Waters™

アプリケーションノート

Separation of Cold Medicine Ingredients using UPLC Technology

Eric S. Grumbach, Diane M. Diehl, Jeffrey R. Mazzeo

Waters Corporation

Abstract

A single chromatographic method was developed for the analysis of common formulation compositions

targeted to relieve symptoms associated with the common cold using a new High Strength Silica (HSS) UPLC stationary phase.

Introduction

Pharmaceutical formulations used to treat the common cold often contain multiple active ingredients to treat different symptoms. These actives can include combinations of decongestants, antihistamines, pain relievers, cough suppressants, and expectorants in addition to numerous excipients, all of which exhibit different chemical properties, including polarity. It is this wide range of analyte polarities that often makes chromatographic methods development difficult.

UPLC Technology was used to develop a single chromatographic method for the analysis of twenty of the most common pharmaceutical formulations targeted to relieve symptoms associated with the common cold. A new High Strength Silica (HSS) UPLC stationary phase was used to develop a single chromatographic method for the analysis of a number of possible formulation compositions. This stationary phase was selected due to its ability to enhance the retention of polar analytes while also having good chromatographic selectivity of hydrophobic species.

Experimental

LC Conditions

LC System:	ACQUITY UPLC System and ACQUITY UPLC TUV Detector
Software:	Empower 2 Build 2154
Column:	ACQUITY UPLC HSS T3, 2.1 x 100 mm, 1.8 µm
Mobile Phase:	A: 0.15% CF_3COOH in H_2O B: 0.02% CF_3COOH in 75:25 (v/v) ACN:MeOH
Flow Rate:	0.6 mL/min

Injection:	1.0 µL
Loop Size:	2.0 µL
Inject Mode:	Partial Loop with Needle Overfill
Temperature:	30 °C
Detection:	UV @ 254 nm
Sampling Rate:	20 Hz
Time Constant:	0.2

Gradient

Time	%A	%B
0.0	99.9	0.1
0.5	99.9	0.1
1.7	87.0	13.0
3.6	67.0	33.0
7.5	0.1	99.0
8.0	0.1	99.0
8.5	99.9	0.1
9.5	99.9	0.1

Sample Preparation

Reference standards were prepared in a solution of 75:25 (v/v) water:methanol containing 0.2% formic acid at a concentration of 25 g/mL for each component, except acetaminophen which was 12.5 g/mL and its

respective impurities, 4-aminophenol, 4-nitrophenol and 4-chloroacetanilide, were prepared at a concentration of 2.5 g/mL

Results and Discussion

A mixture of standards of 20 common components of cold medicine formulations including active ingredients, impurities and counter ions, was separated on a 2.1 x 100 mm, ACQUITY UPLC HSS T3, 1.8 µm Column, as depicted in Figure 1. A listing of elution order, relative retention, and USP resolution of all components is listed in Table 1. Retention factors range from 0.52 to 10.47. All components were baseline separated in less than 7 minutes and had resolution factors of 1.65 or greater.

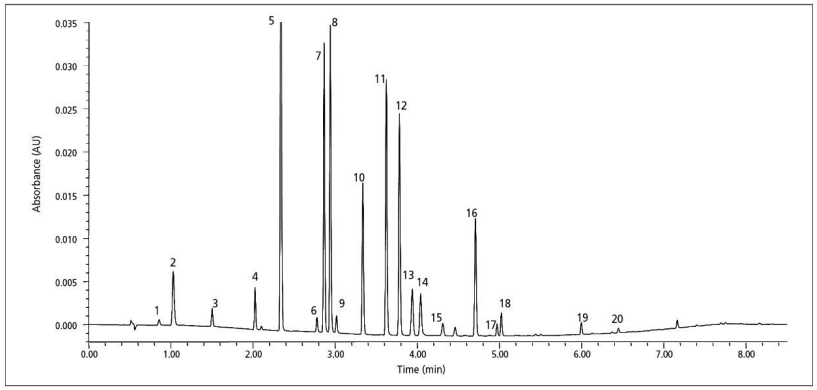

Figure 1. UPLC Technology separation of 20 common cold medicine active ingredients, impurities and counter ions.

Elution Order	K Prime	USP Resolution
1. 4-aminophenol	0.52	
2. Maleate	0.83	4.25
3. Fumarate	1.67	12.68
4. Phenylephrine	2.60	17.59
5. Acetaminophen	3.16	10.69
6. Penylpropanloamine	3.94	14.07
7. Pheniramine	4.10	2.83
8. Doxylamine	4.23	2.62
9. Pseudoephedrine	4.37	2.48
10. Pyrilamine	4.94	9.99
11. Chlorpheniramine	5.45	8.85
12. Brompheniramine	5.73	4.84
13. Guaifenesin	6.01	4.06
14. Acetlysalicylicacid	6.19	2.40
15. 4-nitrophenol	6.67	6.29
16. 4-chloroacetanilide	7.38	9.85
17. Dextromethorphan	7.84	7.65
18. Diphenhydramine	7.94	1.65
19. Clemastine	9.67	30.87
20. Ibuprofen	10.47	14.03

Peaks 1, 15, and 16 are impurities of acetaminophen

Conclusion

A fast, high resolution chromatographic method was developed for pharmaceutical formulations targeted to relieve symptoms of the common cold by utilizing a new High Strength Silica (HSS) UPLC stationary phase. This single chromatographic method can be used to rapidly analyze a number of possible formulation compositions containing different active ingredients.

Featured Products

ACQUITY UPLC System <https://www.waters.com/514207>

ACQUITY UPLC Tunable UV Detector <https://www.waters.com/514228>

Empower Chromatography Data System <https://www.waters.com/10190669>

720002029, July 2007