphoric acid 85% for analysis EMSURE® ACS,ISO,Reag. Ph Eur	1.00573
4	Acetonitrile gradient grade for liquid chromatography LiChrosolv® Reag. Ph Eur	1.00030