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Simultaneous determination of three sulfanilamide artificial sweeteners in foodstuffs by capillary electrophoesis coupled with contactless conductivity detection based on porous aromatic frameworks enhanced solid phase extraction

Shaige Xia[1], Dan Yin[1], Yanlong Chen[1], Zhicong Yang[1], Ying Miao[1], Wenfen Zhang[1], Sheng Chen[1,2], Wuduo Zhao[1,2*], Shusheng Zhang[1,2*]

[1]*College of Chemistry and Molecular Engineering, Kexue Road 100,Zhengzhou University, Zhengzhou 450001, P. R. China*

[2]*Center for Advanced Analysis and Computational Science, Kexue Road 100,Zhengzhou University, Zhengzhou 450001, P. R. China*

Corresponding authors at:

Shusheng Zhang, Email: zsszz@126.com; Phone: +86-0371-67739686.

Wuduo Zhao, Email: zhaowuduo@163.com

Abstract

In this paper, a simple and easy-operating method of solid phase extraction (SPE) followed by capillary electrophoresis (CE) with capacitively coupled contactless conductivity detection (C^4D) is evaluated as a novel approach for the simultaneously determination of acesulfame-K (ACE), sodium saccharin (SAC) and sodium cyclamate (CYC) in foodstuffs without derivatization. In order to reduce the complex matrix interference resulting from the constituents of samples and enrich targets, porous aromatic frameworks (PAFs) enhanced SPE, a suitable sample pretreatment procedure was introduced. Several factors affecting extraction efficiency and electrophoretic separation were investigated. Additionally, The interaction mechanisms of host (PAF–6)–guests (ACE/SAC/CYC) were further studied. Under the optimum conditions, three sulfanilamide artificial sweeteners were baseline separated within 8 min, exhibiting a linear calibration over three orders of magnitude (R^2>0.995); The limits of detection (LOD) and quantification (LOQ) were considered better than those usually obtained by CE with UV and C^4D detection. The proposed SPE–CE–C^4D method has been successfully applied to analyse beverage samples and candied fruits with recoveries in the range of 78.89 – 92.00%.

Keywords: porous aromatic frameworks; solid phase extraction; sulfanilamide artificial sweeteners; foodstuffs;

Introduction

High-intensity sweeteners can be divided into natural sweeteners and synthetic sweeteners according to their source [1]. Sweeteners have been widely used in foodstuffs since entering the food industry back in the 1800's [2], especially artificial high-intensity sweeteners with low calorie. In these so-called non-nutritive sweeteners, acesulfame-K (ACE), sodium saccharin (SAC) and sodium cyclamate (CYC) (Fig. 1B) are mostly common artificial synthetic sweeteners to replace sugar in foods in order to guarantee the safety and good quality of foods, as well as satisfy the needs of consumers, particularly individuals with obesity and diabetes mellitus. Therefore, the consumption of these low-calories foods by the worldwide population has dramatically increased. And it brings the suspicions of adverse health effects of artificial high-intensity sweeteners. The study reported that continuous ingestion of these sweeteners can lead to a metabolic disorder [3,4]. To assure food safety, the World Health Organization (WHO) has placed strictest restriction on its usage and its acceptable daily intake (ADI) value [5], and many countries have also enacted relevant legislations [6-8]. For the determination of individual sweeteners and their combinations, several analytical methods have been proposed including high-performance liquid chromatography (HPLC) [9-11], ion chromatography (IC) [12,13], gas chromatography (GC) [14,15], ion chromatography–mass spectrometry [16], HPLC–MS [17-23], capillary electrophoresis (CE) [24-27] in conjunction with various detectors and so on. Among these methods, HPLC method is widely used due to its simplicity and easy-operating. But, for low-concentrated cyclamate with poor absorbance of ultraviolet (UV), it needs to be derived before analysis [9,10]. It is worthy to be noticed that conductivity detection is an alternative determination method for lacking UV-absorbing ionic sweeteners. Recently,

CE–C^4D [28-30] methods have been successfully used for directly determining ionic sweeteners due to its good sensitivity, simple and inexpensive instrumentation and unrequired derivatization steps. For example, Bergamo et al [29] determined four sweeteners in soft drinks and tabletop sweetener formulations by CE–C^4D. A complete separation of the analytes could be attained in less than 6 min and the method provided an excellent low limit of detection. The prosed method shows CE–C^4D has a great potential in separation of ionic lacking UV-absorbing compounds. However, for various food species with more complicated matrix, it is necessary to develop suitably sensitive and reliable methods for determination of different sweeteners.

Considering the sweeteners' concentration are low, as well as coexistence components in complicated matrix can interfere with the determination of sweeteners. Many sample pre-treatment techniques involving pressurised liquid extraction (PLE) [20], on-line preconcentration [30] and solid phase extraction (SPE) [16,18,21,22,25] were developed by numerous researchers to purify and enrich analytes. Among these methods, SPE has been widely used because of its simplicity, rapidity, low cost, and ability to combine with different detectors in both on-line and off-line mode. To date, a number of commercially available SPE cartridges, such as Oasis HLB, CNW poly-sery PWAX, Oasis MAX and Plexa PAX were introduced to isolate the sweeteners from different matrices [16,18,21,22,25]. However, these commercial SPE absorbents have a limit in effectively extracting multiple targets from complex matrix due to its single interaction mechanism. Therefore, there is considerable interest in developing new selective multi-interaction sorbents for extracting and isolating sweeteners from complicated matrices.

In recent years, porous materials stand out among numerous absorbents on account of their outstanding performance in the sample pretreatment, especially porous aromatic frameworks (PAFs) which has larger surface area and larger π-π conjugate system as well as a simple preparation procedure [31,32]. Our group has been committed to the research of COFs in recent years, and a novel multi-interaction and mixed-mode porous aromatic frameworks PAF–6 has been synthesized [33] and used as SPE adsorbent to extract and determine bisphenol A (BPA) in milk and its packing samples. The results show that PAF–6 has an excellent adsorption capability for BPA based on hydrogen bonding and the inclusion interactions of host–guest. At the same time, the PAF–6 coated magnetic nanoparticles (PAF–6 MNPs) [34] were prepared and used to enrich and remove the trace organic pollutants in water, and the main toxic component in mainstream smoke of cigarette, respectively. The results demonstrate that the PAF–6 MNPs sorbent possesses excellent adsorption of phenols, polycyclic aromatic hydrocarbons (PAHs) and nitroaromatics based on multiple π-π stacking and hydrogen-bond interactions. According to the molecular structures of of PAF–6 (Fig 1A) and ACE, SAC and CYC (Fig. 1B), it is suggested that the *p-p* conjugate interactions, anion exchange interactions and inclusion complexations may exist between PAF–6 and these three sweeteners. Therefore, it is feasible to apply PAF–6 as SPE absorbent to purify and enrich them from foodstuffs before CE–C^4D analysis.

In this work, SPE procedure with PAF–6 as sorbent was optimized for effectively extracting and enriching three sulfanilamide artificial sweeteners in foodstuffs. Gauss theoretical calculations were carried out to assistantly elucidate the multi-interaction sites between PAF–6 and the sweeteners. Based on SPE clean-up procedure, CE–C^4D

method is developed for analysis of the three sulfanilamide artificial sweeteners in different beverage samples and candied fruits with satisfactory results.

Experimental

Reagents and solutions

PAF-6 was synthesized in accordance with the previously published procedures [33], Reagents were all of analytical grade. Tris(hydroxymethyl)aminomethane (Tris), Hexadecyl Trimethyl Ammonium Bromide (CTAB) and Sodium tetraborate were purchased from Shanghai Chemical Reagent Company of China National Pharmaceutical Group (Shanghai, China). ACE, SAC and CYC were purchased from Aldrich (Milwaukee, WI, USA). Deionized water was obtained from a Milli-Q Water Purification System (Millipore, Bedford, MA). Individual stock solution (1 mg mL^{-1}) of each sweetener was prepared by dissolving the corresponding solid reagents in deionized water. Standard solutions used in the analysis were prepared by dilution of the respective stock solutions with deionized water, as required.

Electrophoretic equipment and conditions

All experiments were performed on the $HP^{3D}CE$ system equipped with ChemStation software (Agilent Technologies, Waldbronn, Germany) and a laboratory-made C^4D detector [35]. The C^4D parameters were the same as the previous report [35]. The bare fused-silica capillaries were obtained from Yongnian Optical Fiber Corporation (Hebei, China) with an inner diameter of 50 μm and a length of 50 cm (41.5 cm to the detection window). The

apparent pH was obtained by using a pH meter (Shanghai Weiye Factory, Shanghai, China). A buffer solution (pH 9.74) containing 20 mmol L^{-1} Tris, 20 mmol L^{-1} $Na_2B_4O_7$ and 50 μmol L^{-1} CTAB were used as background electrolyte (BGE) throughout this work. The separation voltage was -20 kV and the injection time was 5 s (at 50mbar). Before the analysis, the capillary was flushed with 1 mol L^{-1} NaOH solution for 10 min, then with deionized water for 15 min, and finally with the BGE for 10 min. After each run, the capillary was flushed with BGE for 3 min.

Sample preparation

A centrifuge (Zhongda Instrument Plant, Jiangsu, China) was used for centrifugal separation. All samples, including 8 beverages (2 carbonated cola drinks, 3 fruit juice drinks, 1 red wine drink, 2 plum grape wine drinks), 6 candied fruits (2 candied mango, 2 candied plum, 2 candied kumquat) were purchased from local market (Zhengzhou, China). They were prepared by the relevant procedures as follows.

For beverages, two carbonated cola drinks were degassed for 5 min in an ultrasonic bath, other six beverages were shaken well. Then, they were diluted with deionized water as required. For candied fruits, take the edible part of the candied fruits and mix homogeneously, a 5 g homogenized sample was dissolved in 20 mL of deionized water and ultrasonicated in an ultrasonic bath for 10 minutes, and followed by centrifugation at 2100 rpm for 10 minutes. The supernatant was transferred into a 50-mL volumetric flask. The precipitate was washed with deionized water and repeated extraction. The supernatants were pooled into the same 50-mL volumetric flask, and deionized water was

added volumetrically to 50 mL level. All sample solutions prepared were stored at 4 ℃, then diluted as required for SPE procedure.

PAF-6 SPE procedure

As shown in Fig. 2, 30 mg of PAF–6 sorbent was packed into a 3 mL SPE cartridge. In total, 50 mL diluting sample solution was passed through the PAF–6 SPE cartridge by gravity, which had been preconditioned with 3mL of MeOH and 3 mL water, respectively. The cartridge was then washed with 3 mL water, and eluted with 5 mL 8% ammoniation ethanol. The eluate was evaporated at ambient temperature under a gentle stream of nitrogen gas until dry and re-dissolved in 1 mL buffer. Each sample was filtered through a 0.22 μm Nylon filter (Agilent, USA) prior to CE–C^4D analysis. All tests were performed in triplicate.

Quantum chemistry calculation

To further understand the mechanism of molecular interactions between the PAF–6 absorbent and target analytes. Geometries of the guest ACE, SAC, CYC and the host PAF–6 were optimized by B3LYP/6–31+G(d) level. The sizes of PAF–6 and the tree sweeteners were calculated using the Gaussian 09 program.

Results and disscussion

Optimizing CE–C^4D conditions

The composition was optimized of the BGE in order to attain the best peak resolution and detectability. Fig. 3 shows electropherogram for a standard solution containing the three target sweeteners. We can note that separation

with good resolution can be obtained in less than 8 min.

The sensitivity of the conductivity detection is directly proportional to the mobility difference between the analytes and the BGE co-ion; the BGE counter-ion also has influence on the instrument response. Moreover, BGE significantly affects the migration time and the separation between targets directly. In the selection of BGE, the main consideration is the ionization characteristic of the analytes. The pKa values for the corresponding acids of the ACE, SAC and CYC are 2.0, 1.8 and 1.9, respectively, which indicated that the analytes have a net negative charge in an aqueous BGE when pH > 2.0, and at pH above 4.0, > 99% are in anionic form. Therefore, in our study, negative polarity separation voltage was used. However, in negative polarity separation voltage mode, the direction of the electroosmotic flow (EOF) was opposite to that of anion electromigration resulted in very poor resolution. So it is favorable to use the EOF modifier to suppress or reverse EOF direction when pH > 4.0. Thus, we chose general CTAB as the EOF modifier. Accordingly in the present work, several electrolytes utilized as the buffer solution that possess a useful pH range from 3.0 to 10.0 were tested, including $Na_2B_4O_7$, $Na_2B_4O_7$–H_3BO_3, Tris–His, Tris–H_3BO_3 and Tris–$Na_2B_4O_7$. Among these tested BGE, 20mM Tris-$Na_2B_4O_7$ provided satisfactory results with the highest resolution relative to the others.

The mixture of Tris and $Na_2B_4O_7$ is used for keeping the background conductivity as low as possible as well as producing the necessary pH buffering. In order to further improve the separation of these three artificial sweeteners, buffer pH and concentration of $Na_2B_4O_7$ in buffer were optimized. The relevant responses were evaluated by the resolutions between ACE and SAC (Rs1) and between SAC and CYC (Rs2). According to the results in table 1, a

BGE containing 20mM $Na_2B_4O_7$, at pH 9.74 adjusted by adding Tris was chosen because it provided the highest resolution relative to the others.

Tests also showed that the efficiency of the separation became good and the migration time became short, when the separation voltage was increased. As known, the higher voltage will result in the peak broadening because of the Joule heating effect, the lower voltage will result in the poor resolution. Therefore, a voltage of - 20 kV when the analytes can observe the minor peak-broadening was selected as the best separation voltage in our study. In addition, the introduction of an organic solvent into a buffer system was considered as a method for improving the separation efficiency because the organic solvent would change the physicochemical nature of the separation system. However, no obvious improvement was observed. So organic solvent will not be added

Optimization of SPE procedure

In this section, the main influence factors (amount of sorbent, kinds of eluent, content of $NH_3 \cdot H_2O$ in eluent and volume of eluent) on the SPE recoveries (n=3) of ACE, SAC, CYC are evaluated in detail to obtain the optimal extraction conditions using simulated samples.

Firstly, the efficiency of the PAF–6 amount on the recovery of analytes was studied. Five absorbent amounts (10, 20, 30, 40, 50 mg) were investigated (Fig. 4A). The results display that the recoveries of sweeteners increased with the rise of the PAF–6 amount from 10 to 30 mg. When the amount of PAF–6 was more than 30 mg, the recoveries of sweeteners remained almost constant. As a result, 30 mg packing was chosen for the subsequent

experiments.

A proper elution is of great importance to reduce interfering substances and improve the recovery. Thus, the influence of the kinds, pH and volume of the elution solution on the extraction of sweeteners was studied. The nitrogen character on piperazine of PAF–6 indicates that adsorption of sweeteners may be relative to weak anion exchange interactions. So the alkaline environment is good to the process of elution. So we added ammonia into eluent solvents. As is shown in Fig. 4B, three kinds of solutions (ammoniation acetonitrile, ammoniation methanol and ammoniation ethanol) all can yield good recoveries. Taking environment protection into account, we chose ammoniation ethanol as eluent solvent.

We subsequently optimized the content of $NH_3 \cdot H_2O$ in ammoniation ethanol. The obtained results (Fig. 4C) showed that 8% ammoniation ethanol yielded the highest recovery. Therefore, the content of $NH_3.H_2O$ need to be adjusted 8% in the actual determination.

In addition, various volumes (1 – 9 mL) of ammoniation ethanol were used for the PAF–6 SPE process. The results (Fig. 4D) showed that when the eluent volume reached 5 mL, the value of recovery was higher than 90%. When the eluent volume was more than 5 mL, the recoveries of sweeteners remained almost constant. Taking reagent saving into account, 5 mL ammoniation ethanol was chosen in this study.

Retention mechanism discussion based on quantum chemistry calculations

PAF–6 demonstrated significant enhanced adsorption ability for ACE, SAC and CYC, indicating the crucial

187 role of the PAF–6. According to the studies developed by our group [33,34], PAF–6 has high surface area and the
188 NLDFT pore size distribution exhibited broad mesoporosity (2 – 5 nm) in its framework. So inclusion complexation
189 should be considered during the process of adsorption. From the results (Fig. 1C) calculated using Gaussian 09
190 program, it can be seen obviously that the inclusion complexation existed in host (PAF–6)–guests (ACE, SAC, CYC)
191 as the sizes of ACE, SAC and CYC are much smaller than that of the channel of PAF–6.

192 ## Method validation

193 ### Linearity, detection limits, and precision

194 The method validation including linearity range, LODs, LOQs and precision was carried out, and were
195 summarized in Table 2. There was an excellent linearity between the peak area (mV) and the concentration of ACE,
196 SAC in the range of 0.5 – 25 μM and CYC in the range of 1 – 50 μM with the correlation coefficients from 0.9949 to
197 0.9973. For the LOD, a signal-to-noise ratio of 3 was evaluated. The LODs were 0.09 μM, 0.12 μM and 0.22 μM,
198 respectively, which were all less than LOD of CZE–UV and common CE–C^4D. For the LOQ, a signal-to-noise ratio
199 of 10 was evaluated. The LOQs were 0.32 μM, 0.37 μM and 0.75 μM, which were all less than the maximum
200 regulatory limits. The inter-day and intra-day analysis precision was tested at 1 μM levels, RSDs were found below
201 4.3% (n= 6), indicating good repeatability.

202 ### Accuracy and recovery test

203 To further evaluate the reliability of this proposed method, Recovery experiments were performed by adding

accurate amounts of ACE, SAC and CYC to the real samples. The standard-spiked samples were subject to the same sample preparation procedure as the real samples. As presented in Table 3, the average recovery data at three different concentrations were in the range of 78.89 – 92.00% with corresponding RSDs of 1.90 – 3.91%. From these results, it was concluded that the developed method was accurate, reproducible and reliable for analysing ACE, SAC and CYC in beverage samples and candied fruits.

Analyses of real samples

The proposed method allowed the quantification of all analytes in the beverages and candied fruits (Table 4) with RSD values lower than 5%. Typical chromatograms of orange juice drink and candied mango A before and after SPE were shown in Figure 5. It is obviously observed that the matrix interference can be minimized after purification using the PAF–6 SPE sorbent, and meanwhile targets achieved enrichment. The results indicated that the developed method was suitable for the determination of the three artificial sweeteners in beverage samples and candied fruits.

Comparison of proposed method with previously reported results

To evaluate the analytical performance of the proposed method, a comprehensive comparison of the proposed method with other reported methods for determination of artificial sweeteners is presented in Table 5. As could be observed, the proposed method can directly accomplish the determination of these three sweeteners without derivation. And it reduced matrix interference as well as provided a low LOD after a SPE clean-up procedure. At the

same time, the prosed method was time saving and cost-effective, it was demonstrated to be rapid, simple, cheap and sensitive for determination of artificial sweeteners in beverage samples and candied fruits.

Conclusion

An analytical method has been developed based on solid-phase clean-up procedure followed by CE–C^4D for the determination of three high-intensity sweeteners in beverage samples and candied fruits. For the first time, a novel home-made multiple-interaction SPE absorbent PAF–6 was used to purify and enrich these sweeteners in foodstuffs containing complicated matrices. By using the SPE pretreatment technique, matrix interference is minimized and excellent detection limits can be achieved, these were much lower than those normal CZE–UV and CE–C^4D methods. The method is suitable for use by the food industry for quality control as well as by health and safety agencies for inspections. We also believe that the SPE–CE–C^4D method can easily be used for analysis of other matrices, such as teas, ice cream, desserts and other foods.

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Compliance with Ethical Standards

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Conflict of interest All authors declare that they have no conflict of interest.

238 **Ethical approval** This article does not contain any studies with human participants or animals performed by any of

239 the authors.

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Figure captions

Fig.1 Chemical structures of (**A)** PAF–6 and **(B)** three sulfanilamide artificial sweeteners and **(C)** optimized geometries of the host (PAF-6)–guests (ACE, SAC, CYC) based on inclusion complexations.

Fig.2 Schematic representation of the solid phase extraction of three sulfanilamide artificial sweeteners in foodstuffs followed by CE–C^4D.

Fig.3 Electropherogram of standard solution containing 1 μM of each sweetener with SPE–CE–C^4D. Peak identification: 1, ACE; 2, SAC; 3, CYC.

Other conditions：BGE: 20 mmol L^{-1} Tris+ 20 mmol L^{-1} $Na_2B_4O_7$+50 μmol L^{-1} CTAB. Separation voltage: - 20 kV; Pressure injection: 50 mbar×5 s; silica capillary with 50 μm inner diameter and 50 cm length (41.5 cm effective).

Fig.4 SPE optimization for three sulfanilamide artificial sweeteners with the PAF–6 sorbent. **(A)** influnce of PAF–6 amount; **(B)** influnce of different kinds of eluent solvents on the recovery; **(C)** influence of different content of $NH_3.H_2O$ in eluent on the recovery; **(D)** influence of different eluent volumes on the recovery.

Fig.5 Electropherograms of real samples. **(A)** orange juice drink, and **(B)** candied mango A with (a) homemade PAF–6 sorbent and (b) without SPE.

1 # Tables

2 **Table 1** The effect of buffer pH and buffer concentration on separation degree.

$Na_2B_4O_7$ Concentration in BGE (mmol/L)	pH	Rs1 (ACE/SAC)	Rs2 （SAC/CYC）
10	9.59	2.17	6.29
15	9.63	2.33	6.74
20	9.74	2.96	6.88
25	9.79	2.65	6.37

3

Table 2 Figures of merit for the ACE, SAC and CYC, based on the areas of the peaks recorded at the CE-C^4D detector (Y and X are expressed in mV and μM, respectively).

Analytes	Regression equation	Evaluated range (μM)	Coefficient of determination, R^2	LOD (μM)	LOQ (μM)	RSD (%) (n=6)	
						Intraday	interday
ACE	y=108.71x+8.573	0.5-25	0.9973	0.09	0.32	3.2	3.9
SAC	y=169.22x-5.835	0.5-25	0.9961	0.12	0.37	3.7	4.1
CYC	y=223.01x-17.63	1-50	0.9949	0.22	0.75	2.9	4.3

Table 3 Recoveries of spiked-standard in real samples.

Analytes	Spiked (μg/g)	Cola drink A			Orange juice drink			Candied mango A		
		Found (μg/g)	Recovery (μg/g)	RSD (%)	Found (μg/g)	Recovery (μg/g)	RSD (%)	Found (μg/g)	Recovery (μg/g)	RSD (%)
ACE	100	262.31	88.02	2.58	194.06	86.96	2.18	191.28	79.88	2.33
	200	332.07	78.89	1.99	291.11	92.00	2.25	277.83	83.21	2.08
	500	600.77	85.30	2.92	559.66	90.51	2.63	561.45	90.01	2.86
SAC	100	211.73	84.32	2.78	87.20	87.20	2.33	152.79	81.28	3.91
	200	292.86	82.73	3.31	177.68	88.84	1.90	244.32	86.40	3.18
	500	538.99	82.32	2.85	455.00	91.00	2.59	512.37	88.17	3.72
CYC	100	193.97	80.70	3.55	90.26	90.26	3.22	80.18	80.18	2.91
	200	282.91	84.82	2.84	175.96	87.98	3.90	172.84	86.42	2.30
	500	512.25	79.80	2.69	458.97	91.79	2.28	427.95	85.59	3.55

Table 4 Assay results of three sulfanilamide artificial sweeteners in real samples (n= 3).

Samples	Average concentration detected (μg/g)		
	ACE	SAC	CYC
Cola drink A	174.29±0.45	127.41±0.28	113.27±0.40
Cola drink B	175.02±0.43	240.26±0.55	640.59±1.55
Orange juice drink	107.10±0.38	n.d.	n.q.
Blueberry juice drink	67.66±0.25	n.d.	245.40±1.14
Grape juice drink	19.64±0.09	n.d	283.15±0.85
Red wine	n.d.	n.d.	n.d.
Plum grape wine A	8.51±0.03	n.d.	123.56±0.34
Plum grape wine B	7.28±0.02	n.q	131.29±0.33
Candied mango A	111.40±0.32	71.51±0.18	n.q.
Candied mango B	120.20±0.35	n.d.	n.q.
Candied plums A	49.11±0.16	n.q.	87.82±0.29
Candied plums B	51.25±0.17	n.q.	621.18±1.43
Candied kumquat A	60.61±0.23	n.d.	n.d.
Candied kumquat B	70.36±0.18	n.q.	n.d.

Note: n.d.= not detected (below LOD); n.q. = detected but not quantified (concentration below LOQ).

Matrix	Analytes	Sample preparation	Determination technique	Run time (min)	LOD	Reference
beverages	CYC	HS-SDME[a]	GC-FID	5	5 μmol/L	[14].
Waste water and surface water	ACE, SAC, CYC, SUC	without pretreatment	HPLC-MS	18	0.5-5.0 ng/L	[17]
river water and wastewater	ACE, ASP, CYC,NHDC,SAC,SUC[b]	SPE	HPLC-MS	13	river water: 0.001-0.04 μg/L waste water: 0.01-0.5 μg/L	[22]
beverages	ASP, CYC, SAC, ACE	without pretreatment	CZE-UV	6	0.5-12.0 mg/L	[26]
soft drinks and tabletop sweetener formulations	ASP,CYC,SAC,ACE	without pretreatment	CE-C^4D	6	1.4-4.2 mg/L	[28].
food samples	ASP,CYC,SAC,ACE	without pretreatment	CE-C^4D with Hydrodynamic	3	3.8-6.5 μmol/L	[29]

			pumping			
Beverages and candied fruits	ACE,SAC,CYC	SPE	CE-C^4D	8	0.09-0.22 μM	Present work

Table 5. Comparison of different methods for the determination of artificial sweeteners.

Note: [a]HS-SDME, headspace single-drop microextraction; [b]ACE: acesulfame-K; ASP: aspartame; CYC: sodium cyclamate; NHDC: neohesperidin dihydrochalcone; SAC: sodium saccharin; SUC, sucralose.

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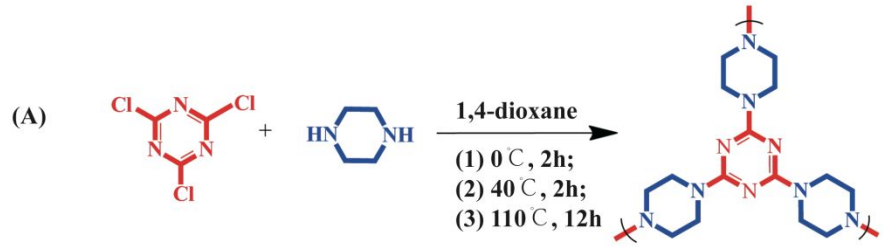
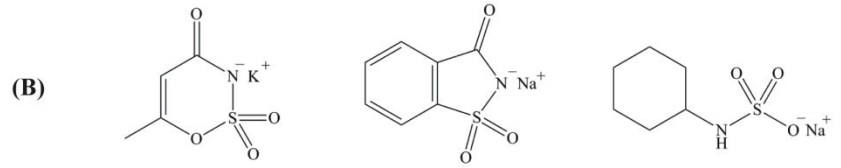
Figure 1



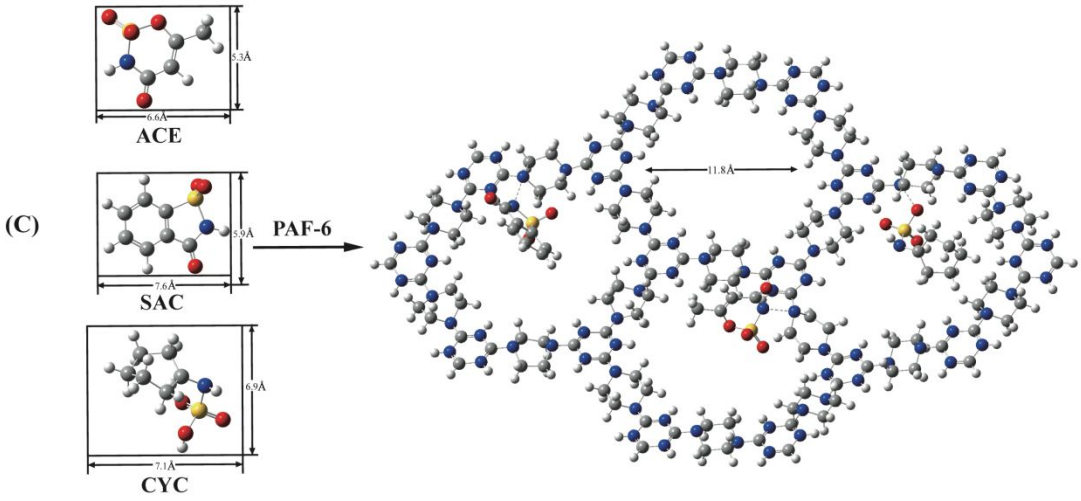
Synthetic procedure of PAF-6 sorbent



Acesulfame-K (ACE)
pKa:2.0

Sodium saccharin (SAC)
pKa:1.8

Sodium cyclamate (CYC)
pKa:1.9



Optimized geometries of the host (PAF-6)–guests (ACE, SAC, CYC) based on inclusion complexation

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Figure 2

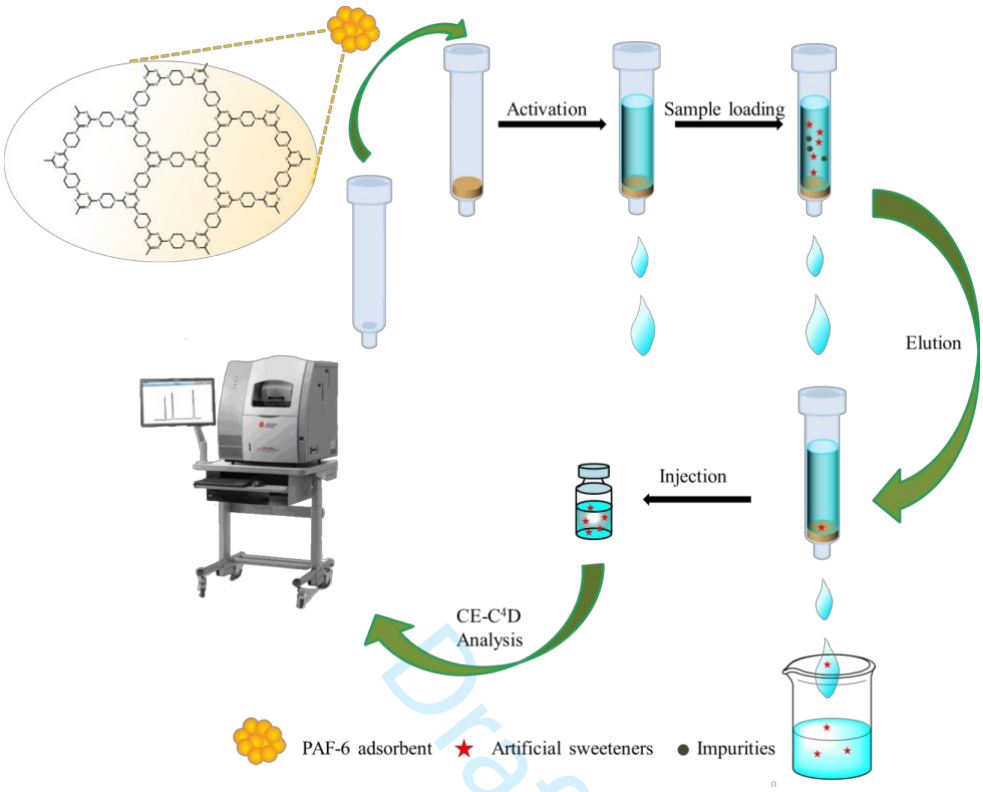

Figure 3

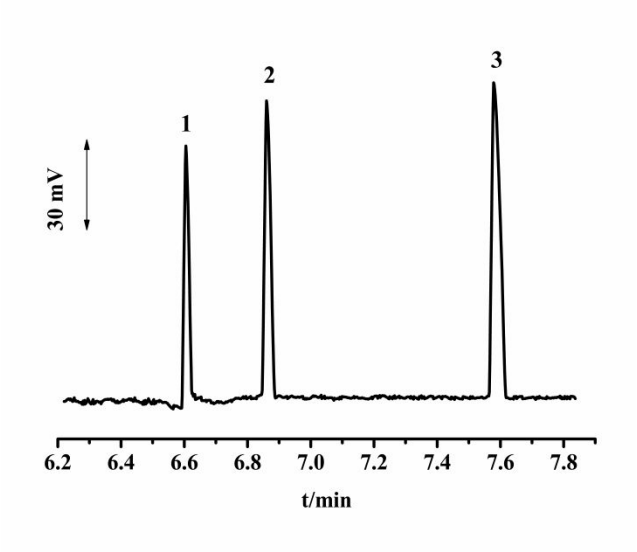

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Figure 4

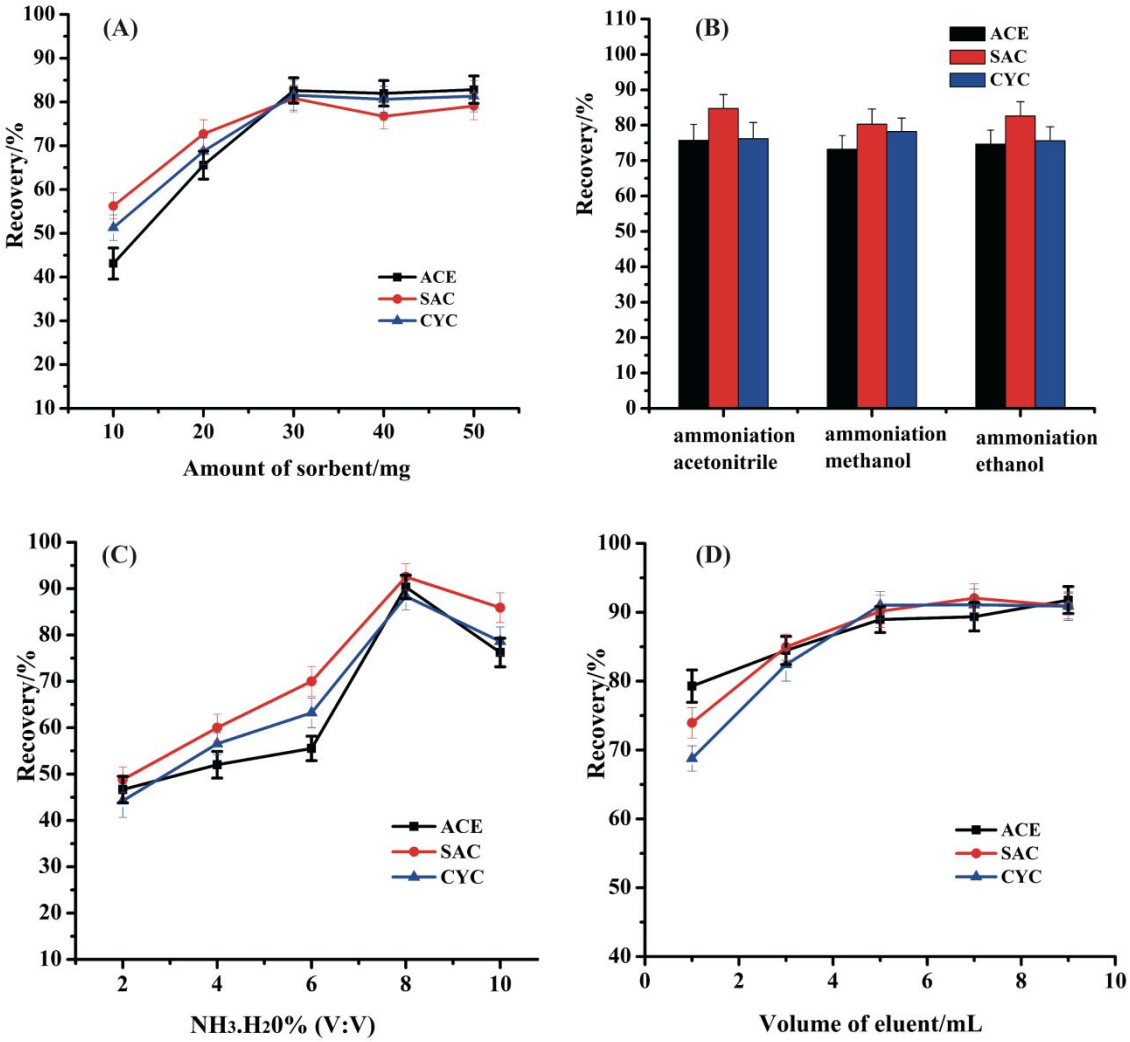

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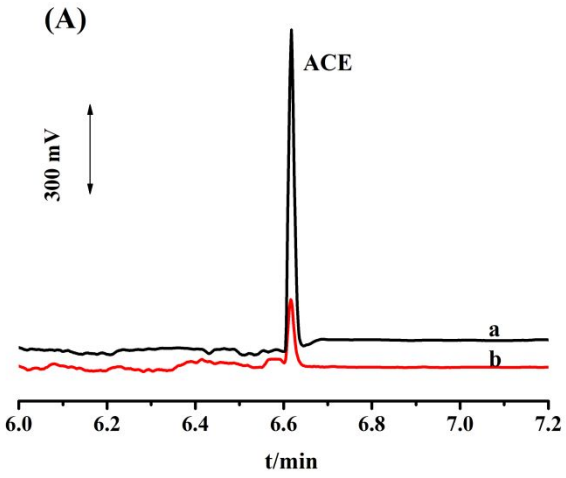
Figure 5



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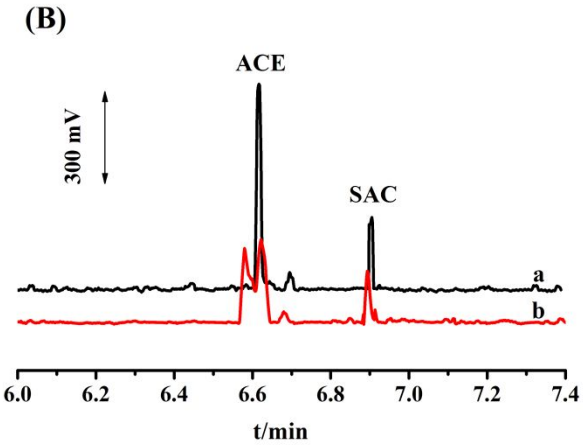

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