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TRANSPORT PROPERTIES OF COMPOSITE POLYMERIC MEMBRANES FOR ARTIFICIAL ORGANS.

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Polymeric membranes represent a fundamental component of many artificial organs, e. g.: artificial kidney and artificial lung; of ibrid artificial organs, e.g.: pancreas and liver, and of endoprostheses such as vascular prostheses and nerve guidance channels for neural regeneration.

This fact should not wonder at all if we consider the mass transport phenomena occurring in the biological systems, where natural membranes play a role of vital importance in regulating the exchanges between cells of various organs, and fluids or gases in the boby. Moreover, the membrane transport phenomena have a determining role, not merely when they are nominated to perform important tasks such as filtration (kidneys) or gases permeability (lung), but also when they act as fluid or tissue containers (vessel, sheath).

It is also interesting to note that evolution in artificial organs, during the last twenty-five years, was dependent on advances made in permselective and microporous polymers with the required characteristic for the critical membrane portion of the device.

In the design of a ideal membrane for artificial organs the following characteristics must be taken into consideration:

1) The biocompatibility, and the hemocompatibility specifically for devices to be placed in contact with blood.
2) The mechanical properties.
3) The mass transport properties.

It is therefore difficult to realize such ideal membrane starting from a single material, also using fabrication processes able to get membranes with different degree of porosity and therefore with different transport properties.

We propose the fabrication of composite membranes using a novel technology that involves blends of synthetic and or natural polymers which are made porous through a combined spraying and phase inversion technique. In our approach, a polymer solution and a nonsolvent (steam or water) are simultaneously deposited through two separate identical ejectors onto a stainless steel rotating cilinder, resulting in a local precipitation of the polymeric material to form membranes with structural characteristics which may be varied over a wide range.

As working materials we selected polymethylmetacrylate-polyurethane (PMMA-PU) blends and polyurethane-polydimethylsiloxane (PU-PDMS) blends. Three different kinds of flat membranes were produced using the following blends: PMMA(30%)-PU(70%), PMMA(50%)-PU(50%), PMMA(80%)-PU(20%) in 2:1 THF-1,4 Dioxane plus acetone, and steam as non-solvent. Cilindrical membranes with different structural characteristics

were also produced using a blend of PU(90%)-PDMS(10%) in 2:1 THF-1,4 Dioxane, and water as non-solvent.

The present work reports of some "in-vitro" transport measurements obtained with such composite membranes potentially utilizable in artificial lungs and artificial kidney (PMMA-PU), and in ibrid artificial pancreas (PU-PDMS).

Membranes for artificial lung and artificial kidney.

We studied the gases transport properties across membranes by an apparatus consisting of two pneumatic circuits connected with a cell separated by the testing membrane. Temperatures and pressures were monitored in each circuit and transmembrane pressures were balanced for permeability determinations. We used helium as carrier gas and oxygen or carbon dioxide for permeability measurements. The three PMMA-PU membranes were compared with some commercial membranes in order to determine the influence of PMMA content on the permeability coeficient $P = N_\infty \cdot l/(A \cdot p)$ [measured at $\Delta p_{cell} = 0$, where: N_∞= Steady flux condition (cm^3/s), l=Membrane thickness (cm); A=Exchange surface (cm^2); p= Pressure of O_2 or CO_2], on the diffusivity D (cm^2/s), and on the selectivity parameters $K_P = PCO_2/PO_2$ and $K_D = DCO_2/DO_2$.

The results of these measurements are showed in Table 1:

TABLE 1
Permeability data, diffusivity data, and selectivity parameters of commercial and PMMA-PU membtranes (T=25 °C).

Membranes	$PCO_2 \cdot 10^{10}$	$PO_2 \cdot 10^{10}$	$DCO_2 \cdot 10^7$	$DO_2 \cdot 10^7$	K_P	K_D
1) Teflon	4.2	11.7	1.52	0.95	0.36	1.6
2) Cardiothane 51®	2.84	23.2	1.03	0.37	0.12	2.78
3) PDMS	609	3354	18.2	30	0.18	0.61
5) PMMA(30)-Card.(70)	24	28	2.4	2.1	0.86	1.14
6) PMMA(50)-Card.(50)	153	145	4.5	4.6	1.06	0.98
7) PMMA(80)-Card.(20)	35	38	2.16	1.98	0.92	1.04

By the examination of the results reported in Table 1, we can derive the following considerations:

- For $\Delta p_{cell} = 0$ the PMMA-PU membranes show both permeability and diffusivity higher than Teflon and Cardiothane 51®, but lower than PDMS which is considered the best material in this application.
- The PMMA-PU membranes differ from all the other examined membranes since they do not show any selectivity characteristic with respect to CO_2 and O_2.
- The variation of the transport properties with the ratio PMMA/PU leaves open the possibility of utilizing these membranes in artificial lungs.

We also studied the solute transport properties across the same membranes by a dialysis apparatus consisting in a two hydraulic circuits connected with a cell separated

by the testing membrane. Temperatures and pressures were monitored in each circuit and transmembrane pressures were balanced for liquids and solutes permeability determinations. We used water as solvent and NaCl and Vitamine B_{12} as solutes.

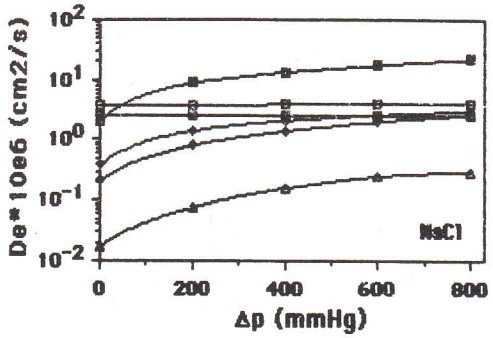

Fig. 1a. De* values vs. Δp of ≠ materials, for NaCl: ▲ PU ; ♦ PU 70 - PMMA 50 ; □ AN 69 ■ PU 50 - PMMA 50 ; ◇ PU 20 - PMMA 80 ; ▪ Cuprophane.

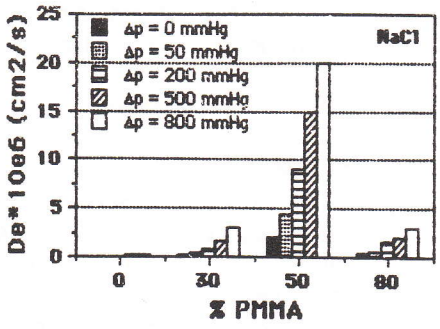

Fig. 1b. De* values vs. % PMMA at ≠ Δp, for NaCl.

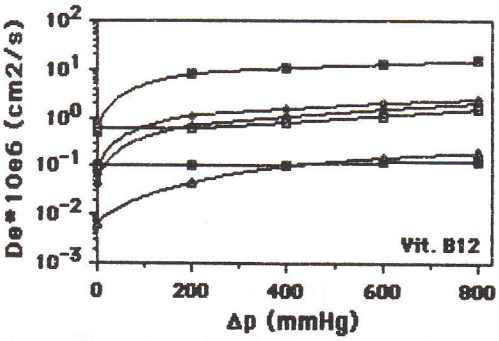

Fig. 2a. De* value vs. Δp of ≠ materials, for Vitamine B_{12} : ▲ PU; ♦ PU 70 - PMMA 30 ; ■ PU 50 - PMMA 50; ◇ PU 20 - PMMA 80; □ AN 69; ▪ Cuprophane.

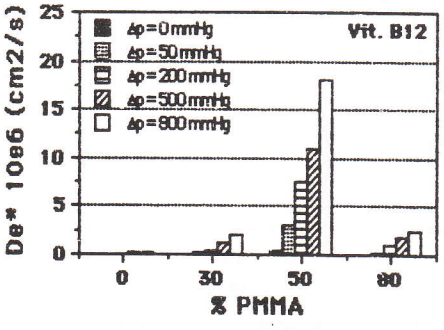

Fig. 2b. De* values vs. % PMMA at ≠ Δp, for Vitamine B_{12}.

For each kind of membrane, both commercial and produced by us, we derived characteristic diagrams in which we reported the **Lp** , **De***, **Jv***, and **Jv*·** γ values as a function of **Δp**. These parameters are normally used to describe the transport properties of homogeneous membranes and according to the theoretical considerations reported in literature, their meaning is : **Lp**= Hydraulic permeability = **Jv/ Dp** ($cm^3/s\ cm^2\ mmHg$); **Jv** = Volumetric flux (cm^3/s); **De***= Apparent effective diffusivity = **Js·l/C_1** (cm^2/s); **Js**= Solute flux (g/s); **C_1**= Solute concentration (g/cm^3); **l**= Membrane thickness (cm); **Jv***= **Jv·l** (cm^2/s); **g** = **Js/Jv·C_1**(adimensional). As an example in Figures 1(a-b) and 2(a-b) we reported **De*** v.s. **Δp** and v.s. the **%** of **PMMA**, for NaCl and Vitamine B_{12}.

The results of the transport properties measurements relative to our PMMA-PU membranes, compared with two commercial membranes [Cuprophane® and AN 69,

polyacrylonitrile (PAN)] show how the % composition of the membranes can markedly affects the membrane transport properties. It is possible to modulate in a wide range, above and below the value of the commercial membranes, the value of D_e^*. Consequentely such new membranes can be easely formulate in order to present higher permeability to small solutes and middle molecules in comparison with Cuprophane® and AN 69, particularly in convective diffusion.

Membranes for ibrid artificial pancreas.

PU-PDMS membranes were processed in order to obtain asymmetric structures with a thin skin on the luminal side and an open trabecular structure in the remaining part of the wall. These membranes were used as tubes, with a 2.5 mm i.d. and a 150 µm wall thickness. Segments of tubes, 15 mm long were first plugged at one end using a polymer solution of the same type as the membranes itself. The chamber so obtained was filled with 1 ml of solution to be tested. The open extremity was then plugged with the same technique. Transport measurements were carried out for D-glucose, ^{125}I-insulin, albumin, immunoglobulin and white blood cells.

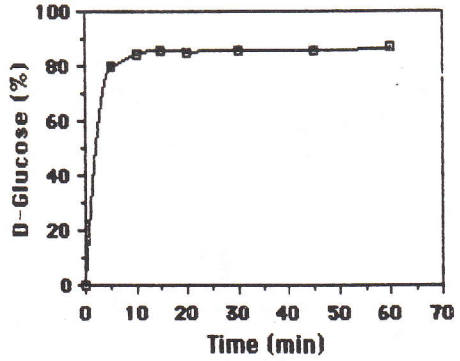

Fig. 3. Diffusion of D-Glucose across the PU-PDMS membrane. The outer glucose concentration at times indicated in abscissa are expressed as a % of the inner concentration.

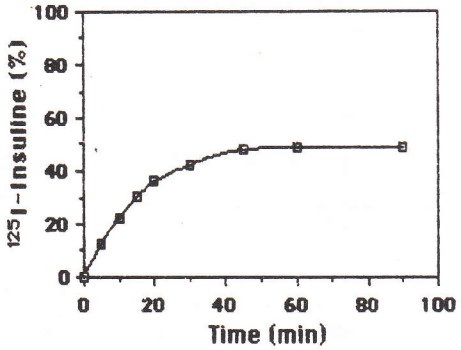

Fig. 4. Diffusion of ^{125}I-Insulin across the PU-PDMS membrane. The amount of insulin diffused out the membrane is expressed as a % of its initial content (240 mU and 282.451 cpm).

Diffusion patterns of D-glucose and ^{125}I-insulin from the chamber to the incubation medium are showed in Fig. 3 and Fig. 4. The diffusion equilibrium of glucose out of the chamber was 85.95 % of the inner concentration. The diffusion equilibrium of ^{125}I-insulin was 48.95 % of the inner concentration. The glucose diffuses much faster, reaching the equilibrium at 10 min with respect to the 45 min of insulin. Albumin, immunoglobulin and white blood cells remained inside the chamber.

The high diffusion rate of D-glucose, together with the good diffusion rate of ^{125}I-insulin across the wall, induce us to propose these permiselective membranes as a potential tool for allo- and xeno-transplantation of islets of Langerhans.

References.

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