Comparison of clonidine and cyproheptadine determination in animal-derived foods by sweeping-micellar electrokinetic chromatography and large volume sample stacking-capillary zone electrophoresis

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ABSTRACT

This study establishes a method for rapid detection of clonidine and cyproheptadine in foods of animal origin. In order to obtain the best detection method, capillary zone electrophoresis (CZE), large volume sample stacking (LVSS), and sweeping-micellar electrokinetic capillary chromatography (sweeping-MEKC) were used respectively. The limits of detection (LODs) of clonidine and cyproheptadine by LVSS-CZE were 0.028 µg mL\(^{-1}\) and 0.034 µg mL\(^{-1}\), and those by sweeping-MEKC were 0.023 µg mL\(^{-1}\) and 0.031 µg mL\(^{-1}\), respectively. Compared with the CZE method, the two online pre-concentration technologies have greatly improved the detection sensitivity and achieved good enrichment results. However, compared with the sweeping-MEKC system, the LVSS system consumed a longer time and was greatly affected by the actual sample matrix. The sweeping-MEKC method was proved to be suitable for real sample analysis. Under the best sweeping-MEKC conditions, clonidine and cyproheptadine could be well separated within 8 min and good linear relationships in the range of 0.1–1.0 µg mL\(^{-1}\) (\(r^2 > 0.99\)) were obtained. This method was successfully applied to the determination of clonidine and cyproheptadine in animal-derived foods with the recoveries of 82.3%–90.1% and the relative standard deviations (RSDs) less than 3.11%. The sweeping-MEKC method is simple to operate and has great potential in the rapid detection of clonidine and cyproheptadine in animal-derived foods.

KEYWORDS

clonidine, cyproheptadine, sweeping-MEKC, LVSS, animal-derived foods, food analysis

INTRODUCTION

Clonidine is an imidazoline derivative and an alpha receptor agonist. It can be used clinically to treat short stature and hypertension [1]. It directly activates the central postsynaptic membrane α2 receptors of the hypothalamus and the oblongata [2]. It also activates inhibitory neurons and reduces the central sympathetic nerve impulse [3]. As a result it can inhibit peripheral sympathetic nerve activity, promote hormone levels, and reduce blood pressure [4]. So it has the effect of increasing the growth rate of animals. Cyproheptadine is a well-known first generation antihistamine that is used in the treatment of allergic disorders [5]. It has alpha-blocking activity and central sedative effect. It can block 5-HT activity in the hypothalamus, get the feeding center excited and cause hunger, also can reduce sugar consumption and utilization [6]. So it will increase animals’ food intake and body mass. For these reasons clonidine and cyproheptadine were incorporated into animal feed by some illegal breeders for the purpose of quickly increasing animals’ growth rate. This leads to clonidine...
and cyproheptadine residues in the animals. Clonidine is easy to accumulate in the human body. Excessive clonidine can cause pale complexion, irregular heartbeat and lower blood pressure. And the residues in high concentration of cyproheptadine can cause toxic symptoms such as shortness of breath, general weakness and even coma. In more severe cases, it can lead to the death of children directly [7]. According to the industry standards of the People’s Republic of China for Entry-Exit Inspection and Quarantine SN/T 5148–201913 [8], clonidine and cyproheptadine are substances that are clearly prohibited in foods. Therefore, it is essential to develop a method for rapid detection of clonidine and cyproheptadine in foods of animal origin.

Several methods have been developed to detect clonidine and cyproheptadine in different samples. Clonidine and cyproheptadine in human plasma and pharmaceutical syrup [9, 10], edible tissue and urine of pigs [11–13] have been analyzed by liquid chromatography coupled with mass spectrometry (LC–MS) and gas chromatography coupled with mass spectrometry (GC–MS) [14]. Methods using HPLC with ultraviolet detection (HPLC-UV) [15, 16] or photodiode array detection (HPLC-DAD) [17] have been developed to analyze them in animal feed and tablet. And there are also methods to detect clonidine or cyproheptadine alone. The method of using an immunochromatographic test strip to test clonidine in pig urine has been established [18]. A non-aqueous capillary electrophoresis with electrochemical and electrochemiluminescence detections (NACE-ECL/EC) method has been reported to detect cyproheptadine [19] in antihistamines. However, the method for simultaneous detection of clonidine and cyproheptadine in animal-derived food by capillary electrophoresis (CE) has not been reported yet.

CE has the advantages of small sample injection volume, high theoretical plate number, fast separation and environmental friendliness. It is an important method for food safety detection. But the traditional capillary zone electrophoresis (CZE) mode has the disadvantage of low sensitivity mainly due to the short path length of optical detection. To solve this problem, online enrichment methods of capillary electrophoresis were developed. Online enrichment technology is a method to improve sensitivity during sample injection or separation. Commonly used online enrichment techniques include sweeping and stacking. The sweeping technique often uses micellar electrokinetic chromatography (MEKC). By applying voltage, the pseudo stationary phase (PSP) penetrates into the sample plug and the analytes in the sample zone is concentrated into a relatively narrow zone under the sweeping of the micelle. The introduction of a large sample zone is integrated into a narrow sample zone to improve the sensitivity. According to reports, the concentration efficiency of sweeping-MEKC can reach 20–5,000 folds [20]. The common stacking methods are large volume stacking (LVSS) and field amplified stacking (FASS) [21, 22]. Stacking technique uses the difference between the conductivity of the buffer solution and the sample matrix. Generally, a sample matrix solution with low conductivity and a buffer solution with high conductivity were chosen. When the sample ions intersect with the buffer solution at the boundary, the movement speed of the sample ions slowed down and sample ions accumulated at the boundary. The accumulated sample ions quickly become a narrow band. When the narrow sample zones pass through the detection window, the signal intensity will increase. According to reports, stacking technology can increase sensitivity by 100 times for some substances [23]. Although the FASS method has high concentration efficiency, it is greatly affected by the actual sample matrix [24]. Therefore, this method will not be discussed in this study. The performance comparison of the sweeping-MEKC method proposed in this study with that of other published methods for clonidine and cyproheptadine determination is collected in Table 1. Although these hyphenated techniques such as LC-MS and GC-MS in Table 1 are several times

| Table 1. Comparison of the results obtained by our method with other methods |
|-----------------------------|------------------|----------|------------------|------------------|
| Method                     | Analytes         | LOD (ng mL⁻¹) | Migration time (min) | References |
| HPLC-UV                    | CLO              | 31        | <7                | [15]          |
|                            | CYP              | 19        | <20               | [16]          |
| HPLC-DAD                   | CYP              | 12        | <6                | [17]          |
| NACE-ECL/EC                | CYP              | 320       | <10               | [19]          |
| LFIA                       | CLO              | 2.5       | <5                | [18]          |
| GC-MS                      | CLO              | 0.026     | <14               | [14]          |
| LC-MS                      | CLO              | 0.15      | <8                | [9]           |
|                            | CYP              | 0.86      | <11               | [10]          |
|                            |                  | 0.48      | <8                | [12]          |
|                            |                  | 0.2       | <5                | [11]          |
| Sweeping-MEKC              | CLO, CYP         | 23, 31    | <8                | This work    |

HPLC-UV: high performance liquid chromatography with ultraviolet detection; HPLC-DAD: high performance liquid chromatography with array detection; NACE-ECL/EC: non-aqueous capillary electrophoresis with electrochemical and electrochemiluminescence detection; LFIA: immunochromatographic; GC-MS: gas chromatography coupled with mass spectrometry; LC-MS: liquid chromatography coupled with mass spectrometry; Sweeping-MEKC: sweeping technique with micellar electrokinetic chromatography; CLO: clonidine, CYP: cyproheptadine.
more sensitive than the sweeping-MEKC method, those techniques are expensive and require highly skilled operators. Therefore, a simple and low cost CE method with reasonable selectivity and sensitivity will offer wider applicability in various analytical laboratories.

In this work sweeping and stacking techniques were used to develop a sensitive CE method for separation and determination of clonidine and cyproheptadine. Key parameters of the two methods are optimized to achieve high sensitivity. The methods were applied to the detection of clonidine and cyproheptadine in animal source foods.

EXPERIMENTAL

Instrumentation

The SCIEX P/ACE™ MDQ plus CE (SCIEX, Fullerton, CA, USA) instrument equipped with UV detector (Beckman, USA) was used for the experiments. Data collection, processing and analysis are performed using the 32 karat software (Beckman) of the system and recorded in Lenovo computer. Uncoated fused-silica capillaries (Yongnian Optical Fiber Factory, Hebei, China) with an inner diameter of 75 μm and total length of 50 cm (effective length 40.2 cm) were used. The temperature was kept at 25°C. A STARTER 3100 pH meter (Shanghai OHAUS Instrument Company, Shanghai, China) was used for pH measurement. A T25 digital ultra turrax homogenizer (IKA Co., Germany) and a Kuansons solid phase extraction device (Kuansens Biotechnology Co., Ltd., Shanghai, China) with PCX mixed cation exchange column (90 mg, 6 mL) were used for sample pretreatment.

Chemicals and materials

Clonidine standard with a purity greater than 98% was purchased from Tanmo Quality Assurance Standards Center (Beijing, China). Cyproheptadine standard with a purity greater than 98% was purchased from Standard Material R&D Center Co., Ltd (Henan, China). The structures of clonidine and cyproheptadine are shown in Fig. 1. Standard stock solutions of clonidine and cyproheptadine at a concentration of 200 μg mL⁻¹ were prepared in methanol (MeOH) and stored at 4°C in a refrigerator. HPLC grade methanol and cetyltrimethylammonium bromide (CTAB) were purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Phosphoric acid, acetonitrile, ammonia, and hydrochloric acid were purchased from Comeo Chemical Reagent Co., Ltd. (Tianjin, China). Sodium dodecyl sulfate (SDS, ≥97.0%) was purchased from Macklin Biochemical Co, Ltd (Shanghai, China). Disodium hydrogen phosphate (Na₂HPO₄·12H₂O, ≥99.0%) and sodium hydroxide (NaOH) were purchased from Sinochem Reagent Co., Ltd. (Shanghai, China). Pork and chicken samples were purchased from a local supermarket.

Sample preparation

The sample processing method is in accordance with the People’s Republic of China Entry-Exit Inspection and Quarantine Industry Standard SNT5148-2019. 2 g of the sample (with accuracy to 0.01 g) were weighed into a 50 mL centrifuge tube then 25 mL of acetonitrile were added and homogenized at 1,000 rpm for 1 min. Then centrifuged for 10 min at 1,000 rpm. The supernatant was transferred to another 50 mL centrifuge tube. Then 2 mL of 0.1% hydrochloric acid solution were added to protonate the analytes. The solution was transferred to an activated PCX column, washed with 5 mL of water and methanol successively, and eluted with 10 mL of 5% ammonia methanol solution. All the eluents were collected and the solvents were evaporated at 40°C with nitrogen. The residues were dissolved in 1 mL 70 mM NaH₂PO₄ solution for sweeping-MEKC or 1 mL 1 mM phosphoric acid for LVSS or 1 mL methanol for CZE and passed through a 0.22 μm filter for CE analysis.

Sweeping-MEKC

Mixed standard solution of 1 μg mL⁻¹ was prepared by diluting the stock solution with 70 mM NaH₂PO₄ solution. Samples were injected at 0.7 psi for 100 s (~1.1 μL) and volume of the capillary was filled about 50%. Buffer solution was consisted of 20 mM NaH₂PO₄, 90 mM SDS and 20% ACN (v/v) at pH 2.4 (Prepared by dilution 1.0 mL 200 mM NaH₂PO₄, 4.5 mL 200 mM SDS and 2.0 mL ACN with water to 10 mL, and adjusted to pH 2.4 with 5 M phosphoric acid). Separation voltage was ~20 kV. To ensure repeatability, the capillary was flushed with 1 M NaOH for 3 min, deionized water for 3 min, and buffer solution for 3 min before each injection.

LVSS

Mixed standard solution of 1 μg mL⁻¹ was prepared by diluting the stock solution with 1 mM phosphoric acid. Samples were injected at 0.7 psi for 130 s (~1.4 μL) and volume of the capillary was filled about 65%. 50 mM phosphoric acid, 20% ACN (v/v) and 2 mM CTAB at pH 2.5 was chosen as background electrolyte (BGE) solution, which was prepared by dilution 0.1 mL 5 M phosphoric acid and 2.0 mL ACN with water to 10 mL. The electroosmotic flow (EOF) was reversed by adding 2 mM CTAB to the BGE, so that the EOF began to move toward the positive electrode. Separation voltage was set at 15 kV. To ensure repeatability, the
capillary was flushed with MeOH for 3 min, deionized water for 3 min, and buffer solution for 3 min before each injection.

**CZE**

Mixed standard solution of 1 mg mL\(^{-1}\) was prepared by diluting the stock solution with methanol. 30 mM NaH\(_2\)PO\(_4\) solution with pH 4.0 was used as buffer solution. Separation voltage was 28 kV. Samples were injected at 0.5 psi for 5 s. To ensure repeatability, the capillary was flushed with 1M NaOH for 3 min, deionized water for 3 min, and buffer solution for 3 min before each injection.

**RESULTS AND DISCUSSION**

In this study two on-line preconcentration CE methods i.e. sweeping and stacking methods were developed and compared in order to develop a sensitive and fast technique for the separation and determination of clonidine and cyproheptadine in animal-derived foods.

**Optimization of Sweeping-MEKC**

Sweeping phenomenon was initially proposed by Quirino and Terabe [25]. In this work SDS was used as the micelles to sweep clonidine and cyproheptadine. During the experiment, it can be seen that the separation and peak shape and peak area of clonidine and cyproheptadine are mainly affected by SDS concentration, organic additive, sample matrix composition and injection time. Therefore, these conditions need to be investigated individually to obtain good separation and satisfactory sweeping results.

**Optimization of SDS concentration.** From the structures of clonidine and cyproheptadine, it can be seen that there are lone pair electrons in nitrogen atoms which can be protonated under acidic condition. Therefore, a sweeping-MEKC method under acidic conditions was investigated. So 20 mM NaH\(_2\)PO\(_4\), 20% ACN (v/v) with different concentrations of SDS (70, 80, 90, 100 mM) at pH 2.4 were used as BGE and 60 mM NaH\(_2\)PO\(_4\) was used as sample matrix. Pressure injection was set at 0.7 psi for 90 s and separation voltage of \(-15\) kV was used. Results are shown in Fig. 2, from which we can see that with the increasing of SDS concentration the migration time and the resolution of clonidine and cyproheptadine gradually increased. While the peak intensity of the analytes did not change obviously, indicating that the retention factor \(k\) was not affected significantly by the concentration of SDS from 70 to 100 mM. In addition, the peak intensity of sample matrix gradually decreased with the increasing of SDS concentration. As the SDS concentration reached 100 mM, the peak of

![Fig. 2. Effect of SDS concentration on the analysis of clonidine and cyproheptadine. MEKC condition: 20 mM NaH\(_2\)PO\(_4\), 20% ACN (v/v), pH 2.4, sample matrix 60 mM NaH\(_2\)PO\(_4\), pressure injection 90 s with 0.7 psi, \(-15\) kV applied voltage. (1. cyproheptadine, 2. clonidine, 1 \(\mu\)g mL\(^{-1}\))](image-url)

![Fig. 3. Effect of the NaH\(_2\)PO\(_4\) concentration as sample matrix on the analysis of clonidine and cyproheptadine. MEKC condition: 20 mM NaH\(_2\)PO\(_4\), 20% ACN (v/v), 90 mM SDS, pH 2.4, other conditions are same as Fig. 2](image-url)

![Fig. 4. Effect of organic modifier on the analysis of clonidine and cyproheptadine. MEKC condition: 20 mM NaH\(_2\)PO\(_4\), 90 mM SDS, pH 2.4, sample matrix 70 mM NaH\(_2\)PO\(_4\), other conditions are same as Fig. 2](image-url)
clonidine tailed obviously. Considering the migration time, the influence on the sample matrix peak and the peak shape, 90 mM SDS was used.

**Optimization of sample matrix composition.** Sample matrix composition determines the conductivity and electric field intensity of the sample zone. According to the literature, the closer the conductivity of the sample matrix and the buffer solution, the better the enrichment effect [26]. However, related reports pointed out that the similarity of conductivity does not directly affect the enrichment factor [27]. In this study, the concentration of the sample matrix was investigated using 60, 70 and 80 mM NaH₂PO₄ (pH 2.4), whose conductivity was lower, similar and higher than that of the buffer solution by means of measuring the current. It can be seen from Fig. 3 that when the concentration of NaH₂PO₄ was 70 mM, the peak area of clonidine and cyproheptadine were larger than those at the concentration of 60 and 80 mM, so the sample matrix concentration was selected as 70 mM.

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![Fig. 5. Effect of injection time on the analysis of clonidine and cyproheptadine. MEKC conditions: 20 mM NaH₂PO₄, 20% ACN (v/v), 90 mM SDS, pH 2.4, 70 mM NaH₂PO₄ sample matrix, other conditions are same as Fig. 2. (1. cyproheptadine, 2. clonidine, 3. sample matrix)](image)

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![Fig. 6. Typical electropherograms of clonidine and cyproheptadine in sweeping-MEKC (A), normal CZE (B) and LVSS-CZE (C). (1. cyproheptadine, 2. clonidine, 1 μg mL⁻¹) A: 20 mM NaH₂PO₄, 20% ACN (v/v), 90 mM SDS, pH 2.4 as BGE, 70 mM NaH₂PO₄ as sample matrix, pressure injection 100 s with 0.7 psi, −15 kV applied voltage, UV detection at 210 nm. B: 30 mM NaH₂PO₄, pH 4.0, pressure injection 5 s with 0.5 psi, 20 kV applied voltage, UV detection at 210 nm. C: 50 mM phosphoric acid, 20% ACN (v/v), 2mM CTAB, pH 2.5 as BGE, 1mM phosphoric acid as sample matrix, pressure injection 130 s with 0.7 psi, 15 kV applied voltage, UV detection at 210 nm)](image)
Optimization of organic modifier. In the previous experiment, it was found that clonidine and cyproheptadine could not be separated when no organic modifier was added. Organic modifier can influence the distribution of the analytes in the micelles and the conductivity of the buffer solution, thus affect sweeping and separation. ACN was used as organic modifier in this work. The addition amount of ACN at 15%, 20% and 25% were investigated. The results were shown in Fig. 4. From Fig. 4 we can see that 20% ACN should be selected considering both migration time and peak area of the analytes.

Optimization of injection time. For the sweeping step, in order to obtain the maximum sensitivity, the sample injection volume should be optimized. The injection time from 90 to 110 s were evaluated with injection pressure of 0.7 psi. The results are shown in Fig. 5. According to Fig. 5, as time increased, the peak area gradually increased. When the injection time was 110 s, the increase in peak intensity was not obvious, while the peak intensity of the sample matrix increased. So 100 s was used as the injection time.

Based on the results above, the optimized sweeping-MEKC conditions were BGE of 20 mM NaH₂PO₄, 90 mM SDS and 20% (v/v) CAN at pH 2.4, sample matrix of 70 mM NaH₂PO₄. Sample was injected by pressure injection at 0.7 psi for 100 s, the voltage was −15 kV. Figure 6A showed the electrophoreogram of clonidine and cyproheptadine in sweeping-MEKC mode under the optimal conditions. Compared with the normal CZE mode (Fig. 6B), the enrichment factors obtained for clonidine and cyproheptadine were 52 and 50, respectively.

Optimization of LVSS

In LVSS mode, due to the conductivity difference between the sample solution and the running buffer sample ions can stack into a narrow band to improve the signal intensity. In this work 1 mM phosphoric acid was used as sample matrix. 50 mM phosphoric acid, 20% ACN (v/v) and 2 mM CTAB at pH 2.5 was chosen as BGE solution. Separation voltage was set at 15 kV. The EOF was reversed by adding 2 mM CTAB and the EOF began to move toward the positive electrode. Thus the long sample plug (sample matrix) could be pumped out and separation as well as concentration efficiency could be improved. The sample injection was carried out using a hydrodynamic technique. The injection time is

![Electropherograms in sweeping-MEKC (A1, B1) of samples: a. spiked with 0.5 μg mL⁻¹ analytes, b. spiked with 0.25 μg mL⁻¹ analytes, c. blank sample, (1), cyproheptadine (2) clonidine; and electropherograms in LVSS (A2, B2) of samples: a. spiked with 0.5 μg mL⁻¹ analytes, b. blank sample, (1) clonidine and cyproheptadine without separation (A1, A2) Pork, (B1, B2) Chicken.](image)
Comparison of sweeping-MEKC and LVSS-CZE

Under optimal conditions, analytical parameters of the sweeping-MEKC, LVSS-CZE and normal CZE methods were evaluated at corresponding concentration ranges. Each standard was analyzed in triplicate using the proposed methodology. Calibration curves were constructed from the peak area. LODs and LOQs were calculated for a signal-to-noise ratio of 3 and 10, respectively. Precision of the both methods were measured in terms of intra-day and inter-day repeatability for migration times and peak areas expressed as the relative standard deviations (%RSD) obtained in the analysis of the standard solutions of the analytes. The results are given in Table 2. From the results we can see that good linear relationships, comparable sensitivities and precisions were achieved for both methods. However, the migration times of the analytes by LVSS-CZE (about 16 and 19 min) were much longer than those (about 5 and 7 min) by sweeping-MEKC.

Sample analysis

In order to further investigate the applicability of sweeping-MEKC and LVSS-CZE methods in real sample analysis, blank and spiked pork and chicken samples were pretreated by solid phase extraction (SPE) and were analyzed with both methods to evaluate the matrix effect. Typical electropherograms are given in Fig. 7. Under the sweeping-MEKC method shown in Fig. 7 A1 and B1, clonidine and cyproheptadine can be effectively separated and detected in actual samples, whereas in the LVSS-CZE mode (Fig. 7 A2 and B2), the peak shape of clonidine and cyproheptadine in the spiked samples had changed a lot, which cannot be well separated and determined in the actual samples, indicating that this method may be greatly affected by matrix changes. Based on the results in Fig. 7, it can be seen that the sweeping-MEKC method is suitable for the detection of clonidine and cyproheptadine in actual samples. Therefore, the sweeping-MEKC method is selected as the final method of this research. The results are shown in Table 3.

CONCLUSIONS

This study established an effective method for analyzing clonidine and cyproheptadine in animal-derived foods. Two online enrichment methods were used, namely sweeping-MEKC and LVSS-CZE methods. The online enrichment

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**Table 2. Validation parameters for proposed sweeping-MEKC method and LVSS-CE method**

| Parameter                      | Clonidine | Cyproheptadine | Clonidine | Cyproheptadine |
|-------------------------------|-----------|----------------|-----------|----------------|
| Calibration curve (μg mL⁻¹)   | \( y = 81,706x + 2,954 \) | \( y = 34,501x - 5,127 \) | \( y = 92,887x + 5,771 \) | \( y = 86,282x + 6,790 \) |
| Lineararity \( (r^2) \)       | 0.9994    | 0.9939         | 0.9996    | 0.9935         |
| Linear range (μg mL⁻¹)        | 0.1–1     | 0.1–1          | 0.1–1     | 0.1–1          |
| LOD (μg mL⁻¹)                 | 0.023     | 0.031          | 0.028     | 0.034          |
| LOQ (μg mL⁻¹)                 | 0.077     | 0.103          | 0.092     | 0.112          |
| Migration time (min)          | 7.100 ± 0.159 | 5.171 ± 0.130 | 16.746 ± 0.429 | 19.229 ± 0.434 |
| \( t_m \) RSD (%) (Intra-day) | 2.25      | 2.51           | 2.56      | 2.26           |
| \( t_m \) RSD (%) (Inter-day) | 2.98      | 3.14           | 3.52      | 3.22           |
| peak area RSD (%) (Intra-day) | 2.52      | 2.98           | 2.86      | 2.82           |
| peak area RSD (%) (Inter-day) | 3.66      | 3.89           | 3.85      | 3.88           |

\( ^a (n = 5). \)

\( ^b \) Values are means of five measurements ±SD.

\( ^c \) Concentration of 1 μg mL⁻¹ individual for clonidine and cyproheptadine were chosen for the assays.

**Table 3. The recoveries of clonidine and cyproheptadine in samples by sweeping-MEKC \( (n = 3) \)**

| Sample | Blank sample (μg mL⁻¹) | Added (μg mL⁻¹) | Found ±SD (μg mL⁻¹) | Recovery (%) | RSD (%) | Found ±SD (μg mL⁻¹) | Recovery (%) | RSD (%) |
|--------|-----------------------|-----------------|---------------------|--------------|--------|---------------------|--------------|--------|
| Chicken | ND                    | 0.50            | 0.44 ± 0.0058       | 87.5         | 2.63   | 0.42 ± 0.0063       | 85.0         | 2.82   |
|        |                       | 0.25            | 0.21 ± 0.0032       | 84.2         | 2.85   | 0.20 ± 0.0023       | 82.3         | 3.11   |
| Pork   | ND                    | 0.50            | 0.45 ± 0.0052       | 90.1         | 1.88   | 0.44 ± 0.0086       | 87.5         | 2.05   |
|        |                       | 0.25            | 0.22 ± 0.0035       | 88.2         | 2.28   | 0.22 ± 0.0039       | 88.5         | 2.31   |

ND: not detected.
multiples of the two methods are not much different. However, the LVSS method was greatly affected by the sample matrix. It was shown that the sweeping-MEKC method could be applied to the determination of clonidine and cyproheptadine in animal-derived foods. Under the sweeping-MEKC method, clonidine and cyproheptadine can be well separated within 8 min. Compared with the ordinary CZE method, the enrichment factor reaches 50. It provides a simple, sensitive and effective way for the detection of clonidine and cyproheptadine in animal-derived foods.

Declaration of competing interest: The authors have declared no conflict of interest.

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