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EXTRACTION AND RECOVERY OF RACEMIC AMLODIPINE VIA  
HOLLOW FIBER SUPPORTED LIQUID MEMBRANE

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A Dissertation Submitted in Partial Fulfillment of the Requirements  
for the Degree of Doctor of Engineering Program in Chemical Engineering

Department of Chemical Engineering

Faculty of Engineering

Chulalongkorn University


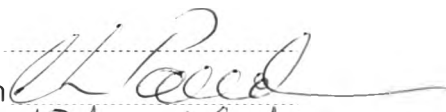
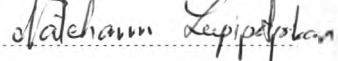
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ด้วยเส้นใยกลวง. (EXTRACTION AND RECOVERY OF RACEMIC  
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งานวิจัยนี้ศึกษาการสกัดและนำกลับราชิมิกแอม โลดีป็นจากสารละลายป้อนซึ่งคือ  
น้ำเสียจากกระบวนการสังเคราะห์ทางเคมีของอุตสาหกรรมเภสัชกรรมด้วยเยื่อแผ่นเหลวที่พุง  
ด้วยเส้นใยกลวง (HFSLM) ปัจจัยที่ศึกษา ได้แก่ ความเป็นกรด-เบส และความเข้มข้นของ  
ราชิมิกแอม โลดีป็นในสายละลายป้อน ชนิดของสารสกัด (สารสกัดที่เป็นไครัล (+)-DBTA  
สารสกัดที่ไม่เป็นไครัล D2EHPA และสารสกัดแบบเสริมฤทธิ์ระหว่าง (+)-DBTA และ  
D2EHPA) ความเข้มข้นของสารสกัด ชนิดของตัวทำละลายอินทรีย์ ชนิดและความเข้มข้นของ  
สารละลายนำกลับ (กรดเบนซีนซัลโฟนิค และเบต้า-ไซโคลเดกซ์ทริน) และอัตราการไหลของ  
สารละลายป้อนและสารละลายนำกลับ กำหนดการไหลของสารละลายป้อนและสารละลาย  
นำกลับแบบสวนทางกันที่อัตราการไหลเท่ากัน จากผลการทดลองพบว่าเมื่อใช้สารสกัดแบบ  
เสริมฤทธิ์ (+)-DBTA 4 mM กับ D2EHPA 4 mM ที่อัตราส่วน 1 ต่อ 1 (v/v) ละลายใน  
1-decanol ค่าความเป็นกรด-เบสของสารละลายป้อนเท่ากับ 5 โดยใช้เบต้า-ไซโคลเดกซ์ทริน  
เป็นสารละลายนำกลับ และอัตราการไหลของสารละลายป้อนและสารละลายนำกลับเท่ากับ  
100 มล./นาที่ สามารถสกัดเอส-แอม โลดีป็นแบบคัดเลือกและนำกลับได้สูงสุดที่ร้อยละ 84  
และ 80 ตามลำดับ ความบริสุทธิ์ของเอส-แอม โลดีป็นที่ได้ในเทอมของ enantiomeric excess  
(% e.e.) เท่ากับ 70% สัมประสิทธิ์การถ่ายเทมวลในสารละลายป้อน ( $k_p$ ) และใน  
เยื่อแผ่นเหลว ( $k_m$ ) ที่คำนวณได้เท่ากับ  $4.87 \times 10^{-2}$  และ  $2.89 \times 10^{-2}$  ซม./วินาที ตามลำดับ  
กล่าวได้ว่าการแพร่ของสารประกอบเชิงซ้อนของเอส-แอม โลดีป็นผ่านเยื่อแผ่นเหลวเป็น  
ขั้นตอนที่ควบคุมอัตราการถ่ายเทมวล (mass-transfer controlling step) และเมื่อศึกษาผลของ  
อุณหภูมิต่อการสกัดได้ค่าพลังงานกระตุ้นของปฏิกิริยาการสกัดเอส-แอม โลดีป็น  
71.10 กิโลจูล/โมล ซึ่งสูงกว่า 40 กิโลจูล/โมล แสดงว่าการสกัดและนำกลับเอส-แอม โลดีป็น  
ผ่าน HFSLM ถูกควบคุมโดยปฏิกิริยาการสกัด (chemical reaction controlled process)  
นอกจากนี้สามารถใช้แบบจำลองการถ่ายเทมวลคำนวณความเข้มข้นของเอส-แอม โลดีป็นใน  
สารละลายป้อนที่ผ่านการสกัด พบว่ามีความคลาดเคลื่อนกับผลการทดลองเพียง 2%

ภาควิชา วิศวกรรมเคมี ลายมือชื่อนิติ   
สาขาวิชา วิศวกรรมเคมี ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์หลัก   
ปีการศึกษา 2555 ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์ร่วม 

# # 5271812521 : MAJOR CHEMICAL ENGINEERING

KEYWORDS : AMLODIPINE / EXTRACTION / RECOVERY / SELECTIVE SEPARATION / HOLLOW FIBER SUPPORTED LIQUID MEMBRANE

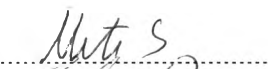
NITI SUNSANDEE : EXTRACTION AND RECOVERY OF RACEMIC AMLODIPINE VIA HOLLOW FIBER SUPPORTED LIQUID MEMBRANE. ADVISOR : ASSOC. PROF. URA PANCHAREON, D.Eng.Sc., CO-ADVISOR : ASST. PROF. NATCHANUN LEEPIPATPIBOON, Dr.rer.nat., 257 pp.

The extraction and recovery of racemic amlodipine from chemical synthesis-based pharmaceutical wastewater as a feed solution via a hollow fiber supported liquid membrane (HFSLM) was studied. The pH and concentration of racemic amlodipine in the feed solution, types of extractants (chiral (+)-DBTA, achiral extractants D2EHPA and the synergistic extractant of (+)-DBTA and D2EHPA), concentrations of the extractants, types of the organic solvents, types and concentrations of the stripping solutions (benzenesulfonic acid and  $\beta$ -cyclodextrin), and the flow rates of feed and stripping solutions were investigated. The feed and stripping solutions at equal flow rates flowed counter-currently in a batch operation. By using the synergistic extraction of chiral-to-achiral mixture (4 mM (+)-DBTA and 4 mM D2EHPA) at equal volumes of 1:1 dissolved in 1-decanol, the feed solution of pH 5.0,  $\beta$ -cyclodextrin as the stripping solution and equal flow rates of feed and stripping solutions of 100 ml/min, it was exhibited that the highest percentages of extraction and stripping were 84 and 80%, respectively, and the enantiomeric excess (% e.e.) of (*S*)-amlodipine of approximately 70% was observed. The aqueous-phase mass-transfer coefficient ( $k_f$ ) in the feed solution and the organic-phase mass-transfer coefficient ( $k_m$ ) in liquid membrane were  $4.87 \times 10^{-2}$  and  $2.89 \times 10^{-2}$  cm/s, respectively, indicating that the diffusion of (*S*)-amlodipine complex through the liquid membrane was the mass-transfer controlling step. According to the investigation of the effect of temperature on the extraction of racemic amlodipine, the activation energy ( $E_a$ ) of the (*S*)-amlodipine extraction reaction was found to be 71.10 kJ/mol. In particular, the  $E_a$  greater than 40 kJ/mol indicating that the extraction and recovery of (*S*)-amlodipine through the HFSLM were controlled by the chemical reaction. Furthermore, by using a mathematical model, the concentration of (*S*)-amlodipine in the feed solution with time can be estimated. The modeled values were found to be in good agreement with the experimental results with the average deviation of approximately 2 %.

Department : ..... Chemical Engineering .....

Field of Study : ..... Chemical Engineering .....

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Student's Signature .....  .....

Advisor's Signature .....  .....

Co-advisor's Signature .....  .....

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## LIST OF ABBREVIATIONS

$A$	effective area of hollow fiber ( $\text{cm}^2$ )
$A, B, C$	constant parameters in the correlated modified Apelblat model
$A.D.$	absolute relative deviation (%)
$A.A.D.$	average absolute relative deviation (%)
$C$	concentration ( $\text{mmol/L}$ )
$c$	calculated result
$D$	density of solvent ( $\text{g/mL}$ )
$D_R$	distribution ratio of ( $R$ )-amlodipine (-)
$D_S$	distribution ratio of ( $S$ )-amlodipine (-)
$e$	experimental data
$f$	feed phase
$\Delta_m H_a^f$	molar enthalpy of fusion ( $\text{kJ/mol}$ )
$H$	constant parameters in the correlated $\lambda H$ model
$H.c.$	$\lambda H$ model calculated result
$i$	inter phase
$J$	flux ( $\text{mol/cm}^3/\text{min}$ )
$K_1$	constant parameters in the empirical formula model
$K_2$	constant parameters in the empirical formula model
$K_{ex}$	extraction equilibrium (-)
$k_f$	aqueous feed mass-transfer coefficient ( $\text{cm/s}$ )
$k_m$	organic mass-transfer coefficient ( $\text{cm/s}$ )
$L$	length of the hollow fiber ( $\text{cm}$ )
$m$	membrane phase
$mA.c.$	modified Apelblat model calculated result
$N$	number of hollow fibers in the module (-)
$P$	permeability coefficient ( $\text{cm/s}$ )
$P_m$	membrane permeability ( $\text{cm/s}$ )
$Q$	volumetric flow rate ( $\text{cm}^3/\text{s}$ )
$R^2$	squared correlation coefficients of the regression
$R_i$	aqueous mass transfer resistance ( $\text{s/cm}$ )
$R_m$	organic membrane mass-transfer resistance ( $\text{s/cm}$ )
$r_i$	internal radius of the hollow fiber ( $\text{cm}$ )
$r_m$	log-mean radius of the hollow fiber ( $\text{cm}$ )



## LIST OF ABBREVIATIONS

$r_o$	external radius of the hollow fiber (cm)
$s$	stripping phase
$S$	experimental solubility data (g/L)
$t$	time (min)
$T$	Temperature (K)
$T_m$	melting temperature (K)
$V_f$	volume of feed phase (cm <sup>3</sup> )
$x$	mole fraction
$0$	initial concentration
( $S$ )	( $S$ )-amlodipine
( $R$ )	( $R$ )-amlodipine
$\tau$	tortuosity of membrane (-)
$\varepsilon$	porosity of membrane (-)
$\eta$	viscosity of the liquid membrane (kg/(s·m))
$\lambda$	constant parameters in the correlated $\lambda H$ model