

ULTRAFILTRATION MEMBRANES FOR MICRODIALYSIS

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Porous asymmetric polysulfone ultrafiltration membranes were prepared via the nonsolvent-induced phase separation process. The composition of the casting solution was optimized to achieve the required transport properties before membranes in the form of hollow fibers were prepared and characterized. The microdialysis probes were fabricated to extract samples from complex media like living tissues.

Keywords: membrane, ultrafiltration, hollow fiber, microdialysis

1. Introduction

Microdialysis enables highly complex samples such as blood or living tissues to be sampled. This technique relies on the selective transfer of analytes through a dialysis membrane into an acceptor solution (dialysate). The selectivity of this transfer is primarily determined by factors such as the material the membrane is composed of, its pore size (cut-off) and the composition of the acceptor solution [1].

The functional part of the microdialysis probe is an ultrafiltration (UF) membrane - in this case polysulfone (PSU) - with suitable surface properties, which is widely used in industrial and laboratory UF membranes, wastewater treatment [2] as well as hemodialysis modules. PSU can also be chemically modified. The membranes are prepared by the nonsolvent-induced phase separation (NIPS) process resulting in an asymmetric porous structure [3]. The porosity of the membrane and thus its permeance can be influenced by the concentration of PSU in the solvent, that is, the higher the concentration, the less permeable the resulting membrane will be.

As the permeance of polysulfone UF membranes is limited, their porosity can be increased by additives, e.g. the nonsolvent-soluble polymer polyvinylpyrrolidone (PVP) [4]-[5]. In addition, PVP enhances hemocompatibility and prevents fouling [6].

The study commenced with membranes in the form of flat films to optimize the casting conditions as well as regulate porosity and other properties. Once the optimum conditions had been determined, probes for microdialysis were developed and prepared.

2. Experimental

2.1. Materials

Polysulfone from Aldrich Mn 22000 from Aldrich, PVP (K90) from Aldrich as well as Dextrans from Pharmacia with average molecular weights of 9.9 (Dextran T10), 35.6 (T40), 74.3 (T70) and 486 kDa (T500).

2.2. Preparation of membranes

The membranes were prepared by the method of controlled coagulation NIPS. Casting solutions of the desired composition were prepared from a stock solution of PSU in N-methylpyrrolidone by diluting it further and adding a weighed amount of PVP while accelerating the process by heating to about 60 °C and stirring. Within a few hours, the solutions appeared to be homogeneous. This method of preparation is faster, the time the solutions are exposed to humid air is shorter and the measurements more reproducible than when a weighed amount of PSU and PVP in N-methylpyrrolidone was dissolved. This was particularly evident during a series of measurements when one of the parameters was changed. The casting solution that was cooled to room temperature and free of air bubbles was poured onto a glass plate and spread into a uniform film using a doctor blade with a 350µm slot. Having been exposed to air for 10 seconds, the glass with the polymer film was immersed in water as a nonsolvent. The polymer, which was insoluble in water, precipitated in the form of an asymmetric microporous membrane before being washed in water for several hours.



Figure 1: Microdialysis probe (22 mm in length) made of polysulfone UF membrane

The membranes for a microdialysis probe are in the form of hollow fibers with one closed end. A special extrusion device was developed to form these membranes. As the support, a glass fiber 0.90 mm in diameter was used, forming a film of the required thickness on the glass surface. Using the optimized composition of the casting solution, tiny membranes were prepared with an outer diameter of 1.10 mm and 15 to 30 mm in length. To fabricate the microdialysis probe, the hollow fiber membranes were adjusted on the tip of a pipette with a capillary to insert the acceptor solution (Figure 1).

2.3. Measurement of transport properties

The properties of the prepared flat sheet membranes were studied on an Amicon stirred cell, which was pressurized with argon to a working overpressure of 2.0 ± 0.1 bar. The total area of the measured membrane was 13.8 cm² and the amount of permeate that flowed through was determined by weighing.

The properties of the prepared microdialysis probes were measured by a device made in the laboratory. The probes were submerged in a stirred vessel containing a measured volume of liquid. The permeate was collected in the tip of a pipette while a negative pressure of 150 mbar was applied to the tip. The amount of permeate was measured on a calibrated scale.

The concentrations of the dextran solutions used in the measurement of the retention coefficients were determined refractometrically using a Mettler Toledo MyBrix refractometer with an accuracy of 0.4 g/l. The retention coefficient (R) of a given membrane for a given dextran solution describing the relative amount of retained molecules is defined as follows:

$$R = 1 - \frac{c_P}{c_R} \quad (1)$$

where c_R denotes the concentration of dextran in the solution above the membrane and c_P represents its concentration in the permeate.

The retention properties of the given membrane were determined for a series of dextran solutions, that is, T10, T40, T70 and T500, each with a starting concentration of 10 g/l. The experiment progressed from the dextran with the lowest molecular weight to the one with the highest. The permeabilities of water and the individual dextran solutions were measured.

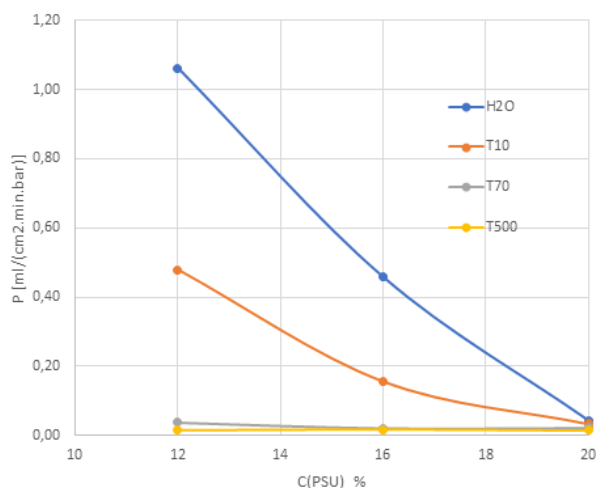


Figure 2: Dependence of the membrane permeance (P) during the ultrafiltration of pure water and aqueous solutions of dextrans on the concentration of PSU in the casting solution (PVP concentration: 4 %)

3. Results and discussion

3.1. Experiments

Changes to the permeation properties of a membrane in the form of a flat film were measured by altering the concentration of PSU and PVP in the casting solution. The dependence on the PSU concentration while the PVP concentration was kept constant at 4 % was studied in detail as shown in Figure 2 and Table 1. As expected, the permeability decreases by increasing the PSU concentration, while retention coefficients for individual dextrans increased. From Table 1, it is also possible to determine the optimal concentration of PSU for the separation of a certain mixture of dextrans or molecules of similar size. For some concentrations of PSU, up to 6 membranes were prepared in order to verify the reproducibility of the preparation process. The accuracy of the permeance measurements and retention coefficients was in excess of 5 %, while the reproducibility was about 10 %.

Next, the dependence of the transport properties on the concentration of PVP in the casting solution was

Table 1: Dependence of the retention coefficients (R) for dextrans on the concentration of PSU in the casting solution (the membranes are identical to those in Figure 2)

| PSU (%) | T10 | T70 | T500 |
|---------|-----|-----|------|
| 12 | 20 | 60 | 99 |
| 16 | 0 | 70 | 95 |
| 20 | 5 | 90 | 99 |

Table 2: Dependence of the retention coefficients (R) for dextrans on the concentration of PVP in the casting solution (the membranes and conditions are identical to those in Figure 3)

| PVP (%) | T10 | T70 | T500 |
|---------|-----|-----|------|
| 0 | 30 | 80 | 99 |
| 2 | 20 | 70 | 99 |
| 4 | 2 | 70 | 95 |
| 6 | 10 | 20 | 90 |
| 8 | 19 | 85 | 99 |

Table 3: Elemental analysis of the prepared dried UF membranes

| Casting solution | | Washed dried membrane | |
|------------------|---------|-----------------------|---------|
| PVP (%) | PSU (%) | N (%) | PVP (%) |
| 0 | 16 | 0 | 0 |
| 2 | 16 | 0.52 | 4.2 |
| 4 | 16 | 0.41 | 3.2 |
| 8 | 16 | 0.88 | 7.0 |

Table 4: Dependence of the retention coefficients (R) for dextrans on the concentration of PSU in the casting solution (the microdialysis probes are identical to those in Figure 4)

| PSU (%) | T40 | T500 |
|---------|-----|------|
| 12 | 23 | 97 |
| 16 | 74 | 99 |

measured while the PSU concentration was kept constant at 16%, as presented in Figure 3 and Table 2. For PVP concentrations lower than 2 %, the permeabilities were very low, in fact only dextrans T10 and T70 passed through the membranes. When the PVP concentration was increased to 4 %, the permeability rose sharply. However, as the PVP concentration increased further, this dependence decreased. By washing water-soluble PVP with a molecular weight of 300,000 out of the membrane, it should become more porous.

The nitrogen contents in the membrane samples, determined by elemental analysis (Table 3), show that part of the added PVP is not removed from the membrane, even when washed with pressurized water in

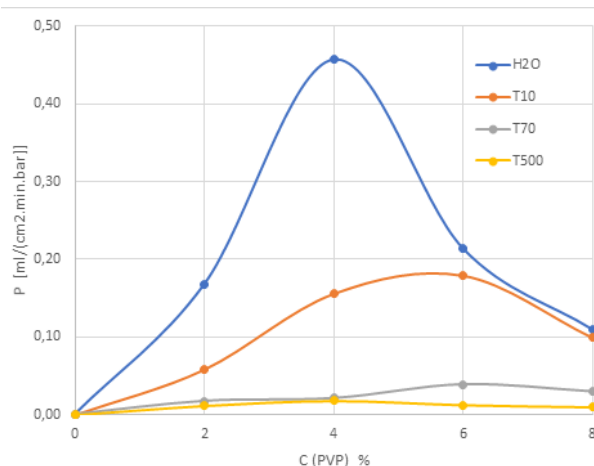


Figure 3: Dependence of membrane permeance (P) during the ultrafiltration of pure water and aqueous solutions of dextrans on the concentration of PVP in the casting solution (PSU concentration: 16 %)

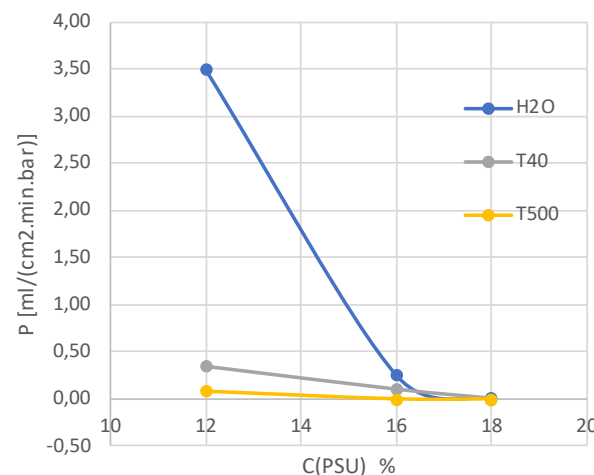


Figure 4: Dependence of the permeance of the microdialysis probe (P) during the ultrafiltration of pure water and aqueous solutions of dextrans on the concentration of polysulfone in the casting solution (PVP concentration: 4 %)

the cell for as long as 100 mins. For example, for a membrane from a casting solution containing 2 % PVP, one third of the added PVP is trapped in its entire profile. However, it is unknown how much of it is captured in the upper "skin" layer directly affecting the permeation properties of the membrane.

The transport properties of microdialysis probes are shown in Figure 4 and Table 4 whereby their dependence on the PSU concentration at a constant PVP concentration of 4 % was measured. Permeabilities are higher than in the case of flat sheet membranes. Although hollow fiber membranes are 60 % thinner, in general, both exhibit similar properties.

4. Conclusions

Porous asymmetric polysulfone ultrafiltration membranes were prepared by the nonsolvent-induced phase separation process. The addition of a certain amount of polyvinylpyrrolidone to the polysulfone casting solution significantly improves the permeation properties of the resulting membranes. The optimized composition consists of 12 to 16 % polysulfone and 4 to 6 % polyvinylpyrrolidone.

Using the optimized composition of the casting solution, tiny membranes in the form of hollow fibers were prepared and characterized before the microdialysis probes were fabricated.

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