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Simultaneous determination of cosmetics ingredients in nail products by fast gas chromatography with tandem mass spectrometry

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ABSTRACT

A rapid and sensitive gas chromatography with tandem mass spectrometry (GC–MS/MS) method has been developed and validated to quantitatively determine cosmetic ingredients, such as toluene, N-methylpyrrolidone, 2,4-dihydroxybenzophenone (benzophenone-1, BP-1), and diethylene glycol dimethacrylate, in nail products. In this procedure, test portions were extracted with acetone, followed by vortexing, sonication, centrifugation, and filtration. During the extraction procedure, BP-1 was derivatized making it amenable to GC–MS analysis, using *N*,*O*- bis(trimethylsilyl) trifluoroacetamide. The four ingredients were quantified by GC–MS/MS in an electron ionization mode. Four corresponding stable isotopically labeled analogues were selected as internal standards, which were added at the beginning of the sample preparation to correct for recoveries and matrix effects. The validated method was used to screen 34 commercial nail products for these four cosmetic ingredients. The most common ingredients detected in the nail products were toluene and BP-1. Toluene was detected in 26 products and ranged from 1.36 to 173,000 μg/g. BP-1 ranged from 18.3 to 2,370 μg/g in 10 products.

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1. Introduction

Nail products for home and salon use are considered cosmetics and regulated by the Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act [1]. Although nail products are not subject to premarket approval by FDA, cosmetics must not be adulterated or misbranded. This means that they must be safe for consumers under labeled or customary conditions of use, and they must be properly labeled.

Although consumers are told to carefully read the label to make sure that they know what ingredients are present in the products they will use, recent investigations by FDA and other government agencies have found inconsistencies between ingredients declared on the label and those actually contained in the product [2]. In order to prevent misbranding and adulteration, analytical methods capable of detecting and quantifying compounds of interest are needed. We therefore have developed a method to simultaneously quantitate four cosmetic ingredients, which are commonly used in nail products and may be potentially harmful [3–7]. These ingredients are toluene, *N*-methylpyrrolidone (also known as *N*-methyl-2-pyrrolidone, NMP), 2,4-dihydroxybenzophenone (benzophenone-1, BP-1) and diethylene glycol dimethacrylate (DEGDMA). The structures of these four compounds are shown in Fig. 1.

Toluene is widely used as a solvent to help nail polish apply smoothly and adhere evenly to nails. NMP, a 5-membered lactam structure, is a clear-yellow liquid miscible with water and other common solvents such as ethyl acetate, chloroform, and benzene. Due to its usefulness as an organic solvent, NMP has been used as a solvent and surfactant in the manufacturing of cosmetic products [8]. BP-1 is used as an ultraviolet filter in nail polish to prevent discoloration when the polish is exposed to sunlight or other forms of ultraviolet light [9]. Methacrylate ester monomers are used as artificial nail builders in nail enhancement products. These monomers undergo rapid polymerization to form a hard material on the nail that is then shaped. While ethyl methacrylate is the primary monomer used in nail enhancement products, other methacrylate esters, such as DEGDMA, are also used [6].

There are many methods, such as gas chromatography-flame ionization detector (GC-FID) [10,11], gas chromatography–mass spectrometry (GC–MS) [12–14], GC–MS/MS [15–17], liquid chromatography (LC) [18,19], LC–MS [20] and capillary electrophoresis (CE) [21–23] to determine individual analytes: toluene [10–12], NMP [13], DEGDMA [14,19,20], BP-1 [15–17,18,21,23] in different matrices including nail polish [10], cosmetic products [18,21–23], water [15,16], Biocef (sandoz) tablets [13], dental

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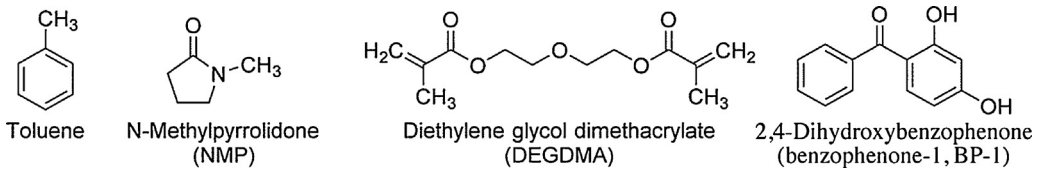

Fig. 1. Structures of the analytes.

materials [14,19,20]. However, no method has been reported to simultaneously determine these four compounds in cosmetic nail products. The published methods suffered poor recoveries and matrix interferences in complex matrices [12,13]. Time-consuming standard addition was required to quantify BP-1in the untreated water samples [15]. Furthermore, the published methods lack the confirmation of the identity of analytes [10,11,16,18,19].

To minimize the interferences from complex matrices of the nail products, a suitable sample preparation procedure without a cleanup step, including derivatization of BP-1, has been developed and optimized in this study. A GC–MS/MS method, which is more selective and sensitive than previously published procedures, has been developed and fully validated to determine these four analytes in nail products. Stable isotopically labeled analogues of the four native compounds were used as internal standards to compensate for matrix effects and correct any recovery issues. Confirmation of the identity of analytes was performed using corresponding confirmatory selected reaction monitoring (SRM) transitions for each analyte. To the best of our knowledge, this is the first approach to simultaneously quantify toluene, NMP, BP-1, and DEGDMA in nail products. This validated analytical method has been used in a survey to screen 34 commercial nail products. This limited survey will allow the FDA to assess the prevalence of the 4 mentioned analytes in nail products and to determine if additional sampling is warranted.

2. Experimental

2.1. Chemicals

Toluene, toluene-d_8, NMP, BP-1, *N,O*-bis(trimethylsilyl) trifluoroacetamide (BSTFA, derivatization reagent for BP-1), and capillary GC grade acetone were purchased from Sigma-Aldrich (St. Louis, MO, USA). DEGDMA, DEGDMA-d_8, and BP-1-$^{13}C_6$ were obtained from Toronto Research Chemicals (Toronto, ON, Canada). NMP-d_9 was purchased from Cambridge Isotope Laboratories, Inc. (Tewksbury, MA, USA). All of the chemicals were used without further purification. Thirty-four nail products were purchased via the internet.

2.2. Preparation of standard solutions

The primary stock solutions of each native analyte and stable isotopically labeled analogue were separately prepared in volumetric flasks at approximately 1000 μg/mL in ethyl acetate. The stock solutions were transferred into amber narrow mouth bottles and stored at −18 °C. Working stock 1 (a mixture of four standards, 200 μg/mL for each analyte) was prepared by dilution of the primary stock solutions in acetone. Working stock 2 (a mixture of four standards, 10 μg/mL for each analyte) was prepared by dilution of Working Stock 1 in acetone. Standard calibration solutions (10 mL in volumetric flasks) were prepared by dilution in acetone using working stocks 1 and 2. The concentration of the calibration standards ranged from 0.100 to 50.0 μg/mL for toluene and BP-1, and 0.100 to 5.00 μg/mL for NMP and DEGDMA, respectively. For toluene and BP-1, the concentrations for standards 1–7 were 0.100, 0.250, 0.500, 1.00, 5.00, 10.0, and 50.0 μg/mL. For NMP and DEGDMA, the concentrations for the standards 1–7 were 0.100, 0.250, 0.500, 0.750, 1.00, 2.50, 5.00 μg/mL. 1 mL of internal standards (a mixture of four standards, 10.0 μg/mL for each analyte) was added to each of the standard solutions at a constant concentration of 1.00 μg/mL for each analyte. 1 mL of BSTFA (derivatization reagent for BP-1) was added to each of the standard solutions at constant concentration of 10.0% (v;v). BP-1was allowed to react with BSTFA at room temperature (~25 °C) for 30 min to form the BP-1 derivative. To help the derivatization of BP-1, the standard solutions were shaken well for three 60-s. The standards were transferred into amber GC–MS vials with crimp top caps and stored at −18 °C.

2.3. Sample preparation

Approximately 100 μL of a nail product was transferred into a 15-mL centrifuge tube in triplicate and accurately weighed (Approximately 100 mg). To each of the tubes 700 μL of acetone, 100 μL of internal standards (a mixture of four standards, 10.0 μg/mL for each analyte), and 100 μL of BSTFA (derivatization reagent for BP-1) were added, which resulted in the final volume of 1.0 mL. The tubes were capped tightly during the sample preparation to minimize the loss of acetone, toluene and NMP. The tubes were first vortexed for approximately 3 min to rinse the walls and disperse the sample, and then sonicated for approximately 20 min. The tubes were again vortexed for 3 min and centrifuged at 11,000 revolutions per min for 10 min using an Eppendorf 5804 centrifuge (Hamburg, Germany). The supernatant was filtered through a 0.2 μm PTFE filter (Pall Life Sciences, Port Washington, NY) directly into a GC/MS sample vial, and 1.0 μL of the filtered extract was injected into the GC–MS/MS.

Since nail products had various formula and content of ingredients, each product was first screened to determine whether the sample needed to be diluted to fit into the calibration range or whether a significant interference existed. If a sample did need to be diluted, acetone, the ISs, and BSTFA were used for dilution without sonication, centrifugation and filtration. BP-1was allowed to react with BSTFA at room temperature (~25 °C) for 30 min to form the BP-1 derivative. The diluted solutions were shaken well for three 60-s. For those samples with significant interferences (e.g., signal to noise ratio of the internal standard was less than 20) or that were difficult to filter, a smaller sample volume (50 μL) and more extraction solvent (1.95 mL acetone, 250 μL of ISs and 250 μL of BSTFA, with a total volume of 2.5 mL) were used to extract the samples with the same procedures as above.

2.4. Instrumentation

The study was carried out on an Agilent 7890A GC System coupled to an Agilent 7000 Triple Quad MS (Santa Clara, CA, USA). The data were acquired and processed using MassHunter GC–MS Acquisition and Quantitative Analysis, respectively. Different columns were tested: Restek Rtx® 5 amine (30 m × 0.25 mm × 0.5 μm, Bellefonte, PA, USA) and Phenomenex ZB-SemiVolatiles (30 m × 0.25 mm × 0.25 μm, Torrance, CA, USA). The ZB-SemiVolatiles column was selected for this study since it resulted in overall best peak shapes for these four analytes. The