



Anal. Bioanal. Chem. Res., Vol. 7, No. 2, 185-195, June 2020.

Fast and Sensitive Determination of Acetic Anhydride in the Air Using Hollow Fiber Method

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(Received 18 May 2019 Accepted 24 October 2019)

This study aimed to introduce a new method based on hollow fiber in order to determination of acetic anhydride (AA) in the air. Hydroxylamine hydrochloride and sodium hydroxide (1:1), were used as an extraction solvent. This method was studied in the laboratory under various conditions. In order to make different concentrations of AA in the air, a standard glass chamber was used. The optimization of the sampling parameters and breakthrough volume was performed using the response surface method (RSM) and Design-Expert software (v.11.0). The results of the study indicated that the optimum sampling rate was 10 ml min⁻¹. The repeatability estimates of the proposed method including intra and inter-day were in the range of 0.079-0.11 and 0.081-0.14, respectively. The limit of detection (LOD) and the limit of quantitation (LOQ) of the examined analytes were 0.003 and 0.009 ng ml⁻¹, respectively. The storage time for the HF sampling method was seven days at laboratory temperature. The overall conclusion is that the HF sampling method showed a great sensitivity for the sampling of AA in the air. It could be assumed that HF sampling method is a fast, reliable and sensitive method and had a proper performance in the sampling AA compared to the National Institute for Occupational Safety and Health (NIOSH)-3506 method.

Keywords: Acetic anhydride, Hollow fiber, Air pollution, Response surface methodology

INTRODUCTION

Acetic anhydride (AA) is flammable and colorless liquid with a sharp odor that is used to produce cellulose acetate. It is also used as a reagent with a purity of >98% in the production of pharmaceutical substances, especially aspirin. Acute exposure to AA involves irritability at the contact point and causes severe eye, skin and respiratory irritation in humans [1]. The National Institute for Occupational Safety and Health (NIOSH) has introduced the exposure limit of 5 ppm for AA; it has an adverse effect on human health even in low amounts [2].

NIOSH has recommended the application of an

impinger for sampling AA; accordingly, a glass impinger containing 10 ml of hydroxylamine hydrochloride and sodium hydroxide as an extraction solvent is connected to a personal sampling pump with a flow rate of 0.2-1 l min⁻¹ and installed nearby the worker's breathing circuit. An identified volume of air containing AA is introduced into the glass impinger, and AA is solved in the hydroxylamine hydrochloride and sodium hydroxide solution. The aforementioned absorber is analyzed utilizing a spectrophotometer in the wavelength of 540 nm [2]. Other methods have also been done for the determination of AA in the air. In the study performed by Diggle *et al.*, photometric measurements are determined after absorption of AA in alkaline hydroxylamine [3]. In another study, a simple procedure was performed to determine AA in the air using

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thin layer chromatography, based on the absorption of AA vapors in a toluene-m-aminophenol solution, followed by a semi-quantitative m-acetyl aminophenol determination, and ultimately its determination by visual scanning [4].

These methods have some advantages and disadvantages. The standard impinger sampling method which proposed by NIOSH interferes with the work of the workers and restricts their mobility and is also likely to be damaged during sampling because of the glass structure [5]. Due to the usage of a high volume of extraction solvent (10-15 ml), this method has many drawbacks such as low sensitivity, high-priced, non-reusable and solvent demands [5,6]. Regarding the drawbacks discussed above, it is necessary to provide an easy and suitable method that does not have difficulties with the above methods. In HF sampling method, a proper solvent fills the HF to provide of the situation to absorb the analytes from the air into HF [5]. In prior studies, the HF method has been strongly used for sampling and analysis of different VOCs from water samples [7-12]. Furthermore, this method is used to extract some of the compounds, such as toluene, styrene, and benzene metabolites from the urine [13-16]. A study by Taheri *et al.* reported that HF sampling method with hydrochloric acid (0.1%) as the extraction solvent could efficiently be used for assessment of 1,1-dimethylhydrazine in the atmosphere [5]. Also, in a study by Partovi *et al.*, hollow membrane fiber was used to determine the maleic anhydride in air, and analysis was performed by high performance liquid spectrophotometric (HPLC). The results of this study showed that the proposed method can be used as a valid, rapid and effective method for sampling of maleic anhydride in the air [17]. Benefits of HF sampling method include a low volume of extraction solvent, less interference with the worker's task, less contact with the extraction solvent, lack of loss of the extraction solvent, high sensitivity of the method due to the low amount of the extraction solvent.

To the best of our knowledge, such studies have not been performed to evaluate the sampling AA in the air using HF sampling method. Consequently, in the present study, the HF sampling method based on hydroxylamine hydrochloride and sodium hydroxide solution was introduced as a new technique for sampling AA in the air. Besides, the impacts of different sampling conditions

including temperature, time, humidity and flow rate on the performance of the HF sampling method was investigated. To assess the quality of the analytical method, the Limit of detection (LOD) and limit of quantification (LOQ) values were estimated. Finally, the recommended method was compared with the standard method recommended by NIOSH-3506.

EXPERIMENTAL

Materials and Instrumentation

Polypropylene hollow fiber (with a 200 μm wall thickness, 0.2 μm pore size, 600 μm internal diameter and 52 cm length) was purchased from the Arvin Tejarat (Tehran, Iran). Hydroxylamine hydrochloride, sodium hydroxide, hydrochloric acid, acetone, ferric chloric and acetic anhydride were obtained from Merck (Germany). A silicone tube with an inner diameter of 1.2 mm was provided from Pars Tajhiz. Just before use, the extraction solvent was obtained with equal volumes of the hydroxylamine hydrochloride and sodium hydroxide solutions mixture (Only 2 h can be used). 10 ml AA and 90 ml acetone in a 100 ml volumetric flask were combined in order to make a stock solution. The study was conducted using a spectrophotometer-UV-Vis (USA, Lambda 950). Personal sampling pump and low flow pump were provided by SKC, USA. In order to present a steady flow in the chamber, a high volume air sampling pump was utilized. In order to add a defined volume of AA inside the chamber and for injecting the extraction solvent into the HF, a syringe pump (JMS SP-510, Japan) and a Hamilton syringe (USA) were utilized, respectively. A heater was used for clogging the HF. The temperature was controlled using a thermometer (Sunward ENG, Korea). In order to control the relative humidity (RH), a hydrometer (Sunward ENG, Korea) was used.

Pilot Study

A glass chamber, made by the researcher, was used to create a standard atmosphere of AA. A syringe pump was used for injections of standard solutions, and a high volume pump was connected to the outlet orifice of the chamber in order to produce constant airflow. In order to adjust the temperature of the sampling air, a small glass chamber

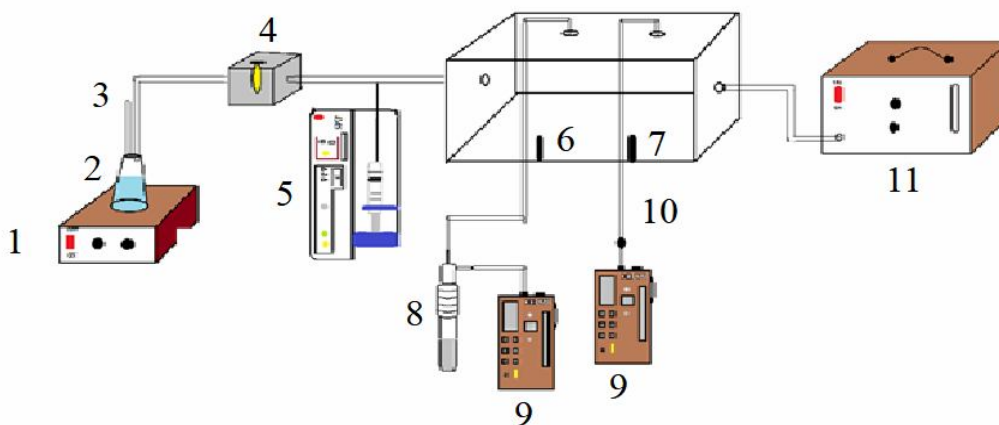


Fig. 1. A simple schematic of chamber; 1, Heater; 2, A chamber for adjusting relative humidity (RH) containing deionized water; 3, A tube for supplying fresh air; 4, A chamber containing light bulb to adjust temperature; 5, Syringe pump; 6, Digital hydrometer; 7, Digital thermometer; 8, Impinger; 9, Low flow pump; 10, Silicone tube containing hollow fiber; 11, High flow vacuum pump.

Table 1. Sampling Parameters and their Levels

Sampling factors	Temperature (°C)	Level 1	Level 2	Level 3
		Flow rate (ml min ⁻¹)	1	5
Relative humidity (%)		50	50	50
Concentration (ppm)		2	5	10
Time (h)		1	2	4

including a lamp inside was used. Also, a temperature sensor was placed inside the chamber for regular temperature monitoring. The relative humidity (RH) in the chamber was fixed to a constant value of 50% and was regularly measured by a digital hydrometer placed in the chamber. As Fig. 1 shows in the upper part of the glass chamber, two orifices were created simultaneously and sampling was carried out concurrently with the HF sampling method and the 3506-method recommended by NIOSH. In throughout analyses, RH was held steady because, according to pretest results, relative humidity had a poor and negligible impact on the sampling performance of

the suggested HF. Hence, we did not consider its effects on HF performance. Sampling parameters and their levels are shown in Table 1.

Preparation of Hollow Fiber

The HF was located in the silicone tube to provide it for sampling. First, the one end of HF was clogged using a heater [5,13,17]. Next using Hamilton syringe a defined volume, 50-100 μl , of absorption solution, was injected inside the HF and ultimately, the other end was sealed. Hollow fiber has two parts; lumen and shell (wall of a porous hollow fiber). The extraction solvent fills 80% of the

lumen volume. The air enters the lumen through the HF shell and thus the extraction solvent absorbs the acetic anhydride. The breakthrough (BT) was investigated using two HFs in sequence. The flow rate of the low flow pump was calibrated using a manual soap-bubble flow meter in the range of 1-10 ml min⁻¹. After the sampling was completed, the absorber solution was collected using a Hamilton syringe and it was carried to a test tube containing 50 µl of the ferric solution and 330 µl of extraction solvent. Finally, the solution at 540 nm wavelengths was analyzed using a spectrophotometer. The amount of AA in the rear section describes the breakthrough. The spectrophotometric analysis has numerous benefits including availability, low cost, simplicity, and no necessity for an experienced operator. The main difficulty of the spectrophotometer is low sensitivity that the great sensitivity of the suggested HF sampling method defeated this difficulty [18].

Experiments

In this study, a full factorial Design-Expert was used to evaluate the impact of different factors and their interactions on sampling efficiency. The response surface methodology (RSM) method consists of mathematical and statistical procedures based on linear or square polynomial functions to determine the optimal conditions of the studied parameters [19-23]. The central composite design (CCD) is used in RSM experimental design [19]. The optimal parameters of the HF sampling method were defined using Design Expert software (v.11.0). In order to predict optimal conditions, the following equation model was used:

$$Y = B_0 + \sum_{i=1}^n B_i X_i + \sum_{i=1}^n B_{ii} X_i^2 + \sum_{1 \leq i < j \leq n} B_{ij} X_i X_j + \varepsilon$$

where the predicted responses are shown by Y, B₀ means a content term, the coefficient of the linear variables expressed by B_i, B_{ii} is the coefficient of quadratic variable, and B_{ij} represents the coefficient of the interaction variable. [20].

In order to optimize the sampling parameters, sampling at different concentrations of analyte from 2 to 10 ppm (0.4-2 times more than the TLV recommended by NIOSH) at sampling time of 1-4 h, under a flow of 1-10 ml min⁻¹ at a temperature of 3, 15, 25 and 35 °C was done, and optimal

conditions for sampling were introduced in the mentioned areas. In introducing optimal sampling conditions, it was noted that the recommended optimal flow rate is below the flow rate leading to the breakthrough volume. The concentration of AA in the standard chamber was 0.4-2 times more than the threshold limit value recommended by NIOSH (5 ppm).

Carryover Effect

For examining the carryover effect, the HF was eluted numerous times with the absorption solution for removing the remaining analyte, and it was again analyzed by the spectrophotometer. The number of washings, after which no absorption was observed, was chosen as the optimal washing number.

Storage Time

In order to examine the storage time of the recommended HF sampling method, after optimization of the sampling conditions, sampling was done in optimal conditions. The samples were placed in sealed bottles and kept in two separate conditions laboratory temperature (24 °C) and refrigerated temperature (3 °C) and analyzed for 1, 3 and 7 days.

Method Validation

In order to estimate the accuracy of the recommended HF sampling method, sampling was performed concurrently with the HF sampling method and NIOSH-3506 method under optimized conditions and the correlation between the two methods was determined and the two methods were compared. The LOD and LOQ are described as the lowest concentration of an analyte in a sample that can be detected and determined with acceptable precision and accuracy. The LOD and LOQ are calculated using LOD = 3.3 (SD/S) and LOQ = 10 (SD/S), which SD and S mean standard deviation and slope of the calibration curve, respectively. [24]. LDR was determined to estimate the proposed method. To examine the inter-day repeatability, the sampling was conducted between days, and for intra-day repeatability, the sampling was done within a day at various concentrations but under a steady sampling condition. To represent the precision of the analysis the relative standard deviation (RSD) was used.

Table 2. Full Factorial Design Expert CCD Matrix for Sampling Parameters

RUNs	Factor 1 Concentration	Factor 2 Flow rate	Factor 3 Time	Factor 4 Temperature
1	0	0	-1	0
2	0	0	0	-1
3	-1	0	0	0
4	+1	0	0	0
5	-1	-1	-1	+1
6	0	0	0	+1
7	0	0	0	0
8	+1	+1	+1	-1
9	0	+1	0	0
10	-1	-1	+1	+1
11	0	0	+1	0
12	-1	+1	-1	+1
13	0	0	0	0

Table 3. Optimum Values and ANOVA Results of Extracted Mass in Sampling of AA with HF

Sampling variables	Parameters	Mass of extraction	Breakthrough
	Optimal temperature (°C)	21.3	23
	Optimal flow (ml min ⁻¹)	10	10
	Optimal time (h)	3.03	3
	R-squared	0.9762	0.987
	Standard deviation (SD)	0.009	0.006
	Coefficient of variant (CV)	12.84	10.74
	Predicted residual sum of squares (PRESS)	0.007	0.0025
	Adeq precision	24.44	29.77

RESULTS AND DISCUSSION

Sampling Parameters

Sine temperature, as an environmental factor, can affect the air sampling, the effect of temperature on the sampling efficiency at 3 levels of 15, 25 and 35 °C was investigated

in this study. The test steps are shown in Table 2.

The results of the ANOVA showed that the quadratic algorithm is significant (Pvalue < 0.0001). The results presented in Table 3 show optimized conditions for sampling the acetic acid in the air. The efficiency of the HF sampling method was assessed within standard deviation

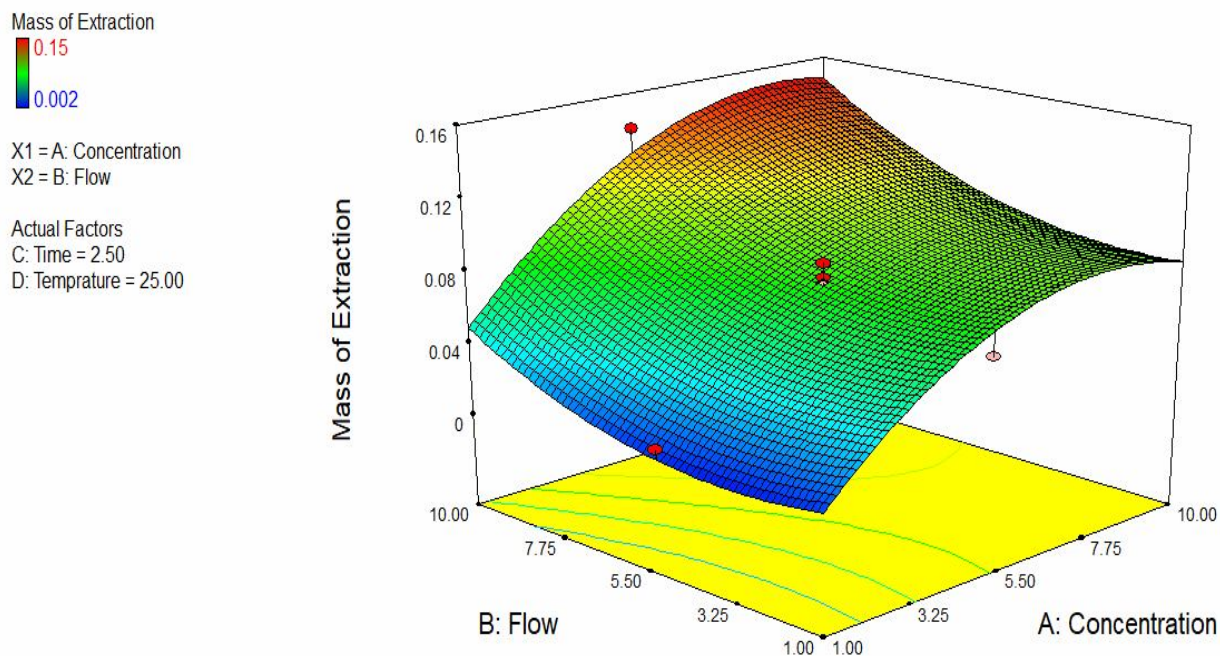


Fig. 2. Effect of interaction between flow rate with concentrations on mass of extraction in sampling of AA by HF.

(SD) and R2. In this study, the R2 was 0.976 and the SD was 0.009, indicating an appropriate fitting of the presented model. As shown in Fig. 2, concentration (A) and flow (B), as well as concentration and flow interaction, had a significant effect on the mass of extraction. This means that with an increase in concentration and flow, the mass of extraction from the hollow fiber is also increased.

The results showed that there is a significant correlation between the predicted results by the Design-Expert software and the results obtained from experiments. After optimization of the sampling conditions, experimental values were compared with the predicted values. As Table 4 shows, there is a large correlation between the experimental values and the predicted values.

Carryover Effect

Carry over is one of the problems that occurs when using a sampler repeatedly. Since HF is a sampler that can be used many times, the carry over of it has been studied [25]. The HF was washed with the absorption solution in order to eliminate the carryover effect. The quantity of extracted analyte after washing the HF is shown in Fig. 3.

The results indicated that washing HF 20 periods with absorption, raised all analytes on it.

Storage Time

Storage capacity is one of the important parameters in determining the quality of a sampling method. Sampling storage was performed in optimal conditions and samples were stored for 1, 3 and 7 days in two separate conditions. The results of Fig. 4 show that there is no significant difference between the mass of extraction from the two HFs on the first day. On the third day, samples kept in the refrigerator had a higher mass of extraction and on the seventh day, there was a greater drop in the amount of mass of extraction in HFs which stored in the laboratory temperature.

Breakthrough

In HF sampling method, the breakthrough volume (BTV) depends on the absorber volume, the length of the HF, temperature, the concentration of the analyte, and the sampling flow rate. The BTV was studied under various concentrations, temperature, and sampling flow rates. The

Table 4. Predicted and Experimental Values of Sampling of AA Using HF

Optimum points	Sampling parameters	Predicted values		Experimental values		
		Mass of extraction	Breakthrough	Mass of extraction	Breakthrough	
1	Concentration (ppm)	6.67	0.0932	0	0.0917	0
	Flow	10				
	Time	3.03				
	Temperature	21.31				
2	Concentration (ppm)	6.80	0.0931	0	0.09157	0
	Flow	10				
	Time	3.03				
	Temperature	21.41				
3	Concentration (ppm)	6.95	0.09315	0	0.0909	0
	Flow	10				
	Time	3.02				
	Temperature	21.12				
4	Concentration (ppm)	6.55	0.093187	0	0.0901	0
	Flow	10				
	Time	2.96				
	Temperature	22.05				
5	Concentration (ppm)	7.14	0.09311	0	0.0914	0
	Flow	10				
	Time	2.92				
	Temperature	26.26				

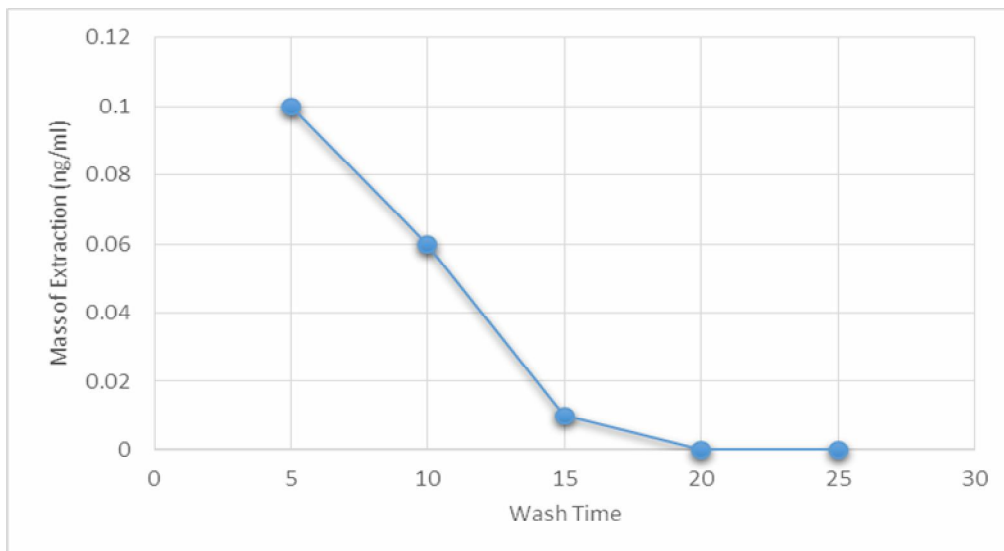


Fig. 3. Evaluation of carryover effect of the suggested HF after washing with absorption solution.

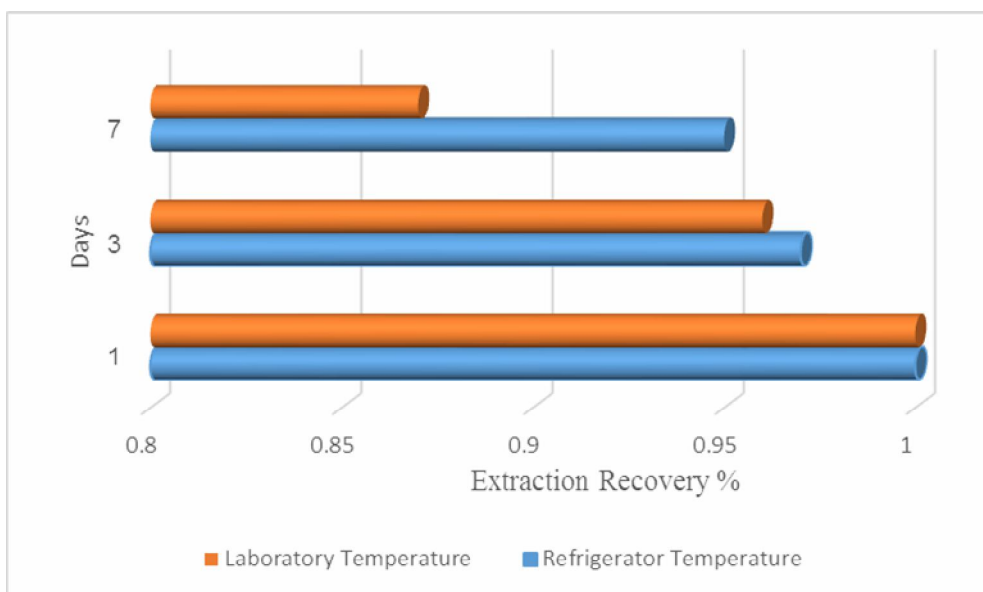


Fig. 4. The storage capacity of the suggested HF.

next equation was utilized to determine the BTV:

$$BTV\% = FT + BT \times 100$$

The extracted mass and BTV were studied at the same time. The experimental runs for modeling and optimization of the

BTV are shown in Table 2. As the results show, by increasing the sampling time and flow rate the BTV will increase. Also, analysis of the interacting parameters showed that the interaction of analyte concentration with sampling flow rate, the interaction of the concentration of the analyte with temperature, and the combined effect of

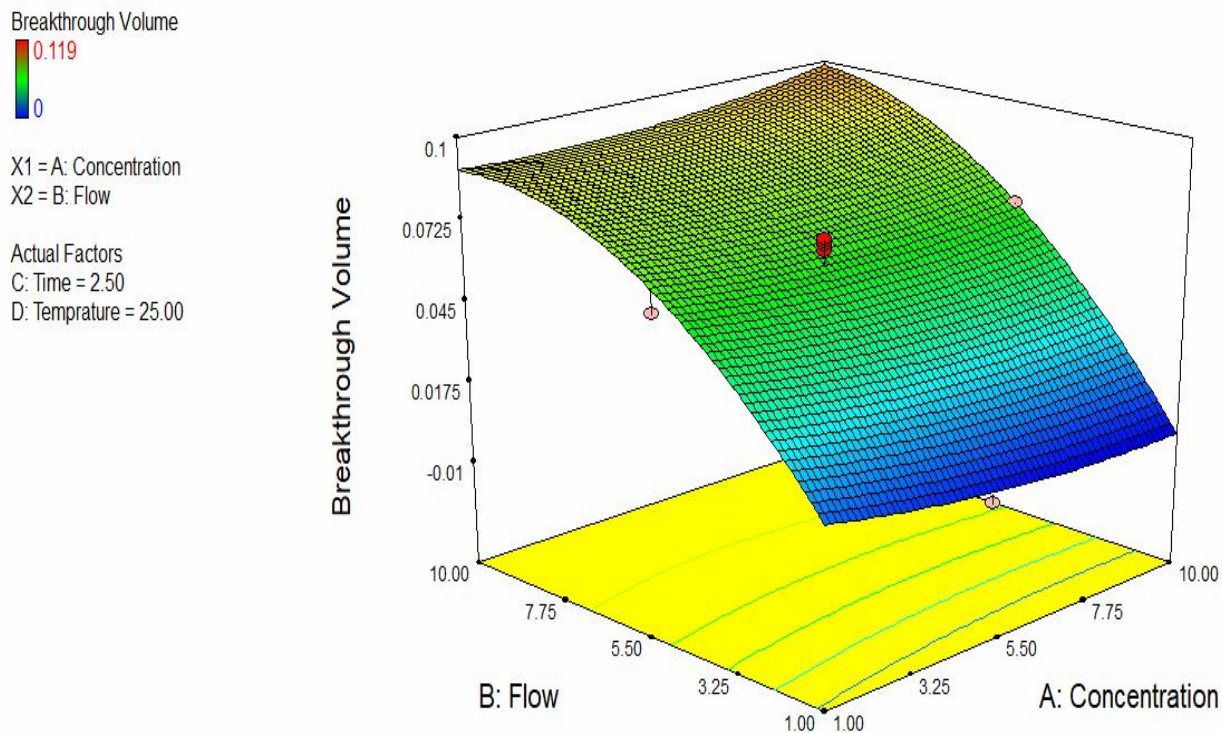


Fig. 5. 1: Effect of interaction between sampling parameters, The interaction between flow rate and concentration, 2: The interaction between time and concentration, 3: The interaction between time and flow.

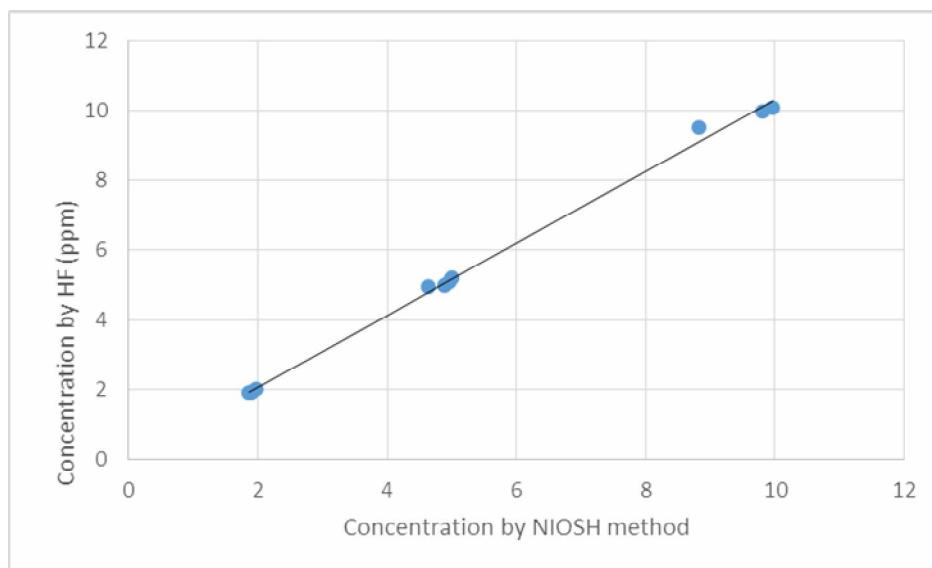


Fig. 6. Correlation between results of sampling with HF and NIOSH-3506 method.

sampling flow rate with time had a significant effect on the increase in BTV. The ANOVA results confirmed that the quadratic model was significant and advised great accuracy and efficiency (Table 3).

Validation of Method

As previously mentioned, to verify the accuracy of the recommended HF sampling method, after optimization of the sampling conditions, sampling was performed concurrently with the HF sampling method and the NIOSH-3506. Next, the results of sampling compared together, and the association between them was 0.998 (Fig. 6). To increase the sampling accuracy, each test was repeated 3 times and averaged. The inter-day repeatability of the method was investigated in two 3-day and 7-day periods and the intra-day repeatability was studied six times in a day. To demonstrate the accuracy of the method relative standard deviation (RSD) was estimated. The RSD for inter-day was 0.079-0.11 and for intra-day it was 0.081-0.14. Under optimal conditions, 10 samples were prepared at a concentration range of 0.25-5 ng ml⁻¹. The concentrations of AA in the chamber were continuously decreased in order to determine LOQ and LOD. The obtained calibration curve was $y = 0.986x - 0.0953$ in which $b = 0.986$ is the calibration curve slope. The standard deviation of the analytic responses was 0.0009. Then, using the equations, the LOD was 0.003 and the LOQ was 0.0091. The results showed that sampling using HF sampling method has high accuracy and high sensitivity for AA sampling. The weaknesses of the HF sampling method as a field sampling method are inapplicability for more than 4-h sampling, the need for replacing several times, the limited capacity of the absorber, HF body vulnerability that results in absorber infusion.

CONCLUSIONS

In this research, for the first time, a novel sampling technique named HF sampling method filled with Hydroxylamine hydrochloride and sodium hydroxide (1:1) extraction solvent is recommended for the sampling of acetic anhydride in the air. The effects of parameters such as temperature, time, humidity and flow on the mass of extraction were investigated. Two important parameters for

choosing a sampler as a field sampler including storage time and breakthrough volume were also investigated. It was found that the proposed method has a high sensitivity in the sampling of acetic anhydride, there is no interference in the work of the worker, and lower LOD of the HF sampling method against the NIOSH-3506, so it can be introduced as a suitable sampling method in the workplace. In the present study, the efficiency of the method was equal to 98-99%, and the efficiency could be increased with further studies. The overall conclusion is that the HF sampling method showed a great sensitivity for the sampling of AA in the air. It could be assumed that HF sampling method is a fast, reliable and sensitive method having a proper performance in the sampling of AA compared to the National Institute for Occupational Safety and Health (NIOSH)-3506 method.

FUNDING

The authors accepted financial assistance from the Student Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran [grant number 9709065180].

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