Journal of Chromatography A, 1516 (2017) 131–134

Contents lists available at ScienceDirect

Journal of Chromatography A

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

Short communication

Determination of iodopropynyl butylcarbamate in cosmetic formulations utilizing pulsed splitless injection, gas chromatography with electron capture detector

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ARTICLE INFO

Article history:
Received 10 October 2016
Received in revised form 13 July 2017
Accepted 18 July 2017
Available online 24 July 2017

Keywords:
Iodopropynyl butylcarbamate
Cosmetics
Preservative
Gas chromatography
Electron capture detector
Pulsed splitless injection

ABSTRACT

Current analytical methodology for iodopropynyl butylcarbamate (IPBC) analysis focuses on the use of liquid chromatography and mass spectrometer (LC–MS), but the high instrumentation and operator investment required has resulted in the need for a cost effective alternative methodology. Past publications investigating gas chromatography with electron capture detector (GC-ECD) for IPBC quantitation proved largely unsuccessful, likely due to the preservatives limited thermal stability. The use of pulsed injection techniques commonly used for trace analysis of thermally labile pharmaceutical compounds was successfully adapted for IPBC analysis and utilizes the selectivity of GC-ECD analysis. System optimization and sample preparation improvements resulted in substantial performance and reproducibility gains. Cosmetic formulations preserved with IPBC (50–100 ppm) were solvated in toluene/isopropyl alcohol and quantified over the 0.3–1.3 μg/ml calibration range. The methodology was robust (relative standard deviation 4%), accurate (98% recovery), and sensitive (limit of detection 0.25 ng/ml) for use in routine testing of cosmetic formulation preservation.

1. Introduction

Fundamental to the preservation of a cosmetic formulation is the preservative's ability to effectively suppress the growth of yeast and mold. IPBC is an effective broad-spectrum fungicide typically used at low ppm concentrations in personal care and cosmetic products [1,2]. The ability to monitor the presence of the active IPBC species is critical to understanding and predicting the stability and/or preservation of a formulation, as the preservative itself is known to undergo hydrolysis at pH greater than 9.0 with the primary hydrolysis product being propargyl butylcarbamate (PBC) [2,3]. Overwhelmingly the determination of IPBC has relied on LC–MS [4], due to IPBC's limited thermal stability. IPBC experiences decomposition at temperatures >85 °C and pH ≥ 9 [3,5]. Several published studies investigating the determination and separation of IPBC have yielded mixed results when utilizing gas chromatography (GC) with flame ionization detector (FID), electron capture detector (ECD) or mass spectrometry (MS) [6,7]. The drawback of these methods is that they either require costly equipment, extensive sample cleanup, or have limited sensitivity. The aim of this presented work was to develop an inexpensive, robust, and reproducible analytical method for the determination of IPBC in a cosmetic product, by addressing and mitigating the sources of IPBC to PBC degradation. The method was carried out using GC-ECD and a programmable injector.

Initial attempts utilizing splitless injection displayed poor reproducibility and signs of component degradation, with a broad peak being noted in the chromatogram, which is thought to be associated with an interference from the product matrix (See Fig. 1). As a result, focus was placed on addressing known issues common to thermolabile compounds [4,8] (peak tailing, low or inconsistent recoveries). The decision to use pulsed injection techniques was dictated by the known thermal instability of IPBC and the complex sample matrix. Cosmetic products are rarely a simple matrix; often formulations are a blend of surfactants, emulsifying oils, foam boosters, humectants, thickeners, fragrance, colorants, and preservatives which have widely varying characteristics and the potential to suppress or enhance the resulting analyte signal. The use of matrix-matched standards was employed to counteract these effects. Cosmetic formulations and blank matrix are both potential sources of active sites in the GC inlet liner. This need for matrix matching was most often present with conditioners, creams, and lotions but not exclusively necessary in isotropic body wash or shampoos. Pulsed injection significantly reduced contamination of

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http://dx.doi.org/10.1016/j.chroma.2017.07.064
0021-9673/

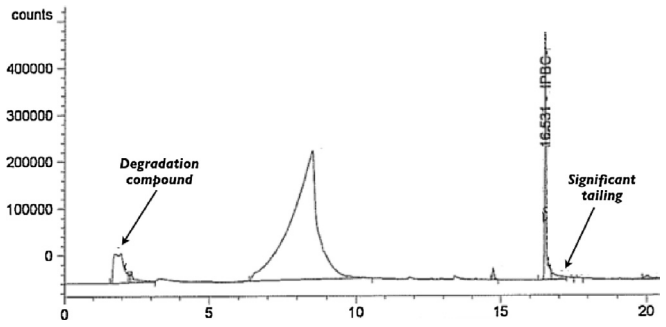

Fig. 1. Initial evaluation of IPBC by GC-ECD, using hot splitless Injection (250 °C), simple 10 °C/min ramp from 50 °C to 300 °C, and skin lotion prepared in methanol. Under these conditions thermal degradation is evident and reproducibility limited.

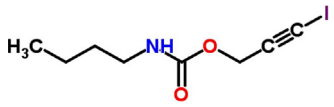

Fig. 2. Chemical structure of Iodopropynyl Butylcarbamate.

the inlet liner. Further addressing this issue, multiple liner designs and manufactures were initially evaluated. The liners were benchmarked based on resistance to active site formation exhibited as enhanced recovery and ability to adequately protect the column. All performed reasonably well using pulsed injection, with Restek SKY™ liner being chosen for the final optimization assessment to achieve suitable recovery, as well as long service life in our studies.

2. Experimental

2.1. Chemicals and materials

Several cosmetic formulations ranging from shampoo to skin lotion containing IPBC and the corresponding blank formulation (preserved with an alternative preservation system free of IPBC) were prepared at laboratory batch scale to evaluate the methodology.

Crystalline IPBC standard (purity 97%) (See Fig. 2) was obtained from Sigma Aldrich. Toluene (HPLC grade) and isopropyl alcohol (IPA) (HPLC grade) were purchased from VWR International.

All dilutions of samples and standards used a premixed solvent blend consisting of 800 ml toluene and 200 ml isopropyl alcohol. The IPBC stock solution ~500 μg/ml was prepared by dissolution of the reference standard with pre-mixed diluent, 80:20 toluene IPA; further dilution yields ~10 μg/ml stock standard. Working standards were prepared from further dilutions of ~10 μg/ml stock standard. Blank formulation was added to the working standards for formulations requiring matrix matching. This was performed by spiking IPBC stock solution into the prepared blank matrix. Working standard concentrations are 0.3 μg/ml–1.25 μg/ml.

2.2. Instrumentation

2.2.1. GC-ECD equipment

Gas chromatographic operations were carried out with an Agilent 6890 plus equipped with electronic pressure controlled (EPC) split-splitless inlet, μ-ECD detector (Agilent cat#G2397A) (Agilent), automatic injector: 7673 type (Agilent), data processor: Waters Empower 3 (Milford, MA, U.S.A). Chromatographic separations were conducted utilizing; Restek Thermolite® Septa (Part# 27143), Restek 4 mm SKY™ split/splitless straight liner with wool (Part# 23300.5), Agilent column HP-5 30.0 m × 250 μm × 0.25 μm (Agilent cat# 19091J-433). Testing utilized helium carrier gas and nitrogen for detector makeup gas.

2.3. Sample preparation

Weighing by difference 0.10 g ± 0.009 g of cosmetic formulation is transferred into a 20 ml scintillation vial. Sample is diluted with 9.9 ml 80:20 toluene:IPA solvent, and vortexed with 5 mm glass beads (Approx. 2 g) for 10 min or until the sample is completely dispersed. Next, the sample mixture is filtered through 0.45 μm PTFE syringe filter (Pall Part#4502) into GC sample vials.

2.4. GC conditions

Pulsed splitless injection; injection pulse pressure: 50 PSI until 0.50 min; purge flow to split vent: 30 ml/min helium at 0.48 min; carrier gas flow rate: helium 1.6 ml/min constant flow mode; ECD gas flow rate: 60 ml/min nitrogen; column temperature: 70 °C (0.5 min)– 20 °C/min–220 °C (0 min), 35 °C/min–310 °C (3.14 min); injection inlet temperature: 250 °C; detector temperature: 330 °C; data rate: 10 Hz; injection volume: 1 μl (whole volume injected).

3. Results and discussion

3.1. Evaluation of optimized method for the measurement of IPBC by GC-ECD

Methodology was evaluated to determine suitability and feasibility for the determination of IPBC in real-life samples by GC-ECD. The choice of system and detector combination was based on meeting multiple criteria; cost, time requirement, sensitivity, and selectivity. The detector was selected due to the low capital requirement of installing an ECD (electron capture detector) to an existing GC, as well as the high sensitivity for halogenated compounds the detector provides. Taking advantage of the high sensitivity and selectivity of the GC-ECD allows for a minimal sample preparation procedure. Through the use of dilution and minimal sample size a very convenient preparation can be utilized, eliminating the need for time consuming and costly sample cleanup.

3.2. Chromatographic separation and optimization

The standard/sample preparation utilizes a solvent mixture of 80:20 toluene: IPA and was selected for its ability to break emulsions in lotions, etc. and adequately disperse the sample matrix, as well as the stabilizing effect it provides to the IPBC molecule as demonstrated during method development. Solvent choice proved critical in this study to allow for dispersion of the entire formulation as well as stability of the analyte once injected into the GC inlet. Several extraction solvents were evaluated. Initially a primary alcohol, methanol was assessed, but it quickly degraded the IPBC within 24 h, liberating free iodine which turned the solution purple. This degradation was reduced, but not eliminated using amber vials. A secondary alcohol, IPA was evaluated as a potentially more stable solvent, but it was not able to fully solubilize the silicone oils in the cosmetic products, so toluene was added to overcome this. Therefore a binary solvent of toluene and IPA was chosen to fully disperse the oil and water components, so a dilute and shoot approach could be used for the analysis. Multiple injection liner styles and manufactures were evaluated, the following designs included; recessed gooseneck, double gooseneck cyclonic, and straight with/without wool. We found the SKY® deactivated 4 mm straight liner with glass wool from Restek provided the best balance of rapid vaporization, sensitivity, and extended maintenance intervals. The use of glass wool helps in preventing column contamination due to non-volatile residues.