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APPLICATION OF NANOFILTRATION MEMBRANE IN THE SEPARATION OF AMOXICILLIN FROM PHARMACEUTICAL WASTEWATER

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ABSTRACT
Separation of amoxicillin from pharmaceutical wastewater by nanofiltration (NF) membrane has been investigated in this study. For this purpose a membrane system including a polyamide spiral wound NF membrane was evaluated for the treatment of amoxicillin wastewater. The effects of operating conditions such as flow rate, pressure and concentration of amoxicillin and COD in the feed, on the efficiency of the membrane were evaluated. The permeation flux and rejection of amoxicillin and COD were the criteria for this evaluation. The rejection of the amoxicillin by the selected NF membrane was adequate and in most cases exceeded 97% whereas COD reached a maximum of 40% rejection and permeation flux was over 1.5 L/min.m^2. The rise in pressure enhanced the transport rate of the solvents. Permeation flux of the NF membrane increased with increasing flow rates. Experimental data also indicated that concentration polarization existed in this membrane separation process. The stable permeation flux and high rejection of amoxicillin indicated the potential of NF for the recovery of amoxicillin from the pharmaceutical wastewater.

Key words: Amoxicillin; Membrane; Nanofiltration; Rejection; Retentate

INTRODUCTION
Amoxicillin (AMX), 6-(*R*-hydroxy-a-amino phenyl acetamido) penicillanic acid is the only phenolic penicillin which is used as an antibacterial drug (Al-Abachi *et al*., 2005). It is a kind of frequently used antibiotic to treat many kinds of infections. Molecular weight of amoxicillin is 365 and it is soluble in water. The molecular structure of amoxicillin is shown in Fig. 1.

The presence of amoxicillin and other kinds of antibiotics in the environment is of concern due to their potential to promote bacterial resistance (Zazouli *et al*., 2010) as well as trigger long term adverse human health effects. Chemical disinfection which is one of the essential water treatment processes may aid in their removal from industrial wastewater but may also form byproducts that can remain biologically active.

Based on amoxicillin characteristics, nanofiltration (NF) which is another water treatment process can be used to separate and recover amoxicillin in order to palliate the amoxicillin's harm to environment and also improve economics. Nanofiltration is the most recent developed pressure driven membrane separation process and its applications have been increasing rapidly in the last decade. It has been widely used in aqueous systems such as the concentration of antibiotic aqueous solutions (Sun *et al*., 2000; Wu, 1997; Zhang *et al*., 2003).

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Removing hardness and dissolved organics from water (Perry and Linder, 1989; Watson *et al*., 1989; Mazloomi *et al*., 2010), arsenic removal from drinking water (Vrijenhoek *et al*., 2000), heavy metal ions recovery from electroplating wastewater (Hafiane *et al*., 2000) and separation of pharmaceuticals from fermentation broths (Christy and Vermant, 2002) are some examples of industrial applications of nanofilteration.

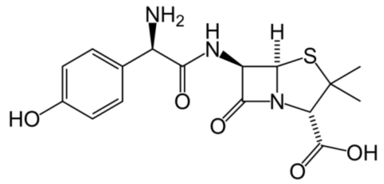

Fig.1: Molecular structure of amoxicillin

NF has properties that lie between ultrafiltration (UF) and reverse osmosis (RO). In general, RO membranes reject both organic matters and salts (Mazloomi *et al.*, 2009; Salahi *et al*., 2010) while UF membranes freely pass all salts and most organic matters. NF membranes, on the other hand, retain matters that can penetrate UF membranes, but some low molecular weight micropollutants that can be rejected by RO membranes. Moreover, NF membranes retain bivalent ions but still are relatively permeable for monovalent ions (Zhu *et al*., 2003). Since all NF membranes have their origins in reverse osmosis (RO) membranes, they are called loose reverse osmosis membranes or tight ultrafiltration membranes with respect to its permeate flux and separation performance (Raman *et al*., 1994); these kinds of membranes have originally served as an attractive economic alternative to RO membranes due to the lower operating pressures involved and higher water permeabiLy.

The nominal molecular weight cut off (MWCO) of NF membranes is in the range of 100–1000 Da (Raman *et al*., 1994; Treffry-Goatley and Gilron, 1993). Therefore the molecular weight of antibiotics is coincident with the range of MWCO of NF membranes and the noticeable difference in molecular weight between amoxicillin and other materials in the amoxicillin wastewater makes it possible for them to be separated effectively with NF membranes.

The objective of this study was to investigate the application of spiral NF membranes in the separation of amoxicillin from amoxicillin wastewater in Dana Pharmaceutical Company, (Tabriz, Iran) producing antibiotics, and to find the optimum operating conditions for the pilot experiments. For this purpose a kind of polyamide NF membrane was used for the concentration of the amoxicillin wastewater. In order to obtain an economically feasible process, it is required that both the flux and the amoxicillin rejection are as high as possible. Therefore, the influence of operating parameters such as feed flow rate, pressure and feed concentration on the permeation flux and rejection of amoxicillin for the selected NF membrane was investigated and this helped obtaining optimal operating parameters.

MATERIALS AND METHODS

Chemicals

The following chemicals were used: amoxicillin waste liquor was provided from the crystallization unit in Dana pharmaceutical company, Tabriz, Iran with the composition of TEA.HCL 4.29 wt%, MIBK 4.22 wt%, amoxicillin 0.9 wt%. Samples were stored at 4°C before tests were conducted. Pure amoxicillin product was also obtained from this company. N,N-dimethyl-p-phenylenediamine, potassium hexacyanoferrate(III), NH_3, NaOH and other chemicals were bought from Merck, Co.(Germany).

Experimental set-up

The experimental NF system was employed to concentrate and separate amoxicillin from its waste liquor. A spiral NF membrane (Film Tec NF4040) with an area of 7.6 m^2 was used for this nanofiltration process. According to the manufacturer's information, the maximum operating pressure and temperature for this NF membrane are 41 bar and 45°C, respectively. The experimental set-up which was used to study the separation performance of the NF membrane are shown in Fig. 2. This membrane unit is mainly comprised of a membrane module, a high pressure pump (SV216, Lowara), a micro filter and a GAC (Granular Activated Carbon) filter for pre-disposing the wastewater to remove big particles and suspended materials that may damage the membrane. A chiller was also used to maintain the NF operation within the temperature range of 27-30 °C.

It can be seen that two streams exist in the NF membrane unit: the concentrate stream containing the species rejected by the NF membrane and the permeate stream made up of the species passing through the membrane.

Measurement of membrane separation performance

The separation performance of membranes depends on the operating conditions. The operating parameters such as flow rate, pressure and concentration of feedstock which have important influences compared to other parameters on the separation performance of the membranes have been investigated in this work. The influence of these operating parameters on the permeation flux and rejection of amoxicillin for polyamide NF membrane was studied.

The solute rejection is a function of concentration across NF membrane, and it has no direct relationship with the operating pressure. Solute rejection can be defined as:

$$R = \left(1 - \frac{C_p}{C_b}\right) \times 100\% \quad (1)$$

Where:

C_p and C_b are concentrations in permeate and bulk feed, respectively.

The permeation flux can be calculated by:

$$\text{Flux} = \frac{V}{t \times S} \quad (2)$$

Where V is the volume of permeate, t the permeate collection time, and S the effective area of the membrane.

In order to test the effect of flow rate on the performance of the membrane, the flow rates were ranged from 10 to 20 L/min, and other parameters were kept constant. Operating pressure

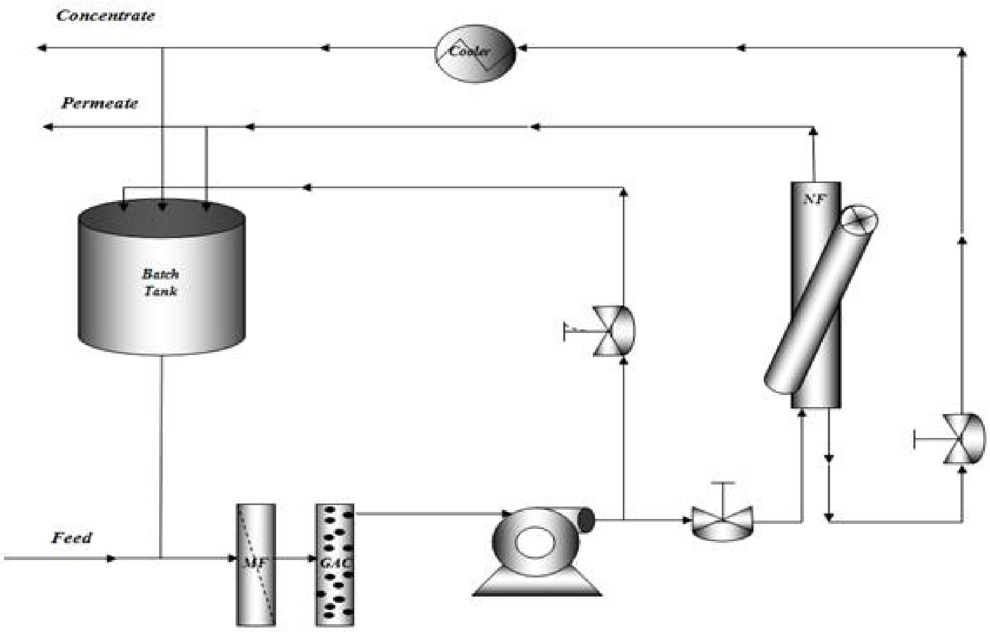

Fig.2: Schematic drawing of the experimental set-up

and pH were kept at 6 bar and 5.9, respectively. Temperature was kept at 28°C by the cooling coil. COD and amoxicillin concentrations in the membrane feed were 24225 mg/L and 1825 mg/L, respectively. The effect of pressure on the performance of the membrane was also studied under the same conditions except that the flow rate was set at 20 L/min and pressure ranged from 3 to 15 bar. For pressure and flow rate experiments both permeate and concentrate streams were returned to the feed tank in order to keep the feed concentration constant.

In order to check whether concentration polarization is significant in this process, the concentration experiments were also carried out in the amoxicillin concentration range from 860 mg/L to 6150 mg/L.

Antibiotic and COD detection

The concentration of amoxicillin in the feedstock and permeate was measured by a UV-Vis spectrophotometer. The method is based on the reaction of amoxicillin with N,N-dimethyl-p-phenylenediamine in the presence of potassium hexacyanoferrate(III) in alkaline medium. The water soluble blue color product was measured at λ_{max} 660 nm (Al-Abachi *et al.*, 2005). The COD of samples was measured by COD chemical oxidation method.

RESULTS

The purpose of this study was to reuse amoxicillin obtained in the concentrate stream and to make the permeate stream of NF membrane suitable for the solvent recovery process, so the rejection of amoxicillin has to be as high as possible in order to improve economics. In addition, the membrane flux has to be as high as possible in order to save energy and investment.

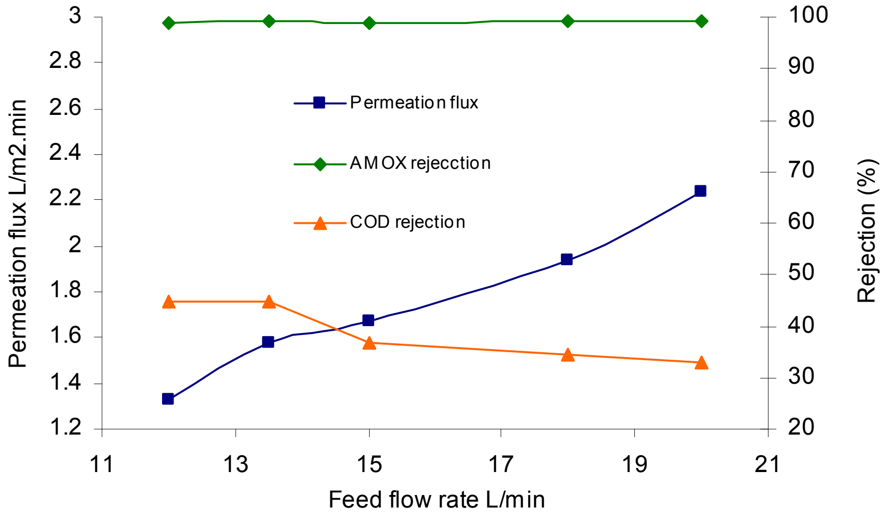

Fig.3: NF Performance against feed flow; pressure: 6 bar, Feed amoxicillin Conc: 1825 mg/L; Temperature: 28ºC; Feed COD: 24225 mg/L; pH: 5.9

Effect of feed flow rates

Flow rate is one of the factors that can affect the membrane performance. To test the effect of flow rate, experiments were conducted with

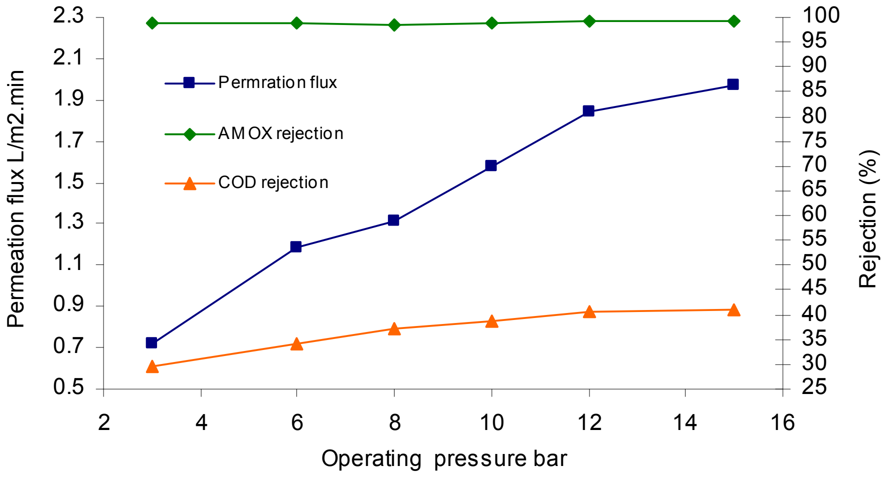

Fig.4: NF Performance against pressure; Feed flow: 20 L/min, Feed amoxicillin Conc=1825 mg/L; Temperature: 28ºC; Feed COD: 24225 mg/L; pH: 5.9

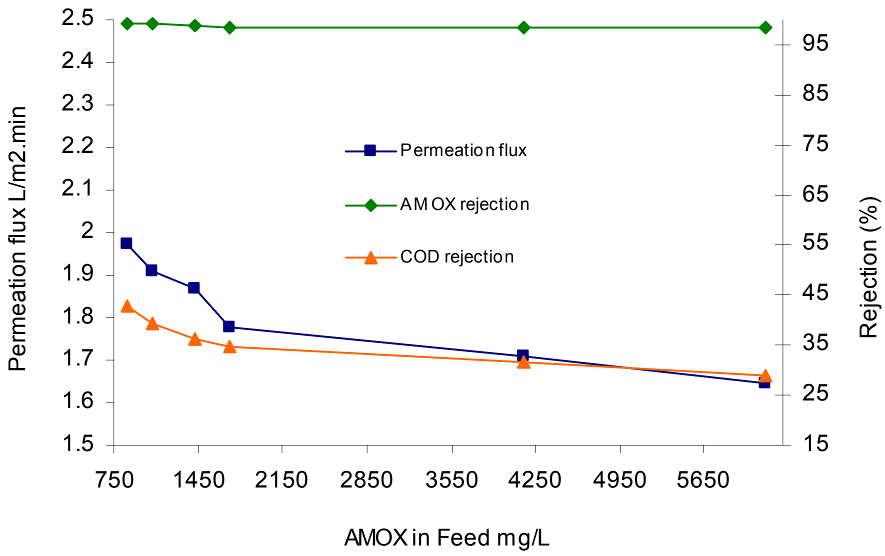

Fig.5: NF Performance against feed concentration (operating time in batch procedure); pressure: 10.5 bar; Feed flow=20 L/min; Temperature: 28º C; Initial pH: 5.9

amoxicillin wastewater under different flow rates ranged from 10 to 20 L/min at fixed pressure and concentration. The results are shown in Fig. 3. This Figure shows that permeation flux increases with increasing flow rate while the flow rate has little influence on amoxicillin rejection.

Effect of pressure

In these series of experiments flux and rejections of the NF membrane were measured with the amoxicillin wastewater under conditions that pressure ranged from 3 to 15 bar at fixed concentration and flow rate. The results of permeation flux, COD rejection and amoxicillin rejection are shown in Fig. 4. It is obvious that flux tends to increase with the operating pressure. Amoxicillin and COD rejections also increase with increasing operating pressure, but amoxicillin rejection is less sensitive to pressure than COD rejection.

Effect of amoxicillin concentration

The effect of amoxicillin concentration on the performance of the NF membrane has also been investigated. For the NF membrane as shown in Fig. 5 amoxicillin rejection exceeds 97% whereas COD reached a maximum of 40% rejection. In many membrane separation processes, the problem of concentration polarization is considerable, so during these experiments the amoxicillin solution used for the measurements of separation performance was diluted to avoid of concentration polarization. As can be seen in the Figure, flux of the NF membrane decreases when concentration increases and also amoxicillin and COD rejections decrease with increasing concentration. COD rejection is more sensitive to concentration than amoxicillin rejection.

DISCUSSION

Effect of feed flow rates

Flow rate (or velocity) of the membrane feed is an important factor affecting membrane flux. As can be seen in Fig. 3, the amoxicillin rejection is high and has not been influenced by the changing of the flow rate while permeation flux of membrane increased with increasing flow rates. This is because a high flow rate can cause an ideal turbulent flow with a favorable flow pattern to reduce the thickness of the boundary layer which exists at the interface of membrane and fluid. The thickness of the boundary layer is related to the viscosity and the flow pattern of fluid. The viscosity is a function of temperature and the operating temperature is fixed at a stable value, but the flow rate of feedstock is a variable in the process. A high flow rate can increase the tangential and radial velocity of fluids. Therefore, increasing the flow rate is an effective way to raise permeation flux especially for those solutions where viscosities are not very low. An increase in feed flow rate may also affect on the membrane fouling. Al-Sofi (Al-Sofi *et al*., 2000) pointed out the water flux increased with increasing flow rate because higher flow rate could deter the membrane fouling.

Effect of pressure

Since NF is a pressure driven process, operating pressure is a very important factor which influences separation performance. Fig. 4 shows that permeation flux tend to increase with increasing pressure, which illustrates that increasing pressure is an effective way for increasing permeation flux. This phenomenon in which the flux increases with pressure has been observed in many cases in the Lerature (Robinson *et al*., 2004; White, 2002). It can also be seen in this Figure that COD and amoxicillin rejections tend to increase with increasing pressure. This may be because the condensed membrane increases the steric resistance and then more solute is rejected which results from the compressing effect of the membrane, as has been observed in other membrane separation processes (Murthy and Gupta, 1997; Zhu *et al*., 2003). All amoxicillin and COD rejections are higher than 98% and 25% respectively. Since the amount of MWCO of the NF membrane is lower than the amoxicillin molecular weight, the amoxicillin molecules are almost rejected while the organic molecules having molecular weight lower than MWCO of NF membrane can penetrate the membrane.

Experiments demonstrated that the operating pressure has great effect on the efficiency of the membrane by increasing the flux of permeate and antibiotic rejection. It also can be seen from Fig. 4 that permeation flux is not in proportion to the operating pressure. In other words, the increasing rate of the permeation flux diminishes during a rise in pressure.

Effect of amoxicillin concentration

As shown in Fig. 5 the permeation flux declined quickly before the concentration reached 1750 mg/L. It shows that concentration polarization exists in this membrane separation process and has an influence on the separation performance of the membrane. When the phenomenon of concentration polarization takes place, a layer is formed at the membrane-liquid interface and the concentration of solute in the layer is higher than that of bulk of the solution on the high pressure side. The concentration polarization layer holds up the transport of each component through the membrane because the increase in osmotic pressure across the membrane reduces the driving force of mass transfer. As a result, permeation flux decreases significantly.

For the selected NF membrane the permeation flux falls slowly with rising concentration when the concentration is over 1750 mg/L. This means that the thickness of the concentration polarization layer tends to a steady value and the separation performance of membranes tends to a stable state. The steady permeation flux is about 1.5 L/ m^2.min at high concentration, which indicates the potential of this polyimide NF membrane for such commercial applications.

Overally, in this study the effect of the flow rates, operating pressure and concentration of amoxicillin on the efficiency of a spiral NF membrane was evaluated. The permeation flux and rejection of amoxicillin were the criteria for this evaluation. The polyamide NF membrane for the concentration of amoxicillin extract showed a suitable separation performance under the test conditions. Permeation flux was over 1.5 L/min. m^2. Amoxicillin rejection was adequate and in most cases exceeds 97%, whereas COD reached a maximum of 40% rejection. This means that NF membrane process is suitable for amoxicillin separation from other organic solvents in the wastewater and amoxicillin concentration can reach the demand of reuse when concentrated with selected NF membrane.

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