Vol. 8, No. 2, 2017
ISSN 2233-4203/ e-ISSN 2093-8950
LETTER www.msletters.org | Mass Spectrometry Letters

Fast Screening of Harmful Disinfectants in Household Products via Low-Temperature Plasma Ionization-Mass Spectrometry

Hyoung Jun Lee,[1,2] Gi Ryang Kweon,[2]* and Yong-Hyeon Yim[1]*

[1]Korea Research Instiute of Standards and Science (KRISS), Daejeon, Korea
[2]Department of Biochemistry, College of Medicine, Chungnam National University, Daejeon, Korea

Received June 17, 2017; Revised June 22, 2017; Accepted June 23, 2017
First published on the web June 30, 2017; DOI: 10.5478/MSL.2017.8.2.44

Abstract : Isothiazolinone derivatives are widely used in consumer products as disinfectants or preservatives, but there are growing concerns about their impact on human health. Therefore, rapid screening of these biocides is very important for proper control and regulation of potentially hazardous substances. To this end, low-temperature plasma (LTP) ionization mass spectrometry (MS) was investigated to demonstrate its potential for direct and selective analysis of isothiazolinones from sprayed aerosol samples. Benzisothiazolinone (BIT) was clearly identified from a commercial fabric deodorant using LTP ionization MS and MS/MS. LTP allowed selective ionization of BIT directly from the simply sprayed aerosol sample and illustrated its potential for fast screening without sample pre-treatments. Selective nature of LTP ionization, on the other hands, implicates use of LTP ionization MS as a general screening method for specific groups of hazardous chemicals in commercial products.

Keywords : low-temperature plasma ionization, benzisothiazolinone, fabric deodorant, fast screening

Introduction

Biocidal substances are used in a wide range of consumer products for antibacterial and preservation purposes.[1] However, there are growing concerns about the potential health hazards of these disinfectant chemicals as evidenced by a recent case of fatal lung fibrosis in Korea caused by exposure to polyhexamethyleneguanidine, a humidifier disinfectant.[2-4] This incident led to a pandemic public response to the use of disinfectants in household products. Isothiazolinone derivatives are commonly used disinfectants known to cause allergic responses including dermatitis, skin rashes, and eye and upper respiratory irritation.[1,5] Recently, there have been serious arguments in Korea over the presence of benzisothiazolinone (BIT) in fabric deodorants and improper labeling relevant to its use in consumer products. For proper control and regulation of biocides, a fast screening method with minimum sample preparation would be very useful.

Liquid chromatography (LC) or gas chromatography (GC) coupled with mass spectrometry (MS) is typically used for qualitative and quantitative analysis of disinfectants in various consumer products.[6,7] Time-consuming sample preparation is usually a requirement, but such work yields more reliable results in return. For rapid screening of hazardous biocides, however, ambient MS without additional sample treatment may be a more convenient choice.[8-11] Low-temperature plasma (LTP) ionization[8,9] is a plasma-based ambient ionization method that is very simple and characterized by low costs. Although LTP is not a universal ionization method for a variety of chemicals, the selective nature of its ionization characteristics may provide advantageous selectivity for a specific group of chemicals such as isothiazolinone derivatives.[8]

In this study, a home-built LTP ionization source that accommodates directly sprayed sample aerosols as well as typical dried sample spots on a glass slide was used to analyze selected disinfectant standards and those included in commercial fabric deodorants. The potential use of the method for fast screening of isothiazolinone derivatives in consumer products is also illustrated.

Experimental

Sample and Reagents

Benzisothiazolinone, methylisothiazolinone (MIT), acetonitrile, water and formic acid (FA) were purchased

Open Access
*Reprint requests to
E-mail: yhyim@kriss.re.kr, mitochondria@cnu.ac.kr

from Sigma-Aldrich (St. Louis, MO, USA). Water and acetonitrile were HPLC-grade quality. The BIT and MIT were dissolved in ethanol and methanol, respectively, to make standard solutions. Benzisothiazolinone standard solutions with 0.1, 0.5 and 1 mM concentrations were prepared to test LTP ionization MS and for quantitative analysis by LC-MS. A fabric deodorant spray was purchased from local market.

Low-Temperature Plasma Ionization Source

An LTP setup described previously in the literature was used with minor modifications (Figure 1).[8] Briefly, the LTP probe consisted of a glass tube with a central ground stainless steel electrode inserted inside the tube using a plastic tee connector, which was also used to allow helium discharge gas to flow through the glass tube. A high AC voltage was supplied to an outer electrode surrounding the tube, which was made by wrapping the tube with Cu tape. The gap between the outer HV electrode and the inner ground electrode was optimized to about 10 mm. An alternating voltage of 0-5 kV and up to 10 kHz frequency was supplied. The He LTP was optimized at an AC supply of 1.2-1.5 kV and a frequency of 10 kHz. Depending on the sample to be analyzed, either the guide tube for the sprayed aerosol sample or the glass slide sample stage was installed.

Mass Spectrometric Analysis

Liquid chromatography MS (LC-MS) and the LTP ionizations MS experiments were all performed using a linear ion trap mass spectrometer (Thermo LTQ; San Jose, CA, USA). For LC-MS, an electrospray ionization (ESI) source was used. For the LTP MS experiments, the ESI source was removed and the LTP ionization source was installed instead. A full MS scan over the 150-600 m/z range was used for the MS analysis. The capillary temperature was set at 270°C. For the MS/MS analysis, a width of 1 Da was used for precursor ion selection with 20-40% collision energy of the full excitation. All of the MS analyses were conducted in positive ion mode.

LC-MS Analysis

The LC-MS conditions were optimized with minor modifications of techniques previously reported in the literature.[7] Chromatrographic separation was performed on a Synergy hydro-RP column (2 mm × 250 mm, 4 mm) (Phenomenex; Torrance, CA, USA). A gradient elution of the mobile phase A (0.1% formic acid in H_2O) and B (0.1 % formic acid in acetonitrile) was used at a flow rate of 0.25 mL/min. The eluent gradient was as follows: 0-1 min (100% A), 1-18 min (100 to 45% A), 18-21 min (45 to 0% A), 21-23 min (0 to 100% A), 23-32 min (100% A). In each case, 5 μL of sample was injected.

Results and Discussion

Analysis of Harmful Disinfectant Standards, BIT and MIT, Using LTP Ionization MS

To investigate the ionization behavior of isothiazolinones in LTP, 500 μM standard solutions of BIT and MIT were

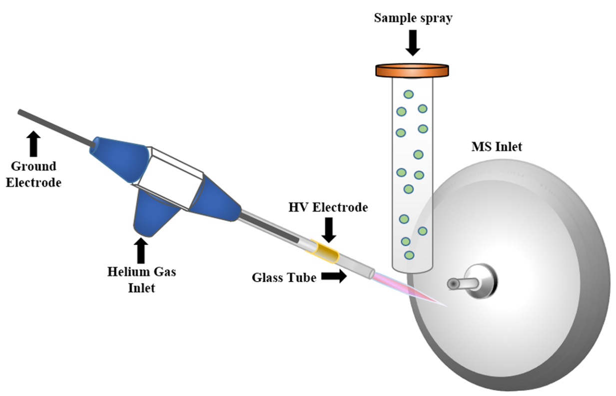

Figure 1. Schematic diagram of the home-built LTP ionization source for the sprayed aerosol samples.

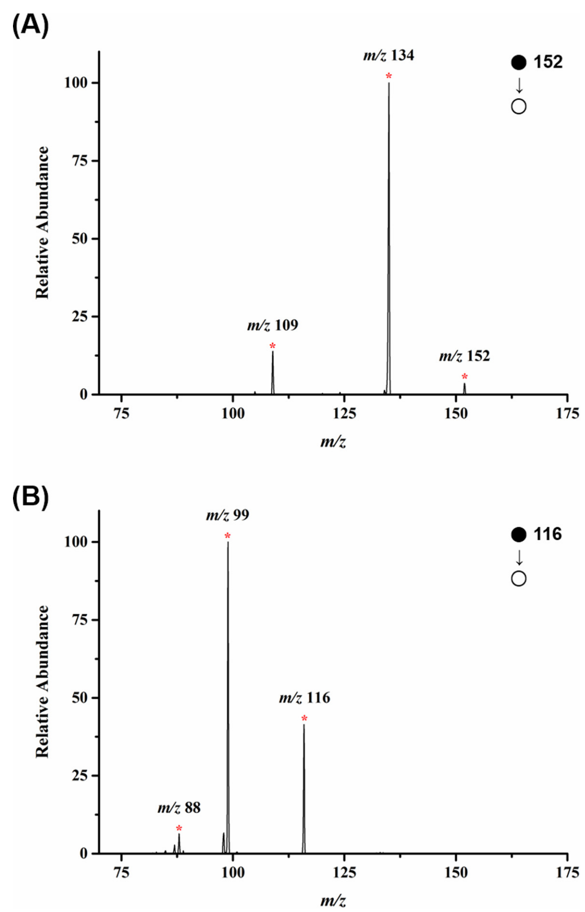

Figure 2. LTP ionization MS/MS spectra for $[M+H]^+$ of (A) BIT and (B) MIT.

loaded and dried individually on a slide glass. Analysis of the standards using LTP in positive ion mode revealed dominants peak at m/z 152 and 116, which correspond to $[M+H]^+$ of BIT and MIT, respectively. MS/MS of the molecular ion of BIT revealed characteristic loss of isocyanic acid yielding fragment ions at m/z 109 as well as fragment ions at m/z 134 resulting from the prevalent loss of water (Figure 2A). $[M+H]^+$ of MIT fragmented into m/z 99, 88, and 84, which are presumed to be generated by the loss of NH_3, CO, and S, respectively (Figure 2B).

Optimization of LC-MS Conditions and Analysis of Selected Isothiazolinone Disinfectants

Liquid chromatography MS analysis of a commercial fabric deodorizer was carried out to identify disinfectants contained within the product. The LC-MS conditions were optimized by modifying those noted by Bester et al.[7] using standard 100 μM solutions of BIT and MIT. Ion chromatograms of BIT and MIT in the optimized LC-MS conditions are shown in Figure 3A. The two isothiazolinone standards, BIT and MIT, are well-separated and show decent chromatographic peaks at 10 and 16 min respectively. The LC-MS analysis of the fabric deodorizer using the same condition demonstrates that BIT is present in the product; the MIT content is negligible (Figure 3B). Based on the brief quantitative analysis of BIT using three-point external calibration, the BIT concentration in the product was estimated to be roughly 1 mM (data not shown).

Fast Screening of a Harmful Disinfectant in a Commercial Product

Fabric deodorizers are typically sprayed as a solution on fabrics. Because spray-generated aerosols may interact with ionizing LTP favorably in ambient conditions, direct sampling and selective ionization of BIT isothiazolinone compounds in the fabric deodorizer have been tested. As shown in Figure 4A, a dominant peak at m/z 152 was observed from the sprayed aerosol samples by LTP ionization MS. The follow-up MS/MS analysis shown in Figure 4B confirmed the identity of m/z 152 as the molecular ion of BIT from its characteristic fragment ions at m/z 152, 134, and 109. A strong peak at m/z 120 corresponds to the major fragment ion of another ingredient of the deodorizer with the same molecular weight. Its presence in the product was confirmed by LC-

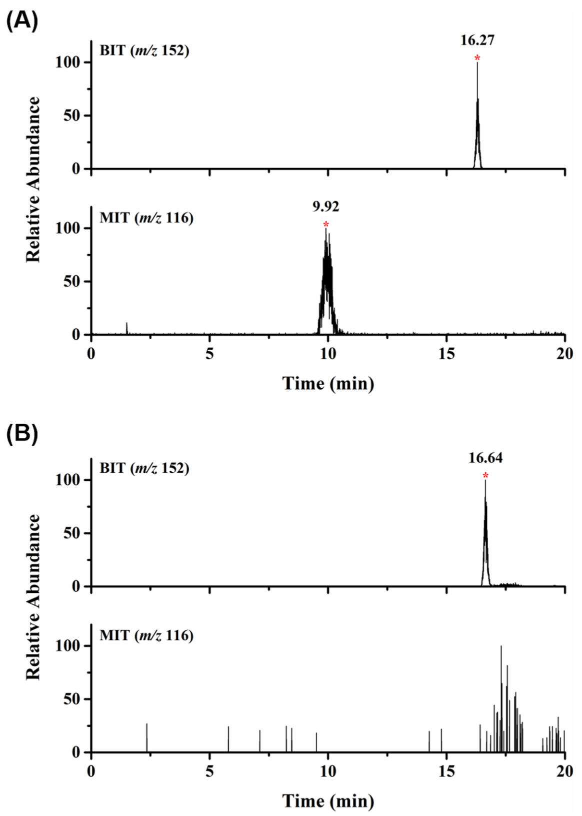

Figure 3. LC-MS ion chromatograms of m/z 152 (BIT) and 116 (MIT) for (A) 100 μM standards and (B) fabric deodorant.

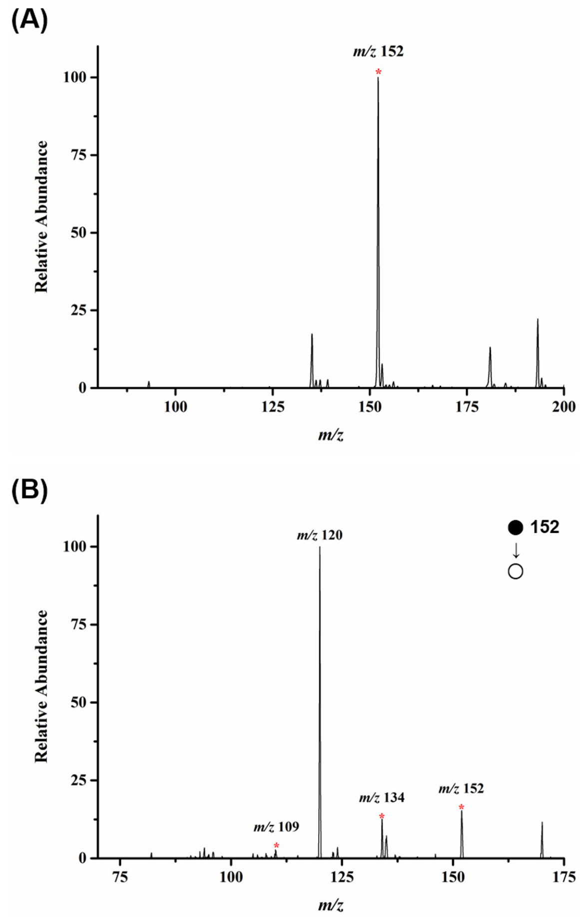

Figure 4. LTP ionization (A) MS spectrum of the commercial fabric deodorant and (B) MS/MS spectrum for molecular ion at m/z 152.

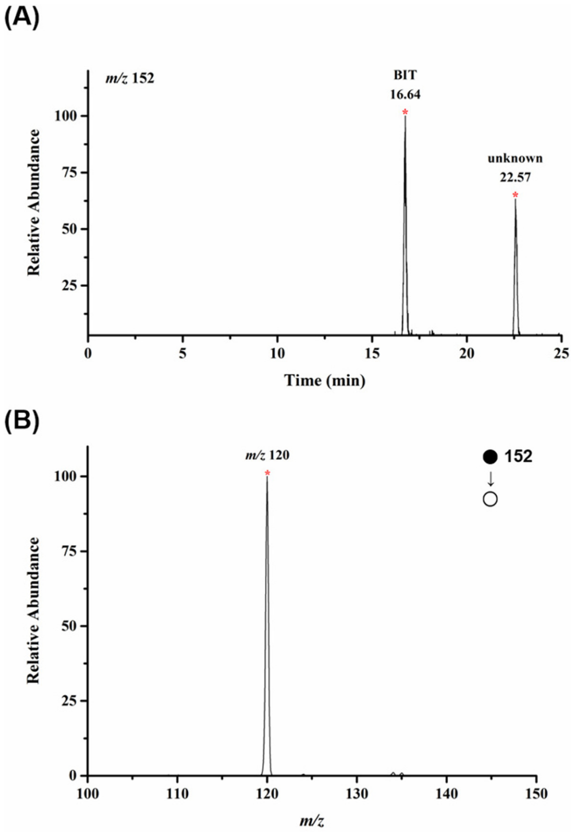

Figure 5. Detailed LC-MS and LC-MS/MS analysis of the commercial fabric deodorant revealed two distinct components producing molecular ions at m/z 152. (A) LC-MS ion chromatogram of m/z 152 obtained from a fabric deodorant shows additional peak at 22.57 min with unknown identity as well as BIT at 16.64 min. (B) LC-MS/MS analysis of m/z 152 at 22. 57 min shows dominant fragment ion at m/z 120.

MS/MS analysis (Figure 5). Although the LTP ionization MS/MS spectrum was obtained without separating two chemicals with molecular ions with the same m/z, the three characteristic fragment ions in the spectrum yielded sufficient information for a brief screening of BIT in the product.

The fabric deodorant product investigated here was found to include only BIT among several isothiazolinone derivatives known to be used in commercial products as disinfectants. As expected, BIT was the only component identified by the LTP ionization MS screening. Even though the general ionization of chemicals is limited in LTP, it implies a potential advantage of the selective ionization for specific group of compounds as a trade-off. Therefore, expanded application of the present method can be used for general screening of isothiazolinone derivatives in commercial products.

Conclusions

A home-built LTP ionization system installed in an ion trap mass spectrometer was used to investigate the potential use of LTP ionization MS as a general screening method for various disinfectants in commercial products. Benzisothiazolinone in a fabric disinfectant was successfully identified by brief analysis of directly sprayed sample aerosols. An additional study is in progress for expanded application of the present method for general fast screening of harmful disinfectants in consumer products.

Acknowledgments

This work was supported by the National Research Council of Science and Technology (NST), Korea via the convergence commercialization research project, 'Rapid identification of microorganisms by mass spectrometry.'

References

1. Garcia-Hidalgo, E.; Sottas, V; von Goetz, N.; Hauri, U.; Bogdal, C. *Contact Dermatitis* **2017**, 76, 96.
2. Kim, K. W.; Ahn, K. et. al. *Am. J. Respir. Crit. Care Med.* **2014**, 189, 48.
3. Kwon, J.-T.; Seo, G.-B.; Kim, H.-M.; Shim, I.; Lee, B., Jung, J. Y.; Kim, P.; Choi, K *Mol. Cell Toxicol.* **2013**, 9, 51.
4. Chang, M.-H.; Park, H.; Ha, M.; Kim, Y.; Hong, Y.-C.; Ha, E.-H. *Environ. Health Toxicol.* **2012**, 27, e2012003.
5. Aerts, O.; Goossens, A.; Lambert, J.; Lepoittevin, J.-P. *Eur. J. Dermatol.* **2017**, 27, 115.
6. Lin, Q. -B.; Wang, T. -J.; Song, H.; Li, B. *Food Addit. Contam.* **2010**, 27, 1775.
7. Bester, K.; Lamani, X. *J. Chromatogr. A* **2010**, 1217, 5204.
8. Lee, H. J.; Oh, J.-S.; Heo, S. W.; Moon, J. H.; Kim, J.-H.; Park, S. K.; Park, B. C.; Kweon, G. R.; Yim, Y.-H. *Mass Spectrom. Lett.* **2015**, 6, 71.
9. Harper, J. D.; Charipar, N. A.; Mulligan, C. C.; Zhang, X. R.; Cooks, R. G. *Anal. Chem.* **2008**, 80, 9097.
10. Takats, Z.; Wiseman, J. M.; Gologan, B.; Cooks, R. G. *Science* **2004**, 306, 471.
11. Cody, R. B.; Laramée, J. A.; Durst, H. D. *Anal. Chem.* **2005**, 77, 2297.

