Multiple headspace-solid phase microextraction for the determination of migrants coming from a self-stick label in fresh sausage

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ABSTRACT

Most fresh sausages are sold with a self-stick adhesive label stuck directly on it. Because of that, the substances in the adhesive could migrate into the fresh sausage. In this work, the multiple headspace-solid-phase microextraction technique has been optimized to quantify the migrants found in the fresh sausage. All the compounds could be analyzed by this technique since its concentration decay exponentially with the number of extractions with good correlation coefficients (0.8258–0.9987). Then, migration assays were carried out and an evaluation of the potential risk for the human health was undertaken with the conclusion that the migration of the compounds from the label does not endanger human health. The results were compared those obtained in migration to casing filled with isooctane used as fat food simulant by Canellas et al. (2014). The values obtained for isooctane (10–600 ng/g) were much higher than the migration values found in the meat stuffed in casing expressed as ng/g of fat content (ranged from 0.02 to 3.3 ng/g of fat content). This finding shows that in some scenarios, it is difficult to simulate the intended contact of materials used in food packaging with simulants.

1. Introduction

Labels in packaging inform about the product and motivate the consumer to buy it. Occasionally, labels are stuck directly on the food. Some examples are fruits, cured cheeses and cold meats.

Adhesives used in labels include a high variety of substances, most of them with a molecular weight lower than 1000 amu that in many occasions migrate from the adhesive to the food (Aznar et al., 2011; Canellas, Aznar, Nerin, & Mercea, 2010; Canellas, Vera, & Nerin, 2015; Stoermer & Franz, 2009; Vera, Canellas, & Nerin, 2013).

These labels have to comply with the Framework Regulation 1935/2004/EC (1935/2004/EC, 2004) that establishes that materials and articles must not transfer their constituents to food in quantities which could endanger human health. In the light of these regulations, it is necessary to study the migration of the compounds from the adhesive to food. Ordinary, migration studies are done following the Framework Regulation 10/2011/EC (10/2011/EC, 2011) that establishes a series of food simulants. The food simulants are liquid solutions that simplify the analytical work required in working with real foods. Nevertheless, this regulation was established for plastic materials that usually cannot be dissolved by the food simulants. In contrast, most of the labels are dissolved by many of these simulants. Because of that it is necessary to study the migration on real food.

Foodstuffs are much more difficult matrices to analyze than food simulants due to the high amount of interferences. The analysis of migrants in foodstuffs usually implies complex extraction processes before the analysis on an analytical instrument (Niu, Zhang, Duan, Wu, & Shao, 2015; Pezo, Wrona, Rodriguez-Lafuente, & Nerin, 2012; Sanches Silva, Cruz, Sendón García, Franz, & Paseiro Losada, 2007; Sendon Garcia, Sanches Silva, Cooper, Franz, & Paseiro Losada, 2006).

Headspace solid-phase microextraction (HS-SPME) is a widely used technique for the analysis of volatile compounds. It is a free solvent technique that allows direct analysis with high sensitivity (Pawliszyn, 2012). In order to analyze volatiles in solid samples using HS-SPME, the multiple HS-SPME technique has been developed (Teresa Tena & David Carrillo, 2007). This technique has been used in the field of food science to determine volatiles in several foodstuffs like herbs, bread, pickles, coffee, mushrooms, cheese, alcoholic beverages or tomato (Bicchi et al., 2011; Costa, Tedone, De Grazia, Dugo, & Mondello, 2013; Lei et al., 2012; Pizarro, Perez-del-Notario, & Gonzalez-Saiz, 2007; Rincón, Pino, Ayala, & Afonso, 2014; Serrano, Beltrán, & Hernández, 2009; Sgorbini et al., 2015; Ye et al., 2011; Ye et al., 2012). Nevertheless, multiple HS-SPME has not been applied yet to analyze migrants in food.

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The multiple HS-SPME technique is based on the multiple headspace extraction (Kolb, 1982). It implies carrying out several extractions of the same sample. The concentration of the analyte decays exponentially and the total peak area can be calculated as the sum of the areas of each extraction. Then, the matrix effect is removed.

In this work, a multiple HS-SPME method for the study of migration of the compounds coming from a label to fresh sausage has been developed.

2. Materials and methods

2.1. Materials

The adhesive used in the labels studied was a pressure sensitive adhesive (PSA). This adhesive is commonly used in labels for direct contact on cheese, cold meats and meat derivatives. The adhesive was supplied by Samtack (Barcelona, Spain).

Labels for direct food contact were made with the adhesive. The labels consisted of 20 g/m^2 of PSA applied over 36 μm thickness polyethylene terephthalate (PET). The labels were supplied by Samtack (Barcelona, Spain).

Natural pork casing and fresh sausage were supplied by Melsa (Graus, Spain). The fresh sausage studied is handmade with approximately a 80% of lean pork meat and smoked bacon, a 20% of jowls and fat, oregano, thyme, clove and nutmeg. The composition of this sausage was: 25% of protein, 27.5% of fat content and 47.5% of water. The sausage studied was 30 cm long and has a diameter of 3.5 cm.

The following reagents: decahydronaphthalene, 3-octanol, 1-methyl-3-methoxy-4-isopropylbenzene and tert-butyldicyclo hexylphosphine were purchased from Sigma–Aldrich Química S.A (Madrid, Spain).

HPLC-MS quality methanol and ultrapurified water were supplied by J.T. Baker (Deventer, The Netherlands). Analytical grade isooctane was supplied by Scharlau Chemie S.A (Sentmenat, Spain).

Polydimethylsiloxane (PDMS) (7 μm), polydimethylsiloxane (PDMS) (100 μm) and divinylbenzene/carboxen/polydimethylsilox ane (DVB/CAR/PDMS) (50 μm) solid phase microextraction fibers were supplied by Supelco (Bellefonte, USA).

2.2. Gas chromatography–mass spectrometry single quadrupole (GC–MS/Q)

The equipment used was a CTC Analytics CombiPal autosampler coupled to an Agilent 6890N gas chromatograph with a mass spectrometer MS 5975B detector. All of them were from Agilent Technologies (Madrid, Spain).

The capillary column used was a HP-5MS (30 m × 0.25 μm × 250 μm) from Agilent Technologies (Madrid, Spain). The oven program was as follows: 40 °C for 2 min, with rate of 10 °C/min up to 300 °C, maintained for 2 min. The injection type was splitless and the helium flow was 1 ml/min. The injector temperature was 250 °C. The acquisition was done in electron impact ionization (EI). The mass detector was set at SCAN mode (in the range m/z 45–350).

2.3. Migration study

The migration studies were carried out as follows. Pieces of 5 cm and 5.5 g of fresh sausage were completely covered by the label (Fig. 1). Then these samples were enveloped with aluminum foil and introduced into the oven at 20 °C for two days. Ten replicates of the migration assay and a blank consisting of fresh sausage without label were prepared. The fresh sausages were controlled gravimetrically before and after the migration study.

Fig. 1. Fresh sausage covered by the label.

After this time, the label was removed and the natural pork casing was separated from the meat mixture stuffed in the sausage in order to find out the amount of migrants that remained in the casing and the amount of migrants that reached the meat mixture stuffed in the sausage. Natural pork casing was cut in approximately 2 mm^2 pieces and meat mixture stuffed in the sausage was cut in approximately 5 mm^2 pieces as it was stuffed into casings.

2.4. Multiple HS-SPME optimization

Firstly, in order to optimize the solid phase microextraction (SPME) conditions, solutions of the adhesive were prepared. 1 g of adhesive was dissolved in 100 g of isooctane. The adhesive contained the compounds showed in Tables 1 and 2. They were identified on the adhesive by Canellas, Vera, and Nerin (2014).

Two kinds of test pieces were prepared. On the one hand, 0.4 g of small pieces of casing were added to 20 mL headspace vials and on the other hand, 2 g of the meat mixture stuffed in the sausage were added to 20 mL headspace vials. Then, 50 μL of the isooctane solution containing the adhesive were added to both types of

Table 1
Compound number, retention times (min), compounds names and correlation coefficient (R) of the exponential decay of the peak areas obtained by multiple HS-SPME of the compounds on the intestine and mixed meat.

N°	Tr (min)	Compound name (Cramer class)	R intestine	R mixed meat
1	21,15	Naphthalene. decahydro-1.6-dimethyl-4-(1-methylethyl)-I)	0.9101	0.9025
2	21,24	Naphthalene. decahydro-2.6-dimethyl-3-octyl	0.9258	0.8956
3	21,32	4.7-dimethyl-1-isopropyl-perhydronaphthalene	0.9105	0.9001
4	21,47	Z.E-2.13-Octadecadien-1-ol	0.8951	0.8856
5	21,53	Z.Z-2.13-Octadecadien-1-ol	0.8854	0.8574
6	21,59	E.Z-2.13-Octadecadien-1-ol	0.8956	0.8258
7	21,79	Dicyclohexylphosphino isomer	0.9987	0.9025
8	21,96	Dicyclohexylphosphino isomer	0.9562	0.9025
9	22,02	Dicyclohexylphosphino isomer	0.9478	0.8999
10	22,17	Dicyclohexylphosphino isomer	0.9211	0.8762
11	22,2	Dicyclohexylphosphino isomer	0.9852	0.901
12	22,4	Dicyclohexylphosphino isomer	0.9789	0.875
13	22,6	Naphthalene. decahydro-1.1-dimethyl-	0.9275	0.91
14	22,76	Dicylcohexylphosphino isomer	0.9901	0.9901
15	23,21	Methyl-3-(3.5-di-tert-butyl-4-hydroxyphenyl)propanoate	0.9568	0.8978

Table 2
Compound number, retention times (min), compounds names and Cramer class, limit of detection (LOD) expressed in ng/g for casing and meat mixture stuffed in the sausage, relative standard deviation (%RSD) of casing and meat mixture stuffed in the sausage migration values, concentration of compounds coming from migration to casing and meat mixture stuffed in the sausage, migration results expressed as ng/g of fat content, estimated daily intake (EDI) expressed as mg/person/day considering that the label covers the 100% of the fresh sausage and estimated daily intake (EDI) expressed as mg/person/day considering that the label covers the 25% of the fresh sausage.

N°	Tr (min)	Compoundname (Cramerclass)	LOD casing (ng/g)	LOD meat (ng/g)	RSD% migration to casing	RSD% migration to meat	Migration ng/g of casing	Migration ng/g of meat	Migration ng/g of fat content in meat	EDI 100% (mg/ person/day)	EDI 25% (mg/ person/day)
1	21,15	Naphthalene. Decahydro-1.6-dimethyl-4-(1-methylethyl)-(I)	0.6	0.6	11	13	17.8	12.1	3.3	0.030	0.008
2	21,24	Naphthalene. decahydro-2.6-dimethyl-3-octyl (I)	0.6	0.6	15	12	10.5	9.8	2.7	0.020	0.005
3	21,32	4.7-dimethyl-1-isopropyl-perhydronaphthalene (I)	0.6	0.6	9	15	10	6.5	1.7	0.017	0.004
4	21,47	Z.E-2.13-Octadecadien-1-ol(I)	0.5	0.5	18	21	0.5	0.1	0.02	0.001	0.001
5	21,53	Z.Z-2.13-Octadecadien-1-ol (I)	0.5	0.5	17	20	7.4	3.6	0.9	0.011	0.003
6	21,59	E.Z-2.13-Octadecadien-1-ol (I)	0.5	0.5	18	19	7.1	3.5	0.9	0.011	0.003
7	21,79	Dicyclohexylphosphinoisomer (III)	0.8	0.8	21	18	195	11.5	3.1	0.207	0.052
8	21,96	Dicyclohexylphosphinoisomer (III)	0.8	0.8	15	17	15.3	9.4	2.5	0.025	0.006
9	22,02	Dicyclohexylphosphinoisomer (III)	0.8	0.8	16	16	24.3	3.2	0.9	0.028	0.007
10	22,17	Dicyclohexylphosphinoisomer (III)	0.8	0.8	15	17	10.1	1.2	0.3	0.011	0.003
11	22,2	Dicyclohexylphosphinoisomer (III)	0.8	0.8	18	18	23.8	3.5	0.9	0.027	0.007
12	22,4	Dicyclohexylphosphinoisomer (III)	0.8	0.8	19	15	17.1	3.3	0.9	0.020	0.005
13	22,6	Naphthalene. decahydro-1.1-dimethyl-(III)	0.6	0.6	21	18	17	7.3	2.0	0.024	0.006
14	22,76	Dicyclohexylphosphinoisomer (III)	0.8	0.8	18	20	9.9	4.3	1.1	0.014	0.004
15	23,21	Methyl-3-(3.5-di-tert-butyl-4-hydroxyphenyl)propanoate (II)	0.7	0.7	15	17	7.6	2	0.5	0.010	0.003

headspace vials. The samples were homogenized using the Vortex agitator for 10 min. Finally, each sample was analyzed by headspace SPME–GC–MS using three different fibers: PDMS (7 μm), PDMS (100 μm) and DVB/CAR/PDMS (50 μm). Then, the selected fiber, DVB/CAR/PDMS (50 μm), and the extraction conditions were optimized. The extraction temperature range studied was 40–80 °C, extraction time range was 5–30 min and desorption time range was 1–5 min at 250 °C. Then, multiple HS-SPME analysis was optimized with the fresh sausage coming from the migration assay. The multiple HS-SPME technique is based on the multiple headspace extraction (Kolb, 1982). The multiple HS-SPME implies carrying out several extractions of the same sample. The concentration of the analyte decays exponentially and the total peak area can be calculated as the sum of the areas of each extraction. Then, the matrix effect is removed.

The natural logarithm of the peak area versus the number of extraction minus one has to be represented to calculate the slope (β) and the regression coefficient (Eq. (1)) (Teresa Tena & David Carrillo, 2007).

$$lnA_i = (i-1)\ln\beta + lnA_1 \quad (1)$$

Finally, the initial mass of the analyte in the sample could be calculated to obtain the total area of each compound in each vial. The total area of each compound in each vial could be calculated using Eq. (2). The constant β was obtained from Eq. (1) through the representation of the natural logarithm of the peak area versus the number of extraction minus one (Teresa Tena & David Carrillo, 2007).

$$A_T = A_1/1-\beta \quad (2)$$

External calibrations (liquid direct injection of standards to GC) can be used to calculate the mass of the migrants in food since the initial mass of the analyte in the sample coming from migration has been obtained with Eq. (2) (Teresa Tena & David Carrillo, 2007). The standards of the compounds present in the adhesive were not commercially available. Therefore, decahydronaphthalene has been used to quantify naphthalene. decahydro-1.6-di methyl-4-(1-methylethyl)-, naphthalene. decahydro-1.6-dime thyl-4-(1-methylethyl)- and 4.7-dimethyl-1-isopropyl-perhydro naphthalene, 3-octanol has been used to quantify Z.E-2.13-Octadecadien-1-ol, Z.E-2.13-Octadecadien-1-ol and E.Z-2.13-Octadecadien-1-ol, 1-methyl-3-methoxy-4-isopropylbenzene has been used to quantify methyl-3-(3.5-di-tert-butyl-4-hydroxyphe nyl)propanoate4 and tert-butyldicyclohexylphosphine has been used to quantify dicyclohexylphosphino isomers.

The sample weight for the multiple HS-SPME analysis was optimized. Different amounts of natural casing ranging from 0.1 g to 0.5 g were placed in headspace vials for its analysis. Besides, different amounts of the meat ranging from 0.2 g to 5 g were placed in headspace vials for analysis.

The samples were extracted with the SPME fiber four consecutive times and analyzed by GC–MS. The natural logarithm of the peak area versus the number of extraction minus one was represented to calculate the slope (β) and the regression coefficient (Eq. (1)).

Finally, 0.5 g of natural pork casing and 2 g of meat mixture stuffed in the sausage coming from the migration specimens were analyzed in order to quantify the migrants on the fresh sausage. The initial mass of the analyte in the sample was calculated from the total area of each compound in each vial using Eq. (2).

3. Results and discussion

The composition of this adhesive was previously studied (Canellas et al., 2014). In that work, it was found that the adhesive contains several volatile and semivolatile compounds including

non-intentionally added substances (NIAS). Moreover, in that work the authors studied the specific migration from the label to pork casing filled with isooctane used as fat simulant. Migration conditions following the European legislation for isooctane were applied (10/2011/EC, 2011). This adhesive is normally used to stick label on sausages, meat derivatives and cold meats, as well as fruits. Because of that it was decided to do the migration assay with a real scenario, a fresh sausage that will be discussed in this work.

3.1. Multiple headspace SPME optimization

Multiple headspace SPME was selected as extraction methodology because it offers the advantages of the high sensitivity of SPME and the absence of matrix effect.

Firstly, the parameters that influence the analysis by headspace SPME were optimized. For that purpose, two kinds of test pieces were prepared, pieces of pork casing and pieces of mixed pork meat used for filling the fresh sausage. All sets of samples were spiked with the isooctane solution of adhesive. Each sample was analyzed by headspace SPME–GC–MS using three different fibers, taking into account the compounds to analyze (Canellas et al., 2014): PDMS (7 μm) (coating designed for non-polar high molecular weight compounds (MW 125–600)), PDMS (100 μm) (coating designed for non polar volatiles (MW 60–275)) and DVB/CAR/PDMS (50 μm) (coating designed for medium polar volatiles and semi-volatiles compounds (MW 40–275)). The extraction conditions were optimized for each fiber coating.

The fiber DVB/CAR/PDMS (50 μm) provided the highest sensitivity for all the adhesive compounds, since this coating fits better than the other two with the polarity and molecular weight of the target compounds here studied. The final extraction conditions that provided the maximum areas of the compounds in both casing and meat mixture stuffed in the sausage were 80 °C extraction temperature, 25 min extraction time and 1 min desorption time at 250 °C.

The multiple HS-SPME optimization was undertaken on the samples coming from the migration study. The sample amount was optimized taking into account the linearity of $\ln A_i$ versus $(i-1)$ plots (Eq. (1)) and the sensitivity. Finally, 0.5 g of natural pork casing and 2 g of meat mixture stuffed in the sausage coming from the migration tests were selected as specimens to be analyzed.

Table 1 shows the correlation coefficients of all the compounds studied in the two kinds of samples studied (pork casing and meat mixture stuffed in the sausage). Since the correlation coefficients were high enough (values ranging 0.8258 to 0.9987), all the compounds were quantified in both samples with this method.

3.2. Migration results

Specific migration of the compounds coming from the label was studied. Conditions of the migration study (20 °C for 2 days) were established to make a comparison with the results obtained for the migration to casing filled with isooctane by Canellas et al. (2014). In this study the authors studied the specific migration from the same label to pork casing filled with isooctane used as fat simulant and migration conditions following the European legislation for isooctane were applied.

Due to the fact that the pork casing and the meat mixture stuffed in the sausage are very different specimens each part of the fresh sausage was studied separately. Fig. 2 shows the chromatograms of casing and meat stuffed in the casing after the migration study. The migrants (retention times from 21.15 to 23.21 min) can be seen in the chromatograms.

In order to calculate the migration values, the multiple-HS-SPME methodology developed in this work has been applied. Then, the initial mass of each compound in the casing and in the meat mixture stuffed in the sausage were calculated according the methodology explained in Section 2.4. They were calculated from the total area of each compound in each vial containing 0.5 g of natural pork casing or 2 g of meat mixture stuffed in the sausage coming from the migration assay. The total area of each compound in each vial was calculated using Eq. (2). External calibrations were used to calculate the mass of the migrants in the fresh sausage.

Table 2 shows the limits of detection (LOD) expressed in ng/g for casing and meat mixture stuffed in the sausage, relative standard deviation (%RSD) of casing and meat mixture stuffed in the sausage migration values, concentration of compounds coming from migration to casing and fr casing and meat mixture stuffed in the sausage, estimated daily intake (EDI) expressed as mg/person/day considering that the label covers the 100% of the fresh sausage and estimated daily intake (EDI) expressed as mg/person/day considering that the label covers the 25% of the fresh sausage.

Good sensitivity was obtained by multiple-HS-SPME since limits of detection ranged from 0.5 to 0.8 ng/g for both casing and meat mixture stuffed in the sausage. Relative standard deviations (%RSD) were calculated for the ten replicates of real samples studied and the values ranged from 9% to 21%. Finally, migration results obtained by the method developed here were the following: migration to casing ranged from 0.5 to 195 ng/g and migration to meat stuffed in casing ranged from 0.1 to 12.1 ng/g.

In order to evaluate the potential risk for the human health, the estimated daily intake values (EDI) expressed as mg/person/day were calculated from the migration values using the Eq. (3) (ILSI, 2002).

$$\mathrm{EDI}_{\text{worst case}}\ (\text{mg/person/day}) = 1\ \text{kg food/person/day} * \text{migration}\ (\text{mg/kg food}) \quad (3)$$

EDI values are calculated taking into account that the label covers the 100% of the area of fresh sausage. Nevertheless, this situation is not the actual situation in the real food, as the label normally covers only 25% of the fresh sausage in the worst case. Because of that EDI values were calculated considering this fact.

These values were compared to the experimental LOAEL (Lowest-observed-adverse-effect level) or NOAEL (No-observed-adverse-effect level) from bibliography. In case these experimental values were not available, the values found were compared to the theoretical values of Human Exposure Threshold (mg/person/day) established by the Threshold of toxicological concern (TTC) according to Cramer toxicity classes (IdeaconsultLtd, 2011).

Values of HET according to the International Life Sciences Institute (ILSI, 2005) are 1.8 mg/person/day for Cramer class I, 0.54 mg/person/day for Cramer class II and 0.09 mg/person/day for Cramer class III. Table 2 shows the Cramer class of the compounds and the EDI calculated for each one. All the EDI values considering the label normally covering only a maximum of 25% of the fresh sausage were below the HET values. Then, it can be concluded that the migration of the compounds coming from this label to fresh sausage does not endanger human health.

On the other hand, the migration results have been compared with the results obtained with casing filled with isooctane made by Canellas et al. (2014). In that work the authors studied the specific migration from the same label to pork casing filled with isooctane used as fat simulant. The results from Canellas et al. (2014) were the following: migration to casing filled with isooctane inside ranged from 540 to 15100 ng/g and migration to isooctane ranged from 10 ng/g to 600 ng/g. Table 2 shows the migration to the meat stuffed in casing expressed as ng/g of fat content taking into account a fat content of 27.5%. The values obtained by Canellas et al. (2014) for isooctane are much higher than the migration values found in the present study meat stuffed in casing expressed as ng/g of fat content (ranged from 0.02 to 3.3 ng/g of fat content). It demonstrates that in some scenarios, it

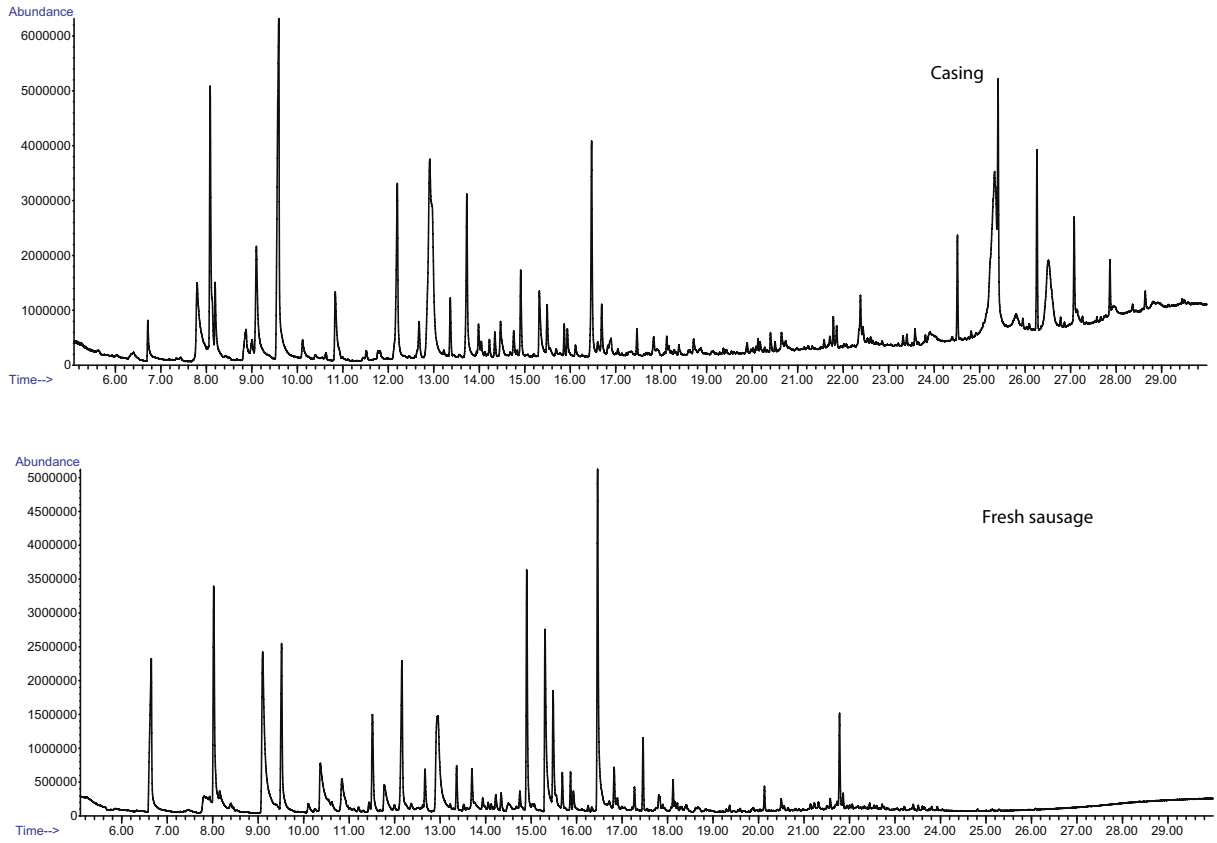

Fig. 2. Chromatograms of the casing and meat stuffed in the casing after the migration assay obtained by SPME–GC–MS.

is difficult to simulate the intended contact of materials used in food packaging with simulants. Because of that it is worth developing a methodology for analyzing real food in order to find out the real migration values.

4. Conclusions

The optimization of the multiple headspace solid-phase microextraction technique for the determination of migrants from an self-stick label in fresh sausage has been carried out in this work. It has been shown that this technique is solvent free and sensitive, and allows volatile compounds coming from a solid meat sample to be quantified. Additionally, this work has demonstrated that in some cases like this one, where a difficult mixture of pork meat, fat, water, salt, spices and pork casing is under test, to replicate with simulants the intended food contact of packaging materials is very difficult and does not represent the real situation. It is therefore necessary to develop a methodology for analyzing real food in order to find out the real migration values.

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