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Chemically modified polymeric filtration membranes for the selective elimination of active pharmaceutical ingredients from water

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Poly(ether sulfone) (PES) filtration membranes were chemically modified by ultraviolet-assisted graft polymerization radical reactions using two monomers, namely acrylic acid (AA) and N-vinyl-2-pyrrolidone (NVP). The reaction kinetics was assessed by applying increasing irradiation durations keeping the monomer concentration constant, and the degree of substitution of the produced materials was monitored by attenuated total reflection-Fourier transform infrared spectroscopy. The selective binding properties of the produced chemically modified membranes of a series of active pharmaceutical ingredients (APIs), namely 4-acetamidophenol (APAP), ofloxacin (OFX), ciprofloxacin (CFX), tetracycline (TC), chloramphenicol (CHPH), (±)-propranolol (PRO) and diclofenac (DF) were evaluated by means of high-performance liquid chromatography. It was observed that native PES membranes showed specific elimination of some of the selected pharmaceuticals (*i.e.* PRO, OFX, CFX and DF), and this elimination was improved after chemical modification with AA (except for DF). After chemical modification by NVP, the binding properties were partially improved for several pharmaceuticals, namely TC, CHPH and PRO, and partially reduced for OFX and CFX. The selective elimination of PRO was significantly improved with both AA- and NVP-modified membranes. The reported results demonstrated that the chemical modification of PES filtration membranes allowed improving significantly their API retention properties. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: PES membrane; UV-assisted graft polymerization; selective elimination; pharmaceutical

INTRODUCTION

The consumption of medications in industrialized countries is undergoing a permanent growth amplified by the emergence of self-medication practices. The use of pharmaceuticals is not limited to humans; indeed, they are also widely used for animals. A relevant number of investigations reported fairly high concentrations of active pharmaceutical ingredients (APIs) in waters.[1,2] A relevant part of APIs is not eliminated by municipal sewage treatment plants and is released into the aquatic environment. Typically, the concentrations of the detected API residues are low; however, some of them were found to be as high as multi μg/L-level[3] and therefore represent a potential risk for human health. To date, a number of processes have been developed for the removal of pharmaceutical from waters; they include activated sludge reactors,[4,5] oxidation by ozone[6] and hydroxyl radicals.[7] Nevertheless, in addition to their high operating costs, their effectiveness is limited. Membrane filtration processes[8] represent a good alternative as they typically require less energy and can be combined with other separation processes.[6,9] Ceramic-based materials are known to be excellent materials for manufacturing membranes; nevertheless, their fairly high production costs limit their application to high added-value products. As an alternative, poly(ether sulfone) (PES) is relevantly cheaper and possesses excellent mechanical properties (*e.g.* high tensile strength and elongation at break), thermal and chemical stabilities; this polymer is widely used to manufacture filtration membranes.[10] Despite these advantages, the drawbacks of PES, mainly related to its hydrophobicity and difficulty of chemical modification, need to be solved. To that end, several surface modification techniques have been reported such as coating,[11] plasma treatment,[12,13] grafting polymerization[14] and blending.[15] In addition, ultraviolet (UV)-assisted graft polymerization has been demonstrated to be a beneficial method because it allows modifying the surface of the material (*i.e.* membrane) without altering its bulk properties. During this processing, polymer chains are grafted onto the surface and in the pores of the membrane.[16] It is worth mentioning that several studies reported that the so-modified membranes possessed good separation ability and enhanced antifouling properties.[14,17–19]

Microfiltration is applied for the treatment of drinking water since 20 years, and the use of ultrafiltration and nanofiltration is also proved to be useful for removal of micropollutants and natural organic matter from water.[6,8] In the present manuscript, we report on our investigations of UV-grafted PES membranes with selective pharmaceutical elimination properties by

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using two different hydrophilic monomers, acrylic acid (AA) and N-vinyl-2-pyrrolidone (NVP). A dead-end filtration equipment was used to assess the elimination of these pharmaceuticals dissolved in water. The degree of grafting (DG) and the influence of the chemical modification on the selective retention of API are discussed.

EXPERIMENTAL

Materials

PES membranes (nominal pore size, $d_p = 0.22$ μm; membrane thickness, $d_m = 110$ μm) were purchased from Tianjin Kava technology (China). 4-acetamidophenol (APAP), ofloxacin (OFX), ciprofloxacin (CFX), tetracycline (TC), chloramphenicol (CHPH), (±)-propranolol (PRO) and diclofenac (DF) were purchased from Sigma-Aldrich (China). All other chemicals were purchased from Sinopharm (China) and used without further purification.

UV-assisted graft polymerization

PES membrane sheets were cut into discs of 12 mm in diameter. These discs were washed with nanopure water and then immersed in nanopure water for 24 h in order to remove the membrane wetting agent (glycerol). Solutions of AA and NVP in water were prepared at a concentration of 5 wt. %. A method slightly modified from that previously described by Pieracci *et al.* was used for the surface modification of PES menbranes.[16] The discs were dipped in the monomer solution (AA or NVP, 5 wt. %) for 10 min and subsequently exposed to UV irradiation under nitrogen using a Scientz03-II UV oven system (254 nm UV, Ningbo Scientz Biotechnology, China). For both monomers, the modification was carried out at different irradiation durations (0.5, 1, 2, 3 and 5 min). After the reaction, the membranes were thoroughly washed in water at 25 °C and dried in air. The so-treated membranes were characterized by attenuated total reflection-flourier transform infrared spectroscopy (ATR-FTIR) (Tensor 27, Bruker). Sixteen scans were taken with a 4 cm^{-1} resolution between 4000 cm^{-1} and 600 cm^{-1}. The DG was evaluated, as previously described,[18] using the following formula:

$$DG = \frac{H_{X,M}}{H_{1487,M}} - \frac{H_{X,U}}{H_{1487,U}}$$

where $H_{X,M}$ and $H_{X,U}$ are the peak heights of the carbonyl group (1662 cm^{-1} for NVP and 1716cm^{-1} for AA) on the modified grafted membrane and the unmodified PES membranes, respectively. $H_{1487,M}$ and $H_{1487,U}$ are the peak heights for the benzene C–C double bond (1487 cm^{-1}) of the modified membrane and the unmodified PES membranes, respectively.

Selective elimination studies

To investigate the selective elimination properties of unmodified and modified membranes, aqueous solutions of the selected pharmaceuticals in water (5 μM for each pharmaceutical) were prepared. The filtration system applied in this work consisted of a syringe pump, a 3 ml syringe and a filter holder where the PES membrane was placed. The mixture of the seven selected pharmaceuticals (1 ml) was supplied by a syringe pump with a constant feed rate of 6 ml · h^{-1}. The filtrate was collected and analyzed using a high-performance liquid chromatography (HPLC) system with a BonChrom-C18 column using a mobile phase consisting of water–acetonitrile–trifluoroacetic acid (95: 5: 0.1, v/v/v), at a flow rate of 2 ml · min^{-1}. The UV detector was set as the same of that previously described by Xiao *et al.* [20] The elimination properties were evaluated by comparing the binding percentages to the membranes, which were defined as the ratio between the concentrations of retained APIs and their initial amount.

RESULTS AND DISCUSSION

ATR-FTIR

PES filtration membranes were chemically modified using a UV-assisted graft polymerization method using two different chemicals, namely AA and NVP, applying increasing UV irradiation durations. The so-produced membranes were characterized by ATR-FTIR; the corresponding spectra are presented in Fig. 1.

The results clearly showed characteristic differences before and after the chemical modification. For instance, from the spectrum of the AA-modified membrane, the most significant change was the appearance of an absorption band at ~1716 cm^{-1}, corresponding to the stretching vibration of carbonyl in –COOH group of AA. For the spectrum of the NVP-modified membrane, the appearance of an absorption band at ~1662 cm^{-1} represents the amide I carbonyl stretch of the NVP five-membered lactam ring. These results clearly confirmed the successful chemical modification of the treated membranes. The DGs, measured for the different modified membranes extracted from the ATR-FTIR spectra, are presented in Fig. 2.

It could be seen that DG values for both modifications, DG_{AA} and DG_{NVP} for AA and NVP modifications, respectively, increased asymptotically with increasing the irradiation time. In the same conditions (*i.e.* monomer concentration and irradiation time), the DG_{AA} is relevantly higher than DG_{NVP}; this can be explained by a higher reactivity of the AA monomer compared to NVP. During the initial phase (0–2 min), the reaction is fairly fast and tends to slow down after 2 min of irradiation. This phenomenon may be attributed to a saturation of the binding sites available at the surface of the polymer and the consumption of the monomer present at the surface. After an irradiation time of 5 min, DG values reach 5.36 and 2.34 for DG_{AA} and DG_{NVP}, respectively.

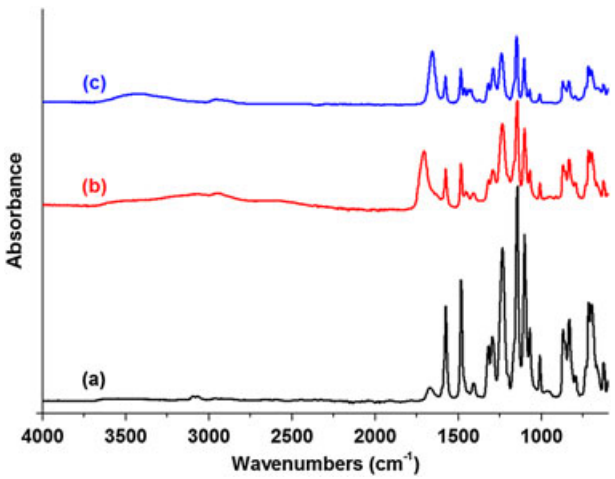


Figure 1. ATR-FTIR spectra of native PES membrane (a), AA modified PES membrane (b) and NVP modified PES membrane (c) 89x63mm (300 x 300 DPI).

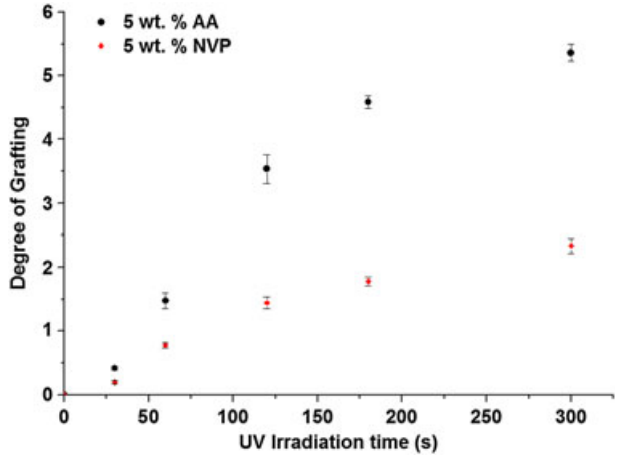


Figure 2. Degrees of grafting of AA and NVP at different UV irradiation time 89x63mm (300 x 300 DPI).

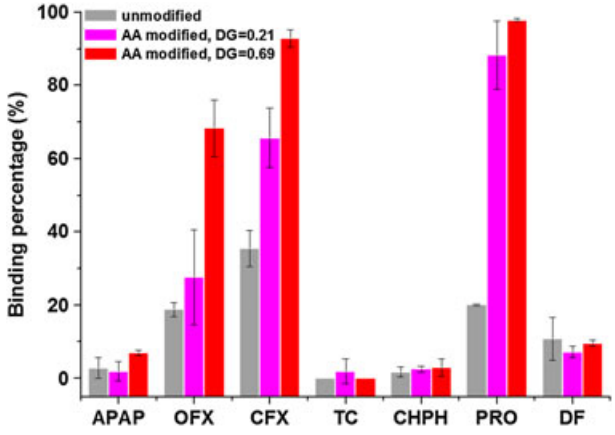
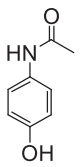
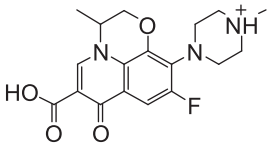
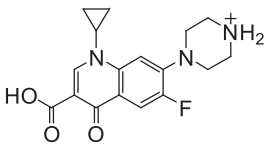
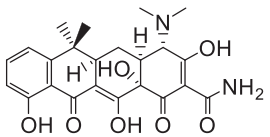
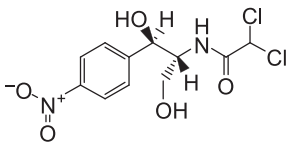
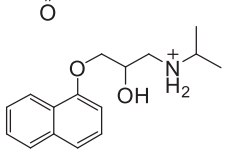
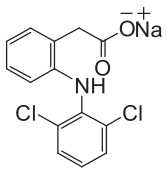


Figure 3. Binding percentages of the studied pharmaceuticals onto unmodified and AA-modified membranes 89x63mm (300 x 300 DPI).

Table 1. Information on the selected chemicals

Abbreviation	Chemical structure [a]	MW, g · mol^{-1}	pK_a	Reference
APAP		151.2	9.56	[21]
OFX		361.4	6.10, 8.28	[22]
CFX		331.3	6.18, 8.76	[23]
TC		444.4	3.31, 7.51, 9.54	[21]
CHPH		323.1	11.0	[24]
PRO		295.8	9.51	[21]
DF		318.1	4.0	[25]

[a]The molecules are presented in their predominant protonation state at pH 6

This set of results is in good agreement with that reported by Taniguchi *et al*.[18]

FILTRATION

The performances of the unmodified and modified membranes in a filtration setup were measured using a mixture of seven selected compounds (5 μM for each compound) that are APAP, OFX, CFX, TC, CHPH, PRO and DF; cf. Table 1. The filtrates were then consecutively analyzed by HPLC. For each type of modification, two types of membranes (two different DG values) were selected.

AA-modified membranes

After filtration, the binding percentages of the tested APIs onto the pure PES membrane and AA-modified membranes were measured, cf. Fig. 3. The results showed that for the tested membranes, OFX, CFX and PRO exhibited higher binding percentages than the other APIs. The unmodified membrane displayed relatively smaller binding capability of DF compared with OFX, CFX and PRO. While for APAP, TC and CHPH, the binding percentages were negligible. Unexpectedly, the affinity between the pure PES membrane and OFX, CFX and PRO was also quite strong. Due to the treatment of PES membranes during manufacturing, the surface of the native PES membrane was negatively charged. At pH 6, DF was in its anionic form while PRO was in cationic form; OFX and CFX existed in both zwitterionic and cationic forms; APAP, TC and CHPH were mainly in neutral forms.[20,24–26] The electrostatic interactions between the tested APIs and the unmodified membrane may contribute to the high affinity for PRO, OFX and CFX. It is worth quoting that, though DF was negatively charged at pH 6, the binding percentage value was approx. 10%. The binding percentages of the other tested APIs were less than 3%. Overall, these results showed that PRO, OFX, CFX and DF were specifically retained by the PES membrane through electrostatic interaction.

After AA grafting onto the membrane, it could be seen that the chemical modification caused a significant increase in retention for PRO, OFX and CFX, while the affinity for the other APIs remained unchanged. These results are in good agreement with that reported by Xiao *et al*.[20,26] Furthermore, greater binding percentages were observed when DG value was higher, highest binding percentage value (92% for CFX and 98% for PRO) was obtained when DG was 0.69. As AA is an anionic monomer at neutral pH (p*Ka* = 4.25),[27] the introduction of AA at the surface of the membrane enhanced the electrostatic interactions with this analyte. Because of the higher negative charge of the membrane, the affinities of PRO, OFX and CFX changed significantly. Higher DG values indicated more AA monomers grafted onto the surface and thus more negative charge. This justified the fact that the binding percentage values are higher when DG was 0.69 than that when DG was 0.21. Comparing the values of PRO, CFX and OFX when the DG was 0.21 with the values obtained from pure membrane, it could also be seen that the value of PRO increased rapidly, then CFX, and OFX. That could be explained by the p*Ka* values of PRO, CFX and OFX being 9.51, 8.8 and 8.28, respectively. Thus, electrostatic interactions between these compounds and AA-modified membrane showed a sequence such as PRO > CFX > OFX, leading the same sequence of affinity. Compared with the unmodified membranes, more PRO, CFX and OFX were eliminated by the AA-modified membranes. This could be attributed to two mechanisms, the specific elimination by the PES membrane itself and the help of AA grafted onto the membrane. For DF, it is expected that the electrostatic repulsion should be improved due to more AA monomers grafted onto the membrane, while the affinity of DF did not change significantly. It is speculated that for DF, the specific elimination was the dominant factor to maintain its binding percentage although electrostatic repulsion was increased.

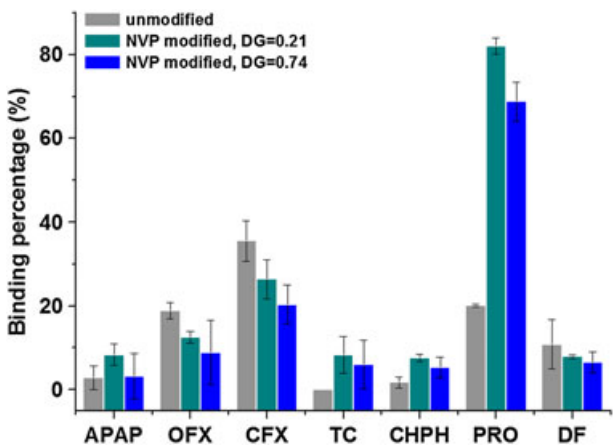


Figure 4. Binding percentages of pharmaceuticals onto unmodified and NVP-modified membranes 89x63mm (300 x 300 DPI).

NVP-modified membrane

The filtration results of NVP-modified membranes with DG_{NVP} values of 0.21 and 0.74 are given in Fig. 4. It showed that after filtration with NVP-modified membranes, the values of binding percentages of APAP, TC and CHPH slightly increased while that of PRO increased significantly, and that of OFX and CFX slightly dropped. In contrast with the results of AA-modified membranes, the binding percentage value of each pharmaceutical when DG is 0.74 is smaller than that when DG is 0.21.

Because of the uncharged nature of the NVP monomer at neutral pH, one can expect that the introduction of NVP at the surface of the membrane did not change its electrostatic properties. From Fig. 4, it could be seen that not all the APIs showed the same tendency after filtration with the NVP-modified membranes. Pieracci *et al*.[16] reported that during the process of grafting NVP by means of UV-assisted graft polymerization, both pore enlargement caused by irradiation and pore obstruction caused by polymer chains grafted onto the membrane surface influenced the performance of filtration. The enhancement of affinity of APAP, TC and CHPH after grafting leads to the assumption that intramolecular hydrogen bonding between these compounds and grafted PVP overcame the effect of pore enlargement previously reported and favors the binding of the APIs. The decrease of binding percentage values of OFX and CFX after filtration with modified membrane could be attributed to the layer of grafted NVP monomer hindering the specific elimination of these two compounds and the pore enlargement intensifying their elution through the membrane. At the same time, hydrogen bond plays a minor role, and not enough to enhance the affinity. For PRO, oppositely, the binding percentage was much higher after filtrating with modified membranes.

Nair *et al*.[28] reported PRO showed extensive hydrogen bonding with PVP. Therefore, one can assume that hydrogen bonding taking place between PVP and PRO was the predominant effect compared to pore enlargement and pore obstruction, and this effect contributed to the high affinity. For DF, the binding percentage changed slightly after filtration through the modified membrane. One can expect that the binding caused by hydrogen bonding and specific elimination onto PES backbone chains balanced out the loss caused by pore enlargement and electrostatic repulsion from the backbone chains. All those lower values of binding percentage at higher DG can be explained by that, though the modified NVP monomer creating a layer that blocks pores and hydrogen bond that binds the compounds; after the completion of the NVP monomer, with continuous irradiation, pore enlarging will be the dominant factor, and the mixed solution of pharmaceuticals will pass through these pores rapidly with less contact with the membrane.

CONCLUSION

A commercial PES membrane was successfully modified with two monomers, AA and NVP, using UV-assisted graft polymerization technique. The selective elimination properties of the so-treated membranes were evaluated by comparing the binding percentages of a series of APIs after filtration.

It was demonstrated that the PES membrane used possessed selective elimination properties of OFX, CFX, PRO and DF. Several characteristics such as electrostatic charge, hydrogen bond, pore enlargement, pore obstruction and specific elimination were shown to have an effect on the filtration performances. Among them, the most important one was specific elimination. Additionally, it is shown that AA modification enhanced the selective elimination property to OFX, CFX and PRO. The affinity for DF did not change significantly. For these three pharmaceuticals, higher affinity was observed with higher DG values. The highest value of binding percentage was $97.90 \pm 0.36\%$ for PRO among all the compounds. The NVP modification enhanced the selective elimination of PRO and decreased that of OFX and CFX while the affinity of DF changed slightly. A lower affinity was found with higher DG value for all pharmaceuticals. The highest value of binding percentage was $82.16 \pm 1.92\%$ for PRO among all the compounds. Overall, the results confirmed that the chemical modification of PES membranes can be used as a valuable strategy to produce filtration membrane with enhanced APIs elimination properties.

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