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Natural-Based Polyurethane Biomaterials for Medical Applications

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1. Introduction

Biomaterials are biologically inert or compatible materials placed inside a patient on a long-term or permanent basis. Advances in engineering and a greater availability of synthetic materials triggered the development of engineered polymers for use in biomaterials medical devices. As for other biomaterials, the basic design criteria for polymers used in the body call for compounds that are biocompatible, processable, sterilizable and capable of controlled stability or degradation in response to biological conditions.

The interdisciplinary field of biomaterials and tissue engineering has been one of the most dynamic disciplines during the last decades (Durairaj, 2001; Grundke, 2005; Norde, 2006; Ohya, 2002; Pilkey, 2005; Thomson, 2005; Vermette et al., 2001). 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.

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.

Polymers from natural sources are particularly useful as biomaterials and in regenerative medicine, given their similarity to the extracellular matrix and other polymers in the human body. Polyester- and polyether-urethanes have been modified with hydroxypropyl cellulose aiming the change of their surface and bulk characteristics to confer them biomaterial qualities (Macocinschi et al., 2008; Macocinschi et al., 2009a; Macocinschi et al., 2009b). 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. Polymeric composites prepared by mixing polyurethanes and natural polymers offer improved mechanical properties and biocompatibility for functional tissue replacements *in vivo*. The biological characteristics in contact with blood and tissues for long periods, in particular good antithrombogenic properties, recommend the use of extracellular matrix components such as collagen, elastin and glycosaminoglycans (GAG) for obtaining biomaterials (Macocinschi et al., 2010a; Macocinschi et al., 2011; Moldovan et al., 2008; Musteata et al., 2010; Raschip et al., 2009). The introduction of biodegradable polymers into a synthetic polymer matrix restricts the action of a fungal, microbial or enzymatic attack (Macocinschi et al., 2010b). Such limitations appear even when the biodegradable component occurs as a continuous phase in the composite material.

Our previous publications presented the synthesis and some properties of new polyurethane-cellulose, (Macocinschi et al., 2008).

Herein the effects of the chemical structure of polyurethanes-cellulose on their surface properties are discussed. Investigations are based on the geometric mean approach of Kälble, Owens and Wendt, Rabel (Kälble, 1969; Owens & Wendt, 1969; Rabel, 1977), on the Lifshitz-van der Waals acid/base approach of Van Oss and co-workers (Van Oss et al., 1988a; Van Oss et al., 1988b; Van Oss, 1994) and on the theoretical methods involving quantitative structure-property relationship (Bicerano, 1996). By scanning electron microscopy surface morphology was investigated. For estimation of the haemocompatibility properties of the obtained materials, water sorption was determined as well as the amount of fibrinogen adsorbed from solution, the amount of fibrinogen adsorbed from blood plasma, and the time of prothrombin consumption.

2. Surface, mechanical and biological characterizations of polyurethane biomaterials

An ideal polymer for medical applications would have adequate surface and mechanical properties to match the application, would not induce inflammation or other toxic response, and would be sterilizable and easily processed into a final end product with an acceptable shelf life. Polyurethanes are good biomaterials due to their high biocompatibility having chemical structure similar to that of proteins and elastomer characteristics.

2.1 Surface properties

Segmented polyurethanes have gained considerable position as useful biomaterials for implants or biomedical devices, (Baumgartner et al., 1997; Hung et al., 2009; Reddy et al., 2008; Wu et al., 2009). Polyurethanes have been widely used for various commercial and experimental blood contacting and tissue-contacting application, such as vascular prostheses, blood pumps and tracheal tubes, mammary prostheses, heart valves, pacemaker

lead wire insulations, intra-aortic balloons, catheters and artificial hearts, because of their generally favorable surface physical properties, together with their fairly good biocompatibility and haemocompatibility characteristics, (Lamba et al., 1997; Lelah & Cooper, 1986; Plank et al., 1987). The balance between the surface hydrophilic and hydrophobic properties is important for achieving an enhanced biocompatibility of polyurethanes. Plasma treatments or other types of stimuli may alter the surface energy of most polymers, thus changing their surface polarity, hydrophilicity and adhesiveness, (Desai et al., 2000; Ozdemir et al., 2002; Ramis et al., 2001). In Table 1 are provided the compositional parameters and the average molecular weights values, polydispersity indices (GPC).

Sample code	Composition macrodiol/MDI/EG/HPC, wt %	M _n	M _w /M _n
PEA-PU	55.56/37.50/6.94/0.0	109613	1.287
PEA-HPC	52.24/36.57/7.27 /3.92	134522	1.865
PTHF-HPC	52.24/36.57/7.27 /3.92	70291	1.590
PPG-HPC	52.24/36.57/7.27 /3.92	72951	1.669

Table 1. Compositional parameters, number-average molecular weights, polydispersity indices

The measurement methods used for determination of surface tension are based on contact angles between the liquid meniscus and the polyurethane surface. The contact angle is a measure of the ability of a liquid to spread on a surface. The contact angle is linked to the surface energy and so one can calculate the surface energy and discriminate between polar and apolar interactions. Table 2 lists the contact angles between double distilled water, ethylene glycol, or CH₂I₂ and polyurethane samples, before and after effecting of high frequency cold plasma treatment.

Polymer code	Untreated samples/ Plasma -treated samples		
	Water	Ethylene glycol	CH ₂ I ₂
PEA-HPC	45/60	40/35	40/29
PTHF-HPC	45/52	36/29	33/29
PPG-HPC	60/50	45/30	32/27

Table 2. Contact angle degrees of different liquids and polyurethane samples before and after plasma treatment

For the calculation of the surface tension parameters, the geometric mean method (Eqns. (1) and (2)), (Kälble, 1969; Owens & Wendt, 1969; Rabel, 1977) the acid/base method (LW/AB) (Eqns. (3)-(5)), (Van Oss et al., 1988a; Van Oss et al., 1988b; Van Oss, 1994), and theoretical method based on the structure-property relationship considering the group contribution techniques (Eqn. (6)), (Bicerano, 1996) , were used.

$$\frac{1 + \cos \theta}{2} \frac{\gamma_{lv}}{\sqrt{\gamma_{lv}^d}} = \sqrt{\gamma_{sv}^p} \cdot \sqrt{\frac{\gamma_{lv}^p}{\gamma_{lv}^d}} + \sqrt{\gamma_{sv}^d}$$

(1)

$$\gamma_{sv} = \gamma_{sv}^d + \gamma_{sv}^p$$

(2)

where θ is the contact angle determined for water, ethylene glycol and CH_2I_2 , subscripts ‘lv’ and ‘sv’ denote the interfacial liquid-vapour and surface-vapour tensions, respectively, while superscripts ‘p’ and ‘d’ denote the polar and disperse components, respectively, of total surface tension, γ_{sv} .

$$1 + \cos \theta = \frac{2}{\gamma_{lv}} (\sqrt{\gamma_{sv}^{LW} \cdot \gamma_{lv}^{LW}} + \sqrt{\gamma_{sv}^{+} \cdot \gamma_{lv}^{-}} + \sqrt{\gamma_{sv}^{-} \cdot \gamma_{lv}^{+}}) \tag{3}$$

$$\gamma_{sv}^{AB} = 2\sqrt{\gamma_{sv}^{+} \cdot \gamma_{sv}^{-}} \tag{4}$$

$$\gamma_{sv}^{LW/AB} = \gamma_{sv}^{LW} + \gamma_{sv}^{AB} \tag{5}$$

where superscripts ‘LW’ and ‘AB’ indicate the disperse and the polar component obtained from the γ_{sv}^{-} electron donor and the γ_{sv}^{+} electron acceptor interactions, while superscript ‘LW/AB’ indicates the total surface tension.

$$\gamma \text{ (298 K)} \approx 0.75 \cdot [E_{coh}/V(298 \text{ K})]^{2/3} \tag{6}$$

where γ is the total surface tension, E_{coh} the cohesive energy and V the molar volume. According to the geometric mean method, the solid surface tension components were evaluated with Eqn. (1), (Van Oss et al., 1989) using the known surface tension components, (Erbil, 1997; Rankl et al., 2003; Strom et al., 1987) of different liquids from Table 3 and the contact angles from Table 2. The total surface tension was calculated with Eqn. (2).

Test liquids	γ_{lv}	γ_{lv}^d	γ_{lv}^p	γ_{lv}^{-}	γ_{lv}^{+}
Water	72.8	21.8	51.0	25.5	25.50
Ethylene glycol	48.0	29.0	19.0	47.0	1.92
Methylene Iodide	50.8	50.8	0.0	0.0	0.72

Table 3. Surface tension parameters (mN/m) of the liquids used for contact angle measurements

Table 4 shows the surface tension parameters for both untreated and plasma-treated polyurethane samples, according to the geometric mean method and to the acid/base method. In this table it was considered that γ_{sv}^{LW} is equivalent to γ_{sv}^d of the geometric mean method, the mean values of γ_{sv}^{-} and γ_{sv}^{+} were calculated with Eqn. (3). Also, the total surface tension was calculated with Eqn. (2). Following the plasma treatment the disperse component of surface tension, γ_{sv}^d , increases in absolute value, while the polar component surface tension γ_{sv}^p , decreases except PPG-HPC sample for which these dependences varies in a less extent (γ_{sv}^p increases from 32.2 to 38.9 mN/m, and γ_{sv}^d increases from 9.1 to 10.7 mN/m). Table 5 shows the contribution of the polar component to the total surface tension obtained from the geometric mean method GM for untreated and plasma treated polyurethanes. Table 5 shows that the polar term γ_{sv}^p in general gives a large contribution to γ_{sv} , due to the large electron donor γ_{sv}^{-} interactions. Before and after plasma treatment all samples exhibits predominant electron donor properties. Table 5 shows that the contribution of the polar component decreases after plasma treatment, except the same PPG-HPC sample. The total, disperse and polar surface tension parameters are influenced by the matrix structure of

polyurethanes possessing various soft segments. Generally, all samples possess high polar surface tension parameters, which decrease after low-pressure plasma treatment, except the PPG-HPC sample.

Polymer code	Untreated samples/ Plasma treated samples				
	γ_{sv}^p	γ_{sv}^d	γ_{sv}^-	γ_{sv}^+	γ_{sv}
PEA-HPC	57.0/24.8	2.1/16.6	55.2/23.6	12.5/4.7	59.1/41.4
PTHF-HPC	53.1/34.7	4.7/12.9	50.7/33.2	10.2/6.6	57.8/47.6
PPG-HPC	32.2/38.9	9.1/10.7	30.7/37.2	6.2/7.4	41.3/49.6

Table 4. Surface tension parameters (mN/m) for untreated and plasma treated HPC-polyurethanes according to the geometric mean method and to the acid/base method

The studied segmented cellulose polyurethanes manifest a hydrophilic character, due to cellulosic component. After HF plasma treatment the hydrophile-hydrophobe balance is changed in the sense of decreasing their hydrophilicity. This can be explained through cross-linking chemical network and by the etching effect, which modifies the rugosity and chemical composition of the surface. The exception is given by the PPG-HPC sample, which is less hydrophilic due to -CH₃ substituent in the soft macromolecular chain that is not favourable for polar interactions. It appears in our case that plasma induces competitive hydrophilic and hydrophobic effects and in the case of PPG-HPC sample these effects are equilibrated, such as the polar component is not changed after plasma treatment.

Polymer code	Untreated samples	Plasma treated samples
	$\gamma_{sv}^p / \gamma_{sv} \cdot 100$ (%)	$\gamma_{sv}^p / \gamma_{sv} \cdot 100$ (%)
PEA-HPC	96.5	60.0
PTHF-HPC	91.9	73.0
PPG-HPC	78.0	78.5

Table 5. Contribution of the polar component to the total surface tension obtained from the geometric mean method for untreated and plasma treated polyurethanes

The total surface tension was estimated from the structure-property relationship, according to Eqn. (6) in the following steps, (Bicerano, 1996):

1. Calculation of the zeroth-order connectivity indices $^0\chi$ and $^0\chi^v$ and of the first-order connectivity indices $^1\chi$ and $^1\chi^v$, according the values of the atomic simple connectivity indices and of the valence connectivity indices (Table 6).
2. Calculation of cohesive energy, by two methods, by applying the group contributions of Fedors, (Bicerano, 1996; Van Krevelen, 1990) and those of Van Krevelen and Hoftyzer, (Bicerano, 1996; Van Krevelen, 1990), (Table 7).
3. Calculation of the molar volume at room temperature (298 K), (Table 7).

Polymer code	$^0\chi$	$^0\chi^v$	$^1\chi$	$^1\chi^v$
PEA-HPC	179.93	139.56	121.34	32.17
PTHF-HPC	175.56	149.16	123.36	90.33
PPG-HPC	180.31	140.74	119.24	84.74

Table 6. Zeroth-order connectivity indices $^0\chi$ and $^0\chi^v$ and first-order connectivity indices $^1\chi$ and $^1\chi^v$

Polymer code	$E_{coh(1)}$, (10^{-5} J/mol)	$E_{coh(2)}$, (10^{-5} J/mol)	V (298 K), mL/mol	$\gamma_{(1)}$, mN/m	$\gamma_{(2)}$, mN/m
PEA-HPC	13.88	15.28	2812	46.89	49.95
PTHF-HPC	12.77	16.39	2613	46.61	54.76
PPG-HPC	12.25	14.75	2560	45.98	51.87

Table 7. Total surface tensions, $\gamma_{(1)}$ and $\gamma_{(2)}$, from the theoretical data calculated for cohesive energies, $E_{coh(1)}$ and $E_{coh(2)}$, and molar volume, V, for studied polyurethanes

The theoretical results are closed to the experimental values, derived from the contact angle measurements.

The hydrophobe-hydrophile balance of untreated and plasma treated polyurethanes has been evaluated by calculation of free energy of hydration, ΔG_w . The ΔG_w values were obtained from Eqn.(7), (Faibish, 2002):

$$\Delta G_w = -\gamma_{lv}(1 + \cos \theta_{water})$$

(7)

where γ_{lv} is the total surface tension of water from Table 3 and θ_{water} is contact angle of water with polyurethanes. The results are presented in Table 8.

Polymer code	Untreated samples/ plasma treated samples	
	ΔG_w (mJ/m ²)	γ_{sl} (mN/m)
PEA-HPC	-124.28/-109.2	10.6/5.0
PTHF-HPC	-124.28/-117.62	6.3/2.7
PPG-HPC	-109.2/-119.59	4.9/2.8

Table 8. Surface free energy between polyurethane and water and interfacial tensions for untreated and plasma treated samples

Generally, the literature (Faibish, 2002; Van Oss, 1994) of the field mentions that for $\Delta G_w < -113$ mJm⁻² the polymer can be considered more hydrophilic while when $\Delta G_w > -113$ mJm⁻² it should be considered more hydrophobic. High frequency cold plasma treatment modifies ΔG_w indicating that the surface becomes more hydrophilic in the case of PPG-HPC sample and less hydrophilic in the case of PEA-HPC and PTHF-HPC samples.

Solid-liquid interfacial tension is defined with the following relation:

$$\gamma_{sl} = (\sqrt{\gamma_{lv}^p} - \sqrt{\gamma_{sv}^p})^2 + (\sqrt{\gamma_{lv}^d} - \sqrt{\gamma_{sv}^d})^2$$

(8)

Free energy of hydration and interfacial tension are very important in that they determines the interactional force between two different media and controls the different processes: stability of the colloidal aqueous suspensions, dynamic of the molecular self-assembling, watability of the surface, space distribution and adhesiveness. The biological and chemical processes, which take place at the level of the surface of the implant, depend on the interfacial interactions between solid and liquid (water).

(1)When the blood-biomaterial interfacial tension is high, the blood proteins will be anchored on many points on the surface, they strongly interact with the surface and thus the solid-liquid interfacial tension decreases. Consequently, the proteins change their conformation. A new interface is formed, between the protein surface and sanguine plasma.

(2) When the blood-biomaterial tension is relatively low, the force, which determines the protein adsorption, will be smaller. Conformation of the proteins initially adsorbed is similar to that found for the proteins in solution. Therefore, the interfacial tension between the protein surface and the sanguine plasma will not be high, not being an appreciable force able to determine the adsorption of sanguine components. This corresponds to a better compatibility of the biomaterial surface with blood comparing with the case (1). The surface of the biomaterial must reduce to minimum the blood-biomaterial interfacial tension such as the modification of the initially adsorbed proteins to be little. Although, apparently an interfacial tension equal to zero would be ideal for realization of the blood compatibility, however this is not desirable in view of the mechanical stability of the blood-biomaterial interface. It is generally considered that the blood-biomaterial interfacial tension should be 1-3 mN/m for a good blood - biomaterial compatibility, as well as a good mechanical stability of the interface.

The values for solid-liquid interfacial tensions are given in Table 8 for untreated and plasma treated samples. It can be observed that the interfacial tensions are in general low, and after plasma treatment become even lower. Moreover, $1 \text{ mN/m} < \gamma_{sl}$ for PTHF-HPC and PPG-HPC samples treated in plasma $< 3 \text{ mN/m}$ which is required for a good biomaterial.

An important goal in material science, biochemistry, cell biology and bioanalytics is to establish a relationship between surface morphology and surface properties of a polyurethane composite on one hand and on the other hand the interconnective interactions synthetic polymer matrix-extracellular matrix natural polymer components (Macocinschi et al., 2010a). The polyurethane was modified with natural polymers aiming the improvement of the surface and bulk properties, to confer good biomaterial qualities. The added natural extracellular matrix polymers determine an increase of the surface tension value for all the biocomposite samples in comparison with starting polyurethane. The fact that the total surface tension values experimentally evaluated for starting polyurethane (untreated and treated in plasma) are less than the theoretical one calculated on the basis of quantitative structure-properties relationships (Bicerano), which can be explained by the complex morphology of polyurethanes with microdomain segregation and network. The complex network morphology gives stability against plasma action. For all the tested biocomposites the values of the total surface tension after plasma treatment are higher, therefore the samples become more hydrophilic except one sample containing chondroitin sulfate, which suggests that chondroitin sulfate component induces further crosslinks and network formation and hence a reducing of hydrophilicity. The evaluated surface tension parameters show that the biocomposites have biomaterial qualities through their increased hydrophilicity. Moreover, plasma treatment decreases the hydration energy while the interfacial tensions fall within 1-3 mN/m, interval required for a good biomaterial. Biocompatible interfaces were constructed based on non-toxic, hydrophilic assembled macromolecular networks, as viable platforms for the affinity of biomolecules. The mechanical strength of the biocomposites decreases in comparison with starting polyurethane but it is higher than that of carotid porcine arteries.

2.2 Scanning electron microscopy

In Fig 1 are illustrated the SEM micrographs corresponding to the treated and untreated polyurethane samples. It is obvious that plasma caused a change in the surface morphology and etching effects are observed.

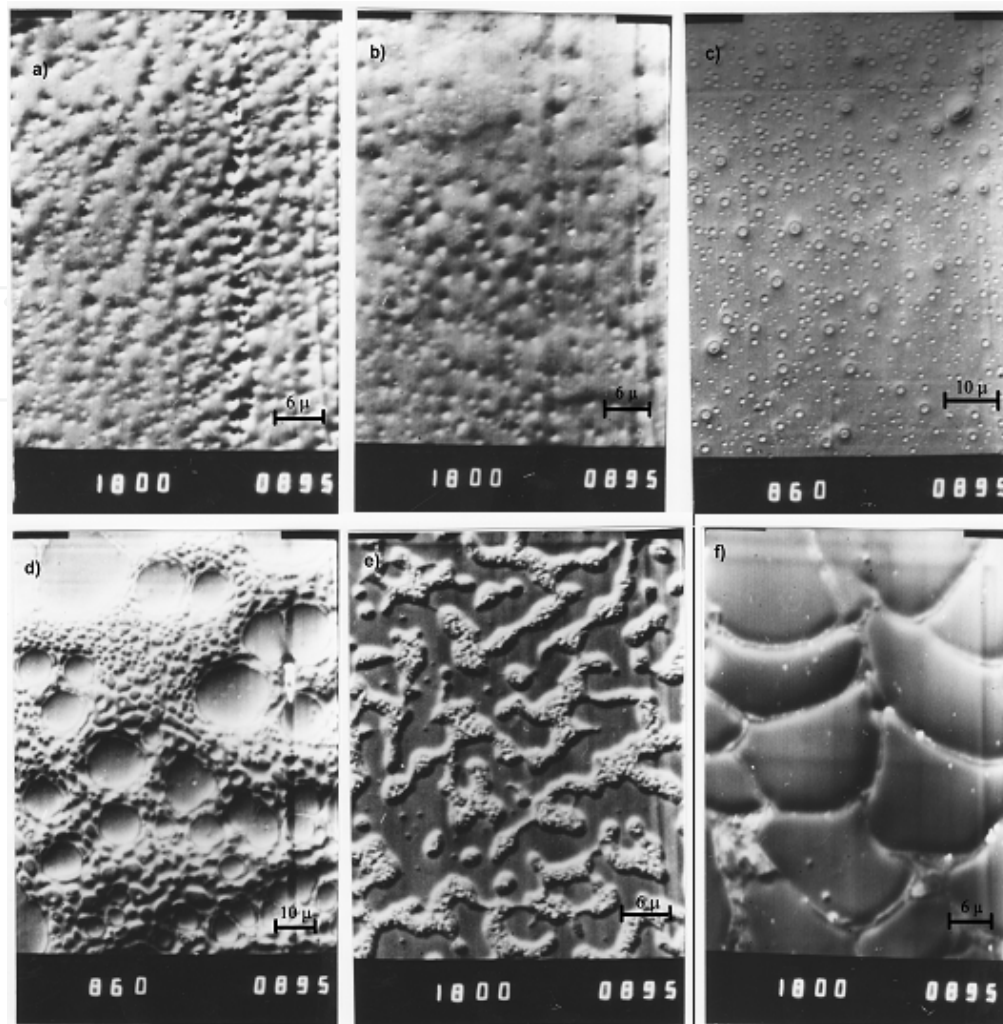


Fig. 1. SEM images of the polyurethane samples untreated and treated in HF cold plasma (PEA-HPC (a,b); PTHF-HPC (c,d); PPG-HPC (e,f))

2.3 Water sorption

The biocompatibility of the materials depend on their ability to swell in aqueous media. A high water level on the surface of the biomaterial provides a low interfacial tension with blood, thus reducing fibrinogen adsorption, cell adhesion and clot formation, (Abraham, 2002; Faibish, 2002; Van Krevelen, 1990; Wang, 2004). The results are presented in Fig 2. It is observed that the water uptake is given by the PEA-PU sample (reference polyurethane sample without hydroxypropylcellulose, PEA/MDI/EG, $M_n=109.613$, $M_w/M_n=1.3$), PEA-HPC and PTHF-HPC samples (151 %, 140 % and 167 %, respectively) and in a less extent by the PPG-HPC (92 %) due to its less polar soft segment having the lateral $-CH_3$ substituent which confer a different geometry to the polyurethane internal microporous structure, unfavorable for water uptake.

2.4 Fibrinogen adsorption

The experimental data related to the amount of adsorbed fibrinogen before and after incubating of polymers with a physiological solution of fibrinogen (3.00 mg/mL) and sanguine plasma (2.98 mg/mL) are presented in Fig 3.

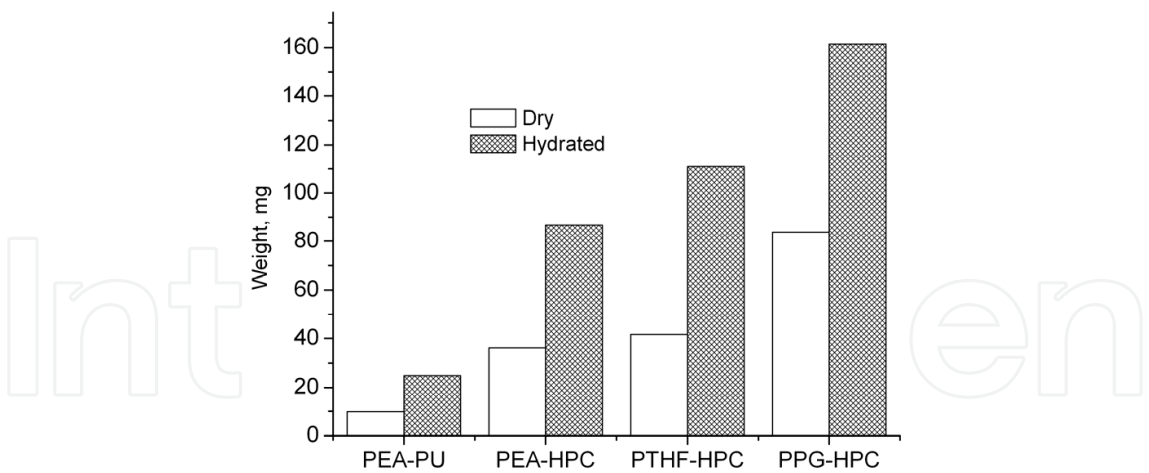


Fig. 2. Weight of polymer sample in dry and maximum hydrated state

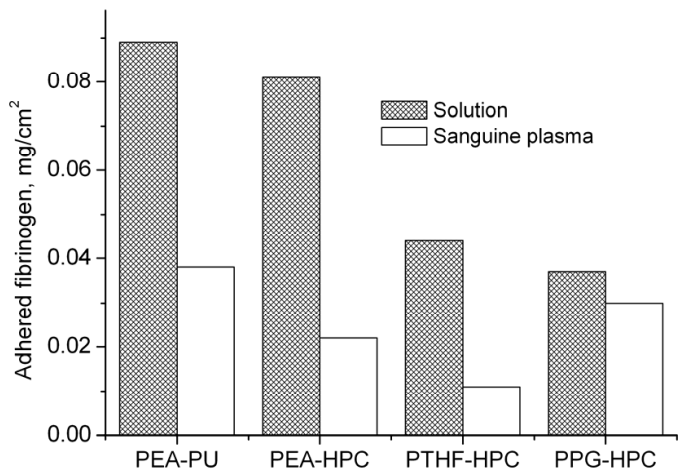


Fig. 3. Amount of adsorbed fibrinogen from physiological solution and sanguine plasma

It is observed that after incubation for 1 h at 37°C of the tested materials, no significant fluctuations of the fibrinogen concentration were recorded in comparison with the reference solution. Incubation of the samples with sanguine plasma realized in the same conditions of the incubation in solution and led to the results from Fig 3. Determination of the adhered fibrinogen from sanguine plasma was coupled with the determination of the prothrombin time, i.e. the time of transformation of the prothrombin in thrombin, followed by transformation of the fibrinogen in fibrin and clot formation. It is observed that the amount of fibrinogen adsorbed from sanguine plasma is less in comparison with that in solution, for all the materials except PPG-HPC, for which the differences are not significant. Also, it is remarked that prothrombin time stand in physiological normal limits (Table 9) so studied polyurethane samples did not affect the clot formation mechanisms. The significant differences between adsorptions of the fibrinogen solution and sanguine plasma, suggest that the fibrinogen adsorption properties of the polyurethane samples, under physiological condition are affected by the concurrent affinities for other plasma proteins, which do not disturb the haemostatic mechanisms. Probably among the plasma proteins that can concur with fibrinogen is albumin, which was investigated in (Lupu et al., 2007a), and it was found that the adsorption value of a sub-physiological solution of serum albumin, (3 mg/ml) to PEA-PU materials was 0.3 ± 0.06 mg/cm².

Parameter	Physiological normal limits, mg/ml	Reference sample (sanguine plasma)	PEA-PU	PEA-HPC	PTHF-HPC	PPG-HPC
Prothrombin time	8.3-11.3	10.43±0.04	11.06±0.4	10.9±0.09	10.9±0.09	10.9±0.07

Table 9. Prothrombin time before and after the contact sanguine plasma with polyurethane samples

2.5 Dynamic contact angle

In Table 10 are presented the dynamic contact angle values (advancing $\theta_{adv,^{\circ}}$ receding $\theta_{rec,^{\circ}}$ and hysteresis H, %) of the film samples in contact with water.

Polymer code		$\theta_{adv,^{\circ}}$	$\theta_{rec,^{\circ}}$	H, %
First immersion	PEA-PU	85.31±1.11	44.21±0.53	36.31
	PEA-HPC	84.85±1.09	54.33±0.59	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

Table 10. Dynamic contact angles values of the film samples in contact with water

From Table 10 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 θ_{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.

In Table 11 are given the experimental values of the surface tension for the polyurethane solutions in DMF and DMF as solvent, by using Wilhelmy plate method. Solutions of the polyurethane sample 4g/dL in DMF were employed and DMF as a starting 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

Table 11. The experimental values of the surface tension for the polyurethane solutions in DMF and DMF as solvent

It is obvious in Table 11 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 $\Delta \gamma$ (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.

2.6 Dynamic mechanical thermal analysis (DMTA)

Polyurethanes are characterized by their high and heterogeneous morphology and by important intermolecular forces that determine their mechanical behavior. 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 behavior. 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. DMTA 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 $\tan \delta$. $\tan \delta$ 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, (Sirear, 1997). The glass transition temperature (T_g) is often measured by DSC (Differential Scanning Calorimetry), but the DMTA technique is more sensitive and yields more easily interpreted data. This is usual as the degree of dependence is specific to the transition type. DMTA 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.

In literature 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, (Heijkants et al., 2005). 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, (Lligadas et al., 2007). 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 $\tan \delta$ graphs the T_g values are less than -50°C, (Mondal, 2006). Gao and Zhang, (Gao & Zang, 2001) found IPNs as a novel kind of material with complex internal friction behavior and thermal dynamic incompatibility: for their semiinterpenetrating networks of castor oil polyurethane and nitrokonjac glucomannan, glass transition temperatures ($T_g \leq 50^\circ\text{C}$) increased with molecular weight of the latter component which affects the storage modulus and shape and position of $\tan \delta$ 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, (Huang & Zhang, 2002), the influence of the NCO/OH molar ratio was studied by DSC and DMTA revealing $T_g = -4.09-23.97^\circ\text{C}$ (DSC) and respectively ($T_g = 6.3-31.1^\circ\text{C}$) 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, (Raschip et al., 2009).

Characteristic temperatures for the studied samples determined from DMTA curves (Figs. 4, 5, 6) are listed in Table 12.

Storage modulus E' is a measure of the stiffness of the material, (Zlatanovic et al., 2002). It appears from the Fig. 4 that the following order of E' values at its drop (at the glass transition from glassy to leathery state) can be stated: $E'_{\text{PEA-HPC}} > E'_{\text{PPG-HPC}} > E'_{\text{PEA-PU}} > E'_{\text{PTHF-HPC}}$. 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 $\tan \delta$. 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 $\tan \delta$ 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 $\log E''$ vs. 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 $\tan \delta$ graph ($T_\beta = -51.4^\circ\text{C}$) 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 $T_\gamma = -128^\circ\text{C}$ and $T_\beta = -81.1^\circ\text{C}$; $\log E''$ graph $T_\gamma = -131.6^\circ\text{C}$ and $T_\beta = -82.5^\circ\text{C}$; $\tan \delta$ graph $T_\gamma = -129.1^\circ\text{C}$ and $T_\beta = -84.4^\circ\text{C}$

Sample	Testing method	Analyzed curve	Temperature transformation, $^\circ\text{C}$			
			$T_g(\text{SS})/T_\alpha$	$T_m(\text{SS})$	$T_m(\text{HC})$	T_β
PEA-PU	DSC		-27.0	52.8	180	-
	DMTA $f=1\text{ Hz}$	$\log E'$	-23.5	65.8	157	-
		$\log E''$	-13.4	63.6	169	-
		$\tan \delta$	15.0	78.5	-	-
PEA-HPC	DSC		-23.0	58.7	189.2	-
	DMTA $f=1\text{ Hz}$	$\log E'$	-17.7	62.3	172	-
		$\log E''$	-9.6	51.7	181	-
		$\tan \delta$	11.7	102.5	-	-
PTHF-HPC	DSC		-41.0	52.6	189.6	-
	DMTA $f=1\text{ Hz}$	$\log E'$	-68.3	52.3	180	-
		$\log E''$	-61.4	62.6	176	-
		$\tan \delta$	16	113.3	-	-51.4
PPG-HPC	DSC		-74	59.5	196	-
	DMTA $f=1\text{ Hz}$	$\log E'$	-37.1	93	-	-
		$\log E''$	-29.3	93.3	-	-82.5
		$\tan \delta$	-8.9	82.2	-	-84.4

$T_m(\text{SS})$ -melting point of soft segment; $T_m(\text{HS})_{\text{dec.}}$ -melting point of hard segment accompanied by decomposition; T_β -secondary transitions below glass transition considered as α -transition (T_α).

Table 12. Characteristic temperatures for the studied samples determined from DMTA and DSC curves

From Fig. 6 $\tan \delta$ values at glass transition peaks show that E' is almost $5E''$ for all the samples, except PTHF-HPC for which E' is almost $10E''$. This result evidences that for all the samples the elastic modulus component is more important than the viscous modulus one.

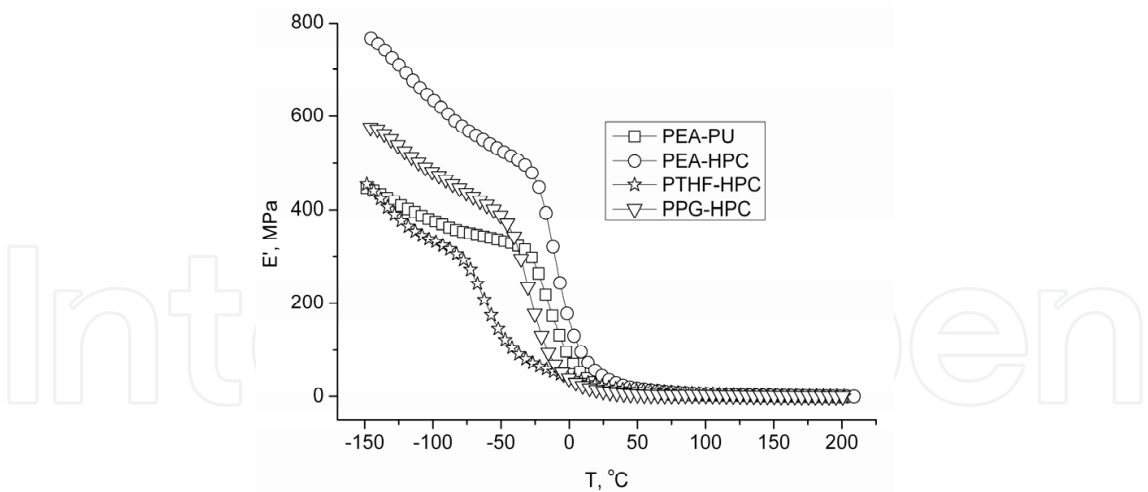


Fig. 4. Storage modulus as a function of temperature for the studied samples

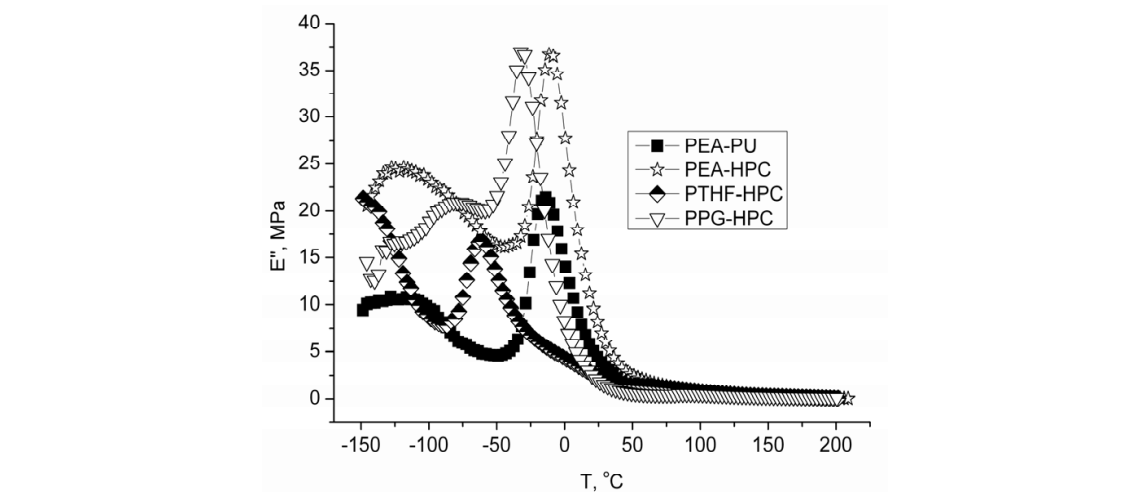


Fig. 5. Loss modulus as a function of temperature for the studied samples

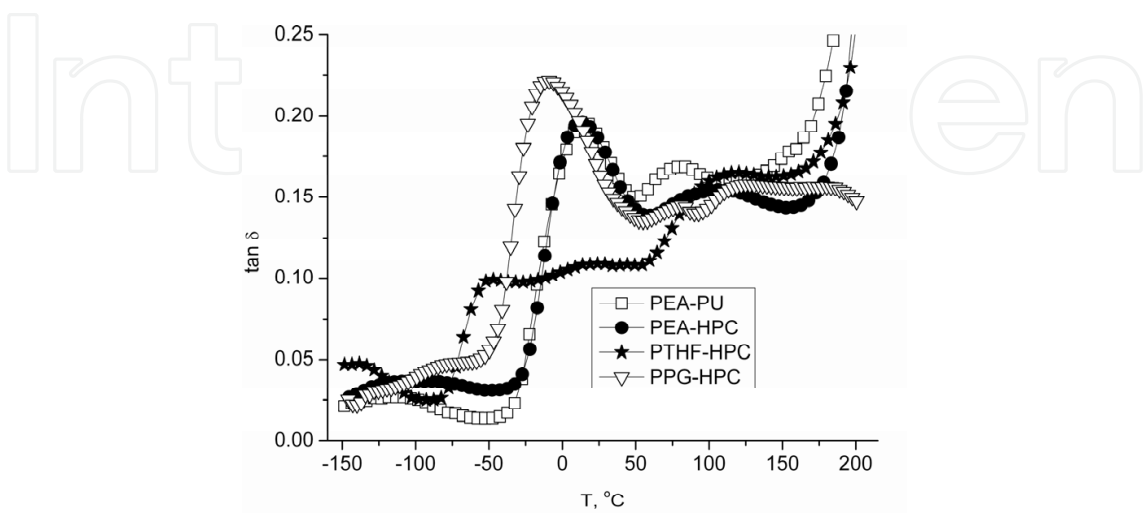


Fig. 6. $\tan \delta$ as a function of temperature for the studied samples

2.7 Mechanical properties

Biological materials have a wide range of mechanical properties matching their biological function. This is achieved via assembly of different size building block segments (soft and hard) spanning many length scales. Due to specific chemical versatility of polyurethanes, different morphologies at different length scales can be obtained and thus different physical properties which satisfy diverse clinical needs have been achieved. The modulability of mechanical properties make polyurethanes excellent candidates for applications in soft tissue engineering. Because of the strong tendency of rigid aromatic moieties to pack efficiently and the presence of hydrogen bonding between urethane and urea groups they tend to self-organize to form semi-crystalline phases within the polymer macromolecular assembly. As the elasticity of the polymers depends on their degree of crystallinity and the degree of hard segment segregation, it is clear that the selection of the diisocyanate monomer will be one of the key parameters that influence polyurethane mechanical characteristics.

The resulted tensile properties are tabulated in Table 13.

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)

Table 13. Mechanical testing results

The stress-strain curves of the studied polyurethanes are plotted in Fig. 7 for dry film samples and in Fig. 8 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.

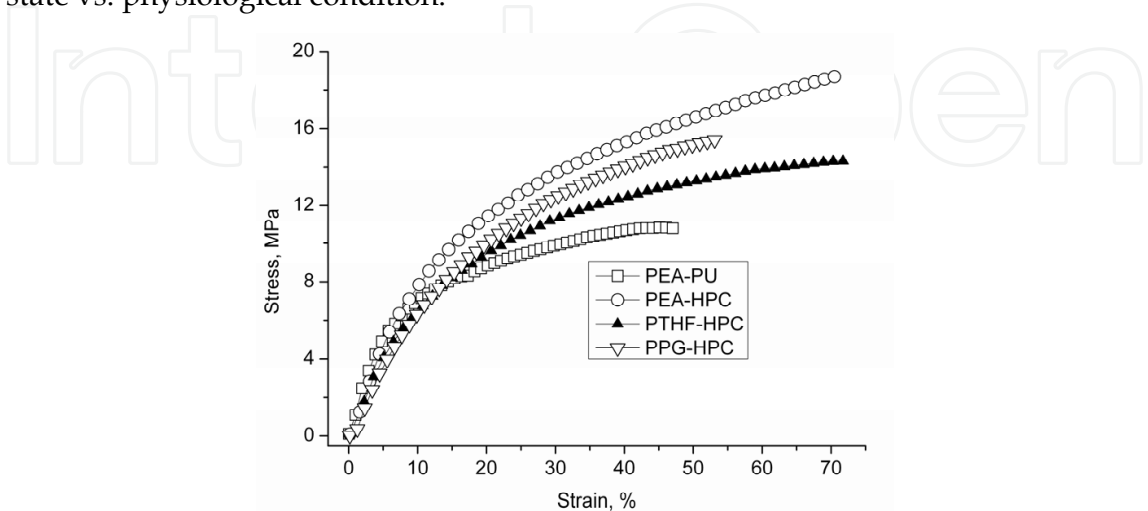


Fig. 7. Stress-strain curves of the dry polyurethanes samples

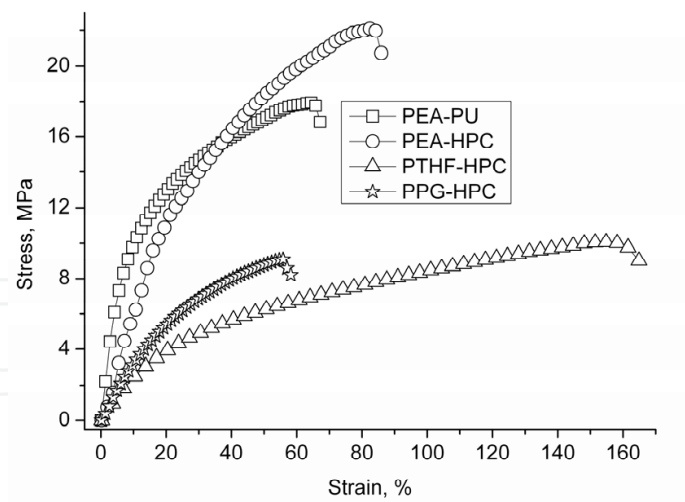


Fig. 8. Stress-strain curves of the polyurethane samples conditioned in saline water

The influence of the physical and chemical cross-links on the elastic behaviour of the polyurethanes is investigated by using Mooney-Rivlin equation, (9), for rubbers, (Sekkar et al., 2000; Spathis, 29) :

$$\sigma / \left(\lambda - \frac{1}{\lambda^2} \right) = 2C_2 \lambda^{-1} + 2C_1 \tag{9}$$

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 (Fig. 9 and Fig. 10) and the values of C_1 and C_2 are obtained (see Table 13). 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.

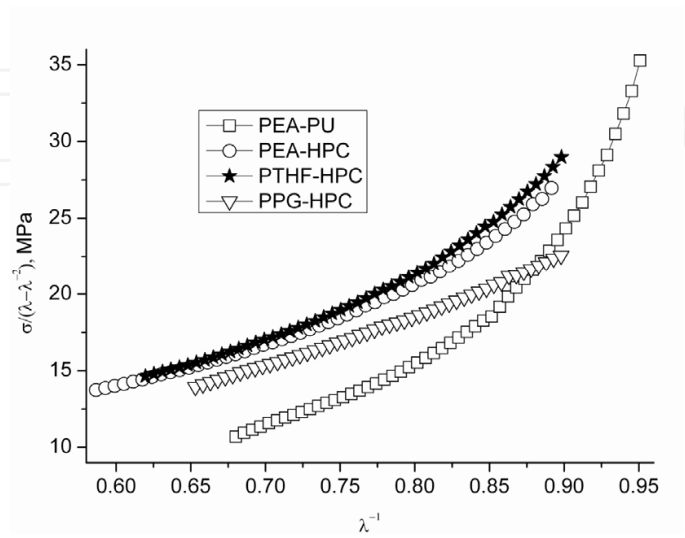


Fig. 9. Mooney-Rivlin plots of the dry polyurethanes samples

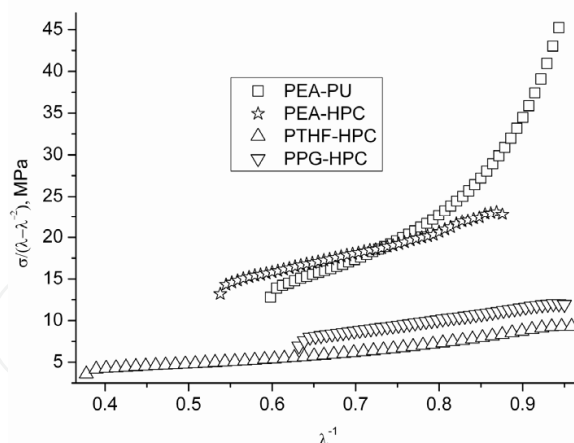


Fig. 10. Mooney-Rivlin plots of the conditioned in saline water polyurethanes samples

Moreover, the Eqn. (9) 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 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 13 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, (Yoon et al., 2005). 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, (Lupu et al., 2007b). 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, (Vermette & Griesser, 2001).

For crosslinked blends of Pellethane and multiblock polyurethanes containing phospholipids, (Yoo & Kim, 2005), it was found for elastic modulus values ranged between 21-47 MPa, whereas for biomaterials based on cross-linked blends of Pellethane and multiblock polyurethanes containing poly(ethylene oxide) it was found for elastic modulus values ranged between 85-246 MPa, (Yoo & Kim, 2004).

2.8 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, (Park et al., 1998).

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 absorption platelet adhesion is diminished which confer to the surface a thromboresistant character, (Bajpai, 2005; Wang et al., 2004).

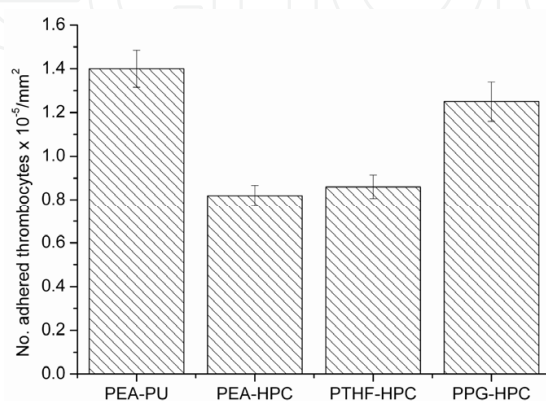


Fig. 11. Platelet adhesion on the studied biopolyurethanes film surfaces

In Fig. 11 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, (Macocinschi et al., 2009a), 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.

From literature for Biospan polyurethane, (Korematsu et al., 1999), the values for adhered thrombocytes found are 101500 adhered thrombocytes per mm². The number of adhered platelet is sensitive also to the soft segment length in the case of fluorinated polyurethanes, (Wang & Wei, 2005). The presence of cellulose in segmented polyurethane matrix indeed inhibits platelet adhesion, (Hanada et al., 2001). For PU/hydrophilic poly(ethylene glycol)diacrylate IPNs, platelet adhesion is suppressed by microseparated IPN structure, (Yoon et al., 2005). 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), (Hsu & Kao, 2005).

3. Conclusion

The effect of the chemical structure of some cellulose derivative based segmented biopolyurethanes and polyurethane biocomposites containing extracellular matrix components on surface properties (static and dynamic contact angle measurements), on dynamical mechanical thermal analysis, mechanical properties was investigated. Specific biological tests were performed (platelet adhesion, protein adsorption tests of fibrinogen) and the results obtained recommend them as biomaterials with enhanced biocompatibility for biomedical applications. Thus, the proper understanding of blood compatibility and the development of prosthetic materials require the investigations of both natural and synthetic materials. Extensive in vitro, ex vivo, and in vivo testing in suitable animals and related differences between the properties of blood components of animals and humans are essential. Future research should be directed in order to clarify the influence of anatomical site of implantation on the behaviour of the implant, with a goal towards the development of site specific implants.

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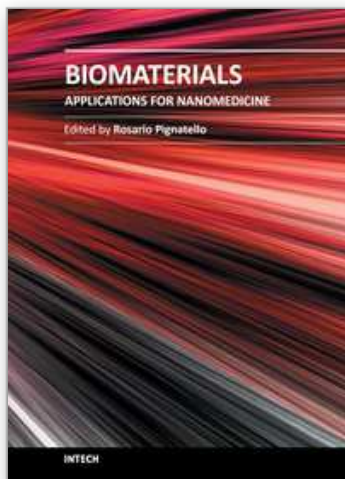
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