Primary aromatic amines in kitchenware: Determination by liquid chromatography-tandem mass spectrometry

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ABSTRACT

The aim of this paper is to develop and validate a methodology with potential for routine analysis that allows a fast and easy quantification of 19 primary aromatic amines (PAAs) in acid simulant (3% (w/v) acetic acid aqueous) in food contact materials (FCM). The main reason for studying these amines was the fact that some of them have a carcinogenic factor according to toxicological studies. To validate the method, the parameters linearity, limit of detection (LOD) and limit of quantification (LOQ), precision and accuracy using an UPLC-MS/MS were evaluated.

This study also analyzed 36 samples of kitchenware obtained from retail markets: 16 were made of polyamide (PA), one was made of polypropylene (PP) and 19 were made of silicone. The origins of samples were Brazil, China and Turkey. Eleven samples had levels of 4,4′diaminodiphenylmethane higher than permitted by legislation and five samples showed values of aniline above the limit.

Considering the Mood test for polyamides, there were significant differences between the samples from Brazil and China, as well as between the colors in the silicone samples. Regarding the polyamides, the Chinese samples showed higher amounts of PAAs than the Brazilian ones, being above that allowed by legislation. Three Chinese silicone samples presented values above the legislation limit. These were all from the same importer.

1. Introduction

Food contact materials (FCM) include all articles and materials intended to come into contact with food, such as containers, packaging, cutlery, kitchen equipment and dishes [1,2].

Primary aromatic amines (PAAs) can migrate from food contact materials and many PAAs are classified as human carcinogens. The World Health Organization's International Agency for Research on Cancer (IARC) classified PAAs into groups such as Group 1: Carcinogenic to humans, Group 2A: Probably carcinogenic to humans, Group 2B: Possibly carcinogenic to humans, Group 3: Not classifiable as to its carcinogenicity to humans [3].

The RASFF (Rapid Alert System for Food and Feed) is a tool that ensures the flow of information to enable swift reaction when risks to public health are detected in the food chain in Europe. A total of 98 notifications were transmitted to the RASFF from different countries of the European Union (EU) regarding primary aromatic amine migration from food contact materials over the last five years. For thus, there were: 25 in 2014, 18 in 2015, 17 in 2016, 13 in 2017 and 25 in 2018 [4].

The main source of PAAs in food contact materials is from kitchenware and multilayer food packaging. Polyurethane (PU) based adhesives are used in multilayer film and they can contain residual aromatic isocyanates that in contact with water can produce primary aromatic amines [5,6]. Residual isocyanates occur when the adhesive is not cured or the ingredients are mixed incorrectly [7]. Thermal treatment such as pasteurization and sterilization are a potential route for producing PAAs, as there are secondary bonds (allophanate and biuret bonds) that can yield neo-formed isocyanic monomers. These monomers in contact with water can lead to PAAs [5,6].

Another source of primary aromatic amines is from kitchenware such as whisks, spoons, tongs, spatulas, slotted spoons, ladles and flippers, made of polyamide, polypropylene and silicone. Polyamides are useful and popular due to their non-scratch proper-

ties, low cost and high temperature resistance [8,9]. The presence of PAAs from kitchenware is due to residues remaining from coloring processes (azodyes), co-monomer addition, degradation of azodyes used as colorants and technical impurities [9–12].

The literature has reports on primary aromatic amines in multilayer films, related with isocyanates in polyurethane adhesives [13–18] and the determination of PAAs in kitchenware utensils [9–12,19,20].

European Union Commission Regulation No. 10/2011 sets out specific requirements that plastic materials and articles shall not release primary aromatic amines, excluding those appearing in Table 1 of Annex I, in detectable quantities into food or food simulants. The LOD is 0.01 mg of substance per kg of food or food simulant. The detection limit applies to the sum of primary aromatic amines released [21].

The technique most used for determining PAAs in food contact materials in plastic is liquid chromatography (LC) coupled to mass spectrometry for the identification and quantification of primary aromatic amines in specific migration assays [10–17,19,22,23]. Gas chromatography/mass spectrometry is also used, but some derivatization needs to be carried out, according to Rubio et al. [20] and Brede et al. [18].

In Brazil (ANVISA) and Mercosul (The Southern Common Market), the only regulation for the primary aromatic amines is Resolution RDC n⁰ 52/10 of ANVISA and GMC 15/10 of Mercosul. These resolutions are related to the purity of colorants, which include compliance with limits for aromatic amines. There are limits for sulfonated and non-sulfonated aromatic amines, as well as for primary aromatic amines such as benzidine, 2-naphthylamine and 4-aminobiphenyl (individual or together) with a limit of 10 mg kg^{-1} [24,25]. Thus, except for colorants, Brazil and the Mercosul have no legislation for primary aromatic amines in plastic.

In this paper, a method for the determination of PAA in acidic food simulants at concentration levels relevant to the enforcement of migration limits was validated using ultra performance liquid chromatography-tandem mass spectrometry (UPLC/MS/MS). The objective of this work was the development of a UPLC-MS/MS method with potential for routine analysis that allows a fast and easy quantification of PAAs in kitchenware.

Thirty-six samples produced in Brazil, China and Turkey were analyzed to determine 19 PAAs from kitchenware of different colors made of polyamide (black, red, blue, gray, white and green), polypropylene (white) and silicone (green, red, yellow, blue, gray, orange and purple).

To the best of our knowledge, it is the first time that samples using polyamide have been evaluated based on colors (black, red, blue and gray) and origin (Brazil and China) and those based on silicone by color (green, red, yellow, blue, gray, orange and purple). In addition the first, second and third migration experiments were carried out.

2. Materials and methods

2.1. Chemicals, reagents and apparatus

The analytical standards of PAAs were from Sigma-Aldrich (USA), except for aniline-d5 which was from Supelco (USA). All amines were > 98.2% pure. Methanol and acetonitrile were HPLC grade and purchased from JTBaker (Mexico), acetone, formic acid and glacial acetic acid were from Merck (Germany) while pentafluoropropinic acid (PFPA) was acquired from Sigma Aldrich (USA). Ultra purified water was from a MilliQ system (Germany and/or its affiliates). Aqueous acetic acid, 3% (w/v), was used as a simulant assuming a density of 1.0 g/cm$^{3.}$

Table 1
Gradient used for the separation of PAAs.

Time (minutes)	% A	% B
0	98	2
0.5	94	6
1.0	92	8
1.5	90	10
2.0	80	20
2.5	70	30
3.0	65	35
4.0	60	40
5.0	50	50
6.0	30	70
7.0	10	90
7.8	98	2
9.0	post run	

For direct infusion into the MS/MS the amines were prepared individually at a concentration of 500 µg L^{-1} in HPLC grade methanol.

For validation and sample quantification, stock standards of each PAA in methanol were prepared using a 5-decimal analytical balance, except for 4,4′-oxydianiline which was dissolved in acetone. The dilution of standards yielded concentrations of 1000 and 5000 µg L^{-1} in methanol. These concentrations (1000 and 5000 µg L^{-1}) were diluted again to obtain concentrations of 0.5 to 300 µg kg^{-1} in 3% (w/v) acetic acid. A stock solution of aniline-d5 (internal standard) in methanol (1,548,450 µg kg^{-1}) was prepared and an intermediate solution of 1052.9 µg kg^{-1} in methanol was obtained. Finally, a dilution in 3% (w/v) simulant acetic acid was made to obtain a concentration of 20 µg kg^{-1}.

2.2. UPLC-MS/MS analysis

The tandem mass spectrometer was a Waters Xevo TQD with a positive mode (ESI+) electrospray source. The source parameters were capillary voltage of 3.5 kV; desolvation temperatures of 450 °C; the desolvatation nitrogen gas flow rate of 800 L h^{-1} and source temperature of 150 °C. For the collision gas, argon was used at a pressure of 3 × 10^{-3} mbar.

For optimization the precursor ions were monitored with cone voltage 20–100 V and for collision energies, 2–80 V were used. Voltage optimization was carried out by direct infusion into the MS at 10 µL min^{-1}, using a concentration of 500 µg L^{-1} individually for PAAs in HPLC grade methanol.

UPLC separation was performed using a Ultra Performance Waters Acquity, with an ACQUITY UPLC BEH C18 column (100 mm x 2.1 mm, 1.7 µm) from Waters. The flow rate was 0.25 mL min^{-1} and the injection volume was 5 µL. The temperature of the column was 40 °C.

To separate the PAAs, some different mobile phases were used in the gradient elution mode as follows: 0.1% (v/v) aqueous acetic acid (A%): acetonitrile (B%); 0.1% (v/v) aqueous acetic acid (A%): methanol (B%); 0.1% (v/v) aqueous formic acid (A%): methanol (B%); water with 4.7 mmol L^{-1} pentafluoropropinic acid (PFPA) (A%): methanol (B%); and water (A%): methanol (B%). The gradient was the same for all mobiles phases according to Table 1.

2.3. Samples

Sixteen polyamides (PA), one polypropylene (PP) and nineteen silicone kitchenware utensils (spoons, ladles, slotted turner, slotted spoons, spatulas and pasta server) were purchased from different retailers in Campinas in the state of São Paulo, Brazil in November and December, 2017, except for sample number 16 that was purchased in Washington D.C., USA in August, 2018. The origin of the PA samples were: seven from Brazil, seven from China and two from

Table 2
Samples analyzed, materials, color, origin and articles of kitchenware.

Sample Number	Retail market	Material	Color	Origin	Articles
1	Campinas/SP- Brazil	polyamide	black	Brazil	slotted turner
2	Campinas/SP- Brazil	polyamide	black	Turkey	slotted turner
3	Campinas/SP- Brazil	polyamide	red	Brazil	ladle
4	Campinas/SP- Brazil	polyamide	blue	Brazil	ladle
5	Campinas/SP- Brazil	polyamide	black	Brazil	ladle
6	Campinas/SP- Brazil	polyamide	black	Brazil	slotted turner
7	Campinas/SP- Brazil	polyamide	gray	Brazil	pasta server
8	Campinas/SP- Brazil	polyamide	red	China	spoon
9	Campinas/SP- Brazil	polyamide	blue	China	ladle
10	Campinas/SP- Brazil	polyamide	black	China	slotted spoon
11	Campinas/SP- Brazil	polyamide	black	China	slotted spoon
12	Campinas/SP- Brazil	polyamide	gray	China	ladle
13	Campinas/SP- Brazil	polyamide	white	Turkey	slotted turner
14	Campinas/SP- Brazil	polyamide	green	China	slotted turner
15	Campinas/SP- Brazil	polyamide	black	Brazil	ladle
16	Washington D. C., USA	polyamide	black	China	spatula
17	Campinas/SP- Brazil	polypropylene	white	China	spoon
18	Campinas/SP- Brazil	silicone	green	China	spoon
19	Campinas/SP- Brazil	silicone	green	China	ladle
20	Campinas/SP- Brazil	silicone	green	China	spatula
21	Campinas/SP- Brazil	silicone	green	China	ladle
22	Campinas/SP- Brazil	silicone	red	China	spoon
23	Campinas/SP- Brazil	silicone	red	China	slotted turner
24	Campinas/SP- Brazil	silicone	red	China	spatula
25	Campinas/SP- Brazil	silicone	red	China	ladle
26	Campinas/SP- Brazil	silicone	yellow	China	ladle
27	Campinas/SP- Brazil	silicone	yellow	China	slotted spoon
28	Campinas/SP- Brazil	silicone	blue	China	slotted spoon
29	Campinas/SP- Brazil	silicone	blue	China	spatula
30	Campinas/SP- Brazil	silicone	blue	China	slotted turner
31	Campinas/SP- Brazil	silicone	gray	China	slotted spoon
32	Campinas/SP- Brazil	silicone	orange	China	spatula
33	Campinas/SP- Brazil	silicone	orange	China	slotted turner
34	Campinas/SP- Brazil	silicone	orange	China	slotted spoon
35	Campinas/SP- Brazil	silicone	purple	China	spatula
36	Campinas/SP- Brazil	silicone	purple	China	slotted spoon

Turkey. The PP and silicone samples were from China. The samples are listed in Table 2.

2.4. Sample preparation

The migration test was carried out following European Standard EN 13130−1:2004 [26] and a technical guide [8] for the migration of PAAs. The area of each kitchenware sample was calculated. The surface-to-volume ratio in the total immersion test is conventionally 600 cm^2 of food contact area to 1000 mL of food simulant, 3% (w/v) acetic acid [26]. The simulant was placed in a beaker or square/rectangular bowl and weighed. The sample was added, covered by two pieces of aluminum foil to avoid evaporation and was then transferred to a preheated oven. After 100 °C/ 2 h, the specimens were removed from the simulant and were allowed to cool. Then, the extract of the sample was transferred to a 10 mL volumetric flask and aniline-d5 was added to a final concentration of 20 µg kg^{-1}. Sample extract was added to complete the flask. After that, the content of each flask was filtered using a fresh 0.2 µm filter and injected into the UPLC-MS/MS. Each kitchenware was analyzed in quintuplicate (five specimens). Since the kitchenware is for repeated use, this experiment was conducted twice more, each time using fresh simulant for the same test specimen, that is, each specimen was left in contact with the food simulant three separate times. These were named 1st migration, 2nd migration and 3rd migration.

2.5. Fourier Transform Infrared Spectroscopy

The infrared spectroscopy analysis was performed using a Perkin Elmer spectrophotometer with Fourier Transform (FT-IR),

Spectrum 100 model. The Attenuated Total Reflectance (ATR) technique was used. The ATR measurement was made with a resolution of 4 cm^{-1}, ranging between 4000−650 cm^{-1} and 16 scans. The spectrum obtained was compared with the reference spectrum (Bio-Rad Laboratories) or an internal library. The samples were identified as polyamide, polypropylene and silicone (Table 2).

2.6. Validation

The validation methodology was performed according to the DOC-CGRE 008 guide from INMETRO [27], which is based on international guidelines (e.g. ISO, IUPAC and EURACHEM).

The LOD and LOQ were obtained by carrying out seven injections from different solutions of the same concentration (0.5 µg kg^{-1}) in 3% (w/v) acetic acid simulant for all amines, except for 4,4′-diaminodiphenylmethane, o-toluidine and 3,3′-dimethylbenzidine, whose concentrations were 1.0 µg kg^{-1} in 3% (w/v) acetic acid simulant, as established by DOQ-CGCRE-008 [27].

The LOD was determined by Eq. 1:

$$LOD = t_{(n-1, 1-\alpha)} \times s \tag{1}$$

where s and t:
   s = standard deviation
   t = Student distribution. The value of t was 3.143 (99% confidence interval, 6 degrees of freedom)
   The LOQ was determined by Eq. 2:

$$LOQ = 10 \times s \tag{2}$$

The linearity was performed using four injections for each level. The levels were 1, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200 and 300 µg kg^{-1} in 3% (w/v) acetic acid (Fig. S5).

Precision tests were performed at one day intervals (repeatability) and three-day intervals (intermediate precision). For repeatability and intermediate precision the simulant 3% (w/v) acetic acid was spiked with three different levels of PAAs (1, 10 and 30 μg kg^{-1}). Seven replicates were used for each concentration, as established by DOQ-CGCRE-008 [27]. The precision was expressed in values of %RSD.

For accuracy (recovery), the simulant 3% (w/v) acetic acid was spiked at three different levels with PAAs (1, 20 and 40 μg kg^{-1}) when in contact with plastic specimens. Seven replicates were used for each concentration, as established by DOQ-CGCRE-008 [27]. The replicates were placed in an oven for 2 h at 100 °C, simulating the expected use of kitchenware.

For all validation solutions, aniline-d5 (internal standard) was added to a final concentration of 20 μg kg^{-1} in 3% (w/v) acetic acid.

2.7. Statistical analysis

The Shapiro-Wilk test for normality, the Anderson-Darling test, the Bartlett test and Levene test for Equality of Variances and the non-parametric Mood test were performed to verify the equality of medians as it was not possible to make an evaluation between the means.

The results considered a 95% confidence interval. The software used was Addinsoft - XLSTAT 2015.06.36749.

The Mood test, also called median test, allowed the median equality between k independent samples to be tested. This test is based on a nonparametric procedure, thus not making any assumption on the distribution of the measurements.

2.7.1. Mood test

Assume that Mi is the median of the i-th sample. The null hypothesis H0 and the alternative Ha associated with the Mood test were:

H0. M1 = M2 = ... = Mk

Ha. At least, one couple (i,j) exists where Mi ≠ Mj

The U statistic of the Mood test was obtained via the following contingency Table (2 x k):

Sample	1	2	...	k	Total
>Median	O_{11}	O_{12}	...	O_{1k}	**a**
≤ Median	O_{21}	O_{22}	...	O_{2k}	**b**
Total	**n$_1$**	**n$_2$**	...	**n$_k$**	**N**

If a large number of ties with the median was detected, XLSTAT will automatically count observations equal to the median with those above so that the following statistic remains computable. Then,

$$U = \frac{N^2}{ab} \sum_{i-1}^{k} \frac{\left(O_{1i} - \frac{n_i a}{N}\right)}{n_i}$$

where N, n, a, b, and O are defined in the contingency table.

This statistic has the property to be asymptotically distributed according to a Khi^2 distribution at a k-1 degree of freedom. When the number of samples k was 2, Yates (1934) proposed a continuity correction for U, denoted by U$_Y$:

$$U_Y = \frac{N \left(\left|O_{11}O_{22} - O_{12}O_{21}\right| - N/2\right)^2}{n_1 n_2 ab}$$

2.7.1.1. Computation of the p-values. To compute the p-values an asymptotic method was used: the p-value was obtained using the asymptotic approximation of the distribution of *U*. The reliability of the approximation depends on the number of observations.

2.7.1.2. Multiple pairwise comparisons. If the p-value was such that the H0 hypothesis had to be rejected, then at least one variable had a different median from the others. To identify which variables were responsible for rejecting H0, a multiple comparison procedure could be used.

3. Results and discussion

Table 3 lists the amines, CAS number, IARC Group, precursor ions (*m/z*), product ions (*m/z*), collision energies and cone energies, used in this study. The most intense transition was used for quantification, and the second most intense was used for confirmation of the analyte (qualification) for each compound.

Fig. 1, shows the total ion chromatogram (TIC) of all the 19 amines from a mixed standard solution at 10 μg kg^{-1} in 3% (w/v) acetic acid, including aniline-d5 (internal standard) at 20 μg kg^{-1}. The mobile phased used was 0.1% (v/v) aqueous acetic acid (A%): methanol (B%). Some different mobile phases were evaluated, but did not present satisfactory ionization. The total ion chromatograms can be seen in the supplementary material (Figs. S1–S4).

This method of separation takes 9 min for 19 PAAs and is faster when comparing with other methods from the literature for analysis of plastic food contact materials containing more than fifteen primary aromatic amines, as for example, 30 min for 22 PAAs [13], 23 min for 22 PAAs [15], 15 min for 20 PAAs [23], 14 min for 18 PAAs [16] and 13 min for 22 PAAs [7]. This new method only one that used 0.1% (v/v) acetic acid as mobile phase for ionization, the others used formic acid [17,22], water [7,10,16], ammonium acetate [12,19] and pentafluoropropinic acid [11,13,15,23].

The results obtained for the LOD were between 0.11 and 0.30 μg kg^{-1} and the LOQ was between 0.36 and 0.95 μg kg^{-1} (Table 4).

The equations of the regression curves and the parameters obtained for each PAA are also shown in Table 4.

Table 5 shows the precision (repeatability) and intermediate precision as RSD at concentrations of 1, 10 and 30 μg kg^{-1}. The lowest value, 1 μg kg^{-1}, was used because it is near the LOQ. The values accepted for precision in the literature [27] are 21% in a range of 10–30 μg kg^{-1} and 30% for 1 μg kg^{-1}.

For the accuracy expressed in percentage (Table 5), for 1 μg kg^{-1} the results obtained were between 45–109%, for 20 μg kg^{-1} were between 75–104% and for 40 μg kg^{-1} were between 73–109%. The values in the percentage range presented in the literature [27] were 40–120% for 1 μg kg^{-1} and 60–115% for 20 and 40 μg kg^{-1}.

The sample preparation for kitchenware is easy, simple, and rapid. In some cases it is only necessary to make a dilution when the sample is very concentrated. Table 6 shows the mean values of the quintuplicate for 1st migration, 2nd migration and 3rd migration.

The specific migration results in Table 6 for PAAs showed that two samples from Brazil (1 and 15) and four samples from China (10, 11, 12 and 16) made of polyamide were above the legislation limit for 4,4-diaminodiphenylmethane for all the migration experiments.

Considering aniline for the polyamide samples, the values showed five samples (1, 10, 11, 15 and 16) above the legislation limit, especially samples 10 and 11, which were 60 times and 30 times higher, respectively, considering the first migration. Even for the second and third migrations, these samples were not in compliance with the legislation for aniline.

Sixteen samples of polyamide were analyzed and seven of them were above the legislation limit, 10 μg kg^{-1}. For two samples, 4,4-diaminodiphenylmethane was responsible for the high value observed while, for five of them, aniline and 4,4-diaminodiphenylmethane were also responsible for the high

Table 3
Amines, CAS number, IARC classification group, precursor and product ions, collision energy and cone voltage.

Amines	CAS number	IARC[1] group	Precursor ion (m/z)	Product ion (m/z)	Collision energy (V)	Cone voltage (V)
4,4'-methylene-bis-(2-chloroaniline)	101-14-4	1	267.0	231.1 140.0	22 30	44
benzidine	92-87-5	1	185.0	151.1 92.8	28 22	42
2-naphthylamine	91-59-8	1	144.0	117.0 77.0	18 30	44
4-aminobiphenyl	92-67-1	1	170.0	143.0 92.6	20 26	42
o-toluidine	95-53-4	1	108.0	90.6 38.9	16 74	40
4-chloro-2-methylaniline	95-69-2	2A	141.9	107.0 89.2	16 30	34
o-dianisidine	119-90-4	2B	245.1	230.1 187.0	20 32	40
o-anisidine	90-04-0	2B	124.0	109.0 65.0	18 20	34
4,4'-diaminodiphenylmethane	101-77-9	2B	199.1	106.0 89.0	26 28	42
2,4-diaminotoluene	95-80-7	2B	123.0	105.7 79.4	14 22	36
2,6-dimethylaniline	87-62-7	2B	122.0	104.7 65.0	14 20	34
4-chloroaniline	106-47-8	2B	127.9	93.0 74.9	14 24	40
aniline	62-53-3	3	94.0	77.0 51.0	16 35	40
3-chloro-4-fluoroaniline	367-21-5		145.9	83.9 73.8	26 38	40
4,4'-oxydianiline	101-80-4	2B	200.9	108.0 80.0	20 36	52
2-methoxy-5-methylaniline	120-71-8	2B	138.0	123.0 106.0	14 20	36
3,3'-dimethylbenzidine	119-93-7	2B	213.1	196.1 180.1	20 35	55
4,4'-diaminodiphenyl sulfide	139-65-1	2B	217.0	124.0 79.9	20 40	48
4,4'-methylene-bis-(2-methylaniline)	838-88-0	2B	227.1	177.8 120.0	36 30	52
aniline-d5 (IS)	4165-61-1		99.0	82.0 54.0	17 30	40

[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.
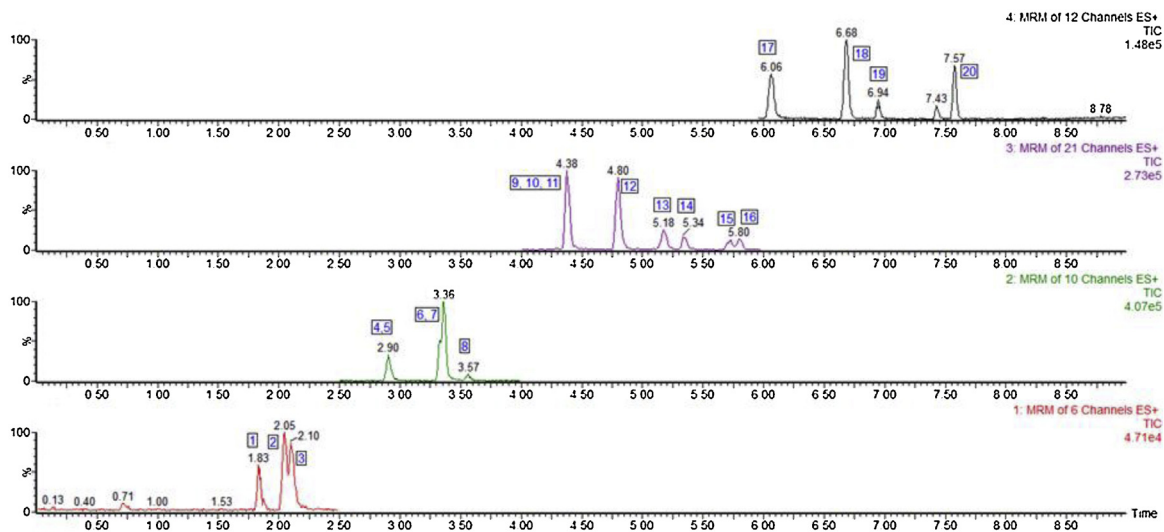
Fig. 1. Total ion chromatogram (TIC) of primary aromatic amines, at a concentration of 10 µg kg^{-1}, except for aniline-d5 (internal standard - IS) with a concentration of 20 µg kg^{-1}. **1**: 2,4-diaminotoluene, **2**: aniline-d5, **3**: aniline **4**: benzidine, **5**: 4,4'-oxydianiline, **6**: o-anisidine, **7**: 4,4'-diaminodiphenylmethane, **8**: o-toluidine, **9**: o-dianisidine, **10**: 3,3'-dimethylbenzidine, **11**: 2-methoxy-5-methylaniline, **12**: 4,4'-methylene-bis(2-methylaniline), **13**: 4-chloroaniline, **14**: 4,4'-diaminodiphenyl sulfide, **15**: 2,6-dimethylaniline, **16**: 2-naphthylamine, **17**: 3-chloro-4-fluoroaniline, **18**: 4-chloro-2-methylaniline, **19**: 4-aminobiphenyl, **20**: 4,4'-methylene-bis(2-chloroaniline).

Table 4
Validation: retention time, limit of detection, limit of quantification, calibration curve, coefficient of regression.

PAAs	R_T (min)	LOD[1] ($\mu g\, kg^{-1}$)	LOQ[1] ($\mu g\, kg^{-1}$)	Analytical curve y = a*x + b	R (1-300 $\mu g\, kg^{-1}$)
4,4'-methylene-bis-(2-chloroaniline)	7.57	0.16	0.51	5.4670 * x -4.0864	0.9958
benzidine	2.92	0.21	0.66	0.0242 * x -0.0346	0.9933
2-naphthylamine	5.80	0.27	0.86	1.0426 * x -0.2171	0.9970
4-aminobiphenyl	6.94	0.20	0.65	0.8050 * x -0.3064	0.9964
o-toluidine	3.56	0.29	0.93	1.0924 * x -1.0606	0.9952
4-chloro-2-methylaniline	6.68	0.11	0.36	7.2575* x -1.1738	0.9958
o-dianisidine	4.28	0.30	0.95	0.0315 * x -0.0517	0.9937
o-anisidine	3.33	0.11	0.36	4.0216 * x -2.2743	0.9960
4,4'-diaminodiphenylmethane	3.39	0.26	0.84	10.0791 * x -0.2244	0.9945
2,4-diaminotoluene	1.83	0.21	0.66	0.4599* x -0.4421	0.9950
2,6-dimethylaniline	5.72	0.19	0.62	2.2558 * x -1.4611	0.9961
4-chloroaniline	5.18	0.21	0.68	4.0480 * x +0.5928	0.9973
aniline	2.10	0.16	0.50	1.4454 * x -0.2697	0.9978
3-chloro-4-fluoroaniline	6.06	0.17	0.53	8.0905* x -2.4563	0.9969
4,4′-oxydianiline	2.90	0.17	0.55	3.7841* x -0.3216	0.9945
2-methoxy-5-methylaniline	4.38	0.11	0.36	10.7844 * x -10.5232	0.9970
3,3'-dimethylbenzidine	4.35	0.26	0.83	0.0592 * x -0.0853	0.9938
4,4'-diaminodiphenyl sulfide	5.34	0.13	0.43	2.1784* x -3.0370	0.9964
4,4'-methylene-bis-(2-methylaniline)	4.78	0.30	0.95	0.3175* x -0.0609	0.9960
aniline-d5 (IS)	2.05	NA	NA	NA	NA

[1] : 7 replicates NA: not applicable.

Table 5
Validation: precision (repeatability), intermediate precision and accuracy for PAAs.

PAAs	Repeatabillity [1] RSD %									Intermediate Precision[1] RSD %			Accuracy[1] (%)		
	1 $\mu g\, kg^{-1}$			10 $\mu g\, kg^{-1}$			30 $\mu g\, kg^{-1}$			1 $\mu g\, kg^{-1}$	10 $\mu g\, kg^{-1}$	30 $\mu g\, kg^{-1}$	1 $\mu g\, kg^{-1}$	20 $\mu g\, kg^{-1}$	40 $\mu g\, kg^{-1}$
	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1, 2 and 3	Day 1, 2 and 3	Day 1, 2 and 3			
4,4'-methylene-bis-(2-chloroaniline)	4	9	7	4	7	6	5	5	5	8	11	9	80	102	109
benzidine	20	30	25	11	14	13	6	16	13	25	18	21	95	96	90
2-naphthylamine	13	11	26	7	11	8	4	4	6	28	11	7	98	98	82
4-aminobiphenyl	13	25	23	7	10	7	5	7	7	22	9	8	87	104	101
o-toluidine	9	20	17	9	6	12	7	4	6	18	11	8	109	78	77
4-chloro-2-methylaniline	7	5	7	7	4	5	4	4	8	15	11	9	45	83	88
o-dianisidine	17	19	30	15	8	10	6	10	12	30	14	21	105	92	90
o-anisidine	15	18	8	6	8	7	6	4	10	19	8	7	58	92	86
4,4'-diaminodiphenylmethane	9	10	11	4	8	6	8	9	6	12	8	9	93	99	103
2,4-diaminotoluene	22	21	12	10	12	8	4	5	7	26	12	11	93	86	83
2,6-dimethylaniline	13	22	12	7	8	6	3	3	5	20	10	8	97	95	101
4-chloroaniline	13	13	8	7	7	9	7	6	10	17	11	8	70	81	73
aniline	7	11	9	5	6	10	5	4	4	11	6	5	75	86	78
3-chloro-4-fluoroaniline	17	19	15	6	10	10	4	4	6	18	14	8	65	75	77
4,4′-oxydianiline	5	27	4	6	5	5	8	10	6	24	6	13	85	103	103
2-methoxy-5-methylaniline	6	11	11	3	7	5	5	4	10	15	6	8	46	84	92
3,3'-dimethylbenzidine	29	25	29	14	16	14	14	13	8	27	18	14	78	83	80
4,4'-diaminodiphenyl sulfide	13	17	5	5	10	6	10	11	11	21	16	12	51	78	85
4,4'-methylene-bis-(2-methylaniline)	15	28	23	12	10	10	6	13	12	23	13	12	83	101	101

[1] : 7 replicates.

value observed. The amines were classified as Group 3 (aniline) and 2B (4,4ʹdiaminodiphenylmethane).

Seven polyamide samples were from China. Four of these samples (57%) showed values for PAAs above the level permitted by legislation. For the Brazilian samples, from a total of seven samples, two samples (29%) showed PAA values above the migration limit.

Considering two samples from Turkey (polyamide), one of them was above the legislation limit for 4,4ʹdiaminodiphenylmethane, while the other was below the LOQ. Both came from the same importer.

For only polypropylene sample (17), at the first migration test the value of 4,4ʹdiaminodiphenylmethane was above the established limit, but in the second and third tests the values decreased and they were in compliance with the legislation.

Three of the silicone samples also showed 4,4ʹdiaminodiphenylmethane above the permitted limit. These three silicone samples (27, 34 and 36) had different colors.

The aniline and 4,4ʹdiaminodiphenylmethane studied in this work were also reported in the literature according to others authors [10–12,19,20,22,23].

Table 6 shows that the values for standard deviation are very high. This can be explained by the fact that the kitchenware does not have batch identification or traceability. Therefore, it is impossible to affirm that one particular specimen of kitchenware will be from the same batch as another piece of kitchenware. The results suggest that the kitchenware was not homogenous.

In general, migration values decreased between the first to the second and the second to the third migrations but this is not a rule. For polyamide samples 15 and 17, the values decreased in the first migration to the second migration, but increased in the third migration for 4,4ʹdiaminodiphenylmethane. Séndon et al. [12] observed the same phenomenon when they studied the total amines in cooking utensils. For silicone samples 27 and 34, the values increased after the third migration and for sample 36, the values increased

Table 6
PAAs concentration obtained in 3% (w/v) aqueous acetic acid for polyamide, polypropylene and silicone kitchenware by UPLC-MS/MS.

Samples (n = 5)*

Concentration in μg kg⁻¹ (Standard Deviation)

Sample Number (origin) Material	PAAs methylaniline	Migration	4-chloro-2-	o-anisidine	4,4'-diaminodiphenylmethane	aniline	3,3'-dimethylbenzidine	benzidine	o-toluidine
1 (Brazil)	polyamide	1st	30 (21)	<LOQ	5222 (1466)	68 (10)	5.6 (3.2)	<LOQ	1.3 (0.3)
		2nd	22 (16)	<LOQ	2648 (705)	57 (13)	4.1 (2.9)	<LOQ	1.2 (0.4)
		3rd	14 (9)	<LOQ	1026 (674)	41 (11)	3.3 (0.9)	<LOQ	<LOQ
2 (Turkey)	polyamide	1st	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd	<LOQ	<LOQ	<LOQ	3.8 (0.4)	<LOQ	<LOQ	<LOQ
3 (Brazil)	polyamide	1st	<LOQ	<LOQ	<LOQ	1.9 (0.4)	<LOQ	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd	<LOQ	<LOQ	<LOQ	1.0 (0.1)	<LOQ	<LOQ	<LOQ
4 (Brazil)	polyamide	1st	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd	<LOQ	2.3 (0.5)	<LOQ	3.1 (1.0)	<LOQ	<LOQ	<LOQ
5 (Brazil)	polyamide	1st	<LOQ	<LOQ	<LOQ	1.5 (0.3)	<LOQ	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd	<LOQ	<LOQ	<LOQ	2.7 (1.0)	<LOQ	<LOQ	<LOQ
6 (Brazil)	polyamide	1st	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd	<LOQ	<LOQ	<LOQ	2.2 (0.3)	<LOQ	<LOQ	<LOQ
7 (Brazil)	polyamide	1st	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd	<LOQ	<LOQ	<LOQ	2.2 (1.1)	2.4 (1.3)	<LOQ	<LOQ
8 (China)	polyamide	1st	<LOQ	<LOQ	<LOQ	1.5 (0.6)	2.0 (0.9)	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	<LOQ	1.3 (0.1)	1.5 (1.1)	<LOQ	<LOQ
		3rd	<LOQ	<LOQ	<LOQ	<LOQ	1.8 (0.8)	<LOQ	<LOQ
9 (China)	polyamide	1st	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd	<LOQ	<LOQ	24133 (2696)	667 (276)	45 (8)	<LOQ	<LOQ
10 (China)	polyamide	1st	<LOQ	<LOQ	17705 (4036)	515 (175)	26 (11)	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	8608 (1947)	267 (85)	14 (8)	<LOQ	<LOQ
		3rd	<LOQ	<LOQ	28483 (7147)	319 (117)	54 (10)	<LOQ	<LOQ
11 (China)	polyamide	1st	<LOQ	<LOQ	13634 (2636)	149 (27)	18 (8)	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	10949 (2246)	142 (32)	17 (5)	<LOQ	<LOQ
		3rd	<LOQ	<LOQ	91 (13)	<LOQ	<LOQ	<LOQ	<LOQ
12 (China)	polyamide	1st	<LOQ	<LOQ	44 (9)	<LOQ	<LOQ	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	32 (12)	<LOQ	<LOQ	<LOQ	<LOQ
		3rd	<LOQ	<LOQ	13 (3)	1.0 (0.1)	<LOQ	<LOQ	<LOQ
13 (Turkey)	polyamide	1st	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	2.6 (1.3)	<LOQ	<LOQ	<LOQ	<LOQ
		3rd	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
14 (China)	polyamide	1st	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

M.Â.F. Perez et al. / J. Chromatogr. A 1602 (2019) 217–227

223

Table 6 (*Continued*)

Samples (n = 5)[*]

Concentration in μg kg^{-1} (Standard Deviation)

Sample Number (origin)	Material	Migration	4-chloro-2-methylaniline (PAAs)	o-anisidine	4,4'-diaminodiphenylmethane	aniline	3,3'-dimethylbenzidine	benzidine	o-toluidine
15 (Brazil)	polyamide	1st Migration	<LOQ	<LOQ	3142 (728)	57 (10)	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	1554 (434)	36 (6)	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	1658 (318)	36 (3)	<LOQ	<LOQ	<LOQ
16 (China)	polyamide	1st Migration	<LOQ	<LOQ	1357 (1615)	34 (18)	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	816 (959)	20 (10)	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	742 (875)	16 (8)	<LOQ	<LOQ	<LOQ
17 (China)	polypropylene	1st Migration	<LOQ	<LOQ	25 (7)	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	4.7 (5.8)	<LOQ	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	7.0 (3.4)	<LOQ	<LOQ	<LOQ	<LOQ
18 (China)	silicone	1st Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
19 (China)	silicone	1st Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
20 (China)	silicone	1st Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	<LOQ	2.7 (0.6)	<LOQ	<LOQ	<LOQ
21 (China)	silicone	1st Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
22 (China)	silicone	1st Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	<LOQ	1.6 (0.1)	<LOQ	<LOQ	<LOQ
23 (China)	silicone	1st Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
24 (China)	silicone	1st Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	<LOQ	1.1 (0.2)	<LOQ	<LOQ	<LOQ
25 (China)	silicone	1st Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	<LOQ	1.0 (0.1)	<LOQ	<LOQ	<LOQ
26 (China)	silicone	1st Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	11 (7)	1.4 (0.3)	<LOQ	<LOQ	<LOQ
27 (China)	silicone	1st Migration	<LOQ	<LOQ	18 (14)	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	26 (24)	<LOQ	<LOQ	<LOQ	<LOQ
		3rd Migration	<LOQ	<LOQ	<LOQ	1.9 (0.6)	<LOQ	<LOQ	<LOQ
28[**] (China)	silicone	1st Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
		2nd Migration	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

			<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
29	(China)	silicone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	<LOQ	2.2 (0.3)	<LOQ	<LOQ	<LOQ
30	(China)	silicone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
31	(China)	silicone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	1.8 (0.2)	<LOQ
			<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	<LOQ	1.2 (0.1)	2.1 (1.1)	<LOQ	<LOQ
32	(China)	silicone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	<LOQ	<LOQ	4.9(1.8)	<LOQ	<LOQ
			<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
33	(China)	silicone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	29 (8)	1.2 (0.3)	<LOQ	<LOQ	<LOQ
34	(China)	silicone	<LOQ	<LOQ	47 (31)	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	61 (30)	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
35	(China)	silicone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	12 (11)	1.3 (0.2)	<LOQ	<LOQ	<LOQ
36	(China)	silicone	<LOQ	<LOQ	35 (36)	<LOQ	<LOQ	<LOQ	<LOQ
			<LOQ	<LOQ	32 (24)	<LOQ	<LOQ	<LOQ	<LOQ

LOQ: Limit of quantification.

* = 5 replicates.

** = 4 replicates.

M.Â.F. Perez et al. / J. Chromatogr. A 1602 (2019) 217–227

225

after the second. However, they decreased in the second to the third migration for 4,4ʹdiaminodiphenylmethane. According to specific requirements set out in EU Commission Regulation No. 10/2011 [21], compliance shall be checked on the basis of the level of the migration found in the third test.

Considering the great variability and nonnormality of samples, a statistical analysis called the Mood test (analysis of median) was applied to observe the difference of colors (only among the polyamide samples and only among the silicone samples from China) and the origin of samples for polyamide (Brazil and China). The results considered the sum of PAAs for all migration experiments.

For the polyamide samples (Table S1), there was a significant difference between the samples from Brazil and China. Considering the colors from the same origin, either Brazil or China, the results showed that even among the colors, there were significant differences for at least one color.

The colors of samples of polyamide from Brazil (Table S1) such as blue (Sample 4), black (Sample 1), black (Sample 5) and black (Sample 15), there were significant differences when compared to the other colors. The difference in sample 4 was because the value for aniline was low. Sample 1 was the only one that had migration of 4-chloro-2-methylaniline, 4,4ʹ-diaminodiphenylmethane, aniline, 3,3ʹ-dimethylbenzidine and o-toluidine, for the Sample 5 it was o-anisidine and for sample 15 the amines that migrated were 4,4ʹ-diaminodiphenylmethane and aniline.

There were significant differences among the other colors in the polyamide samples (Table S1) from China, such as black (Sample 11), black4.1 (Sample 16), gray (Sample 12) and black4.3 (Sample 16). Sample 16 was subdivided into black4.1, black4.2 and black4.3 due to the great variability between specimens. Sample 11 had a high quantity of 4,4ʹ-diaminodiphenylmethane, while sample 16 had an amount of 4,4ʹ-diaminodiphenylmethane and aniline. Moreover, sample 12 had only 4,4ʹ-diaminodiphenylmethane.

The Mood test was applied for all the results and it was observed that for all the silicone samples, the colors had significant differences obtained by the paired multiple comparison test. Table S2 shows these results.

Tables in the supplementary material (S3 and S4) describe the summary for the three migration experiments considering the sum of the PAAs.

For the Brazilian polyamide samples (Table S3), two of them (1 and 15) had median values and high standard deviations (both black) but came from the same manufacturer. The remaining samples were within the limits allowed by the legislation.

For the Chinese polyamide samples (Table S3), three of them (10, 11 and 16) presented high values of medians and standard deviation (all black). They were from different manufacturers. The gray color (sample 12) also presented high values of median and standard deviation.

Comparing the Brazilian and Chinese samples of polyamide (Table S3), it can be observed that the Brazilian median was higher than the Chinese one, but the standard deviation was lower.

For the Chinese silicone samples (Table S4), three of them (27, 34 and 36) presented median values and a high standard deviation in yellow, orange and purple, respectively, all from the same importer.

4. Conclusions

A method was developed and validated for quantification of PAAs in kitchenware. It takes 9 min to separate 19 PAAs using UPLC-MS/MS, being fast and easy, with minimum sample handling, make it suitable for routine analysis. The LOQ ($<1\,\mu g\,kg^{-1}$) were compatible with the specific migration limits of PAAs, $10\,\mu g\,kg^{-1}$, as established by the legislation. Other parameters such as precision

(repeatability), intermediate precision and accuracy were evaluated according to INMETRO.

The primary aromatic amines frequently detected in kitchen utensils were 4,4ʹdiaminodiphenylmethane and aniline, which had a great variability between samples due to a lack of traceability and lack of batch identifications.

It can be concluded the PAAs represent risks to public health in international level and must be monitored and detected in food chain in order to protect consumers health.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.chroma.2019.05.019.

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