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# Simple Determination of Histamine in Cheese by Capillary Electrophoresis with Diode Array Detection

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## ABSTRACT

A capillary electrophoresis method with diode array detection for quantitative analysis of histamine (HIS) in cheese was developed and validated. The electrophoretic conditions studied for method optimization were buffer concentration (25-100 mM) and pH (2.5-6.5), voltage (10-30 kV) and temperature (20-35°C). The effects of these conditions on peak shape, sensitivity and migration time were tested. The optimized method was validated for linearity, sensitivity, accuracy, precision (intraday and interday repeatability) and recovery. The limit of detection (LOD) and limit of quantitation (LOQ) values of the validated method were determined as 20 mg/kg and 61 mg/kg for HIS, respectively. This method was successfully applied for quantitative analysis of HIS in 16 traditional cheese samples obtained from different Turkish markets. Histamine was detected in 15 samples (94%) with a level greater than LOD, and in 2 (13%) samples greater than LOQ, with the values of 91.5 and 65.9 mg/kg.

Key words: biogenic amines, histamine, capillary electrophoresis, cheese, optimization, validation

## INTRODUCTION

Biogenic amines are organic bases of low molecular weight and are formed in foods mainly by the microbial decarboxylation of certain amino acids[1,2]. One of the most studied amines, histamine (HIS) arises in foods by the growth of microorganisms that possess histidine decarboxylase and thus, foods rich in free histidine can contain high level of HIS. Although fish of the families *Scombridae* and *Scomberesocidae* are commonly implicated in incidents of HIS poisoning, non-scombroid fish, cheese and other foods have also been attributed in cases of such poisoning[3].

Besides fish, cheese is the second most significant source of biogenic amines and many organisms may be the cause of amine formation in cheese[3-5]. Several studies have been performed for the identification of lactic acid bacteria capable of producing HIS, and several species have been recovered from cheese, including *Lactobacillus buchneri*, *Lactobacillus bulgaricus*, *Lactobacillus plantarum*, *Lactobacillus helveticus*, *Streptococcus faecium* and *Streptococcus lactis*. Since some of these bacteria are utilized as starter cultures and reach high populations during ripening, their identification as HIS producers is important to the dairy industry[2,3].

The presence of biogenic amines in food constitutes a potential public health concern because of their physiological and toxicological effects[6]. HIS is a powerful biologically active chemical that can directly stimulate the heart, cause extravascular smooth muscle to contract or relax, stimulate both sensory and motor neurons, and control gastric secretion. Therefore, a wide variety of symptoms can be attributed to this type of poisoning[3].

The predominant biogenic amines found in several types of cheese are tyramine, putrescine, cadaverine and histamine[1,3,5]. Amine contents may vary among different types of cheese, and ripened cheeses usually contain higher concentrations of amines than unripened cheeses. This difference can be related to casein proteolysis during ripening[5,7]. Moreover, the duration and conditions of the ripening period and starter culture types used are important factors for the production of amines[5]. Also, bacterial quality of milk, heat treatments applied, pH, salt concentration, and temperature are the other parameters leading to differences among a variety of cheese[3,5].

Due to the impact of biogenic amines on human health and food safety, monitoring their levels in foodstuffs is still gaining importance[6]. Quantitative instrumental analyses developed so far for the analysis of biogenic amines in food samples include thin-layer chromatography, gas chromatography, liquid chromatography, capillary electrophoresis (CE) and biochemical assays. Among these, high performance liquid chromatography (HPLC) by pre- or post-column derivatization is most frequently reported[6,8], and only a few analyses do not require time consuming derivatization procedures, such as enzymic sensor array method detection, HPLC

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with conductometric detection and some CE methods[6]. CE has emerged in recent years as a powerful analytical technique for the separation and quantification of various substances. It possesses many unique advantages, such as small sample values, high separation efficiency, low consumption of reagents, short analysis time and easy conditioning of column. Therefore, CE has been considered an alternative technique to HPLC[9].

Since most of the previously reported HIS analysis methods applying capillary electrophoresis concentrate on fish samples and/or require time consuming derivatization steps[10-12], we aimed to develop a less time consuming, sensitive and easy CE method with diode array detection (DAD) for the assay of HIS in cheese. For this purpose, the influence of buffer concentration, buffer pH, capillary temperature and applied voltage were systemically investigated. The optimized method was evaluated according to a series of validation tests including linearity, sensitivity, precision, accuracy and recovery. Usefulness of the developed and validated method was also investigated with cheese samples available in Turkish markets. The results obtained by the developed method were compared with the literature.

## MATERIALS AND METHODS

### I. *Chemicals*

The reference standard histamine (~97% purity) was purchased from Sigma-Aldrich (Steinheim, Germany). Analytical grade reagents sodium phosphate monobasic dihydrate ($NaH_2PO_4 \cdot 2H_2O$) and sodium hydrogen phosphate dihydrate ($Na_2HPO_4 \cdot 2H_2O$), used for the preparation of buffers were from Riedel-de Haën (Seelze, Germany) and JT Baker (Deventer, Holland), respectively. Phosphoric acid and hydrochloric acid were from Merck (Darmstadt, Germany) and sodium hydroxide 0.1 M used to clean the capillary was supplied from Agilent Technologies (Waldbronn, Germany). Deionized water obtained by the TKA-GenPure water-purifying system (Niederelbert, Germany) was used to prepare the solutions and flush the column.

### II. *Apparatus*

Experiments were performed using an Agilent G1600A model 3D CE system (Waldbronn, Germany) equipped with a 1200 series diode array detector (model G1315B), automatic sample injector, temperature controller and high voltage power supply, and were controlled by ChemStation software. Electrophoretic separations were carried out in an uncoated fused-silica capillary (Agilent Technologies) of 50 μm i.d. and 41 cm total length with a 32.5 cm effective length from inlet to the detector. Before its first use, the new capillary was conditioned by flushing with 1.0 M NaOH, water and 1.0 M phosphoric acid. In order to maintain the capillary in a good condition, it was rinsed with water, 0.1 M phosphoric acid and then the running buffer at the beginning of each working day. Between each run, the capillary was preconditioned with 0.1 M phosphoric acid (8 min), and then with running buffer (12 min), since the components adsorbed onto the capillary surface could change the effective charge on the wall. All injections were made in a hydrodynamic mode over 5 s under a pressure of 50 mbar. Buffer reservoirs were replaced every four runs. Diode array detector for detection of HIS was set at 214 nm.

### III. *Standard and Sample Solutions*

#### (I) *Standard Stock Solution*

The stock solution of HIS (1 mg/mL) was prepared in 0.1 M HCl and kept at 4°C. HIS standard solutions (0.005, 0.01, 0.02, 0.04, 0.06, 0.08, 0.1 and 0.2 mg/mL) were prepared by appropriate dilutions of the stock solution in 0.1 M HCl.

#### (II) *Sample Preparation*

Sixteen traditional cheese samples from different regions of Turkey were obtained randomly from local markets within Ankara (Turkey). The samples were stored in their original packets at 4°C until analyses. A method modified from Cinquina *et al.*[12] and Lange *et al.* for the extraction of HIS from cheese samples,[13] was employed. Five grams of homogenized cheese were mixed with 30 mL of 0.1 M HCl, and the mixture was vortex stirred for 10 min in a centrifuge test tube. The sample was then placed in an ultrasound bath for 10 min, and supernatant was filtered through a Whatman No.1 filter paper after centrifugation at 3°C for 15 min at 10000 rpm. Afterwards, this extraction procedure was repeated once again using 20 mL of 0.1 M HCl. Supernatants were then combined. The final volume was made 50 mL with 0.1 M HCl in volumetric flask and filtered through a 0.45 μm nylon membrane filter prior to injection into the CE-DAD system. Identification of HIS was carried out by comparing retention time and spectral data with standard.

### IV. *Method Development*

For the optimization of the electrophoretic conditions, sodium phosphate buffer at four different concentrations (25, 50, 75 and 100 mM) and five different pH values (2.50, 3.50, 4.50, 5.50 and 6.50) were tested as the running buffer. Different voltages (10, 15, 20, 25 and 30 kV) and separation temperatures (20, 25, 30 and 35°C) were also applied. In each case, several parameters such as peak shape, peak symmetry, peak tailing, peak area and migration time were evaluated, and the conditions giving the best results in terms of these parameters were

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chosen. The detection wavelength was fixed at 214 nm in all above experiments.

V. *Validation of the Method*

Validation of the proposed method was performed with respect to linearity, sensitivity (limit of detection and limit of quantitation), precision (intraday and interday repeatability), accuracy and recovery. These validation criteria were studied under the optimal analysis conditions determined. For the assessment of linearity, calibration curves were constructed by measuring eight calibration points ranging from 0.005 to 0.2 mg/mL for HIS. Aliquots of HIS stock solution were diluted in 0.1 M HCl in order to obtain standard solutions containing histamine in concentrations of 0.005, 0.01, 0.02, 0.04, 0.06, 0.08, 0.1 and 0.2 mg/mL, and three replicates of each calibration point were analyzed. Correlation coefficient was obtained by plotting the average peak area versus concentration.

The limit of detection (LOD) and limit of quantitation (LOQ) were established by analyzing the calibration curves. In order to calculate the LOD and LOQ values, the following equation has been used:

$$C = \frac{K \times SD}{m}$$

where SD is the standard deviation of the y-intercept values, and m is the mean slope value from the three calibration curves constructed. The K values were 3.3 for LOD and 10 for LOQ.

The precision (intraday and interday repeatability) of the system was calculated by making five replicate injections with standard solutions containing HIS at three different concentrations (0.02, 0.06 and 0.1 mg/mL), while keeping the operating conditions identical. Statistical evaluation was expressed as relative standard deviation (RSD). Peak area was measured in all cases. Accuracy of the method has been assessed by calculating the deviation (%) of the concentration data obtained during the precision study from the actual concentrations.

Recovery studies of the method were performed by spiking cheese sample with HIS at two different concentrations (0.05 and 0.1 mg/mL), and samples were treated as described in the procedure for sample preparation. Recovery was determined by comparing the measured responses of HIS obtained from the spiked samples with the responses of calibration standards. Measured HIS levels were corrected for any natural contamination by the analysis of the non-spiked sample.

VI. *Statistical Analysis*

The effect of two different days on peak area values were statistically evaluated by one-way analysis of variance (ANOVA) using the SPSS program, version 13.0. Statistical differences with *P*-values under 0.05 were considered significant.

## RESULTS AND DISCUSSION

I. *Optimization of the Electrophoretic Conditions*

For the development and optimization of the CE method, several parameters were tested to obtain the best peak shape and the highest sensitivity. The influence of temperature on analysis was investigated because of its important effect on CE measurements. HIS standard was injected into the thermostated capillary at four different separation temperatures (20, 25, 30 and 35°C). An increase of the capillary temperature resulted in a decrease of migration times due to smaller electrolyte viscosity. However, small changes in peak shape were observed. The capillary temperature was decided to be kept constant at 30°C.

In order to study the effect of voltage, five different voltages in the range 10-30 kV were applied. System current was considerably high at higher voltage values, resulting in an increased heating inside the capillary. The method performed well between 10 and 20 kV. However, we did not obtain good results at 25 and 30 kV, since voltage over 20 kV resulted in lower resolution and shorter migration times. The best result in terms of peak resolution, peak shape and analysis time, with a good level of baseline noise, was achieved with 15 kV, which was applied in the following studies.

Another important parameter for CE is the buffer system. In this research, the effects of ionic strength and pH of the sodium phosphate buffer, which was used as the running buffer, were also studied. The effect of buffer pH was investigated in the range of pH 2.50 - 6.50. As the buffer pH increased, distortion in peak shapes and a decrease in migration times were observed, particularly at pH 6.50. Choosing the lowest pH value (pH 2.50) enabled not only a good separation, but also reasonable retention time. Therefore, the pH of the running buffer was adjusted to 2.50 for further studies.

When different phosphate buffer concentrations within the range of 25-100 mM were compared at pH 2.50, the system current was too high (nearly 100 μA) with higher phosphate concentrations. The best results regarding peak shape and symmetry were obtained with the concentration of 75 mM. However, peak shape and symmetry failed clearly at higher concentrations (100 mM). So, the buffer concentration giving the best compromise between the parameters considered was 75 mM.

Ultimately, the optimal CE conditions for the separation were determined to be 75 mM phosphate buffer adjusted to pH 2.50, with capillary temperature set at 30°C and voltage of 15 kV. Under the defined conditions, an adequate shape of HIS peak and an easy HIS quantitation could be achieved. Figure 1a shows typical electropherograms belonging to HIS before and after the optimi-

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zation of CE conditions. The migration time of HIS was approximately 3 min. The total time of analysis including preconditioning of the capillary was 25 min.

II. *Validation of the CE-DAD Method*

(I) *Linearity Range*

Under the optimal CE conditions, the method presented linearity in the concentration range of 0.005-0.2 mg/mL. In terms of the dilution factors in sample preparation, this range corresponds to a concentration of 50-2000 mg/kg in the sample. The linearity curve was defined by the following equation: y =677.77x + 2.19, where y is the average peak area and x is the HIS concentration, expressed in mg/mL. Each point in the final calibration curve corresponded to the mean value of three independent measurements. A linear response between peak area and concentration was observed (r = 0.9990). The analytical characteristics of the developed CE method are given in Table 1.

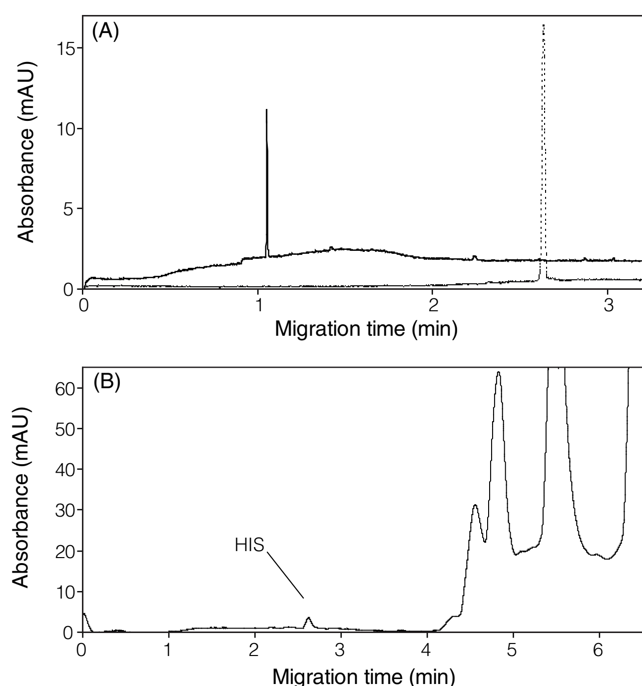


**Figure 1.** (a) Electropherograms of HIS standard solution before (straight line) and after (dashed line) the optimization of CE conditions; (b) Electropherogram of Erzincan Tulum cheese for histamine analysis. Conditions: uncoated capillary, 41 cm × 50 µm i.d.; run buffer, 75 mM phosphate (pH 2.50); injection, 250 mbars; voltage, 15 kV; temperature, 30°C; detection, UV at 214 nm.

(II) *Sensitivity*

The results obtained in the linearity test were used to calculate LOD and LOQ for HIS. LOD, the lowest concentration detectable, was calculated to be 0.0020 mg/mL (Table 1), which can be expressed as 20 mg/kg when the dilution factor in the sample preparation procedure is considered. LOQ is defined as the lowest concentration on the calibration curve that can be quantified with acceptable precision and accuracy, and it was found to be 61 mg/kg for the proposed method.

**Table 1.** Analytical characteristics of the proposed method (n = 3)

| Characteristic | Value |
|---|---|
| Regression equation | y=677.77x +2.19 |
| Correlation coefficient (r) | 0.9990 |
| Standard error of slope | 17.35 |
| Standard error of intercept | 0.24 |
| *LOD (mg/mL) | 0.0020 |
| **LOQ (mg/mL) | 0.0061 |

* LOD: Limit of detection.
** LOQ: Limit of quantification.

**Table 2.** Intraday and Interday repeatability of peak areas (n = 5)

| | Intraday | | | Interday | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Concentration (mg/mL) | | | *Concentration (mg/mL) | | | | | |
| | 0.02 | 0.06 | 0.1 | 0.02 | | 0.06 | | 0.1 | |
| Statistical parameter | Day 1 | Day 1 | Day 1 | Day 1 | Day 2 | Day 1 | Day 2 | Day 1 | Day 2 |
| Mean peak area | 17.32 | 43.66 | 73.08 | 17.32 | 18.28 | 43.1 | 43.82 | 68.08 | 69.8 |
| **SD | 0.77 | 1.25 | 0.97 | 0.76 | 0.83 | 2.10 | 1.80 | 2.90 | 3.07 |
| ***RSD% | 4.42 | 2.86 | 1.32 | 4.37 | 4.55 | 4.86 | 4.10 | 4.25 | 4.40 |

* The effect of two different days on peak area values was found insignificant.
** SD: Standard deviation.
*** RSD: Relative standard deviation (RSD% = (SD / mean) × 100).
Intraday: Repeatability is obtained by the analyses carried out in the same day.
Interday: Repeatability is obtained using the results of different days.

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**Table 3.** Accuracy of the method (n = 5)

| Actual concentration (mg/mL) | Calculated concentration (mg/mL), mean ± *SD | **RSD% | ***Deviation% |
|---|---|---|---|
| 0.06 | 0.0612 ± 0.0018 | 3.01 | 1.97 |
| 0.1 | 0.0972 ± 0.0043 | 4.40 | 2.79 |

* SD: Standard deviation.
** RSD: Relative standard deviation (RSD% = (SD / mean) × 100).
*** Deviation% = (Actual concentration – Mean calculated concentration) / Actual concentration × 100.

(III) *Precision*

The results of intraday repeatability expressed as the relative standard deviation (RSD%) are shown in Table 2, and were found to be 4.42, 2.86 and 1.32% for the concentrations of 0.02, 0.06 and 0.1 mg/mL, respectively. Furthermore, the analysis of HIS standard solutions on two different days showed adequate values of precision (RSD < 5% for each point) considering peak area values (Table 2). The effect of different days on peak area values was found statistically insignificant.

(IV) *Accuracy and Recovery*

Accuracy of the method, defined as its ability to give responses close to the true value, was expressed in terms of deviation % of the mean calculated concentrations from the actual concentrations for HIS standard solutions of 0.06 and 0.1 mg/mL (Table 3). Since the results were within the acceptable range of ± 5%, the method is deemed to be accurate.

The mean percentage recoveries for the spiking levels of 0.05 and 0.1 mg/g were found to be 93.7% and 99.4% respectively, with an average recovery value of 96.6% and RSD of 11.1%. The two concentrations assayed had close recovery percentages, which demonstrated the precision of the analytical procedure.

**Table 4.** Histamine concentration of cheese samples

| Cheese sample | Histamine concentration (mg/kg) |
|---|---|
| Erzincan Tulum | 91.46 |
| İzmir Tulum | 65.89 |
| Antalya Otlu (herbed) | *NQ |
| Denizli Lor | NQ |
| Gaziantep | NQ |
| Bolu Dil | NQ |
| Erzincan Bidon Tulum | NQ |
| Urfa | NQ |
| Balıkesir Mihalıç | NQ |
| Diyarbakır Örgü | NQ |
| Konya Özel Bez | NQ |
| Bolu İsli (smoked) | NQ |
| Denizli Köy | NQ |
| Trakya Eski Kaşar (aged) | NQ |
| White cheese | NQ |
| Balıkesir Yörük | **ND |

* NQ: non quantifiable (histamine level below 61 mg/kg).
** ND: non detectable (histamine level below 20 mg/kg).

III. *Analysis of Cheese Samples*

This optimized CE method was applied to measure HIS in 16 traditional cheese samples, and the amounts of HIS were calculated using the calibration curve obtained. Table 4 shows HIS levels in the 16 cheese samples. According to the results, HIS level was below the LOQ value in most of the investigated cheese samples and could not even be detected in Denizli Yörük cheese. Only two samples were contaminated with a level greater than LOQ at the values of 91.5 and 65.9 mg/kg.

Erzincan Tulum cheese contained the highest level of HIS (91.46 mg/kg) among all types of cheese samples, followed by İzmir Tulum cheese (65.89 mg/kg). Since Tulum cheese is a ripened cheese , it can be concluded that ripened cheeses contain more histamine than fresh cheeses such as Denizli Lor, Bolu Dil, Diyarbakır Örgü and white brined cheese. This can be explained by the formation of free amino acids due to hydrolysis of casein during ripening. These results are also in agreement with the results of Durlu-Özkaya[4], who screened HIS contents of some Turkish cheeses by HPLC, and reported that matured cheeses contained more biogenic amines than fresh cheeses. Authors determined HIS contents of Civil and Mihalıç cheese as 947.6 and 126.4 mg/kg, respectively. On the other hand, in our study HIS levels of some other ripened hard cheese varieties such as Urfa, Balıkesir Mihalıç and Trakya Eski Kaşar were found to be lower than the quantitation limit.

Cheese is an ideal substrate for biogenic amine formation because of the possible presence of decarboxylase-positive microorganisms, the convenience of environmental conditions for the growth of these microorganisms, and the presence of some cofactors[1]. The U.S. and the European Community (EC) have set a maximum limit of 100 ppm for HIS in fish, but not in cheese. However,

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a maximum limit of 900 mg/kg was suggested for tyramine, HIS, putrescine and cadaverine combined[7]. The acceptable level of HIS in cheese was reported as 100 mg/kg by Durlu-Özkaya[4] and Durlu-Özkaya *et al*.[14]. Although the concentration of HIS in all cheese samples analyzed in this study was lower than the acceptable limit, the Erzincan Tulum cheese content was found to be fairly close to the limit. On the other hand, since symptoms of clinical illness have been associated with the consumption of a minimum of 100 to 180 mg of HIS, it seems unlikely that any of the cheeses analyzed in this study could cause intoxication, unless consumed in very large quantities[2].

In another study, Kung *et al*.[15] investigated the histamine contents of some cheese samples from Taiwan, and reported that histamine contents were higher than the 5 mg/100 g limit set by the U.S. Food and Drug Administration for scombroid fish and/or product, in 54.8% and 15.4% of the natural and processed cheese samples, respectively. The average histamine content of natural cheeses was found to be 7.9 mg/100 g.

The electropherogram for Erzincan Tulum cheese is given in Figure 1b. As it can be seen from the figure, a single analysis could be completed in 5 min under the given CE conditions. HIS peak was generally well separated from the other co-extracted components, allowing a clear identification and quantitation, but after many (approximately 7-8) injections some compounds might coeluate with HIS and prevent its identification just by the retention times. This problem might be arising as a result of a decrease in the initial efficiency of the capillary, due to the alteration of the effective charge on the capillary wall by some adsorbed components. In this respect, it can be useful to flush the column at regular intervals with a longer conditioning procedure, besides the preconditioning performed between each run.

Lange *et al*.[13] compared a CE method with HPLC for the determination of HIS and other biogenic amines in various food samples including cheese, and found a good correlation between the two methods. In contrast to HPLC, no laborious sample treatment was necessary with CE, and amines could be separated within a shorter time. In that study, HIS appeared at a migration time of 4.6 min.

## CONCLUSIONS

The results of our study showed that the validated CE technique with DAD detection for the HIS in cheese is reliable and reproducible. The use of CE for HIS analysis seems to be a superior alternative to other methods in terms of being simple (no derivatization or sample preconcentration), rapid, cost-effective and allowing analysis of very small volumes of the sample, making it a useful tool for screening a large number of samples in a short period of time. Optimum separation of HIS was obtained using 75 mM phosphate buffer adjusted to pH 2.50, with a capillary temperature set at 30°C and a voltage of 15 kV. A detection limit of 20 mg/kg was obtained for HIS. Under the optimized conditions, detection of HIS could be achieved accurately and precisely within 5 min. Analysis of cheese samples showed that this method offers a potentially convenient technique for the analysis of HIS in cheese.

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## REFERENCES

1. Novella-Rodríguez, S., Veciana-Nogués, M. T., Trujillo-Mesa, A. J. and Vidal-Carou, M. C. 2002. Profile of biogenic amines in goat cheese made from pasteurized and pressurized milks. J. Food Sci. 67: 2940-2944.
2. Innocente, N. and D’agostin, P. 2002. Formation of biogenic amines in a typical semihard Italian cheese. J. Food Prot. 65: 1498-1501.
3. Stratton, J. E., Hutkins, R. W. and Taylor, S. L. 1991. Biogenic amines in cheese and other fermented foods: A review. J. Food Prot. 54: 460-470.
4. Durlu-Özkaya, F. 2002. Biogenic amine content of some Turkish cheeses. J. Food Process Preserv. 26: 259-265.
5. Novella-Rodríguez, S., Veciana-Nogués, M. T., Izquierdo-Pulido, M. and Vidal-Carou, M. C. 2003. Distribution of biogenic amines and polyamines in cheese. J. Food Sci. 68: 750-755.
6. Önal, A. 2007. A review: Current analytical methods for the determination of biogenic amines in foods. Food Chem. 103: 1475-1486.
7. Flick, G. J. and Granata, L. A. 2004. Biogenic amines in foods. In “Toxins in food”. pp. 121-154. Dąbrowski, W. M. and Sikorski, Z. E. eds. CRC Press. US
8. Loukou, Z. and Zotou, A. 2003. Determination of biogenic amines as dansyl derivatives in alcoholic beverages by high-performance liquid chromatography with fluorimetric detection and characterization of the dansylated amines by liquid chromatography-atmospheric pressure chemical ionization mass spectrometry. J. Chromatogr. A 996: 103-113.
9. Süslü, İ., Demircan, Ş., Altınöz, S. and Kır, S. 2007. Optimisation, validation and application of a capillary electrophoretic method for the determination of zafirlukast in pharmaceutical formulations. J. Pharm. Biomed. 44: 16-22.
10. Su, S. C., Chou, S. S., Chang, P. C. and Hwang, D. F. 2000. Determination of biogenic amines in fish implicated in food poisoning by micellar electrokinetic

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capillary chromatography. J. Chromatogr. B 749: 163-169.
11. Male, K. B. and Luong, J. H. T. 2001. Derivatization, stabilization and detection of biogenic amines by cyclodextrin-modified capillary electrophoresis-laser-induced fluorescence detection. J. Chromatogr. A 926: 309-317.
12. Cinquina, A. L., Longo, F., Calì, A., De Santis, L., Baccelliere, R. and Cozzani, R. 2004. Validation and comparison of analytical methods for the determination of histamine in tuna fish samples. J. Chromatogr. A 1032: 79-85.
13. Lange, J., Thomas, K. and Wittmann, C. 2002. Comparison of a capillary electrophoresis method with high-performance liquid chromatography for the determination of biogenic amines in various food samples. J. Chromatogr. B 779: 229-239.
14. Durlu-Özkaya, F., Alichanidis, E., Litopoulou-Tzanetaki, E. and Tunail, N. 1999. Determination of biogenic amine content of Beyaz cheese and biogenic amine production ability of some lactic acid bacteria. Milchwissenschaft 54: 680-682.
15. Kung, H. F., Tsai, Y. H., Hwang, C. C., Lee, Y. H., Hwang, J. H., Wei, C. I. and Hwang, D. F. 2005. Hygienic quality and incidence of histamine-forming *Lactobacillus* species in natural and processed cheese in Taiwan. J. Food and Drug Anal. 13: 51-56.