Determination of non-volatile components of a biodegradable food packaging material based on polyester and polylactic acid (PLA) and its migration to food simulants

Margarita Aznar, Sara Ubeda, Nicola Dreolin, Cristina Nerín*

Analytical Chemistry Department, GUIA Group, I3A, EINA, University of Zaragoza, Mª de Luna 3, 50018 Zaragoza, Spain

*Corresponding author:

Tel: +34976761873

E-mail address: cnerin@unizar.es

Abstract

Bioplastic materials are increasingly used due to its benefits for the environment preservation. Among them, food packaging materials based on polylactic acid (PLA) are among the most employed. In this work, a sample treatment methodology based on dissolution/precipitation has been optimized, selecting finally dichloromethane/ethanol as solvent/antisolvent system. The extracts obtained were analysed by UPLC-MS(QTOF), that allowed the identification of the main PLA non-volatile components. The recovery results were between 100.9 to 114.0 %. The methodology was applied to the analysis of pellets and films of a PLA-polyester blend sample. A total of 37 different compounds were detected, where the four compounds with the highest intensity in pellet samples were cyclic oligomers coming from the polyester part of the blend and composed by adipic acid (AA), phthalic acid (PA) and butanediol (BD). Migration experiments to 3 food simulants were also performed: ethanol 95% (v/v), ethanol 10% (v/v) and acetic acid 3% (w/v). The results showed that in addition to those compounds previously detected in the film, new compounds coming from the reaction of PLA components with food simulants were present in migration solutions.

Keywords: bioplastics; polylactic acid (PLA); migration; oligomers; non intentionally added substances (NIAS), biopolymers

1. Introduction

Bioplastics encompass those plastics that are biodegradable and/or compostable and also those ones that come from renewable sources [1]. They still account a low percentage of the polymer market, below 1 %. However, the increasing interest in preserving the environment has driven the plastic research towards the study and development of new packaging bio-materials. Poly(lactic acid) (PLA), derived from the fermentation of starch along with starch-based polymers, are the two most important commercial biodegradable polymers, representing about 47% and 41% of the total biodegradable polymer consumption [2]. Other bioplastics that are also being studied are those produced by the bacterial fermentation of starch and glucose such as poly hydroxyl alkanoates (PHA's) or poly hydroxyl butyrates (PHBs) [1].

Bioplastics have been used for different commercial applications such as disposable houseware, medical devices, consumer electronics, bags, automotive or food packaging. When these materials are used for food contact they are expected to protect food and maintain food quality, and it is important to evaluate that they don't transfer any component to food that could modify its sensory properties or imply any risk to consumers health [3].

This work has been focused on the study of a biodegradable PLA based material intended to food packaging. PLA comes from natural sources such as maize, wheat or corn and is also fully biodegradable and compostable with the right temperature and humidity under industrial composting facilities. It has already been used in different packaging applications such as cups for beverages, bowls for salads, bags for potato chips or jars for yogurts.

PLA is a linear aliphatic polyester that is obtained 100% from the fermentation of renewable plant sources. Starch is chemically converted to dextrose and dextrose is fermented to lactic acid followed by polycondensation [4]. Other manufacturing way is the ring-opening polymerization of lactide, a cyclic dimer composed by 2 units of lactic acid (LA). This last methodology provides higher molecular weight polymers and

consequently is more used [5]. Different techniques can be used to transform PLA pellets to the final product such as injection moulding, film extrusion or thermoforming. PLA has very good physical properties, such as mechanical and barrier properties comparable to synthetic polymers like polystyrene (PS) and polyethylene terephthalate (PET)[6]. It is suitable for food contact applications and it has a competitive cost. Nevertheless it has some drawbacks, such as its brittleness and its low resistance to oxygen permeation, that can be solved by blending PLA to other polymers, such as fossil-based polyesters, starch [7] or PHA. For improving its properties, the addition of several plasticizing agents has also been performed, such as glycerol [8], acetyl tributyl citrate [9], tributyl citrate [10] or polyethylene glycol [11]. These compounds are named intentionally added substances (IAS). In addition, there are non-intentionally added substances (NIAS) that can be present in the polymer due to different reasons, such as impurities of the raw materials or degradation and reaction process, that can also migrate to food. IAS as well as NIAS can be transferred to food when the polymer is used as a food contact material and for this reason, migration tests must be performed before its use for a proper risk assessment of the material [12]. Migration studies performed previously in the literature detected lactic acid, lactoyllactic acid and some small oligomers [13] and some NIAS, volatiles [14] as well as non-volatiles such as N,N-diethyldodecanamide, N-[(9Z)-9-octadecen-1-yl] acetamide, 1-palmitoylglycerol or glycerol stearate [15]. Finally, it is important to highlight the presence and likely migration of oligomers, defined as molecules consisting of a few monomer units. The presence of oligomers and its migration to food simulants has been previously studied in different kind of polymers such as polyethylene terephthalate (PET) [16] [17], polyurethanes [18] or polyamides [19]. In PLA, migration of oligomers [20] [21] [22] and how factors such as pH can affect the degradation kinetics [23] has also been studied by different authors. Since PLA is also used in pharmaceutical and surgical devices, oligomers presence has also been determined in these materials [24].

The main aim of this work was to develop a methodology for the determination of the main non-volatile potential migrants, including NIAS, of a biodegradable PLA-polyester blend intended for food contact and its migration to different food simulants.

2. Material and methods

2.1. Reagents

Methanol and water for UPLC-MS analysis (ultra LC-MS quality) were purchased from Baker (Deventer, The Netherlands); ethanol (HPLC quality) and dichloromethane were purchased from Scharlau Chemie S.A. (Sentmenat, Spain) and purified water was obtained with a Milli-Q 185 Plus system (Millipore, Bedford, MA, USA). Acetaminophen, caffeine, reserpine and sulfadimethoxine were purchased from Sigma Aldrich Química (Barcelona, Spain).

2.2 Samples

Samples in pellets and films were provided by a packaging company. They were a blend of PLA and a biodegradable fossil-based polyester. It fulfils the requirements of the European standard DIN EN 13432 for compostable and biodegradable polymers. Its mass density is 1.24-1.26 g/cm^3 and its melt volume rate (190 ºC, 5 Kg) 7.0-11.0 mL/10 min

2.3 Optimization of sample treatment

The dissolution/precipitation methodology used in this work had already been used for the analysis of other polymer's composition [25] [26] [27] [28] [29].

2.3.1. Base sample treatment

For the optimization process, a base sample treatment was used. The steps of this treatment were as follows: 0.25 g of PLA pellets were mixed with 3 mL of the selected solvent and the mixture was placed in an ultrasound bath for 1 hour for its total dissolution. The volume of solvent was selected in order to completely cover the PLA sample. Once the sample was dissolved, the solution was placed in a vial and the antisolvent was added under magnetic agitation (500 rpm). Afterwards, the precipitated was removed and the vial placed in the freezer for 1 hour for a complete polymer precipitation. Finally, the extract was filtered through a 0.25 μm PET, evaporated to dryness under a nitrogen current and redissolved with 1 mL of methanol/water (1/1; v/v).

2.3.2 Optimization and evaluation of the precipitation/redissolution process

First, different solvents were tested for being used as solvent/antisolvent systems according to PLA solubility: dichloromethane/methanol, dichloromethane/ethanol, chloroform/methanol and chloroform/ethanol. They were selected on the basis of previous experiments about PLA solubility [30] [31]. The extracts were analyzed by UPLC-MS(QTOF).

For determining the volume of antisolvent necessary 3 different ratios solvent/antisolvent were checked, they were selected according to the literature: 1/1, 1/2 and 1/3 [25] [26] [27] [28]. Two different procedures were applied to confirm the efficiency of the treatment, the first one based on the weight of precipitate and the second one on the supernatant. Once the polymer was precipitated, the extract was removed and the polymer was dried in an oven until constant weight. While, the weight of the polymer increased around 6 times from ratio 1/1 to 1/2, no significant differences were found between 1/2 and 1/3 ($p<0.01$). For this reason, a ratio 1/2 was used. In order to confirm a complete precipitation, the extract was measured by molecular absorption spectroscopy in the visible range (400-700 nm) and compared to the blank (dichloromethane/ethanol, 1/2) to confirm the absence of light scattering. In presence of particles or colloids in the solution the incoming light would be scattered and higher absorbance would be observed. No differences were observed between the blank and the extract.

Then, the effect of performing a washing step in the precipitated polymer was checked. For this purpose, 3 mL of ethanol were added over the precipitated polymer and it was manually shaken. Then, the ethanol was removed and mixed with the previous extract, and the base sample treatment continued.

To calculate possible losses due to the evaporation process, recovery percentages as well as the possible matrix effects the following experiments were performed. For the study, a surrogate solution of acetaminophen, caffeine, reserpine and sulfadimethoxine (20 mg/Kg) in methanol was used. These compounds were selected in order to have compounds from different chemical families and with different molecular weights that could represent different kind of sample components. The extracts were analyzed by ULPC-MS(QqQ) and the areas of the peaks were measured *(A)*:

- *Experiment 1:* A solution of 1 mL methanol/water (1/1, v/v) was spiked with 100 µL of the standards solution (A_{E1})

- *Experiment 2:* A solution of DCM (1 mL) + EtOH (3 mL) was spiked with 100 µL of the standards solution, concentrated to dryness and redissolved with 1 mL of methanol/water (A_{E2}).
- *Experiment 3:* 1 mL of PLA solution was precipitated using the base protocol and the final methanol/water extract (1 mL) was spiked with 100 µL of the standards solution (A_{E3}).
- *Experiment 4.1*: 1 mL of PLA solution was spiked with 100 µL of the standards solution and analyzed using the base protocol ($A_{E4.1}$).
- *Experiment 4.2:* 1 mL of PLA solution was spiked with 100 µL of the standards solution and analyzed using the base protocol with the washing step ($A_{E4.2}$).

All the experiments were performed in triplicate.

2.4. Optimized sample treatment

This protocol was used for pellet samples as well as for films or trays. An amount of 0.25 g of sample was weighted and 3 mL of dichloromethane were added. The mixture was shaken in an ultrasound machine during 1 hour until it was dissolved. For the precipitation of the polymer, 6 mL of ethanol were added to the dissolved sample was added with 6 mL of ethanol under magnetic stirring (500 rpm, 15 min). After this time, the solvent was removed and stored in a vial. Afterwards, the precipitated polymer was washed with 3 mL of ethanol and the mixture was manually shaken. Then, the polymer was gently pressed with a glass bar and the solvent was removed and mixed to the previous extract. The final extract was filtered through a 0.25 µm PET filter, concentrated to dryness under a gentle nitrogen current and reconstituted with 1 mL of methanol/water (1/1; v/v).

2.5. Migration tests

Migration tests were performed by total immersion of samples into the simulants. Cut-offs of 5 x 1 cm were placed in 20 mL vials and immersed in 3 different food simulants: ethanol 10% (v/v) (simulant A), acetic acid 3% (w/v (simulant B) and ethanol 95% (v/v) (substitute of simulant D2). Vials were filled in according to the rate 6 dm^2 contact surface/kg of simulant, established by the Regulation EU/10/2011 [32]. Afterwards, vials were placed in an oven at 60 ºC during 10 days.

All the migration experiments were performed in triplicate and according to the European Regulation for food contact materials EU/10/2011 [32].

2.6. UPLC-MS analysis

Chromatography was carried out using an Acquity system and a UPLC BEH C18 column of 1.7 μm particle size (2.1 x 100 mm), both from Waters (Milford, MA, USA). Chromatography was carried out at 0.4 mL min^{-1} column flow, 40 ºC column temperature and using an injection volume of 10 μL. The mobile phase was composed by 2 phases, water with 0.1 % formic acid v/v/ (phase A) and methanol with 0.1 % formic acid (v/v) (phase B). Chromatography started at 98/2 phase A/phase B (1 minute), changed to 0/100 in 7 minutes and stayed at 0/100 for additional 2 minutes.

For ULPC-MS(QTOF) analysis, the UPLC was connected with an ESI probe to a Xevo G2 QTOF mass spectrometer also from Waters. Instrument configuration was as follows: capillary at 2.5 kV, sampling cone at 30 V, extraction cone at 4 V, source temperature at 120 ºC, desolvation temperature at 450 ºC, cone gas flow at 20L $hr^{-1}$and desolvation gas flow at 500L hr^{-1}. Acquisition was carried out in sensitivity and MS^E mode. MS^E mode allows the acquisition at low and high collision cell energies (CE) during the same run. Even though most of the compounds are detected at 30 V of cone voltage, analyses were also performed at 70 V to not lose any information. Data were recorded using MassLynx v4.1 software. The identification of the compounds detected was carried out following the methodology previously described by the authors [33] [12].

For quantitative purposes, ULPC-MS(QqQ) was used, where the UPLC was connected to an ESI probe to a TQ mass spectrometer from Waters. Instrument configuration was as follows: capillary at 2.5 kV, sampling cone at 40 V, extraction cone at 3 V, source temperature at 120 ºC, desolvation temperature at 450 ºC, cone gas flow at 60L $hr^{-1}$and desolvation gas flow at 600L hr^{-1}. Acquisition was carried out in SIR (selected ion recording) mode and the protonated masses of the molecular ions were recorded: acetoaminophen [MH+] = 152.1, caffeine [MH+] = 195.1, sulfadimethoxine [MH+] = 311.1 and reserpine [MH+] = 609.3.

3. Results and Discussion

3.1. Optimization of PLA sample treatment by dissolution/precipitation

The four solvent/antisolvent systems studied (dichloromethane/methanol, dichloromethane/ethanol, chloroform/methanol and chloroform/ethanol) provided good results in terms of dissolution and polymer precipitation and no significant differences were found when they were analyzed by UPLC-MS(QTOF). Since these extracts were expected to be used as well in GC-MS in future experiments, solvent properties for GC-MS analysis were taken into account in the decision. Dichloromethane was selected versus chloroform since it was eluted at a shorter retention time in the GC-MS analysis and therefore, it allows detecting more compounds with high volatility. Ethanol was selected as antisolvent versus methanol, since it had a lower expansion volume and therefore it was more appropriate for GC-MS. Finally, the system dichloromethane/ethanol was selected for PLA sample analysis.

The possible compound losses due to the evaporation to dryness process were evaluated comparing the areas obtained from experiments 1 and 2. The results showed that there were no losses for the reference compounds since no significant differences were observed in the measured areas for any compound.

The calculation of matrix effect was performed with the results obtained from experiments 1 and 3 using the following equation:

$$Matrix\ effect\ (\%) = 100 \times A_{E3} / A_{E1}$$

The results are shown in table 1. All the values obtained for the reference compounds, except for caffeine, were in the range from 80 to 120 %, which implies that no matrix effects should be considered.

The calculation of recovery data was carried out with results obtained from experiments 3, 4.1 and 4.2 using the following equation:

$$Recovery\ (\%) = 100 \times A_{E4} / A_{E3}$$

The best recoveries were found when the washing step of the precipitated polymer was performed, with values between 100.9 to 114.0 % (table 1).

In order to have a better sensitivity, in the final sample treatment protocol the whole PLA solution was used, maintaining the same solvents rates than in the optimization process for polymer precipitation and the washing step.

3.2. Composition of PLA pellets and film

The optimized protocol was applied to the analysis of pellets and film PLA samples. Three replicates of each were dissolved and analyzed. Figure 1 shows a chromatogram of a PLA pellets extract.

Table 2 shows the main compounds found in PLA samples (pellets and film) and in migration solutions. A total of 37 different compounds were detected. Initially, 23 were detected in pellet samples and afterwards, 19 out of them were also detected in films. No new compounds were detected in films with regard to those found in pellets. This fact would mean that the extrusion process from pellets to film did not generate any new compound but some of them disappeared. With regard to migration results, 14 out of the 19 compounds found in the film were finally detected in any of the food simulants. In addition, 14 new compounds were also found, probably generated from the reaction between the components of the packaging material and the simulants.

The initial compounds screening was performed in positive mode and 30V of cone voltage, since according to previous studies it provided the best sensitivity [33]. Chromatograms obtained at 70 V did not show any new compound and only 14 out of the 23 detected at 30 V were detected. Among them, only 4 were detected at 70 V with a higher intensity.

The four compounds detected with the highest intensity in pellet samples were cyclic oligomers composed by adipic acid (AA), phthalic acid (PA) and butanediol (BD), which corresponded to the formula $[AA\text{-}BD]_2$ (7.21_401.2183), [PA-BD-AA-BD] (7.71_443.1676), $[AA\text{-}BD]_3$ (7.84_601.3229) and [PA-BD-AA-BD-AA-BD] (8.20_643.2741). Common fragments were observed for these structures in high collision mass spectra, such as 221.0818 and 149.0234 in those containing PA or 201.112, 255.1580 and 183.1013 in those containing only AA and BD. All masses had been previously detected by Bradley in biobased materials used for food contact applications [5] but they had not been identified. Since samples were a blend of PLA and polyester, these compounds came from the polyester component. These compounds showed also the highest intensity in films and afterwards in migration experiments, which implies that the polyester part of the blend had a critical role in the risk assessment of this kind of materials.

Among the compounds detected with medium intensity in pellets it is important to highlight 3 PLA cyclic oligomers composed by lactic acid monomers (LA): $[LA]_6$,

276 $[LA]_7$ and $[LA]_9$. $[LA]_5$ and $[LA]_8$ which were also detected but at lower intensity. In
277 this case, even though they maintain the same intensity in films they were not detected
278 in migration in any case, probably because they reacted with food simulants, inducing a
279 cycle opening and formation of new compounds. Five more compounds were also
280 detected with medium intensity such as 2 plasticizers with adipate structure
281 (5.77_313.162 and 6.92_513.2671); a glycol (4.59_259.1160), probably also used as
282 PLA plasticizer or a compound with piperidine structure (5.68_281.1480), probably
283 added as light stabilizer. All of them had been previously detected by Bradley in
284 biobased materials [5] but they had not been identified.

285 Among the compounds with the lowest intensities, some plasticizers, PLA oligomers
286 and compounds defined as indirect additives for food contact materials by the U.S.
287 Food&Drug administration were also found [34].

288 Figure 2 shows the comparison of area intensity between pellets and films for those
289 compounds detected in the PLA-polyester blend. The results showed very similar values
290 for pellets and films. Only 4 compounds were detected just in pellets and were not
291 present in films. These compounds were: 4.59_259.1160, 4.88_303.1421,
292 5.29_391.1943 and 6.19_269.1373. The Pearson correlation factor was calculated
293 taking out these four compounds. The factor value obtained, 0.996, indicates a good
294 correlation between pellets and film composition.

295

296 **3.3. Composition of migration solutions**

297 Migration was tested in 3 different simulants in order to predict the behavior of this
298 material with different kinds of food, from aqueous to fat. Figure 3 shows a
299 chromatogram of migration in ethanol 95%, ethanol 10% and acetic acid 3%. The first
300 observation was that not all the compounds present in the film were detected in
301 migration, as expected based on previous experience [35-37]. A total of 19 compounds
302 were detected initially in the film but only 14 of them were present in any of the food
303 simulants; 13 in ethanol 95%, 9 in ethanol 10% and 5 in acetic acid 3%. None of the
304 cyclic PLA oligomer detected in the material (6.40_383.0955, 6.80_455.1155,
305 7.05_527.1373, 7.30_599.1591, 7.44_671.1793) migrated to food simulants.

306 Figure 4 shows the area intensity of the peaks detected in migration in the different food
307 simulants. The highest migration values were found in ethanol 95% as food simulant for
308 two cyclic oligomers coming from the polyester part of the blend: $[AA\text{-}BD]_2$,
309 (7.21_401.2183) and [PA-BD-AA-BD] (7.71_443.1676).

310 Section "a" of figure 4 shows the compounds that had been previously detected in the
311 film (14) and "b" those only detected in migration (14). Those ones only detected in
312 migration were probably formed as a consequence of the reaction between the PLA
313 components and the food simulants. Six linear PLA oligomers with two hydroxyl
314 groups corresponding to the formula $HO\text{-}[LA]_n\text{-}H$ (n= 3-8) were found as a
315 consequence of the reaction with aqueous food simulants (ethanol 10% or acetic acid
316 3%). In all cases the intensity was higher in acetic acid 3% than in ethanol 10%. The
317 compound 3.60_331.0711 was only found in acetic acid 3% but it was not possible to
318 identify it. When PLA was in contact with food simulants with ethanol content (ethanol
319 95% or ethanol 10%) 7 different linear PLA oligomers with an additional C_2H_4O were
320 detected. Different structures can be proposed for these oligomers: $CH_3\text{-}O\text{-}[LA]_n\text{-}CH_3$,
321 $C_2H_5\text{-}O\text{-}[LA]_n\text{-}H$ or $C_2H_5\text{-}[LA]_n\text{-}OH$. Since the first option was previously described by
322 Badia et al in PLA samples [38], it was chosen as the principal candidate. In all cases
323 the intensity of these oligomers was higher in ethanol 95% than in ethanol 10%.

324 In order to determine the weight of the film components and the reaction components in
325 migration, the relative percentage of area intensity of each detected peak related to the
326 total area in migration was calculated. It was observed that 44.6% of the total intensity
327 corresponded to peaks previously detected in the film and 55.4 % to peaks detected only
328 in migration. When considering each simulant individually, different behaviors were
329 observed. In ethanol 95%, 65.6 % of the total area corresponded to compounds already
330 detected in the film, which would mean that these compounds have a slight higher
331 weight in migration that the new-formed. In the case of ethanol 10%, similar results
332 were found for each kind of compounds, 45.5 and 54.5 %. In acetic acid 3%, only a
333 15.4% of the area corresponded to compounds already detected in films, and 84.6 %
334 corresponded to new-formed compounds, what would mean that in this food simulant
335 the new-formed compounds have a very relevant role.

336

337 **4. Conclusions**

The dissolution/precipitation sample treatment developed in this work followed by the analysis of extracts by UPLC-MS(QTOF) showed to be an efficient methodology for the analysis of non-volatile components present in a biodegradable PLA-polyester blend. Very similar composition was found in PLA pellets and films, since no new compounds were formed during the extrusion and only 4 disappeared during this process. The compounds with the highest intensities in PLA blend samples as well as in migration studies came from the polyester part of the blend and corresponded to cyclic oligomers composed by adipic acid, phthalic acid and butanediol. Even though several cyclic oligomers had been detected in pellets and film samples with medium intensity, they were not detected in migration solutions. In contrast, new linear oligomers formed as a consequence of a cycle opening were identified. Furthermore, some plasticizers as well as other additives were found, both in samples and migration. It is important to remark that in addition to the screening in the film samples, a screening study in the migration solutions is necessary in order to have a comprehensive information about the migrants present in the food simulants. A future quantification of the compounds detected would allow establishing a correct risk assessment of the material.

Acknowledgements: The authors acknowledge Projects AGL2015-67362-P from MINECO (Spain) and FEDER funds and Project RYC-2012-11856 (Ramón y Cajal Research Program). The authors thank the Aragon Government and European Social Funds for the financial help given to GUIA group T-10.

References

[1] N. Jabeen, I. Majid, G.A. Nayik, Bioplastics and food packaging: A review, Cogent Foods and Agriculture, 1 (2015) 1-6.
[2] S.A. Ashter, Commercial Applications of Bioplastics, in: Introduction to Bioplastics Engineering, Elsevier, 2016.
[3] European-Commission, Regulation (EC) No 1935/2004 of the European Parliament on materials and articles intended to come into contact with food (2004).
[4] S. Inkinen, M. Hakkarainen, A.C. Albertsson, A. Sodergard, From Lactic Acid to Poly(lactic acid) (PLA): Characterization and Analysis of PLA and Its Precursors, Biomacromolecules, 12 (2011) 523-532.
[5] E.L. Bradley, Biobased materials used in food contact applications: an assessment of the migration potential, in, The Food and Environment Research Agency, York, 2010, pp. 201.
[6] R.A. Auras, B. Harte, S. Selke, R. Hernandez, Mechanical, physical, and barrier properties of poly(lactide) films, Journal of Plastic Film & Sheeting, 19 (2003) 123-135.
[7] J. Muller, C. Gonzalez-Martinez, A. Chiralt, Combination of Poly(lactic) Acid and Starch for Biodegradable Food Packaging, Materials, 10 (2017).

[8] Z.O. Erdohan, B. Cam, K.N. Turhan, Characterization of antimicrobial polylactic acid based films, J Food Eng, 119 (2013) 308-315.
[9] M.B. Coltelli, I. Della Maggiore, M. Bertold, F. Signori, S. Bronco, F. Ciardelli, Poly(lactic acid) properties as a consequence of poly(butylene adipate-co-terephthalate) blending and acetyl tributyl citrate plasticization, J Appl Polym Sci, 110 (2008) 1250-1262.
[10] N. Ljungberg, B. Wesslen, The effects of plasticizers on the dynamic mechanical and thermal properties of poly(lactic acid), J Appl Polym Sci, 86 (2002) 1227-1234.
[11] K.M. Choi, M.C. Choi, D.H. Han, T.S. Park, C.S. Ha, Plasticization of poly(lactic acid) (PLA) through chemical grafting of poly(ethylene glycol) (PEG) via in situ reactive blending, Eur Polym J, 49 (2013) 2356-2364.
[12] C. Nerin, P. Alfaro, M. Aznar, C. Domeno, The challenge of identifying non-intentionally added substances from food packaging materials: A review, Anal. Chim. Acta 775 (2013) 14-24.
[13] R. Auras, B. Harte, S. Selke, An overview of polylactides as packaging materials, Macromolecular Bioscience, 4 (2004) 835-864.
[14] E. Canellas, P. Vera, C. Nerin, Migration assessment and the 'threshold of toxicological concern' applied to the safe design of an acrylic adhesive for food-contact laminates, Food Additives and Contaminants Part a-Chemistry Analysis Control Exposure & Risk Assessment, 34 (2017) 1721-1729.
[15] M.J. Martinez-Bueno, M.D. Hernando, S. Ucles, L. Rajski, S. Cimmino, A.R. Fernandez-Alba, Identification of non-intentionally added substances in food packaging nano films by gas and liquid chromatography coupled to orbitrap mass spectrometry, Talanta, 172 (2017) 68-77.
[16] M. Hoppe, R. Fornari, P.d. Voogt, R. Franz, Migration of oligomers from PET: determination of diffusion coefficients and comparison of experimental versus modelled migration., Food Addit Contam A, (2017) 1-10.
[17] D.J. Kim, K.T. Lee, Determination of monomers and oligomers in polyethylene terephthalate trays and bottles for food use by using high performance liquid chromatography-electrospray ionization-mass spectrometry, Polym Test, 31 (2012) 490-499.
[18] S. Ubeda, M. Aznar, P. Vera, C. Nerín, L. Henríquez, L. Taborda, C. Restrepo, Overall and specific migration from multilayer high barrier food contact materials – Kinetic study of cyclic polyester oligomers migration, Food Addit Contam A, (2017).
[19] M. Heimrich, H. Nickl, M. Bönsch, T.J. Si, Migration of Cyclic Monomer and Oligomers from Polyamide 6 and 66 Food Contact Materials into Food and Food Simulants: Direct Food Contact, Packag Technol Sci, (2014).
[20] M. Mutsuga, Y. Kawamura, K. Tanamoto, Migration of lactic acid, lactide and oligomers from polylactide food-contact materials, Food Addit Contam A, 25 (2008) 1-14.
[21] Y. Bor, J. Alin, M. Hakkarainen, Electrospray Ionization-Mass Spectrometry Analysis Reveals Migration of Cyclic Lactide Oligomers from Polylactide Packaging in Contact with Ethanolic Food Simulant, Packag Technol Sci, 25 (2012) 427-433.
[22] S. Dopico-Garcia, A. Ares-Pernas, J. Otero-Canabal, M. Castro-Lopez, J.M. Lopez-Vilarino, V. Gonzalez-Rodriguez, M.J. Abad-Lopez, Insight into industrial PLA aging process by complementary use of rheology, HPLC, and MALDI, Polym Advan Technol, 24 (2013) 723-731.
[23] S. Lazzari, R. Codari, G. Storti, M. Morbidelli, D. Moscatelli, Modeling the pH-dependent PLA oligomer degradation kinetics, Polym Degrad Stabil, 110 (2014) 80-90.

[24] I. Osaka, A. Yoshimoto, M. Watanabe, M. Takama, M. Murakami, H. Kawasaki, R. Arakawa, Quantitative determination of cyclic polylactic acid oligomers in serum by direct injection liquid chromatography tandem mass spectrometry, J Chromatogr B, 870 (2008) 247-250.
[25] F.L. Bayer, Polyethylene terephthalate recycling for food-contact applications: testing, safety and technologies: a global perspective, Food Additives and Contaminants Part a-Chemistry Analysis Control Exposure & Risk Assessment, 19 (2002) 111-134.
[26] T.H. Begley, H.C. Hollifield, Liquid-chromatographic determination of residual reactants and reaction by-products in polyethylene terephthalate, Journal of the Association of Official Analytical Chemists, 72 (1989) 468-470.
[27] J.C. Poulakis, C.D. Papaspyrides, Dissolution/reprecipitation: A model process for PET bottle recycling, Journal of Applied Polymer Science, 81 (2001) 91-95.
[28] B. Li, Z.W. Wang, Q.B. Lin, C.Y. Hu, Study of the Migration of Stabilizer and Plasticizer from Polyethylene Terephthalate into Food Simulants, Journal of Chromatographic Science, 54 (2016) 939-951.
[29] S. Ubeda, M. Aznar, C. Nerín, Determination of oligomers in virgin and recycled polyethylene terephthalate (PET) samples by UPLC-MS-QTOF, Anal Bioanal Chem, 41 (2018) 2372-2384.
[30] S. Kalia, L. Avérous, Biopolymers: Biomedical and Environmental Applications, Wiley, Scrivever, Salem, MA, 2011.
[31] L. Xiao, B. Wang, G. Yang, M. Gauthier, Poly(Lactic Acid)-Based Biomaterials: Synthesis, Modification and Applications, in: D.N. Ghista (Ed.) Biomedical Science, Engineering and Technology, IntechOpen, 2010.
[32] European-Commission, Commision Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food, (2011).
[33] M. Aznar, P. Alfaro, C. Nerin, E. Jones, E. Riches, Progress in mass spectrometry for the analysis of set-off phenomena in plastic food packaging materials, J Chrom A, 1453 (2016) 124-133.
[34] U.S.F.D. Administration, https://www.fda.gov/Food/IngredientsPackagingLabeling/PackagingFCS/IndirectAdditives/default.htm, 2018.
[35] E. Canellas, M. Aznar, C. Nerin, P. Mercea, Partition and diffusion of volatile compounds from acrylic adhesives used for food packaging multilayers manufacturing, J Mater Chem., 20 (2010) 5100-5109.
[36] E. Canellas, P. Vera, C. Nerin, UPLC-Q-TOF-MSE and GC-MS identification and quantification of non-intentionally added substances coming from biodegradable food packagings, Anal Bioanal Chem, 407 (2015) 6781-6790.
[37] E. Canellas, P. Vera, C. Nerin, Migration assessment and the Threshold of Toxicological Concern applied to the safe-design of an acrylic adhesive for food contact laminates, Food Addit Contam A, 34 (2017) 1721-1729.
[38] J.D. Badia, E. Stromberg, A. Ribes-Greus, S. Karlsson, Assessing the MALDI-TOF MS sample preparation procedure to analyze the influence of thermo-oxidative ageing and thermo-mechanical degradation on poly (Lactide), Eur Polym J, 47 (2011) 1416-1428.

Figure captions

Figure 1. Chromatogram obtained by UPLC-MS(QTOF) analysis of PLA pellet samples overlaid with a blank sample.

Figure 2. Area intensity of the non-volatile components of PLA-polyester blend pellets and films.

Figure 3. Chromatogram obtained by UPLC-MS(QTOF) analysis of migration solutions from PLA-polyester blend films to different food simulants: ethanol 95% (a), ethanol 10% (b) and acetic acid 3% (c), overlaid with blank samples.

Figure 4. Area intensity of the non-volatile components detected in migration from PLA-polyester blend to 3 different food simulants. Section “a” shows the compounds that had been previously detected in the film and “b” those only detected in migration.

Table 1: Recovery data and matrix effect for PLA-polyester sample treatment by dissolution/precipitation

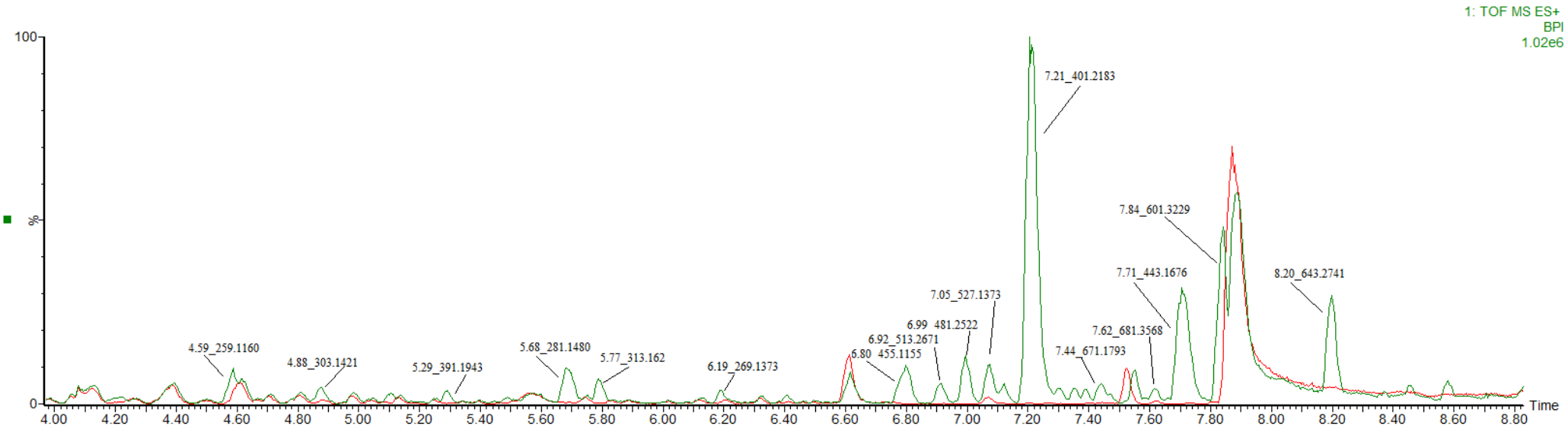
	Acetoaminophen	**Caffeine**	**Reserpine**	**Sulfadimethoxine**
Recovery Without washing (%)	53.0	55.6	30.3	34.1
Recovery With washing (%)	120.4	113.1	81.3	79.7
Matrix effect (%)	103.4	131.7	100.9	114.0

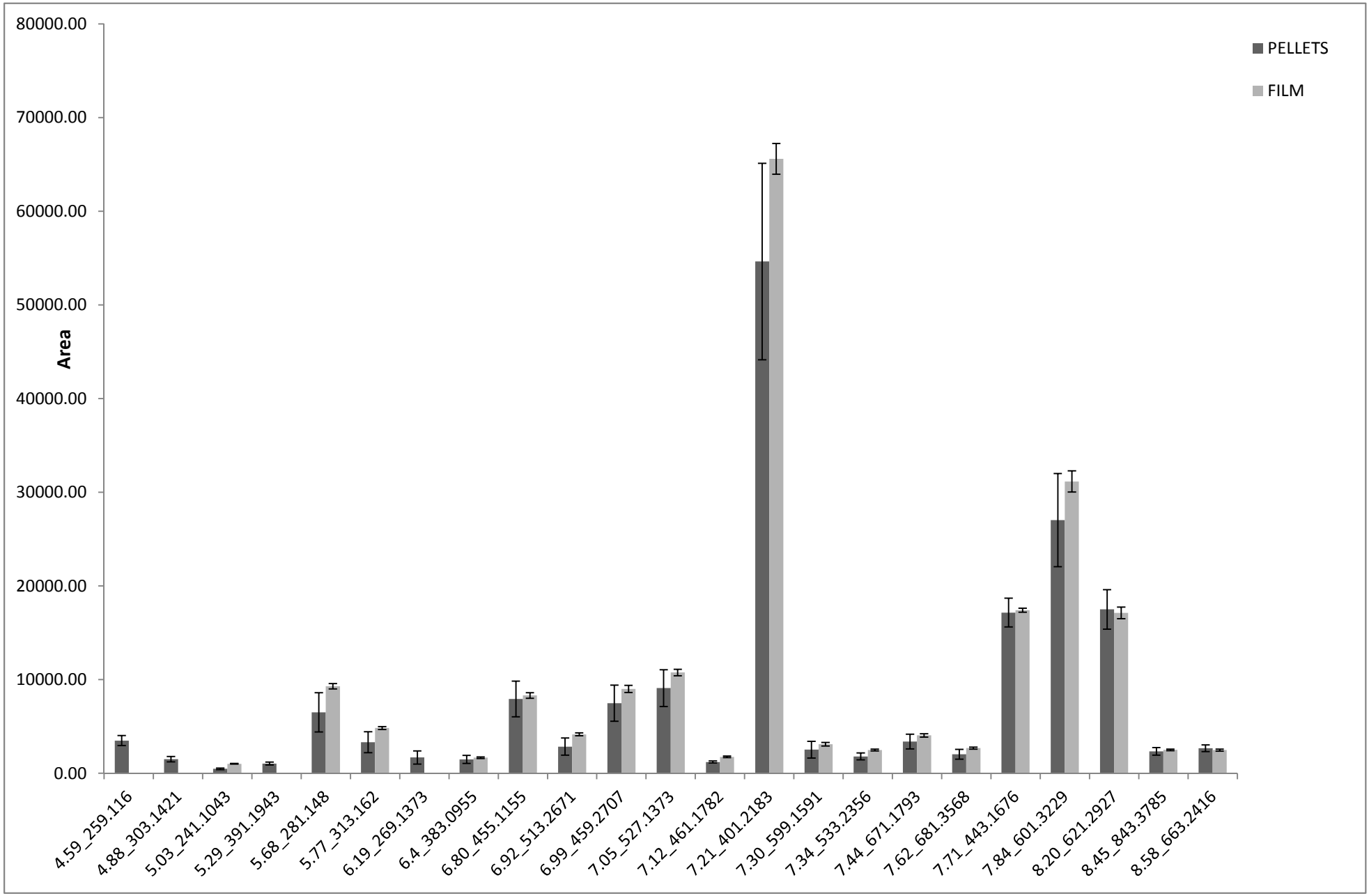
Table 2: Compounds detected in pellets, films and migration and its areas intensity (1 high, 2 medium, 3 low) at 30V cone voltage; molecular formula; proposed candidates; remarks, main fragments in the high collision energy mass spectrum and its scores (S) obtained by MassFragmet®.

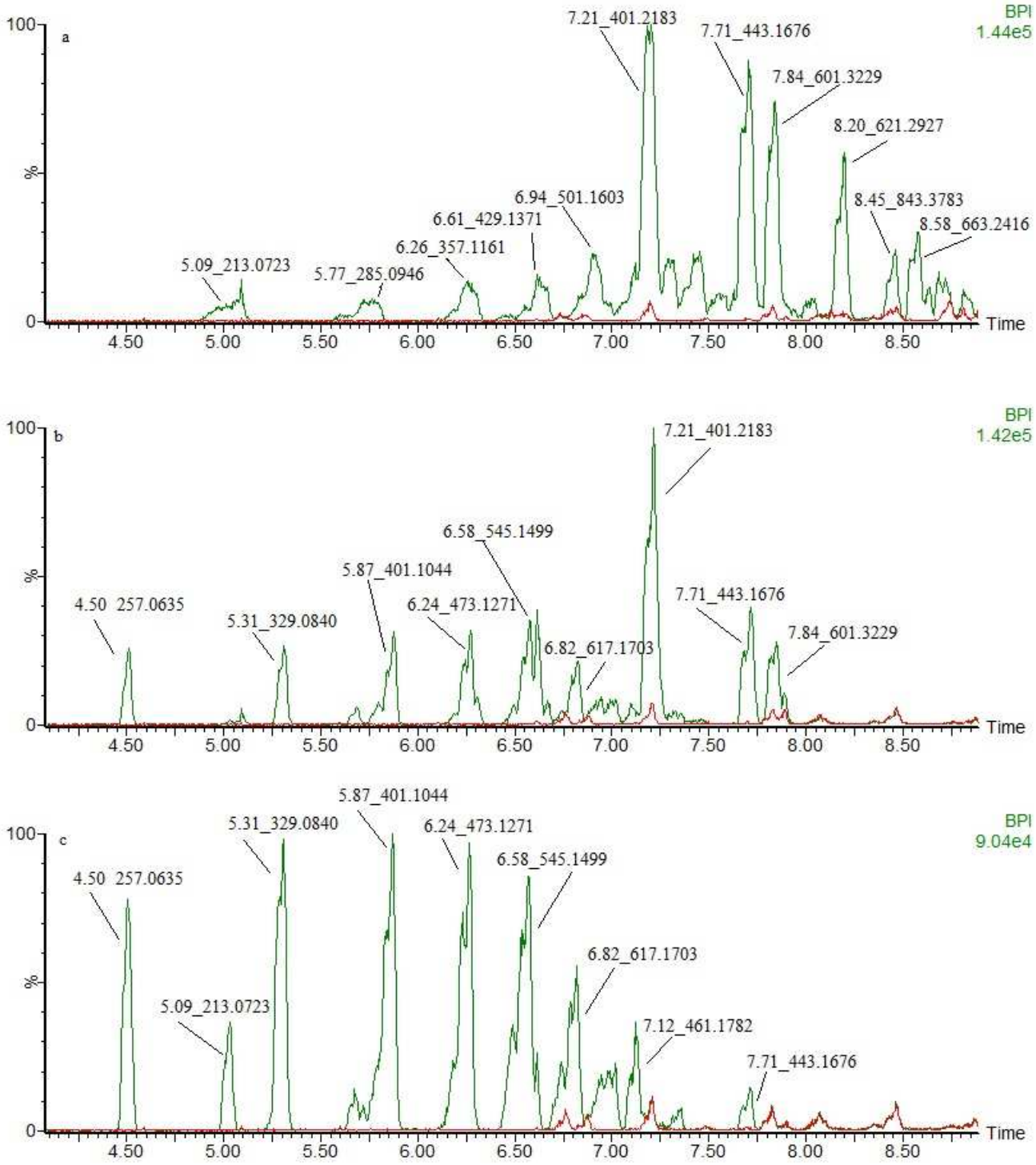
Code rt_mass	I pellets	I film	I mig	Adduct	Molecular formula	Candidates	Remarks/Fragments (scores)
3.60_331.0711	nd	nd	1	$[MNa]^+$	$C_{22}H_{12}O_2$	No candidates	167.0027, 185.0129
4.50_257.0635	nd	nd	2	$[MNa]^+$	$C_9H_{14}O_7$	HO-$[LA]_3$-H *(linear)*	PLA oligomer
4.59_259.1160	2	nd	nd	$[MNa]^+$	$C_{10}H_{20}O_6$	1,3,6,9,11,14-Hexaoxacyclohexadecane CAS 74485-37-3 (Glycol)	PLA plasticizer 103.0392 (S2); 131.0706 (S2); 87.0438 (S2)
4.88_303.1421	1	nd	nd	$[MNa]^+$	$C_{12}H_{24}O_7$	Poly(trimethylolpropane adipate) CAS 28301-90-8	Indirect additives by FDA [23] 131.0705 (S2)
4.98_241.1043	1	1	2	$[MNa]^+$	$C_{10}H_{18}O_5$	Diethylene glycol, dipropionate CAS 6942-59-2	PLA plasticizers
5.09_213.0723	nd	nd	2	$[MNa]^+$	$C_8H_{14}O_5$	CH_3-O-$[LA]_2$-CH_3 *(linear)*	PLA oligomer
5.29_391.1943	1	nd	nd	$[MNa]^+$	$C_{16}H_{32}O_9$	No candidates	
5.31_329.0840	nd	nd	2	$[MNa]^+$	$C_{12}H_{18}O_9$	HO-$[LA]_4$-H *(linear)*	PLA oligomer
5.68_281.1480	2	2	1	$[MNa]^+$	$C_{12}H_{22}N_2O_4$	Piperidine family	Detected by Bradley in PLA [5] Hindered piperidines are light stabilizer
5.71_285.0946	nd	nd	2	$[MNa]^+$	$C_{11}H_{18}O_7$	CH_3-O-$[LA]_3$-CH_3 *(linear)*	PLA oligomer
5.77_313.162	2	2	2	$[MNa]^+$	$C_{14}H_{26}O_6$	Bis(2-ethoxyethyl) adipate CAS 109-44-4	Detected by Bradley in starch and cellulose [5] 111.0440 (S1); 101.0597 (S1.5); 129.0545 (S1); 73.0651 (S0.5)
5.87_401.1044	nd	nd	2	$[MNa]^+$	$C_{15}H_{22}O_{11}$	HO-$[LA]_5$-H *(linear)*	PLA oligomer
6.19_269.1373	1	nd	nd	$[MNa]^+$	$C_{12}H_{22}O_5$	2,2'-(oxybis((methyl-2,1-ethanediyl)-oxymethylene)) bisoxirane CAS 41638-13-5	Indirect additives by FDA [23] 83.0493 (S2); 101.0601 (S1.5)
6.24_473.1271	nd	nd	2	$[MNa]^+$	$C_{18}H_{26}O_{13}$	HO-$[LA]_6$-H *(linear)*	PLA oligomer
6.26_357.1161	nd	nd	2	$[MNa]^+$	$C_{14}H_{22}O_9$	CH_3-O-$[LA]_4$-CH_3 *(linear)*	PLA oligomer
6.40_383.0955	1	1	nd	$[MNa]^+$	$C_{15}H_{20}O_{10}$	$[LA]_5$ *(cyclic)*	PLA oligomer 217.0704 (S2); 145.0494 (S2)
6.58_545.1499	nd	nd	2	[MNa]+	$C_{21}H_{30}O_{15}$	HO-$[LA]_7$-H *(linear)*	PLA oligomer
6.61_429.1371	nd	nd	2	$[MNa]^+$	$C_{17}H_{26}O_{11}$	CH_3-O-$[LA]_5$-CH_3 *(linear)*	PLA oligomer
6.80_455.1155	2	2	nd	$[MNa]^+$	$C_{18}H_{24}O_{12}$	$[LA]_6$ *(cyclic)*	PLA oligomer 217.0704 (S2); 145.0494 (S2); 289.0922 (S2)
6.82_617.1703	nd	nd	2	$[MNa]^+$	$C_{24}H_{34}O_{17}$	HO-$[LA]_8$-H *(linear)*	PLA oligomer

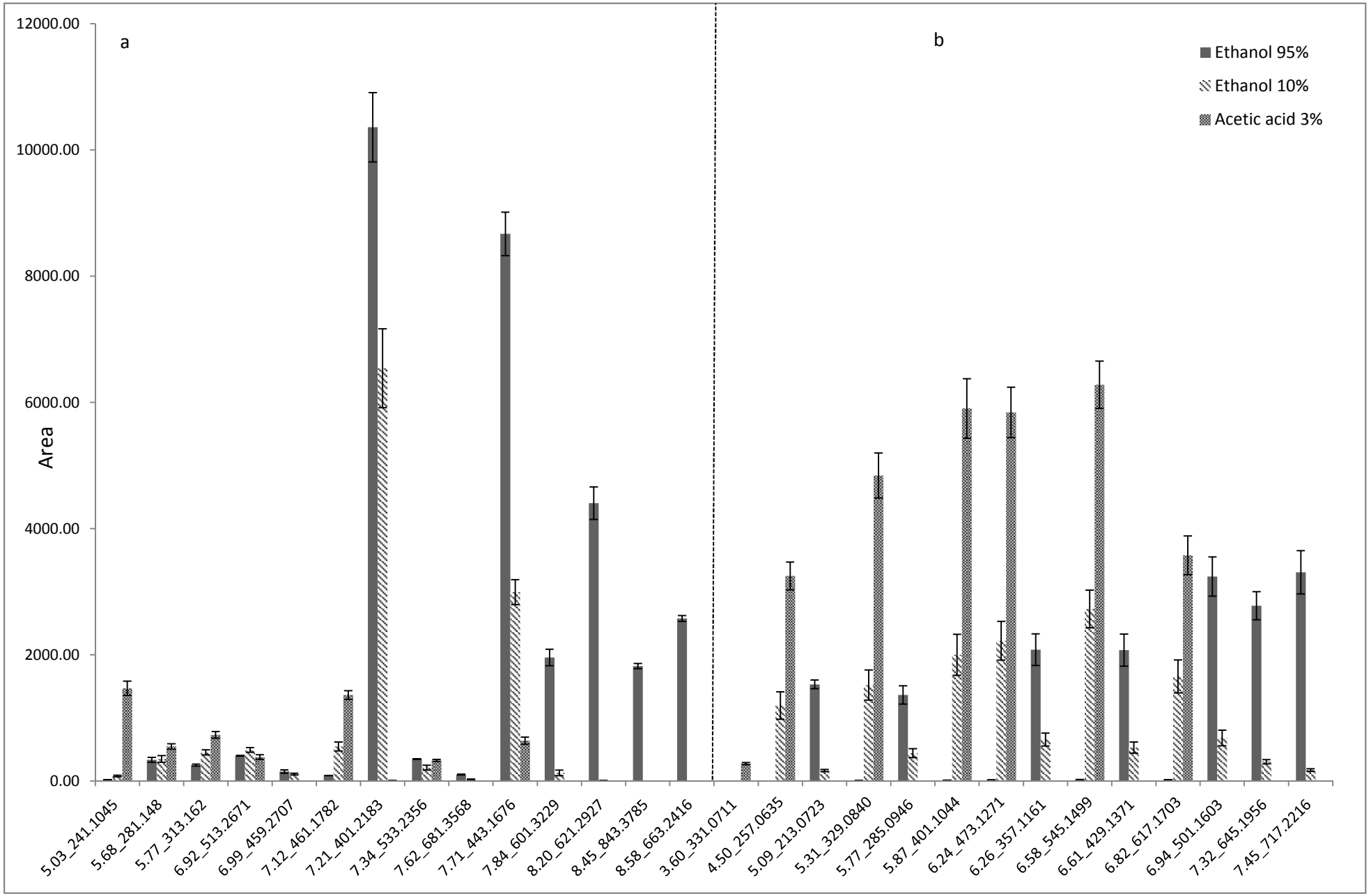
6.92_513.2671	2	2	1	$[MNa]^+$	$C_{24}H_{42}O_{10}$	Bis[1-(2-butoxyethoxy)-1-oxo-2-propanyl] adipate	Detected by Bradley [5] 201.1120 (S1.5); 111.0440 (S1); 101.0597 (S1.5); 129.0545 (S1)
6.94_501.1603	nd	nd	2	$[MNa]^+$	$C_{20}H_{30}O_{13}$	CH_3-O-$[LA]_6$-CH_3 *(linear)*	PLA oligomer
6.99_481.2522	2	2	1	[MNa]+	$C_{22}H_{38}N_2O_8$	Urethane dimethacrylate UDMC CAS 72869-86-4	Detected by Bradley [5] 129.0548 (S0.5); 241.1543 (S1.5)
7.05_527.1373	2	2	nd	$[MNa]^+$	$C_{21}H_{28}O_{14}$	$[LA]_7$ *(cyclic)*	PLA oligomer 217.0708 (S2); 289.0913 (S2); 361.1119 (S2)
7.12_461.1782	1	1	2	$[MNa]^+$	$C_{22}H_{30}O_9$	No candidates	Detected by Bradley [5]
7.21_401.2183	3	3	3	$[MH]^+$	$C_{20}H_{32}O_8$	$[AA\text{-}BD]_2$ *(cyclic)* CAS 78837-87-3	Polyester oligomer. Detected by Bradley [5] 201.1120 (S2);129.0547 (S2); 111.0443 (S2); 255.1580 (S2); 183.1013 (S2)
7.30_599.1591	1	1	nd	$[MNa]^+$	$C_{24}H_{32}O_{16}$	$[LA]_8$ *(cyclic)*	PLA oligomer 361.1119 (S2); 433.1345 (S2)
7.32_645.1956	nd	nd	2	$[MNa]^+$	$C_{26}H_{38}O_{17}$	CH_3-O-$[LA]_8$-CH_3 *(linear)*	PLA oligomer
7.34_533.2356	1	1	1	$[MNa]^+$	$C_{26}H_{38}O_{10}$	No candidates	221.0818 (S2); 149.0234(S2); 167.0339 (S2); 111.0443 (2)
7.44_671.1793	2	2	nd	$[MNa]^+$	$C_{27}H_{36}O_18$	$[LA]_9$ *(cyclic)*	PLA oligomer 361.1133(S2);433.1345 (S2); 505.1565 (S2)
7.45_717.2216	nd	nd	2	$[MNa]^+$	$C_{29}H_{42}O_{19}$	CH_3-O-$[LA]_9$-CH_3 *(linear)*	PLA oligomer
7.62_681.3568	1	1	1	$[MNa]^+$	$C_{38}H_{50}N_4O_6$	No candidates	349.1647; 381.2684
7.71_443.1676	3	3	3	$[MNa]^+$	$C_{22}H_{28}O_8$	[PA-BD-AA-BD] *(cyclic)*	Polyester oligomer. Detected by Bradley [5] 221.0818 (S2); 149.0234(S2); 167.0339 (S2); 111.0443 (2)
7.84_601.3229	3	3	2	$[MH]^+$	$C_{30}H_{48}O_{12}$	$[AA\text{-}BD]_3$ *(cyclic)* CAS 1135871-65-6	Polyester oligomer. Detected by Bradley [5] 201.1124 (S2); 329.1581 (S2); 255.0549 (S2); 183.1017 (S2)
8.20_643.2741	3	3	3	$[MNa]^+$	$C_{32}H_{44}O_{12}$	[PA-BD-AA-BD-AA-BD] *(cyclic)*	Polyester oligomer. Detected by Bradley [5] 421.1862 (S2); 221.0818 (S2); 149.0234 (S2); 129.0548 (S2)
8.45_843.3785	1	1	2	$[MNa]^+$	No formula	No candidates	621.2953; 421.1875
8.58_663.2416	1	1	2	$[MNa]^+$	$C_{34}H_{40}O_{12}$	No candidates	Detected by Bradley [5] 369.0979; 441.1561

nd: non detected; LA: lactic acid; AA: adipic acid; PA: phthalic acid; BD: butanediol;


1: TOF MS ES+
BPI
1.02e6
100
%
0
4.59_259.1160
4.88_303.1421
5.29_391.1943
5.68_281.1480
5.77_313.162
6.19_269.1373
6.92_513.2671
6.80 455.1155
6.99 481.2522
7.05_527.1373
7.21_401.2183
7.44_671.1793
7.62_681.3568
7.71_443.1676
7.84_601.3229
8.20_643.2741
4.00 4.20 4.40 4.60 4.80 5.00 5.20 5.40 5.60 5.80 6.00 6.20 6.40 6.60 6.80 7.00 7.20 7.40 7.60 7.80 8.00 8.20 8.40 8.60 8.80
Time


80000.00
70000.00
60000.00
50000.00
40000.00
30000.00
20000.00
10000.00
0.00
Area
PELLETS
FILM
4.59_259.116
4.88_303.1421
5.03_241.1043
5.29_391.1943
5.68_281.148
5.77_313.162
6.19_269.1373
6.4_383.0955
6.80_455.1155
6.92_513.2671
6.99_459.2707
7.05_527.1373
7.12_461.1782
7.21_401.2183
7.30_599.1591
7.34_533.2356
7.44_671.1793
7.62_681.3568
7.71_443.1676
7.84_601.3229
8.20_621.2927
8.45_843.3785
8.58_663.2416


a
BPI
1.44e5
7.21_401.2183
7.71_443.1676
7.84_601.3229
8.20_621.2927
8.45_843.3783
8.58_663.2416
6.94_501.1603
6.61_429.1371
6.26_357.1161
5.77_285.0946
5.09_213.0723
b
BPI
1.42e5
7.21_401.2183
6.58_545.1499
5.87_401.1044
7.71_443.1676
4.50 257.0635
6.24_473.1271
5.31_329.0840
7.84_601.3229
6.82_617.1703
c
BPI
9.04e4
5.87_401.1044
5.31_329.0840
6.24_473.1271
4.50 257.0635
6.58_545.1499
6.82_617.1703
5.09_213.0723
7.12_461.1782
7.71_443.1676
100
%
0
Time
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50


a
b
Ethanol 95%
Ethanol 10%
Acetic acid 3%
Area
12000.00
10000.00
8000.00
6000.00
4000.00
2000.00
0.00
5.03_241.1045
5.68_281.148
5.77_313.162
6.92_513.2671
6.99_459.2707
7.12_461.1782
7.21_401.2183
7.34_533.2356
7.62_681.3568
7.71_443.1676
7.84_601.3229
8.20_621.2927
8.45_843.3785
8.58_663.2416
3.60_331.0711
4.50_257.0635
5.09_213.0723
5.31_329.0840
5.77_285.0946
5.87_401.1044
6.24_473.1271
6.26_357.1161
6.58_545.1499
6.61_429.1371
6.82_617.1703
6.94_501.1603
7.32_645.1956
7.45_717.2216