RESTEK

clinical/forensic

Applications note

GC Analysis of Phenylpropanolamine in Cold Medications Using an Rtx®-5Amine Column

Until recently, phenylpropanolamine was an ingredient in prescription and over-the-counter medications. It primarily was used as a nasal decongestant, but also was used in over-the-counter appetite suppression preparations for weight control. However, a study by researchers at the Yale University School of Medicine[1] reported that phenylpropanolamine could increase the risk of hemorrhagic stroke in women. In November 2000, the Food and Drug Administration (FDA) issued a public health advisory requesting that all manufacturers of products containing phenylpropanolamine voluntarily discontinue manufacturing and marketing them. Although the risk of stroke is very low, the FDA determined that the serious medical effects associated with stroke outweighed the benefits derived from phenylpropanolamine. In addition, its use is not so important because a number of other medications can be substituted for phenylpropanolamine, especially for treating colds and sinus congestion.

Cold and sinus medication can be analyzed for the presence of phenylpropanolamine using a simple extraction procedure followed by analysis using capillary gas chromatography (GC). We surveyed the most commonly available cold medications, and chose two for testing. Brand A contained phenylpropanolamine at a concentration of 1.25mg/mL and guaifenesin at a concentration of 10mg/mL. Brand B contained only guaifenesin at a concentration of 20mg/mL. Each medication was supplied as a syrup. Extraction was performed by adding 100uL of syrup to a screw-cap culture tube and making it basic by adding 1.4mL of 2.5% ammonium hydroxide. The sample was mixed thoroughly before adding 3mL of extraction solvent (methylene chloride:isopropanol, 90:10). Each sample was mixed by gently rocking the tube for 5 minutes. The layers were allowed to separate and the top aqueous layer was aspirated to waste. The bottom organic layer was transferred to a clean glass culture tube and evaporated to dryness under a stream of dry nitrogen at room temperature. The extracts were reconstituted for analysis with 100µL of methanol.

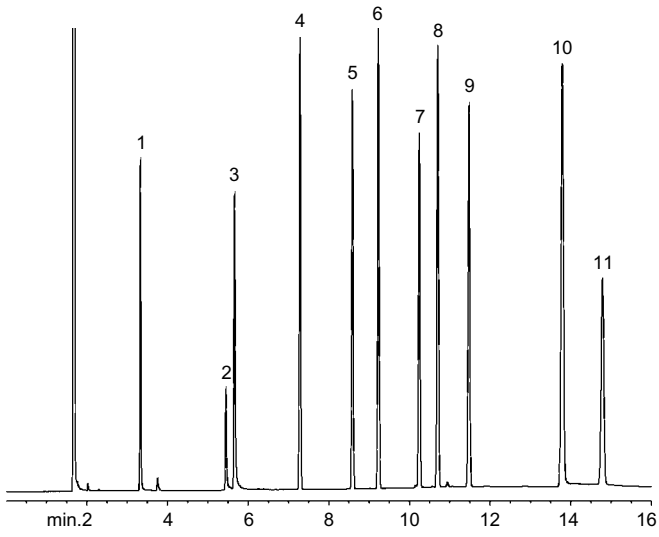
Most of the compounds in the target list, including phenylpropanolamine, are basic compounds that have a pKa greater than 8.0. After passing through the extraction protocol described above, these compounds are in the free base form in the reconstituted extract. Free bases can exhibit tailing peak shapes and reduced response on columns that are poorly deactivated or not designed specifically for use with basic compounds. Because of its superior performance analyzing free bases, an Rtx®-5 Amine column was chosen for this separation. A wide bore, thick-film column was needed for increased sample capacity because most of the cold medications had analyte concentrations well above 1mg/mL.

The Rtx®-5 Amine column provides excellent resolution of all the compounds commonly found in most cold medications (see **Figure 1**). Phenylpropanolamine (peak 1) is separated easily from the rest of the compounds. All of the target analytes exhibit good peak shape, even when in the free base form. Additionally, the analysis is complete in less than 15 minutes, which allows for quick turn-around of multiple samples.

Figure 1: The Rtx®-5Amine column provides excellent resolution of compounds in cold medications.

Rtx®-5Amine Column
30m, 0.53mm ID, 1.00µm df
(cat.# 12355)

Oven temp.:	175°C to 280°C @ 10°/min. (hold 5.5 min.)
Inj./det. temp.:	250°C/280°C
Carrier gas:	helium
Linear velocity:	40cm/second
Sample size:	1uL
Split vent flow:	88mL/min.
Split ratio:	20:1



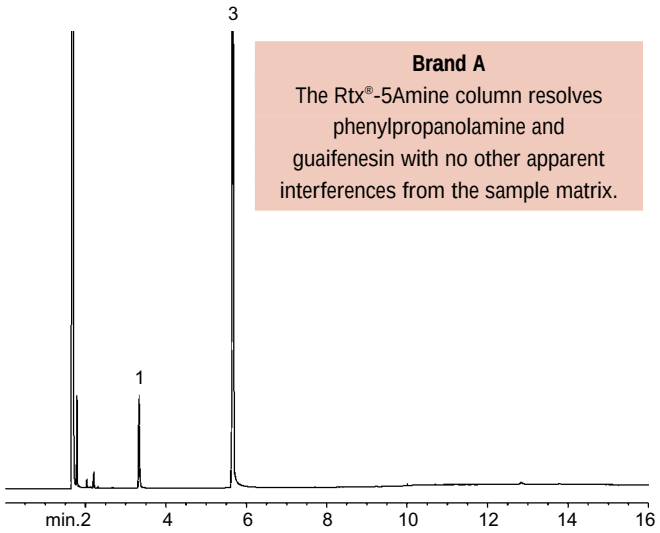
Peak List:
1. phenylpropanolamine
2. phenylephrine
3. guaifenesin
4. pheniramine
5. phenyltoloxamine
6. chlorpheniramine
7. brompheniramine
8. dextromethorphan
9. pyrilamine
10. codeine
11. hydrocodone

clinical/forensic

Figure 2 shows the analysis of Brand A and Brand B medications, respectively, using an Rtx®-5Amine column. Phenylpropanolamine and guaifenesin are well resolved from each other with no apparent interferences from the sample matrix. Based on the response of phenylpropanolamine in Brand A, concentrations as low as 10µg/mL can be detected by adjusting the sample size in the extraction procedure.

Cold and sinus medications can be checked quickly and easily for the presence of phenylpropanolamine using the procedure described above. Complete resolution of all analytes, and optimized peak shape and response can be achieved by selecting the appropriate column phase and dimensions.

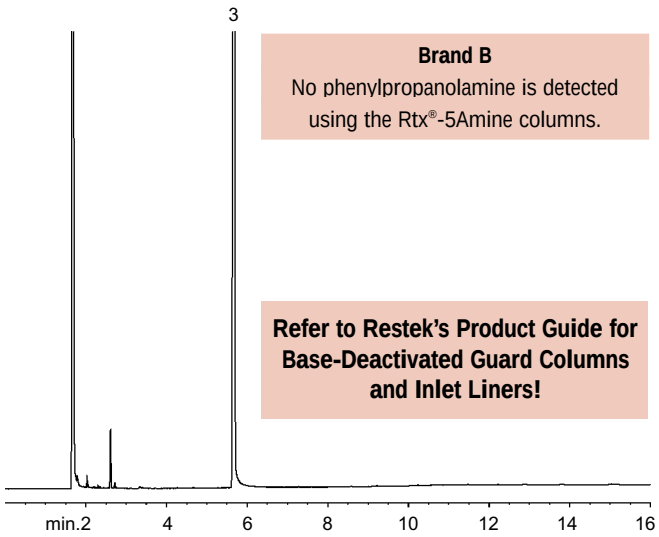
Figure 2: The analysis of Brand A and Brand B medications using an Rtx®-5Amine column.



Brand A
The Rtx®-5Amine column resolves phenylpropanolamine and guaifenesin with no other apparent interferences from the sample matrix.

Brand A and Brand B:
Rtx®-5Amine Column
30m, 0.53mm ID, 1.00µm df (cat.# 12355)

Oven temp.:	175°C to 280°C @ 10°/min. (hold 5.5 min.)	**Linear velocity:**	40cm/second
Inj./det. temp.:	250°C/280°C	**Sample size:**	1uL
Carrier gas:	helium	**Split vent flow:**	88mL/min.
		Split ratio:	20:1



Brand B
No phenylpropanolamine is detected using the Rtx®-5Amine columns.

Refer to Restek's Product Guide for Base-Deactivated Guard Columns and Inlet Liners!

Brand A and Brand B:
Peak List:
1. phenylpropanolamine
2. phenylephrine
3. guaifenesin
4. pheniramine
5. phenyltoloxamine
6. chlorpheniramine
7. brompheniramine
8. dextromethorphan
9. pyrilamine
10. codeine
11. hydrocodone

Rtx-5Amine (Fused Silica) (Crossbond® 5% diphenyl/95% dimethylpolysiloxane) Stable to 340°C

ID:	df (µm)	temp. limits	15-meter	30-meter
0.25mm	0.50	-60 to 300/315°C	12335	12338
	1.00	-60 to 300/315°C	12350	12353
0.32mm	1.00	-60 to 300/315°C	12351	12354
	1.50	-60 to290/305°C	12366	12369
0.53mm	1.00	-60 to 290/305°C	12352	12355
	3.00	-60 to 280/295°C	12382	12385

1. R. Horwitz, MD, L. Brass, MD, W. Kernan, MD, C. Viscoli, PhD, "Phenylpropanolamine and Risk of Hemorrhagic Stroke: Final Report of The Hemorrhagic Stroke Project", May 10, 2000.