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Direct Identification of Prohibited Substances in Cosmetics and Foodstuffs Using Ambient Ionization on a Miniature Mass Spectrometry System

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Abstract

Significantly simplified work flows were developed for rapid analysis of various types of cosmetic and foodstuff samples by employing a miniature mass spectrometry system and ambient ionization methods. A desktop Mini 12 ion trap mass spectrometer was coupled with paper spray ionization, extraction spray ionization and slug-flow microextraction for direct analysis of Sudan Reds, parabens, antibiotics, steroids, bisphenol and plasticizer from raw samples with complex matrices. Limits of detection as low as 5 µg/kg were obtained for target analytes. On-line derivatization was also implemented for analysis of steroid in cosmetics. The developed methods provide potential analytical possibility for outside-the-lab screening of cosmetics and foodstuff products for the presence of illegal substances.

Graphical Abstract

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Keywords

Ambient ionization; Slug-flow microextraction; Paper Spray; Extraction Spray; Miniature ion trap mass spectrometer; Cosmetics; Foodstuffs; Steroids; Sudan Red; Parabens; Plasticizer

INTRODUCTION

In this study, we developed methods using a miniature mass spectrometer and ambient ionization for direct analysis of prohibited substances in food and cosmetic products. Food safety has been drawing public attention due to its relevance to the public health. Although restrictive regulations are enforced worldwide, highly publicized incidents occur from time to time [1, 2]. Safety of cosmetic products typically is not getting much public attention, but it is also of a significant concern for public health, simply because of the wide and routine use of these products. Cosmetics cover a wide range of materials that are applied in contact with the human body for cleansing purposes or for altering appearance. Cosmetic products worldwide play an important role in people's daily lives. In addition to the use by adults, cosmetics have also been increasingly used in the care of infants and toddlers. The cosmetic industry represents a tremendous global market, with total sales of about 168 billion Euros in 2014 in the European Union, the United States, China, and Japan [3].

Voluntary addition of illicit substances to lower the costs of production is the most common problem in both the food and cosmetics industry [4–9]. For cosmetic products, illicit substances are also added to enhance short-term cosmetic effectiveness. Common banned additives include antibiotics [10, 11], corticosteroids [12–15], sexual hormones (oestrogens [16], progestogens [16], androgen [17]), pharmacologically active substances [16–18], prohibited preservatives (parabens [19–22], methylidibromoglutaronitrile [23]), whitening agents [13, 24], phthalates [25–28], and nitromusk fragrances [25, 28]. Long-term exposure to these substances could cause adverse effects such as skin irritation, allergic reactions, and antibiotic resistance, which represents a severe risk to public health.

The need to enforce product safety and regulatory compliance in both the food and cosmetics industries, calls for the development of effective and convenient methods to identify illicit ingredients with high molecular specificity and sensitivity. The analytical techniques that have been reported for the chemical analysis of foods and cosmetic products include thin layer chromatography [29, 30], capillary electrophoresis [22, 31], gas chromatography (GC) with flame ionization detection [21, 32] or coupled with various types of mass spectrometers [19, 20, 23, 25, 26, 28, 33–36], high-performance liquid

chromatography (HPLC) using ultraviolet [10, 12, 16, 17, 24, 37], electrochemical detection [38] or coupled with various types of mass spectrometers [1, 11–17, 26, 35, 39]. These methods are typically implemented in analytical laboratories and performed by experienced chemists using bench-top equipment. Sample preparation is usually achieved through multi-step, laborious and time-consuming processes, which also require laboratory procedures such as solvent extraction, dilution, reagent mixing, sonication, heating, centrifugation, and filtration. Although these analytical processes work well for analysis of large numbers of samples at centralized locations, it is also highly desirable to develop fast and easy-to-use methods for on-site screening, especially for situations when rapid decision making is required by inspectors in the field [40, 41].

As already demonstrated, MS is a highly sensitive and selective technology which is suitable for both qualitative and quantitative chemical analysis. Conventional laboratory-scale mass spectrometers are bulky and typically used in combination with GC or HPLC, which limits their usage for in-field applications. As opposed to traditional chemical analysis work flow, where samples are brought to the laboratory for analysis, miniaturized mass spectrometers can now be brought to the samples in the field [42, 43]. A wide variety of small mass spectrometers have been developed, with a weight as low as 4 kg [44]. However, not all of them are suitable for analysis of food or cosmetic products, for which a majority of the target analytes are non-volatile. The miniature MS instruments with internal ionization sources, which relies on sample introduction through GC, [45] membrane, [46] solid-phase microextraction (SPME) [45, 47] or sorbents, [48] typically can only analyze non- or semi-volatile compounds. To enable the coupling with in-air ionization methods, such as electrospray ionization that is suitable for ionizing non-volatile compounds, atmospheric pressure interface (API) is required for transferring the ions into the mass analyzer under vacuum. Small mass spectrometers with APIs have been developed, among which the Mini 10/11/12 series of instruments [44, 49, 50] used the discontinuous APIs [51] to achieve the ion transfer without requiring additional pumping capacity. The miniature ion trap instruments also have an advantage of performing MS/MS analysis, which provides additional confirmation of the chemical identity and improved sensitivity for analysis of complex mixtures. [42, 52]

Sample pretreatment is typically required prior to MS analysis, which would also need to be done quickly in the field to minimize the matrix effects. Ambient ionization has been developed for direct MS analysis of the analytes in untreated samples, and this represents a promising solution for simplification or elimination of sample preparation procedures in on-site analysis [53]. Since desorption electrospray ionization (DESI) [54] and direct analysis in real time (DART) [55] were reported in 2004 and 2005, respectively, more than 40 ambient ionization methods have been developed [53, 56]. Sample pretreatment and chromatographic separation, traditionally required for MS-based analysis, can now be bypassed. Notably, a set of ambient ionization methods, e.g., paper spray [57, 58], extraction spray [59], or low temperature plasma [60], have been coupled with miniature mass spectrometers, with promising results obtained for on-site applications in food safety [61, 62], product authentication [44], environmental monitoring [48, 63, 64], biomolecule analysis [65, 66], homeland security [67] and biomedical diagnosis as well as in forensic investigations [68].

In this study, direct identification of illicit ingredients in food and cosmetic products has been explored by coupling a miniature ion trap mass spectrometry system with ambient ionization methods (Figure 1). Versatile procedures using paper spray [57, 58], extraction spray [59, 69], and slug-flow microextraction [70] were developed for direct analysis of a wide variety of cosmetic products. In comparison with traditional methods requiring sample pretreatment and separation steps, the methods reported here enable a research to identify illicit ingredients in cosmetics with significantly improved throughput.

EXPERIMENTAL

Chemicals and reagents

Sudan Red I (1), Sudan Red II (2), Sudan Red III (3), Sudan Red IV (4), phenylparaben (8), chloramphenicol (10), metronidazole (11), and bis(2-ethylhexyl)phthalate(14) were purchased from Sigma-Aldrich (St. Louis, MO, USA); isopropylparaben (5), isobutylparaben (6), benzylparaben (9), and bisphenol A (13) were purchased from AccuStandard (New Haven, CT, USA); pentylparaben (7) was purchased from Alfa Aesar (Ward Hill, MA, USA); epitestosterone (12) was purchased from Steraloids (Newport, RI, USA). All reference standards had purities greater than 96%, except for Sudan Red II and IV (both 90%). The chemical information for the analytes is listed in Table S1. Ethanol, dichloromethane, methanol, and ethyl acetate of HPLC grade were purchased from Merck (Darmstadt, Germany). Ultrapure water was obtained from a Millipore Milli-Q integral water purification system (Bedford, MA, USA). Other chemicals used in the experiment were purchased from Sigma-Aldrich (St. Louis, MO, USA). The Grade 1 Chr (0.18 mm thickness), Grade 3MM Chr (0.34 mm thickness), Grade 4 Chr (0.21 mm thickness), Grade 31ET Chr (0.50 mm thickness) cellulose chromatography papers and the Grade SG81 (0.27 mm thickness) ion exchange paper were purchased from Whatman (Piscataway, NJ, USA) and used without further chemical treatment to prepare sample substrates for paper spray ionization. Stock standard solutions were prepared by dissolving each analyte with solvents. Sudan Red I, II, III and IV were dissolved in dichloromethane:ethanol (40:60); all other reference standards were dissolved in methanol. A variety of untreated cosmetic samples of different categories were collected from local stores, including the face powder (L.A. COLORS® Mineral Blush), lipstick (L.A. COLORS® Purely Matte Lipstick), cream (April Bath & Shower Cold Cream), shampoo (PANTENE® Pro-V Classic All Hair Types Shampoo), and lotion (LANCOME® Redefining Lifting Beauty Lotion). Stock solutions of the analytes were further diluted and spiked into 0.1 g of raw cosmetic samples, which were weighed into 2.0-mL Eppendorf Safe-Lock tubes. The mixtures were vortex mixed thoroughly and let dry overnight for subsequent analysis.

Instrumentation

In this study, rapid analyses for cosmetic and food samples were carried out using a Mini 12 desktop miniature mass spectrometry system [50]. The integrated Mini 12 system had a weight of 25 kg, an outer dimension of 19.6×22.1×16.5 in., and consumed less than 100 W of power. The pumping system consisted of a two-stage diaphragm roughing pump (KNF Neuberger, Trenton, NJ, USA) and a HiPace 10 turbomolecular pump (Pfeiffer Vacuum, Nashua, NH, USA). The manifold pressure could be pumped down to below 1×10^{-5} Torr.

Ions from the ambient ionization source were drawn in a pulsed fashion through the inlet capillary of the discontinuous atmospheric pressure interface (DAPI) [49, 51] into a rectilinear ion trap (RIT) located inside the vacuum manifold. For each scan, the DAPI was opened briefly for about 15 ms for ion introduction and closed during the rest of the time in each scan cycle. Due to the special mode of ion introduction using the DAPI, residual air was used as the collision gas instead of helium, which is typically used for commercial lab-scale ion trap instruments. The portability of the miniature MS system, however, was improved by eliminating the need for helium gas cylinders. Mass analysis was performed in a mass-selective instability scan mode to generate mass spectra using an rf of 1 MHz. A supplementary dipolar AC excitation at 350 kHz with its amplitude being ramped with the rf scan was applied to achieve resonance ejection. The frequency and the amplitude of the excitation signal used for CID are shown in Table 2. A scan speed of 10,000 m/z per second was used. The user interface for instrument control and data acquisition was developed in-house.

RESULTS AND DISCUSSION

Analysis of Powders and Lipstick Samples using Paper Spray

A significantly simplified protocol for direct analysis of powders and lipstick samples demonstrated the use of the miniature mass spectrometer system with paper spray ionization. Sudan Red dyestuffs (Sudan Red I, II, III and IV), an exemplary class of prohibited substances of great concern for regulatory control [71], were selected for method development and validation. Each sample of face powder, makeup, eye shadow or lipstick was approximately 1 mg and contained Sudan Red spiked at a concentration of 50 $\mu\text{g/kg}$. Each sample was loaded simply by smudging or swabbing it onto a piece of Grade 31ET chromatography paper substrate, which was then cut into a small triangle with a sharp tip (0.5 cm base width, 0.75 cm height and top angle 30°). A solid copper mini-alligator clip (Mueller, Ballinger, TX, USA) was used to hold the paper triangle with its tip about 5 mm from the DAPI inlet of the Mini 12. The metal clip was connected to a Bertan 205B-05R high voltage power supply (Hauppauge, New York, USA); 20 μL of dichloromethane:ethanol:formic acid (40:60:0.1) was applied as the wetting and spray solvent to induce a spray from the tip of the paper triangle. The MS analysis was performed in positive ion mode with a spray voltage at 4.0 kV. Based on the observed signal-to-noise ratio (S/N) of the most intense MS/MS fragment peaks and using the $S/N = 3$ as a criterion, the limits of detection (LODs) are estimated to be between 5 to 30 $\mu\text{g/kg}$ for the four prohibited Sudan Red dyestuffs in powders and lipstick samples (Figure 2).

As discussed in previous studies [72], paper spray involves three-steps: the extraction of analytes from the deposited sample by the spray solvent, the transport of extracted analytes across the paper substrate, and the generation of charged droplets due to the high voltage applied. The improvement in sensitivity with optimized paper spray conditions is more important for miniature mass spectrometers than for the commercial lab-scale instruments, since the performance of miniature instruments could be compromised due to the less sophisticated atmospheric pressure interfaces supported by their much smaller vacuum systems.

The selection of proper spray solvent and paper substrate is critical to the analytical performance of the paper spray MS analysis. The composition of the solvent not only affects the efficiency of extracting analytes from the sample matrix on paper, but also the efficiencies for their transfer across the paper and of ion formation during the spray event. In an attempt to optimize the overall elution/ionization efficiency for Sudan Red dyestuffs spiked in powdery and lipstick samples, the composition effect of the spray solvent was first evaluated by testing a series of pure solvents of different polarities, including hexane, tetrahydrofuran, ethyl acetate, chloroform, dichloromethane, acetone, acetonitrile, isopropanol, ethanol, methanol, and water. With a spray voltage of 4.0 kV, the highest signal intensities were observed with dichloromethane and ethanol, which have moderate solvent polarities (Figure S1a, b).

Solvent properties, such as the polarity, volatility and surface tension, also have a significant impact on the electrospray process. Typically, relative concentrations of the components in a mixture of solvents are adjusted to optimize the spray process for analysis of the target class of analytes [73]. As paper spray is expected to share similar spray characteristics with electrospray, a follow-up experiment for spray optimization was performed using a set of dichloromethane/ethanol mixture solvents at different mixing ratios. It was found that a mixture of dichloromethane:ethanol at 40:60 gave the maximum signal responses (Figure S1c, d). Addition of formic acid or acetic acid was also found to enhance the sensitivity in the positive ionization mode, with a most significant improvement obtained with formic acid (Figure S1e, f). The actual optimum concentration of the formic acid was determined to be 0.3%, through experimental testing of different concentrations between 0.1% and 2.0% (Figure S1g, h).

The nature of the paper substrate also plays a key role in the process of paper spray, since analyte elution and migration on paper are also dependent on the interactions between the analyte and the paper substrate, which acts somewhat like a stationary phase. As a porous and hydrophilic material, cellulose paper allows liquid flow over the surface and wicking through the inside microchannels by capillary action. Both the physical and chemical nature of the paper substrate might impact the migration behavior of the analytes, the ionization efficiency, and ultimately the analysis results. A variety of paper substrates, including cellulose chromatography papers (Grade 1 Chr, Grade 3MM Chr, Grade 4 Chr, Grade 31ET Chr) and ion exchange paper (Grade SG81), have been investigated in this study (Figure S2a, b). Upon the application of the optimized elution solvent of dichloromethane:ethanol:formic acid (40:60:0.3) and a spray voltage of 4.0 kV, Grade 31ET chromatography paper was identified as the best paper substrate with the highest signal intensities delivered.

Analysis of Shampoo and Cream Samples Using Extraction Spray

Another ambient ionization method, extraction spray, was used to develop a simple sampling/ionization method for the analysis of the prohibited paraben preservatives and antibiotics in the shampoo and cream products. Five paraben preservative (isopropyl-, isobutyl-, pentyl-, phenyl- and benzyl-) and two antibiotics [71] (chloramphenicol and metronidazole) were spiked into the samples. The paraben preservatives have been

forbidden for use in cosmetics because of their doubtful toxicological profiles [74]. Samples were gently picked up using a metal wire probe (approximately 1 mg loaded), and then inserted into a borosilicate glass capillary (1.5 mm o.d., 0.86 mm i.d., 5 cm length) with a pulled tip, which had been pre-filled with 10 μ L methanol:water:ammonia solution (60:40:0.5) for parabens) for analysis of parabens or 10 μ L methanol:water:ammonia solution (80:20:1.0) for antibiotics analysis. The nanoESI capillary was then placed in front of the DAPI inlet of Mini 12 with a voltage of 2.5 kV applied via the metal wire, to produce the spray ionization for immediate MS analysis. The MS/MS spectra recorded for samples spiked with analytes at 50 μ g/kg are shown in Figure 3. Based on the observed signal-to-noise ratios of the most abundant fragment peaks in MS/MS spectra and using the $S/N = 3$ as a criterion, the LODs are estimated to be between 5 and 25 μ g/kg for the five parabens in shampoo and 20 or 10 μ g/kg for chloramphenicol or metronidazole in cream, respectively.

The solvent composition for the extraction spray ionization was also optimized. A range of solvents with different polarities, including tetrahydrofuran, acetone, acetonitrile, isopropanol, ethanol, methanol, water, were first compared. Among the solvents investigated, methanol gave the highest intensities as a pure solvent (Figure S3a, b). The experimental results demonstrated that the addition of water could help disperse shampoo or cream samples into the solvent and improve the extraction and ionization efficiency. The optimal proportions of water in methanol were identified to be 40% for the analysis of parabens in shampoo (Figure S3e, f) and 20% for the analysis antibiotics in cream (Figure S4e, f). Addition of ammonia was found to further improve the signal intensities in the negative ionization mode (Figure S3c, d and Figure S4c, d) with the best concentration of 0.5% for parabens (Figure S3g, h) and 1.0% for antibiotics (Figure S4g, h).

Analysis of Milk, Beverage and Lotion Samples Using Slug-Flow Microextraction

We used slug-flow microextraction (SFME) nanoESI [70], a newly developed method for direct analysis of liquid samples, such as milk and beverage, in a simple, one-step process. Ethyl acetate and an aqueous solution of sample, each of 10 μ L, were sequentially injected into a borosilicate glass capillary (1.5 mm o.d., 0.86 mm i.d., 5 cm length) with a pulled tip. Liquid-liquid extraction of the analytes from the sample phase into the organic phase was expected, but at a fairly low efficiency because of the small interfacial area. However, as previously demonstrated [70], the analyte extraction speed could be significantly increased with slug flows induced by the movement of the two liquid plugs, which could be facilitated by tilting the capillary or applying a push-and-pull force through air pressure. Due to the friction with the capillary wall, internal circulations were formed inside each plug, transferring the analytes towards and away from the liquid-liquid interface, therefore significantly improving the extraction efficiency. After the extraction process, a stainless-steel wire was then inserted through the biofluid sample to reach the organic solvent plug and a high voltage applied to generate the nanoESI for MS analysis.

This method was applied to analyze milk samples spiked with bisphenol A (BPA) and beverage samples spiked with industrial plasticizer. BPA is an endocrine disruptor used as the monomer for the manufacture of polycarbonate plastics that is widely used for making containers and packaging materials; however, BPA has hormone-like properties and

therefore is forbidden for use in making infant milk bottles [75]. Bis(2-ethylhexyl)phthalate is a plasticizer that has been used as a substitute for palm oil, the clouding agent in beverage, to lower the cost [7]. In this study, the BPA and bis(2-ethylhexyl)phthalate were spiked into the whole milk (Dean's, Dean Dairy, Sharpsville, PA 16150) and Gatorade G2 Perform Fruit Punch (PepsiCoInc., Purchase, NY 10577), respectively, at a concentration of 50 µg/kg. The MS and MS/MS spectra recorded are shown in Figure 4. The LOD was estimated to be 10 µg/kg for BPA in milk and 5 µg/kg for bis(2-ethylhexyl)phthalate in the fruit punch.

Chemical derivatization is an effective way of altering the properties of the target analytes to improve the efficiency of separation or ionization for MS analysis. For instance, epitestosterone is a type of corticosteroid forbidden in cosmetics [71], which can be expected to be extracted and preconcentrated into the organic phase using the SFME method; however, the efficiency of the subsequent ionization by nanoESI is relatively low due to the poor proton affinity of the epitestosterone. The reaction with hydroxylamine has previously been shown to improve the ionization efficiency of the steroids [76], and therefore was used in this study. A liquid plug of 10 µL water containing 100 mM hydroxylamine was injected between 10 µL ethyl acetate and 10 µL water-based lotion sample spiked with epitestosterone at 50 µg/kg. In comparison with the slug-flow microextraction and nanoESI without the derivatization, a significantly improved sensitivity was observed. The CID of the reaction product ion m/z 304 yielded characteristic fragment ions at m/z 112 and 124 (Figure 5). The LOD of this method is estimated to be about 5 µg/kg based on the S/N values of peaks attributed these two fragment ions.

CONCLUSIONS

In this study, three ambient ionization methods were used with a miniature mass spectrometer to develop simple procedures for direct analysis of illicit substances in food and cosmetic products. Paper spray is suitable for analysis of powders or dried sample spots, extraction spray can be used for lotion or gel samples, and slug-flow microextraction can be applied for direct analysis of aqueous samples. LODs at low parts-per-billion levels can be achieved with the miniature ion trap mass spectrometer using MS/MS experiments. Specialized analysis with target analytes is expected to be a major field of applications for the miniature MS systems. The future implementation of the ambient ionization methods for direct sampling ionization can be done through disposable kit containing a sample cartridge and small volumes of solvents. [50, 77, 78] The optimization of the solvent for sample extraction and spray ionization was shown to have significant impact on the overall analytical performance in this study. This information would be useful for future design of the sampling kits for on-site analysis of cosmetic and foodstuff samples.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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HIGHLIGHTS

- Miniature ion trap analytical system with ambient ionization capability for direct chemical analysis
- Direct analysis of condensed-phase samples in the forms of powder, aqueous mixtures, and cream
- Optimal conditions identified for real-time sample extraction and analyte ionization

Figure 1. Paper spray ionization, extraction spray ionization, slug-flow microextraction, and Mini 12 desktop ion trap mass spectrometer for the rapid identification of prohibited substances in cosmetics, milk, and beverage samples

Figure 2.

Procedures for the analysis of (a) powder and (b) lipstick samples by paper spray ionization. MS/MS spectra for (a) Sudan Red I (precursor m/z 249) and (d) Sudan Red II (precursor m/z 277) spiked in powder and (e) Sudan Red III (precursor m/z 353) and (f) Sudan Red IV (precursor m/z 381) spiked in lipstick, each at 50 $\mu\text{g/kg}$.

Figure 3.

(a) Procedure for the analysis of cream and shampoo samples by extraction spray ionization. Product ion MS/MS spectra for (b) pentylparaben (precursor m/z 207) and (c) benzylparaben (precursor m/z 227) spiked in shampoo, and (d) chloramphenicol (precursor m/z 322) and (e) metronidazole (precursor m/z 170) spiked in cream, each at 50 $\mu\text{g/kg}$.

Figure 4.

(a) Procedure for the analysis of milk and beverage samples using slug-flow microextraction nanoESI-MS and product ion MS/MS spectra for bisphenol A (precursor m/z 227) spiked in milk(b and c), and bis(2-ethylhexyl) phthalate(precursor m/z 392) spiked in beverage(d and e), each at 50 $\mu\text{g/kg}$.

Figure 5.

(a) Procedure for the analysis of (a) lotion samples using reactive slug-flow microextraction. Product ion MS/MS spectra for analysis of epitestosterone spiked in lotion at 50 $\mu\text{g/kg}$, (b) without and (c) with on-line derivatization using hydroxylamine.

Table 1

Experimental conditions for Analysis

Compound	Matrix	Ambient Ionization	LODs ($\mu\text{g/kg}$)	Spray Solvent
Sudan Red I	Powder	Paper Spray	5	6:4 EtOH-DCM containing 0.3% formic acid
Sudan Red II	Lipstick	Paper Spray	5	6:4 EtOH-DCM containing 0.3% formic acid
	Powder	Paper Spray	15	
Sudan Red III	Lipstick	Paper Spray	15	6:4 EtOH-DCM containing 0.3% formic acid
	Powder	Paper Spray	30	
Sudan Red IV	Lipstick	Paper Spray	30	6:4 EtOH-DCM containing 0.3% formic acid
	Powder	Paper Spray	20	
Isopropylparaben	Lipstick	Paper Spray	20	6:4 MeOH-water containing 0.3% ammonia
	Shampoo	Extraction Spray	10	
Isobutylparaben	Shampoo	Extraction Spray	25	6:4 MeOH-water containing 0.3% ammonia
Pentylparaben	Shampoo	Extraction Spray	25	6:4 MeOH-water containing 0.3% ammonia
Phenylparaben	Shampoo	Extraction Spray	5	6:4 MeOH-water containing 0.3% ammonia
Benzylparaben	Shampoo	Extraction Spray	20	6:4 MeOH-water containing 0.3% ammonia
Chloramphenicol	Cream	Extraction Spray	20	8:2 MeOH-water containing 1.0% ammonia
Metronidazole	Cream	Extraction Spray	10	8:2 MeOH-water containing 1.0% ammonia
Epitestosterone	Lotion	Slug-Flow Microextraction	5	EtOAc-100 mM Hydroxylamine
Bisphenol A	Milk	Slug-Flow Microextraction	10	EtOAc
Bis(2-ethylhexyl)phthalate	Beverage	Slug-Flow Microextraction	5	EtOAc

Table 2

Source voltage, SWIFT notch, CID AC voltage and AC frequency for analytes

Compound	Source voltage (kV)	SWIFT notch (kHz)	CID AC voltage (V)	AC frequency (kHz)
Sudan Red I	4.0	232–240	0.42	124.8
Sudan Red II	4.0	204–212	0.36	111.7
Sudan Red III	4.0	155–163	0.72	87.0
Sudan Red IV	4.0	142–150	0.72	80.4
Isopropylparaben	2.5	382–390	0.65	178.2
Isobutylparaben	2.5	332–340	0.62	164.0
Pentylparaben	2.5	297–305	0.65	152.0
Phenylparaben	2.5	285–293	0.75	147.4
Benzylparaben	2.5	262–270	0.55	137.7
Chloramphenicol	2.5	171–179	0.46	95.6
Metronidazole	2.5	442–450	0.42	188.8
Epitestosterone	2.5	183–191	0.68	101.4
3-Oxime-epitestosterone	2.5	194–202	0.68	106.9
Bisphenol A	2.5	262–270	0.72	137.7
Bis(2-ethylhexyl)phthalate	2.5	138–146	0.65	78.1