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Influence of fluid viscosity on membrane permeability: considerations for extending standard testing

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Abstract: The ISO 7198:2016 standard requests permeability testing for medical cover materials but does not consider for physiological viscosity. This study examines the impact of fluid viscosity on the permeability of polymer membranes under static pressure conditions. A specialized test bench was used to evaluate the permeability of two membrane materials with water and a water-glycerol mixture. The appropriate water-glycerol ratio was determined by rheometric analysis to match physiological viscosity. Permeability was assessed at four static pressure levels using a flow sensor, following ISO 7198:2016. Permeability increased with pressure for both test fluids. However, permeability with the water-glycerol mixture was significantly lower than with water. The application of water alone for permeability testing may not represent the materials behavior under physiological conditions. Including permeability measurements with fluids of physiological viscosity could improve the reliability of standardized testing, ensuring more accurate material characterization for medical applications. On the other hand, the use of pure water represents a worst-case scenario if low permeability of the membrane is required.

Keywords: permeability, viscosity, membranes

1 Introduction

Medical applications utilize a wide range of polymeric and biomaterial-based covers, serving functions such as blood component filtration, drug delivery, or covering on a stent graft [1]. Consequently, these materials must meet specific requirements, which are assessed according to standardized testing procedures. Ensuring a physiologically relevant testing environment is crucial for obtaining application-oriented permeability data. The ISO 7198:2016 standard for tubular vascular grafts and vascular patches specifies certain requirements regarding the testing procedure for the integral water permeability. Within sect. 8.7.2.1.2 and in annex A.5.1.3, test requirements for investigation of the integral water permeability are defined [2]. However, the standard requests testing with particle free water at room temperature, which does not particularly consider for the physiological viscosity of blood [2]. In contrast, ISO 5840-1:2021 references a blood-mimicking fluid with a kinematic viscosity of $\nu = 3.5$ cSt as relevant for mimicking physiological conditions for hydraulic measurement of heart valve prosthesis [3]. This discrepancy highlights a potential gap in the characterization of membranes for cardiovascular implants under physiological conditions. To the best of the authors knowledge, there are no published studies concerning the investigation or comparison respectively of the impact of a different viscosity on membrane permeability under static pressure conditions.

Within the current study, a test bench was employed to evaluate the permeability properties of two different membrane materials depending on the fluid viscosity under static pressure conditions. The permeability was determined and compared using two test fluids with distinct viscosities: water and a water-glycerol mixture.

2 Materials and methods

2.1 Rheometric fluid investigations

As a reference for selecting a suitable viscous test fluid in comparison to water, the blood substitute fluid specified in ISO 5840-1:2021, sect. H.3.3.6, was considered [2]. Borowski et al. (2022) implemented this requirement using a glycerol-saline mixture, with a mixing ratio on physiological conditions for hydraulic measurement of heart valve prosthesis at $\theta = 37$°C [4]. To experimentally determine an appropriate water-glycerol ratio at $\theta = 21$°C, rheometric measurements were performed using a rotational rheometer (HAAKE

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RheoStress 1, Thermo Fisher Scientific, Germany). A composition of water (ρ = 0.998 g/cm³) and glycerol (ρ = 1.261 g/cm³) was analyzed with n = 3 measurements per test solution, resulting in an experimentally determined mixing ratio of $m_{Glycerol}/m_{Total}$ = 0.4 with a density of the blood substitute fluid of ρ = 1.089 g/cm³ and a kinematic viscosity of ν = 3.51 cSt (see also Table 1).

Table 1: Mixing ratios for a water-glycerol mixture with the corresponding kinematic viscosities (θ = 21°C, n = 3)

Mixing ratio Water/Glycerol	Mixture density ρ [g/cm³]	Kinematic viscosity ν [cSt]
50/50	1.141	5.213 ± 0.018
58/42	1.094	3.779 ± 0.021
59/41	1.091	3.653 ± 0.019
60/40	1.089	3.510 ± 0.108
70/30	1.065	2.375 ± 0.178

2.2 Experimental setup for measuring membrane permeability

For this study a customized experimental setup for the assessment of integral water permeability in compliance with ISO 7198:2016, was used. During testing, the sample is exposed to pressure while the amount of fluid passing through is measured. To achieve this, the samples (membranes) were fixed within a custom made sample holder. Each test membrane was stamped out into a circular segment with a diameter of 20 mm. After fixation into the sample holder, the diameter of the wetted surface is D = 10 mm.

To collect the fluid permeating the sample, the holder is positioned above a collection reservoir. Test fluid is pumped through the system using a centrifugal pump (IPD-30.1-50-01, Levitronix, Zürich, Switzerland), which directs the flow through a monitoring flow sensor (LEVIFLOW LFS-008-Z, Levitronix, Zürich, Switzerland, measurement error < 1 % RD within the range of 1 to 800 ml/min). The test fluid is then guided into the inflow of the sample holder. At the outflow of the system, a pressure sensor (type 86A, TE Connectivity, Galway, USA, measurement error < 2 mmHg within the range of 0 mmHg to 286 mmHg and < 3 mmHg within the range of 0 mmHg to 800 mmHg) is installed to record the system pressure and adjust the pump power as the input variable of the control loop.

Before testing, the sample holder is filled and air was removed. Because the sample is tightly sealed within the holder, fluid can only pass through the membrane. The test temperature was θ = 21°C (room temperature). An illustration of the experimental setup is provided in Figure 1.

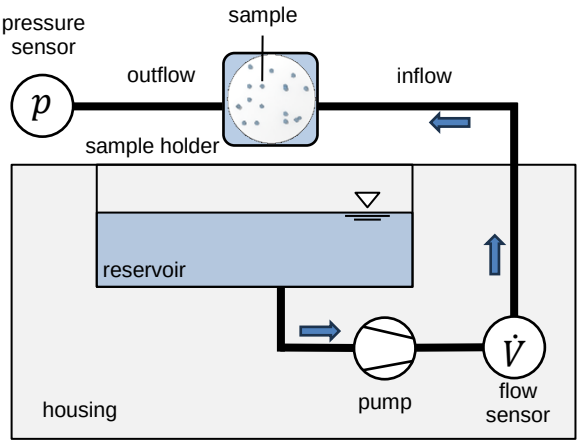

Figure 1: Schematic illustration of the customized test setup for testing water permeability of membranes

2.3 Measurement procedure

For the investigation of the influence of viscosity on the permeability behavior, two representative polymer membranes (*M1* = polyethylene terephthalate (PET) - membrane with 1.2 µm pore size; *M2* = polyethersulfone (PES) - membrane with 0.2 µm pore size), which can be used as cover materials, were used in this study. For both materials, permeability was determined using water as well as a water-glycerol mixture as test fluid.

The test setup allows for pressure-controlled experiments under different conditions. To simulate the physiological vascular pressure range of the human body, four static pressure levels (80 mmHg–200 mmHg; Δp = 40 mmHg) were applied to the test sample [5]. After an initial equilibration phase of 30 seconds, each pressure level was maintained for 60 seconds (holding time) while the flow $\dot{V}$ was measured simultaneously by the flow sensor. The equilibration phase was intended to ensure sufficient wetting of the sample and to compensate for any latent material behavior affecting permeability.

Permeability Q was then calculated using equation (1) according to ISO 7198:2016 and averaged over the 60-second holding time. Each experiment was repeated three times for each material and test fluid [2].

$$Q = \frac{\dot{V}}{\pi \cdot \frac{D^2}{4}} \quad [ml \cdot cm^{-2} \cdot min^{-1}] \qquad (1)$$

3 Results

Figure 2 presents exemplary the calculated permeability and measured pressure as a function of the time for the tested membranes with different fluids. The graphs show the considerably shift of permeability due to viscosity change of the test fluid. For *M1*, the water permeability decreases over time for each pressure step and does not stabilize within the predetermined time. (Figure 2: red line). When using a more viscous medium, the permeability stabilizes much faster for each pressure step (Figure 2: yellow line). This behavior is less pronounced for *M2*. Here relatively constant plateaus are established for both test fluids (Figure 2: blue and green line).

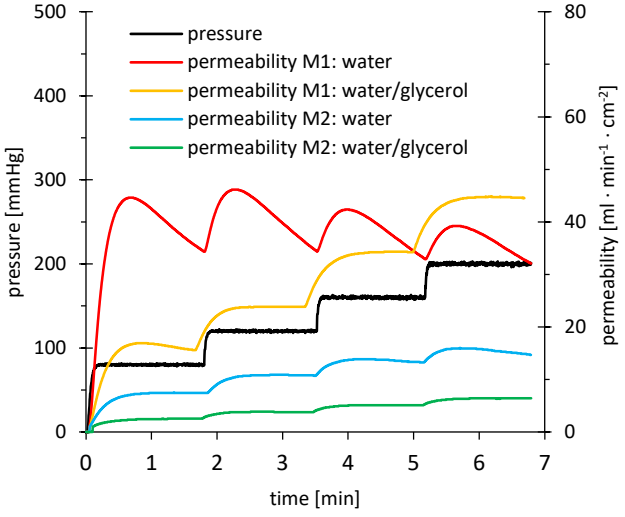

Figure 2: Exemplary presentation of permeability behavior for both materials M1 and M2 with water and water-glycerol at different pressure steps

The permeability measurements of the tested materials (*M1* and *M2*) using both water and the water-glycerol mixture as test fluids are summarized in Table 2 and Table 3. Figures 3 and Figure 4 provide graphical representations of the permeability behavior across different pressure steps.

Table 2: Quantitative results of the permeability for material M1 (PET-membrane) using water and water-glycerol test fluid

Pressure step [mmHg]	Permeability with water [ml · min^{-1} · cm^{-2}]	Permeability with water/glycerol [ml · min^{-1} · cm^{-2}]
80	36.61 ± 3.72	18.67 ± 1.91
120	38.25 ± 3.28	25.33 ± 1.88
160	38.37 ± 2.91	33.36 ± 2.19
200	39.44 ± 4.59	41.97 ± 2.95

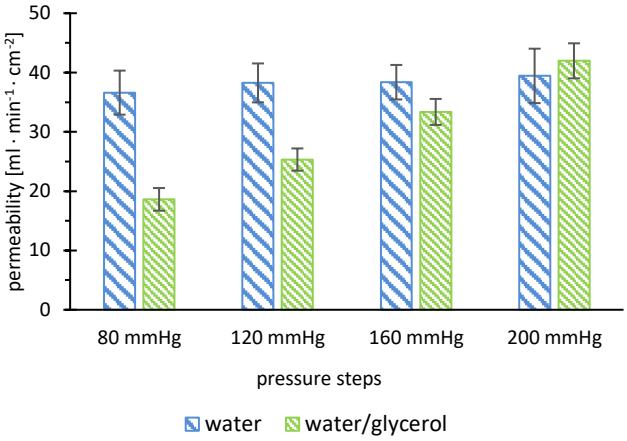

Figure 3: Permeability for material M1 (PET-membrane) using water and water-glycerol test fluid

Table 3: Quantitative results of the permeability for material M2 (PES-membrane) using water and water-glycerol test fluid

Pressure step [mmHg]	Permeability with water [ml · min^{-1} · cm^{-2}]	Permeability with water/glycerol [ml · min^{-1} · cm^{-2}]
80	7.64 ± 0.25	2.30 ± 0.19
120	11.18 ± 0.44	3.53 ± 0.29
160	14.03 ± 0.81	4.73 ± 0.39
200	15.85 ± 1.40	5.83 ± 0.60

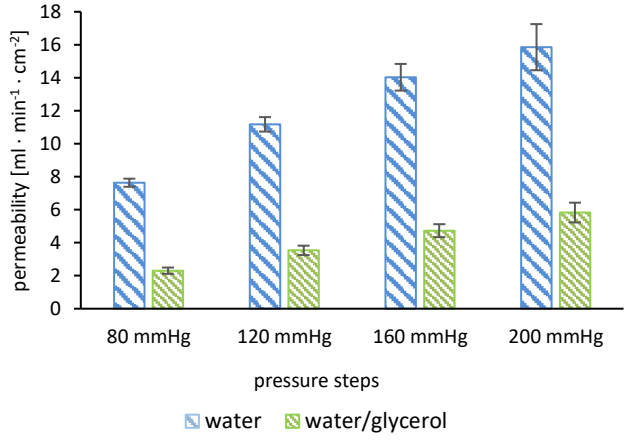

Figure 4: Permeability for material M2 (PES-membrane) using water and water-glycerol test fluid

The permeability increases with increasing pressure for both test fluids. However, there is a distinct difference between

water and the water-glycerol mixture. At lower pressures, the permeability measured with the more viscous test fluid is significantly lower than with water. This difference is particularly pronounced at 80 mmHg, where permeability values with the water-glycerol mixture are approximately 49 % lower for *M1* and 70 % lower for *M2* compared to water.

As the applied pressure increases, the difference in permeability between the two test fluids for *M1* decreases. At 200 mmHg, the permeability values for the water-glycerol mixture approach those measured with water, where the values are nearly converging.

For material *M2*, the ratio of permeability between water and the water-glycerol mixture remains nearly constant across all pressure levels. However, *M2* exhibits considerably lower permeability values compared to *M1* when tested with water. This indicates that the permeability of the material plays a major role in determining fluid transport properties, and the absolute reduction due to viscosity could be more evident in membranes with initially higher permeability, such as *M1*.

4 Conclusion

Within the current study, the permeability properties of two membrane materials were investigated depending on the viscosity of the test fluid. In addition to water, a water-glycerol mixture was used to represent a more physiological test medium in terms of viscosity.

The results of this study highlight that permeability measurements of membranes can be significantly affected by the viscosity of the test fluid. The experimental data show that the use of a more viscous, blood-mimicking test fluid results in significantly lower permeability values in the pressure range of 80–200 mmHg, particularly at lower pressure levels. This suggests that viscosity-dependent fluid transport properties play a critical role in material performance, which may not be adequately captured when testing with water alone.

The observed differences in permeability between water and the water-glycerol mixture vary depending on the material's intrinsic permeability. In highly permeable membranes, the impact of viscosity appears to decrease with rising pressure, while in less permeable materials, the ratio between water and water-glycerol permeability remains relatively stable across all pressure levels.

Given the critical role of cover membranes in medical applications, particularly in vascular prostheses and covering on a stent graft, it is recommended to ensure physiological test conditions from a hydraulic perspective. Therefore, supplementing standardized water-based permeability testing with additional measurements using fluids of physiological viscosity, could enhance the reliability and applicability of permeability data. This adjustment would bridge the gap between standardized testing protocols and actual physiological conditions, ultimately contributing to the improved evaluation and selection of materials for medical applications. Blood is a suspension in which blood plasma has the viscosity of water and components such as erythrocytes primarily determine the viscosity of blood. Water-glycerol is a solution, not a suspension.

The present study highlights the potential of considering test fluids with physiological viscosity when assessing the permeability of cover membranes. The results demonstrate that using water alone may not provide a comprehensive assessment of a material's behavior under conditions which are more representative of its intended medical application. An extension of the permeability test to include a more viscous test fluid in addition to ISO 7198:2016 may be considered [2]. On the other hand, the use of pure water represents a worst-case scenario if low permeability of the membrane is required.

Author Statement

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