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SEPARATION OF AMOXICILLIN FROM PHARMACEUTICAL WASTEWATERS VIA A HOLLOW FIBER SUPPORTED LIQUID MEMBRANE

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อะม็อกซีซิลลินเป็นยาปฏิชีวนะที่นิยมใช้กันมากในรักษาอาการติดเชื้อแบคทีเรียในคนและสัตว์ วงแหวนเบต้าแรคตัมในตัวยาออกฤทธิ์ยับยั้งหรือทำลายโครงสร้างผนังเซลของแบคทีเรียทำให้แบคทีเรียตายหรือไม่สามารถเจริญเติบโตได้ อะม็อกซีซิลลินที่ตกค้างในน้ำเสียส่งผลให้เชื้อแบคทีเรียพัฒนาความต้านทานต่อยาจึงควรแยกอะม็อกซีซิลลินในน้ำเสียก่อนปล่อยออกสู่สิ่งแวดล้อม จากคุณสมบัติที่เด่นของเยื่อแผ่นเหลวที่พยุงด้วยเส้นใยกลวงในการแยกสารจึงได้นำเสนอการสกัดและนำกลับอะม็อกซีซิลลินออกจากน้ำสังเคราะห์ด้วยระบบเยื่อแผ่นเหลวที่พยุงด้วยเส้นใยกลวง ปัจจัยที่ศึกษา ได้แก่ ชนิดและความเข้มข้นของสารสกัด (Aliquat 336, D2EHPA และ Alamine336) ชนิดของตัวทำละลายในเฟสเยื่อแผ่นเหลว (1-decanol, benzene, dichloromethane, ethylene dichloride และ chloroform) ค่า pH ของสารละลายป้อน ความเข้มข้นของสารละลายป้อนและนำกลับ อัตราการไหลของสารละลายป้อนและนำกลับ ระยะเวลาปฏิบัติการ จำนวนมอดูล อุณหภูมิที่ใช้ในการทดลอง ผลการศึกษาพบว่าความเข้มข้นของ Aliquat 336 (6 มิลลิโมลต่อลิตร) ในตัวทำละลาย 1-decanol ค่า pH=8.0 ของสารละลายป้อน ความเข้มข้นของสารละลายป้อน (6.0 มิลลิโมลต่อลิตร) ความเข้มข้นของสารละลายนำกลับ (6.0 มิลลิโมลต่อลิตร) อัตราการไหลของสารละลายป้อนและนำกลับเท่ากันที่ 100 มิลลิลิตรต่อนาที ระยะเวลาปฏิบัติการ 100 นาที อุณหภูมิเท่ากับ 318 เคลวิน จำนวนสองมอดูลต่อแบบอนุกรม รูปแบบการไหลวนแบบต่อเนื่อง สามารถสกัดอะม็อกซีซิลลินได้ร้อยละ 95.25 และได้ร้อยละการนำกลับเท่ากับ 89.74

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TEERAPON PIROM: SEPARATION OF AMOXICILLIN FROM PHARMACEUTICAL WASTEWATERS VIA A HOLLOW FIBER SUPPORTED LIQUID MEMBRANE. ADVISOR: DISTINGUISHED PROF. URA PANCHAROEN, D.Eng.Sc., CO-ADVISOR: ASST. PROF. NATCHANUN LEEPIPATPIBOON, Dr.rer.nat., 178 pp.

Amoxicillin is an antibiotic used in the treatment of bacterial infections in humans beings and animals. The beta-lactum ring of the drug can inhibit or destroy the cell walls of the bacteria causing the bacteria to die. Amoxicillin residues, however, can be found in water resources. Therefore, there is a need to treat wastewater containing amoxicillin residues before releasing it into the environment. To prevent this problem, the hollow fiber supported liquid membrane (HFSLM) system had been employed to extract and recover amoxicillin out of synthetic wastewater. Factors studied included type and concentration of the extractants (Aliquat 336, D2EHPA and Alamine336) and type and concentration of the solvent in the liquid membrane phase (1-decanol, benzene, dichloromethane, ethylene dichloride and chloroform). Concentration of both feed and stripping solutions as well as the pH of feed solution was also investigated together with flow rate of feed and stripping solutions, operating temperature and operating time. The results showed that the concentration of Aliquat 336 (6 mmol / L) dissolved in 1-decanol, feed solution pH = 8.0, concentration of the feed solution (6.0 mmol per liter), concentration of the stripping solution (6.0 mmol per liter), flow rate of both feed and stripping solution equal to 100 ml per minute, operating temperature of 318 K and operating time 100 min. Two modules were connected in series and circulating continuous flow. Extraction and recovery of amoxicillin reached 95.25% and 89.74%, respectively.

Department:	Chemical Engineering	Student's Signature .....
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CHAPTER 1
INTRODUCTION

1.1 The rationale of research problem

Amoxicillin is an antibiotic that is widely used nowadays [1]. It is an effective drug which can inhibit the growth of bacterial and enables the body to fight infections [2]. The drug is used to treat infections in the respiratory tract, gastro-intestinal and urinary tract. It is effective against micro-organisms such as Streptococcus, Pneumococcus, Salmonella and Hemophilic influenza [3].

Amoxicillin is effective because it cannot be destroyed by stomach acid but can be well absorbed in the gastro-intestinal tract. Thus, because the drug is absorbed in the intestine, it is used as an oral agent and can be used before or after meals. However, Amoxicillin may cause allergic reactions and may interfere with normal bacteria in the digestive tract. The demand for drugs like amoxicillin ensures a huge increase in industrial production [4]. Amoxicillin will always remain in the urine or feces. The production of amoxicillin increases the quantity of chemicals in the environment [5]. Over time, bacteria develop resistance to the drug, leading to an increased dose [6, 7]. Thus, treatment with the amoxicillin drug will not be effective anymore [8]. Getting rid of amoxicillin residues in the environment is an important issue and has been interesting in the pharmaceutical industry [9, 10]. The pharmaceutical industry needs to treat wastewater with amoxicillin residue before releasing it to the water resources of the community [11, 12]. It is necessary to extract and recover amoxicillin from wastewater.

The Ministry of Health of Thailand allows the production of amoxicillin capsules (500 mg) to enter the market at an average of 100,000 tablets per day. Water usage

per month during production reaches a capacity of 140 liters while the effluent containing amoxicillin residues is concentrated around 400-500 mg per liter [13].

In 1997, GC Sahoo et al. studied the separation of antibiotics such as Cephalexin using a bulk liquid membrane (BLM) method [14]. In 1998, he continued to develop methods to separate emulsion liquid membrane extraction [15]. This program was costly because it used large quantities of solvents. However, a separate process with an efficient extraction method was developed resulting in extraction separation by membrane type with support, i.e. (Supported Liquid Membrane) [16]. Another extraction system proved successful, especially the hollow fiber supported liquid membrane (HFSLM). HFSLM had a higher surface area compared to most types of support plates (Flat Sheet) [17] and Spiral Wound [18] as well as lower power consumption. The hollow fiber supported liquid membrane system can be easily adapted and expanded and can be applied on an industrial scale [19].

1.2 Separation of Amoxicillin in synthetic wastewater via HFSLM

1.2.1 General information on amoxicillin substances

1.2.1.1 Trade name: Ibis A Campbell (Ibiamox), Amoxicillin, Amoxy, Actimoxi, Alphamox, Amocla.

1.2.1.2 Formula: (2S,5R,6R)-6-{[(2R)-2-amino-2-(4-hydroxy-phenyl)-acetyl]amino}-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid or a-amino-p-hydroxybenzylpenicillin [20].

1.2.1.3 Structure

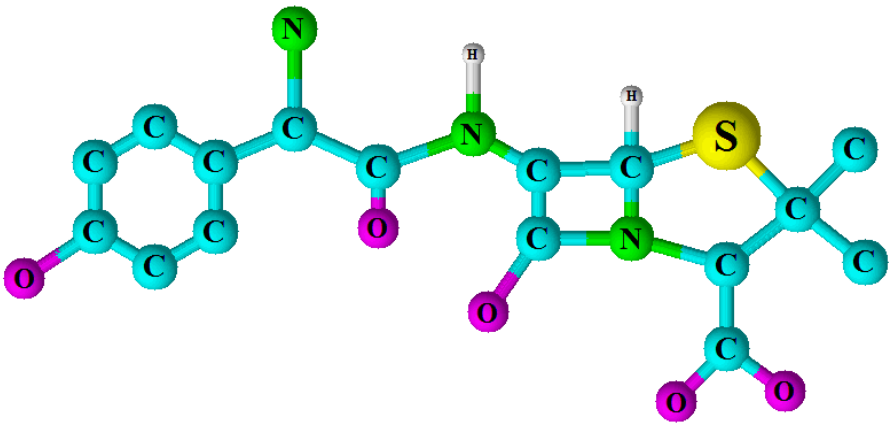

Figure 1.1 Amoxicillin structure [21]

1.2.1.4 Properties

The amoxicillin drug is allied with ampicillin which belongs to the penicillin group. Penicillin is better absorbed through the intestine than ampicillin and is used instead of ampicillin in all cases.

Amoxicillin is used in the treatment of some types of bacterial infections [22], especially in the following cases:

1. Respiratory complications, such as fever, bacterial infection, tonsillitis, bronchitis, bronchiolitis, pneumonia and sinusitis.

2. Ears such as acute otitis media.

3. Skin such as eczema, ulcers, boils, blisters and pustules.

4. Prevention and treatment of anthrax.

5. Tract such as dysentery, typhoid, ulcers, inflammation of the gums and tooth extraction.

6. Urinary tract and reproductive organs, such as cystitis, pyelonephritis, urethritis and gonorrhea.

1.2.1.5 Toxicity to environment

Amoxicillin causes environmental pollution, mainly due to human waste (medication), animals farming [23] and the pharmaceutical industry. The amoxicillin residues in the environment is causing bacteria to develop resistance to amoxicillin [24]. As a result, amoxicillin is less effective and will not be able to overcome the bacteria.

The mechanisms by which micro-organisms exhibit resistance to antimicrobials are as follows: drug inactivation or modification, alteration of metabolic pathway, alteration of target site and decreasing drug permeability or increasing active efflux of the drugs across the cell surface. Drug resistance can lead to many things, such as an increase in higher infection rates, longer hospital stays, higher treatment costs and a greater number of deaths [25].

1.2.2 Mass-transport mechanisms of amoxicillin in HFSLM

The hollow fiber system consists of three parts, i.e. feed phase, liquid membrane phase and stripping phase. The feed stage contains the target ions. The organic membrane stage contains the carrier dissolved in the solvent. The stripping stage recovers the target ions in the feed solution which is transferred through the membrane.

The mass transfer is divided into 2 types, depending on the type of reaction that occurs between the hydronium ion (H^+) in the feed solution and complexation of target ions in the membrane [26].

1.2.2.1 Co-transport

Co-transport is the means whereby the negatively charged target ions $[MY]^{n-}$ and hydronium ions in the feed solution move through the membrane in the same direction. Negatively charged target ions and hydronium ions react with the basic extractant (R_3N) in the membrane of the complexes (R_3NH^+ $[MY]^{n-}$) as in Eq. (1.1):

$$[MY]^{n-} + H^+ + R_3N \longrightarrow R_3NH^+ [MY]^{n-} \quad (1.1)$$

The complexes diffuse to the other side of the membrane due to the difference in the concentration of complexes. At the interface between the membrane phase and the recovering solution, the complexes react with the recovery solution. Then, the purpose ions are recovered into the recovering solution while the carrier diffuses back to the organic membrane phase as shown in Eq. (1.2).

$$R_3NH^+ [MY]^{n-} \longrightarrow [MY]^{n-} + H^+ + R_3N \quad (1.2)$$

1.2.2.2 Counter-transport

Counter-transport is the means whereby the positive by charged target ions $[M]^{n+}$ in the feed solution and hydronium ions in the stripping solution move through the membrane in the opposite direction as shown in Eq. (1.3):

$$M^{n+} + nRH \longrightarrow MR_n + nH^+ \quad (1.3)$$

The complexes diffuse to the other side of the membrane due to the difference in the concentration of complexes. At the interface between the membrane phase and the stripping solution, the complexes (MR_n) react with the hydronium ions. At that point, the purpose ions are recouped into the recovering solution while the carrier diffuses assist to the organic membrane phase as indicated in Eq. (1.4) [27].

$$MR_n + nH^+ \longrightarrow M^{n+} + nRH \quad (1.4)$$

Amoxicillin (negative charge) was extracted and recovered by the mechanism of ion-exchanged. It reacts with quaternary amine (Aliquat 336, QCl). The mole ratio between amoxicillin ($AMOX^-$) and quaternary amines is 1:1. The reaction of the extraction and recovery of amoxicillin is shown in Eq.s (1.5) and (1.6), respectively. Fig. 1.1 showed the mass transfer of amoxicillin:

$$AMOX^-_{(f)} + Q^+Cl^-_{(o)} \longleftrightarrow Q^+AMOX^-_{(o)} + Cl^-_{(f)} \quad (1.5)$$

$$Q^+AMOX^-_{(o)} + Cl^-_{(s)} \longleftrightarrow AMOX^-_{(s)} + Q^+Cl^-_{(o)} \quad (1.6)$$

Amoxicillin is a particle that has both positive and negative charge with pKa_1 = 2.68, pKa_2 = 7.49. The condition of the particle is controlled by the pH of the arrangement; pH of 6 is a negative charge and pH of 3.5 is in the middle [28]. Extraction occurs via two mechanisms, i.e. extracted ion coupling and ion exchange.

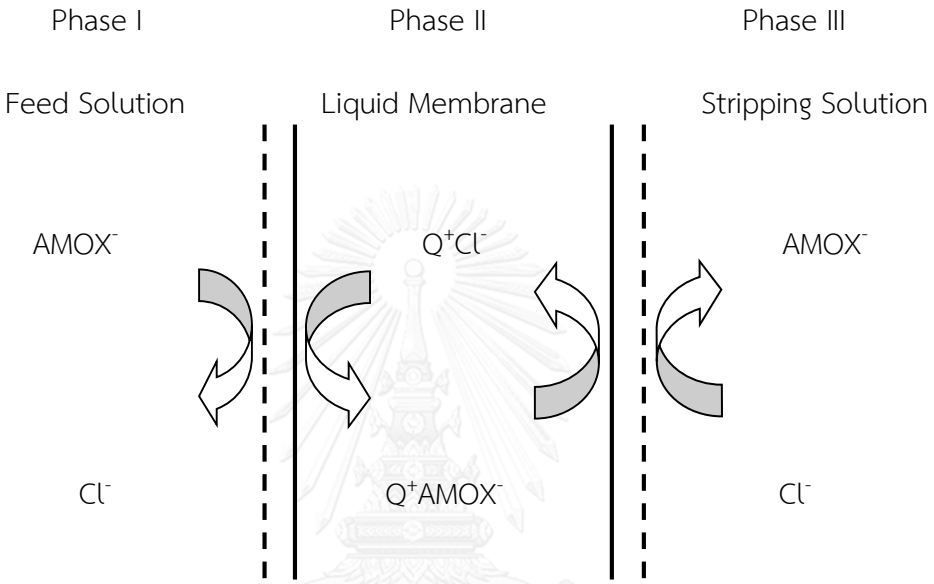

Figure 1.2 The mass transfer of amoxicillin as the counter-transport

1.3 The factors affecting separation of amoxicillin

1.3.1 The influences of carrier

1.3.1.1 The type of extractant

Extractants used in the liquid membrane process are divided into 5 groups as follows:

A: Acidic extractants

An acidic extractant consists of the functional groups: -COOH, =P(O)OH, $-SO_3H$. Thus, the metal ions react with the acidic extractant [29]. The complexes are neutral and are soluble in organic solvents as shown in Eq. (1.7):

$$M^{n+} + nRH \leftrightarrow MR_n + nH^+ \quad (1.7)$$

The acidic extractant is found to be very useful in the commercial extraction of metal ions. These include “organic derivatives of phosphorous acids” and “mono-carboxylic acids” in which the extract is acid alkyl-phosphoric acid. Alkyl-phosphoric acids are the most active, especially 2-ethyl hexyl phosphoric acid (D2EHPA).

B: Chelate extractants

A chelate extractant can react with metal ions. Complexes are neutral and can be soluble in organic solvents. Extracts of chelating (chelation) with metal ions are positively charged. The extractants containing chelating are among the anion (donor groups) which can form complexation (bidentate complexes) with metal ions. Extracts of commercial chelating are limited to two types:

(a) Type 2-hydroxy group benzophenones, (2-hydroxy benzophenone oximes), manufactured by Henkel Corporation (General Mills Inc. USA.) under the name LIX Acorga extractants manufactured by Imperial Chemical USA and SME extracts manufactured by Shell Chemical USA.

(b) 8-hydroxy group Aquino's (8-hydroxyquinoline) manufactured by Sherex (Ashland Chemical Company USA) under the trade name Kelex. These extracts are manufactured specifically for the extraction of copper ions from acid solution, the process of leaching (acidic leach liquors) and alkaline solution.

The simplified Eq. (1.8) shown below is for the extraction of a metal cation with a $^{+}2$ charge.

$$[2\mathrm{RH}]_{\mathbf{org}} + [\mathrm{M}^{2+}\mathrm{SO}_4^{=}]_{\mathbf{aq}} \leftrightarrow [\mathrm{R}_2\mathrm{M}]_{\mathbf{org}} + [2\mathrm{H}^{+} + \mathrm{SO}_4^{=}]_{\mathbf{aq}} \quad (1.8)$$

C: Solvating extractants

A solvating extractant or a neutral extractant can extract only an anion. In general, extractions with solvating extractants are limited. This is due to the ability of metal to form neutral complexes with anions, the co-extraction of acid at high acid concentrations and the solubility of the organometallics complex in the organic carrier as shown in Eqs. (1.9) and (1.10) [26]:

$$\mathrm{MX_n} + \mathrm{yS} \leftrightarrow \mathrm{MX_nS_yMX_n} + \mathrm{yS} \leftrightarrow \mathrm{MX_nS_y} \quad (1.9)$$

$$\mathrm{HMX_{n+1}} + \mathrm{xS} \leftrightarrow (\mathrm{HS_x})^{+}(\mathrm{MX_{n+1}})^{-} \quad (1.10)$$

D: Ligand substitution extractants

Ligand substitution extractants are the same as neutral or solvating extractants that they give an electron pair to a metal ion [30]. However, these

extractants are diverse that they form inner shell complexes with metals and, in so doing, will remove different ligands. For instance, consider the extraction of Pd from an acidic palladium chloride solution by a mono-oxime as depicted by the following Eq. (1.11):

$$2R_2C = NOH + PdCl_4^{=} \leftrightarrow (R_2C = NOH)_2PdCl_2 + 2Cl^- \quad (1.11)$$

E: Ion-pair extractants

Ion-pair extractants are based on the rule of ion association whereby a large, positively charged organic moiety causes the extraction of an anionic metal complex into the organic phase, with corresponding ejection of a typical anion into the aqueous phase. Alamine and Aliquat are examples of ion-pair extractants [31].

Alamine reagents contain a basic nitrogen capable of forming amine salts with a wide variety of inorganic and organic acids. Tertiary amines of the general equation R_3N (where R represents a variety of hydrocarbon chains) are largely used in metal recovery preparing by solvent extraction. The equations below are illustrative of the extraction chemistry of the alamine series of reagents.

The Aliquat series of reagents is based on the quaternization of the particular alamine reagent by methyl chloride. Since a quaternary amine is positively charged, anion extraction with Aliquat reagents is not pH dependent as it is with tertiary amines. Thus, some basic metal leach solutions may be successfully treated by Aliquat reagents without pH adjustment. Eq. (1.12) represents amine salt formation and Eq. (1.13) represents true ion exchange:

$$[R_3N]_{org} + [HA]_{aq} \leftrightarrow [R_3NH^+A^-]_{org} \quad (1.12)$$

$$[R_3NH^+A^-]_{org} + [B^+]_{aq} \leftrightarrow [R_3NH^+B^-]_{org} + [A^-]_{aq} \quad (1.13)$$

1.3.1.2 The concentration of carrier

Typically, the concentration of an extractant has a direct effect on the percentage of extraction and stripping. When concentration of an extractant is increased, the reaction tends to be forward reaction, according to the rules of the Le Chatelier.

1.3.2 The influences of organic diluents

The stability of the membrane and the liquid membrane varies according to the type of organic solvent [32]. The solvent properties and the transport properties are interrelated, depending on the types of solvent in the liquid membrane [33, 34]. The polarity index and the viscosity properties seem to be important in their effects on transport [35]. The diffusion coefficient depends on the viscosity according to Stokes-Einstein relation (Eq. 1.14).

$$D_m = kT/(6\pi\eta r) \quad (1.14)$$

In this study, several diluents with different polarity indexes can enhance extraction performance: alcohol > alkyl > halide > hexane [36, 37].

1.3.3 The influences of separation time

Operating time increases the retention time in reaction to the extraction and the separation of amoxicillin. For instance, the percentage of extraction of amoxicillin in the feed solution increased when the retention time increased [38, 39].

1.3.4 The influences of concentration polarization

The concentration of amoxicillin in feed solution causes the concentration polarization [40], and thereby the boundary layer thickness increases [41]. Thus, mass transfer of amoxicillin is hindered.

1.3.5 The effects of feed and stripping flow rates

The flow rates of feed and stripping solutions have the direct effects on the extraction and recovery of target ions. When the flow rate of feed is increased, it reduces the residence time to extract and recover the target ions [42].

1.3.6 The effects of pH of feed and stripping solutions

The pH of feed solution affects the seperation of amoxicillin ions. The pH in the range of pKa1 and pKa2 is suitable to extract anion amoxicillin by Aliquat336. When the pH is greater than 9.0, amoxicillin disintegrates [43].

1.3.7 The influences of temperature

During the experiment, the temperatures ranged between 278.15 and 318.15 K. The reaction is endothermic extraction. According to van der Waal's forces and hydrogen bonding, when the temperature is increased, the intermolecular attractions between the solute molecules and water molecules are interrupted leading to higher extraction and stripping [44]. On the other hand, if the reaction is exothermic extraction, an increase in temperature results in a decrease in forward reaction. When the temperature is higher than 50 K, amoxicillin disintegrates [45].

1.4 The systems used to separate amoxicillin in HFSLM

There are three types of systems used to separate amoxicillin via HFSLM:

1.4.1 Mass transport

The fundamental mass-transfer rates through the hollow fiber supported liquid membrane are the diffusion steps. The ability of amoxicillin transport through the feed diffusion layer and the organic phase is shown by k_i (Eq. 1.15) and k_m (Eq. 1.16), respectively, and is estimated by the equation of the Sherwood-Graetz [46]. The mass transfer across the membrane phase proved to be the rate controlling step because k_m (the mass transfer coefficient of the organic membrane) is less than k_i (the mass transfer coefficient of amoxicillin through the feed diffusion layer).

$$\mathrm{Sh} = \frac{\mathrm{k}_i \mathrm{d}_i}{\mathrm{D}_{aq}} \tag{1.15}$$

$$k_m = \frac{\varepsilon D_m}{\tau r_i \ln(\frac{r_o}{r_i})} \quad (1.16)$$

To find out the outlet concentration of amoxicillin via HFSLM system, Eq. (1.17) has to be developed based on Fick's first law of relation. Modeling of the diffusive mass-transport flux is performed under the following assumptions:

a) The framework is thought to be at a pseudo-steady state;

b) The extraction reaction takes place at the interface between the aqueous solution and the liquid membrane. The impact of the interface curvature in the mass-transfer rate can be viewed as insignificant;

c) No solute transport happens through the non-permeable parts of the organic membrane;

d) The solvency of both liquids in one another is insignificant; and

e) Mass transfer is depicted by simple film-type mass-transport coefficients.

The objective of the mathematical model to predict the amoxicillin concentration, is defined as follows [47]:

$$[\text{Amoxicillin}]_{f(t)} = -\frac{R_f[\overline{QCl}]_0}{R_m} + ([\text{Amoxicillin}]_{f(0)} + \frac{R_f[\overline{QCl}]_0}{R_m}).\exp(\frac{-A}{2R_f V_f} t) \quad (1.17)$$

1.4.2 Kinetics

Kinetics was used to determine the order of reaction and reaction rate constant for extraction and recovery of amoxicillin by applying an integral equation to plot the

graph to determine the relationship of the concentration of the target ion versus time. The integral concentrations with respect to zero, first and second orders were plotted between C_A, $\ln(C_{A0}/C_A)$ and $1/C_A$ against time at the optimum condition. The linear line of each reaction order is presented by the squared correction coefficients (R^2). Furthermore, Pancharoen's model [48] can predict the outlet concentration of the target ions in feed solution. This equation is defined as follows:

1. The inside and the outside diameters of a hollow fiber are little. Along these lines, the membrane thickness is very thin; in this way, the radial concentration profile of amoxicillin is constant;

2. Just the complex species happening from the reaction, not amoxicillin, diffuse through the membrane phase;

3. The extraction reaction is irreversible that implies just the forward reaction of Eq. (1.5) is considered; and

4. Because of very thin membrane thickness, it is assumed that the reaction occurs only in the axial direction of the hollow fibers. Mass flux of amoxicillin exists in the axial direction.

$$\bar{C}_A^*(0,t-\tau_0)=\frac{(V_{FT}-V_F)\bar{C}_A(0,t)+V_F\bar{C}_A(L,t)}{V_{FT}} \tag{1.18}$$

Furthermore, the experimental data can be used to determine the activation energy of amoxicillin extraction in the temperature range between 278.15 K and 318.15 K. This factor can be resolved by linearizing the mathematical statement (Eq. 1.19). By plotting the flux (ln *J*) versus (*1/T*) [49, 50], a straight line with the slope equivalent to $-E_a/R$ can be gotte:

$$\ln J = \ln A - \frac{E_a}{R}\frac{1}{T} \tag{1.19}$$

1.4.3 Thermodynamics

The extraction and the stripping of amoxicillin via the HFSLM system, in the temperature range between 278.15 K and 318.15 K, was investigated. The thermodynamic factors were dictated by Van't Hoff's mathematically model [51]. This demonstrates the relationship between the impacts of the equilibrium extraction constant (K_{ex}) and the temperature amid amoxicillin extraction. Eq. (1.20) is the Van't Hoff mathematically model in linearized structure.

$$\ln K_{\mathrm{ex}} = -\frac{\Delta H^0_{ex}}{RT} + \frac{\Delta S^0_{ex}}{R} \tag{1.20}$$

As per Eq. (1.20), a plot of ln K_{ex} versus $1/T$ gives a straight line whose slope and interception can be utilized to focus ΔH^0_{ex} and ΔS^0_{ex} [52]. Gibbs free-energy change (ΔG^0_{ex}) is related to the standard enthalpy (ΔH^0_{ex}) and the extraction entropy changes (ΔS^0_{ex}) via Gibb-Helmholtz mathematical statement as indicated in Eq. (1.21):

$$\Delta G_{ex}{}^0 = \Delta H_{ex}{}^0 - T\Delta S_{ex}{}^0 \tag{1.21}$$

The values of enthalpy change indicate that the separation of amoxicillin can be endothermic reaction. The positive estimations of entropy change suggests that the extraction procedure is forward response.

1.5 The objectives of the dissertation

1.5.1 To study the extraction and the recovery of amoxicillin via hollow fiber supported liquid membrane system;

1.5.2 To study the influences of parameters which affect the extraction and the recovery of amoxicillin via HFSLM;

1.5.3 To investigate the optimum condition for the extraction and the recovery of amoxicillin via HFSLM.

1.6 The scope of the dissertation

1.6.1 The extraction and the stripping of amoxicillin from synthetic wastewater via the hollow fiber supported liquid membrane system were investigated.

1.6.2 The parameters investigated include:

- the types of flow patterns of the feed phase and the stripping phase, i.e. circulating flow and continuous flow;

- the pH of feed phase;

- the concentrations of the carrier;

- the pH of the stripping phase;

- the concentrations of stripping phase;

- the flow rates of the feed phase and the stripping phase;

- the operating temperatures.

1.7 The expected results

1.7.1 High extraction and stripping of amoxicillin

1.7.2 A simple and effective system for separation of amoxicillin from wastewater

1.7.3 Highly accurate reaction flux model and mass-transfer flux model

1.8 The descriptions of dissertation

Part I

This study was undertaken to learn the basic principles and functioning of the hollow fiber supported liquid membrane system. Di-(2-ethylhexyl) phosphoric acid diluted in kerosene was used as an extractant in order to separate cobalt and manganese ions from sulphate media via HFSLM. This solution is also a suitable one at low concentrations and separation performance as well as low cost. The research started with the introduction of Co and Mn in sulfate media designated as the feed solution. D2EHPA dissolved in kerosene was used as an extranctant, then packed in micropore of hollow fiber module serves as a liquid membrane. The stripping solution of HCl was used at a concentration of 0.2M. Hollow fiber supported liquid membrane in the oil phase acts as a barrier between the aqueous of feed phase and the aqueous of stripping phase. The circulating continuous flow was used as the flow pattern in the experiment. To find the optimum conditions for extraction of the parameters are the pH values of the feed phase, the Co(II) and Mn(II) concentrations, the D2EHPA concentrations, the hydrochloric acidic stripping concentrations, the feed and the stripping flow rates and the number of hollow fiber modules. When the system is in

equilibrium, the sample is collected to analyze the concentrations of Co and Mn by an atomic absorption spectrophotometer (AAS). The percentage of extraction is a value that indicates the ability to separate the target ion. In addition, permeability as a function of flow rates of the feed and the stripping together with the extractant concentration was developed. The extraction and the stripping of cobalt and manganese ions from sulphate media were investigated by multi-module HFSLM. A reaction flux model (Pancharoen's model [48]) was also used to predict the outlet concentration. The model results were verified by the experimental data by measuring the deviation equal to 2.24%.

$$C_A(L,t) = \bar{C}_A^*(0, t-\tau_0)\cdot u(t-\tau_0)e^{-k_f\tau_0} \qquad (1.22)$$

The plot between the concentrations of amoxicillin against time led to find the reaction order and the reactions constants. The details are presented in Chapter II and available in the published articles of Journal of Industrial and Engineering Chemistry (pages 1532-1541, volume 20 and year 2014) [53].

Part II

In Chapter III, the HFSLM system was employed to reduce the impact of resistance from the discharge of industrial wastewater containing amoxicillin to the environment; following the guidelines from the Ministry of Health for the separation of amoxicillin using trioctylmethylammonium chloride via HFSLM. Amoxicillin is used as the feed solution by pH controlling with diluted buffer solution. Aliquat336 dissolved in a solution of 1-decanol was served as an extractant in liquid membrane phase, and NaCl dissolved in the buffer solution was served as a stripping solution. The circulating

continuous flow was used as the flow pattern in the experiment. The variables used to design the best conditions were the pH of the feed solution, the amoxicillin concentrations of feed solution, the carrier concentrations (Aliquat336), the NaCl concentrations of stripping solution, and the flow rates of feed phase and stripping phase. The examples were taken out toward the end of every investigation from the feed and stripping reservoirs, and the state of being concentrated of amoxicillin were measured by HPLC (high performance liquid chromatography). The variables indicating the process performance were presented as the percentages of extraction and recovery of amoxicillin, the distribution ratio, the permeability coefficient and the mass-transfer coefficient. The permeation of amoxicillin can be communicated regarding the permeability coefficient (*P*), as prefered by Danesi [54] in Eqs. (1.23) and (1.24):

$$-\mathrm{V_f}\ln\left(\frac{\mathrm{C_f}}{\mathrm{C_{f,o}}}\right)=\mathrm{A}P\frac{\beta}{\beta+1}\mathrm{t} \tag{1.23}$$

the permeability coefficient, which is utilized to focus the mass-transfer coefficients for amoxicillin separation by HFSLM, relies on upon mass-transfer resistance which is the equal of the mass-transfer coefficients [55], as takes after:

$$\frac{1}{P}=\frac{1}{k_{\mathrm{f}}}+\frac{r_{\mathrm{i}}}{r_{\mathrm{lm}}}\frac{[\mathrm{Cl}^-]}{K_{ex}\,k_m[\overline{\mathrm{QCl}}]} \tag{1.24}$$

where k_m is the mass-transfer coefficient of the organic membrane phase, and k_f is the mass-transfer coefficient of the feed phase.

The diffusion flux mathematically model developed to predict the state of being concentrated of amoxicillin is defined as follows :

$$[Amoxicillin]_f = -\frac{R_f[\overline{QCl}]_m}{R_m} + \left([Amoxicillin]_{f0} + \frac{R_f[QCl]_m}{R_m} \right) \cdot \exp\left(\frac{-A}{2R_f V_f} t \right) \quad (1.26)$$

The model results were verified by the experimental data as described in detail in the published articles of Journal of Industrial and Engineering Chemistry (year 2014) [56].

Part III

This part studied the influences of temperature affecting the extraction and the recovery from amoxicillin synthesized via the HFSLM system. The objective of this research is to find the best condition for the extraction and recovery amoxicillin, that is, the pH value of feed solution of 8.0, the pH value of stripping solution of 6.0, the flow rates of feed and stripping solutions of 100 mL/min, the concentration of feed solution of 6.0 mmol/L, the concentration of the extractant (Aliquat 336) of 6.0 mmol/L and the concentrations of recovery solution (NaCl) of 6.0 mmol/L. The temperatures used in the present study ranged from 278.15 to 318.15 K. According to the Van't Hoff model (Eq. 11), the values of ln K_{ex} and 1/T were plotted in order to determine the slope and interception of the straight line for calculations of ΔH^0_{ex} (the standard enthalpy) and ΔS^0_{ex} (extraction entropy changes), respectively [52].

$$\ln K_{\text{ex}} = -\frac{\Delta H^0_{ex}}{RT} + \frac{\Delta S^0_{ex}}{R} \quad (1.27)$$

Gibbs free-energy change (ΔG^0_{ex}) is related to ΔH^0_{ex} and ΔS^0_{ex} via Gibb-Helmholtz mathematical statement as indicated in Eq. (1.28):

$$\Delta G_{ex}{}^{0} = \Delta H_{ex}{}^{0} - T\Delta S_{ex}{}^{0} \quad (1.28)$$

The effects of temperature were investigated to improve the separation efficiency for amoxicillin separation via the HFSLM system since the temperature has a significant effect on chemical reactions as denoted by the Arrhenius equation.

The linearizing the flux equation (Eq. 1.29) Applied for the Activation energy of amoxicillin via HFSLM system. By plotting the temperature term (1/T) versus the flux term (ln J)[49, 50], the slope of straight line equal to $-E_a/R$ can be obtained:

$$\ln J = \ln A - \frac{E_a}{R}\frac{1}{T} \quad (1.29)$$

In general, the main transport mechanism can be determined by the value of activation energy, that implies the diffusion or the reaction are the rate limiting step [57]. The details are presented in Chapter IV and available in the published articles of Chemical Engineering Journal (pages 75-83, volume 265 and year 2015) [58].

Part IV

The results from research in Chapter II - IV were applied to study the removal of amoxicillin from synthetic wastewater using Aliquat336 as a carrier via double-

module HFSLM. The optimum condition was composed of 6 mmol/L of Aliquat336 in 1-decanol, the pH value of 8.0, the temperature of 318.15 K, the flow rate of feed phase of 100 ml/min and the flow rate of stripping phase of 100 ml/min. The mass-transfer parameters (k_i, k_m) were approximated by the Sherwood-Graetz correlation as shown in Eq. (1.30, 1.31) [46, 59].

$$\mathrm{Sh} = \frac{k_i d_i}{D_{aq}} \tag{1.30}$$

$$k_m = \frac{\varepsilon D_m}{\tau r_i \ln(\frac{r_o}{r_i})} \tag{1.31}$$

The mass-transfer coefficients of amoxicillin in the feed phase (k_i) of 1.65 × 10^{-4} cm/s and the membrane phase (k_m) of 6.89 × 10^{-5} cm/s were found. In addition, the extraction reaction order (n) was found to be 1.00 and the reaction rate constant (k_f) were found to be 0.0344 min^{-1}. The application of the thermodynamic techniques, the endothermic reaction can realized from the positive values of enthalpy change while the extraction process is forward reaction can realized from the positive values of entropy change. Furthermore, the value of activation energy (Ea) of amoxicillin extraction implied that the chemical reaction was the mass-transfer controlling step. This study was presented in Chapter V. The details are available in the published articles of the Korean Journal of Chemical Engineering (year 2015) [60].

CHAPTER 2

SEPARATION OF Co(II) AND Mn(II) FROM SULPHATE MEDIA VIA A HFSLM: REACTION FLUX MODEL AND EXPERIMENTAL VERIFICATION

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2.1 Abstract

Separation of Co(II) and Mn(II) from sulphate media through triple HFSLM in series using D2EHPA was explored. Mn(II) was extracted preferentially over Co(II) with best conditions obtained at pH value 5, 100 ppm of Co(II) and Mn(II), 5% (v/v) of D2EHPA, 0.2M HCl. The highest extraction percentage of Mn(II) was 98.14%, and Co(II) remained at 94.05% in the raffinate stream. The reaction order (n) and the reaction rate constant (k_f) were found to be 1.00 and 0.0180 min^{-1}, respectively. Furthermore, the reaction flux model proved to be in good agreement with the experimental data at an average deviation of 2.24%.

Keywords: Separation; Co(II); Mn(II); D2EHPA; HFSLM.

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2.2 Introduction

Cobalt and manganese demands have been increasing in recent years driven by the soaring growth of the world steel-making industry. However cobalt and manganese naturally appear in compound forms such as $CuSO_4$, $MnSO_4$. There is a growing interest in the investigation of new processes for their extraction and recovery from various sources [1]. For instance, Co(II) and Mn(II) in the industrial metallurgical processes contain both valuable and toxic metals in high concentrations [2, 3]. If the latter are not disposed with proper arrangements, they can have a negative effect on the environment owing to their non-biodegradability, high toxicity and ecological aspects [4]. Co(II) and Mn(II) have many applications in various fields, viz. steel production, preparation of dietary additives, non-ferrous alloys, fertilizers, carbon-zinc batteries, etc., owing to their outstanding advantages of deoxidizing, sulfur-fixing, and alloying properties [5]. This makes their recovery from secondary sources economically viable such as spent alkaline batteries, catalysts [6] and industrial metallurgical processes. Previously used methods for the separation of Co(II) and Mn(II) were iron-functionalized sepiolite [7], electrocoagulation [4], ammonia-ammonium carbonate leaching [8], solvent extraction [9], redox leaching and solvent extraction [10], ion exchange [11] together with chemical oxidation and reduction [12]. These methods, however, have some limitations in dealing with low metal concentrations [13]. In this study, the separation method used was the hollow fiber supported liquid membrane (HFSLM) since this method has the outstanding advantages and can resolve a shortcoming problem of the conventional methods, i.e. high selectivity [14], high surface-per-volume ratios [15,16], lower capital and operating costs [17,18], low energy consumption [19], easily large-scalability [20] along with relatively high mass-transfer rates [21,22].

HFSLM is considered a more effective method to overcome the drawbacks of conventional separation methods since it has many advantages in separating metal ions [23]. In particular, many researchers have attempted to separate metal ions via

HFSLM. Mamba et al. [24] focused on the removal of copper and cobalt by *Shewanella spp.* via biosorption. Their study removed Co(II) and Cu(II) from aqueous solutions, and at the optimum condition, the percentages of Co(II) and Cu(II) removal were 44.00% and 33.00%, respectively. Katsiapi et al. [8] investigated the recovery of cobalt from mixed Co(II) and Mn(II) hydroxide precipitates by ammonia-ammonium carbonate leaching technique. At the optimum condition of pH 10.5, temperature of 25°C and using 5 M NaOH (a neutralizing agent), Co(II) and Mn(II) were precipitated by 99.90% and 99.50%, respectively. In 2011, Hossain et al. [9] studied the selective separation of Mn(II) from high tenor cobalt electrolyte solution. The study used co-D2EHPA in solvent-extraction system. The McCabe-Thiele diagram showed that 100% manganese can be extracted through four stages using an O/A ratio of 0.65. Feng et al. [10] focused on the process of redox leaching and solvent extraction for the recovery of Mn(II), Ni(II) and Co(II) from manganese modules. The optimum condition can be summarized as temperature of 90°C; time of 4 h; H_2S0_4 concentration of 1.25 mol/L; charge ratio of 3:2; liquid-to-solid ratio of 2:1 and stirring speed of 300 rpm. The recovery rates for Mn(II), Co(II) and Ni(II) are 85.00%, 75.00% and 78.00%, respectively.

In recent years, HFSLM has followed certain rules for the choice of the promising pre-separation and pre-concentration methods and has a large application range because of the aforementioned advantages [25-27]. It has attracted a lot of researchers who have studied the liquid-membrane configuration to remove trace metal ions from aqueous solutions containing Co(II), Mn(II) and other impurities. Marchese et al. [28] investigated the extraction and recovery of Co(II), Ni(III) and Cu(II) via a flat-sheet supported liquid membrane. Youn et al. [29] intensively carried out studies to remove Co(II) across a supported liquid membrane containing 2-ethylhexyl hydrogen phosphonate (EHP) as an extractant. In addition, selective methods of extraction and recovery of Co(II) and Mn(II) were applied and were summarized in Table 2.1.

Table 2.1 The reviewed methods for cobalt and manganese ion removal

Authors	Target ions	Extractants	Methods	%Extraction/%Stripping
Youn et al. [30]	Co(II), Ni (II)	D2EHPA	SLM	N/A
Gega et al. [31]	Co(II), Ni (II)	D2EHPA, Cyanex 272,301,302	SLM, HLM	N/A
Bukhari et al. [32]	Co(II), Ni (II)	TEA	SLM	80.00%/-
Alguacil et al. [33]	Co(II), Mn(II)	DP-8R	SLM	N/A
Parhi et al. [34]	Co(II),Ni (II)	LIX 84I, TOPS-99 and Cyanex 272	SLM	N/A
José et al. [35]	Co(II), Mn(II)	DP-8R	SLM	44.00% for Co(II), 90.00% for Mn(II)/-
Sadyrbaeva et al. [36]	Mn(II)	D2EHPA	ELM	88.00%/-
Hossain et al. [9]	Mn(II)	Co-D2EHPA	LL	100.00%/-
Tsakiridis et al. [37]	Co(II), Mn(II), Ni(II), Mg(II)	Cyanex 301	LL	99.80% for Co(II), 99.60% for Ni(II)/-
Devi et al. [38]	Co(II), Mn(II)	D2EHPA , PC-88, Cyanex 272	LL	N/A
Prakorn et al. [39]	Co(II)	D2EHPA	HFSLM	N/A
This work	Co(II), Mn(II)	D2EHPA	HFSLM	98.64% for Mn(II), 6.05% for Co(II)/ 85.32% for Mn(II), 5.15% for Co(II)

Note: LL = liquid-liquid extraction; BLM = bulk liquid membrane; SLM = supported liquid membrane; HLM = hybrid liquid membranes; HFSLM = hollow fiber supported liquid membrane; TEA = Triethanolamine; DP-8R = di(2-ethylhexyl)phosphoric acid; SW = synthetic wastewater

This work presented the transport and selectivity of Co(II) and Mn(II) from mixed manganese and cobalt sulphate via HFSLM arranged D2EHPA-triple hollow fiber

modules in series systematically investigated. The prime objectives were to obtain the best condition affecting the transport of Co(II) and Mn(II) via HFSLM. Variable influencing transport of Co(II) and Mn(II) were investigated, i.e. pH values of the feed phase, Co(II) and Mn(II) concentrations, D2EHPA concentrations, hydrochloric acidic stripping concentrations and the number of hollow fiber modules. In addition, permeability as a function of flow rate of the feed and stripping together with the extractant concentration was developed. Finally, raffinate concentrations were predicted by the reaction flux model of Pancharoen et al. [40] and compared with the experimental data.

2.3 Theory

2.3.1 Hollow fiber supported liquid membrane (HFSLM)

The HFSLM system consists of three main phases (solution): feed, membrane and stripping phases. The membrane phase is an embedded organic extractant which acts as a semi-barrier between the feed and stripping phases. Nevertheless, this phase only allows for the diffusing target ions and impedes other ions. Schematic representation of the microporous HFSLM was illustrated in Fig. 2.1.

2.3.2 Facilitated transport mechanism and separation of Co(II) and Mn(II)

The descriptive schematic mechanisms were the counter-transport mechanism via HFSLM. In Fig.2.2, the concentration profile for the system was shown. The gradient of proton concentration yielded high enrichment factors for metal ion [41]. The driving force of the process is the proton concentration gradient in the feed phase and stripping phase.

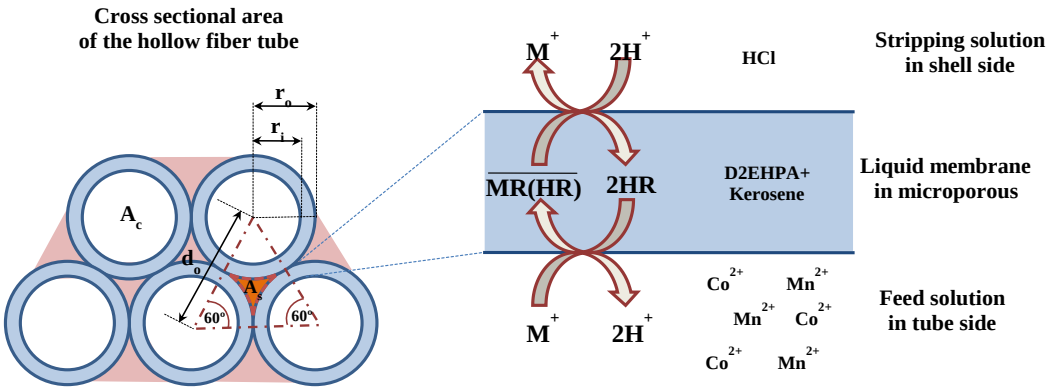

Figure 2.1 Schematic representation of the microporous hollow fiber supported liquid membrane

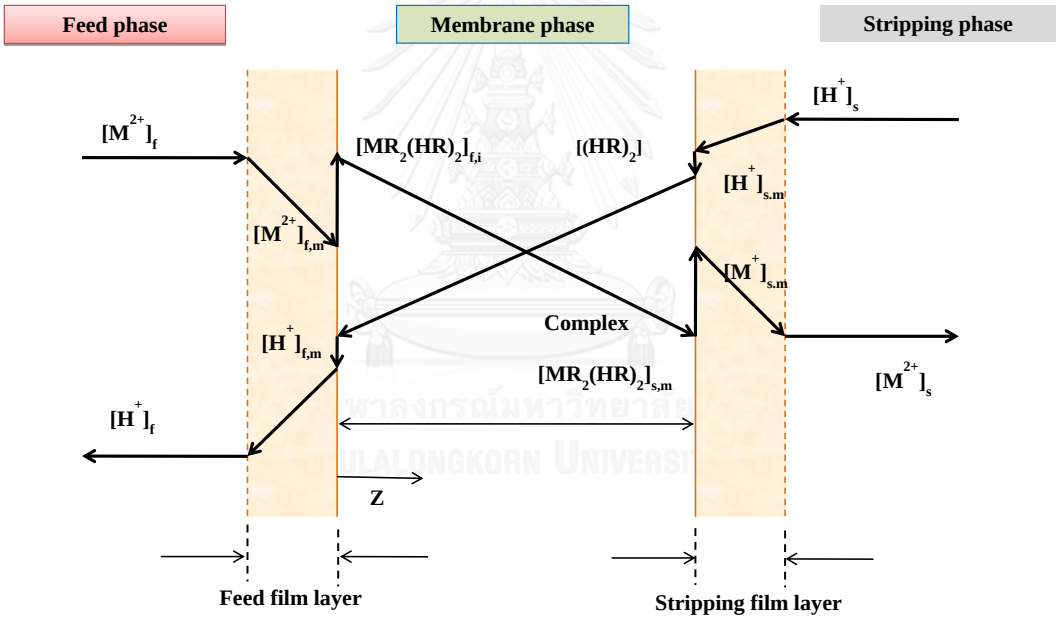

Figure 2.2 Schematic concentration profile for the system M^{2+}: Mn(II) or Co(II); HR: active substance of the carrier

D2EHPA, an acidic extractant, plays the role of an accelerator for the transport of specific components from the feed phase to the stripping phase. The analysis of permeation rates of Co(II) and Mn(II) through the HFSLM method was carried out via the following steps.

Step I: Co(II) and Mn(II) in the feed solution were transported to a contact interface between the feed phase and the liquid membrane phase. Subsequently, Co(II) and Mn(II) reacted with the D2EHPA (*HR*) to form the complex species ($MR_2(HR)_2$) [42] and hydrogen ion H^+ was released as described in Eq. (2.1)

$$M^{2+} + 2(\overline{HR})_2 \overset{K_{eq}}{\leftrightarrow} \overline{MR_2(HR)_2} + 2H^+ \quad (2.1)$$

where K_{eq} is the extraction equilibrium constant, and the overbar refers to the organic phase. *"M^{2+}"* is Co(II) or Mn(II), *"HR"* is an active substance of the carrier (D2EHPA). Meanwhile, ($MR_2(HR)_2$) is the Co(II) or Mn(II) complex species.

Step II: The Co(II) and Mn(II) complex species ($MR_2(HR)_2$) diffused to the interface between the membrane phase and the stripping phase by the concentration gradient.

Step III: The hydrogen ion, H^+, from the stripping phase diffused to the membrane-stripping interface. H^+ reacted with the Co(II) and Mn(II) complex species ($MR_2(HR)_2$) at the interfaces between the membrane phase and the stripping phase and then Co(II), Mn(II) and $(HR)_2$ were released as shown in Eq. (2.2).

$$\overline{MR_2(HR)_2} + 2H^+ \rightarrow M^{2+} + 2(\overline{HR})_2 \quad (2.2)$$

Step IV: Co(II) and Mn(II) transfers into the stripping phase while the extractant $(HR)_2$ diffuses back to the membrane phase by the concentration gradient and reacted again with the target ions Co(II) and Mn(II).

2.3.3 The equilibrium constants

The relationships of equilibrium constant, K_{eq}, for Mn(II) extraction and recovery though the HFSLM are given by:

$$K_{eq} = \frac{\left[\overline{MR_2\left(HR\right)_2}\right]\left[H^+\right]^2}{\left[M^{2+}\right]\left[\left(\overline{HR}\right)_2\right]^2} \tag{2.3}$$

2.3.4 Permeability and mass-transfer coefficient

The permeation rates of Co(II) and Mn(II) and hydrogen ions at the aqueous boundary layers are represented by the permeability depending on the mass-transfer resistance which is reciprocal to the mass transfer and is given by Merchese et al. [28] as shown in Eq. (2.4).

$$P = \left[\frac{R_m}{\left(\left[H^+\right]_f^{-2} + \left[H^+\right]_s^{-2}\right)K_{eq}C_{HR}^2} + R_i + R_s\right]^{-1} \tag{2.4}$$

where $[H^+]_f$ is hydrogen ion concentration in the feed phase; $[H^+]_s$ is hydrogen ion concentration in the stripping. R_m, R_i and R_s are the organic-membrane phase, feed-phase and strip-phase resistances, respectively, and are defined as:

$$R_m = l_{ef} / D'_{MR_2(HR)_2} = 1/k_m \tag{2.5}$$

$$R_i = 1/k_i \tag{2.6}$$

$$R_s = 1/k_s \tag{2.7}$$

where l_{ef} is the effective thickness of the membrane; $D'_{MR2(HR)2}$ is the effective diffusion coefficient of the metal complex in the organic phase. k_m, k_i and k_s are mass-transfer coefficients of the membrane, the feed and the stripping phases, respectively.

In the experiment, the hydronium concentrations in both feed and stripping sides were kept constant and $[H^+]_f << [H^+]_s$, so the overall permeability of the metal can be rewritten as [43]:

$$P = \left[B + \frac{1}{k_i} + \frac{1}{k_s} \right]^{-1} \tag{2.8}$$

and B is calculated by Eq. (2.9)

$$B = \left[\frac{l_{ef}}{D'_{MR_2(HR)_2} K_{eq} C_{HR} [H^+]_f^{-2}} \right] \tag{2.9}$$

$$l_{ef} = r_i \ln \frac{d_0}{d_i}$$

Where: K_{eq} is the extraction equilibrium constant,

C_{HR} is the initial concentration of the carrier and

l_{ef} is calculated from the following correlation:

r_i is the radius of the fiber in the hollow-fiber module,

d_0 and d_i are the outer and inner diameters of the fiber, respectively.

Given

$$D'_{mem} = \frac{\varepsilon D_{mem}}{\tau} \tag{2.10}$$

where D'_{mem} is similar to $D'_{MR2(HR)2}$. D_{mem} can be calculated by the Stokes-Einstein equation. The tortuosity ($\boldsymbol{\tau}$) and the porosity ($\boldsymbol{\varepsilon}$) of the hollow fiber are shown in Table 2.1. From the experiment, the value of permeability, P_{ex} was defined by Eq. (2.11) [44]

$$P_{ex} = \frac{q_s \left[M^{2+} \right]_{out,2}}{A_m \left[M^{2+} \right]_{m,1}} \tag{2.11}$$

The experimental mass balance with the assumption of instantaneous stripping reaction [45] was calculated by:

$$q_f \left(\left[M^{2+} \right]_{in,1} - \left[M^{2+} \right]_{out,1} \right) = q_s \left[M^{2+} \right]_{out,2} \tag{2.12}$$

The average value of $[M^{2+}]_{m,1}$ is given by:

$$\left[M^{2+}\right]_{m,1} = \frac{\left(\left[M^{2+}\right]_{in,1} - \left[M^{2+}\right]_{out,1}\right)}{\ln\left(\left[M^{2+}\right]_{in,1} / \left[M^{2+}\right]_{out,1}\right)} \tag{2.13}$$

After substituting Eq. (2.11) in Eq. (2.12) and (2.13), Eq. (2.14) was obtained:

$$P_{ex} = \frac{q_f \ln\left(\left[M^{2+}\right]_{in,1} / \left[M^{2+}\right]_{out,1}\right)}{A_m} \tag{2.14}$$

where q_f and q_s are the volumetric flow rate of feed phase and stripping phase, respectively.

2.3.5 Reaction flux model for extraction stream

The target metal-ion extraction was theoretically and experimentally evaluated. The theoretical evaluation referring as Pancharoen's model [40] was developed for outlet concentration prediction at any time based on the assumptions for the reaction flux model given as follows:

$$-\frac{q}{A_c}\frac{\partial C_A(x,t)}{\partial x} - r_A(x,t) = \frac{\partial C_A(x,t)}{\partial t} \tag{2.15}$$

where $r_A(x,t)$ and $C_A(x,t)$ are the reaction rate and the concentration of Mn(II) at any time, respectively.

In the Case n = 1, the solution of Eq. 2.15 can be expressed as:

$$C_A(L,t) = \bar{C}_A^*(0,t-\tau_0)\cdot u(t-\tau_0)e^{-k_f\tau_0} \tag{2.16}$$

Where: $u(t-\tau_0)$ is a shifting unit function and

$$\tau_0 = \frac{A_C L}{q}$$

Where

$C^*_A(x,t)$ is the average concentration of target metal ion in the feed reservoir (mg/L). A_c is the cross-sectional area of hollow fiber (dm^2). L is the length of hollow fiber (dm). q is a volumetric flow rate (mL/min). C is the concentration of target metal ion (mg/L).t is time (min) and n is the order of the reaction.

In case of a batch system, the feed concentration of Mn(II) is the average concentration in the reservoir before feeding back into the process. It can be calculated from Eq. (2.17).

$$\bar{C}_A^*(0,t-\tau_0) = \frac{(V_{FT}-V_F)\bar{C}_A(0,t)+V_F\bar{C}_A(L,t)}{V_{FT}} \tag{2.17}$$

where:

$$\bar{C}_A(0,t) = C_A(0,t) - C_A(0,0)$$

$$\bar{C}_A(L,t) = C_A(L,t) - C_A(L,0)$$

where V_{FT} and V_F are the total volume of solution in the feed reservoir and the volume of feed solution, respectively. $C_A(0,t)$ and $C_A(L,t)$ are the average concentration of metal ion in the feed concentration of metal ion (ppm) and the concentration of metal ion (ppm) at the outlet, respectively.

2.3.6 The percentage of metal ion extraction, recovery

The percentage of metal ion extraction and recovery from the experiments and the model were calculated by Eq. (2.18) and Eq. (2.19) respectively.

$$\%Extraction = \frac{C_{in} - C_{raf}}{C_{in}} \times 100 \quad (2.18)$$

where C_{in} and C_{raf} are the inlet feed and raffinate concentrations of metal ions

$$\%\,\text{Recovery} = \frac{C_{st,out} - C_{st,in}}{C_{in}} \times 100 \quad (2.19)$$

where $C_{st,in}$ and $C_{st,\,out}$ are the inlet and outlet stripping concentrations of metal ions, respectively.

2.3.7 The separation factor and standard deviation

The separation factor "$S_F(AB)$" is the ratio of concentrations A and B in the permeate and retentate[46]. That was calculated by Eq. (2.20).

$$S_F(AB) = [C_A/C_B]_{Permeate} / [C_A/C_B]_{Retentate} \quad (2.20)$$

where C_A and C_B are the concentrations Mn(II) and Co(II).

The percentage absolute error of the extraction efficiency of Mn(II) in the feed solution obtained by experimental runs and model simulation is defined as:

$$A.E.(\%) = \frac{\left|D_{Exp} - D_{Mod}\right|}{D_{Mod}} \times 100 \quad (2.21)$$

where *A.E.* (%) is percentage absolute error, D_{Exp} is the experimental data, D_{Mod} is the model calculated value from the mathematical model.

The value of the validity of the mathematical model was the percentage of standard deviation (*S.D.* (%)) between the model calculated value from the mathematical model and the experimental results is defined as;

$$S.D.(\%) = 100 \times \sqrt{\frac{\sum_{i=1}^{N}\left\{\left(\frac{D_{Exp}}{D_{Mod}}\right) - 1\right\}^2}{N-1}} \quad (2.22)$$

where D_{Exp} is the experimental data, D_{Mod} is the model calculated value from the mathematical model and N is the number of experimental points.

2.4 Experimental

2.4.1. Chemicals and reagents

The feed solution was prepared by dissolving cobaltous sulfate and manganese sulfate in distilled water. Hydrochloric acid was used to adjust the pH value in order to keep it at pH 5.0. The stripping solution was 0.2 M hydrochloric acid from Merck Ltd. D2EHPA in the presence of kerosene from Fluka was used as the extractant. All chemicals used were A.R. grade.

2.4.2. Apparatus

The Liqui-Cel® Laboratory Liquid/Liquid Extraction System was composed of gear pumps, variable speed controllers, rota meters and pressure gauges as shown in Fig. 2.3.

This HFSLM module is Celgard® microporous polyethylene fibers that are woven into fabric and wrapped around a central-tube feeder that supplies the shell-side fluid. Woven fabric allows more uniform fiber spacing which in turn leads to higher mass-transfer coefficients than those obtained with individual fibers. The properties of the hollow fiber module are as shown in Table 2.2. The fiber is potted into a solvent-resistant polyethylene tube sheet and the shell casing is polypropylene.

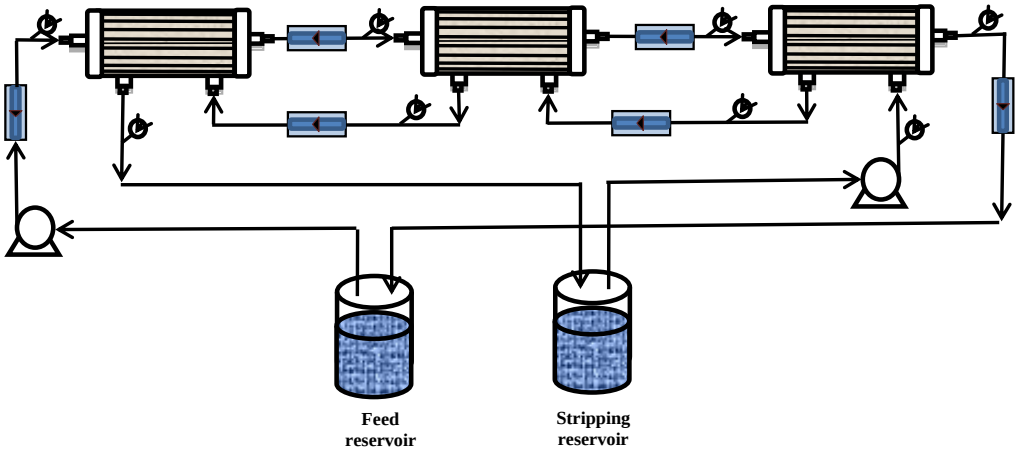

Figure 2.3 Schematic counter-current flow diagram for triple hollow fiber modules

2.4.3 Analytical instruments

The measurement of Co(II) and Mn(II) concentration in the aqueous phases was monitored by periodically sampling both extracted solutions at steady state. Then, it was analyzed after appropriate dilution by an Atomic Absorption Spectrophotometer, Model IL551, AA/AE Spectrophotometer from Instrumentation Laboratory Inc. The atomic absorption spectrometry has produced a rapid and relatively inexpensive method for the determination of metal concentrations in a wide variety of samples [47]. The measurements were made in duplicate and the difference between the two values was less than 2.0%. The pH of the aqueous phase was measured by a SevenMulti™ modular pH meter with expansion unit (Mettler-Toledo, Greifensee, Switzerland).

2.4.4 Procedure

First, the liquid membrane is prepared by dissolving D2EHPA in kerosene. The organic solution was then fed into the tubes and shell of the HFSLM at the same time for 50 min. to ensure that the extractant was embedded in the micropores of the

hollow fibers. Thereafter, the feed solution was pumped into the tube side. Simultaneously, the stripping solution was counter-currently pumped into the shell side and a circulating-flow pattern operation was used. A schematic counter current flow diagram of single [45], double and triple hollow fiber modules was set up in an identical experiment but the number of hollow fiber modules were differed. In this work, triple hollow fiber modules were illustrated as in Fig. 2.3.

Table 2.2 Physical characteristics of the hollow fiber module (Membrana-Charlottle Company, USA)

Properties	Descriptions
Inside diameter of hollow fiber	240 μm
Outside diameter of hollow fiber	300 μm
Effective length of hollow fiber	15 cm
Number of hollow fibers	35,000
Average pore size	0.03 μm
Porosity	30 %
Effective surface area	1.4×10^4 cm^2
Area per unit volume	29.3 cm^2/cm^3
Module diameter	6.3 cm
Module length	20.3 cm
Contact area	30%
Tortuosity factor	2.6
Operating temperature	1-60°C

2.5 Results and discussion

2.5.1 Effect of the pH of the feed phase

The pH gradient between the feed and stripping phases is an important driving force for the extraction and recovery of metal ions through supported liquid membrane [47]. The effects of feed-phase pH on the transport of Co(II) and Mn(II) were studied by varying the pH in the range of 2-7, carried out using a stripping phase of 0.2 M hydrochloric acid. The concentration of the carrier is 5% (v/v) in kerosene. Hydrochloric acid was used to maintain the feed phase pH according to the previously mentioned range. The principle of counter-transport mechanism in case of Co(II)and Mn(II) transport is shown in Fig. 2.1. The transport process is driven by the concentration gradient of hydrogen in the stripping solution as compared with that in the feed phase [33].

The extraction percentages of Mn(II) from Co(II) in sulphate mixture attained maximum at a feed phase pH of 5.0 at 75.14% for Mn(II) and 3.35% for Co(II). The maximum percentages of recovery of Mn(II) and Co(II) were 62.32% and 2.12%, respectively. As the pH value of feed solution approached neutral region, it apparently does not favor the acidic extractant D2EHPA. As such, extraction efficiency became decreasing when pH is reported to be more than 5. This is consistent with the Zn(II) and Mn(II) extraction using D2EHPA an extractant, reported by Hosseini et al. [49]. They reported that the highest Mn(II) extraction percentages is obtained at pH 5. Fig. 2.4 presented the experimental results according to this study where Mn (II) was preferentially extracted over Co(II). This preferential extraction was in line with experimental works by Devi et al. [38]. The Figure was incorporated with the error bar, derived from reproducibility over the same experiment.

2.5.2. Effect of initial concentration of Co(II) and Mn(II) in the feed phase

The effects of initial feed concentration on the transport of Co(II) and Mn(II) were studied by varying the feed concentration in the range of 50-1,000 ppm. Fig. 2.5 shows the effects of initial feed concentration on the transport of Co(II) and Mn(II). The initial feed concentration 50 ppm yielded the highest extraction of Mn(II) at 76.21%. However, it dropped to 47.01% at the initial feed concentration of 1,000 ppm. This could be explained by the effect of the concentration polarization [50,51]. With an increase of metal ions in the feed, the concentration polarization also increase at the boundary layer with the liquid membrane thus hindering mass transfer. Subsequently, the feed mass-transfer coefficient (k_f) in Eq. (2.8) became smaller. This resulted in reducing the permeability. However, the same 100 mg/L Co(II) and Mn(II) concentration was used in further experiments owing to convenient preparations and corresponding to the concentration level of real wastewaters.

2.5.3 Effect of carrier concentration in the membrane phase

A study of the Co(II), Mn(II) and D2EHPA systems has been made previously and published elsewhere [38]. The concentration of carrier in the organic phase had a significant effect on the transport of metal ions [52] through HFSLM.

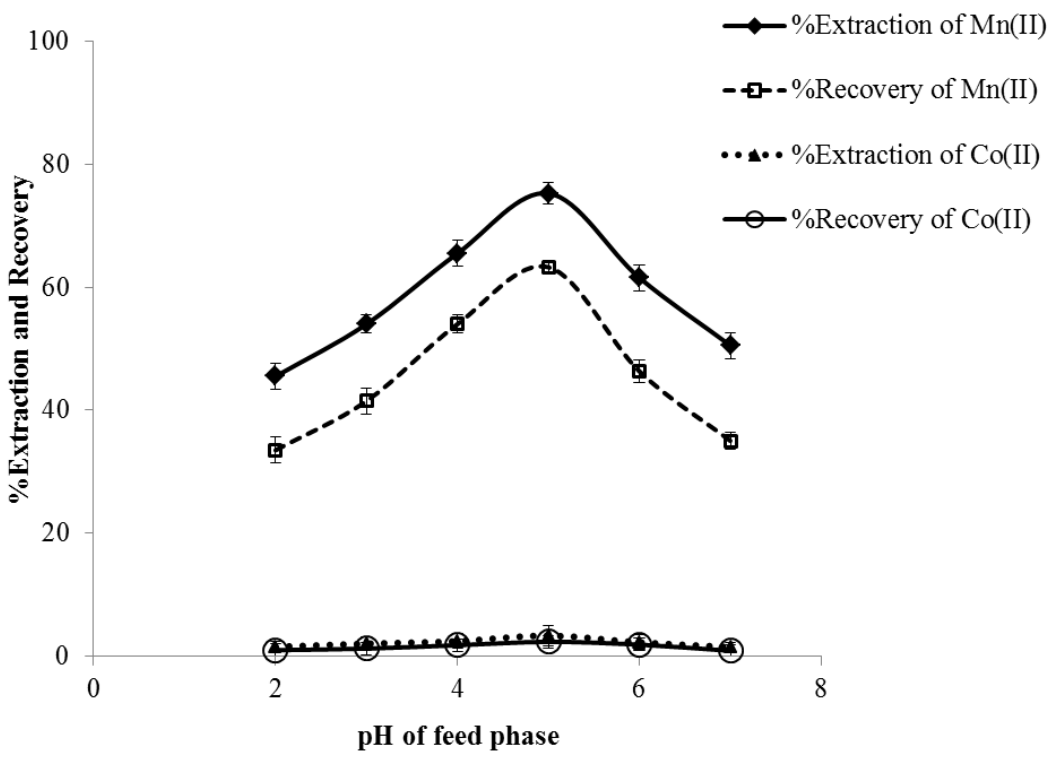

Figure 2.4 The effects of feed phase pH on the separation of Co(II) and Mn(II), feed concentration = 100 mg /L, stripping agents = 0.2 M HCl, carrier concentration = 5% (v/v), the flow rate of feed and stripping solution = 100 mL/min, operating time = 120 min in single hollow module

This work studied the influence of the D2EHPA in the concentration ranges of 0.5-20% (v/v). The results were graphically presented in Fig. 2.6. This showed that the percentage of extraction and recovery of Mn(II) increased with increasing carrier concentrations. The optimum concentration of carrier concentration was 5% (v/v). It was noted that the trend of extraction and recovery percentage decreased when the carrier concentration was higher than 5% (v/v). This could be attributed to an increase in viscosity of the liquid membrane (LM) from an increase of D2EHPA

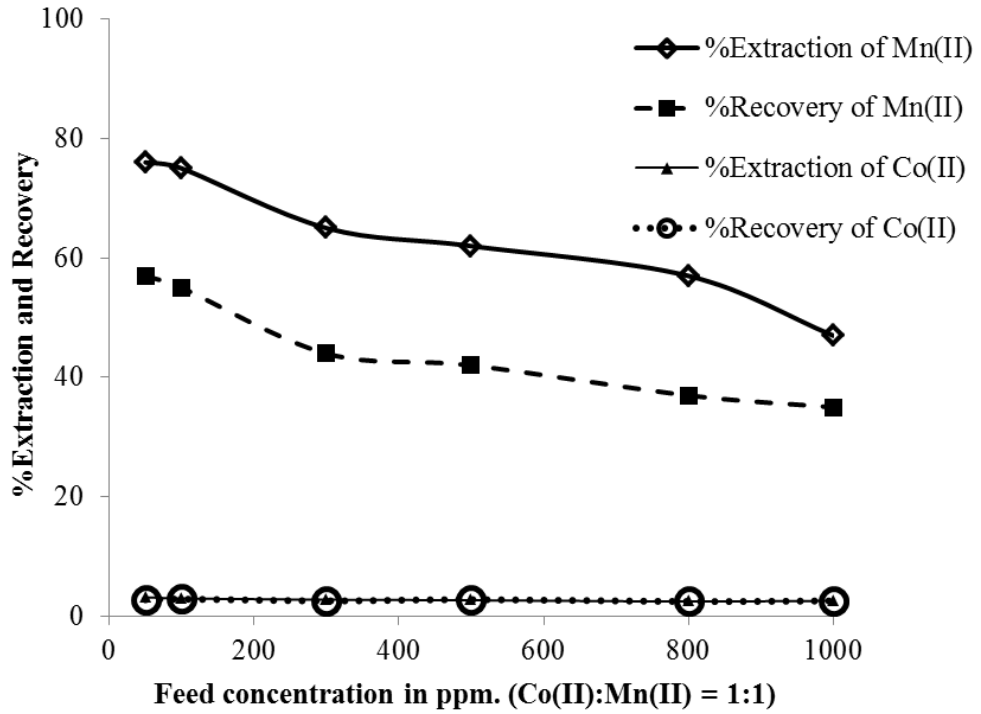

Figure 2.5 The effects of initial feed concentration on the transport of Co(II) and Mn(II), feed phase pH = 5, stripping agents = 0.2 M HCl, carrier concentration = 5% (v/v), the flow rate of feed and stripping solution = 100 mL/min, operating time = 120 min in single hollow module

concentration [53]. As diffusivity was inversely proportional to viscosity, an increase of LM viscosity caused the reduction of ion diffusivity which eventually decreased the recovery percentage of Co(II) and Mn(II). The percentage of extraction of Mn(II) was 75.33% (removing from Co(II) in sulphate mixture) by D2EHPA at 5% (v/v). The recovery percentages of Mn(II) and Co(II) were 56.11% and 2.64%, respectively.

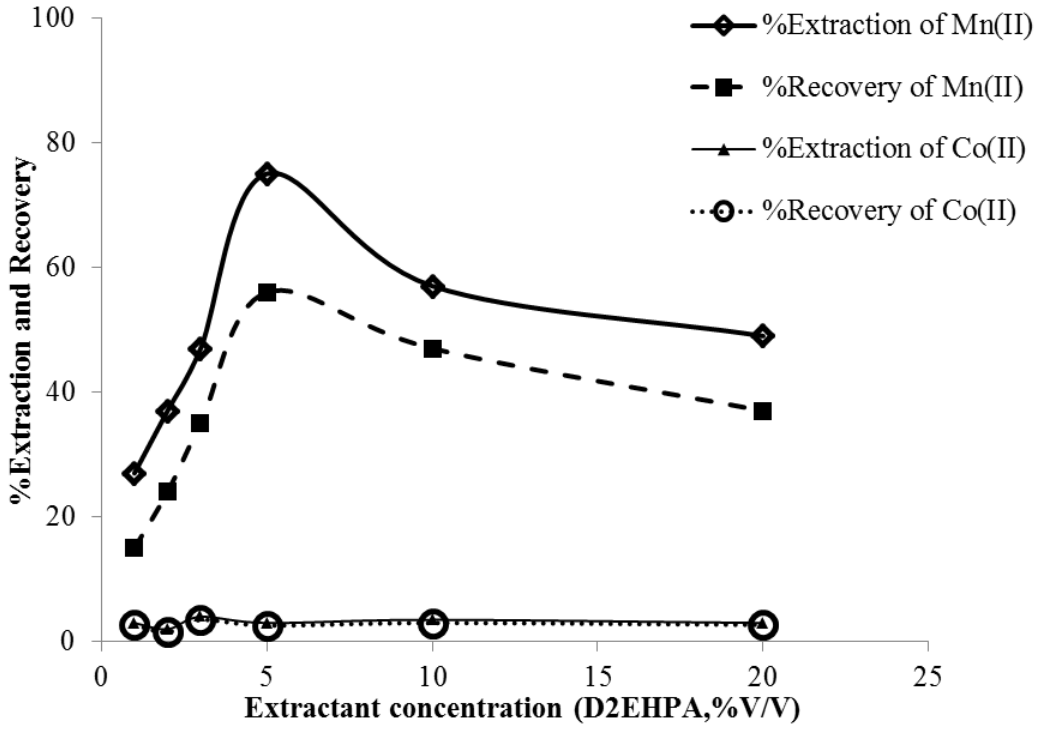

Figure 2.6 The effects of various carrier concentration, feed concentration = 100 mg/L, stripping agents = 0.2 M HCl , feed phase pH = 5, the flow rate of feed and stripping solution = 100 mL/min, operating time = 120 min in single hollow module

2.5.4 Effect of stripping-phase concentration

The influence of the stripping phase concentration played an important role on the separation of the mixture of Co(II) and Mn(II) as carried out by varying the HCl concentration in the range of 0.1-0.5 M, in single hollow module and the feed pH of 5.0. Fig. 2.7 showed the effect of the stripping phase concentration on the transport of the mixture of Co(II) and Mn(II). It was observed that the extraction of Mn(II) increased with the increasing in HCl concentration up to 0.2 M HCl. This result was in agreement with the fact that the driving force for the present coupled transport is supplied by the proton concentration gradient between the feed and the stripping phase. However, the extraction of Mn(II) reduced at a higher stripping phase concentration than 0.5 M because Co(II) could precipitate at a high HCl concentration and the precipitates could

also block the membrane pores. Maximum extractions of 74.28% for Mn(II) and 3.32% for Co(II) in the sulphate mixture were obtained at the stripping concentration at 0.2 M HCl. The percentages of recovery of Co(II) and Mn(II) were 2.94% and 59.52%, respectively.

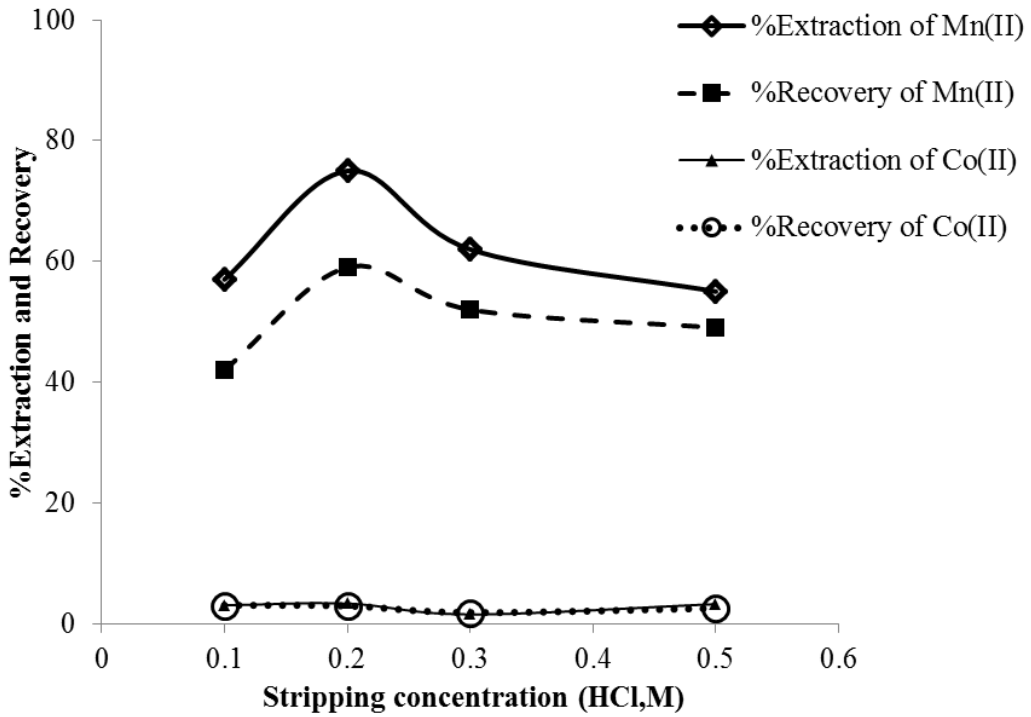

Figure 2.7 The effects of stripping phase concentration, feed concentration = 100 mg/L, feed-phase pH = 5, carrier concentration = 20% (v/v), the flow rate of feed and stripping solution = 100 mL/min, operating time = 120 min in single hollow module

2.5.5 Influence of the different feed composition of Co(II) and Mn(II) in the feed phase

Separation of the mixture at two different feed compositions (Mn(II) =100 mg/L and Co(II) =100 mg/L; Mn(II) =100 mg/L and Co(II) = 20 mg/L) were studied. The percentages of Mn(II) extraction of 76.12% (high Co(II)) and 67.14% (low Co(II)) from a

4-hour operation were reported and presented in Fig. 2.8. The results showed that the extraction percentage of Mn(II) in the feed stream for both feed compositions was almost the same. It can be stated that the presence of Co(II) does not influence the extraction of Mn(II). Extraction of Mn(II) increases up to 75% at 120 min. after that, when the time is increased to 240 min. the percentage of extraction does not change.

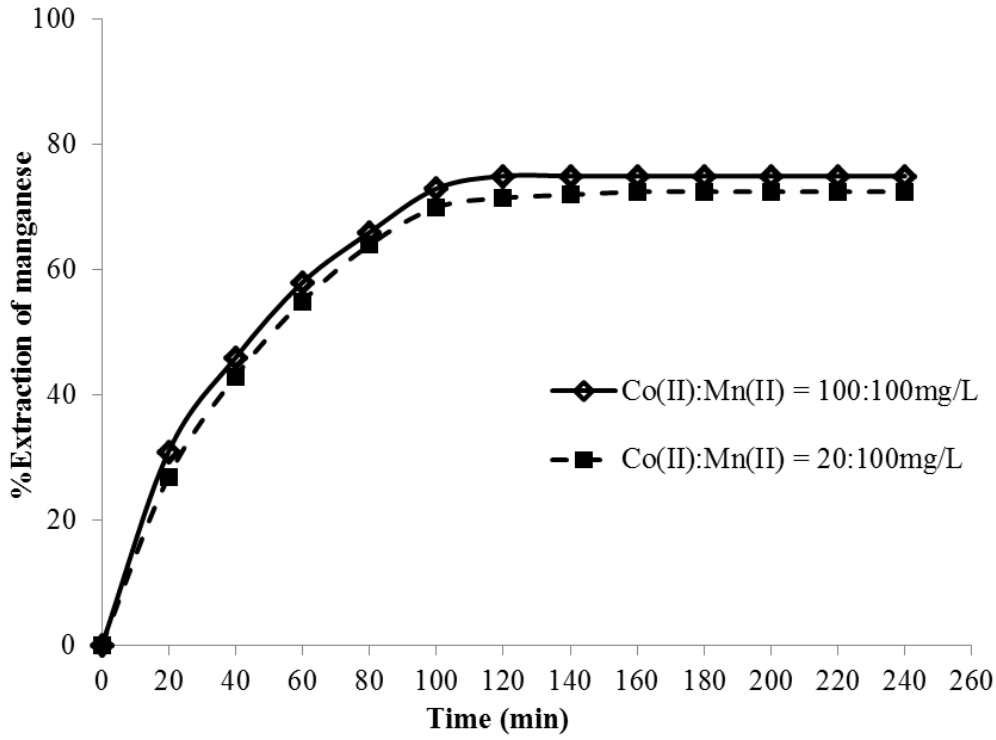

Figure 2.8 Separation of mixture of cobalt and manganese at various feed compositions in terms of Mn(II) extraction percentages at feed pH = 5, carrier concentration = 5% (v/v), stripping concentration = 0.2 M HCl, experiment time = 240 min in single hollow module

2.5.6 Effect of the number of hollow fiber modules

In this experiment, the investigation of a suitable number of hollow fiber modules in the selective extraction and recovery of Co(II) and Mn(II) – that was, a single module, double modules and triple modules in series – was carried out. The optimum

conditions of the experiment was studied including 5% (v/v) D2EHPA in the presence of kerosene, the pH value of 5, the concentrations of Co(II) and Mn(II) in feed phase of 100 mg/L, 0.2 M HCl, feed and stripping flow rate of 100 ml/min in the single hollow fiber module. The flow pattern was the circulating operation. The single-module HFSLM operation was shown in Fig. 2.4, and the results as illustrated in Fig. 2.9 indicates

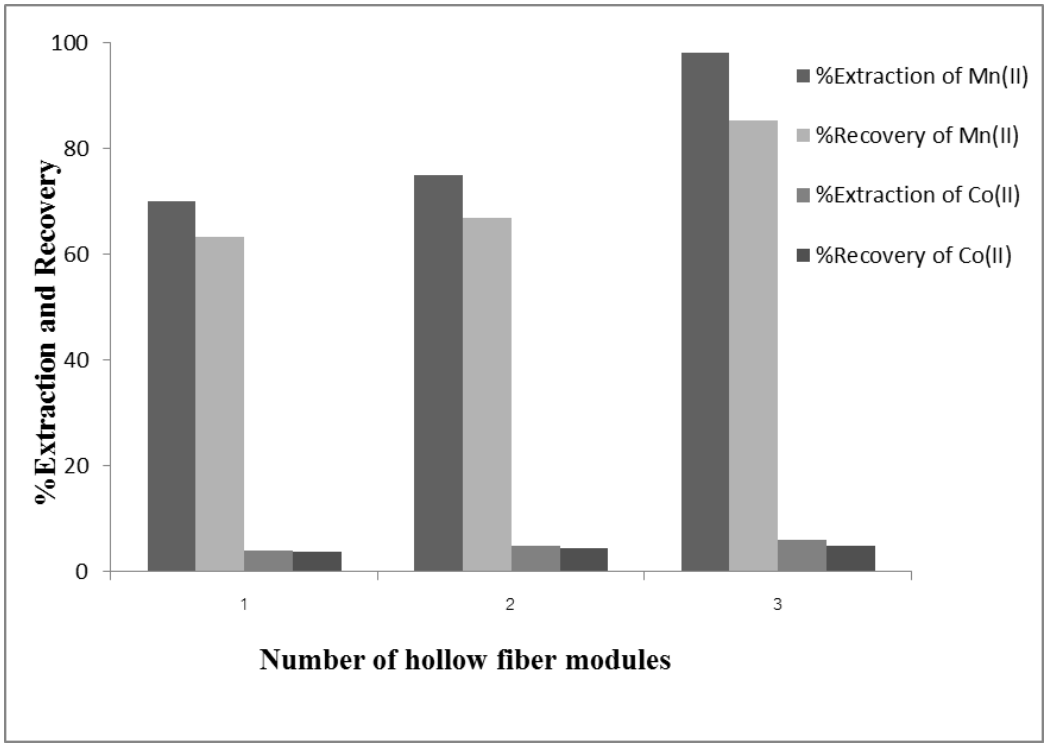

Figure 2.9 The percentages of metal-ion extraction and recovery against the number of hollow fiber modules using the D2EHPA as an extractant and 0.2 M HCl as the stripping solution

that the percentages of Mn(II) extraction and recovery reached 70.05% and 63.24%, respectively. The results showed that the addition of the number of modules viz. the double and triple hollow fiber modules leads to an increase in the percentages of extraction and recovery due to an increase in the contact time in the system corresponding to Eq. (2.17) and (2.18) [40]. Therefore, the highest extraction and recovery percentages of Mn(II) from the triple-hollow fiber modules at 98.14% and

85.32%, respectively, were obtained as shown in Fig. 2.9 at the same optimum condition. In contrast, the percentages of extraction and recovery of Co(II) were very low because reaction of D2EHPA and Co(II) at the feed-membrane interface were very slow corresponding to the previous work “Experiments using extracts D2EHPA, PC 88A, Cyanex 272 suggested that the extent of extraction of compounds with manganese over cobalt” [38]. The triple modules were efficient in the extraction and recovery Mn(II) at best conditions.

2.5.7 Permeability

The permeability of Co(II) and Mn(II) were studied with D2EHPA as the extractant in triple hollow fiber modules placed in series. The permeability of Co(II) and Mn(II) concentrations were calculated from Eq. (2.14). The results were shown in Fig. 2.10 and 2.11. It was observed that permeability decreased as the feed concentration increased [54]. An excessive increase in feed concentration generates a lower diffusion speed of the species [55]. This could be due to the membrane fouling and concentration polarization at the interface between the aqueous feed solution and the liquid membrane [56]. The existence of boundary layers in the aqueous phase showed that the permeability of metal ion increased with the increase in flow rate.

2.5.8 The determination of the reaction order and the reaction rate constant for Mn(II)

The transport kinetic mechanisms through the liquid membrane were controlled by the rate of chemical changes.

The reaction order (n) and the reaction rate constant (k_f) for Mn(II) extraction were determined. The integral concentrations with respect to zero, first and second

orders were plotted against times at optimum conditions which were shown in Table 2.3. The linear line of each reaction order was presented by the squared correlation coefficients (R^2).

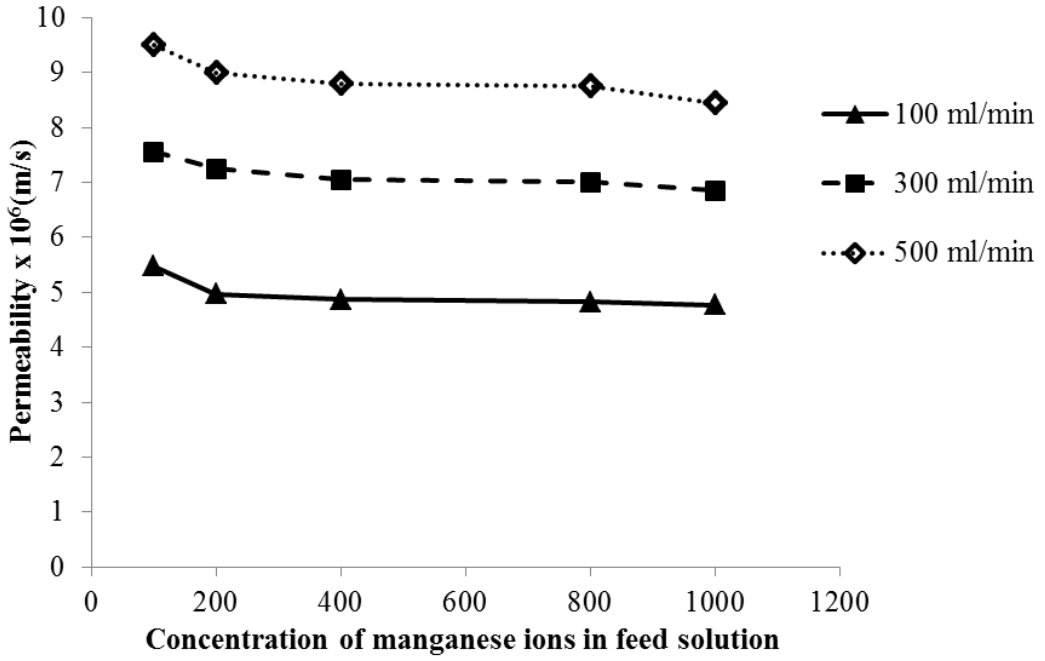

Figure 2.10 The permeability against feed concentration for Mn(II) using feed pH =5, carrier concentration = 5% (v/v), stripping concentration = 0.2 M HCl, experiment time = 120 min. in triple hollow modules placed in series

The results from the plot between integral concentration of Mn(II) in feed solution versus time as shown in Fig. 2.12 indicated that the linear line with respect to the first-order reaction (n = 1) provided the best line fitting. The reaction rate constant ($k_{e,f}$) of 0.0180 min^{-1} for Mn(II) extraction was obtained.

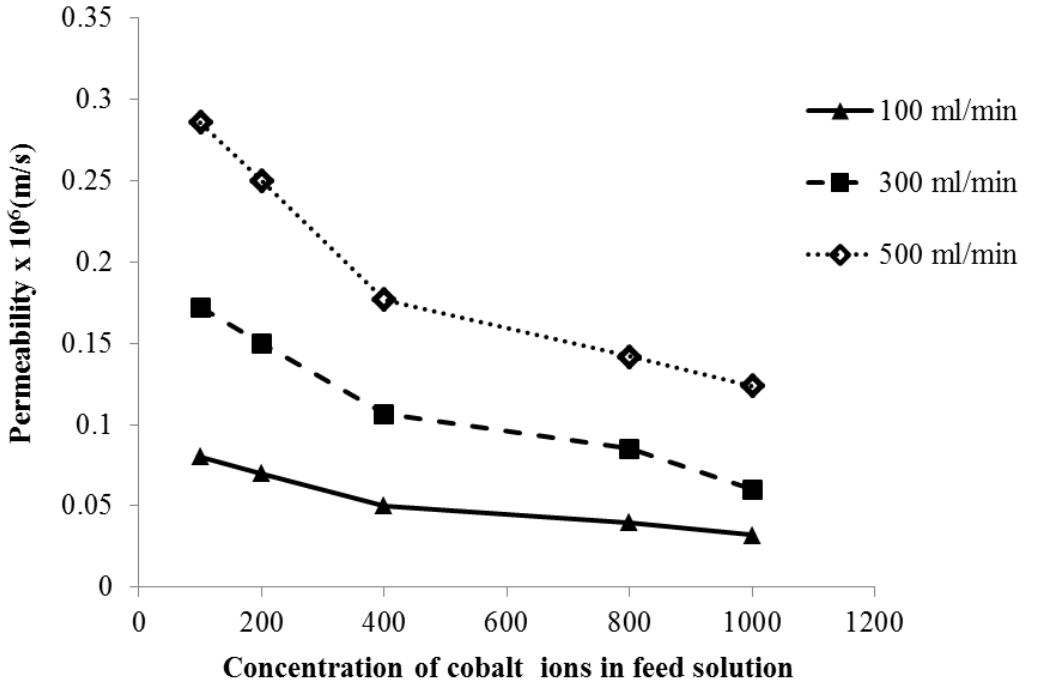

Figure 2.11 The permeability against feed concentration for Co(II) using feed pH =5, carrier concentration = 5% (v/v), stripping concentration = 0.2 M HCl, experiment time = 120 min. in triple hollow modules placed in series

2.5.9 Separation factor

The separation factor was obtained from the experimental parameters used in quantifying the separate elements of the two substances by the relationship between the terms of the concentration of Mn(II) and Co(II) in the permeate and retentate.

Table 2.3 The values of the reaction orders (n) and the reaction rate constant (k_f)

n	Plot	k_f	*R*-square	Acceptability
0	C_A vs. t	0.098 mg/L min	0.6870	No
1	$\ln(C_{A0}/C_A)$ vs. t	0.018 min^{-1}	0.9870	Yes
2	$1/C_A$ vs. t	0.0048 L/mg·min	0.7980	No

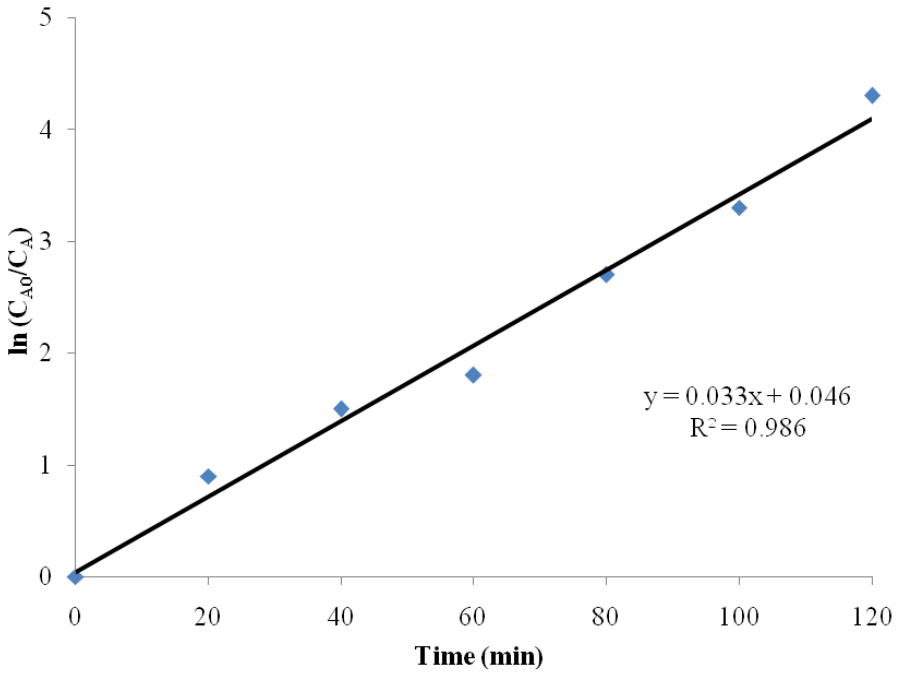

Figure 2.12 The plot of integral concentrations of Mn(II) in term of $\ln(C_{A0}/C_A)$ versus time

The separation factor as shown in Table 2.4 used the experimental conditions similar to Fig. 2.12 where the separation factor had a flow rate of 100 mL / min. using a single, double and triple hollow fiber modules with 74, 144 and 1,591, respectively.

2.5.10 Reaction flux model for extraction of Mn(II)

A reaction flux model representation of the HFSLM system, where the amount of the extractant is the input and the target ion extraction percentage is the output, would be useful for the modeling and the analysis of the processes.

Table 2.4 The separation factor for validation

Hollow fiber modules	Flow rate, L/min	Separation factor, S_F(MnCo)
single	0.5	74
	1.0	74
	1.5	65
	2.0	59
	2.5	53
double	0.5	115
	1.0	144
	1.5	146
	2.0	121
	2.5	93
triple	0.5	1,083
	1.0	1,591
	1.5	225
	2.0	120
	2.5	87

Therefore, the reaction flux model as in Eq. (2.17) had been applied to estimate the concentration of Mn(II) at any time from feed solution. It can be compared with the experimental data as shown Fig. 2.13. The reaction flux model for the triple, double and single hollow fiber modules were in good agreement with the experimental data at an average standard deviation of 2.24%, 3.32% and 3.42%, respectively. The results implied that the transport of complex species in the membrane phase was influenced by the reaction flux.

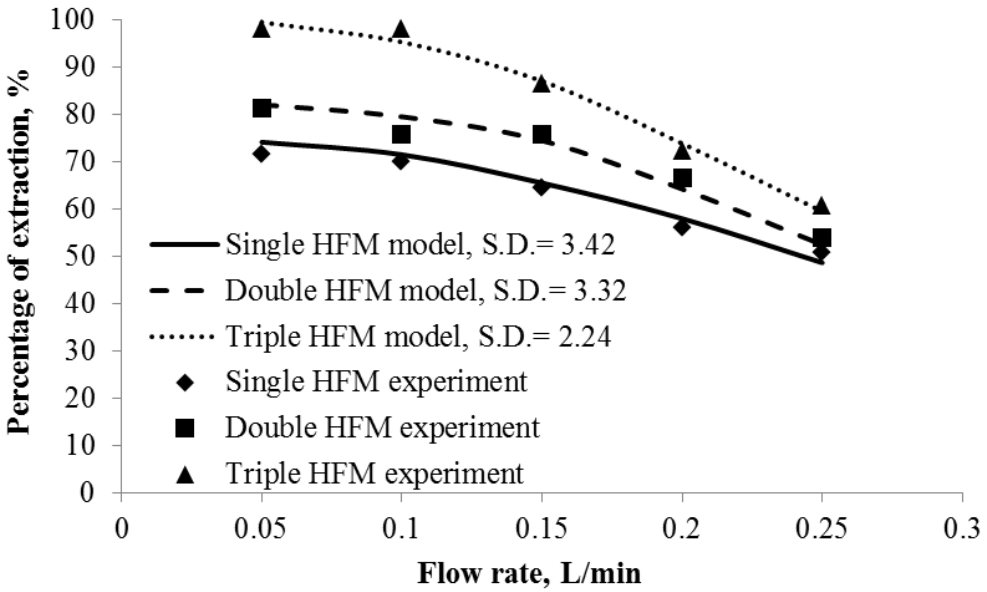

Figure 2.13 The modeling plot of flow rate versus the percentage of extraction and experimental data validation in the triple, double and single hollow fiber modules placed in series

2.6 Conclusion

The transport and selectivity of Co(II) and Mn(II) from synthetic feed solution in the sulphate media via HFSLM arranged D2EHPA-triple hollow fiber modules in series were investigated. The Mn(II) percentages of 70.05% extraction and 63.24% recovery were achieved at 5% (v/v) D2EHPA, 0.2 M HCl in the single hollow fiber module. In order to efficiently enhance the percentage performance of extraction and recovery, double and triple hollow fiber modules were used. The highest extraction and recovery percentages of Mn(II) for the triple hollow fiber modules at 98.14% and 85.32% respectively were obtained at the same optimum condition as in the single hollow fiber module. High separation percentages of 94.05% Co(II) in the raffinate stream and 85.32% Mn(II) in the stripping stream were achieved at the optimum variable. Therefore, the development of the HFSLM system for the separation of manganese (Mn(II)) from mixed manganese and cobalt (Co(II)) sulphate has attracted

great attention, both for environmental protection and resource conservation. Moreover, the reaction flux model based on the facilitated transport mechanism via the HFSLM for the raffinate concentration prediction proved to be in good agreement with the experimental data at an average standard deviation of 2.24%.

2.7 Nomenclature

A_c : cross-sectional area of hollow fiber [m^2]

A_m : mean surface of mass transfer [m^2]

A_s : cross-sectional area of stripping phase [m^2]

A.E. (%) : percentage absolute error

B : term defined in Eq. (9)

C_{in} : concentrations of feed

C_{raf} : concentrations of raffinate

$C_{st,in}$: concentrations of inlet strip

$C_{st,\,out}$: concentrations of outlet strip

$C_A(0,t)$: average concentration of metal ion in the feed (ppm)

$C_A(L,t)$: concentration of metal ion (ppm) at the outlet

$C_A(x,t)$: concentration of A

$C^*_A(x,t)$: average concentration of target metal ion in the feed reservoir (mg/L)

C^0_{HR} : initial concentration of the extractant [M]

d : diameter [m]

d_i : inner diameters of the fiber

d_0 : outer diameters of the fiber

D_{aq} : aqueous diffusion coefficient of the metal salt [m^2s^{-1}]

D_{Exp} : experimental result

D_{mem} : diffusion coefficient through in liquid membrane [m^2s^{-1}]

D'_{mem} : effective diffusion coefficient in liquid membrane [m^2s^{-1}]

D_{Mod} : model calculated result

F_v : volumetric flow [m^3s^{-1}]

K_{eq} : the extraction equilibrium constant

k_i : mass-transfer coefficient of the feed phase [m s^{-1}]

k_m : mass-transfer coefficient of the membrane phase [m s^{-1}]

k_s : mass-transfer coefficient of the stripping phase [m s^{-1}]

L : length of fiber [m]

l_{ef} : membrane thickness [m]

N : number of experimental points.

n : order of the reaction

P : permeability [m s^{-1}]

q_f : the volumetric flow rate of feed solution

q_s : volumetric flow rate of stripping phase

$r_A(x,t)$: reaction rate of A

r_i : inner radius of the fiber [m]

r_o : outer radius of the fiber [m]

R_f : aqueous feed-phase resistance [s m−1]

R_m : organic-phase resistance [s m^{-1}]

R_s : aqueous stripping-phase resistance [s m^{-1}]

S.D. (%) : percentage of standard deviation

t : time (min)

V_F : volume of feed solution

V_{FT} : total volume of solution in the feed reservoir

ε : porosity

τ : support tortuosity

2.8 Acknowledgements

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CHAPTER 3

SEPARATION OF AMOXICILLIN USING TRIOCTYLMETHYLAMMONIUM CHLORIDE VIA A HOLLOW FIBER SUPPORTED LIQUID MEMBRANE: MODELING AND EXPERIMENTAL INVESTIGATION

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3.1 Abstract

The separation experiments of amoxicillin via HFSLM were performed under various operating conditions to find the optimal parameters, i.e. pH, feed concentration, carrier concentration, and flow rates of feed and stripping solution. Percentages of extraction and recovery of amoxicillin from the feed phase reached 85.21% and 80.34%, respectively. The aqueous-phase mass transfer coefficient (k_f) and organic-phase mass transfer coefficient (k_m) were reported to be 3.57×10^{-2} and 0.70×10^{-2} cm/s, respectively. Furthermore, a mathematical model was developed to predict the concentration of amoxicillin at different times. The results showed promising agreement with experimental data.

Keywords: Separation; Amoxicillin; Hollow fiber supported liquid membrane; Trioctylmethylammonium chloride; Model

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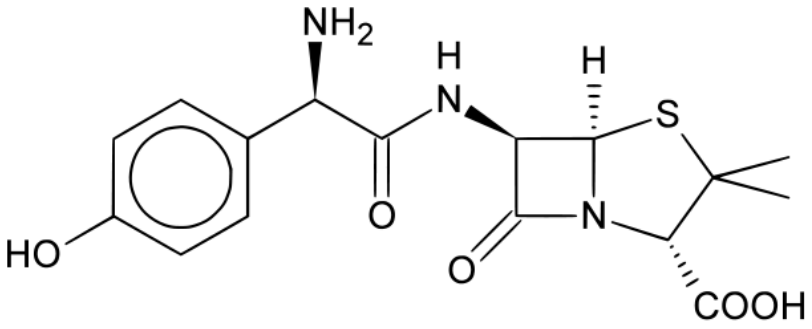
3.2 Introduction

Amoxicillin, 6-(R-hydroxy-a-amino phenyl acetamido) penicillanic acid, is the only phenolic penicillin which is used as an antibacterial drug [1]. Amoxicillin is a β-lactam antibiotic that has a broad in vitro spectrum against gram negative and gram

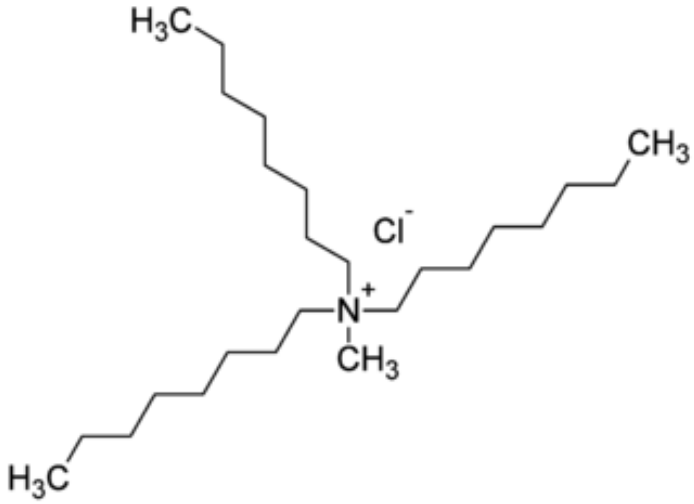
positive bacteria, as well as good absorption and penetration into tissues. It is a kind of frequently used antibiotic to treat many kinds of infections [2]. The molecular weight of amoxicillin is 365 and it is soluble in water. The molecular structure of amoxicillin is shown in Fig. 3.1(a). The presence of amoxicillin and other kinds of antibiotics in the environment is of concern due to their potential to promote bacterial resistance [3] 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 by-products that can remain biologically active. Amoxicillin wastes can cause unpleasant odor, skin disorder, and may cause microbial resistance among pathogen organisms or the death of microorganisms which are effective in wastewater treatment [4]. The resistant bacteria may cause disease that cannot be treated by conventional antibiotics. For these reasons, amoxicillin waste needs to be treated before being disposed to the environment.

There are many methods for the removal of amoxicillin from wastewater, such as sand filtration [5], chemical coagulation or flocculation [6], chlorination [7], ultraviolet (UV) radiation [8], ozonation and advanced oxidation processes (AOP), adsorption and membrane process [9]. Techniques that have been gaining attention in the past few years are membrane process and liquid membrane process. Hollow fiber supported liquid membrane (HFSLM) is a system based on the liquid membrane process and membrane process. HFSLM technique has specific characteristics of simultaneous extraction and stripping processes of low concentrations of target species in one single stage [10]. Some other advantages of the hollow fiber contactor over traditional separation techniques include lower capital and operating costs [11], lower energy consumption [12], less solvent used and high selectivity [13]. These advantages render the HFSLM system more suitable for the treatment or separation of amoxicillin.

The present work studied the effects of parameters which influence the effective separation of amoxicillin by using HFSLM technology based on trioctylmethyl ammonium chloride (Fig. 3.1(b)) as an extractant. In addition, the experimental data of amoxicillin concentrations in the outlet feed solution were compared with the results from the mathematical model based on HFSLM batch separation system.



(a)



(b)

Figure 3.1 The structures of (a) amoxicillin, (b) trioctylmethylammonium chloride (aliquat 336)

3.3. Theoretical background

3.3.1 Transport mechanism and separation of amoxicillin

In a hollow fiber supported liquid membrane (HFSLM) system, the supported liquid membrane is embedded in an organic extractant which separates the feed from the stripping phases. At the feed-membrane interface, the amoxicillin reacts with the extractant to form complex species. Subsequently, the complex species diffuse across the liquid membrane to react with the stripping solution at the membrane-stripping interface. Then, they are stripped into the stripping phase. The separation of amoxicillin was studied using the extractant trioctylmethylammonium chloride (Aliquat 336 Cl) and involves their facilitated coupled counter-transport across HFSLM as illustrated in Fig. 3.2.

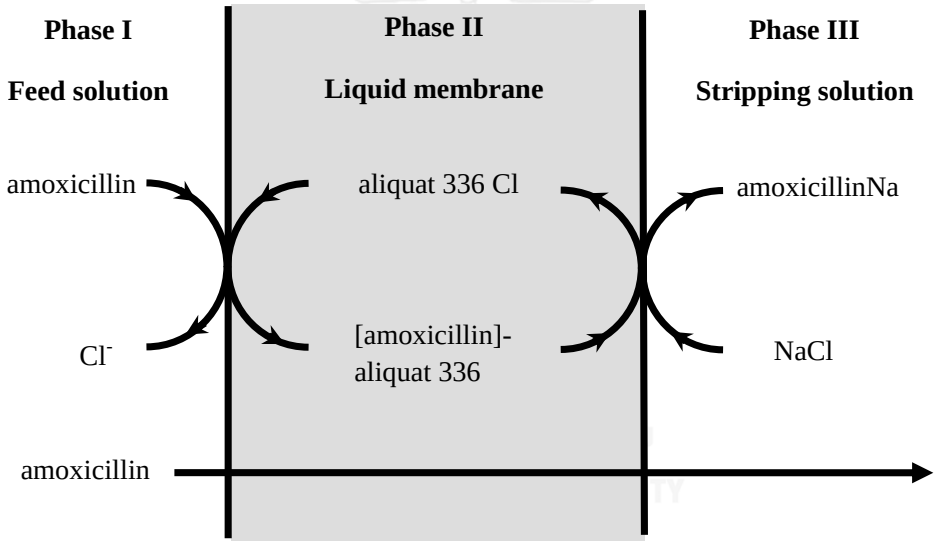


Figure 3.2 The counter transport mechanism of amoxicillin using aliquat 336 Cl as the extractant

The mechanism using the extractant is described in the following steps:

Step 1: Amoxicillin (Amox) in the feed phase is transported to the interface between the feed and liquid membrane phases. Then, it reacts with the extractant (QCl) to form the complex species (QAmox) and releases chloride ions into the feed phase.

Step 2: The complex species diffuses to the interface between the liquid membrane and stripping phases by its concentration gradient.

Step 3: The complex species reacts with the stripping solution to recover amoxicillin into the stripping phase while the extractant transports back to the opposite side and reacts again with the amoxicillin in the feed phase. Thus, both amoxicillin and chloride ions are counter-transported across HFSLM.

When the diffusion steps in the facilitated transport are slower than the chemical reaction steps, the transport is described as the diffusion transport regime. On the other hand, when the chemical reaction steps are slower, it is described as the chemical reactions kinetic transport regime [14, 15].

In developing the reliable mathematical model in order to describe the transport mechanism of the target species across liquid membrane, general models based on diffusion or chemical reaction were taken into consideration [16, 17]. The diffusional process through a liquid membrane is affected by the porosity and tortuosity of the polymeric support [18]. The basic parameter of the transport regime to determination of transport parameters was the diffusion coefficient [18-20]. The type of movements associated with the migration of the complexes through the organic phases of the liquid membrane is indicated by the diffusion coefficient [19-21].

1. The diffusion coefficient in the range of 10-6-10-5 cm2 s-1 indicated movement of pure diffusion for a very stable complex in an organic phase [21].

2. The diffusion coefficient in the range of 10-5-10-4 cm2 s-1 indicated composed movement for unstable complexes in the organic phase of the liquid membrane [21].

Another method is used to verify the transport regime by using the value of parameter α[18]. If $\alpha<1$, the transport is primarily controlled by the diffusion of the complex; while the transport is mainly limited by the reaction rate in the case where $\alpha>1$.The calculation of α can be determined by Eq. (3.1) as follows:

$$\alpha = \frac{1/\varepsilon k}{h_m / D_m} \tag{3.1}$$

where **α** is a dimensionless parameter which relates diffusion-limited transport to kinetically limited transport, h_m is the layer film (or membrane support) thickness, k is the rate of reaction, **ε** is the porosity of the membrane support and D_m is the diffusivity of the amoxicillin complex.

The removal reaction of amoxicillin with Aliquat 336 can be concluded as [22]:

$$Amox + \overline{QCl} \leftrightarrow \overline{QAmox} + Cl^- \tag{3.2}$$

The recovery reaction of amoxicillin with sodium chloride solution [22] is schematically described in Eqs. (3.3) as follows:

$$\overline{QAmox} + NaCl \leftrightarrow \overline{QCl} + AmoxNa \tag{3.3}$$

The over bar denotes the species in the liquid membrane phase.

The reaction rate of amoxicillin removal can be described by Eq. (3.4):

$$r_f(x,t) = -k_r[\mathrm{Amox}(x,t)]^n \tag{3.4}$$

where *x* is any distance along the axis of hollow fibers (dm, $0 \leq x \leq L$), *t* is the

processing time (min), k_r is the reaction rate constant, $[Amox(x,t)]^n$ is the concentration of amoxicillin as a function of x and t (mg/dm^3) and n is the reaction order.

3.3.2 Extraction equilibrium constant and distribution ratio

From the extraction reaction described in Eq. (3.2), the extraction equilibrium constant (K_{ex}) of amoxicillin extracted by Aliquat 336 can be expressed as:

$$K_{ex} = \frac{[\overline{QAmox}][Cl^-]}{[Amox][\overline{QCl}]} \quad (3.5)$$

The distribution ratio (D) for amoxicillin, is given by:

$$D = \frac{[\overline{QAmox}]}{[Amox]} \quad (3.6)$$

According to Eq. (3.6), the distribution ratio could then be derived as a function of the extraction equilibrium constant, as follows:

$$D = K_{ex}\frac{[\overline{QCl}]}{[Cl^-]} \quad (3.7)$$

From the stripping reaction described in Eq. (3.3), the stripping equilibrium constant (K_{st}) can be expressed as:

$$K_{st} = \frac{[\mathrm{AmoxNa}][\overline{\mathrm{QCl}}]}{[\overline{\mathrm{QAmox}}][\mathrm{NaCl}]} \tag{3.8}$$

where the values of K_{ex} for amoxicillin extracted with Aliquat 336, and K_{st} for amoxicillin stripped with sodium chloride solution were found to be 1.4172 and 1.0079, respectively.

3.3.3 Permeability coefficient

The permeation of amoxicillin can be expressed in terms of the permeability coefficient (P), as proposed by Danesi [23] in Eqs. (3.9) and (3.10):

$$-\mathrm{V_f}\ln\left(\frac{\mathrm{C_f}}{\mathrm{C_{f,o}}}\right) = \mathrm{A}P\frac{\beta}{\beta+1}\mathrm{t} \tag{3.9}$$

where

$$\beta = \frac{\mathrm{Q_f}}{P\mathrm{L}\varepsilon\pi\mathrm{N}r_i} \tag{3.10}$$

where P is the permeability coefficient (cm/s), V_f is the volume of the feed (mL), $C_{f,0}$ is the amoxicillin concentration (mmol/L) at initial time (t = 0), C_f is the amoxicillin concentration at time t (mmol/L), A is the effective area of the hollow fiber module (cm^2), t is the time (min), Q_f is the volumetric flow rate of the feed solution (mL/s), L is the length of the hollow fiber (cm), $\boldsymbol{\varepsilon}$ is the porosity of the hollow fiber (%), N is the number of hollow fibers in the module, and r_i is the internal radius of the hollow fiber module (cm). The value data is shown in Table 3.1.

AP(ß/(ß+1)) is the slope of the plot between $-V_f \ln (C_f / C_{f,0})$ versus t in Eq. (3.9), and then P can be obtained. To determine the mass transfer coefficients for amoxicillin separation by HFSLM, the mass transfer model and permeability coefficient (P) are employed. The permeability coefficient depends on mass transfer resistance which is the reciprocal of the mass transfer coefficients [24], as follows:

$$\frac{1}{P} = \frac{1}{k_f} + \frac{r_i}{r_{lm}} \frac{1}{P_m} + \frac{r_i}{r_o} \frac{1}{k_s} \tag{3.11}$$

where r_{lm} is the log-mean radius of the hollow fiber, r_o is the external radius of the hollow fiber (cm), k_f is the aqueous mass transfer coefficient on the tube side, k_s is the stripping mass transfer coefficient on the shell side, and P_m is the membrane permeability coefficient.

The relation between P_m and the distribution ratio (D) [25] is as follows:

$$P_m = D k_m \tag{3.12}$$

Combining Eq. (3.7) and Eq. (3.12), thus:

$$P_m = K_{ex}\, k_m \frac{[\overline{QCl}]}{[Cl^-]} \tag{3.13}$$

where k_m is the mass transfer coefficient of the membrane. The value of the liquid membrane permeability coefficient (P_m) from Eq. (3.13) is substituted into Eq. (3.11).

Assuming that the stripping reaction is instantaneous and the contribution of the stripping phase is neglected, Eq. (3.11) becomes:

$$\frac{1}{P} = \frac{1}{k_f} + \frac{r_i}{r_{lm}} \frac{[Cl^-]}{K_{ex}\, k_m [\overline{QCl}]} \tag{3.14}$$

where k_f is the mass transfer coefficient of the feed solution

In this research, the extractability of amoxicillin was determined by the percentage of extraction:

$$\%\text{Extraction} = \frac{C_{f,in} - C_{f,out}}{C_{f,in}} \times 100 \tag{3.15}$$

The percentage of recovery was calculated by:

$$\%\text{Stripping} = \frac{C_{s,out}}{C_{f,in}} \times 100 \tag{3.16}$$

where $C_{f,in}$ and $C_{f,out}$ are the inlet and outlet feed concentrations of component i (mmol/L), and $C_{s,in}$ and $C_{s,out}$ are the inlet and outlet stripping concentrations of component i (mmol/L).

3.3.4 Diffusion flux model for amoxicillin concentration in feed solution

This section shows the analysis of the diffusion flux model in order to estimate the outlet concentration of amoxicillin in the feed solution after reacting with Aliquat 336. Modeling of the diffusive mass transport flux is performed under the following assumptions:

a) The system is considered to be at a pseudo-steady state.

b) The extraction reaction takes place at the interface between the aqueous solution and the liquid membrane. The influence of the interface curvature in the mass transfer rate can be considered negligible.

c) No solute transport occurs through the non-porous parts of the membrane.

d) The solubility of both fluids in each other is negligible.

e) Mass transfer is described by simple film-type mass-transport coefficients.

The objective of the mathematical model is to predict the overall mass transport flux (J) of the solute from the feed solution to the organic phase which is defined as follows [26]:

$$J = J_{\mathrm{f}} = J_{\mathrm{m}} = J_{\mathrm{s}} \tag{3.17}$$

$$J_f R_f = [Amoxicillin]_{f,0} - [Amoxicillin]_{f,m} \tag{3.18}$$

$$J_m R_m = [Amoxicillin]_{m,f} - [Amoxicillin]_{m,s} \tag{3.19}$$

$$J_s R_s = [Amoxicillin]_{s,m} - [Amoxicillin]_{s,0} \tag{3.20}$$

where $R_f = 1/k_f$ and $R_m = 1/k_m$ are the aqueous and membrane mass-transfer resistance, respectively, and $[\text{Amoxicillin}]_{f,0}$, $[\text{Amoxicillin}]_{f,m}$ are the concentrations of the amoxicillin complexes in the feed solution and at the interface between aqueous feed solution and membrane phase at subsequent time *t*.

Considering the extraction reaction in Eq. (3.19), $[\text{Amoxicillin}]_{f,m}$ is the concentration of the amoxicillin in the interface between the aqueous feed phase and membrane phase and $[\text{Amoxicillin}]_{m,f}$ is the concentration of the amoxicillin complex in the membrane phase, respectively, as follows:

$$[Amoxicillin]_{m,f} = [\overline{QAmox}]_m \tag{3.21}$$

From Eq. (3.5), $[\text{Amoxicillin}]_{m,f}$ is defined in terms of the equilibrium constant K_{ex},

$$[Amoxicillin]_{m,f} = K_{ex}[Amoxicillin]_{f,m}\frac{[\overline{QCl}]}{[Cl^-]} \tag{3.22}$$

The flux equation of the diffusion of the [Amoxicillin]-[Aliquat 336] complex through the membrane phase can be written as per Eq. (3.19). The concentration of the stripping solution can be neglected [27]. Therefore:

$$J_m R_m = [Amoxicillin]_{m,f} \tag{3.23}$$

$[\text{Amoxicillin}]_{m,f}$ from Eq. (3.22) was substituted into Eq. (3.23) to obtain the following expression:

$$[Amoxicillin]_{f,m} = \frac{J_m R_m [Cl^-]}{K_{ex}[\overline{QCl}]} \tag{3.24}$$

By substituting $[Amoxicillin]_{f,m}$ from this expression into Eq. (3.18) and under the pseudo-steady-state condition assumption that $J_m = J_f = J$, the equation flux can be expressed as follows:

$$\frac{J_m R_m [Cl^-]}{K_{ex}[\overline{QCl}]} = [Amoxicillin]_{f,0} - J_f R_f \tag{3.25}$$

From Eq. (3.25), the flux of amoxicillin in the feed phase can be rewritten as follows:

$$J = \frac{K_{ex}[\overline{QCl}][Amoxicillin]_{f,0}}{R_f K_{ex}[\overline{QCl}] + R_m [Cl^-]} \tag{3.26}$$

The carrier thereby reacts totally with the amoxicillin to form the complex species when they are at low concentration. Consequently, the concentration of the complex species is equal to the initial carrier concentration ($[QCl]_0$) and determined by Eqs. (3.5) and (3.18) as follows:

$$[\overline{QCl}] = \frac{[\overline{QCl}]_0 [Cl^-]}{K_{ex}[Amoxicillin]_{f,m}} \tag{3.27}$$

Substituting Eq. (3.27) in Eq. (3.26), the flux of amoxicillin in the feed phase can be rewritten as follows:

$$J = \frac{[\overline{QCl}]_0[Amoxicillin]_{f,0}}{R_f[\overline{QCl}]_0 + R_m\left([Amoxicillin]_{f,0} - J_f R_f\right)} \tag{3.28}$$

Hence, rearranging Eq. (3.28) in the form of a quadratic equation gives:

$$J^2 R_f R_m - J(R_m[Amoxicillin]_{f,0} + R_f[\overline{QCl}]_0) + [\overline{QCl}]_0[Amoxicillin]_{f,0} = 0 \tag{3.29}$$

To determine the flux of amoxicillin, Eq. (3.29) is rearranged into a quadratic equation and solved for flux of amoxicillin in the feed phase as shown in Eq. (3.30).

$$J = \frac{(R_m[Amoxicillin]_{f,0} + R_f[\overline{QCl}]_0) \pm \sqrt{\left(R_m[Amoxicillin]_{f,0} + R_f[\overline{QCl}]_0\right)^2 - 4R_f R_m[\overline{QCl}]_0[Amoxicillin]_{f,0}}}{2R_f R_m} \tag{3.30}$$

Considering Eq. (3.30), we have

$$\sqrt{\left(R_m[Amoxicillin]_{f,0} + R_f[\overline{QCl}]_0\right)^2 - 4R_f R_m[\overline{QCl}]_0[Amoxicillin]_{f,0}} << R_m[Amoxicillin]_{f,0} + R_f[\overline{QCl}]_0 \tag{3.31}$$

Thus, the term of $\sqrt{\left(R_m[Amoxicillin]_{f,0} + R_f[\overline{QCl}]_0\right)^2 - 4R_f R_m[\overline{QCl}]_0[Amoxicillin]_{f,0}}$ is neglected and the flux of amoxicillin becomes

$$J_f = \frac{[Amoxicillin]_{f,0}}{2R_f} + \frac{[\overline{QCl}]_0}{2R_m} \quad (3.32)$$

From the definition of flux given in Reference [28], the equation flux of amoxicillin can be presented as:

$$J = -\frac{d[Amoxicillin]_f}{dt}\frac{V}{A} \quad (3.33)$$

where V is volume of the feed solution (mL) and A is membrane area (cm^2). In accordance with the relationship between the flux equation in Eq. (3.32) and Eq. (3.33) thus it becomes:

$$-\frac{d[Amoxicillin]_f}{dt}\frac{V}{A} = \frac{[Amoxicillin]_{f,0}}{2R_f} + \frac{[\overline{QCl}]_0}{2R_m} \quad (3.34)$$

Finally, by integrating with initial conditions t = 0 and $[Amoxicillin]_f$ = $[Amoxicillin]_{f,0}$, the equation for amoxicillin concentration can be expressed as:

$$[\text{Amoxicillin}]_{f(t)} = -\frac{R_f[\overline{QCl}]_0}{R_m} + ([\text{Amoxicillin}]_{f(0)} + \frac{R_f[\overline{QCl}]_0}{R_m}).\exp(\frac{-A}{2R_fV_f}t) \quad (3.35)$$

3.4 Experimental

3.4.1 Chemicals and reagents

The feed solution was amoxicillin, of pharmaceutical grade, obtained from the Government Pharmaceutical Organization (GPO) of Thailand. The extractant Trioctylmethylammonium chloride (Aliquat 336) was purchased from Sigma-Aldrich, United states. Sodium tetraborate, hydrochloric acid, citric acid, sodium citrate, 1-decanol and sodium chloride, all of analytical reagent grade, were purchased from Merck, Germany. All reagents used in this experiment were of GR grade (Merck). Aqueous solutions were prepared using Milli-Q® deionized water (Millipore, Billerica MA, USA). Doubly deionized water was used throughout the experiments.

3.4.2 Liquid membrane

A hollow fiber module is composed of an outer shell, which is a single nonporous material, through which the materials inside cannot be transported. Inside the shell, there are many thin fibers (polymeric micropores) running through the length of the shell, all in rows. The feed phase is piped through the system, and the pores in the fibers themselves are filled with the organic solution of an extractant (carrier). The carrier, in that phase, transports the feed across to the stripping phase. Then, the stripping phase is forced out through the sides of the shell. Fig. 3.3 shows a schematic diagram of the experimental setup of a hollow fiber supported liquid membrane process.

The Liqui-Cel® laboratory liquid/liquid extraction system (Celgard [formerly Hoechst Celanese], Charlotte NC, USA) was composed of two gear pumps, two variable speed controllers, two rotameters and four pressure gauges. A Liqui-Cel Extra-Flow module was used as support material. This module uses Celgard® microporous polyethylene fibers that are woven into fabric and wrapped around a central tube feeder that supplies the shell-side fluid. Woven fabric allows more uniform fiber spacing which in

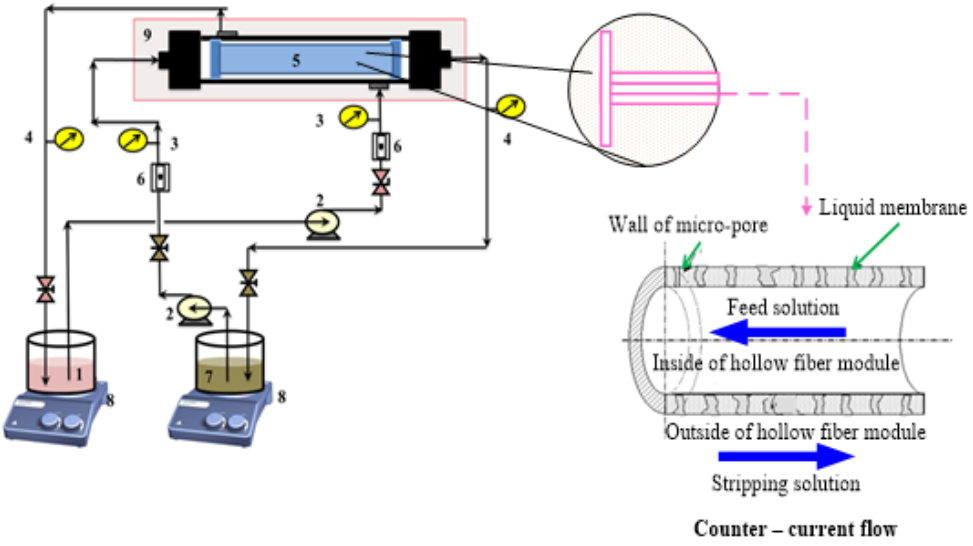


Figure 3.3 Schematic representation of the counter-current flow diagram for batch-mode operation in HFSLM: (1) stripping reservoir, (2) gear pumps, (3) inlet pressure gauges, (4) outlet pressure gauges, (5) the hollow-fiber module, (6) flow meters, (7) feed reservoir, (8) stirrer with temperature controller, and (9) temperature control box

turn leads to higher mass transfer coefficients than those obtained with individual fibers. The properties of a hollow fiber module were shown in Table 3.1. The fiber was potted into a solvent-resistant polyethylene tube sheet and the shell casing is polypropylene.

3.4.3 Membrane supporter

A polymeric membrane using microporous polyethylene fibers was used as the support for the organic liquid phase. The physical characteristics of this support material were summarized in Table 3.1.

3.4.4 Procedure

First, the liquid membrane was prepared by dissolving the extractant (Aliquat 336) in 1-decanol (500 mL). This was then fed into the tube and shell sides of the HFSLM at the same time, for 40 min, to ensure that the extractant became embedded in the micropores of the hollow fibers [29]. Thereafter, the feed solution was pumped into the tube side whereas the stripping solution was pumped into the shell side of the module in counter-current direction. A schematic diagram of counter-current flow direction for recirculation mode in the HFSLM module was shown in Fig. 3.3. In order to prevent the leakage of the liquid membrane from the micropores of hollow fibers [24] as well as to enhance the effective transport of amoxicillin under recirculation mode, the flow rates of feed and stripping solutions was controlled by the gear pump. The operating time of 50 min. for each run was selected as recommended by Sunsandee et al. [30].

Samples of 2 mL were taken out at the end of each experiment from the feed and stripping tanks and the concentrations of amoxicillin determined by high-performance liquid chromatography (HPLC). Each experiment was duplicated under identical conditions, with a standard deviation within 2%.

3.4.5 Analytical instruments

The chromatographic system consisted of an Agilent 1100 series compact LC system (Agilent Technologies, Palo Alto CA, USA) and equipped with a built-in solvent degasser, quaternary pump, column compartment, photodiode array detector with

Table 3.1 The properties of the hollow-fiber module

Properties	Descriptions
Material	Polypropylene
Inside diameter of hollow fiber	240 μm
Outside diameter of hollow fiber	300 μm
Effective length of hollow fiber	15 cm
Number of hollow fibers	10,000
Average pore size	0.03 μm
Porosity	30%
Effective surface area	1.4×10^4 cm^2
Area per unit volume	29.3 cm^2/cm^3
Module diameter	6.3 cm
Module length	20.3 cm
Contact area	30%
Tortuosity factor	2.6

variable injector, and an auto sampler. Data analysis was carried out using Agilent's ChemStation version B.04.01 software.

The analytical system was performed follow the United States Pharmacopeia 35. The chromatographic procedure was carried out using an Eclipse XDB-C18 column (5 μm, 4.6 ×250 mm) [31]. The column was thermo stated at 298.15 ± 1 K using a column heater. The flow rate of the mobile phase was 1.5 mL/min; injection volume was 10 μL. The relative retention times of amoxicillin was about 5.9 min. as detected by a spectrophotometer set at UV 230 nm. The analysis time was set at 25 min. per sample to eliminate potential interference from late eluting peaks. The pH of the aqueous phase was measured with a SevenMulti™ modular pH meter with expansion unit (Mettler-Toledo, Greifensee, Switzerland).

3.5 Results and discussion

3.5.1 Effect of the (initial) pH of the feed phase

The effect of pH on the separation of amoxicillin was studied in recirculation mode operation of the HFSLM system with 6 mmol/L of Aliquat 336 in 1-decanol solvent and 6 mmol/L amoxicillin. The pH is an important factor, as pH has an impact on the ionized form of amoxicillin. Amoxicillin is a molecule that contains both positive and negative ions. In aqueous solutions, pK_{a1} and pK_{a2} of amoxicillin are 2.68 and 7.49, respectively; the state of the ions is determined by the pH of the solution [10, 32]. When the pH value was 6, the solution is in neutral polarity. When the pH value was 8 the solution is in negative polarity. A maximum of the extraction value up to 85.21% in aqueous phase was reached at pH = 8 as shown in Fig. 3.4. The possible reason may be that the negative polarity of amoxicillin increases because of the increase in pH value [4, 28].

3.5.2 Effect of amoxicillin concentration in the feed phase

To investigate the influence of initial concentrations of amoxicillin, different values of amoxicillin concentrations studied were 2, 4, 6, 8 and 10 mmol/L. The results

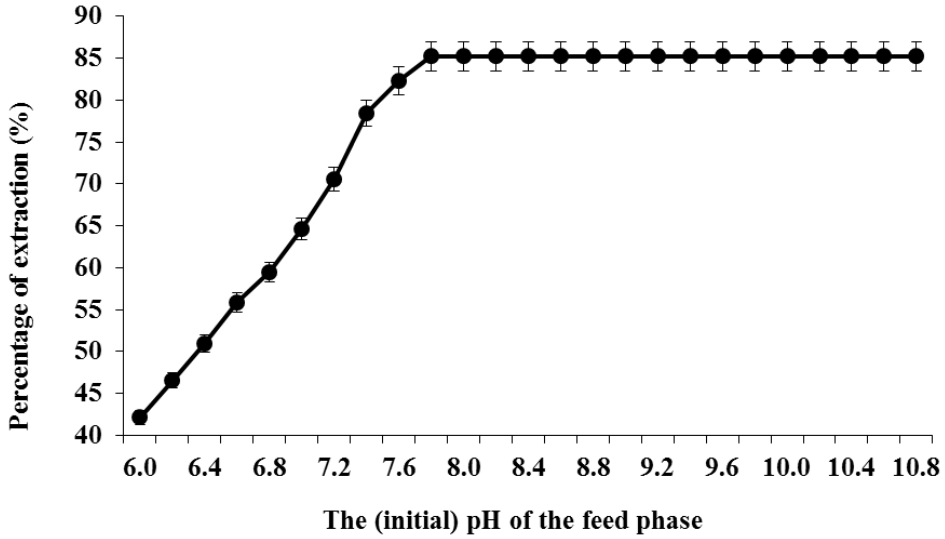


Figure 3.4 Effect of the (initial) pH of the feed phase on percentages of extraction of amoxicillin

as illustrated in Fig. 3.5 indicated that the percentages of extraction and stripping of amoxicillin can be achieved by increasing the concentration of the initial feed concentration. This was due to an increase in initial concentration in the feed phase, resulting in higher fluxes [33]. Optimum concentration was found to be 6 mmol/L where the extraction of amoxicillin reached 85.21%. On the other hand, the percentages of extraction decreased slightly at higher concentrations above 6 mmol/L. This was because of the increase in film viscosity resulting in lower fluxes [34]. These experimental results were consistent with an earlier report by Sunsandee et al. [35]. Therefore, for all subsequent experiments, the concentration of amoxicillin was fixed at 6 mmol/L.

3.5.3 Effect of extractant concentration in the membrane phase

The concentration of extractant is an important parameter influencing the

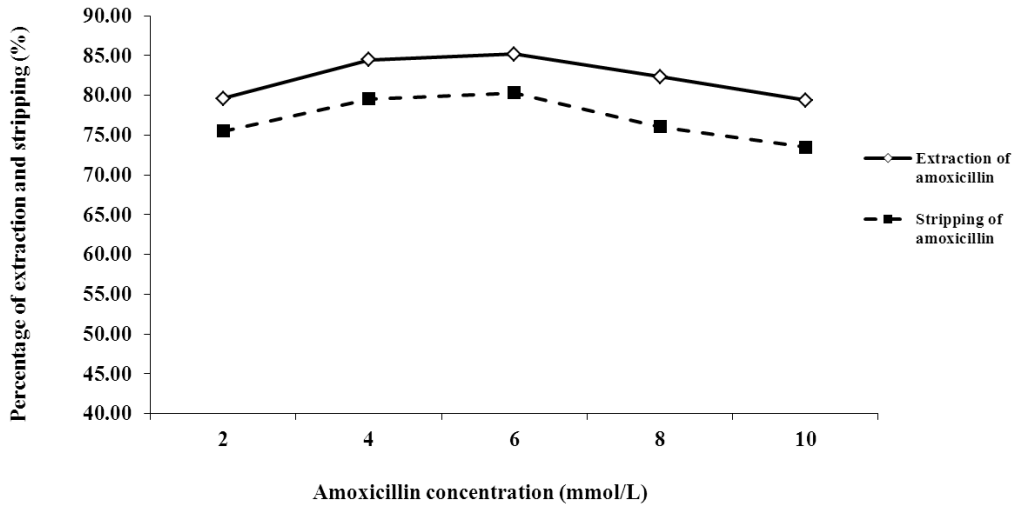


Figure 3.5 Effect of amoxicillin concentration in the feed phase on percentages of extraction and recovery of amoxicillin

transport efficiency of target compounds [36]. In order to study the influence of the concentration of Aliquat 336 on the transport of amoxicillin, different concentrations of the extractant at 2, 4, 6, 8 and 10 mmol/L were tested. Results, as illustrated in Fig. 3.6, demonstrated that the percentages of amoxicillin extraction increased when the concentration of extractant increased. The highest percentages of amoxicillin extraction reached 85.21% at a concentration of 6 mmol/L Aliquat 336 and then decreased. This fact could be explained by Le Chatelier's principle which states that an increase of extractant concentration in the liquid membrane causes higher fluxes. However, above 6 mmol/L, the flux decreases because the viscosity of the film between the feed solution and the liquid membrane increased, resulting in obstruction of the mass transfer of amoxicillin as well as a decrease in the diffusion coefficient [37]. Similar results were found in previous work by Sunsandee et al. [35].

According to these results, 6 mmol/L Aliquat 336 was employed in further experiments the HFSLM system.

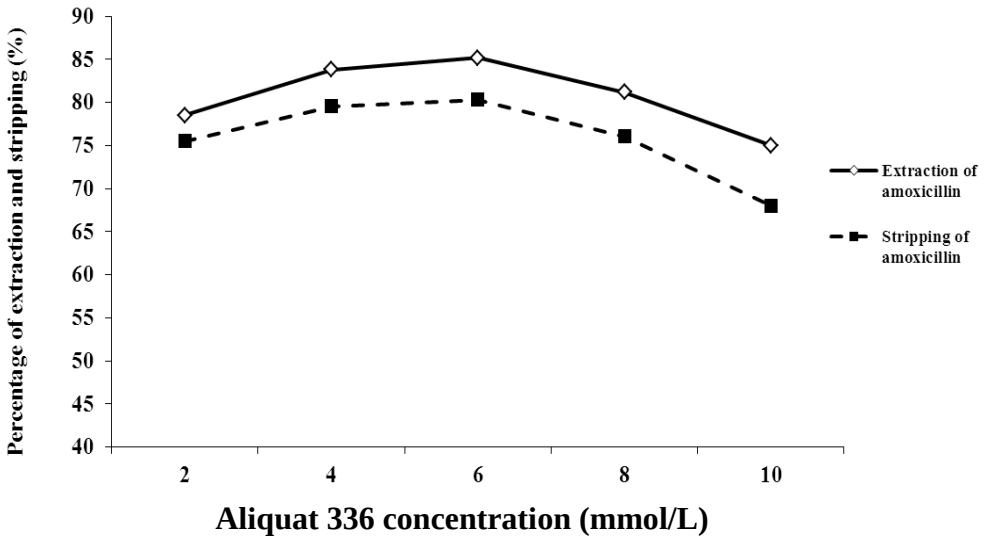


Figure 3.6 Effect of extractant concentration in the membrane phase on percentages of extraction and recovery of amoxicillin

3.5.4 Effect of receiving concentration in the stripping phase

An investigation of the influence of stripping solution on the efficiency of amoxicillin stripping was studied with regards to the liquid membrane consisting of 6 mmol/L

Aliquat 336 as the extractant and sodium chloride as the stripping solution. The concentration of sodium chloride varied in the range of 2, 4, 6, 8 and 10 mmol/L. Results are shown in Fig. 3.7 indicating that the percentages of amoxicillin stripping increased when there was an increase in the concentration of the stripping solution.

This can be explained by using the rate of stripping reaction obtained from correlations in Eq.(3.3) as follows:

$$R_s(x,t)=-k_s[NaCl]^m \quad (3.36)$$

Thus, when the concentration of NaCl was increased from 2 to 6 mmol/L, the reaction would shift forward, resulting in an increase in percentages of amoxicillin stripping. This could be explained by Le Chatelier's principle [38, 39]. However, at concentrations of stripping agents higher than 6 mmol/L, the percentages of stripping remained constant. This was because of being obstructed by concentration polarization [40-42] as well as being limited owing to the amount of complex species which reacted with the stripping solution at the interface of the liquid membrane – stripping [29]. According to the molecular kinetic interpretation by Stokes and Einstein, the increase in high stripping concentration leads to lower diffusion coefficient. This reason was published with the earlier report by Chakrabarty et al. [43] and Wannachod et al. [44]. Consequently, this implied that maximum concentration of sodium chloride solution for reaction with the complex species was 6 mmol/L.

3.5.5 Effect of the flow rates of feed solution

Investigation of the optimal flow rates of feed solution is significant for the separation of target compounds across HFSLM for better recovery and scaling-up of the process[45]. The relationship between the percentage of extraction and stripping of amoxicillin at different flow rates of feed and stripping solutions which operated a counter-flow pattern was reported by adjusting flow rates at 50, 100, 150, 200, 250 and 300 mL/min. Results are illustrated in Fig. 3.8. The results indicated that by using

a flow rate of feed solution of 100 mL/min, the extraction of amoxicillin reached the highest percentage of about 85.21%.

On the other hand, higher flow rates result in less resident time of the solutions with the extractant (Aliquat 336) or less contact time of the relevant molecule in the reaction in the HFSLM process. For instance, at too high a flow rate (especially at 300 mL/min) the membrane system may deteriorate. This can be seen from both poor

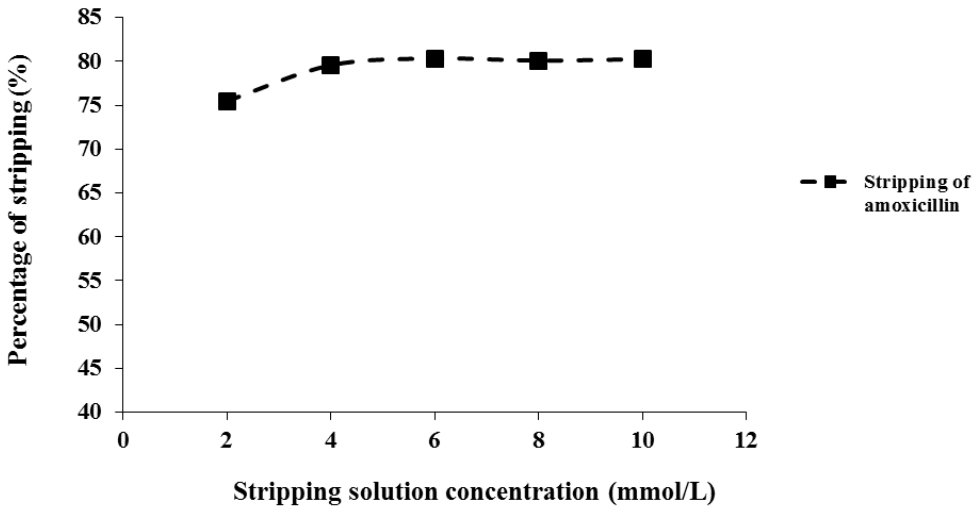


Figure 3.7 Effect of receiving concentration in the stripping phase on percentages of recovery of amoxicillin

liquid membrane stability and lower percentage of extraction [46].Therefore, it can be concluded that the flow rates of feed solutions play an important role in the percentages of extraction and stripping of amoxicillin.

3.5.6 Effect of the flow rates of stripping solution

The results as illustrated in Fig. 8 demonstrated that at lower flow rates of stripping solution, in particular 50 mL/min, the efficiency of extraction was lower than

at 100 mL/ min owing to the difficulty in supplementing amoxicillin in the hollow fiber module. Furthermore, increasing the flow rate from 50 to 100 mL/min leads to a thinner aqueous boundary layer, high shear force and higher turbulence; consequently, the mass transfer resistance is reduced [47]. The highest percentages of stripping solution observed reached 80.34% at 100 mL/min. However, the percentage of amoxicillin extraction and stripping decreased with an increase of the flow rates of feed and stripping solutions due to resident time of solutions in the hollow fiber module [45]. Moreover, Leepipatpaiboon et al., [48] reported that higher flow rates can cause the liquid membrane to leak out of the micro-pores of hollow fibers and destroy the liquid membrane system.

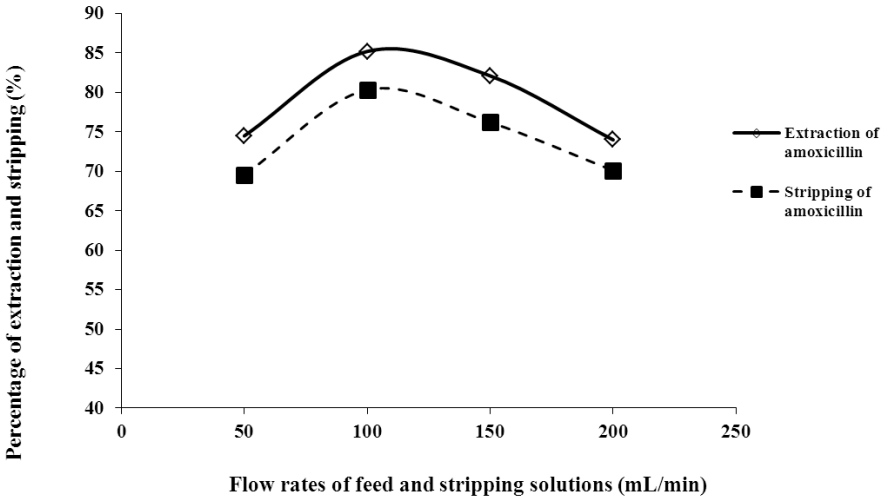


Figure 3.8 Effect of the flow rates of stripping solution on percentages of extraction and recovery of amoxicillin

3.5.7 Extraction equilibrium constant and distribution ratio

The extraction equilibrium constant (K_{ex}) was calculated by the slope of the graph in Fig. 3.9 and was found to be 1.4172. The stripping equilibrium constant (K_{st}) was calculated by the slope of the graph in Fig. 3.10 and was found to be 1.0079. The

distribution ratio (*D*) at an Aliquat 336 concentration of 6 mmol/L was calculated by Eq. (3.6), as shown in Table 3.2. It was noted that the distribution ratio increased with the extractant concentration, as seen in an earlier report by Sunsandee et al. [35].

3.5.8 Permeability and mass transfer coefficients

The permeability coefficients of amoxicillin as a function of concentration

Table 3.2 The distribution ratios (D) at the aliquat 336 concentrations of 2, 4, 6, 8 and 10 mmol/L

[aliquat 336] (mmol/L)	2	4	6	8	10
The distribution ratios	6.74	8.59	11.34	14.17	17.72

of Aliquat 336 from 2 to 10 mmol/L were calculated by the slope obtained in Fig. 3.11, as shown in Table 3.3. The results showed that the permeability coefficient increased when extractant concentration increased as noted in the earlier report by Sunsandee et al. [35]. Eq. (13) was obtained by substituting the membrane permeability coefficient (P_m) in Eq. (3.12) into Eq. (3.10), assuming that the stripping reaction of amoxicillin was instantaneous and that there was no contribution of the stripping phase [27]. Eq. (3.13) was used to calculate the aqueous mass transfer coefficient (k_f) and the membrane mass transfer coefficient (k_m).

By plotting $1/P$ as a function of $1/[\text{ amoxicillin}]_f[\text{Aliquat 336}]_m$ for different carrier concentrations of Aliquat 336, a straight line with slope $r_i/(r_{lm} \cdot K_{ex} \cdot k_m)$ and Y-intercept $1/k_f$ for the calculation is obtained (Fig. 3.12). Thus, the values of k_f and k_m were found to be 3.57×10^{-2} and 0.70×10^{-2} cm/s, respectively. Since the membrane mass transfer

coefficient (k_m) is less than the aqueous feed mass transfer coefficient (k_f), it can be concluded that the mass transfer across the membrane phase is the rate-controlling step.

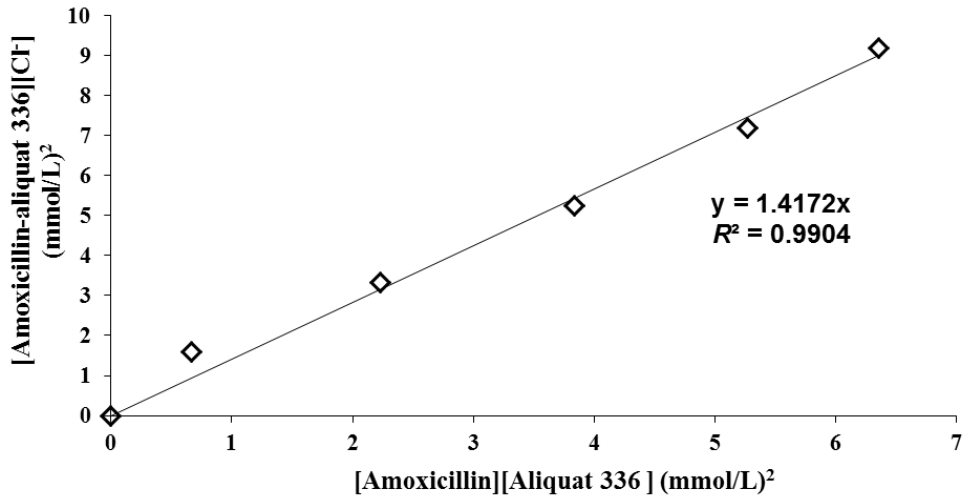


Figure 3.9 The amoxicillin extraction with aliquat 336 as a function of equilibrium [amoxicillin][aliquat336]

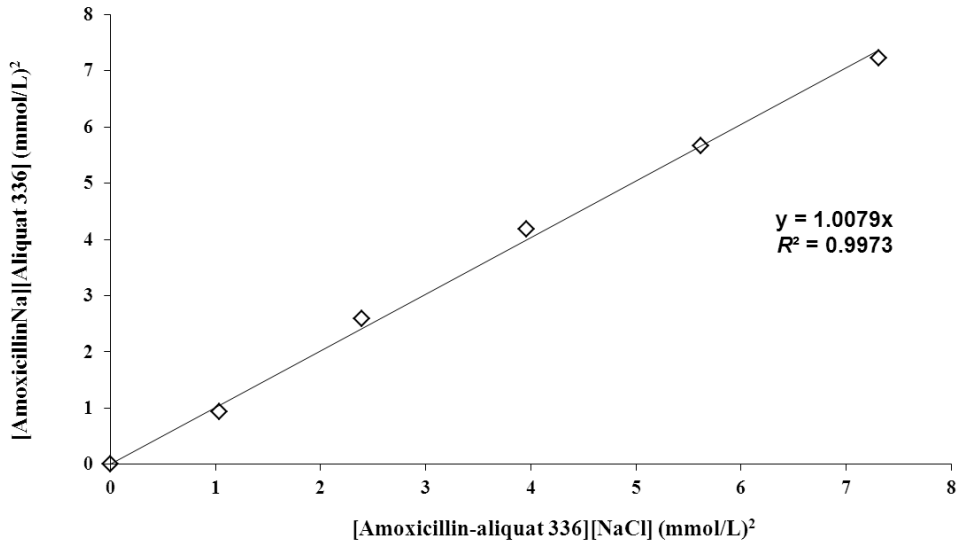


Figure 3.10 The amoxicillin recovery with NaCl solution as a function of equilibrium [amoxicillin][NaCl]

3.5.9 The mathematic modeling of amoxicillin concentration

The mean value of the diffusion coefficient of amoxicillin was found to be 4.62 $\times 10^{-5}$ cm^2s^{-1}[49]. The value indicated that the transport of amoxicillin is described as the pure diffusion transport. Moreover, the calculated valve of α as shown in Eq (3.1) is 0.1263 which indicates that diffusion controls the transport. Therefore, a mathematical model based on a diffusion flux model was developed as demonstrated in Eq. (3.35). The amoxicillin concentration profile through HFSLM is shown in Fig. 3.13.The mass transfer reaction of amoxicillin through hollow fiber supported liquid membrane was assessed by diffusion flux modeling, as represented in Fig. 3.14. Eq. (3.35) was used to calculate the percentage of amoxicillin extraction as a function of time for carrier concentrations at 2, 4, 6, 8 and 10 mmol/L. The computational results were shown by the solid line which was in good agreement and fitted well with the experimental data. The diffusion process is explained by Fick's law of diffusion. Mass transfer flux was presented in this model. Therefore, it can be concluded that the diffusion flux model was satisfactory for the extraction of amoxicillin through hollow fiber supported liquid membrane.

Table 3.3 The permeability coefficients (P) at aliquat 336 concentrations of 2, 4, 6 and 8 mmol/L

[aliquat 336] (mmol/L)	Permeability coefficients (×100 cm/s)
2	2.11
4	2.34
6	2.57
8	2.67

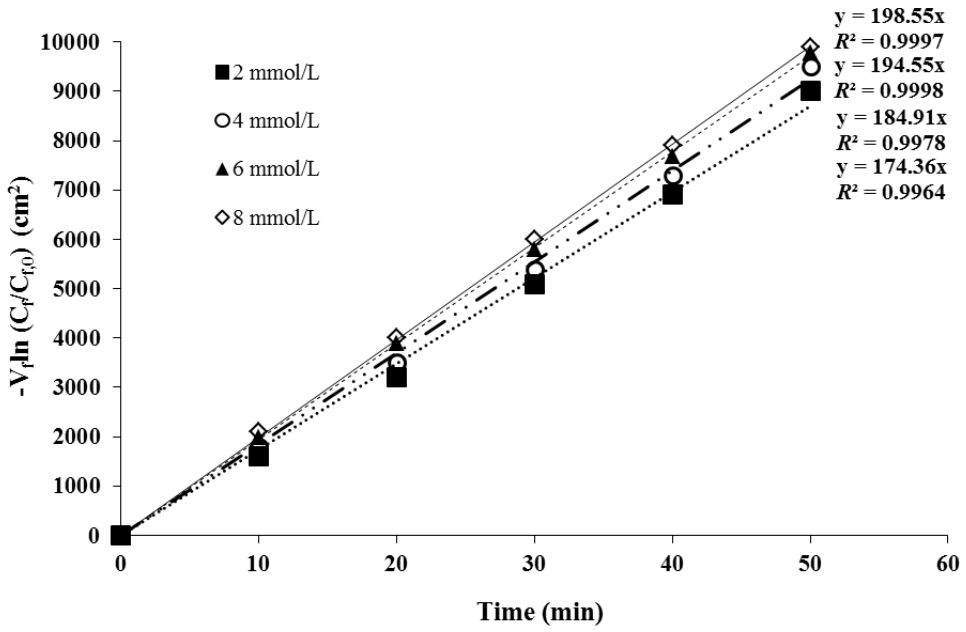


Figure 3.11 The plot of $-V_f \ln(C_f/C_{f,0})$ of amoxicillin in the feed solution against time with different aliquat 336 concentrations

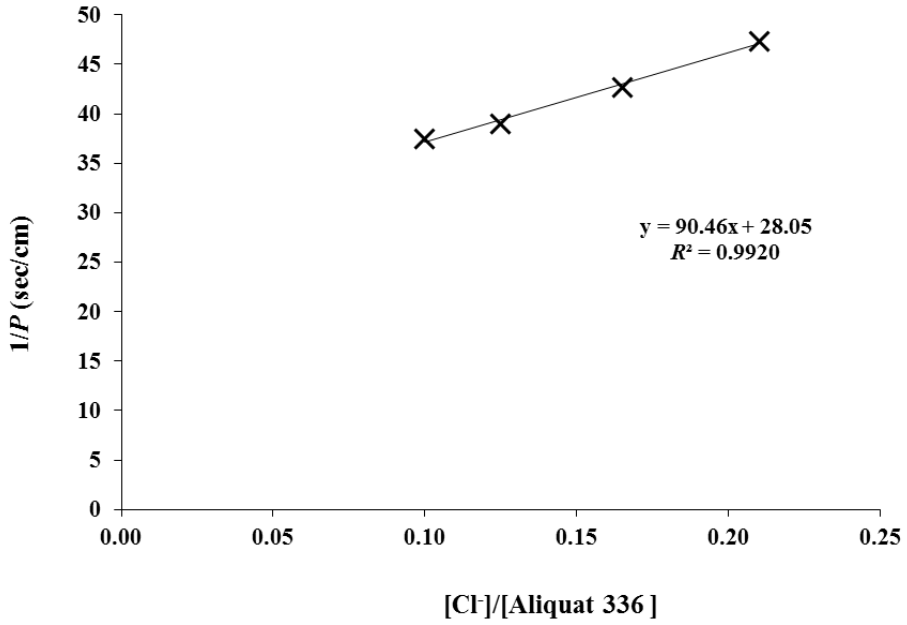


Figure 3.12 The plot of 1/P as a function of $1/[\text{amoxicillin}]_f[\text{aliquat 336}]_m$

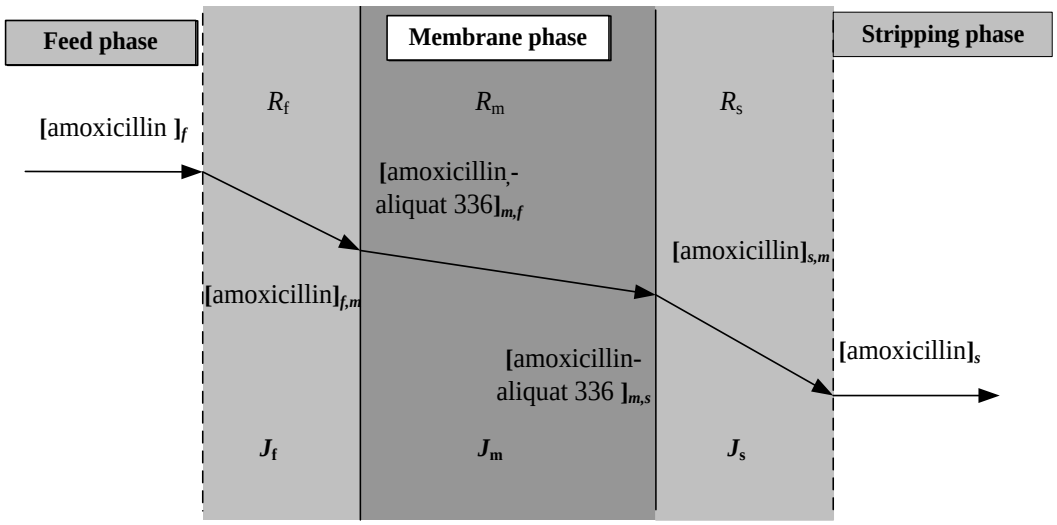


Figure 3.13 Mass transfer of amoxicillin with aliquat 336 and concentration profile in HFSLM

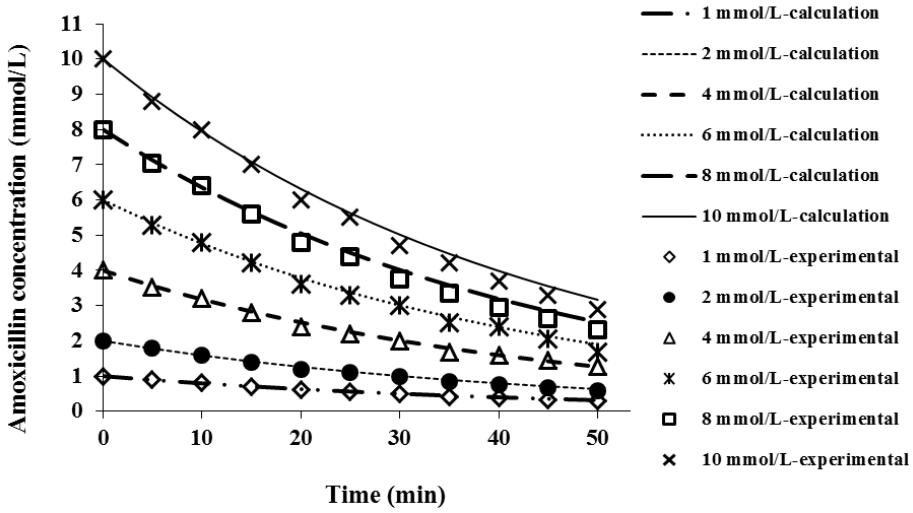


Figure 3.14 Different concentrations of amoxicillin in the feed phase plotted as a function of time

3.6 Conclusion

Separation of amoxicillin has been a subject of increasing research in the pharmaceutical and chemical industries. Optimum parameters were applied to separate amoxicillin in order to attain high yields. After a run of 50 min. in the HFSLM system, the amoxicillin percentages of cumulative extraction and cumulative stripping reached 85.21% and 80.34%, respectively, from an initial concentration of feed solution of 6 mmol/L, 6 mmol/L Aliquat 336, and 100 mL/min of feed and stripping solutions. The aqueous-phase mass transfer coefficient (k_f) and organic-phase mass transfer coefficient (k_m) were reported to be 3.57×10^{-2} and 0.70×10^{-2} cm/s, respectively. The results demonstrated good agreement between experimental and calculated data via a hypothetical concept. The model was found to be a very useful design equation and was able to operate satisfactorily.

3.7 Nomenclature

[Amox(x,t)]	concentration of amoxicillin as a function of x and t (mg/dm3)
$[\text{Amoxicillin}]_{f,0}$	concentrations of the amoxicillin complexes in the feed solution
$[\text{Amoxicillin}]_{f,m}$	concentrations of the amoxicillin complexes at the interface between aqueous feed solution and membrane phase at subsequent time t
$[\text{Amoxicillin}]_{m,f}$	concentration of the amoxicillin complex in the membrane phase
A	effective area of the hollow fiber module (cm^2)
C	concentration (mmol/L)
C_f	amoxicillin concentration at time t (mmol/L)
$C_{f,0}$	amoxicillin concentration (mmol/L) at initial time (t = 0)

$C_{f,in}$	inlet feed concentrations of component i (mmol/L)
$C_{f,out}$	outlet feed concentrations of component i (mmol/L)
$C_{s,in}$	inlet stripping concentrations of component i (mmol/L)
$C_{s,out}$	outlet stripping concentrations of component i (mmol/L)
D	distribution ratio
D_m	diffusivity of the amoxicillin complex.
h_m	layer film (or membrane support) thickness
J	mass transport flux (mol/cm^3/min)
k_f	aqueous feed mass transfer coefficient (cm/s)
k_m	organic mass transfer coefficient (cm/s)
K_{ex}	extraction equilibrium (-)
K_{st}	stripping equilibrium (-)
L	length of the hollow fiber (cm)
N	number of hollow fibers in the module
n	reaction order
P	permeability coefficient (cm/s)
P_m	membrane permeability (cm/s)
Q	volume metric flow rate (cm^3/s)
R_m	organic membrane mass transfer resistance (s/cm)
R_i	aqueous mass transfer resistance (s/cm)
r_i	internal radius of the hollow fiber module (cm)

r_{lm}	log-mean radius of the hollow fiber (cm)
r_o	external radius of the hollow fiber (cm)
t	time (min)
V_f	volume of feed phase (cm^3)
x	distance along the axis of hollow fibers (dm, $0 < x < L$)

Greek letters

τ	tortuosity of membrane (-)
ε	porosity of membrane (-)
α	dimensionless parameter which relates diffusion-limited transport to kinetically limited transport

Subscripts

f	feed phase
s	stripping phase
m	membrane phase
i	inter phase
0	initial concentration

3.8 Acknowledgements

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CHAPTER 4

THE EFFECT OF TEMPERATURE ON MASS TRANSFER AND THERMODYNAMIC PARAMETERS IN THE REMOVAL OF AMOXICILLIN VIA HOLLOW FIBER SUPPORTED LIQUID MEMBRANE

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4.1 Abstract

The influence of temperature on the separation of amoxicillin via HFSLM containing the carrier Aliquat 336 was systematically investigated. Mass-transfer parameters including distribution ratio and flux as well as thermodynamic properties namely ΔH and ΔG were also determined at different temperatures ranging from 278.15 K to 318.15 K. The positive value of the enthalpy change (24.5778 kJ/mol) indicated that the extraction process is endothermic reaction. Further, the positive value of the entropy change (112.0145 J/molK) and the negative value of the Gibbs free-energy indicated that the extraction process is forward reaction. It was found that by increasing the temperature of the system from 278.15 to 318.15 K, extraction of amoxicillin increased from 81.81 to 89.65% and the stripping of amoxicillin increased from 76.63 to 84.70 % respectively. Activation energy (E_a) of amoxicillin extraction was found to be 44.28 kJ/mol. This implied that the chemical reaction was the mass transfer controlling step. The mass transfer coefficients in the membrane phase were found to be less than the mass transfer coefficients in the feed phase within the range of temperatures i.e. 278.15 K to 318.15 K. This implied that the mass transfer process in the membrane phase was the rate controlling step.

Keywords: Thermodynamic parameters; Mass transfer; Amoxicillin; HFSLM; Antibiotics

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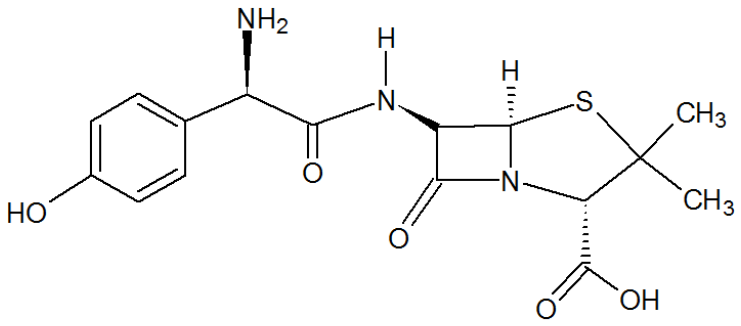
4.2 Introduction

Amoxicillin ($C_{16}H_{19}N_3O_5S$) is an antibiotic which is widely used to treat various infections in both human beings and animals [1, 2]. However, when amoxicillin is released into the environment, it is a major problem. When amoxicillin, for example, is introduced into surface water and groundwater, a change in aquatic ecosystems takes place [3, 4]. This is owing to insufficient removal of amoxicillin in the conventional water and wastewater treatment plant. Thus, bacteria develop causing resistance to these drugs in humans and further failure of treatment with antibiotics [5-7]. Many applications for antibiotic removal from wastewater are available including ion exchange, adsorption, ultraviolet radiation, chemical coagulation and flocculation, ozonation, chlorination, membrane reverse osmosis and ultra-filtration, and biological degradation [8-10].

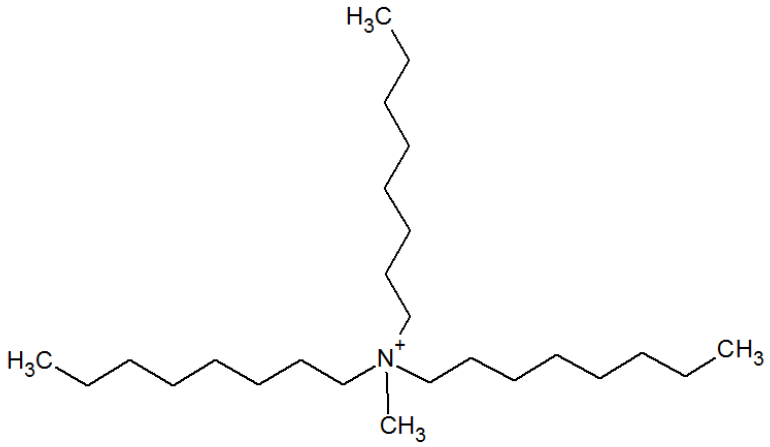
Membrane technology has attracted much research for industrial wastewater treatment [11–13]. Recently, hollow fiber supported liquid membrane (HFSLM) has emerged as the technology of interest for chemical and environmental engineers in the treatment of wastewater containing low concentrations of metal ions, pharmaceuticals and organic compounds [14-16]. The principle of HFSLM is based on the simultaneous extraction and stripping of contaminant compounds with appropriate solvents in a single stage operation [17]. The advantages of such a system over other techniques include high treatment efficiency and selectivity, low energy costs, less solvent used and it is a simple design amenable to scaling up for industrial applications [18-22].

It is clear therefore that the HFSLM system should be suitable for the treatment of wastewater containing amoxicillin. Based on the literature, temperature was cited as one of the important operating parameters since it affected the performance of the mass transfer process during extraction and stripping [23-24]. Moreover, the effect of temperature is of significance to chemical reactions as denoted by the Arrhenius equation. Yet, few researchers have reported on the effect of temperature and

thermodynamic parameters i.e. ΔG and ΔH on the mass transfer process in HFSLM [25-26]. Thus, the objective of this work is to investigate the effect of temperature on the mass transfer process during the extraction and stripping of amoxicillin via HFSLM. The work also employs Van't Hoff Model analysis of selectivity values derived from variable temperatures in order to assess the thermodynamic functions of separation.



Amoxicillin



b) Aliquat 336

Figure 4.1 Chemical structures: a) amoxicillin and b) Aliquat 336

4.3 Theory

The extraction and recovery of the botanical extract amoxicillin (AMOX) [27] and Aliquat 336 (QCl) is shown in Eqs. (4.1) and (4.2), respectively. Fig. 4.2 shows the

mechanism and transport kinetics scheme of amoxicillin through the hollow fiber supported liquid membrane. As shown in Eq. (4.1), amoxicillin in anionic form reacts with the extractant (i.e. QCl) to form complexes which will be recovered according to Eq. (4.2) with NaCl as stripping solution. Fig. 4.2 illustrates the use of HFSLM to separate amoxicillin from feed solution.

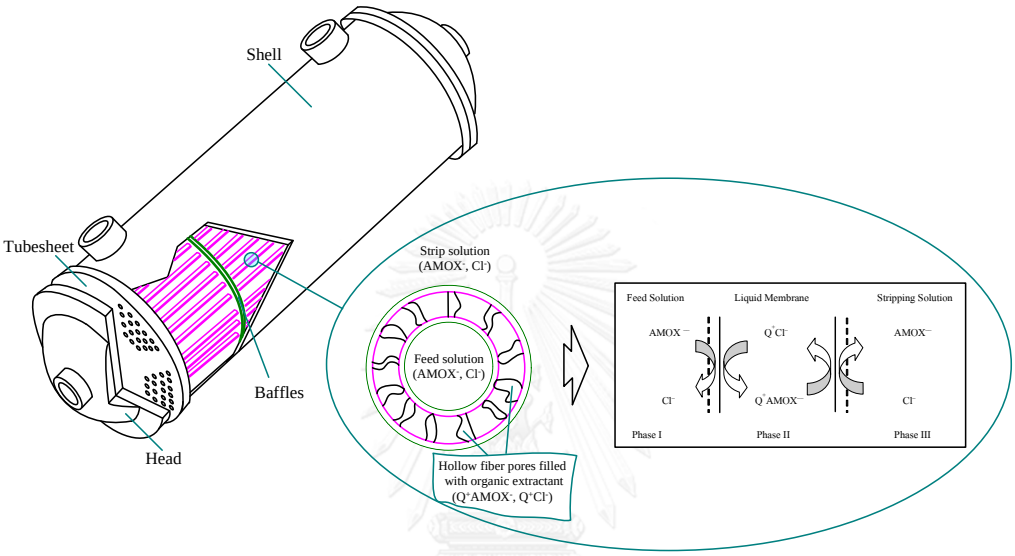


Figure 4.2 Transport scheme for amoxicillin in HFSLM

$$AMOX^{-}_{(f)} + Q^{+}Cl^{-}_{(m)} \underset{k_2}{\overset{k_1}{\longleftrightarrow}} Q^{+}AMOX^{-}_{(m)} + Cl^{-}_{(f)} \tag{4.1}$$

$$Q^{+}AMOX^{-}_{(m)} + Cl^{-}_{(s)} \underset{k_4}{\overset{k_3}{\longleftrightarrow}} AMOX^{-}_{(s)} + Q^{+}Cl^{-}_{(m)} \tag{4.2}$$

where k_1 and k_2 are the apparent rate constants of the feed-membrane interfacial transport and membrane-strip interfacial transport of amoxicillin, respectively, while k_3 and k_4 are the apparent rate constants of the feed-membrane interfacial transport and the membrane-strip interfacial transport, respectively. The suffixes *f*, *m* and *s* represent feed, membrane and stripping phases.

4.3.1 Extraction equilibrium and distribution ratio

The extraction equilibrium (K_{ex}) of amoxicillin by QCl and the distribution ratio of amoxicillin (D), extracted from the feed phase to membrane phase, can be written according to Eqs. (3) and (4), respectively:

$$K_{ex} = \frac{\left[Q^{+}AMOX^{-}\right]_{m}\left[Cl^{-}\right]_{f}}{\left[Q^{+}Cl^{-}\right]_{m}\left[AMOX^{-}\right]_{f}} \tag{4.3}$$

$$D = \frac{\left[Q^{+}AMOX^{-}\right]_{m}}{\left[AMOX^{-}\right]_{f}} \tag{4.4}$$

The distribution ratio for the extraction equilibrium constant as shown in Eq. (4.5) is derived from Eq. (4.4):

$$D = K_{ex}\frac{\left[Q^{+}Cl^{-}\right]_{m}}{\left[Cl^{-}\right]_{f}} \tag{4.5}$$

In the present study, the percentages of extraction and stripping were calculated according to Eqs. (4.6) and (4.7):

$$\alpha = \frac{k_S}{k_R}$$

$$\%\text{Extraction} = \frac{C_{f,0} - C_{f,t}}{C_{f,0}} \times 100 \tag{4.6}$$

$$\%\text{Stripping} = \frac{C_{s,t}}{C_{f,0}} \times 100 \tag{4.7}$$

where $C_{f,o}$ and $C_{f,t}$ are the initial feed concentrations at time *t* for component *i* (mmol/L), respectively while $C_{s,t}$ is the concentration of stripping phase at time *t* for component *i* (mmol/L).

4.3.2 Influence of temperature on extraction equilibrium

Van't Hoff Model shows the relationship between the temperature and the effect of the equilibrium extraction constant (K_{ex}) during amoxicillin extraction. This equation also relates to the standard Gibbs free-energy equation [28]. The extraction is calculated by the Gibbs free-energy change as follows:

$$\Delta G_{ex}^{0} = -RT \ln K_{ex} \tag{4.8}$$

$$\ln K_{ex} = -\frac{\Delta G_{ex}^{0}}{RT} \tag{4.9}$$

Gibbs free-energy change (ΔG^{0}_{ex}) is related to the standard enthalpy and extraction entropy changes (i.e. ΔH^{0}_{ex} and ΔS^{0}_{ex}) via Gibb-Helmholtz equation as shown in Eq. (4.10):

$$\Delta G_{ex}{}^{0} = \Delta H_{ex}{}^{0} - T\Delta S_{ex}{}^{0} \tag{4.10}$$

Eq. (4.11) is the Van't Hoff Model in linearized form which can be obtained by substituting Eq. (4.8) into Eq. (4.10):

$$\ln K_{ex} = -\frac{\Delta H_{ex}^{0}}{RT} + \frac{\Delta S_{ex}^{0}}{R} \tag{4.11}$$

According to Eq. (4.11), a plot of ln K_{ex} versus $1/T$ gives a straight line whose slope and interception can be used to determine ΔH^0_{ex} and ΔS^0_{ex} [39, 30]. Previous works also applied similar methodology for obtaining ΔH^0_{ex} and ΔS^0_{ex} [28, 31].

4.3.3 Permeability coefficient

The permeability coefficient (P) of amoxicillin can be expressed based on the work of Kandwal [32] as shown in Eq. (4.12) where P is the permeability coefficient (cm/s), $C_{f,0}$ is initial amoxicillin concentration (mmol/L), C_f is amoxicillin concentration at time t (mmol/L), A is the effective area of the hollow fiber module (cm^2) and V_f is the volume of the feed (cm^3):

$$-V_f \ln\left(\frac{C_f}{C_{f,o}}\right) = AP\frac{\beta}{\beta+1}t \qquad (4.12)$$

The value of β in Eq. (12) can be calculated by Eq. (4.13) as follows:

$$\beta = \frac{Q_f}{P_L \varepsilon \pi N r_i} \qquad (4.13)$$

where Q_f is the volumetric flow rate of the feed solution (cm^3/s), L is the length of the hollow fiber module (cm), ε is the porosity of the hollow fiber (%), N is number of hollow fibers in the module and r_i is the internal radius of the hollow-fiber module (cm). Thus, a plot of $-V_f \ln (C_f / C_{f,0})$ and t in Eq. (4.12) gives a straight line with a slope of $AP(\beta/(\beta+1))$ which in turn can be used to determine the permeability coefficient.

The mass-transfer coefficient for amoxicillin removal in HFSLM is dependent on the mass-transfer model and permeability coefficient. The permeability coefficient of amoxicillin is influenced by the sum of the mass transfer resistance of each phase

i.e. feed, liquid-membrane and stripping solvent which is the reciprocal of the mass-transfer coefficient. The permeability coefficient, written in terms of the mass transfer resistance, is as shown in Eq. (4.14):

$$\frac{1}{P} = \frac{1}{k_f} + \frac{r_i}{r_{lm}}\frac{1}{P_m} + \frac{r_i}{r_o}\frac{1}{k_s} \tag{4.14}$$

where P_m is the membrane permeability coefficient, r_{lm} is the log-mean radius of the hollow fiber, r_o is the external radius of the hollow fiber module (cm), k_f is the feed mass-transfer coefficient in the tube side and k_s is the stripping mass-transfer coefficient in the shell side. Eq. (4.14) can be utilized to evaluate the overall mass transfer coefficient from the experimental data.

The relationship between P_m and the distribution ratio (D) is as follows:

$$P_m = Dk_m \tag{4.15}$$

combining Eq. (4.5) and Eq. (4.15) gives the expression of P_m as shown in Eq. (4.16):

$$P_m = k_m K_{ex} \frac{\left[Q^+Cl^-\right]}{Cl^-} \tag{4.16}$$

Assuming that the stripping reaction is instantaneous and the contribution of the stripping phase is neglected [33], Eq. (4.14) becomes:

$$\frac{1}{P} = \frac{1}{k_f} + \frac{r_i}{r_{lm}}\frac{\left[Cl^-\right]}{k_m K_{ex}\left[Q^+Cl^-\right]} \tag{4.17}$$

4.3.4 Activation energy

An Arrhenius equation shows the relationship of the activation energy (E_a) with temperature changes. In general, mass transfer due to diffusion is the main transport mechanism when activation energy is lower than 20 kJ/mol. However, when activation energy is greater than 40 kJ/mol, the rate of diffusion is significantly less than the reaction rate; thus, reaction becomes the rate limiting step [34]. Activation energy of amoxicillin transport in the HFSLM system can be determined by linearizing the flux equation (Eq. 4.18) to obtain Eq. (4.19). By plotting the flux (ln *J*) versus (*1/T*) [35, 36], a straight line with the slope equal to $-E_a/R$ can be obtained:

$$J = Ae^{-E_a/RT} \tag{4.18}$$

$$\ln J = \ln A - \frac{E_a}{R}\frac{1}{T} \tag{4.19}$$

The flux of amoxicillin can be presented based on the definition by Lin and Juang [37] as follows:

$$J = -\frac{d[AMOX^-]_f}{dt}\frac{V}{A} \tag{4.20}$$

where *V* is the volume of the feed solution (cm^3) and *A* is the membrane area (cm^2).

4.4 Experiment

4.4.1. Chemicals and reagents

Pharmaceutical grade amoxicillin was provided by the Government Pharmaceutical Organization (Thailand). Aliquat 336 (QCl) was obtained from Sigma-Aldrich, United states. Analytical grade reagents including sodium tetraborate ($Na_2B_4O_7{\cdot}10H_2O$), hydrochloric acid (HCl), citric acid ($C_6H_8O_7$), sodium citrate ($C_6H_7NaO_7$),

1-decanol ($C_{10}H_{22}O$) and sodium chloride (NaCl) were purchased from Merck (Germany). Aqueous solutions were prepared with distilled water throughout the experiment.

4.4.2 Apparatus

The micro-porous polypropylene hollow fiber module (Liqui – Cel® Extra) was manufactured by Hoechst Celanese, Charlotte, NC, USA. Detailed specifications of the hollow fiber module are depicted in Table 4.1.

4.4.3 Procedure

A schematic diagram showing transport of amoxicillin across HFSLM in a single step operation is illustrated in Fig. 4.3. First, the extractant Aliquat 336 was dissolved in 1-decanol (500 mL) and then was fed into both shell and tube sides of the hollow fibers by different flow rates and recirculation mode. The flow rate in the tube side was set higher than the flow rate in the shell side to construct pressure gradient across the membrane phase for pushing the extractant into the micro-pores of the hollow fibers. The process was operated for 40 min. [38] to ensure that the extractant was fully embedded in the micro-pores of the hollow fibers. Thereafter, the concentrated feed solution was prepared by dissolving amoxicillin in distilled water and then diluted with an aqueous buffer solution in order to adjust the pH range between 8.0-9.0 using a mixture of sodium tetra borate and hydrochloric acid. The concentrated stripping solution was prepared by dissolving sodium chloride in distilled water and simultaneously was diluted with an aqueous buffer solution to adjust the pH range between 4.0-6.0 using a mixture of citric acid and sodium citrate [15]. Subsequently, feed solution containing amoxicillin and stripping solution containing NaCl solution was fed into the tube and shell sides of the module. After that, the concentration of amoxicillin in both outlets, feed and stripping, was analyzed at intervals by HPLC. In order to enhance the performance of the HFSLM system, the concentration of

Table 4.1 Physical characteristics of the hollow fiber module

Properties	Descriptions
Material	Polypropylene
Inside diameter of hollow fiber	240 μm
Outside diameter of hollow fiber	300 μm
Effective length of hollow fiber	15 cm
Number of hollow fibers	35,000
Average pore size	0.03 μm
Porosity	30 %
Effective surface area	1.4×10^4 cm^2
Area per unit volume	29.3 cm^2/cm^3
Module diameter	6.3 cm
Module length	20.3 cm
Tortuosity factor	2.6
Operating temperature	278-318 K

Aliquat336 was increased from 3 to 6 mmol/L, operating time from 20 to 100 min. and operating temperature from 278.15 to 318.15 K.

For study on the amoxicillin extraction at equilibrium, the solvent extraction method was carried out [39]. 20 mL of feed solution with the concentration of amoxicillin at 6 mmol/L was mixed with 20 mL of membrane solution (6 mmol/L of Aliquat 336 dissolving in 1-decanol) in the shaker. The process was operated for 100 min. that was the equilibrium time for the amoxicillin separation in the HFSLM system. Thereafter, the feed and membrane phases were separated by a separation funnel. The feed samples were withdrawn and analyzed using HPLC.

4.4.4 Analytical Method

The quantity of amoxicillin, in both feed and stripping solutions, was measured by using high performance liquid chromatography (HPLC, Agilent 1100 series compact

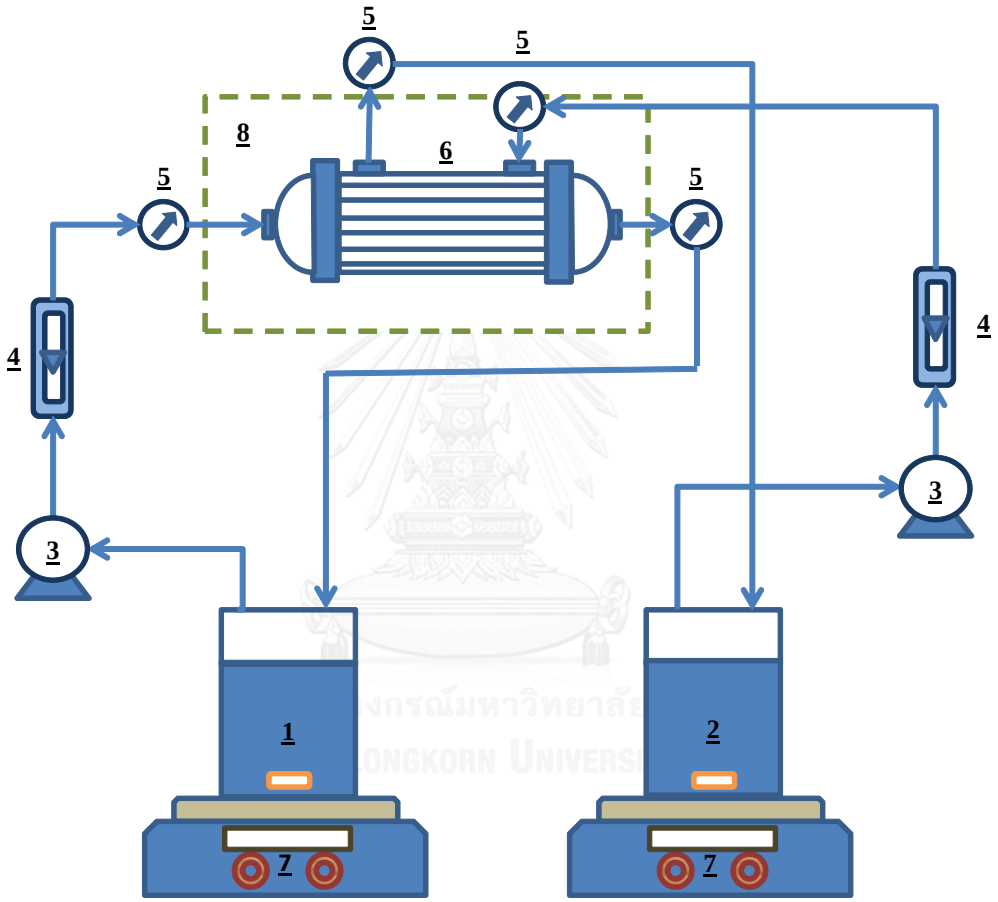


Figure 4.3 Schematic counter-current flow diagram for a single-module operation in the hollow fiber supported liquid membrane: 1) feed reservoir, 2) stripping reservoir, 3) Gear pump, 4) Rota meter, 5) Pressure gauge, 6) Hollow fiber module, 7) stirrer with temperature control and 8) temperature control box

LC system, USA). The data (10 min. per sample) was analyzed by Agilent's Chem Station version B.04.01. HPLC was carried out using an Eclipse XDB-C18 column (5 μm,

4.6 ×150 mm) [40]. The column was maintained at 298.15 K by a column heater. The mobile phase, which was a mixture of deionized water and methanol at 90:10 %v/v, was maintained at a volumetric flow rate of 1.0 mL/min. Relative retention times of amoxicillin were approximately 3.5 min. The pH of the solutions was measured with pH meter (SevenMulti™, Mettler, Switzerland).

4.5 Results and discussion

4.5.1 Optimization of extraction for amoxicillin via HFSLM

To obtain the highest efficient extraction of amoxicillin via HFSLM, many factors have to be considered: the pH of feed, concentration of feed, flow rate of feed, concentration of carrier, concentration of stripping, flow rate of stripping and cycles of extraction.According to a previous study [41], optimal operating parameters for extraction of amoxicillin included the following: an initial pH of feed phase of 8.0, an initial pH of stripping phase of 6.0, the concentration of feed phase of 6.0 mmol / L, feed and stripping solution flow rates of 100 mL / min., concentrations of 6.0 and 6.0 mmol / L for the carrier (Aliquat 336) and stripping phase (NaCl), respectively. These optimal conditions are illustrated in Table 4.2.

4.5.2 Effect of temperature on the percentages of extraction and stripping

The influence of temperature on the extraction and stripping of amoxicillin is demonstrated in Fig. 4.4. The HFSLM system was operated at optimal condition, specifically maintaining feed pH of 8.0, feed and stripping concentrations at 6 mmol/L, concentration of extractant (QCl) at 6 mmol/L, feed and stripping flow rates at 100 mL/min and an

Table 4.2 Optimized operation of separation of amoxicillin using HFSLM.

Phase	Chemical reagent	Concentration	Flow rate
Feed	amoxicillin	6.0 mmol/L	100 mL/min
Membrane	Aliquat 336	6.0 mmol/L	-
Stripping	Sodium chloride	6.0 mmol/L	100 mL/min

operating time of 100 min. When the temperature increased from 278.15 to 318.15 K, percentages of amoxicillin extraction were observed to increase from 81.81 to 89.65%. This was attributed to the fact that a fast diffusion rate occurred at higher temperature, resulting in a decrease in viscosity of the target solution which improved the penetration of the aqueous matrix and the extraction [42]. In addition, the higher temperature can reduce the intermolecular force between the solute and distilled water in the feed phase. It contributed to the easier interaction of solute with the extractant at the feed-membrane interface [43]. In the case of the stripping side, as temperature increased, results showed that at the temperature of 318.15 K, percentages of stripping of amoxicillin of 84.70% were obtained.

4.5.3 Effect of temperature on enthalpy, entropy and Gibbs free-energy change

Van't Hoff Model was plotted according to Eq. (4.11) resulting in a straight line with the slope and interception which can be used to calculate ΔH_{ex}^{0} and ΔS_{ex}^{0}, respectively (Fig. 4.5). The values of ΔH_{ex}^{0} and ΔS_{ex}^{0} for amoxicillin extraction were determined at

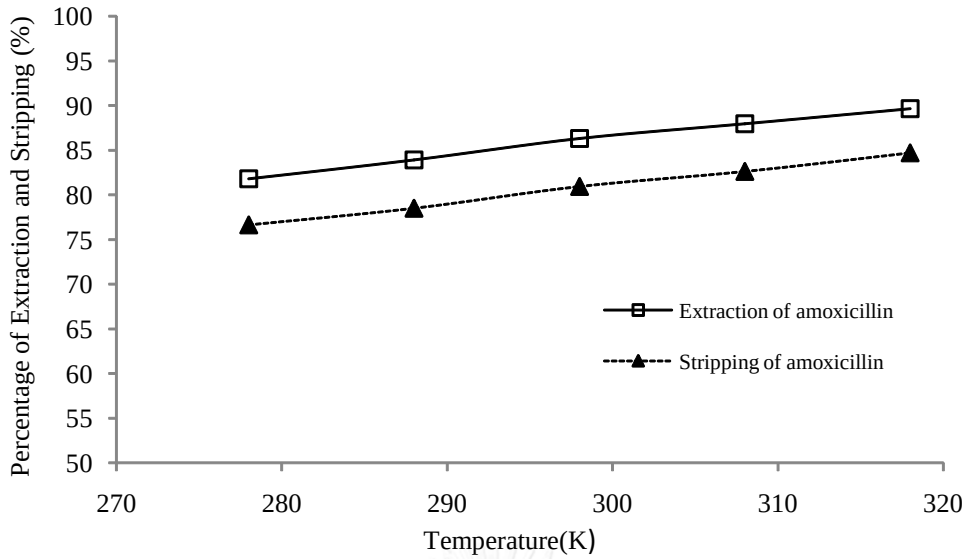


Figure 4.4 Influence of temperature on percentages of extraction and stripping of amoxicillin.

24.5778 kJ/mol and 112.0145 J/mol·K. The positive values of enthalpy change indicated that amoxicillin extraction is endothermic reaction while the positive values of entropy change implied that the extraction process is forward reaction. The Gibbs free-energy change (ΔG_{ex}^{0}) during the extraction process was calculated according to Eq. (4.10) providing negative values (Table 4.3). These results implied that the extraction process was able to proceed.

4.5.4 Permeability and mass transfer coefficients

Permeability coefficients were determined by using the slope of Eq. (4.12) as shown in Fig. 4.6 (a-e). The results were then plotted according to Eq. (17) whose slope and *y*-interception were employed to calculate the mass transfer coefficients of amoxicillin in the

Table 4.3 Thermodynamic data for amoxicillin extraction across a hollow fiber supported liquid membrane

Temperature(K)	K_{ex}	ΔG_{ex} (J/mol)	ΔH_{ex} (kJ/mol)	ΔS_{ex} J/(mol-K)
278	17.7329	-6,562.19		
288	23.8374	-7,682.33		
298	34.7693	-8,802.48	24.5778	112.0145
308	46.8285	-9,922.62		
318	67.5123	-11,042.77		

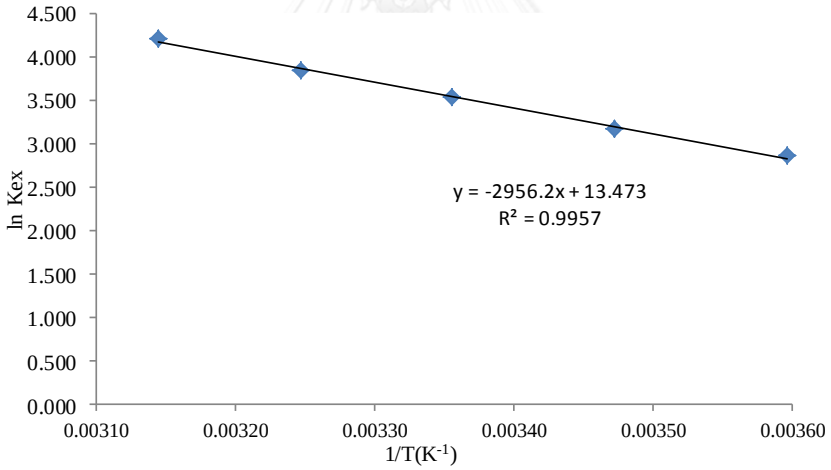
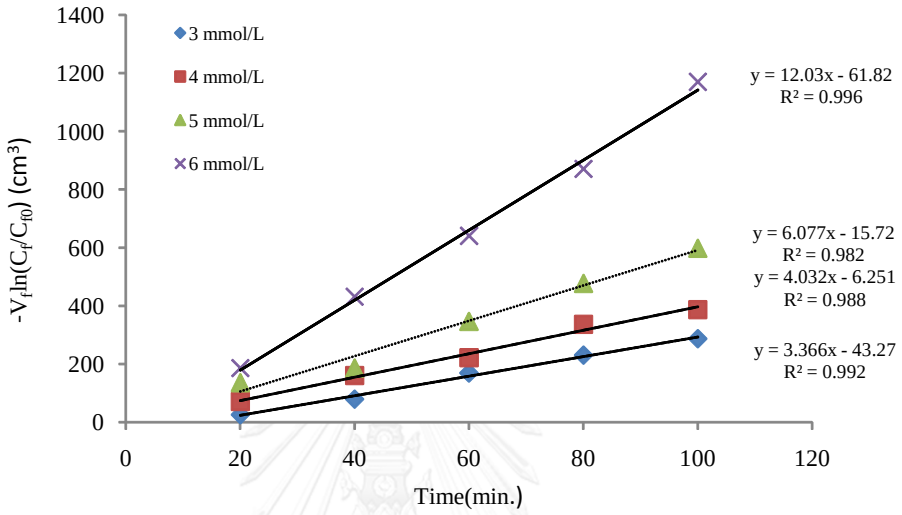


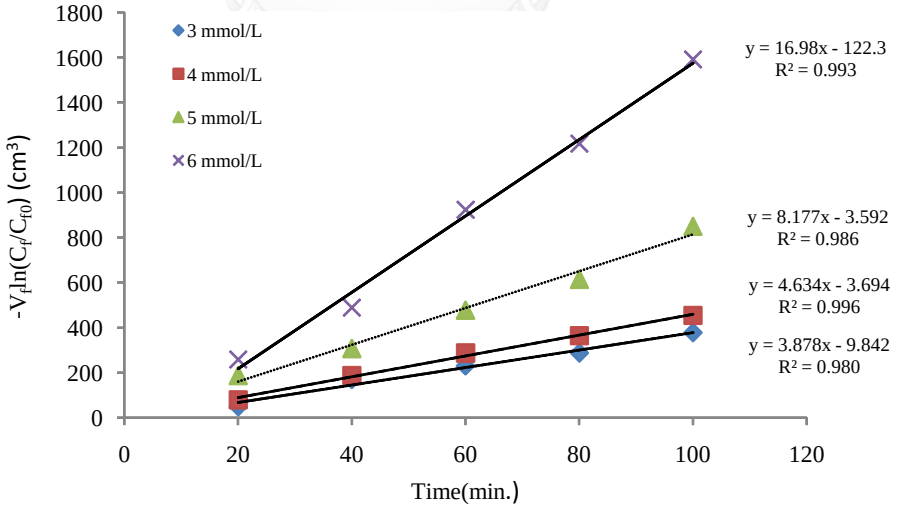
Figure 4.5 Plot of extraction equilibrium constant versus temperature

feed phase (k_f) and that in the membrane phase (k_m), respectively. The results obtained are illustrated in Fig. 4.7 and tabulated in Table 4.4. The extraction equilibrium constant (K_{ex}) was calculated for each temperature based on Eq. (4.3). It was found that K_{ex} increased linearly from 17.7329 to 67.5123 within the range of temperatures (i.e. 278.15 K to 318.15 K) being tested. It should be noted also that the mass transfer coefficient in the membrane phase (k_m) was less than that of the feed

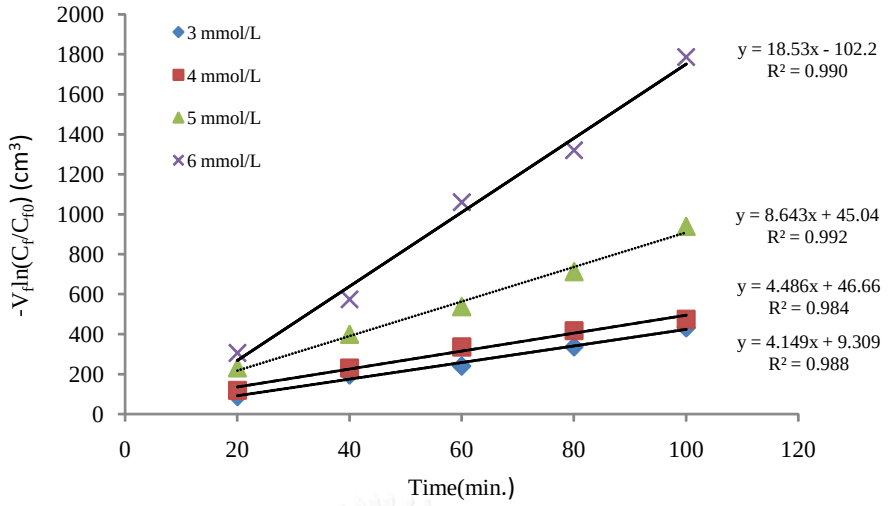
phase (k_f). This implied that the mass transfer in the membrane phase was the rate controlling step.



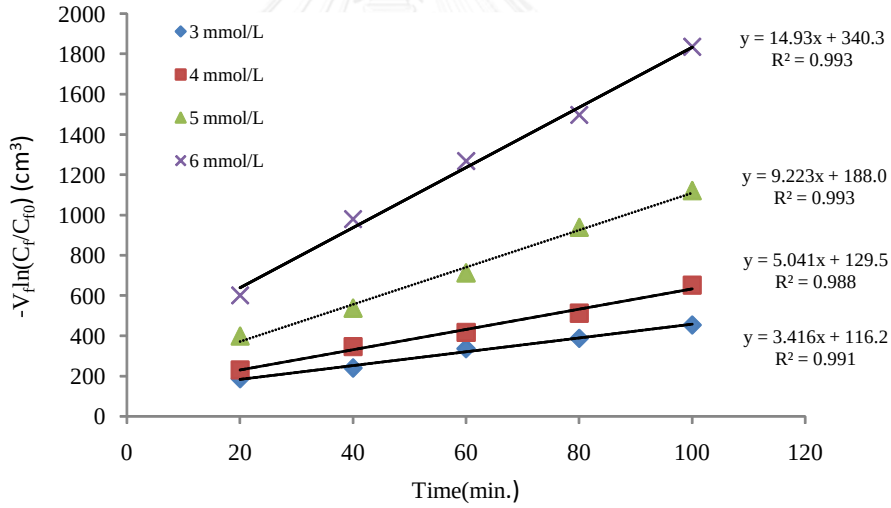
(a) 278 K



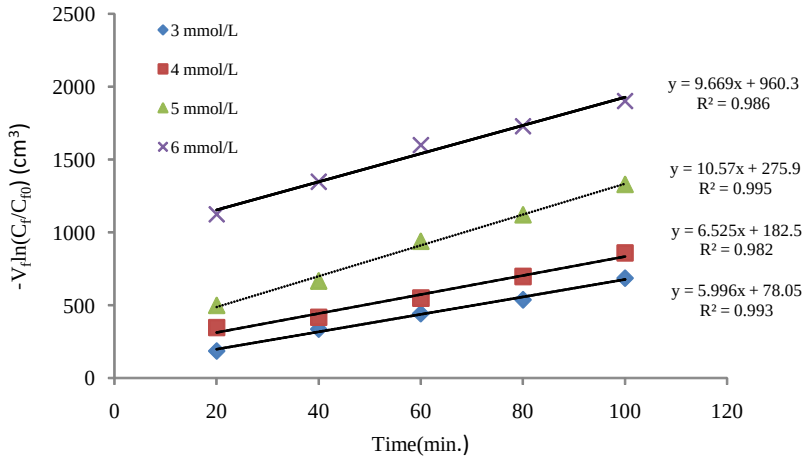
(b) 288 K


3 mmol/L
4 mmol/L
5 mmol/L
6 mmol/L
y = 18.53x - 102.2
R² = 0.990
y = 8.643x + 45.04
R² = 0.992
y = 4.486x + 46.66
R² = 0.984
y = 4.149x + 9.309
R² = 0.988
-V_t ln(C_t/C_f0) (cm³)
Time(min.)

(c) 298 K


3 mmol/L
4 mmol/L
5 mmol/L
6 mmol/L
y = 14.93x + 340.3
R² = 0.993
y = 9.223x + 188.0
R² = 0.993
y = 5.041x + 129.5
R² = 0.988
y = 3.416x + 116.2
R² = 0.991
-V_t ln(C_t/C_f0) (cm³)
Time(min.)

(d) 308 K



(e) 318 K

Figure 4.6 (a-e) Plot of $-V_f \ln (C_f / C_{f,0})$ versus time as function of carier concentration at temperature 278 to318 K

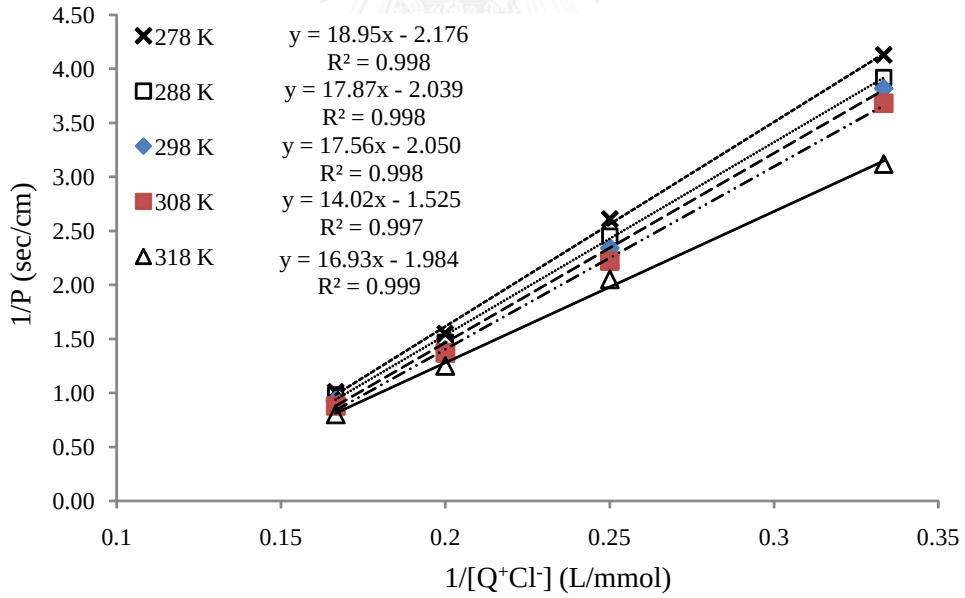


Figure 4.7 Plot of 1/P as a function of $1/[\text{aliquat 336}]_m$ at temperature 278,288, 298, 308 and 318 K

Table 4.4 Influence of temperature on extraction equilibrium (K_{ex}), aqueous mass transfer coefficient (k_f) and membrane mass transfer coefficient (k_m)

Temperature (K)	K_{ex}	Slope	Interception	k_m	k_f
278	17.7329	9.013	0.324	0.0056	3.086
288	23.8374	8.684	0.277	0.0043	3.610
298	34.7693	8.295	0.243	0.0032	4.115
308	46.8285	7.965	0.213	0.0024	4.694
318	67.5123	7.741	0.194	0.0017	5.154

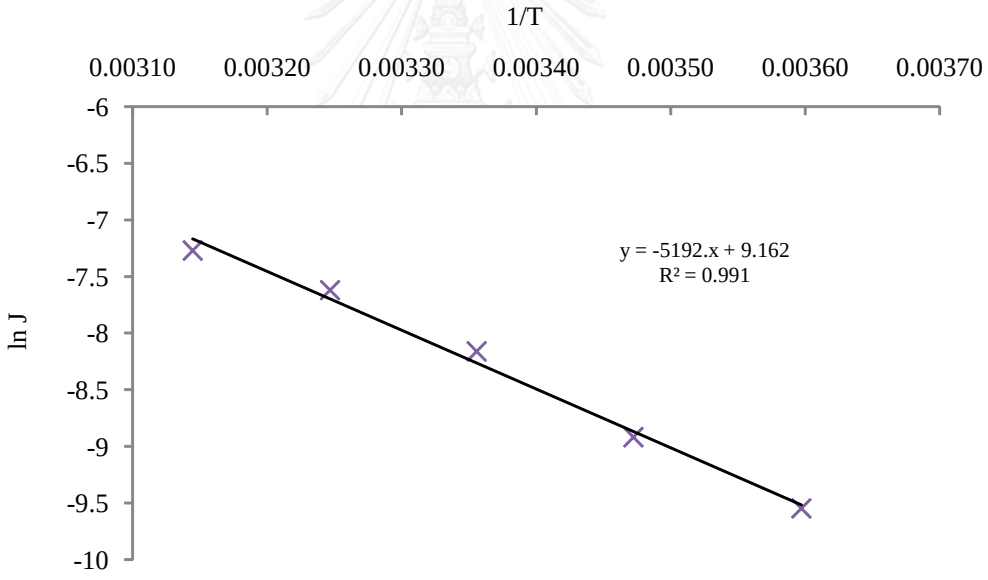


Figure 4.8 Arrhenius plot of amoxicillin transport

4.5.5 Arrhenius plot of amoxicillin transport

An Arrhenius plot of amoxicillin flux in the HFSLM system was prepared for the temperature range from 278.15 K to 318.15 K (Fig. 4.8). Clearly, the flux of amoxicillin

fitted in well with the Arrhenius model as can be confirmed by the R^2 value which was greater than 0.98. The activation energy (E_a) i.e. (44.28 kJ/mol) obtained in this study for amoxicillin extraction process was found to be greater than 40 kJ/mol; therefore implying that chemical reaction is the rate limiting step [34].

4.6 Conclusion

This work focused on the influence of temperature on mass transfer by operating across a hollow fiber membrane in a single step operation. Temperature strongly affected K_{ex}, k_f, k_m, % extraction and % stripping. Thus, temperature proved to be an influential tool for governing and adjusting the performance for the separation of amoxicillin. When temperature was increased, the percentage of extraction and stripping increased. Although temperature changes affected the mass transfer coefficients in the membrane phase as well as in the feed phase, the mass transfer coefficients in the membrane phase were found to be less than the mass transfer coefficients in the feed phase. This implied that the mass transfer in the membrane phase was the rate controlling step. The enthalpy change (24.5778 kJ/mol) and the entropy change (112.0145 J/molK) indicated that the extraction process is endothermic reaction and forward reaction, respectively. The activation energy of amoxicillin was calculated as 44.28 kJ/mol. These results demonstrated that the chemical reaction controlled process is the rate limiting step for the transport of amoxicillin across HFSLM. This indicated that temperature has a significant role on the mass transfer of amoxicillin through HFSLM.

4.7 Nomenclature

A	effective area of the hollow fiber module (cm^2)
C	concentration (mmol/L)
D	distribution ratio of amoxicillin

D	distribution ratio of amoxicillin (-)
Ea	activation energy (kJ/mol)
J	flux (mol/cm^3/min)
K_{ex}	extraction equilibrium (-)
k_f	aqueous feed mass transfer coefficient (cm/s)
k_m	organic mass transfer coefficient (cm/s)
k_s	stripping mass-transfer coefficient in the shell side
L	length of the hollow fiber (cm)
N	number of hollow fibers in the module (-)
P	permeability coefficient (cm/s)
P_m	membrane permeability (cm/s)
Q	volumetric flow rate (cm^3/s)
R_i	aqueous mass transfer resistance (s/cm)
R_m	organic membrane mass transfer resistance (s/cm)
r_i	internal radius of the hollow fiber (cm)
r_m	log-mean radius of the hollow fiber (cm)
r_o	external radius of the hollow fiber (cm)
T	Temperature (K)
t	time (min)
V_f	volume of feed phase (cm^3)
ΔG^0_{ex}	Gibbs free-energy change (J/mol)
ΔH^0_{ex}	standard enthalpy change (kJ/mol)
ΔS^0_{ex}	extraction entropy change (J/(mol-K)

Greek letters

τ	tortuosity of membrane (-)
ε	porosity of membrane (-)

Subscripts

f	feed phase
s	stripping phase
m	membrane phase
0	initial concentration

4.8 Acknowledgements

The authors gratefully acknowledge financial support given by the 90th anniversary of Chulalongkorn University Fund (Ratchadaphiseksomphot Endowment Fund) as well as the Integrated Innovation Academic Center Chulalongkorn University Centenary Academic Development Project (CU56-FW13). Thanks are again extended to the Separation Laboratory, Department of Chemical Engineering, Faculty of Engineering, Chulalongkorn University for chemical and apparatus support.

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CHAPTER 5

PERFORMANCE OF DOUBLE HFSLM ON THE REMOVING OF AMOXICILLIN USING ALIQUAT336 AS A CARRIER

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5.1 Abstract

Double hollow fiber supported liquid membrane in series containing the extractant Aliquat336 was employed for the separation of amoxicillin. Important variables affecting the transport of amoxicillin at optimum conditions were obtained at 6 mmol/L Aliquat336 in 1-decanol, pH value of 8.0, temperature of 318.15 K, feed and stripping flow rate of 100 ml/min. Thus, the highest amoxicillin extraction percentages of 95.25 and stripping percentages of 89.74 were achieved. The mass transfer coefficients of amoxicillin in the aqueous feed phase (k_i) and that in the organic membrane phase (k_m) were found to be 1.65×10^{-4} and 6.89×10^{-5}cm/s, respectively. The extraction of reaction order (n) and the reaction rate constant (k_f) were found to be 1.0 and 0.0344 min^{-1}, respectively.

Keywords: Separation; Kinetic; Aliquat336; Amoxicillin; HFSLM

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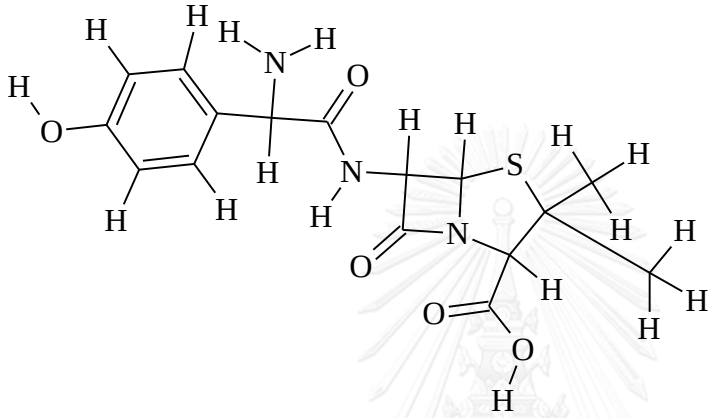
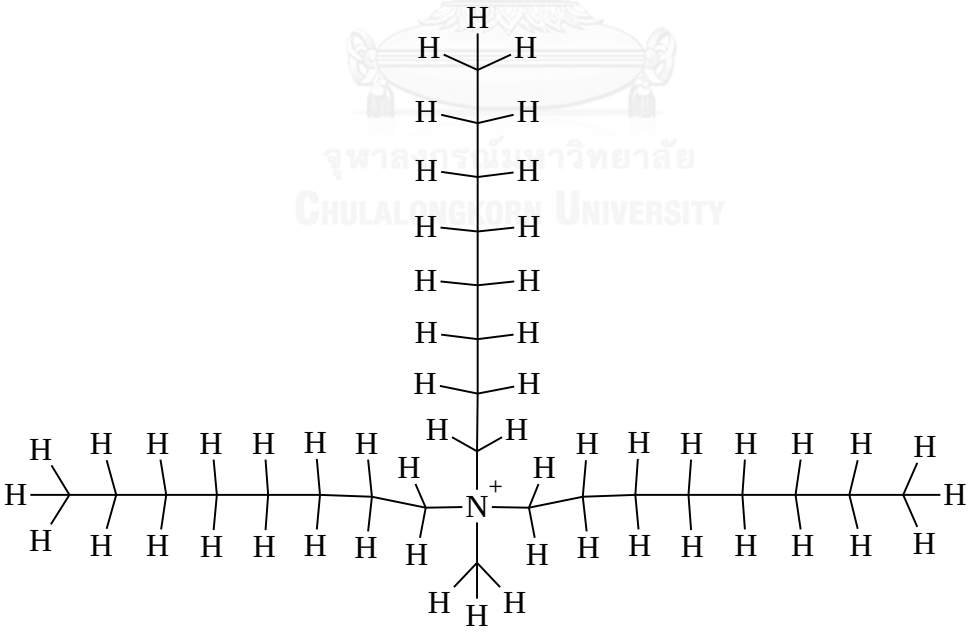
5.2 Introduction

Amoxicillin is known as one of the most important antibiotics, due to its useful ability of anti-bacterial-growth. This pharmaceutical drug is used world-wide as a treatment agent for both humans and animals. It can be used to treat many infected diseases, such as respiratory tract, skin and urinary tract [1]. Besides, it can be used as growth promoters in livestock farming and used in plant agriculture to control bacterial diseases [2]. The formula is $C_{16}H_{19}N_3O_5S$ and the molecular structure is demonstrated in Fig. 5.1 [3, 4]. Since the widespread usage of antibiotics, these substances have been

reported in various environmental samples such as in hospital liquid waste, wastewater from treatment plant, surface waters, groundwater, soil, sediment and drinking water [5]. The crucial issue about the residual antibiotics effect on the environment is the development of resistant antibiotic action which is considered a threat to the usefulness of antibacterial substances [6]. Thus conventional antibiotics will be no longer able to defeat the bacteria. The volume of amoxicillin accumulation in the environment increases every day and needs to be curtailed.



Amoxicillin [20].



Aliquat336 [21].

Figure 5.1 Structures of amoxicillin and Aliquat 336

In previous research, several methods used to separate antibiotics are shown in Table 5.1.

Recently, hollow fiber supported liquid membrane (HFSLM) has been used widely in the separation process of diluted ions from many solutions. The HFSLM system overcomes conventional methods for several reasons. It has, for example, lower energy consumption [16], lower capital and operating costs, less solvent used [17],

Table 5.1 research related to the separation of antibiotics

Author	Method	Feed Solution	Extractant/ Carrier	Solvent	% Separation
Derakhsheshpoor et al. (2013) [6]	Nanofiltration	Amoxicillin	Polysulfone membrane	-	85
Ghauch et al. (2009) [7]	microscale nanoscale	Amoxicillin, Ampicillin	Iron particle	-	80.9, 74.25
Ornelas et al. (2010) [8]	Adsorption	Amoxicillin	Activated carbon	-	NA
Shahtalebi et al. (2011) [9]	Nanofiltration	Amoxicilin in wastewaters	Polyamide spiral wound	-	97
Elmolla et al. (2011) [10]	Sequencing Batch Reactor	Amoxicillin, Cloxicillin	UV/TiO2/H2O 2	-	89
Kawasaki et al. (1996) [11]	SLM	Erythomycin	1-Decanol	-	NA
Saira et al. (2012) [12]	ELM	Cefadroxil	cyanex301	Toluene	82
Michael et al. (2009) [13]	SLM with Strip dispersion	Cephalexin	Aliquat 336	1-Decanol Isopar L	99
Naksang et al. (2013) [14]	HFSLM	Rac-phenylalanine	D2EHPA, Aliquat 336	n-octanol	98
Sunsandee et al. (2013) [15]	HFSLM	(S)-amlodipine &(R)-amlodipine	DBTA	1-Decanol	82
This Research	HFSLM	Amoxicillin	Aliquat 336	1-Decanol	95

SLM: Supported liquid membrane, ELM: Emulsion liquid membrane,

HFSLM: Hollow fiber supported liquid membrane

high surface per volume ratios causing high separation rates [18]. The modules can also be applied in series for high capacity. Consequently, the HFSLM method was chosen for this work. The focus of this study is the separation of amoxicillin at very low concentration by using counter-current flow in a double module of HFSLM which applies Aliquat336 as a carrier. The application of one module of HFSLM used in experiments is limited and therefore by connecting two modules in series extraction is increased [19]. The prime objective is to acquire the best conditions influencing the transport of amoxicillin via HFSLM. Parameter influences on transport of amoxicillin were examined viz. pH of the feed phase, amoxicillin concentrations in feed solution, extractant concentration, working temperature, operating time, the flow rate of feed solution and the flow rate of stripping solution.

5.3 Theory

5.3.1 Hollow fiber supported liquid membrane

The HFSLM system is set up as in Fig. 5.2, from which the two modules are connected in series to provide higher mass transfer area. There is a feed reservoir tank and associated pump to provide continuous feed throughput for the module. Likewise, there is a stripping reservoir tank and its pump to provide stripping solution feed in a counter flow against the feed. The modules are filled with extractant solution, acting as liquid membrane or organic phase to separate the two aqueous phases, i.e. feed and stripping phase, from contact.

5.3.2 Separation and facilitated transport mechanism of amoxicillin

The unmistakable schematic systems are the counter-transport mechanisms through HFSLM; the concentration profile for the framework is indicated in Fig. 5.3. The gradient of target ion concentration yielded high improvement components for

amoxicillin [22]. The main thrust of the procedure is the target ion concentration gradient in the aqueous feed solution and aqueous stripping solution. The mechanism of the counter-transport system HFSLM is indicated in Fig. 5.3.

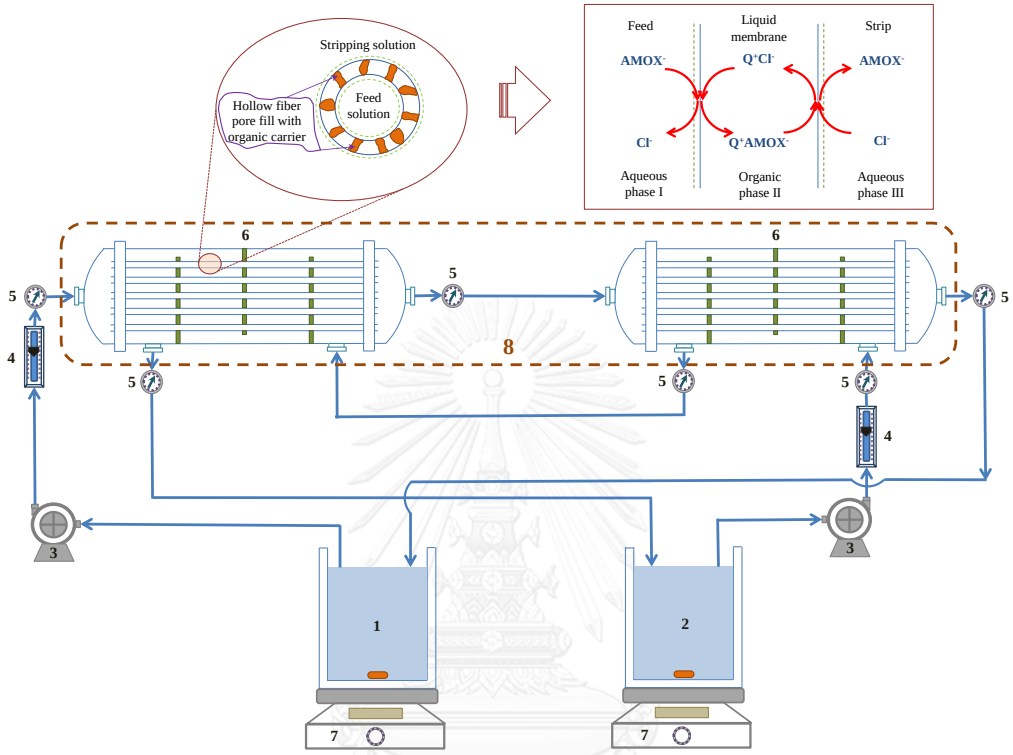


Figure 5.2 Schematic diagram for a double-module operation in the HFSLM system: 1) feed tank 2) stripping tank 3) Gear pump 4) Rota meter 5) Pressure gauge 6) Hollow fiber module 7) magnetic stirrer with temperature control and 8) temperature control box

The transport of amoxicillin through the HFSLM system is divided into the following steps.

Step 1: surface contact between the feed solution and liquid membrane solution. When amoxicillin in the feed solution moved to the affected area, it reacted with the extractant (Aliquat336-Cl) and changed to amoxicillin complex. This is called the extraction reaction as illustrated in Eq. 5.1:

$$AMOX^-_{(f)} + Q^+Cl^-_{(m)} \xleftrightarrow{k_f} [Q^+AMOX^-]_{(m)} + Cl^-_{(f)} \quad (5.1)$$

where K_{eq} is the extraction equilibrium constant, $AMOX^-$ is amoxicillin, Q^+Cl^- is an active substance of the extractant (Aliquat336), Q^+AMOX^- is the amoxicillin complex species.

Step 2: amoxicillin complex moves through the liquid membrane from the interface of the feed solution to the interface of the stripping solution; as a result of the difference in concentration which act as the driving force.

Step 3: skin contacts between the liquid membrane and the stripping solution. Chloride ions in the aqueous solution react with the amoxicillin complex and release amoxicillin into the stripping phase. This reaction is called the stripping reaction as shown in Eq. 5.2.

$$[Q^+AMOX^-]_{(m)} + Cl^-_{(s)} \xleftrightarrow{k_s} AMOX^-_{(s)} + Q^+Cl^-_{(m)} \quad (5.2)$$

Step 4: the extractant (Aliquat336) combines with chloride ions and changes to Aliquat336-Cl^-.

5.3.3 The equilibrium constants

The equilibrium constants K_{eq} relative with the extraction of amoxicillin via HFSLM are given by:

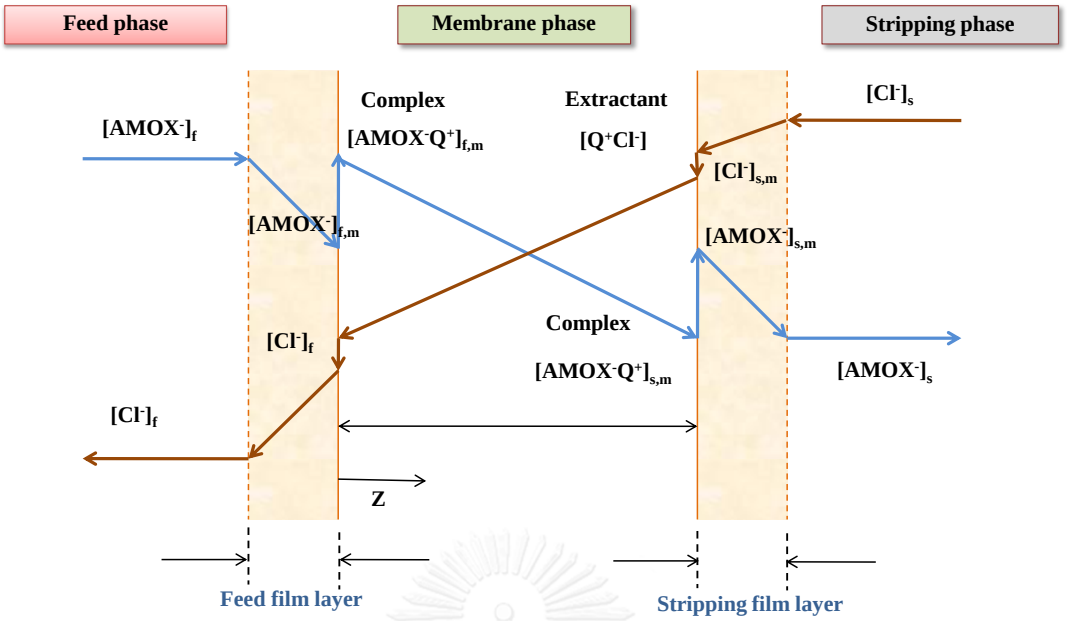


Figure 5.3 Schematic concentration profile for the system [$AMOX^-$]:amoxicillin; [Q^+Cl^-]: active substance of the carrier

$$K_{eq} = \frac{[AMOX^-Q^+][Cl^-]}{[AMOX^-][Q^+Cl^-]} \tag{5.3}$$

5.3.4 Influence of temperature on extraction equilibrium

Van't Hoff Model demonstrates the relationship between the temperature and the impact of the equilibrium extraction constant (K_{ex}) amid amoxicillin extraction. This mathematical statement likewise identifies with the standard Gibbs free-energy equation [23, 24]. The extraction is figured by Gibbs free-energy change as takes after:

$$\Delta G^0_{ex} = -RT\ln K_{ex} \tag{5.4}$$

$$\ln K_{ex} = -\frac{\Delta G^0_{ex}}{RT} \tag{5.5}$$

Gibbs free-energy change (ΔG^0_{ex}) is identified with the standard enthalpy change (ΔH^0_{ex}) and extraction entropy change (ΔS^0_{ex}) by means of Gibb-Helmholtz equation as demonstrated in Eq. (5.6):

$$\Delta G_{ex}{}^0 = \Delta H_{ex}{}^0 - T\Delta S_{ex}{}^0 \tag{5.6}$$

The Van't Hoff Model or Eq. (5.7) can be gotten by substituting Eq. (5.4) into Eq. (5.6):

$$\ln K_{ex} = -\frac{\Delta H^0_{ex}}{RT} + \frac{\Delta S^0_{ex}}{R} \tag{5.7}$$

As per Eq. (5.7), a plot between ln K_{ex} and 1/T gives a straight whose interception and slope can be utilized to focus (ΔS^0_{ex}) and (ΔH^0_{ex}) [25]. Previous works also applied similar methodology for obtaining (ΔH^0_{ex}) and (ΔS^0_{ex}) [26].

5.3.5 Percentage of extraction, percentage of recovery and standard deviation

The percentage of target ion extraction and recovery from examinations and the model were figured by Eqs. (5.8) and (5.9) individually:

$$\%Extraction = \frac{C_{in} - C_{raf}}{C_{in}} \times 100 \tag{5.8}$$

$$\%\,\mathrm{Recovery} = \frac{C_{st,out} - C_{st,in}}{C_{in}} \times 100 \tag{5.9}$$

where C_{in}, C_{raf}, $C_{st,in}$, and $C_{st,\,out}$ are inlet feed concentration, raffinate concentration, inlet concentration and outlet stripping concentration, respectively.

5.4 Experimental

5.4.1 Chemicals and reagents

Amoxicillin (pharmaceutical grade) was given by the Government Pharmaceutical Organization Thailand. Aliquat 336 (extractant) was procured from Sigma-Aldrich, United states. Analytical reagents grade including hydrochloric acid (HCl), sodium tetraborate ($Na_2B_4O_7{\cdot}10H_2O$), sodium citrate ($C_6H_7NaO_7$), citric acid ($C_6H_8O_7$), 1-decanol ($C_{10}H_{22}O$) and sodium chloride (NaCl) were obtained from Merck, Germany. All experiment were prepared the aqueous solutions with distillation water.

5.4.2 Apparatus

The hollow fiber suppored liquid membrane system which comprises of two gear pumps, two flow rate controllers, four pressure gauges and two rota meters were utilized. The hollow fiber module (Liqui-Cel® Extra-Flow module) as indicated in Fig. 5.2, was utilized as support material.

Table 5.2 Physical characteristics of the hollow fiber module (Membrana-Charlottle Company, USA)

Properties	Descriptions
Material	Polypropylene
Inside diameter of hollow fiber	240 μm
Outside diameter of hollow fiber	300 μm
Effective length of hollow fiber	15 cm
Number of hollow fibers	35,000
Average pore size	0.03 μm
Porosity	30 %

This module uses micro-porous polyethylene fibers that are woven into fabric and wrapped around a focal tube feeder that supplies the shell side liquid. Woven fabric permits more uniform fiber spacing, which thusly prompts higher mass-transfer coefficients than those got with individual fibers. The properties of the hollow fiber module are exhibited in Table 5.2.

5.4.3 Analytical instruments

The concentration of amoxicillin in feed and stripping phase was measured by utilizing HPLC (high performance liquid chromatography, Agilent 1100 series), United State of America. The data of the sample was investigated by Agilent's Chem Station version B.04.01. HPLC was finished using (5 μm, 4.6 ×150 mm) an Eclipse XDB-C18 column [27]. The column heater was kept up at 298.15 K of the column. A mixture of deionized water and methanol at 90:10 %v/v (the mobile phase) was retain at a volumetric flow rate of 1.0 mL/min and the relative retention times of amoxicillin were about 3.5 min. The pH of the solutions was measured with pH meter (Mettler), Switzerland.

5.4.4 Procedure

First, the liquid membrane is prepared by dissolving Aliquat336 in 1-deccanol. Then, it is fed into the tube and shell sides of the double HFSLM in series for 50 min [28]. This is to ensure that the carrier goes into the micro-pores of the hollow fibers. Starting there, the tube side pumped with the feed solution. At the same time, the shell side pumped with the stripping solution at counter-currently flow direction, and a circular flow pattern was situated up. The double hollow fiber modules for the extraction and recovery of amoxicillin was exhibited in Fig. 5.2.

5.5 Results and discussion

5.5.1 Effect of pH on the feed phase

The pH gradient between the feed solution and stripping solution is a basic central purpose for the extraction and stripping of amoxicillin through supported liquid membrane [29]. The effect of the pH of the feed solution on the transport of amoxicillin was carried out by changing the pH in the scope of 6.0–9.0, utilizing a stripping phase of 6.0 mmol/L sodium chloride. Phosphate buffer was used to keep up the feed phase pH as indicated by the previously mentioned range. The impact of feed phase pH on the percentage of extraction and recovery of amoxicillin through HFSLM is demonstrated in Fig. 5.4. The highest extraction of amoxicillin in the feed solution was achieved at feed pH of 8.0 reaching a maximum of 87.64%. However, the maximum percentage of recovery of amoxicillin was 80.32%.

The transport procedure presented to be well driven by the concentration gradient between the phosphate buffer and amoxicillin with pH in the scope of 6.0-8.0. Yet, transport performance decreased when the pH is higher than 8.5 [30] because the amoxicillin disintegrated.

5.5.2 Effect of initial concentration of amoxicillin in the feed phase

The impact of initial feed concentration on the transport of amoxicillin was contemplated by fluctuating the initial feed concentration in the scope of 2-10 mmol/L. The study was conducted on the condition that 6 mmol/L Aliquat336, in the presence of 1-dacanol, was used as the carrier in the liquid membrane while 6 mmol/L NaCl solution was used as the stripping

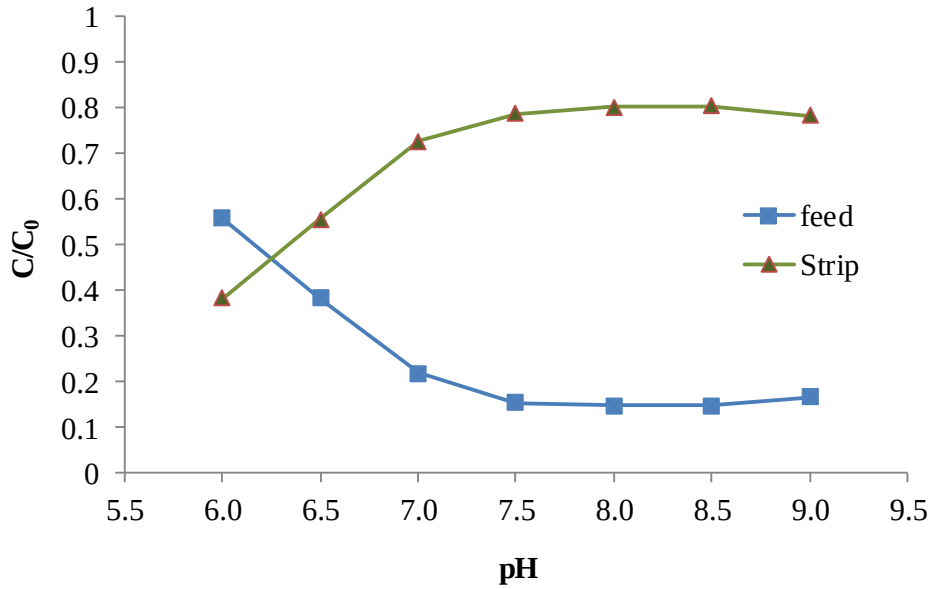


Figure 5.4 Plot of C/C_0 versus pH

solution. Fig. 5.5 demonstrates the impact of initial feed concentration on the extraction of amoxicillin. The concentration of feed solution (6 mmol/L) yielded the highest percentage extraction of amoxicillin at 85.24. However, it dropped to 76.01% at an initial feed concentration of 10 mmol/L. This could be clarified by the impact of concentration polarization [30, 31]. The concentration polarization also increases thus hindering mass transfer of system due an increase of amoxicillin in the feed.

5.5.3 Effect of carrier in the membrane phase

The concentration of carrier in the organic phase has a huge impact on the transport of amoxicillin through HFSLM. This work concentrated on the impact of the extractant in the concentration scope between 2.0 to 10.0 mmol/L. The outcomes are graphically introduced in Fig. 5.6. Results demonstrated that the concentration of amoxicillin in feed solution diminished when carrier concentration expanded: optimum concentration of carrier was 6 mmol/L. It was noted that the pattern of extraction percentage and stripping percentage diminished when the aliquat336 concentration was higher than 6 mmol/L. This could be ascribed to an increase in viscosity of the

membrane phase when Aliquat336 concentration increased [32]. As diffusivity is inversely corresponding to viscosity, an increase of liquid membrane viscosity causes the decrease of particle diffusivity.

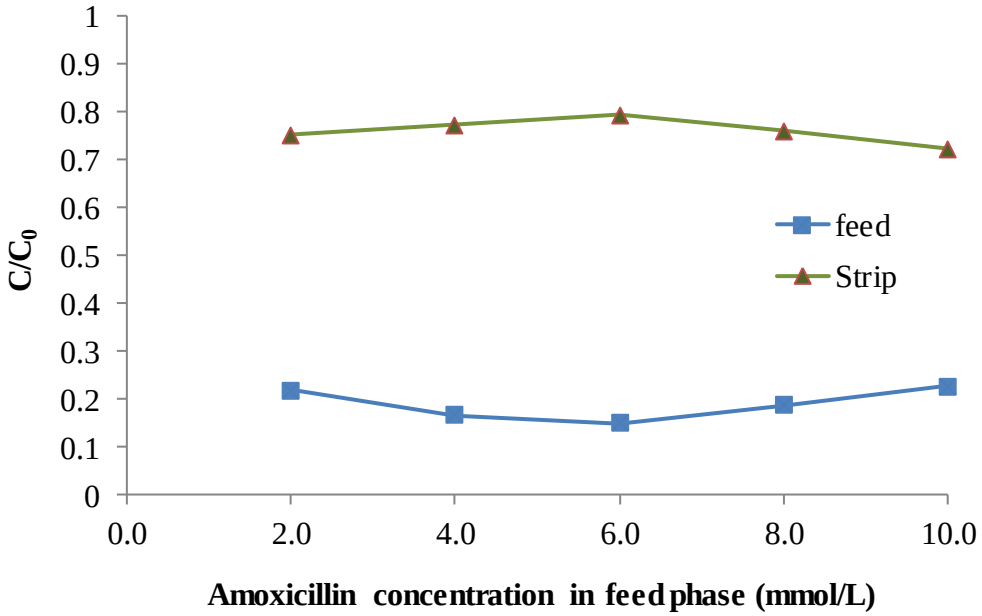


Figure 5.5 Plot of C/C0 versus amoxicillin concentration in feed phase

5.5.4 Effect of organic diluents

Organic diluents have an impact on the execution of numerous liquid membrane systems. Part of the diluent is not just to enhance the physical properties of the liquid Membrane system, but also to improve the amoxicillin complex. This needs be considered in the choice of diluents [33]. As is known from liquid membrane theory, the principle variable influencing liquid membrane stability is the type of diluent used [34]. In this study, several diluents with different polarity indexes were chosen: 1-decanol (1.8), benzene (2.7), dichloromethane (3.1), ethylene dichloride (3.5) and chloroform (4.1) [35, 36]. From Fig. 5.7, we can see the extraction percentage of the various types of organic diluents: alcohol > alkyl >halide > hexane; their performance might be related to interaction of different organic solvents with the

solute and the polarity. The relationship between the polarity of diluents and the percentage of extraction indicated that 1-decanol is a suitable organic diluent for the extraction of amoxicillin.

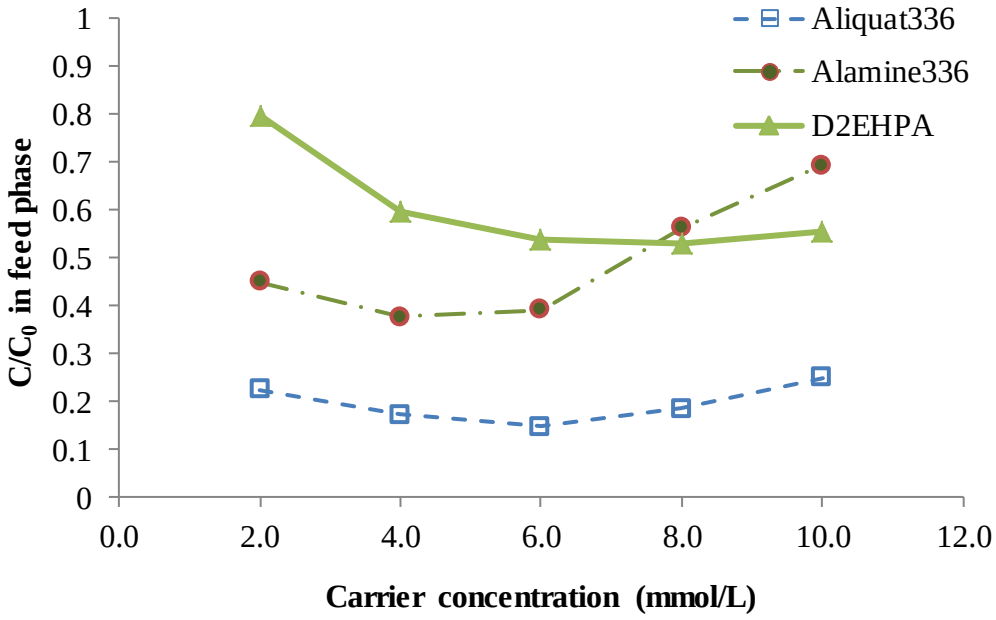


Figure 5.6 Plot of C/C0 in feed phase versus carrier concentration

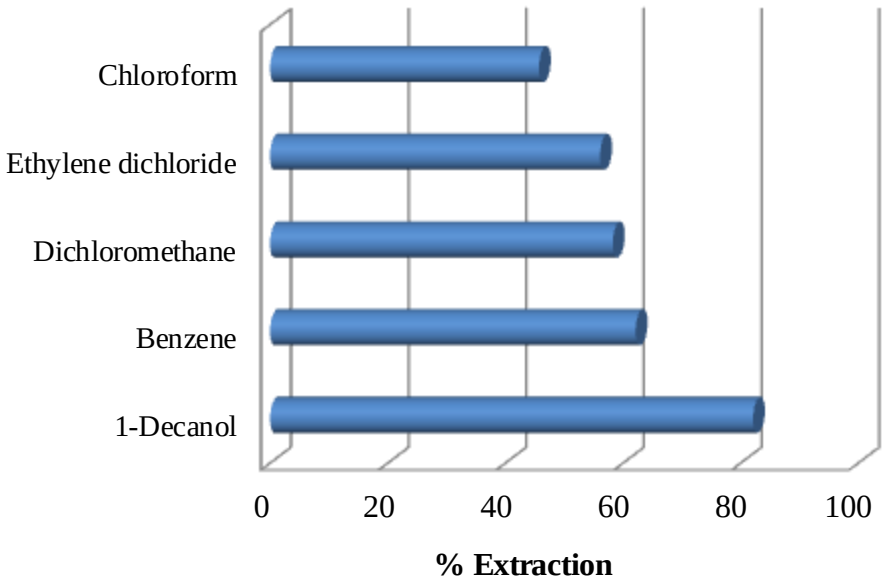


Figure 5.7 Effect of organic diluents on percentages of extraction of amoxicillin

5.5.5 Effect of operating time

The extraction and recovery of amoxicillin was accomplished at optimum conditions as follows: double hollow fiber module, 6 mmol/L Aliquat336 dissolved in 1-decanol, the pH value of 8.0, 6 mmol/L NaCl, feed phase flow rate of 100 ml/min and stripping phase flow rate of 100 ml/min. The concentration of amoxicillin in the feed solution decreased when retention time increased. In the aqueous phase, the maximum extraction of amoxicillin was attained at 100 min. as demonstrated in Fig. 5.8 below.

5.5.6 Effect of the operating temperature

The impact of temperature on the extraction and stripping of amoxicillin in terms

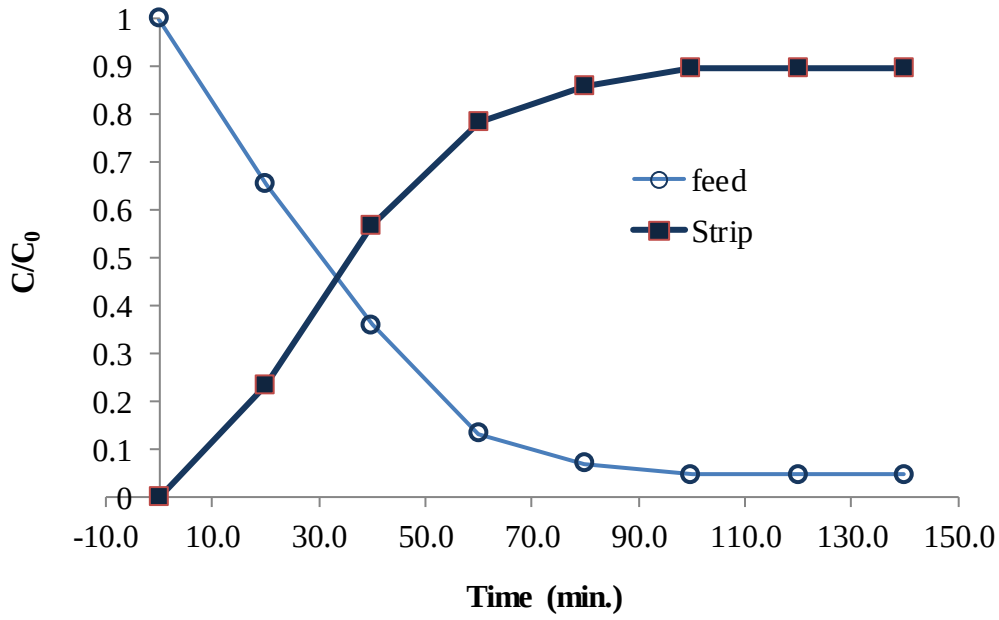


Figure 5.8 Influence of operating time on C/C_0.

of the concentration is shown as in Fig. 5.9. The HFSLM system was worked at best condition, particularly keeping up pH of 8.0, concentration of aliquat336 at 6 mmol/L, feed concentrations at 6 mmol/L, stripping concentrations at 6 mmol/L, feed flow rates at 100 mL/min and stripping flow rates at 100 mL/min and operation time 100

min. When the temperature expanded from 278.15 to 318.15 K, the concentration of amoxicillin in the feed solution was seen to decrease, consequently a decrease in viscosity of the target solution which improved the extraction [37]. Furthermore, at the higher temperature, intermolecular attractions between water molecules and the solute molecules, hydrogen bonding and van der Waal's forces were obstructed, prompting to the higher capacity of the organic extractant dissolving the amoxicillin [38]. On account of the stripping side, as temperature expanded, results demonstrated that the percentages of stripping of amoxicillin of 89.74 were acquired at 318.15 K.

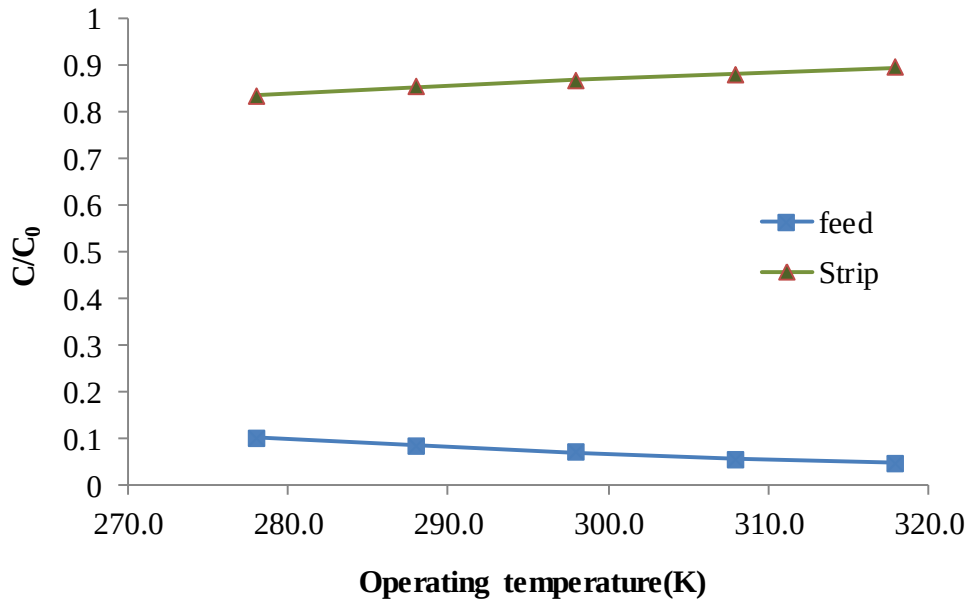


Figure 5.9 Influence of operating temperature on C/C_0.

5.5.7 Effect of temperature on enthalpy, entropy and Gibbs free-energy change

From Van't Hoff Model, Eq. (5.7), was connected to plot the straight line which then was utilized to calculate ΔH^0_{ex} (enthalpy change) and ΔS^0_{ex} (entropy change) is shown as in Fig. 5.10. The values of ΔH^0_{ex} and ΔS^0_{ex} for amoxicillin extraction were determined at 6.8614 kJ/mol and 27.6350 J/mol·K., respectively. The positive estimations of ΔH^0_{ex} demonstrated that the extraction is endothermic reaction while

the positive values of ΔS^0_{ex} implied that the extraction is forward reaction. The Gibbs free-energy change (ΔG^0_{ex}) during this procedure was computed by Eq. (5.10) providing negative values as demonstrated in Table 5.3. These results suggested that the extraction procedure was able to proceed.

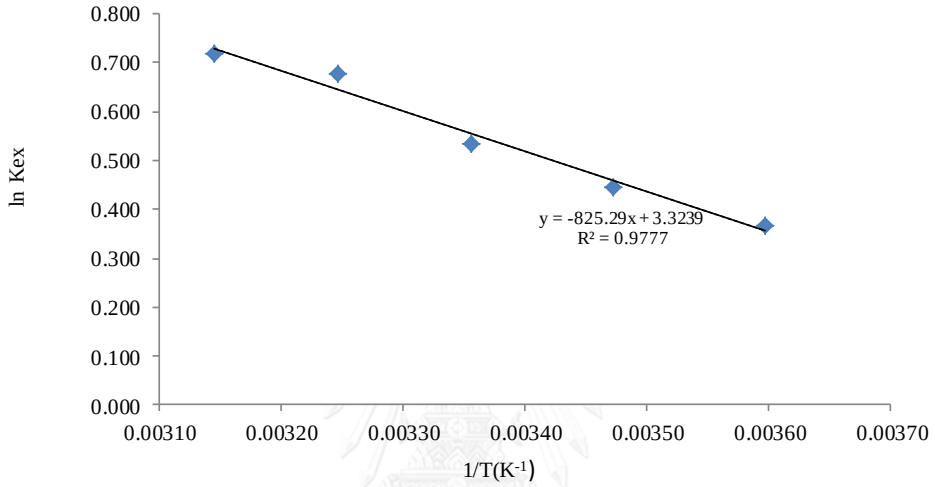


Figure 5.10 Plot of ln K_{ex} versus 1/T

Table 5.3 Thermodynamic data for amoxicillin extraction across a hollow fiber supported liquid membrane

Temperature (K)	K_{ex}	ΔG_{ex} (J/mol)	ΔH_{ex} (kJ/mol)	ΔS_{ex} (J/(mol-K))
278	1.4428	-821.04		
288	1.5598	-1,097.39		
298	1.7075	-1,373.74	6.8614	27.6350
308	1.9705	-1,650.08		
318	2.0473	-1,926.43		

5.5.8 Determination of the reaction order and the reaction rate constant for amoxicillin

The rate of chemical changes controlled the transport kinetic mechanisms through the hollow fiber membrane. The extraction of reaction rate constant ($k_{e,f}$) and the extraction of reaction order (n) for amoxicillin extraction were resolved. At optimum conditions, the integral concentrations with respect to the zero, first and second orders were plotted against time which are indicated in Table 5.4. The squared correction coefficients (R^2) exhibited the straight line of each reaction order. The outcomes indicated in Fig. 5.11, demonstrate that the straight with respect to the extraction of first-order reaction (n = 1) provided the best line fitting. The extraction of reaction rate constant ($k_{e,f}$) of 0.0344 min^{-1} for amoxicillin extraction is gotten.

Table 5.4 Values of the extraction of reaction orders (n) and the reaction rate constant ($k_{e,f}$)

n	Plot	$K_{e,f}$	R-square	Acceptability
0	C_A vs. t	0.9330 mg/L min	0.9047	No
1	$\ln(C_{A0}/C_A)$ vs. t	0.0344 min^{-1}	0.9968	Yes
2	$1/C_A$ vs. t	0.8457 L/mg·min	0.8402	No

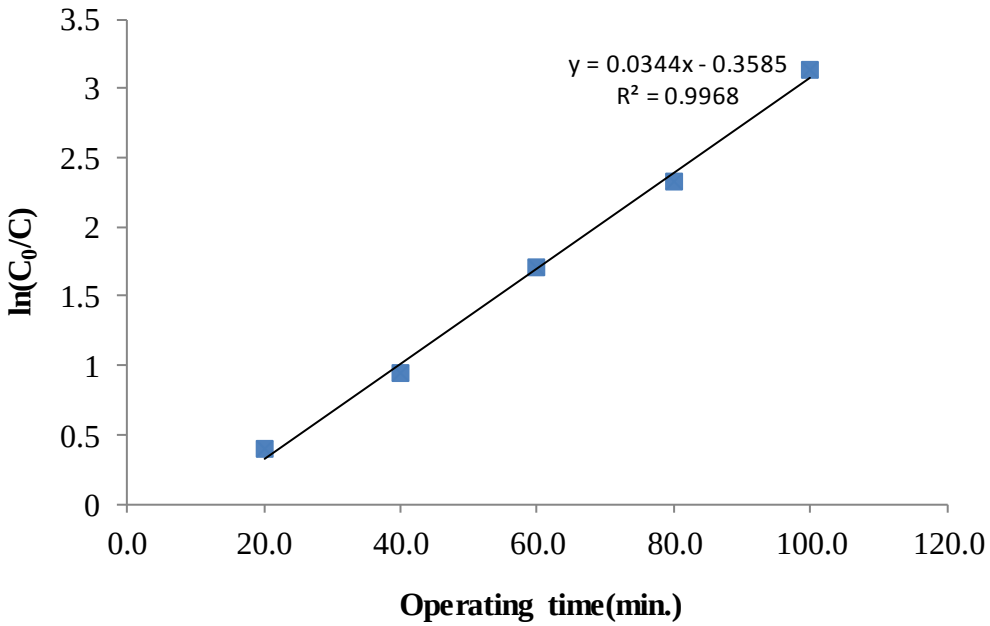


Figure 5.11 Plot of ln (C/C_0) versus operating time

At the best conditions of stripping reaction, the integral concentrations concerning the zero, first and second orders were plotted against time which are indicated in Table 5.5.

Table 5.5 Values of the stripping of reaction orders (n) and the stripping reaction rate constant ($k_{r,f}$)

n	Plot	$k_{r,f}$	R-square	Acceptability
0	C_A vs. t	0.0445 mg/L min	0.9937	Yes
1	$\ln(C_{A0}/C_A)$ vs. t	0.0134 min^{-1}	0.9526	No
2	$1/C_A$ vs. t	0.0005 L/mg·min	0.8746	No

The outcomes from the plot between integral concentration of amoxicillin complex in the organic membrane stage versus time as demonstrated in Fig. 5.12, show that the straight line with respect to the stripping of zero-order reaction (n = 0) procured the best line fitting. It demonstrates that the reaction does not rely on upon the initial concentration and increasing the initial concentration will not expand the reaction rate. The stripping of reaction rate constant ($k_{s,f}$) of 0.0445 mg/L.min for [Q^+AMOX^-] stripping reaction is obtained.

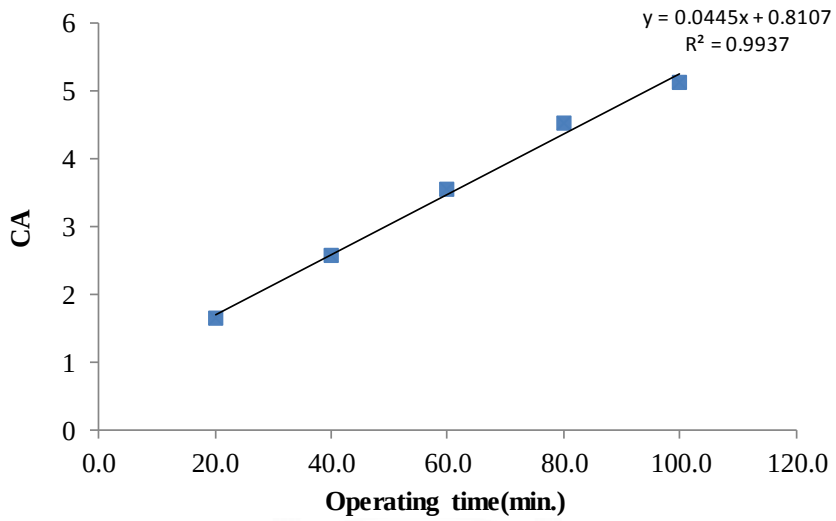


Figure 5.12 Plot of C_A versus operating time

5.5.9 Estimation of mass transfer coefficient

The fundamental mass transfer rates through the hollow fiber supported liquid membrane are the diffusion steps. They are the mass transfer coefficient of amoxicillin through the feed diffusion layer(k_i), the mass transfer coefficient of amoxicillin-carrier complexes through the organic phase (k_m), and the mass transfer coefficient of amoxicillin through the stripping diffusion layer (k_s), as indicated in Fig. 5.3. Since the stripping reaction is instantaneous, the distribution of the stripping phase will be ignored. It is essential that k_s values are very high when compared with k_i and k_s values [39]. Theoretically, laminar flow is through the tube side of the hollow fiber; hence the

mass-transfer coefficient of the aqueous feed stage (k_i) which flows in the tube side can be estimated depending on the Sherwood–Graetz dealing [40]:

$$Gz = \frac{d_i^2 \upsilon}{LD_{aq}} \tag{5.10}$$

$$Sh = mGz^n \tag{5.11}$$

$$Sh = \frac{k_i d_i}{D_{aq}} \tag{5.12}$$

where Sh is Sherwood number; Gz is Graetz numbers; d_i is the inner diameter of fiber (cm); L is the length of hollow fiber (cm); v is the linear velocity of the feed solution in the lumen side (cm/s); and D_{aq} is the diffusion coefficient of amoxicillin in the aqueous phase, which is estimated based on the Wilke–Chang equation , equal to 2.238×10^{-6} cm^2/s. Theoretically, at fast chemical reaction for a diffusion process m = 1.62, n = 0.33 expect by Leveque [41]. The estimation of k_i from Sherwood–Graetz correlation is 1.65×10^{-4} cm/s. The individual mass transfer coefficient in the membrane phase, k_m, can be approximated as follows [42]:

$$k_m = \frac{\varepsilon D_m}{\tau r_i \ln(\frac{r_o}{r_i})} \tag{5.13}$$

Where **ε** and **τ** are the porosity and tortuosity of the fiber membrane; D_m is the diffusivity of the amoxicillin–carrier complex in the membrane phase, $1.052\times10^{-6}cm^2/s$; and r_i and r_o are the inside and external radious of the fiber (cm), individually. The k_m value is estimated 6.89×10^{-5}cm/s. The mass-transfer coefficient in organic membrane (k_m) is much less than the mass-transfer coefficient in aqueous feed (k_i). From these results, the mass transfer across the membrane phase proved to be the rate control.

5.6 Conclusion

The transport of amoxicillin from synthetic feed solution via HFSLM using Aliquat336 in a double hollow fiber module in series was investigated. Amoxicillin percentages of 95.25% extraction and 89.74% recovery were achieved at 6 mmol/L Aliquat336, 6 mmol/L NaCl and temperature of 318.15 K. A compelling device for overseeing and altering the performance for the separation of amoxicillin was proved by the temperature. When the temperature was expanded, the percentage of extraction and the percentage of stripping increased. The enthalpy change (6.8614 kJ/mol) showed that the extraction process is endothermic reaction and the entropy change (27.6350 J/molK) showed that forward reaction. The first order reaction and the extraction reaction rate constant ($k_{e,f}$) 0.0344 min^{-1} were obtained. The mass transfer in the organic membrane phase was the rate controlling step due to the mass transfer coefficient in organic membrane (k_m) being much less than the mass transfer coefficient in aqueous feed phase (k_i). Therefore, the development of the HFSLM system for pharmaceutical wastewater has attracted great attention for resource conservation and environmental protection.

5.7 Acknowledgements

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5.8 Nomenclature

C_{in} : concentrations of feed (mmol/L)

C_{raf} : concentrations of raffinate (mmol/L)

$C_{st,\,out}$: concentrations of outlet strip (mmol/L)

$C_{st,in}$: concentrations of inlet strip (mmol/L)

d : diameter [m]

D_{aq} : aqueous diffusion coefficient of the t salt [m^2s^{-1}]

D_m : diffusion coefficient through in liquid membrane [m^2s^{-1}]

Gz : Graetz numbers

K_{eq} : the extraction equilibrium constant

k_i : mass transfer coefficient of the feed phase [m s^{-1}]

k_m : mass transfer coefficient of the membrane phase [m s^{-1}]

k_s : mass transfer coefficient of the stripping phase [m s^{-1}]

L : length of fiber [m]

n : reaction order

r_i : inner radius of the fiber [m]

r_o : outer radius of the fiber [m]

Sh : Sherwood number

t : time (min)

v : linear velocity of the feed solution in the lumen side (cm/s)

ΔG^0_{ex} : Gibbs free-energy change (J/mol)

ΔH^0_{ex} : standard enthalpy change (kJ/mol)

ΔS^0_{ex} : extraction entropy change (J/(mol-K)

Greek letters

τ : tortuosity of membrane (-)

ε : porosity of membrane (-)

Subscripts

f : feed phase

s : stripping phase

m : membrane phase

0 : initial concentration

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CHAPTER 6
CONCLUSION

6.1 Conclusion

This work shows that amoxicillin can be separated via a hollow fiber supported liquid membrane (HFSLM) system using Aliquat336 as a carrier. Temperature and a double hollow fiber module proved to be persuasive for overseeing and altering the execution for the separation of amoxicillin from synthetic wastewater. Optimum conditions affecting the transport of amoxicillin using double modules were obtained at 6 mmol/L Aliquat336 dissolved in 1-decanol, pH value of 8.0, temperature of 318.15 K, feed solution flow rates of 100 ml/min and stripping solution flow rates of 100 ml/min. It was noted that percentages of amoxicillin as regards extraction and stripping reached 95.25% and 89.74 %, respectively. Mass-transfer coefficients of amoxicillin in the feed phase (k_i) and mass-transfer coefficients of amoxicillin in the organic membrane phase (k_m) were found to be 1.65×10−4 and 6.89×10−5cm/s. The extraction reaction order (n) and the reaction rate constant (k_f) were 1.00 and 0.0344 min^{-1}. The positive values of enthalpy change (ΔH^0_{ex}= 6.8614 kJ/mol) demonstrated that endothermic reaction of amoxicillin extraction while the values of entropy change (ΔS^0_{ex}= 27.6350 J/mol·K) indicated that the extraction process is forward reaction. The negative value of Gibbs free-energy change (ΔG^0_{ex}) implied that the extraction reaction was able to proceed. The activation energy (E_a) of amoxicillin was calculated to be 44.28 kJ/ mol (one module). A reaction flux model was used to calculate the outlet amoxicillin concentration and ended up being in great concurrence with the experimental data.

In this study, the first experiment presents a new approach by using Di-(2-ethylhexyl) phosphoric acid (D2EHPA) diluted in kerosene as an extractant in order to separate cobalt and manganese ions from sulphate media via the hollow fiber supported liquid

membrane (HFSLM) system as presented in Chapter II. Not only were the extraction and stripping of cobalt and manganese ions from sulphate media by multi module HFSLM investigated, but a reaction flux model was used to predict outlet concentration and the model results were compared with the experimental data. At pH value of the feed phase of 5, 100 ppm [Co(II)] and [Mn(II)], the concentration of 5% (v/v) for the carrier [D2EHPA], 0.2M HCl and 3 hollow fiber modules, the highest extraction percentage of Mn^{2+} and Co^{2+} wer found to be 98.14%, and 94.05%, respectively. Reaction order (n) was found to be 1.00 and the reaction rate constant (k_f) was found to be 1 0.0180 min^{-1}. Besides, the reaction flux model turned out to be in great concurrence with the experimental data at an average deviation of 2.24%.

In Chapter III, a second experiment was presented. Separation experiments of amoxicillin via HFSLM were performed under various operating conditions to find the optimal parameters. The latter were applied to separate amoxicillin in order to attain high yields from an initial concentration of feed phase of 6 mmol/L, the concentration of extractant (Aliquat 336) of 6 mmol/L, feed solution flow rate of 100 mL/min and stripping solution flow rate of 100 mL/min. Amoxicillin extraction percentage reached 85.21 and stripping percentage reached and 80.34. Besides, the feed phase mass transfer coefficient (k_f) was reported 3.57×10^{-2} cm/s and the membrane phase mass transfer coefficient (k_m) was reported to be 0.70×10^{-2} cm/s. In addition, a mathematical model was developed to predict the outlet concentration of amoxicillin at each times. The results demonstrated good consent between the experimental and calculated data.

In Chapter IV, the extraction and stripping of amoxicillin, in a temperature range from 278.15 K to 318.15 K via the HFSLM system, were investigated. The mass transfer parameters and thermodynamic parameters were also reported. At pH of feed 8.0, 6 mmol/L [amoxicillin], 6 mmol/L [Aliquat336], 6 mmol/L [NaCl] and 318.15 K, the highest percentage of amoxicillin extraction reached 89.65%. The mass transfer coefficients of amoxicillin in the aqueous feed phase (k_f) and the mass transfer coefficients of amoxicillin in the organic membrane phase (k_m) were found to be 5.154 and 0.546 cm/s, respectively. The positive estimations of enthalpy change (ΔH)

demonstrated that amoxicillin extraction is endothermic reaction and the positive estimations of entropy change inferred that the extraction procedure is forward reaction. Furthermore, the activation energy (E_a) of amoxicillin extraction was found to be 44.28 kJ/mol. This implied that the chemical reaction was the mass transfer controlling step.

In Chapter V, the novel application of the double modules of the HFSLM system for extraction and stripping of amoxicillin was presented. This proved to be most effective because the percentage of extraction of amoxicillin increased compared with one module increasing from 89.74 to 95.25% (Chapter III). In the study, important parameters affecting the transport of amoxicillin at optimum conditions were obtained at 6 mmol/L Aliquat336 in 1-decanol, pH value of 8.0, temperature of 318.15 K, feed solution flow rate of 100 ml/min and stripping solution flow rate of 100 ml/min. The mass-transfer coefficients of amoxicillin in the aqueous feed phase (k_i) was found to be 1.65×10^{-4} cm/s and the mass-transfer coefficients of amoxicillin in the organic membrane phase (k_m) was found to be 6.89×10^{-5}cm/s. The extraction reaction order (n) was found to be 1.0. The reaction rate constant (k_f) was found to be 0.0344 min^{-1}.

6.2 Limitations of dissertation

1. Amoxicillin is an organic structure and has low stability. When conditions change such as light, temperature or pH etc.it can change or decompose easily.

2. All experiments should contain the pH of feed and stripping solution because they have a direct impact on the product.

3. An analysis of amoxicillin by HPLC has high accuracy, but it should be careful of contamination by other substances e.g. oil.

4. Extraction and stripping of amoxicillin via the HFSLM system is slow. Continuous mode run is not recommended.

5. Kinetic and mass transfer model can predict many parameters only when run in circulating mode.

6. The extractant in each experiment can only be used 3 times because it is lost in the cleanup process.

6.3 Recommendations for future research

1. The separation process should be applied to industrial wastewater and analysis of amoxicillin by UV Spectrophotometry because it is low cost and easy to analyze contamination substances.

2. The separation of amoxicillin should be run via HFSLM with a strip dispersion system because this increases stability and extends the useful life of the extractant.

3. The separation process should be applied to extract and recover other antibiotics.

APPENDIX

Diffusion flux model

Diffusion flux model is developed for estimate the outlet concentration of amoxicillin in the feed solution. Modeling of the diffusive mass transport flux is performed under the following assumptions:

a) The system is considered to be at a pseudo-steady state.

b) The extraction reaction takes place at the interface between the aqueous solution and the liquid membrane. The influence of the interface curvature in the mass transfer rate can be considered negligible.

c) No solute transport occurs through the non-porous parts of the membrane.

d) The solubility of both fluids in each other is negligible.

e) Mass transfer is described by simple film-type mass-transport coefficients.

Flux of Amoxicillin through the feed boundary layer (J_f) is

$$J_f R_f = [Amoxicillin]_{f,0} - [Amoxicillin]_{f,m} \quad (1)$$

Flux of a complex species through liquid membrane phase (J_m) is

$$J_m R_m = \overline{[\text{Amoxicillin}]}_{m,f} - \overline{[\text{Amoxicillin}]}_{m,s}$$

or

$$J_m R_m = \overline{[\text{QAmoxicillin}]}_{m} - \overline{[\text{Amoxicillin}]}_{m,s} \quad (2)$$

$\overline{[Amoxicillin]}_{m,s}$ is neglected, thus, Eq. (2) is

$$J_m R_m = \overline{[\text{Q}\,Amoxicillin]}_{m} \quad (3)$$

The equilibrium constant (K_{ex}) is

$$K_{ex} = \frac{[Amoxicillin]_{m,f}[Cl^-]}{[\overline{QCl}\ ]\ [Amoxicillin]_{f,m}} \quad (4)$$

$$[Amoxicillin]_{m,f} = \frac{K_{ex}[Amoxicillin]_{f,m}[\overline{QCl}]}{[Cl^-]} \quad (5)$$

Substitute Eq. (5) in Eq. (3):

$$J_m R_m = \frac{K_{ex}[Amoxicillin]_{f,m}[\overline{QCl}]}{[Cl^-]} \quad (6)$$

$$[Amoxicillin]_{f,m} = \frac{J_m R_m [Cl^-]}{K_{ex}[\overline{QCl}]} \quad (7)$$

Substitute Eq. (7) in Eq. (1):

$$J_f R_f = [Amoxicillin]_{f,0} - \frac{J_m R_m [Cl^-]}{K_{ex}[\overline{QCl}]} \quad (8)$$

$$J_f R_f = \frac{[Amoxicillin]_{f,0} K_{ex}[\overline{QCl}] - J_m R_m [Cl^-]}{K_{ex}[\overline{QCl}]} \quad (9)$$

$$J_f R_f K_{ex}[\overline{QCl}] = [Amoxicillin]_{f,0} K_{ex}[\overline{QCl}] - J_m R_m [Cl^-] \quad (10)$$

$$J_f R_f K_{ex}[\overline{QCl}] + J_m R_m [Cl^-] = [Amoxicillin]_{f,0} K_{ex}[\overline{QCl}] \quad (11)$$

Under the pseudo-steady-state assumption:

$$J = J_f = J_m \tag{12}$$

Thus, rewrite Eq. (11):

$$J(R_f K_{ex}[\overline{QCl}] + R_m[Cl^-]) = [Amoxicillin]_{f,0} K_{ex}[\overline{QCl}] \tag{13}$$

$$J = \frac{K_{ex}[\overline{QCl}]\,[Amoxicillin]_{f,0}}{R_f K_{ex}[\overline{QCl}] + R_m[Cl^-]} \tag{14}$$

Let

$$[\overline{QCl}]_0 = [\overline{QCl}]_{free} + [Amoxicillin]_{m,f} \tag{15}$$

At low concentration of Aliquat336, all of Aliquat336 will react with Amoxicillin. Thus, Eq. (15) can be rewritten as:

$$[\overline{QCl}]_0 = [Amoxicillin]_{m,f} \tag{16}$$

Substitute Eq. (16) in Eq. (5):

$$[\overline{QCl}]_0 = \frac{K_{ex}[Amoxicillin]_{f,m}[\overline{QCl}]}{[Cl^-]} \tag{17}$$

$$[\overline{QCl}] = \frac{[\overline{QCl}]_0[Cl^-]}{K_{ex}[Amoxicillin]_{f,m}} \tag{18}$$

Substitute Eq. (18) in Eq. (14):

$$J = \frac{K_{ex}\dfrac{[\overline{QCl}]_0[Cl^-]}{K_{ex}[Amoxicillin]_{f,m}}[Amoxicillin]_{f,0}}{R_f K_{ex}\dfrac{[\overline{QCl}]_0[Cl^-]}{K_{ex}[Amoxicillin\ ]_{f,m}} + R_m[Cl^-]} \tag{19}$$

$$J = \frac{\dfrac{[\overline{QCl}]_0[Cl^-]}{[Amoxicillin]_{f,m}}[Amoxicillin]_{f,0}}{\dfrac{R_f[\overline{QCl}]_0[Cl^-] + R_m[Cl^-]\ [Amoxicillin]_{f,m}}{[Amoxicillin\ ]_{f,m}}} \tag{20}$$

$$J = \frac{[\overline{QCl}]_0[Cl^-]\ [Amoxicillin]_{f,0}}{R_f[\overline{QCl}]_0[Cl^-]\ + R_m[Cl^-]\ [Amoxicillin]_{f,m}} \tag{21}$$

$$J = \frac{[\overline{QCl}]_0[Cl^-]\ [Amoxicillin]_{f,0}}{(R_f[\overline{QCl}]_0 + R_m[Amoxicillin]_{f,m})[Cl^-]} \tag{22}$$

$$J = \frac{[\overline{QCl}]_0[Amoxicillin]_{f,0}}{(R_f[\overline{QCl}]_0 + R_m[Amoxicillin]_{f,m})} \tag{23}$$

Rewrite Eq. (1) to determine $[Amoxicillin]_{f,m}$:

$$[Amoxicillin]_{f,m} = [Amoxicillin]_{f,0} - J_f R_f \tag{24}$$

Substitute Eq. (24) in Eq. (23):

$$J = \frac{[\overline{QCl}]_0 [Amoxicillin]_{f,0}}{R_f [\overline{QCl}]_0 + R_m ([Amoxicillin]_{f,0} - R_f J_f)} \quad (25)$$

$$J = \frac{[\overline{QCl}]_0 [Amoxicillin]_{f,0}}{R_f [\overline{QCl}]_0 + R_m [Amoxicillin]_{f,0} - R_m R_f J_f} \quad (26)$$

$$J(R_f [\overline{QCl}]_0 + R_m [Amoxicillin]_{f,0} - R_m R_f J_f) = [\overline{QCl}]_0 [Amoxicillin]_{f,0} \quad (27)$$

When $J = J_f$;

$$R_f [\overline{QCl}]_0 J + R_m [Amoxicillin]_{f,0} J - R_m R_f J^2 - [\overline{QCl}]_0 [Amoxicillin]_{f,0} = 0 \quad (28)$$

$$-R_m R_f J^2 + (R_m [Amoxicillin]_{f,0} + R_f [\overline{QCl}]_0) J - [\overline{QCl}]_0 [Amoxicillin]_{f,0} = 0 \quad (29)$$

$$R_m R_f J^2 - (R_m [Amoxicillin]_{f,0} + R_f [\overline{QCl}]_0) J + [\overline{QCl}]_0 [Amoxicillin]_{f,0} = 0 \quad (30)$$

Rewrite Eq. (30) into a quadratic equation:

$$J = \frac{R_m [Amoxicillin]_{f,0} + R_f [\overline{QCl}]_0 \pm \sqrt{\left(R_m [Amoxicillin]_{f,0} + R_f [\overline{QCl}]_0\right)^2 - 4R_f R_m [\overline{QCl}]_0 [Amoxicillin]_{f,0}}}{2R_f R_m} \quad (31)$$

Let

$$\sqrt{\left(R_m [Amoxicillin]_{f,0} + R_f [\overline{QCl}]_0\right)^2 - 4R_f R_m [\overline{QCl}]_0 [Amoxicillin]_{f,0}} << R_m [\text{Amoxicillin}]_{f,0} + R_f [\overline{QCl}]_0$$

Thus, Eq. (31) becomes

$$J = \frac{R_m [Amoxicillin]_{f,0} + R_f [QCl]_0}{2R_f R_m} \quad (32)$$

$$J = \frac{[Amoxicillin]_{f,0}}{2R_f} + \frac{[\overline{QCl}]_0}{2R_m} \tag{33}$$

The mass balance of Amoxicillin in feed phase in the case of diffusion transport regime is

$$J = -\frac{d[Amoxicillin]_{f,0}}{dt}\frac{V_f}{A} \tag{34}$$

Substitute Eq. (34) in Eq. (33):

$$-\frac{d[Amoxicillin]_{f,0}}{dt}\frac{V_f}{A} = \frac{[Amoxicillin]_{f,0}}{2R_f} + \frac{[\overline{QCl}]_0}{2R_m} \tag{35}$$

$$-\frac{d[Amoxicillin]_{f,0}}{dt}\frac{V_f}{A} = \frac{2R_m[Amoxicillin]_{f,0} + 2R_f[\overline{QCl}]_0}{4R_fR_m} \tag{36}$$

$$-\frac{d[Amoxicillin]_{f,0}}{dt}\frac{V_f}{A} = \frac{2(R_m[Amoxicillin]_{f,0} + R_f[\overline{QCl}]_0)}{4R_fR_m} \tag{37}$$

$$-\frac{2R_fR_mV_f}{A}\frac{d[Amoxicillin]_{f,0}}{dt} = R_m[Amoxicillin]_{f,0} + R_f[\overline{QCl}]_0 \tag{38}$$

$$\frac{d[Amoxicillin]_{f,0}}{R_m[Amoxicillin]_{f,0} + R_f[\overline{QCl}]_0} = -\frac{A}{2R_fR_mV_f}dt \tag{39}$$

$$\int_{[Amoxicillin]_{f(0)}}^{[Amoxicillin]_{f(t)}} \frac{d[Amoxicillin]_{f,0}}{R_m[Amoxicillin]_{f,0} + R_f[\overline{QCl}]_0} = \frac{-A}{2R_f R_m V_f}\int_0^t dt \tag{40}$$

$$\frac{1}{R_m}(\ln\frac{R_m[Amoxicillin]_{f(t)} + R_f[QCl]_0}{R_m[Amoxicillin]_{f(0)} + R_f[QCl]_0}) = \frac{-A}{2R_f R_m V_f}t \tag{41}$$

$$R_m[Amoxicillin]_{f(t)} + R_f[\overline{QCl}]_0 = (R_m[Amoxicillin]_{f(0)} + R_f[\overline{QCl}]_0)\cdot\exp\left(\frac{-A}{2R_f V_f}t\right) \tag{42}$$

$$R_m[Amoxicillin]_{f(t)} = -R_f[\overline{QCl}]_0 + (R_m[Amoxicillin]_{f(0)} + R_f[\overline{QCl}]_0)\cdot\exp\left(\frac{-A}{2R_f V_f}t\right) \tag{43}$$

$$[Amoxicillin]_{f(t)} = -\frac{R_f[\overline{QCl}]_0}{R_m} + \left([Amoxicillin]_{f(0)} + \frac{R_f[QCl]_0}{R_m}\right)\cdot\exp\left(\frac{-A}{2R_f V_f}t\right) \tag{44}$$

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VITA

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