High flux nanocomposite hollow fiber membrane for hemodialysis

Surendra Kumar Verma1, Akshay Modi1, Atul Kumar Singh2, Rohit Teotia3 and Jayesh Bellare1,2,4*

1Department of Chemical Engineering, 2Centre for Research in Nanotechnology & Science, 3Department of Biosciences and Bioengineering, and 4Wadhwani Research Center for Bioengineering, Indian Institute of Technology Bombay, Mumbai-400076, India
*Corresponding author: jb@iitb.ac.in, Phone: +919820605364

ABSTRACT

Nanocomposite zeolite based hollow fiber membranes (HFMs) were synthesized using polyethersulfone (P) as a base polymer, vitamin E TPGS (T) as an additive, and nano-zeolite (NZ) as a filler. Such membranes would have widespread applications, but one goal was to improve outcomes in hemodialysis for kidney failure patients. The resulting nanocomposite membranes materials (called PT-NZ) were spun based on dry-wet spinning method based on phase inversion. The additive and filler helped nodular organization of the polymer into nano-sized domains with numerous pores inbetween, and improved transport properties. They also helped with presenting a more biocompatible surface to the blood and thereby improved hemocompatibility. The PT-NZ membranes were used to fabricate modules consisting of bundles of fibers, and the modules were, in turn, fabricated into mini dialysers. The ultrafiltration coefficient of such PT-NZ HFM-based module (of about 274 mL/m²-hr-mm of Hg) was about 1.5-times higher than that of the commercial (F60S) membrane (about 152 mL/m²-hr-mm of Hg). The bovine serum albumin BSA rejection in aqueous mixtures was found 93.98 %. The toxin clearance performance of lab-scale PT-NZ HFM-based hemodialyzer with uremic toxin spiked goat blood was remarkably higher (about 5X more reduction ratio) than that of commercial F60S hollow fibers. Hence, the synthesized PT-NZ HFMs can be a potential membrane material for the hemodialysis application. The newly made HFMs reported here could help in decreasing the total treatment time and reducing side-reactions during dialysis for those end stage kidney disease (ESRD) patients dependent on hemodialysis.

Keywords: Nanocomposite hollow fiber membrane; hemocompatibility; ultrafiltration coefficient; solute rejection; uremic toxin clearance

1 INTRODUCTION

Chronic kidney disease (CKD) is one of the major diseases that the World population is facing today. Lakhs of people die annually due to lack of affordable treatment available. In addition to this, there is a tremendous shortage of donor organs compared to the required ones. So, dialysis is the most promising alternative solution to these patients.
2.2 Fabrication of HFMs

Polymer dope solution of specified composition was prepared to fabricate HFMs using indigenous pilot plant using dry-wet spinning method based on liquid-liquid phase separation [10]. The process parameters were listed in Table 1.

Table 1: Process parameters for HFMs manufacturing

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>25</th>
</tr>
</thead>
<tbody>
<tr>
<td>R.H. (%)</td>
<td>50-60</td>
</tr>
<tr>
<td>Dope comp. (% w/w)</td>
<td></td>
</tr>
<tr>
<td>Samples</td>
<td>PES</td>
</tr>
<tr>
<td>PT</td>
<td>18</td>
</tr>
<tr>
<td>PTN-25</td>
<td>18</td>
</tr>
<tr>
<td>PTN-50</td>
<td>18</td>
</tr>
<tr>
<td>PTN-75</td>
<td>18</td>
</tr>
<tr>
<td>Bore comp.</td>
<td>DI water + 33% (v/v) NMP</td>
</tr>
<tr>
<td>Dope/bore temperature (°C)</td>
<td>25</td>
</tr>
<tr>
<td>Dope/bore flow rate (ml/min)</td>
<td>2</td>
</tr>
<tr>
<td>Air gap (cm)</td>
<td>45</td>
</tr>
<tr>
<td>Coagulation/rinse bath composition</td>
<td>DI water</td>
</tr>
<tr>
<td>Coagulation bath temperature (°C)</td>
<td>45</td>
</tr>
</tbody>
</table>

2.3 HFMs Characterization

Surface morphology of HFMs was studied using scanning electron microscopy (SEM) (JEOL JSM-7600F, Japan).

2.4 Fabrication of Lab-scale HFM-based Hemodialyzer

Lab-scale modules of PT, PTN-25, PTN-50, PTN-75 and F60S HFMs were made by potting HFM ends with Araldite® and sealing fibers in the Teflon™ tube. These modules were used in ultrafiltration coefficient and BSA solute rejection. Next, these modules were then housed in an acrylic pipe to make lab-scale HFM-based hemodialyzers, and the two ends were then sealed using Araldite®. The exposed surface area was kept constant in all dialyzers. The prepared hemodialyzers were used for the uremic toxin clearance study with toxin spiked goat blood. The representative picture of the lab-scale hemodialyzer is shown in Figure 1.

2.5 Hemocompatibility studies of HFMs

The prepared HFMs were studied for the hemocompatibility (hemolysis and platelet adhesion) as per the protocols followed in our previous study [11]. The blood was taken from a healthy donor as per the prescribed institute norms. Also, HFM samples were equilibrated with NSS.

Hemolysis: The hematocrit obtained from the centrifuged human blood was incubated with HFM samples for 1 h at 37 °C and 5 % CO₂ in incubator (Thermo Scientific™). DI water and NSS were used as positive and negative controls, respectively. Then, the samples were centrifuged at 1000x g for 5 min. RBC lysis was quantified to calculate hemolysis ratio (HR).

Platelet adhesion: The supernatant having PRP obtained from the centrifuged human blood was collected and was incubated with HFM samples for 2 h at 37 °C and 5% CO₂ in incubator. The samples were gently washed with NSS, and fixed with 3% glutaraldehyde. Then, the samples were dried with ethanol-water solutions. The samples were coated with Au/Pd using sputter coater (JEOL JFC-1600, Japan), and the cell attachment and activation on different HFM samples were observed under SEM.

2.6 Separation Performance

The ultrafiltration coefficient and BSA solute rejection were measured following the protocols and equations mentioned in our previous study [12]. The cross flow filtration system was used for the studies.

Ultrafiltration coefficient: DI water was pumped at a constant flow rate of 60 ml/min through the lumen of the HFM-based module for 2 h, with the collection of permeate at a regular interval of 15 min., maintaining the pressure difference across the membrane module as 50 kPa.

BSA solute rejection: BSA stock solution (1 g/l) was pumped at a constant value of flow rate (60 ml/min) through the lumen of HFM-based module for 30 min., keeping the transmembrane pressure 50 kPa. After 30 min., permeate was collected and the amount of BSA was determined using BSA analysis kit (Micro BCA Protein Assay Kit, Pierce Biotechnology, IL, United States).

Toxin clearance study with toxin-spiked goat blood: The goat blood was collected as per the standard protocol, and the values of urea, creatinine and phosphate in goat blood were spiked up to the respective levels in CKD stage-5 patients, or popularly known as end-stage renal disease.

Figure 1: The representative pictures of lab-scale HFM-based hemodialyzer.
(ESRD) patients. Dialysis procedure and the dialysis circuit were the same as mentioned in the section “Hemodialysis using a simulated solution” of IS/ISO 8637:2004. Pre-and post-dialysis blood samples were collected and sent to an ISO 9001:2008 certified pathology laboratory for the biochemistry tests to determine the values of toxins (urea, creatinine and phosphate).

3 RESULTS AND DISCUSSION

3.1 HFM Characterization

Figure 2 shows the SEM images of the different asymmetric HFM samples (PT, PTN-25, PTN-50 and PTN-75) prepared in this study. The finger-like structures in the skin layer of the HFMs and the presence of micro to macro voids in the layer towards support layer are also visible. HFMs are predominantly porous.

3.2 Hemocompatibility studies of HFMs

Hemolysis: Sheer-force generates due to the flow of blood, which may lead to the rupturing of red blood cells (RBCs) when blood comes in contact with hemodialyzer membrane. It releases hemoglobin in the hemodialyzer membrane. It releases hemoglobin in the hemodialyzer membrane. It releases hemoglobin in the hemodialyzer membrane. Percentage hemolysis was calculated to determine their suitability for the hemodialysis application. The percentage hemolysis less than 5 is regarded as non-toxic according to ASTM F-756-08 standard. Clearly, the percentage hemolysis values reported are well within the permissible limit which indicated the blood-contact suitability of the prepared HFMs in this study, with PTN-50 HFMs being the best membrane material among all HFMs (Figure 3).

3.3 Separation Performance

Ultrafiltration coefficient: \(K_{UF}\) determines the flux of a dialyzer, and usually high value of \(K_{UF}\) is desirable for kidney dialysis. In this study, with increase in the NZ content in HFMs, the value of \(K_{UF}\) increased from 51 mL/m²-hr-mm Hg to 379 mL/m²-hr-mm Hg (Figure 5A). The hydrophilic nature of NZ altered the interfacial polymerization kinetics and membrane structure resulting in enhanced membrane permeability [15].

BSA solute rejection: The efficacy of a membrane material for the hemodialysis application was studied using BSA solute rejection which corroborates to retention of the albumin present in the blood during hemodialysis. Figure 5B shows the comparative performance of all the
membranes tested in the study. % BSA solute rejection for PT, PTN-25 and PTN-50 is comparable to that of the F60S. However, the value is considerably less for PTN-75 which may be attributed to the increased pore size in PTN-75 which resulted in significant loss of BSA. Thus, although the higher value of $K_{UF}$ was achieved with PTN-75 HFMs but the low solute rejection may hinder its use for the hemodialysis application. So, PTN-50 HFMs was chosen for the uremic toxins removal experiment with goat blood, alongwith PT and F60S HFMs.

The superior performance of PTN-50 HFMs to that of F60S HFMs may be corroborated to the following reasons: (1) Vit. E TPGS improved the hemocompatibility, i.e., less hemolysis, low platelet adhesion and minimal activation leading to less side-reactions during hemodialysis. and (2) incorporation of NZ particles improved the porous structures of PT-NZ HFMs desired for hemodialysis resulting in increased separation performance.

4 CONCLUSIONS

PTN HFMs with high $K_{UF}$, and improved hemocompatibility were indegenously fabricated without affecting the BSA rejection and high value of $K_{UF}$ resulting in decreased treatment time. It implies the safer usability of PTN HFMs for hemodialysis. The toxin reduction ratio was significantly higher (5-times) for PTN HFMs than that for F60S HFMs which is due to incorporation of vit. E TPGS to improve the hemocompatibility, and incorporation of NZ particles to improve the porous structures of PT-NZ HFMs desired for hemodialysis resulting in increased separation performance. Thus, PT-NZ HFMs may be a potential hemodialyzer material for hemodialysis application.

REFERENCES