Overall and specific migration from multilayer high barrier food contact materials – Kinetic study of cyclic polyester oligomers migration

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Abstract
Most multilayer high barrier materials used in food packaging have a polyurethane adhesive layer in their structures. In order to assess the safety of these materials, it is important to determine the compounds intentionally added to the adhesives (IAS) as well as those non-intentionally added substances (NIAS). During the manufacture of polyurethane adhesives, some by-products can be formed, such as cyclic polyester oligomers coming from the reaction between dicarboxylic acids and glycols. Since these compounds are not listed in the Regulation 10/2011/EU, they should not be found in migration above 0.01 mg/kg of simulant. In this study two flexible multilayer packaging materials were used and migration was evaluated in simulant A (ethanol 10 % v/v), simulant B (acetic acid 3% w/v) and simulant ethanol 95% v/v during 10 days at 60 ºC. Identification and quantification of non-volatile compounds was carried out by UPLCMS-QTOF. Most of migrants were oligomers such as cyclic polyesters and caprolactam oligomers. Overall migration and specific migration of adipic acid-diethylene glycol and phthalic acid-diethylene glycol were monitored over time and analysed by UPLCMS- TQ. In most cases, ethanol 95% v/v was the simulant with the highest concentration values. Overall migration kinetics followed a similar pattern than specific migration kinetics.

Keywords: Non-intentionally added substances, cyclic polyester oligomers, overall migration, specific migration, kinetics.

Introduction
Nowadays, food packaging is widely used and its main function is minimizing the incidence of external factors and thus protecting the integrity of the product, preserving its quality and nutritional, sensory and health characteristics. Food packaging contains intentionally added substances (IAS) and it can also contain non-intentionally added substances (NIAS), coming from degradation processes and/or impurities present in the raw materials, that can migrate to food and compromise food safety. If a large quantity of migrants is transferred to foodstuffs, they can reach levels that are harmful to health and can also affect the composition and properties of food such as color, smell, taste and appearance, affecting the shelf life of the product. Therefore, it is important to control them in order to assure food quality and safety. Migrants identification is very difficult and it is necessary to use highly sensitive advanced analytical techniques, especially for non-volatile compounds (Nerin et al. 2013).
Most of multilayer high barrier materials used in food packaging have an adhesive layer, often based on polyurethane. Although the adhesives are not in the food contact side of the packaging, their components can also migrate to food due to diffusion and partition processes (Tehrany and Desobry 2004). Previous works have described the presence of adhesive components in food migration (Aznar et al. 2011, Vera et al. 2011).

Polyurethane is usually produced using polyesters and di-isocyanate compounds. In addition, several additives such as antioxidants, surfactants, biocides or catalysts can be included in the adhesive to improve their properties. At the same time, linear polyesters necessary for polyurethane manufacture, are produced by reaction of polyols and aliphatic and/or aromatic carboxylic acids. When the reaction proceeds under equilibrium conditions, linear polyesters are produced. As the reaction continues, it can unbalance and favors the formation of short chain cyclic polyesters, commonly referred as lactones, that are considered by-products of the polyurethanes manufacture and can migrate to food (Carrizo et al. 2015, Nerin et al., 2013). One of the most difficult tasks is the identification and quantification of these by-products, as none of the chemical database includes oligomers (Heimrich et al. 2015, Hoppe and Franz 2016, Paseiro-Cerrato et al.2016). To ensure the food safety, food packaging must comply with legislation. Food contact materials and articles, including adhesives, must comply with the Regulation (EC) 1935/2004 (EC 2004) and must not transfer their constituents to food in quantities which could endanger human health. Regulation (EU) no. 10/2011 (EC 2011) applies on plastic materials and articles intended to come into contact with food. This regulation includes a positive list of substances that can be present in migration at concentration values below its specific migration limit (SML). If the substances are not included in this list, their migration should not be found above 0.01 mg/kg of food/simulant. This is the case of some cyclic polyester oligomers, and therefore, the determination of its migration to food is very relevant. The first aim of this study was to identify and quantify the non-volatile compounds present in migration to three food simulants in contact with two high barrier food packaging multilayer materials. Migration kinetic plays a critical role in the final food packaging migration and may affect the migration of oligomers. For this reason, the second important objective of this study was to evaluate the migration kinetics in the studied materials, both in overall and specific migration of two cyclic polyesters coming from polyurethane adhesives (Isella et al. 2013). Finally, the last aim of the work was to study the cyclic polyesters stability in acidic medium, in order to know the variation o their concentration overtime. Liquid chromatography coupled to high resolution mass spectrometry was used for these purposes, as it is the required powerful tool to identify non-volatile compounds.

Material and methods

Reagents

Caprolactam (CAS 105-60-2) was purchased from Merck (Madrid, Spain). Bis(2-etilhexil) adipate 99% (CAS 103-23-1), acetyl tributyl citrate (CAS 77-90-7), 1-stearoylrac- glycerol (CAS 123-94-4), butyl 4-hydroxybenzoate (CAS 94-26-8), dioctyl phthalate (CAS 117-81-7), Irganox 1010 (CAS 6683-19-8) and acid acetic (CAS 64-19-7) were supplied by Sigma-Aldrich Química S.A. (Madrid, Spain). Cyclic esters composed by diethylene glycol (DEG) and adipic acid (AA) or phthalic acid (PA), AA-DEG and AADEG- PA-DEG, were synthetized and provided by an adhesives company. Ethanol was purchased from Panreac (Barcelona, Spain). Ultrapure water was obtained from a Millipore Milli-QPLUS 185 system (Madrid, Spain). Milli-Q water (18 M·Ω·cm) was used to prepare all solutions. Methanol and water for UPLC analysis (ultra LC–MS quality) were supplied by Baker (Deventer, The Netherlands).

Samples

Two flexible multilayer materials used for cured meat products packaging were tested. Both were provided by the company Alico S.A. (Medellín, Colombia). Multilayers were manufactured with PET: polyethylene terephthalate (PET), aluminium foil (Al),

polyamide (PA) and cast polypropylene (CPP), joint by polyurethane (PU) layers. CPP was in both cases the food contact side (FCS). Their structures were:
• Material 1: [PET//PA//CPP]FCS Material thickness was 105 μm and PU grammage was 2 g per square meter of laminate (g/m2) - (PET: 10; PA: 15; CPP: 80 μm).
• Material 2: [PET//Al//PA//CPP]FCS Material thickness was 113 μm and PU grammage was 2 g per square meter of laminate (g/m2) - (PET: 12; Foil: 9; PA: 25; CPP: 80 μm).

Instrumental analysis

Ultra-performance liquid chromatography (UPLC)

Chromatography was carried out in an Acquity system supplied by Waters (Milford, MA, USA). A UPLC BEH C18 column of 1.7 μm particle size (2.1 x 100 mm) from Waters was used. Chromatography was carried out at 0.3 mL/min column flow and 35 ºC column temperature. Mobile phase A was water (with 0.1% v/v formic acid) and mobile phase B was methanol (with 0.1% v/v formic acid). Chromatography started at 95:5 (A:B) and changed to 5:95 (A:B) in 6 min and maintained for 2 min. Injection volume was 10 μL.

Mass spectrometry detection with quadrupole-time-of-flight mass analyzer (MS–QTOF)

A Xevo G2 QTOF mass spectrometer supplied from Waters (Milford, MA, USA) was used for the analysis by MS-QTOF. This system was coupled to the UPLC system with an ESI probe. The experimental instrument parameters were as follows: positive and negative ionization (ESI+ y ESI-), sensitivity mode, capillary voltage 2.5 kV, cone voltage 30 and 70 V, extraction cone 4 V, source temperature 120ºC, desolvation temperature 450 ºC, cone gas flow 20 L/h, and desolvation gas flow 700 L/h. Acquisition was performed in MSE mode to allow using low and high collision energy (CE) in the collision cell during the same run. The mass spectrum at low energy (CE 4 V) provides information about the precursor ion (function 1) and the mass spectrum at high energy (CE ramp: from 15 to 30 V) information about fragment ions (function 2).

Identification of compounds detected by UPLC–MS-QTOF

From the spectra obtained in function 1 the elemental formula was obtained. Once the molecular formula of each accurate mass was known, it was necessary to use a database of chemical compounds in order to propose the most likely candidate. Chemspider (ChemSpider 2014) and SciFinder (Finder 2014) were used to obtain a list of candidates. Then, with the use of function 2, the fragmentation spectra were obtained and the proposed structures were checked through MassFragment® software from Waters. This software enabled us to evaluate and confirm whether the product ions detected in the high collision energy spectrum could be linked to the fragments generated from the chemical structures of the candidates proposed. Furthermore, when possible, the standards were purchased and the compounds were confirmed by a comparison of the retention time and mass spectrum.

Mass spectrometry detection with triple quadrupole mass analyzer (MS-QqQ)

A TQ triple quadrupole mass spectrometer supplied by Waters (Milford, MA, USA) was used for quantification purposes. The UPLC system was coupled to an ESI probe to the QqQ. The experimental instrument parameters used were as follows: positive ionization and SIR (selected ion recording) acquisition mode, capillary voltage 2.5 kV, cone voltage 30 V, extraction cone 3 V, source temperature 120ºC, desolvation temperature 450ºC, cone gas flow 30 L/h, and desolvation gas flow 650 L/h. The ions monitored were 217.1 [MH+] for AA-DEG, 259.1 [MNa+] for PA-DEG and 129.3 [MNa+] for DEG. AA was

measured under the same conditions but in negative mode, ion monitored was 145.05 [H-].
For building the calibration curves, solutions of the cyclic ester AA-DEG standard were prepared and injected before each analysis. MassLynx v.4.1 and QuanLynx software (Waters, Milford MA, USA) were used to analyze the samples.

Migration test
For the migration experiments, bags made with materials described before were manufactured by thermosealing. Afterwards, they were filled with different food simulants. The materials were tested in ethanol 10% v/v (simulant A) and acetic acid 3% w/v (simulant B) as aqueous simulants and in ethanol 95% v/v as fat simulant. Meat used in this study was "cured meat" that in most cases does not require refrigeration and it has a long time storage. EU/10/2011 established that for contact times above 30 days at room temperature and below the specimen shall be tested in an accelerated test at elevated temperature for a maximum of 10 days at 60 °C. For this reason, the bags were maintained in an oven the forced convection at 60 ºC for 10 days. Simulants and test conditions used for the migration assays were chosen according to the European Regulation 10/2011. The samples were analyzed by UPLC-MS-QTOF. All the concentrations were corrected according to the rate of 6 dm2 of packaging material per 1kg of simulant, in accordance with European Regulation 10/2011 (EC 2011) .

Identification and quantification of migrants in food simulants
For the identification of the main migrants, migration solutions of simulant D samples were gently concentrated under a nitrogen current (x5) and they were injected in a UPLCMS- QTOF system. For migrant quantification, calibration curves were performed with the pure standards at different concentration levels. When the standards were not available, the quantification was done with a standard with similar chemical structure.

Hydrolysis of AA-DEG oligomer in acetic acid 3 % (w/v) overtime
This study was carried out to see the behavior of the cyclic ester AA-DEG in acidic medium. Firstly, an aqueous solution of the cyclic ester of 1µg/g was prepared. Half of dissolution was added with acetic acid to have a final 3% v/v acetic acid concentration. Three aliquots of 20 mL of this solution were placed in glass vials and introduced in the oven at 60º for 10 days. A 600 µl aliquot was taken at 1, 6, 24, 72, 144, 192 and 240 hours and analyzed by UPLC-MS-QqQ. A parallel experiment was performed with aqueous solutions (without acetic acid) and AA-DEG at the same concentration.

Kinetic study
The kinetic migration study was performed for overall migration and specific migration of two cyclic esters, AA-DEG and PA-DEG. During migration test, migration aliquots were evaluated at six different times: 1, 6, 24, 72, 144, 192 and 240 hours. For overall migration, a gravimetry analysis of migration residues was performed. For specific migration, a 1 ml aliquot of migration samples was taken and analyzed by UPLC-MSQqQ.
In all cases, three independent replicates of each sample were analyzed.

Results and discussion

Identification and quantification of non-volatile migrants in UPLC-MS-QTOF.

Table 1 and 2 summarize the identification and quantification of compounds which migrated from [PET//PA//CPP]FCS and [PET//Al//PA//CPP]FCS materials respectively. For those compounds listed in the Regulation EU/10/2011 the specific migration limit (SML) is shown. Migration of compounds not listed in the Regulation must be below 0.010 mg/kg. The analytical characteristics of the standards used for quantification are shown in table 3.

Many migrants were identified from both materials, both IAS such as antioxidants, plasticizers and monomers (caprolactam) and NIAS, such as oligomer esters coming from PU adhesive. In most cases, the migration values were higher in ethanol 95 % v/v than in ethanol 10% v/v or acetic acid 3% w/v.

In the migration tests from material [PET//PA//CPP]FCS (table 1), 17 compounds were identified, most of them were oligomers. Caprolactam, the monomer of polyamide 6 (PA 6) was detected in the three simulants, but at lower concentration of that allowed in the European Regulation (15 mg/kg). Four caprolactam oligomers (n=2, 3, 4 and 5) were also detected in ethanol 95% v/v simulant, what reveal a higher tendency of these kind of compounds to migrate to fat simulants than to aqueous ones. Since these compounds are not present in the positive list, their migration concentration should be below 0.01 mg/kg. Oligomer n=4 showed the highest concentration migration values. Oligomers coming from polyurethane adhesives were also found. They were cyclic esters made up of phthalic acid (PA) and diethylene glycol (DEG) in combination 1:1 (PA-DEG) or 2:2 (PA-DEG-PA-DEG). Several additives were also found such as plasticizers (tributyl acetyl citrate, dioctyl phthalate or bis(2-etilhexil) adipate), antioxidants (oxidation products of butylhydroxytoluene, Irganox 1010 and 3,5-di-tertbutyl- 4-hydroxybenzaldehyde), lubricants based on glycerol (Glycerol monotridecanoate, Glycerol monoheptadecanoate, Glycerol monononadecanoate).

Table 2 shows migration from material [PET//Al//PA//CPP]FCS. Caprolactam and its oligomers were also found in migration from this material. As it happened in the previous material, oligomer n=4 showed the highest values. This material showed a high quantity of polyurethane oligomers in migration, made up of diacids such as adipic acid (AA) or phthalic acid (PA), and diols such as diethylene glycol (DEG), neopentyl glycol (NPG), dipropylene glycol (DPG), dihydroxyalkyl ethers (dHAE), ethylene glycol (EG), propylene glycol (PG), butylene glycol (BD) or hexanediol (HD). None of them was confirmed with standards, because the commercial standards were not available. It was not possible either to confirm by MassFragment since sodium adducts were formed and no fragmentation was observed. Therefore, the identification was based on the possible combination among di-acid and diol compounds and taking into account their characteristic molecular mass. Only compounds with migration values above 0.01 mg/kg are shown. It is notable that some compounds were only found in migration to acetic acid 3%, such as 3.00_257.0999, 4.33_255.1207 and 4.55_299.1463 (retention time_mass). Figure 1 shows the chromatograms of migration solutions after 10 days at 60ºC in acetic acid 3% w/v and ethanol 10% v/v. According to their mass, these compounds corresponded to the cyclic oligomers AA-DEG, AA-NPG and AA-dHAE plus H2O. They could be the consequence of the hydrolysis of the cyclic esters and the opening of the ring due to the acidic medium. This hypothesis is in agreement with previous studies (Carrizo, et al., 2015). Figure 2 shows the high collision energy spectra for AA-DEG (a) and its hydrolyzed form AA-DEG + H2O (b). Fragments observed successfully matched with the proposed structure. Even though opening of the ring could take place in both the ether and the ester oxygen, the first option was selected as the most likely one. The second option would produce an acid and the analysis in ESI- mode did not show any carboxylic compound. This behavior was found also for the oligomers AA-NPG and AA-dHAE

(C7). These results showed that the hydroxylation, and therefore the opening of the cycle, is more likely when the oligomer was made up of adipic acid rather than phthalic acid and when only 1 diacid and 1 diol composed the oligomer. Three antioxidants were also detected in migration from this material: Agidol 110, Irganox 1310 and Irganox 1010.

Hydrolysis of AA-DEG oligomer in acetic acid 3 % (w/v) overtime

The analysis of AA-DEG and its hydrolyzed formed AA-DEG+H2O in the acetic acid 3% simulant over time showed a progressive reduction of the amount of lactone (figure 3). In contrast, the hydrolyzed lactone started increasing after 1 day of storage. To measure these compounds, the oligomer AA-DEG standard was used. Its working range was 0.033-2264 µg/g and 0.011 µg/g was its limits of detection (LOD). Lactone AA-DEG decreased by 52 % (1046-506 ng/g) after 10 days and hydrolyzed lactone increased to 74.60 ng/g. On the other hand, in water medium no changes in AA-DEG concentration were observed. The injection of the acidic solutions in the UPLC-MS-QTOF, both in positive and negative mode, did not show any additional compound. In addition, the monomers that made up the lactone, adipic acid and diethylene glycol, were also analyzed by UPLC-MS-QqQ in order to check if they were also the resulting reaction products of lactones hydrolyzation. The results showed that none of the monomers was present above the limits of detection (LOD DEG= 3 ng/g, LOD AA=13 ng/g). Transformations of lactones to their opened form decrease its theoretical toxicity in most cases. Lactone AA-NPG belongs to class I but AA-DEG and AA-dHAE (C7) belong to class III Cramer group, what means the highest theoretical toxicity, having a maximum daily intake of 0.09 mg/person/day according to Cramer. However, their opened hydrolyzed forms belong to class I, what means lower toxicity and a higher allowed daily intakes (1.8 mg/person/day).

Kinetic study of migration

Since kinetics play a critical role in the final food packaging migration, migration kinetic study, both specific and overall migration, were performed from both materials. Figures 4a and 4b show the results for overall migration of materials [PET//PA//CPP] and [PET//Foil//PA//CPP] respectively. In both cases overall migration was higher with ethanol 95% v/v as simulant, reaching values after 10 days of 7.5 and 6.6 µg/g while for ethanol 10% v/v and acetic acid 3% w/v very similar kinetic behaviour was obtained over time, reaching values always below 5 µg/g. In most cases the maximum migration values and thus inertia to transfer non-volatile substances from both packaging materials was reached after 144-192 hours (days 6-8) and afterwards they remained stable. Small differences between the migration values reached between material 1 and 2 were found, attributed mainly to the presence of aluminium foil as functional barrier. Finally, in both cases, the established limit for global migration was achieved in the Regulation of the European Commission 10/2011 of 60 mg/kg.

The kinetic study of specific migration was performed for the cyclic ester PADEG in [PET//PA//CPP] (figure 4c) and the cyclic ester AA-DEG in [PET//Al//PA//CPP] (figure 4d). Specific migration of both lactones increased over time until 144-192 hours (days 6-8) where they reached maximum values and afterwards they remained constant. It is interesting to remark that the profile of overall and specific migration is very similar, what means that no other compounds different from oligomers migrate from the materials at a significant concentration. As happened for overall migration, the simulant with the highest migration values was ethanol 95% v/v. However, in this case, ethanol 10% v/v and acetic acid 3% w/v showed different values, especially for AA-DEG. This was probably due to the hydrolyzation of the cyclic ester in acidic medium, which decreased

its concentration in acetic acid over time, as it was observed in the results from section 3.2. The results showed a different kinetic pattern for this compound, since a slight decrease over time was observed.
Comparing migration of PA-DEG and AA-DEG, it can be observed that PA-DEG migration values in aqueous simulants (ethanol 10% v/v, acetic acid 3% w/v) was more similar to ethanol 95% v/v than in the case of AA-DEG, what could be attributed to the higher polarity of PA-DEG.

Conclusions

UPLC-MS-QTOF has been demonstrated to be a powerful tool for identifying compounds and NIAS migrated from the adhesives used to laminate food packaging materials. In these materials, cyclic esters coming from PU adhesives were the main migrants in all simulants, which corroborates the migration from internal material layers and the importance of NIAS screening.
A comparison between migration values in the three simulants showed in most cases that ethanol 95% v/v was the simulant with the highest values. Ethanol 95% was used as substitute of simulant D2 (vegetal oil), proposed for food with free fats at the surface. Nevertheless, simulant D1 (ethanol 50%, v/v) that it has been also proposed for fatty food, was not evaluated in this study and it probably would provide less migration concentration values. According to the results obtained, these materials should be used more cautiously with food with free fats at the surface but probably could be safely used with lower fat content food. Finally, overall migration kinetics followed a similar pattern than specific migration kinetics, what confirms that the equilibrium was reached in both cases under the selected experimental conditions.
The results from degradation of cyclic oligomers in acidic media showed that the concentration of some cyclic oligomers coming from PU adhesives can decrease over time if they are in acidic media. The resultant reaction products showed in most cases a lower theoretical toxicity, what is very positive for health consumers safety.

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Table 1. Compounds detected in migration from $[PET//PA//CPP]_{FCS}$ multilayer material. Retention time (rt) and measured mass (mass), type of ion found (adduct), compound candidate, molecular formula (MF), quantification standard (QS). Migration values in different food simulants and specific migration limit (SML) according to EU/10/2011 Regulation.

	rt mass	Adduct	Candidate MF	QS	EtOH 95% µg/Kg	EtOH 10% µg/Kg	HAc 3% µg/Kg	SML mg/Kg	Remarks
1	2.52 249.1589	$[MNa]^+$	Caprolactam oligomer (n=2) C12H22N2O2	1	271 ± 40	<LOD	<LOD		Polyamide oligomer
2	2.74 114.0918	$[MH]^+$	Caprolactam✓✓ C6H11NO	1	69.9 ±14.6	129 ±10	122 ±29	15	Polyamide oligomer
3	3.25 362.2425	$[MNa]^+$	Caprolactam oligomer (n=3) C18H33N3O3	1	2600 ± 280	<LOD	<LOD		Polyamide oligomer
4	3.72 475.3268	$[MNa]^+$	Caprolactam oligomer (n=4) C24H44N4O4	1	3450 ± 317	<LOD	<LOD		Polyamide oligomer
5	4.05 588.4082	$[MNa]^+$	Caprolactam oligomer (n=5) C30H55N5O5	1	169 ± 34	<LOD	<LOD		Polyamide oligomer
6	4.31 259.0588	$[MNa]^+$	PA-DEG C12H12O5	2	779 ± 142	240 ± 28	222 ± 39		Polyurethane oligomer
7	5.22 495.1267	$[MNa]^+$	PA-DEG-PA-DEG C24H24O10	3	71.5 ± 7.9	32.3 ± 5.8	28.9 ± 7.3		Polyurethane oligomer
8	5.60 269.0617	$[MNa]^+$	Anhydride of monomethyl succinate C10H14O7	6	57.7 ± 2.0	6.55 ± 2.89	<LOD		
9	6.02 311.2203	$[MNa]^+$	Glycerol monotridecanoate✓ C16H32O4	6	3.59 ± 0.11	<LOD	<LOD		Lubricant
10	6.38 233.1536	$[M-H]^-$	3,5-di-tert-butyl-4-hydroxybenzaldehyde✓✓ C15H22O2	10	2.89 ± 0.56	<LOD	<LOD		
11	6.46 383.2782	$[MNa]^+$	Erythriol monopalmitate C20H40O5	6	9.28 ± 0.33	<LOD	<LOD		
12	6.84 425.2158	$[MNa]^+$	Tributyl acetylcitrate✓✓ C20H34O8	5	29.8 ± 1.0	<LOD	<LOD	60	Plastizicer
13	7.19 679.4187	$[MNa]^+$	Irganox 1010✓✓	9	1602 ± 358	<LOD	<LOD	No SML	Antioxidant
14	7.63 391.2831	$[MH]^+$	Dioctil phthalate✓✓ C24H38O4	8	53.3 ± 3.7	<LOD	<LOD		Plastizicer
15	7.88	$[MNa]^+$	Glycerol monoheptadecanoate✓	6	19.5 ± 3.3	<LOD	<LOD		Lubricant

	367.2822		C20H40O4						
16	8.11 393.2999	$[MNa]^+$	Bis(2-etilhexil) adipate✓✓ C22H42O4	4	47.1 ± 2.3	<LOD	<LOD	18	Plastizicer
17	8.59 395.3137	$[MNa]^+$	Glycerol monononadecanoate✓ C22H44O4	6	10.3 ±1.3	<LOD	<LOD		Lubricant

LOD: detection limit; LOQ: quantification limit PA: phthalic acid; DEG: diethylene glycol; EMG: ethylmethylglycol
ni: non identified; ✓confirmed by MassFragment; ✓✓confirmed by internal standard

Table 2.- Compounds detected in migration from $[PET//Al//PA//CPP]_{FCS}$ multilayer material. Retention time (rt) and measured mass (mass), type of ion found (adduct), compound candidate, molecular formula (MF), quantification standard (QS). Migration values in different food simulants and specific migration limit (SML) according to EU/10/2011 Regulation.

No	rt mass	Adduct	Candidate MF	QS	EtOH 95% (µg/Kg)	EtOH 10% (µg/Kg)	HAc 3% (µg/Kg)	SML (mg/Kg)	Remarks
1	2.73 114.0922	$[MNa]^+$	Caprolactam✓✓ C6H11NO	1	1300±127	882±44	1040±170	15	Polyamide oligomer
2	3.00 257.0999	$[MNa]^+$	AA-DEG +H_2O C10H18O6	2	<LOD	<LOD	51.2±10.1		PU oligomer
3	3.23 362.2425	$[MNa]^+$	Caprolactam oligomer (n=3) C18H33N3O3	1	18.4±6.2	20.9±4.7	<LOD		Polyamide oligomer
4	3.55 239.0905	$[MNa]^+$	AA-DEG✓✓ C10H16O5	2	759±72	366±38	57.9±11.9		PU oligomer
5	3.71 475.3269	$[MNa]^+$	Caprolactam oligomer (n=4) C24H44N4O4	1	35.5±11.3	28.0±7.0	<LOD		Polyamide oligomer
6	4.03 588.4092	$[MNa]^+$	Caprolactam oligomer (n=5) C30H55N5O5	1	31.8±10.1	18.8±5.1	<LOD		Polyamide oligomer
7	4.25 701.5039	$[MNa]^+$	Caprolactam oligomer (n=6) C36H66N6O6	1	8.34±0.98	13.3±2.5	<LOD		Polyamide oligomer
8	4.33 255.1207	$[MNa]^+$	AA-NPG + H_2O C11H20O5	2	<LOD	<LOD	12.80 ± 1.2		PU oligomer
9	4.55 299.1463	$[MNa]^+$	AA-dHAE (C_7) +H_2O C13H24O6	2	<LOD	<LOD	13.52 ± 0.68		PU oligomer
10	4.70 267.1219	$[MNa]^+$	AA-DPG C12H20O5	2	9.65±1.19	17.6±0.2	2.65±0.52		PU oligomer

11	4.76 455.1890	$[MNa]^+$	AA-DEG-AA-DEG $C_{20}H_{32}O_{10}$	3	5.87±0.94	4.49±0.20	<LOD		PU oligomer
12	4.93 237.1108	$[MNa]^+$	AA-NPG $C_{11}H_{18}O_4$	2	1.50±0.30	1.98±0.70	<LOD		PU oligomer
13	5.10 475.1592	$[MNa]^+$	AA-DEG-PA-DEG✓✓ $C_{22}H_{28}O_{10}Na$	3	12.1±2.1	8.87±0.41	<LOQ		PU oligomer
14	5.18 495.1298	$[MNa]^+$	PA-DEG-PA-DEG $C_{24}H_{24}O_{10}$	3	<LOD	<LOD	<LOQ		PU oligomer
15	5.23 281.1380	$[MNa]^+$	AA- dHAE (C_7) $C_{13}H_{22}O_5$	2	687±55	344±13	40.2±10.0		PU oligomer
16	5.50 445.1492	$[MNa]^+$	PA-EG-AA-PG $C_{18}H_{20}O_8$	3	45.5±4.8	34.8±0.9	7.99±1.36		PU oligomer
17	5.63 453.2098	$[MNa]^+$	AA-DEG-AA-NPG $C_{21}H_{34}O_9$	3	25.1±2.6	25.7±0.8	<LOQ		PU oligomer
18	5.96 473.1801	$[MNa]^+$	PA-DEG-AA-NPG $C_{23}H_{30}O_9$	3	60.1±6.1	38.8±1.6	7.84±1.52		PU oligomer
19	6.27 443.1696	$[MNa]^+$	PA-EG-AA-HD $C_{22}H_{28}O_8$	3	48.7±5.1	8.83±0.3	<LOQ		PU oligomer
20	6.58 471.1994	$[MNa]^+$	PA-DEG-PA-BD $C_{24}H_{32}O_8$	3	43.3±5.6	<LOQ	<LOQ		PU oligomer
21	6.08 395.2433	$[M-H]^-$	Agidol 110 $C_{22}H_{36}O_3$	7	2.29±0.45	4.46±0.17	<LOQ		Antioxidant
22	6.28 277.1809	$[M-H]^-$	Irganox 1310 $C_{17}H_{26}O_3$	7	18.1±2.6	9.81±0.50	<LOQ		Antioxidant
23	6.39 233.1532	$[M-H]^-$	3,5-di-tert-butyl-4-hydroxybenzaldehyde✓✓ $C_{15}H_{22}O_2$	10	6.25±1.1	<LOD	<LOD		
24	10.47 1199	$[MNa]^+$	Irganox 1010 ✓✓ $C_{73}H_{108}O_{12}$	9	1010±142	<LOD	<LOD	no SML	Antioxidant

LOD: detection limit; LOQ: quantification limit ; AA: adipic acid; PA: phthalic acid; DEG: diethylene glycol; NPG: neopentilglycol; EG: ethylene glycol; dHAE: dihydroxyalkyl ether; DPG: Dypropylen glycol; PG: propylene glycol ; BD: butylene glycol; HD: hexanediol; PU: polyrethane

ni: non identified; ✓confirmed by MassFragment; ✓✓confirmed by internal standard

Table 3. Standards used for quantification in migration analysis, working range, determination coefficient (R^2) and limits of detection (LOD) and quantification (LOQ)

No	Compound	Working range (µg/g)	R^2	LOD (µg/g)	LOQ (µg/g)
1	Caprolactam	0.21 - 6.40	0.9986	0.07	0.21
2	Oligomer AA-DEG	0.04 - 1.27	0.9922	0.01	0.04
3	Oligomer AA-DEG-IPA-DEG	0.03 - 1.70	0.9921	0.01	0.03
4	Diethylhexyl adipate	0.03 - 0.59	0.9921	0.01	0.03
5	Tributy acetylcytrate	0.04 - 0.60	0.9963	0.01	0.04
6	Glycerol monostearato	0.04 - 1.95	0.9907	0.01	0.04
7	Butyl 4-hydroxybenzoate	0.05 - 2.53	0.9971	0.02	0.05
8	Dioctyl phtalate	0.03 - 1.19	0.9970	0.01	0.03
9	Irganox 1010	0.03 - 0.31	0.9984	0.01	0.03
10	3,5-di-tert-butyl-4-hydroxybenzaldehyde	0.02 - 1.56	0.9960	0.004	0.02

Figure caption

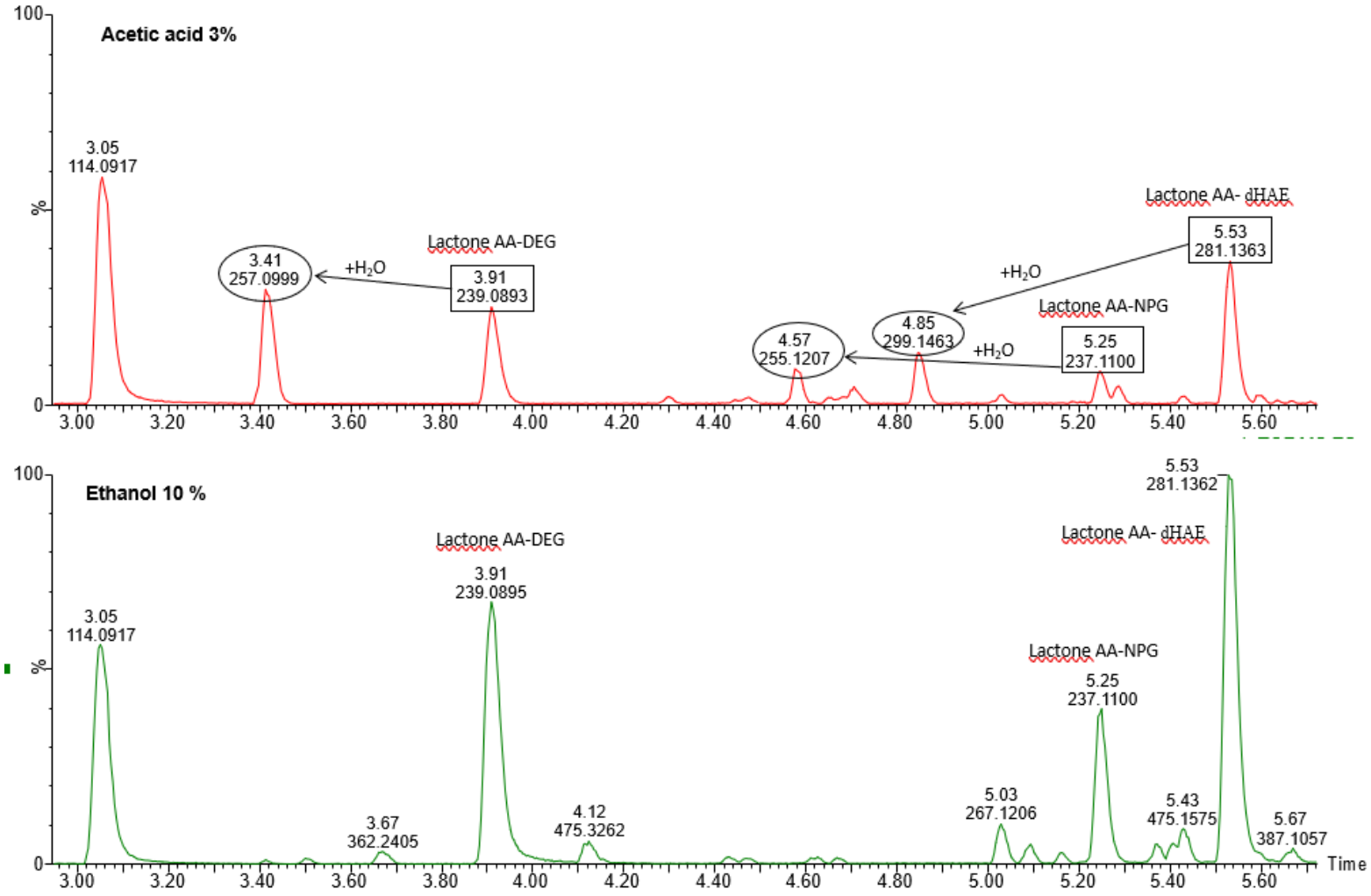

Figure 1 Chromatograms of migration test in acetic acid 3 % (w/v) (up) and ethanol 10 % (v/v) (down) after 10 days at 60ºC.

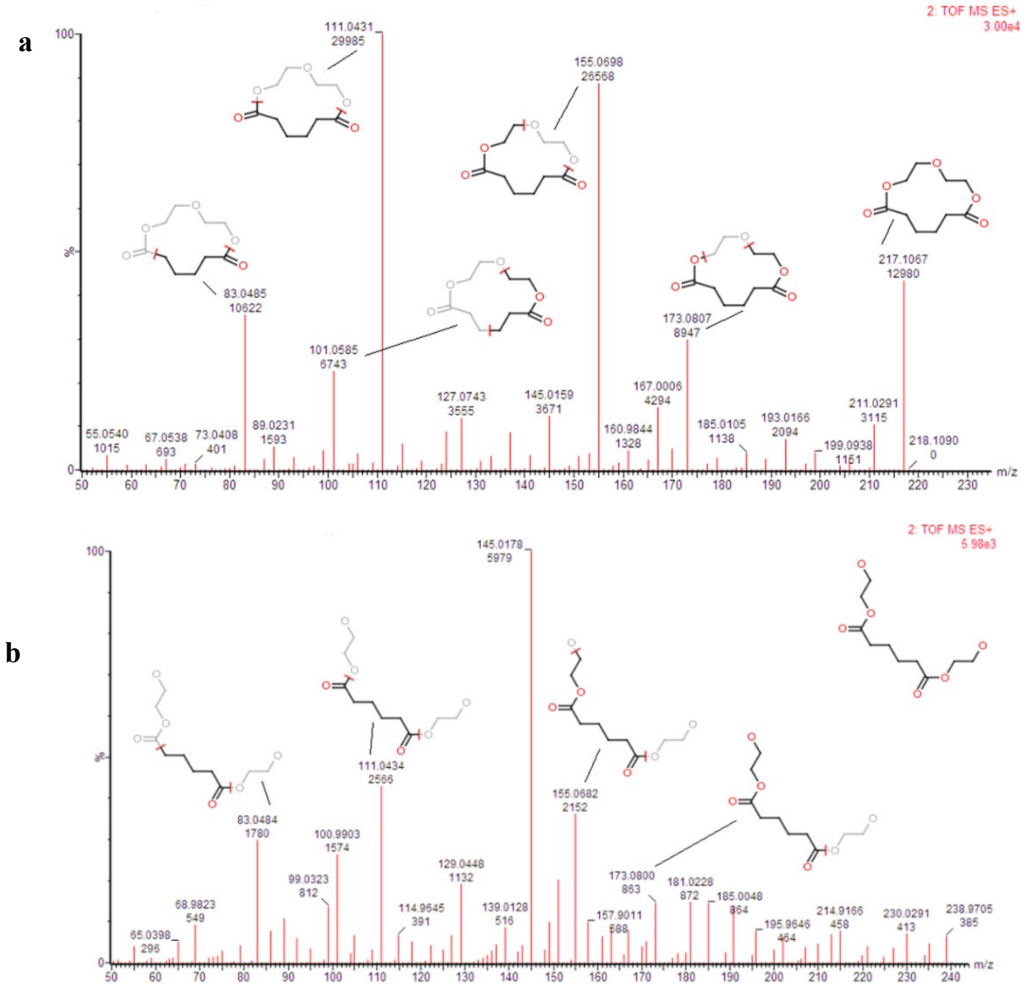

Figure 2 The high collision energy spectra for AA-DEG (a) and its hydrolyzed form (b) with their fragments.

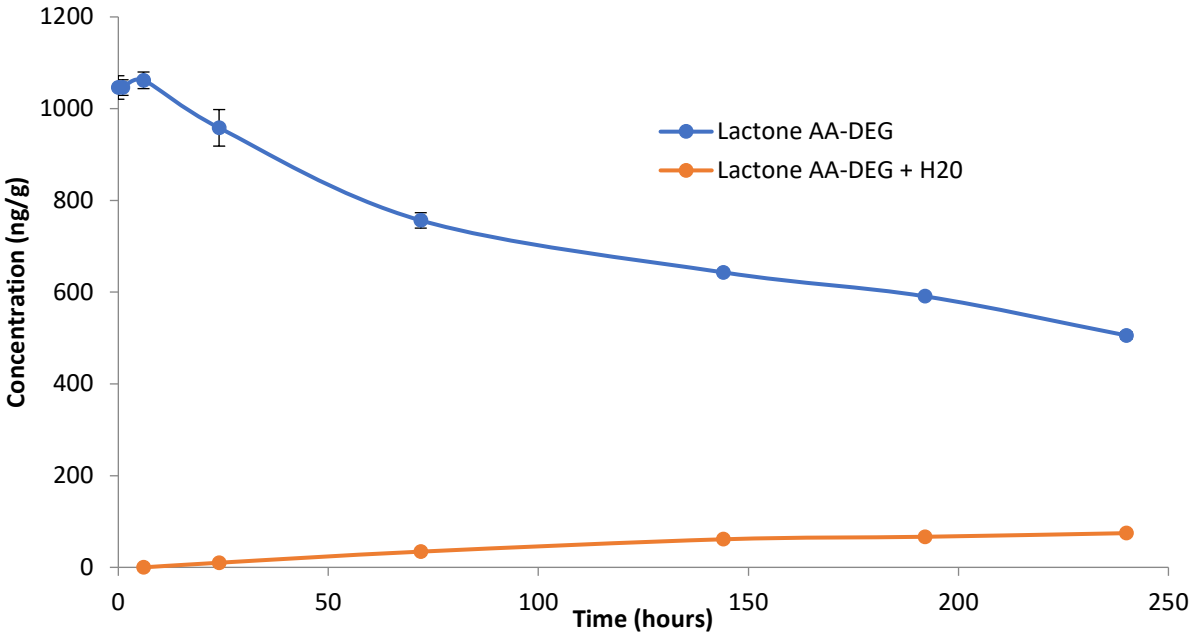

Figure 3 Evolution of concentration of lactone AA-DEG and hydrated lactone AADEG in acid medium over time.

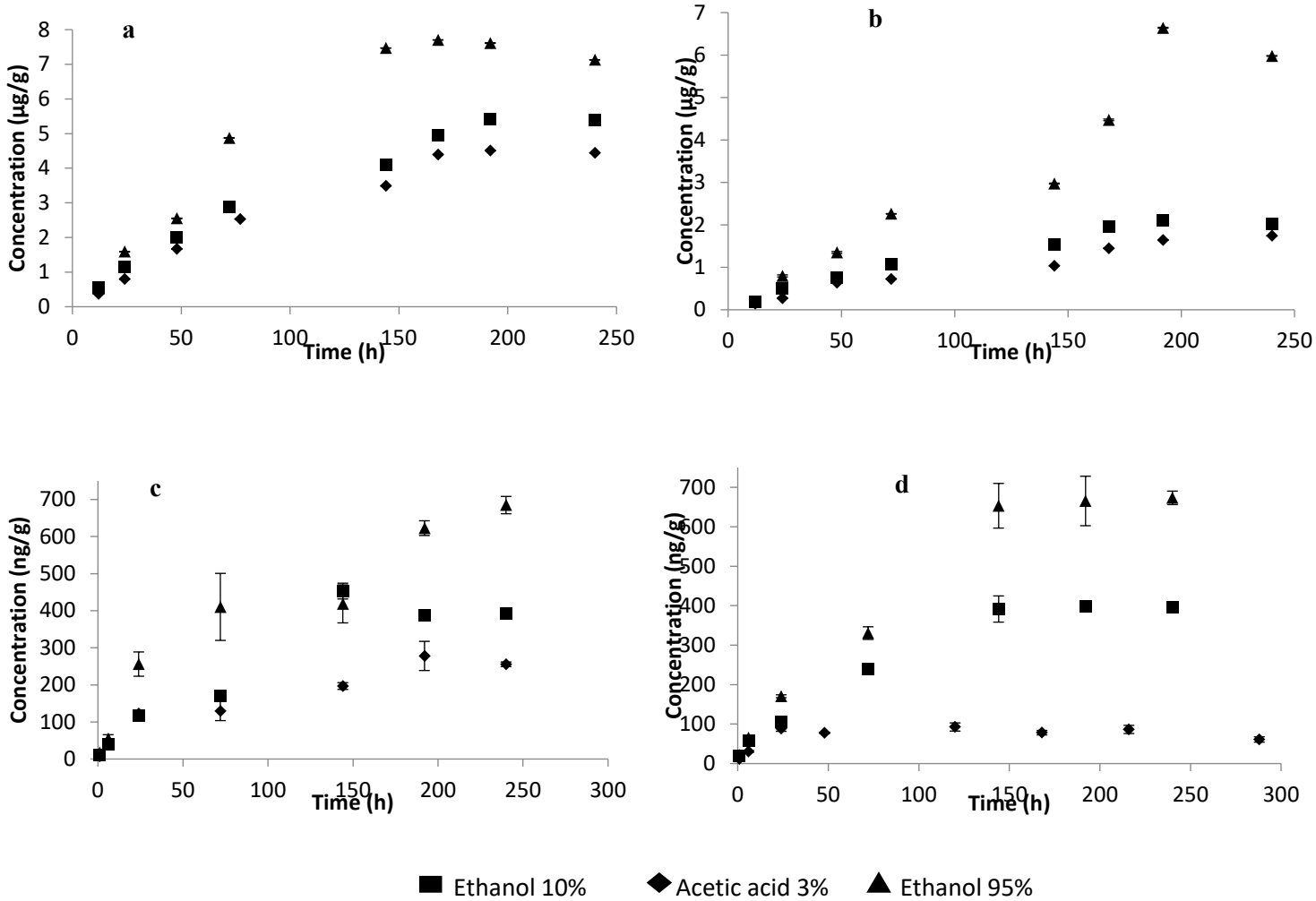

Figure 4 Kinetic study for overall migration of [PET//PA//CPP] material (a) and [PET//Foil//PA//CPP] material (b) and kinetic study of specific migration of the cyclic ester PA-DEG in [PET//PA//CPP] (c) and the cyclic ester AA-DEG in [PET//Al//PA//CPP] (d) in three simulants.