TSKgel ODS-140HTP, 2.3µm Columns for the Fast and Reliable Separation of Drugs Used in Cold and Sinus OTC Medicines

TSKgel
APPLICATION NOTE

Introduction

Since the USA Patriot Act* has been enacted, many pharmaceutical companies have reformulated their over the counter (OTC) drug products with phenylephrine (a nasal decongestant) as a substitute for pseudoephedrine. Phenylephrine comes as a tablet, a liquid, or a dissolving strip to take orally - all as a treatment for cold symptoms[1]. Besides phenylephrine, most pharmaceutical formulations for common cold and sinus medications often contain multiple active ingredients to treat different types of symptoms in addition to numerous excipients. From an analytical perspective, the challenge is to develop chromatographic conditions that allow quantitative analysis of a variety of excipients that vary widely in hydrophobic properties.

We used a 2.1mm ID x 5cm TSKgel ODS-140HTP, 2.3µm reversed phase column to address the need to revalidate the test methods for new phenylephrine formulations with the overall goal to reduce retention time of the APIs (active pharmaceutical ingredients). Six different drug standards were selected covering a wide range of hydrophobicities, all of which are commonly used as APIs in many cold and sinus medicines. We report for the first time the separation of these six drug standards within a 4 minute analysis time using a conventional HPLC system.

Experimental Conditions

LC System: HP-1100 HPLC with Chemstation (ver B.03.01)
Column: TSKgel ODS-140HTP, 2.3µm, 2.1mm ID x 5 cm
Mobile Phase: A: water with 0.15% TFA
B: 100% ACN with 0.15% TFA

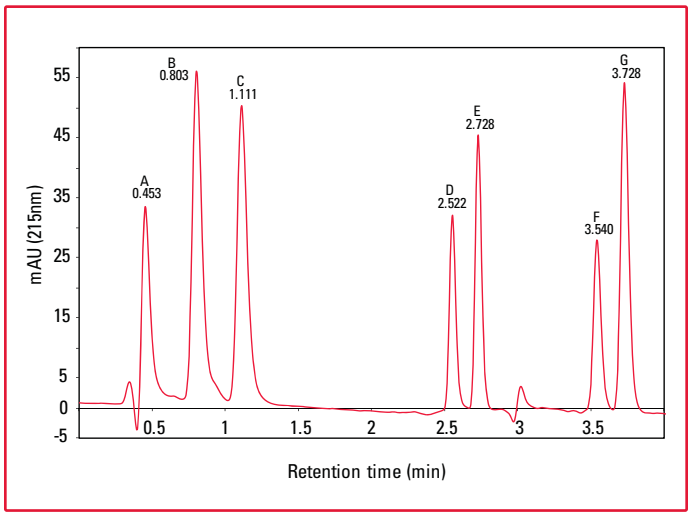
Gradient:

Time (min)	Solvent B (%)	Flow (mL/min)
1.4	2.0	0.6
1.5	24.0	1.4
2.1		1.4
2.2		0.8
4.	25.0	0.8
4.1	1.0	0.6

Temperature: 50°C
Injection volume: 10µL
Detection: UV@215nm

High purity Sigma brand chemicals were used for the preparation of stock solutions of phenylephrine, acetaminophen, doxylamine succinate, chlorpheniramine maleate, dextromethorphan hydrobromide and diphenhydramine hydrochloride in 50% methanol (HPLC grade from Fisher). To avoid solvent mismatch at the time of injection, the working standards were prepared by diluting the stock standards in mobile phase A. The final concentration of each drug standard was 0.8µg/mL in the drug cocktail. The standards were filtered through a 0.45µm membrane prior to injection.

Figure 1. Analysis of six cold and sinus drug standards: phenylephrine (B), acetaminophen (C), doxylamine succinate (D), chlorpheniramine maleate (E), dextromethorphan HBr (F) and diphenhydramine HCl (G) using a TSKgel ODS-140HTP column. The peak (A) was a maleate peak, which was proven to be associated with drug standard (E).



Results and Discussion

Six cold and sinus drug standards *(Figure 1)* containing phenylephrine (B), acetaminophen (C), doxylamine succinate (D), chlorpheniramine maleate (E), dextromethorphan HBr (F) and diphenhydramine HCl (G) could be separated as sharp peaks with good resolution within 3.8 minutes using a TSKgel ODS-140HTP column. The peak labeled (A) was identified as maleate originating from the drug standard chlorpheniramine maleate (E). The pressure drop over the 5cm column was 12.5MPa at the beginning and 16.3MPa at the end of the gradient run. The retention time of diphenhydramine is considerably lower than that reported using an ACQUITY UPLC® system[2]. The goal of most HPLC methods is to achieve baseline separations with a resolution of 1.5 or more for all key analytes - which was achieved in this study. The two drug substances diphenhydramine and dextromethorphan have very similar and strong hydrophobic properties with a tendency to co-elute or elute with considerable overlap. In this study they were separated with a resolution of 1.9. The number of theoretical plates for drug standards D, E, F, and G were greater than 15,000. The reproducibility of the method was confirmed by calculating %RSD for retention time for 13 consecutive injections (data not shown).

Conclusions

In this study, it is clearly demonstrated that a TSKgel ODS-140HTP, 2.3µm column can successfully be employed using a conventional HPLC system with operational pressure limit of 41.4MPa to obtain a simple, fast and reliable separation of a wide variety of drugs used in common cold and sinus OTC medicines with remarkable reduction of overall run time. Decreased run times help reduce the amount of solvent waste as well as analysis cost, which is particularly important during this time of acetonitrile shortage.

References

1. http://www.nlm.nih.gov/medlineplus/druginfo/meds/a606008.html#brand-names
2. Mazzeo JR, LCGC Asia Pacific, Volume 10, Issue 1, May1, 2007

*Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001

TOSOH

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TOSOH Bioscience LLC
3604 Horizon Drive, Suite 100
King of Prussia, PA 19406
Orders & Service: (800) 366-4875
Fax: (610) 272-3028
www.separations.us.tosohbioscience.com
email: info.tbl@tosoh.com

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