EXTRACTION OF ACETAMINOPHEN FROM AQUEOUS SOLUTION BY EMULSION LIQUID MEMBRANE

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EXTRACTION OF ACETAMINOPHEN FROM AQUEOUS SOLUTION BY EMULSION LIQUID MEMBRANE

by

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LIST OF SYMBOLS

M	Molar	-
W	Watt	-
%	Percent	-
ng/L	nanogram per litre	-
µg/L	microgram per litre	-
mg/L	miligram per litre	-
kg/m^3	kilogram per meter cube	-
cP	centiPoise	-
d_{32}	Sauter mean diameter	cm
ε	Membrane breakage	%
V_i	Initial volume of the internal phase	L
V_s	volume of the internal phase leaked into external phase	L
µ	Viscosity	mPa.s
E	extraction efficiency	%
C_o	initial concentration of ACTP	mg/L
C_f	Final concentration of ACTP	mg/L
Hz	Hertz	-
rad/s	Radian per second	-
K_D	distribution coefficient	-
$C_{i,II}$	ACTP-complex concentration in organic solution	mg/L
$C_{i,III}$	ACTP concentration in feed phase	mg/L
wt%	weight percentage	-

Subscripts

i	Responding variable
n	Order of membrane flux registered
1,2	Component/species to be evaluated

LIST OF ABBREVIATIONS

ACTP	Acetaminophen
Adogen 283	Di-tridecylamine
Adogen 381	Tri-isooctylamin
Adogen 383	Tri-isodecylamine
Adogen 464	Tri (C8-C10) methylammonium chloride
Alamine 336, TOA	Tri-octylamine
alkyl poly	Ethylene oxide
Amberlite LA-1	N-5,5,7,7-tetramethylocten-2-yl-1,1,3,3,5,5,-hexamethylhexylamine
BLM	Bulk liquid membrane
$C_{24}H_{44}O_6$	Span 80
CEC	contaminant of emerging concern
CH_3COOH	acetic acid
CTAB	cetyltrimethylammonium bromide
D2EHPA	di(2-ethylhexyl)phosphoric acid
DoD	Department of Defense
ELM	Emulsion Liquid Membrane
EPA	Environmental Protection Agency
HCl	Hydrochloric acid
HLB	hydrophile-lipophile balance
HNO_3	nitric acid
HOE F 2562	Di-isotridecylamine
KCl	potassium chloride
Na_2CO_3	Sodium Carbonate
$NaHCO_3$	Sodium Bicarbinate
NaOH	Sodium Hydroxide
NH_3	ammonia
OWO	organic-water-organic
Peimene JMT	1,1,3,3,5,5,7,7,9,9- decamethyldecyl amine
poly	propylene oxide

PP	propylprarabane
PPCP	pharmaceuticals and personal care products
rpm	radian per minute
SDS	sodium dodecylsulfate
SLM / ILM	supported or immobilized liquid membrane
Span 80	Sorbitan Monooleate
TBP	Tributyl-phosphate
TCC	Taylor-Couette Column
TDA	Tri-dodecylamine
TDA	tridodecylanmine
TOA	Trioctylamine
TOPO	trioctylphosphine oxide
USGS	United States Geological Survey
UV-Vis	Ultra Violet Visible
W/O	water-in-oil
WOW	water-organic-water
WWTP	waste water treatment plants

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PENGEKSTRAKAN ASETAMINOFEN DARI LARUTAN BERAIR MENGGUNAKAN MEMBRAN CECAIR EMULSI (ELM)

ABSTRAK

Kesedaran mengenai pencemaran alam sekitar menerusi bahan cemar farmaseutikal telah meningkat sejak beberapa tahun lalu. Pencemaran ini adalah sangat meluas, dengan beratus-ratus jenis dadah perubatan boleh didapati pada kadar kepekatan yang rendah di dalam sungai. Salah satu bahan farmaseutikal yang paling banyak digunakan ialah asetaminofen (ASTP). Proses rawatan konvensional yang digunakan oleh loji rawatan air sisa gagal untuk menyingkirkan sebatian farmaseutikal secara sepenuhnya. Di antara kaedah yang sedia ada, salah satu kaedah yang berpotensi untuk menyingkirkan ASTP adalah membran cecair emulsi (MCE). MCE terdiri daripada fasa dalaman dan fasa membran yang membentuk emulsi A / M (air dalam minyak) utama, yang kemudiannya akan diserakkan di dalam fasa luaran. Kajian telah dijalankan bagi mencari rumusan MCE dengan agen pembawa, agen pencair, dan agen perlucutan yang sesuai. Kesan parameter perumusan ini juga telah dikaji untuk mendapatkan rumusan MCE yang terbaik bagi penyingkiran ASTP. Pemilihan komponen MCE yang sesuai, penggunaan pengemulsian ultrabunyi, dan Turus Taylor-Couette (TTC) dijangka dapat meningkatkan kecekapan pengekstrakan ASTP. Kesan bagi beberapa keadaan pengendalian seperti kepekatan agen surfaktan, agen pembawa dan agen perlucutan, kekuatan ultrabunyi, nisbah isipadu, tempoh pengemulsian, nisbah rawatan, kepekatan awal dan kepekatan asid, tempoh adunan, dan kelajuan adunan telah dikaji. Keputusan eksperimentasi menunjukkan bahawa rumusan yang paling sesuai bagi pembentukan membran cecair bagi penyingkiran ASTP adalah dengan menggunakan kerosin sebagai agen pencair, trioktilamina (TOA) sebagai agen pembawa, dan ammonia (NH_3) sebagai agen perlucutan. Keadaan optimum bagi

proses emulsifikasi telah didapati pada peratus berat TOA dan Span 80 sebanyak 6%, kepekatan agen perlucutan pada kadar 0.1M, tempoh pengemulsian selama 15 minit, nisbah isipadu pada kadar 3: 1, kuasa prob ultrabunyi pada nilai 20W, kepekatan awal pada kadar 10 bahagian per juta (ppm), kepekatan HCl pada kadar 0.1M, tempoh pengekstrakan dengan menggunakan TTC selama 5 minit dengan nisbah sudut frekuensi pada kadar 1.0, dan nisbah rawatan pada kadar 3:1. MCE yang dihasilkan didapati berkesan untuk menyingkirkan 85% ion ASTP daripada larutan akua. Oleh itu, proses MCE merupakan teknologi yang berpotensi untuk mengekstrak ASTP daripada air sisa pengeluaran farmaseutikal.

EXTRACTION OF ACETAMINOPHEN FROM AQUEOUS SOLUTION BY EMULSION LIQUID MEMBRANE

ABSTRACT

In recent years there is an increasing awareness of pharmaceutical contaminants in the environment. Pharmaceutical contamination in rivers is widespread with hundreds of drugs found at low concentrations. One of the main abundantly used pharmaceuticals are acetaminophen (ACTP). The application of conventional treatment process in wastewater treatment plants is unable to completely remove the residues. Thus, among the existing methods, one of the promising methods for ACTP removal is by emulsion liquid membrane (ELM). ELM comprises internal and membrane phase which form primary W/O (water-in-oil) emulsion. The formulation of ELM was investigated to find suitable carrier, diluent and stripping agent. The effect of emulsion formulation parameters of ELM was investigated in order to obtain its best formulation for removal of ACTP. Selection of suitable ELM components, use of ultrasound emulsification and Taylor-Couette Column (TCC) are expected to increase the extraction efficiency. The influence of several parameters such as carrier, surfactant and stripping agent concentration, ultrasonic power, volume ratio, emulsification time, treat ratio, initial and acid concentration, stirring time and stirring speed were investigated. The results show that kerosene as a diluent, Trioctylamine (TOA) as carrier or extractant and ammonia (NH_3) as stripping agent were the most suitable for the liquid membrane formulation of ACTP removal. The optimum condition for the emulsification study was found at 6 wt.% of TOA and Span 80, 0.1 M concentration of stripping agent, 15 minutes of emulsification time, volume ratio of 3:1, 20 W power of ultrasonic probe, 10 ppm of initial concentration, 0.1M of HCl concentration, 5 minutes of extraction time using TCC with a frequency angular ratio of 1.0 and treat ratio of 3:1. The prepared ELM was found to effectively remove

85% of ACTP ions from aqueous solution. Thus, ELM process is a promising technology to extract ACTP from pharmaceutical production wastewater.

CHAPTER 1

INTRODUCTION

1.1 Research Background

For centuries environmental pollution has existed but started to be notable in consequence of the industrial revolution in the 19th century. This in turn has raised many critical issues on a vast and unprecedented scale around the globe. Pollution occurs when there is an introduction of contaminants into the natural environment where it harms humans and other living species as well as causes damage to the environment. It is one of the major challenges that the globe is presently facing and increases day by day causing irreversible damage to Mother Earth. Thus, as our environment changes, so does the need to become increasingly aware of the problems that surrounds it.

While present generation resumes to exert themselves in order to minimize traditional contaminants in environment, diverse "emerging" environmental contaminants are warranting attention and is labelled as 'contaminants of emerging concerns' or CECs (Richardson and Kimura, 2017). These contaminants are widespread in the aquatic and terrestrial environments, including anthropogenic and naturally occurring chemicals, pharmaceuticals and personal care products (PPCPs), illicit drugs, engineered nanomaterials, and antibiotic resistance genes. Even though it is not yet circulated in drinking water supplies and not monitored in the environment, these contaminants have the potential to cause harmful ecological and human health effects (Noguera-Oviedo and Aga, 2016).

PPCPs is one of the most common emerging pollutants present in wastewater and drinking water. This is because it is initiated not only by humans, but through

veterinary usage too resulting in their endless release to environment. The presence of pharmaceutical CECs in environmental waters are due to incomplete removal in wastewater treatment or diffuse-source contamination, which are threats to drinking waters which leads to estrogenic possibility and harmful effects to both wildlife and human. The major concern of pharmaceuticals CECs is that it is usually specifically designed to target certain metabolic, enzymatic or cell-signalling mechanisms as well as maximise their biological activity at low doses. Several research studies stated that over 30 mg/L of pharmaceutical waste was discharged daily (Fawell and Ong, 2012). Some of the most abundantly used pharmaceuticals are cimetidine, diltiazem, carbamazepine, acetaminophen, and six sulfonamide related antibiotics. According to Al-Odaini et al. (2013), acetaminophen has the highest concentration detected in Langat River, Malaysia with value as high as 350.3 ng/L. The same phenomenon was also noted to occur internationally such as in Spain with concentration of 250 ng/L and 1µg/L in UK.

The removal of PPCPs from wastewater and drinking water is really challenging since there are no comprehensive method in removing it. Removals of these pollutants in the wastewater treatment processes are generally good. Nevertheless, reports on the inability of the application of conventional treatment processes in wastewater treatments plants (WWTPs) to remove pharmaceutical contaminants in water completely have been well documented (Chaouchi and Hamdaoui, 2014). To some extent, the accumulated chemicals were simply discharged into the groundwater while some were not treated properly in the WWTPs (Jarrett, 2017). This is due to the notable concentrations remaining in the final effluents owing to the relatively high influent concentrations encountered. Some specific treatments have been implemented to eliminate PPCPs such as biodegradation, photocatalysis, ozonation and Fenton process

(Kyzas et al., 2015). However, some disadvantages have arisen from these methods including high investment and maintenance cost, formation of secondary pollutants and complex operation procedures (Grassi et al., 2012).

Therefore, integration of advance separation technology with conventional wastewater treatments such as liquid membranes has become a great interest for many. To enhance this process, liquid membrane separation was looked at in this study to be utilized in separating ACTP from contaminated water. Emulsion Liquid Membrane (ELM) which was invented by Li (1968) has shown to have a promising potential for the application of extraction of ACTP. Currently, ELM is introduced as an alternative technique to the separation process where it consists of three main stages which are emulsification, extraction and demulsification. ELM fulfils the promise of providing several attractive characteristics such as high interfacial area to volume ratio for mass transfer, economical, low energy consumption, simultaneous extraction and stripping process, efficient for low solute concentration and requirement of small quantity of solvent. Besides, it is also estimated that ELM is about 40% cheaper than the conventional extraction processes (Kislik, 2010). With these advantages, ELM has been widely studied for industrial applications such as for the separation of various types of metal ions (Zhao et al., 2010, Alaguraj et al., 2009, Ahmad et al., 2013), organic compound (Ng et al., 2010, Lee, 2011) and inorganic compound (Lichang et al., 2016).

1.2 Problem Statements

These chemical compounds, such as acetaminophen, carbamazepine, diclofenac, ibuprofen, and salicylic acid can be easily detected in water (Kim et al., 2007). While the levels of individual pollutants are low, little is known about the long-

term health implications. To make matter worse, there is some concern regarding potential ‘cocktail’ effects of different species of pharmaceutical contaminants mixed together. Thus, even though these compounds existed in trace amount, and at insignificant degree, finding an effective method to prevent further pollution of our water sources are of a major and emerging concern.

Emulsion liquid membrane was given more attention due to having high interfacial area which able the system to selectively recover solute. Thus, it is a suitable method to implement in order to remove acetaminophen CECs in water. Unfortunately, emulsion stability remains as a great challenge that would hinder its wide applications. Emulsion instability occurs through various physical mechanisms such as swelling, breakage and coalescence. It is usually governed by membrane breakage in ELM systems which involves the rupture of the emulsion and leakage of internal phase and extracted solute to the external phase causes the decrease in volume of the stripping phase (Ho and Kamalesh, 1992). This causes the driving force for mass transfer, concentration gradient reduced and increases the external feed concentration, thereby lowering the extraction efficiency. The instability may cause by the emulsion formulation and condition of emulsification (Djenouhat et al., 2008). Therefore, the effects of several factors on liquid membrane formulation together with its effectiveness in removing ACTP were investigated in this study.

In order to obtain high performance of acetaminophen extraction, the selectivity of ELM formulation is very important. According to Chiha et al. (2010), carrier and surfactant concentration, emulsification time and W/O volume ratio have greatly influenced the efficiency and the stability of ELM. Besides that, investigation on process parameters during extraction are important to understand the process of acetaminophen extraction using ELM process. Attempts to reduce emulsion instability

have been made including the usage of Taylor-Couette column (TCC) to disperse the system. The unit was designed to minimize emulsion instability while maintaining high extraction performance (Park et al., 2004).This column improves the stability of the emulsion in such a way that it provides relatively low and uniform fluid shear.

1.3 Research Objectives

The focus of this study is to develop an emulsion liquid membrane system for acetaminophen extraction from aqueous solution using Taylor-Couette Column. Listed below are the measurable objectives:

i. To formulate emulsion liquid membrane for acetaminophen extraction.

ii. To investigate the affecting parameters of acetaminophen extraction using emulsion liquid membrane.

iii. To evaluate the effectiveness of emulsion liquid membrane formulation on acetaminophen removal.

1.4 Scope of Research

The aim of this study is to develop Emulsion Liquid Membrane system for the extraction of acetaminophen from an aqueous solution. Firstly, an ELM was formulated where suitable components in the systems are required for selectively extract acetaminophen from the aqueous solution. Thus, the formulation was initiated by the screening of liquid membrane components where the compatibility of diluent with the other membrane phase components (carrier, surfactant and stripping solution) will be looked at before selection is made for the optimal ELM formulation.

The chosen carrier, diluent and stripping solution must comply with the reaction in the interface of the membrane to support the simultaneous processes of extraction and stripping. Also, the stoichiometry of the extraction reaction and the optimum operating conditions will be determined. Therefore, influence of operating conditions such as carrier concentration, surfactant concentration, stripping agent concentration, volume ratio, ultrasound power, emulsification time, treat ratio, angular frequency ratio and time using TCC will be investigated. These parameters were investigated to obtain the best emulsion formulation hence, a stable emulsion and maximum acetaminophen removal efficiency could be achieved.

1.5 Significance of Current Work

Due to increasing demand of acetaminophen in many applications, it is essential to extract acetaminophen from biological production waste. ELM was implemented as promising alternative separation technology to the existing conventional technique such as electrochemical, ozonation and solar photoelectro-Fenton oxidation. It provides tremendous advantages where the extraction offers high interfacial area to volume ratio for mass transfer, economical, low energy consumption, simultaneous extraction and stripping process, efficient for low solute concentration and requirement of small quantity of solvent. This study will be significant in wastewater treatment due to its high efficiency in removing desired contaminants. Besides that, it is also beneficial to industry and treatment plants as it is an alternative economical way in dealing with emerging contaminants. In addition, it will also serve as reference to new researchers to achieve higher and better extraction efficiency.

1.6 Organization of Thesis

This thesis contains five chapter, which are presented in a sequential order.

Chapter 1: In this chapter, as an introduction it presents a brief overview of the study, introduction of the research background, problem statement, research objectives and scopes, and significance of study.

Chapter 2: This chapter describes the literature of this research. This includes a review of acetaminophen characteristics and applications, ELM technology, stability and extraction of acetaminophen.

Chapter 3: The methodology for the overall research was discussed in detail. The chapter outline starts with the materials and methods including chemical and reagents used for the experiment. It was then followed by experimental procedure for liquid membrane component screening and emulsion liquid membrane extraction. The analytical equipment used throughout this study were also discussed in detail.

Chapter 4: This chapter presents the results and discussions were presented following the number of set of experiments discussed in methodology. The optimal condition in achieving minimal membrane instability and highest removal efficiency will be made and discussed.

Chapter 5: In this chapter, the findings of the current work were summarized and relates with the research objectives. Significant findings were highlighted, and recommendations were given for future work.

CHAPTER 2

LITERATURE REVIEW

2.1 Prologue

This chapter starts with a literature review on the pharmaceutical waste especially focused on acetaminophen, followed by an overview on liquid extraction and liquid membrane treatment technique, and a brief review on liquid membrane classification. The role of crucial parameters of a liquid membrane system such as diluents, surfactants and carriers have been described and an overview of solute transport properties and mechanism through liquid membrane is presented. A literature survey on extraction of contaminants by emulsion liquid membrane technique is presented.

2.2 Emerging Contaminants

Diverse chemicals are being introduced by society in vast quantities for a range of purposes including agricultural, industrial, household as well as for human and animal healthcare. These chemicals are referred to collectively as 'contaminants of emerging concern' (CECs). Emerging contaminants are defined by several definitions. According to U.S. Environmental Protection Agency (EPA) and U.S Department of Defense (DoD) as "a chemical or materials which is characterized by a perceived, potential or real threat to human health or the environment or lack of published health standards". It can also be defined as "any synthetic or naturally occurring chemical or any microorganism that is not commonly monitored in the environment but has the potential to enter the environment and cause known or suspected adverse ecological and/or human health effects" by The United States Geological Survey (USGS). The term does not necessarily correspond to newly discovered compound in the environment due to analytical developments, but also refers to compounds that are

recently been categorised as contaminants (Lapworth et al., 2012). CECs has emerged as an environmental problem and it may have adverse effects on aquatic ecosystem.

Many CECs are present at extremely low concentrations from nanogram per litre (ng/L) up to microgram per litre (µg/L) concentration, making detection and assessments of it challenging. However, recent advances have given researchers the ability to detect wide range of contaminants in environment at extremely low concentrations which encouraged researchers to advance on this research topic(Martha J.M. Wells et al., 2009). There are several groups of compounds that emerged which are algal and cyanobacterial toxins, brominated flame retardants, disinfection by-products, gasoline additives, hormones and other endocrine disrupting compounds, organometallics, organophosphate flame retardants and plasticisers, perfluorinated compounds, pharmaceuticals and personal care products, polar pesticides and their degradation/transformation products and surfactants and their metabolites (Petrovic et al., 2008).

2.3 Pharmaceutical as Emerging Contaminants

Over the past few years, there has been an increasing awareness of pharmaceutical CECs in aquatic environment at concentrations capable of causing detrimental effects towards aquatic organisms. This is because it is introduced not only by humans but also through veterinary usage resulting in their continuous release to the environment (Noguera-Oviedo and Aga, 2016).

Improper treatment of these chemicals will eventually cause major environmental pollution (Mohammadi M. et al., 2009). According to Alistair (2004), pharmaceutical wastes are released to the environment by various routes as shown in Figure 2.1. The residues during manufacturing process are released into wastewater

which may directly enter surface water and adsorbed by the soil. The presence of pharmaceutical CECs in environmental waters are due to incomplete removal in wastewater treatment or diffuse-source contamination, which are threats to drinking waters, estrogenic possibility and also adverse effects to both humans and wildlife. The major concern of pharmaceuticals CECs is that they were usually designed specifically to maximise their biological activity at low doses and target certain metabolic, enzymatic or cell-signalling mechanisms (Ahmad et al., 2012). Though residues of the chemicals were detected in natural waters, however outputs of Waste Water Treatment Plants (WWTP) were identified as the main source of pharmaceuticals introduction into the ecosystem. Recently, 44 pharmaceuticals have been developed in a common priority list which are relevant for the water cycle based on consumption, physicochemical properties, toxicity, occurrence, persistance and resistance to treatment (Boleda et al., 2011). In fact, number of sources of water at high risk of contamination is expected to escalate as human population density increases. This is due to the fact that, these chemicals disrupt the endocrine balance in various ecological species and can adversely affect fish and other aquatic species living in the contaminated water (Jarrett, 2017).

The usage of medicines in human and animals are also passage of pharmaceutical residues entering the environment through the excretion process since medicines are not completely adsorbed into the body. Besides, the development of bacterial resistance from release of antibiotics and the decrease in biodegradation of leaf and other plants which serves as primary food source for aquatic livings are also one of the major concerns of pharmaceutical CECs (Chaouchi and Hamdaoui, 2014). Application of manure and slurry as fertilizer in livestock treatments also causes the residues to indirectly enter the environment. Other entry of pharmaceuticals CECs are

through the inappropriate disposal of used containers and unused medicines. Besides that, it may also enter the environment through disposal of unused and emissions from manufacturing process of the products (Stackelberg et al., 2007).

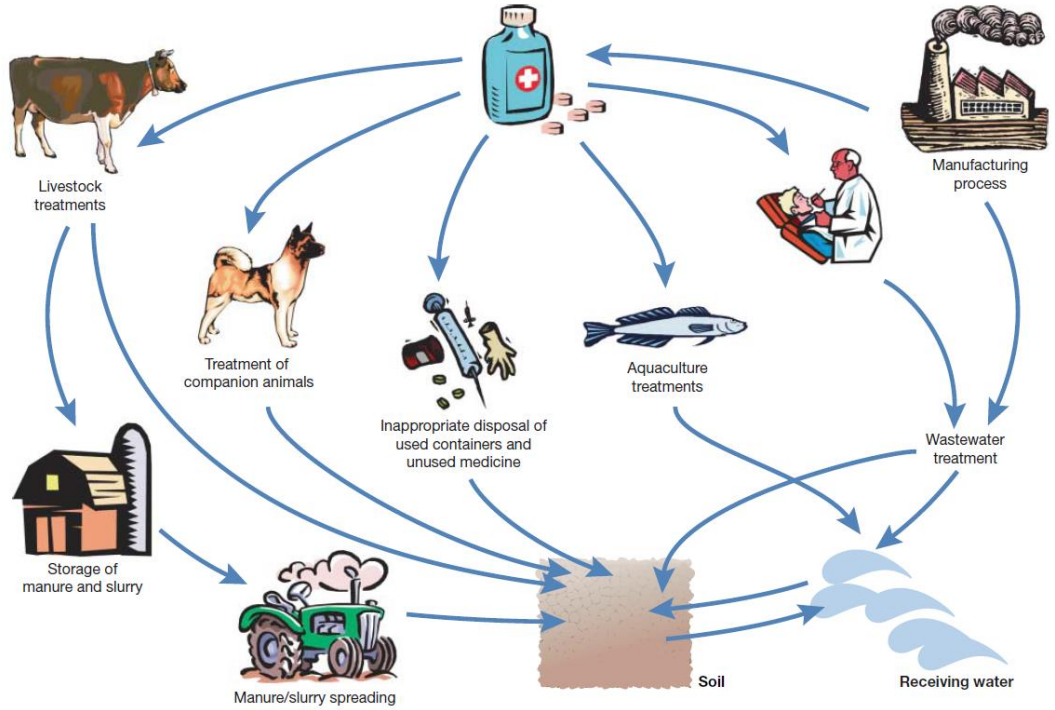


Figure 2.1 Routes of pharmaceuticals entering environment (Stackelberg et al., 2007)

The presence of pharmaceuticals is one of the most studied group of emerging contaminants that has been widely reported in the aquatic environment at the low ng/L to the µg/L range (Ternes et al., 2002, Mompelat et al., 2009, Nikolaou et al., 2007, Zuccato and Castiglioni, 2009). It is estimated that approximately 3000 different substances are used as pharmaceuticals ingredients including pain-killers, antibiotics and impotence drugs. This includes more than 4000 molecules with different physico-chemical and biological properties and distinct modes of biochemical reaction. Most medical substances are administrated orally whereas some drugs are metabolised while others remain intact before excreted (Monteiro and Boxall, 2010). Therefore, mixture

of pharmaceuticals and their metabolites will enter municipal sewage and sewage treatment plants.

Easily detected compounds in the contaminated water include acetaminophen, carbamazepine, diclofenac, ibuprofen and salicylic acid (Stackelberg et al., 2007). Several types of pharmaceutical CECs that have been detected in Langat River, Malaysia is shown in Table 2.1. According to Lyons (2014), global review found that 713 pharmaceuticals (of which 142 are transformation products) have been looked for in the environment and it was reported that 631 (of which 127 are transformation products) are above their detection limits.

Table 2.1 Pharmaceutical occurrence in Langat River and the concentration detected (Al-Odaini et al., 2013).

Pharmaceutical	Concentration Detected (ng/L)
Acetaminophen	350.3
Atenol	86.6
Furosemide	239.4
Glibenclamide	3.2
Atenol	19.7
Loratadine	9.1
Mefanamic acid	82.7
Metformin	189.6
Metorprolol	190.7
Nifedipine	12.3
Perindopril	12.4
Salbutamol	4.5
Salicylic acid	131.2

2.3.1 Acetaminophen

Among widely used pharmaceuticals is Acetaminophen (ACTP), also known as Paracetamol, which is primarily used as analgesics and antipyretics. It is a drug used to relieve pain and to suppress inflammation in a way similar to steroids without side effects. Although the anti-inflammatory effect is weak, the impact on the environment is not different from others. The molecular structure of ACTP consists of benzene ring

core substituted by one hydroxyl group and nitrogen atom of an amide group in the para (1,4) pattern as shown in Figure 2.2 while Figure 2.3 shows two-dimension molecular structure with 0.368 nm^2 of two-dimensional areas. Table 2.2 shows the physicochemical properties of acetaminophen.

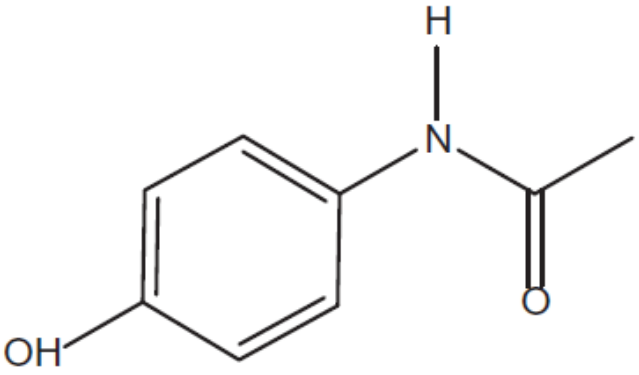


Figure 2.2 Molecular Structure of Acetaminophen (Mestre et al., 2014)

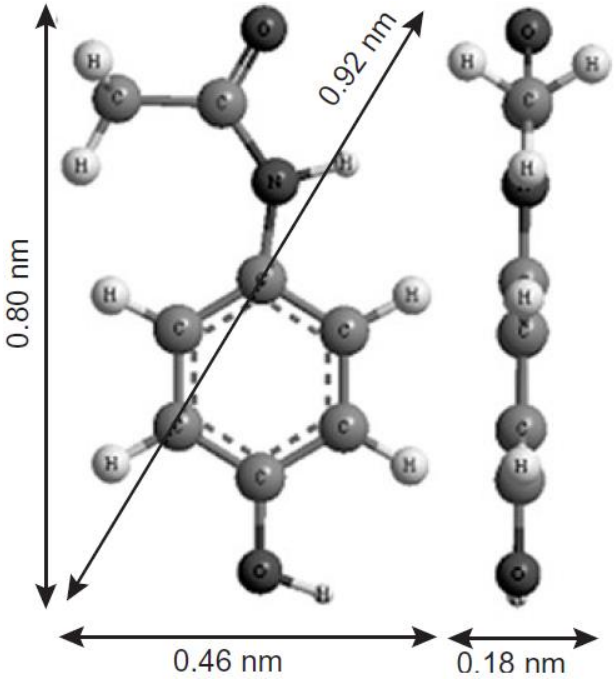


Figure 2.3 Two-dimension molecular structure of Acetaminophen (Sabina Beninati et al., 2008)

Table 2.2 Physicochemical properties for Acetaminophen (Monteiro and Boxall, 2010, El-Obeid and Al-Badr, 1985)

Formula	$C_8H_9NO_2$
Molecular Weight	151.2
pK_a	9.38
Log k_{ow}	0.46
Water solubility (mg/L)	1.40×10^4
Melting Point (^oC)	169-170.5
pH	A saturated solution has a pH of about 6.

The water solubility of ACTP is high, resulting in its easily accumulation in aquatic environment (Wu S et al., 2012). As reported by Kim et al. (2007), ACTP is one of the most frequently detected pharmaceuticals in sewage treatment plant effluents, drinking water or surface water. According to Petrie et al. (2015) the prescription of ACTP is estimated to be more than 2000000 kg whereby 20% of the excretion unchanged resulting with a mean maximum amount of contaminants found on surface water around 2382 ng/L. Yue Zhao et al. (2015) stated that in a previous study, during therapeutic use of ACTP, about 58-68% of the dose could not be absorbed by the body and are released into the environment through excretion process. Even though this compound existed in trace amount, and at insignificant degree, finding an effective method to prevent further pollution of our water sources is a major concern. With that, paracetamol is categorized as one of the alarming CECs (Ebele et al., 2017).

2.3.2 Conventional Removal Method

Major portion of the pharmaceutical's products were removed by conventional wastewater treatment processes. ACTP wastewater is mainly treated by chemical oxidation processes such as electrochemical, ozonation, H_2O_2/UV oxidation, TiO_2 photocatalysis and solar photoelectro-Fenton oxidation (Skoumal et al., 2006). However, conventional treatment process applied to wastewater treatment plants fail to completely remove pharmaceutical compounds. In addition, according to Chaouchi and Hamdaoui (2014), reports on the inability of the conventional treatment processes applied in wastewater treatment plants to remove pharmaceutical compounds in water completely have been well documented. Large number of different trace organic polluting compounds have been found in WWTP for which conventional treatment technologies have not been specifically designed (Gros et al., 2010). The use of chlorine in conventional wastewater treatment in a study to remove acetaminophen have been reported by Rivera-Utrilla et al. (2013) and it is found that the reaction between chlorine and acetaminophen have formed numerous sub-products which are identified as toxic compound such as diclofenac chlorination and chloramines. Notable concentrations remain in final effluents owing to the relatively high influent concentrations encountered (Ooi et al., 2015). To some extent, the accumulated chemicals were simply discharged into the groundwater while some were not treated properly in the WWTPs (Jarrett, 2017).

Several methods have been investigated to remove pharmaceuticals from contaminated water (Kyzas et al., 2015). Among the hydrometallurgical methods available, solvent extraction provides an effective and simple separation method (Hosseinzadeh et al., 2014). Therefore, integration of conventional wastewater

treatments with advanced technologies has become of great interest especially liquid membranes.

2.4 Liquid Membrane

A membrane where it can be homogeneous, heterogeneous, symmetric, asymmetric, solid or liquid, is a semipermeable barrier which separates two phases and restricts the transport of various chemical species in a rather specific manner (Porter, 1990). Membranes are used commercially for various applications such as water purification, gas applications, chemical, biotechnology, and biomedical applications.

Recently, liquid membrane systems are being extensively studied by researches due to its advantages over solid membranes and liquid-liquid extraction. In addition, it also gained increasing attention due to its huge potential in replacing conventional technique available for solute separation. Like most developments, this separation operation has various names such as "liquid membranes", liquid pertraction", "carrier-mediated extraction", "facilitated transport" and "two-stage" (Boyadzhiev and Lazarova, 2003). Liquid membrane system consists of processes where liquid-liquid extraction and membrane separation were incorporated simultaneously. It involves an immiscible liquid with the source (feed phase) and receiving (product) solutions that serves as a semipermeable barrier between these two liquid and gas phase. There are three types of liquid membrane which are bulk liquid membrane (BLM), supported or immobilized liquid membrane (SLM or ILM) and emulsion liquid membrane (ELM) transport as shown in Figure 2.4. The differences of these liquid membranes are in the aspect of design, formulation as well as way of contact with feed phase (Parhi, 2013). In contrast, these three configurations of liquid membrane are similar in a way that all of them require the assistance of an extracting reagent, either stagnant or flowing

between the feed and the internal phase to specifically remove the targeted solute (Kislik, 2010).

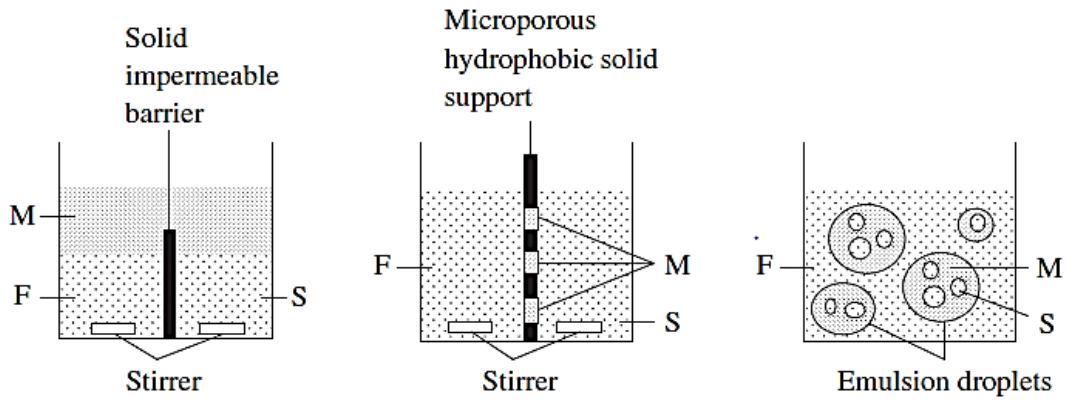


Figure 2.4 Configuration of liquid membrane (a) Bulk (b) Supported (c) Emulsion (Chang, 2013). F is the source or feed phase, M is the liquid membrane, and S is the stripping phase.

2.4.1 Bulk Liquid Membrane

Bulk Liquid Membrane (BLM) consists of bulk aqueous feed and receiving phases which are separated by a bulk organic, water immiscible liquid phase. The membrane phase consists of carrier which is responsible in solute extraction as it helps to transport the solute into the stripping phase as shown in Figure 2.5. BLM is the simplest form of liquid membrane which shows superior membrane stability but inferior fluxes which are caused by small interfacial area per unit volume, long transportation path (requires high amount of solvent which contributes to high operational cost) and high membrane resistance (Chang, 2015).

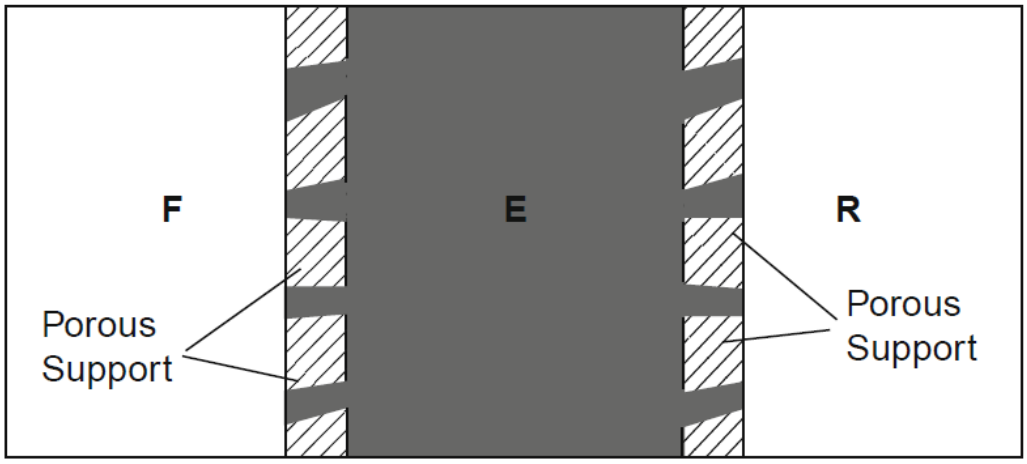


Figure 2.5 Configurations of liquid membrane systems: Bulk (BLM). F is the source or feed phase, E is the liquid membrane, and R is the receiving phase(Kislik, 2010).

2.4.2 Supported Liquid Membrane

SLM, in a rather primitive configuration, was reported for the first time by Scholander (1960) who used thin cellulose acetate filters impregnated with an aqueous hemoglobin solution for oxygen transport. In supported liquid membrane (SLM) a thin microporous filter is installed as a support by forming a thin layer of organic membrane phase which is responsible in separating the feed and stripping phases as shown in Figure 2.5. The support is impregnated by an organic carrier (also named as facilitator, modifier or mobilizer) to modify the extraction process (Dżygiel and Wieczorek, 2010). The main advantage of supported liquid membranes is the insignificant amount of organic phase required for impregnation of the support matrix while the main SLM disadvantage is the low stability of the membrane, caused by leakage or losses of membrane phase components during transport process. The great potential for energy saving, low capital and operating cost, and the possibility to use expensive extractants due to the low consumption of the membrane phase, make SLM technique noticeable and interesting (Kocherginsky et al., 2007). In addition, supported liquid membrane

extraction is the most versatile membrane extraction technique for analytical sample preparation compared with other LM configurations (Jönsson and Mathiasson, 2000).

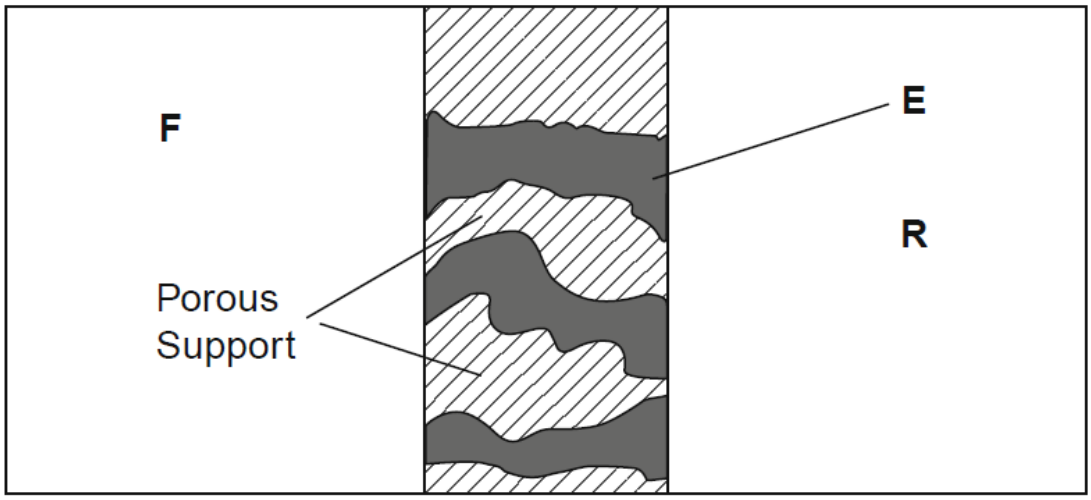


Figure 2.6 Configurations of liquid membrane systems: Supported (immobilized) (SLM or ILM). F is the source or feed phase, E is the liquid membrane, and R is the receiving phase. (Kislik, 2010)

2.4.3 Emulsion Liquid Membrane

Li (1968) invented a different type of liquid membrane in which the stripping phase was emulsified in an immiscible liquid membrane. ELM may be in the form of water-organic-water (W/O/W) or organic-water-organic (O/W/O). In emulsion liquid membrane (ELM) mass transfer takes place by dispersion of emulsion in the feed solution. Figure 2.7 illustrates Emulsion Liquid Membrane (ELM) system which consists of feed (F) and receiving (R) phase and they were separated by immiscible organic membrane (E) phase. ELM extraction ability can be enhanced by using carriers, chemical reagents and electric impulses(Chakraborty et al., 2010).

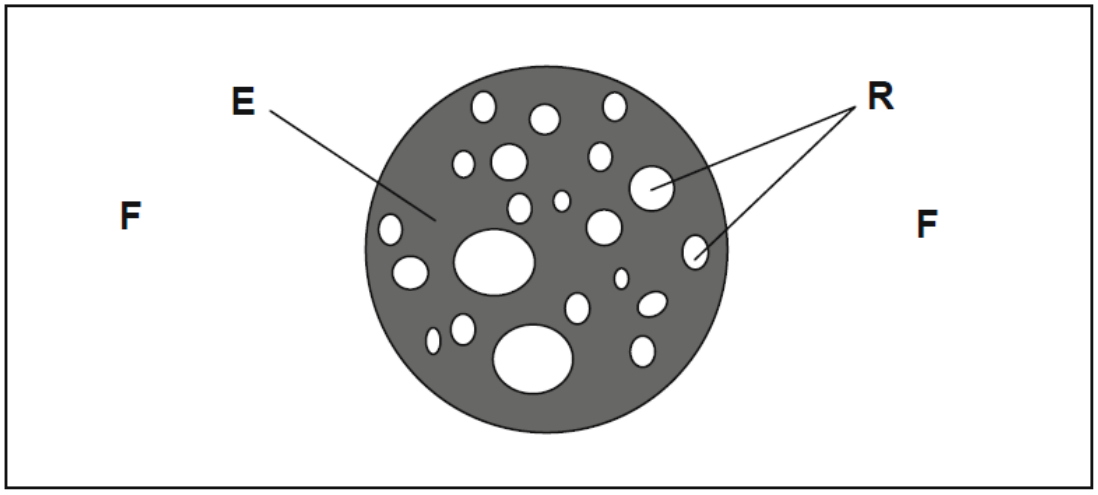


Figure 2.7 Configurations of liquid membrane systems: Emulsion (ELM). F is the source or feed phase, E is the liquid membrane, and R is the receiving phase. (Kislik, 2010)

As the historically first application of liquid membrane in wastewater treatment, ELM has been studied and investigated for many years by numerous researchers and scientists. ELM is relatively cheap with high flux rate, high extraction efficiency and environmental-friendly (Ahmad et al., 2013) but coalescence and emulsion swelling resulting in low emulsion stability are considered as its disadvantages. ELM process involves four main steps which are emulsion preparation, solute extraction, emulsion separation and demulsification. ELM system is created by forming a primary emulsion which consists of organic and aqueous phase stabilized by surfactant. The concept of ELM separation is a solute-carrier complex formed when the carrier selectively combines with solute ions at the external membrane phase. Therefore, ELM still can work appropriately even in the low concentration of solute.

2.5 Transport Mechanism of Emulsion Liquid Membrane

2.5.1 Simple Diffusion

The solute permeates through the membrane layer due to its solubility in the membrane phase and this selective transport took place from a region of high concentration to the lower one (Kislik, 2010). When the concentration equilibrium is reached, the transportation of solute will stop. No reaction is involved in this mechanism and the solute (X) remains in the same form as in the feed, stripping or membrane phase.

2.5.2 Facilitated Transport

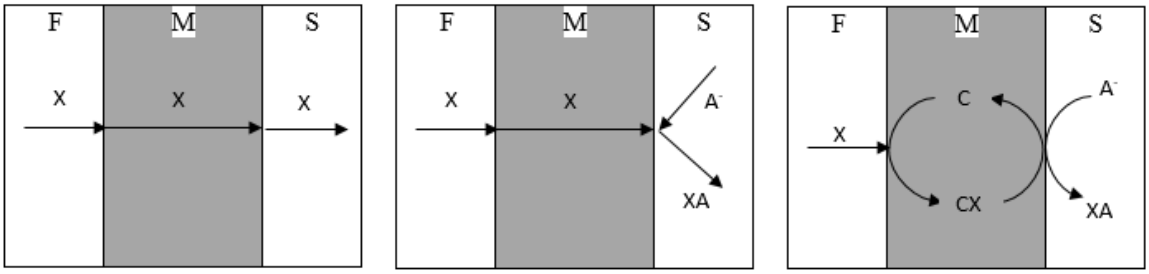
a) Type I

In Type I Facilitated Transport mechanism system, a solute must be soluble in all the three phases (external phase, liquid membrane phase and stripping phase) so that a solute can diffuse across the membrane phase to the internal stripping phase. A modification was made as from the simple diffusion by introducing a stripping agent in the opposite side of the membrane phase to enhance the mass transfer rate. The stripping agents (A) will react with the transferred solute (X) in the membrane phase and yield an insoluble compound (XA) as illustrated in Figure 2.8. This stripping process causes the reaction product unable to diffuse back through the membrane phase. The solute concentration in the internal stripping phase is also maintained zero by the reaction. In type I, the reaction only involves the solute and stripping agent without the presence of carrier.

b) Type II

Type II ELM system involves the facilitated transport of a solute across the membrane phase with the presence of a carrier agent. This mechanism was named as "carrier-mediated" transport as carrier plays an important role in facilitating the diffusion of the targeted solute across the membrane phase (Teng et al., 2014). In this system, a solute is insoluble in the membrane phase, thus a carrier agent is required to transport the solute across the membrane. Two reactions involve with a carrier take place at the external interface between the external and membranes and at the internal interface between the membrane and the internal phases. The solute (X) turned into a solute-carrier complex (CX) via a reversible reaction before it can be transported into the internal stripping phase. The reaction product diffuses across the membrane layer to the membrane-internal interface and dissociates, discharging the solute into the internal phase. The unchanged carrier (C) will diffuses back to the membrane-external interface to continue the same cycle.

The driving force in Type II is the concentration gradient of the solute-carrier complex at the external and internal interface. According to Wan et al. (1997), the concentration gradient of the solute-carrier complex across the membrane phase is maximized by reaction with a stripping agent at the membrane-internal interface since the solute is insoluble in the membrane phase. Apart from that, pH difference between internal and external phases also affect the removal of solute (Kargari et al., 2006). This mechanism allows the carrier molecules to transport the solute as many times as necessary hence reducing the amount of carrier required in the membrane phase.



(a) (b) (c)

Figure 2.8 Transport Mechanism of solute in liquid membranes (a) Simple (b) Type I Facilitated (c) Type II Facilitated, where F is feed phase, M is membrane phase and S is stripping phase (Kislik, 2010).

2.6 Emulsion Formulation

The development of ELM system can be considered as a simple process however, it is hard to maintain ELM for long application. For an efficient separation, the emulsion must have a high viscosity, neutral buoyancy for emulsion suspends in the external phase and large concentration of surfactant for emulsion stability (Hiroshi, 1990). Therefore, the ELM formulation which include carrier, diluents and stripping agents are important. The success of an ELM process always depends on the choice of components in its formulation since indirectly it will affect the extraction efficiency. Besides, ELM formulation is also needed to produce a stable emulsion which is able to effectively entrap the solute in the feed phase. Thus, ELM must be optimally stable to ensure a high extraction efficiency.

Some of emulsion liquid membrane formulations for various solute extraction are summarized in Table 2.3. Studies on extraction of pharmaceutical contaminants in table below are acetaminophen, penicillin G and propylpraben. The maximum extraction of pencilin G was achieved by Lee (2000) by altering the surfactant composition of Span 80 and non-ionic polyamine PARABAR 9551. Chaouchi and Hamdaoui (2014) studied the extraction of acetaminophen (known as paracetamol)

from aqueous solution where the study used hexane as diluent, Aliquat 336 as carrier, potassium chloride, KCl as stripping agent and Span 80 as surfactant. As a result, almost all of the ACTP contaminants were successfully extracted from the aqueous solution. Besides that, Chaouchi and Hamdaoui (2015) also studied the extraction of endocrine disrupting compound propylprarabane (PP) from water. The study showed promising method to remove PP contaminants using trioctylphosphine oxide (TOPO) as carrier, hexane as diluent, Sodium Carbonate, Na_2CO_3 as stripping agent and Span 80 as surfactant.

It can be concluded that ELM is a tailor-made formulation which means that different formulation is applied depending on the solute of ion extract. Basically, there are 3 main phases in ELM system which are internal, membrane and external phase. The primary emulsion which consists of membrane and internal phase normally have a diameter ranging from 0.01 to 0.1 mm (Matsumiya et al., 2006).