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Novel perfluorinated nanofiltration membranes for isolation of pharmaceutical compounds

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ABSTRACT

Polymeric membranes for separation of pharmaceutical intermediates/products by organic solvent nanofiltration (OSN) have to be highly resistant to many organic solvents including high-boiling polar aprotic ones, e.g., N-methyl-2-pyrollidone (NMP), dimethylsulfoxide (DMSO), dimethylformamide (DMF). Unless cross-linked, few polymers resist swelling or dissolution in such solvents; however particular perfluoropolymers are resistant to almost all solvents except perfluorosolvents. One such polymer, designated AHP1, a glassy amorphous hydrophobic perfluorinated polymer, has been studied here. Additional perfluoropolymers studied here are hydrophilically modified (HMP2 and HMP3) versions to enhance the flux of polar aprotic solvents. OSN performances of three types of membranes including the hydrophilically modified ones were studied via solvent flux and solute rejection at pressures up to 5000 kPa. The solutes were four active pharmaceutical ingredients (APIs) or pharmaceutical intermediates having molecular weights (MWs) between 432 and 809 Da and three dyes, Oil Blue N (378 Da), Sudan Black B (456 Da), Brilliant Blue R (826 Da). Solvents used were: ethyl acetate, toluene, n-heptane, *iso*-octane, DMSO, tetrahydrofuran (THF), DMF, acetone, NMP, methanol. Test cells included stirred cells and tangential flow cells. Pure solvent fluxes through three membrane types were characterized using a particular parameter employing various solvent properties. All three membranes achieved high solute rejections around 91–98% at ambient temperatures. HMP2 membrane achieved 95% solute rejection for an API (809 Da) in DMSO at a high temperature, 75 °C. A two-stage simulated nanofiltration process achieved 99%+ rejection of a pharmaceutical intermediate (MW, 432 Da) in 75v% NMP-25v% ethyl acetate solution.

1. Introduction

Quite a few biopharmaceuticals of large molecular weights (MWs) especially monoclonal antibodies (MW $\geq$ 150,000 Da) have come into the marketplace in the last 10–15 years. An overwhelming majority of pharmaceuticals however have MW in 200–1000 + Da range and are produced by organic solvent-based synthesis. The organic synthesis process may involve anywhere from 4 to 20 reaction steps [1]. After each step, one or more of the following steps is often executed: solvent exchanged with another solvent [2–4]; catalyst recovered [5]; the intermediate/product may need to be concentrated/purified [6]. The latter step may involve removal of byproducts, impurities and undesired solvents via liquid–liquid extraction and distillation followed by crystallization for the pure product. A variety of studies [7–10] have recently focused on membrane separation of organic solvents from compounds in the MW range of 200–1000 including pharmaceutical intermediates and active pharmaceutical ingredients (APIs); separation has been studied with organic solvent-resistant nanofiltration (NF) membranes for solvent exchange as well as byproduct removal. Many separation studies have been implemented with different organic solvent-resistant membranes [11–18].

This study is focused on lab-scale study/demonstration of separation of both hydrophilic and organophilic solvents from actual APIs using novel solvent resistant membranes. In conventional pharmaceutical processing, thermal methods [2] utilizing vacuum distillation are employed for solvent removal in the presence of APIs most of them being thermally labile. This becomes impractical especially for high-boiling polar aprotic solvents e.g., DMF, DMAc, DMSO, NMP. Organic solvent

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nanofiltration (OSN) for solvent removal is attractive for such solvents due to room temperature operation.

Nanofiltration of aqueous solutions is an established commercial process [19–21]. Nanofiltration of organic solutions was commercialized first for solvent dewaxing [22] in the petroleum industry. Very few polymers are capable of resisting all pharmaceutically relevant solvents. To develop solvent resistance, most polymers undergo crosslinking reactions of one kind or another. It would be useful to have a polymer which is intrinsically resistant to all solvents of interest in pharmaceutical processing. One such polymer is the glassy amorphous copolymer, PDD-TFE (perfluoro-2,2-dimethyl-1,1,3-dioxole copolymerized with tetrafluoroethylene) [23–25]. The maximum swelling encountered for polymers of this kind with a variety of pharmaceutically relevant organic solvents is less than 2.5% [26–27]. This perfluoropolymer is dissolved only by perfluorosolvents.

Pervaporative dehydration of polar aprotic solvents, DMSO, DMF, DMAc was successfully implemented using a particular variety of this polymer identified as CMS-3 [23]. Organic solvent nanofiltration of dye solutes, Safranin O (MW, 351 Da) and Brilliant Blue R (MW, 826 Da), was successfully studied using another somewhat more open variety of this polymer called CMS-7 [26]. It was found that this highly hydrophobic polymer has very low permeability for polar aprotic solvents [27]. Therefore, small flat membranes developed from hydrophilically modified perfluorinated polymers were studied for OSN of polar aprotic solvents such as DMSO, NMP and DMF. A non-hydrophilically modified perfluorinated polymer also studied here was different from the CMS-7 variety studied earlier. The separation performances of these membranes were characterized in a stirred cell for four APIs and pharmaceutical intermediates having MWs of 432, 546, 629 and 809; all compounds were in solutions of polar aprotic solvents. OSN performances of a few other solvents were also determined. In addition, the following dye solutes, Oil Blue N, Sudan Black B, and Brilliant Blue R having MWs ranging between 378 and 826, were used to characterize the performances of such membranes.

Since tangential flow configurations are often used to limit the effect of concentration polarization, such a configuration was also investigated for particular solutes and solvents. Lastly, the scaled-up performance of one of the membranes in a spiral-wound module having an active membrane area of 1.5 m^2 was evaluated using a dye solute.

2. Experimental

2.1. Materials and chemicals

Two types of perflourinated membranes with prefixes of 106 and 255 (Compact Membrane Systems, Wilmington, DE) were studied. Membranes designated 106 are made of an amorphous hydrophobic perfluorinated polymer with a polyacrylonitrile (PAN) support whereas membranes designated 255 membrane are based on a hydrophilically modified perfluorinated polymer with an expanded polytetrafluoroethylene (ePTFE) support. The 106 membrane is also designated AHP1. The 255 membranes are divided into two groups: HMP2 membranes are used for polar aprotic solvents with high boiling points and HMP3 membranes are used for moderately polar solvents. In addition, HMP2 membranes which were ion-exchanged with an aqueous 0.1 N aluminum nitrate are called pre-treated HMP2 membranes.

The solvents used for pure solvent flux study included toluene (Fisher Scientific, 99.8%), n-heptane (Acros Organics, 99%), ethyl acetate (Acros Organics, 99%), *iso*-octane (Solvent Grade, Fisher Chemical), N-methylpyrollidone (NMP) (Acros Organics, 99%), tetrahydrofuran (THF) (Sigma Aldrich, greater than 99.9%), dimethylsulfoxide (DMSO) (Certified, Fisher Scientific), acetone (Certified, Fisher Scientific) and dimethylformamide (DMF) (EMDMillipore, greater than 99.8%). The dyes used were: Oil Blue N (MW, 378 Da; dye content 96%, Sigma–Aldrich, St. Louis, MO); Sudan Black B (MW, 456 Da, certified by the Biological Stain Commission, Sigma–Aldrich, St. Louis, MO); Brilliant Blue R (MW, 826 Da; dye content 90%, Sigma–Aldrich, St. Louis, MO). Three active pharmaceutical ingredients obtained from GlaxoSmithKline US (Collegeville, PA) were: compound A (MW, 809 Da); compound B (MW, 546 Da); compound C (MW, 629 Da). Of these compounds, API A is an amphoteric molecule whereas API B is neutral; API C is a cocrystal. The fourth compound D, a pharmaceutical intermediate, was obtained from Bristol-Myers Squibb (New Brunswick, NJ) and has a MW of 432 Da; it does not have any charge. Table 1 provides a list of these compounds, their sources and molecular weights.

2.2. Methods

For pure solvent permeation studies, the solvent was introduced into a stirred cylindrical cell (Model HP 4750, Sterlitech, Kent, WA) on the feed side of the membrane from a stainless steel solvent reservoir of 300 cm^3 volume; this liquid was pressurized by a N_2 cylinder (Fig. 1a). The N_2 gas pressure was varied between 2500 and 4000 kPa. First, pure solvent permeation studies were conducted. The pure solvents studied included: ethyl acetate (EtAc), toluene, n-heptane, and *iso*-octane for 106 membranes; DMSO, ethyl acetate, THF, DMF, acetone, and NMP for 255 membranes. The temperature of permeation was 25 °C. The effective area of the membrane in the stirred cell was 14.6 cm^2. A feed volume of ~150 cm^3 was loaded in the stirred cell; the permeate volume collected was ~5 cm^3; the stirring speed was ~350 rpm.

Then, solvent-resistant nanofiltration was conducted with either an individual dye or a pharmaceutical compound present in different solvents. The temperature was 25 °C unless otherwise mentioned. For compound A, the temperature was 75 °C since its solubility in DMSO is quite low. The feed pressure was varied from 3000 to 5000 kPa. The rejection study employed the following solute–solvent combinations: Oil Blue N and Sudan Black B in *iso*-octane; Sudan Black B, Brilliant Blue R, compound A and compound B in DMSO; compound C in NMP. The feed concentrations of all the dyes in solvents were approximately 0.001 mol/L. Feed concentrations of compounds A, B, C, and D were 0.12, 0.24, 0.20, and 0.23 mol/L, respectively for the stirred cell configuration. Feed concentration of compound D was 0.116 mol/L for the cross-flow configuration. Feed and permeate concentrations of all solutes used in the solvent-resistant nanofiltration study were determined by a UV-Vis spectrophotometer (Cary 50 Bio UV-Vis, Varian). In addition, the feed and permeate concentrations of compounds A, B, and C were determined by NMR; those concentrations of compound D were also determined by HPLC.

Supplementary Information (SI) section provides the UV-Vis calibration curves for the following systems: Figure S1 (Oil Blue N in *iso*-octane); Figure S2 (Sudan Black B in *iso*-octane); Figure S3 (Sudan Black B in DMSO); Figure S4 (Brilliant Blue R in DMSO); Figure S5 (compound A in DMSO); Figure S6 (compound B in DMSO); Figure S7 (compound C in NMP); Figure S8 (compound D in 75v% NMP-25v% ethyl acetate). Additional calibration curves provided in SI are as follows: Figure S9 (NMR peak assignment and acquisition parameters); Figure S10 (HPLC method for compound D). Section S1 provides details of the NMR method.

Most of the experiments were carried out in the stirred cell. Some of the solvent-resistant nanofiltration experiments were carried out in a

Table 1
List of pharmaceutical compounds studied.

Compound property and source	Compound identification			
	Compound A	Compound B	Compound C	Compound D
Molecular weight, Dalton	809	546	629	432
Source	GSK*	GSK*	GSK*	BMS**

* GlaxoSmithKline USA.
** Bristol-Myers Squibb.

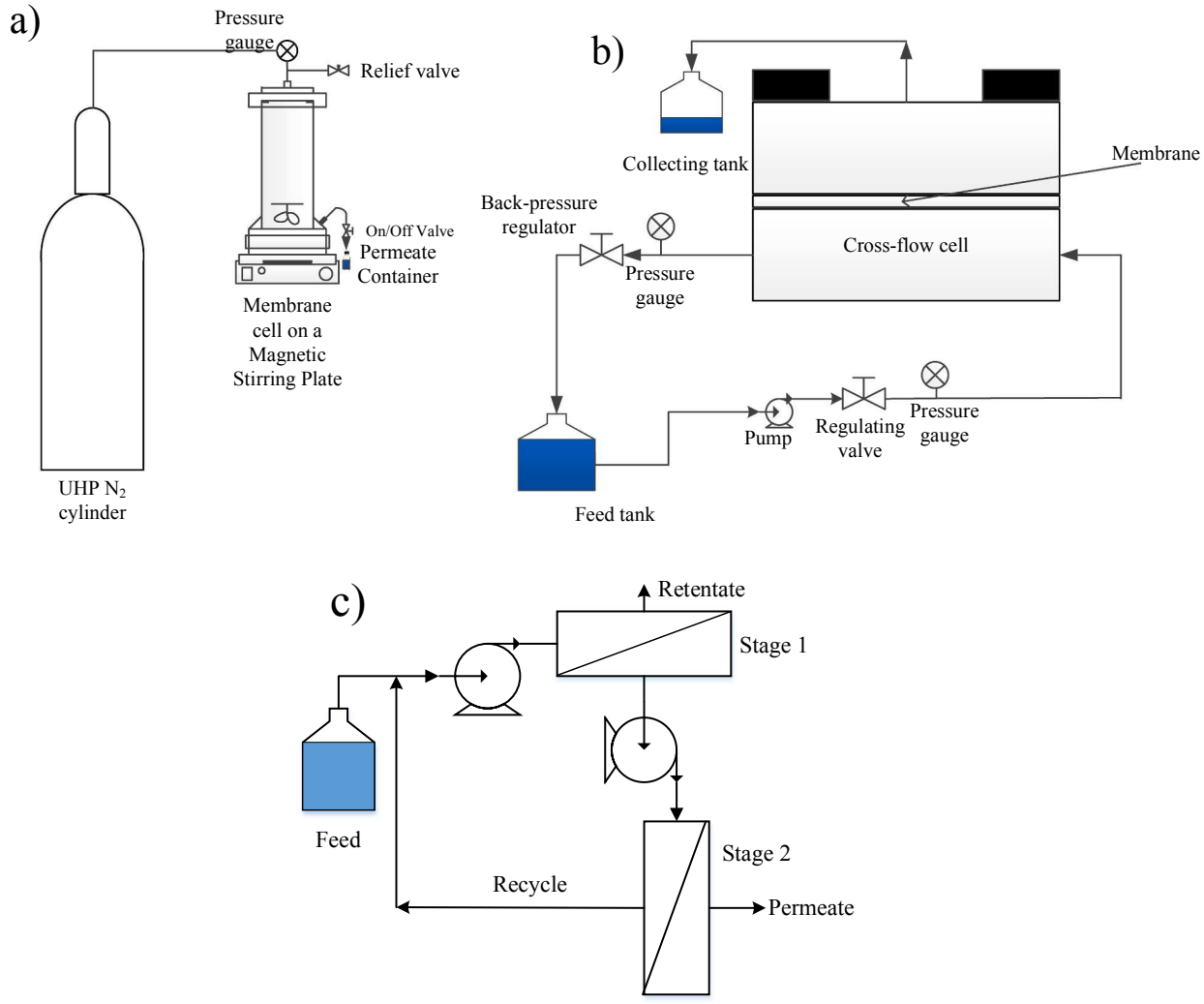

Fig. 1. Schematics of a) the stirred cell with 2500 to 5000 kPa feed pressure and 350 rpm stirring speed, b) the cross-flow OSN set up with ~ 3450 to 4830 kPa feed pressure and 500 cm^3/min recirculation rate, and c) a conceptual continuous two-stage OSN configuration whose batch version was used in this study.

cross-flow cell (Model CF016, Sterlitech, Kent, WA) (Fig. 1b). The flow rate in the recirculation pump was 500 cm^3/min. The effective area of the membrane in the cross-flow cell was 20.6 cm^2. In order to achieve 97+% overall rejections of some compounds, a two-stage nanofiltration process was carried out using the stirred cell (Fig. 1c). The simulated two-stage nanofiltration process carried out in this study was as follows. Permeate from the first stage was not used as the feed for the second stage. A new feed solution was made with almost the same concentration as the collected permeate from the first stage and was used in the study. Finally, rejection study of 1 mM Sudan Black B in hexane solution was carried out using a spiral-wound module of HMP-3 membrane having an active area of 1.5 m^2 at 4136 kPa (600 psi) and 25 °C. The membrane rejection R_i of a solute species i is defined as

$$R_i = \left[1 - \left(C_{ip}/C_{if}\right)\right] \quad (1)$$

Here C_{ip} and C_{if} are respectively the concentrations of the solute i in the permeate and the feed.

3. Results and discussion

We will first present the data on contact angles for the three different membranes studied here.

Table 2 shows that AHP1 is quite hydrophobic. Its contact angle is however significantly smaller than that of the perfluorinated OSN membrane CMS-7 studied earlier namely, 113° [26]. The hydrophilically–modified varieties of perfluorinated polymers HMP2 and HMP3 have even smaller contact angle values than that of AHP1; these two membranes are only mildly hydrophobic with contact angles slightly larger than 90°.

Table 2
Contact angles of water for various membranes.

Membrane	Contact Angle (^{0})
AHP1	104.6 ± 0.5
HMP2	96 ± 1.5
HMP3	96.6 ± 1.1

Fig. 2 illustrates the results of thermogravimetric analysis of the three membranes. The AHP1 membrane starts degrading around 300 °C and around 80% of the weight is lost by around 575 °C; after that the rate of loss is very slow till about 800 °C. No measurements were made beyond 800 °C. This behavior is somewhat similar to that of another fluoropolymer, ethylene chlorotrifluoroethylene (ECTFE) whose degradation starts around 250 °C and is almost complete by 525 °C [28]. On the other hand, both HMP2 and HMP3 membranes show initiation of degradation much later around 500 °C and are completely degraded by around 625 °C.

We will now present permeances of various pure solvents through

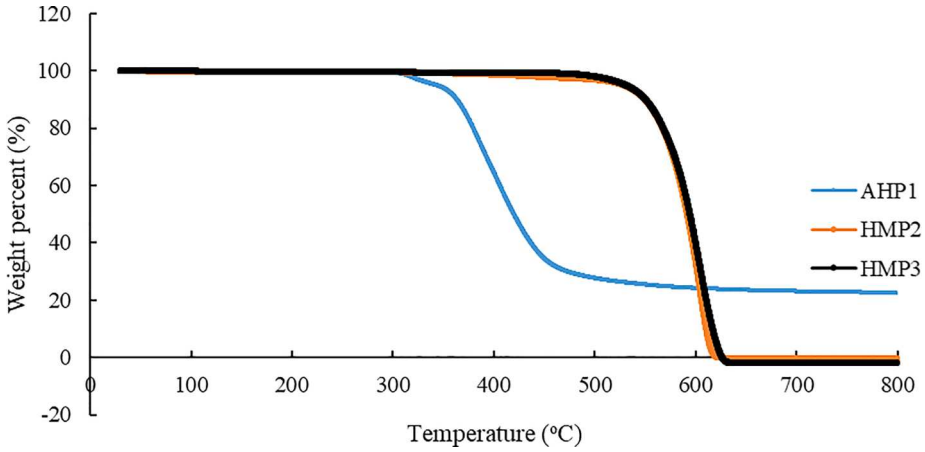

Fig. 2. Thermogravimetric analysis of the three membranes used in the study.

three membranes, AHP1, HMP2 and HMP3 (Fig. 3). The solvents are: ethyl acetate (EtAc), toluene, n-heptane, and *iso*-octane for the AHP1 membrane; DMSO, NMP, DMF and *iso*-octane for the HMP2 membrane; EtAc, THF, acetone, and *iso*-octane for the HMP3 membrane. The feed pressure was varied from 2500 to 4000 kPa. Pure solvent fluxes for a few systems are shown in Fig. 4.

Fig. 4 shows that as the feed pressure increases, the flux increases for both membranes. Fluxes for HMP2 membrane with the polar protic solvents are low but reasonable. Table 4 in reference [7] provides an extensive collection of data of OSN membrane performances for a wide variety of membranes and solvents including some data for DMF with cross-linked PI and a few other membranes which have capacity to resist polar aprotic solvents like DMF. The values of DMF permeance reported there in L/m^2-hr-bar for various membranes including cross-linked PI membranes vary between 0.2 and 2.8 with a number of values around 1.6. These values converted to fluxes for the operating pressures used here will be around twice the value reported here for DMF. On the other hand, the HMP3 membrane yields significant permeate fluxes especially for moderately polar solvents, ethyl acetate and acetone.

Fig. 5 a,b,c show that permeances of all solvents generally increase as the solvent property parameter ($\delta_p{*}\eta^{-1}{*}d_m^{-2}$) increases for each of the three membranes: HMP2 (Fig. 5(a)); HMP3 (Fig. 5(b)); AHP1 (Fig. 5(c)). The increase is much less for AHP1 membrane. This solvent property parameter employs solvent viscosity,η, the solvent solubility parameter due to dipole forces, δ_p, and the diameter d_m of solvent molecules (assuming a spherical model) and was useful also for characterizing permeance through a polar hydrophilic membrane [29]. Fig. 5(b) shows that the permeances of membrane HMP3 with moderately polar solvents happen to be the highest of all membranes studied here. As Fig. 5(a) shows, the permeances of many polar aprotic solvents through HMP2 membranes are considerably lower. The linear correlation is weakest for AHP1 membrane (Fig. 5(c)). We conclude that for the membranes of this study, this type of correlation [29] may be useful only to some extent. We need to exercise significant caution.

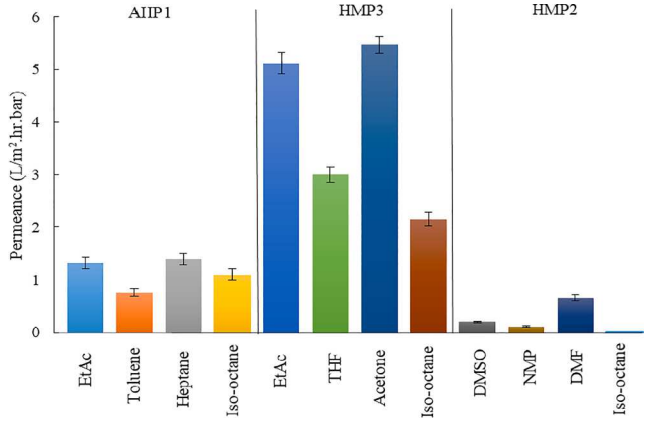

Fig. 3. Pure solvent permeances for three types of perflourinated membranes.

Fig. 6 shows rejections of dyes, Oil Blue N (MW, 378 Da) and Sudan Black B (MW, 456 Da), in *iso*-octane solution for membranes (a) AHP1 and (b) HMP3. It is clear that, as expected, solute rejections increase with solute molecular weight and increasing feed pressure. Both membranes reject at least 91% of the dyes at a feed pressure of 3000 kPa. As the feed solvent pressure increases, solute rejections are enhanced significantly. The rejection values for the lower molecular weight Oil Blue N goes up to 93% for AHP1 membrane whereas that for HMP3 membrane goes up to 94%. The larger MW solute Sudan Black B exhibits a high rejection value of 97.5% for the AHP1 membrane and 96.5% for the HMP3 membrane.

Fig. 7 is focused on solute rejections of the HMP2 membrane for the polar aprotic solvent DMSO in the pressure range of 3000–4000 kPa. The solute MW range varies between 378 and 826 Da. Solute rejection trends as a function of solute molecular weight and feed pressure are similar to those in Fig. 6. Solute rejection increases with increasing molecular weight and increasing feed pressure. HMP2 membrane can reject at least 91% of all solutes studied at 3000 kPa feed pressure. It can reject more than 97% of Brilliant Blue R (MW 826 Da) at a feed pressure of 4000 kPa. All such runs were carried out at 25 °C except for compound A.

Nanofiltration separation for compound A in DMSO (Fig. 7) was done at 75 °C; otherwise compound A would have had a much lower solubility. Its rejection of ~95% by the membrane is remarkable since hot organic solutions coming out of reactors are usually cooled down before carrying out OSN [30]. Higher temperature operations are not carried out also with reverse osmosis and NF membranes for aqueous solutions to avoid significant reduction in solute rejection. Current commercial OSN membranes are recommended for operation below 50 °C. Recent literature reports identify membranes that have high temperature capabilities with polar aprotic solvents. Membranes formed with interpenetrating polymer networks incorporating polydopamine and polybenzimidazole (PBI) were developed successfully for a variety of polar aprotic solvents on porous PBI support for organic solvent nanofiltration; these have high solvent permeance and can withstand up to 100 °C [31]. Thin film polyamide composite membranes on a porous support prepared from a thermally rearranged polymer were also found to have a high permeance for DMF at a high temperature of 90 °C [32].

It is of interest to compare the solvent flux values of DMSO at such a high temperature with those at a lower temperature for this membrane. Table 3 provides the data for pure solvent flux of DMSO at 25 °C for three feed pressures. The table also provides solvent flux data obtained during OSN with compound A at 75 °C. It is clear that the solvent fluxes

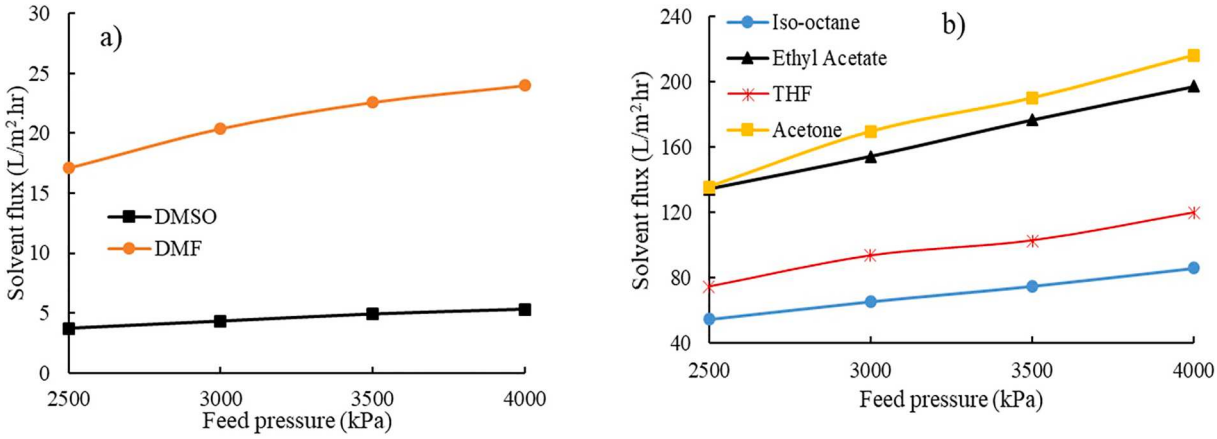

Fig. 4. Pure solvent fluxes for a) HMP2 and b) HMP3 membranes at different feed pressures.

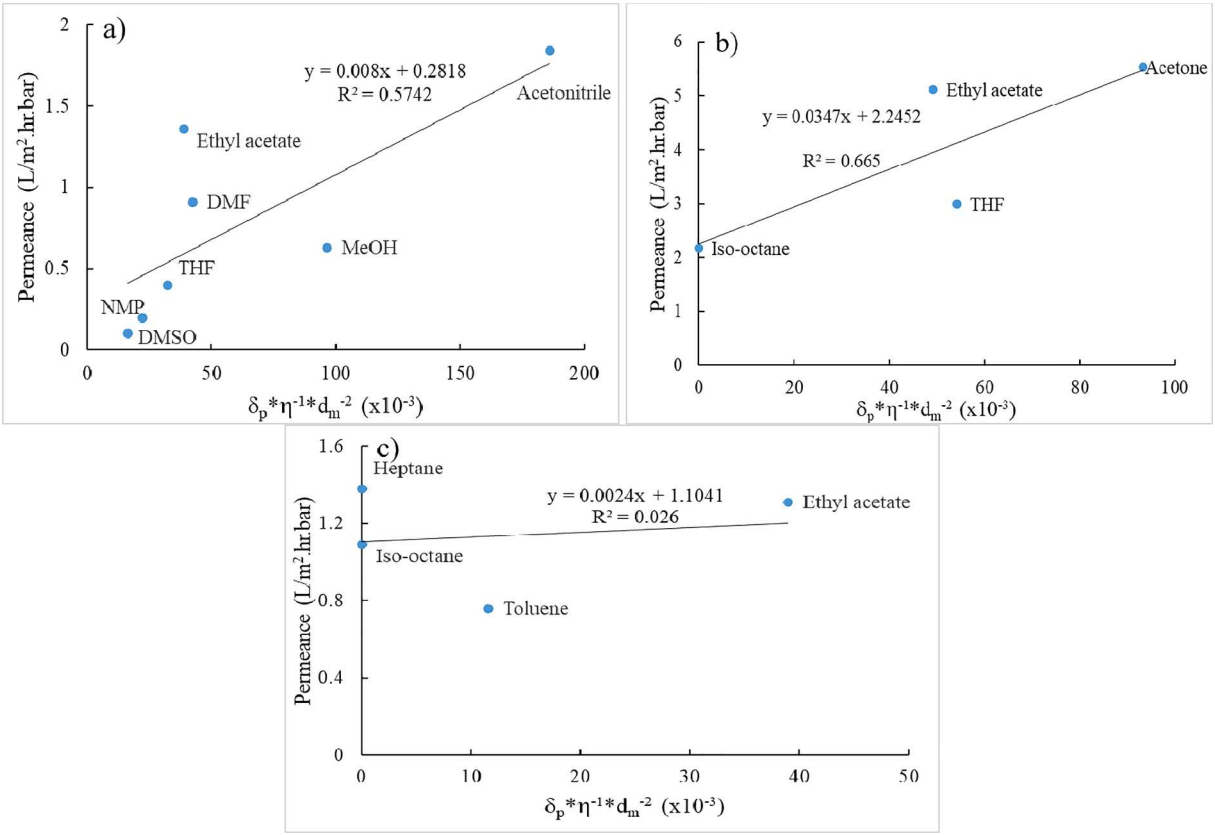

Fig. 5. Permeances of various solvents against the combined solvent property parameter ($\delta_p*\eta^{-1}*d_m^2$) for three membranes: (a) HMP2 membrane for polar aprotic solvents with methanol included; (b) HMP3 membrane for moderately polar solvents with that for *iso*-octane included; (c) AHP1 membrane for nonpolar solvents with ethyl acetate permeance included.

at 75 °C during OSN are higher than those at 25 °C by about 2–3 times with the API rejection being ~ 95%.

Fig. 8 illustrates the observed solute rejection values of compound B (API; MW, 546 Da) in DMSO for 1st stage, 2nd stage and overall purification at different feed pressures; the stirred cell was used. For the 1st stage purification, the HMP2 membrane can reject ~90% of the API. In addition, the solute rejection values estimated by UV–Vis and NMR are comparable. For the 2nd stage purification with much more dilute solutions, the rejection values are not as high as the 1st stage; the value increases with increasing feed pressure. After a 2-stage purification process, the membrane rejected more than 97% of compound B at a feed pressure of 3000 kPa.

Similarly, rejections of compound D (MW, 432 Da) in a 75v% NMP-25v% ethyl acetate solution was studied by a simulated 2-stage OSN process using a pre-treated HMP2 membrane. The results plotted in Fig. 9 show that the pre-treated HMP2 membrane can reject at least 92% of the compound D at lower pressures; at 5000 kPa, the rejection increases to 94%+. The values obtained by both UV–Vis and HPLC are comparable. After a simulated 2-stage NF process, 99%+ of compound D was rejected. Pre-treating the HMP2 membrane improves solute rejections significantly. Therefore, to achieve a high recovery of this pharmaceutical intermediate, a 2-stage NF process is necessary for this membrane. The solvent flux values are provided in Table S1.

A word about multistage processing in OSN is useful. Here we have

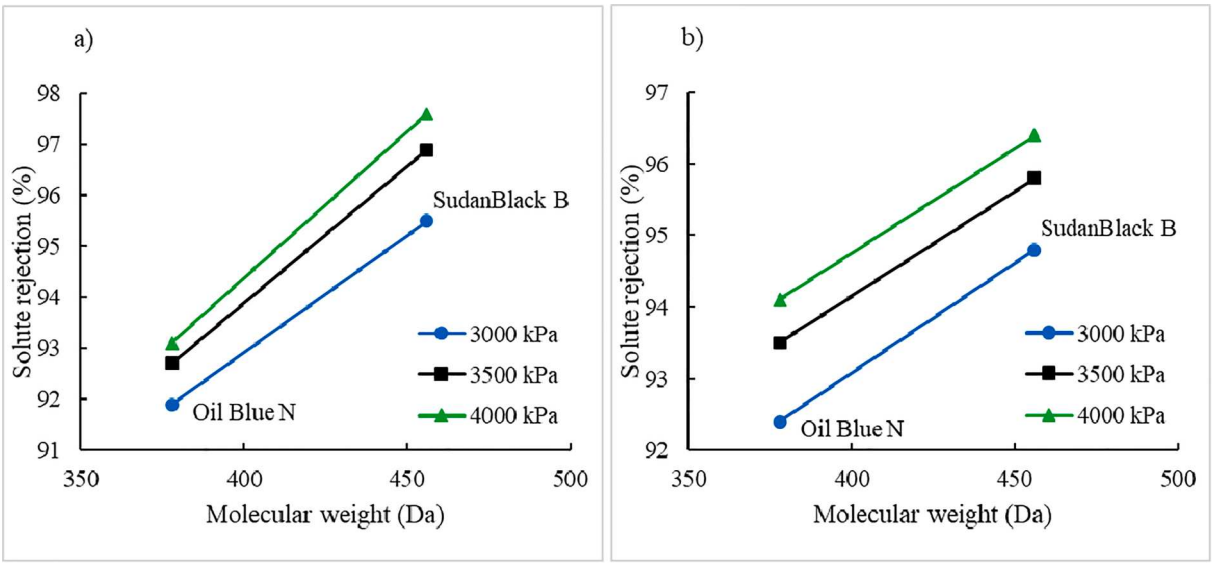

Fig. 6. Solute rejections of dyes, Oil Blue N and Sudan Black B, in *iso*-octane for (a) AHP1 and (b) HMP3 membranes. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

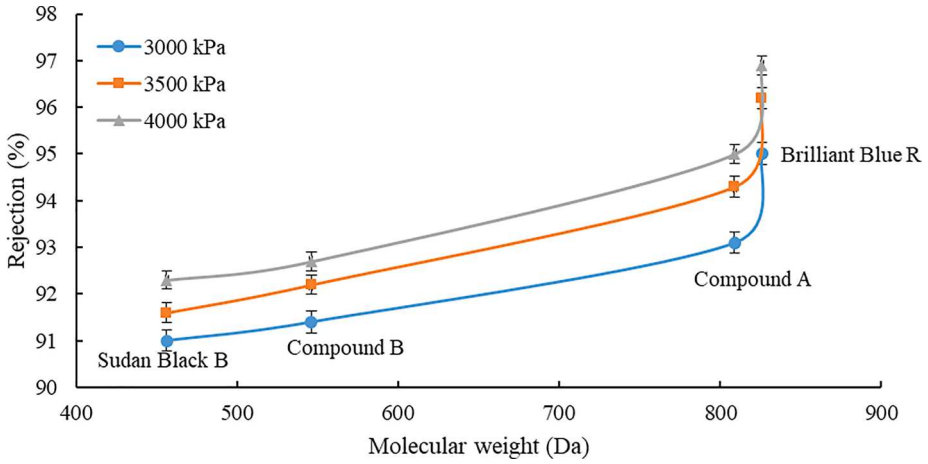

Fig. 7. Solute rejections in DMSO for a HMP2 membrane.

Table 3
Solvent flux of DMSO through HMP2 membrane at different temperatures.

Feed pressure (kPa)	Solvent flux (L/m^2.hr)	
	Pure DMSO at 25 °C	Rejection study of compound A in DMSO at 75 °C
3000	4.3	8.5
3500	4.9	12.0
4000	5.3	14.8

focused on one solute recovery via sequential separation using two stages even though we used a simulated feed for the second stage as feed. Multistaging has been used in the literature for a number of objectives: (1) using a membrane cascade to separate two solutes since the membrane rejection behavior in one stage is not sharp enough [33]; (2) for separation of a two-component mixture, a three-stage organic solvent nanofiltration (OSN) process was used: here 2-stages were used for separation of two solutes with the third stage being used to recycle solvent [34].

Studies on rejections of compound D (MW, 432 Da; a pharmaceutical intermediate) in 75v% NMP-25v% ethyl acetate solution for different

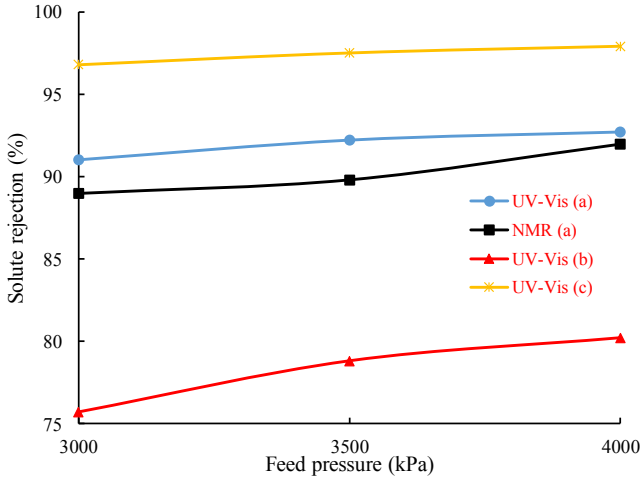

Fig. 8. Rejections of compound B (MW, 546 Da) in DMSO: (a) one stage purification; (b) second stage purification; (c) overall purification for a HMP2 membrane.

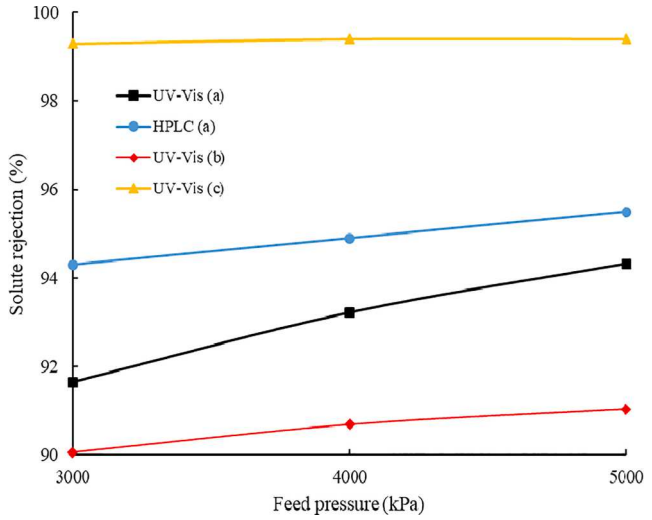

Fig. 9. Rejections of compound D (MW, 432 Da) in 75v% NMP-25v% ethyl acetate by a pre-treated HMP2 membrane: (a) one stage purification; (b) second stage purification; (c) overall purification by two stages.

feed concentrations by a pre-treated HMP2 membrane were also carried out in a cross-flow cell. The results are illustrated in Fig. 10 which shows that rejections increase with increasing feed pressure. In addition, the rejections decrease somewhat as the feed solute concentration becomes much lower via dilution. The rejections obtained for no-dilution feed in the cross-flow cell are comparable to those obtained in the stirred cell shown in Fig. 9. This suggests that in a batch nanofiltration process to remove solvent from a solution of an API/pharmaceutical compound, separation improves as the process progresses since solute concentration will increase with time. However, if the process involves solvent exchange without change in solute concentration, then no benefit is expected since solute concentration is invariant. Solvent fluxes for this case have been shown in Table S2.

Results of rejection studies of API compound C (a cocrystal; MW, 629 Da) in NMP using a HMP2 membrane are shown in Figure S11. The solute rejection values are significantly lower than 90% even though this membrane should easily achieve rejection values around 92–95% for a compound with a MW of 629. Apparently this cocrystal shows significant dissociation in NMP, a polar aprotic, yielding a smaller MW API and the coformer. The molar ratio of coformer/host increased significantly from ~1 mol-eq in the feed to ~1.9 mol-eq in the permeate indicating higher permeation of the coformer, which is likely due to its lower MW (~0.5 x MW of the host). This result indicated that compound C, which was initially thought to be a salt, is actually a co-crystal; this result was

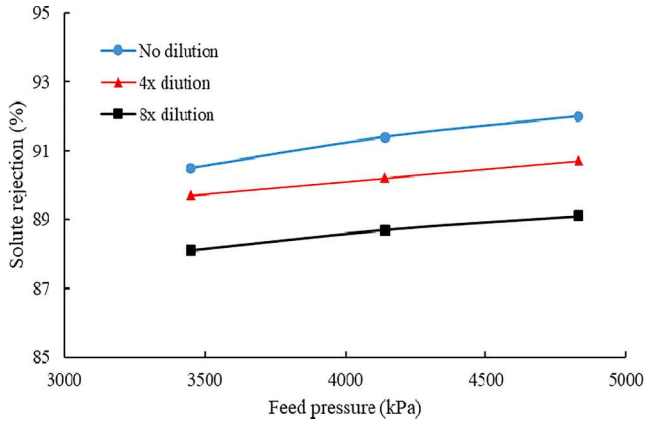

Fig. 10. Rejection of compound D (MW, 432 Da) in 75v% NMP-25v% ethyl acetate at different feed concentrations in a cross flow cell by a pre-treated HMP2 membrane.

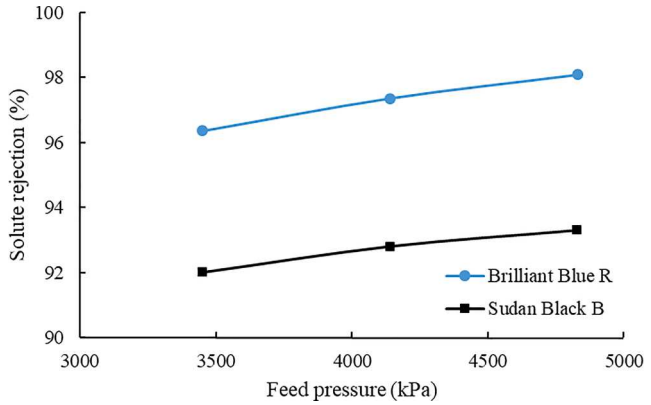

Fig. 11. Brilliant Blue R (MW, 826 Da) and Sudan Black B (MW = 456 Da) rejections in DMSO in a cross flow cell for a pre-treated HMP2 membrane. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

confirmed later with SCXRD.

Studies on rejection of dyes in DMSO were also carried out in a cross-flow cell using a pre-treated HMP2 membrane; the results are plotted in Fig. 11. It shows that rejection values of Brilliant Blue R in DMSO are much larger than those of Sudan Black B due to larger molecular weight of Brilliant Blue R. The pre-treated HMP2 membrane can reject 98%+ and 93%+ of Brilliant Blue R and Sudan Black B respectively at ~4800 kPa feed pressure.

Fig. 12a and 12b provide data on extended term performances of two membranes AHP1 and HMP3 respectively. The runs were carried out at 3450 kPa for around 7 days. The feed solution used was: 0.1 mM Sudan Black B in the solvent hexane. In each case, the solute rejection was always greater than 98%. In each case, there are some gaps in actual data taking due to Covid-19 related shutdown during extended weekends; no one is allowed in the buildings under certain conditions while the run was continuing. The performances appear to be stable.

Lastly, 99+% of Sudan Black B (MW, 456 Da) in hexane solution was rejected in the spiral-wound module of HMP3 membrane at 4136 kPa and 25 °C. The solvent permeance was ~3.61 L/m^2.hr.bar. The run was carried out for 6 hr.

4. Concluding remarks

We have successfully characterized the OSN performances of the glassy amorphous perfluorinated polymer, AHP1, and two types of its hydrophylically modified versions, HMP-2 and HMP-3 over a pressure range of 2500–5000 kPa. HMP2 membranes produced reasonable permeate flux for aprotic solvents e.g., DMSO and DMF. HMP3 membranes yielded very high permeate flux for ethyl acetate and acetone ~140 L/m^2-hr at 2500 kPa feed pressure. The permeances of various solvents through these perfluoromembranes may be characterized as increasing approximately linearly with an increase in the solvent property parameter ($\delta_p{}^*\eta^{-1}{}^*d_m^{-2}$). However, this correlation is quite weak and one should exercise caution. These two types of membranes rejected 92%+ of solutes having MWs larger than 378 Da over the studied pressure range. In addition, remarkably HMP2 membrane could withstand high temperature and achieve 95% rejection of the API compound A (MW, 809 Da) in DMSO solution at 75 °C and 4000 kPa. Further, the solvent fluxes were approximately 2–3 times higher than those at 25 °C. A two-stage simulated nanofiltration process studied to enhance API recovery could recover 99%+ of the pharmaceutical intermediate compound D (MW, 432 Da) in 75v% NMP-25v% ethyl acetate solution using a pre-treated HMP2 membrane. The solvent flux for the first stage of this system was around 3.5–7.0 L/m^2.hr depending on the type of nanofiltration cell used and the applied pressure difference.

Rejections of Brilliant Blue R (MW, 826 Da) and Sudan Black B (MW,

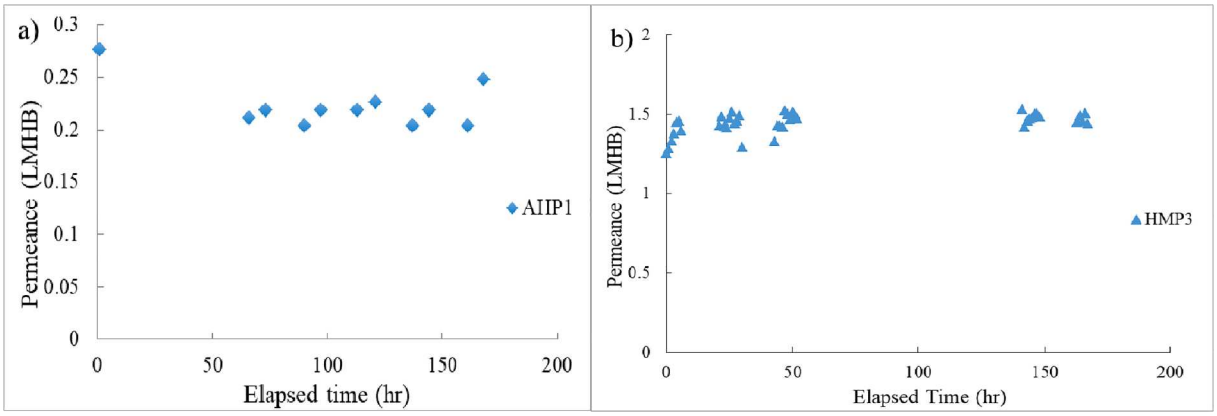

Fig. 12. Extended term studies for (a) AHP1 and (b) HMP3 membranes of 0.1 mM Sudan Black B in hexane solution at ~ 3450 kPa with 98%+ rejection.

456 Da) in DMSO and compound D (MW, 432, Da) in 75v% NMP-25v% ethyl acetate at different feed concentrations were also studied in a cross-flow cell using a HMP-2 membrane. Dye rejections in DMSO in the cross-flow cell were comparable to those obtained using the stirred cell.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.seppur.2020.117944.

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