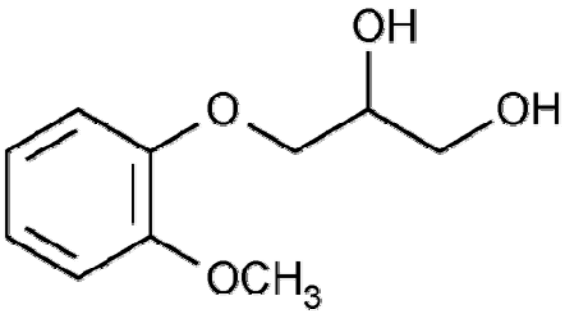
Guaifenesin

USP Method Guaifenesin Assay



Original Manufacturer: FDA approved in 1952

Brand Name: Humibid, Humibid LA, Robitussin, Organidin NR, Fenesin, Mucinex, Cheratussin, Benylin, DayQuil Mucous Control, Meltus, and Bidex 400.

Guaifenesin or guaiphenesin, also glyceryl guaiacolate, is an expectorant drug and usually taken by mouth that promotes elimination of mucus from the lungs. Hence it assist the bringing up (expectoration) of phlegm from the airways in acute respiratory tract infections.

Guaifenesin is sold as pills or syrups under many brand names. Single-ingredient formulations of guaifenesin are available, and it is also included in many other over-the-counter cough and cold remedy combinations (usually in conjunction with dextromethorphan and/or pseudoephedrine or phenylephrine and/or acetaminophen).

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Guaifenesin

USP34 – NF29 S1

USP Columns:

Nucleosil C18 Assay and Chromatographic purity 4.6 mm x 25 cm, 5 µm

Equivalent Column:

Purospher®STAR RP-18 endcapped (5 µm) 250x4.6 mm (1.51456.0001)

Recommended Solvents and Reagents:

Acetonitrile gradient grade for liquid chromatography LiChrosolv® (1.00030)

Water Water for chromatography LiChrosolv® (1.15333)
or freshly purified water from Milli-Q water purification system

Acetic Acid Acetic acid (glacial) 100%. Use ACS reagent grade

USP Standards

Guaifenesin (200 mg) USP Product Number:1301007
Guaiacol (1 g) USP Product Number:1300004

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Assay
Solution A: Prepare a mixture of water and glacial acetic acid (990:10).
Solution B: Use acetonitrile.

Mobile phase
Use variable mixtures of Solution A and Solution B as directed for Chromatographic system.
Make adjustments if necessary (*see System Suitability under Chromatography 621*).

Resolution solution
Prepare a solution in Solution B containing about 0.5 mg of USP Guaifenesin RS and 0.02 mg of USP Guaiacol RS in each mL.

Standard preparation
Prepare a solution of USP Guaifenesin RS in Solution B with known concentration of about 0.5 mg per mL.

Assay preparation
Transfer about 25 mg of Guaifenesin, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with Solution B to volume, and mix.

Chromatographic system (*see Chromatography 621*)
The liquid chromatograph is equipped with a 276-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1 mL per minute. Gradient programmed as follows:

Time (min)	Solution A (%)	Solution B (%)	Elution
0-32	80→50	20→50	Linear gradient
32-35	50→80	50→20	Linear gradient

Chromatograph the Resolution solution, and record the peak responses as directed for Procedure: the relative retention times are about 0.9 for guaifenesin isomer, 1.0 for guaifenesin, and 1.3 for guaiacol; and the resolution, R, between guaifenesin and guaiacol is not less than 3.

Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the relative standard deviation for replicate injections is not more than 1.0%.

USP Method Guaifenisin Assay

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 peak responses.
Calculate the quantity of $C_{10}H_{14}O_4$ in the portion of Guaifenesin taken by the formula:

$$50C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Guaifenesin RS in the Standard preparation; and r_U and r_S are the peak areas obtained from the Assay preparation and the Standard preparation, respectively.
Calculate the percentage of $C_{10}H_{14}O_4$ in the portion of Guaifenesin taken.
To this value, add the percentage of guaifenesin isomer found in the test for Chromatographic purity.

Solution A, Solution B, and Mobile phase *(Proceed as directed in the Assay.)*

Chromatographic system (*Proceed as directed in the Assay*)
To evaluate the system suitability requirements, use the Resolution solution and the Standard preparation prepared as directed in the Assay.

Test solution
Dissolve about 20 mg of Guaifenesin in 10 mL of Solution B.

Diluted test solution
Transfer 1.0 mL of Test solution to a 100-mL volumetric flask, dilute with Solution B to volume, and mix.

Separately inject equal volumes (about 10 µL) of the Test solution and the Diluted test solution into the chromatograph, record the chromatograms, and measure the areas for the major peaks. All of the peaks are baseline resolved. Calculate the percentage of each impurity in the portion of Guaifenesin taken by the formula:

$$F(r_i / r_S)$$

in which F is a response factor equal to 0.63 for the guaiacol peak, having a relative retention time of 1.4, and 1.0 for all other impurities; r_i is the area of each peak, other than that of the main guaifenesin peak, obtained from the Test solution; and r_S is the area of the main peak obtained from the Diluted test solution: not more than 1.5% of 2-(2-methoxyphenoxy)-1,3-propanediol (guaifenesin isomer), the peak for which occurs at a relative retention time of about 0.9, is found; not more than 0.03% of guaiacol is found; not more than 0.5% of any other individual impurity is found; and not more than 1.0% of total impurities, excluding guaifenesin isomer and guaiacol, is found.

USP Method for Guaifenisin Assay

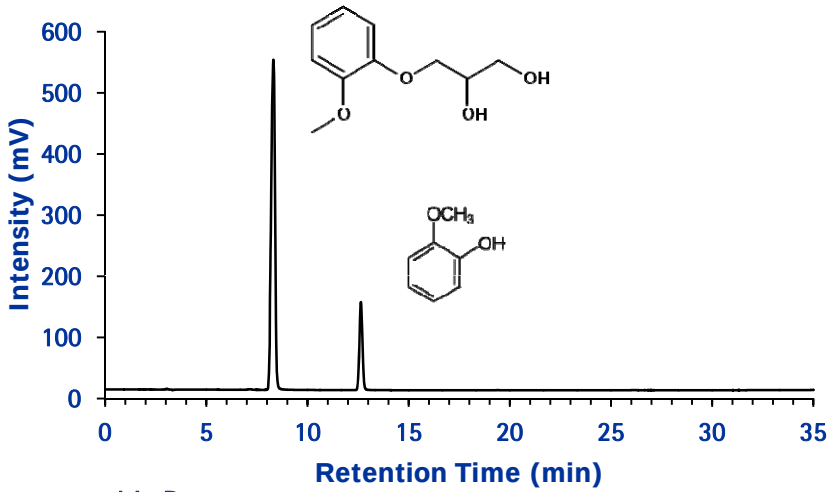
Purospher®STAR RP-18 endcapped

Chromatographic Conditions

Column:	Purospher®STAR RP-18 endcapped (5 µm) 250x4.6 mm	1.51456.0001
Injection:	10 µL	
Detection:	Shimadzu Prominence 2010, UV@276 nm	
Cell:	8 µL	
Flow Rate:	1.0 mL/min	
Mobile Phase (v/v):	Solution A: Glacial acetic acid and water (10:990) Solution B: Acetonitrile	
Gradient:	See Table:	

Time (min)	Solution A (%)	Solution B (%)	Elution
0-32	80→50	20→50	Linear gradient
32-35	50→80	50→20	Linear gradient

Temperature:	30° Celsius
Diluent	mobile phase
Sample:	500 ppm (0.5 mg/mL) Guaiphenesin and 20 ppm (0.02 mg/mL) Guaiacol
Pressure Drop:	142 Bar (2059 psi)



Chromatographic Data

No.	Compound	Time (min)	Tailing Factor (TUSP)	Relative Retention Time (RRT)	Resolution (Rs)
1	Guaifenesin beta isomer	7.2	1.0	0.9	
2	Guaifenesin	8.3	1.0	1.0	
3	Guaiacol	12.6	1.1	1.5	4.8
4	Impurity 1	19.4	1.1		
5	Impurity 2	26.1	1.3		

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