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Polyurethane urea membranes for membrane blood oxygenators: synthesis and gas permeation properties

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Abstract—A custom-made set-up was constructed and optimized for the measurement of the gas permeation properties of membranes at constant temperature. Integral asymmetric membranes and dense symmetric membranes of poly(ester urethane urea) were synthesized and characterized in terms of: i) structure by Scanning Electron Microscopy (SEM), and ii) gas permeation properties for N₂, CO₂ and O₂ in the custom-made set-up. The membranes were synthesized by a modified version of the phase inversion technique where polyurethane and polycaprolactone-diol prepolymers react in a solvent mixture of dimethyl formamide and diethyl ether. The total polymer to solvent weight ratio, the solvent evaporation time and the polycaprolactone quantity were varied.

I. INTRODUCTION

Blood oxygenators are one of the main components of the perfusion system, and like natural lungs they are responsible for the gas exchanges. Patients need to be connected to these systems during cardiac surgeries where cardiopulmonary bypass (CPB) is performed and in Extracorporeal membrane oxygenation (ECMO) where pulmonary and/or cardiac functions are artificially supported for long periods of time (days to weeks) [1]. The membrane blood oxygenators (MBOs) are the only type of oxygenators in use today. The ideal MBO has to fulfil a two-fold goal: i) promote efficient gas exchange and ii) be blood compatible or hemocompatible [2]. Despite the widespread use and the 70 years of continuous developments of MBOs, several aspects related to the membrane/blood interactions, circulating blood flow conditions and equipment design still need to be improved [3]. Polyurethanes, having extensive structure and property diversity are one of the most bio- and blood compatible material [4]. Polyurethanes structure is composed of hard segment (HS) urethane linkages (and urea linkages) and soft segments (SS) polyol chains characterized by the high mobility. The chemical composition of polyurethanes backbones is strongly dependent on the composition, type and molecular weights of the SS, degree of hydrogen bonding between groups and the HS/SS ratio [5]. Further increase of the tunability of polyurethanes properties were attained by Zhao that introduced a second type of SS on the polyurethane structure, creating the bi-soft segment polyurethanes [6]. Bi-soft segment polyurethane urea membranes have been thoroughly studied by Professor de Pinho research group [7], [8].

Regarding the established use in vascular tissue engineering, polycaprolactone (PCL) was selected as second SS with the objective of improving the polyurethanes hemocompatibility [9]. Characterization studies of the dense symmetric bi-soft segment poly(ester urethane urea) (PU) membranes showed that the variation of the PCL content effects the surface energy, morphology, topography and hemocompatibility. The PU membranes were found to be nonhemolytic and the in-vitro thrombosis degree was between 27% and 42% for a blood contact time of 15 minutes [10]. Despite the very promising results in terms of hemocompatibility, the gas permeability of the PU membranes did not achieve the minimum required to assure physiological needs of a patient connected to a MBO. To increase the gas permeabilities and simultaneously preserve the enhanced hemocompatibility these membranes were synthesized as integral asymmetric bi-soft segment poly(ester urethane urea) (PEU) membranes, that are composed of a very thin top dense layer and by a bottom thicker porous support layer [11]. The top dense surfaces of the PEU membranes can be tailored with different morphologies when the ratio of the two SSs varies. The increase of the PCL content in the PEU membranes results in lower platelet deposition and inhibition of extreme states of platelet activation. These results are indications that the hemocompatibility properties of the PU dense symmetric membranes are conserved in the PEU membranes [12], [13]. The effect of the solvents weight ratio and the solvent evaporation time used in the preparation of the PEU membranes were studied by Faria et al. [14]. It was concluded that increasing the amount of most volatile solvent in the casting solution results in a decreasing of the dense layer thickness. The membranes prepared with the higher amount of most volatile solvent and the lowest evaporation times were the ones that showed higher permeabilities. The literature reveals that the versatility of polyurethane synthesis is a strong asset on the design of membrane material properties. In the present work, this versatility is further extended to membrane gas permeation properties by the variation of the casting parameters involved in the synthesis of integral asymmetric membranes of bi-soft segmented polyurethanes. The main objectives of this work are: Build and validate a novel experimental set-up capable of measuring the evolution of pressure online, at constant temperature, for extended periods of time; Synthesis of PEU and PU membranes and characterization of the membranes surface and cross-section structures by SEM; Determination of the permeation properties of the PEU and PU membranes towards CO₂, O₂ and N₂.

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II. MASS TRANSPORT PHENOMENA IN DENSE MEMBRANES

The mass transport in dense polymer membranes is assumed to occur by a solution-diffusion-desorption mechanism. The steady state diffusive flux in the y -direction, J_{Ay} , is described by the Fick's First Law (1):

$$J_{Ay} = -D_{Am} \frac{dc_{Am}}{dy} \quad (1)$$

where J_{Ay} is the flux of species A in terms of moles per unit of time and unit of membrane surface area. The gradient of concentration along the membrane thickness is dc_{Am}/dy with c_{Am} being expressed as the molar concentration of solute A in the polymer. The quantity D_{Am} is the diffusion coefficient and can be regarded as a proportionality between the flux and the concentration gradient [15]. Integrating the Ficks First Law over the total membrane thickness, δ , considering that the concentration inside the polymer is proportional to the applied pressure and Henry's law can be applied, and considering the Solution-diffusion model, where the Permeability P_A is the product of Diffusivity D_A and Solubility S_A , (2) is obtained:

$$J_A = \frac{P_A}{\delta} (p_f - p_p) \quad (2)$$

Equation (2) shows that the flux of a component through a membrane is proportional to the pressure difference across the membrane and inversely proportional to the membrane thickness [16]. Usually, Permeability is represented in units of Barrer $\left[10^{-10} \left(\frac{\text{cm}^3 \text{cm}}{\text{cm}^2 \text{scmHg}}\right)\right]$. The transient state diffusive flux is described by the Fick's Second Law (3):

$$\frac{\partial c_{Am}}{\partial t} = D_A \frac{\partial^2 c_{Am}}{\partial y^2} \quad (3)$$

Solving this equation for the following conditions:

$$cc_{Am}(y, 0) = 0 \quad (4.1)$$

$$c_{Am}(0, t) = c_{Am0} \quad (4.2)$$

$$c_{Am}(\delta, t) = c_{Am\delta} \cong 0 \quad (4.3)$$

The Ficks second Law can be solved by a commonly used method of assuming a solution in the form of Fourier series assigning coefficients to meet the boundary and initial requirements [17]. A Solution of the Second Fick's Law is obtained, which for very long times can be approximated to an expression that allow to obtain the diffusivity of the gas in the membrane by a graphical method, known as time-lag method. The plot of permeate pressure versus time, in conjunction with the plot of the asymptotic linear permeation flow in steady state, results in an intercept on the time axis, denoted by t_c (characteristic time). Obtaining t_c from the experimental data, D_A can be obtained from (5).

$$t_c = \frac{\delta^2}{6D_A} \quad (5)$$

III. EXPERIMENTAL

A. Materials

For the membrane synthesis it was used a poly(propylene oxide)-based polyurethane (PUR) prepolymer with a molecular weight of 3500 Da and a prepolymer PCL-diol with a molecular weight of 530 Da. The solvents used were dimethylformamide (DMF) (w / w% grade, 99.8%) and diethyl ether (DEE) (w / w% grade, 99.7%). Tin-Octoate ($C_{16}H_{30}O_4Sn$) (wt.%, 95%) was used as the catalyst for the prepolymers reaction. Permeation tests were performed using N_2 (purity 99.999%), CO_2 (purity 99.98%) and industrial O_2 (purity 99.5%). All gases were used as received.

B. Synthesis of poly(ester urethane urea) membranes

Integral asymmetric PEU membranes, were synthesized by a modified version of the phase inversion technique where the prepolymers PUR and PCL-diol reacted in a solvent system of DMF and DEE in presence of the Tin-Octoate catalyst for two hours. In a second step, the casting solution was spread on a glass plate using a 250 μm casting knife. After a solvent evaporation step, the glass plate was introduced into the coagulation bath (distilled water) where it was left for about 12 hours. When removed from the bath, the membranes were dried in an oven (35 $^\circ C$) for at least 36 hours. The PEU membranes, were synthesized varying the total polymer to total solvent weight ratio, solvent evaporation time (SET) and the PCL content.

The dense symmetric PU membranes were synthesized by the solvent evaporation method, varying the PCL content. Table I shows the chemical composition, solvent time evaporation and total polymer to total solvent weight ratio of the PEU, and PU membranes.

TABLE I: Weight % of PCL, soft segments (SSs), solvent evaporation time (SET) and total polymer (Pol.) to total solvent (Solv.) weight ratio of the PEU and PU membranes.

Membrane	PCL (wt.%)	SET (min)	Pol./Solv.
PEU1	0	0.5	2/3
PEU2	5	0.5	2/3
PEU3	10	0.5	2/3
PEU4	0	0.5	1/1
PEU5	0	0.5	3/2
PEU-1-100	0	1	1/1
PEU-5-100	0	5	1/1
PEU-10-100	0	10	1/1
PEU-15-100	0	15	1/1
PEU-1-95	5	1	1/1
PEU-1-90	10	1	1/1
PEU-1-85	15	1	1/1
PEU-5-95	5	5	1/1
PEU-5-90	10	5	1/1
PEU-5-85	15	5	1/1
PU100	0	n.a.	1/1
PU95	5	n.a.	1/1
PU85	15	n.a.	1/1

C. Set-up for Gas Permeation Measurements

An in house built set-up was used for gas permeation measurements by the pressure method at constant temperature. A temperature controlled unit was built and calibrated to perform gas permeation tests where pressure variation is recorded online. Fig. 1 represents a diagram of the set-up where PfT is the feed pressure sensor and PpT is the permeate pressure transmitter. The permeate chamber volume was $27.7 \pm 0.1 \text{ cm}^3$. In each measurement, a sample of membrane was placed in the permeation cell, after which, a single pure gas (N_2 , CO_2 or O_2) was fed at constant pressure, and all the outlet valves were closed. The pressure at the permeate side was measured as a function of time by the PpT sensor.

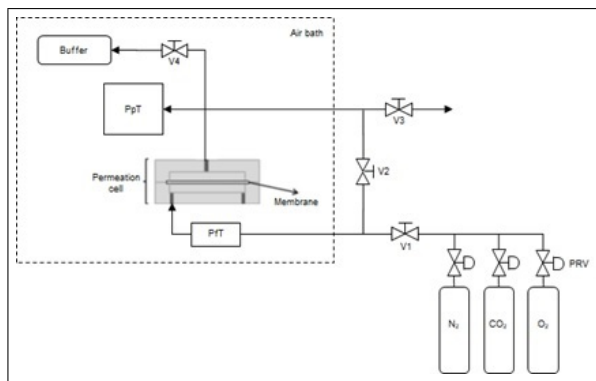


Fig. 1: Scheme of the set-up used in the gas permeation measurements

IV. RESULTS AND DISCUSSION

A. Characterization of the integral asymmetric PEU membranes by SEM

1) *Variation of the total polymer to total solvent weight ratio:* The PEU1, PEU2 and PEU3 integral asymmetric membranes, containing 0, 5 and 10% wt. of PCL, respectively, were synthesized with total polymer to total solvent weight ratio of 2/3 and SET of 30 seconds. It was not verified the formation of homogeneous films. Further membrane synthesys were attained by varying the total polymer to total solvent ratio in 2/3, 1/1 and 3/2. Comparing the morphology and the SEM micrographs of the PEU1, PEU4 and PEU5 integral asymmetric membranes prepared only with PUR and 30 seconds of SET it was determined that, for the materials used, the most suitable total polymer to total solvent ratio is 1/1.

2) *Variation of the solvent evaporation time:* PEU-1-100, PEU-5-100, PEU-10-100 and PEU-15-100 membranes, containing only PUR, were prepared with a polymer/solvent ratio of 1/1, varying the SET in 1, 5, 10 and 15 minutes. It was observed that all of these membranes presented structural sustainability, were homogeneous and elastic. SEM micrographs of the cross-section of these membranes showed that the upper denser layer becomes more distinct with the increase of the SET. In the same order, it is verified an apparent increase of the membrane thickness.

3) *Variation of the PUR to PCL weight ratio:* The PEU-1-100, PEU-1-95, PEU-1-90 and PEU-1-85 membranes were synthesized with a SET of 1 minute and varying the PCL content. SEM micrographs show that the number of pores and its diameter on the membranes top surface decreases with the amount of PCL. The PEU-5-100, PEU-5-95, PEU-5-90 and PEU-5-85 membranes were synthesized with a SET of 5 minutes and varying the PCL content. Fig. 2 shows SEM images of top surface, bottom surface and cross-section of the PEU-5-95, PEU-5-90 and PEU-5-85 membranes prepared with a solvent evaporation time of 5 minutes and PCL wt.% of 5, 10 and 15%, respectively. The membranes appears to have a distinct cross section structure with no visible dense layer but instead two porous regions: close to the upper and bottom surface small pores in large number are observed, while in the most inner part of the membrane is observed a thicker phase with larger pores and less numerous. It is observed that the upper denser layer becomes more distinct, the number of pores and their diameter in the inner region decreases with the increase of the PCL content.

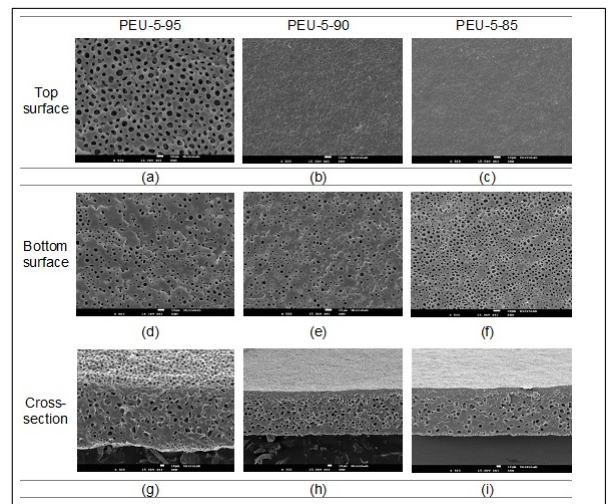


Fig. 2: SEM images of samples of PEU-5-95: (a) top, (b) cross-section, (c) bottom; PEU-5-90: (d) top, (e) cross-section, (f) bottom; PEU-5-85: (g) top, (h) cross-section, (i) bottom.

B. Characterization of the dense symmetric PU membranes by SEM

1) *Variation of the PUR to PCL weight ratio:* The dense symmetric PU membranes prepared were translucent, glassy and very sticky. Fig. 3 shows the SEM images of the top surface and cross-section of the PU100 membrane. The PU100 membrane is completely dense with no visible pores. The same was observed for the PU95 and PU85 membranes.

C. Gas Permeation Properties of the PEU and the PU membranes

The permeance of the PEU-5-95, PEU-5-90 and PEU-5-85 membranes to CO_2 , O_2 and N_2 were measured in the were

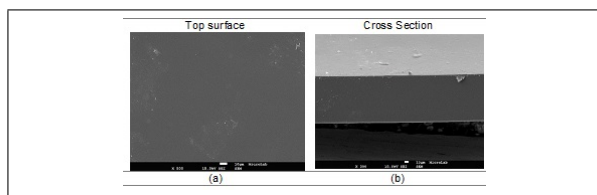


Fig. 3: SEM images of samples of PU100 membrane: (a) top and (b) cross-section.

performed in the custom made set-up. Results show that the permeance values of CO_2 for the PEU membranes were one order of magnitude higher than O_2 permeance values and two orders of magnitude higher than N_2 permeance (Table II).

TABLE II: Average permeance of N_2 , CO_2 and O_2 , obtained for PEU membranes.

Membrane	Perm N_2	Perm CO_2	Perm O_2
PEU-5-100	0.003	0.14	0.011
PEU-5-95	0.006	0.11	0.008
PEU-5-90	0.004	0.12	0.010
PEU-5-85	0.004	0.13	0.015

Permeance (Perm) has units of $10^{-3} \text{cm}^3 \text{cm}^{-2} \text{s}^{-1} \text{cmHg}^{-1}$

The permeation properties of the PU membranes to CO_2 were measured in the set-up. The well known thickness of the dense symmetric PU membranes allow to obtain the permeability of the PU100, PU95 and PU85 membranes to CO_2 that were 163, 94 and 218 barrer, respectively. The Diffusivity and Solubility of CO_2 was determined by the time-lag method for the PU95 membrane. Results show that the diffusion coefficient were $5.6 \times 10^{-7} \text{cm}^2 \text{s}^{-1}$ and the solubility coefficient was $1.9 \times 10^{-2} \text{cm}^3_{\text{CO}_2} \text{cmHg}^{-1} \text{cm}^3_{\text{memb}}$.

V. CONCLUSIONS

A novel experimental set-up capable of recording the evolution of pressure online, at constant temperature was built and validated. Integral asymmetric membranes and dense symmetric membranes were synthesized and characterized by SEM, showing that the upper denser layer of the PEU membranes becomes more distinct with the increase of the PCL content and of the SET. The gas permeation measurements showed that there is no direct relation between the PCL quantity and the permeance of the membranes to a given gas. Considering the gas permeation measurements, a MBO constituted by the PEU-5-85 membrane, to ensure adequate CO_2 fluxes, must have a membrane surface area of 3.4 m^2 , which is in the order of magnitude of the commercial MBOs. A considerably bigger membrane area is required when making this estimation for the O_2 fluxes. Strategies for minimization of the dense layer thickness of the PEU membranes and for enhancement of the circulation conditions in a gas/membrane/liquid system surrogate of MBO must be applied to improve the mass transfer and consequently the reduction of the membrane area that ensure the O_2 and CO_2 fluxes physiologically required.

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