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Short communication

Thermal desorption extraction proton transfer reaction mass spectrometer (TDE-PTR-MS) for rapid determination of residual solvent and sterilant in disposable medical devices

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ABSTRACT

Thermal desorption extraction proton transfer reaction mass spectrometer (TDE-PTR-MS) has been exploited to provide rapid determination of residual solvent and sterilant like cyclohexanone (CHX) and ethylene oxide (EO) in disposable medical devices. Two novel methods are proposed for the quantification of residual chemicals in the polyvinyl chloride infusion sets with our homemade PTR-MS. In the first method, EO residue in the solid infusion sets (y, mg set^{-1}) is derived through the determination of EO gas concentration within its packaging bag (x, ppm) according to the correlative equation of $y = 0.00262x$. In the second one, residual EO and CHX in the solid infusion sets are determined through a time integral of their respective mass emission rates. The validity of the proposed methods is demonstrated by comparison with the experimental results from the exhaustive extraction method. Due to fast response, absolute concentration determination and high sensitivity, the TDE-PTR-MS is suggested to be a powerful tool for the quality inspection of disposable medical devices including the quantitative determination of residual solvent and sterilant like CHX and EO.

1. Introduction

For a considerable time, most disposable medical devices (DMDs) such as catheters, syringes and dialysis sets have been made of polyvinyl chloride (PVC) [1]. It was estimated that the medical PVC usage in Europe took up about 26% of the total medical polymers in 2005. However, some chemicals including the solvent cyclohexanone (CHX) and the sterilant ethylene oxide (EO) are frequently used in the manufacturing processes of DMDs. CHX is an adhesive solvent commonly used to bond different parts in assembling DMDs [2]. It can remain in the joints and subsequently migrate into the stored solutions or leach to the internal airspace of medical devices [3–5]. A very recent animal experiment reported that the clinical CHX exposure can produce cardiovascular, neurological and edema morbidities [6], and it is potentially tumorigenic and mutagenic upon exposure [4]. However, to our knowledge, there is no official law or regulation for the limit of CHX residues in medical devices except that a limit of 5 mg CHX for a 250 mL plastic containers in parenteral medical use was recommended by the European Pharmacopoeia [7]. In addition to CHX, EO is often applied in the sterilizing course of medical devices [8]. Currently, EO sterilization accounts for around 50% of the market in the USA due to its effectively bactericidal, sporicidal, and virucidal activity [9]. Studies have indicated that EO is carcinogenic and mutagenic upon exposure [10]. In view of its toxicity, the ISO 10993-7:2008(E) [11], a standard concerning the biological evaluation of medical devices, specifies the allowable amounts of EO residue in various medical devices. Thus, DMDs have a potential health risk arising from the residue of CHX and EO.

Due to the potential harm, the determinations of total CHX and EO residues are of importance for quality assessment of medical devices. The analytical methods for residual CHX in medical devices mainly include gas chromatography (GC) [3], gas chromatography–mass spectrometry [5] and high performance liquid chromatography [4]. Quantifying residual EO in medical devices is based on GC technique combined with a variety of pretreatments including vacuum extraction [12], simulated-use extraction [11,13], exhaustive extraction [11,14] and solid-phase microextraction [15]. The extraction steps involved in the aforementioned methods make the CHX and EO residual analysis considerably complicated and time consuming.

In our previous study [16], proton transfer reaction mass spectrometry (PTR-MS) was used to rapidly discriminate and inspect

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whether the CHX is used in DMDs like infusion sets through the direct detection of gaseous CHX within the packaging bag. However, the total CHX residues in the solid PVC medical devices remain unknown. In this paper, two novel methods are proposed for the determination of CHX and EO residues in the solid infusion sets based on thermal desorption extraction PTR-MS (TDE-PTR-MS), which is similar to the aerosol analysis by PTR-MS described by Holzinger et al. [17]. In the first method, as long as the concentration of gaseous EO within the packaging bag of the infusion set is measured, the total EO residue in the solid infusion set can be derived according to a correlative equation associating gaseous EO concentration within the packaging bag with the EO residue in the solid infusion set. Due to CHX mainly presenting nearby the joints of infusion sets, this method is not suitable to obtain the residual CHX in the solid infusion set. Thus, the second strategy is brought forward, i.e., the CHX and EO residues in the solid infusion set can be directly obtained through a time integral of the chemical residue mass emission rates monitored by PTR-MS. The validity of the proposed methods is evaluated by comparison with the experimental results from the standard exhaustive extraction method. With TDE-PTR-MS technique, the determination of residual CHX and EO in the DMDs can be achieved with little sample pretreatment and no calibration. This shows that TDE-PTR-MS can apply to the quality inspection of DMDs.

2. Experimental

2.1. PTR-MS apparatus

The present study was performed using a homemade PTR-MS apparatus as described in our previous work [16,18] and a detailed description of PTR-MS technique can be found elsewhere [19–22]. Briefly, in the PTR-MS the reactant ions H_3O^+ were produced by a hollow cathode discharge through water vapor, and then were injected to the drift tube. When a sample gas including analyte M was introduced to the drift tube, M can undergo proton transfer reaction with H_3O^+ if the proton affinity of M exceeded that of H_2O. After passing through a differentially pumping intermediate chamber, the ions at the end of drift tube were leaked into the vacuum chamber and detected by the quadrupole mass spectrometer. According to the well-established ion-molecular reaction kinetics, the absolute concentrations of analyte M can be determined even if its concentration is rather high [16,19].

For typical experimental conditions, the pressure in the drift tube was kept at 1.0 Torr and the reduced-field E/N was set to be about 140 Td (1 Td = 10^{-17} V cm^2 molecule^{-1}). The inlet gas was at a flow rate of 6 mL min^{-1}.

2.2. DMDs and chemical agents

As typical examples of DMDs, two kinds of PVC infusion sets were used and labeled as Brands A and B. The infusion sets of Brand A were sterilized for 12-h by the manufacturer with 99% EO kept at 50 °C and 60% relative humidity. The Brand B was obtained from a pharmacy, and it also had been sterilized with EO as described on its package bag. In some cases, the gaseous EO concentration within the packaging bag of the infusion set greatly exceeded the upper detectable limit of PTR-MS, so the 10 mL gas from the packaging bag was sampled with a gastight syringe and injected to a 1.44 L flask where it was thoroughly mixed before introduction to the PTR-MS. In addition, the packages containing the infusion sets were punctured directly via a syringe needle at the inlet of PTR-MS.

In the experiments, pure EO gas and ethylene glycol (EG) diluted in nitrogen were used to confirm and discriminate the origin of ionic mass spectra in the PTR-MS measurements, and these gases were purchased from the Nanjing Special Gas Co. (Nanjing, China).

2.3. Exhaustive extraction with thermal desorption

Previous studies showed that the exhaustive extraction method performs with better accuracy than the simulated-use extraction method to determine the residual EO within solid medical devices [13], so in present measurement the exhaustive extraction with thermal desorption method was utilized according to the standard ISO 10993-7:2008(E). The EO residues in the solid infusion sets were determined immediately after quantification of the gaseous EO concentration in the internal airspace of the packaging bag. A complete infusion set was firstly weighed using an electronic balance with the precision of ±0.01 mg, and then some small slices of solid material taken from the infusion set were also weighed. In order to avoid the loss of EO due to volatilization, the weighing operations were completed as quickly as possible. The small slice of solid material was rapidly sealed into a 1.44 L flask, followed by 30 min thermal extraction at a temperature of 50 °C. After that, the flask was naturally cooled to room temperature, and the gaseous EO inside the flask was measured by PTR-MS. The same procedures were repeated with 99.999% nitrogen evacuation for the same slice of solid material until the EO concentration in the flask was less than 10% of the first measurement.

2.4. Residue determination via mass emission rate

To measure the residual CHX or EO in the solid infusion set, another method was used. A whole infusion set was swept using ambient air as carrier gas at a flow rate Q (m^3 h^{-1}) so as to take out CHX or EO released from the infusion set. Then the mass emission rate $m(t)$ of CHX or EO can be expressed as $m(t) = c(t)Q$ with a unit of mg h^{-1}, where $c(t)$ (mg m^{-3}) is the concentration of CHX or EO in the carrier gas. Thus, the residual CHX or EO can be in principle derived by a time integral of the mass emission rate. In the measurement, a complete infusion set of Brand A, containing 0.50 mg EO as predetermined by exhaustive extraction method, was placed into a 1.44 L flask with three ports for carrier gas inlet, sample placement and carrier gas outlet to the PTR-MS. Meanwhile, the gas inside the flask was well mixed with a magnetic stirrer. The flow rate of the carrier gas Q was 0.018 m^3 h^{-1}, and the concentration of CHX or EO, leached from the infusion set in the flask and involved in the outlet carrier gas, was monitored in real-time by the PTR-MS.

3. Results and discussion

3.1. Identification of CHX and EO

The diluted gas inside the packaging bag of Brand A was measured by PTR-MS, and the mass spectra are shown in Fig. 1a. The mass spectra of the gas leached from a small slice of solid material after thermal desorption are given in Fig. 1b. It can be seen that the two spectra are nearly same, suggesting that the gas in the package originated from the emission of chemical compounds in the solid infusion set. In general, in PTR-MS spectra the impurity ions mainly include NO^+, O_2^+ and $H_3O^+(H_2O)$, which can be observed at m/z 30, 32 and 37, respectively. The ionic peaks at m/z 81, 99 and 117 arose from residual solvent CHX according to our previous PTR-MS investigation [16]. And the peak at m/z 45 was assigned as the protonated EO, $C_2H_4OH^+$.

In addition, there is a weak peak at m/z 63. The corresponding ions may be the cluster ions $C_2H_4OH^+(H_2O)$ formed through the ligand switching reaction of EO with H_3O^+ (H_2O) [19], and this was evidenced through detecting EO gas in our PTR-MS measurement.

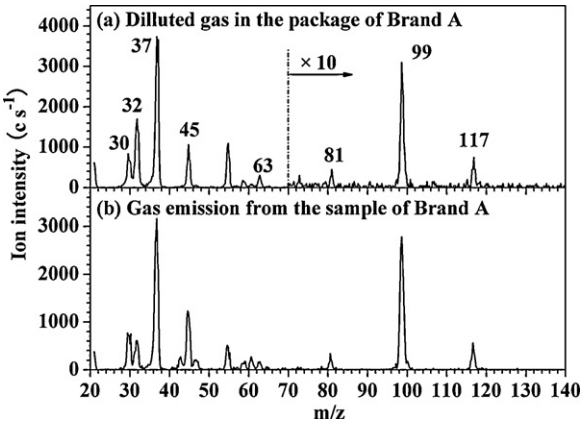

Fig. 1. Mass spectra measured by PTR-MS from Brand A for (a) the diluted gas in the package (b) the gas releasing from the small slice of solid material in the flask after it was extracted for 30 min at 50 °C.

Table 1
Study of extraction temperature effect on EO residues in the slices of Brand A.

Extraction temperature (°C)	EO residues (ng mg^{-1})			Mean (RSD%)
	Slice 1	Slice 2	Slice 3	
37	29.1	9.6	7.9	15.5 (75.8)
50	33.2	31.3	27.9	30.8 (8.7)
70	22.0	17.5	29.9	23.1 (27.1)
100	21.5	32.7	38.5	30.9 (28.0)

The other possibility is that the ions at *m*/*z* 63 is the protonated EG because previous study showed that the EG, with a molecular weight 62, usually exists in EO sterilized medical devices [23]. But when the EG gas was measured in our PTR-MS experiments, the protonated EG was not observed probably due to collision-induced dissociation, thus the possibility of *m*/*z* 63 belonging to the protonated EG was excluded.

3.2. Extraction time and temperature

To obtain an appropriate temperature of thermal desorption in the exhaustive extraction experiments, the 12 weighed slices were taken from the same infusion set of Brand A and were divided into four groups, and the slices in the four groups were thermally extracted for 60 min in the flask at temperature 37, 50, 70 and 100 °C, respectively. The EO residues inside the slices are shown in Table 1. It can be seen that the efficiency of exhaustive extraction at 37 °C was the worst. Considering the highest EO residues and reproducibility, the optimum extraction temperature was chosen to be 50 °C.

Likewise, the extraction time was optimized at an extraction temperature of 50 °C. The measurement results are listed in Table 2. It can be seen that the extraction time of 10 min resulted in the lowest EO residues inside the slices. However, no significant differences were found using the longer extraction time, from which the shortest extraction time of 30 min was selected for fast measurements. Thus, to minimize potential errors caused by the extraction time and temperature, the sample slices were thermally extracted for 30 min at 50 °C.

Table 2
Study of extraction time effect on EO residues in the slices of Brand A.

Extraction time (min)	EO residues (ng mg^{-1})			Mean (RSD%)
	Slice 1	Slice 2	Slice 3	
10	1.4	11.7	12.2	8.4 (72.3)
30	39.5	41.5	36.6	39.2 (6.3)
50	32.6	33.7	27.8	31.4 (10.0)
70	32.4	34.6	38.5	35.2 (8.8)

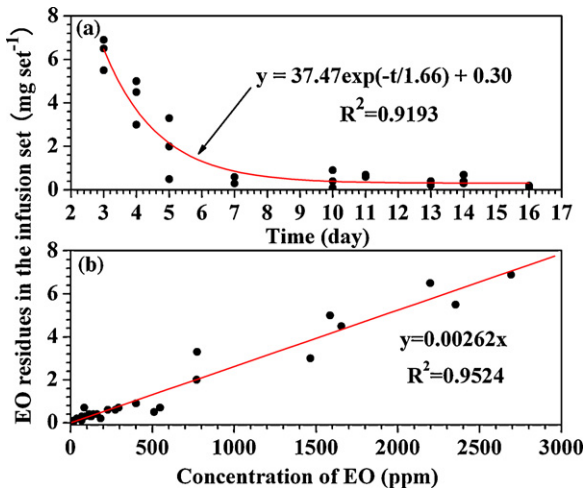

Fig. 2. In the infusion set of Brand A, (a) the EO residues variation along with stock time and (b) the correlation between EO residues and the concentration of EO gas within the packaging bag.

3.3. Determination of residual EO with two methods

3.3.1. EO residues obtained via determining concentration of EO in the package

The variation of the total EO residues in the solid infusion set of Brand A along with stock time was obtained via exhaustive extraction method and the results are shown in Fig. 2a. According to Fig. 2a, the total EO residues decrease exponentially with the time after sterilization. So, in order to reach the allowable EO residue <4 mg set^{-1} as mandated by the ISO 10993-7:2008(E), the Brand A should be placed in normal conditions for at least 4 days before use.

Moreover, it was discovered that the EO residues inside the solid infusion set was positively correlated to the concentration of gaseous EO in the package (see Fig. 2b). Their correlative equation is $y = 0.00262x$, where y (mg set^{-1}) is the total EO residues in the solid infusion set and x (ppm) is the EO concentration within the packaging bag of the infusion set. This may result from the fact that the EO gas in the package of the infusion set quickly gets into equilibrium between adsorption and desorption in normal conditions. Therefore, it is possible to carry out fast detection of EO residues in DMDs by direct determination of EO gas in the package. In order to check the validity of this method, a comparison of the EO residues of Brand B from the correlative equation and exhaustive extraction is given in Table 3. As can be seen in Table 3, the EO residues obtained from the correlative equation are slightly smaller than those determined with exhaustive extraction, and the quantitative agreement is satisfactory with relative error from 4% to 27%. However, it should be noted that the correlative equations might be a little different for the DMDs from different manufacturers, because they may use different raw materials and production techniques. To summarize, as long as the correlative equation of the EO residues in the DMDs and the concentration of EO in the package is obtained, it is easy to determine the residual EO in DMDs quickly and accurately by direct determination of EO gas in the package.

3.3.2. EO residues measurement via emission test

Fig. 3a shows the emission process of residual EO in the complete infusion set of Brand A with 0.50 mg EO residues predetermined through exhaustive extraction method. However, the emission rate in our measurements could not be well fitted by an empirical model

Table 3
The EO residues in the solid infusion set of Brand B measured with two methods.

Infusion set No.	Concentration of EO in the package (ppm)	EO residues via exhaustive extraction (mg set^{-1})	EO residues from correlative equation (mg set^{-1})	Relative error
Infusion set 1	93	0.33	0.24	27%
Infusion set 2	82	0.29	0.22	24%
Infusion set 3	95	0.26	0.25	4%

[24]. Thus, a new modified model was adopted as expressed by Eq. (1).

$$(t)=Qc(t)=Q\{A[1-\exp(-Bt)]-C[1-\exp(-Dt)]-E[1-\exp(-Ft)]\} \quad (1)$$

where $c(t)$ is the concentration in the flask at a given time t (h), parameters A, C and E are the linear parameters (mg m^{-3}) and B, D and F are the rate parameters (h^{-1}). Therefore, the residual EO inside the solid infusion set can be calculated through definite integral of the mass emission rate, $m(t)$, on time t from 0 to 16.8 h where $c(t)$ decayed to zero (see red line in Fig. 3a). (For interpretation of the references to color in text, the reader is referred to the web version of the article.) Through the integral method, the EO residues inside the solid infusion set were 0.47 mg, which was consistent with the value gained by exhaustive extraction method. Therefore, this method can be applied to accurately determine the residual EO in DMDs.

3.4. Determination of residual CHX via emission test

To the best of our knowledge, there is no standard method to determine the residual CHX in the DMDs. In current research we also tried to do the same exhaustive extraction with thermal desorption to obtain the CHX residues inside the solid infusion set. Six weighed slices taken from the different parts of the same infusion set of Brand A were respectively placed in a sealed flask and then heated at 100 °C for 1 h. The obtained results (CHX residues inside the slices from 72 to 671 ng mg^{-1}) show that the amount of CHX residing in the joints is far higher than that in the other parts of the infusion set. This is because the CHX solvent is only applied at the joints of infusion sets. Therefore, the residual CHX in the infusion set cannot be quantified through the exhaustive extraction method.

It has been confirmed above that the EO residues inside the solid infusion set can be accurately measured through the integral of EO mass emission rate. Therefore, the similar emission experiment was also done to determine the residual CHX in the solid infusion set of Brand A. The emission rate and the fitted equation are shown in Fig. 3b. Through the same calculation method, 0.73 mg CHX residues were obtained.

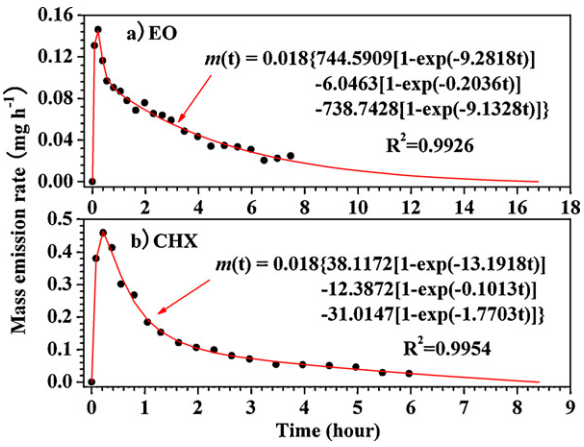

Fig. 3. The mass emission rate of EO and CHX released from a complete infusion set of Brand A as a function of time.

4. Conclusion

The potential of using TDE-PTR-MS for the determination of residual CHX and EO in the solid PVC infusion sets was demonstrated. There are two novel methods proposed to quantify residual chemicals in the solid infusion sets. (1) Based on the correlative equation between the residual EO in the solid infusion set and the concentration of EO gas in packaging bag of the infusion set, the EO residues in the infusion sets can be quickly measured through determining EO gas in the package. (2) By time integral of the chemical residues emission rate, the amount of residual EO and CHX inside solid infusion sets can be obtained. These two methods have been validated by comparison with the exhaustive extraction method. The analytical procedures are quick, sensitive and reproducible with little sample preparation. Thus, TDE-PTR-MS is very promising to become a powerful tool for the quality control of the DMDs including the inspection of residual solvent and sterilant like CHX and EO.

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References

[1] X. Zhao, J.M. Courtney, Update on Medical Plasticised PVC, iSmithers, UK, 2009.
[2] J. Mraz, E. Galova, H. Nohova, D. Vitkova, Uptake, metabolism and elimination of cyclohexanone in humans, Int. Arch. Occup. Environ. Health 66 (1994) 203–208.
[3] R.P. Snell, Gas-chromatographic determination of cyclohexanone leached from hemodialysis tubing, J. AOAC Int. 76 (1993) 1127–1132.
[4] F. Khalfi, T. Dine, M. Luyckx, B. Gressier, C. Brunet, L. Ballester, M. Cazin, J.C. Cazin, Determination of cyclohexanone after derivatization with 2,4-dinitrophenyl hydrazine in intravenous solutions stored in PVC bags by high performance liquid chromatography, Biomed. Chromatogr. 12 (1998) 69–72.
[5] D.A. Story, J. Leeder, P. Cullis, R. Bellomo, Biologically active contaminants of intravenous saline in PVC packaging: Australasian, European, and North American samples, Anaesth. Intensive Care 33 (2005) 78–81.
[6] C.S. Thompson-Torgerson, H.C. Champion, L. Santhanam, Z.L. Harris, A.A. Shoukas, Cyclohexanone contamination from extracorporeal circuits impairs cardiovascular function, Am. J. Physiol.: Heart Circul. Physiol. 296 (2009) H1926–H1932.
[7] J.N. Cammack, R.D. White, D.M. Wilson, J.C. Gonder, P. Hoet, Assessment of proposed cyclohexanone limits for containers, Int. J. Toxicol. 18 (1999) 157–158.
[8] G.C.C. Mendes, T.R.S. Brandao, C.L.M. Silva, Ethylene oxide sterilization of medical devices: a review, Am. J. Infect. Control 35 (2007) 574–581.
[9] http://www.anpro.com/support/indexeto.htm, January 2011.
[10] G.C.D. Mendes, T.R.D. Brandao, C.L.M. Silva, Ethylene oxide potential toxicity, Expert Rev. Med. Dev. 5 (2008) 323–328.
[11] ISO 10993-7, Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals, International Organization for Standardization, 2008.

[12] J.A. Mogenhan, Je. Whitbour, R.R. Ernst, Determination of ethylene oxide in surgical materials by vacuum extraction and gas chromatography, J. Pharm. Sci. 60 (1971) 222–224.
[13] D.T. Centola, K.I. Ayoub, N.T. Lao, H.T.C. Lu, B.F.J. Page, Variables affecting simulated use determination of residual ethylene oxide in medical devices, J. AOAC Int. 84 (2001) 512–518.
[14] A.D. Lucas, K. Merritt, V.M. Hitchins, T.O. Woods, S.G. McNamee, D.B. Lyle, S.A. Brown, Residual ethylene oxide in medical devices and device material, J. Biomed. Mater. Res. B 66B (2003) 548–552.
[15] M.P. DiCicco, B. Lang, T.I. Harper, Optimization of a novel headspace-solid-phase microextraction-gas chromatographic method by means of a Doehlert uniform shell design for the analysis of trace level ethylene oxide residuals in sterilized medical devices, Biomed. Chromatogr. 23 (2009) 647–657.
[16] Y.J. Wang, H.Y. Han, C.Y. Shen, J.Q. Li, H.M. Wang, Y.N. Chu, Control of solvent use in medical devices by proton transfer reaction mass spectrometry and ion molecule reaction mass spectrometry, J. Pharm. Biomed. Anal. 50 (2009) 252–256.
[17] R. Holzinger, J. Williams, F. Herrmann, J. Lelieveld, N.M. Donahue, T. Rockmann, Aerosol analysis using a thermal-desorption proton-transfer-reaction mass spectrometer (TD-PTR-MS): a new approach to study processing of organic aerosols, Atmos. Chem. Phys. 10 (2010) 2257–2267.
[18] C.Y. Shen, J.Q. Li, H.Y. Han, H.M. Wang, H.H. Jiang, Y.N. Chu, Triacetone triperoxide detection using low reduced-field proton transfer reaction mass spectrometer, Int. J. Mass spectrom. 285 (2009) 100–103.
[19] W. Lindinger, A. Hansel, A. Jordan, On-line monitoring of volatile organic compounds at pptv levels by means of proton-transfer-reaction mass spectrometry (PTR-MS) – medical applications, food control and environmental research, Int. J. Mass Spectrom. 173 (1998) 191–241.
[20] J. de Gouw, C. Warneke, Measurements of volatile organic compounds in the earths atmosphere using proton-transfer-reaction mass spectrometry, Mass Spectrom. Rev. 26 (2007) 223–257.
[21] S.P. Jin, J.Q. Li, H.Y. Han, H.M. Wang, Y.N. Chu, S.K. Zhou, Proton transfer reaction mass Spectrometry for online detection of trace volatile organic compounds, Prog. Chem. 19 (2007) 996–1006.
[22] R.S. Blake, P.S. Monks, A.M. Ellis, Proton-transfer reaction mass spectrometry, Chem. Rev. 109 (2009) 861–896.
[23] P.R. Hari, C.P. Naseerali, K. Sreenivasan, A sensitive estimation of residual ethylene glycol in ethylene oxide sterilized medical devices by HPLC with electrospray ionization mass spectrometric detection, J. Chromatogr. B 877 (2009) 328–332.
[24] A. Colombo, M. Debortoli, E. Pecchio, H. Schauenburg, H. Schlitt, H. Vissers, Chamber testing of organic emission from building and furnishing materials, Sci. Total Environ. 91 (1990) 237–249.