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Fast screening of short-chain chlorinated paraffins in indoor dust samples by graphene-assisted laser desorption/ionization mass spectrometry

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ABSTRACT

As an important class of emerging chemical contaminants, short-chain chlorinated paraffins (SCCPs) are considered as one of the most challenging groups of compounds to analyze. In this paper, we report a new method for fast screening of SCCPs based on matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) with graphene as a matrix and 2,5,6,9-tetrachlorodecane as an internal standard. We found that the use of graphene as MALDI matrix generated high peak intensities for SCCPs while producing few background noises. The ion fragmentation mechanisms of SCCPs in MALDI are discussed in detail. Under the optimized conditions, much lower detection limits of SCCP congeners (0.1–5 ng/mL) than those reported previously were obtained. Other distinct advantages such as short analysis time and simplified sample preparation procedures are also demonstrated. The method was successfully applied in fast screening of SCCPs in indoor dust samples and monitoring of human exposure levels to SCCPs, and the results were verified by gas chromatography coupled to negative chemical ionization quadrupole time-of-flight high-resolution mass spectrometry. This work not only offers a new promising tool for SCCP studies, but also further demonstrates the promise of graphene as a new generation of MALDI matrix.

1. Introduction

Chlorinated paraffins (CPs), also called polychlorinated *n*-alkanes, are widely used as lubricants, plasticizers, and additives in a great variety of industrial and consumer products due to their thermal stability, variable viscosity, flame resistance, and low vapor pressure [1,2]. The production volume of CPs in China was estimated to be 260 kt/year in 2006 [3] and over 1 million t/year in 2013 [4]. CPs are classified into three categories according to the length of the carbon chain: short-chain (SCCPs, C_{10}-C_{13}), medium-chain (MCCPs, C_{14}-C_{17}), and long-chain CPs (LCCPs, C_{17}-C_{30}) [5,6]. Among them, SCCPs are most concerned because of their potential toxicity to human and organisms, long-range migration, and long-term persistence in the environment [7]. SCCPs have been identified as persistent organic pollutants (POPs) by the Persistent Organic Pollutants Review Committee (POPRC) in 2017 [8] and have also been added into the list of toxic chemicals by the U. S. Environmental Protection Agency (USEPA) [9]. However, current understanding of the environmental occurrence and fate of SCCPs is still limited due to the extreme difficulty in the analysis of SCCPs in environmental media.

Due to the presence of thousands of isomers and homologues, SCCPs are regarded as “the most challenging groups of substances to analyze and quantify” [10]. Currently, analysis of SCCPs mainly rely on gas chromatography coupled with electron capture negative ionization low-resolution or high-resolution mass spectrometry (GC-ECNI-LRMS or GC-ECNI-HRMS) [7,11]. However, the GC-MS methods cannot fully separate SCCPs. In fact, due to the extremely complex family of CPs, even by using two-dimensional gas chromatography coupled to electron capture negative ionization high-resolution time-of-flight mass spectrometry (GC × GC-ECNI-HRTOF-MS), complete separation of SCCPs is still impossible [12]. Another disadvantage of GC-ECNI-MS methods is that the instrument response of SCCPs closely depend on their chlorination degree, so adequate reference standards of SCCPs are required to calibrate the analytical results. To achieve congener group-level

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quantification of SCCPs, mathematical deconvolution methods were developed to resolve congener groups of SCCPs from the mass spectra data [13–16]. To shorten the analysis time, Bogdal et al. recently reported a direct injection atmospheric pressure chemical ionization quadrupole time-of-flight high-resolution mass spectrometry (APCI-qTOF-HRMS) method with deconvolution for analysis of CPs with no chromatographic separation [13]. Gao et al. used a negative chemical ionization quadrupole time-of-flight high-resolution mass spectrometry (GC-NCI-qTOF-HRMS) to extract accurate masses of SCCPs to eliminate interferences from other compounds [17]. However, all currently available methods for analysis of SCCPs require laborious and time-consuming sample clean-up procedures [13]. The low throughput of these methods also limits their application in environmental health or exposomic studies. Therefore, new techniques capable of fast analyzing SCCPs in complex samples are highly desired.

The aim of this study is to develop a fast method for screening of SCCPs. To this end, we used for the first time matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) to analyze SCCPs without any column purification procedures or time-consuming chromatographic separation. MALDI-TOF MS is a simple and high-throughput MS technique that uses a matrix to transfer the laser energy and promote the laser desorption/ionization (LDI) process of analytes. This technique is normally only applicable for qualitative analysis of large molecules due to the strong background noises in low-mass regions caused by organic matrices and poor reproducibility resulting from the inhomogenous co-crystallization process of analytes with the matrix. To overcome these problems, we herein used graphene, a novel two-dimensional carbon nanomaterial [18–20], as a MALDI matrix and 2,5,6,9-tetrachlorodecane as an internal standard (IS). Graphene-based materials have been shown to be useful MALDI matrices due to the exceptional properties of graphene, such as strong optical absorption, efficient energy transfer, and unique two-dimensional structures [21–26]. Here we show that graphene could effectively facilitate the LDI process of SCCPs while producing few background noises in low-mass regions. Furthermore, the use of an IS could greatly improve the accuracy of MALDI analysis. Several selected SCCP congener groups could be well resolved by MALDI-TOF MS with LODs at sub-ppb levels. This method was successfully applied in rapid screening of SCCPs in indoor dust samples and monitoring the exposure levels of SCCPs to human body. The results were verified by GC-NCI-qTOF-HRMS method. Therefore, this method provides a valuable complementary to GC-MS methods for SCCP studies.

2. Experimental section

2.1. Chemicals and materials

Chemically converted graphene (purity > 98 wt%; single layer ratio ~80%; thickness 0.8–1.2 nm; diameter 0.5–2 μm; see Fig. S1) and graphene oxide (GO; purity > 99 wt%; single layer ratio ~ 99%; thickness 0.8–1.2 nm; diameter 0.5–5 μm) were purchased from XFNANO (Nanjing, China). Fluorographite (F% > 56%) was bought from CarFluor Chemicals (Shanghai, China). The standards of individual SCCP congener groups, including 1,1,1,3,8,10,10,10-octachlorodecane ($C_{10}Cl_8$), 1,1,1,3,10,11-hexachloroundecane ($C_{11}Cl_6$), and 1,1,1,3,12,13-hexachlorotridecane ($C_{13}Cl_6$), were bought from Sigma-Aldrich (St. Louis, MO). 2,5,6,9-Tetrachlorodecane ($C_{10}Cl_4$), 1,2,5,6,9-pentachlorodecane ($C_{10}Cl_5$), 1,2,5,6,9,10-hexachlorodecane ($C_{10}Cl_6$'), 1,2,4,5,9,10-hexachlorodecane ($C_{10}Cl_6$''), 1,1,1,3,9,10-hexachlorodecane ($C_{10}Cl_6$'''), and three mixed SCCP standards (C_{10}–C_{13} containing 51%, 55.5%, and 63% chlorine; 100 μg/mL in cyclohexane) were obtained from Dr. Ehrenstorfer (Augsburg, Germany). Cyclohexane, *n*-hexane, and isooctane of HPLC grade were from J. T. Baker (Phillipsburg, NJ). α-Cyano-4-hydroxycinnamic acid (CHCA) was from Sigma. Ultrapure water was prepared by using a Millipore Milli-Q system (Billerica, MA, USA). All reagents were of analytical grade unless otherwise noted.

2.2. Sample preparation procedures

For GC-NCI-qTOF-HRMS measurements, the samples were prepared according to the procedures reported previously [17,27]. Briefly, 0.1 g of dust sample was mixed with 15 g of anhydrous sodium sulfate. The mixture was extracted with dichloromethane/hexane 1:1 (v/v) on a Thermo (Dionex) ASE 350 accelerated solvent extractor system. The extract was evaporated to ~ 1 mL and then purified by a 1.5 cm composite column consisting of 3 g of Florisil, 2 g of neutral silica gel, 5 g of acid silica gel, and 4 g of anhydrous sodium sulfate. The column was pre-activated with 50 mL of *n*-hexane, and then eluted with 40 mL of *n*-hexane, 50 mL of dichloromethane, and 50 of mL *n*-hexane in sequence. The fractions of the final dichloromethane and *n*-hexane solution were collected, evaporated to nearly dryness under gentle nitrogen flow, and re-dissolved in 1 mL of cyclohexane. The detailed conditions for GC-NCI-qTOF-HRMS measurements are given in the Section 1.2 in Supporting information.

For MALDI-TOF MS measurements, two sample preparation strategies (i.e., with and without column purification) were compared. Besides the sample preparation procedures described above, we also tested the procedures without column purification as follows: first, 0.1 g of dust sample was extracted by 5 mL of dichloromethane/cyclohexane 1:1 (v/v) for 30 min with the aid of ultrasonication. Then, the mixture was centrifuged at 9000 rpm for 3 min and the supernatant was collected and concentrated to 1 mL under the gentle stream of N_2.

2.3. MALDI-TOF MS

MALDI-TOF MS was performed on a Bruker Daltonics Autoflex III Smartbeam MALDI-TOF mass spectrometer working in reflector mode and controlled by the FlexControl software. The detection was carried out in positive ion mode. 2,5,6,9-Tetrachlorodecane was used as an IS for quantification of SCCPs. The matrix dispersion was prepared by dispersing graphene in water at 1 mg/mL with the aid of ultrasonication. The sample solution, IS solution (10 μg/mL in cyclohexane), and matrix dispersion were mixed at a ratio of 1:1:2 (v/v/v). The mixture was well blended by vortex generator and 2 μL of it was placed on a stainless steel MTP target frame III (Bruker Daltonics) followed by air drying. A Nd:YAG laser with the frequency of 100 Hz was used. The laser power was set to 31%. The spectra were recorded by summing 200 laser shots. The FlexAnalysis 3.4 software was used for data processing.

2.4. Real sample analysis

The indoor dust samples were collected by using a household vacuum cleaner (Puppy D-530, Beijing) in different apartments and offices (n = 20) in Beijing, China. The intake nozzle of the aspirator was covered by a nylon membrane, which was refreshed after each sampling to avoid cross contamination. The samples were sieved by using a 100 mesh sieve, wrapped in aluminum foil, and stored at −20 °C.

3. Results and discussion

3.1. Selection of MALDI matrix

For MALDI-TOF MS, a suitable matrix is critical for obtaining good analytical performance. Generally, a good MALDI matrix should have the following properties: (1) capable of embedding and isolating analytes (e.g. by co-crystallization); (2) soluble in solvents compatible with analytes; (3) stable in vacuum; (4) can adsorb the laser energy; (5) can cause co-desorption of analytes upon laser irradiation; and (6) can promote the analyte ionization. Conventional organic matrices used in MALDI can produce strong background noises in low-mass regions that greatly interfere the detection of small molecules. Recent development

of new matrices makes MALDI also capable of analyzing small molecules [21,28–32]. Particularly, graphene-related materials have been shown to be highly efficient MALDI matrices [21–26]. Thus, herein, we tested three types of matrices (including a conventional matrix CHCA, graphene, and GO) in MALDI analysis of SCCPs. The characterization of graphene and GO was similar to that in previous reports [26,32] and the results are also shown in Fig. S1.

Four individual SCCP congener standards, $C_{10}Cl_4$, $C_{10}Cl_5$, $C_{10}Cl_5$, and a mixed standard ($C_{10}Cl_8$, $C_{11}Cl_6$, and $C_{13}Cl_6$), were used as model analytes (see Table S1 for chemical structures). These congeners were selected for the following reasons: $C_{10}Cl_4$ is a lowly chlorinated congener that is difficult to be analyzed by conventional GC-MS [33,34]. $C_{10}Cl_5$ is a low-content congener in technical SCCP formulations and it was used as a congener requiring high analytical sensitivity. $C_{10}Cl_6$ is one of the most widely used SCCP congener groups [17,27,35,36]. Mixed standards of congeners with different carbon chain lengths and chlorine contents ($C_{10}Cl_8$, $C_{11}Cl_6$, and $C_{13}Cl_6$) were used as an artificial SCCP formulation. Note that SCCPs are abbreviated as C_nCl_m (n and m are numbers of C and Cl atoms in molecular formula) with H atoms being omitted.

Fig. 1 shows the mass spectra for $C_{10}Cl_6$ using different materials as MALDI matrices. The mass spectra for other congeners are given in Figs. S2-S4. It can be seen from Fig. 1A and S2 that without using matrix no signals were observed in the spectra. With CHCA as a matrix (Fig. 1B and S3), no peaks corresponding to SCCPs could be obtained either. When using GO as a matrix (Fig. 1C and S4), peaks of SCCPs could be detected but the intensities were low. Only with graphene as a matrix (Figs. 1D and 2), high peak intensities were obtained for all SCCP congeners, indicating that graphene is an excellent matrix for MALDI analysis of SCCPs. The detection was also performed with a blank sample and no target analytes could be detected (Fig. S5), indicating that the observed MS signals in Fig. 2 were from SCCPs. It should be noted that SCCPs could be detected in both negative and positive ion mode on the graphene matrix. However, positive ion mode yielded much stronger peak intensities and lower background noises than negative ion mode. Thus, positive ion mode was used in the following experiments.

To further explain the results obtained above, we investigated the morphology of matrices in MALDI. In previous reports using graphene in MALDI [23–26], aggregation of graphene was often observed at the surface of MALDI target, resulting in low LDI efficiency and poor analytical reproducibility. However, in this study, we found that the aggregation of graphene was greatly suppressed and a uniform film could be obtained at the MALDI target surface (Fig. S6A). The reason may be that in this study the sample was dissolved in a nonpolar solvent (i.e., cyclohexane) that could assist in dispersing graphene and improve the homogeneity of the resulting film. The homogenous film was favorable to obtain high LDI efficiency and reproducible analytical results. In contrast, CHCA formed numerous discrete “hot spots” with a large part of the surface of MALDI target being exposed due to the inhomegeous co-crystallization process (Fig. S6B). For GO, the large delocalized π-electron system of graphene was disrupted by the heavy oxidation to produce many defects on the surface [26,31,37], which might seriously compromise the laser absorption and energy transfer capability. In addition, we have also tested fluorographene (FG) that has recently been shown to a useful MALDI matrix [31]. We found that graphene was a better matrix than FG for SCCPs (see Fig. S7). The reason may be that FG needs to self-assemble into a honeycomb-like film in aqueous solution to exert its best performance in MALDI [31]. However, in this study, the sample was dissolved in organic solvent that might disturb the self-assembly of FG (see Fig. S8).

Fig. S9 shows the analysis of a mixed C_{10}–C_{13} SCCP formulation on graphene matrix. All SCCP congener groups could be readily identified in the mass spectra with no significant signal suppression effect. Therefore, graphene is suitable not only for individual SCCP congener groups but also for complex SCCP formulations. Based on the results mentioned above, graphene was selected as a matrix in the MALDI screening of SCCPs.

3.2. Ion formation mechanism of SCCPs

The ion fragmentation mechanism of SCCPs in positive-ion MALDI was investigated in detail. The peaks for SCCPs are labeled in Fig. 2 and their corresponding ions are listed in Table S2. It should be noted that, due to the nature of MALDI-TOF MS, the mass values obtained in MALDI were not as accurate as in GC-ECNI-MS. So, in addition to masses, the peaks in MALDI-TOF MS were further identified by the presence of isotopic peaks and spiking standards into the samples. Generally, we obtained three types of peaks of SCCPs in MALDI, including $[M - H + 2Na]^+$, $[M - nCl + (n + 1)Na]^+$, and $[M - nCl + (n - 1)Na]^+$. For example, as shown in Fig. 1D, the peaks at m/z 301.1, 334.4, 359.3, and 393.3 are assigned to $[M - 2Cl + Na]^+$, $[M - 3Cl + 4Na]^+$, $[M - Cl + 2Na]^+$, and $[M - H + 2Na]^+$ of $C_{10}Cl_6$, respectively. Their isotopic peaks are shown in Fig. 2E-F. This suggests that the

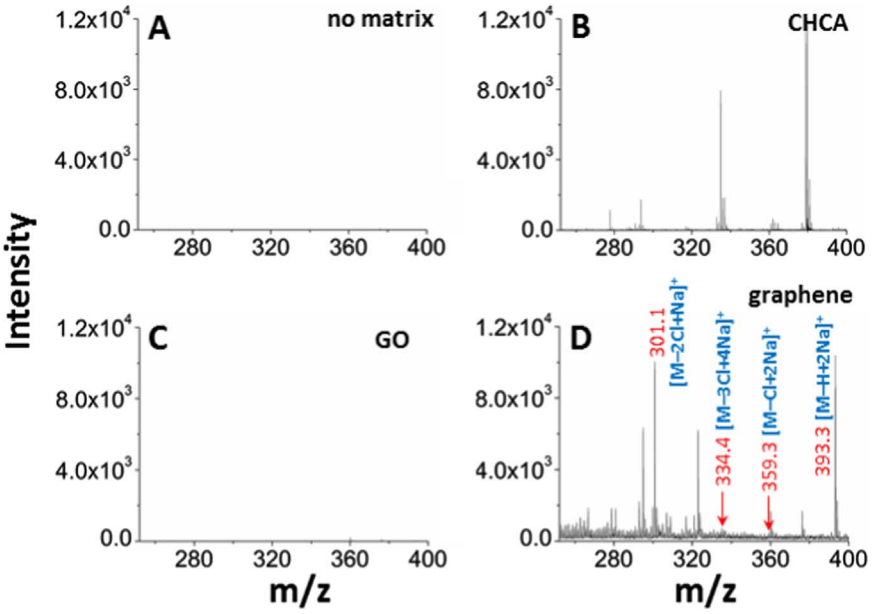

Fig. 1. Analysis of $C_{10}Cl_6$ by MALDI-TOF MS using different matrices. (**A**) Without matrix, (**B**) using CHCA, (**C**) GO, and (**D**) graphene as matrix. The peaks corresponding to the analytes are labeled in the mass spectra. Analyte concentration: 1 μg/mL. The standard sample of $C_{10}Cl_6$ was mixed with the matrix dispersion at a ratio of 1:1 (v/v) and 1 μL of the mixture was used for MALDI-TOF MS measurement.

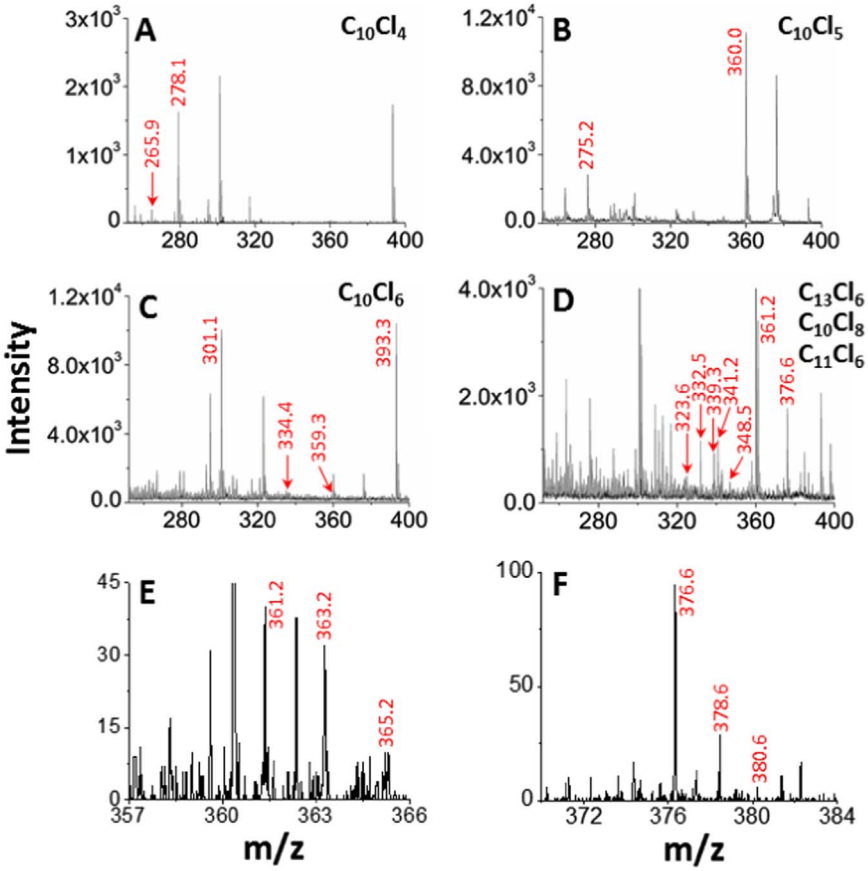

Fig. 2. Analysis of different SCCP congeners by MALDI-TOF MS using graphene as a matrix. (**A**) $C_{10}Cl_4$, (**B**) $C_{10}Cl_5$, (**C**) $C_{10}Cl_6$, and (**D**) mixture of $C_{10}Cl_8$, $C_{11}Cl_6$, and $C_{13}Cl_6$. (**E**,**F**) Zoom-in spectra showing the isotopic patterns of $[M - 2Cl + 3Na]^+$ ion of $C_{11}Cl_6$ (**E**) and $[M - 3Cl + 4Na]^+$ ion of $C_{13}Cl_6$ (**F**). Analyte concentration: $C_{10}Cl_4$, 10 μg/mL; $C_{10}Cl_5$, 0.1 μg/mL; $C_{10}Cl_6$, 1 μg/mL; $C_{10}Cl_8$, 0.33 μg/mL; $C_{11}Cl_6$, 0.33 μg/mL; and $C_{13}Cl_6$, 0.33 μg/mL. The peaks corresponding to the analytes are labeled in the mass spectra.

cationization of SCCPs in positive-ion MALDI follows a chloride-to-alkali exchange mechanism, which has also been observed in previous reports [38–41]. The singly charged alkali cations substitute a H atom or multiple Cl atoms in a SCCP molecule and the redundant alkali cations make the resulting adduct positively charged. Interestingly, the ion of $[M - nCl + (n - 1)Na]^+$ is not frequently observed in MALDI-TOF MS and its formation mechanism is still not very clear. We speculate that it may be related to the formation of dimers of SCCPs in MALDI. For example, the $[M - 2Cl + Na]^+$ ion may result from the formation of $[2M - 4Cl + 2Na]^{2+}$ ion (see Fig. S10). This speculation was also supported by the observation of SCCP dimers in the mass spectra (Fig. S11). In addition, some unassigned noise peaks were also observed in the mass spectra, which might be produced from the matrix or unidentified ion fragments of SCCPs.

We also characterized the isomers of SCCPs by MALDI-TOF MS. Fig. S12 shows the mass spectra for three different isomers of $C_{10}Cl_6$ as an example. The MS was unable to directly separate SCCP isomers due to their same mass. However, different peak patterns were observed for different isomers in MALDI, suggesting that the ion fragmentation of SCCPs was affected by the location of Cl atoms in the carbon chain.

3.3. Selection of internal standard

MALDI often suffers from its unsatisfactory reproducibility, so it is important to use a proper IS for calibration. In general, an IS should have similar properties with target analytes but do not interfere with the detection of target analytes. In previous reports, $^{13}C_{10}$-*trans*-chlordane was normally used as an IS for SCCPs [27,36,42]. However, this isotope-labeled compound is not easily available and still has some different nature from SCCPs. Here we propose a new idea for the selection of IS in SCCP analysis. Since SCCPs include numerous congeners, it is possible to select a specific individual SCCP congener as an IS as long as it satisfies the following requirements: first, it has good MS responses and does not interfere with the detection of other SCCP congeners; second, it does not present or is not found in the samples. For the second requirement, one may need to make a pre-screening of the samples to check whether the selected SCCP congener is present in the samples. Such a pre-screening is very easy to perform with MALDI-TOF MS due to the simple and high-throughput nature of MALDI-TOF MS technique. In this way, the IS will have a higher similarity with the target analytes than $^{13}C_{10}$-*trans*-chlordane (because itself is a SCCP congener) to ensure a better calibration. In this study, we found that $C_{10}Cl_4$ could well satisfy the requirements mentioned above, so it was used as an IS for analysis of SCCPs. Note that in other applications with different real samples, different SCCP congeners may be used as IS depending on which congener can meet the requirements mentioned above.

3.4. Optimization of amount of matrix and IS

To obtain optimal analytical results, the effects of the amount of matrix and IS were investigated (Fig. 3 and Table S3). Fig. 3A shows the critical role of the IS in MALDI. Without using IS, the linearity of the MS response with the analyte concentration was rather poor ($R = 0.756$). Once the IS was used (even at a low concentration), excellent linearity was obtained with all R values > 0.98. This clearly demonstrates the effectiveness of the use of $C_{10}Cl_4$ as an IS in MALDI analysis of SCCPs. Increasing the IS concentration did not affect the linearity but slightly increased the slope of the calibration curve. Considering that the environmental concentration of SCCPs may reach a high level, the IS concentration was set at a relative high concentration (10 μg/mL). From Fig. 3B, increasing the amount of graphene matrix from 0.5 to 2 μg did not exert significant effect on the calibration curve, and 1 μg of graphene was used as matrix in each measurement.

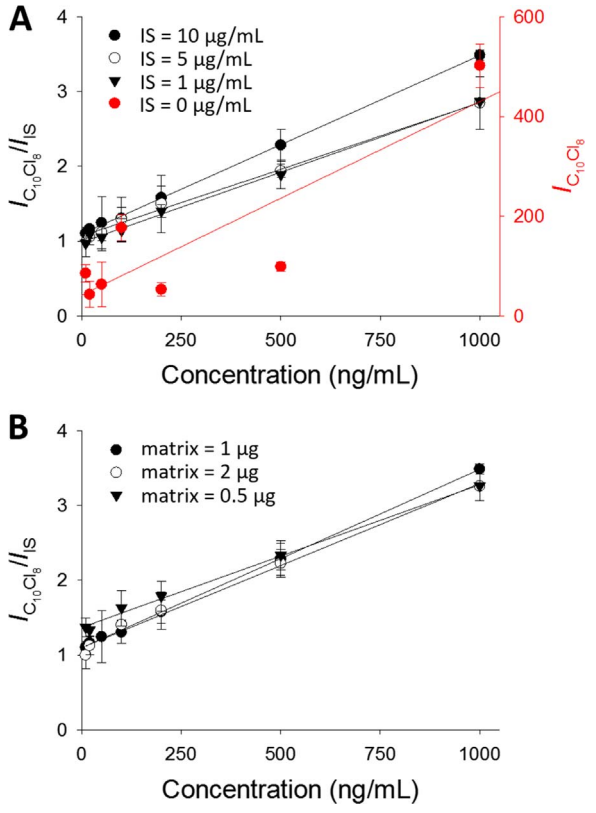

Fig. 3. Effects of the amount of IS (**A**) and graphene matrix (**B**) on the calibration curve of $C_{10}Cl_8$. The amounts of graphene matrix and IS were in the range of 0.5–2 μg and 0–10 μg/mL, respectively. In **A**, the calibration curve and *y*-axis for IS = 0 μg/mL (i.e., with no IS) is marked in red. The parameters for the calibration curves are given in Table S3. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

3.5. Analytical performance

The aim of this study is to provide a rapid screening method for SCCPs rather than to accurately quantify SCCPs or to fully resolve SCCP congener groups. So we selected limited SCCP congener groups as target analytes rather than giving a comprehensive congener profile of SCCPs. Here we did not use any chromatographic techniques to separate SCCP congener groups (in fact, there have been no instrumental methods capable of full separating or differentiating SCCP congener groups even by GC × GC). Notably, different SCCP congener groups produced different fragment ion patterns (see Fig. 2 and Table S2). Thus, it is possible to achieve a congener group-level screening of SCCPs by selecting proper *m/z* values. This may be a special ability of MALDI differing from GC-MS, which avoids the use of mathematical deconvolution methods to eliminate the interferences [13–16]. The peaks used in screening are marked in Table 1. These peaks were selected to avoid interference from background noises and other congener groups as much as possible.

Table 1 lists the analytical figures of merit for the selected SCCP congeners under the optimized conditions. For all congeners, excellent linearity ($R > 0.98$) was obtained over a concentration range wider than three magnitudes. The detection limits (LODs), defined as the concentrations at S/N = 3, for all SCCP congeners were lower than ppb levels (0.1–5 ng/mL). These LODs can fully meet the demand for routine monitoring of SCCPs in environmental media [43,44]. The shot-to-shot ($n = 20$) and sample-to-sample RSDs ($n = 15$) obtained on the graphene matrix were in the range of 16.0–26.8% and 22.1–31.6%, respectively. These results should be satisfactory taking into account the general concern about the reproducibility of MALDI-TOF MS. It should also be noted that, in previous reports using graphene as a MALDI matrix, poor reproducibility was usually obtained due to the aggregation of graphene [26,31,45]. In this study, better reproducibility was obtained than that in previous reports due to the improved homogeneity of the matrix (see Fig. S6).

We have also compared the present method with previously reported methods for the analysis of SCCPs [7,11–13,17]. As listed in Table 2, the LODs were lower than those obtained with all other methods. As analytical sensitivity is still a major concern in analysis of SCCPs, such an improvement should be of high value for SCCP studies. Noteworthily, these LODs were achieved by direct MALDI-TOF MS with no sample enrichment, and they may be further lowered by integrating preconcentration procedures in the methodology development (e.g., using a surface-enhanced laser desorption/ionization (SELDI) probe) [46–50].

More importantly, MALDI-TOF MS provides a much faster and higher-throughput method for screening of SCCPs than other techniques. It can be applied to directly screen complex real samples without column purification (see Fig. S13). Column purification has been included in all previously reported methods for analysis of SCCPs. As column purification is a rather time-consuming and laborious step, the present method can cut much time for analysis of SCCPs in complex samples. As shown in Table 2, the instrumental time of MALDI-TOF MS for a single sample can be less than 30 s (*Note*: if the sample preparation, sample loading, and data processing are included, the whole analysis time is less than 1.5 h). Although the instrumental time for the APCI-qTOF-HRMS method is also short (< 1 min), rigorous sample purification is still required, which actually significantly extends the total analysis time. At the same time, GC-MS methods can provide better reproducibility and more accurate mass values than MALDI-TOF MS. Therefore, with some compromise in reproducibility and but higher sensitivity and throughput, the MALDI-TOF MS method should be particularly suitable for fast and preliminary screening of samples.

In addition to SCCPs, we have also examined the application potential of this method for MCCPs and LCCPs. The results are shown in Fig. S14. The method has been successfully applied in detection of an MCCP and two LCCP formulation group. The application potential of

Table 1
Analytical figures of merit for typical SCCP congeners obtained by MALDI-TOF MS.

Congener	*m/z*[a]	Linear range (ng/mL)	R^2	LOD (ng/mL)[b]	Shot-to-shot RSD ($n = 20$)[c]	Sample-to-sample RSD ($n = 15$)[d]	Recovery (%)[e]
$C_{10}Cl_5$	275.2; 360.0*	2–1 × 10^3	0.995	0.5	23.2%	28.0%	88.4
$C_{10}Cl_6$	301.1; 334.4*; 359.3; 393.3	1–2 × 10^3	0.984	0.1	16.0%	22.1%	119.7
$C_{10}Cl_8$	332.5*; 341.2	5–1 × 10^3	0.998	0.6	24.8%	31.6%	93.4
$C_{11}Cl_6$	323.6*; 361.2; 348.5	10–5 × 10^3	0.999	1	20.3%	29.1%	110.2
$C_{13}Cl_6$	339.3; 376.6*	50–1.5 × 10^4	0.990	5	26.8%	23.3%	111.9

[a] The peaks used for quantification are marked with asterisk.
[b] The LODs presented here were instrumental LODs obtained based on the highest peaks of the analytes.
[c] The shot-to-shot RSDs were measured based on 20 shots at different locations on the matrix. The analyte concentration was the same as in Fig. 2.
[d] The sample-to-sample RSDs were measured based on 15 samples in different batches. The analyte concentration was the same as in Fig. 2.
[e] The recoveries were determined with indoor dust samples ($n = 3$). The spike concentration was the same as in Fig. 2.

Table 2
Comparison of analytical performance of the present method with previously reported methods.

Method	LOD	RSD	Instrumental analysis time[a]	Column chemistry	Throughput
MALDI-TOF MS (this work)	0.1–5 ng/mL	16.0–26.8%	< 30 s	no	high
HRGC-EI/HRMS [7]	33 ng/g	≤ 10%	70 min	yes	low
GC-ECNI MS [11]	2.9–9.2 ng/g	13%	46 min	yes	low
GC × GC-ECNI-HRTOF-MS [12]	3.7 ng/g	2–10%	85 min	yes	low
APCI-qTOF-HRMS [13]	20–1.2 × 10^3 ng/mL	1–10%	1 min	yes	low
GC-NCI-qTOF-HRMS [17]	24–81 ng/mL	> 10%	35 min	yes	low

[a] The instrumental analysis time refers to the time that the instrument is running in a single analysis and does not include the sample preparation, sample loading and data processing time.

the present method in the analysis of MCCPs and LCCPs needs to be further verified in future studies.

3.6. Fast screening of SCCPs in indoor dust samples

To show the real application of the method, we used it to screen SCCPs in indoor dust samples. Modern people spend most of time indoors and dust is an important indicator of the indoor environment to assess the human exposure to indoor pollutants [11,35,51–54]. Therefore, indoor dust was used as a target sample matrix in this study. The samples were collected from 20 apartments and offices in Beijing. As shown in Fig. 4A, a large number of peaks were detected from *m/z* 252–400 in MALDI-TOF MS. Among them, we have successfully identified 5 SCCP congener groups at *m/z* 275.2, 360.0; 323.6, 361.2; 332.5, 341.2; 339.3, 376.6; and 334.4, 359.3, 393.3, corresponding to $C_{10}Cl_5$, $C_{11}Cl_6$, $C_{10}Cl_8$, $C_{13}Cl_6$, and $C_{10}Cl_6$, respectively. The $C_{10}Cl_4$ (i.e., the IS) was not detected in unspiked samples (Fig. S15). The concentrations of these SCCP congener groups were determined to range from 0 to 117 μg/g (see Table S4). This concentration range was at the same level as that reported in previous reports [11,35]. Furthermore, we have compared two sample preparation strategies (i.e., with and without column purification) in analysis of indoor dust samples. Column purification could reduce some background noises in the mass spectra (Fig. S13), but it did not significantly affect the screening results of SCCP congeners (see Fig. S16). The recoveries of SCCP congener groups determined in indoor dust samples were in the range of 88.4–119.7% (Table 1). These results demonstrate the capability of MALDI-TOF MS to directly analyze real samples.

To verify the screening results obtained by MALDI-TOF MS, we also measured the concentrations of the SCCP congeners in indoor dust samples by GC-NCI-qTOF-HRMS (see Section 1.2 in Supporting information for experimental conditions). The concentrations determined by GC-NCI-qTOF-HRMS are also given in Table S4. As shown in Fig. 4B and Table S5, an excellent consistency was obtained between the concentrations determined by these two techniques ($R > 0.996$ with the slope 0.98 ± 0.09), definitely demonstrating that the screening results with MALDI-TOF MS were highly accurate. The successful verification of the results by GC-NCI-qTOF-HRMS (with column purification) and

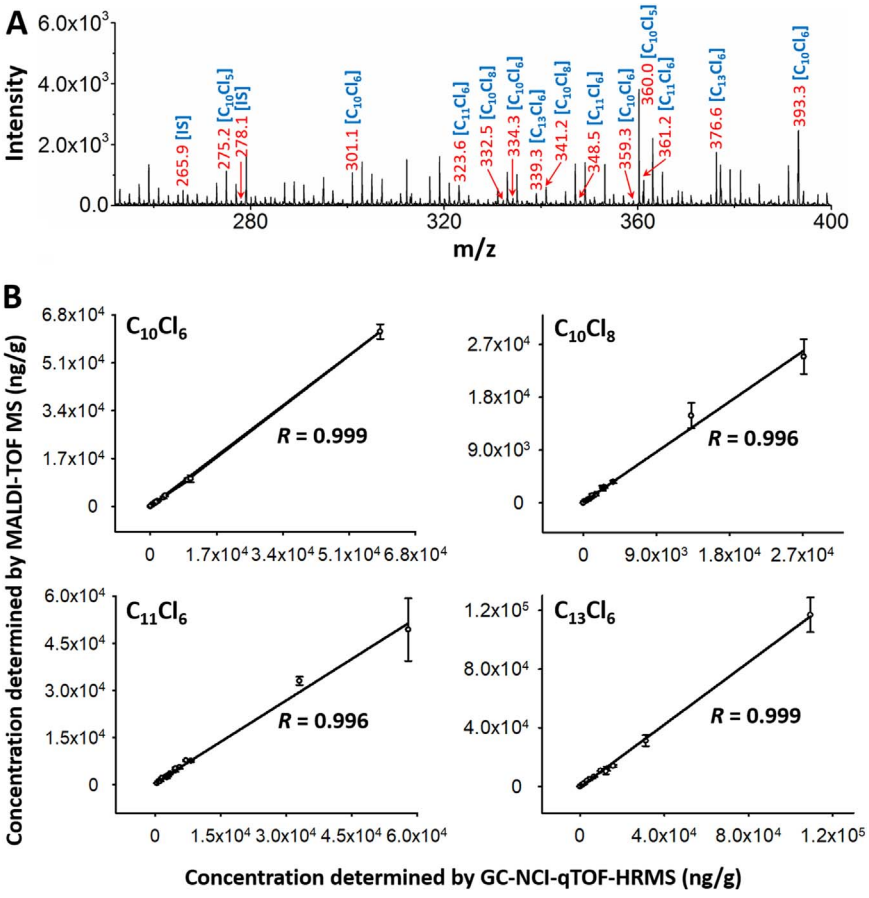

Fig. 4. Rapid screening of SCCPs in indoor dust samples by MALDI-TOF MS with graphene as a matrix. (**A**) A typical mass spectrum for an indoor dust sample. The peaks for the identified SCCP congeners are labeled in the mass spectrum. (**B**) Comparison of the concentrations of SCCP congeners determined by using MALDI-TOF MS and GC-NCI-qTOF-HRMS. The parameters for the calibration curves are given in Table S5.

the satisfactory recoveries (88.4–119.7%) proved that there was no significant matrix interference to the analysis of SCCPs in this study.

The MALDI-TOF MS method permits a fast and high-throughput monitoring of human exposure levels to SCCPs. Based on the obtained concentrations of SCCP congeners, we made a preliminary assessment of the human exposure to SCCPs via indoor dust ingestion (see Section 1.3 and Table S6 in Supporting information for the details for exposure assessment) and calculated the daily intake (EDI; ng/kg bw/day) of SCCP congeners through dust ingestion (see Table S7). The concentration of individual SCCP congener groups in indoor dusts could reach 1.2 $\times$ 10^2 ug/g. However, the calculated EDI values of SCCP congeners were overall lower than the oral reference dose of SCCPs (100 mg/kg bw/day) established by the European Parliament Council [44], suggesting that the exposure of SCCPs via the indoor dusts in Beijing may have low risk for human health.

4. Conclusions

In summary, we have developed a MALDI-TOF MS method for fast screening of SCCPs in indoor dust samples. The use of graphene as a MALDI matrix and 2,5,6,9-tetrachlorodecane as an IS greatly enhanced the LDI efficiency and improved the accuracy of analysis. Compared with previously reported methods for analysis of SCCPs, the present method has the following distinct advantages: (1) high speed (instrumental analysis time < 30 s for single run) and high throughput; (2) capable of directly analyzing real samples with no need of column purification; (3) high sensitivity (LODs at sub-ppb levels); and (4) high accuracy. Therefore, it provides a promising tool for SCCP studies. Furthermore, by using such a complex group of compounds as target analytes, this work demonstrates the potential of graphene to be a new generation of matrices in MALDI-TOF MS.

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Notes

The authors declare that they have no conflict of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.talanta.2017.11.055.

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