Available online at www.sciencedirect.com
SCIENCE DIRECT®

Polymer 45 (2004) 805–813

polymer

www.elsevier.com/locate/polymer

Prevention of plasticizer leaching from PVC medical devices by using organic–inorganic hybrid coatings

M. Messori[a,*], M. Toselli[b], F. Pilati[a], E. Fabbri[a], P. Fabbri[a], L. Pasquali[a], S. Nannarone[a]

[a]*Dipartimento di Ingegneria dei Materiali e dell'Ambiente, Università di Modena e Reggio Emilia, Via Vignolese 905A, 41100 Modena, Italy*
[b]*Dipartimento di Chimica Applicata e Scienza dei Materiali, Università di Bologna, Viale Risorgimento 2, 40136 Bologna, Italy*

Received 4 April 2003; received in revised form 20 November 2003; accepted 2 December 2003

Abstract

α,ω-triethoxysilane terminated poly(ethylene oxide) (PEO-Si) was prepared and used to produce organic/inorganic hybrids by the sol–gel approach. These hybrids were used as coatings for flexible PVC tubes in order to reduce the plasticizer leaching from PVC medical devices. Extraction tests carried out with hexane indicated that all coating composition investigated are able to strongly reduce (about one order of magnitude) the leaching of di-ethylhexyl phthalate in hexane. The best results were obtained by an accurate balance of organic and inorganic phases content. XPS analysis showed a preferential segregation of silica onto the outer surface suggesting that a high inorganic content at the coating–extraction medium interface was present.

Keywords: Organic–inorganic hybrids; Poly(vinyl chloride); Plasticizer leaching

1. Introduction

Plasticized poly(vinyl chloride) (PVC) is widely used in the production of a number of array of medical devices. PVC covers more than 25% of all plastic materials used in medical applications [1]. Major medical uses of PVC include intravenous fluid bags and tubing, blood and plasma bags, enteral feeding and dialysis equipment, catheters, and gloves. Notwithstanding the availability of several plasticizers on the market, the largest group are the phthalate esters [2]. Of 25 different phthalate esters, di-ethylhexyl phthalate (DEHP or DOP) is the one most commonly used in the production of medical devices for its processing advantages.

Over the past 30 years, studies have demonstrated that DEHP can leach to varying degrees from medical devices into patients [3,4]. Despite two decades of research into patient exposures and DEHP toxicity, the human health risks posed by medical devices containing DEHP are uncertain and disputed.

A complete and critical review on the health risks by use of DEHP plasticized PVC has been recently published by Tickner et al. [5] Authors concluded that, in some instances, humans are exposed to clinically important levels of DEHP through PVC medical devices and experimental evidence suggests that DEHP exposures resulting from medical care may lead to adverse health effects in certain groups of patients.

Many studies have been reported about the possibility to use plasticizers alternative to DEHP, such as tris-octyl trimellitate [6], di(*n*-decyl)phthalate [7] or, more recently, polyadipates and poly(ethylene oxide) based block copolymers [8]. However, this approach does not prevent the possibility of plasticizer leaching from the flexible PVC compound.

An alternative approach is represented by the application on the surface of the medical device of a coating with appropriate barrier properties with respect to the migration of relatively low molecular weight PVC additives. Chemical vapour deposition (CVD) is an excellent technique to coat complex substrates like fibres or inner surfaces of tubes [9]. Unfortunately, CVD often suffers from high coating temperatures, which makes it impossible to coat temperature-sensitive materials like polymers. Recently, a plasma-assisted CVD process was developed to coat PVC at very low temperatures with titanium-based layers [10], which seems to have the potential to prevent leaching of plasticizers from PVC. Of course plasma techniques present

---

[*] Corresponding author. Tel.: +39-09-2056212; fax: +39-09-2056243.
E-mail address: messori.massimo@unimore.it (M. Messori).

0032-3861/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.polymer.2003.12.006

drawbacks such as cost, poor adhesion with the substrate, loss of transparency and are limited to small item dimensions.

In this respect, the coating of polymeric surfaces by a wet chemical process can be in most cases an interesting alternative and the preparation of organic–inorganic hybrids by sol–gel process, with its associated mild conditions, represents one of the preferred approach. Organic–inorganic hybrids, also named *ceramers* according to the definition suggested by Wilkes and co-workers [11, 12], represent a class of materials which can be produced by using monomers able to form inorganic network structures (glass-like) and organic networks. As already mentioned, they can be prepared by the sol–gel process starting from liquid precursors such as metal alkoxides (typically tetraethoxysilane and tetramethoxysilane) and organic oligomers preferably with suitable reactive groups [13]. In fact, the intimate mixing favoured by the covalent bonding between organic and inorganic components can prevent the formation of macroscopically separate phases. This may lead to molecular composite materials, having domain sizes in the nanometric scale [14], which cannot be prepared by conventional methods such as mixing of glass with organic polymers because of temperature restraints. Molecular composites have the potential to combine certain structural properties of different classes of materials in ways not accessible by mixtures of macroscopic phases as in the case of classical composites (e.g. glass-fibre reinforced polymers).

Ceramers have a huge potential for applications in a variety of advanced technologies [15,16], especially in the field of functional coatings of several substrates. Ceramers have been already recognised as barrier coating materials to obtain high barrier properties for oxygen, water vapour and volatile organic compounds permeation in the field of polymeric packaging materials [17,18]. In principle, the same barrier properties can be usefully employed to suppress the plasticizer leaching phenomena from plasticized PVC, while preserving transparency thanks to the nanosizes of organic and inorganic domains.

With respect to the reactive oligomers that originate the organic domains, several commercial polymers such as poly(tetramethylene oxide), hydroxy terminated aliphatic polyesters, poly(ethylene-*co*-vinyl alcohol), etc. can be good candidates to be tested. However, in this preliminary work, poly(ethylene oxide) (PEO) was chosen as organic polymer because it is a cheap commercially available aliphatic polyether which can be linear or branched and available in a broad range of molecular masses from less than a few hundred to several million [19]. Another important feature of PEO is its solubility in water and alcohols (typical solvents for tetraethoxysilane and non-solvents for PVC). Finally the presence of ether linkages in PEO may lead to intermolecular association complexes with PVC due to the strong hydrogen bonding character of the ether oxygens and this ability can be usefully employed to obtain a better adhesion to PVC substrate.

Furthermore, PEO is usually characterized by primary hydroxyl end-groups which can be used to obtain oligomers able to react with sol–gel reactants such as metal alkoxides.

The present study deals with preparation and characterization of hybrid materials based on α,ω-triethoxysilane terminated PEO, their application as protective coatings on plasticized PVC substrates and the evaluation of their effect in terms of plasticizer leaching reduction.

2. Experimental

2.1. Materials

α,ω-hydroxyl terminated poly(ethylene oxide) (PEO, purchased from Fluka and with a number average molecular weight of about 600 g/mol), 3-isocyanatopropyltriethoxysilane (ICPTES, Fluka), tetraethoxysilane (TEOS, Aldrich), hydrochloric acid at 37% concentration (Carlo Erba) and ethanol (EtOH, Carlo Erba) were used without further purification.

Poly(vinyl chloride) (PVC) in form of tube was a commercial plasticized product, K70 type, with a DEHP plasticizers contents of 33 wt% and a glass transition temperature of about 272 K (determined by DSC).

^{1}H NMR signals and assignments of PEO and ICPTES are reported in Table 1.

Table 1
^{1}H NMR signals and assignments of (1) poly(ethylene oxide) (PEO), (2) 3-isocyanatopropyltriethoxysilane (ICPTES) and (3) α,ω-triethoxysilane terminated poly(ethylene oxide) (PEO-Si) (s: singlet; t: triplet; q: quadruplet; m: multiplet)

i)	$[\underset{a}{CH_2}-\underset{a}{CH_2}-O]_n$ *a*: 3.6 ppm, (4n)H, s
ii)	$(\underset{a}{CH_3}-\underset{b}{CH_2}-O)_3Si-\underset{c}{CH_2}-\underset{d}{CH_2}-\underset{e}{CH_2}-NCO$ *a*: 1.2 ppm, 9H, t; *b*: 3.8 ppm, 6H, q; *c*: 0.65 ppm, 2H, t; *d*: 1.7 ppm, 2H, m; *e*: 3.3 ppm, 2H, t
iii)	$\sim O[\underset{a}{CH_2}-\underset{a}{CH_2}-O]_{n-1}-\underset{a}{CH_2}-\underset{b}{CH_2}-O-CO-NH-\underset{c}{CH_2}-\underset{d}{CH_2}-\underset{e}{CH_2}-Si(O-\underset{f}{CH_2}-\underset{g}{CH_3})_3$ *a*: 3.6 ppm, (4n-2)H, s; *b*: 4.15 ppm, 4H, m; *c*: 3.15 ppm, 4H, m; *d*: 1.6 ppm, 4H, m; *e*: 0.6 ppm, 4H, t; *f*: 3.8 ppm, 12H, q; *g*: 1.2 ppm, 18H, t

2.2. Preparation of α,ω-triethoxysilane terminated poly(ethylene oxide) (PEO-Si)

α,ω-triethoxysilane terminated poly(ethylene oxide) (PEO-Si) was prepared by bulk reaction of PEO with ICPTES (molar ratio of 1:2). The reaction was carried out in a 50 ml glass flask equipped with a calcium chloride trap and under magnetic stirring, at 120 °C, for 3 h.

The progress of the reaction between hydroxyl terminated PEO and ICPTES was monitored using FT-IR spectroscopy by comparing the broad absorption band of the hydroxyl groups of PEO-OH (at about 3500 cm^{-1}) to the absorption band of the urethane groups (at about 3380 cm^{-1}) and following the disappearing of the absorption band related to isocyanate groups (at 2270 cm^{-1}). It was found that, under the experimental conditions used in this study, the reaction goes to completion within 3 h.

^{1}H NMR signals and assignments of PEO-Si are reported in Table 1.

2.3. Preparation of PEO/silica hybrids (unsupported)

PEO-Si/TEOS mixtures were dissolved in EtOH at a concentration of 40% wt/vol, then water (for the hydrolysis reaction) and hydrochloric acid (as catalyst) were added at the following molar ratios with respect to ethoxide groups of PEO-Si and TEOS: $\text{EtO}-:\text{H}_2\text{O}:\text{HCl} = 1:1:0.1$.

A typical preparation was as follow: 2.0 g of a PEO-Si/TEOS mixture were added to 3 ml of EtOH in a screw-thread glass vial and mixed until a homogeneous solution was obtained. Then water and HCl (37% wt solution) were added under vigorous stirring at room temperature for about 10 min. The closed vial was placed in air circulating oven at the temperature of 70 °C for 3 h in order to allow the progress of the sol–gel reaction. The clear solution was then cast into a closed Petri dish and the solvent was slowly evaporated at room temperature for about 1 week. The samples were also typically post-cured at 60 °C for 24 h under vacuum.

The final hybrids were coded as PEO-Si/SiO$_2$ $x:y$ wt/wt, in which $x:y$ represents the nominal weight ratio of organic and inorganic components assuming the completion of the following sol–gel reactions:

$$\text{Si(OEt)}_4 + x\text{H}_2\text{O} \rightarrow \text{Si(OEt)}_{4-x}(\text{OH})_x + x\text{EtOH}$$

$$(\text{EtO})_3\text{Si–PEO-Si(OEt)}_3 + (x+y)\text{H2O} \rightarrow (\text{EtO})_{3-x}(\text{HO})_x$$

$$\times \text{Si–PEO-Si(OEt)}_{3-y}(\text{OH})_y + (x+y)\text{EtOH}$$

$$\sim \text{Si–OH} + \text{EtO–Si} \sim \rightarrow \sim \text{Si–O–Si} \sim + \text{EtOH}$$

$$\sim \text{Si–OH} + \text{HO–Si} \sim \rightarrow \sim \text{Si–O–Si} \sim + \text{H}_2\text{O}$$

The PEO-Si/SiO$_2$ weight ratio was ranged from 4:1 to 1:1.

2.4. Deposition of PEO/silica hybrids onto PVC substrate

PEO-Si/TEOS sol–gel solutions were prepared according to the procedure described above. Before coating application, the sol–gel reaction was allowed to proceed at 70 °C for 3 h. Then the PEO-Si/silica hybrids solution was deposited onto small pieces of PVC tubes (15 mm length, 7 and 8 mm internal and external diameter) and films (15×15 mm^2), previously washed with EtOH, by manual dip-coating. Samples, after a period of 30 min at room temperature, were subjected to a thermal post-treatment at 60 °C for 24 h under vacuum. A further post-curing treatment at 100 °C for 2 h was carried out in some cases.

In all cases, no variation of the original shape and dimension of the tube was observed.

2.5. Leaching tests

Weighted samples of coated and uncoated PVC tubes were completely immersed in 5 ml of a hexane solution containing toluene (2% wt/vol) as HPLC internal standard. The system was maintained at room temperature under mechanical stirring for various times and the amount of plasticizer leached by PVC samples was measured by HPLC, according to a procedure recently proposed for the determination of DEHP in PVC packaging [20].

2.6. Characterization

FT-IR analysis was performed with a Brucker IFS48 spectrometer. A minimum of 64 scans with a resolution of 2 cm^{-1} was used. Samples were analysed as thin films cast on sodium chloride window.

^{1}H NMR analysis was performed with a Bruker FT NMR Avance DPX200 instrument by using CDCl$_3$ as solvent and tetramethylsilane as internal reference.

Differential scanning calorimetry (DSC) was performed with a TA DSC2010 instrument in the range -100 to $+150$ °C with a heating rate of 10 °C min^{-1}. Melting temperature and degree of crystallinity were determined on the basis of the thermograms collected during the first heating scan. A second heating scan was performed in the case of hybrids in order to evaluated the presence of further sol–gel reaction or melting transitions.

Coated tubes were fractured in liquid nitrogen and fracture surfaces were gold-coated and examined by Scanning electron microscopy (SEM) using a Philips XL-40 instrument.

High performance liquid chromatography (HPLC) analysis was performed using a Waters Isocratic HPLC 1515 metering pump operating at room temperature with a Waters Simmetry® C$_{18}$ column (4.6×150 mm, 5.0 μm). The injected volume was of 20 μl and the eluent was monitored at 270 nm with a Waters UV Absorbance 2487 detector. Separation was performed with a mobile phase consisting of an acetonitrile/methanol mixture (9:1 v/v), pumped at a flow rate of 0.8 ml min^{-1}. Calibration was carried out with standard solutions of DEHP in hexane/toluene mixture having concentrations ranging from 0.5 to 10 g l^{-1}.

During leaching tests, fixed volumes of extracting liquid (20 μl diluted with 400 μl of acetonitrile/methanol 9:1 vol/vol elution mixture) were taken and injected in the HPLC apparatus. Tests were carried out on two or three different coated tubes for each coating composition and the average concentration data are reported.

XPS measurements were carried out on the vacuum-side surface using a V.G. ADES 400 hemispherical analyser and a single-channel detector system. The Mg $K\alpha_{1,2}$ line from a V.G. XR3 dual anode X-ray tube was used as the source, operated at 210 W (14 kV and 15 mA). High-resolution spectra of carbon 1s (C_{1s}), silicon 2p (Si_{2p}) and oxygen 1s (O_{1s}) core level for each sample were acquired. Data were collected at 20° takeoff angle between the sample and the analyser corresponding to a sampling depths of approximately 10–20 Å. Binding energies were referenced to the C–H level at 285.0 eV.

3. Results and discussion

3.1. Preparation of α,ω-triethoxysilane terminated poly(ethylene oxide) (PEO-Si)

Preparation of PEO/silica organic–inorganic hybrid materials by sol–gel approach has been extensively reported in the literature [21,22]. In particular, the crystallization behaviour of hydroxyl terminated PEO in silica networks has been recently investigated by Jiang et al. [23] Authors showed that PEO in the hybrid is able to crystallize when its weight content is higher than 50%. Of course the crystallization of the polymeric phase may result in transparency loss, which in turn can be problematic for several applications. It is widely accepted [14,24,25], that the introduction of triethoxysilane end-groups on the polymeric chains is essential in order to have a better interconnection between organic and inorganic phases and thus to the suppression of crystallization also for high organic contents, thanks to the higher reactivity/miscibility of triethoxysilane groups with respect to the hydroxyl counterpart. For this reason, in this work α,ω-hydroxyl terminated commercial PEO was first functionalized by using ICPTES in order to obtain α,ω-triethoxysilane terminated PEO.

The reaction between PEO and ICPTES was quantitative without the formation of undesired by-products as it was confirmed by ^{1}H NMR spectra. In particular, the complete conversion of isocyanate groups into urethane groups, as indicated by FT-IR analysis, is also confirmed by comparing ^{1}H NMR signals (e) and (c) of Table 1, for (ii) and (iii) structures respectively, corresponding to the methylene groups adjacent to nitrogen atom of isocyanate and urethane groups.

The extent of reaction between hydroxyl end-groups of PEO and ICPTES can be evaluated from the signal (b) in Fig. 1 and in Table 1 for (iii) structure, related to the methylene groups of the polyether linked to urethane groups. Furthermore, the ratio between signals (a) and (b) was consistent with a complete conversion of the hydroxyl end-groups of PEO according to its molecular weight of about 600 g/mol.

Furthermore, it is interesting to note the complete absence of any hydrolysis reaction under the used conditions. In fact, the ratio between ^{1}H NMR signals (g) and (d) or (e) is equal to 4.5 according to completely non-hydrolyzed triethoxysilane end-groups. Alternatively, in the case of hydrolysis reaction the formation of volatile EtOH and Si–OH groups should decrease the above mentioned signal ratio.

3.2. Curing of PEO/silica hybrids (unsupported)

As already mentioned the samples were typically post-cured at different temperatures (room temperature, 60 and 100 °C, respectively) under vacuum.

DSC analysis (first heating scan) carried out on α,ω-hydroxyl terminated PEO and α,ω-triethoxysilane terminated PEO-Si showed melting transitions with T_m values of 20.9 and 4.5 °C, respectively. The degrees of crystallinity (only referred to the PEO segment and determined considering a melting enthalpy of the PEO homopolymer of 195 J g^{-1}) [26] were 71% for PEO and 39% for PEO-Si. As expected, a depression of both melting temperature and degree of crystallinity is noted when hydroxyl end-groups were replaced by bulky triethoxysilane end-groups.

Contrary to PEO-Si precursor, all the prepared PEO-Si/SiO_2 hybrids were fully transparent and DSC analysis showed the absence of melting transitions in the temperature range from − 100 to 30 °C. Both evidences can be assumed as an indication of the formation of a nanocomposite hybrid structure in which PEO and silica phases are intimately interconnected with dimensions less than the wavelength of visible light and that PEO chains bonded to silica domains are not able to organize themselves into crystalline domains or that only very small crystallites are formed.

Different curing treatments were used in order to investigate the effect of the extent of the sol–gel reaction (i.e. the crosslinking degree) on barrier properties and adhesion and properties of the coating. The different curing conditions were: (a) 24 h at room temperature, (b) 24 h at 60 °C and (c) 24 h at 60° plus 2 h at 100 °C. In all cases curing was carried out under vacuum.

A typical DSC thermogram (first heating run) of a PEO-Si/SiO_2 hybrid (cured at room temperature for 24 h) collected in the temperature range from − 100 to 150 °C is reported in Fig. 2. While, as above-mentioned, no melting peaks are present in the low temperature region, a large

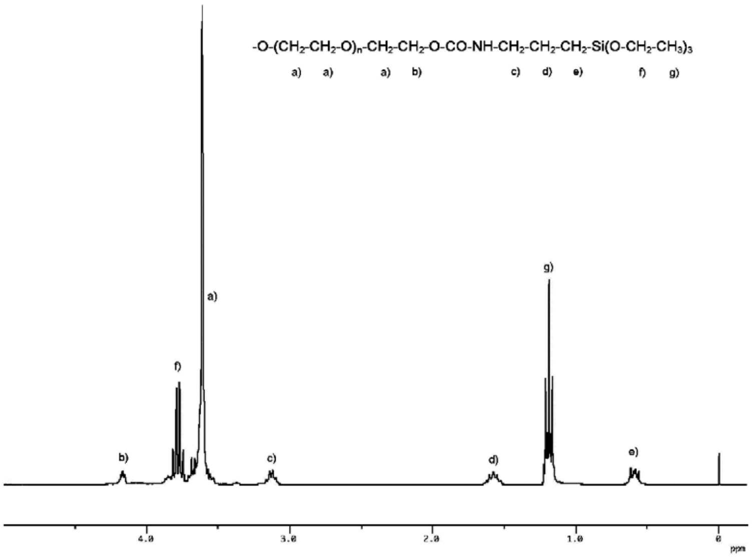

Fig. 1. ^{1}H NMR spectrum of PEO-Si (crude product).

broad endothermic peak is detected starting from room temperature. This peak, which can be attributed to the combined effects of evaporation of residual volatile products (water and EtOH) previously added and/or formed during the sol–gel reaction, is an indication that the condensation reactions are not complete after curing. Such a deduction is supported by further analysis on hybrids subjected to different post-curing treatments as reported in Fig. 3. The thermogram (a) of Fig. 3 is referred to the first heating run on a PEO-Si/SiO$_2$ 1:1 wt/wt hybrid after a post-curing at 60 °C for 24 h. Thermogram (b) is referred to the first heating run on the same sample subjected to a double treatment at 60 °C for 24 h and at 100 °C for 2 h. In this case a marked decrease of the endothermic peak area can be noted with respect to the previous sample due to the post-curing conditions that lead to a further extent of the sol–gel reaction. A completion of the sol–gel reaction was observed after the first heating cycle, in fact the thermograms for the second heating scan were free from any endothermic peaks (see thermogram (c) in Fig. 3).

It is interesting to note that the organic/inorganic ratio had a great influence on the final properties of the hybrid which passed from brittle to flexible film by increasing the PEO-Si/SiO$_2$ ratio.

3.3. PEO/silica hybrids coated onto PVC substrate

Short pieces of PVC tubes were coated with PEO-Si/silica hybrids by manual dip-coating.

Preliminary visual inspections indicated that inorganic-rich hybrid coatings (with a SiO$_2$ content higher than 50% by weight) were characterized by a very poor adhesion to

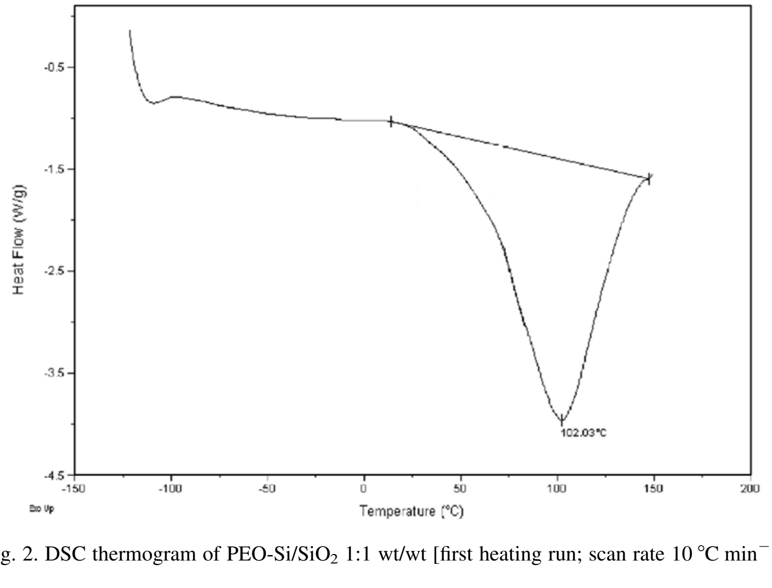

Fig. 2. DSC thermogram of PEO-Si/SiO$_2$ 1:1 wt/wt [first heating run; scan rate 10 °C min^{-1}].

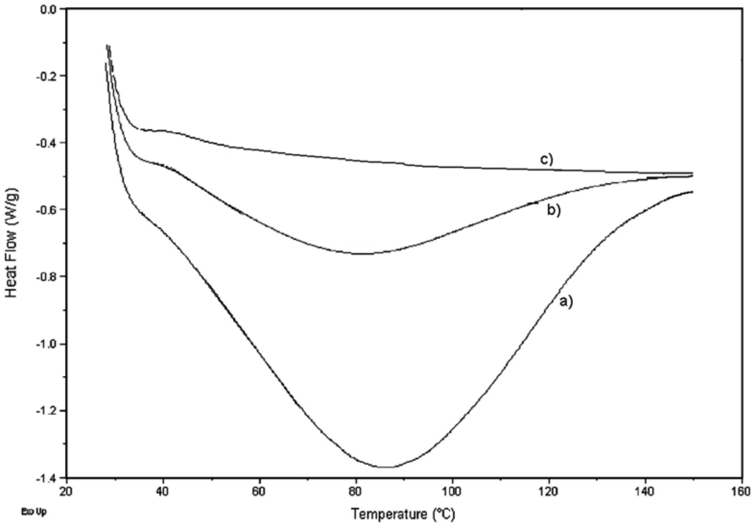

Fig. 3. DSC thermogram of PEO-Si/SiO_2 1:1 wt/wt: (a) post-cured at 60 °C for 24 h [first heating run]; (b) post-cured at 60 °C for 24 h and at 100 °C for 2 h [first heating run]; (c) second heating run of sample (b) [scan rate 10 °C min^{-1} for all runs].

PVC substrate leading to coated tubes with poor aesthetic properties. On the contrary, by increasing the organic phase content in the hybrid a marked improvement in terms of coating flexibility and adhesion was clearly evident. On the basis of these evidences, only coating compositions with an organic phase of 50% by weight or higher were prepared and applied onto PVC substrates. For these samples, the thickness of the coatings and their adhesion with the substrate were investigated by SEM analysis. Typical micrographs are shown in Fig. 4 for PVC tubes coated with PEO-Si/SiO_2 2/1 and 4/1 wt/wt, respectively, and fractured in liquid nitrogen. From these figures it appears that compact and homogenous coatings having a good adhesion with the substrate were obtained. Similar results were obtained also for other reaction conditions. Coating thicknesses ranging from 3 to 7 μm was observed and an average value of 5 μm can be assumed for all samples.

3.4. XPS surface characterization of coatings

Information about the surface chemical composition of coated PVC films were obtained by XPS analysis. Due to the presence of a typical hydrocarbon contamination, only spectra of Si_{2p} and O_{1s} core level were used to evaluate the surface chemical composition. Results are reported in terms of Si/O atomic ratio after correction by appropriate sensitivity factors calculated on the basis of a pure SiO_2 sample used as reference. Of course, in the calculation the Si/O atomic ratio was taken as 0.5 for pure SiO_2.

From the surface composition data reported in Table 2, a strong silica surface enrichment compared to the correspondent bulk composition was noted for almost all the investigated samples indicating a preferential segregation of silica domains onto the air-coating interface.

The preferential segregation of SiO_2 onto the outer surface, makes the very surface of the coating almost

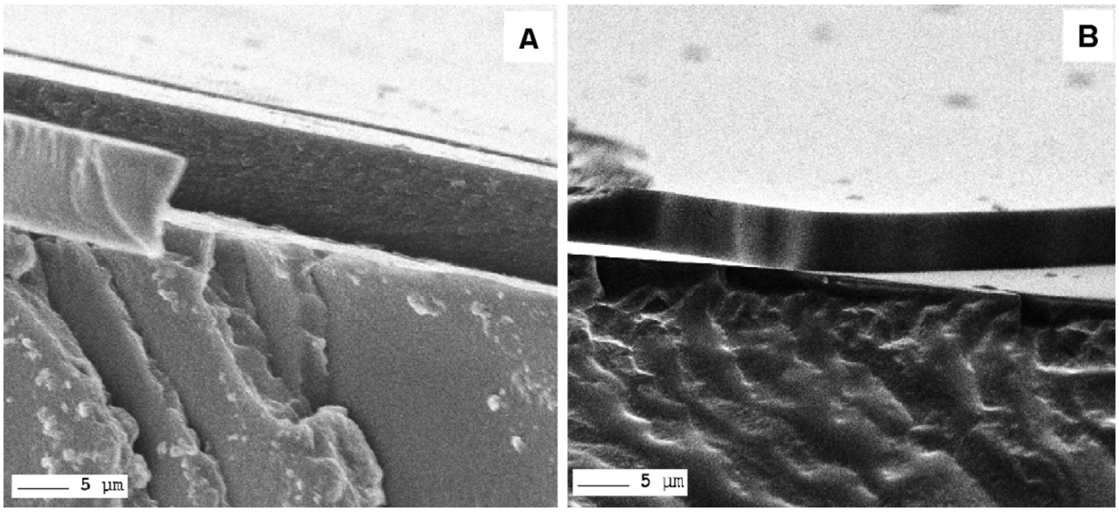

Fig. 4. SEM micrographs of the edge view of fracture surface of PVC tubes coated with PEO-Si/SiO_2 2/1 wt/wt (A) and PEO-Si/SiO_2 4/1 wt/wt (B).

Table 2
XPS analysis of outer surface of PVC films coated with PEO-Si/SiO_2

Coating composition	Si/O atomic ratio	
	Surface[a]	Bulk[b]
PEO-Si/SiO_2 4:1 wt/wt	0.25	0.20
PEO-Si/SiO_2 3:1 wt/wt	0.42	0.22
PEO-Si/SiO_2 2:1 wt/wt	0.45	0.26
PEO-Si/SiO_2 1:1 wt/wt	0.43	0.33

[a] From XPS analysis.
[b] From initial composition.

completely inorganic and should contribute to greatly improve the barrier properties of the hybrid. On the other hand, an enrichment of the organic phase may result at the coating–PVC interface due to the greater chemical affinity of PEO and PVC, leading to an improvement of adhesion between the coating and the substrate.

3.5. Plasticizer leaching tests

In the literature, several factors are discussed that influence the rate of extraction of a plasticizer in the presence of a particular medium. At constant temperature, the surface area of the test specimen and the diffusion rate of the plasticizer through PVC control the plasticizer's extraction rate. The efficiency at which a given test medium can remove plasticizer from the surface of a test specimen represents the first level of control on the rate of plasticizer extraction or migration.

Additionally, the ability of the medium to permeate into the flexible PVC device can be an additional factor influencing the diffusion rates of the plasticizer and its compatibility with PVC.

Very low plasticizer extraction rates were evidenced by preliminary leaching tests carried out with physiological solutions due to the poor thermodynamic affinity of plasticizer and water and to the small surface/volume ratio of investigated tubes. For this reason, in the present study the plasticizer leaching was evaluated by using another solvent. However, it has to be emphasized that even though PEO is recognized to be a very hydrophilic polymer, we did not observe swelling or removal of ceramers from ceramer-coated PVC tubes, also after long times of dipping in such aqueous solutions. According to the literature [20] we used hexane as extraction medium, a good solvent for DEHP. Even if hexane extraction could not be representative of a real medical exposure medium, the use of a such aggressive extraction agent (more aggressive of other proposed media such as water, soapy water, and mineral oil) was preferred in order to obtain a fast preliminary indication of the possibility to use organic–inorganic hybrid coatings for the prevention of plasticizer leaching. Indeed, in our systems hexane was able to extract all the plasticizer of the uncoated specimens in less than 30 h.

Leaching test results are shown in Fig. 5 in which the amount of DEHP leached (expressed as percentage of the total plasticizer content) is plotted against the extraction time and reported as average values over two HPLC runs for each of two or three different tubes.

First of all, it has to be emphasized that extraction tests for all coating compositions investigated showed a strong reduction of the leaching of DEHP with respect to the uncoated reference. This is particularly interesting in view of the very different mechanical behaviour of pure ceramer films containing different percentages of silica (from brittle to relatively tough, decreasing the percentage of silica) and because also ceramer coatings with an amount of silica as low as 20 wt% proved to be a good barrier against leaching.

In particular the best performances were obtained for intermediate coating compositions (PEO-Si/SiO_2 2:1 wt/wt and 3:1 wt/wt), which showed the highest decrease of the amount of extracted DEHP with respect to the reference (about one order of magnitude for the extraction time range investigated). These results seem to indicate that an accurate balance of organic and inorganic phases is required to obtain the best performance of the coating. Probably, a proper amount of PEO is necessary to obtain good adhesion between coating and PVC substrate while a minimum amount of silica phase is necessary to improve barrier properties towards to DEHP migration: the best behaviour for our investigated systems was shown by a coating with a silica weight content ranging from 25 to 33%.

It is also interesting to note that, according to the XPS results reported in Table 2, the very surface composition of the coatings seems to play a relevant role with respect to DEHP extraction. In fact, the coatings PEO-Si/SiO_2 2:1 wt/wt and PEO-Si/SiO_2 3:1 wt/wt, which showed the highest barriers against DEHP removal, have a surface composition similar or higher than that of the silica-richest sample PEO-Si/SiO_2 1:1 wt/wt.

The poorer anti-leaching properties showed by the organic-richest coating PEO-Si/SiO_2 4:1 wt/wt can be explained on the basis of its surface chemical composition in which the inorganic component content is too low to impart the desired barrier properties. On the other hand, also the inorganic-richest coating PEO-Si/SiO_2 1:1 wt/wt exhibited low performance notwithstanding a strong silica surface enrichment. In this case the low adhesion between coating and substrate, typical for hybrids with high silica content, and the brittleness of the coating that may lead to surface cracks may play a negative role on the final anti-leaching characteristics.

As demonstrated by DSC curves, curing of the ceramers at 60 °C for one day does not allow a complete reaction of alkoxy groups and a progress of the reaction by a further heating at a higher temperature could be a way to modify the barrier properties of the coatings. In order to verify if the performance of the coatings can be improved by an increase of crosslinking density, a second post-curing treatment (2 h 100 °C) was applied to the investigated system and leaching tests were repeated.

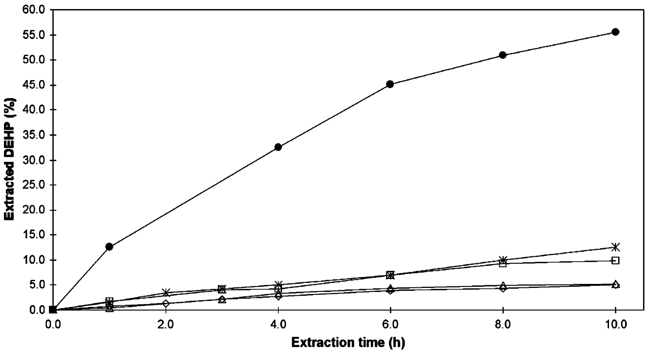

Fig. 5. Amount of leached plasticizer (expressed as percentage with respect to the maximum extractable DEHP) vs. extraction time (coating composition: ●: uncoated PVC; □ PEO-Si/SiO_2 1:1 wt/wt; △ PEO-Si/SiO_2 2:1 wt/wt; ∗ PEO-Si/SiO_2 3:1 wt/wt; ∗ PEO-Si/SiO_2 4:1 wt/wt).

The amount of leached plasticizer after 6 h of extraction in hexane for different post-curing conditions are reported in Table 3.

Contrary to what expected, in the case of the inorganic-richest hybrid coating (PEO-Si/SiO_2 1:1 wt/wt) a further post-curing treatment led to a marked worsening of the anti-leaching properties with an amount of extracted DEHP after 6 h which increases from 7 to 17%. Presumably, in this case the increase of crosslinking density led to very brittle coatings that may crack on cooling or handling and probably with a poorer adhesion to the substrate. This in turn affect negatively the anti-leaching properties.

For the other coating compositions, the presence of a higher amount of organic phase seems to be able to impart a sufficiently high flexibility to the coating films and a further progress of the reaction resulted in better barrier properties for PEO-Si/SiO_2 4:1 wt/wt as it is clearly evidenced in Table 3.

4. Conclusions

Ceramers with different organic/inorganic ratios were prepared by the sol–gel approach by reacting α,ω-triethoxysilane terminated PEO (PEO-Si) with TEOS. Visual transparency and DSC data were in agreement with the formation of a nanocomposite structure with a high level of interpenetration between PEO and silica phases. PEO-Si/SiO_2 ceramers were subsequently used to dip-coat PVC tubes in order to verify if these coatings are able to prevent or reduce the plasticizer leaching from PVC medical devices and extraction tests with hexane were carried out for this purpose. The results indicated that all coating composition investigated are able to strongly reduce the leaching of DEHP with respect to the uncoated control even when the content of inorganic phase was as low as 20 wt%.

This important result suggests that barrier and mechanical properties can be properly adjusted to optimise performances by a suitable choice of reactants, reactants concentration and reaction conditions. Indeed, the best results were obtained for intermediate coating compositions indicating that a fundamental role for final performance of the coating was played by an accurate balancing of organic and inorganic phases content, which probably controls the adhesion and the barrier properties.

Even though the results obtained are probably far to be optimised for application to biomedical devices (for this purpose an extended work has to be done to understand the effects of chemical nature of the organic and inorganic phase, of molecular weight of the oligomer, of coating thickness and of reaction conditions), they gave interesting indication of the role of some important variable such as organic/inorganic ratio and extent of reaction.

In addition, these results suggest that a relevant role with respect to an effective barrier against plasticizer diffusion is played by the surface segregation of silica occurring during curing. In fact, XPS results combined with leaching-test data support the evidence that a high inorganic content at the coating–extraction medium interface contribute to improve barrier properties toward plasticizer extraction.

Table 3
Amount of leached plasticizer (expressed as percentage with respect to the maximum extractable DEHP) after 6 h of extraction for different curing conditions

Coating composition	Extracted DEHP after 6 h (%)	
	Curing: 24 h at 60 °C	Curing: 24 h at 60 °C, 2 h at 100 °C
PEO-Si/SiO_2 4:1 wt/wt	6.9	4.9
PEO-Si/SiO_2 3:1 wt/wt	4.0	4.0
PEO-Si/SiO_2 2:1 wt/wt	4.4	3.7
PEO-Si/SiO_2 1:1 wt/wt	6.9	17.0

References

[1] Huber W, Grasl-Kraupp B, Schulte-Hermann R. Crit Rev Toxicol 1996;26:365–481.

[2] Plasticizers. Chemical economics handbook, Palo Alto: Stanford Research Associates (SRI) International; 1996.

[3] Jaeger R, Rubin R. Lancet 1970;2:778.

[4] Hillman L, Goodwin S, Sherman W. N Engl J Med 1975;292(8): 381–6.

[5] Tickner JA, Schettler T, Guidotti T, McCally M, Rossi M. Am J Ind Med 2001;39(1):100–11.

[6] Smith A, Thrussell IR, Johnson GW. Clin Nutr 1989;8(3):173–7.

[7] Shimizu T, Kouketsu K, Morishima Y, Goto S, Hasegawa I, Kamiya T, Tamura Y, Kora S. Transfusion 1989;29(4):292–7.

[8] Jin HL, Kyeong OK, Young MJ. J Biomed Mater Res 1999;48(3): 328–34.

[9] Rees WS. CVD of nonmetals. Weinheim: Wiley; 1996.

[10] Breme F, Buttstaedt J, Emig G. Thin Solid Films 2000;377–378: 755–9.

[11] Huang HH, Orler B, Wilkes GL. Polym Bull 1985;14:557–64.

[12] Huang HH, Wilkes GL, Carlson JG. Polymer 1989;30:2001–12.

[13] Brinker CJ, Scherer GW. Sol–gel science. Boston: Academic Press; 1990.

[14] Messori M, Toselli M, Pilati F, Fabbri E, Fabbri P, Busoli S, Pasquali L, Nannarone S. Polymer 2003;44(16):4463–70.

[15] Haas KH, Wolter H. Curr Opin Solid State Mater Sci 1999;4:571–80.

[16] Uhlmann DR, Teowee G. J Sol–Gel Sci Technol 1998;13:153–62.

[17] Amberg-Schwab S, Katschorek H, Weber U, Hoffmann M, Burger A. J Sol–Gel Sci Technol 2000;19(1–3):125–9.

[18] Amberg-Schwab S, Hoffmann S, Bader S, Gessler M. J Sol–Gel Sci Technol 1998;13(1–3):141–6.

[19] Bailey FE, Koleske JV. Polyoxyalkylenes, 6th ed. Ullmann's encyclopedia of industrial chemistry, Wiley-VCH; 2003. Release 2003.

[20] Aignasse MF, Prognon P, Stachowicz M, Gheyouche R, Pradeau D. Int J Pharm 1995;113(2):241–6.

[21] Wojcik AB, Ting A, Klein LC. Mater Sci Engng C, Biomimetic Mater, Sensors Syst 1998;C6(2,3):115–20.

[22] Klein LC, Beaudry CL, Wojcik AB, Mandanas M. Ceram Trans 1998; 81:273–80.

[23] Jiang S, Yu D, Ji X, An L, Jiang B. Polymer 2000;41:2041–6.

[24] Kohjiya S, Ochiai K, Yamashita S, Yamashita S. Polym Gels: Fundamentals and Biomedical Applications. New York: Plenum; 1991.

[25] Tian D, Dubois Ph, Jerome R. Polymer 1996;37:3983–7.

[26] Miller RL. Crystallographic data and meting points for various polymers. In: Brandrup J, Immergut EH, Grulke EA, editors. Polymer handbook, 4th ed. New York: Wiley; 1999. Section VI-1.