Letter

Simultaneous preconcentration and desalting of organic solutes in aqueous solutions by bubble bursting

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Simultaneous preconcentration and desalting of organic solutes in aqueous solutions by bubble bursting

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ABSTRACT: Significant efforts are being made to develop more practical and versatile approaches for the preconcentration and purification of complex chemical samples. Inspired by the naturally occurring enrichment of organic compounds in sea aerosols, in this study we demonstrate the potential of induced bubble bursting as an approach for the pre-concentration of organic solutes in various aqueous solutions. Apart from the pre-concentration of organics, notable decrease in the concentration of metal salt components was discovered for the first time. Based on a series of model experiments, the phenomenon has been attributed to inter-molecular competition at the surface interface of rising bubbles. Overall, our results indicate the high versatility and simplicity of the bubble bursting approach for the simultaneous preconcentration and desalting of organic solutes in aqueous solutions for mass spectrometry, chromatography, optical detection and other fields of analysis.

INTRODUCTION

Characterization of trace organic compounds in environmental, biological and synthetic matrices using mass spectrometry (MS), optical spectroscopy, nuclear magnetic resonance (NMR), colorimetry, electrochemistry and various other techniques commonly requires analyte preconcentration as well as the removal of solute interferences. Efficient sample purification often requires multiple stages of chromatographic separation, chemical extraction, lyophilization, recrystallization, solute precipitation, dialysis, ultrafiltration, *etc*.[1-4] The multi-stage pretreatment procedures are usually laborious, time-consuming, and expensive in operation and commonly suffer from sample losses and chemical contamination. Significant efforts are being made to develop more practical and versatile approaches for chemical preconcentration and purification relying on the recent advances in adsorbent materials,[5-7] microfluidics,[8] nanotechnology,[9] micro-extraction,[10] crystallization,[11] electrospray ionization (ESI)[12-14] and matrix-assisted laser desorption/ionization (MALDI).[15-17]

It has been earlier discovered that the concentration of organic solutes in bursting bubble aerosols above the sea surface is increased by more than two orders of magnitude relative to the bulk seawater whereas the chemical enrichment of inorganic constituents (including Na^+, Mg^{2+}, Ca^{2+}, K^+, Cl^-, and SO_4^{2-}) is limited to a few percent if occurs at all.[18-23] The effect has been attributed to the high surface activity of organic compounds, which allows them to gradually partition to the gas–liquid interface of rising bubbles in sea water.[19,20] Upon bubble bursting at the ocean surface these compounds are released into the atmosphere in tiny droplets.[24-27] Chemical partitioning has been also documented in the bursting bubbles of Champagne and other sparkling wines.[28-30] Inspired by the naturally

occurring selective enrichment of organic compounds in bursting bubbles, in this study we demonstrate the potential of induced bubble bursting as a simple and versatile analytical approach for the preconcentration of organic compounds in aqueous solutions.

METHODS

Bursting bubbles were generated at ambient conditions either by sonicating aqueous analyte solutions (10-500 mL) pre-saturated with CO_2 gas (dry ice, ~ 100 mg/mL) or by feeding gas through the porous surface (i.d. 100 µm) at the bottom of the analyte solution. The bursting bubble aerosol was collected using a slanted glass slide fixed above the liquid surface (Figure S-1). Typically, ca. 100 µL of aerosol was collected within 5 min from 500 mL bulk solution. Other experimental details are available in Supporting Information.

RESULTS AND DISCUSSION

A series of model experiments showed the increase of analyte signal intensity (I) in the collected aerosol relative to the bulk solution ($R = I^{bubble}/I^{bulk} > 1$) for all the tested organic compounds either when analyzed independently (Tables 1, S-1) or from a mixture (Figures 1, S-2, Table 2). In sharp contrast, the concentration of metal salts (CsI, NaCl and $AgNO_3$) did not observably change in the collected aerosol relative to bulk ($R \approx 1$) when analyzed independently (Tables 1, S-1) and notably decreased ($R < 1$) in the presence of certain organic components (Figures 1, S-3, Table 3). To our knowledge this is the first evidence for the depletion of inorganics content in bursting bubbles.

Based on a series of model experiments with varied composition of analyte solutions and bubble bursting parameters (Tables 1, 2, 3, S-1, S-2), we propose a simple model of chemical partitioning in bursting bubbles summarized in Figure 2. At a low solute concentration,

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molecular enrichment factor (R) is mainly determined by the surface activity and grows with the bubble path in solution. However, starting from a certain value further increase in the path length causes the decrease of R values (Table S-2). The optimal path length in our experiments was ca. 90 cm, enabling the R-value > 100 for some analytes. The occurrence of the optimal path length can be rationalized by taking into account the fact that rising bubbles gradually increase in diameter as a result of bubble coalescence. The average bubble diameter at the 10 cm path length was ca. 0.7 mm, and the average bubble diameter at the 100 cm path length was ca. 2.2 mm. Larger bubbles release more water molecules upon bursting, resulting in the dilution of collected aerosols and the decrease of R values at long path lengths. The decrease of sea-to-air flux of organics via bubble bursting upon the increase of bubble size was also documented in earlier studies.[24]
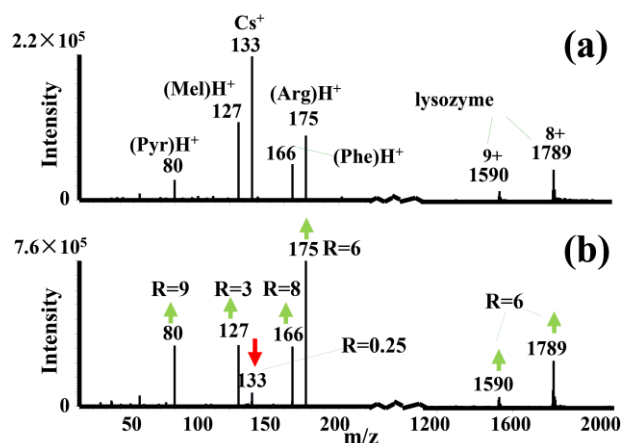

Figure 1. a) Direct-infusion ESI-MS analysis of a model aqueous solution (500 mL) containing arginine (Arg, 80 μM), pyridine (Pyr, 5 μM), lysozyme (Lyz, 30 μM), phenylalanine (Phe, 500 μM), melamine (Mel, 300 μM) and cesium iodide (CsI, 400 μM) ; b) direct-infusion ESI-MS of a bubble aerosol (100 μL) collected from the same original solution over 5 min and analyzed under identical MS parameters. The numbers above each peak in the mass spectra correspond to the mass-to-charge ratio (m/z) of detected ions. Enrichment factor for each signal is calculated as the ratio between its intensity in the second spectrum and its intensity in the first spectrum (R = I^{bubble}/I^{bulk}). Bubbles were produced by ultrasound (Figure S-1a). Bubble path length was 20 cm.

At a high solute concentration, bubble is saturated with organic compounds before it reaches the liquid surface, resulting in lower R-values (Table 2). Further chemical partitioning upon bubble saturation is largely determined by inter-molecular competition for the bubble surface (Figure 2). As a result of such competition, metal salts are gradually expelled from the surface of rising bubbles by the organic compounds with higher surface activity (Table 3). This effect has not been observed in sea aerosols, which is probably related to the relatively low concentration of surface-active organics in sea water (Figure 2). We also found that chemical partitioning of certain analytes was strongly dependent on the molecular composition of gas inside the rising bubbles (Table S-3). Although this curious phenomenon is yet to be explored in detail, the data suggest that gas composition can be an important factor to tailor

chemical selectivity of the bursting bubble approach. The use of mixed gas composition might also provide an optimized enrichment for two or more different solute compounds simultaneously.

Table 1. Signal enrichment (R = I^{bubble}/I^{bulk}) of chemicals by bursting bubbles in single-analyte aqueous solutions. Bubbles were produced by ultrasound (Figure S-1a) from 500 mL solution. Bubble path length was 20 cm. Pyr = pyridine (50 μM); Mel = melamine (100 μM); Phe = phenylalanine (100 μM); Arg = arginine (30 μM); Qui = quinine (50 μM); Lys = lysozyme (1 μM). The data for other analytes is shown in Table S-1.

	Pyr	Mel	CsI	Phe	Arg	Qui	Lyz
R	13±2	37±13	1.1±0.1	56±15	23±5	34±12	27±8

Table 2. Chemical enrichment for the chemicals in water solution (50 μM Pyr; 3 mM Mel; 4 mM CsI; 5 mM Phe; 1 mM Arg; 300 μM Qui) diluted in water by D = 1, 10 and 100 times before bubbling (the same bubbling conditions as in Table 1).

D	R_{Pyr}	R_{Mel}	R_{CsI}	R_{Phe}	R_{Arg}	R_{Qui}
×1	6±1	5±1	0.5±0.1	2.2±1	1.5±0.5	10±2
×10	10±2	6.3±1	0.9±0.1	10±2	5±1	16±3
×100	20±5	13±2	1.25±0.1	23±3	12±3	25±4

Table 3. Signal enrichment for CsI (100 μM) and organic component ([M] = 10 μM) in various aqueous M-CsI mixtures (the same bubbling conditions as in Table 1).

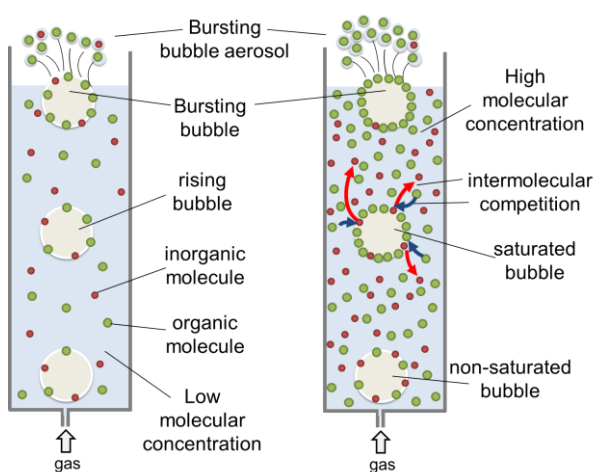| M	Pyr	Mel	Phe	Arg	Lyz
R_{CsI}	0.85±0.1	0.86±0.1	0.61±0.1	0.75±0.1	0.55±0.1
R_M	12±3	19±4	40±5	15±4	20±3

Figure 2. Schematic representation for the proposed mechanism of chemical enrichment in bursting bubbles.

Bursting bubble approach can be used to pre-concentrate trace organic solutes covering a broad range of molecular

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polarity, hydrophobicity, volatility, size, solubility and other molecular properties (Table S-1). Figures S-3 and S-4 show model applications of the approach to increase the sensitivity and speed of targeted MS detection for codeine drug in urine and isovaleric acid differential metabolite in *Staphylococcus aureus* bacterial culture. Figure 3 shows the application of bursting bubble approach to non-targeted gas chromatography mass spectrometry (GC-MS) screening, allowing the increased number of molecular identifications in a complex sample (mosquito spray, Liu Shen, Shanghai, China).
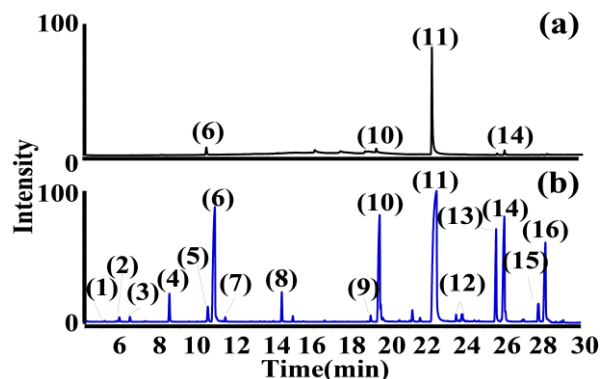

Figure 3. GC-MS analysis for the low-polarity fraction of a mosquito spray (30% water, 65% ethanol) extracted into hexane from a) the original spray solution; b) bubble aerosol collected from the same original solution. Identical experimental conditions were used. Signals were identified via NIST library search (Table S-4). Peak labels correspond to their entry number in Table S-4. Bubbles were produced by ultrasound (Figure S-1a). Bubble path length was 20 cm.

As the metal salts are very common interferences in bioanalysis,[1] desalting effect of the bubble bursting approach has an added value for the pretreatment of biological samples. Figure S-5 shows that the bursting bubble pretreatment of lysozyme (1 μM) in aqueous buffer solution (20 mM NH₄Ac) containing 1 mM NaCl yields more than 10-fold increase in the signal-to-noise ratio of protein signals in the mass spectrum. Moreover, substantial peak narrowing is evident owing to the reduction of protein-salt clustering. The considered examples illustrate the high versatility of bubble bursting approach as a pretreatment step for the chemical analysis by MS and chromatography.

In addition to the applications in MS and chromatography, we further demonstrate the applied potential of bursting bubble approach in optical detection. Many chromophore molecules have a high surface activity and can be very efficiently pre-concentrated by bursting bubbles. In addition to the preconcentration effect, optical visibility of chromophores can be increased owing to the partial depletion of inorganic components in bursting bubbles. Metal salts are ubiquitous fluorescence quenchers and can also seriously affect spectral shape and color of chromophore moieties, thereby complicating data interpretation. Figure 4 shows ca. 100-fold enhancement of quinine fluorescence in the collected aerosol from the bulk aqueous solution with a high concentration of fluorescence quencher (Cl⁻ anion, 40 mM NaCl) and organic solutes (10 mM Phe). The interplay of preconcentration and desalting effects by the bursting bubble approach is expected to be beneficial for a wide range of optical methods, such as fluorescence sensing, colorimetry, UV-Vis absorption spectroscopy, *etc*.
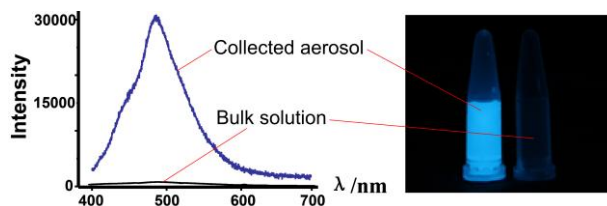

Figure 4. Fluorescence of quinine in aqueous solution containing 40 mM NaCl and 10 mM Phe (black line) and in the collected aerosol from the same solution (blue line). Bubbles were produced by ultrasound (Figure S-1a). Bubble path length was 20 cm.

Using ambient ionization techniques,[31,32] bursting bubble aerosol can also be analyzed directly without collection. Ambient MS approach for the rapid molecular fingerprinting of beer has been recently demonstrated in which neutral beer aerosol was formed by bubbling gas through the bulk volume of untreated beer and ionized *in situ* by primary electrospray droplets.[33] Despite the relatively poor efficiency of ambient ionization, many low-abundance nonvolatile chemicals in beer were readily detected, which could be related to the chemical enrichment occurring in bursting bubbles. Here we present additional evidence showing more than 10-fold increase in EESI-MS signal intensities and signal-to-noise ratios of a raw fragrant solution when sampled by bursting bubble approach vs. volatile sampling (Figure S-6). The results indicate that induced bubble bursting significantly extends the sensitivity and molecular range of chemical sampling.

In an inverse problem, bubble bursting can be applied to purify bulk solutions from organic impurities, e.g. disinfection by-products. Simple calculations (see Supporting Information) show that the bulk concentration of an organic solute (C) is decreasing during the bubbling process as $C = C_0(1 - \Delta V/V_0)^{R-1}$, where C_0 is the original solute concentration, V_0 – original bulk volume, ΔV – volume removed from the bulk solution by bursting bubbles, R – concentration enrichment factor for the specific solute in bursting bubbles. The bulk concentration of analyte with $R \approx 100$ is expected to decrease by ca. 7-times upon the removal of only 2% bulk volume ($\Delta V/V_0 = 0.02$) and by ca. 10^5-times upon the removal of 10% volume. These estimates well agree with the results of our model experiments (Figure S-7). Importantly, the bursting bubble approach works well for volatile and semi-volatile compounds, which are very difficult to remove from water using standard distillation procedure. However, it should be noted that the partial loss of volatile solutes might still be expected due to evaporation from the aerosol droplets. The loss of water by evaporation in our experiments was estimated to be < 10% (see Experimental in SI). To minimize sample losses by evaporation one can consider cooling down working solution or using shorter distances between working solution and collection glass slide.

There is no principal limitation on the time of bubbling process, so that larger volumes of aerosols can be collected. The speed of preconcentration can be increased by using higher bubbling rates.[24] However, it should be noted that the distance from the solution surface to the

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collection glass slide is gradually increasing as the bulk volume is decreased by bubbling. Significant increase in the distance may lead to the lower efficiency of aerosol collection, because fewer bursting droplets will reach the glass slide. In this case, the bulk solution should be regularly replenished to the original volume during the bubbling process.

CONCLUSION

Bubble bursting has been demonstrated as a simple and versatile approach for the simultaneous preconcentration and desalting of organic solutes in aqueous solutions. We hope that our results will energize deep investigation of bubble chemistry using various approaches. The process of chemical partitioning at the bubble surface of complex solutions is still poorly addressed, and the improved mechanistic understanding should further increase the applied value of bubble bursting approach in organic chemistry, analytical biochemistry, environmental research, forensic science, quality control applications, etc.

ASSOCIATED CONTENT

Supporting Information

Experimental description. Mathematical representation of chemical partitioning during bubble bursting process. Supplementary tables showing the chemical enrichment of various complex samples. Supplementary figures as noted in the main text. This information is available free of charge via the Internet at http://pubs.acs.org/.

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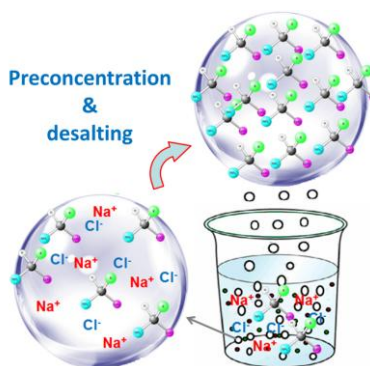
Notes

The authors declare no competing financial interest and no conflicts of interest.

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