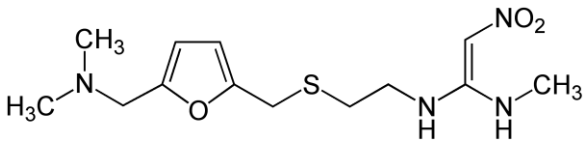
Ranitidine Hydrochloride Tablets (USP)



Ranitidine is a histamine H2-receptor antagonist that inhibits stomach acid production.
It is used in treatment of peptic ulcer disease and gastroesophageal reflux disease.
Ranitidine is used alongside fexofenadine, and other antihistamines, for the treatment of hives and other skin conditions.

Common brand name: Zantac

Drug dissolution of ranitidine tablets is normally conducted by determining the amount of C13H22N4O3S dissolved with UV measurements at 314 nm using filtered portions of the solution under test in comparison with a standard solution with a known concentration of USP Ranitidine Hydrochloride RS in the same medium.

Here we present an alternative HPLC procedure based on the normal dissolution test and the assay test under Ranitidine Injection. In this new alternative method, drug binding has also been tested with Nylon, PTFE and PVDF syringe filters.

The new method proposal is very fast, with an analysis time less than 3 minutes.
It meets all system suitability requirements.
Drug dissolution has a tolerance higher than 80% after 45 minutes and with no prominent drug binding from the sample solution to any of the filters tested.

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Dissolution <711>

HPLC

Medium: water; 900 mL.
Apparatus 2: 50 rpm.
Time: 45 minutes.

Procedure: Determine the amount of $C_{13}H_{22}N_4O_3S$ dissolved from UV absorbance at the wavelength of maximum absorbance at about 314 nm using filtered portions of the solution under test, suitably diluted with water, if necessary, in comparison with a Standard solution having a known concentration of USP Ranitidine Hydrochloride RS in the same medium.

Tolerances—Not less than 80% (Q) of the labeled amount of $C_{13}H_{22}N_4O_3S$ is dissolved in 45 minutes.

Assay (from Ranitidine Injection)
Mobile phase: Prepare a filtered and degassed mixture of methanol and 0.1 M aqueous ammonium acetate (85:15). Make adjustments if necessary (see System Suitability under Chromatography 621).
Standard preparation: Dissolve an accurately weighed quantity of USP Ranitidine Hydrochloride RS in Mobile phase to obtain a solution having a known concentration of about 0.112 mg (equivalent to 0.100 mg of ranitidine base) per mL.
System suitability solution: Dissolve accurately weighed quantities of USP Ranitidine Hydrochloride RS and USP Ranitidine Related Compound C RS in Mobile phase to obtain a solution having known concentrations of about 0.112 mg per mL and 0.01 mg per mL, respectively.
Assay preparation: Dilute an accurately measured volume of Injection, quantitatively and stepwise if necessary, with Mobile phase to obtain a solution having a concentration of 0.1 mg of ranitidine per mL.

Chromatographic system (see Chromatography 621)

Detection: UV at 322 nm
Column: a 4.6 mm × 20 to 30 cm column, packing L1.
Flow rate: about 2 mL per minute.

Suitability requirements
Tailing factor: NMT 2.0
Column efficiency: NLT 700 theoretical plates (measured from the ranitidine hydrochloride peak)
Relative standard deviation: NMT 2.0%

Chromatograph the System suitability solution, and record the peak responses as directed for Procedure: the resolution, R, between ranitidine hydrochloride and N-[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]sulfinyl]ethyl]-N-methyl-2-nitro-1,1-ethenediamine (ranitidine related compound C) is not less than 1.5.
Chromatograph the Standard preparation, and record the peak responses as directed for Procedure.

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Dissolution <711> HPLC

Procedure: Separately inject equal volumes (about 10 µL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the area responses for the major peaks.

Calculate the quantity, in mg, of C13H22N4O3S in the portion of Injection taken by the formula:

(314.40 / 350.87)(L / D)(C)(rU / rS)

where 314.40 and 350.87 are the molecular weights of ranitidine and ranitidine hydrochloride, respectively

L is the labeled quantity of ranitidine in the Injection taken;
D is the concentration, in mg per mL, of ranitidine in the Assay preparation on the basis of the labeled quantity and the extent of dilution;

C is the concentration, in mg per mL, of USP Ranitidine Hydrochloride RS in the Standard preparation; and rU and rS are the peak area responses obtained from the Assay preparation and the Standard preparation, respectively.

The new method proposal include the following:

Chromatographic system
Detection: UV at 314 and 322 nm
Column: a 100x4.6 mm column, packing L1.
Flow rate: about 1.0 mL/minute.
Filter: Either Millex PVDF, Millex PTFE or Millex Nylon

The drug recovery after dissolution was calculated according to the following equation:

$$\text{Result} = (rU/rS) \times (CS/L) \times V \times 100$$

rU = peak response from the Sample solution
rS = peak response from the Standard solution
CS = concentration of the Standard solution (mg/mL)
L = label claim (mg/Capsule)
V = volume of Medium, 900 mL

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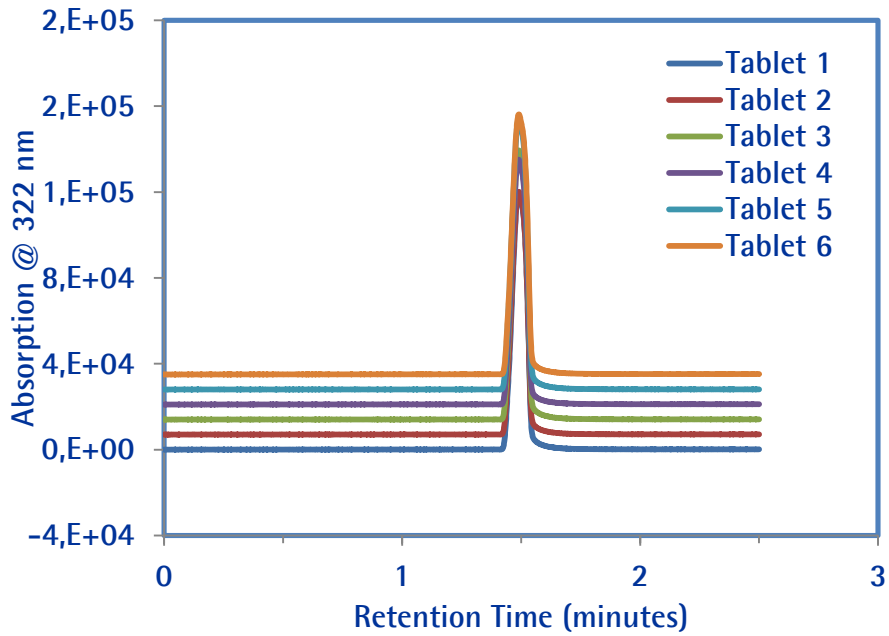
Chromolith® HighResolution RP-18 endcapped

Chromatographic Conditions

Column:	Chromolith® HighResolution RP-18 endcapped, 100x4.6 mm	1.52022.0001
Injection:	2 µl	
Detection:	UV detection @ 314 nm and 322 nm	
Cell:	10 µL	
Flow Rate:	1.0 mL/min	
Medium:	Water, 900 ml for 45 min	
Apparatus 2:	50 rpm	
Mobile phase:	0.1 M Ammonium acetate in water + methanol 15:85 (v/v)	
Temperature:	35°C	
Diluent:	Mobile phase	
Standard Solution:	Dissolve accurately weighed quantity of Ranitidine Hydrochloride USP in mobile phase. Dilute as necessary.	
Sample Solution:	Filter portions of solution under study using appropriate 0.45 µm pore size syringe filter	
Pressure Drop:	173 bar (2500 PSI)	



Chromatographic Data: Standard

No.	Compound	Retention Time (min)	Tailing factor	Theoretical plates
1	Ranitidine hydrochloride	1.48	1.00	1557

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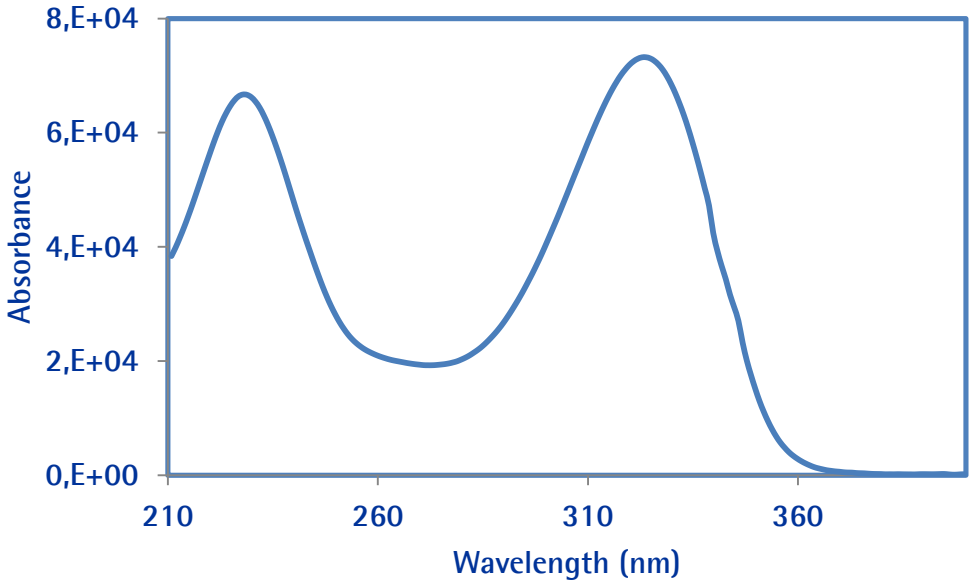
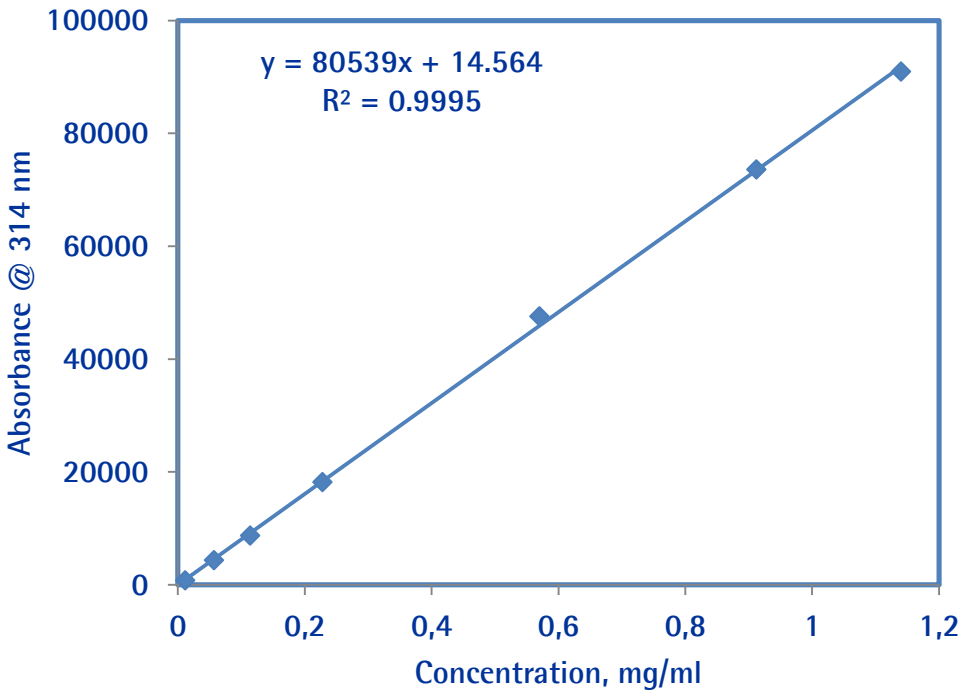
Chromolith® HighResolution RP-18 endcapped





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Chromolith® High Resolution RP-18 endcapped

Result = (rU/rS) × (CS/L) ×V× 100

Filtrate Used	Syringe Filter Used		
	Millex PTFE	Millex Nylon	Millex PVDF
1st ml	107.6	122.8	106.8
2nd ml	117.5	120.8	122.5
3rd ml	119.6	121.6	122.7
5th ml	118.1	121.0	122.6

Did you know?

A quick way to speed-up the preparations for your dissolution tests and to improve the precision in your results is to utilize the automatic volumetric water dispense function on modern Milli-Q water systems.

Automatic volumetric water dispensing
Volumetric water dispensing is set on the base of the POD unit.
You can adjust the volume to be delivered with the (+) and (-) keys, and then press the volumetric dispensing button to start delivery of the selected volume, with excellent accuracy (< 1 %) and reproducibility (cv < 1 %).

The mast and the arm supporting the Q-POD® and E-POD® dispensers are designed to accommodate all commonly used glassware — from a 250 mL Erlenmeyer flask to a 5 L calibrated flask — and even a 20 L carboy!

For hands-free water delivery, an optional footswitch can be connected to the base of the POD dispensers or directly to the Milli-Q® Integral system. Press once to start and once to stop.