



# Analysis of low-molar-mass materials in commercial rubber samples by Soxhlet and headspace extractions followed by GC–MS analysis

N. Delaunay-Bertoncini<sup>a,1</sup>, F.W.M. van der Wielen<sup>b</sup>, P. de Voogt<sup>b</sup>,  
B. Erlandsson<sup>c</sup>, P.J. Schoenmakers<sup>a,\*</sup>

<sup>a</sup> *Polymer-Analysis Group, Department of Chemical Engineering (ITS), Faculty of Science, University of Amsterdam, Nieuwe Achtergracht 166, 1018 WV Amsterdam, The Netherlands*

<sup>b</sup> *Department of Environmental and Toxicological Chemistry, Institute for Biodiversity and Ecosystem Dynamics, University of Amsterdam, Nieuwe Achtergracht 166, 1018 WV Amsterdam, The Netherlands*

<sup>c</sup> *AstraZeneca, R&D Södertälje, Analytical Development, S-151 85 Södertälje, Sweden*

Received 10 October 2003; received in revised form 23 March 2004; accepted 26 March 2004

Available online 23 July 2004

## Abstract

Very tight regulations apply to materials used for pharmaceutical packaging and for administering drugs. In this paper, we describe a simple and reliable procedure involving both gas- and liquid-phase extraction steps followed by an analysis step to identify the low-molar-mass materials in commercial-rubber samples. Representative commercial rubbers, that could be used for pharmaceutical packaging, have been selected and cryogenically powdered. Headspace and Soxhlet extractions have been carried out and the key parameters are discussed. The obtained extracts have been analyzed by gas chromatography (GC)—mass spectrometry (MS). More than 100 compounds have been detected and identified. Headspace allowed to extract the more-volatile compounds, whereas Soxhlet extraction recovered less-volatile compounds, but induced a loss of the volatile ones. Thus, both extraction techniques are required to fully characterize the low-molar-mass compounds present in rubber.

© 2004 Elsevier B.V. All rights reserved.

*Keywords:* Soxhlet extraction; Headspace extraction; Rubbers; Polymers

## 1. Introduction

Nowadays, with the ever-increasing amount of legislation on emission of volatile organic chemicals into

the workplace and the environment in general, and on potential contamination of drugs and food through the packaging in particular, there is a need to know the nature and amounts of low-molar-mass extractables in rubber down to trace levels. Indeed, the contamination of drug solutions with compounds originating from rubber closures has already been observed, and evaporated or leached materials can seriously alter the physical appearance or even the chemical and biological properties of the dosage forms [1,2].

\* Corresponding author. Tel.: +31-20-525-6642x6515;  
fax: +31-20-525-6638.

E-mail address: [pjschoen@science.uva.nl](mailto:pjschoen@science.uva.nl) (P.J. Schoenmakers).

<sup>1</sup> Present address: Laboratoire des Sciences Analytiques, UMR 5180, CPE, Université Claude Bernard Lyon I, 43 Boulevard du 11 Novembre 1918, 69622 Villeurbanne Cedex, France.

All three major compendia, the United States Pharmacopoeia, the European Pharmacopoeia, and the Japanese Pharmacopoeia have published monographs specifically dealing with solvent extractables from closures intended for parenteral use [3]. The majority of the tests described are non-specific in nature in that they measure a particular chemical class (acid/base/reducing agent/metal), but do not separate or identify the extractables. As an example, measuring the turbidity of the extract of rubber in water or isopropanol is not useful for evaluating the potential contamination of drug solutions. Similarly, the significance of the pH change is limited, because a stopper with equal amounts of extractable acids and bases (or large amounts of neutral contaminants) may yield a small change in pH, but a large amount of extracted material. To circumvent this lack of specificity, the US Food and Drug Administration asks for an exhaustive identification of the low-molar-mass compounds potentially present in a polymer used for human drug packaging and a demonstration with simulation tests that no drug contamination occurs [4]. To be able to adequately determine which low-molar-mass compounds might migrate to a formulated drug, an extensive characterization of all low-molar-mass compounds present in the rubber material is of considerable value.

Numerous types of rubber closures with varying compositions are available for drug packaging. The complex formulations consist of elastomers and additives introduced to prevent degradation, both during processing and use, and to optimize specific product properties. Common additives are vulcanizing (or cross-linking) agents, plasticizers, antioxidants, antioxidants, accelerators, and retarders. They belong to many compound classes and represent a wide range of molar mass, volatility, and polarity. Moreover, many additives are labile and contain impurities, are introduced in complex mixtures in rubbers, and at quite low concentrations (<1–5%). Finally, traces of residual solvents, of monomers and oligomers, encapsulated in the polymeric matrix without having reacted, and potential contaminants originating from the environment may also be present in rubbers. This explains why the identification of low-molar-mass compounds in rubbers is complicated.

In some specific cases, rapid analysis of additives can be carried out without extensive pretreatment

steps. Direct spectroscopic methods, such as UV, IR, fluorescence or phosphorescence, and X-ray fluorescence can be used. However, generally these methods suffer from a lack of specificity [5]. Therefore, a more desirable approach for most additives packages and other low-molar-mass components is the separation and determination of each individual compound in the polymer. This requires extraction of the components followed by (usually) chromatographic determination. Extraction is often the most difficult and time-consuming step in the analysis of low-molar-mass compounds present in rubbers, especially when quantitation is required.

A variety of thermal methods for the analysis of polymer and additives has been proposed, most often based on pyrolysis [6–13]. The pyrolysis method induces degradation or decomposition of the polymers at high temperatures. This method is more appropriate to study the degradation products of a polymer than to study the low-molar-mass components present initially. Thus, this technique has been avoided in this study. Conversely, the static headspace extraction technique may induce the direct desorption of volatile compounds from samples in a very straightforward and soft (non-destructive) way. Surprisingly, reports on the use of this method with rubbers have been scarce, even if encouraging results have been obtained [14–16].

In order to extract compounds with a low volatility, a liquid-phase extraction technique has to be used. Different liquid-phase extraction techniques are nowadays available, and many of these have been used to extract compounds from polymers, such as polypropylene and polyethylene, and sometimes rubbers. The conventional methods include stirring [17,18], refluxing [5,19,20], Soxhlet [11,21–27], and sonication [28]. More recently, accelerated-solvent extraction (ASE) [29–31] and microwave-assisted solvent extraction (MASE) [32] have been introduced.

Various authors have shown that the use of smaller particles results in higher extraction rates [20,33,34]. The enhanced efficiency of extraction for a given extraction time arises from an increase in the overall rate of mass transfer, due to an increased surface area and a reduced (average) diffusion path length. Thus, to identify as many extractables as possible, it is desirable to grind the polymer samples before the extraction and analysis steps. The polymer may be ground

into small particles in a mortar, but the use of a grinder should give more reproducible and homogeneous samples. Some authors have frozen the polymer with liquid nitrogen before grinding it. This prevents the loss of additives due to volatilization or thermal decomposition during the milling process [29,30,35–37]. Also, grinding will be much easier at temperatures below the glass-transition point ( $T_g$ ), where the rubber is no longer elastic.

In this study, we describe a procedure to extract as much as possible of different low-molar-mass materials present in commercial rubber samples. This was achieved by utilizing a new procedure involving both gas- and liquid-phase extraction steps, followed by an analysis step, to identify the low-molar-mass materials in commercial, cryogenically ground rubber samples. A headspace and a Soxhlet method have been selected because both methods feature a relatively low number of operating parameters and both have a good reputation as standard methods.

## 2. Experimental

### 2.1. Chemicals

All the extraction solvents: acetone, isopropanol, chloroform, and toluene were of analytical quality (HPLC grade) and were obtained from Rathburn (Walkerburn, Scotland, UK). Two commercial butyl rubbers (isobutylene and isoprene mixture in a ratio close to 0.99:0.01), P1 and P2, used as stoppers in drug packaging, were used. This kind of rubber is well-known to be quite resistant to the action of some destructive factors, particularly heat, light, oxygen, and ozone.

### 2.2. Cryogenic grinding

The rubbers under study were ground after being frozen using a 6750 Freezer Mill (SPEX CertiPrep, Metuchen, NJ, USA). This system is a cryogenic laboratory mill, which chills samples in liquid nitrogen and pulverizes them with a magnetically driven impactor. Each sample was placed in a closed grinding vial along with a steel impactor, and the vial was then inserted in the coil assembly and lowered into the liquid nitrogen. Thus there was no cross-sample

contamination, and the low temperature of the sample was maintained during grinding. When the sample was thoroughly chilled (after 5 min) grinding was started. The magnetic coil shuttled the impactor rapidly back and forth, pulverizing the sample against the end plugs of the vial. When the two grinding cycles were complete (2 min each with an intermediary cooling period of 2 min), the vial was removed from the mill, emptied, and cleaned. The ground rubber samples were stored in a freezer until used.

### 2.3. Headspace extraction

A static-headspace unit was used. It was part of a Combi PAL system (CTC Analytics, Zwingen, Switzerland). It consisted of an incubator oven (25–200 °C) and a heated headspace syringe of 2.5 ml (25–150 °C, injection speed 100–1000  $\mu$ l/s). It was a syringe only concept, without sample loops, transfer lines or valves. 20 ml vials, containing 1 g of the sample and sealed with crimp caps of silicone rubber and PTFE faced septa (Chrom. Tech., Apple Valley, MN, USA) were placed in the incubator oven. The temperature of the incubator oven was fixed at 110 °C, in order to induce the transfer from solid- to gas-phase of the volatile compounds and to prevent decomposition or degradation of the rubber itself as much as possible. At this temperature, the vials pressure increased to 1.3 atm. Heating times of 5, 20, and 50 min were applied for each type of rubber. After the incubation period, a heated headspace syringe took 2.5 ml of the gas-phase and injected it into the gas chromatography (GC) spectrometer system at a speed of 1000  $\mu$ l/s in order to analyze the leached volatile compounds.

### 2.4. Analysis by GC–MS of the headspace extracts

The analytes were separated and detected using a GCQ (ThermoFinnigan, formerly Finnigan MAT, Kungens Kurva, Sweden) gas chromatography spectrometer, equipped with an ion-trap detector, linked to the Combi PAL system. The GC conditions were as follows: splitless injection; column, HP-5MS (Agilent Technologies, Amstelveen, Netherlands), 60 m  $\times$  0.32 mm i.d., stationary phase 5% phenyl, 95%-dimethylsiloxane copolymer, 250 nm film thickness; carrier gas, helium. The MS conditions were as follows: full scan mode,  $m/z$  40–550 amu; positive

electron-impact (EI)-ionization mode; ion-source temperature, 200 °C; capillary interface heated at 270 °C. The column temperature was programmed from 50 to 300 °C at 5 °C/min, initial time 5 min.

### 2.5. Soxhlet extraction

The two rubbers under study have been extracted with the above-listed HPLC-grade solvents. A blank experiment (with no polymer being introduced) has been performed in parallel for each extraction. The procedure always involved cleaning of the set-up first. Three hundred and fifty milliliters of HPLC-grade solvent were introduced in a 500 ml round-bottom flask. One centimeter height of deactivated silica and around 5 cm height of glass wool were successively introduced into a glass container, which had a compressed glass filter at the bottom and the glass container was introduced in the thimble. The flask was heated and therewith the Soxhlet process commenced. After 3–4 h, the heater was switched off and the solvent was removed from the set-up and discarded.

This was followed by the procedure of polymer extraction. The 350 ml of HPLC-grade solvent were again introduced in the 500 ml round-bottom flask. After having carefully removed the 5 cm height of glass wool, 2 g of ground rubber sample were introduced into the glass container, and the glass wool was put back. The glass container was then introduced in the thimble. To carry out a blank extraction, the two previous steps were omitted. The flask was then appropriately heated and therewith the Soxhlet process, with a cycle of about 15 min, commenced. After 16 h, the solvent was evaporated from the set-up by opening a gate connected to a funnel localized just above the thimble. It was assumed that the extraction was complete and that the non-volatile analytes were all in the flask. When around 100 ml of the solvent remained in the flask, the thimble was replaced by a Kuderna–Danish evaporator. The evaporation was stopped when 10–50 ml of extract remained and the final extract was stored in a fridge.

Some turbid extracts were obtained with isopropanol, which was the most polar solvent used. This turbidity was probably due to the increased concentration, through evaporation of the solvent, of compounds that were only slightly soluble in this polar solvent.

### 2.6. Analysis by GC–MS of the Soxhlet extracts

The analytes were separated and detected using a Trace GC 2000 (ThermoFinnigan) gas chromatograph equipped with an AS2000 autosampler, combined with a Trace MS mass spectrometer, which had a quadrupole separator. The GC conditions were as follows: cold on-column injection; column, J&W Scientific (Agilent Technologies, Amstelveen, The Netherlands), 60 m × 0.32 mm i.d., DB-5 stationary phase, 250 nm film thickness; precolumn, 2 m × 0.53 mm i.d., DPTMDS deactivated retention gap; carrier gas, helium; injection volume, 1.5 µl. The ramp and the total duration of the temperature program were optimized. The resulting program ranged from 120 to 320 °C at 5 °C/min, initial time 4 min, final time 20 min, total duration 64 min. The MS conditions were as follows: full scan mode,  $m/z$  40–550 amu; positive EI-ionization mode; ion-source temperature, 200 °C; capillary interface heated at 270 °C. Xcalibur was used as software for controlling the analytical equipment.

The extracts obtained in toluene ( $B_p = 111$  °C) or in isopropanol ( $B_p = 82$  °C) were injected into the GC–MS, without any manipulation. The 0.5 ml of the each extract obtained in chloroform ( $B_p = 61$  °C) or in acetone ( $B_p = 56$  °C) was introduced in a vial and 1 ml of toluene was added. Then, an evaporation step under a stream of nitrogen was carried out until the volume was again equal to 0.5 ml. The resulting extracts were then injected in the GC–MS set-up.

## 3. Results and discussion

### 3.1. Headspace extractions

The static-headspace-extraction technique was used to extract the volatile compounds from ground rubber samples. The resulting extracts were analyzed by GC–MS. As the caps used to seal the 20 ml vial were made of silicone rubber with PTFE-faced septa, headspace extractions with empty vials were carried out to determine potential interference with the rubbers under study. Around 40 peaks were detected that resulted from compounds leached from the caps or from the GC capillary column. An excellent repeatability of the pattern of leached compounds was observed. An increase in the incubation time induced

an increase in the area of some peaks, which seems to indicate that they correspond to compounds originating from the vial caps.

Fig. 1A presents a typical chromatogram obtained by GC–MS analysis of a headspace extract of a poly-isobutylene-based rubber. The number of de-

tected peaks in this chromatogram is around 125, excluding interference from the blank. In the enlarged chromatogram (Fig. 1B), it is obvious that some of these peaks represent several co-eluting compounds. This indicates that a large number of compounds have been volatilized during the headspace extraction.

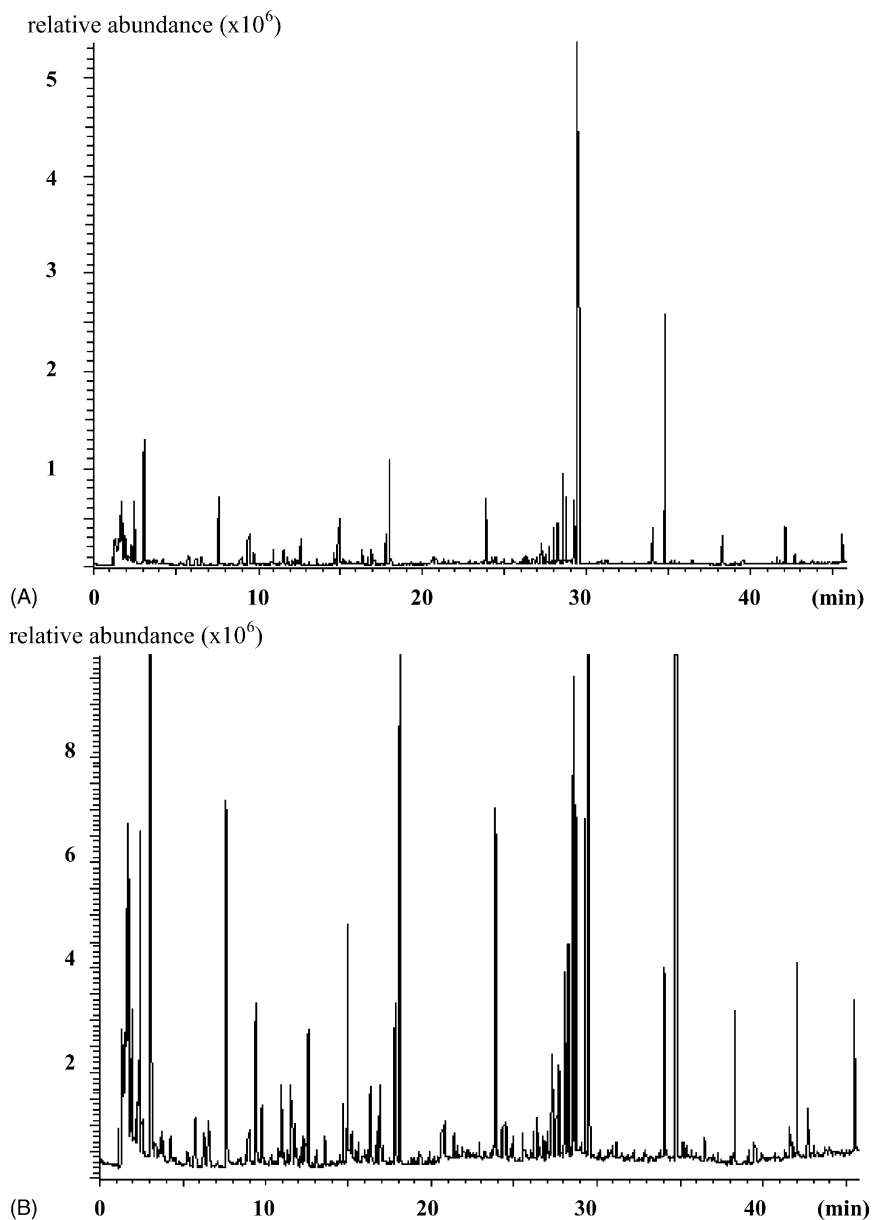


Fig. 1. GC–MS chromatograms obtained by analysis of the headspace extract of polymer P1 obtained after 20 min of heating time. (A) Full scale. (B) Enlarged scale. (See Section 2 for other details.)

Table 1

Boiling point, Hildebrand solubility parameter, and ability to participate in hydrogen-bonding interactions of the solvents selected for Soxhlet extractions [44,45]

	$B_p$ (°C)	$\delta$ (cal/ml) <sup>0.5</sup>	H
Toluene	111	9.57	P
Chloroform	61	9.88	P
Acetone	56	10	S
Isopropanol	82	11.5	S

P: poor; S: strong.

### 3.2. Soxhlet extractions

In order to extract the more polar and/or the less volatile compounds, Soxhlet extractions of the ground rubber samples have been carried out. The key parameter of this extraction is the choice of the solvent. It has to dissolve the analytes, while not interfering with the analysis step. Cross-linked rubbers can not be dissolved, but swelling is expected. Table 1 presents the boiling points, the Hildebrand solubility parameters, and the ability to participate in hydrogen-bonding interactions of four different selected solvents [38,39]. These parameters are expected to affect the extraction yields depending on the nature of the extractables.

Cyclohexane ( $\delta = 8.5$  (cal/ml)<sup>0.5</sup>) is considered to be an excellent solvent for poly-isobutylene rubber, benzene ( $\delta = 9.17$  (cal/ml)<sup>0.5</sup>) a moderate one, and dioxane ( $\delta = 10.13$  (cal/ml)<sup>0.5</sup>) is a non-solvent [40]. The swelling power for cross-linked rubbers may be expected to correspond to the solvent strength for non-cross-linked rubbers of the same type (i.e. based on poly-isobutylene). According to the Hildebrand solubility parameters, toluene is thus supposed to provide here the greatest extent of swelling. A good swelling is necessary to facilitate the diffusion of the analytes from the rubber to the extraction solvent. Another important parameter is the ability of the solvent to dissolve the analytes. This is why other solvents with higher Hildebrand solubility parameters have also been selected. Maybe, these solvents provide a better compromise between swelling of the polymer and dissolving (certain classes of) low-molar-mass extractables.

Fig. 2 shows a typical chromatogram (full-scale and enlarged) obtained by GC–MS analysis of a rubber Soxhlet extract, here the polymer P1 extracted in

toluene. Around 155 peaks are present, some of which represent co-eluting components.

### 3.3. Interpretation of the mass spectra

A chromatogram provides information regarding the complexity (number of components) of samples, and on the quantity (peak height or area) and identity (retention parameter) of the components present. In this latter respect, identification based solely on retention is impossible, when the nature of the initial components is completely unknown, as it is the case in this study. This is why the hyphenation of GC with mass spectrometry (MS) is necessary. The mass spectrometer is a virtually universal detector for gas chromatography, since, almost any compound that can pass through a gas chromatograph is converted into ions in the mass spectrometer. The electron-impact ionization mode is the most frequently used in GC–MS. Several factors contribute to the popularity of this ionization technique: stability, ease of operation, simple ionization, and a narrow kinetic-energy spread of the ions formed. The molecular peak and the fragment peaks form a typical pattern that can be interpreted or compared with reference spectra contained in available libraries, which allows the compounds to be identified.

A mass spectrum was obtained for each peak in each chromatogram corresponding to the analysis of a Soxhlet or a headspace extract of a polymer. In order to identify the structures of the extracted and eluted compounds, each mass spectrum has then been submitted to a library-search program.

The mass-spectral library used was that of the National Institute of Standards and Technology (NIST) (<http://www.nist.gov/srd/nist1a.htm>). This library contains 107,886 compounds with spectra. In this study, numerous compounds have been tentatively identified with this library. Compounds from various classes have been found: alkanes, alkenes, phenolic compounds, a large variety of aromatic compounds with one or more aromatic rings, phthalates, carboxylic acids (from C14 to C18), cyclic sulfur compounds and other sulfur-containing compounds, ketones, esters, di-esters, etc.

Using the NIST library, between 20 and 45% of the peaks representing between 18 and 60% of the total area, were readily identified in the different chromatograms. These results are encouraging, but

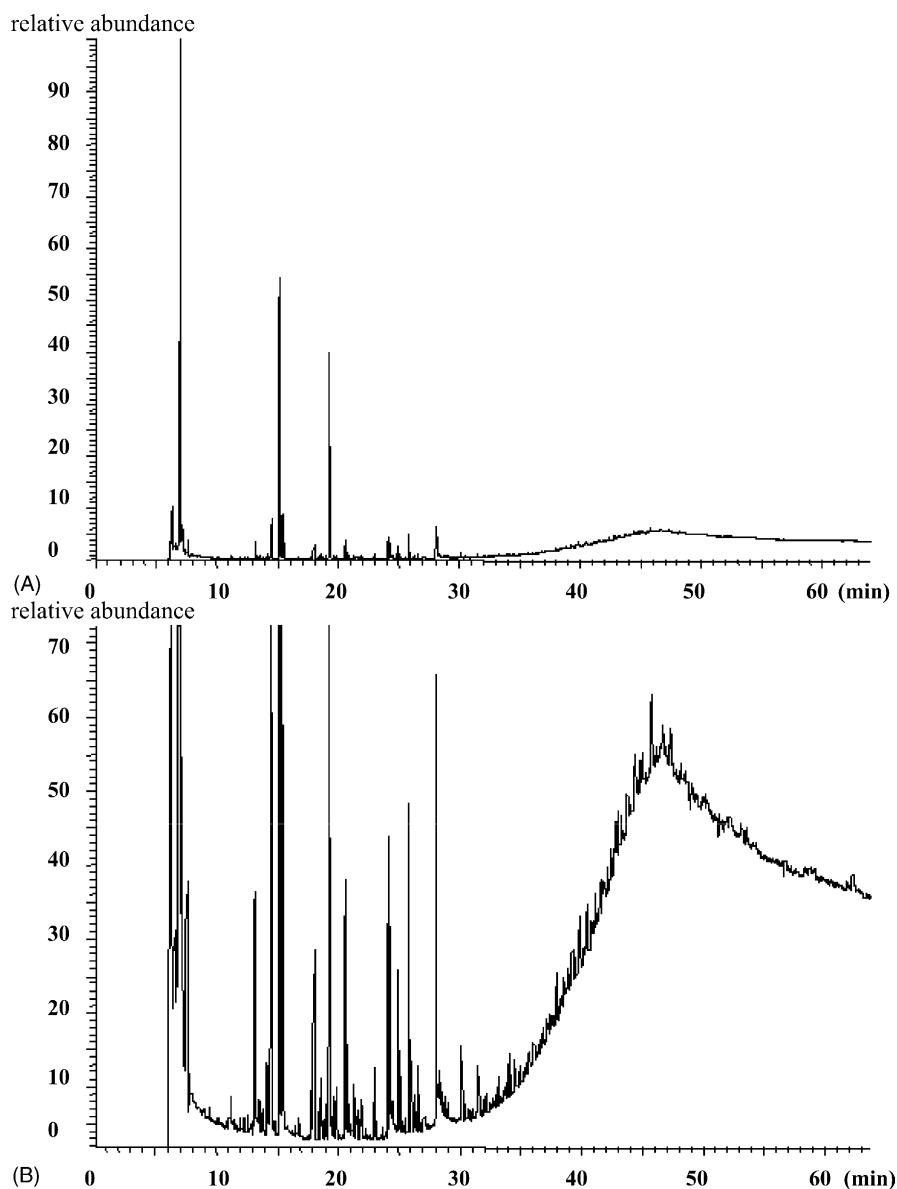


Fig. 2. GC-MS chromatograms obtained by analysis of the toluene Soxhlet extract of polymer P1. (A) Full scale. (B) Enlarged scale. (See Section 2 for other details.)

not sufficient, especially as some major peaks could not be identified using the library.

It was observed that the mass spectra of many unidentified peaks had similar patterns, as is illustrated in Fig. 3. Indeed, similar fragments are observed in each spectrum at  $m/z$ : 55, 57, 97, 99. As numerous peaks show mass spectra with these characteristic

fragments, whatever the polymer, the extraction technique, the extraction solvent, or the extraction time, they may arise from the degradation of the polymer rather than from additives. The basic structure of 99% of the rubbers is based on isobutylene monomers. Sawaguchi et al. [41] observed two main scission mechanisms of this kind of polymer (back-biting

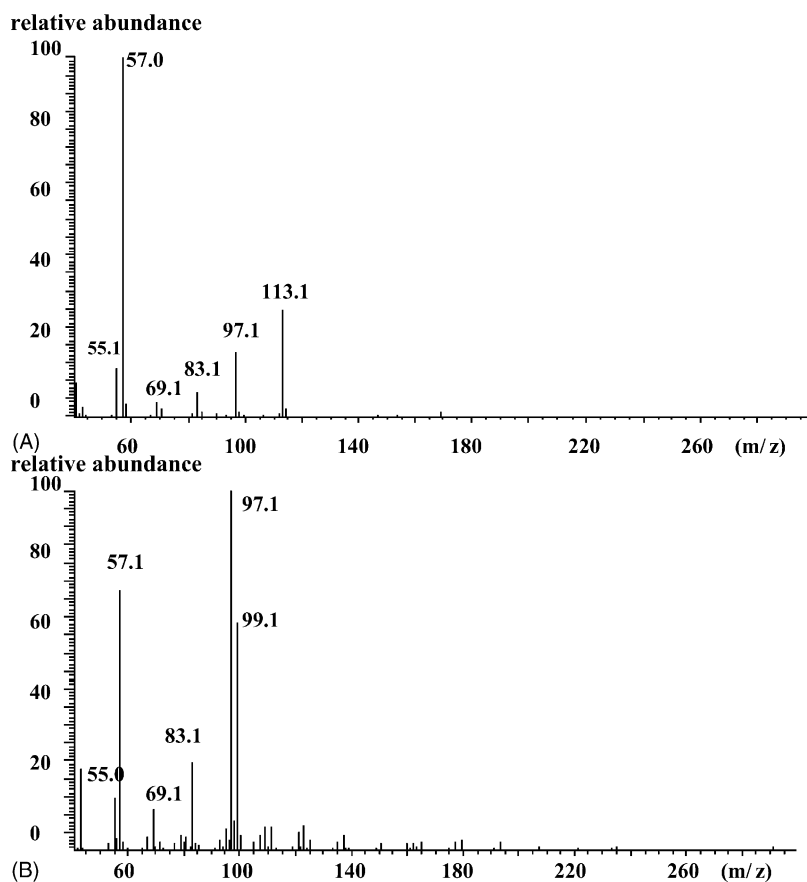


Fig. 3. Mass spectra of the peaks at retention times of: (A) 12.0 min and (B) 41.2 min obtained in the GC–MS analysis of the chloroform Soxhlet extract of polymer P1.

reactions). Depending on the position of the hydrogen abstraction, two types of mono-olefins with a *tert*-butyl end-group and two types of mono-olefins with an isopropyl end-group are formed. Those main fragments have been identified by GC–MS with electron-impact in the positive ionization mode. Fig. 4 presents the mass spectra obtained for each fragment by Sawaguchi et al. [41]. The mass spectra of Fig. 3 can be seen as combinations of the different mass spectra presented in Fig. 4. This permits us to conclude that many of the previously unidentified peaks result from degradation fragments of the basic structure of the rubbers.

The characterization problems are aggravated by the fact that the complex polymer structure leads to such a variety of products that even if a GC peak appears to be resolved, it may comprise several iso-

meric structures or structures that are not present in the database library. The co-elution of the degradation fragments is explained by their similar structures and molecular weights:  $56(n+2)$  for the fragment having the *tert*-butyl end-group and  $56(n+2) - 14$  for the fragments having the isopropyl end-group, where  $(n+2)$  is the initial number of isobutylene groups, which constitute 99% of the rubbers. They will be called oligomers in the remainder of this paper, even if this name is not rigorously correct.

Fig. 5 presents an example of a tentatively interpreted chromatogram of a Soxhlet extract. All the peaks presenting the typical patterns previously observed have been identified as oligomers. With the NIST library and the identification of the degradation products of the rubbers, between 42 and 100% of the



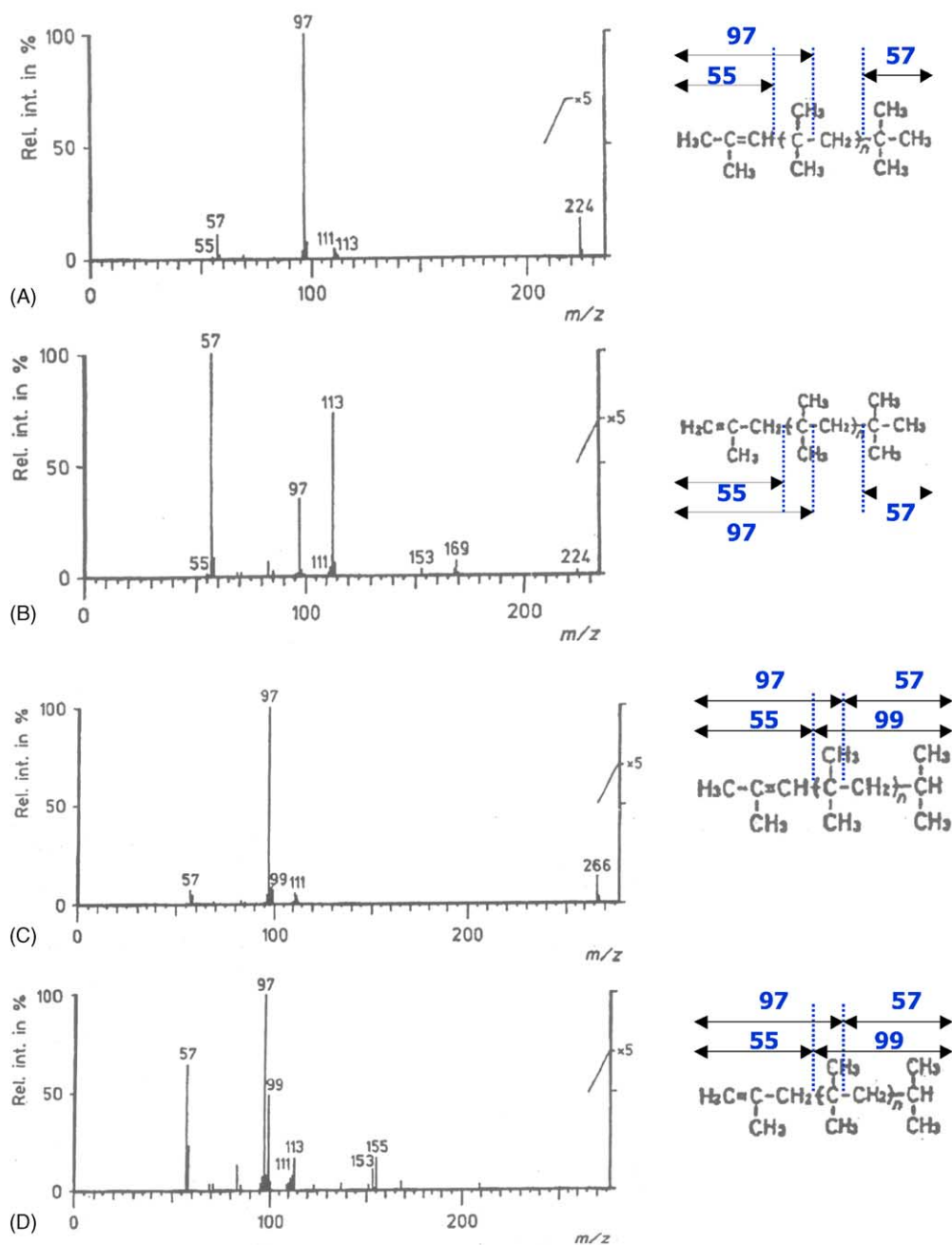


Fig. 4. Mass spectra of the fragments resulting from the chain scission of poly-isobutylene rubbers (A and B) at the terminal *tert*-butyl group or (C and D) at the terminal isopropyl group and indication of the formation of the main ion peaks in each spectrum. Adapted from [41].

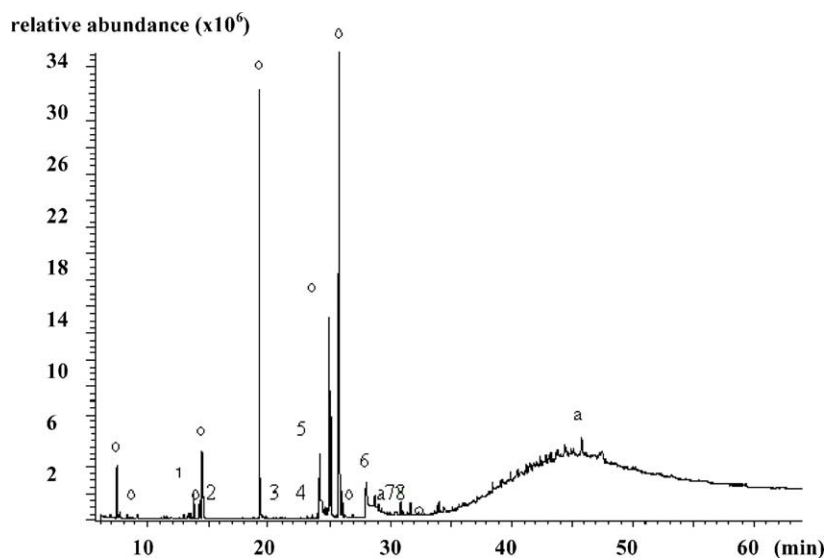


Fig. 5. Chromatogram corresponding to the GC–MS analysis of the chloroform Soxhlet extract of polymer P2. a: alkanes. o: oligomers. 1: 2,6-di-*tert*-butyl-*p*-benzoquinone ( $t_R = 13.8$  min). 2: 2,6-di-*tert*-butyl-*p*-cresol ( $t_R = 14.8$  min). 3: 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde ( $t_R = 20.5$  min). 4: di-isobutyl phthalate ( $t_R = 22.5$  min). 5: palmitic acid ( $t_R = 24.3$  min). 6: stearic acid ( $t_R = 28.0$  min). 7: methyl-10-oxonadecanoate ( $t_R = 30.5$  min). 8:  $\tau$ -stearolactone ( $t_R = 30.8$  min).

total area has currently been identified, with an average of 82%, which is quite satisfactory (this is only a rough indication of the fraction of the total mass of the sample identified, because of the variation in response factors between individual analytes).

### 3.4. Origin of the compounds

The presence of residual monomers was confirmed by the experimental data. Isobutylene, sometimes in dimeric or tetrameric forms, has been identified in the extracts of the rubbers under study. Also, numerous detected compounds are deduced to result from the degradation of the rubber by scission of the polymeric chain. This degradation could have occurred during processing and storage or during the extraction step. Indeed, during the extraction step in the gas or the liquid phase, the rubber samples are exposed to hot media. Such rough conditions may induce the extraction of the compounding ingredients, but also aging of the rubber itself. Aging processes that affect the rubbers may involve oxygen, so-called rubber poisons, heat, or hot media. The extraction conditions that were used involved quite high temperatures. The extractions were carried out

in the presence of oxygen and, consequently, they may have induced a partial degradation of the rubber samples. The products of degradation may be, for example, the so-called oligomers, aldehydes, or ketones [42].

Some aromatic compounds (e.g. toluene, xylene, bibenzyl, and diphenylethylene) have been detected in the toluene Soxhlet extracts and in the headspace extracts. These compounds may also result from the degradation of the rubbers [10,11]. It has been conjectured that degradation processes may arise in two ways: (i) random scission reactions, which will produce oligomers; (ii) secondary reactions, in which primary products decompose or react to form other components, such as aromatic compounds. Some mechanisms to generate aromatic compounds have been proposed, involving for example Diels–Alder reactions. Fuh and Wang [6] described the formation of styrene by an intramolecular process via thermal rearrangement. The aromatic compounds have only been detected in the extracts obtained with headspace or with Soxhlet in toluene, which means at the highest used extraction temperatures (110 and 111 °C, respectively), which induce more degradation or thermal rearrangement.

Among the most relevant compounds detected in the different extracts of the rubber samples, some can be identified as common additives for rubbers. As an example, fatty acids, and especially stearic acid (low cost, wide availability), are common additives, which have been leached from the rubbers under study. Stearic acid is an accelerator activator of the vulcanization process when zinc oxide is used [43,44]. It improves processibility and filler distribution, which are important for the properties of vulcanizates. Fatty acids and fatty-acid esters are also processing aids and they are used as dispersion agents or lubricants.

The detection of 2,6-di-*tert*-butyl-*p*-cresol is consistent with the presence of antidegradants in the rubbers. This compound offers protection against oxygen and heat and, to some extent, heavy-metal rubber poisons, but it shows little or no effect against flex cracking and none against ozone cracking [45]. This compound is widely used. However, because of its high volatility, it is an effective antioxidant only at relatively low temperatures.

Numerous phenolic compounds have been identified. The mono- and difunctional phenols are added as antioxidants in the compounding of rubbers, and they are also used as stabilizers in polymer production. Polymers can be damaged thermo-oxidatively during processing (e.g., during drying) and must therefore be protected. Besides direct protection during production, stabilizers also protect the polymers during storage and use. The stabilizers are generally pure antioxidants, but combinations of non-staining antioxidants with organic phosphates, such as the tri-phenyl phosphate or tri-butyl phosphate detected in some of the extracts, are also used. These kinds of compounds have already been identified as potentially leached material from rubber stoppers [1,3].

Dibenzyl ether has been detected in each rubber under study. This compound is a synthetic plasticizer, which has a limited effect because of its volatility. The detection of phthalate structures in the rubbers under study indicates the presence of additional plasticizers. Some trace aldehydes and ketones detected may be attributable to a slight oxidation of the materials. The aromatic compounds detected in the toluene Soxhlet extracts and in the headspace extracts for the rubbers would also be consistent with the introduction of aromatic oils as plasticizers. Indeed,  $\pi$ - $\pi$  electron interactions between aromatic analytes and solvent may

occur in toluene (the only aromatic solvent used). Hence, from the solvents used only toluene would be able to extract these properly from the material. Thus, it is difficult to draw conclusions about the origin of these compounds: degradation of the polymeric chain or additives.

More than 20 compounds extracted from the rubbers under study can be identified as common additives for rubbers. A number of other peaks may also be due to additives or to degradation products of additives. To conclude, the detected compounds result both from the rubbers themselves and from additives, either in their original forms or as degradation products.

### 3.5. Influence of heating time in headspace extractions

During headspace extractions, the extraction temperature was fixed at 110 °C, which is a temperature sufficient to volatilize the compounds of interest, without degrading the rubber too much and, thus, without generating too many interferent peaks in the chromatograms.

The heating time is one of the key parameters of a headspace extraction. It has to be long enough to allow volatilization of the compounds, but not so long as to waste time. With the rubber P1, three extraction times have been tested: 5, 20, and 50 min. Fig. 6 shows the area of the chromatographic peaks obtained in GC-MS for different compounds leached from the rubber.

For each compound, the maximum area has been obtained with an extraction time of 20 min. An extraction time of 5 min seems insufficient to reach the equilibrium between the gaseous phase and the solid sample. An extraction time of 50 min results in consistently lower recoveries, whereas equal or higher recoveries were to be expected if the equilibrium had not been reached in 20 min. This indicates a loss of analyte components, maybe through the septum or in the pores of the septum, or analyte degradation. Thus, an extraction time of 20 min seems more appropriate in this case.

### 3.6. Influence of the solvent in Soxhlet extractions

As already said, the key parameter of a Soxhlet extraction is the choice of the solvent. Four solvents have been used: toluene, chloroform, acetone,

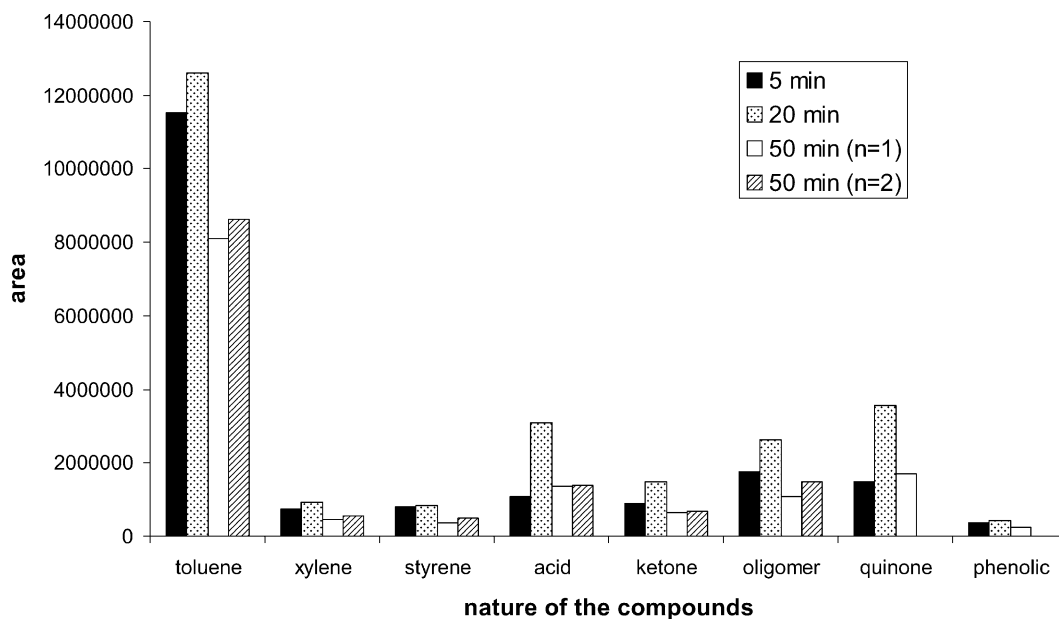


Fig. 6. Influence of the duration of the static headspace extraction on the area of the chromatographic peaks obtained in GC–MS for different compounds leached from rubber P1.

and isopropanol. Some of their properties have been listed in Table 1. Fig. 7 summarizes the influence of the solvent used for the Soxhlet extractions of: (A) P1 and (B) P2 rubbers on the area of the chromatographic peaks detected in GC–MS. In Fig. 7, it appears clearly that different classes of compounds have been detected in the Soxhlet extracts depending on the extraction solvent.

The highest extraction recoveries of acids have been obtained with chloroform, of phenols with toluene, chloroform, and acetone, of oligomers with toluene or chloroform, and of alkanes with toluene or chloroform. To extract phthalates, the four solvents performed equivalently. Thus, the most appropriate extraction solvent for this kind of rubber is chloroform, as it is the best compromise to extract both apolar compounds, such as alkanes and oligomers, and compounds having a polar moiety, such as fatty acids.

### 3.7. Headspace versus Soxhlet extractions

In order to determine the low-molar-mass materials in commercial rubber samples, both gas- and liquid-phase extractions have been carried out. At this point, it is interesting to know if it was necessary to

do both. If only a single extraction is sufficient to fully characterize the low-molecular-mass compounds in rubbers, a waste of time and money should be avoided. Moreover, a headspace extraction requires a minimal sample preparation, induces no analytical interference from the solvent or solvent artefacts, is environmentally friendly, and cost-effective compared to a liquid-phase extraction technique.

In order to verify whether it is really useful to carry out both techniques in parallel for each sample, Table 2 presents the nature of some of the compounds identified by GC–MS in the headspace and Soxhlet extracts of the polymers under study. It appears that some compounds, such as 2,6-di-*tert*-butyl-*p*-cresol, 2,6-di-*tert*-butyl-*p*-benzoquinone, and a ketone with a molecular weight equal to 198, can be extracted and detected by both techniques. This is not the case for other compounds, such as the alkanes, oligomers, aromatic compounds, and fatty acids. Liquid-phase extraction is better for recovering the less-volatile compounds than gas-phase extraction. However, as expected, it induces losses in volatile ones. For compounds of intermediate volatility, both methods are equivalent. Thus, the two extraction techniques that have been performed in this study are complementary.

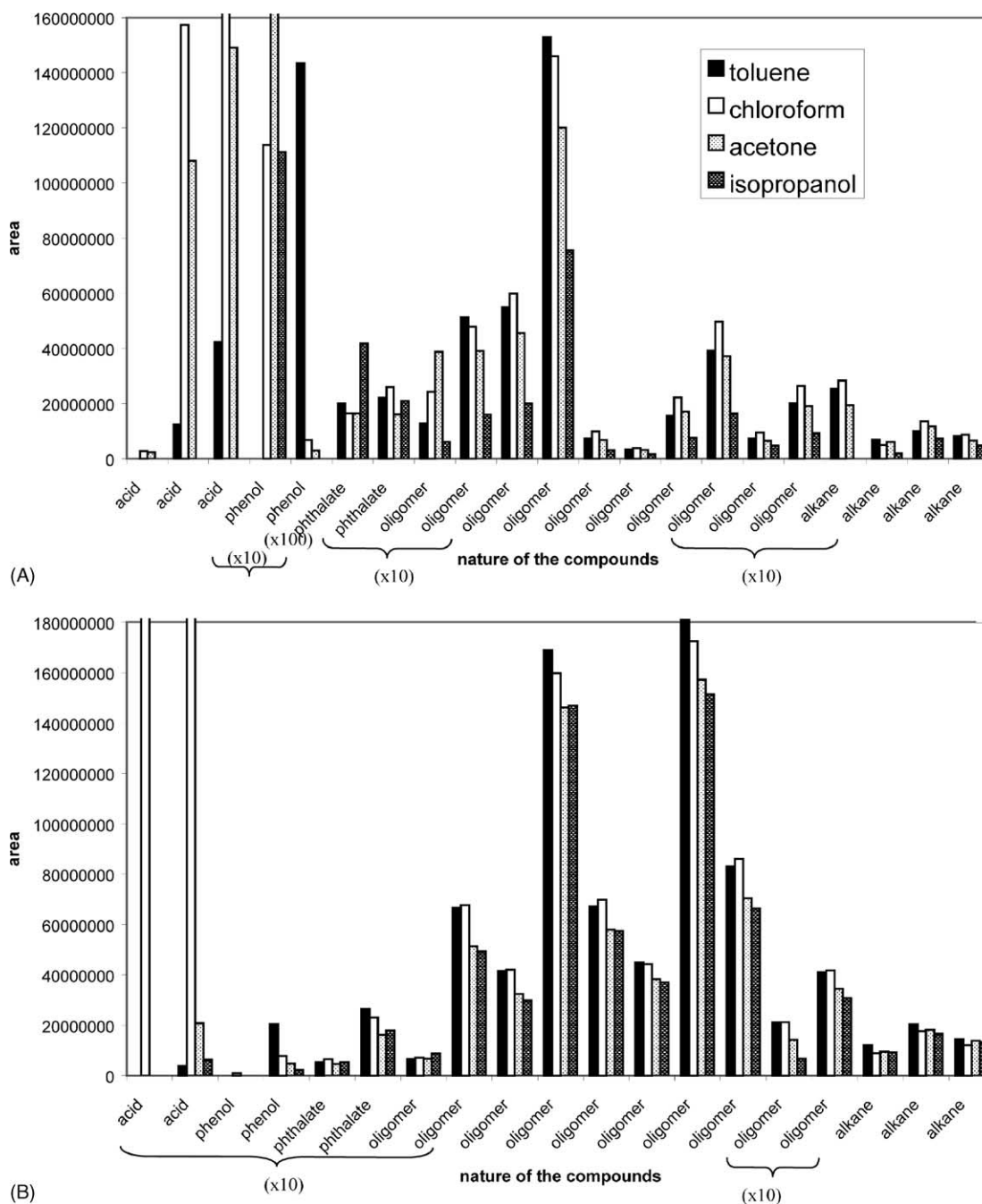


Fig. 7. Influence of the solvent used for the Soxhlet extractions of: (A) P1 and (B) P2 on the area of the chromatographic peaks of different classes of compounds detected in GC-MS.

Table 2

Nature of the compounds identified by GC–MS in the headspace and Soxhlet extracts of the three rubbers under study

	Compounds identified in the extracts obtained with	
	Headspace	Soxhlet
Alkanes	C5 and higher	C9–C30
Oligomers	$T_{\max}$ (elution) = 235 °C	$T_{\max}$ (elution) = 280 °C
Aromatics	92 < MW < 132	168 < MW < 182
Fatty acids	No	228 < MW < 352
Esters	No	Yes
2,6-di- <i>tert</i> -Butyl- <i>p</i> -cresol	Yes	Yes
2,6-di- <i>tert</i> -Butyl- <i>p</i> -benzoquinone	Yes	Yes
Ketone	MW = 198	MW = 198

#### 4. Conclusion

The purpose of the study was to develop a method to identify as many of different low-molar-mass compounds as possible, that can be extracted from rubbers used as packaging materials, in this case butyl rubbers. To a large extent this objective has been reached. Conventional gas- (headspace) and liquid-phase (Soxhlet) extractions have been carried out, which were followed by gas-chromatographic analysis of the extracts. Mass spectrometry allowed tentative identification of most of the extracted compounds, thanks to the use of a library and to knowledge of the degradation mechanism of the basic structure of the rubbers under study. On average, more than 82% of the total peak area has been identified. More than one hundred different compounds have been found and their origins have been explained. It has also been demonstrated that gas- and liquid-phase extraction techniques are complementary for this kind of application.

This study dealt with the identification of the low-molar-mass materials extracted from rubber samples and, therefore, has been performed from a qualitative point of view. It creates the possibility to address quantitative aspects. For environmental and economic reasons it may also be valuable to try and reduce the required amount of organic solvent for a Soxhlet extraction by studying recently introduced extraction methods, such as ASE or MASE. In the future, LC–MS analysis of the liquid extracts has to be performed to analyze and identify the less volatile and/or the more polar (e.g., water extractable) low-molar-mass materials potentially present in rubber samples.

#### References

- [1] X.K. Zhang, R.C. Dutky, H.M. Fales, *Anal. Chem.* 68 (1996) 3288–3289.
- [2] F. Chrzanowski, P.J. Niebergall, R. Mayock, J. Taubin, E. Sugita, *J. Pharm. Sci.* 65 (1976) 735–736.
- [3] C.J. Milano, L.C. Bailey, *PDA J. Pharm. Sci. Technol.* 53 (1999) 202–210.
- [4] Guideline for Submitting Documentation for Packaging for Human Drugs and Biologics, [www.fda.gov/cder/guidance/package.htm](http://www.fda.gov/cder/guidance/package.htm).
- [5] G. Di Pasquale, L. Giambelli, A. Soffientini, R. Paiella, *J. High Resol. Chromatogr.* 8 (1985) 618–622.
- [6] M.-R.S. Fuh, G.-Y. Wang, *Anal. Chim. Acta* 371 (1998) 89–96.
- [7] S.-S. Choi, *J. Anal. Appl. Pyrol.* 55 (2000) 161–170.
- [8] J.A. Hiltz, *J. Anal. Appl. Pyrol.* 55 (2000) 135–150.
- [9] N. Dadvand, R.S. Lehrle, I.W. Parsons, M. Rollinson, I.M. Horn, A.R. Skinner, *Polym. Degrad. Stab.* 67 (2000) 407–419.
- [10] R.S. Lehrle, N. Dadvand, I.W. Parsons, M. Rollinson, I.M. Horn, A.R. Skinner, *Polym. Degrad. Stab.* 70 (2000) 395–407.
- [11] W. Kaminsky, C. Mennerich, J.T. Andersson, S. Gotting, *Polym. Degrad. Stab.* 71 (2001) 39–51.
- [12] M.J. Forrest, *Polym. Test* 20 (2001) 151–158.
- [13] S.-S. Choi, *J. Anal. Appl. Pyrol.* 62 (2002) 319–330.
- [14] J.B. Pausch, I. Sockis, *Rubber Chem. Tech.* 50 (1977) 828.
- [15] E.R.J. Wils, A.G. Hulst, A.L. de Jong, *J. Chromatogr.* 625 (1992) 382–386.
- [16] J.C.J. Bart, *Polym. Test* 20 (2001) 729–740.
- [17] J.D. Vargo, K.L. Olson, *Anal. Chem.* 57 (1985) 672–675.
- [18] J.D. Vargo, K.L. Olson, *J. Chromatogr.* 353 (1986) 215–224.
- [19] C.G. Juo, S.W. Chen, G.R. Her, *Anal. Chim. Acta* 311 (1995) 153–164.
- [20] D.E. Korte, *J. AOAC* 50 (1967) 840–844.
- [21] F. Sevinci, B. Marcato, *J. Chromatogr.* 260 (1983) 507–512.
- [22] M.W. Raynor, K.D. Bartle, I.L. Davies, A. Williams, A.A. Clifford, J.M. Chalmers, B.W. Cook, *Anal. Chem.* 60 (1988) 427–433.
- [23] R. Moulder, J.P. Kithinji, M.W. Raynor, K.D. Bartle, A.A. Clifford, *J. High Resolut. Chromatogr.* 12 (1989) 688–691.

- [24] D. Dilettato, P.J. Arpino, K. Nguyen, A. Bruchet, J. High Resolut. Chromatogr. 14 (1991) 335–342.
- [25] R.P. Lattimer, R.E. Harris, C.K. Rhee, H.-R. Schulten, Anal. Chem. 58 (1986) 3188–3195.
- [26] V. Janda, J. Kriz, J. Vejrosta, K.D. Bartle, J. Chromatogr. A. 669 (1994) 241–245.
- [27] D. Munteanu, A. Isfan, C. Isfan, I. Tincul, Chromatographia 23 (1987) 7–14.
- [28] N. Yagoubi, A. Baillet, C. Mur, D. Baylocq-Ferrier, Chromatographia 35 (1993) 455–458.
- [29] X. Lou, H.-G. Janssen, C.A. Cramers, Anal. Chem. 69 (1997) 1598–1603.
- [30] H.J. Vandenburg, A.A. Clifford, K.D. Bartle, S.A. Zhu, J. Caroll, I.D. Newton, L.M. Garden, Anal. Chem. 70 (1998) 1943–1948.
- [31] L.Y. Zhou, M. Ashraf-Khorassani, L.T. Taylor, J. Chromatogr. A 858 (1999) 209–218.
- [32] B. Marcato, M. Vianello, J. Chromatogr. A 869 (2000) 285–300.
- [33] M. Ashraf-Khorassani, J.M. Levy, J. High Resolut. Chromatogr. 13 (1990) 742–747.
- [34] M. Ashraf-Khorassani, D.S. Boyer, J.M. Levy, J. Chromatogr. Sci. 29 (1991) 517–521.
- [35] H. Daimon, Y. Hirata, Chromatographia 32 (1991) 549–554.
- [36] X. Lou, H.-G. Janssen, C.A. Cramers, J. Chromatogr. Sci. 34 (1996) 282–290.
- [37] A.M. Pinto, L.T. Taylor, J. Chromatogr. A 811 (1998) 163–170.
- [38] J. Brandrup, E.H. Immergut, E.A. Grulke, Polymer Handbook, Wiley-Interscience, 1999.
- [39] A. Townshend (Ed.), Encyclopedia Anal. Sci., Academic Press, London, UK, 1995.
- [40] J.I. Kroschwitz, J.J. Kroschwitz (Eds.), Concise Encyclopedia of Polymer Science Engineering, Wiley, New York, USA, 1990.
- [41] T. Sawaguchi, T. Takesue, T. Ikemura, M. Seno, Macromol. Chem. Phys. 196 (1995) 4139.
- [42] S. Jipa, M. Giurginca, T. Setnescu, R. Setnescu, G. Ivan, I. Mihalcea, Polym. Degrad. Stab. 54 (1996) 1–6.
- [43] J. Leveque, Caoutchoucs et Plastiques 601 (1980) 91–94.
- [44] S. Hawkins, W. Russey, G. Schulz, B. Elvers (Eds.), Ullmann's Encyclopedia of Industrial Chemistry, fifth ed., VCH, New York, USA.
- [45] S.J. Wright, M.J. Dale, P.R.R. Langridge-Smith, Q. Zhan, R. Zenobi, Anal. Chem. 68 (1996) 3585–3594.