Separation and Purification Technology 158 (2016) 308–312

Contents lists available at ScienceDirect

Separation and Purification Technology

journal homepage: www.elsevier.com/locate/seppur

Separation and analysis of pharmaceuticals in cold drugs using green chromatography

Brahmam Kapalavavi [a], Yu Yang [a,*], Ronita Marple [b], Chris Gamsky [b]

[a] Department of Chemistry, East Carolina University, Greenville, NC 27858, United States
[b] Global Analytical Capability Organization, The Procter & Gamble Company, Cincinnati, OH 45241, United States

ARTICLE INFO

Article history:
Received 3 November 2015
Received in revised form 12 December 2015
Accepted 21 December 2015
Available online 22 December 2015

Keywords:
Green chromatography
Subcritical water chromatography
Cold drug
Pharmaceuticals
Acetaminophen
Guaifenesin

ABSTRACT

Subcritical water chromatography (SBWC) can replace traditional HPLC for separation and analysis of pharmaceuticals. Because hazardous organic solvents are eliminated from the SBWC mobile phase, subcritical water chromatography is a green separation technique. In addition, SBWC is economical since the purchasing of organic solvents and waste disposal costs required for HPLC can be saved. In this work, pharmaceuticals present in cold drugs including Vicks formula 44 custom care, Alka-seltzer plus, and CVS multi-symptom severe cold relief were successfully separated using subcritical water chromatography on an Alltech Adsorbosil C18 column. Both gradient elution and programmed temperatures were employed to achieve the best SBWC separation of pharmaceuticals contained in the cold drug samples studied. The recoveries of pharmaceuticals in the three real-world cold drug samples achieved by SBWC range from 94% to 105% with less than 5% RSD.

1. Introduction

Subcritical water chromatography (SBWC) has gained greater attention due to its green nature and low cost [1–16]. While a majority of the SBWC research has been done in academia, several industrial applications of subcritical water chromatography have also been reported [17–23]. We recently collaborated with The Proctor & Gamble Company and tried to replace the company's existing HPLC methods with subcritical water chromatography for separation and analysis of niacinamide, preservatives, and sunscreens in skincare products [17–19].

Common cold is a disease of upper respiratory tract due to viral infections. Common cold is not caused by a single microorganism infection, rather by the infection from a group of viruses belong to different families [24]. Medications belong to antipyretics, decongestant, antihistamine and antitussives are available in the market to treat several problems of common cold [24,25].

Combinations of drugs are normally used in the treatment of cold. Antihistamines such as pyrilamine maleate and chlorpheniramine maleate are used in combination to treat allergic reactions associated with cold [26]. Pheniramine maleate (antihistamine) combined with pseudoephedrine hydrochloride (decongestant) is used in the treatment of cold, sinusitis, bronchitis, and respiratory allergies [27]. Dextromethorphan hydrobromide (antitussive) combined with guaifenisin (expectorant) is used to treat the cough associated with cold [28]. These cold medications are available in the market as syrups, sachets, capsules and tablets [28,29].

It is necessary to accurately analyze the active pharmaceutical ingredients (APIs) present in various cold drugs for quality control, product release, and other regulatory purposes. The separation and analysis of the APIs by HPLC involve hazardous solvents such as methanol [30–33]. The development of SBWC methods for separation of analytes is necessary to completely eliminate the toxic organic solvents from mobile phase.

In this work, several green SBWC methods were developed for separation and analysis of pharmaceuticals including dextromethorphan hydrobromide; chlorpheniramine maleate; doxylamine succinate; phenylephrine hydrochloride; acetaminophen; and guaifenesin present in cold drugs. The stationary phase used in this work was Alltech Adsorbosil C18. Cold drugs studied for the pharmaceuticals SBWC separations include Vicks formula 44 custom care, cough and cold PM; Alka-seltzer plus, night, cold and flu formula; and CVS multi-symptom severe cold relief, daytime, non-drowsy.

2. Experimental

2.1. Reagents and materials

Dextromethorphan hydrobromide, chlorpheniramine maleate, acetaminophen, doxylamine succinate, phenylephrine hydrochlo-

* Corresponding author.
E-mail address: yangy@ecu.edu (Y. Yang).

http://dx.doi.org/10.1016/j.seppur.2015.12.036
1383-5866/

ride, guaifenesin, and 4-acetamidophenol were received from Sigma–Aldrich Chemical (Milwaukee, WI, USA). HPLC-grade methanol, ortho phosphoric acid and formic acid (90%) were purchased from Fisher Scientific (Fair Lawn, NJ, USA). Deionized water (18 MΩ cm) was obtained in our laboratory using a Sybron/Barnstead system (Sybron/Barnstead, Boston, MA, USA).

GD/X PVDF membrane filters (0.45 μm) were purchased from Whatman (Florham Park, NJ, USA). Glass vials were acquired from Supelco (Bellefonte, PA, USA). Real-world samples of Vicks formula 44 custom care, cough and cold PM; Alka-seltzer plus, night, cold and flu formula; and CVS multi-symptom severe cold relief, daytime, non-drowsy were purchased at a local store. Adsorbosil C18 (4.6 × 150 mm, 5 μm) was obtained from Alltech Associates, Inc. (Deerfield, IL, USA).

2.2. Preparation of internal standard and calibration standard solutions

Different internal standards were used for the analysis of pharmaceuticals in three real-world cold drugs. Phenylephrine hydrochloride served as the internal standard for Vicks formula 44 custom care, benzyl alcohol for CVS multi-symptom severe cold relief, and chlorpheniramine maleate for Alka-seltzer plus. Each internal standard solution was prepared by adding 0.05 g (accurately weighed) of an appropriate internal standard to a 50-mL volumetric flask and then diluted to the mark with methanol.

A stock standard solution was prepared by adding Q mg (accurately weighed) of each pharmaceutical compound in cold drugs to a 50-mL volumetric flask and then diluted to the mark with methanol. Then a series of five calibration standard solutions were prepared from this stock standard solution with an appropriate amount of internal standard solution. Methanol was used as the solvent.

2.3. Preparation of sample solutions

Each cold drug sample was mixed well before sampling. For Vicks formula 44 custom care (syrup) analysis, a diluent was used as the solvent in sample preparation. This diluent was prepared by adding approximately 11 g of calcium chloride to a 50-mL volumetric flask and then diluted to the mark with deionized water. Then the Vicks pharmaceutical sample was prepared by adding 1.00 mL of each syrup and phenylephrine hydrochloride internal standard to a 25-mL volumetric flask and diluted to the mark with the diluent. This solution was then vortexed to obtain a homogeneous sample mixture and filtered through a 0.45 μm Whatman GD/X filter into a 2-mL sample vial for chromatographic analysis.

For CVS multi-symptom severe cold relief (caplet) and Alka-seltzer plus (capsule) analysis, one caplet or capsule was added to a 50-mL volumetric flask and diluted to the mark with methanol. In case of caplet, it was broken down into pieces before adding it to the 50-mL volumetric flask for faster sample preparation. This mixture was then vortexed to obtain a homogeneous mixture. Then a sample solution was prepared by transferring 2.00 mL of homogeneous mixture and 1.00 mL of appropriate internal standard solution to a 25-mL volumetric flask and diluted to the mark with methanol. This solution was again vortexed and filtered through a 0.45 μm Whatman GD/X filter into a 2-mL sample vial for chromatographic analysis.

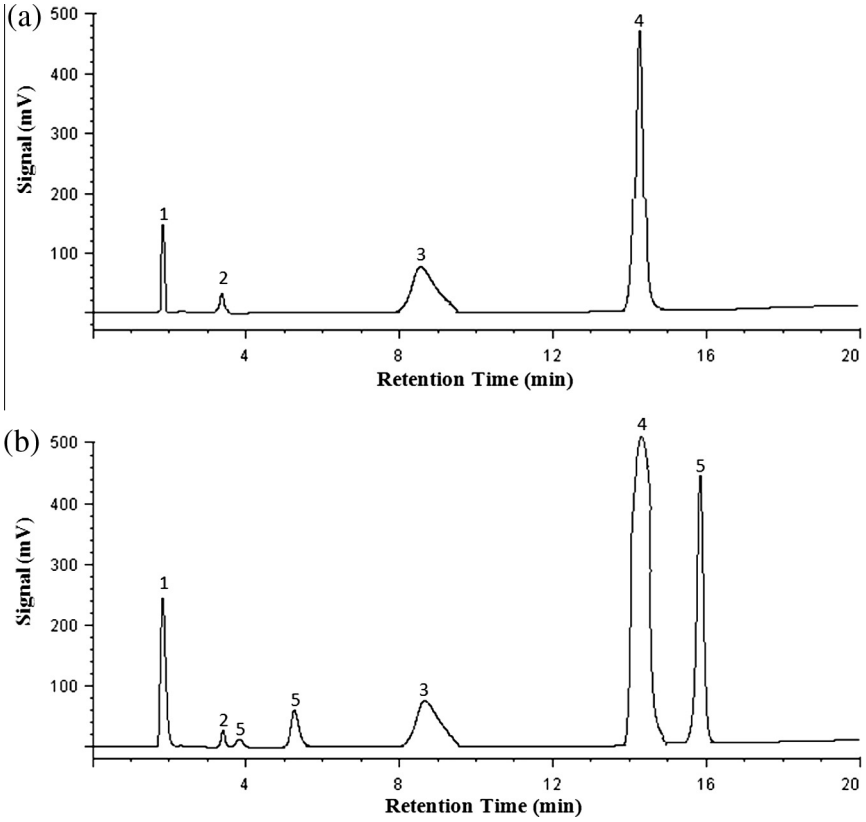

Fig. 1. Subcritical water chromatography chromatograms of pharmaceuticals obtained on the Alltech Adsorbosil C18 column with 1.0 mL/min using programmed temperatures. (a) Pharmaceuticals standard mixture; (b) Vicks formula 44 custom care cough and cold sample. UV detection: 210 nm. Mobile phase: A, deionized water; B, 100 mM phosphoric acid. Gradient: 100% water for 1 min and then 100% 100 mM phosphoric acid for the remainder of the run. Programmed temperatures: Initial temperature of 25 °C for 3 min and then increased at 15 °C/min to 150 °C and maintained at 150 °C for the remainder of the run. Peak identification: 1, dextromethorphan hydrobromide; 2, chlorpheniramine maleate; 3, phenylephrine hydrochloride; 4, acetaminophen; 5, matrix peak.