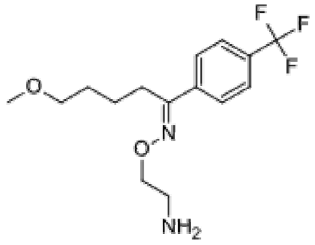
Fluvoxamine and Related Substances (USP)



Fluvoxamine

Fluvoxamine is a medication which functions as a selective serotonin reuptake inhibitor (SSRI) and σ1 receptor agonist. Fluvoxamine is used primarily for the treatment of obsessive-compulsive disorder (OCD), and is also used to treat major depressive disorder (MDD), and anxiety disorders such as panic disorder and posttraumatic stress disorder (PTSD).Fluvoxamine CR (controlled release) is approved to treat social anxiety disorder. Common commercial brand names: Floxyfral, Luvox, Fevarin.

The current USP monograph method for Fluvoxamine maleate and related substances specifies the use of a 250x4.6 mm column with L7 (RP-8) packing as stationary phase (no particle size mentioned), and with identical experimental conditions as described in the assay method. System suitability requirements for related substances are provided by means of relative retention time (RRT) for identified and known impurites, see tabulated impurites in chromatography performance table. In addition, for the assay method, the column efficiency should be not less than 5000 theoretical plates and the tailing factor is not more than 2.0.

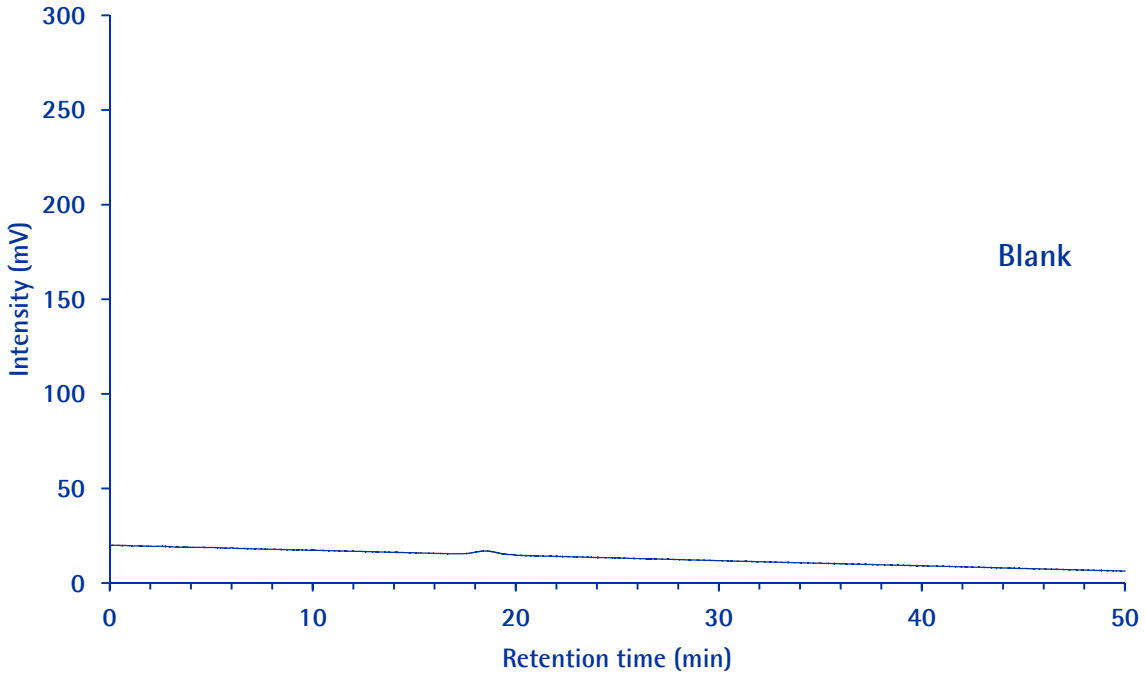
The following pages illustrate that the acceptance critera are being met for the Fluvoxamine maleate and related substances methods by following the current USP monograph and using identical matched column. Using a 250x4.6 mm Purospher® STAR RP-8 endcapped (5 µm) column it is possible to comply with the requirement for Fluvoxamine maleate and related substances analysis.

Fluvoxamine and Related Substances (USP)

Purospher® STAR RP-8 endcapped

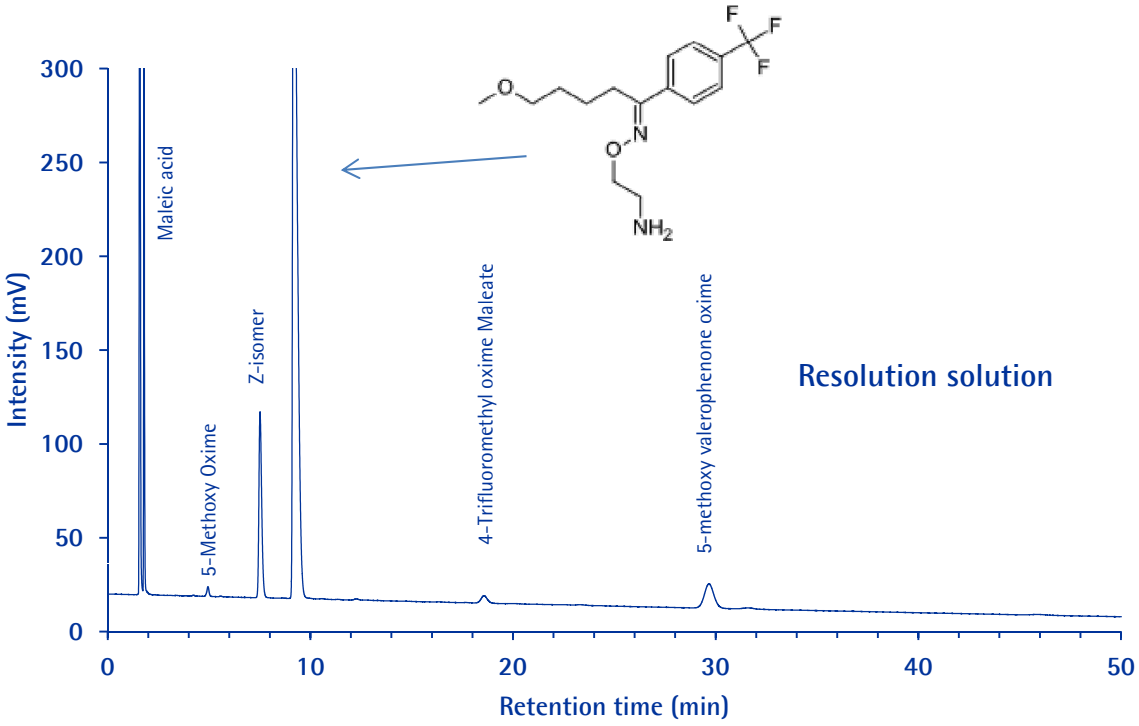
Chromatographic Conditions

Column:	Purospher® STAR RP-8 endcapped (5µm) Hibar® 250x4.6 mm	1.51454.0001
Injection:	20 µL	
Detection:	UV 234 nm	
Cell:	10 µL	
Flow Rate:	1.7 mL/min	
Mobile Phase:	Buffer: dissolve about 5 g of 1-pentanesulfonic acid sodium salt and 0.7 g of monobasic potassium phosphate in 620 mL of water. Adjust with phosphoric acid to a pH of 3.00 ± 0.05. Mix buffer and acetonitrile 62:38 (v/v)	
Temperature:	40 °C	
Diluent:	Mobile phase	
Resolution Solution:	Transfer about 6 mg of Fluvoxamine Maleate to a 50-mL volumetric flask. Heat the sample at 120 for 10 minutes. Cool down to room temperature, add 3.0 mL of 0.1 N hydrochloric acid. Heat the solution in a water bath for 10 minutes. Cool down to room temperature, add 50 mg of Fluvoxamine Maleate, and dissolve in 25 mL of Mobile phase. Dilute with Mobile phase to volume, and mix.	
Pressure Drop:	179 Bar (2596 psi)	



Fluvoxamine and Related Substances (USP)

Purospher® STAR RP-8 endcapped



Chromatographic Data : Sample

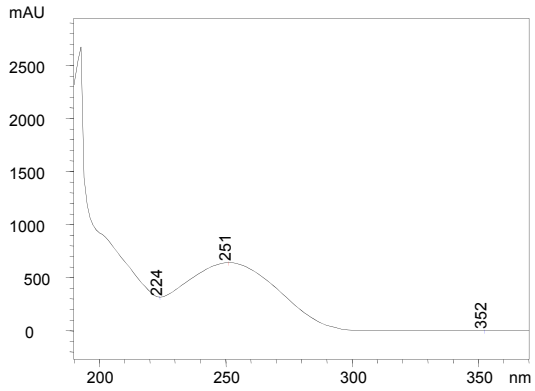
No.	Compound	Retention Time (min)	Resolution	Observed RRT	Approx RRT USP guideline
1	Maleic acid	1.6		0.17	0.19
2	5-Methoxy Oxime	4.9		0.54	0.50
3	Z- Isomer	7.5	11.6	0.82	0.79
4	Fluvoxamine	9.2	5.1	1.00	1.0
5	4-Trifluoromethyl oxime Maleate	18.6		2.02	2.00
6	5-methoxy valerophenone oxime	29.7		3.23	3.45

In the analyzed samples neither:
5-Methoxy-4¢-(trifluoromethyl)valerophenone(E)-O-(2-aminoethyl)aminoethyl oxime maleate (RRT 0.67);
4¢-(Trifluoromethyl)valerophenone(E)-O-2-(2-aminoethyl)aminoethyl oxime maleate (RRT 1.18);
(E)-O-2-(2-Aminoethyl)-4-(trifluoromethyl)- -phenylacetophenone oxime maleate (RRT 1.74) nor
5-Methoxy-4¢-(trifluoromethyl)valerophenone ketone (RRT 4.2) could be found!

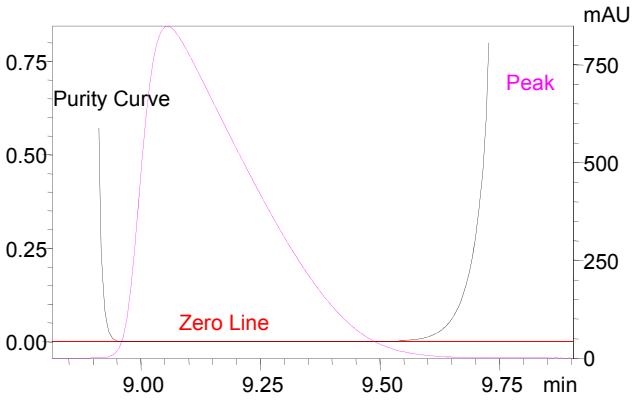
Fluvoxamine and Related Substances (USP)

Purospher® STAR RP-8 endcapped

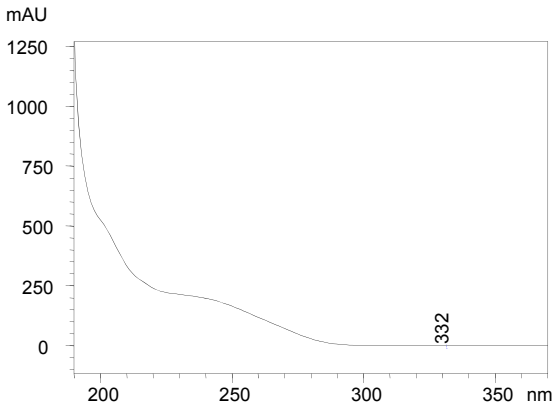
UV spectra: Fluvoxamine



Peak purity curve: Fluvoxamine



UV spectra: Z-isomer



Peak purity curve: Z-isomer