Migration of unknown non-volatile compounds from hot melt adhesives used in food packaging materials characterized by ultra-performance liquid chromatography coupled to quadrupole time-of- flight mass spectrometry.

Paula Vera[1], Elena Canellas[1], and Cristina Nerín[1]*

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

pvera@unizar.es; elenac@unizar.es; cnerin@unizar.es

Keywords:

Adhesives, food packaging, migration, UPLC-MS/QTOF

Abstract.

The identification of unknown non-volatile migrant compounds from adhesives used in food contact materials is a very challenging task because of the number of possible compounds involved, given that adhesives are complex mixtures of chemicals. The use of ultra-performance liquid chromatography coupled to quadrupole time-of-flight mass spectrometry (UPLC- MS/QTOF) is shown to be a successful tool for identifying non-targeted migrant compounds from two hot melt adhesives used in food packaging laminates. Out of the seven migrants identified and quantified, five were amides and one was a compound classified in Class II of the Cramer toxicity. None of the migration values exceeded the recommended Cramer exposure values.

1. Introduction

Adhesives are complex formulations of substances as a polymer, antioxidants, tackifiers, inhibitors, fillers, solvents, diluents, plasticizers, etc. [1] which provide specialized functions. It is very difficult even for adhesive producers to know in detail the formulas of their products due to the presence of impurities from raw materials or by-products as result of a side reaction between different ingredients [2].

Adhesives are commonly used in the manufacture of food packaging materials, for example to form multilayer packaging materials (laminates) [3]. Although all components of food contact materials must comply with the Framework Regulation (EC) Nº 1935/2004 [4], there is no specific legislation in the EU for adhesives. Manufacturers currently follow the provisions of the European ‘‘Plastics Directive’’ [5], while in Spain recent legislation governing food contact materials [6], has come into force. Both regulations provide positive lists of authorized substances, their specific migration limits (SML) or global migration limits (GML).

The migration of volatile compounds from adhesives has been widely studied in the framework of the European research project MIGRESIVES [2, 7-11] and a great variety of migrant compounds have been identified. However, the migration of non-volatile compounds has scarcely been studied as it was assumed that they would not migrate [12-15].

The screening of unknown non-volatile and non-targeted compounds in complex samples poses a significant analytical challenge. Mass spectrometry such as single and triple quadrupole or ion trap does not provide sufficient sensitivity in scan or full scan mode for these complex samples. In contrast, the time-of-flight mass (TOF) analyzer combined with quadrupole provides the sensitivity and selectivity required for screening these types of samples. This is one of the most powerful techniques because it provides the possibility of acquiring full scan mass spectra with high sensitivity and elevated mass accuracy of any ionizable components in the sample. In addition, this combination gives accurate masses for both parent and fragment ions providing more structural information and enhancing selectivity . Therefore, this technique is very attractive for the non-targeted analysis commonly used in environmental and food safety analysis [11, 16-22].

The aim of this paper is to identify unknown non-volatile migrants from two hot melt adhesives used in common multilayer food packaging materials. Ultra-performance liquid chromatography coupled to quadrupole time-of-flight mass spectrometry (UPLC-ESI-MS/ QTOF) was used to provide the structural information for this screening purpose. Once identified, the migrant concentrations were quantified in order to study the possible risk for consumers.

2. Materials and methods

2.1. Reagents

The standards tetradecanamide (638-58-4), hexadecanamide (629-54-9), 9-Octadecenamide, (9Z) (301-02-0), 3,5-di-tert-butyl-4-hydroxybenzaldehyde (1620-98-0), hexamide (628-02-4), 2,6-di-tert-butyl-4-(1-methylpropyl)-phenol (17540-75-9) and formic acid were purchased from Sigma-Aldrich Química S.A (Madrid, Spain). All were of analytical quality. Dicloromethane, water and methanol of HPLC grade were supplied by Scharlau Chemie S.A (Sentmenat, Spain). Tenax TA 80/100 mesh was supplied by Supelco (Bellefonde, USA).

An A solution of hexamide at 200 µg/g in methanol was used as internal standard for ESI (+) mode and a B solution of 2,6-di-tert-butyl-4-(1-methylpropyl)-phenol at 200 µg/g in methanol was used as internal standard for ESI (-) mode.

Solution C contained four standards (tetradecanamide, hexadecanamide, Octadecenamide, (9Z), 3,5-di-tert-butyl-4-hydroxybenzaldehyde) at 20 µg/g in methanol
.

2.2. Adhesive samples and laminates.

Two hot melt adhesives were studied, both supplied by the same adhesive company. Hot melt1 (HM1) was based on EVA (ethylene vinyl acetate) and hot melt 2 (HM2) was based on an amorphous polyolefin APAO enriched in propene. Both adhesives contained tackifiers and an antioxidant, but no more precise information about their formulation can be supplied for confidentiality reasons.

The adhesives were studied both individually and as part of laminates whose structures [Substrate- Adhesive- Substrate] are commonly used for packaging dry food such as salt, sugar, cakes, cookies, etc.

These laminates were manufactured in the laboratory. The adhesives are solid polymers (films, granules or pellets) at room temperature. To manufacture the laminates, the hot-melt adhesive was heated at 160-180ºC to be cured and was then applied as a coating

layer on a 10 x 10 cm substrate forming a uniform layer (10x10 cm). An extender machine was used for this purpose. When the adhesive was slightly dry, the second substrate was placed on the coated adhesive and some pressure was applied to facilitate the laminate formation.

Two types of substrates were used: cardboard (CB) of 380 µm thickness and polypropylene laminated cardboard (ppCB) of 380+30 µm thickness. The quantity of adhesive applied was 30 ±2.5 g/m^2 per laminate, which was weight controlled. Finally, the laminate was stored in the laboratory at 23ºC.

Using these procedures the following laminates were manufactured:

- Laminate 1: [CB-HM1 -CB]
- Laminate 2: [ppCB-HM1-ppCB]
- Laminate 3: [CB-HM2-CB]
- Laminate 4: [ppCB-HM2-ppCB]

2.3. UPLC separation.

Chromatography was carried out in an Acquity^{TM} system using an Acquity UPLC BEH C18 column of 17 µm particle size (2.1 mm x 100 mm), both from Waters (Milford, MA, USA). The solvents used as mobile phase were water and methanol both with 0.1 % formic acid. The column flow was 0.3 mL/min and the column temperature was 35ºC. The gradient used here was 5-95% methanol 0.1% formic acid (0-24min) and the volume of sample injected was 5 µL.

2.4. Mass spectrometry detector/ QTOF

The detector was an API source (atmospheric pressure ionization) with an electrospray interface (ESI) coupled to a Xevo G2 mass spectrometer consisting of a hexapole, a quadrupole, a collision cell and a time of flight analyzer (QTOF) supplied by Waters (Milford, MA, USA).

The electrospray probe was used in positive (ESI+) and negative (ESI-) modes as well as sensitivity analyzer mode. The mass range considered was from 10 to 1000 Da. The

corona voltage was 2.5 kV for (ESI+) and 0.5 kV for (ESI-). The sampling cone voltage was optimized between 20 and 50V. Finally, 30 V was selected for the migration screening because more peaks were detected. Other MS parameters were as follows: the source temperature was 150º C, the desolvation gas temperature 450ºC and the desolvation gas flow 650Lh^{-1}.

MS^E mode was selected for the acquisition, and collision ramp energy from 5 to 40 V was used. This was optimized for each migrant compound in order to obtain the maximum fragment ions for each mass in the function 2 (Table 1).

MassLynx v.4.1 software (Waters, Milford MA, USA) was used to analyze the samples and CromaLynx (Waters, Milford MA, USA) was used to deconvolve the spectra.

2.5. Screening and identification of migrant compounds from adhesives.

The first aim of this work was the screening of the potential migrant compounds from the adhesives used in the manufacture of laminates used for food packaging. For this purpose, a qualitative migration test of these laminates and their respective substrates was carried out using Tenax ® as a food simulant. These kinds of laminates are commonly used for dry food packaging for which Tenax ® is the recommended simulant in migration tests. Before the migration test, the Tenax ® was purified by soxhlet extraction with acetone for 6 hours.

The migration test was performed following the procedure optimized by Vera et al [7]. Cutouts of each laminate and substrate, 5 x 5 cm in size, were placed in Petri dishes and covered with 1 gram of Tenax forming a uniform layer (4 g Tenax per dm^2 laminate in accordance with UNE-EN 14338 [23]). The Tenax was applied on the side of the laminate that will be in contact with food. This system was kept in the oven at 40 ºC for 10 days [23]. After that, it was extracted two consecutive times with 3.4 mL of methanol. The total solution was concentrated under a stream of N_2 to 200 µL. Finally, the extracts were analyzed by UPLC-MS/QTOF using the same method explained above with the electrospray probe in ESI (+) and ESI (-) mode. Two replicates of each laminate and substrate were studied.

The identification of the compounds was carried out using the Chromalynx XS, Elemental composition and Mass Fragment ™ software tools. These helped in the structural elucidation of the unknown compounds. It was necessary to work in MS^E mode, a method of data acquisition that records exact mass precursor and fragment ion information in the same run. It alternates between two functions: function 1 acquiring low-energy exact mass precursor ion spectra and function 2 acquiring elevated-energy exact mass fragment ions. The parameters selected for Chromalynx XS software tool were (non targeted analysis, mass tolerance ±20 mDa, retention time ±0.2 min and ions abundance above 1000).

To determine the migrant compounds coming from the adhesives, a comparison between the chromatograms of each laminate with their respective substrates was carried out using the Chromalynx XS software tool in non-targeted mode.

Once the different ions from adhesives were determined, their identification was carried out by the Elemental Composition tool within MassLynx 4.1. This software provides the most probable formula for the ion under investigation, considering that the molecules are formed with the most common elements selected by the analyst (C, H, O, N, Cl, S and Na as adduct). This tool is based on the exact mass measurement and the isotopic ratios.

Once the different options for the elemental composition of each accurate mass were known, the molecular structures were searched in chemical databases such as Chemspider [www.chemspider.com] or Scifinder [scifinder.cas.org]. Finally, MS^E high energy fragment ion data (function 2) was utilized for further confirmation of unknown migrant compounds. Where the structures of the proposed candidates were fragmented and compared with the spectra of the unknown compounds, also fragmented by function 2. If the accurate masses of the fragments of one candidate coincided with the unknown compound, the identification was almost confirmed. To check this identification, the pure standards of these candidates were compared for their retention times and mass spectra with the compounds found.

Before the last step, the collision energies (MS^E high energy fragment) were optimized for each mass in order to obtain the maximum fragments of each ion and thus make efficient use of the MassFragment software.

2.6. Determination of initial concentration of the migrants in the adhesives.

The initial concentration test was only carried out with the HM2 adhesive since no migrant compounds were detected in the HM1 adhesive.

For this study, the HM2 adhesive was heated at 160-180ºC until it was melted. It was then applied on a flat surface (silicone paper) and cooled to room temperature, simulating the curing process. The cured adhesive was cut into strips to be extracted.

The extraction step was optimized. For this purpose, 0.5 grams of HM2 adhesive were extracted with 2.5 mL of two solvents with different polarities: dichloromethane and methanol at 40ºC during 24 hours. Finally, diclorometh**a**ne was considered the most appropriate solvent because it dissolved completely the adhesive. In contrast methanol showed low recoveries.. The final extraction method was as follows. 0.5 g of HM2 adhesive was extracted twice with diclorometh**a**ne. Each extraction was carried out at 40ºC during 24 hours. The extracts were then mixed together obtaining the total solution. The final solution was diluted 1/80 in methanol where the polymer precipitated. 10 µL of internal standard solutions A and B were added, and finally the solutions were filtered and analyzed by UPLC-MS/QTOF (in ESI (+) and (-) mode). Three replicates of HM2 adhesive were analyzed.

For building the calibration curves, solutions of the compounds at different concentration levels were prepared in methanol. 10 µL of solution A and B were added as internal standards. The solutions were analyzed by UPLC-MS/QTOF. Three replicates of each concentration level were analyzed.

2.7. Quantitative migrant values.

Once the migrants were identified and the initial concentration of the migrant in the HM2 adhesive was determined, the quantitative migration tests were performed. Firstly, the number of extractions of Tenax ® was optimized. For this purpose, a recovery experiment was carried out. Two samples of Tenax (1g) were spiked with 100 µL of solution C and afterwards extracted 3 consecutive times with .4 mL methanol. Each extract was separately analyzed by UPLC-MS/QTOF. The final extraction method was as follows. 1 gram of Tenax ® was extracted two consecutive times with 3.4 mL of methanol each

time. The solutions were put together and 10 µL of internal standard solution A and B were added. The solutions were then concentrated under a stream of N_2 to 200 µL and finally analyzed by UPLC-MS/QTOF. Recoveries above 90% were obtained for all the compounds.

The migration test of the laminates (lam_03 and lam_04) was performed as described in section 2.5. Three replicates of the migration test were carried out and analyzed by UPLC-MS/QTOF.

3. Results

3.1. Screening and identification of migrant compounds from adhesives

For the migration of compounds from laminates 1 and 2 made with the EVA hot melt, no different ions were found with respect to their substrates in either the ESI (+) or the ESI (-) modes. However, for laminates 3 and 4 made with the APAO hot melt adhesive, five different ions were found in the ESI (+) mode and 2 ions in the ESI (-) mode, the same ions for both laminates.

The Chromalynx software showed the several deconvoluted ions and their retention times. The different peaks corresponding to these ions were highlighted in the chromatograms. Figure 1 shows these several peaks in the chromatograms for laminate 3 compared to their substrate of cardboard for both ESI (+) and ESI (-) modes.

Table 1 shows the measured exact mass of the ions found (Da), their retention times, their proposed molecular formulas and their theoretical mass (Da),iFit (%) and the identified compounds

Figure 2 shows an example of the MS^E fragment ion spectrum for the precursor ion 282.2804 (9-Octadecenamide, (9Z)), and includes the fragment ion structure proposed by the MassFragment software.

For the second compound detected (Table 1), the candidates with the formula C13H29N3O3 were discarded due to the differences between the fragmentation spectra and the unknown compound. The molecular formula selected was C16H31NO. For this formula, one compound had similar fragmentation spectra to the unknown compound,

although this could not be confirmed because of the lack of a standard. The candidate for this compound was 2-Pyrrolidinone, 1-dodecyl- (CAS 2687-96-9). For the seventh compound, the candidate proposed with a large number of references and similar fragmentation was heptaethylene glycol (CAS 5617-32-3), but it was confirmed that the unknown compound did not correspond to this compound.

The identified migrated compounds found in the HM2 adhesive were four amides (Tetradecanamide, 9,12-Octadecadienamide, (9Z,12Z), Hexadecanamide and 9-Octadecenamide, (9Z) known as oleamide). According to the bibliography, these are slipping and antiblocking additives used in polyolefin films to reduce friction resistance [24-29]. The compound identified by ESI (-), 3,5-di-tert-butyl-4-hydroxybenzaldehyde, could derive from the degradation of Irganox 1010, which is commonly used as an antioxidant in polyolefin adhesives.

3.2. Determination of initial concentration.

The initial concentration and migrant quantitative test were only carried out with the HM2 adhesive since no migrant compounds were detected in the HM1 adhesive.

Table 2 shows the analytical parameters for UPLC-MS/QTOF. Good results were obtained in terms of linearity, limits of detection (LOD) and reproducibility. The LOD values were between 0.004 $\mu g/dm^2$ (9-Octadecenamide, (9Z)) and 0.23 $\mu g/dm^2$ (Hexadecanamide). The RSD values were below 6.32 %.

The values of initial concentrations are also shown in Table 2. The most abundant compound was 9-Octadecenamide (9Z) with a concentration below 7000 $\mu g/dm^2$ of laminate.

3.3. Determination of migrant concentration.

The number of extractions of the compounds that migrated to Tenax ® was optimized. It was found that two extractions were sufficient to obtain recoveries above 90%.

The migration values for both laminates manufacture with HM2 are shown in Table 2. Slightly higher values were found in laminate 4 than in laminate 3 for most of the

compounds. Laminate 4 was manufactured with cardboard as the substrate with the same grammage and thickness as the substrate used for laminate 3, but the former was covered by polypropylene.

In the case of volatile compounds, the diffusion through the pores of the paper is produced in the air entrapped between them, so that the diffusion is fast. However, for nonvolatile compounds, diffusion involves dissolution of particles in the pulp and in the case of polypropylene coating in the polymer, therefore the diffusion is lower.

Lower values of migration would be expected for laminate 4 than for laminate 3 because the presence of a PP layer on the cardboard reduces migration processes by limiting diffusion [7, 9]. However, the opposite occurred.

This could be explained by the fact that the migration depends on the partition coefficient that is the ratio of the migrant concentration at equilibrium between the substrate and the adhesive and on the diffusion coefficient of the compound in both surfaces [7, 8, 30, 31]. As mentioned, the diffusion coefficients for volatile compounds are reduced in the substrate by the PP layer [7, 9] [32]. However, the partition coefficients could be increased by the PP layer, promoting the migration of compounds to the substrate.

The partition coefficient depends on the Hildebrand solubility parameter (δ), a numerical value that indicates the relative solvency behavior of a specific compound. The solubility of two materials is only possible when their intermolecular attractive forces are similar, and therefore similar δ values are required for good solubility [30, 33, 34]. The solubility value of substrate PP is 16.5 $MPa^{1/2}$ according to the bibliography [35, 36] and the solubility of the amides is >25 $MPa^{1/2}$ [35]. Therefore, they would not have a tendency to migrate to the ppCB substrate.

The solubility of the APAO adhesive was not known, but it is a polymer made by polymerizing an alpha-olefin proving a structure similar to polypropylene. Therefore, its solubility will be very similar to this. The migrant compounds, which have the tendency to reach equilibrium, are distributed uniformly in both the adhesive and the substrate. For this reason, the migrants would increase in the laminate 4 made of paper coated with PP as substrate.

In order to study the possible human risk, the legislation of plastics [5, 6] was examined to see if the compounds were specified in the lists of authorized substances. Only the 9-Octadecenamide (9Z) appeared in these lists without specific migration limits (SML).

For the rest of the newly identified compounds, the estimated daily intake (EDI) established by the FDA (Food and Drug Administration of United States) [37] were calculated using the following equation:

$$EDI\left(\frac{mg}{personxday}\right) = migration\ \left(\frac{mg}{Kg}\right) x3Kg(food\ intake\ per\ person\ and\ day)xCF \quad [1]$$

where CF is the fraction of the daily diet expected to be in contact with a specific packaging material (for adhesives this is 0.14).

In order to check the possible human risk, these migrant values (EDI) were compared with the maximum values recommended for human exposure (mg per person per day) established by Cramer for each toxicity class. The values of daily intake for class I, II and III are 1.8, 0.54 and 0.09 mg per person per day, respectively [38]. The amides come within class I according to Cramer while 3,5-di-tert-butyl-4-hydroxybenzaldehyde belongs to class II.

To calculate the EDI values, the values of migration were first converted into mg of compound per kg of food (assuming a cube with a surface area of 6dm^2 in contact with 1 Kg of food). None of the migration values exceeded the recommended Cramer exposure values.

Conclusion

The non volatile migrants from two hot melt adhesives used in food packaging materials have been identified and quantified. The study has been carried out using UPLC-MS/QTOF. The technique has been shown as a powerful technique for the elucidation of unknown compounds based on the measurement of exact and accurate mass for both molecular ions and their fragments by means of a collision cell and a TOF analyzer. Therefore, using the exact mass and additional exact fragments with the structural elucidation tools, most of the migrants have been identified. No migrant compound was found in the HM1 adhesive, while seven compounds were identified as migrants in the

HM2 adhesive. These included several amides and one compound of class two toxicity. None of the migration values exceeded the recommended Cramer exposure values.

Acknowledgements

P. Vera acknowledges a grant from the Gobierno de Aragón (Spain). The authors thank the suppliers of the market samples provided for this work and Grupo T-10, Grupo Consolidado de Investigación recognized by the Gobierno de Aragón (Spain), for financing the research.

References

1. Edward M. Petrie. 1st ed. 2000 Chapter 9, p. 319-341: McGraw Hill handbooks.
2. J.S. Félix, F. Isella, O. Bosetti, and C . Nerín. Anal. Bioanal. Chem., 2011. 403: p. 2869–2882.
3. R. J. Ashley, M. A. Cochran, and K. W. Allen. Int. J. Adhesion and Adhesives 1995. 15 p. 101-108.
4. Regulation (EC) Nº 1935/2004 of the European Parliament and the Council of 27 October 2004 on materials and articles intended to come into contact with food and repealing Directives 80/590/EEC and 89/109/EEC.
5. Commission regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and article intended to come into contact with food.
6. Real Decreto 847/2011, de 17 de junio, por el que se establece la lista positiva de sustancias permitidas para la fabricación de materiales poliméricos destinados a entrar en contacto con los alimentos.
7. P. Vera, M. Aznar, P. Mercea, and C. Nerin. J. Mater. Chem., 2011. 21(2): p. 420-431.
8. E. Canellas, M. Aznar, C. Nerin, and P. Mercea. J. Mat. Chem., 2010. 20(24): p. 5100-5109.
9. M. Aznar, P. Vera, E. Canellas, C. Nerin, P. Mercea, and A. Stormer. J. Mater. Chem., 2011. 21(12): p. 4358-4370.
10. Paula Vera, Blanca Uliaque, Elena Canellas, Ana Escudero, and Cristina Nerin. Anal. Chim. Acta, 2012. 745C: p. 53-63.
11. E. Canellas, P. Vera, C. Domeno, A. P. Alfaro, and C. Nerin. J. Chromatogr. A, 2012. 1235: p. 141-148.

12. C. Nerin, E. Canellas, M. Aznar, and P. Silcock. Food Addit. Contam. Part A-Chem, 2009. 26(12): p. 1592-1601.

13. M. Aznar, E. Canellas, and C. Nerin. J. Chromatogr. A, 2009. 1216(27): p. 5176-5181.

14. B. Athenstadt, M. Funfrocken, and T. C. Schmidt. Rapid Commun. Mass Spectrom., 2012. 26(16): p. 1810-1816.

15. R. Sendon, A. Sanches-Silva, J. Bustos, P. Martin, N. Martinez, and M. E. Cirugeda. J. Sep. Sci., 2012. 35(10-11): p. 1319-1326.

16. J. Zweigenbaum. Agro Food Ind. Hi-Tech, 2011. 22(5): p. 4-6.

17. M. J. Martinez Bueno, Maria M. Ulaszewska, M. J. Gomez, M. D. Hernando, and A. R. Fernandez-Alba. J. Chromatogr. A, 2012. 1256: p. 80-8.

18. I. Bobeldijk, J. P. C. Vissers, G. Kearney, H. Major, and J. A. van Leerdam. J. Chromatogr. A, 2001. 929(1-2): p. 63-74.

19. Y. Pico, M. La Farre, N. Tokman, and D. Barcelo. J. Chromatogr. A, 2008. 1203(1): p. 36-46.

20. F. Hernandez, J. V. Sancho, M. Ibanez, and S. Grimalt. Trac-Trends Anal. Chem., 2008. 27(10): p. 862-872.

21. Y. Pico and D. Barcelo. Trac-Trends Anal. Chem., 2008. 27(10): p. 821-835.

22. Y. Pico, M. la Farre, C. Soler, and D. Barcelo. J. Chromatogr. A, 2007. 1176(1-2): p. 123-134.

23. UNE-EN-14338, AENOR. Papel y cartón para contacto alimentario. Condiciones para la determinación de la migración desde el papel y cartón utilizando óxido de polifenileno modificado (MPPO) como simulante, 2004.

24. A. Maltby. The effects of polyolefin formulation and processing variables on slip agent performance (I). 1999, Tappi Press: Atlanta. p. 349-358.

25. B. L. Chen. Surface properties of corona-treated polyethylene films containing N-(2-hydroxyethyl) erucamide as slip agent for enhanced adhesion of water-based ink. 1997, Tappi Press: Atlanta. p. 427-438.

26. C. L. Swanson, D. A. Burg, and R. Kleiman. J. Appl. Polym. Sci., 1993. 49(9): p. 1619-1624.

27. A. J. Maltby and M. Read, in Tappi Polymers, Laminations & Coatings Conference, Vols 1 and 2. 1999, Tappi Press: Atlanta. p. 1079-1087.

28. A. R. Zahedi, A. Ranji, and S. Asiaban. J. Plast. Film Sheeting, 2006. 22(3): p. 163-176.

29. L. Walp and H. Tomlinson. J. Plast. Film Sheeting, 2004. 20(4): p. 275-287.

30. E. A. Tehrany and S. Desobry. Food Addit. Contam., 2004. 21(12): p. 1186-1202.

31. P. Dole, A. E. Feigenbaum, C. De la Cruz, S. Pastorelli, P. Paseiro, T. Hankemeier, Y. Voulzatis, S. Aucejo, P. Saillard, and C. Papaspyrides. Food Addit. Contam., 2006. 23(2): p. 202-211.

32. G. W. Horgan. Geoderma, 1999. 88(1-2): p. 55-71.

33. John B. Durkee. Met. Finish., 2004. 102(1): p. 39-42.

34. John B. Durkee. Met. Finish., 2004. 102(4): p. 42-50.

35. AIC. Vol. three. 1984, volume three: The American Institute for Conservation.

36. Allan F.M. Barton. 2nd ed. 1991: CRC PRESS. 69-149.

37. FDA, 1995. Food and Drug Administration. Recommendations for Chemistry Data for Indirect Food Additive Petitions.

38. Threshold of toxicological concern (TTC). ILSI Europe concise monograph series, 2005.

Table 1: Number of the peak in the chromatogram, retention time (RT), ion found, measured mass, formula of the compounds proposed, theoretical mass, Δm(Da), iFit(%),collision energy optimized for function 2 and the identified compound by UPLC–MS/QTOF.

Nº	RT	Ion	Measure mass (Da)	Formula proposed	Theoretical mass (Da)	Δm (Da)	iFit(%)	Collision energy (eV)	Identified compounds
1	18.92	$[M+H]^+$	228.2325	C14H30NO	228.2307	-0.2	100	30-40	Tetradecanamide
2	19.27	$[M+Na]^+$	276.2303	C16H31NONa	276.2303	0.0	78.53	15-30	Ni
		$[M+H]^+$		C13H30N3O3	276.2288	1.6	15.91		
3	19.66	$[M+Na]^+$	302.2457	C18H33NONa	302.2460	-0.3	74.11	20	9,12-Octadecadienamide, (9Z,12Z)
		$[M+H]^+$		C18H32N3O3	302.2444	1.3	19.68		
4	20.08	$[M+H]^+$	256.2639	C16H34NO	256.2640	-0.1	100	30-40	Hexadecanamide
5	20.29	$[M+H]^+$	282.2804	C18H36NO	282.2797	0.7	100	15-30	9-Octadecenamide, (9Z)
6	16.15	$[M-H]^-$	233.1542	C15H21O2	233.1542	0.0	100	15-30	3,5-di-tert-butyl-4-hydroxybenzaldehyde
7	20.27	$[M-H]^-$	325.1849	C14H29O8	325.1862	-1.3	100	15-30	Ni

Ni: non identified compound

Table 2: Analytical parameters of the UPLC-MS/QTOF method, initial concentration (Cp_0) and migration results expressed as µg/dm^2 of laminate

Compounds	**Equation**	**R^2**	**Linear range (µg/dm^2)**	**LOD (µg/dm^2)**	**LOQ (µg/dm^2)**	**RSD (%)**	**Cpo µg/dm^2**	**Migration Laminate 3 µg/dm^2**	**Migration Laminate 4 µg/dm^2**
Tetradecanamide	Y=3.7539x+0.0667	0.9989	0.15-22.9	0.05	0.15	4.21	346±21	6.67±0.07	8.7±1.1
9,12-Octadecadienamide, (9Z,12Z)*							460±110	28.5±1.4	37±3.7
Hexadecanamide	Y=3.5933x+0.1099	0.9999	0.79-23.1	0.23	0.79	3.14	1670±240	29.7±2.3	40±4.2
9-Octadecenamide, (9Z)	Y=3.7162x+0.0689	0.9985	0.01-21.8	0.004	0.01	6.32	7350±910	243±1.9	260±4.1
3,5-di-tert-butyl-4-hydroxybenzaldehyde	Y=2.1922x-0.0101	0.9994	0.27-5.55	0.08	0.27	1.87	14.0±2.9	0.60±0.1	0.50±0.1

*compound quantified with 9-Octadecenamide, (9Z) as standard

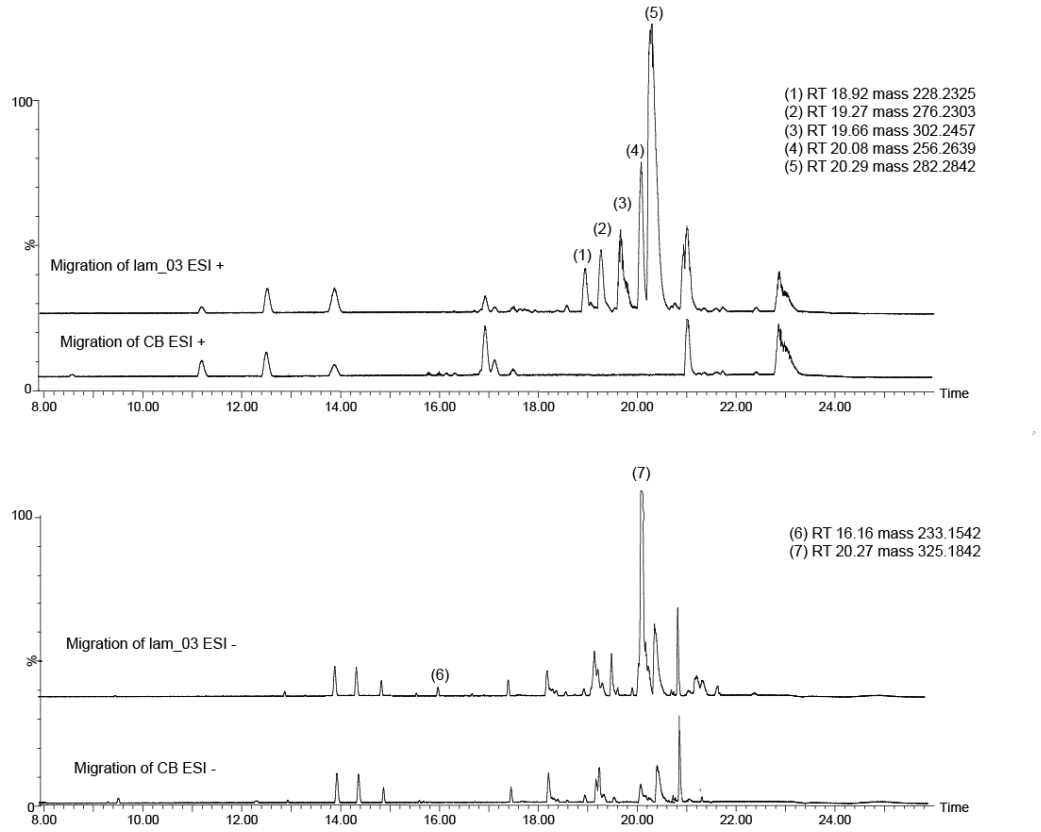

Figure 1: Chromatograms of migration of laminate 3 made with HM2 adhesive and CB analyzed by UPLC-MS/QTOF with ESI + (on the top) and by ESI – (on the bottom).

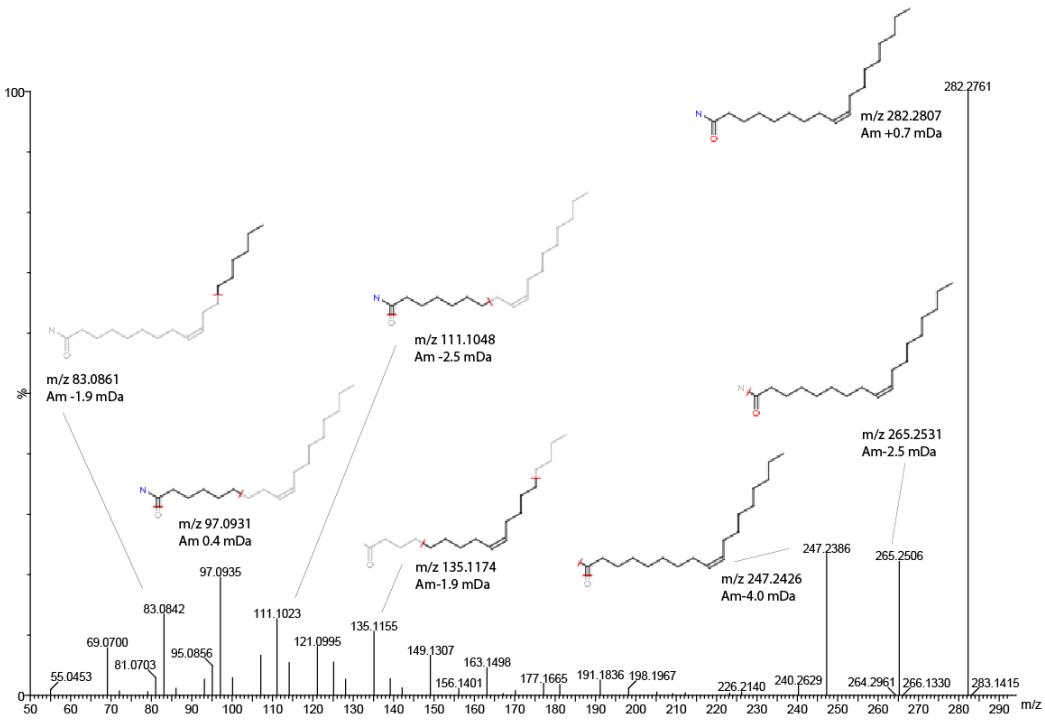

Figure 2: MS^E high energy fragment ion spectrum for the ion 282.2804 (9-Octadecenamide, (9Z)), with the proposed fragment ion structures taken from MassFragment Software.