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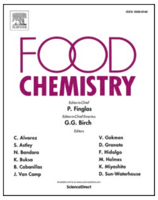

Determination of primary aromatic amines from cooking utensils by capillary electrophoresis-tandem mass spectrometry

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Benzidine (PubChem CID: 7111)
2-Naphthylamine (PubChem CID: 7057)
4-Aminobiphenyl (PubChem CID: 7102)
o-Toluidine (PubChem CID: 7242)
4-Chloro-2-methylaniline (PubChem CID: 7251)
4-Aminoazobenzene (PubChem CID: 6051)
o-Anisidine (PubChem CID: 7000)
4,4′-Diaminodiphenylmethane (PubChem CID: 7577)
2,4-Diaminotoluene (PubChem CID: 7261)
2,6-Dimethylaniline (PubChem CID: 6896)
4-Chloroaniline (PubChem CID: 7812)
4,4′-Oxydianiline (PubChem CID: 7579)
2-Methoxy-5-methylaniline (PubChem CID: 8445)
3,3′-Dimethylbenzidine (PubChem CID: 8413)
4,4′-Diaminodiphenyl sulfide (PubChem CID: 8765)
4,4′-Methylene-bis-(2-methylaniline) (PubChem CID: 13283)
Aniline (PubChem CID: 6115)
2,6-Diaminotoluene (PubChem CID: 13205)
3-Chloro-4-fluoroaniline (PubChem CID: 9708)

ABSTRACT

This paper describes a fast, sensitive, environment-friendly method for the determination of 19 primary aromatic amines (PAAs) in cooking utensils by capillary zone electrophoresis coupled with tandem mass spectrometry. The best electrophoretic separation of PAAs was obtained in 0.1 mol l^{-1} formic acid (pH 2.4) as the background electrolyte, fused silica capillary (67 cm) with a run time below 6 min. The proposed method presented a linear calibration with correlation coefficients higher than 0.99 and reproducibility in a range of 1–25%. Limits of detection were in the range of 0.2–1.3 μg kg^{-1} and recoveries were in a range of 85–120% for all the PAAs. The validated method was employed to determine PAAs on 36 samples of cooking utensils using acetic simulant. The results showed that 4,4′-diaminodiphenylmethane and aniline being the most frequently found PAAs in these samples and 28% of cooking utensils were not compliant.

1. Introduction

Primary aromatic amines (PAAs) are organic compounds characterized by the presence of a primary amine group attached to an aromatic ring. They are widely used as intermediates in the synthesis of azo dyes, pharmaceuticals and antioxidants in consumer goods including rubber products (Radomski, 1979). Several PAAs are classified by The World Health Organization's International Agency for Research on Cancer

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(International Agency for Research on Cancer, 2020) as carcinogenic or possibly carcinogenic to humans (International Agency for Research on Cancer, 2020). Therefore, PAAs represent a health risk and their presence in different matrices has been studied, especially in materials that have direct contact with food, due to the possibility of contamination by migration (Kiroska-Petreska, Popovska, Gjorgjev, Kostikj, & Petrovska, 2014; Schubert, Kappenstein, Luch, & Schulz, 2011; Trier, Okholm, Foverskov, Binderup, & Petersen, 2010; Wang & Chen, 2009).

Today, colorful kitchen utensils such as ladles, slotted spoons and skimmers made from different materials are widely used for cooking due to their high temperature resistance and low cost. However, chemical substances can migrate from these articles to food, contributing to food contamination (Shepherd, 1982). The migration of PAAs from cooking utensils to food may occur due to the presence of azo dyes residues from the coloring process as well as the addition of comonomer (Campanella, Ghaani, Quetti, & Farris, 2015; McCall, Keegan, & Foley, 2012). In order to protect consumer health, Brazilian legislation has established a specific migration limit for materials and articles of plastic used in contact with food. The Brazilian Regulation No. 326/2019, which describe the positive list of additives for the preparation of plastic materials and polymeric coatings intended to come into contact with food sets a detection level of 0.01 mg kg^{-1} in food or food simulant (Brazil, 2019). The migration of materials for repeated use is determined in three sequential tests in the same specimen (Brazil, 2010). Due to that, several methods for the determination of PAAs at low concentration levels in migration assays have been developed, and the spectrophotometric method– initially adopted for the determination of PAAs– has been replaced by more sensitive and selective techniques (Kolado & Balcerzak, 2009; Paseiro-Cerrato, Noonan, & Begley, 2014; Sanllorente, Sarabia, & Ortiz, 2016).

Gas chromatography with flame ionization (GC-FID) or mass spectrometric detection (GC–MS) (Brede, Skjevrak, & Herikstad, 2003; Jain, Reddy-Noone, Pillai, & Verma, 2013; Rubio, Sanllorente, Sarabia, & Ortiz, 2014) and liquid chromatography with ultraviolet detection (LC–UV), tandem mass spectrometric (LC–MS/MS) or high resolution mass spectrometric detection (Lambertini et al., 2014; Mattarozzi, Lambertini, Suman, & Careri, 2013; OuYang, Luo, Wang, & Yang, 2014; Pezo, Fedeli, Bosetti, & Nerin, 2012; Sanchis, Coscollà, & Yusà, 2019; Sanchis, Coscollà, Roca, & Yusà, 2015; Yang et al., 2016) are the most explored techniques for the determination of PAAs. Whereas gas chromatographic analysis of the PAAs always requires derivatization of the sample, liquid chromatography uses other approaches. PAAs are very polar compounds that are ionized at low pH, and it is difficult to find a suitable stationary phase capable of retaining small and charged molecules in reversed-phase liquid chromatography, which results in loss of resolution and poor peak shape. To overcome this problem, some strategies such as increasing the pH of the mobile phase or of the sample and the use of ion-pairing chromatography have been adopted, but the high pH impairs ionization in the mass spectrometer, thereby decreasing the detectivity of the method (Aznar, Canellas, & Nerín, 2009; Lambertini et al., 2014; McCall et al., 2012; Mortensen, Trier, Foverskov, & Petersen, 2005; Sanchis et al., 2015; Sendón, Bustos, Sánchez, Paseiro, & Cirugeda, 2010; Yavuz, Valzacchi, Hoekstra, & Simoneau, 2016).

Free zone capillary electrophoresis (CE) is another important technique used to analyze PAAs, because it uses the ionic nature of these compounds to separate them. CE has several advantages over other separation techniques, including high peak resolution, short separation time, and minimal reagent and organic solvent consumption, which makes CE an environmentally friendly separation technique. An additional advantage is that CE can be performed with relatively simple instrumentation, and with very low running costs. However, CE sensitivity is low when compared to LC or GC. To overcome this limitation, CE can be used in combination with online preconcentration techniques, which has already been used for PAAs analysis with ultraviolet detection (CE-UV) (Liu, Wang, Chen, & Sun, 2012; Yang et al., 2016) or high sensitivity detectors such as laser-induced fluorescence (CE-LIF) (Asthana, Bose, Durgbanshi, Sanghi, & Kok, 2000; Li et al., 2013) or electrochemical ones (CE-EC) (Huang, You, Li, Yang, & Wang, 1999; Shin et al., 2004; Sun et al., 2009).

Another interesting combination, that could be used in the determination of PAAs is using of CE coupled to the mass spectrometer as a detection method. This provides significant advantages, combining the high separation efficiency of CE with the identification power of sequential MS. However, to the best of our knowledge, there is no report in the current literature on the determination of PAAs using capillary electrophoresis coupled to tandem mass spectrometric (CE-MS/MS). Thus, the aim of this work was to develop a quick, sensitive and selective method for the determination of nineteen PAAs originating from cooking utensils in food simulant using CE-MS/MS.

2. Material and methods

2.1. Chemicals, materials and standards

All the reagents were of analytical grade. Sodium hydroxide, formic acid and methanol were purchased from Sigma-Aldrich (St. Louis, MO, USA). Methanol was also J.T. Baker (Ecatepec, Mexico), while glacial acetic acid and acetone were acquired from Merck (Darmstadt, Germany). The standards of PAAs were from Sigma-Aldrich (St. Louis, MO, USA and Bellefonte, PA, USA), purity >98.2%. The internal standard, aniline-d5, was from Supelco (Bellefonte, PA, USA), purity 99.9%. The solutions were prepared with 18 MΩ cm deionized water (Millipore Milli-Q Direct). All amines were weighed using a 5-decimal analytical balance and stock standard solution were prepared individually in methanol, except 4,4′-oxydianiline which was dissolved in acetone.

Cooking utensil samples were purchased in Campinas, São Paulo, Brazil and in Washington D.C., USA. The thirty-six samples of kitchenware were acquired on the retail market in quintuplicate and were classified as polyamides (sixteen: seven from Brazil, seven from China and two from Turkey), polypropylene (one: from China) and silicone (nineteen: all from China). The samples are listed in Table 1. All samples were first identified by Fourier Transform Infrared Spectroscopy (Perez, Padula, Moitinho, & Bottoli, 2019). One polyamide-based sample and one silicone-based sample, in which none of the PAAs were found, were used as blanks for the matrix effect test.

2.2. Instrumental

The CE-MS system was an Agilent 7100CE coupled to an Agilent 6430 triple-quadrupole mass spectrometer equipped with an Agilent electrospray ionization (ESI) source (Agilent Technologies, Santa Clara, CA, USA). New capillaries were preconditioned by flushing with 0.1 mol l^{-1} NaOH solution (5 min), deionized water (10 min), and background electrolyte (BGE) (10 min). The standard solutions and samples were hydrodynamically injected at 100 mbar for 15 s (≈35 nl) with a previous flushing step with BGE for 30 s before each new injection. The PAAs separation by capillary electrophoresis was achieved using 0.1 mol l^{-1} formic acid, pH 2.4, as background electrolyte (BGE), and 1:1 (v/v) methanol with 0.01 mol l^{-1} formic acid/water, pH 2.4, as sheath liquid at a flow rate of 5 µl min^{-1}. The experiments were performed using a 67 cm long, 50 µm i.d., 360 µm o.d. fused-silica capillary, at 25 °C, with +28 kV at injection point.

Others experiments to separation of PAAs were used such as: BGE, 0.05 mol l^{-1} formic acid, time of injection (20 s), capillary fused-silica capillary (67 cm long, 50 µm i.d.), +28 kV at injection point; BGE, 0.1 mol l^{-1} formic acid, time of injection (20 s), capillary fused-silica capillary (67 cm long, 50 µm i.d.), +28 kV at injection point; BGE, 0.1 mol l^{-1} formic acid, time of injection (12 s), capillary fused-silica capillary (102 cm long, 75 µm i.d.), +29 kV at injection point; BGE, 0.1 mol l^{-1} acetic acid, time of injection (15 s), capillary fused-silica capillary (67 cm long, 50 µm i.d.), +28 kV at injection point; and BGE, 0.1 mol l^{-1} formic acid, time of injection (15 s), capillary polyvinyl

Table 1
Samples analyzed, material, origin, other information.

Sample #	Material	Color	Origin	Photograph	Manufacturer Specification	Food Symbol
1	polyamide	black	Brazil		BPA free, Nylon, Resistant up to 180ºC, Dishwasher safe	Yes
2	polyamide	black	Turkey		BPA free	No
3	polyamide	red	Brazil		Nylon utensils, Dishwasher safe, Resistant up to 180ºC	Yes
4	polyamide	blue	Brazil		(-)	No
5	polyamide	black	Brazil		Nylon utensils, Dishwasher safe, Resistant up to 180ºC	Yes
6	polyamide	black	Brazil		Resistant to high temperatures	No
7	polyamide	gray	Brazil		Nylon, Stainless steel shank, Polypropylene handle, Dishwasher safe, Resistant up to 180°C	Yes
8	polyamide	red	China		Plastic material, Dishwasher safe, Avoid exposure to direct heat sources	No
9	polyamide	blue	China		(-)	No
10	polyamide	black	China		Utensil with inox cable, 50% Polyamida, 50% Inox	No
11	polyamide	black	China		Black nylon, Dishwasher safe	No
12	polyamide	gray	China		Resistant from -40°C until 220ºC, Dishwasher safe, Nylon	Yes
13	polyamide	white	Turkey		Resistant up to 220ºC, Dishwasher safe PPA	Yes
14	polyamide	green	China		(-)	No
15	polyamide	black	Brazil		BPA free, Nylon, Dishwasher safe, Resistant up to 180°C	Yes
16	polyamide	black	China		Nylon, Heat resistant to 400°F, Dishwasher safe	No
17	polypropylene	white	China		PP plastic, non toxic, PVC free, Resistance from -20°C up to 100ºC, Dishwasher safe	Yes
18	silicone	green	China		Silicone, Inox cable	Yes
19	silicone	green	China		Easy to clean nonstick resistant, Silicone utensils	No
20	silicone	green	China		Silicone, Dishwasher safe, Resistant up to 180°C, Do not place in direct heat or open flame	No
21	silicone	green	China		Silicone	No
22	silicone	red	China		Silicone, Inox cable	Yes
23	silicone	red	China		Silicone utensils, Use neutral detergent, Dishwasher safe	No

(*continued on next page*)

acetate (PVA) (67 cm long, 50 μm i.d.), +28 kV at injection point. Another parameters were kept identical as 1:1 (v/v) methanol with 0.01 mol l^{-1} formic acid/water, pH 2.4, as sheath liquid at a flow rate of 5 μl min^{-1}, at 25 °C.

Nitrogen nebulizer pressure was 55158,1 Pa, drying gas was nitrogen at a flow rate of 5 L min^{-1} and temperature at 350 °C. The inlet capillary voltage was 4.5 kV. The instrument was operated in positive multiple reaction monitoring (MRM) mode using two specific transitions for each PAA. Table 2 describes the MS/MS acquisition parameters used for the determination of PAAs. The most intense transitions were used for quantification and the others were used as qualifying ions for the confirmation of the analysis.

Table 1 (*continued*)

24	silicone	red	China		Silicone, Dishwasher safe, Resistant up to 180°C, Do not place in direct heat or open flame	No
25	silicone	red	China		Silicone	No
26	silicone	yellow	China		Silicone utensils, Easy to clean nonstick resistant	No
27	silicone	yellow	China		Silicone	No
28	silicone	blue	China		Silicone utensils, Easy to clean nonstick resistant	No
29	silicone	blue	China		Silicone, Dishwasher safe, Resistant up to 180°C, Do not place in direct heat or open flame	No
30	silicone	blue	China		Silicone	No
31	silicone	gray	China		Silicone, Inox cable	Yes
32	silicone	orange	China		Silicone utensils, Easy to clean nonstick resistant	No
33	silicone	orange	China		Silicone and metal, Do not place in direct heat or open flame	No
34	silicone	orange	China		Silicone	No
35	silicone	purple	China		Silicone utensils, Easy to clean nonstick resistant	No
36	silicone	purple	China		Silicone	No

(-) without information.

2.3. Migration test

According to the rules specified for migration testing, the relative density for all simulants was conventionally assumed to be '1'. Therefore, 1 kg of food simulant is taken as having a volume of 1 L (European Committee for Standardization, 2004). Basically, the area of samples was measured, and the food simulant volume calculated to follow the ratio of 100 ml to 0.6 dm^2 of sample area. The kitchen utensils submerged in a 3% (w/v) aqueous acetic acid solution were submitted to the boiling point of the simulant (100 °C ± 3 °C) for 2 h (until +5 min) as recommended by the technical guide (Simoneau, 2009). To avoid evaporation, two pieces of aluminum foil were used over the top of the beaker or bowl and the evaporation was controlled by weighting before and after the heating. After this procedure, the samples were removed from the simulant and the liquid was transferred to a 10 ml volumetric flask to which aniline-d5 at a final concentration of 20 $\mu g\ kg^{-1}$ was added. The extracts were filtered using a 0.2 µm membrane filter prior to CE-MS/MS analysis.

Kitchen utensils are articles of repeated use and for this reason the procedure described was repeated twice more with the same specimen, using fresh food simulant, totaling three repetitions (1st migration, 2nd migration and 3rd migration). For each kitchenware, five specimens were used, and the results of each migration test refer to the average of the obtained values for these specimens.

2.4. Validation

The validation of the method was performed according to the guideline EUR 24105 outlined by the European Union Reference (EUR) for food contact materials (Bratinova et al., 2009). The limit of detection (LOD) was calculated from the standard deviation of the blank. According to the guideline EUR 24105, LOD at 3 times the standard deviation of the lowest concentration level, are defined as:

$$LOD = 3 \cdot s_{Bl}$$

where: S_{Bl} is the standard deviation of the analysis.

The limit of quantification (LOQ) was calculated as:

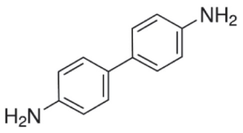
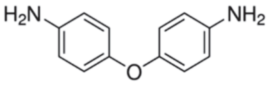
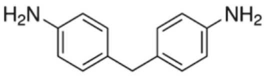
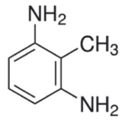
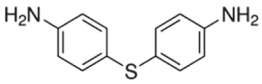
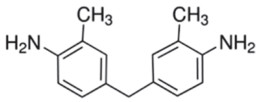
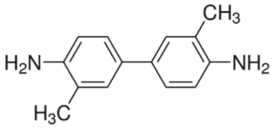
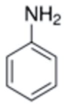
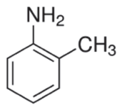
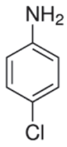
$$LOQ = 3 \cdot LOD$$

For the analytical curves, concentrations of 5, 10, 20, 30, 40, 50, 60, 70, 80, 90 and 100 $\mu g\ kg^{-1}$ and 100, 200, 300, 400 and 500 $\mu g\ kg^{-1}$ in 3% (w/v) aqueous acetic acid solution were prepared and injected in triplicate. Repeatability and reproducibility were performed at one day and three-day intervals, respectively, and using three different concentrations (5, 10 and 30 $\mu g\ kg^{-1}$) that were spiked into 3% (w/v) aqueous acetic acid solutions. Ten replicates were used for each concentration, and the precision was obtained as a percentage of RSD.

Trueness (recovery) was obtained from recovery using three different concentrations (5, 20 and 40 $\mu g\ kg^{-1}$). The plastic specimens were kept in contact with solutions of these three concentrations in 3% (w/v) aqueous acetic acid solution at 100 °C for 2 h. Ten replicates were used for each concentration and the values were expressed as percentages.

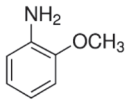
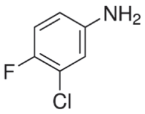
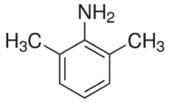
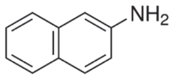
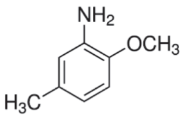
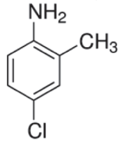
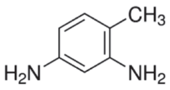
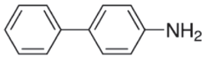
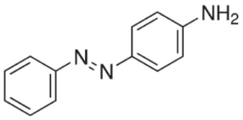
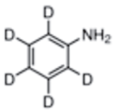
Matrix-matched calibration curves were prepared in polyamide and silicone matrix extracts at the same concentration levels as the analytical curve prepared in 3% (w/v) aqueous acetic acid solution. Sample 14, and sample 18 were used blank sample matrices for polyamide and silicone, respectively. These samples were maintained in a preheated

Table 2
Primary aromatic amines, CAS number, IARC group, migration time, pka and optimized MRM parameters.

Number	PAAs	CAS number	IARC[1] group	Migration time (min)	pka	Q1[a] (*m/z*)	Q3[b] (*m/z*)	CE[c] (V)	FE[d] (V)
1	benzidine 	92-87-5	1	3.23	3.65 4.73	185.1	167.0 139.1	36 64	136
2	4,4′-oxydianiline 	101-80-4	2B	3.24	3.76 4.64	201.2	108.2 80.3	20 40	141
3	4,4′-diaminodiphenylmethane 	101-77-9	2B	3.25	3.92 4.83	199.2	106.1 89.3	20 40	121
4	2,6-diaminotoluene 	823-40-5	–	3.37	2.80 5.28	123.1	106.2 79.3	20 20	96
5	4,4′-diaminodiphenyl sulfide 	139-65-1	2B	3.42	3.35 4.24	217.1	124.0 80.2	24 60	136
6	4,4′-methylene-bis-(2-methylaniline) 	838-88-0	2B	3.46	4.68 3.81	227.2	120.1 77.3	40 80	141
7	3,3′-dimethylbenzidine 	119-93-7	2B	3.48	3.55 4.58	213.1	198.1 181.1	20 24	125
8	aniline 	62-53-3	2A	3.68	4.64	94.1	77.2 51.3	20 40	31
9	o-toluidine 	95-53-4	1	3.85	4.48	108.2	91.1 65.3	20 40	170
10	4-chloroaniline 	106-47-8	2B	3.87	3.49	128.0	93.1 75.2	20 40	71

(continued on next page)

Table 2 (*continued*)

11	o-anisidine 	90-04-0	2A	3.87	4.42	124.0	109.0 80.1	20 40	81
12	3-chloro-4-fluoroaniline 	367-21-5	–	3.98	3.03	146.0	111.1 74.2	24 52	101
13	2,6-dimethylaniline 	87-62-7	2B	3.98	4.31	122.2	105.1 77.3	20 40	135
14	2-naphthylamine 	91-59-8	1	3.99	4.25	144.1	127.4 117.1	24 24	116
15	2-methoxy-5-methylaniline 	120-71-8	2B	3.99	4.63	138.1	123.4 106.1	16 40	111
16	4-chloro-2-methylaniline 	95-69-2	2A	4.05	3.41	142.0	106.1 89.1	40 16	121
17	2,4-diaminotoluene 	95-80-7	2B	4.15	2.91 5.58	123.0	106.0 79.0	20 24	61
18	4-aminobiphenyl 	92-67-1	1	4.16	4.28	170.1	153.0 128.0	20 25	136
19	4-aminoazobenzene 	60-09-3	2B	4.87	3.06	198.2	93.3 77.3	18 20	101
IS	aniline-d5 	4165-61-1	–	3.68	4.64	99.1	82.3 54.3	24 36	36

[1] IARC classification groups: 1 = carcinogenic to humans; 2A = probably carcinogenic to humans; 2B = possibly carcinogenic to humans; 3 = not classifiable as carcinogenic to humans. [a] Precursor ion (Q1), [b] Fragment ion (Q3), [c] Collision energy, [d] Fragmentor energy. Internal Standard (IS).

oven at 100 °C for 2 h. For more details in sample preparation, see item 2.3. After that, the matrix of polyamide or silicone was added to the mixture of amines in the concentrations of 10, 100, 200, 300 and 400 μg kg^{-1}, with three replicates per level. Aniline d-5 was added at the final concentration of 20 μg kg^{-1} and the solution was filtered using a 0.2 μm membrane filter.

The statistic test applied for normality was Shapiro-Wilk, and, later, a *t* test (Student) was run to compare the slopes of the analytical curves. The results considered a 95% confidence interval. The software used was Action 2.9.29.368.534 June/2015, version R:3.0.2 (Estatcamp).

3. Results and discussion

Although, different conditions were used to separate the PAAs, such as BGE, injection time, size of capillary and voltage at injection point, the choice was based on the best separation, shape of peak, migration time and better intensity of signal.

Fig. 1 illustrates the total ion electropherogram (TIE) and the extracted multiple reaction monitoring (MRM) electropherogram of the PAAs at 100 μg kg^{-1} each. As expected, doubly charged amines have small migration times, because of the higher electrophoretic mobilities.

The smallest value of LOD was 0.2 μg kg^{-1}, and the highest LOD was 1.3 μg kg^{-1} (Table 3). The LOD is compatible with the limit of detection considering the sum of primary aromatic amines released (10 μg kg^{-1}) (Brazil, 2019). The analytical curves were constructed considering the concentration range of 5–100 μg kg^{-1} and 100–500 μg kg^{-1}, and the determination coefficient (R^2). All amines had determination coefficients higher than 0.99.

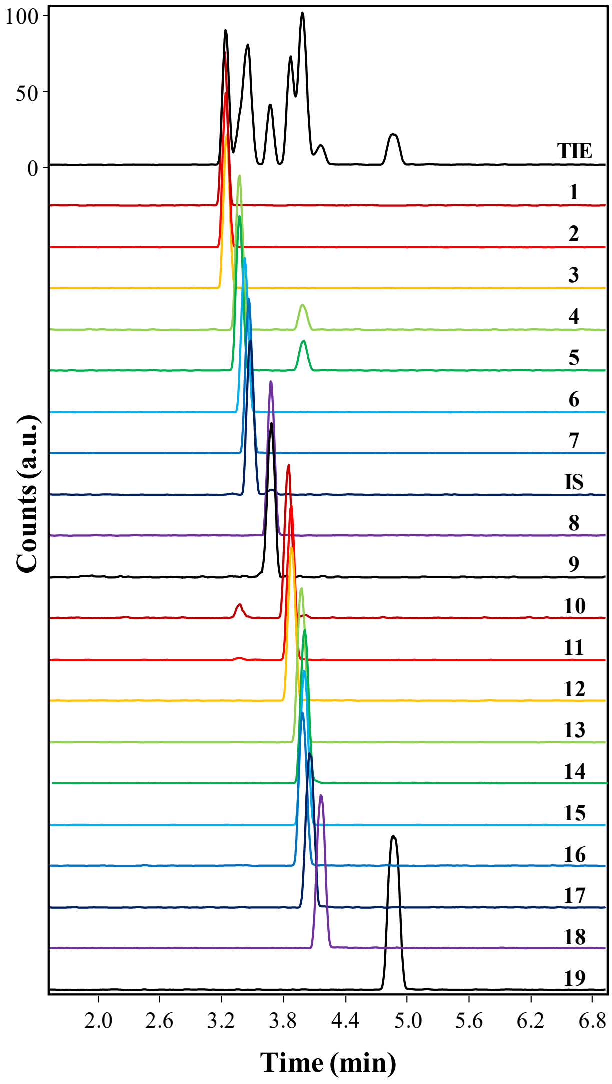


Fig. 1. Total ion electropherogram (TIE) and extracted MRM of PAAs at 100 μg kg^{-1} each. The migration order is the same shown in Table 2.

The results for precision (repeatability and reproducibility) are showed in Table 3. Considering repeatability (RSD%) for all amines, the range obtained was 1–23% (5 μg kg^{-1}), 1–21% (10 μg kg^{-1}) and 1–27% (30 μg kg^{-1}). The reproducibility for all amines was 1–25% (5 μg kg^{-1}), 7–20% (10 μg kg^{-1}) and 8–15% (30 μg kg^{-1}). The values accepted in the guideline EUR 24105 (Bratinova, Raffael, & Simoneau, 2009; Horwitz & Albert, 2006; Thompson, 2000) are up to 35.2% for 5 μg kg^{-1}, up to 31.7% for 10 μg kg^{-1}, and up to 26.9% for 30 μg kg^{-1}. Table 3 also shows the recovery, expressed in %. For a concentration of 5 μg kg^{-1}, the range was 85–120%. For a concentration of 20 μg kg^{-1}, the range was 91–112%, and for a concentration of 40 μg kg^{-1}, the range was 95–106%. The ranges accepted in guideline EUR 24105 (Bratinova et al., 2009) are 40–120% for concentrations ≤10 μg kg^{-1} and 60–110% for concentrations between 10 and 100 μg kg^{-1}.

Considering the analytical curves in three replicates per level – three curves for 3% (w/v) aqueous acetic acid solution, three curves of polyamide and three curves of silicone – the normality test of Shapiro-Wilk was applied. The 19 amines studied showed p-value ≥0.05, demonstrating that the results had a normal distribution. The *t* tests were applied comparing the analytical curve for 3% (w/v) aqueous acetic acid solution versus polyamide, and 3% (w/v) aqueous acetic acid solution versus silicone. Comparing the slopes of the analytical curves, the results showed the p-value ≥0.05 for all amines, which indicates no matrix matched effect. The only exception was for 3-chloro-4-fluoroaniline which showed a matrix effect in silicone when compared to 3% (w/v) aqueous acetic acid solution, with around 11% silicone matrix-related ion suppression. According to Sanchis, Coscolla, Roca, & Yusa (2015) values between 0 and 20% were not considered matrix matched effect.

3.1. *Sample analysis*

The 3% (w/v) aqueous acetic acid simulant is considered to be the simulant representing the worst case conditions to evaluate PAAs migration from food packaging (Lambertini et al., 2014).

The results of the specific migration of PAAs in cooking utensils are presented in Table 4. The absence of traceability and batch identification for cooking utensils makes it impossible to guarantee that the 5 specimens of each sample have been manufactured from the same batch of polyamide. This justifies the high standard deviations observed for the samples.

From a total of 16 polyamide samples, the presence of PAAs was not detected in nine of them. At least one PAA was detected and quantified in the remaining samples (identified in Table 4 as 1, 10, 11, 12, 13, 15 and 16). Aniline was found in five samples and in all of then the value found after the third migration was greater than 10 μg kg^{-1}, which is the maximum limit established for the sum of all amines present in the material. However, aniline (classification 2A) is probably carcinogenic to humans by the International Agency for Research on Cancer (IARC).

4,4′-Diaminodiphenylmethane was detected in seven polyamide samples and, with the exception of sample 13, whose concentration was 7.0 μg kg^{-1}, in all other samples the concentrations were higher than 10 μg kg^{-1}, with values ranging from 115 to 29,288 μg kg^{-1} for the first migration test and from 25 to 9793 μg kg^{-1} for the third migration test. This primary amine is classified as possibly carcinogenic to humans by IARC.

For samples number 1, 10, and 11, 3,3′-dimethylbenzidine was found at concentrations ranging from 13 to 64 μg kg^{-1} for the first migration values, and exceed the value set by the Brazilian Regulation No. 326/2019 (Brazil, 2019). This amine is also classified as possibly carcinogenic to humans by IARC.

Only sample 1, presented 4-chloro-2-methylaniline, o-toluidine and

Table 3
Analytical figures of merit for the method developed.

Compound	LOD* μg kg^{-1}	LOQ* μg kg^{-1}	R^2 5–100 100–500 μg kg^{-1}	Repeatability** (1 day), RSD %			Reproducibility** (3 days), RSD %			Trueness** (Recovery), %		
				5 μg kg^{-1}	10 μg kg^{-1}	30 μg kg^{-1}	5 μg kg^{-1}	10 μg kg^{-1}	30 μg kg^{-1}	5 μg kg^{-1}	20 μg kg^{-1}	40 μg kg^{-1}
Benzidine	0.7	2.0	0.998 0.992	12	6	15	12	12	13	100	103	101
4,4′-Oxydianiline	1.1	3.4	0.994 0.995	6	5	8	8	12	12	111	94	105
4,4′-Diaminodiphenylmethane	0.5	1.4	0.991 0.995	7	8	7	10	9	13	96	109	104
2,6-Diaminotoluene	0.7	2.0	0.998 0.994	1	1	1	1	7	8	114	98	97
4,4′-Diaminodiphenyl sulfide	0.4	1.1	0.993 0.993	10	7	8	12	8	14	106	96	104
4,4′-Methylene-bis-(2-methylaniline)	1.3	4.0	0.993 0.995	12	6	13	12	13	14	99	112	104
3,3′-Dimethylbenzidine	0.2	0.6	0.993 0.995	7	4	6	6	12	11	111	99	97
Aniline	1.0	3.0	0.992 0.992	11	3	16	12	9	14	120	107	99
o-Toluidine	1.0	3.0	0.993 0.994	17	10	17	17	17	15	113	103	104
4-Chloroaniline	1.0	3.1	0.998 0.996	9	6	13	10	12	14	99	97	105
o-Anisidine	0.4	1.1	0.997 0.994	9	12	13	16	14	13	85	108	95
3-Chloro-4-fluoroaniline	0.6	1.7	0.997 0.994	9	4	10	8	12	13	92	91	96
2,6-Dimethylaniline	0.7	2.2	0.995 0.991	9	15	18	16	16	13	88	93	102
2-Naphthylamine	0.6	1.8	0.991 0.992	8	6	9	9	10	13	112	109	106
2-Methoxy-5-methylaniline	0.5	1.6	0.998 0.993	23	21	27	25	20	14	95	98	97
4-Chloro-2-methylaniline	0.9	2.6	0.998 0.991	11	15	11	14	12	12	98	100	100
2,4-Diaminotoluene	1.0	3.0	0.995 0.995	2	1	3	6	8	9	112	108	99
4-Aminobiphenyl	0.2	0.7	0.997 0.993	9	13	11	13	14	11	101	100	100
4-Aminoazobenzene	0.7	2.0	0.992 0.997	10	11	8	11	8	12	102	104	103

*: 7 replicates.
**: 10 replicates.

2,6-dimethylaniline amines with values in the first migration of 27 μg kg^{-1}, 6.9 μg kg^{-1}, and 8.0 μg kg^{-1}, respectively. 4-Chloro-2-methylaniline is classified as probably carcinogenic to humans, while o-toluidine is classified as carcinogenic to humans, according to IARC. In no other sample were these amines observed. Although only 4-chloro-2-methylaniline was observed at concentration above 10 μg kg^{-1} after performing the third migration test, the presence of these other two amines should be monitored.

Considering that 16 polyamide samples were analyzed and that, for six of them, the levels were above 10 μg kg^{-1} after the first migration, one can conclude that 38% of them were out of compliance according with Regulation No. 326/2019 (Fig. 2A). Classifying the polyamide samples according to their origin it is possible to state that 29% of the Brazilian samples and 57% of the Chinese samples presented problems and did not comply with the requirements for use in contact with food. Still regarding the six polyamide samples that exceeded the limit of 10 μg kg^{-1} for PAAs, five of them were black while just one sample was gray, which suggests that the polyamide black utensils higher concentrations of PAAs. This conclusion agrees with Sendón et al. (2010) citing that "4,4′-diaminodiphenylmethane was used in the manufacture of some types of polyamide, apparently as a comonomer, to increase the stability of the plastic at high temperatures". Nowadays, this substance is not allowed by Regulation No. 56/2012 (Brazilian Resolution regarding monomer and polymers for food contact) for polyamides (Brazil, 2012). "It has also been suggested that 4,4′-diaminodiphenylmethane is used to produce the azo dyes that give the utensils their black color" (Sendón et al., 2010).

The only polypropylene sample presented values above 10 μg kg^{-1} for 4,4′-diaminodiphenylmethane during the first and second migration tests, but the result for the third migration was below the LOQ. Even though, according to Brazilian legislation this sample is not approved.

The results of the specific migration of PAAs in silicone cooking utensils are also presented in Table 4. From 19 silicone samples, PAAs were not detected in 16 of them. Only 4,4′-diaminodiphenylmethane was found in the other three silicone samples at concentrations above 10 μg kg^{-1}, even after the third migration test. These three samples (number 27, 34 and 36) are from the same importer, but of different colors (yellow, orange, and blue). Considering that 19 silicone samples were analyzed and three of them were above 10 μg kg^{-1}, this means that 16% of them were out of compliance (Fig. 2B).

It is worth noting that in 36 samples analyzed, of different materials and origins, in 11 of them at least one PAA was detected and considering the all migration tests (first, second and third migration), 10 of these samples were non-compliant, which represents 28% of the total samples (Fig. 2C).

Table 4
Results of quantitative analysis of PAAs in kitchenware samples by CE-MS/MS.

Sample Number	Assay	Concentration (μg kg^{-1}), average of 5 specimens of samples, and standard deviation							Total conc. (μg kg^{-1})
		4-Chloro-2-methylaniline	4,4′-Diaminodiphenylmethane	Aniline	3,3′-Dimethylbenzidine	o-Toluidine	4,4′-Oxydianiline	2,6-Dimethylaniline	
1	1st Migration	27 (20)	4775 (381)	68 (9)	13 (11)	6.9 (3.4)	29 (9)	8.0 (4.3)	Σ = 4927
	2nd Migration	24 (13)	2842 (158)	44 (4)	8.4 (7.6)	4.9 (2.5)	18 (5)	5.1 (2.7)	Σ = 2946
	3rd Migration	12 (10)	1309 (176)	24 (5)	<LOQ	<LOQ	10 (4)	<LOQ	Σ = 1355
10	1st Migration	ND	26,794 (3544)	785 (35)	64 (6)	ND	74 (11)	ND	Σ = 27,717
	2nd Migration		12,362 (1370)	477 (44)	50 (6)		59 (10)		Σ = 12,948
	3rd Migration		7725 (4224)	300 (39)	18 (8)		49 (3)		Σ = 8092
11	1st Migration	ND	29,288 (3304)	251 (24)	46 (13)	ND	64 (13)	ND	Σ = 29,649
	2nd Migration		13,052 (1923)	142 (25)	36 (8)		40 (2)		Σ = 13,270
	3rd Migration		9793 (1227)	115 (15)	26 (8)		21 (2)		Σ = 9955
12	1st Migration	ND	115 (2)	ND	ND	ND	ND	ND	Σ = 115
	2nd Migration		31 (3)						Σ = 31
	3rd Migration		25 (22)						Σ = 25
13	1st Migration	ND	7.0 (3.3)	ND	ND	ND	ND	ND	Σ = 7.0
	2nd Migration		<LOQ						<LOQ
	3rd Migration		<LOQ						<LOQ
15	1st Migration	ND	4968 (3213)	61 (9)	ND	ND	21 (5)	ND	Σ = 5050
	2nd Migration		2913 (1525)	41 (9)			15 (8)		Σ = 2969
	3rd Migration		2668 (1059)	38 (4)			11 (7)		Σ = 2717
16	1st Migration	ND	1564 (486)	43 (62)	ND	ND	ND	ND	Σ = 1607
	2nd Migration		871 (224)	15 (8)					Σ = 886
	3rd Migration		668 (179)	11 (8)					Σ = 679
17	1st Migration	ND	17 (6)	ND	ND	ND	ND	ND	Σ = 17
	2nd Migration		12 (1)						Σ = 12
	3rd Migration		<LOQ						<LOQ
27	1st Migration	ND	15 (3)	ND	ND	ND	ND	ND	Σ = 15
	2nd Migration		17 (7)						Σ = 17
	3rd Migration		18 (7)						Σ = 18
34	1st Migration	ND	20 (5)	ND	ND	ND	ND	ND	Σ = 20
	2nd Migration		24 (10)						Σ = 24
	3rd Migration		33 (16)						Σ = 33
36	1st Migration	ND	15 (4)	ND	ND	ND	ND	ND	Σ = 15
	2nd Migration		23 (12)						Σ = 23
	3rd Migration		17 (7)						Σ = 17

LOQ: Limit of quantification, ND: not detected.

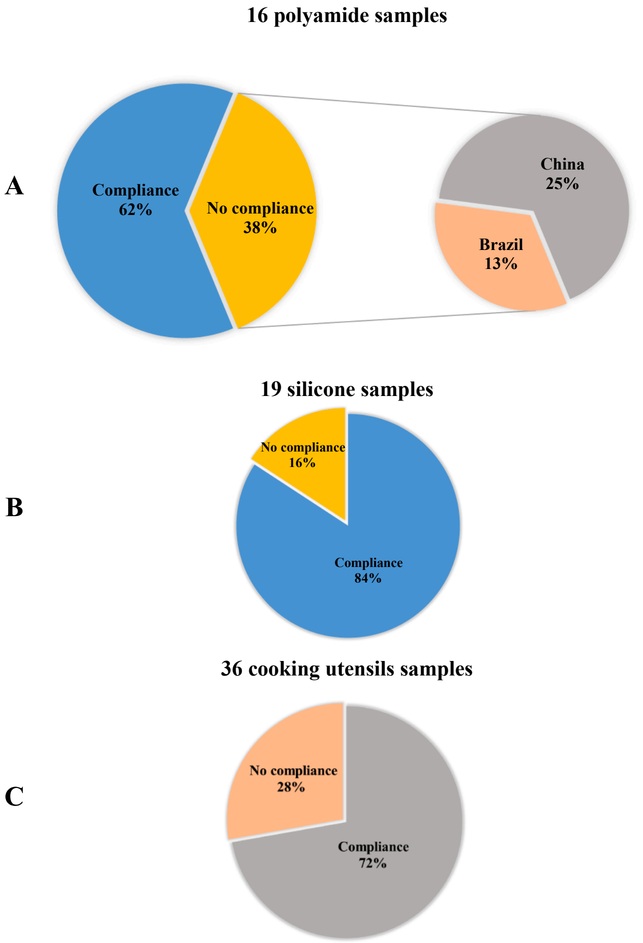


Fig. 2. Compliance and not compliance according Regulation No. 326/2019 (limit of detection of 10 μg kg^{-1} the sum of PAAs) for the analyzed samples. 2A: polyamides samples, 2B: silicone samples, C: all samples of cooking utensils.

4. Conclusion

For the first time CE-MS/MS has been applied to determine PAAs in cooking utensils, based on the specific migration of these analytes into food simulants. The proposed method has been demonstrated to be reliable, fast and simple, allowing the simultaneous determination of 19 PAAs from cooking utensils in less than 6 min. This method presents good linearity and repeatability. The developed and validated method for the determination of PAAs by CE-MS/MS has potential to be used as a routine approach because it is more cost-effective due to the use of relatively less expensive capillaries, when compared to chromatographic columns, and to the small amounts of organic solvents, sample and reagents required. Additionally, low waste generation makes the developed method consistent with green chemistry principles. The proposed method, with LOD lower than 1.3 μg kg^{-1}, has lower detectivity than chromatographic methods employed for this same analysis, but it is sufficiently sensitive to attend to the requirements set by the Brazil Regulation No. 326/2019 on the criteria of plastic materials and articles intended to come into contact with food.

The results obtained for the analysis of 36 cooking utensils samples, purchased in the Campinas (Brazil) and Washington (USA) retail market, revealed that 28% of the samples are out of compliance, some have PAAs concentrations up to 2900 times higher than the value approved by Brazilian legislation.

CRediT authorship contribution statement

Mary Ângela Favaro Perez: Validation, Formal analysis, Writing - original draft, Writing - review & editing, Resources. **Daniela Daniel:** Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Marisa Padula:** Conceptualization, Resources, Writing - review & editing, Funding acquisition. **Claudimir Lucio do Lago:** Methodology, Resources, Writing - reviewing & editing, Funding acquisition. **Carla Beatriz Grespan Bottoli:** Conceptualization, Resources, Writing - reviewing & editing, Supervision, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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