Poll Res. 40 (3) : 978-985 (2021)

ISSN 0257–8050

ANTIBIOTICS SEPARATION FROM PHARMACEUTICAL WASTEWATER USING CERAMIC TIO_2 NANOFILTRATION MEMBRANE

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(Received 30 April, 2021; Accepted 1 June, 2021)

ABSTRACT

The presence of antibiotics can be detected in the drains of both sewage units and industrial wastewater units, in additions to the possibility of their presence in drinking water treatment units. These compounds about concern might actuate dangerous impacts on various aquatic organisms and in a form that can cause a negative impact on the biological balance of the aquatic environment. Experimental set-up for bench scale of new highly performance ceramic membrane filtration was designed. An experimental study is carried out using Amoxicillin and Flagel (Metronidazole) as a model contamination in order to determine the separation and fouling behavior of these two modeled from pharmaceutical wastewater using 0.9 nm tubular titanium dioxide ceramic nano-filteration membrane. The lowest and highest rejection behavior of 50 and 250 mg l^{-1} Amoxicillin and Falgel concentrations were found to be (85% and 77%) and (64% and 52%) at applied trans-membrane pressure of 5.0 bar, respectively. The permeation flux for both antibiotics was over 13 l m^{-2} hr^{-1} and the linear stability of this flux was indicated good potential for recovery of Amoxicillin and Metronidazole from pharmaceutical wastewater. The present work suggested a concentration of 500 mg l^{-1} for both antibiotics to study the fouling behavior by measuring the membrane permeation volume flux as a function of filtration time (up to 32 hr). Experiments were carried out the same operating conditions and it is found that the fouling rate of Amoxicillin was higher than that of metronidazole. It was also observed that concentration polarization of solute existed in this separation process.

KEY WORDS: Ceramic membranes, Nanofiltration, Rejection, Fouling, Antibiotics

INTRODUCTION

The applications of nanofiltration membrane () have been widely increased due to offers unique specifications such as a low working pressure, high permeate volume flux, high rejection of multivalent ion salts and organic molecules at low operation and maintenance costs (Hoffman, 2003). NF membranes represent the most recently developed membrane process for liquid phase separation compared to other types of membranes (Bartels, 2008).

The membrane can be considered as the heart of any filtration system where the cost of the membrane unit is about 2025 percent of total capital cost. As a result, any continuous long term effective membrane process should involve the reduction of membrane fouling (Weber *et al.*, 2003; Timmer, 2001). A decrease in membrane performance over a period of time resulting from this fouling leads to reduction in water permeate flux across the membrane (Shirazi *et al.*, 2010). Scale formation on the membrane surface is a genuine issue that might lead to reduce permeates flux, increase feed pressure, decrease product quality and ultimately shortens the membrane life. Consequently, membrane fouling incredibly expands those operation costs by increasing: vitality consumption, framework down time, necessary membrane area, construction, labor and material cost for backwashing and cleaning processes. According to many researchers, the titanium dioxide membranes have received significant attention because of their unique characteristics compared to other mineral oxides such as, orThese characteristics can be summarized as follows (Zhang *et al.*, 2006; Hagen *et al*., 2003; Lee *et al*., 2008) good resistance to fouling, stability and chemical resistance under harsh conditions towards extreme range, commercial availability, ease of preparation and lower fabrication costs due to their reduced sintering temperatures.

Wastewater of pharmaceutical industry is characterized by high organic matter contents, toxicity, deep color, and high salt contents. The treatment of pharmaceutical wastewater treatment (PWW) involved the following problems: diverse characteristics and different medicines produce different type of waste; variable amount of products and highly variable pH; mixing of pharmaceutical waste with other type of waste.

The removal of these substances from the pharmaceutical waste water has been a huge assignment of the most industrial wastewater treatment plants (Kirubanandam *et al.*, 2017). Basically, the selection of any treatment water method depends mainly upon the quantity, needed quality and cost. The conventional treatment methods of PWW can be divided to (Lee *et al.*, 2008): physical, chemical, thermal and biological treatment. According to many authors, the biological treatment is a very good option to achieve the treatment of PWW; nevertheless in certain cases this type of treatment cannot be fully achieved. Numerous pharmaceuticals are very hydrophilic and, consequently; their adsorption onto sludge is limited, inhibiting the degradations of the compounds by microscopic organisms during the treatment process. In addition, pharmaceuticals compounds, are not easily degraded because of their structure which protect them against any biological attack and thus may have long-term ecological impacts which lead to significant persistency.

In this research 0.9 nm pore size of tubular ceramic titanium dioxide membrane has been selected to determine the separation and fouling behavior of antibiotics from pharmaceutical wastewater. This membrane was selected for different reasons which are: it has mechanical, chemical and thermal constancy; low fouling tendency; possibility of back flushing and steam sterilization; high abrasion resistance; high flux and durability; bacterial resistance; regeneration possibility and dry storage after cleaning (Li, 2007; Burggraaf *et al.*, 2005). Amoxicillin (AMX) and Metronidazole (MTZ) or Flagyl are a kind of frequently used antibiotics to treat many types of infections, therefore have been selected as models for this study.

MATERIALS AND METHODS

Materials

Membrane module

A composite mono-channel tubular ceramic titanium dioxide NF membrane with mean pore size of 0.9 nm supported by aluminum dioxide sub-layers (produced by Inopor® GmbH, Veilsdorf-Germany) was used in this work as seen Fig.1. According to the manufacturer's information, the main specifications of this membrane are (Inopor® GmbH): number of channels: 1; external diameter (mm): 10; inner channel diameter (mm): 7; total length (mm): 190; porosity: 30 - 40 %; mean pore diameter (nm): 0.9; filtration area (m^2):4.178 x 10^{-3}; Inflow area per tube (mm^2): 38; maximum temperature: above 300 ^{o}C.

A laboratory scale tubular ceramic (TiO_2) membrane vertical module (see Fig. 2, all the

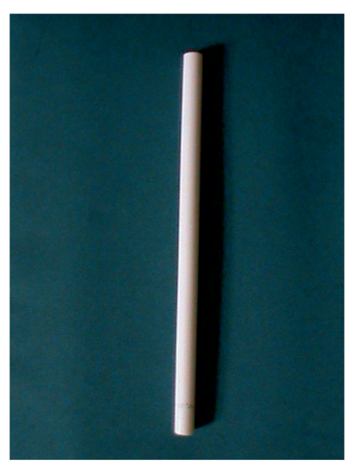

Fig. 1. Virgin ceramic TiO_2 NF membrane with pore size of 0.9 nm.

dimensions in mm)was used in this research. This module of membrane was tested by Amer Ahmed (2012). The module structure was divided into three main parts: inlet section, middle section, outlet section. The middle section was made from Perspex (a transparent material, in order to monitor the accumulation of the cross flow solutes permeate droplets), while the inlet and outlet sections were made from Poly Vinyl Chloride (PVC) with same inner diameter of the titania NF membrane in order to give same velocity and flow pattern inside the membrane. The module was tested and proved to be capable of tolerating relatively high pressures (up to 8.0 bars). This range covered the typical working pressure for the pressure driven NF membranes (5.0 – 6.0 bar) (Scott *et al*., 1996).

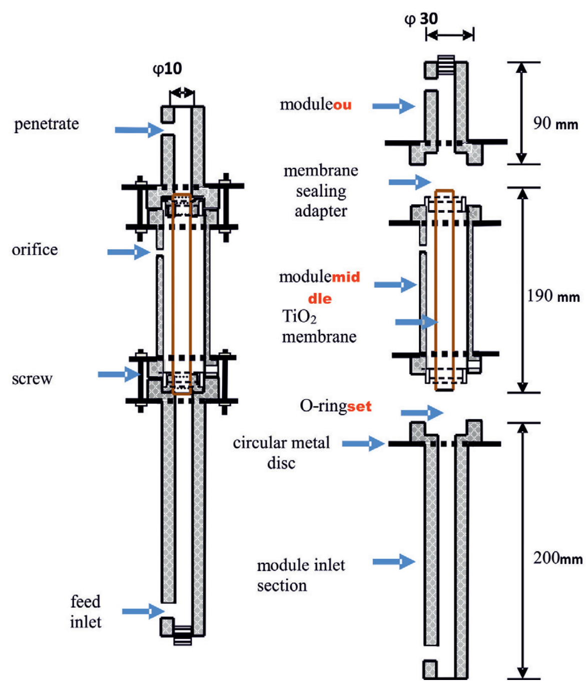

Fig. 2. Schematic diagram of tubular titanium dioxide NF membrane module with three structures of main three sections.

Amoxcillin

Amoxcillinis an antibiotic used to treat a number of bacterial infections with chemical structure as shown in Fig. 3. Pure Amoxicillin vials (trade name Strimox 500 mg, Strides Arcolub Ltd. company, India) were purchased from pharmaceuticals. Chemical formula $C_{16}H_{19}N_3O_5S$and formula weight 365.4. The IUPAC name is (2*S*,5*R*,6*R*)-6-[[(2*R*)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

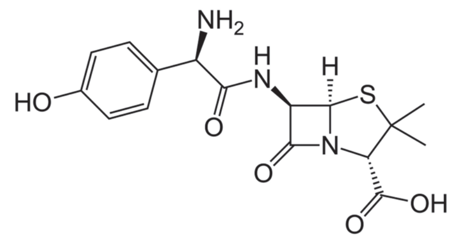

Fig. 3. Chemical structure of Amoxicillin (Pub, Chem. Amoxicillin, 2021).

Metronidazole

Metronidazole is a prescription medicine used to treat the symptoms of bacterial infectionswith chemical structureas shown in Fig. 4. Pure Metronidazole vials (trade name Flagyl 500 mg in 100 ml, parenteral Drugs Ltd., India) were purchased from pharmaceuticals. Chemical formula of Flagyl $C_6H_9N_3O_3$ and its formula weight 171.15. The IUPAC name is 2-(2-methyl-5-nitro-1H-imidazol-1-yl) ethanol.

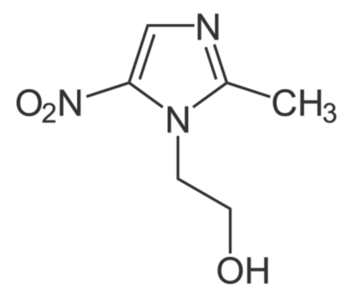

Fig. 4. Chemical structure of Metronidazole (Pub. Chem. Metronidazole, 2021).

NaOH

0.01 M of sodium hydroxide (NaOH) (Anala R, BDH, UK) was used as a chemical cleaning agent for membrane regeneration after each set of experiments.

Experimental methods

Analysis

The concentrations of antibiotics (Amoxicillin and Metronidazole) in the solution were measured usinga high performance liquid chromatography (HPLC) (Sykam, S4011, Germany). Stock standard solutions were prepared by dissolving 25 mg of antibiotics in 50 mL of methanol and serial dilutions of these stock solutions were prepared. A thrice replication of 20 µl from these dilutions were injected into the column. Calibration curves of antibiotics with a range of 1– 50 µg ml^{-1} were constructed. These curves were plotted using average peak area (of three chromatograms) versus concentrations of dilutions.

Methodology

Antibiotics rejection and fouling experiments

To determine the retention efficiency of the two antibiotics (Amoxcillin and Flagyl) at a range of initial concentrations (50, 100, 150, 200, and 250 mg l^{-1}) with fixed applied trans-membrane pressure of 5.0 bar, experiments were carried out by dissolving a certain amount of antibiotics in ultra-pure demonized water. The mixture was shaken in 5 liters glass container using a MTOPO CH 30 stirrer (Human Lab Instrument CO, Korea) at a speed of 500 r.p.m. this experiment were carried out at room temperature of 25 °C for a certain period of time to assure the full solubility of antibiotic.

The rejection of solutes (*R*) and permeate flux by ceramic titanium Nanofiltration membrane was calculated as follows (Schäfer *et al.*, 2005):

$$R = \left(1 - \frac{C^{permeate}}{C^{feed}}\right) \times 100\% \quad .. (1)$$

$$Permeate\ flux = \left(\frac{V}{t \times S}\right) \quad .. (2)$$

Where C^{fe} and C^{permeg} are the feed and permeate concentrations of antibiotics in the solution respectively (mg l^{-1}), *V* is the volume of permeate (m^3), *t* is the permeate collection time (hr), and *S* is the effective area of the ceramic membrane (m^2).

A laboratory bench scale membrane filtration rig (see Fig. 5, section A-A not applied in this study), which has been developed at the ministry of science and technology- Baghdad,was usedto study the rejection and fouling behavior of two selected antibiotics at room temperature. A high pressure centrifugal pump (BADOR- RELIANCE, Super E motor, ^{CEM35,US}) was switched onwith the required inlet flow rate of antibiotics solution (360 l. hr^{-1}, LZT, 1005–Chin) and applied pressure was set at 2.0 bar for about 10 min. by regulating the back pressure valve. Throughout this time the retenate and permeate fluxes were continuously monitored to guarantee that the framework is stable after getting rid of all the air bubbles that could exist inside those system. It was notice that the rejection was conducted at applied trans-pressure of 5.0 bar. The concentration of solute permeation (20 ml) was measured using HPLC as described above. The rejection and permeate flux of solute equation 1 and 2 was calculatedrespectively. The cross flow velocities for streaming potential measurements were conducted at 0.85 m.s$^{?1}$ which corresponded to a Reynolds number of about 6000 (turbulent flow).

Regeneration of ceramic membrane experiments

The general procedure that has been used in the present work for the cleaning and a re-generation of the Titania ceramic membrane after each rejection or fouling experiment can be summarized as follows**:**

Five liters of 0.01 sodium hydroxide solution was fed and re-circulated in the rig. At the beginning of the re-generation process the pressure was set to be less than 0.5 b to ensure that the system is stable after getting rid of all the air bubbles that might have existed inside the system. Then, the pressure was increased to 2.0 and the permeate flux was monitored and measured every 15 min. until reaching the same pure water permeate flux at the pressure of 2.0. In order to clean the system (piping and equipment) from the traces of solution, centrifugal pump was switched on again to re-circulate the deionized water with required pressure for 5 hr. The performance of the regeneration was characterized using 'regeneration efficiency', obtained by comparing the permeation of the pure water before and after the re-generation process.

RESULTS AND DISCUSSION

To study the rejection behavior for Amoxicillin and Metronidazole, experiments were carried out with 0.9 nm tubular ceramic TiO_2 NF membrane at 5.0 bar applied trans-membrane pressure. Fig.6 shows that the percentage rejection of these antibiotics using Equation (1) at a range of initial concentrations (50 – 250 mg l^{-1}). It is clear from Figure 6 that the rejection was decreased from 85.2 to 77.6% for Amoxicillin and from 64 to 52.6% for Metronidazole as the antibiotics initial concentration increased from 50 to 250 mg l^{-1}. It also evident from this figure that the percent rejection of amoxicillin higher than that of Metronidazole. Similar result was found by Reza *et al.* (2013) for 85% rejection percent of Amoxicillin. Generally; in nanofiltration membranes, there are three main effects related to the transport of solutes, which are: convection, diffusion and charge effect. The rejection of uncharged solutes are generally governed by the combination of a sieving effect and fractional forces, a convection effect due to pressure

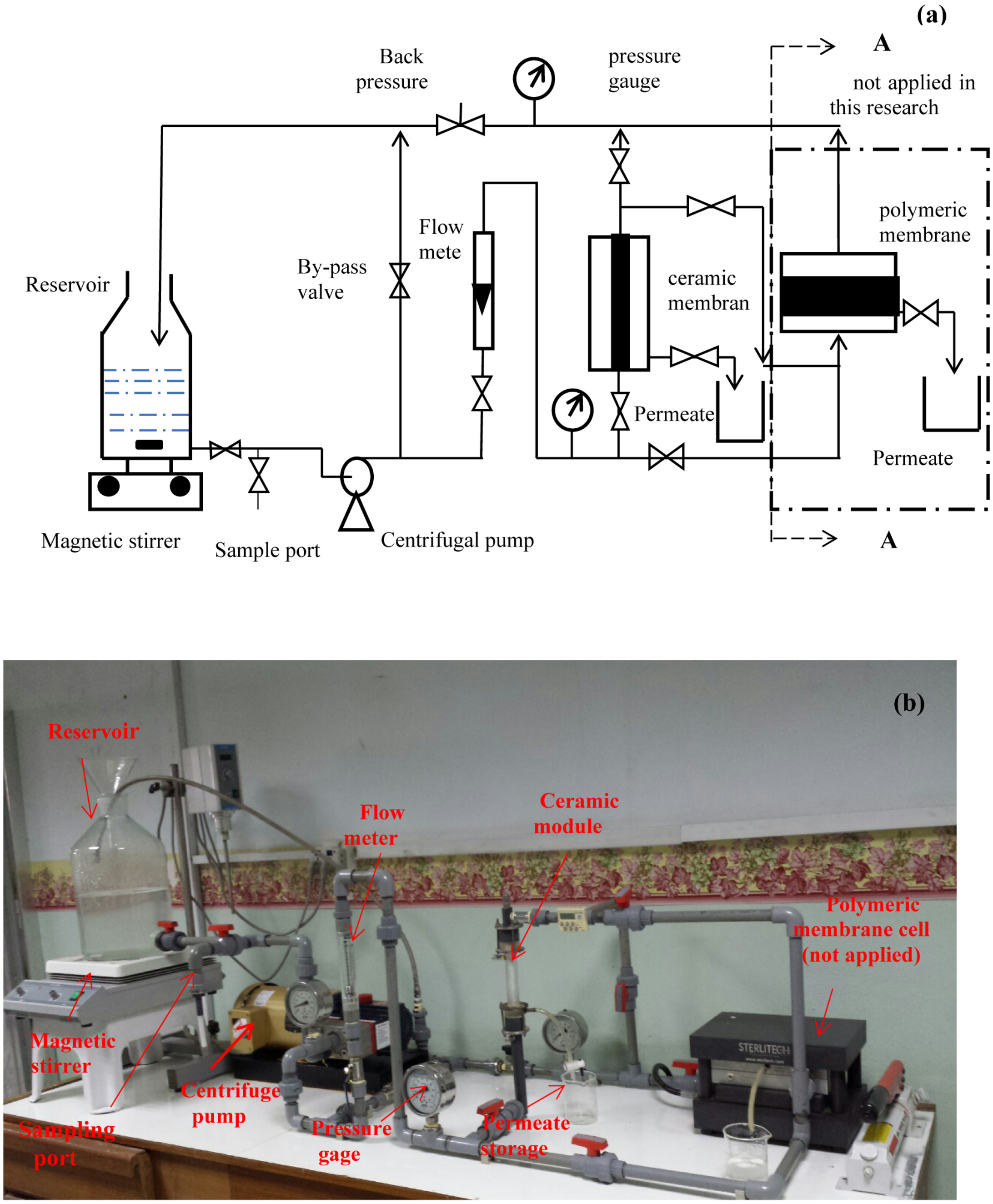

Fig. 5. (a) Schematic diagram and (b) annotated photograph of laboratory bench scale membrane filtration for pharmaceutical wastewater treatment.

difference, and by a diffusion effect as a result of the concentration gradient across the membrane. Sieving (or steric hindrance) is a function of size exclusion where the solutes with a large molecular weight cut off (MWCO) will be retained. The molecular weight (M.Wt.) of AMX is 365.4 g mol^{21} while that for MTZ is 171.15 gmol^{21}. This difference in molecular weight might explain the effect of steric hindrance and why the rejections of AMX were higher than that of MTZ.

The convection effect which mainly related to applied pressure difference might have an effect on the rejection in ceramic NF membranes, in other words increased applied pressure can play an important role on increasing solutes rejection. Also, the adsorption of solute particles that might occur

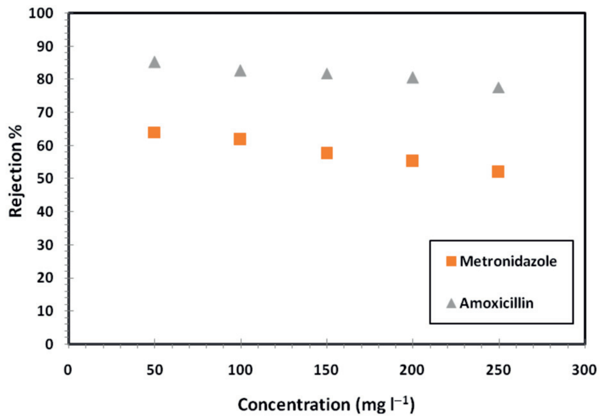

Fig. 6. Effect of initial concentration of Amoxicillin and Metronidazole on rejection percentof 0.9 nm tubular ceramic TiO_2NF membrane for applied trans-membrane pressure of 5.0 bar.

inside membrane pores or on membrane surface should have an effect on antibiotics rejection. As antibiotic concentration increases, the effect of solute adsorption by the membrane increases which might have a negative effect on the rejection due to the increase in the possibility of membrane fouling.

Regarded to MTZ, the chemical structure of this antibiotic developed a positive and negative charge. In this case another important factor might effect on the rejection of such drugs in ceramic Nanofiltration membranes. Most ceramic nanofiltration membranes are either negatively or positively charged, (present work titania ceramic membrane developed a negative change for pH solutions above 5) thus, when brought in contact with an aqueous solution acquired an electrical charge as a result of the dissociation of functional groups or adsorption of charged species from the solution into membrane pores. In the case of nanofiltration membranes where the pores are very small, the electrostatic interaction between the charged groups in aqueous solution and membrane material can play a very important role on the electrolyte transport through membrane pores.

The combination of very small pore diameters (less than 2 nm for NF membranes) with electrically charged membrane materials indicate that the separation mechanisms of NF membranes involve both steric effect (size exclusion) and electrical effect (Donnan exclusion). This combination could explain the reasonably rejection (up to 64%) of MTZ in present work ceramic NF membranes in spite of its low molecular weight compared MTZ, taking in consideration that this rejection ratio can be increased based on changing the operating conditions of the present work filtration rig or by choosing another concentrations of this antibiotic.

The permeation flux (l m$^{?2}$ hr$^{?1}$) for deionized water was calculated using Equation (2) at different applied trans- pressure (up to 5.0 bar) as shown in Fig. 7, where the effective ceramicTiO_2 NF membrane area is 4.178 x 10$^{?3}$ m^2. It is clear observed from this figure that the relationship between the applied pressure and permeation flux was linear. This flux was also determined for AMX and MTZ as a function of filtration time (up to 32 hr.) at initial concentration of 500 mg l$^{?1}$as shown in Fig. 8 and 9, respectively.The stability of permeation flux indicated the TiO_2 NF membrane has potential for removal of AMX and MTZ from the pharmaceutical wastewater.

It can be seen from Fig. 8 and 9 that the permeate volume flux for AMX and MTZ was 13.16 and 13.88 l m^{-2} hr^{-1}, respectively at 32 hr. filtration time. This could be a possible indication that the fouling has been taken place for both antibiotics especially when comparing this results with that of pure water at same operating conditions (14.84 l m^{-2} hr^{-1}, see Fig. 7). It is also observed that permeation flux for AMX and MTZ are declined with filtration time up to 32 hr and to be the same for the first four hours of filtration. This behavior can be explained based to the occurring of concentration polarization phenomenon and similar result was found by Shahtalebi *et al.* (2011). Bian *et al*. (2000) defined the concentration polarization (CP) as the accumulation of the solutes (or particles) immediately adjacent to the membrane surface being higher than that in the bulk side. This phenomenon can lead to serious problems during membrane operation processes

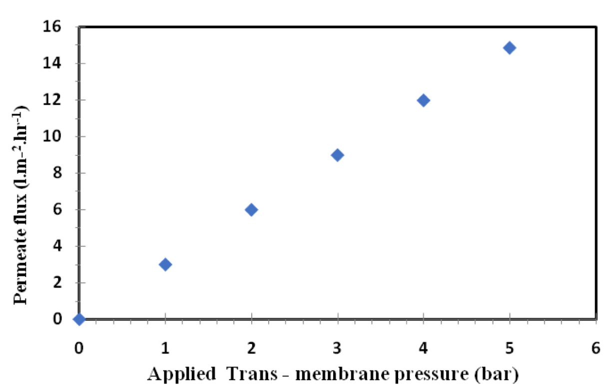

Fig. 7. The relationship between deionized water permeates flux and applied trans-membrane pressure using ceramic TiO_2 NF membrane.

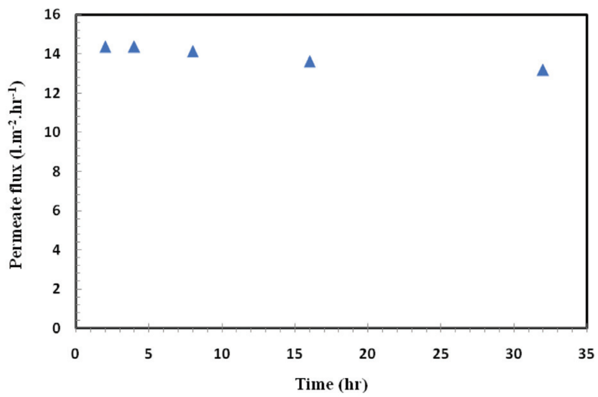

Fig. 8. Permeate flux of Amoxicillin at 500 mg l^{-1} initial concentration using 0.9 nm ceramic TiO_2 NF membranes as a function of time.

such as: deterioration in the quality of permeates, increase in the risk of fouling and possibility of scale development, furthermore, it increases the overall resistance to solute flow and thus decreases the permeate flux.When the concentration polarization taken place, a layer is structured at the membrane - solute interface and the concentration of solute in the layer is higher than that of bulk of the solution on the high pressure side.

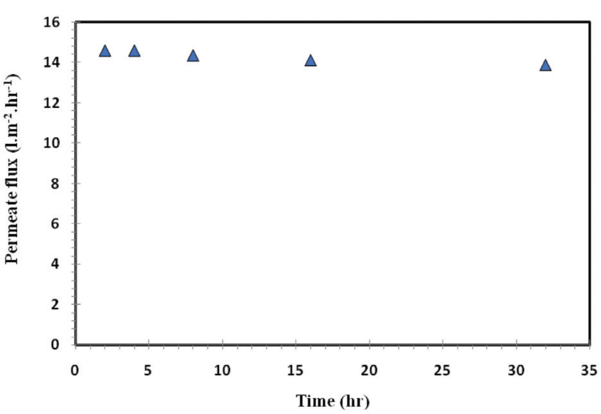

Fig. 9. Permeate flux of Metronidazole at 500 mg l^{-1} initial concentration using 0.9 nm ceramic TiO_2 NF membrane as a function of time.

CONCLUSION

The pharmaceutical waste water treatment process using 0.9 nm tubular ceramic TiO_2 membrane was found to be highly performance and effective for separation of antibiotics (AMX and MTZ). Theeffects of antibiotics molecular weights and concentrations on the efficiencies of membrane separation process were investigated in order to study the rejection performance and fouling behavior. It was found that the rejection decreased as the antibiotics concentration increased. The experimental results showed that the rejection and fouling rate of Amoxicillin were higher than that of Metronidazole at the same operating conditions due to effect of sieving or steric hindrance as result of M.Wt difference of both antibiotics.It is also find that the relationship between the applied pressure and permeation flux was linear. The stable permeation flux of antibiotics indicated the potential of ceramicTiO_2 NF membrane for removal of AMX and MTZ from the pharmaceutical wastewater.

The present study shows that the concentration polarization phenomena occurred in this separation process, a layer is formed at the membrane-solute interface and often means flux decline significantly which causes a decrease of nanofilteration performance. Further work is also needed such as: study the effects of flow rate, pressure, pH on the percentage rejection and investigate another selected pharmaceutical modelin order to improve the process performance and to enable treatment of higher antibiotic concentration.

ACKNOWLEDGMENT

The authors would like to acknowledge theIraqi Ministry of Science and Technology (MOST) / directorate of environment and water research and also the Ministry of Higher Education and Scientific Research / Alkarkh University of Science for their support. I would like to thank all participants of laboratory membrane staff and thanks must go to the technicians in MOST specially Mr. Mahmood Najem.

Conflict of interest: the authors declare no conflict of interest

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