



# Ultra-high performance liquid chromatography coupled to ion mobility quadrupole time-of-flight mass spectrometry for the identification of non-volatile compounds migrating from 'natural' dishes



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## ABSTRACT

Although most new biomaterials for food industry applications are labelled '100% natural fabrication' and 'chemical-free', certain compounds may migrate from those materials to the food, compromising the organoleptic characteristics and safety of the product. In this work, the degree of compound migration from dishes made with four different biomaterials: bamboo, palm leaf, wood and wheat pulp was investigated. Migration tests were carried out using three food simulants, 10% ethanol (simulant A), 3% acetic acid (simulant B), and 95% ethanol (simulant D2). Unequivocal identification of non-intentionally added substances (NIAS) is challenging even when using high-resolution mass spectrometry techniques however, a total of 25 different non-volatile compounds from the migration tests were identified and quantified using Ultra-high performance liquid chromatography coupled to ion mobility quadrupole time-of-flight mass spectrometry (UPLC-IMS-MS). In the bamboo samples three oligomers, cyclic diethylene glycol adipate, 3,6,9,16,19,22-hexaoxabicyclo[22.3.1]-octacosane-1(28),24,26-triene-2,10,15,23-tetrone and 1,4,7,14,17,20-hexaoxacyclohexacosane-8,13,21,26-tetrone exceeded the specified limits of migration.

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## 1. Introduction

Given the excessive usage of plastics, particularly single-use plastics, governments and society as a whole are taking action against the environmental impact these materials [1,2]. In particular, petroleum-based plastic pollution is becoming of increasing global concern [3]. The search for alternatives to plastics has seen a drive towards dishes developed from materials termed as natural (biomaterials) and biodegradable substances made from vegetable resources including bamboo, palm leaf, wood and wheat pulp [4].

Some components, such as fibres of vegetable origin, have relevance in the development of new materials for contact with food, as is the case of single-use dishes made with biomaterials [5]. Most

of these new biomaterials have achieved a great interest in the fast food and catering sector which is now the primary consumer of tableware based on these components [6]. These new materials have very interesting characteristics such as their ability to be used in ovens, microwaves and freezers, combined with the fact that they are biodegradable. Studies carried out on wood-based materials show interesting properties related to resistance to oil, fats, aroma, and oxygen due to the presence of hemicellulose, an abundant component in this type of material [7]. In a similar fashion, bamboo is considered to be an attractive material from which to produce materials and packaging destined to be in contact with food due to its low price, easy acquisition, and ability to degrade in the environment [6].

Although in the food industry most of these new biomaterials are marketed under '100% natural' and 'chemical-free manufacture' labels, it is possible that non-intentionally added substances (NIAS) and intentionally added substances (IAS) are present in the materials [8,9]. IAS are generally used to improve the physical-chemical properties of materials, such as their plasticity or

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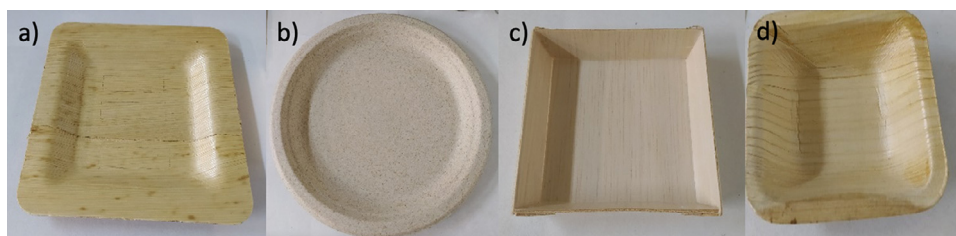


Fig. 1. Dishes under study, made from a) bamboo, b) wheat pulp, c) wood and d) palm leaf.

moldability [6]. The presence of NIAS may originate from impurities in the raw material itself, degradation compounds that occur during manufacturing process or substances resulting from the interaction with reagents [10]. Unfortunately, NIAS and IAS can migrate from the biomaterial to the food they are used to package [3,6]. The identification of non-volatile NIAS is a highly challenging task [8,9] to which sophisticated techniques have been applied. Such techniques include, ultra-high performance liquid chromatography coupled to time-of-flight mass spectrometry<sup>Elevated Energy</sup> (UPLC-QTOF-MS<sup>E</sup>) [11–13], liquid chromatography coupled to quadrupole-orbitrap mass spectrometry (LC-Q-Orbitrap-MS) [14] and ion mobility quadrupole time-of-flight mass spectrometry coupled to ultra-high pressure liquid chromatography (UPLC-IMS-MS) [15–19].

Travelling wave ion mobility separation (TWIMS) is a relatively new gas-phase separation technique, which involves the separation of ionized molecules in a drift cell containing a buffer gas (normally nitrogen or helium) under the influence of a weak electric field [20]. The mobility of ions through the drift cell depends on their size, shape and charge, since more compact ions tend to move faster than those with a larger rotational cross-section due to the fact that they interact less with the buffer gas [21–23]. In addition to being able to separate ions by their drift-time (the time taken to traverse the drift cell), ion mobility offers other benefits. For example, since ions can be aligned both in terms of retention-time and drift-times there are less interfering ions in the resulting low and high energy spectra which facilitates the spectral interpretation. Additionally, using a suitable ion-mobility calibration, collision cross section (CCS) values can be determined from the drift times. The ion mobility derived CCS value is related to the size and shape of a molecule, and can provide complementary structural information for analytes [20,22–24].

To the best of our knowledge, UPLC-IMS-MS has not been used for the analysis of 'natural' bio-dishes to ensure their safety. Therefore, the main objective of this research was to explore the applicability of UPLC-IMS-MS to determine whether non-volatile compounds, including NIAS, can migrate from a range of dishes made from natural materials. Migration tests were performed using liquid simulants on dishes made from the pulp of wheat, wood, palm leaf and bamboo that satisfy EU recommendations. The work explores the applicability of UPLC coupled to IMS for the screening, qualitative and quantitative analysis of a wide range of chemicals migrating from complex matrices.

## 2. Materials and methods

### 2.1. Reagents

Methanol (LC-MS, CAS 67–56–1) was purchased from Honeywell (Barcelona, Spain). Ethanol absolute (GC-MS, CAS 64–27–5) and acetonitrile (CAS 75–05–8) were obtained from PanReac, AppliChem (Germany). Acetic acid ( $\geq 99.7\%$ , CAS 64–19–7) and formic acid (CAS 64–18–6) were supplied by Sigma-Aldrich (Madrid, Spain). The Vion Test Mix and leucine enkephalin

(CAS 64,963–01–5) were supplied by Waters (Barcelona, Spain). Ultrapure water was obtained from a Wasserlab Ultramatic GR system (Barbatáin, Spain). The following standards were also purchased from Sigma-Aldrich (Madrid, Spain): (+)-lactose (CAS 63–42–3); 1,4-cyclohexanedicarboxylic acid (CAS 1076–97–7); 1,5-diphenylcarbazide (CAS 140–22–7); 3,5-di-tert-butyl-4-hydroxyphenyl propionic acid (CAS 20,170–32–5); N,N-dimethylhexadecylamine (CAS 112–69–6); N,N-diethanololeamide (CAS 93–83–4); dioctyl terephthalate (CAS 6422–86–2); dinonyl phthalate (CAS 28,553–12–0); diphenyl-(2,4,6-trimethylbenzoyl) phosphine oxide (CAS 75,980–60–8); cyclic diethylene glycol adipate (CAS 6607–34–7); deoxycholic acid (CAS 83–44–3).

### 2.2. Samples

Three samples of each dishes made from bamboo, palm leaf, wood and wheat pulp were studied and photographs of the samples are shown in Fig. 1. All samples were acquired from a Spanish supplier, and currently, they are available on the market for food applications, mainly in catering services. The manufacturer's specifications indicate that some of them (bamboo, palm leaf and wheat pulp) can also be used in an oven or microwave and can be heated up to 170 °C.

### 2.3. Migration tests

Regulation (EU) No 10/2011 [25] and its fifteen amendments establish the use of three types of simulants for migration studies: A (10% (v/v) ethanol), B (3% (v/v) acetic acid) and D2 (95% (v/v) ethanol) which together can simulate most types of food. In accordance with this regulation, a 6 dm<sup>2</sup> of food contact material per 1 kg of food or food simulant were used for migration tests. For simulants A and B, the plate samples were cut into strips of 1 × 5 cm, placed in a 20 mL vial and 18 mL (18 g) of simulant was added. In the case of simulant D2, 1 × 4 cm strips were immersed in 18 mL (14 g) of simulant. Both samples and simulants were gravimetrically controlled. Blank samples (simulants) were prepared in each case and subjected to the same time and temperature conditions as the migration samples and all samples were prepared in triplicate.

Time and temperature conditions were established to carry out the appropriate migration tests for each simulant. In the case of simulants, A and B, the migration tests were carried out at 70 °C for 2 h and in the case of simulant D2, the tests were carried out at 40 °C for 30 min. The samples were then cooled and injected directly into the UPLC-IMS-MS.

### 2.4. UPLC-IMS-MS analysis

The Acquity<sup>TM</sup> UPLC chromatography system coupled to Vion<sup>®</sup> ion mobility-quadrupole/time of flight (IMS-QTOF) mass spectrometer together with an electrospray interface (ESI), from Waters (Manchester, UK) was used for the analysis of the migration extracts. The column, a CORTECS C18 UPLC column (2.1 × 100 mm,

1.6  $\mu\text{m}$  particle size, 90  $\text{\AA}$  pore size), was maintained at a temperature of 35  $^{\circ}\text{C}$ . Phase (A), 0.1% (v/v) formic acid in water, and phase (B), 0.1% (v/v) formic acid in methanol, were used as mobile phase in gradient mode. The elution conditions were as following: Initially 95% A and 5% B; from 7 to 11 min 0% A and 100% B; at 11.10 min 95% A and 5% B until 13 min. The mobile phase flow rate was 0.3 mL/min and the injection volume was 5  $\mu\text{L}$ . The ESI interface was used in positive mode (ESI+), and data were acquired in 'sensitivity mode' with a capillary voltage of 1 kV and a sampling cone voltage of 30 V. The source temperature was 120  $^{\circ}\text{C}$  and the desolvation temperature was 500  $^{\circ}\text{C}$ . The gas flow rate was 800 L/h. The system was calibrated a lock mass solution of 100 pg/ $\mu\text{L}$  leucine enkephalin solution in 50:50 water/acetonitrile (v/v) with 0.1% formic acid was used for real-time mass correction. The Vion test mix (nine component mixture) was used as a comprehensive reference standard: the name,  $m/z$ , retention time and CCS values of the nine compounds have been described in a previous study [16]. Data were acquired over a  $m/z$  range of 50 to 1000. The data were acquired using data independent analysis (DIA) in high definition MS<sup>E</sup> mode (HDMS<sup>E</sup>) with scan time of 0.200 s and collision energy ramp of 6–40 eV. Analyser mode was set to sensitivity. This method of data acquisition allows the simultaneous collection of data at low and high collision energies [26,27].

## 2.5. Qualitative analysis

Qualitative analysis of non-volatile compounds was performed using the UNIFI scientific library (v1.9.4) with an embedded library of food contact chemicals created by GUIA group (University of Zaragoza, Spain) [27]. It should be highlighted that this library has limited number of compounds what is connected with availability of standards in laboratory. Acquisition of compounds in library was performed using the same chromatographic conditions as the analyses performed here. The spectral library was created to facilitate the qualitative analysis in the field of the analytical chemistry of food packaging. When a candidate substance within the sample matches any target compound in the analysis method, the compound was automatically identified, associating each peak of the chromatogram with the most probable compound from UNIFI spectral library.

Identification using external online library was based on UNIFI's Elucidation toolset which include automated elemental composition and database searching through ChemSpider. The UNIFI software can separate recognized compounds (known) and unknown masses (unknown) that have not been assigned using the in-house library. To determine the unknown compounds to submit to the identification process a binary comparison of the candidate masses in the sample and a reference blank was performed. Compounds that were unique to the sample or had a higher response in the sample were then identified using the ChemSpider database using the discovery tools [28]. Limitations in qualitative analysis based on external database is connected with possible presence of uncommon compound in sample that may not be present in database.

It should be highlighted that the applied technique combined at the same time parameters such as retention time, drift time, accurate mass of precursor and product ions resulted in accurate peak identification.

## 2.6. Quantitative analysis

Quantitative analysis was performed using an external standard calibration. Solutions of standards were prepared using each simulant (A, B, D2) in over a range of concentrations (see results Section 2.2. Qualitative analysis) and injected into UPLC-IMS-MS

using the same chromatographic conditions as the samples. Detected compounds were quantified using the corresponding standards. In absence of corresponding standards in the laboratory, a similar compound was used for semi-quantification. In such cases the applied standard has been indicated in footnotes of Table 3. The results are expressed as mean concentration  $\pm$  standard deviation.

The following analytical parameters of the UPLC-IMS-MS method were determined by the signal-to-noise method; linearity, limits of detection (LOD) and limits of quantification (LOQ). Linearity was tested in the range of the calibration curve using the correlation coefficient ( $r$ ).

## 2.7. Risk assessment

The migration tests were used to determine specific levels of migration. The amount of a specific, identifiable substance that is transferred to food can be established from the data, and a risk assessment of the material can be performed. If the substances found are not present in the positive list of Regulation (EU) No 10/2011, no observed adverse effect level (NOAEL) is applied. However, for analytes to which a toxicity value can be attributed, the threshold of toxicological concern (TTC) approach and Cramer classification, recommended by the European food safety authority (EFSA) [29], is applied. Cramer separates the toxicity of molecules into three toxicity classes (I–III) based on their chemical structure. Molecules identified during migration assays were assigned Cramer classes using Toxtree® (v3.1.0.1851), a flexible open-source software application predicting toxic effect of chemicals by applying decision tree approaches.

Class I corresponds to the less harmful compounds, characterized by simple chemical structures, which are assigned a maximum estimated daily intake (EDI) of 1.80 mg/person/day. Class II corresponds to the compounds with medium toxicity, having structures that are less innocuous than those from Class I, and have a maximum EDI of 0.54 mg/person/day. Finally, class III corresponds to the highly toxic compounds with a maximum EDI of 0.09 mg/person/day. Therefore, for European people eating 1 kg food per day, the specific migration limit (SML) based on the TTC approach will be as following:  $\text{SML}_{\text{Class I}} = 1.80 \text{ mg/kg of food/food simulant}$ ;  $\text{SML}_{\text{Class II}} = 0.54 \text{ mg/kg of food/food simulant}$ ;  $\text{SML}_{\text{Class III}} = 0.09 \text{ mg/kg of food/food simulant}$  [30,31].

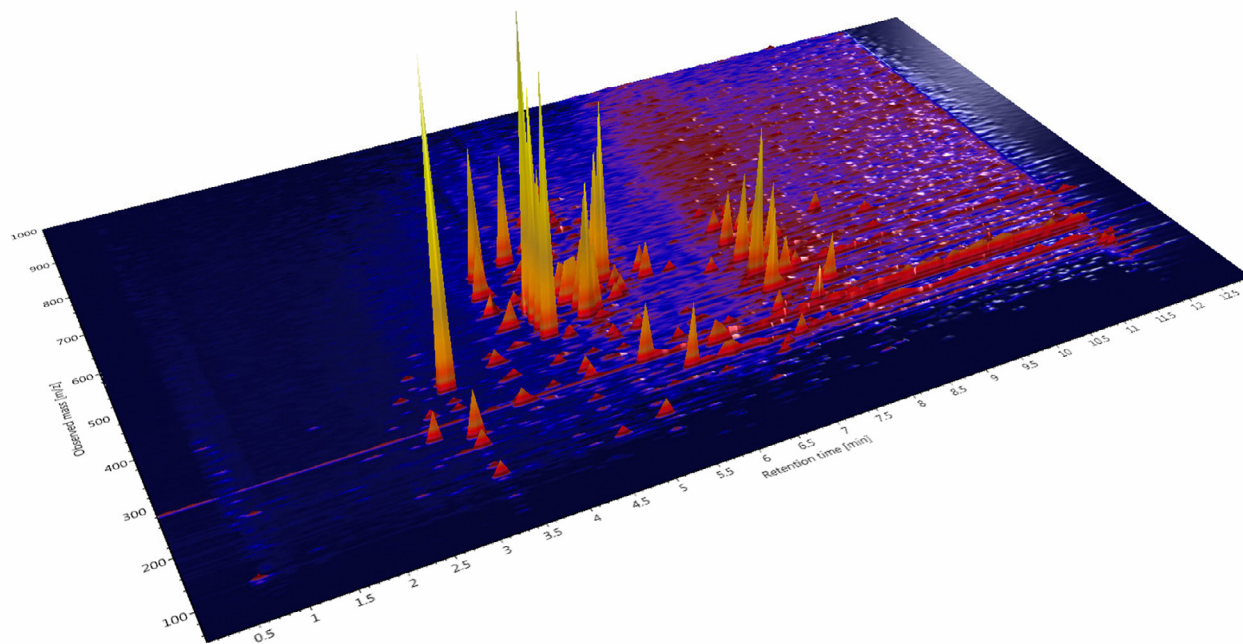
# 3. Results and discussion

## 3.1. Qualitative analysis

The use of ion mobility technology enables the effects of co-elution of compounds to be minimised, helps to avoid misidentification of isomers and enables fragment ions to be aligned to their precursors. Without ion-mobility, phenomena such as coelution often hinder, and sometimes even prevent, the separation and proper identification of analytes. In this case, unprecedented peak identification was possible due to application of CCS values and reduce spectral interferences due to drift time alignment.

The data from which the compounds are identified can be represented by 3D chromatogram shown in Fig. 2.

Data-independent acquisition was applied to record the fragmentation information useful for the structural elucidation of migrants. Precursors and fragmentation ions are aligned for both retention time and drift time for ion mobility in HDMS<sup>E</sup>. Thus, the high-energy spectra do not contain ions with different drift times from the co-eluting compounds or the background. As a result, qualitative analysis is easier and more accurate. Fig. 3 shows the comparison of low- and high-energy spectra with and without drift time alignment for 1,4,7,14,17,20-hexaoxacyclohexacosane-



**Fig. 2.** 3D neat chromatogram of migration from bamboo sample into 95% ethanol acquired by UPLC-IMS-MS where (x) is the observed  $m/z$  fragment, (y) the retention time and (z) the intensity of the fragment.

8,13,21,26-tetrone (455.1883  $m/z$ , retention time 4.9456 min) that has migrated into simulant D2 from the bamboo plate samples. It can be clearly seen that spectra using drift-time alignment are cleaner and displays peak ions associated only for the selected analyte.

In addition, Fig. 4 shows the comparison of scatter-plots for the low- and high-energy data with and without drift time alignment for 1,4,7,14,17,20-hexaoxacyclohexacosane-8,13,21,26-tetrone migrating into simulant D2 from bamboo plates.

In Fig. 4 the drift time, in milliseconds is on the y-axis and is plotted against  $m/z$  on the x-axis. The low-energy scatter plots show regions of interest, indicating the position of isotope clusters for the selected analyte. In turn, identified fragments are plotted as dots on the high-energy scatter plots. It can be clearly seen that the number of ions aligned in drift time as well as retention time has been significantly reduced. This highlights the advantage of working with IMS technology, leading to better identification of compounds in the non-target screening of migrants from complex samples such as 'natural dishes'.

Table 1 shows the results obtained of the identification of migrating non-volatile compounds by UPLC-IMS-MS from dishes made from four different biomaterials (bamboo, palm leaf, wood and wheat pulp). Table 1 contains the list of all compounds detected in the three food simulants without specifying of each of the simulants. The migration of each compound into specific food simulant 10% ethanol, 3% acetic acid and 95% ethanol is presented as part of the results for the quantitative analysis (Table 3).

The inclusion of CCS as an identification parameter in this study, aids the identification of compounds, especially those that elute closely to each other (see Table 1). As an example, heptadecanoic acid, diphenyl-(2,4,6-trimethylbenzoyl) phosphine oxide, deoxycholic acid (compounds 23, 24 and 25 respectively in Table 1) are present in the same samples with very close retention times but different CCS values. However, they have different  $m/z$  values therefore CCS is not the only differentiator in this case.

The results obtained in Table 1 show the compound diphenyl-(2,4,6-trimethylbenzoyl) phosphine oxide (TPO) migrates from all

four of the biomaterials studied. This compound is likely to be present in the migration extracts since it is used by the packaging industry as an ultraviolet curing agent for resins and polyesters. TPO is also used as a coating whitener, a component of printing inks and wood coatings [32]. TPO may also be present due to cross-contamination occurring in the dish manufacturing industry itself, since it is possible that the production of other types of packaging from other materials took place in the same production area. Moreover, its addition may have been intentional, as it may have been used as a bleaching agent on the biomaterials to achieve a more attractive color for the consumer [32].

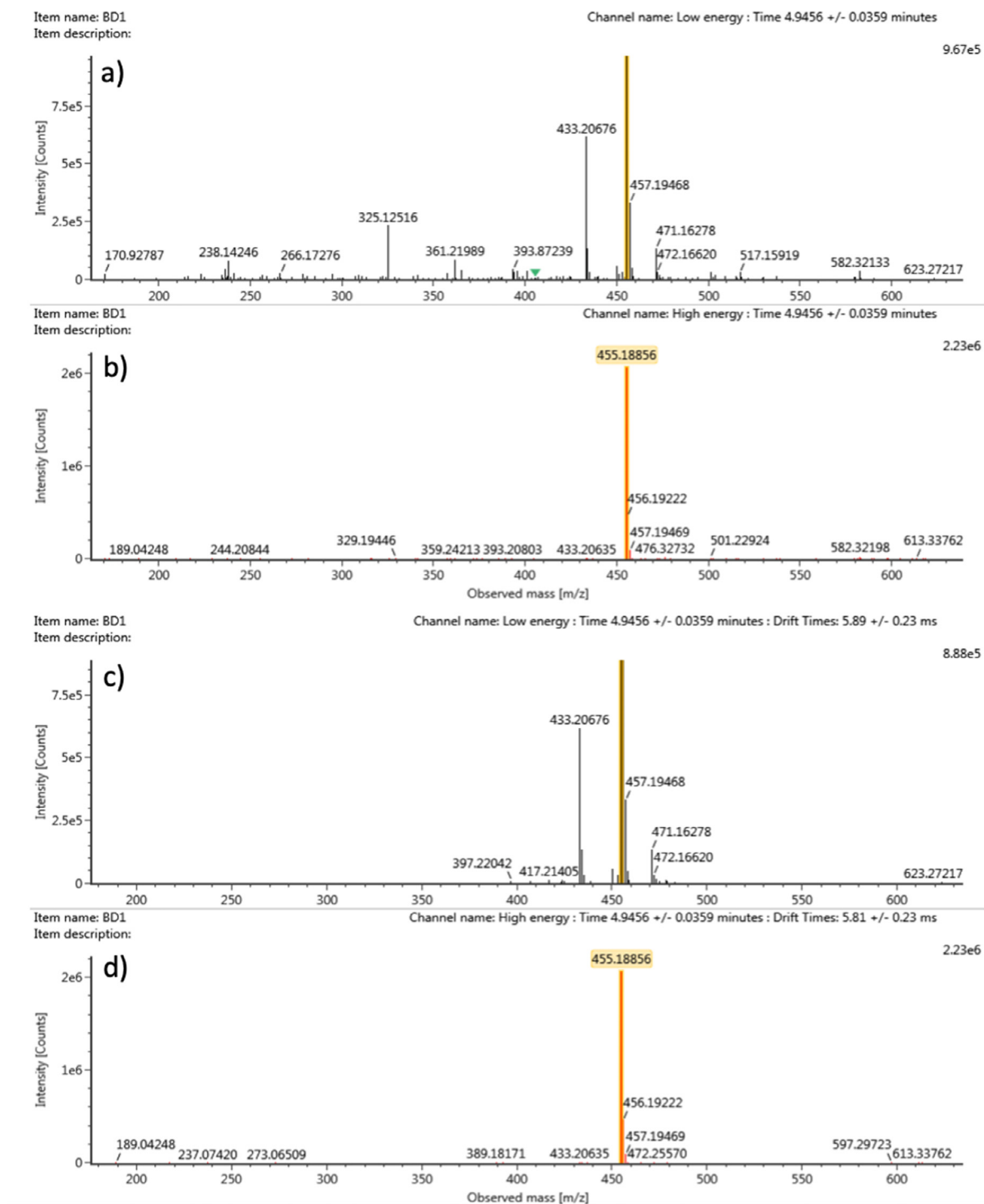
It should be highlighted that some of the identified compounds are included in Regulation (EU) No 10/2011 [25] and therefore have assigned SML that must not be exceeded in the migration from the biomaterial to the food. The SMLs apply to the following compounds: D(+)-glucose, 1,4-cyclohexanedicarboxylic acid, 2,2'-dihydroxy-4-methoxy benzophenone, bis-(2-ethylhexyl) phthalate, palmitoleic acid and oleic acid.

The presence of the palmitoleic and oleic acids (fatty acids) may be due to the natural origin of the analysed materials, since they form part of the plant matter. On the other hand, both substances are also used in the manufacturing process of food contact materials (FCMs). In the case of oleic acid, there are references that classify it as a surfactant [32] and a plasticizer in the production of biodegradable materials [34].

Another compound that may originate naturally from plant matter is the monosaccharide D(+)-glucose. However, it can be also intentionally added during the manufacture of FCMs [32].

In respect of the rest of the compounds of interest, it should be noted that 2,2'-dihydroxy-4-methoxy benzophenone can be used either as an UV absorber or as photo initiator, coating or adhesive [35] and bis-(2-ethylhexyl) phthalate as a plasticizer and technical support agent in plastic FCMs. This phthalate is of additional importance because it is directly related to negative effects on reproduction, reducing the level of foetal testosterone [36].

Fig. 5 shows three compounds assigned to candidate masses from the bamboo samples, as a result of the elucidation process



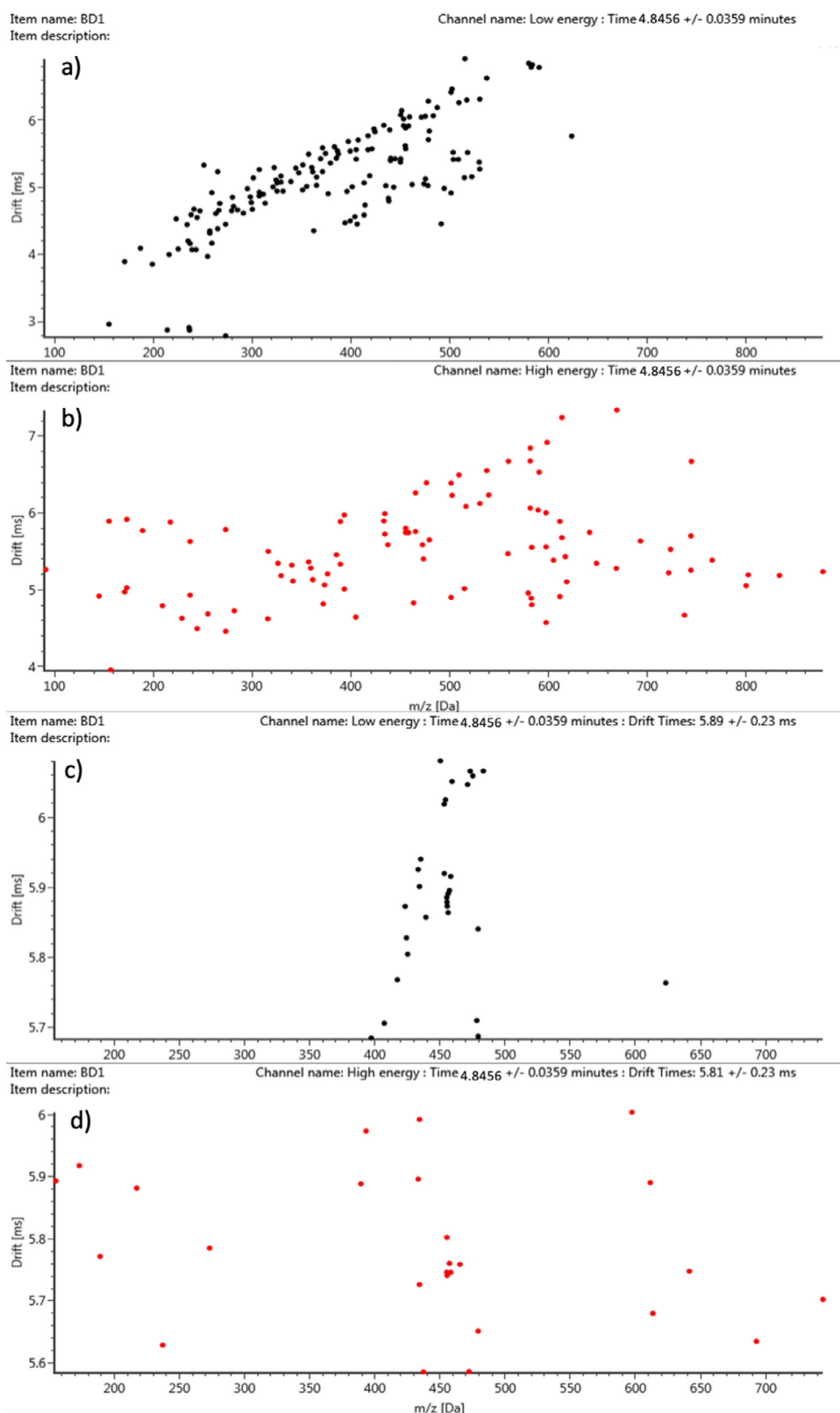
**Fig. 3.** Comparison of HDMS<sup>E</sup> spectra of a) low energy and b) high energy without drift time alignment; c) low energy and d) high energy with drift time alignment for 1,4,7,14,17,20-hexaoxacyclohexacosane-8,13,21,26-tetrone in D2 simulant migrating from bamboo plates.

within UNIFI library which were present in all three simulants. Their masses and retention times were not found in the system's spectral library, therefore, identification through external online libraries was used. The software established a list of possible related compounds and those with a higher affinity were assigned resulting in the identification of 3,6,9,16,19,22-hexaoxabicyclo[22.3.1]-octacos-1(28),24,26-triene-2,10,15,23-tetrone, 1,4,7,14,17,20-hexaoxacyclohexacosane-8,13,21,26-tetrone and 1,4,7-trioxacyclotridecane-8,13-dione (cyclic diethylene glycol adipate). The latter two compounds are oligomers related to the

manufacture of polyurethane adhesives and plastic containers [37]. Their identification was also confirmed by their CSS values. Moreover, a standard of cyclic diethylene glycol adipate was acquired and injected to confirm the identification and enable quantification to be performed.

### 3.2. Quantitative analysis

Table 2 shows the analytical parameters determined from data acquired using the UPLC-IMS-MS, and Table 3 shows the results



**Fig. 4.** Scatter plots showing drift time, in milliseconds, on the y-axis against  $m/z$  on the x-axis. a) low energy and b) high energy without drift time alignment; c) low energy and d) high energy with drift time alignment for 1,4,7,14,17,20-hexaoxacyclohexacosane-8,13,21,26-tetrone migrating from bamboo plates into simulant D2.

**Table 1**

Qualitative analysis of migrating non-volatile compounds using UPLC-IMS-MS. The '•' symbol indicates the compound has been detected in that sample. Blank cells in table mean no detected compounds. Key: B – bamboo; P – palm leaf; W – wood; WP – wheat pulp.

N°	RT (min)	Molecular formula	Compound	CAS	Experimental <i>m/z</i>	Adduct	CCS (Å <sup>2</sup> )	Samples				Applications <sup>a</sup>
								B	P	W	WP	
1	0.67	C <sub>12</sub> H <sub>22</sub> O <sub>11</sub>	lactose	63–42–3	365.1045	[M+Na] <sup>+</sup>	171.3	•	•			FCM
2	0.69	C <sub>6</sub> H <sub>12</sub> O <sub>6</sub>	D(+)-glucose	50–99–7	203.0522	[M+Na] <sup>+</sup>	143.5	•				FCM
3	0.89	C <sub>16</sub> H <sub>18</sub> O <sub>2</sub>	bisphenol B	77–40–7	265.1188	[M+Na] <sup>+</sup>	169.5	•				Bisphenols
4	3.00	C <sub>8</sub> H <sub>12</sub> O <sub>4</sub>	1,4-cyclohexanedicarboxylic acid	1076–97–7	173.0806	[M + H] <sup>+</sup>	131.2	•				IFCA
5	3.37	C <sub>10</sub> H <sub>16</sub> O <sub>5</sub>	1,4,7-trioxacyclotridecane-8,13-dione	6607–34–7	217.1068	[M + H] <sup>+</sup>	144.6	•				Formation plastic packaging/adhesive
6	4.66	C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O	1,5-diphenylcarbazine	140–22–7	265.1069	[M+Na] <sup>+</sup>	165.7	•				–
7	4.78	C <sub>14</sub> H <sub>12</sub> O <sub>4</sub>	2,2'-dihydroxy-4-methoxy benzophenone	131–53–3	245.0806	[M + H] <sup>+</sup>	149.4	•				UV absorber
8	4.85	C <sub>15</sub> H <sub>10</sub> O <sub>6</sub>	kaempferol	520–18–3	287.0544	[M + H] <sup>+</sup>	158.4		•			Phenolics
9	4.94	C <sub>20</sub> H <sub>32</sub> O <sub>10</sub>	1,4,7,14,17,20-hexaoxa cyclohexacosane-8,13,21,26-tetrone	314,254–68–7	455.1883	[M+Na] <sup>+</sup>	192.2	•				Component of adhesive
10	5.31	C <sub>22</sub> H <sub>28</sub> O <sub>10</sub>	3,6,9,16,19,22-hexaoxabicyclo[22.3.1]octacosane-1(28),24,26-triene-2,10,15,23-tetrone	1,394,013–66–1	453.1753	[M + H] <sup>+</sup>	196.5	•				Formation of plastic packaging/component of adhesive
11	5.42	C <sub>16</sub> H <sub>22</sub> O <sub>4</sub>	dibutyl phthalate	84–74–2	301.1405	[M+Na] <sup>+</sup>	183.6	•				Plasticizers
12	5.98	C <sub>22</sub> H <sub>28</sub> O <sub>10</sub>	1,6,13,18-tetraoxacyclotetrasane-7,12,19,24-tetraone	78,837–87–3	401.2167	[M + H] <sup>+</sup>	189.1	•				Reaction products between adipic acid and 1,4-butanediol
13	6.56	C <sub>17</sub> H <sub>26</sub> O <sub>3</sub>	3,5-di-tert-butyl-4-hydroxyphenyl propionic acid	20,170–32–5	301.1772	[M+Na] <sup>+</sup>	175.6	•				Degradation product of antioxidants
14	6.77	C <sub>18</sub> H <sub>39</sub> N	N,N-dimethylhexadecylamine	112–69–6	270.3315	[M + H] <sup>+</sup>	190.7			•	•	Emulsifier/surfactant/antistatic agent
15	7.78	C <sub>22</sub> H <sub>43</sub> NO <sub>3</sub>	N,N-diethanololeamide	93–83–4	392.3135	[M+Na] <sup>+</sup>	208.7	•				Emollient/antistatic agent
16	7.98	C <sub>55</sub> H <sub>104</sub> O <sub>6</sub>	2-stearoglycerol	2190–27–4	381.2969	[M+Na] <sup>+</sup>	202.7			•	•	Emollient/lubricant
17	8.08	C <sub>21</sub> H <sub>42</sub> O <sub>4</sub>	glyceryl monostearate	123–94–4	381.2979	[M+Na] <sup>+</sup>	203.8	•	•			Emollient/antistatic agent
18	8.09	C <sub>24</sub> H <sub>38</sub> O <sub>4</sub>	dioctyl terephthalate	6422–86–2	413.2665	[M+Na] <sup>+</sup>	216.4			•	•	Plasticizers
19	8.15	C <sub>24</sub> H <sub>38</sub> O <sub>4</sub>	bis(2-ethylhexyl)phthalate	117–81–7	413.2663	[M+Na] <sup>+</sup>	218.4	•				Plasticizers
20	8.19	C <sub>16</sub> H <sub>30</sub> O <sub>2</sub>	palmitoleic acid	373–49–9	277.2149	[M+Na] <sup>+</sup>	180.1		•			Lubricants
21	8.33	C <sub>18</sub> H <sub>34</sub> O <sub>2</sub>	oleic acid	112–80–1	283.2635	[M + H] <sup>+</sup>	219.8				•	Lubricants
22	8.41	C <sub>26</sub> H <sub>42</sub> O <sub>4</sub>	dinonyl phthalate	28,553–12–0	441.2981	[M+Na] <sup>+</sup>	226.4	•				Plasticizers
23	8.72	C <sub>17</sub> H <sub>34</sub> O <sub>2</sub>	heptadecanoic acid	506–12–7	271.2635	[M + H] <sup>+</sup>	182.9		•			Lubricants
24	8.75	C <sub>22</sub> H <sub>19</sub> O <sub>2</sub> P	diphenyl-(2,4,6-trimethylbenzoyl) phosphine oxide	75,980–60–8	349.1356	[M + H] <sup>+</sup>	197.1	•	•	•	•	Adhesives (crosslinker)/Wood manufacturing
25	8.80	C <sub>24</sub> H <sub>40</sub> O <sub>4</sub>	deoxycholic acid	83–44–3	393.2984	[M + H] <sup>+</sup>	172.2	•	•			FCM

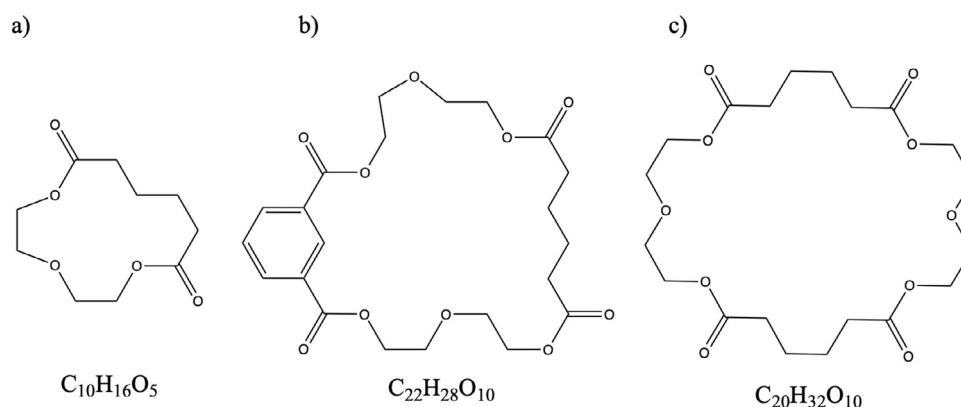
The list of applications has been summarised from CompTox Chemicals Dashboard of EPA [33], IFCA – Indirect Food Contact Additives.

obtained from the quantitative analysis together with the migration limits.

It can be seen that the extent migration of non-volatile substances to the three types of liquid simulants depends on the material from which the samples were made. The results show that the dishes from which the highest level of migration was observed were those made from bamboo. These were followed in terms of the extent of migration by dishes made from palm leaves. Dishes made from wood and wheat pulp exhibited lower levels of compound migration to the simulants.

The migration of non-volatile compounds is dependent upon the chemical properties of food simulants and nature of migrants. The highest level of migration of non-volatile compounds was observed in simulant A, followed by simulants B and D2. It is anticipated that this is due to the fact that most migrating compounds detected are hydrophilic. This tendency is the opposite to that observed for volatile compounds detected in migration tests from biodegradable dishes previously published [3].

The results for the bamboo dishes show that most of the identified compounds are detected with concentrations below the limits established for each substance, whether those limits are SML,



**Fig. 5.** Chemical structures and elemental composition of three oligomers detected in the migration samples from bamboo: a) 1,4,7-trioxacyclotridecane-8,13-dione (cyclic diethylene glycol adipate) b) 3,6,9,16,19,22-hexaoxabicyclo[22.3.1]-octacosane-1(28),24,26-triene-2,10,15,23-tetrone c) 1,4,7,14,17,20-hexaoxacyclohexacosane-8,13,21,26-tetrone.

**Table 2**

Analytical parameters determined from data acquired using the UPLC-IMS-MS, where A, B, D2 are food simulants.

No	Standard	$r^2$ , (linearity range) ( $\mu\text{g}/\text{kg}$ )			LOD ( $\mu\text{g}/\text{kg}$ )			LOQ ( $\mu\text{g}/\text{kg}$ )		
		A	B	D2	A	B	D2	A	B	D2
1	lactose	$r = 0.9980$ (1–992)	$r = 0.9980$ (1–921)	–	432	13	–	1439	45	–
2	1,4-cyclohexanedicarboxylic acid	$r = 0.9995$ (1106–5002)	$r = 0.9980$ (1499–6139)	–	134	965	–	448	3216	–
3	1,4,7-trioxacyclotridecane-8,13-dione	$r = 0.9945$ (527–2032)	$r = 0.9977$ (526–2000)	$r = 0.9985$ (364–2091)	73	78	135	243	260	451
4	1,5-diphenylcarbazide	$r = 0.9995$ (245–993)	$r = 0.9279$ (110–887)	$r = 0.9970$ (49–851)	603	341	1241	2009	1138	4138
5	3,5-di-tert-butyl-4-hydroxyphenylpropionic acid	$r = 0.9995$ (3–1131)	–	–	42	–	–	142	–	–
6	N,N-dimethylhexadecylamine	–	–	$r = 0.9951$ (1–869)	–	–	68	–	–	228
7	N,N-diethanololeamide	$r = 0.9995$ (6–995)	–	–	245	–	–	817	–	–
8	dioctyl terephthalate	$r = 0.9980$ (1–446)	$r = 0.9995$ (1–953)	–	1	2	–	3	6	–
9	dinonyl phthalate	$r = 0.9995$ (1–1124)	–	–	10	–	–	33	–	–
10	diphenyl-(2,4,6-trimethylbenzoyl) phosphine oxide	$r = 0.9995$ (1–1059)	$r = 0.9995$ (1–999)	$r = 0.9951$ (1–948)	1	16	5	5	53	17
11	deoxycholic acid	$r = 0.9995$ (1–1060)	$r = 0.9980$ (1–999)	–	1	19	–	3	64	–

NOAEL values or Cramer classification. It is important to highlight that there is one compound, 1,4-cyclohexanedicarboxylic acid, that exceeds its SML set according to Regulation (EU) No 10/2011, by at least 7 times in the simulant in which it was detected. The migration levels of 1,4-cyclohexanedicarboxylic acid to simulants A and B was quantified as  $53 \pm 1$  mg/kg and  $36 \pm 1$  mg/kg, respectively, and this compares to the SML limit of 5 mg/kg. This compound is classified as an indirect additive to FCMs, which may explain its presence in the bamboo dishes.

There are eight compounds, which do not have SML or NOAEL values. Compounds classified as Cramer III, Cramer II and Cramer I, should not exceed EDIs of 0.09 mg/kg, 0.54 mg/kg and 1.80 mg/kg, respectively, but four compounds exceed their EDI values. It should be highlighted that, compounds such as 3,6,9,16,19,22-hexaoxabicyclo[22.3.1]-octacosane-1(28),24,26-triene-2,10,15,23-tetrone and 1,4,7,14,17,20-hexaoxacyclohexacosane-8,13,21,26-tetrone are present only in the bamboo sample. They were found to be at very high concentrations in simulants A and D2. These two oligomers, as previously mentioned, are related to the manufacture of polyurethane adhesives and plastic containers [38], they do not have SML or NOAEL value, but are classified as Cramer III, so they should not exceed 0.09 mg/kg. It is therefore

very important to control the extent of their migration and to confirm its possible origin in bamboo dishes.

In the case of lactose and glucose no limits were applied as they are degradation products of chains of cellulose and are considered as food.

Six compounds were found to migrate from the wooden dishes and those identified were at low concentrations. The wheat pulp dishes show the least migration with only 5 compounds detected in the simulants and none of these exceeded the migration limits or established NOAEL values.

Considering all the results obtained in this work together, a series of follow-up action are proposed. It is necessary to continue studying tableware articles made from natural materials from other Spanish, European, and world suppliers, in order to ensure they are safe to use. The current lack of migration studies on these types of natural materials make it impossible to compare results. The migration results indicate that the manufacture these types of natural materials are not totally free of chemicals. It would be interesting to know if the production lines in the factories where natural materials are produced are also used for the manufacture of items from plastic materials. If so, this could indicate that the presence of some substances in the dishes made from natural materials is due to cross-contamination.



**Table 3**

Results of quantitative and semi-quantitative analysis and the migration limits. Blank cells in table mean no detected compounds.

RT (min)	Compound	Concentration (mg/kg)			Migration Limits (mg/kg)		
		A	B	D2	SML	NOAEL	Cramer
<b>Bamboo</b>							
3.00	1,4-cyclohexanedicarboxylic acid	53 ± 1	36 ± 1		5		
3.37	1,4,7-trioxacyclotridecane-8,13-dione	< LOD	6.4 ± 0.4	< LOD			0.09
4.66	1,5-diphenylcarbazine	< LOD	0.90 ± 0.04	0.29 ± 0.03			0.09
4.78	2,2'-dihydroxy-4-methoxybenzophenone <sup>(a)</sup>	< LOD				60	
4.94	1,4,7,14,17,20-hexaoxacyclohexacosane-8,13,21,26-tetrone <sup>(b)</sup>	282 ± 33	173 ± 23	< LOD			0.09
5.31	3,6,9,16,19,22-hexaoxabicyclo[22.3.1]octacosane-1(28),24,26-triene-2,10,15,23-tetrone <sup>(b)</sup>	15 ± 3	7.3 ± 0.8	< LOD			0.09
5.42	dibutyl phthalate <sup>(c)</sup>	0.0072 ± 0.0001			0.3		
5.98	1,6,13,18-tetraoxacyclotetracosane-7,12,19,24-tetraone <sup>(a)</sup>	< LOD	< LOD				1.80
6.56	3,5-di-tert-butyl-4-hydroxyphenylpropionic acid	< LOD					0.54
7.78	N,N-diethanololeamide <sup>(a)</sup>	< LOD				1000	
8.08	glyceryl monostearate <sup>(a)</sup>	< LOD					1.80
8.15	bis(2-ethylhexyl)phthalate <sup>(d)</sup>	< LOD			1.5		
8.41	dinonyl phthalate	0.30 ± 0.01			1.5		
8.75	diphenyl-(2,4,6-trimethylbenzoyl) phosphine oxide	0.10 ± 0.02	0.076 ± 0.001	0.029 ± 0.001		50	
8.80	deoxycholic acid	0.0063 ± 0.0001					0.09
<b>Palm leaf</b>							
0.67	lactose		0.044 ± 0.001				
0.69	D(+)-glucose <sup>(d)</sup>		0.036 ± 0.001				
0.89	bisphenol B <sup>(a)</sup>	< LOD					1.80
4.85	kaempferol <sup>(a)</sup>	< LOD					1.80
8.08	glyceryl monostearate <sup>(a)</sup>	< LOD					1.80
8.09	dioctyl terephthalate	< LOD			60		
8.19	palmitoleic acid <sup>(a)</sup>		< LOD		60		
8.72	heptadecanoic acid <sup>(a)</sup>			< LOD			1.80
8.75	diphenyl-(2,4,6-trimethylbenzoyl) phosphine oxide	0.050 ± 0.001	0.079 ± 0.003	0.031 ± 0.001		50	
8.80	deoxycholic acid		< LOD				0.09
<b>Wood</b>							
0.67	lactose	0.054 ± 0.002					
0.69	D(+)-glucose <sup>(d)</sup>			7.7 ± 0.3			
6.77	N,N-dimethylhexadecylamine			< LOD		40	
7.98	2-stearoglycerol <sup>(a)</sup>			< LOD			1.80
8.09	dioctyl terephthalate		< LOD		60		
8.75	diphenyl-(2,4,6-trimethylbenzoyl) phosphine oxide	0.072 ± 0.001	0.077 ± 0.002	0.030 ± 0.001		50	
<b>Wheat pulp</b>							
6.77	N,N-dimethylhexadecylamine			< LOD		40	
7.98	2-stearoglycerol <sup>(a)</sup>			< LOD			1.80
8.09	dioctyl terephthalate		< LOD		60		
8.33	oleic acid <sup>(a)</sup>		< LOD		60		
8.75	diphenyl-(2,4,6-trimethylbenzoyl) phosphine oxide	< LOD	0.034 ± 0.001	0.030 ± 0.002		50	

Semi-quantified using the following standards (a) 1,5-diphenylcarbazine (b) 1,4,7-trioxacyclotridecane-8,13-dione (c) dinonyl phthalate (d) lactose.

## Conclusions

Application of UPLC-IMS-MS allowed the identification of non-volatile compounds migrating from 4 natural raw materials into a variety of food simulants. The identified compounds were mainly additives and food contact substances that are generally used to improve the properties of commercial dishes.

It has been seen that the migration of non-volatile substances to three types of liquid simulants is different depending on the

material from which the tableware was made. The results show that the dishes from which the highest levels of migration was observed were those made of bamboo. Decreasing levels of migration were observed from dishes made from palm leaves, wood and wheat pulp, respectively.

This analysis, has enabled the level of migration of non-volatile compounds from dishes made of four natural materials (bamboo, palm leaf, wood and wheat pulp) to be quantified. Most of the quantified compounds do not exceed either the SML limits set out

in Regulation (EU) No 10/2011, NOAEL values or limits established using Cramer rules. Therefore, their presence does not pose a health problem for consumers. However, three compounds, 1,4-cyclohexanedicarboxylic acid, 3,6,9,16,19,22-hexaoxabicyclo[22.3.1]-octacos-1(28),24,26-triene-2,10,15,23-tetrone and 1,4,7,14,17,20-hexaoxacyclohexacosane-8,13,21,26-tetrone, found to migrate from the bamboo dishes, did exceed the EDI level established by Cramer. As such, this work shows that manufacturing FCMs from natural materials does not guarantee of food safety, since they may be manufactured with additives and are also susceptible to cross-contamination. It is recommended that tableware from different origins and of different brands should be studied and clear rules for these FCMs established.

The current absence of studies on these kinds of materials has prevented a conclusive comparison. Therefore, it is important, and necessary, to continue these types of investigation to enable future comparison and to check that the legal levels of compound migration are not exceeded.

### Declaration of Competing Interest

The authors declare no conflict of interest.

### CRediT authorship contribution statement

**Magdalena Wrona:** Conceptualization, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Supervision. **Ana Román:** Methodology, Validation, Investigation, Data curation. **Xue-Chao Song:** Conceptualization, Methodology, Validation, Investigation, Data curation, Writing – original draft. **Cristina Nerín:** Conceptualization, Resources, Writing – review & editing, Supervision, Project administration, Funding acquisition. **Nicola Dreolin:** Writing – review & editing. **Jeff Goshawk:** Writing – review & editing. **Esther Asensio:** Methodology, Investigation, Conceptualization, Resources, Writing – review & editing, Supervision, Project administration, Funding acquisition.

### Data availability

Data will be made available on request.

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