J Mater Sci: Mater Med (2009) 20:1659–1668
DOI 10.1007/s10856-009-3731-3

Segmented biopolyurethanes for medical applications

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Received: 5 January 2009 / Accepted: 4 March 2009 / Published online: 19 March 2009

Abstract Polyurethanes are one of the most popular groups of biomaterials applied for medical devices. Their segmented block copolymeric character endows them a wide range of versatility in terms of tailoring their physical properties, blood and tissue compatibility. Polyester- and polyether-urethanes have been modified with hydroxypropyl cellulose aiming the change of their surface and bulk characteristics to confer them biomaterial qualities. In this respect, dynamic contact angle measurements, dynamic mechanical analyses accompanied by mechanical testing have been done. Platelet adhesion test has been carried out in vitro and the use of hydroxypropyl cellulose in the polyurethane matrix reduces the platelet adhesion and therefore recommends them as candidates for biocompatible materials.

1 Introduction

The selection of the materials used in the construction of prostheses and implants is basically focused on their ability to maintain mechanical, chemical and structural integrity and on various characteristics which allow this function to substitute any organ or tissue properly and exhibit safe, effective performance within the body. Biocompatibility has been defined as the ability of a material to perform with an appropriate host response in a specific application. Any material used satisfactorily in orthopedic surgery may be inappropriate for cardiovascular applications because of its thrombogenic properties. Any deleterious effects may be encountered if used under stress–strain conditions. Biocompatibility of a material can be simulated by comparing its behaviour to reference materials in standardized experimental condition. Biocompatibility is in fact, complex being interpreted as a series of events of interactions happening at the tissue/material interface, allowing the identification of those materials with surface characteristics and/or polymer chemistry more biocompatible; these interactions are influenced by intrinsic characteristics of the material, the confrontational circumstances related to the bioactive and biocooperative responses.

Blood contact assays have been developed and include tests investigating the adhesion or activation of blood cells, proteins, and macromolecules such as those found in the complement or coagulation cascade. Other biocompatibility tests have been tentatively proposed and involve analytical testing or observations of physiological phenomena, reactions or surface properties attributable to a specific application such as protein adsorption characteristics.

Blood compatibility of polyurethane polymers have been widely used for biomedical applications such as artificial hearts, intraortic ballons, pacemaker leads, heart valves and haemodialysis membranes [1–8]. Polyurethane is the general name of a family of synthetic copolymers that contain the urethane chemical group in their chemical structure. Their huge diversity of applications (elastomers, foams, paints, adhesives, etc.) originates from the tailorable chemistry of polyurethanes, i.e. chemical composition by choosing different raw materials, different proportions and molecular weights, processing conditions, able to

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accommodate specific requirements. As to biomaterials, segmented block-copolyurethanes are frequently synthesized, starting from a polyol, which is the soft segment, a diisocyanate and a chain extender. The combination of the chain extender and the diisocyanate components is referred to as the hard segment of the polymer. The diisocyanate can react with either the polyol or chain extender. In linear polyurethanes the three components have a functionality of two. If a branched or cross-linked material is desired, multifunctional polyols, isocyanates, and chain extenders can be incorporated into the formulation. The statistical nature of copolymerization leads to a distribution in segment length and molecular weight. Conventional polyols are usually polyethers (–R–O–R′–) or polyesters (–R–CO–O–R′–) with end-capped hydroxyl groups. It was soon realized that biocompatibility is intimately related to their microphase separated structure composed of hard and soft segment domains [9–13]. The relationship between blood response and hard/soft segment for Biomer^{TM} showed that hard segment of polyurethane were highly thrombogenic in platelet retention experiments [14]. Two reasons were proposed to explain the high thrombogenicity of hard segment: the high crystallinity of the polymers and strong hydrogen bonding of their surface. Surface mobility may play a role in the interaction of polymers with biological systems [15].

Hydrophilicity describes a surface characteristic promoting water absorption in the polymer which has been associated with blood response. An optimization of the hydrophobic–hydrophilic ratio as surface modification has been shown to improve blood compatibility by reducing platelet adhesion, biostability and antithrombogenicity characteristics [16, 17].

Our previous publications [18, 19], presented the synthesis and properties of a series of new polyurethanes having incorporated hydroxypropyl cellulose. The present paper is dealing with the effect of the chemical structure of segmented biopolyurethanes on surface properties (dynamic contact angle measurements), on dynamical mechanical thermal analysis, mechanical properties and platelet adhesion.

2 Experimental part

2.1 Materials

Poly(ethylene adipate)diol (PEA, $M_n = 2{,}000$ g/mol) was purchased from Fibrex SA Savinesti, Romania; Polytetrahydrofuran (PTHF, $M_n = 2{,}000$ g/mol) and poly (propylene)glycol (PPG, $M_n = 2{,}000$ g/mol) are commercial products purchased from BASF; 4,4′-Diphenylmethane diisocyanate (MDI, Merck) was distilled, prior to utilization, under reduced pressure; Hydroxypropyl cellulose LF (HPC, Klucel) and ethylene glycol (EG, Merck) was used as received.

2.2 Preparation of polyurethanes

The polyurethanes were prepared by solution polymerization using *N*,*N*-Dimethylformamide (DMF, Fluka) as solvent. First, the NCO-terminated prepolymer was prepared by dehydrating the macrodiol for 3 h at 90°C under vacuum followed by adding MDI to the vigorously stirred macrodiol. The reaction between diisocyanate and macrodiol took place for 1.5 h under nitrogen atmosphere at 90°C. The temperature was lowered to 70°C and the ethylene glycol was added. The reaction continued for 1 h, at 70°C. At the end a solution of hydroxypropyl cellulose in 10 ml DMF was added and the stirring continued for another 0.5 h. One polyurethane sample was prepared without adding at the end the cellulose derivative, just for comparison (PEA–PU). For the other polyurethane samples, PEA–HPC, PTHF–HPC and PPG–HPC, the sample code is referring at the soft segment and hydroxypropyl cellulose. The resulting polymers were precipitated in water and dried under vacuum for several days.

In Table 1 are provided the compositional parameters and the average molecular weights values, polydispersity indices (GPC) and glass transition temperatures (DSC).

2.3 Preparation of polyurethane film samples

The polyurethane film samples were prepared by precipitating in warm water of polyurethane solution resulted after

Table 1 Compositional parameters, number-average molecular weights, polydispersity indices and glass transition temperatures

Sample code	Composition macrodiol/MDI/E.G/HPC (wt%)	% N^a	M_n	M_w/M_n	T_g^b (°C)
PEA-PU	55.56/37.50/6.94/0	3.83	109,613	1.287	−27
PEA-HPC	52.24/36.57/7.27/3.92	3.5	134,522	1.865	−23
PTHF-HPC	52.24/36.57/7.27/3.92	3.4	70,291	1.590	−74
PPG-HPC	52.24/36.57/7.27/3.92	3.35	72,951	1.669	−41

[a] From elemental analyses

[b] From DSC second heating run, 10°C/min

synthesis, followed by drying, for several days at room temperature and under vacuum for further 12 h. All these films were used for the research investigations presented in this paper.

2.4 Measurements

Gel permeation chromatography (GPC) measurements were carried out by employing a PL-EMD 950 Evaporative Mass Detector instrument using DMF as eluent after calibration with polystyrene standards.

A Perkin–Elmer DSC-7 was used for thermal analysis and operated under nitrogen atmosphere with a heating rate of 10°C/min and temperature range −150°C to 250°C.

Dynamic contact angle were performed by the Wilhelmy plate technique, using a Sigma 700 precision tensiometer, produced by KSV Instruments. The sample plate dimensions were 50 × 8 mm and rate of immersion-emersion was 5 mm/min in water. Immersion depth was 5 mm in standard conditions. All measurements were the average of 3 contact angle measurements of samples. Also, Wilhelmy plate method utilizes the interaction of a platinum plate with the surface being tested. This is a method for determination of the surface tension. Solutions of the polyurethane sample 4 g/dl in DMF were employed and DMF as a starting solvent. Generally low values of contact angle indicate that liquid spreads or wets well, while high values indicate poor wetting. If the angle is less than 90° the liquid is said to wet the solid, and when it is greater than 90° it is said to be non-wetting. The value of static contact angles are found to depend on the recent history of the interaction. When the drop has recently expanded the angle is said to represent the 'advanced' contact angle. When the drop has recently contracted the angle is said to represent the 'receded' contact angle. These angles fall within a range with advanced angles approaching a maximum value and receded angles approaching a minimum value. If the three phase (liquid/solid/vapor) boundary is in actual motion the angles produced are called Dynamic Contact Angles and are referred to as 'advancing' and 'receding' angles. The difference between 'advancing' and 'receding' is that in the static case motion is incipient in the dynamic case motion is actual. The difference between the maximum (advancing) and minimum (receding) contact angle values is called the contact angle hysteresis. A great deal of research has gone into analysis of the significance of hysteresis. When wetting with water, hydrophobic domains will pin the motion of the contact line as the liquid advances thus increasing the contact angles. When the water recedes the hydrophilic domains will hold back the draining motion of the contact line thus decreasing the contact angle. From this analysis it can be seen that, when testing with water, advancing angles will be sensitive to the hydrophobic domains and receding angles will characterize the hydrophilic domains on the surface. Tensiometry involves measuring the forces of interaction as a solid is contacted with a test liquid.

Dynamic mechanical experiments were made using a Diamond Perkin–Elmer instrument that applies a sinusoidal stress to the sample and measures the resulting strain. The force amplitude used was well within the linear viscoelastic range for all investigated samples. The thermomechanical properties were evaluated for a heating rate of 4°C/min and a frequency of 1 Hz, under nitrogen atmosphere. Temperature investigated range −150°C to 200°C. The variations of the storage modulus E', loss modulus E'' and tension loss tangent, tanδ as a function of temperature were obtained. Polyurethanes are characterized by their high and heterogeneous morphology and by important intermolecular forces that determine their mechanical behaviour. In such way that the forces applied to polymers in general and the deformations produced by those are not thoroughly local. Consequently the response of the polymer to the foreign solicitations is extended in a wide time interval (relaxation time), originating its peculiar viscoelastic behaviour. While energy supplied to a perfectly elastic material is stored and a purely liquid dissipates it, polymeric materials dissipate a part of energy that excites to them. DMA is a sensitive technique used to study and characterize macroscopic responses of the materials as well local internal motions. By monitoring property changes with respect to the temperature and/or frequency of oscillation, the mechanical dynamic response of the material is referred to two distinct parts: an elastic part (E', storage modulus) and a viscous component (E'', loss modulus). The damping is called tan delta, loss factor or loss tangent, tan $\delta = E''/E'$. With increasing temperature different physical states are revealed: glass, leathery, rubbery and elastic of rubbery flow, viscous flow. The glass transition is easily identified from dynamical mechanical data because of the sharp drop in storage modulus, peaks of loss dispersion modulus or tan δ. Tan δ peak may occur at higher temperatures than those given by E' drop or E'' peak, because it responds to the volume fraction of the relaxing phase, its shape and height depends on the amorphous phase, being a good measure of the 'leather like' midpoint between glassy and rubbery state [20]. The glass transition temperature (T_g) is often measured by DSC (Differential Scanning Calorimetry), but the DMA technique is more sensitive and yields more easily interpreted data. This is usual as the degree of dependence is specific to the transition type. DMA can also resolve sub-T_g transitions, like beta, gamma, and delta transitions, in many materials that the DSC technique is not sensitive enough to pick up. The magnitude of the low temperature relaxations is much smaller than that of α-relaxation considered as the glass transition. These relaxations are due to local mode (main chain)

relaxations of polymer chains and rotations of terminal groups or side chains, or crankshaft motion of a few segments of the main chain.

Stress–strain measurements were performed on dumbbell-shaped cut from thin films on a TIRA test 2,161 apparatus, Maschinenbau GmbH Ravenstein, Germany. Measurements were run at an extension rate of 50 mm/min, at room temperature, 25°C. All samples were measured three times and the averages were obtained. Dry polyurethane film samples and conditioned in warm saline water (37°C, 0.9% w/v NaCl, 24 h) were analysed by mechanical testing.

The platelet adhesion tests were realized by using methods described in literature [21]. Therefore, small pieces of polymer were employed (5 × 5 mm, with a total exposed surface area of 50 mm^2). Initially, the small film pieces of polyurethane were incubated in phosphate buffered saline solution, pH 7.4, at 37°C, for 24 h, and then after removing the buffer solution, were incubated for 1 h in 0.5 ml platelet-rich plasma, obtained through centrifuging of the collected blood originating from a healthy human donors at 250*g* for 10 min at a temperature of 4°C. Collecting of the blood was realized in vials with sodium citrate, 3.8% (9/1 v/v), for each tested polymer, a set of three samples was employed along with the reference sample. In order to find the number of thrombocytes adhered onto surface of the polymer, the thrombocytes no. before and after incubation of the biomaterial in plasma was determined. To eliminate from the calculation of the destroyed thrombocytes during incubation or those adhered on the vial wall, the difference was done between the polymer and reference samples in the same identical experimental conditions. Reading of the thrombocyte number was realized with a Laboratory Flow-Cytometer whereas the number of the adhered thrombocytes was determined with the formula (1):

$$N(\text{adhered cells/surface unit}) = (N_0 - N_1)xS^{-1} \quad (1)$$

where N_0 is the number of thrombocytes before incubation and N_1 is the number of thrombocytes after incubation, S is the total exposed surface area of the polyurethane samples.

3 Results and discussion

3.1 Dynamic Contact Angle

In Table 2 are given the dynamic contact angle values (advancing $\theta_{adv,}$° receding $\theta_{rec,}$° and hysteresis H, %) of the film samples in contact with water.

From Table 2 it is observed that at first immersion θ_{adv}° are less than 90° which concludes that the polyurethane materials show hydrophilicity. These film samples have been prepared through precipitating in water making them microporous and enough hydrophile at surface through orientation of the hydrophile groups towards surface. The evaluated receding contact angles are 44–48% less, except PEA–PU which is the polyurethane without HPC in its composition. Thus, HPC reduces the $\theta_{rec.}$ At the second immersion the hysteresis for PEA–PU is significantly less comparing with all samples having HPC. It appears that a polar material induces a low hysteresis, and the polarity of the soft segment in the polyurethane influences the results, considering additionally at second immersion the water up-take within the microporous layer disposed at surface. Advancing contact angles at second immersion are less than at first immersion, thus the material is better wet. Of all the polyurethane samples, PTHF–HPC evidences the lowest dynamic contact angles, both advancing and receding angles, at first and second immersion, which recommends it for biomedical applications.

Table 2 Dynamic contact angles values of the film samples in contact with water

Polymer code	θ_{adv} (°)	θ_{rec} (°)	H (%)
First immersion			
PEA–PU	85.31 ± 1.11	54.33 ± 0.59	36.31
PEA–HPC	84.85 ± 1.09	44.21 ± 0.53	47.89
PTHF–HPC	77.40 ± 1.12	42.91 ± 0.49	44.56
PPG–HPC	85.63 ± 1.08	44.81 ± 0.51	47.67
Second immersion			
PEA–PU	51.01 ± 0.55	54.06 ± 0.56	5.64
PEA–HPC	52.57 ± 0.49	43.67 ± 0.49	16.93
PTHF–HPC	31.61 ± 0.41	42.26 ± 0.45	25.20
PPG–HPC	60.33 ± 0.59	44.07 ± 0.52	26.95

In Table 3 are given the experimental values of the surface tension for the polyurethane solutions in DMF and DMF as solvent, by using Wilhelmy plate method.

It is obvious in Table 3 that γ_{DMF} decreases only with 7.62% by solving the PEA–PU polymer. When PEA–HPC is solved, due to cellulose derivative, OH groups and hydrogen bonding, the decrease is found to be somewhat higher. For polyether-urethanes, PTHF–HPC and PPG–HPC, there is found a much more significant $\Delta\gamma$

Table 3 The experimental values of the surface tension for the polyurethane solutions in DMF and DMF as solvent

Polymer solution	γ (mN/m)	γ_{DMF} (mN/m)	$\Delta\gamma$ (%)
PEA–PU	33.44 ± 0.045	36.19 ± 0.038	7.62
PEA–HPC	33.19 ± 0.042	36.45 ± 0.051	8.96
PTHF–HPC	29.26 ± 0.035	37.36 ± 0.044	21.69
PPG–HPC	29.51 ± 0.031	37.34 ± 0.041	20.96

(21.69%, respectively 20.96%), and this is due to the polyether nature of the soft segment. This can be explained by the fact that when polar polymers like poly(ester urethane)s are solved in a polar solvent like DMF reduces in some extent the surface tension, while a somewhat less polar polymer like poly(ether urethane)s in the same solvent reduces more.

3.2 Dynamic Mechanical Thermal Analysis (DMTA)

For polyurethanes based on poly(epsilon caprolactone) and 1,4-butane diisocyanate with different soft segment lengths and constant hard segment length it was evidenced by DMTA additional transitions at room temperature due to crystalline fraction of PCL while the hard segment crystallinity influence the rubber plateau [22]. For poly(ether urethane) networks prepared from renewable resources: epoxidized methyl-oleate polyether polyol and 1,3-propandiol by using L-lysine diisocyanate, it was found very well differentiated both from DSC and DMTA, two glass transitions for the soft segment (−17–1°C; 9–22°C) and respectively hard segment (35, 44°C; 45, 58°C) explainable through phase segregated morphology [23]. Three kinds of polyurethane mixed blocks (polycaprolactone glycol, polypropylene glycol, polytetramethylene glycol) and 4,4′-diphenylmethane diisocyanate extended with 1,4-butane diol were studied by DMTA and it was revealed that soft chain mobility affects the glassy state modulus. From E' and tan δ graphs the T_g values are less than −50°C [24]. Gao and Zhang [25], found IPNs as a novel kind of material with complex internal friction behaviour and thermal dynamic incompatibility: for their semiinterpenetrating networks of castor oil polyurethane and nitrokonjac glucomannan, glass transition temperatures ($T_g \leq 50$°C) increased with molecular weight of the latter component which affects the storage modulus and shape and position of tan δ by changing the degree of order and motion of molecules through concentration fluctuations of molecular structural units. For graft-interpenetrating polyurethane networks and natural polymers such as nitrolignin [26], the influence of the NCO/OH molar ratio was studied by DSC and DMA revealing $T_g = -4.09 - 23.97$°C (DSC) and respectively ($T_g = 6.3 - 31.1$°C) which increase with NCO/OH molar ratio through formation of three-dimensional allophanate or biuret networks. DMTA and DSC investigations on new blends of hydroxypropylcellulose and polyurethane (poly (ethylene glycol) adipate-4,4′-diphenylmethane diisocyanate-ethylene glycol) reveals glass transitions ranging between (−17–11.8°C) by DMTA and T_m for soft segments (41.6–49.7)°C by DSC [27].

Characteristic temperatures for the studied samples determined from DMTA curves (Figs. 1, 2, 3) are listed in Table 4. Storage modulus E' is a measure of the stiffness of the material [28]. It appears from the Fig. 1 that the following order of E' values at its drop (at the glass transition from glassy to leathery state) can be stated: $E'_{PEA-HPC} >$

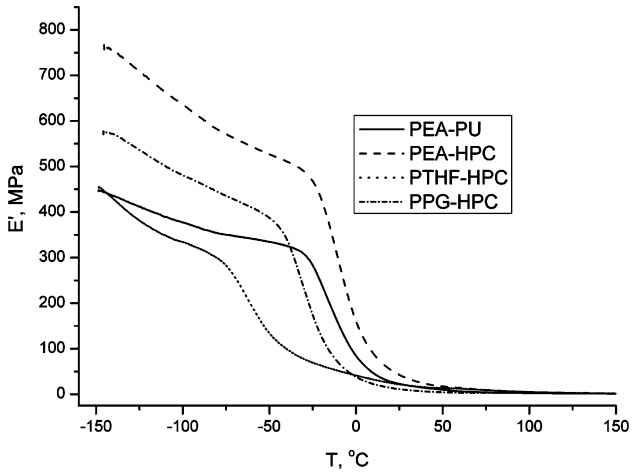

Fig. 1 Storage modulus as a function of temperature for the studied samples

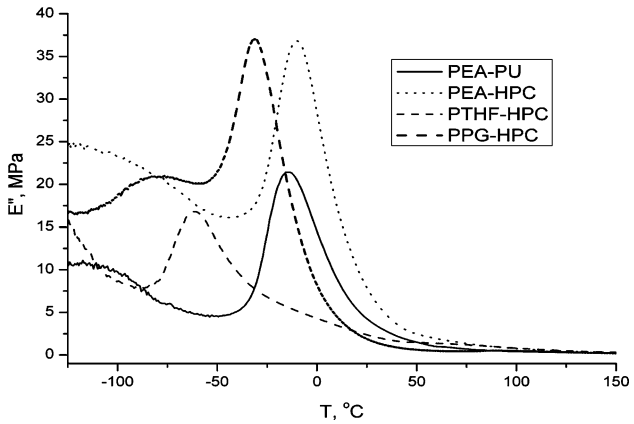

Fig. 2 Loss modulus as a function of temperature for the studied samples

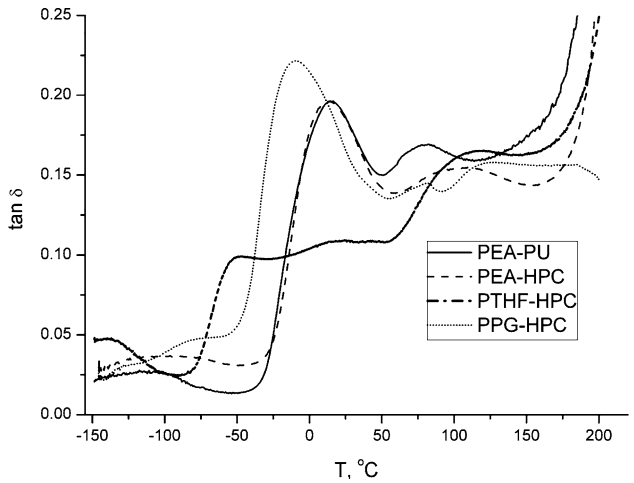

Fig. 3 Tan δ as a function of temperature for the studied samples

$E'_{PPG-HPC} > E'_{PEA-PU} > E'_{PTHF-HPC}$. This is related to the crystalline domains or physical/chemical network/entanglements which constraint molecular motions in amorphous state. For all the samples E' is less than 10^9 Pa, being generally known that when $E' > 10^9$ Pa the material is glassy. In addition we recall that for an amorphous linear polymer the decline of E' in the glass transition range amounts three orders of magnitude in a narrow temperature span. In particular for our samples the decline found for E' is about two orders of magnitude, polyester urethanes are expected to be stiffer, than polyether, cellulose derivative induces also stiffness to the material, while lateral methyl groups in amorphous atactic PPG provokes constraints in the mobility of the soft segment. PTHF macromolecular chain is more mobile with a low stiffness and low tan δ. The glass transition of the soft segment (SS) was determined from DMTA curves as follows: from the intersection of tangents to the E' (log E') curves from the glassy region and the transition "leathery" region, from E'' (log E'') peaks and tan δ peaks. T_g of the soft segment from DSC was evaluated from the second heating scan. It can be noticed that T_g from DSC are close to those from DMTA, for poly(ester urethanes) while for poly(ether urethanes) are different and this can be explained by the sensitivity of DMTA technique to the mobility of the macromolecular segment. And we referred here to the T_g values evaluated from E' (log E') graphs. The log E' or log E'' versus E' or E'' evidence better the biphasic behaviour of the samples by revealing the melting phenomena related to the soft and hard segment. We remark slope changes on log E' descent and the right edge of the E'' peak has a descent trend which indicate a possible overlapping of the melting of the soft phase with a glass transition of the hard phase. The broadening of the glass transition reveals large distribution of the relaxation times that implies a heterogeneous structure with a soft phase constraint by a hard phase which reduces its mobility. Poly(ether urethanes) samples evidence secondary relaxations of the soft segment, attributed to local relaxations in glassy state, which may imply few methylene groups or the motion of $-CH_3$ attached to the backbone or crankshaft motion: for PTHF–HPC sample below glass transition of the soft segment β relaxation is evidenced by tan δ graph ($T_\beta = -51.4$°C) while for PPG–HPC sample β and γ relaxations arised probably at the level of the main chain and lateral $-CH_3$ groups (E'' graph $T_\gamma = -128$°C and $T_\beta = -81.1$°C; log E'' graph $T_\gamma = -131.6$°C and $T_\beta = -82.5$°C; tan δ graph $T_\gamma = -129.1$°C and $T_\beta = -84.4$°C).

From Fig. 3 tan δ values at glass transition peaks show that E' is almost $5E''$ for all the samples, except PTHF–HPC for which E' is almost 10 E''. This result evidences that for all the samples the elastic modulus component is more important than the viscous modulus one.

3.3 Mechanical properties

The stress–strain curves of the studied polyurethanes are plotted in Fig. 4 for dry film samples and in Fig. 5 the stress–strain curves of the film samples previously conditioned in warm (37°C) saline water (NaCl, 0.9% w/v, pH = 7.4) for 24 h, then blotted with absorbent filter paper, are presented. We compare in this way, the mechanical properties of the films in dry state vs. physiological condition. The resulted tensile properties are tabulated in Table 5.

The influence of the physical and chemical cross-links on the elastic behaviour of the polyurethanes is investigated by using Mooney–Rivlin equation, (2), for rubbers [29, 30]:

$$\sigma/(\lambda - \frac{1}{\lambda^2}) = 2C_2\lambda^{-1} + 2C_1 \quad (2)$$

where σ is the stress, λ is the extension ratio (L/L_0) and C_1, C_2 are the Mooney–Rivlin constants.

From the stress–strain experimental data, the Mooney–Rivlin curves are plotted (Figs. 6, 7) and the values of C_1 and C_2 are obtained (see Table 5). C_1 can be obtained by extrapolating the linear portion of the curve to $\lambda^{-1} = 0$, and C_2 from the slope of the linear portion. The elastic behaviour depends on the size and the distribution of the hard domains into the soft matrix and is more or less reflected in the deviation from the Mooney–Rivlin equation.

Moreover, the Eq. 2 has been used to analyze the effects of different environments on the tensile behaviour of the polyurethane film samples. It has been suggested that the Mooney–Rivlin constants C_1 and C_2 are respectively associated with the network structure and the flexibility of the network. In case of dry biopolyurethanes samples it appears that polyurethane PPG-HPC shows an almost linear behaviour when comparing with PEA–PU, PEA–HPC and PTHF–HPC samples. In these block-copolymers the number of physical and chemical cross-links depends on the nature of the macrodiol used, the hydroxypropyl cellulose which generates chemical cross-links in the matrix and on the feed ratio. In the case of polyester-based matrix, PEA–HPC dry sample, the low value of C_1 evidences clearly that the more polar ester groups lead to a matrix dominated by physical cross-links. Therefore, C_1 is different for HPC polyether- and polyester-urethanes (C_1 is lower for polyester- than polyether-urethanes). At higher strains a disrupting of the physical cross-links is taking place and C_1 becomes lower. C_2 is not so sensitive relative to the nature of soft segment but shows the presence of both physical and chemical cross-links specific to a polyurethane network. The effect of conditioning in saline water (0.9% w/v, 24 h, 37°C) is clearly revealed by C_1

Table 4 Characteristic temperatures from DSC and DMTA for the studied samples

PEA–PU		
DSC	$T_g = -27°C$; T_m (SS) = 52.8°C; T_m (HS) dec. = 180°C	
DMTA	E'	$T_g = -29.7°C$; melting phenomena are not evidenced
	log E'	$T_g = -23.5°C$; T_m (SS) = 65.8°C; T_m (HS) = 157°C
	E''	$T_g = -13.4°C$; T_m (SS) = 68.0°C
	log E''	$T_g = -13.4°C$; T_m (SS) = 63.6°C; T_m (HS) = 169°C
	tan δ	$T_g = 15°C$; T_m (SS) = 78.0°C
PEA–HPC		
DSC	$T_g = -23°C$; T_m (SS) = 58.7°C; T_m (HS)dec. = 189.2°C	
DMTA	E'	$T_g = -21.4°C$; melting phenomena are not evidenced
	log E'	$T_g = -17.7°C$; T_m (SS) = 62.3°C; T_m (HS) = 172°C
	E''	$T_g = -9.6°C$; melting phenomena are not evidenced
	log E''	$T_g = -9.6°C$; T_m (SS) = 51.7°C; T_m (HS) = 181°C
	tan δ	$T_g = 11.7°C$; T_m (SS) = 102.5°C
PTHF–HPC		
DSC	$T_g = -41°C$; T_m (SS) = 52.6°C; T_m (HS)dec. = 189.6°C	
DMTA	E'	$T_g = -76.2°C$; T_m (SS) = 65.4°C
	log E'	$T_g = -68.3°C$; T_m (SS) = 52.3°C; T_m (HS) = 180°C
	E''	$T_g = -61.4°C$; T_m (SS) = 63.3°C
	log E''	$T_g = -61.4°C$; T_m (SS) = 62.6°C; T_m (HS) = 176°C
	tan δ	$T_\beta = -51.4°C$; $T_g = 16°C$; T_m (SS) = 113.3°C
PPG–HPC		
DSC	$T_g = -74°C$; T_m (SS) = 59.5°C; T_m (HS)dec. = 196°C	
DMTA	E'	$T_g = -42.4°C$; melting phenomena are not evidenced
	log E'	$T_g = -37.1°C$; T_m (SS) = 93°C; no melting of the hard segment
	E''	$T_\gamma = -128°C$; $T_\beta = -81.1°C$; T_g (SS) = $-30.8°C$ T_m (SS) = 63.3°C
	log E''	$T_\gamma = -131.6°C$; $T_\beta = -82.5°C$; $T_g = -29.3°C$ T_m (SS) = 93.3°C no melting of the hard segment
	tan δ	$T_\gamma = -129.1°C$; $T_\beta = -84.4°C$; $T_g = -8.9°C$; T_m (SS) = 82.2°C

T_m (SS)—melting point of soft segment

T_m (HS)dec.—melting point of hard segment accompanied by decomposition

T_β, T_γ—secondary transitions below glass transition considered as α-transition

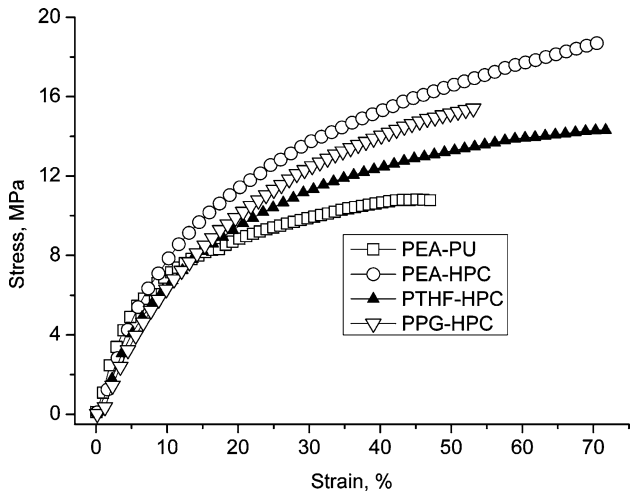

Fig. 4 Stress–strain curves of the dry polyurethanes samples

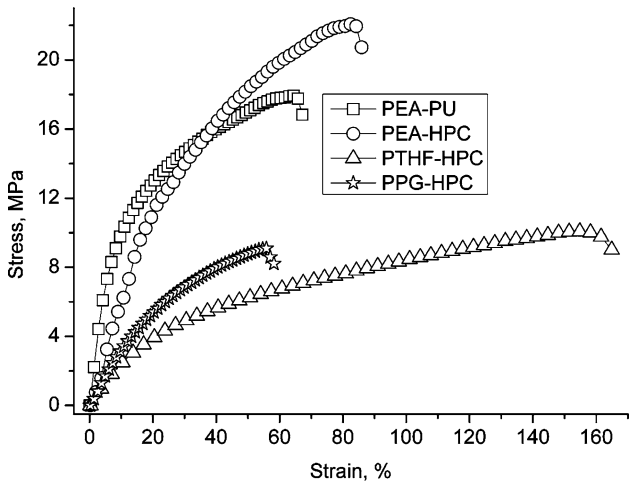

Fig. 5 Stress–strain curves of the polyurethane samples conditioned in saline water

Table 5 Mechanical testing results

Sample	Young modulus (MPa)	Elongation at break (%)	Tensile strength at break (MPa)	Toughness (MJ/m^3)	C_1 (MPa)	C_2/C_1
PEA–PU	166/186	47/66	11/18	4.0/9.4	9.2/7.3	2.3/3.2
PEA–HPC	90/113	71/84	19/22	9.3/13.1	2/0.64	7.3/18.83
PTHF–HPC	70/30	72/159	14/10	7.7/11.8	3.7/0.91	4.7/3.28
PPG–HPC	75/39	53/56	15/9	5.6/3.5	4.3/0.42	4/16.03

'/' means dry/conditioned (37°C, saline water 0.9% w/v, 24 h)

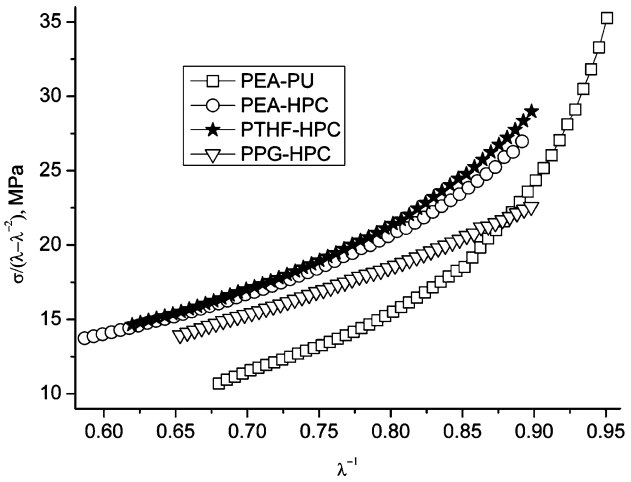

Fig. 6 Mooney–rivlin plots of the dry polyurethanes samples

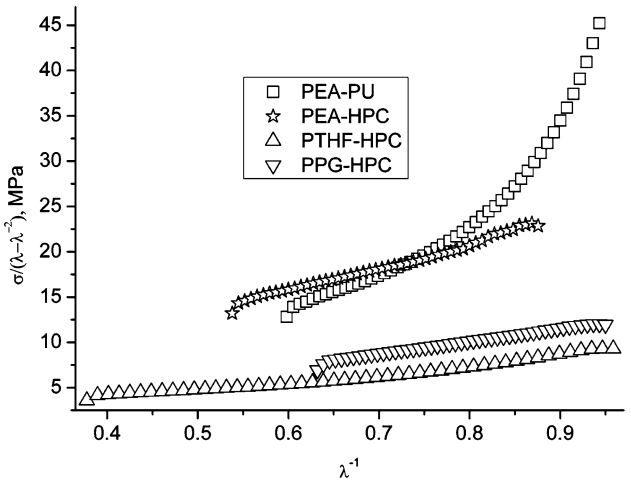

Fig. 7 Mooney–rivlin plots of the conditioned in saline water polyurethanes samples

which is found lower for all the samples evidencing that after conditioning the physical network is affected as well as its flexibility.

The toughness representing the energy absorbed before the sample breaks is higher as expected for PEA–HPC sample than for the PPG–HPC and PTHF–HPC samples, both for dry and conditioned samples. Moreover it can be noticed that the cellulose derivative makes that this absorbed energy to be much higher in case of dry samples. Hydration of samples leads to the increase of toughness except PPG–HPC sample due to amorphous and atactic soft segment structure.

Hydration of the semicrystalline, more or less ordered structures like polyurethanes, have as main result the disrupting of the physical bonding, and the plasticizing of the biopolyurethane matrix, affecting strain behaviour. Water may penetrate within interstitials of the microporous structure favoring biological interactions. The heat is also important in softening the material acting upon the soft segment and physical hydrogen bonding. From Table 5 one can notice that for polyether-urethanes (PTHF–HPC, PPG–HPC), Young modulus decreases after conditioning in saline water at 37°C for 24 h, the material achieve more flexibility, which may bring as advantage for realization of biopolyurethane tissular structures, such heart valves and leather grafts.

Hydrogen bonding is known as an important driving force for the phase separation of a hard segment from a soft-segment matrix consisting of polyether or polyester polyol. The separated hard segment acts as physical cross-links and filler particles for the soft-segment matrix. Microphase separation of segmented polyurethanes is probably the single most influential characteristic of these materials. The degree of phase separation plays a key role in determining mechanical properties and blood compatibility [9]. The heterogeneous morphology of polyurethanes will determine the surface composition exposed to a polar environment (water or blood) or to a nonpolar environment (air or vacuum). The surface segregation phenomenon reflects the difference in surface energy between the polar and nonpolar components [31]. The surface composition constitutes a crucial parameter for a biomedical material in contact with blood. The mobility of polymer chains coupled with environmental changes can lead to surface composition and properties that are time-dependent and dependent on the contacting medium, temperature, that the polymer experiences. It is, however, an unresolved question as to whether an air-stored polyurethane surface indeed adapts to the aqueous environment on biomedical usage. As the polyurethane biomaterial is placed into contact with a physiological medium, such as blood or

tissue, its surface layers will undergo motions in order to accommodate the new interfacial situation. In contact with aqueous environments, it is obviously favorable for hydrophilic constituents of the polymer to become enriched at the interface [2].

For crosslinked blends of Pellethene and multiblock polyurethanes containing phospholipids [12], it was found for elastic modulus values ranged between 21 and 47 MPa, whereas for biomaterials based on cross-linked blends of Pellethene and multiblock polyurethanes containing poly(ethylene oxide) it was found for elastic modulus values ranged between 85 and 246 MPa [32].

3.4 Platelet adhesion

In vitro platelet adhesion experiments were conducted to evaluate the preliminary blood compatibility. It is very well known that the surface properties particularly platelet adhesion of the biomaterials is very important with respect to their haemocompatibility, especially when they are used as cardiovascular devices [21].

It is well known that when blood is in contact with a synthetic material, firstly the latter one adsorbs onto its surface blood plasma proteins, and secondly attract and activate the thrombocytes. In function of the type of the adsorbed plasma proteins (fibrinogen or albumins) this phenomenon can exert in a more or less extent. In case of the preferentially fibrinogen adsorption (important protein in endogenous haemostasis), platelet adhesion is increased followed by thrombus activation and clot formation. In case of albumin absorbtion platelet adhesion is diminished which confer to the surface a thromboresistant character [33, 34].

In Fig. 8 platelet adhesion corresponding to the studied polyurethane samples is given. It can be noticed that when comparing PEA–PU with PEA–HPC the no. of adhered thrombocytes is much lower for PEA–HPC and this is due to the cellulose derivative which confers improved biomaterial qualities. Among the PPG–HPC, PTHF–HPC and PEA–HPC samples the most promising thromboresistant ones are PTHF–HPC and PEA–HPC. In our previous paper, the fibrinogen adsorption tests [19], revealed that PTHF–HPC and PEA–HPC polyurethanes proved to be indicated for thromboresistant devices, and the polyether-urethane PTHF–HPC proved to have more relevant haemocompatible material qualities.

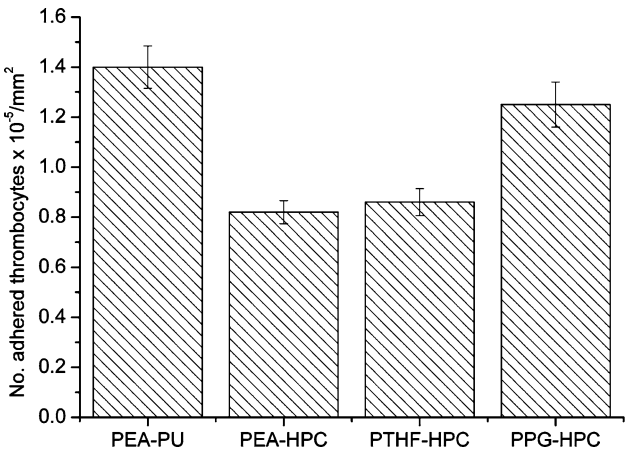

Fig. 8 Platelet adhesion on the studied biopolyurethanes film surfaces

From literature for Biospan polyurethane [35], the values for adhered thrombocytes found are 101,500 adhered thrombocytes per mm^2. The number of adhered platelet is sensitive also to the soft segment length in the case of fluorinated polyurethanes [11]. The presence of cellulose in segmented polyurethane matrix indeed inhibits platelet adhesion [13]. For PU/hydrophilic poly(ethylene glycol)diacrylate IPNs, platelet adhesion is suppressed by microseparated IPN structure [9]. For poly(carbonate urethane)s with various degree of nanophase segregation the number of platelet adhered found was 5.33×10^6 up to 10.67×10^6 (for Pellethane is 8×10^6) [10].

4 Conclusions

Segmented polyurethane block-copolymers manifest thromboresistant qualities and adequate mechanical properties to be use as various medical devices. Segmented biopolyurethanes based on natural renewable polymer resources have been prepared. The phase segregated structure is favourable for biomedical applications. Introducing of natural polymer is expected to improve the biomaterial qualities.

The type of the soft segment induces different elastic properties and defines the glass transition of the polyurethane biomaterial. The hydrophobe block assures the corresponding mechanical strength whereas the hydrophilic one assures the wetting and separation capability absolute necessary for biocompatible requirements. In this respect the poly(ether urethane) PTHF–HPC sample proved the best surface characteristics revealed by dynamic contact angle determinations as well as the blood response by platelet adhesion test. Evaluation of the mechanical flexibility by DSC and DMTA as well as mechanical elastic modulus determinations dry versus physiological conditions recommends this material for a better haemodynamics to assure the transmitting pulse wave in cardiovascular model systems.

Acknowledgements The authors are grateful for the financial support, to Ministry of Education and Research—Exploratory Research Projects, Code: PN-II-ID-PCE-988/2008.

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