

**SYNTHESIS OF IRON AND COBALT CONTAINING
IONIC LIQUIDS AND THEIR APPLICATION IN
MICROEXTRACTION AND ADSORPTION**

BY

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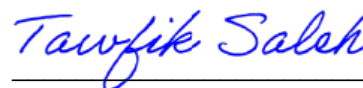
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DEDICATED

TO

My beloved parents, brothers, sisters, wife, and daughter for their continuous support,
prayers and love all my life. |

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LIST OF ABBREVIATIONS

IL	:	Ionic Liquid
OCPs	:	Organochlorine Pesticides
GC-MS	:	Gas Chromatography-Mass Spectrometry
UV	:	Ultraviolet
μ-SPE	:	Micro-Solid-Phase Extraction
SB-μSPE	:	Stir-Bar Supported Micro-Solid-Phase Extraction
D-μSPE	:	Dispersive Micro-Solid Phase Extraction
MIL	:	Magnetic Ionic Liquid
[OA]FeCl₄	:	(Z)-octadec-9-en-1-aminium tetrachloroferrate (III)
[OA]CoCl₃	:	(Z)-octadec-9-en-1-aminium trichlorocobaltate (II)
[OA]Cl	:	(Z)-octadec-9-en-1-aminium chloride
CLOM	:	Clomipramine
CBZ	:	Carbamazepine
KETO	:	Ketoprofen
LOP	:	Loperamide
R²	:	Correlation Coefficient

RSD	:	Relative Standard Deviation
LOD	:	Limit of Detection
LOQ	:	Limit of Quantification
DFT	:	Density-Functional Theory
RB	:	Rose Bengal
MB	:	Methylene Blue
SPE	:	Solid-Phase Extraction
SPME	:	Solid-Phase Micro-Extraction
DLLME	:	Dispersive Liquid-Liquid Microextraction
SLME	:	Supported Liquid Membrane Extraction
SDME	:	Single Drop Micro-Extraction
HFSLME	:	Hollow Fiber Supported Liquid Membrane
LCMS	:	Liquid Chromatography–Mass Spectrometry
MALDI	:	Matrix-Assisted Laser Desorption/Ionization
NSAIDs	:	Nonsteroidal Anti-Inflammatory Drugs
RTILs	:	Room Temperature Ionic Liquids
FILs	:	Frozen Ionic Liquids

DCM	:	Dichloromethane
AAS	:	Atomic Absorption Spectrometry
¹HNMR	:	Proton Nuclear Magnetic Resonance
FT-IR	:	Fourier-Transform Infrared Spectroscopy
XRD	:	X-Ray Powder Diffraction
TGA	:	Thermogravimetric Analyzer
SEM	:	Scanning Electron Microscopy
EDX	:	Energy Dispersive X-Ray
POPs	:	Persistent Organic Pollutants
MEPs	:	Micro Extraction by Packed Sorbent
MSPE	:	Magnetic Solid Phase Extraction
[4-MA][FeCl₄]	:	4-methylbenzenaminium tetrachloroferrate (III)
[1-NA][FeCl₄]	:	1-naphthyl ammonium tetrachloroferrate (III)
EPR	:	Electron Paramagnetic Resonance
SERS	:	Surface-Enhanced Raman Spectroscopy
PP	:	Polypropylene
EF	:	Enrichment Factor

DI	:	Deionized
HPLC-DAD	:	High-Performance Liquid Chromatography Diode-Array Detector
PF	:	Preconcentration Factor
PPMS	:	Physical Property Measurement System
HOMO	:	Highest Occupied Molecular Orbital
LUMO	:	Lowest Unoccupied Molecular Orbital
ESI-MS	:	Electrospray Ionization Mass Spectrometry
[P₆₆₆₁₄]	:	Trihexyltetradecylphosphonium
[Bmim]	:	1-Butyl-3-methylimidazolium hexafluorophosphate
[C10mim]	:	1-Decyl-3-methyl-1H-imidazol-3-ium
[Nbmim]	:	1-butyronitrile-3-methylimidazolium

ABSTRACT

Full Name : Ahmed Abdi Hassan
Thesis Title : Synthesis of iron and cobalt-containing ionic liquids and their application in microextraction and adsorption.
Major Field : Chemistry
Date of Degree : April 2021

[This research involves the synthesis of cobalt- and iron-containing ionic liquids (ILs) from readily available and cheap amines as useful materials for the microextraction of pharmaceuticals and organochlorine pesticides (OCPs) and the adsorption of cationic and anionic dyes, respectively, coupled with HPLC, GC-MS and UV-Vis as detection techniques. ILs containing transition elements such as iron and cobalt can respond to an external magnetic field and increase the surface area of the material. Due to the easy modifiability of ILs, they can be used for the extraction of both hydrophilic and hydrophobic analytes. Moreover, they can be easily separated from the sample after extraction by magnet (if the magnetic property is strong), membrane separation, filtration, and centrifugation. Therefore, in this study, we successfully synthesized and characterized IL, 4-methylbenzenaminium tetrachloroferrate (III) and used it for the extraction of organochlorine pesticides (OCPs) from environmental water samples. This is the first time that IL is used in stir bar assisted membrane protected micro solid phase extraction and analyzed in gas chromatography-mass spectrometry (SB- μ -SPE-GC-MS). Various parameters affecting the extraction were optimized and the analytical figures of merit for the nineteen target OCPs were studied and determined as follows: Different linear ranges (1-100, 4-100, 10-100 $\mu\text{g/L}$), correlation coefficients between 0.9943 and 0.9992. Intraday

and interday RSD% were between 3.9 and 12.5%. The detection limits were found to be 0.25 to 3.4 µg/L. The developed method was tested on real agricultural wastewater samples for pre-concentration and determination of OCPs.

Also, a simple and efficient method based on D-µ-SPE-HPLC was developed for the preconcentration and quantification of the drug carbamazepine in environmental water and urine samples. Magnetic ionic liquids, (Z)-octadec-9-en-1-aminium tetrachloroferrate (III) and (Z)-octadec-9-en-1-aminium trichlorocobaltate (II) were prepared and used as sorbents at room temperature. A linearity range of 1-1000 µg/L was obtained with a correlation coefficient of 0.9989, relative standard deviation for intraday 0.4% and interday 2.1%. The detection limit was found to be 0.51 µg/L.

The same magnetic ionic liquid (Z)-octadec-9-en-1-aminium tetrachloroferrate (III) sorbent was extended to simultaneous extraction and preconcentration of three categories of pharmaceutical products clomipramine, ketoprofen and loperamide in wastewater and urine samples. The correlation coefficients (R^2) obtained were 0.9974, 0.9967 and 0.9967 for CLOM, KETO and LOP, respectively. The RSD% for intraday and interday were found to be 2.7 and 3.1%, 3.3 and 2.6% and 3.7 and 3.0% for CLOM, KETO and LOP, respectively. The LODs obtained were 2.3 µg/L for CLOM, 2.4 µg/L for KETO and 2.9 µg/L for LOP.

Finally, 1-naphthylammonium tetrachloroferrate (III) was also synthesized and used as an adsorbent for the removal of methylene blue (MB) and rose bengal (RB) dyes from aqueous solutions. The adsorption capacity of the adsorbent at equilibrium was found to be 6.443 mg/g for MB and 20.70 mg/g for RB. The adsorption kinetics followed a pseudo-second order kinetic model with R^2 value above 0.99. Moreover, the density functional theory

calculation (DFT) confirmed an excellent correlation between the experimental results and the theoretical studies.

Therefore, in this research work, readily available and environmentally friendly amines were used as starting compound for the preparation of ILs and then their suitability for the microextraction of pharmaceutical products, OCPs and adsorption of dyes were investigated. The extraction enhanced with ILs sorbent is inexpensive, easy to handle and efficient. In this research work, several factors were also optimized and with the adjusted parameters, method validation was also studied which showed higher extraction efficiency and adsorption capacity. The methods developed here in this study were compared with other related published works.]

ملخص الرسالة

الاسم الكامل: أحمد عابدي حسن

عنوان الرسالة: تصنيع السوائل الأيونية المحتوية على الحديد والكوبالت وتطبيقاتها في الإستخلاص الدقيق و الإدمصاص

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يتضمن هذا البحث تصنيع السوائل الأيونية المحتوية على الكوبالت و الحديد من أمينات متوفرة ورخصية الثمن والتي تعتبر بدورها مواد قيمة للإستخلاص الدقيق للمواد الصيدلانية و مبيدات الكلور وعضوية وبالمثل إدمصاص الصبغ الكتيونية و الأيونية ويتصل مع GC-MS, HPLC, UV-VIS و التي تمثل تقنيات الكشف بالترتيب. السوائل الأيونية التي تحتوي على عناصر إنتقالية مثل الحديد و الكوبالت يمكن أن تستجيب لمجال مغناطيسي خارجي و تزيد بدورها مساحة سطح المادة. سهولة تعديل السوائل الأيونية يجعل من السهل إستخدامها في كلتا المواد الكارهة و المحبة للماء. بالإضافة لذلك يمكن فصلها بسهولة من العينة بعد عملية الإستخلاص بإستخدام المغناطيس (في حالة الخاصية المغناطيسية القوية)، الفصل بالغشاء، الترشيح والطررد المركزي . لذلك، تم بنجاح تصنيع و تشخيص السوائل الأيونية، 4- ميثيل بنزين أمونيوم رباعي حديدات (III) و تم إستخدامه للإستخلاص مبيدات الكلور وعضوية من عينات مياه بيئية. وهذه أول مرة يتم فيها توظيف السوائل الأيونية في قطب تحريك مدعوم بغشاء للإستخلاص الدقيق في الطور الصلب و تم تحليله عن طريق كروماتوغرافيا الغاز - مطياف الكتلة (SB- μ -SPE-GC-MS). تمت دراسة عدة متغيرات ذات تأثير على الإستخلاص و قيم مزايا التحليل والتي تم اختبارها و وجدت كالتالي بالنسبة لتسعة عشر عينة من عينات مبيدات الكلور وعضوية ؛ عند إستخدام نطاقات خطية مختلفة من (1-100, 4-100 و 10-100 ميكرو جرام /لتر)، كانت معاملات الارتباط في المدى بين 0.9943 و 0.992. الإنحراف المعياري النسبي داخل اليوم الواحد و بين الأيام يتراوح بين 3.9 - 12.5 %. و كانت حدود الكشف من 0.25 - 3.4 ميكرو جرام /لتر. تم إختبار هذه الطريقة علي عينات حقيقية علي مياه صرف صحي زراعية لتركيز و تعيين مبيدات الكلور و العضوية .

و تم أيضاً تطوير طريقة بسيطة وذات كفاءة عالية بناءً على (D- μ -SPE-HPLC) لتركيز و تقدير كمية عقار الكاربامازيبين في عينات بيئية من المياه و البول. تم تحضير السوائل الأيونية المغناطيسية (Z)- أوكتا ديك-9-ين-1-أمينيوم رباعي كلورو حديدات (III) و (Z)- أوكتا ديك-9-ين-1-أمينيوم ثلاثي كلورو كوبالتات (II) و تم توزيعها كمواد إمتصاص في درجة حرارة الغرفة. تم التحصل على معامل ارتباط 0.9989 للنطاق خطي 1-1000 ميكرو جرام /لتر، تم تسجيل الإنحراف المعياري النسبي في داخل اليوم الواحد بنسبة 0.4% و 2.1 % كنسبة بين الأيام. ووجد أن حد الكشف يساوي 0.51 ميكرو جرام /لتر. إضافة لذلك تم استخدام نفس السائل الأيوني (Z)- أوكتا ديك-9-ين-1-أمينيوم رباعي كلورو حديدات (III) في الإستخلاص والتركيز الآني لثلاثة منتجات صيدلانية كلومبيرامين، كيتوبروفين ولوبراميد الموجوده في عينات مياه الصرف الصحي والبول. تم التحصل علي معاملات الارتباط 0.9974، 0.9967 و 0.9967 للعينات كلومبيرامين، كيتوبروفين ولوبراميد على التوالي. تم تسجيل الإنحراف المعياري النسبي في داخل اليوم الواحد و كنسبة بين الأيام 2.7 و 3.1%، 3.3 و 2.6%، 3.7 و 3.0 % للعينات كلومبيرامين، كيتوبروفين ولوبراميد على التوالي. و حدود الكشف كانت 2.3، 2.4 و 2.9 ميكرو جرام /لتر للعينات كلومبيرامين، كيتوبروفين ولوبراميد على التوالي.

وأخيراً، تم تحضير 1-نفثالين أمينيوم رباعي كلورو حديدات (III) واستخدامه كمادة ادمصاص لإزالة صبغات الميثايلين بلو و الروزبنغال من محاليل مائية. وقد وجدت سعة الأدمصاص عند الأتزان تساوي 6.443 و 20.70 ملي جرام/جرام لعينات الميثايلين بلو و الروزبنغال على التوالي. وتتبع حركية الأدمصاص نموذج حركية الرتبة الثانية الكاذبة بقيمة (R^2) اعلى من 0.99. إضافة لذلك أكدت حسابات نظرية الكثافة الوظيفية (DFT) صلة عالية بين النتائج العملية المتحصل عليها و الدراسات النظرية.

لذلك، في هذا البحث تم استخدام أمين متوفر وصديق للبيئة كمادة أساسية لتحضير السوائل الأيونية، ومن ثم تم اختبار مدى صلاحيتها في الاستخلاص الدقيق في المنتجات الصيدلانية، المبيدات الكلور وعضوية و أدمصاصها للأصباغ. الاستخلاص المعزز بالسوائل الأيونية يعتبر رخيص الثمن، سهل التعامل و ذو كفاءة عالية. في هذا البحث، تم ايضا ضبط عدة عوامل، و باستخدام المتغيرات المثلى، وتم التحقق من صحة الطريقة لتظهر كفاءة استخلاص و سعة إدمصاص عالية. تمت مقارنة هذه الطرق المطورة في هذه الدراسة بدراسات ذات صلة منشورة مسبقاً.

CHAPTER 1

INTRODUCTION

1.1 Background Information

Pollutants, whether pesticides, pharmaceuticals, dyes, or synthetic organic compounds, have continuously become a major challenge in modern times and are mostly found in the aquatic environment [1]. Organic pollutants have become a major threat because they can only be partially removed during wastewater treatment and pose a threat to humans and animals through drinking water. In particular, the pharmaceutical industry dealing in human, poultry and fish medicines contributes to the environmental hazard and it is estimated that there are more than 3000 different ingredients that can easily enter the environment [2]. In addition, dyes in aqueous medium also contribute significantly to environmental pollution, and recently more than 9000 different types of dyes have been included in the color index. Many industries use dyes; however, the textile industry is the main user because the market demands attractive fabrics [3]. Therefore, investigating the fate of these chemical contaminants and ensuring safe drinking water is crucial. In this regard, developing a suitable, efficient, simple, accurate and reliable method is equally important. The concentrations of these contaminants, such as drugs and pesticides, are in the trace range and require a pre-concentration step to be detected by a suitable instrument. A commonly used method is solid phase extraction (SPE) to isolate them from the water matrix [4]. However, there is still a need to develop suitable, efficient, and economical methods not only for environmental samples but also for biological and food samples.

Biological samples are usually complex as they contain blood and blood derivatives, tissues, and urine, etc., which contain proteins in significant amounts and therefore require appropriate sample preparation before analysis is carried out [5]. The traditional method is no longer practical as it is expensive, time consuming, labor intensive and outdated in modern science. To address this challenge of traditional methods and classical approach, many innovations have been successfully developed in recent decades to improve the existing techniques, especially in solid phase microextraction (SPME) so that it can be directly applied to biological and complex matrices for pharmacokinetic studies as well as drugs and in vivo applications, but this has not been successful in many cases [6]. Therefore, researchers have been striving for several years to develop fast, reliable, selective, sensitive, and accurate methods that can also be automated to detect and quantify analytes at trace levels, but despite great technological advances in the analytical field with little success, especially the direct introduction of samples into analytical instruments is still a major challenge. Therefore, an additional step is required to isolate the analyte from the main matrix without losing, affecting, or changing the composition and concentration. Therefore, proper sample preparation is inevitable to pre-concentrate the analytes and extract, purify and modify them from the matrix to the limit of detection to achieve the desired instrument compatibility [7]. All these reduce errors and provide reliable results in the analysis. Therefore, it is important to develop a suitable microextraction method that also meets green chemistry standards [8]. Thus, microextraction is not only important in analytical chemistry but is also increasingly used in research in almost all disciplines such as biochemistry, chemistry, genetics, chemical engineering, environmental science, molecular biology, medicine, toxicology, pharmacology, pharmaceuticals, food and flavor,

and even social sciences [9]. Microextraction is an integral part of science in general and has a decades-long tradition. Many techniques such as dispersive liquid-liquid microextraction (DLLME), discovered by Rezaee and coworkers in 2006, remain popular and were first used to determine organic contaminants in water [10]. Electromediated extraction has also gained importance, especially for cations and anions by applying an electric field to the supported liquid membrane (SLM) [11], solid phase microextraction [9] and micro solid phase extraction [12] are other techniques that are widely used. However, all these techniques have weaknesses and there is room for improvement and development of tailored, simple, environmentally friendly, and low-cost methods with high enrichment factor.

Moreover, microextraction and preconcentration of analytes from aqueous media require the selection of a suitable excellent sorbent with the following properties: low solubility in water, a chemical structure that gives a high partition coefficient of the analyte, low vapor pressure, thermal instability, and high polarity, since most analytes belong to polar compounds. Most of these mentioned properties are fingerprints of ionic liquids (ILs) [13].

Over the decades, ILs have attracted immense attention from researchers both in science and engineering as evidenced by the high number of citations especially in analytical and organic chemistry and other related fields [14]. ILs are basically salts with organic or inorganic anions and organic cations, with low melting point of less than 100 °C [15]. The main advantage of ILs is their low cost, easy isolation, and possibility of reuse. Besides, several ions are available for selection in their synthesis, and they are often referred to as “model solvents” due to their appealing chemical and physical properties such as viscosity, low melting points, thermal stability, density, and even low solubility in water and some other solvents [16]. Furthermore, compared to other available conventional solvents, ILs can be fine-tuned to achieve the desired chemical and physical properties, which makes them very powerful in sample preparation and many other applications. Such superior properties are electrical conductivity, volatility, hydrophobicity, hydrophilicity, lubricant for polymers, catalyst and extraction properties, solubility in organic and inorganic compounds, acidity, and basicity etc. All these fascinating properties led scientists to develop interest in the application of ILs for extraction purposes in dispersive liquid-liquid microextraction (DLLME) [7], single droplet microextraction (SDM) [17], solid phase extraction (SPE) [9], solid phase microextraction (SPME) [18] and hollow fiber supported liquid membrane extraction (HF-SLME) [19]. Recently, many literatures have also reported ILs as potential adsorbents for the removal of various types of dyes [20]–[25].

Nevertheless, ILs have a major challenge which is phase separation, especially when solvent-based extraction is involved. However, the effects are reduced by centrifugation and the solvent is evaporated only for those solvents that have a density higher than water this approach is not cost-effective [26]. Therefore, ILs with magnetic properties have attracted the attention of scientists as they provide faster and good phase separation that can be easily performed by applying an external magnetic field to isolate the sorbent or extractant with the analyte from the aqueous medium, which can be desorbed, purified, and reused, making the material environmentally friendly, easy to handle, efficient and cost-effective. However, the separation depends on the strength of the magnetic property of the material [27].

Recently, ILs with magnetic property have become a landmark in phase separation, which increases the efficiency in extraction and adsorption applications and even attracts scientists in the field of physics and other disciplines [28]. In the case where magnetic metals are incorporated externally, they form magnetic nanoparticles, and the main challenge is that poorly functionalized ILs can easily leave the surface of the magnet during adsorption and desorption, which makes complete separation difficult, especially in solid phase extraction and adsorption. This problem was overcome by incorporating the ILs with metal ions such as Fe, Mn, Co, Gd, etc., forming magnetic ionic liquids (MILs) with cation and anion content, which made the separation much easier than using externally incorporated metals [29]. Based on this, researchers have moved to incorporate the metals into the ILs and develop MILs to obtain anion and cation parts rather than using them externally. These compounds can be easily dispersed in a sample solution and easily isolated by centrifugation or filtration if they do not respond to a strong external magnetic field, which minimizes time and energy consumption and further increases efficiency [30].

Therefore, the aim of this work is to synthesize and characterize cobalt- and iron-containing ILs from simple, cheap, and readily available amines and to apply them in the microextraction of environmental pollutants OCPs and various categories of pharmaceutical products from wastewater and biological samples, as well as in the adsorption of dyes from aqueous solutions. We chose amines because they are less toxic, more available, and cheaper compared to other cationic groups. They have lone pair of electrons, easily form basic ammonium salts as intermediates in reaction with hydrochloric acids, play nucleophilic role in most reactions and presence of aromatic rings with π - π bonding interactions becomes an additional advantage for extraction and adsorption, all these properties make amines more attractive for researchers [31], [32].

1.2 General objectives

The aim of this study is to develop a simple, novel, and sensitive technique for the instant extraction, preconcentration and detection of various pharmaceutical compounds and OCPs in a complex matrix such as wastewater and urine samples. Similarly, adsorption of dyes from aqueous media. These techniques require a simple, manageable extraction and adsorption setup that includes a magnetic stirrer or a shaker to allow contact between analytes and sorbent in a small beaker, with a different time frame for the extraction and adsorption process, immediately followed by separation of the sorbent-rich analytes by centrifugation. This is followed by ultrasonic treatment for desorption and finally direct

injection into the HPLC or GCMS or UV-Vis instruments for detection and quantification of the respective analytes.

The main objective of this research work is to study various parameters affecting the extraction and adsorption efficiency such as equilibrium time, pH of sample solution and ionic strength. To evaluate the applicability of the synthesized cobalt and iron containing ILs for extraction and adsorption of OCPs, drugs and dyes to study quantitative aspects like recovery and reuse of ILs.

1.2.1 Specific objectives

- i. Synthesis, characterization, and investigation of a new class of ILs containing iron and cobalt from simple, cheap, and readily available amine compounds.
- ii. To assess the performance of the prepared ILs for D- μ -SPE of carbamazepine drug from biological and environmental water samples.
- iii. To investigate potential applications of the ILs in SB- μ -SPE of OCPs in environmental samples.
- iv. To evaluate the synthesized ILs for the adsorption of rose bengal (RB) and methylene blue (MB) dyes from aqueous solutions.
- v. Recycling and reuse of these ILs for cost-effectiveness and environmental protection.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

Recently, pharmaceutical, and other environmental pollutants, including pesticide contamination of food, have become a major problem in the world. Pharmaceuticals contribute most to water pollution due to incomplete treatment of the compounds [33]. Drug abuse by drug addicts which reach high concentrations in the body due to excessive consumption beyond the recommended amount, leading to severe life-threatening consequences, is becoming more eminent [34]. These compounds contain several unique substituents that behave differently in the environment, whether in waste or drinking water. Some form more complex and difficult products, by-products, and metabolites by reacting with other substances when dissolved. The presence of these pharmaceutical products in humans, vegetation, wildlife, and aquatic environments needs to be monitored and regulated for transport and fate to meet internationally established standards. Therefore, urgent, and rapid measures are required for the treatment, extraction, and adsorption of these products from the main matrix [35]. Therefore, microextraction techniques such as solid-phase and liquid-liquid microextraction have become essential for the treatment processes. However, some of the reported methods are expensive, demanding, time consuming and environmentally harmful as they generate excessive organic solvents [36]. Moreover, these compounds have very large molecular weight, especially pharmaceuticals

and dyes, so their diffusion through materials by adsorption becomes difficult unless a special material is designed and synthesized for their specific extraction and adsorption process [37].

The currently existing techniques are very expensive and require derivatization of the compounds, especially when using gas chromatography (GC). Derivatization is not only expensive, but it can also affect the accuracy of the method utilized, lead to loss of analytes and incomplete reaction of derivatization, making it difficult to determine trace levels. Organic pollutants are the most important environmental pollutants as they are generated by our daily activities such as households, hospitals, farms, and industrial disposals. Pharmaceuticals are other pollutants that are first metabolized and excreted in their respective metabolites or parent form, and in some cases these metabolites are even more toxic than the parent compounds in the environment. The development of selective and sensitive analytical techniques in the last decades has made a remarkable contribution to the detection and quantification of these compounds, but there is still a need to establish a more reliable, precise, and accurate detection technique for the efficient extraction of these compounds and their metabolites [38]. LCMS is an excellent technique that reduces the effect of derivatization, but analytical problems arise when using wastewater, as the sensitivity decreases, and a purification step becomes necessary [39]. GC-MS offers better sensitivity and specificity for volatile, non-polar and low molecular weight compounds and is still considered the gold standard for broad screening. HPLC coupled with a UV detector can be an excellent alternative that provides results based on the signal to background ratio, which is due to the superior selectivity and precision of the detection system and is therefore preferred for the quantification of drugs and drug-related analytes. In addition, HPLC can determine a large number of compounds with large molecular weights simultaneously [40].

Recently, there has been good progress in environmentally friendly extraction techniques such as SPE and SPME which are time saving and require less effort and organic solvents. The most commonly used technique is SPE where the separation depends on the interaction of analytes with the stationary phase, washout from the mobile phase and finally the release of analytes for detection. All these parameters affect the limits of detection (LODs) and recoveries, thus requiring optimization during extraction, which is challenging when compounds are determined simultaneously [41]. The most interesting part of SPE is its ability to be automated, resulting in better accuracy and speed by performing conditioning, washing, and elution of analytes simultaneously [42]. Common solvents used for these steps are usually methanol, ethanol, acetonitrile, and ethyl acetate.

SPME is another technique that has attracted the interest of many researchers working on organic compounds in aqueous media, including pharmaceuticals. Basically, SPME extracts the target compound through the absorption layer, which consists of fibers coated with sorbents, until equilibrium is reached by convection or stirring, followed by desorption by solvent or thermally. SPE provides quantitative extraction as the entire sample passes through the sorbent cartridge, but SPME technique is gaining importance due to its speed, time efficiency, small sample volume and reusability of the fibers [43]. Selection and synthesis of the right sorbent material for SPME are important, and amine-based MILs can be an excellent option. The group of Santos and Albo have synthesized several MILs from different amines and studied their chemical and physical properties as well as their application. In 2009, they reported chiral ionic liquids derived from amino acids [44], in 2013 they were used for CO₂ separation [45], and recently they reported variable MILs that are hydrophobic and derived from amines for MALDI analysis [46]. Therefore, synthesis and use of MILs are well established and several literatures have reported MILs used for microextraction of various analytes, especially by modifying commercially available ionic liquids (**see Table 1**).

Therefore, the synthesis and characterization of ILs containing the transition elements cobalt and iron, derived from readily available and cheap amines, for various microextraction applications and dye adsorption is an interesting area to be explored.

Table 1: Summary of some literature in microextraction using MILs.

Analyte	Extraction Technique	MILs	Instrument	Ref.
Triazines	MIL-DLLME	[C _{6mim}] [FeCl ₄]	HPLC-UV	[47]
Phenolic compounds & Acidic pharmaceuticals	SADBME	{N _{8,8,8,+} }[FeCl ₄]	HPLC-DAD	[48]
Arsenic	MIL-DLLME	[P _{6,6,6,14}]FeCl ₄	ETAAS	[49]
Volatile PAHs	SBDLME	[P _{6,6,6,14}][Ni(hfacac) ₃ ⁻]	GCMS	[50]
Pesticides	MIL-MSPD	[P ₆₆₆₁₄₊][Co(II)(hfacac) ₃ ⁻]	HPLC-DAD	[51]
Paraben	MIL-DLLME	{N _{8,8,8,+} }[FeCl ₄]	HPLC-UV	[52]
Estrogens	MIL-DLLME	[P _{6,6,6,14+}] ₂ [MnCl ₄ ²⁻]	HPLC-DAD	[53]

In this research work, we first identified commonly prescribed pharmaceutical products like nonsteroidal anti-inflammatory drugs (NSAIDs) such as ketoprofen [54] and carbamazepine, which was detected in wastewater [55], as well as clomipramine, which is abused by drug addicts, and loperamide (**Fig. 1**) for preconcentration and determination in environmental water and urine samples [56], [57].

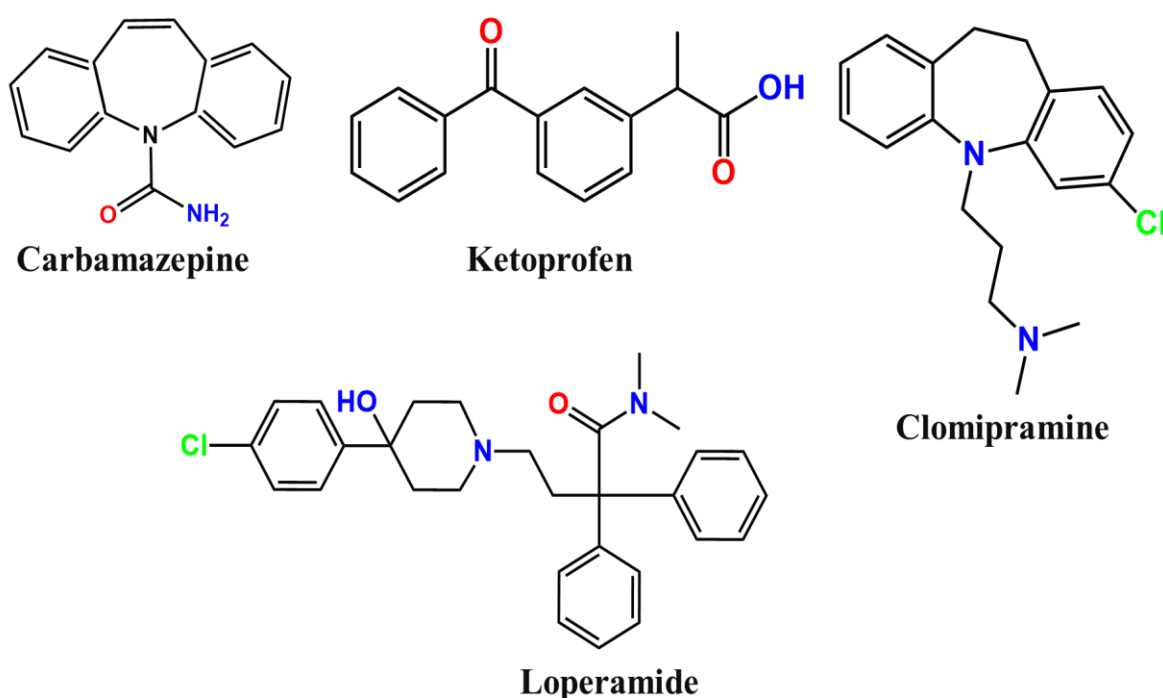


Figure 1: Selected pharmaceutical products for the study.

Undoubtedly, there is a need to study these pharmaceutical products and their metabolites in the aquatic environment and in biological samples, as they may ultimately pose a threat to the sustainability of our ecosystem. In terms of analytical methods, there have been advances in the identification and quantification of the compounds, especially LC-MS and

GC-MS, which have played a crucial role, but further scientific research in this direction is needed to provide relevant answers and solutions for the simultaneous extraction and pre-concentration of these compounds.

The other major area of interest is pesticides pollution. These are toxic and hazardous substances that are intentionally released into the environment to kill organisms such as rodents, fungi, weeds, and insects. In addition, these pollutants are used by public health to control vector diseases and are also used in electrical appliances such as refrigerators [58]. They are designed to be toxic and can be harmful to humans and other living things even at low concentrations if not handled properly.

Exposure to pesticides can cause various diseases such as cancer, hypersensitivity, allergies, asthma, hormonal problems, birth defects and in extreme cases death. Due to these associated health problems, the study and extraction of these compounds is important and warranted [59]. The most important pesticide pollutants are organochlorines (OCPs) **(Fig. 2)**. Although they are banned worldwide, they are still used in some developing and underdeveloped countries, and their residues are still in the environment and must be properly removed because they are toxic to all species and have significant physiological effects on the body, whether on the reproductive, circulatory, or nervous systems [60]. They can also remain in the environment for a very long time due to their low rate of biodegradation [61].

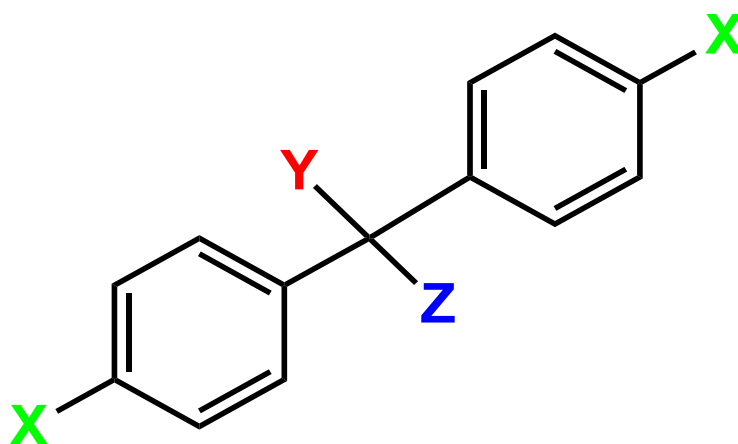


Figure 2: General structure of OCPs where X is Cl, F, C₂H₅ and OCH₃, Y is OH, H and whereas Z is CCl₃, CCl₂, CHCl₂, COOC₂H₅, CH(NO₂) C₂H₅ and CH₃

Thus, in summary, we considered the study of membrane-protected micro-solid phase extraction coupled with GC-MS for OCPs in environmental water samples and dispersive micro-solid phase extraction of carbamazepine, loperamide, clomipramine, and ketoprofen in wastewater and urine samples.

2.2 Existing Microextraction Techniques

There are various techniques and methods for extraction of pharmaceutical products and their metabolites listed in USEPA method-521 such as solid phase extraction (SPE) [62], liquid-liquid extraction (LLE) [63], [64], steam distillation and solid phase microextraction (SPME) [65]. Solid-phase extraction (SPE), which involves several steps of labor-intensive sample extraction, uses a relatively large number of solvents, which is expensive and contributes to environmental pollution. Another challenge is the SPE cartridges, which are not reusable, making the extraction techniques more cumbersome and costly [66]. LLLE is equally challenging in terms of solvent consumption and effectiveness, which leads to more environmental pollution; moreover, it takes longer time especially the pre-concentration step and generally the whole experiment may require up to about 20 hours to be completed.

Solventless extraction such as SPME is gaining the interest of researchers due to its environmental friendliness as there is no solvent waste and the technique is time saving as both extraction and sample preparation are done simultaneously. However, the technique also has drawbacks such as loss of sorbent coating on the fiber, which is expensive, fragile, and entails carryover effects [67]. Steam distillation is usually used only for volatile pollutants from industrial wastes and environmental samples [68]. No doubt, LLE is still required for the enrichment of distillates, and a complex setup is inevitable, excessive solvent generation in the process and longer analysis time make it difficult. Therefore, to overcome these drawbacks, researchers have worked on various micro solid phase extraction (μ -SPE) techniques; be it dispersive, pipette tip, spin column, membrane protected, etc. In this study, we investigated the efficiency of membrane-protected micro solid phase extraction of OCPs in environmental water samples and dispersive micro solid phase extraction of carbamazepine, loperamide, clomipramine and ketoprofen in wastewater and urine samples.

2.3 Dye pollution

Dyes are also environmental pollutants in aqueous medium, and recently over 9000 different types of dyes have been included in the Dye Index. Many industries use dyes; however, textile processing industry is the major user as the market demands attractive fabric dyes [3]. Various techniques have been used to remove dyes from the environment; such approaches can be summarized as adsorption [69], [70], electrocoagulation [71],

reverse osmosis [72], electrochemical oxidation [73], ion exchange [74], Fenton oxidation [75], and ozonation [76]. However, adsorption is considered the best process, but unfortunately the availability of cheap effective sorbents is still a problem. Activated carbon (AC), which is commercially available, is considered an excellent option, but the high cost associated with it is a major drawback [77]. Therefore, in this study, we investigated the adsorption performance of rose bengal and methylene blue dyes in aqueous solutions using the synthesized IL.

2.4 Ionic Liquids (ILs)

Ionic liquids (ILs) are a mixture of oppositely charged ions with low interactions that result in low melting point and liquids at low temperatures, such as the [BMIM] cation and the NTf₂ anion. The compound is liquid at room temperature (27 °C) and is therefore called room temperature ionic liquid (RTIL). ILs have long names and are usually abbreviated. They have several properties such as electrically conducting free ions, solvent specific such as carbon dioxide, chemically stable and low vapor pressure, making them safer to use, easier to recycle and more efficient.

ILs are naturally produced by ants, with one ant producing the toxin and the other producing formic acid as an antidote to neutralize the ILs, rendering them harmless [78]. However, the first synthesis in humans was performed in 1888 using ethanol ammonium nitrate with a melting point of 52-55 °C by S. Gabriel and J. Weiner [79]. Thirty years later, in 1914, Paul Walden synthesized ethyl ammonium nitrate with a melting point of 12 °C,

in which the hydroxyl group is substituted by a methyl group, which reduces the overall attraction and thus lowers the melting point, like how water forms hydrogen bonds [80]. In the 1970s and 1980s, pyridinium cations were synthesized with halogen anions and used as electrolytes in batteries, but they decomposed in aqueous acidic and alkaline environments and proved to be unstable. In the 1990s, neutral ILs were synthesized that were more stable, such as the phosphorus hexafluoride anion (PF_6^-) and boron tetrafluoride anion (BF_4^-) by Wilkes and Zawarotko, but they were toxic [81]. In 2004, the first magnetic ionic liquid (MIL), 1-butyl-3-methylimidazolium tetrachloroferrate (III) $[\text{BMIM}]\text{FeCl}_4$, was synthesized by Satoshi Hayashi at the University of Tokyo and opened a new direction in this field [13]. Therefore, current research focuses on reducing toxicity, increasing stability, and improving environmental friendliness.

ILs can be used as solvents in non-aqueous reactions such as Friedel-Crafts and they are also used as catalysts in the synthesis of branched alkenes by dimerization of shorter alkenes in a deeper salt process. The first industrial application was the Basel process, an acid-free pure product in which ILs were used to remove acid residues [82]. ILs can be used in the dissolution of cellulose, e.g., in woods, in the production of biofuels from algae, in the processing of nuclear and normal wastes, and in the capture of carbon dioxide [45], [83]. Therefore, ILs can be considered as an ecofriendly process with high efficiency and little or no production of toxic substances, which makes ILs green solvents for the future.

Therefore, ILs are compounds whose melting point is equal to or lower than $100\text{ }^\circ\text{C}$ and usually consist of bulky organic ions [84]. Inorganic salts such as sodium chloride (NaCl) have melting points higher than $800\text{ }^\circ\text{C}$. If one replaces a part with a bulky organic ion, the melting point decreases due to the poor coordination between the inorganic ions and the

large organic molecule. When ILs have a melting point less than or equal to 25 °C at a vapor pressure of zero, they are called room temperature ionic liquids (RTILs) and when they have a melting point between -100 and 25°C, they are called frozen ionic liquids (FILs) [85]. Generally, the cation part is selected from imidazolium, ammonium, pyridinium, phosphonium, picolinium, oxazolium, pyrrolidinium, sulfonium, thiazolium and pyrazolium ions, while the other part, the anion, can be inorganic or organic, e.g., nitrate, tetrafluoroborate, which are used as counterions [86], [87]. **(Fig. 3)** illustrates the different pathways of ionic liquids from synthesis process to application and recycling. **(Fig. 4)** shows the most common anions and cations used in the synthesis of ionic liquids.

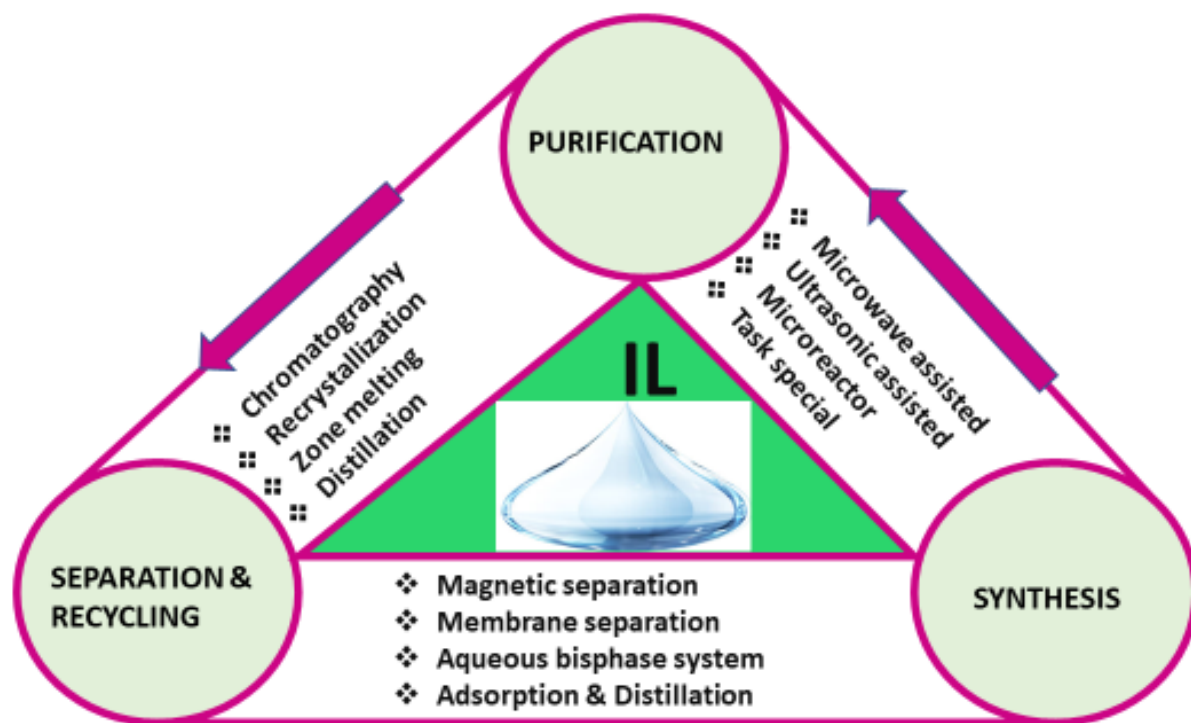


Figure 3: Pathways of Ionic Liquids

In many applications, ionic liquids became attractive for several techniques such as extraction, mass spectrometry, gas chromatography because they are easily tunable by just changing either cation or anion part of the salt, therefore, it changes the properties of the compound by increasing or decreasing the hydrophobicity or hydrophilicity. Ionic liquids have several excellent advantages of both physical and chemical properties such as good solubility in organic and inorganic compounds, low vapor pressure, low melting point, high thermal stability, high viscosity, hydrophobic, non-flammable, and high extractability for trace metals and organic compounds [88].

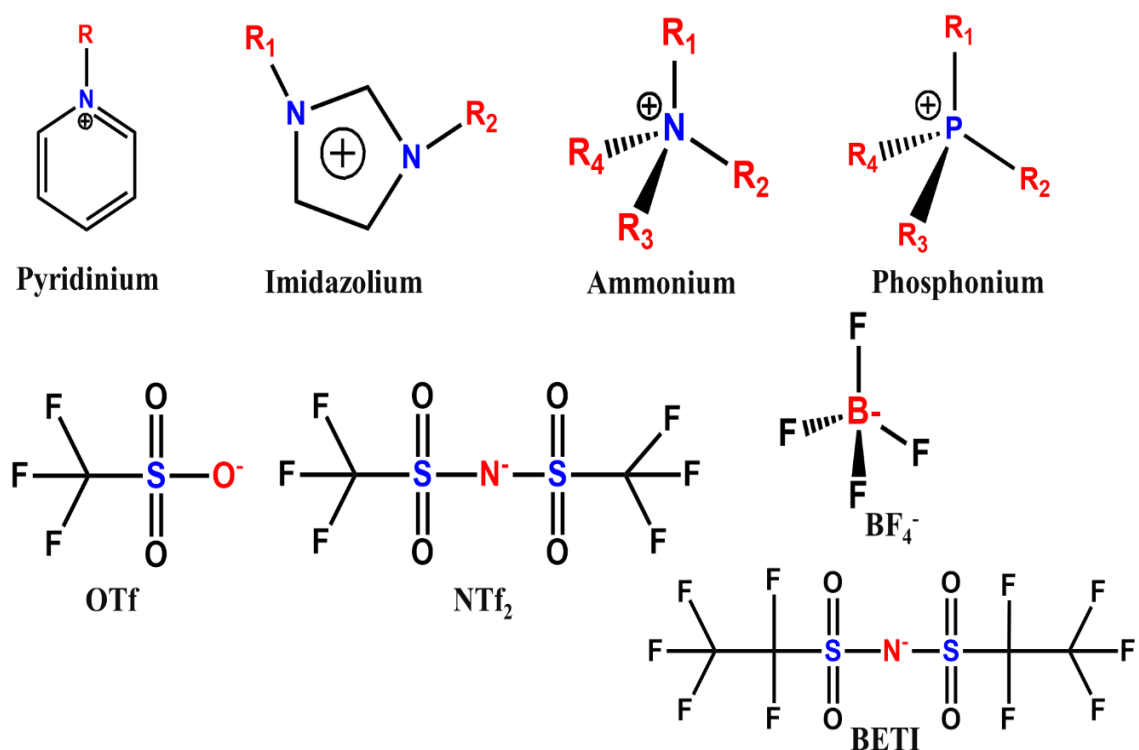


Figure 4: Common anions and cations used for ILs synthesis.

2.5 Magnetic Ionic Liquids Solid-Phase Extraction

There are several drawbacks associated with ILs microextraction, namely the selection of appropriate dispersing solvents. The common ones that have been reported are acetonitrile, methanol, acetone, propanol, and butanol [89]. Isolation of the ionic liquids from the aqueous phase is another problem, and some of the ionic liquids may be lost during the process, resulting in low recoveries of the analytes. To overcome these challenges, a new direction was developed that combines ionic liquids with magnetic properties that are efficient and fast in analytical samples. Yilmaz and his group demonstrated the use of magnetic ionic liquids for the microextraction of lead II from environmental samples [88]. Solid phase extraction with magnetic ionic liquids is a new approach gaining importance in the field of microextraction and involves the synthesis of tailored magnetic ionic liquids for the appropriate analyte of interest. The paramagnetic properties of MILs arise from the anion, with the cation part being either hydrophobic or hydrophilic, and these types of ILs usually contain a transition metal. Therefore, magnetic metals such as Fe, Mn, Co, etc. are incorporated into the part of MIL that forms the anion and cation part. MILs can be easily dispersed in solution and easily separated with analytes by using an external magnetic field to eliminate the centrifugation step, although not all MILs respond completely to the external magnetic field. ILs containing the transition elements iron and cobalt allow sensitive and selective extraction of organic pollutants and pharmaceuticals contaminants, as well as adsorption of dyes. This type of approach is cheap, time efficient, requires little solvent, is reusable and easy to synthesize as they are readily available, cheap amines without complex extraction or adsorption setups, which makes them more attractive and

desirable. Also, the IL-based extraction and adsorption devices that were used were simple instruments in the lab such as vials, flasks, shakers, and magnetic stirrers, which makes the process much cheaper compared to commercially available devices. To the best of our knowledge, there is no much research on microextraction and adsorption of various analytes using synthesized ILs containing iron and cobalt, especially in environmental, wastewater and biological matrices. All existing microextraction and adsorption studies have used commercially available ILs or their modification [90].

2.6 Synthesis and Characterization of MILs

Simplicity in synthesis and reusability make ILs potential adsorbent/material for many applications. For example, 1-butyl-3-methylimidazolium hexafluorophosphate can be easily prepared by mixing only two solvents, water, and dichloromethane (DCM), and a reaction between 1-butyl-3-methylimidazolium chloride and sodium hexafluorophosphate can be easily achieved by the same procedure.

In this study, the methods reported in the literature were adopted but with considerable modifications [44], [46], [91]. In general, the synthesis process used in this work involves two main steps. In the first step, the amine is dissolved in diethyl ether/dichloromethane (DCM)/ethanol or other organic solvent depending on the solubility. Hydrochloric acid is then added, and the mixture is stirred vigorously for 3 to 4 hours to accelerate the formation of the intermediate quaternary salt, and the excess acid is washed out thoroughly with deionized or distilled water to pH range of 4 to 6. The water is then removed by lyophilization or carefully pipetted off and the organic solvent evaporated with a rotary evaporator. The resulting quaternary intermediate salt is further washed several times to get rid of the residual HCl and organic solvents. The second step is the introduction of the anionic moiety, where iron (III) chloride (FeCl_3) or cobalt (II) chloride (CoCl_2) are dissolved in 5.0 mL of methanol or ethanol, depending on the solubility, in a 1:1 ratio equimolar with the quaternary intermediate salt with vigorous stirring for 24-30 hours. The solvent is then evaporated using a rotary evaporator to obtain the resulting IL containing the iron or cobalt. The product is then washed thoroughly with double distilled or deionized water to pH 3 or pH 4.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Instrumentation

Currently, there are several detection methods for various pharmaceuticals, pesticides, and dyes, however, the most common ones used for ILs-based extracted analytes are chromatography and spectroscopy such as HPLC and AAS, respectively [49], [53], [92]–[94]. In this work, chemiluminescence-based detection was avoided because the NH_3 group readily decays upon electronic excitation and can interfere with the analytes, it also requires a high level of expertise in operation and interpretation and has very high maintenance cost [95]. However, spectroscopic techniques such as Raman and FT-IR were used to characterize the materials. Therefore, HPLC, UV-Vis and GCMS detection techniques without derivatization with remarkable efficiency and high sensitivity up to $\mu\text{g/L}$ range were chosen for this study and a similar pattern is also reported in the literature [53], [92] [92].

The most important parameter in HPLC is compatibility, since ILs are analyte-rich and must be successfully desorbed into an organic solvent and injected directly into the instrument, which reduces the risk of errors and shortens the analysis time. In addition, the desorption solvent must be compatible with the mobile phase of the HPLC to minimize interference and contamination. Finally, the most important factor in the UV detector is the

absorption range of the ILs, which must not coincide with the absorption range of the analyte to avoid interference and possible residues of the ILs during the desorption process [90]. To overcome this challenge, in our study, all the materials and the absorption range of the analyte were scanned using the UV-Vis spectroscopy instrument, which is a cheap, simple, and fast technique before running in HPLC. In addition, the UV-Vis instrument is used for the detection and quantification of some analytes, such as dyes. To our knowledge, it has never been used for IL-based extraction and adsorption, which reduces the cost and use of excessive solvents as in HPLC.

3.2 Reagents and Synthesis of ILs

The reagents, chemicals, standards, and analytical grade solvents used in this study were obtained from different suppliers and all dilutions were done using deionized/distilled water from Millipore Milli-Q system. The various standard solutions of analytes were prepared by dissolving in water, acetonitrile or non-polar solvents like hexane and toluene etc. depending on the application. The synthesis of ILs followed previous literature reports but with modifications [44]–[46], [91]. Generally, the process involves two main stages, in the first stage, a simple amine is selected, which is then dissolved in a relevant solvent with hydrochloric acid for 3 to 4 hours with vigorous stirring to accelerate the formation of the intermediate quaternary salt, and then the excess acid is washed away with deionized or double distilled water after evaporation of the solvent. In the second part, FeCl_3 or CoCl_2 is added in methanol or ethanol in an equimolar ratio of 1:1 and stirred for a long time, up to 24-30 hours, so that the iron- and cobalt-containing ILs are formed. Then the solvent is

removed using a rotary evaporator (**Fig. 5**). The synthesized ILs were tested in the microextraction of various pharmaceutical products such as carbamazepine, clomipramine, loperamide and ketoprofen, OCPs and adsorption of rose bengal and methylene blue dyes to investigate the applicability and efficiency of the synthesized iron and cobalt containing ILs.

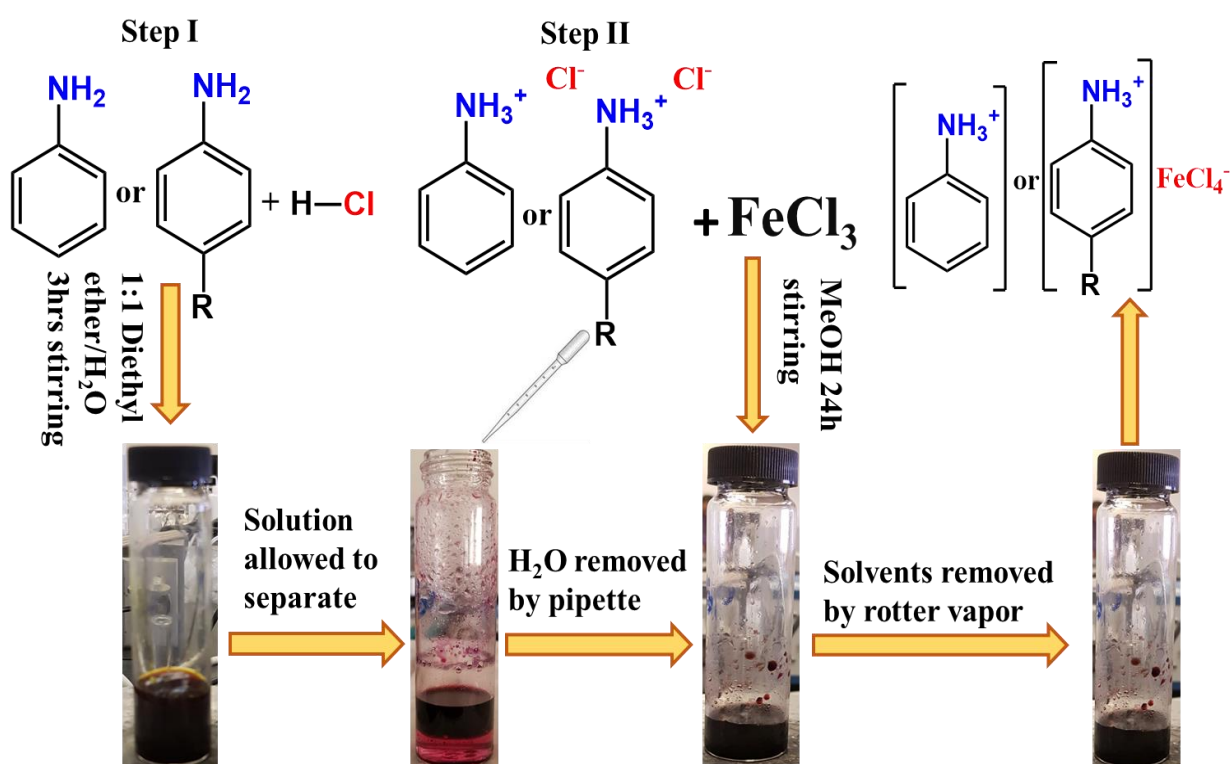


Figure 5: Synthesis procedure of the ILs containing iron and cobalt.

3.3 ILs Characterization

All synthesized cobalt- and iron-containing ILs were subjected to thorough characterization to confirm their physical, chemical, and structural properties, and if the material does not meet expectations, the procedure is repeated, and the parameters are adjusted. In this study, several characterizations were performed to confirm the expected product such as. Proton nuclear magnetic resonance ($^1\text{HNMR}$), mass spectrometry (MS), ultraviolet-visible spectroscopy (UV-Vis), Fourier transform infrared spectroscopy (FT-IR), zeta potential, thermogravimetric analysis (TGA), X-ray diffraction (XRD), scanning electron microscopy (SEM) and energy dispersive X-ray (EDX) and Raman spectroscopy. Magnetic susceptibilities and paramagnetic properties have also been investigated. In addition, physical properties such as melting points were also measured [96].

3.4 ILs Recycling and Reuse

ILs are interesting compounds with a promising different academic and industrial applications, because recycling the material for commercial use is very cheap but still with few industrial applications due to difficulty in reuse. Although several researchers have attempted to investigate the recycling and reuse of ILs with magnetic properties, further research is needed [97]. In this study, all synthesized ILs were desorbed, purified, reused, and recycled to be economical, cost effective and environmentally friendly. Some ILs may pose serious health hazards in landfills by forming other complex compounds if not

properly managed. However, cobalt- and iron-containing ILs derived from hydrophobic quaternary ammonium have been tested on human colon cancer cells and normal human skin fibroblasts, indicating less toxicity than when the element gadolinium was used [98], [99]. To avoid any risk posed by these synthesized ILs, a simple recycling and reuse approach was adopted to minimize waste disposal, hence reduce exposure.

3.5 Application of the synthesized ILs in real samples

The urine samples were collected from willing, healthy individuals and wastewater samples were collected from private date farms from the city of Al Hofuf in Saudi Arabia and the National Water Company's sewage treatment plant Al-Khobar. To prepare the urine sample, the urine is first centrifuged at 3500 to 4000 rpm for 5 to 7 min and diluted with deionized water at a ratio of 1:9 v/v. The sample is then transferred directly into sterilized tubes and stored at -20 °C until analysis. To avoid interference and prevent variation in the results obtained, all urine samples were analyzed within three to four days.

Several ILs containing cobalt and iron in milligram amounts are dispersed in 10 mL of the sample solution containing the analyte in different concentrations and then stirred or shaken to allow contact between the ILs and the analyte and to achieve equilibrium. The mixture is then centrifuged to isolate the ILs-rich analytes and desorb with various solvents. In the case of HPLC, polar solvents such as acetonitrile and for GC-MS, non-polar solvents such as hexane were used by sonication for 5 to 60 minutes of desorption time.

3.6 General mechanism

The general mechanism can be summarized in **(Fig. 6)**. First, the amine is used as the starting material, which has unshared electron pairs that form the N-H bond. The N-H bond is not available for the nucleophilic reaction, so amine hydrochloride salts (quaternary intermediates) are formed. When excess acid is added, the reaction stops. Therefore, the reaction was carefully monitored with ^1H MNR until the complete chemical shift is observed without additional peaks to avoid contamination.

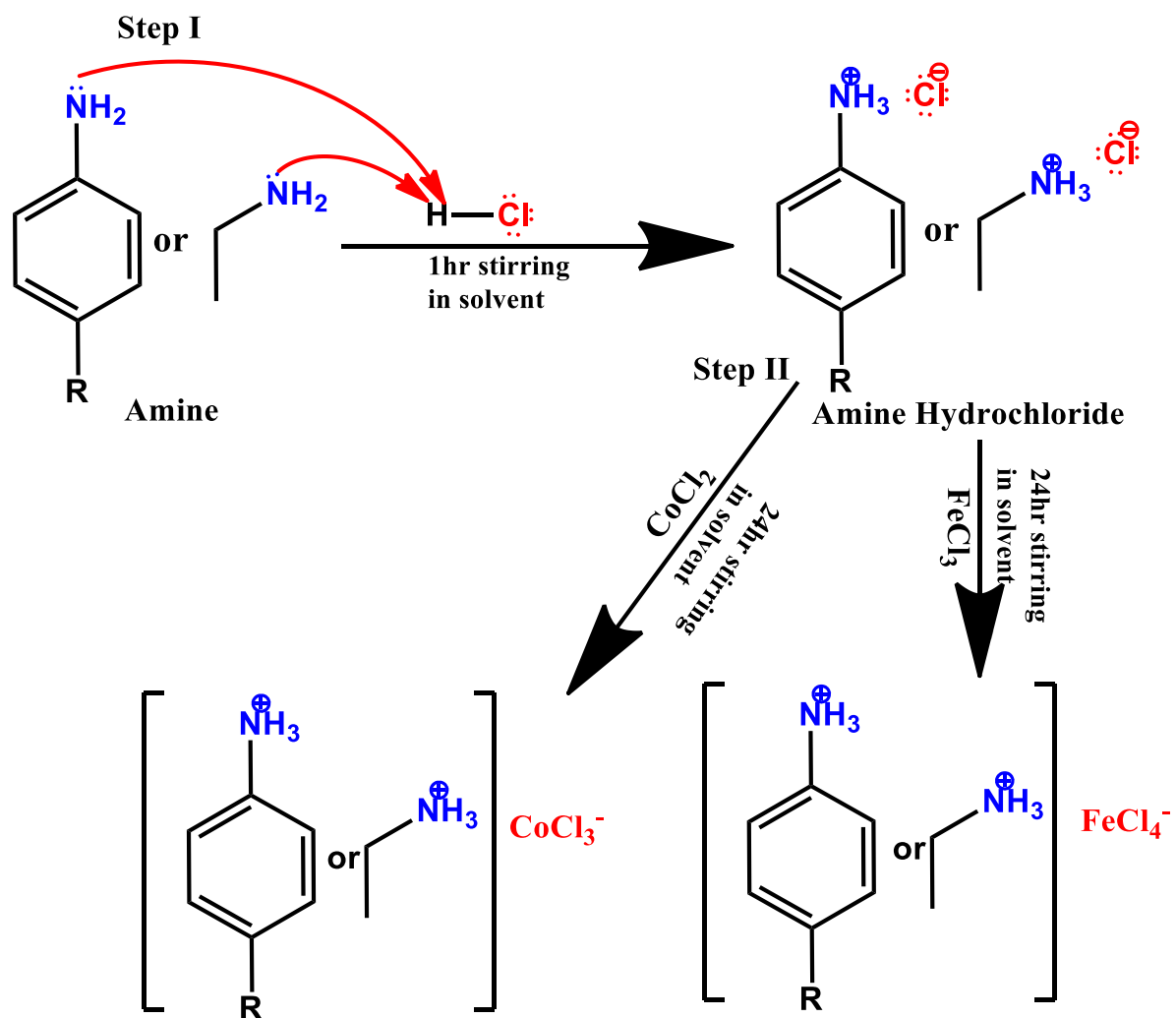


Figure 6: Proposed general reaction mechanism.

CHAPTER 4

IONIC LIQUID-BASED MEMBRANE-PROTECTED MICRO-SOLID-PHASE EXTRACTION OF ORGANOCHLORINE PESTICIDES IN ENVIRONMENTAL WATER SAMPLES¹

4.1 Introduction

Organochlorine pesticides (OCPs) are classified as persistent organic pollutants (POPs) due to their persistent nature and tendency to bioaccumulate in lipophilic tissues [100]. Although OCPs are synthesized to disrupt the physiological functions of target organisms, their toxic effects can also severely affect non-target species, including humans and wildlife [101]. They induce a variety of health complications in humans, ranging from noncarcinogenic to carcinogenic. OCPs were used indiscriminately as agrochemicals before 1970. However, due to increasing concerns about their toxicity and health effects, they were banned in many developed countries in 1970. Unfortunately, they are still synthesized and used in many non-developed countries. Due to their low rate of biodegradation, they can remain in the environment for a very long time. They can be transported long distances and may be present in areas where they have never been used.

¹ This chapter has been published in “Microchemical Journal”.

A study suggests that only a fraction (0.1%) of the applied pesticides reaches the target pests, while the rest is dispersed in different parts of the environment [61]. Moreover, exposure to OCPs occurs via inhalation from the contaminated environment or ingestion of contaminated food. Since they do not decompose after accumulation in fats, they increase to many folds. The above facts provide the background that all food and drinking water resources should be subjected to careful examination before consumption. Therefore, the development of sensitive, accurate and efficient analytical methods for the detection of OCPs is required.

Classical sample preparation methods are based on techniques such as liquid-liquid extraction (LLE) and solid-phase extraction (SPE). LLE and SPE are the most widely used techniques but consume large amounts of hazardous organic solvents and subsequently produce significant amounts of waste that is unsafe for both workers and the environment [102]. This provides the basis for the development of new sample preparation techniques that are either solvent-free or consume only small amounts. Thus, several miniaturized sample preparation techniques have been developed in the last three decades. Solid phase microextraction (SPME) [103], [104], hollow fiber liquid phase microextraction (LPME) [105], [106], single droplet microextraction (SDME) [107], [108], membrane protected micro solid phase extraction (μ -SPE) [109], [110], dispersive liquid-liquid microextraction (DLLME) [10], [111], dispersive solid-phase microextraction (DSPME) [112], [113], microextraction by packed syringes (MEPS) [114], [115] and many of their modified versions are among the top performers in this category. A variety of sample preparation methods have been used for the extraction of OCPs in environmental water samples. SPME

[116]–[118], magnetic solid phase extraction (MSPE) [119], DLLME [120], static LPME (SDME) [121], MEPS [122] and μ -SPE [123] can be mentioned here.

In porous membrane-protected micro-solid phase extraction (μ -SPE), a very small amount of solid phase is packed into a membrane bag by heat sealing the flat membrane film to form like an envelope. The extraction material is adequately protected inside the porous membrane bag and is suitable for extraction from complex liquid samples, as matrix components and macromolecules cannot penetrate the sorbent enclosed by the membrane bag. Analytes can be desorbed by immersing the membrane bag in a suitable solvent using ultrasound [110]. Due to its ease of fabrication, low cost, simplicity of operation, and protection of the sorbent from the complex matrix, the μ -SPE and its various versions are widely used for the extraction of analytes from environmental [124], biological [125], and food samples [126], [127]. In some cases, the μ -SPE device begins to float on the surface of the sample solution or sticks to a wall of the sample vessel during extraction. The stir bar assisted μ -SPE (SB- μ -SPE) was developed to overcome these difficulties. In SB- μ -SPE, a tiny stir bar is packed into the membrane bag along with the sorbent. This increases the effective surface area of the sorbent exposed to the sample solution by continuous agitation and rotation. Also, the choice of sorbent is critical in SB- μ -SPE [125]. In addition to improvements in the design and operation of μ -SPE, the synthesis and application of new sorbents according to the nature of the analytes is a growing area of research.

Ionic liquids (ILs) are salts that have melting points below 100 °C. They are typically composed of organic cations and organic or inorganic anions. They are characterized by their low melting points, high thermal and chemical stability, negligible volatility, and low flammability. They are emerging as green alternatives to conventional organic solvents

[128]. The composition of IL forming ions can be fine-tuned to obtain desired properties such as viscosity, melting points, solubility, etc. Depending on their composition, they can dissolve a wide range of inorganic and organic analytes, which is why they are also referred to as "designer solvents". In analytical sample preparation, ILs are either used as a liquid extraction phase or applied to other supports to work as a solid extraction phase [90], [129]. ILs are used in sample preparation as well as in other areas of analytical chemistry [130]–[132]. In addition, magnetic ionic liquids (MILs) and polymeric ionic liquids have also attracted much interest in the field of microextraction [30], [90], [133]. However, phase separation is still a challenge because some MILs do not respond strongly to an external magnet. Some ILs can also exist as a solid at a temperature below their melting point. Thus, there is a possibility to use them as a sorbent phase.

In this work, we synthesized two new ILs (4-methylbenzenaminium tetrachloroferrate (III) and 1-naphthylammonium tetrachloroferrate (III)) and used them for the extraction of OCPs in aqueous environmental samples. The synthesized ILs can interact with OCPs through hydrophobic and electrostatic interactions. To the best of our knowledge, this is the first time that ILs have been used as sorbents in porous membrane-protected micro-solid phase extraction. This combines the advantages of the extraction properties of ILs with the unique procedural advantages of μ -SPE.

4.2 Experimental

4.2.1 Materials and chemicals

The analytical grade solvents diethyl ether, dichloromethane, tetrachloromethane, n-hexane, methanol, and toluene were purchased from Sigma-Aldrich. An analytical standard containing a mixture of OCPs was acquired from Resteck. In total 19 analytes (Alpha-lindane, Beta-lindane, Delta-lindane, Heptachlor, Aldrin, Heptachlor Epoxide, Trans-chlordane, Endosulfan I, Cis-chlordane, Dieldrin, 4,4'-DDE, Endrin, Endosulfan II, 4,4'-DDD, Endrin Aldehyde, Endosulfan Sulfate, 4,4'-DDT, Endrin Ketone, Methoxychlor) were considered in this study. The reagents 4-methylaniline, 1-Naphthylamine, hydrochloric acid, ferric chloride, and sodium chloride were obtained from Sigma-Aldrich. The polypropylene (PP) membrane sheet with pore size 0.2 μm and thickness of 157 μm was acquired from Membrana (Wuppertal, Germany).

4.2.2 Synthesis of ILs

In this work, two new ILs (4-methylbenzenaminium tetrachloroferrate (III) and 1-naphthylammonium tetrachloroferrate (III)) were synthesized. The synthesis of the ILs was carried out in two main steps. In the first step, 1-naphthylamine or 4-methylaniline is dissolved in diethyl ether and water (1:1 v/v, 5 mL each) followed by hydrochloric acid. The mixture is stirred vigorously for 3 hours to accelerate the formation of an intermediate. The amines are soluble in diethyl ether; the excess acid is washed away with the water. The water is then slowly pipetted off. The resulting intermediate was washed 6 to 8 times, then

the diethyl ether was removed by lyophilization. In the second step, the intermediate and FeCl_3 are dissolved in 5.0 mL of methanol at an equimolar ratio of 1:1 with vigorous stirring for 24 hours. The solvent is then evaporated using a rotary evaporator to obtain IL. **(Fig. 7)** shows the various steps involved in the synthesis of IL from 4-methylaniline. The chemical reactions involved in the synthesis of ionic liquids, 4-methylbenzenaminium tetrachloroferrate (III) and 1-naphthylammonium tetrachloroferrate (III) are shown in **(Fig. 8 and 9)**, respectively.

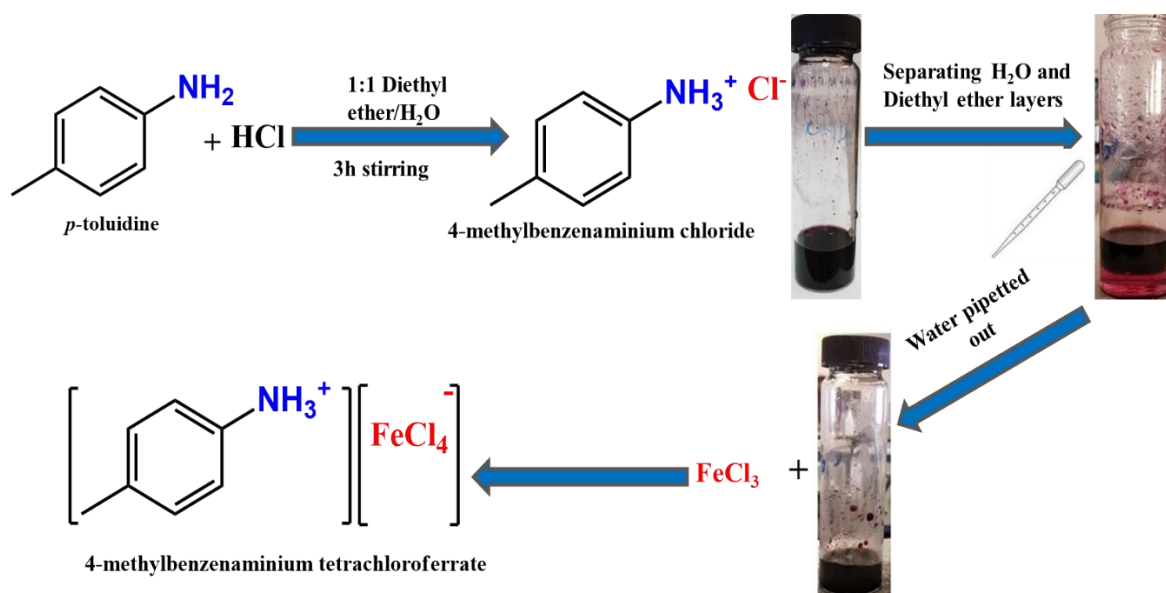


Figure 7: Procedural steps involved in the synthesis of 4-methylbenzenaminium tetrachloroferrate (III).

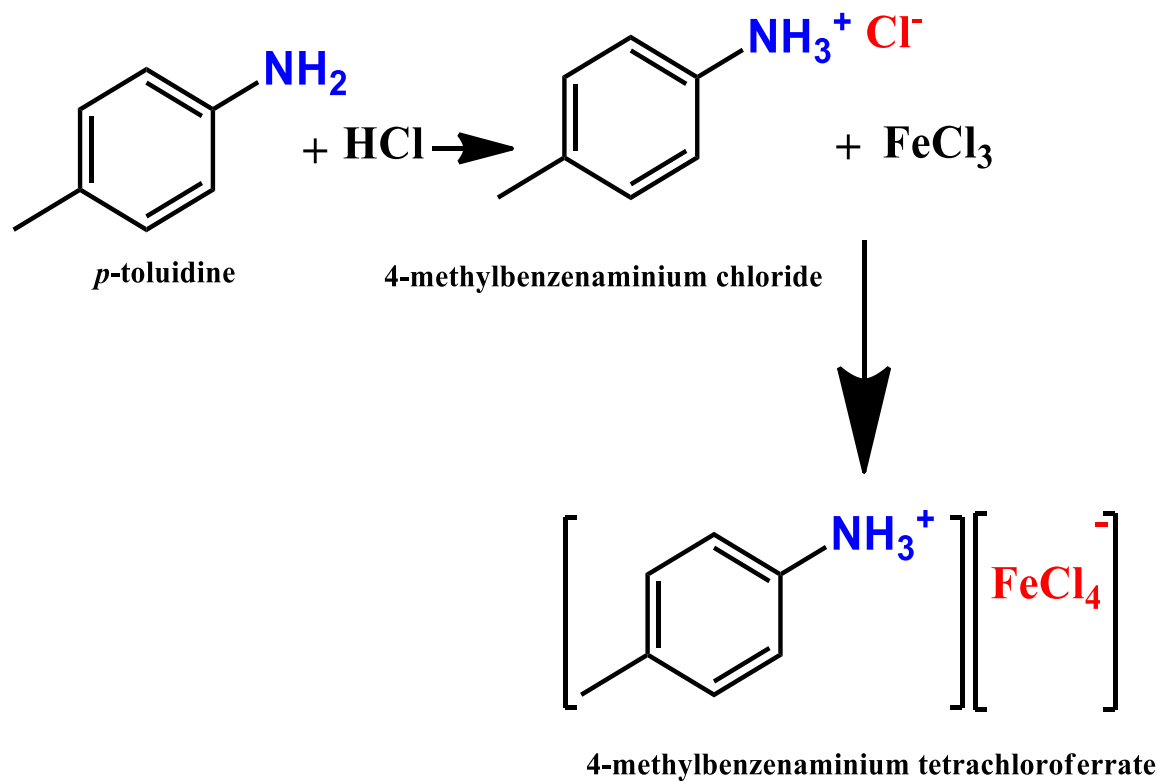


Figure 8: Synthesis scheme of IL 4-methylbenzenaminium tetrachloroferrate (III)

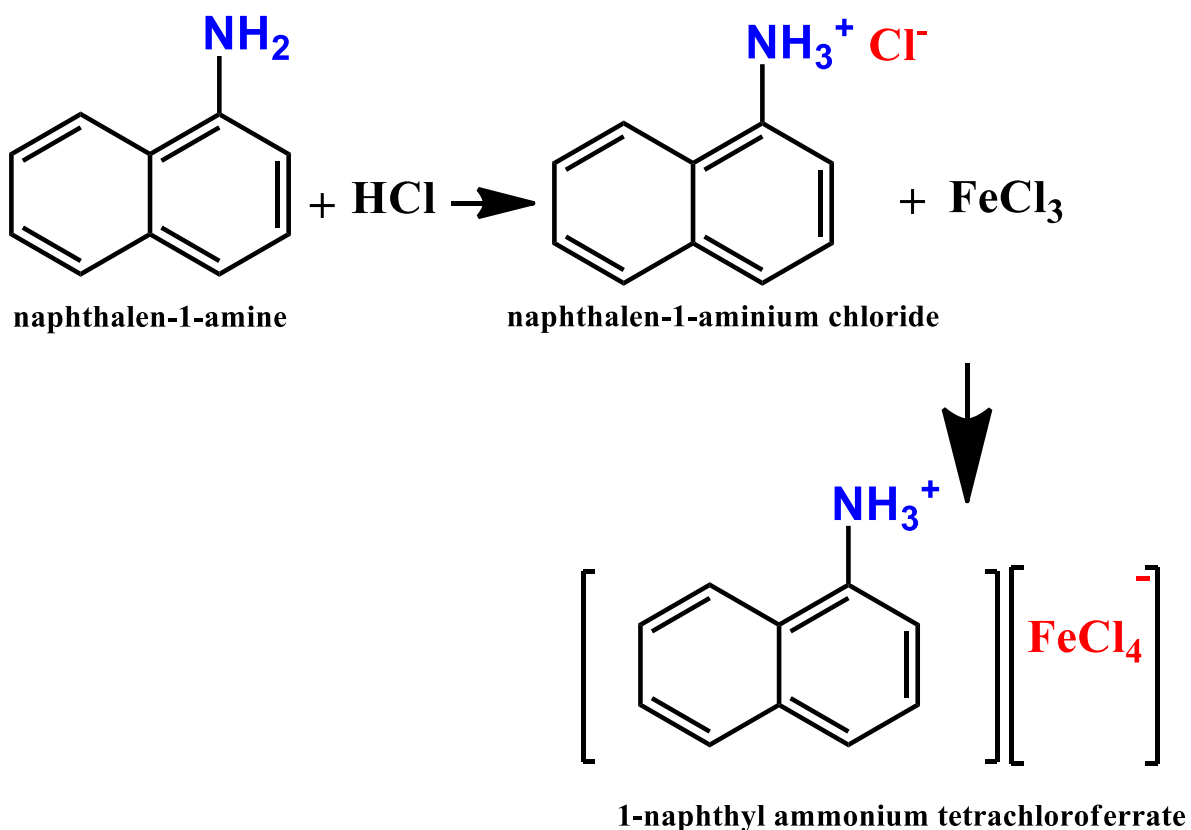


Figure 9: The synthesis scheme of IL 1-naphthyl ammonium tetrachloroferrate (III)

4.2.3 Characterization of ILs

The characterization of ILs was performed using various techniques such as fourier-transform infrared spectroscopy, UV-Vis spectroscopy, scanning electron microscopy, proton nuclear magnetic resonance, x-ray diffraction, and electron paramagnetic resonance. The UV-Vis measurement was performed using Thermo scientific Genesys 10S UV-Vis spectrophotometer. The SEM analysis was performed using FESEM Quarto S

instrument. XRD was performed by Rigaku instrument UltimaIV X-Ray diffractometer model with D/teX Ultra 2 detector, X-ray 40 kV, 40 mA, scan speed/duration time was 5.0000 deg./min, scanning angle was 5 to 90 degrees, and Cu-K α radiation ($\lambda=1.5418$ Å). EPR Adani spectrometers MiniScope model (X-band, 9.3 - 9.55 GHz) was used for the EPR analysis.

4.2.4 Extraction procedure

In the first step, a membrane pouch was prepared using an electric heat sealer according to a previously described procedure [134]. Briefly, a membrane piece was cut from the PP membrane roll and folded in half. All edges of the folded membrane piece were heat sealed to form it like an envelope with one end open. The sorbent material (1 mg [4- MA] [FeCl₄]) was packed together with a tiny stir bar (7 mm $\times$ 2 mm) from the open end and then heat sealed. All protruding edges were cut off. This sorbent containing bag was named as "SB- μ -SPE device". The dimensions of the SB- μ -SPE device were 0.5 cm x 2.0 cm (**Fig. 10**).

The SB- μ -SPE device was immersed in 10 mL of the sample solution or spiked aqueous solution (50 ng/mL) and then stirred for 15 min. After extraction, the SB- μ -SPE device was removed from the sample solution, washed with deionized water, and then dried with a lint-free cloth. The SB- μ -SPE device was then transferred to a glass vial and 200 μ L of n-hexane: Toluene mixture added for desorption. The desorption was assisted with ultrasound for a time of 30 min.

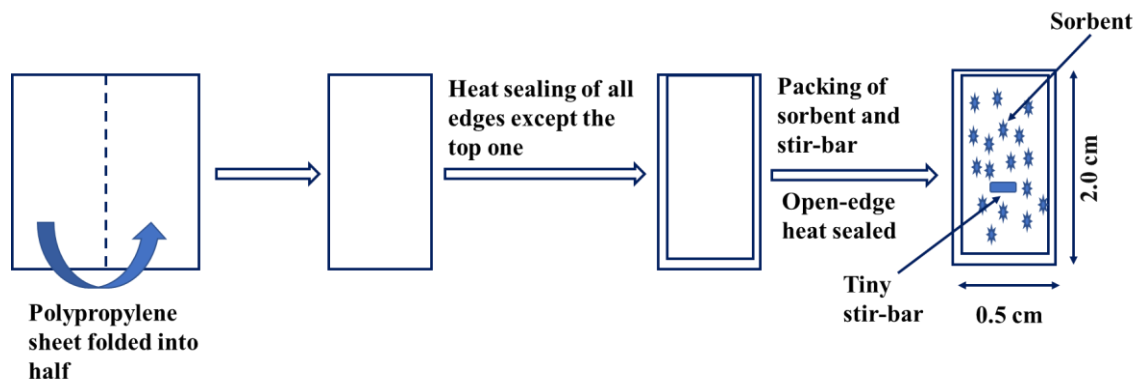


Figure 10: Fabrication of SB- μ -SPE device.

4.2.5 GC-MS

A GC-MS system (consisting of GC: 7890A, MS: MS-5975C inert MSD with a triple-axis detector, Autosampler: GC-Sampler 80 from Agilent) was employed for chromatographic separation and quantification of target compounds. HP-5 (30 m x 320 μ m x 0.25 μ m) column was employed for the separation of analytes. High purity helium was used as carrier gas at a flow rate of 1.4 mL/min. The samples were injected using split mode with a split ratio of 10:1. The temperatures of GC-injection port, GC-MS interface, ion source, and MS quadrupole were adjusted to 200 °C, 250 °C, 230 °C, and 150 °C, respectively. The oven temperature programming was as follows: an initial temperature of 50 °C, which was then to 180 °C at 20 °C/min and held for 1.5 min. This was then increased to 200 °C 3 °C/min and held for 3 min. Finally, it was increased to 230 °C at 5 °C/min and held for 5 min. The total run time was 28.667 min. SCAN mode in the m/z range of 40–550 was used for qualitative data acquisition and SIM mode was employed for quantitative data acquisition. The m/z values of selected ions are listed in **Table 2**.

Table 2: Target analytes, their retention times, and selected m/z values.

S/N	Analytes	Retention time	Selected m/z values		
1	Alpha-lindane	9.062	183	181	219
2	Beta-lindane	9.796	219	181	109
3	Delta-lindane	10.478	181	183	109
4	Heptachlor	11.842	100	272	274
5	Aldrin	12.997	66	263	79
6	Heptachlor Epoxide	14.571	81	353	355
7	Trans-chlordane	15.567	33	375	377
8	Endosulfan I	16.092	241	239	195
9	Cis-chlordane	16.302	373	375	377
10	Dieldrin	17.404	79	81	82
11	4,4'-DDE	17.613	246	318	248
12	Endrin	18.61	81	79	263
13	Endosulfan II	19.187	195	241	237
14	4,4'-DDD	19.922	235	237	165
15	Endrin Aldehyde	20.184	67	345	250
16	Endosulfan Sulfate	21.391	387	272	274
17	4,4'-DDT	21.758	235	237	165
18	Endrin Ketone	23.437	67	317	315
19	Methoxychlor	24.696	227	228	

4.3 Results and discussion

4.3.1 Characterization of the sorbent

The FT-IR spectra ($500\text{--}4000\text{ cm}^{-1}$) of the starting materials, intermediates and the corresponding complexes were compared. The intermediates were found to be very similar to the starting material, as the addition of a hydrogen atom does not generate a new functional group but causes some broadening and sharpening of some peaks in both spectra (**Fig. 11**). The anions of the ILs do not show any significant chemical shift; however, a broad OH group is observed overlapping with the N-H region, which can be attributed to the hygroscopic nature of FeCl_4 . The peaks observed in some cases at 2700 cm^{-1} to 2900 cm^{-1} are attributed to the hydration of the NH^{3+} group, with the water oxygens taking up protons from the ammonium to form H-bonds leading to the formation of aromatic ammonium.

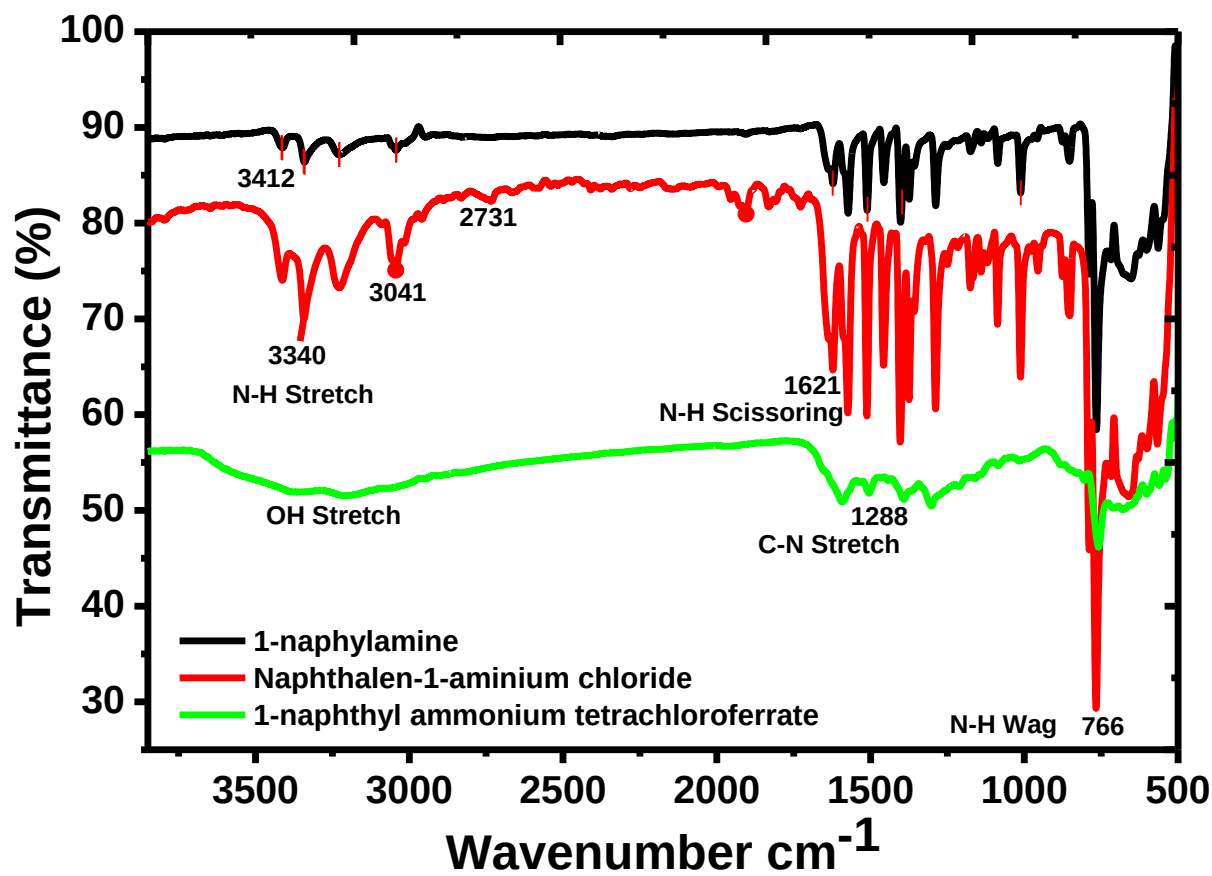


Figure 11: The FTIR spectra of a) $[1\text{-NA}]^+[\text{FeCl}_4]^-$

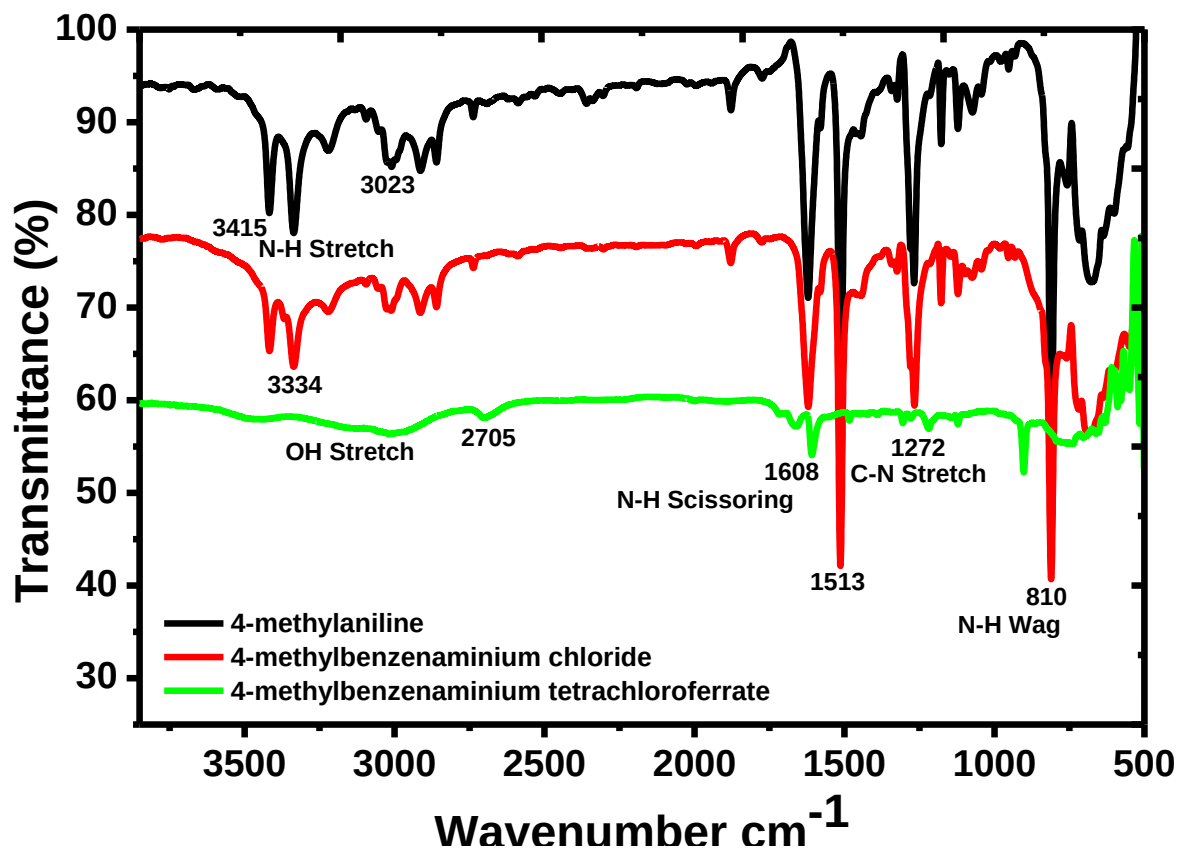


Figure 12: The FTIR spectra of $[4\text{-MA}]^+[\text{FeCl}_4]^-$

UV-Vis measurements were carried out in methanol as solvent (**Fig. 13 and 14**). In the UV region, two sets of absorption bands are observed at about 230 nm and 250 nm, which is associated with the tetrahedral coordination of the anion moiety FeCl_4^- . UV-Vis shifts to lower energy levels in both ILs when ferric chloride is introduced, this hypochromic shift is attributed to an increase in the rigidity of the benzene rings of the complex. In general, both ILs showed very low absorbance, which makes them better alternatives for the extraction of various analytes from aqueous media and for analysis by UV detection techniques.

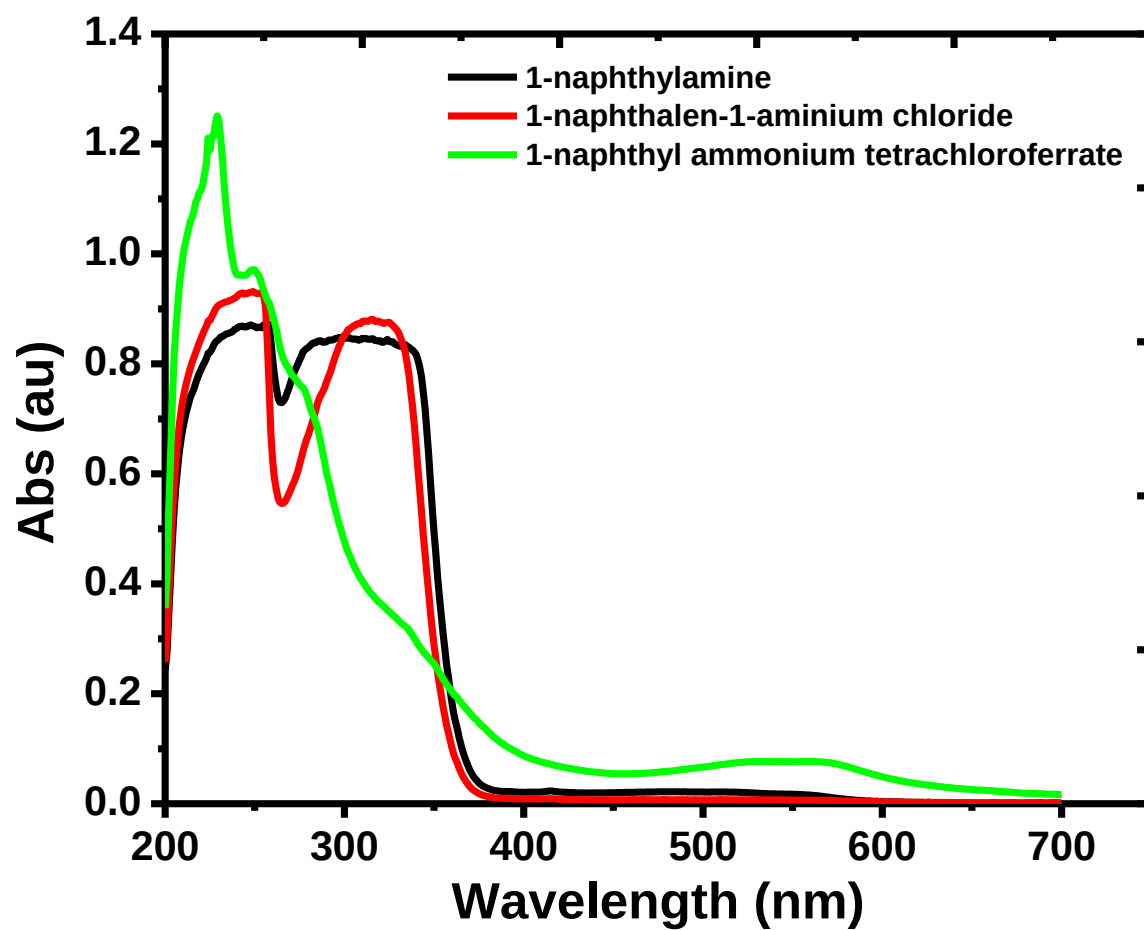


Figure 13: The UV-Vis spectra of a) $[1\text{-NA}]^+[\text{FeCl}_4]^-$

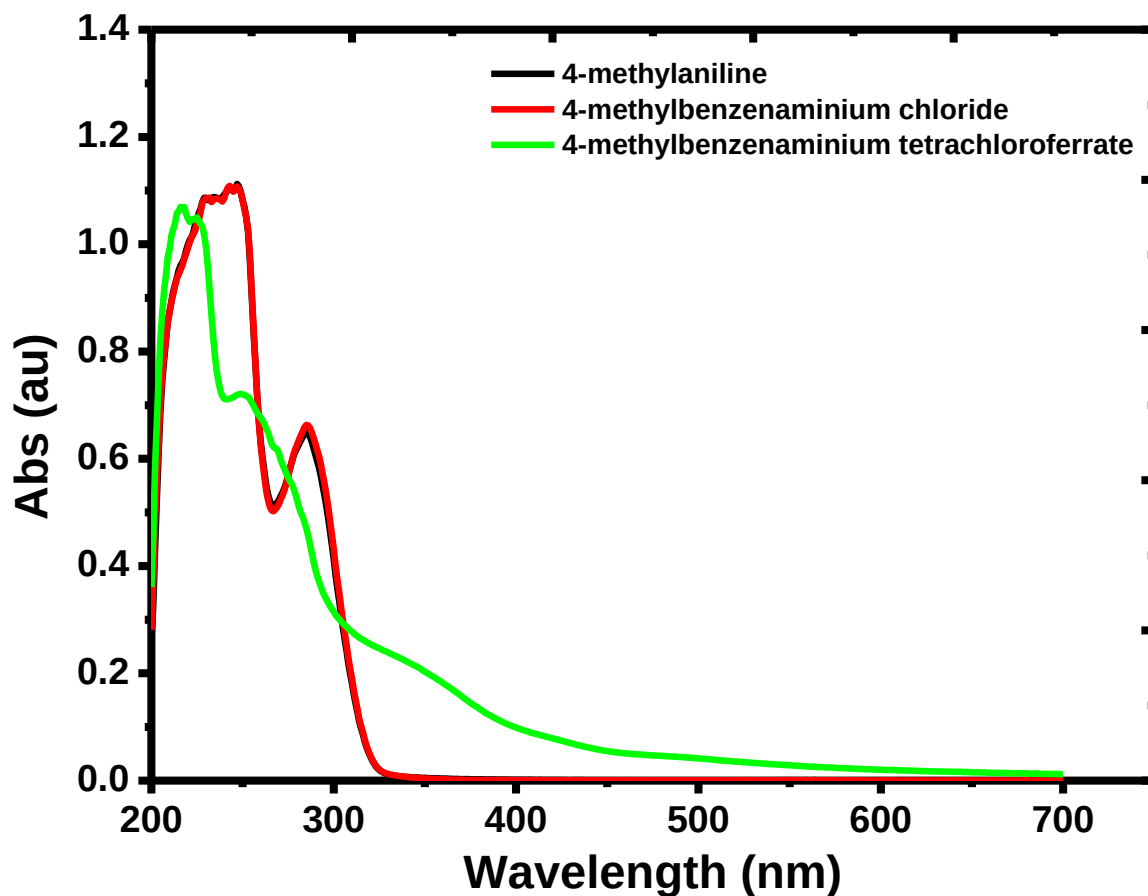


Figure 14: The UV-Vis spectra of a) $[1\text{-NA}]^+[\text{FeCl}_4]^-$ and b) $[4\text{-MA}]^+[\text{FeCl}_4]^-$

The ^1H NMR spectra confirmed the purity and the structure of the cationic intermediates of the two ILs is shown in (**Fig. 15, Fig. 16, Fig. 17, and Fig. 18**). The spectra show peaks consistent with the number of hydrogen atoms present, with negligible shift. Moreover, no additional peak was observed for any of the intermediates, indicating that they were synthesized.

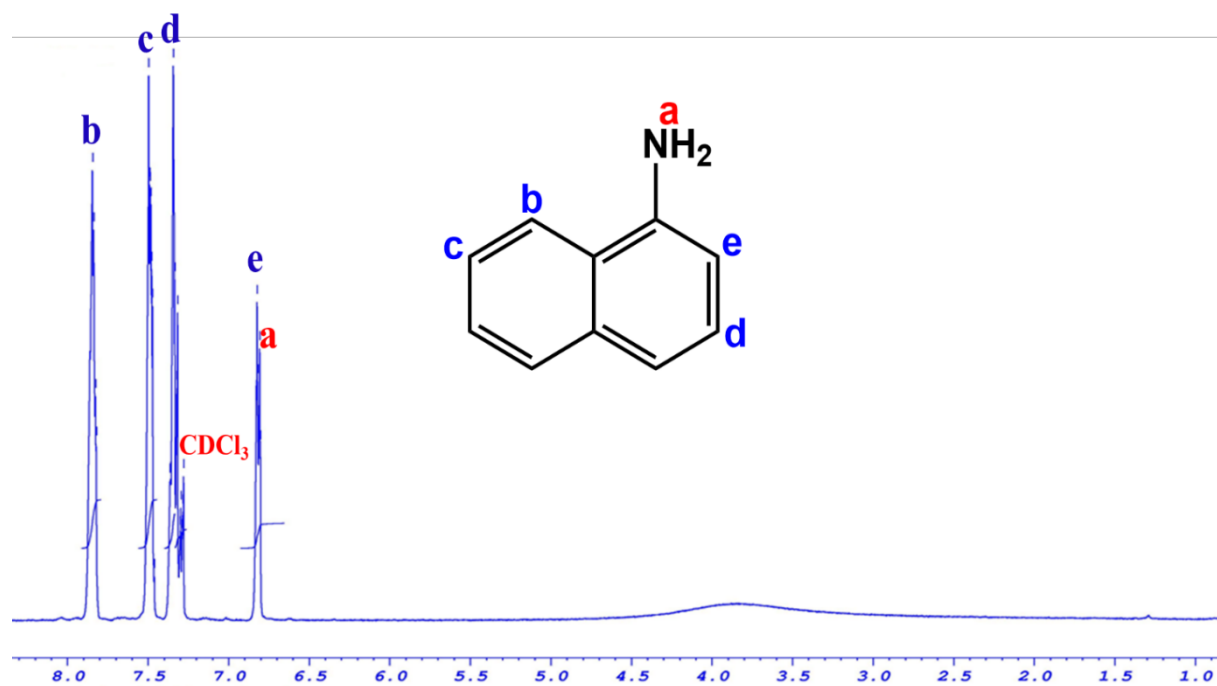


Figure 15: The ^1H NMR spectra of 1-Naphthylamine

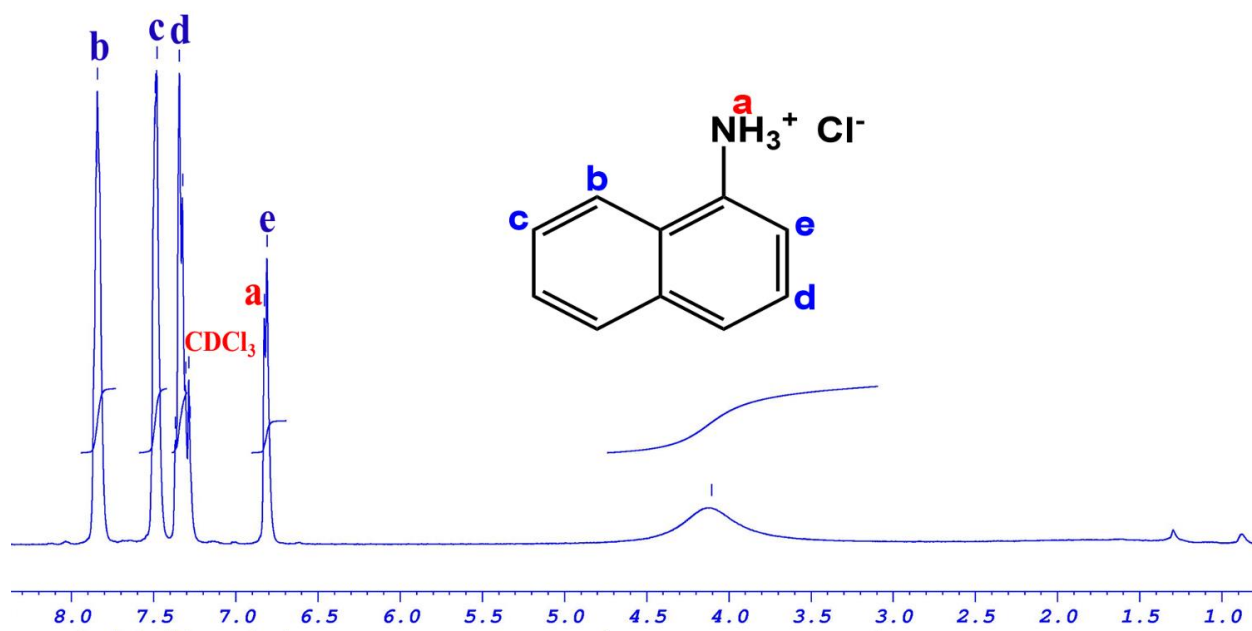


Figure 16: The ^1H NMR spectra of intermediate naphthalen-1-aminium chloride.

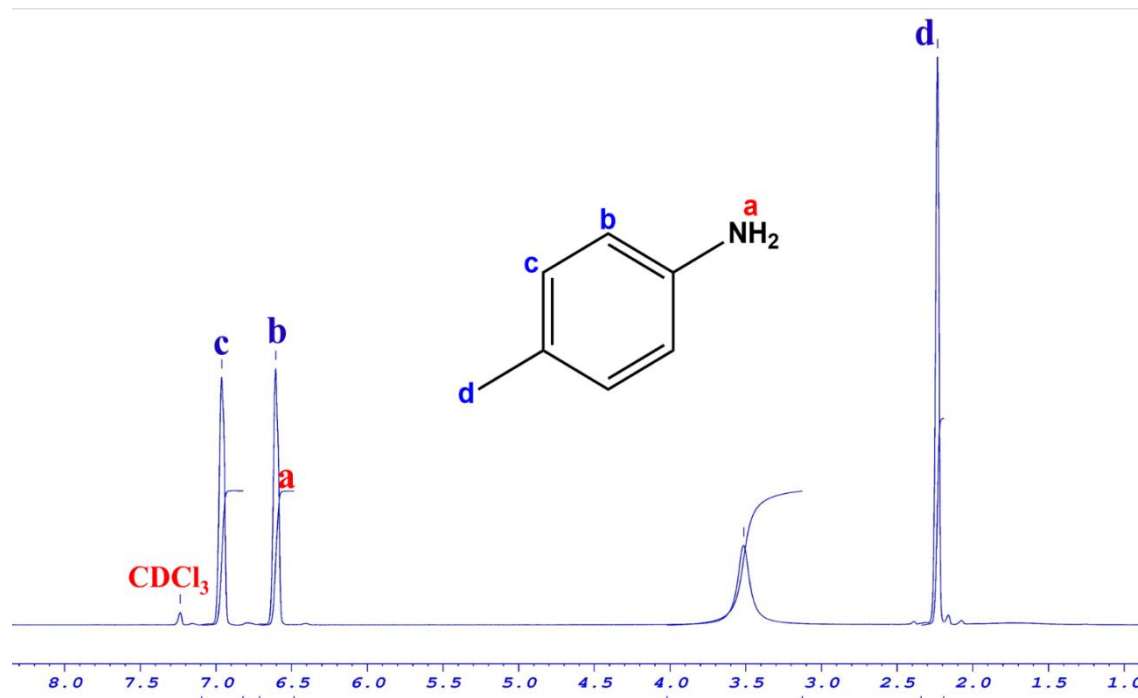


Figure 17: The ^1H NMR spectra of 4-methylaniline

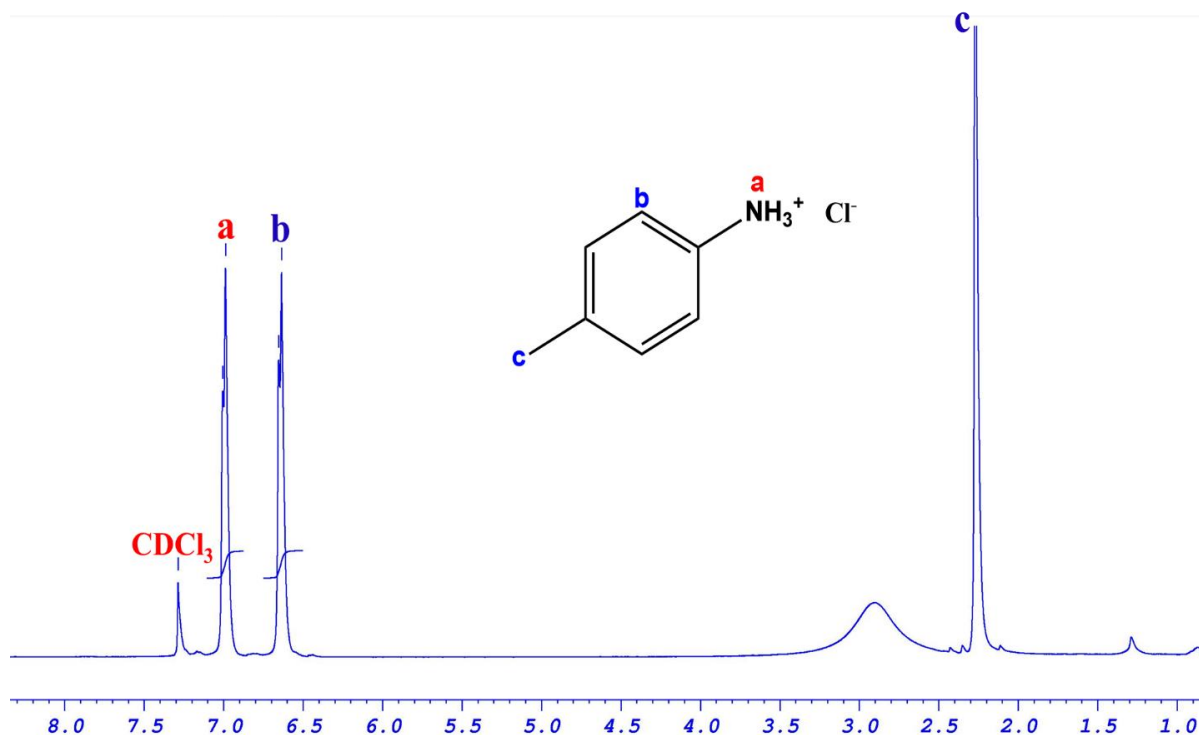


Figure 18: The ^1H NMR spectra of intermediate 4-methylbenzenaminium chloride

Both ILs appeared as solids at room temperature, and their melting points were determined using an electrothermal melting point apparatus and were about 62 °C and 65 °C for [1-NA][FeCl₄] and [4-MA][FeCl₄], respectively, **Table 3**. A slight increase in the melting point for [4-MA][FeCl₄] was observed.

Table 3: Melting points of parent and resulting IL compounds.

Compounds	MP (°C)	MW
1-NA	301	143.19
[1-NA][FeCl ₄]	62	340.7
4-MA	44	107.15
[4-MA][FeCl ₄]	65	304.85

The SEM analysis was performed to investigate the surface morphology of the ILs. Porous spherical structures were observed in both ILs (**Fig. 19**). However, in the case of 4-methylbenzenaminium tetrachloroferrate (III) (**Fig. 19c and d**), greater porosity is evident, making it more favorable for extraction applications than 1-naphthylammonium tetrachloroferrate (III) (**Fig. 19a and b**). Analytes, such as OCPs, can likely be trapped between the pores. The bright structures seen could be attributed to the charged ferrous material composition. In some cases, micropores are found in (**Fig. 19c and d**). Possibly due to hydrogen bonding between two adjacent amine groups on the surface of the material, typically resulting in smaller pores. SEM images show that the material is porous; however, this may not be solely responsible for the extraction. Hydrophobic interactions between aromatic rings as well as electrostatic interactions may contribute to the extraction of OCPs. There is a likelihood of ionic interactions between the OCPs and 4-

methylbenzenaminium tetrachloroferrate (III), which forms a smaller positive charge. Compared to 1-naphthylammonium tetrachloroferrate (III), the former is expected to have better extractability as it forms a larger positive charge. The ionic charge formation in the molecule is also enhanced by the presence of an electron withdrawing group such as chlorine in the OCP.

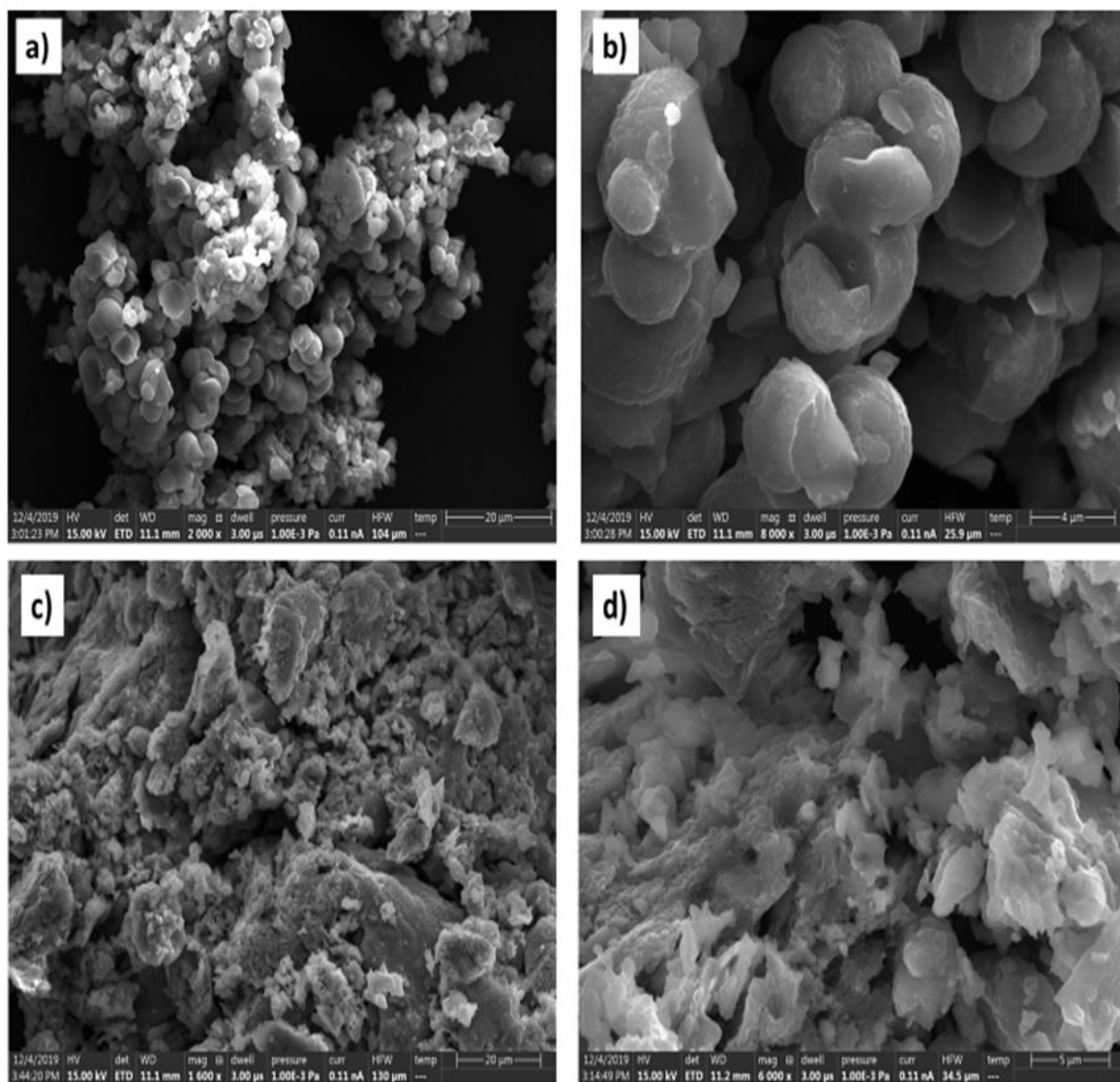


Figure 19: SEM images of 1-naphthyl ammonium tetrachloroferrate (III) (a,b) and 4-methylbenzenaminium tetrachloroferrate (III) (c,d).

To better understand the crystallographic orientation of the material, X-ray diffraction (XRD) analysis of the starting material, intermediate, and product was performed (**Figs. 20 and 21**). X-ray diffraction showed well-resolved peaks with high intensity for both starting materials, indicating excellent crystallinity. However, low peaks with complete loss of intensity were observed for the final products, 1-naphthylammonium tetrachloroferrate (III) and 4-methylbenzenaminium tetrachloroferrate (III), indicating a lack of crystallinity when FeCl_4^- was formed. Normally, changes in bonding and magnetic property have a strong effect on the crystallinity of the material, which is why the peaks decreased. No shift or additional peaks are observed, indicating non-covalent bonding between the anion and cation moieties, as most ionic liquids have H-bonds, ionic and van der Waals forces as intermolecular interactions.

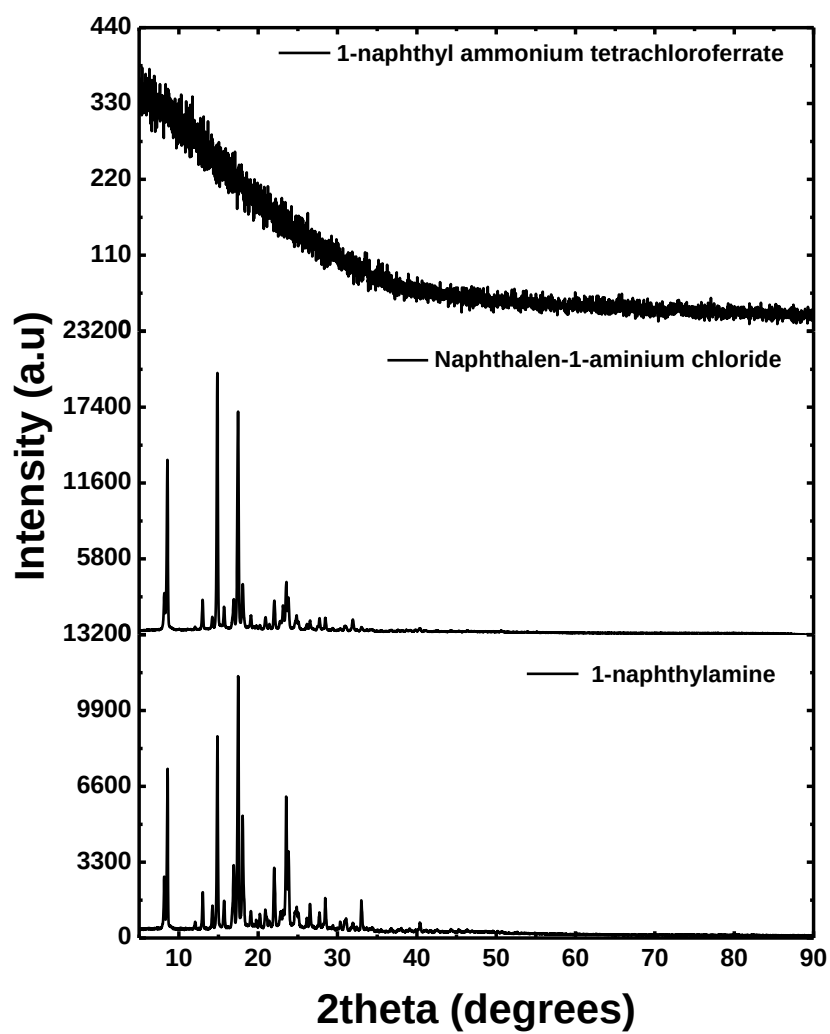


Figure 20: XRD of 1-Naphthylamine, Naphthalen-1-aminium chloride, and 1-naphthyl ammonium tetrachloroferrate (III).

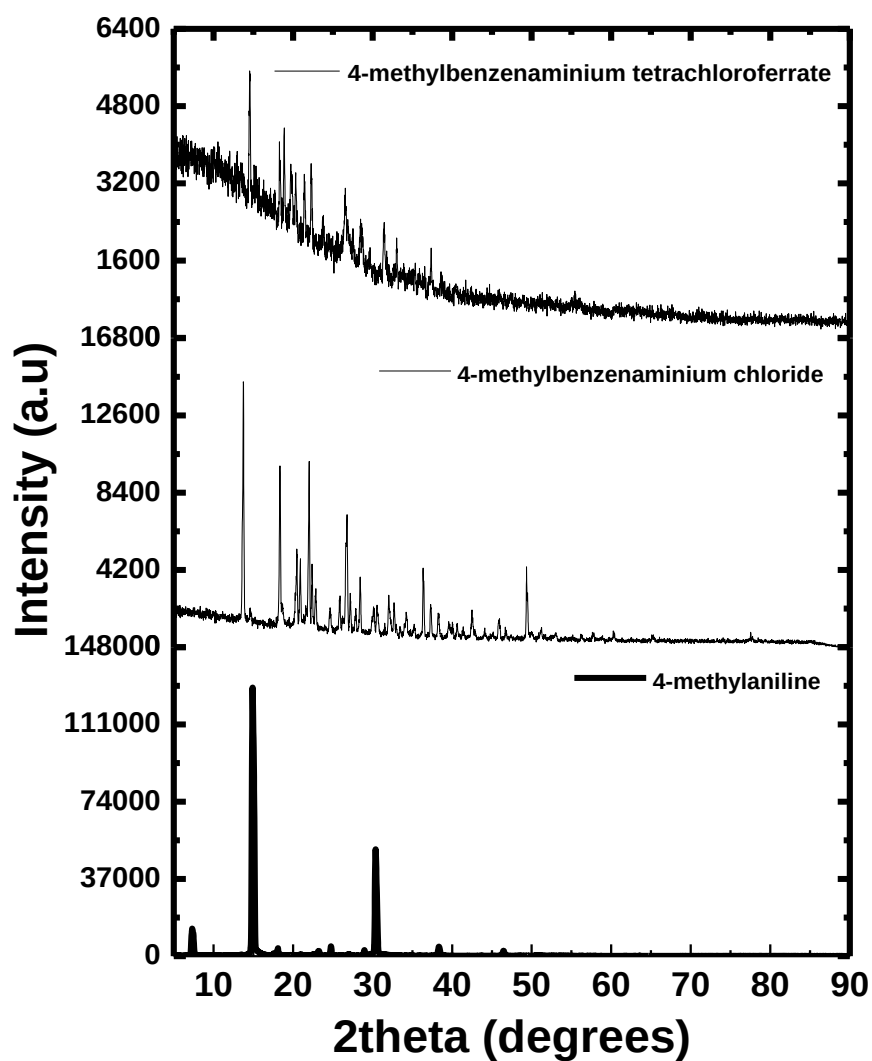


Figure 21: XRD of 4-methylaniline, 4-methylbenzenaminium chloride and 4-methylbenzenaminium tetrachloroferrate (III).

Due to the presence of magnetic anionic components, the ILs were also investigated for their magnetic behavior. The ILs did not exhibit sufficient magnetism to be extracted from aqueous solutions. Electron paramagnetic resonance (EPR) of both ILs was performed to

check the unpaired electron of FeCl_4^- as it spins and resonates, giving the material paramagnetic properties. The spectra for both materials showed a similar pattern, indicating paramagnetic behavior (**Fig. 22**). A sharp singlet g value was observed at 2.01804 and 2.01726 for 1-naphthylammonium tetrachloroferrate (III) and 4-methylbenzenaminium tetrachloroferrate (III), respectively, showing the presence of Fe^{3+} ions in both ILs.

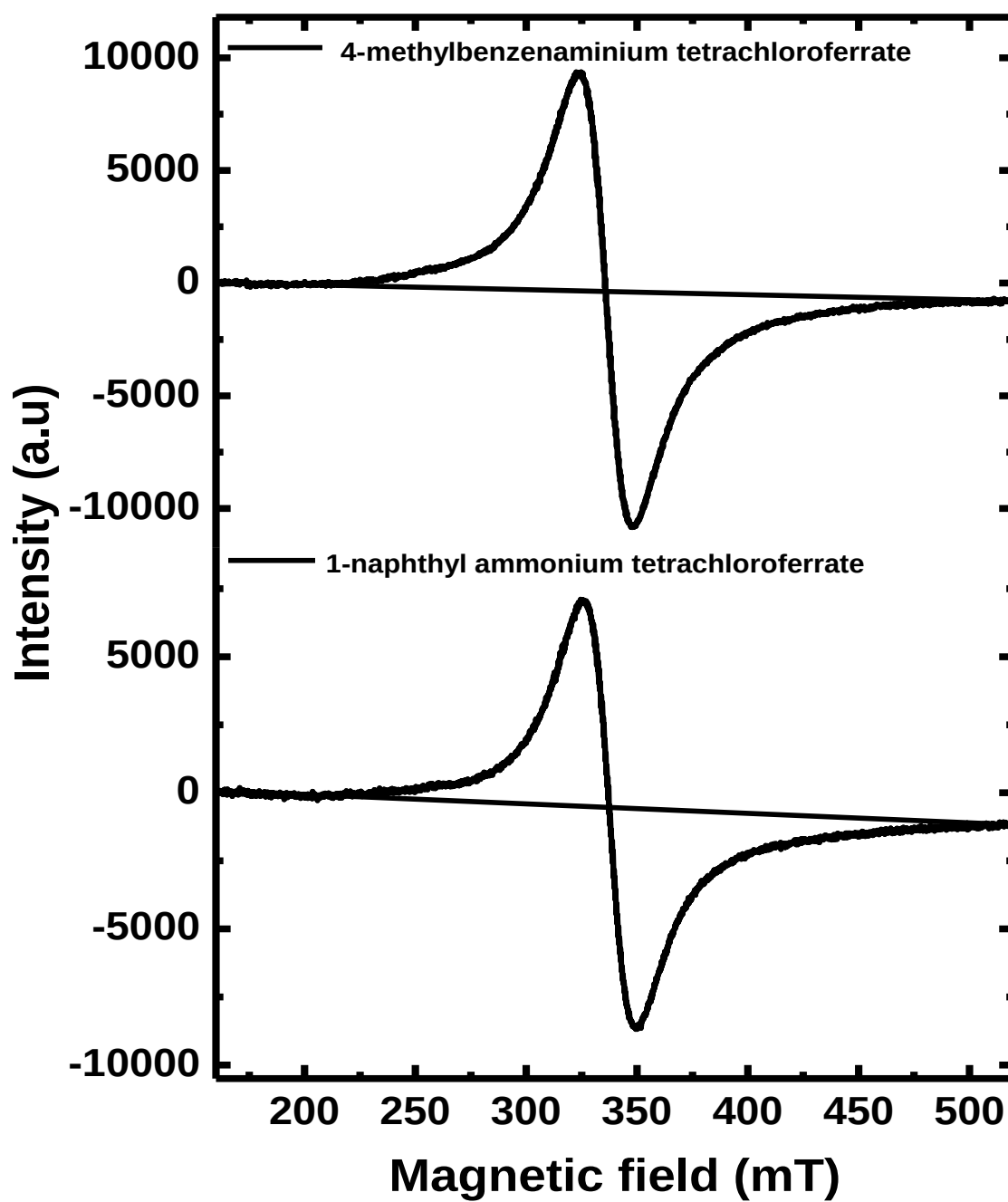


Figure 22: EPR spectra analysis 4-methylbenzenaminium tetrachloroferrate (III) and 1-naphthyl ammonium tetrachloroferrate (III).

The spectroscopy for surface-enhanced Raman spectral scattering (SERS), model LabRam, was recorded from 100 cm^{-1} to 1000 cm^{-1} . A 633 nm laser in a dark environment was used as the excitation source. A dominant sharp broad peak was observed between 300 and 400 in both ILs, which can be associated with symmetric bond stretching vibrations originating from Fe-Cl of FeCl_4^- (**Fig. 23**).

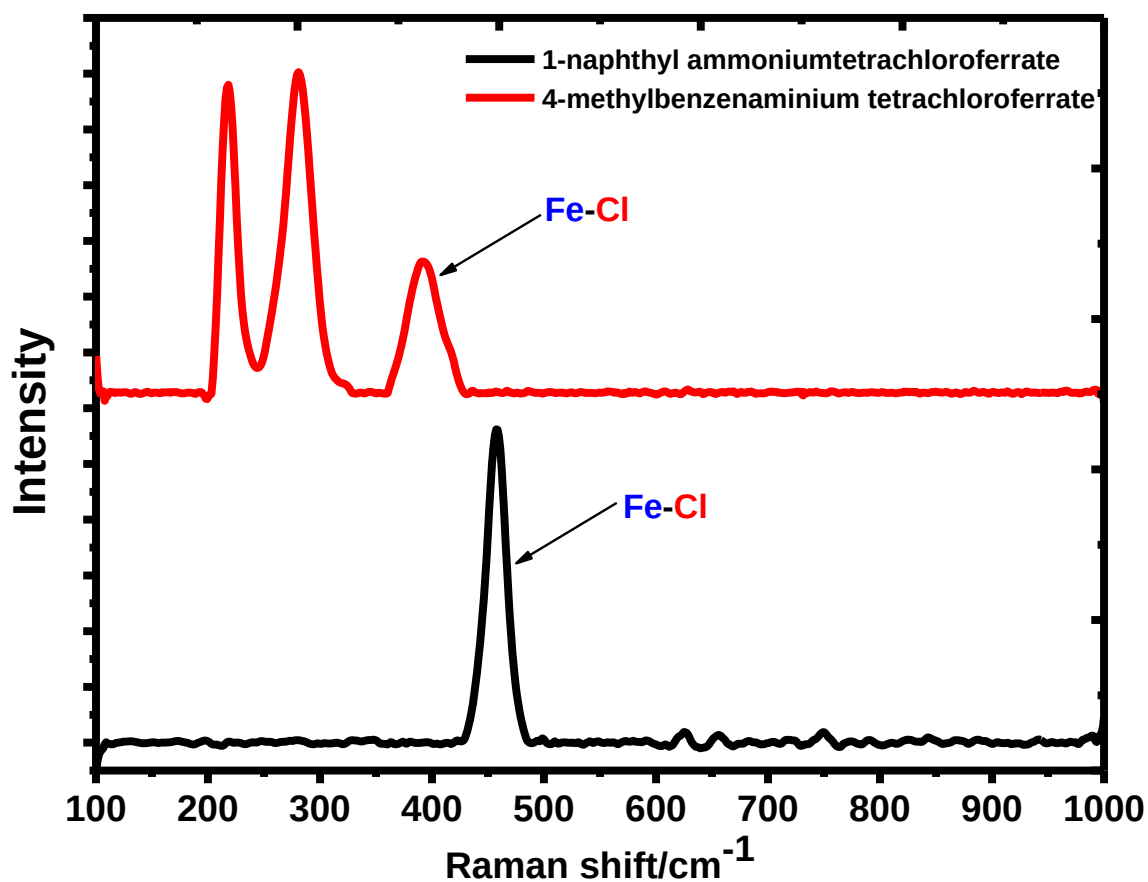


Figure 23: Raman spectra analysis 4-methylbenzenaminium tetrachloroferrate (III) and 1-naphthyl ammonium tetrachloroferrate (III).

4.3.2 Optimization of the extraction procedure

Optimization of extraction parameters was performed using 10 mL aqueous samples containing 50 ng/mL of a mixture of OCPs. **Table 4** lists the extraction parameters, the initial values, the range studied and the optimal values.

Table 4: Information on the optimization of SB- μ -SPE.

Variables studied	Initial value	Range investigated	Optimum value
Sorbent type and amount		1 – 20 mg of [1-NA] [FeCl ₄] and [4-MA] [FeCl ₄]	1 mg of [4-MA] [FeCl ₄]
Desorption solvent	n-hexane	n-hexane, toluene, carbon tetrachloride, and n-hexane: toluene	n-hexane: toluene
Volume of Desorption solvent (μ L)	200	100 – 500	200
Amount of salt (g)	1	1 – 2.5	2
Extraction time (min)	30	15 – 75	15
Desorption time (min)	30	10 – 50	30
Stirring rate	Level 2	Level 1 – 3	Level 2

4.3.2.1 Ionic liquid and its amount

Both ILs were evaluated for the extraction of OCPs in water samples. For this purpose, different amounts of both sorbents (1, 2.5, 5, 10, 20 mg) were tested for the extraction of the target compounds. [1-NA][FeCl₄] showed better extraction performance for most of the compounds with an amount of 2.5 mg, except alpha-lindane and heptachlor, which were better extracted with 5 mg (**Fig. 24**).

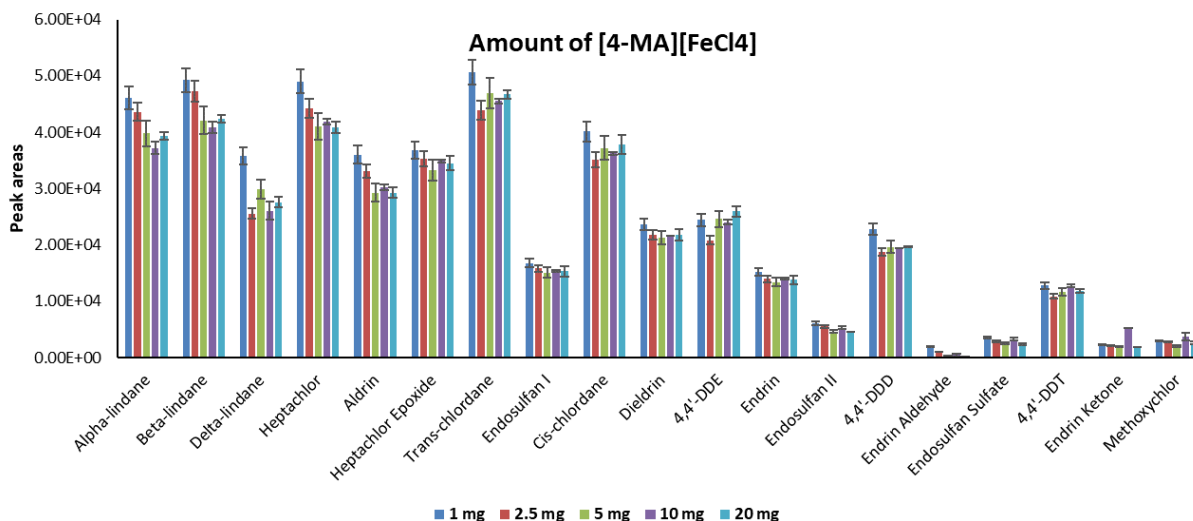


Figure 24: Effect of sorbent amount on the extraction of OCPs.

[4-MA] [FeCl₄] showed the highest extraction efficiency for all target substances with an amount of 1 mg. As the sorbent amount increased, the extraction decreased and, in some cases, remained unaffected with increasing sorbent amount (**Fig. 25**). In order to select an IL as the optimal sorbent for further experiments, the extraction efficiencies of the two ILs were compared at the sorbent amounts where they showed the best extraction results. The extraction efficiency of 1 mg [4-MA] [FeCl₄] was higher than that of 2.5 mg [1-NA] [FeCl₄] except in the case of trans-chlordane, cis-chlordane, 4,4'-DDE, 4,4'-DDT and methoxychlor (**Fig. 24**). The small amount of sorbent is sufficient to adsorb the analyte concentration present from the sample solution. The second reason could be the difficulty of desorption from the larger amount of sorbent. The most likely interactions between OCPs and the proposed ILs are both hydrophobic and electrostatic interactions.

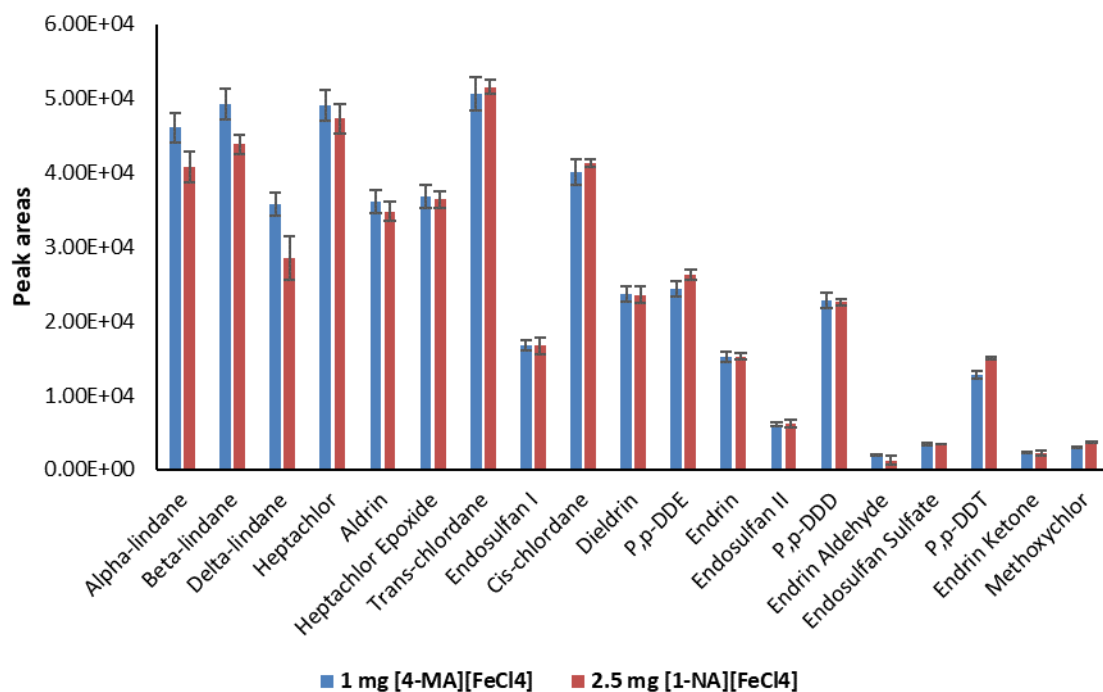


Figure 25: Comparison of the extraction of OCPs using an optimum amount of two different ILs.

4.3.2.2 Desorption solvent and its volume

To achieve the goal of high extraction efficiency, the selection of the appropriate desorption solvent is of great importance. In this work, different solvents such as n-hexane, carbon tetrachloride and toluene were investigated. The reason for selecting toluene as one of the solvents along with the non-polar solvents n-hexane and carbon tetrachloride was our previous experience. It was found that toluene dilates the pores of the membrane PP better and somehow facilitates the transport of analytes across the membrane. Therefore, we planned to study it both singly and in combination with n-hexane in a 1:1 ratio. The extraction performance of n-hexane and toluene was almost comparable. However, in the

case of their combination, the highest chromatographic peak areas were obtained for all target compounds (**Fig. 26**). This can be attributed to the combination of the hydrophobicity of n-hexane and the dilatancy of the toluene solvent.

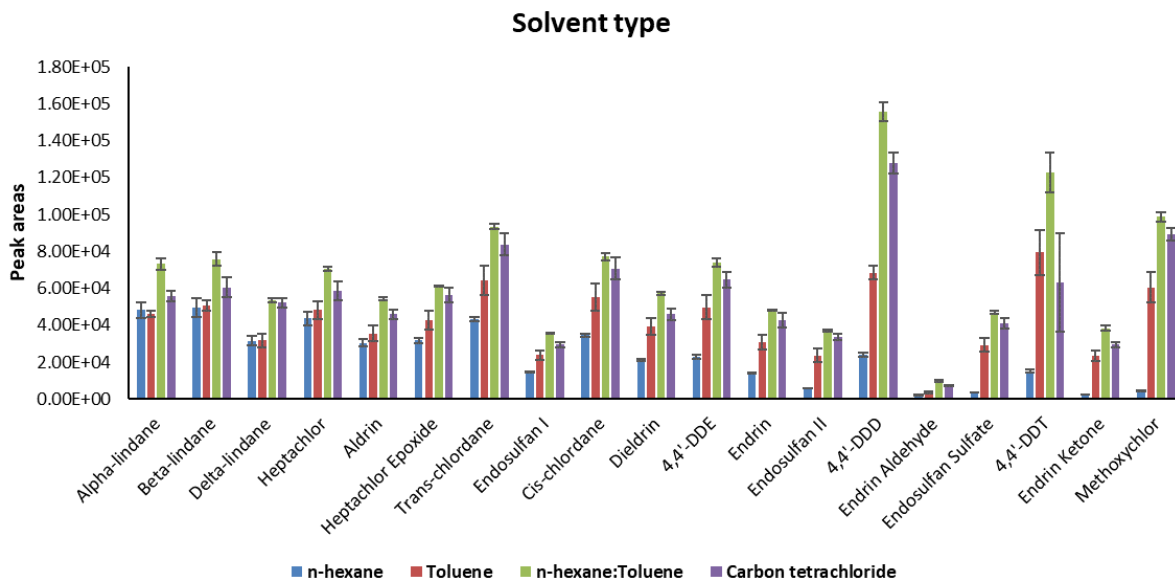


Figure 26: The influence of solvent type on the extraction of OCPs.

The volume of desorption solvent should be carefully optimized, as it can have a significant effect on the sensitivity and reproducibility of extraction results. Complete immersion of the SB- μ -SPE device in the desorption solvent is critical to obtain reproducible extraction. Any volume more than that required for immersion will dilute the analytes and compromise the sensitivity of the method. The volumes that do not properly immerse the SB- μ -SPE instrument will not provide reproducible extraction data. Therefore, different volumes of

desorption solvent ranging from 100 to 500 μL were investigated. The best extraction results were obtained with 200 μL , in agreement with the assumptions postulated above (Fig. 27).

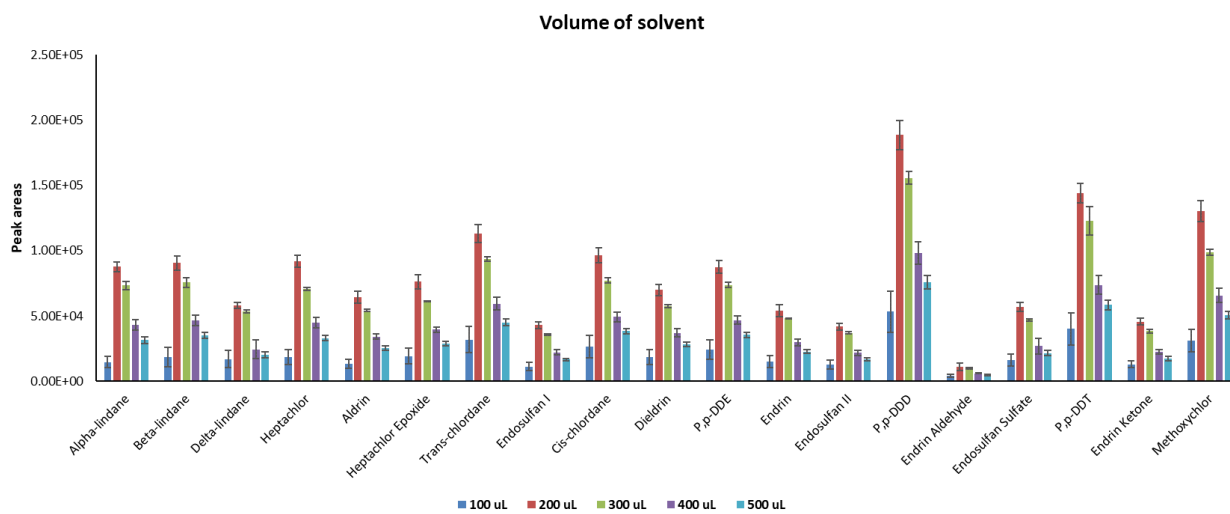


Figure 27: The influence of volume of solvent on the extraction of OCPs.

4.3.2.3 Addition of salt

The salting-out effect is a well-known phenomenon in analytical extractions. The addition of salt (NaCl) to the aqueous samples decreases the solubility of the organic analytes and extracts them more efficiently into the organic phase. Therefore, different amounts of salt ranging from 0-2.5 g (0 -25%) were investigated. Different behavior was observed for different OCPs. Out of the nineteen compounds studied, thirteen showed the highest

extraction efficiency at 2.0 g salt addition. Some compounds showed the highest extraction at 1.5 g. In some cases, the addition of salt may negatively affect the extraction process (**Fig. 28**). This is due to an increase in the viscosity of the sample solution, which may hinder mass transfer of the target compounds. However, this effect can be different for different compounds, and it is enormously complex to study it for each compound. Therefore, 2.0 g NaCl was chosen as the optimal amount for the upcoming experiments.

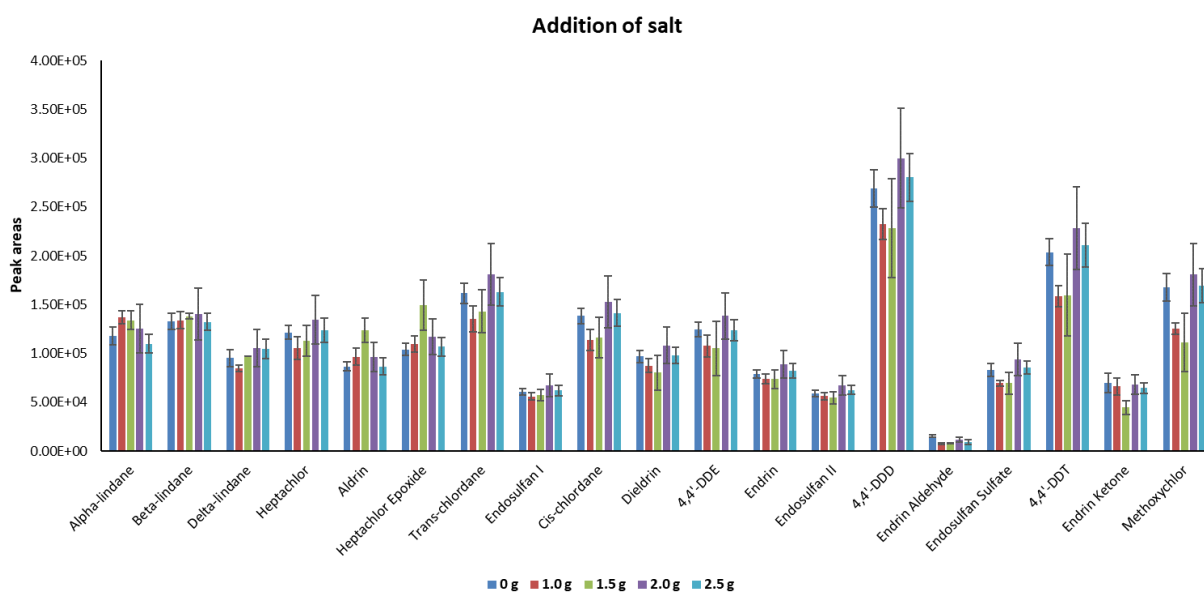


Figure 28: Effect of salt addition on the extraction of OCPs.

4.3.2.4 Extraction time

The μ -SPE is an equilibrium-based method in which the equilibrium setting depends on both the mass transfer rate and the extraction time. The mass transfer rate can be increased by stirring, and equilibrium can be reached in a relatively short time. The extraction time was evaluated between 15-75 min. The chromatographic peak areas of the extracted compounds showed that 15 min was sufficient time to extract most of the target compounds (**Fig. 29**), and this was chosen as the optimum extraction time for the subsequent experiments. After 15 min, a slight decrease in extraction was observed for some analytes, possibly due to re-extraction of the analytes into the sorbent, but this needs further investigation.

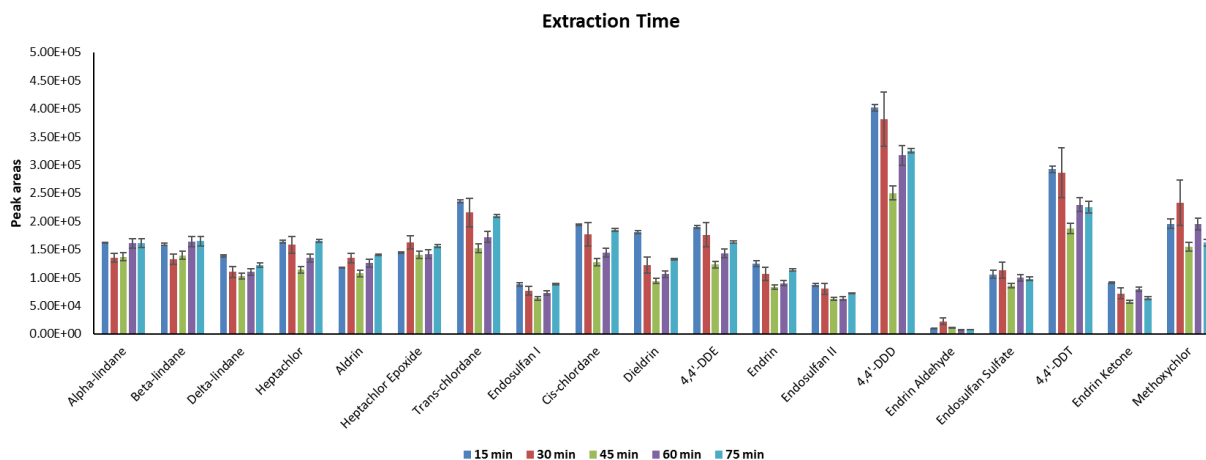


Figure 29: Effect of extraction time on the extraction of OCPs.

4.3.2.5 Desorption time

As described earlier, after adsorption of the analytes, desorption is carried out in a suitable solvent. The process of desorption is assisted by sonication. To effectively elute the analytes from the adsorbent, the desorption time should be optimized. Thus, the desorption time between 10 and 50 min was investigated. The chromatographic peak areas increased with an increase in time from 10 to 30 min (**Fig. 30**). A further increase in sonication time resulted in a decrease in the peak areas of the target compounds. This could be due to the fact that longer sonication times cause an increase in temperature and evaporation of the target compounds into the headspace. Therefore, a time of 30 min was chosen as the optimal desorption time.

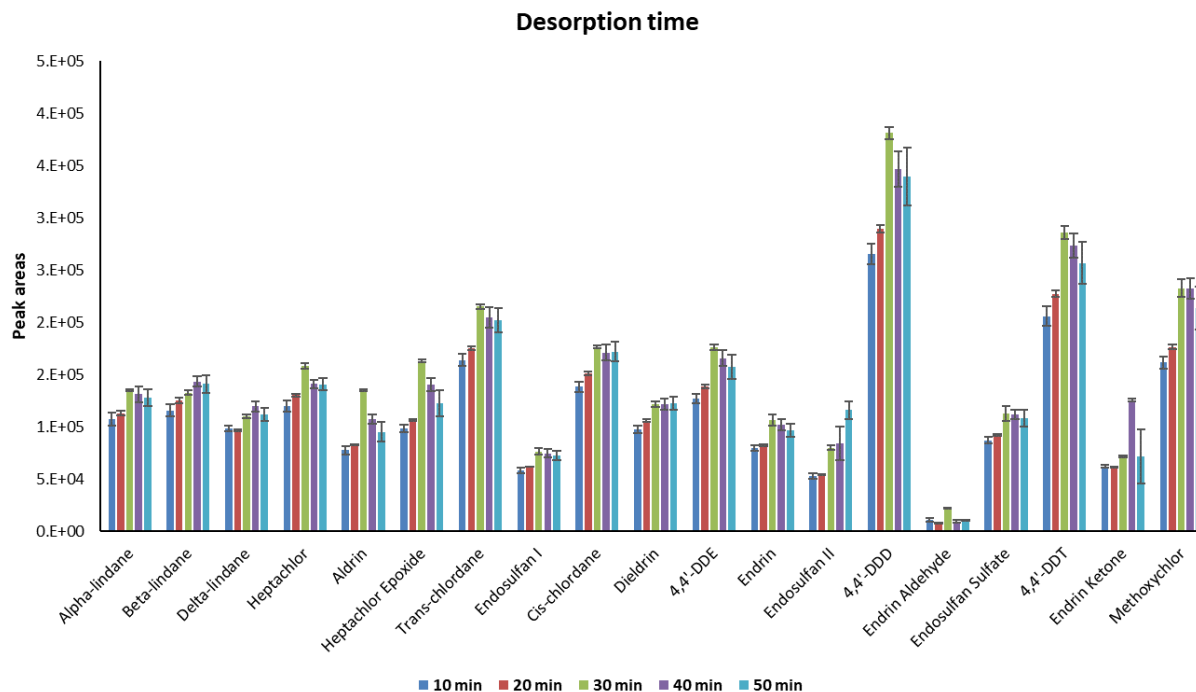


Figure 30: The influence of desorption time on the extraction of OCPs.

4.3.3 The analytical figures of merit and analysis of real samples

The analytical properties of the proposed method are summarized in **Table 5**. Calibration plots were made using six aqueous standards subjected to the proposed extraction technique under optimized conditions. The performance of the method was evaluated based on its linearity, sensitivity, precision, enrichment factors and relative recoveries.

Sensitivity was determined using limits of detection (LODs) calculated based on a signal-to-noise ratio of 3. LODs ranged from 0.25 ng/mL (for 4,4'-DDD) to 3.4 ng/mL (for

endrin). The lower range of linearity represents the limits of quantitation (LOQs) of the method. The upper range of linearity was maintained at 100 ng/mL for all analytes.

Intra-day and inter-day precision were expressed as relative standard deviations (%RSDs) calculated at a concentration closer to the method's limit of quantification (10 ng/mL). For intraday reproducibility studies, seven samples spiked with the same concentration on the same day were extracted and injected into the instrument, and the RSD for the signal was calculated. For the interday reproducibility studies, the same procedure was repeated on seven different, non-consecutive days. The RSDs ranged from 3.9 to 12.5%. RSDs were also measured at intermediate (25 ng/mL) and high (100 ng/mL) calibration levels, and the results were better than the level of LOQ (values not shown in **Table 5**). Enrichment factors (EFs) were determined after extraction of aqueous samples spiked at 25 ng/mL. The EF was calculated using the same data obtained during the precision studies **Equation 1**:

$$EF = \frac{\text{The final concentration of analyte in the eluent}}{\text{Initial concentration of analyte in the sample solution}} \quad (1)$$

The final concentration is calculated from the instrumental calibration curve (prepared without extraction). EF values indicate the enrichment obtained by the proposed method. The EFs ranged from 16.1 to 45.1.

Table 5: Analytical figures of merit for the developed method.

Analytes	Linear range (ng/mL)	R ²	%RSDs at 10 ng/mL (n=7)		LODs (ng/mL)	EFs (n=3)
			Intra-day	Inter-day		
Alpha-lindane	1-100	0.9979	6.2	7.1	0.34	35.0
Beta-lindane	1-100	0.9992	3.9	4.2	0.28	31.0
Delta-lindane	4-100	0.9952	12.5	13.2	1.35	27.8
Heptachlor	1-100	0.9974	10.7	11.4	0.36	35.9
Aldrin	1-100	0.9978	4.4	8.1	0.39	45.1
Heptachlor	1-100	0.9943	5.5	6.7	0.32	37.4
Trans-chlordane	1-100	0.9959	9.5	9.5	0.29	33.6
Endosulfan I	4-100	0.9964	9.6	11.2	1.29	35.1
Cis-chlordane	1-100	0.9958	9.8	12.3	0.33	32.5
Dieldrin	1-100	0.9985	8.8	8.9	0.36	30.6
4,4'-DDE	1-100	0.9974	8.9	9.6	0.33	40.6
Endrin	10-100	0.9965	10.4	10.2	3.4	37.1
Endosulfan II	4-100	0.9984	11.5	12.1	1.41	36.1
4,4'-DDD	1-100	0.9981	10.9	11.5	0.25	41.9
Endrin Aldehyde	4-100	0.9977	5.3	8.1	1.27	23.6
Endosulfan Sulfate	4-100	0.997	12.2	12.5	1.39	31.7
4,4'-DDT	1-100	0.9969	7.5	8.2	0.34	37.6
Endrin Ketone	4-100	0.9978	11.5	12.1	1.37	16.1
Methoxychlor	1-100	0.9984	10.9	11.8	0.26	39.3

After optimizing the influence parameters and evaluating the analytical merits, the applicability of the proposed method was extended to the analysis of real samples. To verify the accuracy of the developed method, analyte-free real samples were spiked at three different concentrations and the relative recoveries were calculated. The relative recoveries of the target substances were in the range of 89-105%. **(Fig. 31)** shows a GC-MS chromatogram of a real spiked sample extracted under optimal extraction conditions. Agricultural wastewater samples were analyzed and no traces of OCPs were detected. The peak areas of the analytes in the real sample and in DI water were compared, and the values of the percent relative extraction were significantly close, indicating the insensitivity of the method to matrix interference.

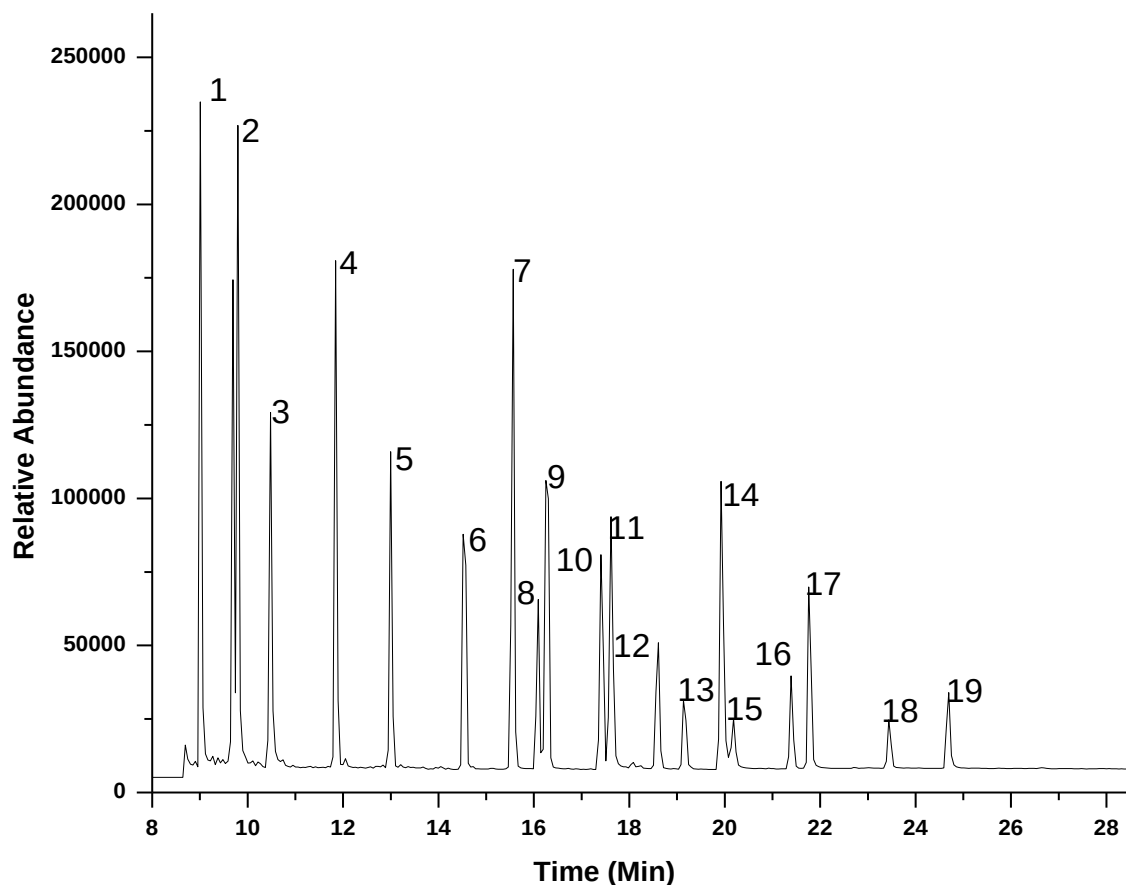


Figure 31: GC-MS trace of OCPs extracted from spiked (at 25 ng/mL) agricultural wastewater sample. (1) Alpha-lindane (2) Beta-lindane (3) Delta-lindane (4) Heptachlor (5) Aldrin (6) Heptachlor Epoxide (7) Trans-chlordane (8) Endosulfan I (9) Cis-chlordane (10) Dieldrin (11) 4,4'-DDE (12) Endrin (13) Endosulfan II (14) 4,4'-DDD (15) Endrin Aldehyde (16) Endosulfan Sulfate (17) 4,4'-DDT (18) Endrin Ketone (19) Methoxychlor

The proposed method was compared with previously published literature **Table 6** and it was found that this method has some advantages in terms of required sample volume, amount of sorbent and extraction time. The sample volume required was 10 mL, which was equal to or less than the volume used in other reports. The amount of sorbent 1 mg was much less than that used in other studies, which makes this method environmentally

friendly and cost effective. The sample preparation time was 45 min, which is better than SPME methods but higher than MSPE. The %RSDs and recoveries were also comparable to published methods. LOD is an important factor in determining the sensitivity of the method, and therefore the LOD values obtained could be compared with the existing literature. In some cases, they are higher than the reported values. Nevertheless, the values were comparable with some methods **Table 6**.

Table 6: Comparison of IL- μ -SPE with published literature

Method	Instrument	Number of OCPs	Sample volume (mL)	Amount of sorbent (mg)	Sample preparation time (min)	RSDs (%)	LODs	Recoveries (%)	Ref.
IL- μ -SPE	GC-MS	19	10	1	45	3.9 – 12.5	0.25 – 3.4	89 – 105%	– This work
NH ₂ -MIL-53(Al)-SPME	GC-MS	8	10	30 μ m thickness	65	3 – 12	0.051 – 0.97	77.4 – 117	[116]
OPAC-Fe-SPME	GC- μ ECD	2	10	10	10	4.6 – 6.8	7.3 – 8.6	98.6 – 103.5	[119]
PPy MSPE Biosorbent-SPME	GC- ECD	6	15		87	3 – 14	ng/L 0.19 – 0.71	60 – 113	[117]
AuNPs-SPME	GC- ECD	7	15	3 μ m thickness	63	8.67 –	0.13 – 0.24	85 – 97.1	[118]
DLLME	GC- μ ECD	20	5		5	21.3 – 1.9	ng/mL 0.21 – 11.65	73.9 – 116.2	– [120]
Static LPME (SDME)	GC- ECD	8	3		25	3.2 – 10.7	0.02 – 0.2	90.4 – 98.3	– [121]
MWCNTs-MEPS	GC-MS	5	10	6	20 draw eject cycles	3.3 – 8.5	0.02 – 0.19	81 – 118	[122]
MIL (101)- μ -SPE	GC-MS	5	10	4	55	4.2 – 11	0.0025 – -	87.6 – 98.6	– [123]
							0.016		

4.4 Conclusion

In this work, two ILs, namely 1-naphthylammonium tetrachloroferrate (III) and 4-methylbenzenaminium tetrachloroferrate (III), were successfully synthesized and characterized. 4-Methylbenzenaminium tetrachloroferrate (III) was used as a sorbent in SB- μ -SPE for the extraction of OCPs from environmental water samples because it has relatively better performance than 1-naphthylammonium tetrachloroferrate (III). The extraction properties of 4-methylbenzenaminium tetrachloroferrate (III) are due to its porous structure and the likelihood that it forms both hydrophobic and electrostatic interactions with the target OCPs. SB- μ -SPE showed excellent performance in terms of analytical figure of merits. The LODs of the method ranged from 0.25 to 3.4 ng/mL. This method has great potential for application in the analysis of real samples, as demonstrated by the excellent recoveries of analytes from spiked samples.

CHAPTER 5

Iron and cobalt-containing magnetic ionic liquids for dispersive micro-solid phase extraction coupled with HPLC-DAD for the preconcentration and quantification of Carbamazepine drug in urine and environmental water samples²

5.1 Introduction

In recent years, an exponential increase of about 600 pharmaceutical compounds has been reported mainly in surface waters, leading to contamination of drinking water due to the high demand for these drugs for both human and veterinary use [135]. Generally, when pharmaceutical products are used, the active ingredient remains intact and is not metabolized or are active metabolites that are normally excreted from the body in the form of sulfates and glucuronides via urine or feces [136]. In addition, the source of the compounds may be from the disposal of expired and unused drugs. These drugs are mobile and rigid in the environment and can easily leach into groundwater [137]–[139]. One of the most used drugs in the world is carbamazepine (CBZ), an anticonvulsant used for primary treatment of neuropathic pain and as a first-line choice drug in epilepsy therapy due to its safety profile and efficacy in both children and adults [140]. The drug is degraded in the body by secretion from bile and partially metabolized to CBZ 10, many derivatives

² This chapter has been published in journal of molecular liquids.

and 11 epoxides [141]. The drug has been frequently detected in high concentrations in wastewater, as 2 to 3% of it is directly excreted as a parent compound in urine [142]. The drug is considered one of the most resistant compounds to photodegradation and biodegradation. It is also among the most important persistent pharmaceutical products in the aquatic environment as well as in chlorinated water treatment processes [143]. The main challenge in the analysis of CBZ is that the analyte is present in its matrix at very low concentrations, which makes detection difficult even with the most sensitive analytical instruments. Therefore, the development of a suitable analytical method for sample preconcentration is urgently needed.

To understand and diagnose CBZ in terms of overdose, abuse and other diagnostic exclusions, a suitable, relevant, sensitive, and selective analytical method is required to monitor, detect, and quantify the analyte in human urine and environmental water samples. In this context, several studies have been devoted to the extraction of CBZ, such as dispersive liquid-liquid microextraction (DLLME) [144], [145], membrane-protected solid-phase microextraction [146], dispersive solid-phase microextraction [138], hollow fiber liquid-phase microextraction [140], and solid-phase microextraction [147]. Although these techniques are useful, they still have drawbacks and challenges. Therefore, dispersive solid phase microextraction was considered more attractive compared to other miniaturized extraction methods due to its simplicity, direct interaction of sorbents with the analyte matrix, and efficiency, as well as speed and kinetic favorability in terms of extraction and desorption [148]. However, the most difficult step in dispersive micro solid phase extraction is the selection of a suitable, stable, and selective sorbent.

Magnetically modified sorbents for dispersive micro solid phase extraction are strongly favored because they reduce sample preparation time. They are also less difficult to prepare and modify, require a minimal amount of organic solvents, and can be easily recovered and reused [149]. After extraction, sorbents can be easily separated from the sample solution by an external magnet if the particles respond to a magnetic field. Centrifugation and filtration are other options for separating the sorbents, leading to a reduction in sample preparation time [150].

Recently, magnetic ionic liquids (MILs) have received much attention from researchers in the field of microextraction due to their easy tunability, which allows them to be modified and used for extraction in both hydrophilic and hydrophobic media [90]. Various cationic liquids such as imidazolium, phosphonium and pyrrolidinium have been used for the synthesis of MILs [30], [151]. However, quaternary ammonium cations are preferred due to their flexibility as well as physicochemical properties besides ease of adaptation and lower toxicity [152]. Recently, our group has demonstrated the ability of quaternary ammonium cation-based ionic liquids as sorbents for the extraction of organochlorine pesticides from water samples [153] and for the adsorption of rose bengal and methylene blue dyes from aqueous solutions [154]. In this study, the advantages of magnetic properties and ionic liquids in extraction technology were combined to develop a MIL of quaternary ammonium cations as sorbents for the extraction of CBZ. CBZ analysis was performed by liquid chromatography (LC). The LC became the preferred and suitable technique for pharmaceutical and drug separations due to its high molecular weights [155], [156]. However, the detection of these compounds in water samples is difficult due to their

trace level concentrations and interference from the matrix effect, making sample preparation of paramount importance [157].

Therefore, in this work, we successfully synthesized two MILs ((Z)-octadec-9-en-1-aminium tetrachloroferrate (III) and (Z)-octadec-9-en-1-aminium trichlorocobaltate (II)) and used them as sorbents at room temperature for dispersive micro solid phase extraction of CBZ drug from human urine and wastewater samples.

5.2 Experimental

5.2.1 Reagents and chemicals

All chemicals and reagents were used as received from the company. Acetonitrile (analytical grade) was purchased from Carlo Erba reagents. Ethanol, methanol, hydrochloric acid, sodium hydroxide, sodium chloride, oleylamine, cobalt (II) chloride hexahydrate, and deuterated chloroform were received from Sigma-Aldrich. Acetone (analytical grade) was received from Merck, Germany. Ferric chloride was received from Fluka Analytical, the carbamazepine standard was acquired from Merck, phosphoric acid was purchased from ReAgents, and potassium phosphate monobasic was obtained from the Cole-Parmer scientific expert.

5.2.2 Sample preparation

A stock solution of 100 ppm of the analyte was prepared and stored in a refrigerator at approximately 4 °C. The working solutions were mixed in deionized water as the model analyte was prepared at different concentrations. Both urine and wastewater samples were collected in a clean, sterile glass container. The urine samples were obtained from two healthy individuals who were not administered the drug under study and then stored at approximately -20 °C until use. First, 3 mL of the urine sample was centrifuged at 3500 rpm for 7 min and then diluted with deionized water in a ratio of 1:9 v/v. The effluent was carefully filtered with a filter paper to remove suspended solids, stored at 4 °C and used directly without dilution. The pH of both urine and effluent samples was adjusted to 7 before each extraction.

5.2.3 Instrumentation and operating conditions

The chromatographic separation was performed in HPLC-DAD system Agilent technologies 1260 Infinity equipped with quaternary pump (G1311C), autosampler (G1315D), and detector DAD (G1315D) controlled and managed through Chemstation software powered by Agilent technologies. The separation column that was used was eclipse XDB-C18 (4.6 mm ID × 250 mm). The mobile phase was composed of 45% acetonitrile, 50% deionized water, and 5% 50 mM phosphate buffer solution, at a pH 3.5 maintained using 0.1M NaOH and 0.1M phosphoric acid. The mobile phase was pumped

at a flow rate of 1 mLmin⁻¹ in an isocratic mode, and 20 µL of the sample was injected. The CBZ was detected at a wavelength of 230 nm.

5.2.4 Synthesis of MILs

The synthesis of the two MILs ((Z)-Octadec-9-en-1-aminium tetrachloroferrate (III) and ((Z)-Octadec-9-en-1-aminium trichlorocobaltate (II)) was carried out according to the reported procedure with modifications [153]. Briefly, 5 mL of oleylamine was dissolved in 5 mL of ethanol and an equimolar amount of HCl acid was added dropwise. The mixture was vigorously stirred for 4 hours to form the intermediate (Z)-octadec-9-en-1-aminium chloride ([OA]Cl). The mixture was then subjected to a rotary evaporator to remove the ethanol solvent, and the intermediate was confirmed by ¹H NMR. Then, the intermediate and iron (III)chloride/cobalt (II)chloride hexahydrate were mixed in equimolar ratio in 10 mL of ethanol solvent and stirred for 24 hours in a strong magnetic stirrer. Then the ethanol solvent was removed using a rotary evaporator and washed thoroughly with deionized water and lyophilized by freeze drying to remove the water. The products obtained were sonicated and centrifuged at 7800 rpm in acetonitrile solvent several times until the solution became clear, indicating the absence of unreacted FeCl₃/CoCl₂ and starting material. The dark, sticky, and highly hygroscopic compound (**Fig. 35b**) was stored in an oven at 80 °C for 72 hours to remove all traces of water molecules and solvent droplets. The steps of the reaction mechanism of the synthesis are shown in (**Fig. 32**).

The reaction mechanism begins with a simple Lewis acid-base reaction between the oleylamine and hydrochloric acid to form the intermediate ammonium salt (Z)-octadec-9-en-1-aminium chloride. This is followed by the addition of $\text{FeCl}_3/\text{CoCl}_2$, which acts as a stable acceptor for the free chlorine ion and forms the anion moieties of MIL. Thus, Fe^{3+} and Co^{2+} are surrounded by four and three Cl^- , respectively. The cation part of MIL, (Z)-octadec-9-en-1-aminium, forms the NH_3^+ .

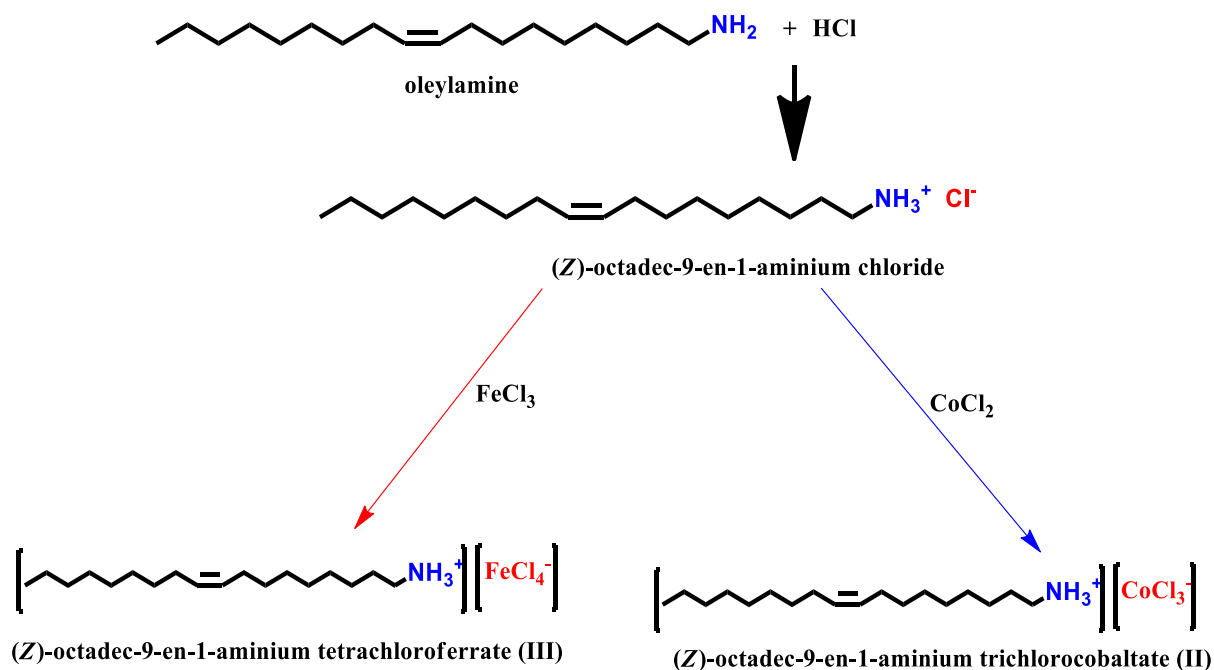


Figure 32: Synthesis steps of (z)-octadec-9-en-1-aminium tetrachloroferrate (III) and (z)-octadec-9-en-1-aminium trichlorocobaltate (II)

5.2.5 Extraction procedure

First, 40 mg MIL solid was dispersed at room temperature in a 10 mL sample solution containing 300 µg/L and 10% NaCl w/v using a magnetic stirrer at a constant speed of 700 rpm. The pH was adjusted to 2.8. The extraction was performed at different times: 5-60 min, after which the solution was centrifuged at a constant speed of 7800 rpm for 5 min to isolate the sorbent, and the liquid was carefully decanted. Then, 500 µL of acetonitrile was used as solvent to desorb the analyte from the sorbent by ultrasonication for 45 min. Finally, the solution was centrifuged again for 5 min to separate the sorbent and the analyte-rich supernatant and transferred to HPLC tubes for HPLC-UV analysis. A flow chart showing the procedure is shown in **(Fig. 33)**.

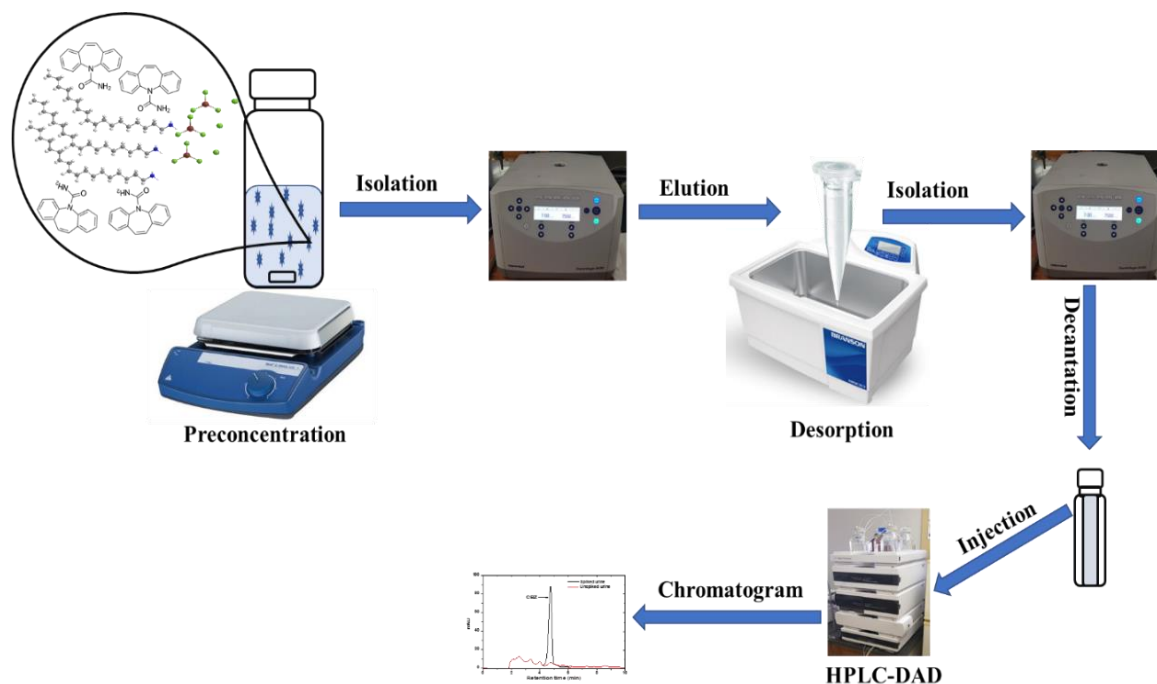


Figure 33: Steps involved in the dispersive micro-solid phase extraction procedure of the CBZ.

5.3 Results and discussion

5.3.1 Synthesis of MILs

In this study, $[\text{OA}]\text{FeCl}_4$ and $[\text{OA}]\text{CoCl}_3$ MILs were successfully synthesized and used as sorbents at room temperature for the extraction and preconcentration of the drug CBZ from human urine and wastewater samples. The synthesized MILs readily interact with the aromatic rings of CBZ analyte by predominant electrostatic (induce dipole moment)

interaction as the sorbent forms micelles in water with a hydrophobic core and a hydrophilic perimeter, as shown in (Fig. 35a. Fig. 34a) also shows the main structure of CBZ in water indicating hydrogen bonding with less resonance, which gives better chances for extraction between analyte and sorbent. (Fig. 34b) shows the structure in acetonitrile, indicating resonance that promotes dipole-dipole moment and reduces the induced dipole-moment interaction between the hydrophilic end of the MIL and CBZ to allow easy desorption of the analyte from the sorbent.

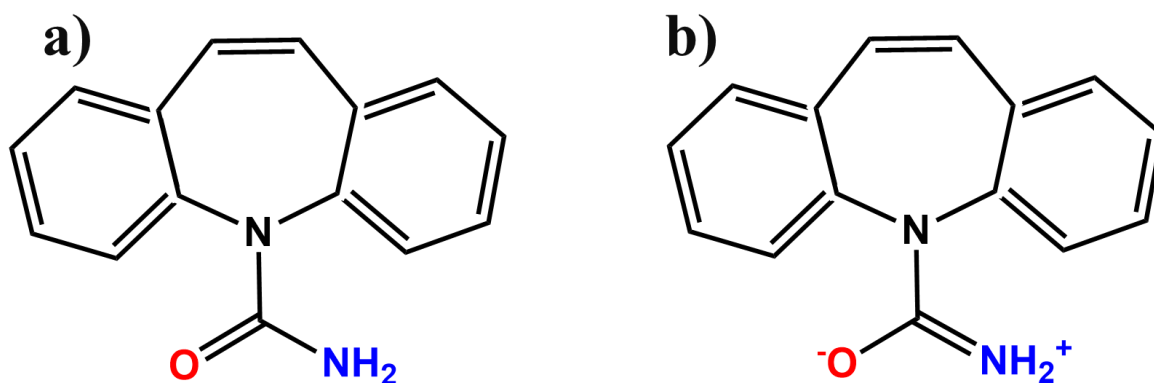


Figure 34: a) CBZ in water b) CBZ in acetonitrile

Important parameters for extraction and desorption such as sorbent type, pH, sorbent dosage, extraction time, desorption time, salinity, desorption solvent and desorption solvent volume were optimized. The study shows that [OA]FeCl₄ can be used as a sorbent

for the extraction of CBZ from both human urine and wastewater samples and has better efficiency than $[\text{OA}]\text{CoCl}_3$. This may be due to the fact that the orbital of $\text{Co}(\text{II})$ (d^7) is in a low spin, making the complex less stable and repelled by the free electron than the Fe complex with (d^6), which is more stable.

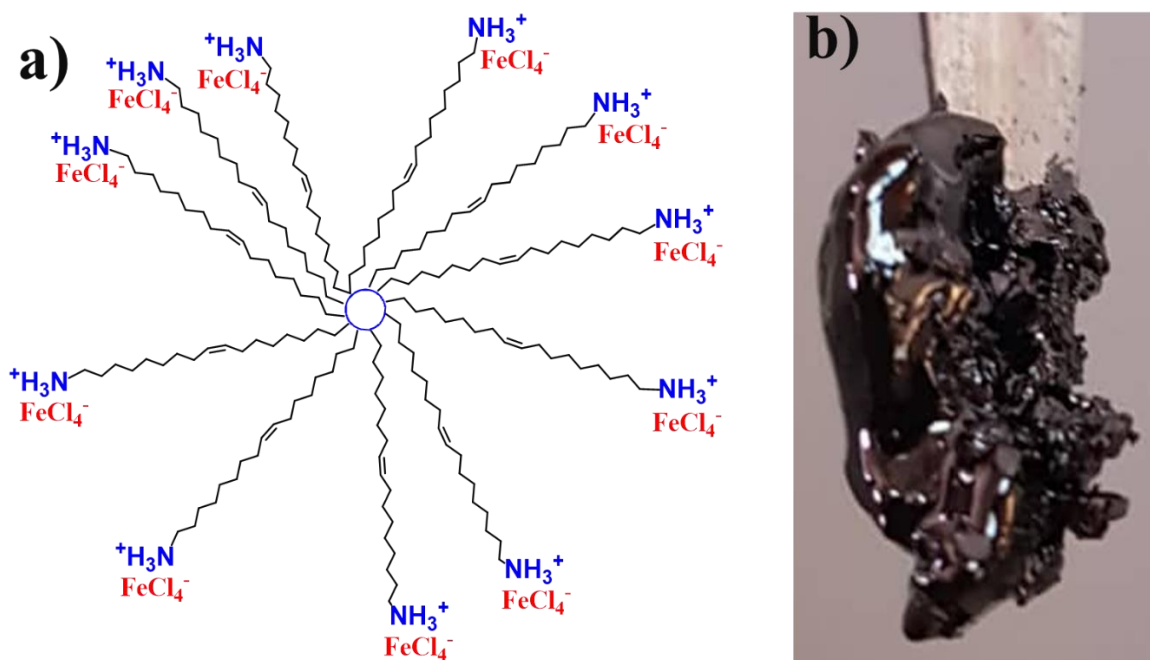


Figure 35: a) Micelle of $[\text{OA}]\text{FeCl}_4$ in water b) picture of the MIL

5.3.2 Characterization of the MILs

The characterization of MILs is very important because their physical properties are easily affected by the presence of impurities and the structure of the compound [96]. On this basis, the following characterizations were carried out.

5.3.2.1 Proton nuclear magnetic resonance (^1H NMR) spectra of [OA]Cl intermediate

The formation of the (Z)-octadec-9-ene-1-aminium chloride intermediate resulting from the protonation of the amino group of the oleylamine reactant by HCl acid solution was confirmed by ^1H NMR. The ^1H NMR spectra were recorded using a JEOL spectrometer (JNM-LA 500 MHz, JEOL USA Inc.). The observed chemical shift of the ^1H NMR spectrum of oleylamine from 0.38, 0.59, 0.81, 0.92, 1.58, 2.15, 4.81 and 4.92 ppm (**Fig. 36**) downward to 0.98, 1.39, 1.51, 2.03, 2.88, 3.93, 5.32 and 5.40 ppm (**Fig. 37**) was indicative of the successful protonation of the oleylamine reactant to form the quaternary [OA]Cl intermediate. The ^1H NMR spectra also showed an integral peak area directly proportional to the number of hydrogen atoms present in the compounds at various shifts with negligible error range. No additional peaks were also observed for the intermediate compound indicating high purity. The peak observed at about 7.2 ppm is due to deuterated chloroform (CDCl_3) as solvent.

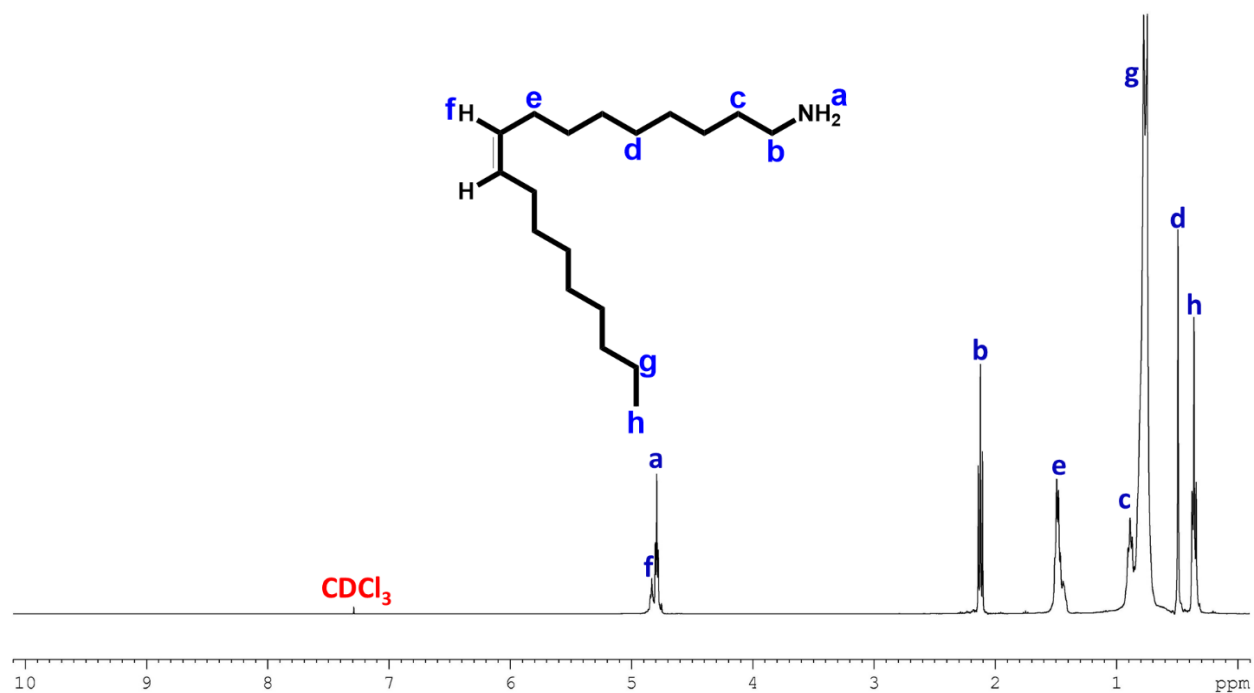


Figure 36: ^1H NMR of oleylamine

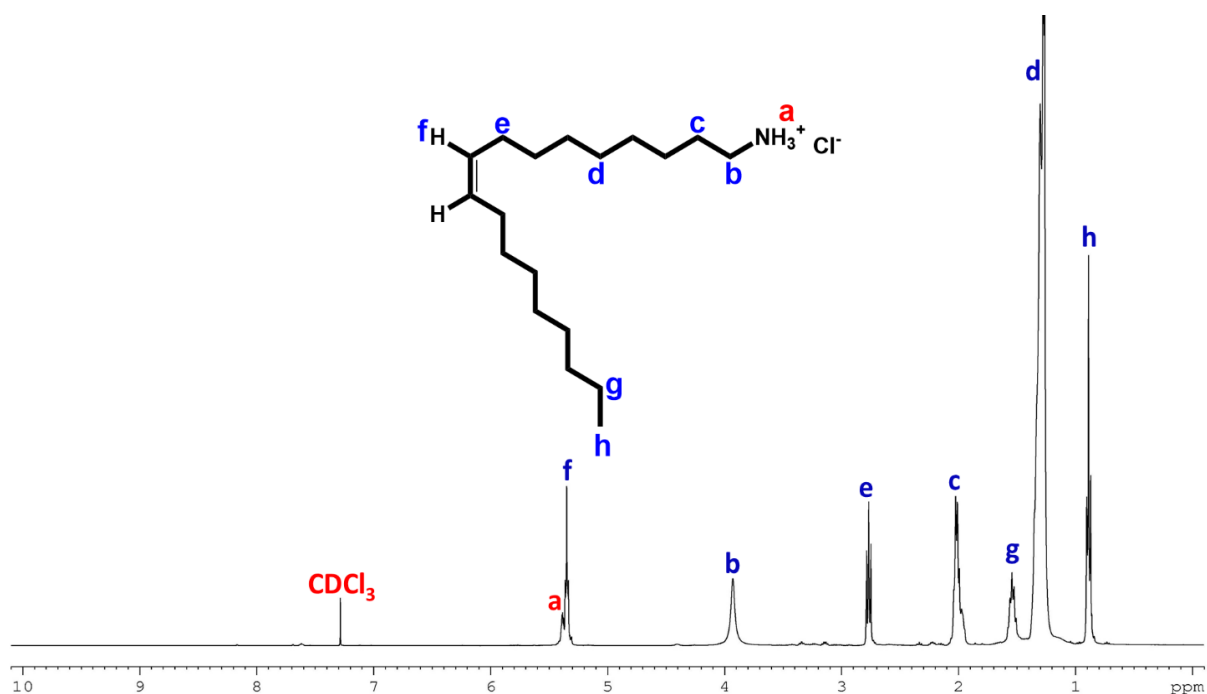


Figure 37: ^1H NMR of intermediate [OA]Cl

5.3.2.2 FTIR spectra of the MILs

FT-IR spectra were recorded in the range 400 cm^{-1} to 4000 cm^{-1} using the Smart iTR NICOLET iS10 model from Thermo Fisher Scientific. Both the oleylamine, [OA]Cl intermediate and [OA]FeCl₄ MIL showed similar FTIR spectra (**Fig. 38a and b**). The appearance of absorption bands at 1631.6 cm^{-1} and 3355.7 cm^{-1} indicates the presence of C=C and N-H, respectively. Moreover, the 1631.6 cm^{-1} can also be attributed to the combined motion of N-H bending and NH₂ shear. The broadened absorption band between

3500 cm^{-1} and 3300 cm^{-1} seen in **(Fig. 38c and d)** is due to the hygroscopic or deliquescent behavior of FeCl_4^- or CoCl_3^- , or perhaps can be attributed to the coordination between the oleylamine amine group and FeCl_4^- or CoCl_3^- . The absorption bands at 2850.4 cm^{-1} and 2950.4 cm^{-1} were assigned to the in-plane asymmetric C-H stretching and terminal asymmetric CH_3 stretching, respectively, or the same bands could be assigned to the hydration of the $-\text{NH}^{3+}$ group in the complex. In general, the analysis of the FT-IR spectra shows that the anions of the product have little effect on the chemical shift, while the cationic structures show a similar pattern.

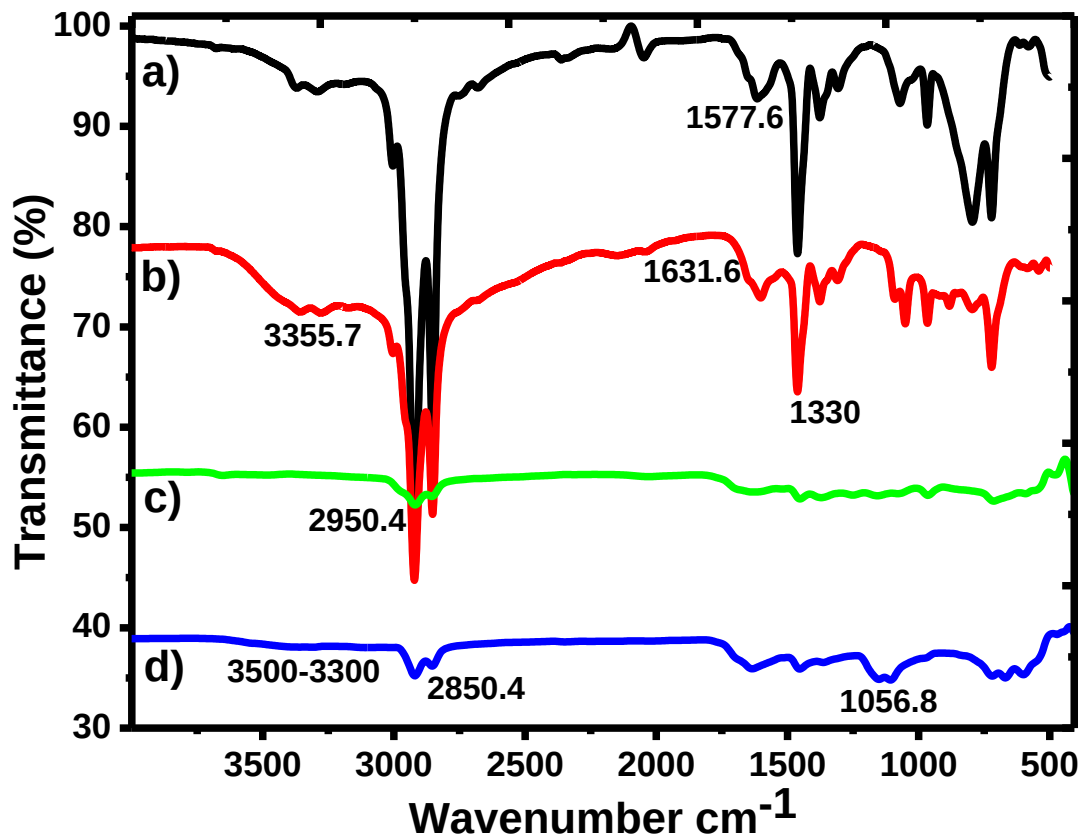


Figure 38: FTIR spectra of a) oleylamine b) intermediate [OA]Cl c) [OA]FeCl₄ d) [OA]CoCl₃

5.3.2.3 Raman spectroscopy of the MILs

Raman spectra were recorded in a range from 100 cm⁻¹ to 700 cm⁻¹ using the surface-enhanced Raman scattering spectroscopy (SERS), model LabRam. The excitation laser source used was 633 nm. Sharp dominant peaks were observed at about 327.4 cm⁻¹ and 349.7 cm⁻¹ for [OA]FeCl₄ and [OA]CoCl₃, respectively (**Fig. 39**). In addition, peaks at about 120 cm⁻¹ can be seen (indicated by arrows), which were assigned to the symmetric

bond stretching vibrations originating from Fe-Cl of FeCl_4^- and Co-Cl of CoCl_3^- . Similar observations have been previously reported for FeCl_4^- containing ionic liquids [96], [158]–[160]. Moreover, well-resolved broad peaks at 204.8, 250 and 300 cm^{-1} are seen in the case of $[\text{OA}]\text{CoCl}_3$, and a similar pattern has been reported in the literature with CoCl_3 [161].

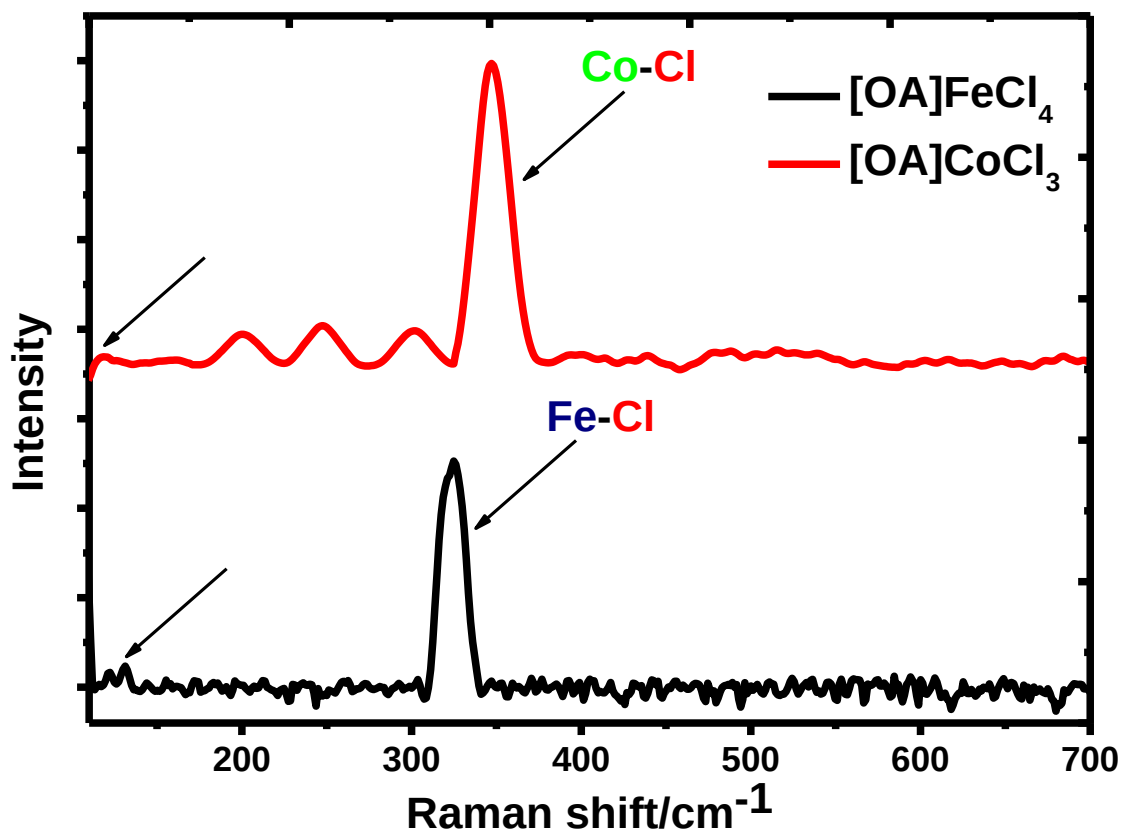


Figure 39: Raman spectra of $[\text{OA}]\text{FeCl}_4$ and $[\text{OA}]\text{CoCl}_3$ MILs

5.3.2.4 Scanning electron microscopy (SEM) of MILs

The morphology and surface characterization of the MILs were studied using the JEOL JSM-6610LV model SEM. The images of the MILs are shown in **(Fig. 40a and b)**. It was found that both MILs did not have regular particle structure and particle size, but the particles were well dispersed. This dispersion resulted in efficient diffusion of the analyte into the surface of the sorbents. EDX elemental analysis **(Fig. 40c and d)** confirmed the presence of all elements in the MILs.

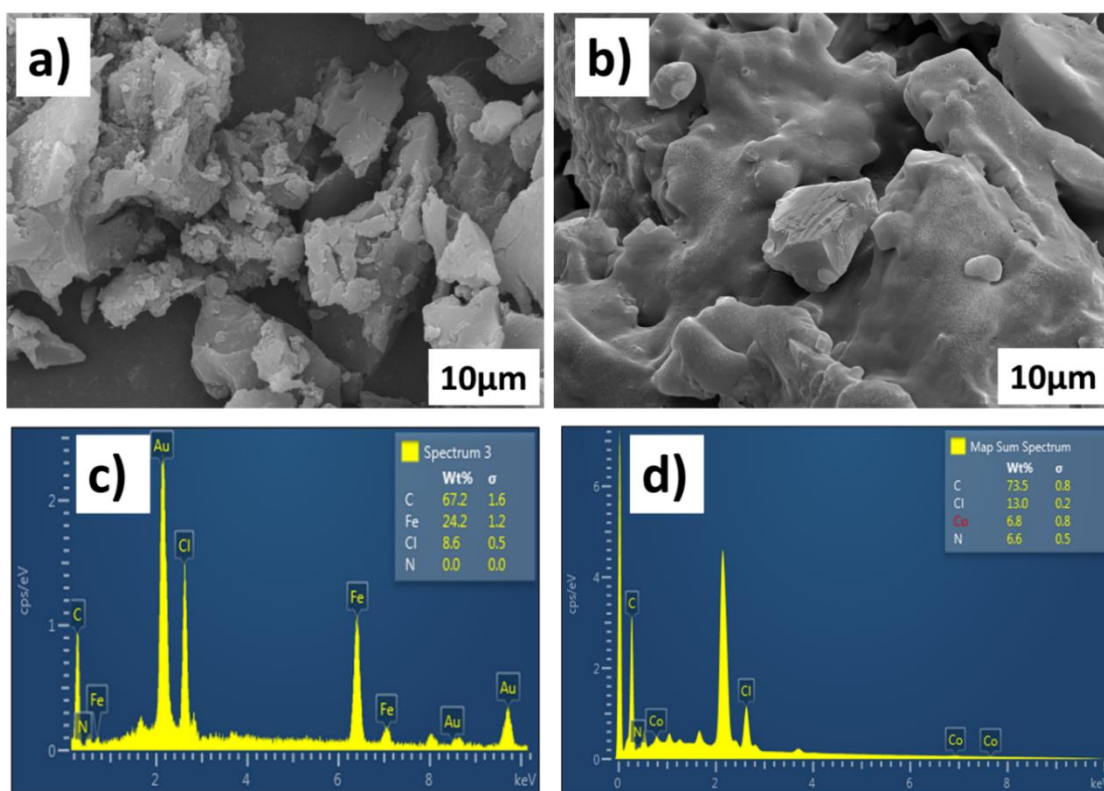


Figure 40: SEM image of a) [OA]FeCl₄ 10 μm b) [OA]CoCl₃ 10 μm, c) and d) respective elemental analysis in EDX.

5.3.2.5 Thermogravimetric (TGA) analysis of the MILs

A thermogravimetric analyzer, model SDT Q600, was used to analyze the two MILs. About 8.1 mg of the MIL were heated over a range of temperatures (from 30 to 900 °C) in an alumina pan with a ramp of 10 °C/min and a nitrogen flow of 50 mL/min to obtain the decomposition curve. The MIL [OA]CoCl₃ showed good thermal stability up to 300 °C compared to [OA]FeCl₄ at 243.3 °C, while the stability of [OA]FeCl₄ was maintained up to 500 °C with less than 50% weight loss. Both started to decompose, although [OA]CoCl₃ decomposed faster than [OA]FeCl₄ at higher temperatures (**Fig. 41a**). The endothermic peak seen at about 57.5 °C in both MILs can be attributed to the melting point of the complexes. The decomposition mechanism was initiated by a nucleophilic attack from the anion to the cation part of the complexes [162]. The first step, the loss of the coordinated chlorine and solvents at slightly below 300 °C, followed by the tail of the complexes at about 450 °C, at about 600 °C the loss of the amine moiety and the entire organic backbone to form the respective oxides. A similar observation was reported for cobalt and iron containing complexes [163]. The TGA result showed that the [OA]FeCl₄ and [OA]CoCl₃ MILs sorbent exhibited excellent thermal stability with minimal weight loss even at very high temperatures and within the range reported in the literature [164].

5.3.2.6 Zeta potential of the MILs

The zeta potential of the two MILs was studied in six different pH ranges of 2, 4, 6, 8, 10 and 12 in deionized water using the model PALS Zeta Potential Analyzer. The zeta potential is an essential parameter to determine the stability of the MILs during dispersion in a particular medium. It was observed that the materials exhibited positive charge at low pH and negative potential at higher pH (**Fig. 41b**). The negative surface charge was due to the presence of CoCl_3^- and FeCl_4^- . Moreover, the positive charge at low pH was from the (Z)-octadec-9-ene-1-aminium cation of the MILs. The isoelectric point of the complexes was determined at pH values of about 3.4 and 9.6 for $[\text{OA}]\text{FeCl}_4$ and $[\text{OA}]\text{CoCl}_3$, respectively. It was confirmed that the compound has both negative and positive charges on the surface.

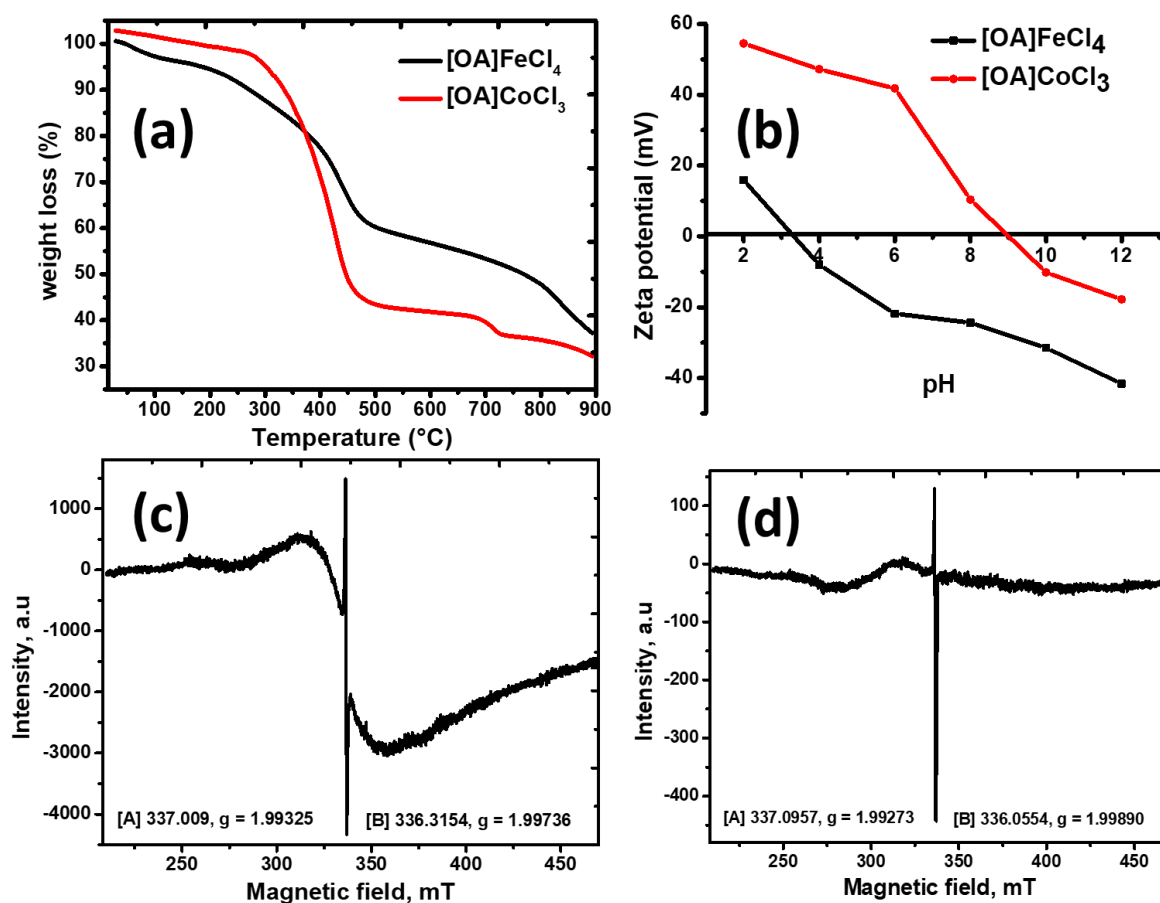


Figure 41: (a) TGA analysis curve; (b) Zeta potential vs. pH; (c) EPR spectra of [OA]FeCl₄ and (d) EPR spectra of [OA]CoCl₃ of the MILs.

5.3.2.7 Electron paramagnetic resonance (EPR) analysis of the MILs

EPR spectra were performed using a miniscope model of a benchtop EPR spectrometer, and it was found that the EPR analysis of the two MILs consistently follows a similar trend upon temperature treatment, and this can be confirmed in the comparable g-factors, which vary around 1.999. The g-factor, which is also known as Land'e factor, is an excellent value

to determine the paramagnetic property of compounds in spectroscopic technique, it indicates the unique signature of the compound, and it is generally calculated using **Equation 2**. Here $h\nu$ is the radiation energy, B_0 is the value of the resonance field, and the magnetic field is directly proportional to the maximum adsorption. First, a spin can be excited from the resting ground state to a higher energy level by supplying electromagnetic radiation, which must satisfy Planck's law.

$$g = \frac{h\nu}{\beta e B_0} \quad (2)$$

A neutral iron and cobalt atom give up its 4s electrons by ionization, and the subsequent ionization goes to the 3d orbitals. After ionization, the unpaired valence electrons form the net spin. Therefore, these high-spin atoms of iron and cobalt are responsible for the formation of the corresponding anion complexes such as tetrachlorocobaltate and tetrachloroferrate, which are the cause of the paramagnetic behavior observed in MILs. A similar pattern is also reported in the literature [154], [165].

5.3.3 Optimization of the extraction conditions

To understand the effectiveness of the extraction method, various key experimental parameters such as sorbent type, pH, sorbent dosage, extraction time, desorption time, ionic

strength, desorption solvent and desorption volume were evaluated and studied. All experiments were carried out in triplets for each parameter at room temperature.

5.3.3.1 Sorbent type and dosage

The selection of the correct sorbent in extraction is of paramount importance in all method developments and determines the extraction performance and efficiency of the method. In this study, polar sorbents, [OA]FeCl₄ and [OA]CoCl₃ MILs, were compared for the extraction of CBZ drug. It is observed that [OA]FeCl₄ exhibits higher extraction efficiency than [OA]CoCl₃ (**Fig. 42**). The performance can be attributed to the hydrophobic formation in combination with the D(z²) orbital of Co (II) (d⁷) in a low spin, which is less stable compared to the Fe complex with (d⁶). Therefore, [OA]FeCl₄ was selected for the extraction of CBZ present in human urine and water samples. The polarity of [OA]FeCl₄ in water (as shown in **Fig. 35a**) produced an induced dipole moment in the aromatic rings of CBZ, and this resulted in the attraction of CBZ by the sorbent [OA]FeCl₄ MIL. The effect of sorbent dosage for both MILs on the extraction efficiency was also investigated using a range (between 10-50 mg) of sorbent dosage while maintaining the other experimental conditions. The highest extraction efficiency was observed when 40 mg of sorbent was used for extraction. However, 50 mg sorbent showed similar results without significant improvement. Therefore, the [OA]FeCl₄ sorbent dosage was kept constant at 40 mg for the rest of the study.

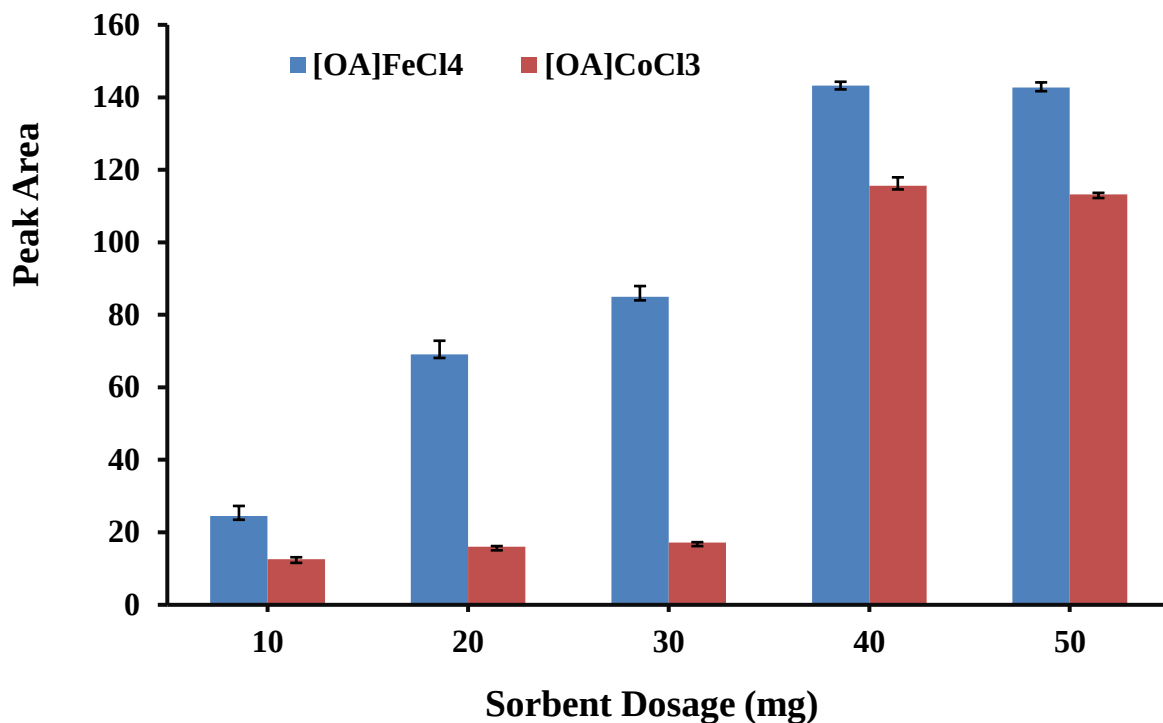


Figure 42: Effect of sorbent type.

5.3.3.2 Effect of pH

The pH of the sample solution plays a crucial role in extraction, as it affects the present form of both the sorbent and the target analyte. It also affects the surface charge and density [166]. Therefore, the pH of the solution was adjusted between 2 and 9 and it was observed that CBZ was highly and efficiently extracted at neutral pH 7 as shown in **(Fig. 43a)**. This was confirmed by the isoelectric point of the zeta potential (3.4), which is well below pH 7. The surface of the sorbent [OA]FeCl₄ MIL was rich in negative charges compared to

[OA]CoCl₃ MIL, which had a larger positive charge of 9.6. However, both positive and negative charges were present on the surface of the sorbent [OA]FeCl₄ MIL at different pH values. Thus, the extraction behavior can be attributed to the electrostatic interactions (inducing dipole-dipole) between the sorbent [OA]FeCl₄ MIL and CBZ at neutral pH. Although CBZ is a neutral compound in all pH ranges studied, the basic hydrolysis of the amide group of CBZ probably formed the carboxylate ion, and the negative charge of the carboxylate ion further repelled the negative surface charge of the sorbent [OA]FeCl₄ MIL at high pH, further reducing the extraction efficiency. Similarly, the acidic hydrolysis of CBZ may have led to a reduction in recovery in acidic media. The extraction behavior of CBZ may be attributed to hydrophobic interactions as it exhibits higher dissociation values ranging from 7 to 13.9 compared to the isoelectric point, as reported in the work of Jones *et al* [167]. Moreover, CBZ tends to show higher tendency to organic solvents upon desorption. Therefore, pH 7 was chosen as the most suitable value for the extraction of CBZ. A similar trend was reported when ionic liquids were used for the extraction of drugs like CBZ [168].

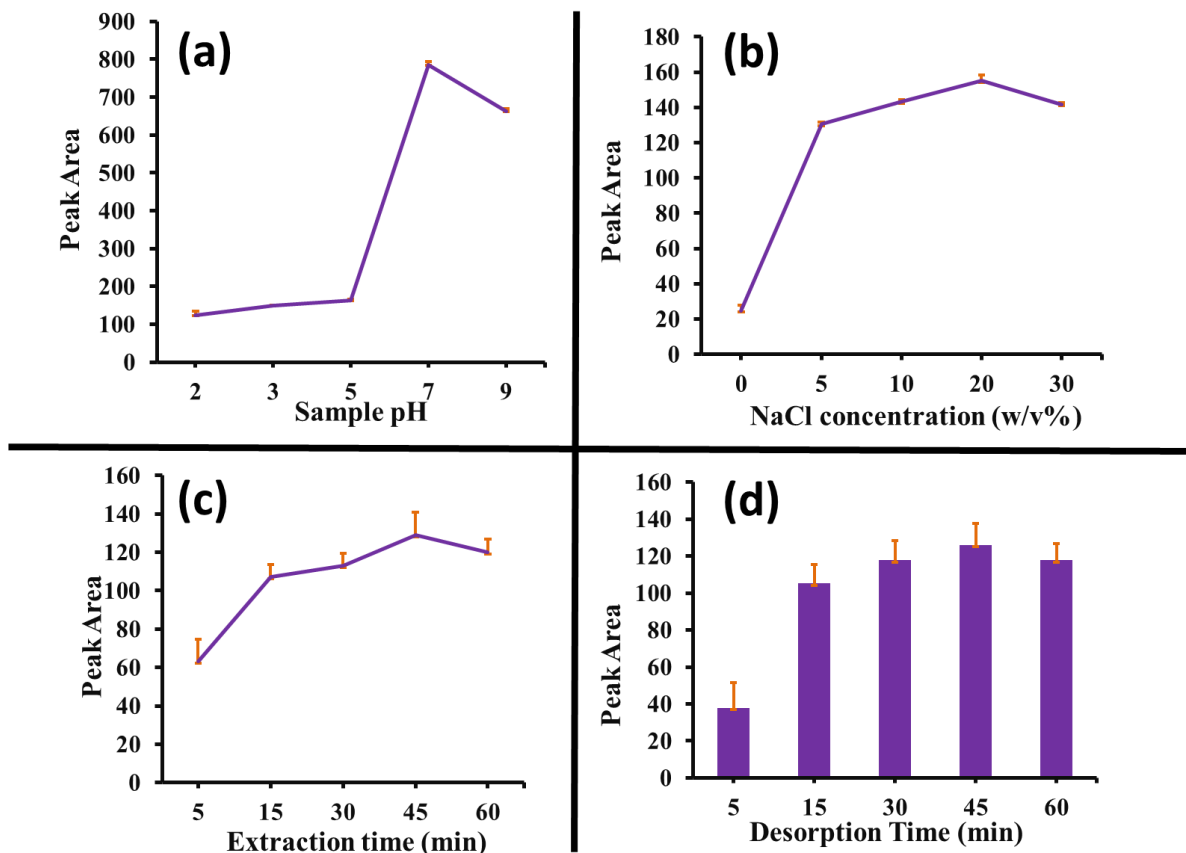


Figure 43: Effect of a) sample pH, b) NaCl concentration, c) extraction time and d) desorption time on the extraction performance of CBZ on [OA]FeCl₄ MIL sorbent. All optimizations were performed in a 10 mL deionized water sample solution, spiked with 300 µg/L of the analyte.

5.3.3.3 Effect of sodium chloride salt concentration

The effect of NaCl on the efficiency of CBZ extraction was carried out by monitoring the recovery rate at different salt concentrations of 5, 10, 20 and 30% w/v in the sample solution. The addition of NaCl had a great effect on the extraction of the drugs as it affects

the ionic strength of the sample matrix and thus reduces the solubility. In **(Fig. 43b)**, it was observed that the extraction efficiency improved equally with increasing concentration of salt. However, the optimum condition was reached at 20 % w/v.

5.3.3.4 Effect of extraction and desorption time

The time required for the sorbent [OA]FeCl₄ MIL to fully adsorb the CBZ analyte was critical to the extraction process. To understand the optimal contact time, a series of experiments were performed at different extraction times of 5, 15, 30, 45, and 60 min as shown in **(Fig. 43c)**. It was found that the adsorption efficiency improved with increasing time. However, the best extraction time was 45 min at which adsorption equilibrium was achieved. Similarly, the time for desorption of analytes from the sorbent was studied using an ultrasonic water bath. The desorption time was varied from 5 to 45 min and it was found that 45 min was the most suitable time for desorption of CBZ **(Fig. 43d)**. Therefore, 45 min was chosen as the most suitable time for CBZ desorption for this study.

5.3.3.5 Effect of desorption solvent type and its volume

A good desorption solvent is of paramount importance in optimizing extraction because it has a high tendency to target the analyte and shows better quantitative kinetic recovery in a much shorter desorption time. In this study, the following solvents, acetone, ethanol,

methanol, and acetonitrile were used for the desorption of CBZ from the surface of the sorbent [OA]FeCl₄ MIL. The solvent desorption plot (**Fig. 44a**) showed that acetonitrile was the most suitable solvent for the desorption of CBZ. The superiority of acetonitrile as a desorption solvent could be due to its interaction with CBZ. As shown in (**Fig. 44b**), the acetonitrile promoted a stronger dipole-dipole moment in CBZ, and this stronger electrostatic interaction between acetonitrile and CBZ made the desorption process easier and faster than in the other solvents. Therefore, acetonitrile was chosen as the preferred desorption solvent. In addition, the effect of desorption volume was investigated, and it was found that 400 μ L of acetonitrile was the best volume for the desorption of CBZ from the sorbent (**Fig. 44b**).

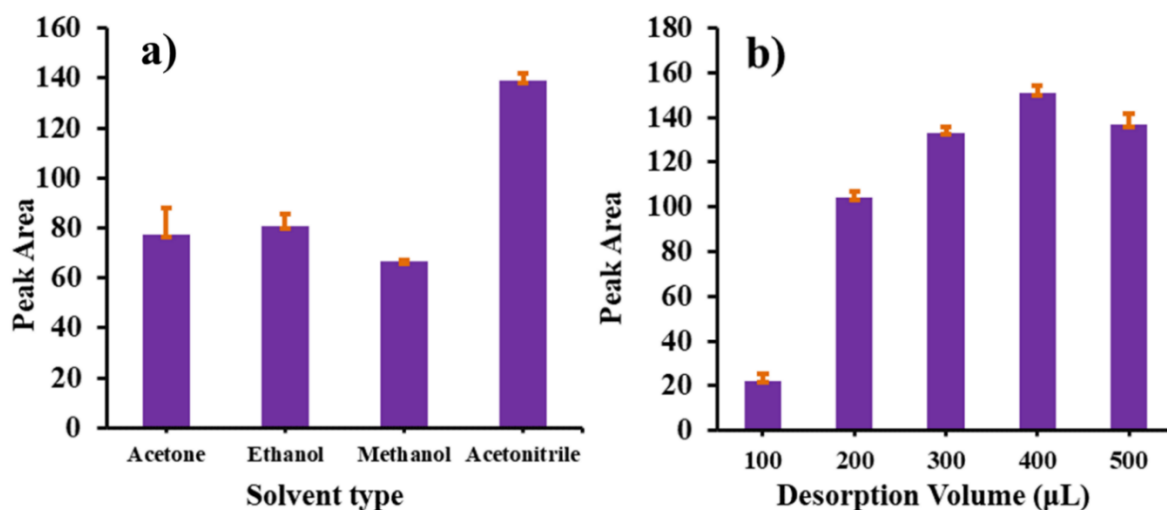


Figure 44: Effect of a) solvent type, and b) desorption volume. Optimization was performed in a 10 mL deionized water sample solution, spiked with 300 μ g/L of the analyte.

5.3.3.6 Method validation

The quantitative parameters of the method were evaluated in terms of linearity, dynamic range (LDR), limit of quantification (LOQ), limit of detection (LOD), pre-concentration factor, average recovery %, intraday and interday RSD %. The analytical parameters of the method were summarized in **Table 7**. The calibration curve was constructed using seven broad concentration ranges of CBZ standard, as 1, 100, 250, 500, 750, 1000, 1500 µg/L in 10 mL deionized water. The calibration plots were prepared by linear least squares regression analysis and the obtained correlation coefficient R^2 was 0.9989. The sensitivity of the method was further evaluated by calculating the LOD value using a signal to noise ratio of 3.0 and it was found to be 0.51 µg/L while the lowest number of the linear dynamic range was selected as LOQ value. Moreover, the average percentage recovery was calculated as the ratio of the final concentration to the found concentration multiplied by 100, which was 95.4%. The summary output of the regression statistics and ANOVA are shown in **Table 8**.

Table 7: Analytical method performance of the proposed D- μ SPE-HPLC

Analytical parameters	Obtained values
Correlation coefficients (R^2)	0.9989
Limit of detection (LOD) $\mu\text{g/L}$	0.51
Limit of quantification (LOQ) $\mu\text{g/L}$	1
Intra-day RSD, %	0.4
Inter-day RSD, %	2.1
Average recovery, %	95.4
Preconcentration factor (PF)	25
LDR, $\mu\text{g/L}$	1-1000

Table 8: Summary output

<i>Regression Statistics</i>	
Multiple R	0.999596
R Square	0.999193
Adjusted R Square	0.998991
Standard Error	22.37825
Observations	6

<i>ANOVA</i>					
	<i>Df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>
Regression	1	2479443	2479443	4951.1	2.44E-07
Residual	4	2003.145	500.7863		
Total	5	2481446			

	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>	<i>Upper 95%</i>	<i>Lower 95.0%</i>	<i>Upper 95.0%</i>
Intercept	12.61322	14.412	0.875188	0.430878	-27.4009	52.62735	-27.4009	52.62735
X Variable 1	1.809235	0.025712	70.36405	2.44E-07	1.737846	1.880625	1.737846	1.880625

Interday and intraday precision was demonstrated in terms of RSD. To investigate the reproducibility of the intraday method, six samples of deionized water were spiked with the same concentration and extracted at the same time, analyzed, and the RSD was calculated. For intraday RSD, the same procedure was repeated on different days and RSD was calculated. The values for intraday and interday RSD were 0.4 and 2.1%, respectively. The value of the pre-concentration information was obtained in the form of the pre-concentration factor (PF), which was calculated as the ratio of the volume of the sample solution to the final desorption solvent volume.

5.3.3.7 Application of D- μ SPE-HPLC on human urine and wastewater samples

After all extraction parameters were optimized, the method was tested on human urine and wastewater samples to evaluate its efficiency in complex matrices. To investigate the accuracy of the developed method, three separate samples were spiked with the CBZ standard at different concentrations and the percentage RSD and relative recoveries were calculated. It was found that the relative recoveries were in the range of 85.5 - 98%, with RSD in the range of 2.1-4.1 **Table 9. (Fig. 45)** shows the chromatograms of the two samples of human urine and wastewater after extraction under optimized conditions. The obtained result was compared with the extraction performed in deionized water and showed similar values, indicating that the proposed method can be used for complex and real samples.

Table 9: Determination of CBZ in spiked real samples

Sample type	Added, ng/mL	Found, ng/mL	Recovery %	RSD, %
Wastewater	1	0.855	85.5	4.1
	250	243.9	97.6	2.7
	750	727.3	97.0	2.7
Human urine	1	0.873	87.3	2.4
	250	244.5	97.8	2.1
	750	734.9	98.0	2.4

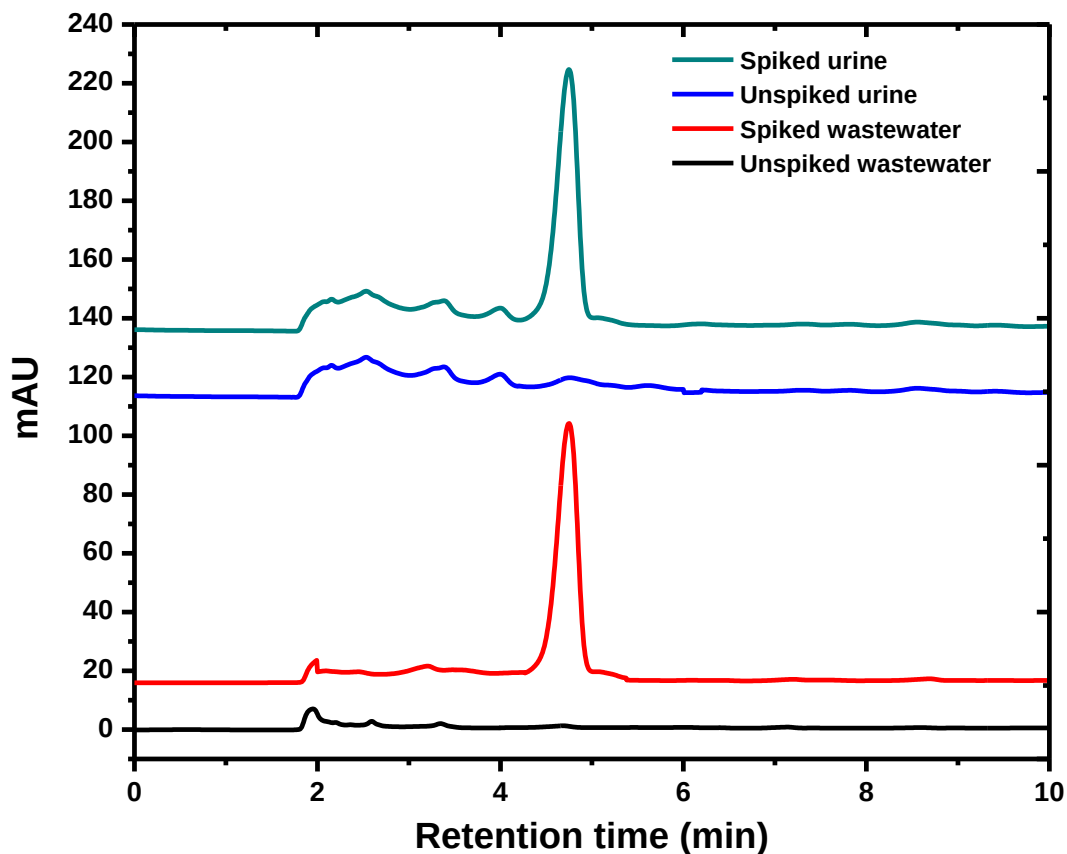


Figure 45: HPLC chromatograms showing unspiked and spiked 300 µg/L real samples under optimized conditions. The peak at 4.7 min is corresponding to CBZ.

5.3.3.8 The proposed method and its comparison with published literature

The proposed method was also compared with other published literature as shown in **Table 10**. The samples used were not contaminated as CBZ was not detected in both real samples. The method shows better selectivity for CBZ with a wider linearity range indicating excellent proportionality between the concentration and the signal, with a comparable LOD

value as well as a much lower RSD. The other important factor that distinguishes this method is the reuse of the sorbent at least five times, showing a similar recovery rate of more than 90% (**Fig. 46**), which is the goal of microextraction method development. During reuse, the sorbent was washed several times and analyzed with deionized water for any CBZ residues and dried in an oven overnight at 40 °C before reuse. This greener approach increases the environmental friendliness of MIL. In addition, the reusability of MIL was compared with work also published. Behbahani *et al.* recently reported an amine-modified mesoporous silica sorbent that could be used five times in the ultrasound-assisted D- μ SPE method for the extraction of carbamazepine and lamotrigine [169]. Also, Kahkha *et al.* demonstrated an amino-functionalized metal-organic framework containing zirconium as a sorbent for five cycles in the determination of the drug carbamazepine from water and urine samples [170].

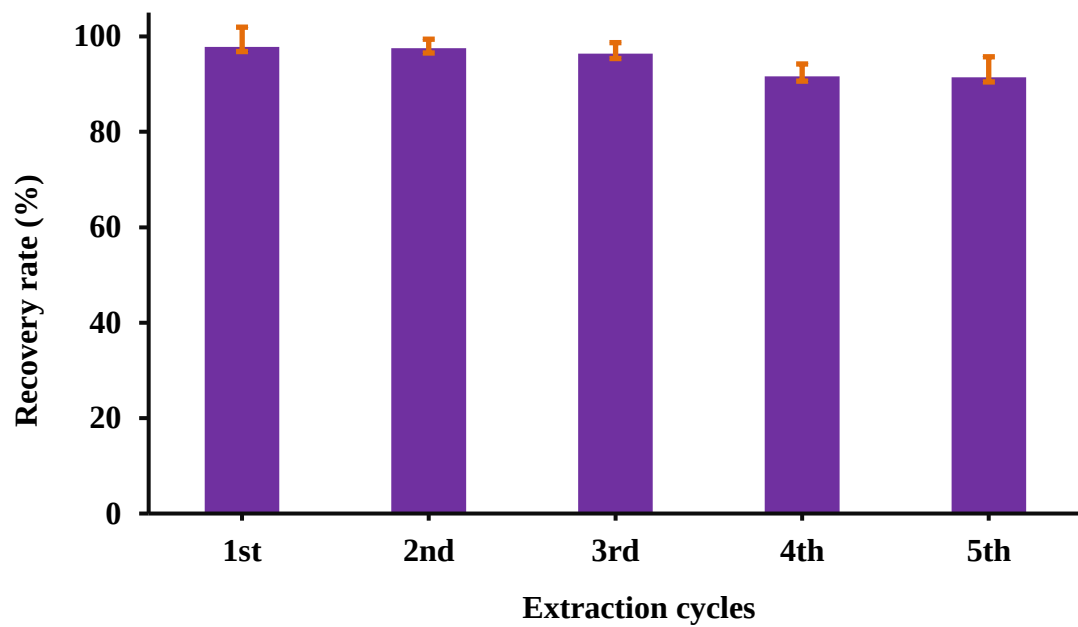


Figure 46: Recycling experiments of MIL ([OA]FeCl₄) sorbent for the extraction of CBZ.

Table 10: Comparison of [OA]FeCl₄ sorbent with other reported methods for CBZ determination

Method	Matrix	DLR	LOD	Extraction time (min)	RSD (%)	Ref.
Two-phase HF-LPME	Aqueous & plasma	5–500 µg/L	2.8 µg/L	30	4.4	[140]
CTAB coated Cu NCs-based fluorimetric assay	Exhaled breath condensate	200–20000 µg/L	80 µg/L	10	3.9	[171]
Surface molecularly imprinted polymers-DSPE-HPLC-UV	Human plasma	0.5–500 µg/L	0.1 µg/L,	5	3.6	[172]
Ultrasonic assisted-DSPE-HPLC-DAD	Wastewater	0.3–800 µg/L	0.08 µg/L	17.5	1.4	[173]
MIL	River water	5–500 µg/L	1.5 µg/L	3	9.2	[174]
MIL ([OA]FeCl ₄)	Wastewater & Human urine	1–1000 µg/L	0.51 µg/L	45	0.4	This work

5.4 Conclusion

Magnetic ionic liquids, (Z)-octadec-9-en-1-aminium tetrachloroferrate (III) and (Z)-octadec-9-en-1-aminium trichlorocobaltate (II) were successfully synthesized and used as sorbents at room temperature for dispersive micro solid phase extraction (D- μ -SPE) coupled with high performance liquid chromatography-ultraviolet (HPLC-DAD) for the separation, preconcentration and determination of CBZ drugs in real human urine and wastewater samples. It was observed that (Z)-Octadec-9-en-1-aminium tetrachloroferrate (III) showed better extraction performance of CBZ from wastewater and urine samples, which may be related to both hydrophobicity and advantage arising from stable Fe complex with (d^6) compared to unstable $D(z^2)$ orbital of Co (II) (d^7) in a low spin. When this method was compared with other existing techniques, it offered better linearity of 1-1000 $\mu\text{g/L}$, much lower RSD of 0.4% and comparable LOD value of 0.51 $\mu\text{g/L}$. The proposed method offered simple, sensitive, efficient, and selective determination of CBZ drug, also easy preparation of sorbent and limited consumption of organic solvents. This work paves the way for a new direction of future studies by investigating potential applications of tunable MILs as sorbents at ambient conditions for the extraction and pre-concentration of complex trace contaminants and pharmaceutical products in the environment.

CHAPTER 6

Magnetic ionic liquid (Z)-octadec-9-en-1-aminium tetrachloroferrate (III) for dispersive micro-solid phase extraction coupled with high-performance liquid chromatography for the simultaneous preconcentration of three pharmaceutical compounds in wastewater and human urine samples

6.1 Introduction

Sample preparation is a crucial step in pharmaceutical product analysis because it reduces matrix influence, increases selectivity and sensitivity, and improves column protection [175], [176]. Liquid-liquid is one of the classical analytical techniques used for sample preparation. However, it has major drawbacks such as excessive use of toxic organic solvents, high time consumption, purification, and evaporation to pre-concentrate analytes for analytical detection. To overcome these challenges, dispersive liquid-liquid microextraction (DLLME) was developed, which is simple, inexpensive, provides better preconcentration factor and excellent recovery, and requires only small amounts of solvent [10], [177]–[179]. However, DLLME is not efficient when dealing with complex matrices and not suitable for solvents with higher densities than water [180]. Since then, there has been a continuous search for improved sample enrichment methods, such as. solid phase microextraction protected by a porous polypropylene membrane [110], dispersive solid

phase microextraction (D-SPME) [181], hollow fiber liquid phase microextraction (HF-LPME) [182], Solid Bar Microextraction (SBME) [183], [184], Effervescent Assisted Liquid Phase Microextraction (EA-LME) [185], Sorbent Packed Device [186], [187], Headspace Solid Phase Microextraction [188], and so on. All these techniques have proven useful for various applications, but dispersive solid phase microextraction (D- μ -SPE) is preferred due to its higher efficiency, simplicity, etc. [148].

Although dispersive solid phase microextraction is attractive to many scientists, choosing the right sorbent for pre-concentration of target analytes remains a major challenge. In recent years, environmentally friendly ionic liquids (ILs) have gained tremendous attention for applications in numerous research areas, including analyte preconcentration. ILs are low melting point salts characterized by high thermal stability, low vapor pressure, high viscosity, and excellent reusability [189]. Recently, magnetic ionic liquids (MILs) have emerged as promising sorbents for analytical applications because they can be easily separated from the sample matrix by using a strong external magnet [90]. Our group has recently reported iron-containing ionic liquids for the microextraction of 19 organochlorine pesticides and the adsorption of cationic and anionic dyes [153], [154]. Thus, this study takes advantage of MILs as sorbents at room temperature for the simultaneous extraction of three different types of drugs from wastewater and human urine samples.

Emerging contaminants are becoming a major concern in both private and public sectors, especially for water resources. These contaminants include various types of drugs that enter the water body through widespread use by humans and animals. One such drug is clomipramine (CLOM), a tricyclic antidepressant used to treat various diseases. It is one of the pharmaceutical substances most likely to be found in the environment [190]. It

undergoes various conversion steps but is mainly metabolized in the liver via the demethylation process to desmethylclomipramine and 66% is excreted from the body via urine. Recently, the drug has gained interest in forensics and clinical trials due to its high suicide risk [191]. Another problem in the waters is loperamide (LOP), which is given to patients to relieve diarrhea, short bowel syndrome, as well as inflammatory stomach disorders. The drug and its metabolites are largely excreted from the body through feces and end up in sewage. It is also reported to be one of the most abused drugs, resulting in higher concentrations of the compounds in sewage systems [192]. Ketoprofen (KET) is another pharmaceutical contaminant commonly used in non-steroidal anti-inflammatory drugs (NSAIDs) and has both antipyretic and analgesic effects that are common in human and veterinary medicine. It is associated with side effects such as blood clotting, stomach irritation, and liver and kidney toxicity. It is also used by slaughterhouses in high doses before slaughter to deceive buyers by making the meat appear pale and healthy, but this endangers the lives of consumers [193]. The main problem for these drugs in the environment is that they are present in trace concentrations, and the creation of reliable analytical techniques that pre-concentrate and detect them is vital [157].

The most commonly used technique for the analysis of pharmaceuticals and biomedical compounds is high liquid chromatography (HPLC), as it achieves excellent precision, specificity as well as accuracy simultaneously. It is usually equipped with UV and photodiode array (PDA) detectors with a wide range of scanning wavelengths [156].

Therefore, in this work, magnetic ionic liquid (Z)-octadec-9-ene-1-aminium tetrachloroferrate (III) was synthesized and used as a sorbent at ambient conditions in conjunction with HPLC-DAD for dispersive micro solid phase extraction of

pharmaceutical compounds CLOM, KET and LOP from wastewater and human urine samples.

6.2 Materials and methods

6.2.1 Materials

Analytical grade solvents such as acetonitrile, methanol, ethanol, and acetone were purchased from Sigma-Aldrich. Other chemicals obtained from the same company include hydrochloric acid (HCl), sodium hydroxide (NaOH), sodium chloride (NaCl), oleylamine and deuterated chloroform (CHCl_3). Ferric chloride (FeCl_3) was purchased from Fluka. Analytical and analytical drug standards were purchased from Merck. Phosphoric acid and potassium phosphate monobasic were also purchased from Sigma-Aldrich.

6.2.2 Sample preparation procedure

First, 100 ppm stock solutions were prepared from the three drug analytes and stored at 4 °C. The wastewater and human urine were sampled in clean containers. The urine sample was obtained from a healthy person who did not receive the drugs in this study and then stored at -20 °C. The urine sample was first diluted 1:9 v/v with double distilled water after being centrifuged at 4000 rpm for 5 min. For the wastewater samples, a similar procedure was followed but without dilution, but filtered with a filter paper to remove suspended solid

particles and stored at 4 °C. All samples were adjusted to the optimized pH 7 before an extraction procedure was performed.

6.2.3 Instrumentation and chromatographic conditions

Separation and quantification of analytes were performed on an Agilent USA 1260 HPLC system equipped with an autosampler, a detector DAD and a separation column G1315D, G1315D and XDB-C18 with a length of 4.6×250 mm and 5 µm, respectively. The system was controlled and operated by the software Agilent Technologies' Chemstation. The mobile phase of the device consisted of double distilled water, acetonitrile, and phosphate buffer solution at a ratio of 50%, 45%, and 5%, respectively. The flow rate was maintained at 1 mL/min, a sample injection volume of 20 µL and a UV wavelength of 230 nm during all runs in isocratic mode.

6.2.4 Synthesis of MIL (Z)-octadec-9-en-1-aminium tetrachloroferrate (III)

The synthesis of MIL (Z)-Octadec-9-en-1-aminium tetrachloroferrate (III) was carried out according to our previously reported procedure, but with significant modifications and changes [153]. First, 5 mL of the parent amine compound, oleylamine, was mixed with 5 mL of ethanol and treated dropwise with an excess of 1M HCl acid. The mixture was vigorously stirred with a strong magnetic stirrer for 3 hours 30 min and the solvent was evaporated with a rotary evaporator to form the intermediate quaternary (Z)-octadec-9-en-

1-aminium chloride ([OA]Cl). Subsequently, [OA]Cl and FeCl₃ were mixed in an equimolar ratio and stirred in ethanol for 30 hours. The solvent was evaporated. The solvent was then removed using a rotary evaporator. The final dark, sticky material was washed extensively with double-distilled water to neutral pH, freeze-dried, and stored in an oven at about 70 °C for 72 hours to remove residual solvent and water droplets. The synthesis reactions are shown in (Fig. 47).

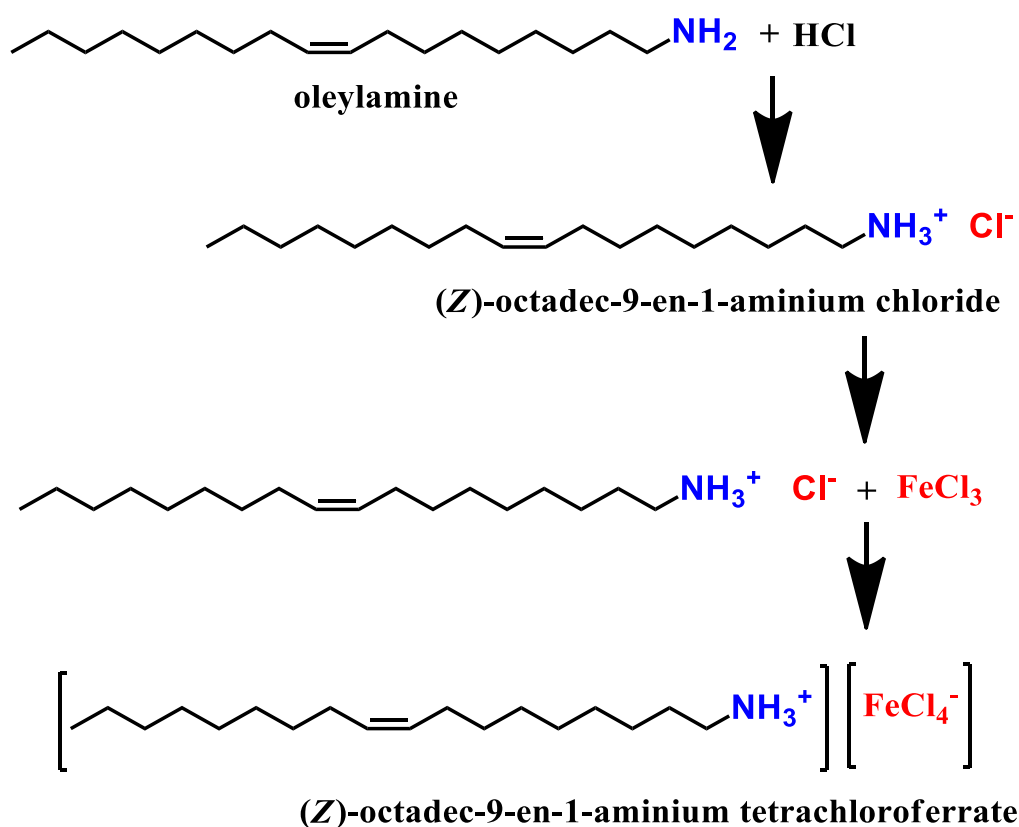


Figure 47: Synthesis reactions for the formation of MIL (Z)-octadec-9-en-1-aminium tetrachloroferrate (III)

6.2.5 The dispersive micro solid-phase extraction procedure

A 10 mL sample solution containing a known concentration of the three drug analytes was prepared in a 50 mL cap bottle, and then 40 mg of the synthesized [OA]FeCl₄ sorbent was added. The pH was adjusted to 3 and the mixture was continuously magnetically stirred at 700 rpm for 45 min to ensure good dispersion of MIL and diffusion of the analytes to its surface for their extraction. After extraction, the analyte-rich sorbents were isolated from the aqueous solution by centrifugation at a speed of 7000 rpm and the aqueous phase was carefully decanted. The analytes were desorbed with 0.4 mL of acetonitrile in an ultrasonic water bath for 45 min, and the sorbent was separated by centrifugation at the same speed. The acetonitrile after desorption was transferred to HPLC vials for analysis. A stepwise procedure for dispersive micro solid phase extraction is shown in **(Fig. 48)**.

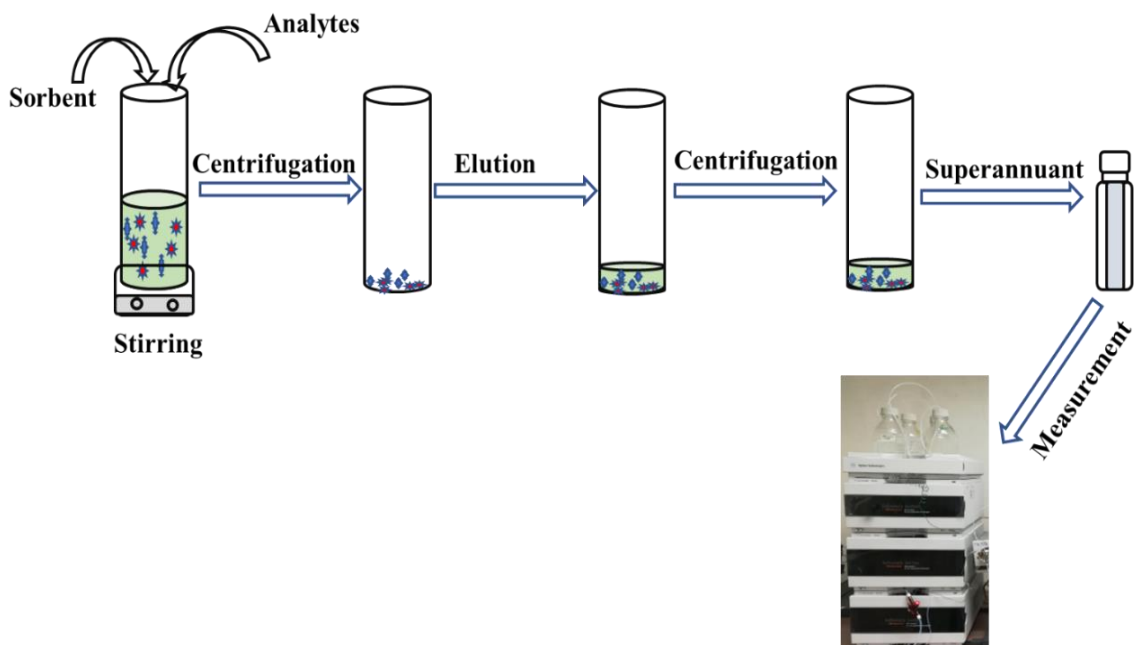


Figure 48: Dispersive micro-solid phase extraction procedure.

6.3 Results and discussion

MIL (Z)-octadec-9-en-1-aminium tetrachloroferrate (III) was prepared and used as a sorbent at ambient conditions for the microextraction and preconcentration of three different categories of pharmaceutical products such as CLOM, KET and LOP in wastewater and human urine samples (**Fig. 49**). The interaction of the hydrophobic moiety with the long chain of MIL and the dipole-dipole interaction between OH and the carbonyl group of LOP with the cationic NH^{3+} center of MIL at neutral pH are responsible for the successful extraction of the drug. Also, deprotonation of OH group of KETO promoted both electrostatic and hydrophobic interaction between MIL and analyte. CLOM is also

effectively extracted by hydrophobic interaction due to the long carbon chains of the sorbent and π - π interaction due to the presence of benzene rings of the drug at neutral pH.

Important factors affecting the dispersive micro solid phase extraction such as elution solvent, pH, elution solvent volume, desorption time, sorbent type and dosage, extraction time and salt concentration were optimized. It was found that the [OA]FeCl₄ sorbent can be successfully used for the extraction of the three categories of drugs from both wastewater and human urine samples.

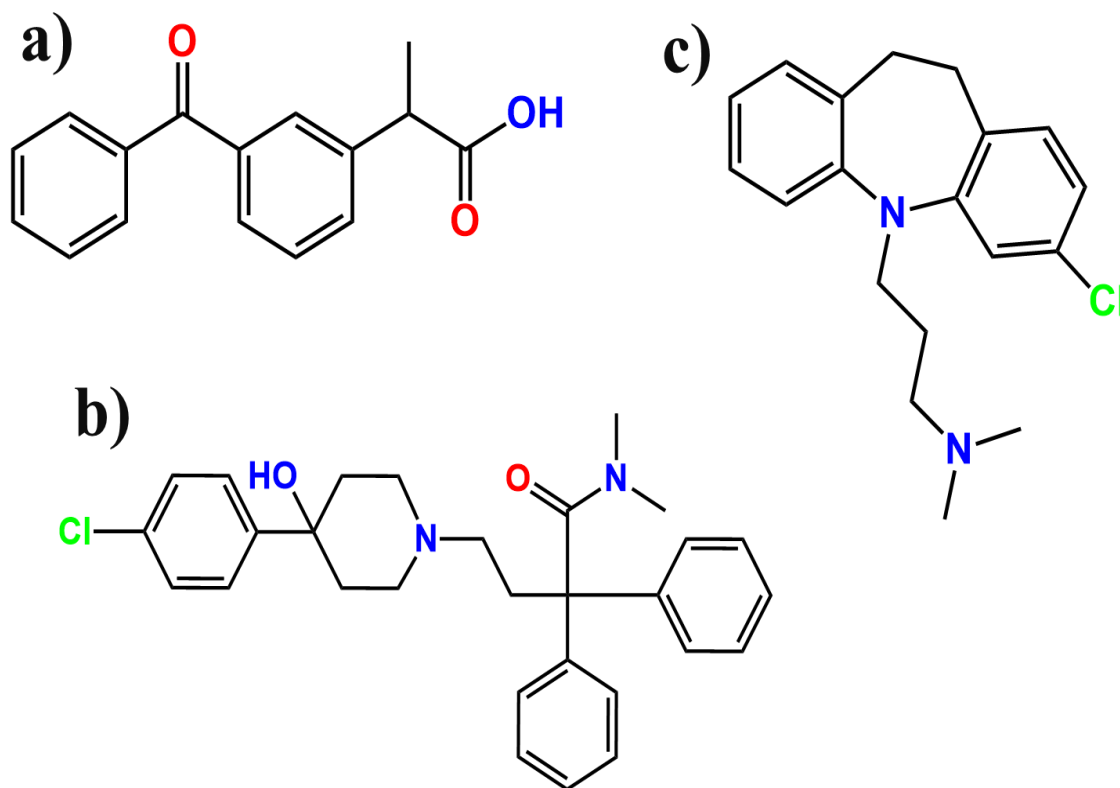


Figure 49: a) KETO b) LOP c) CLOM structures.

6.3.1 Characterization of the MIL sorbent and the intermediate compound

The characterization of MILs is of fundamental importance because their physical properties can be easily affected by impurities and structural changes [96], [194]. Therefore, various analytical methods are used to determine both their chemical and physical properties. Although it is difficult to quantify the content of impurities, the characterizations help to confirm the structure of MILs. A good example is the contamination of MIL with lithium chloride, since both ions do not appear in standard mass spectrometry, although their trace contamination does not have a major impact on elemental analysis. The most common contaminants or impurities in MILs can be categorized into water, unreacted starting materials, residual solvents, metals, and halides [87]. In this context, some of the characterization techniques used in this study such as Fourier transform infrared spectroscopy (FT-IR), zeta potential, magnetic property measurement systems (MPMS), proton nuclear magnetic resonance (^1H NMR), thermogravimetric analysis (TGA), scanning electron microscopy, energy dispersive X-ray analysis (SEM EDX) and Raman scattering spectroscopy can be summarized.

6.3.1.1 ^1H NMR spectra

The ^1H NMR spectra were recorded using a JEOL spectrometer (JNM-LA 500 MHz, JEOL USA Inc.). The ^1H NMR of both the starting material (oleylamine) (**Fig. 50**) and the quaternary intermediate [OA]Cl (**Fig. 51**) were performed to investigate the protonation of

the amine group in the starting compound after addition of HCl. The ^1H NMR spectra showed a downward in the chemical shift of the proton from 4.81 ppm to 5.40 ppm. This shift is due to the hydrogen bonding between the amine group of oleylamine and the hydrogen ion of HCl acid. It can also be deduced that the electronic structure of the long hydrophobic chain cation forms acidic carbons at the corresponding carbon numbers. No other peaks were observed, indicating the purity of the intermediate. The peak observed at about 7.2 is due to the deuterated standard solvent chloroform (CDCl_3).

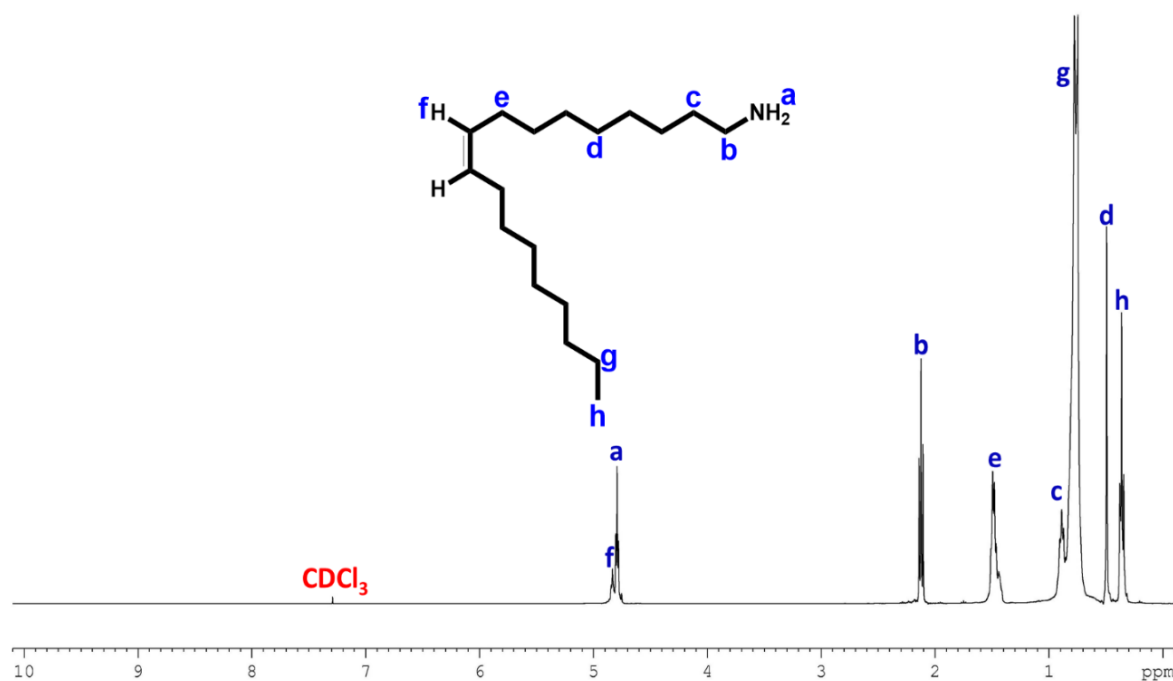


Figure 50: ^1H NMR of oleylamine

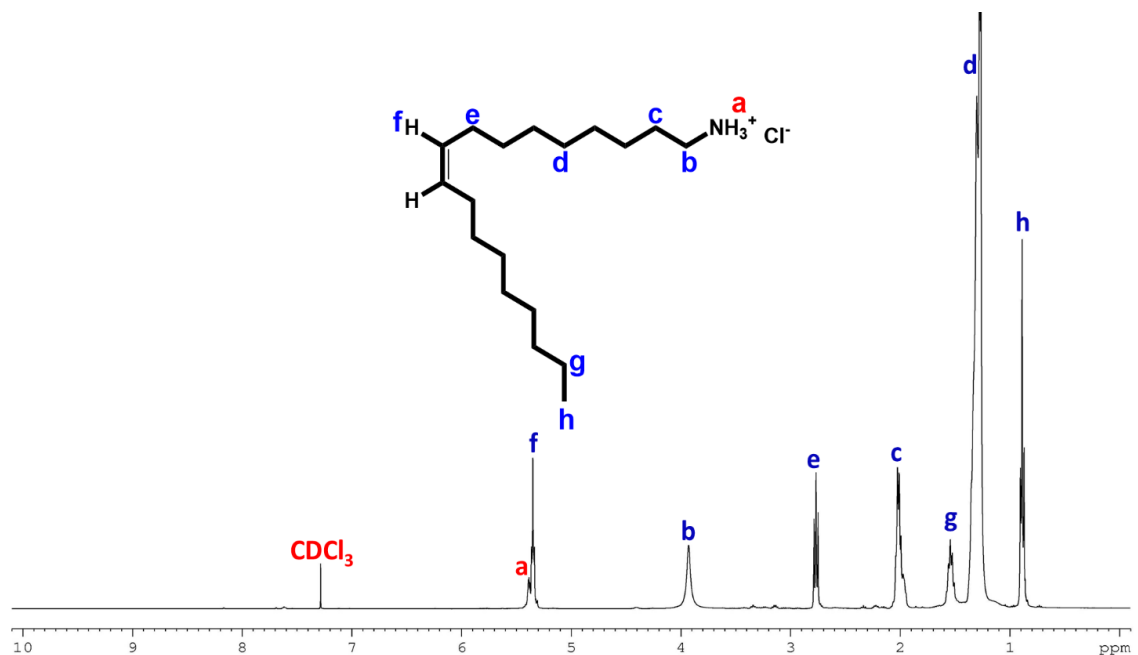


Figure 51: ^1H NMR of intermediate [OA]Cl

6.3.1.2 FT-IR spectra

To understand the functional groups of the sorbent MIL, FT-IR between 500 cm^{-1} to 4000 cm^{-1} was performed using the Smart iTR NICOLET iS10 model instrument from ThermoFisher scientific. The FTIR of the parent compound oleylamine, intermediate [OA]Cl and final product [OA]FeCl₄ was compared. Oleylamine shows sharp dominant peaks at about 2917.7 cm^{-1} and at about 2800 cm^{-1} , which are due to the asymmetric methyl stretching of CH₃ and CH₂, respectively (**Fig. 52a**). A peak at 1614.1 cm^{-1} is attributed to the combined motions of NH₂ shear vibration and N-H bending. The N-H shear vibration is seen at about 750 cm^{-1} and the N-H bending vibration is observed at 900 cm^{-1} . In

addition, N-H stretching vibrations were observed at 3392.2 cm^{-1} . Similar peaks were observed in the FT-IR spectrum of the intermediate (**Fig. 52b**), but a slight broadening was observed, which can be attributed to the addition of the proton. The FT-IR spectrum of the final complex (**Fig. 52c**) shows a broad band extending from 3500 cm^{-1} to 3300 cm^{-1} (circled) covering the NH_3 stretching region, which may be related to the hygroscopic behavior of the FeCl_4 bond.

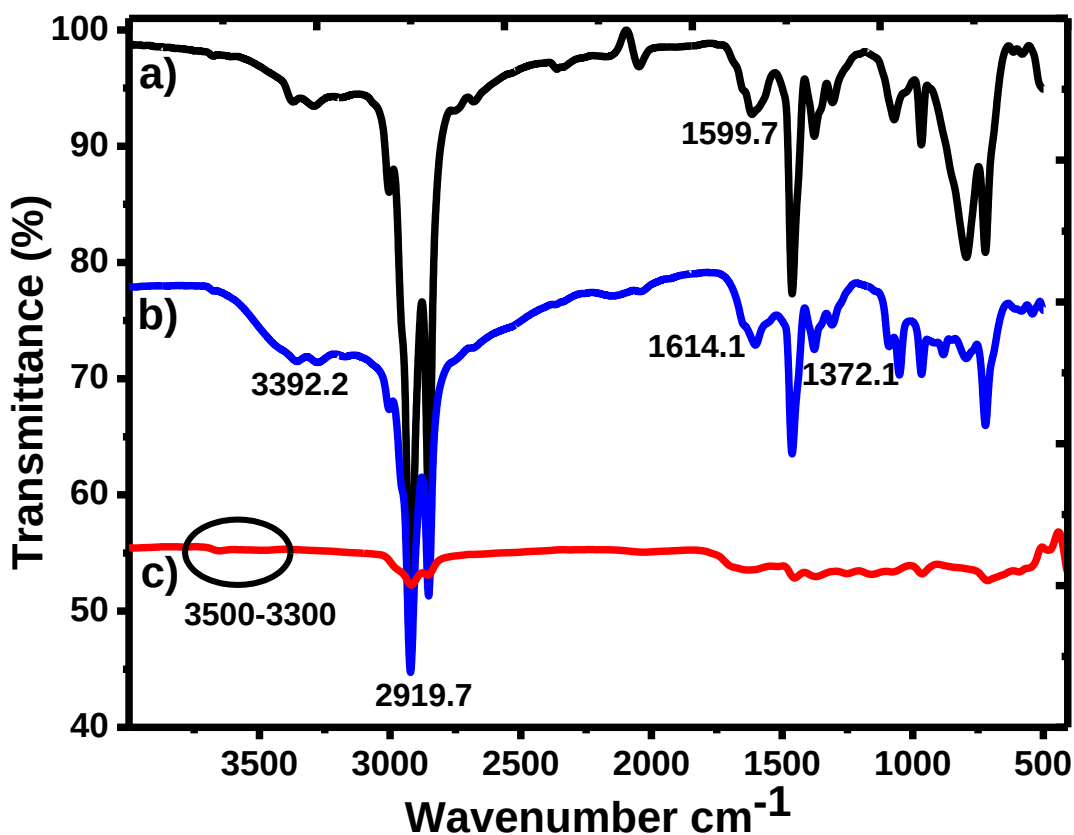


Figure 52: FT-IR spectra of a) oleylamine b) intermediate $[\text{OA}]\text{Cl}$ c) MIL $[\text{OA}]\text{FeCl}_4$

6.3.1.3 Raman spectroscopy

Raman scattering of functional groups MIL from 100 cm^{-1} to 1000 cm^{-1} was recorded with a laser excitation wavelength of 633 nm using the Raman spectroscope model LabRam. A dominant sharp broad peak is seen at 332.4 nm (**Fig. 53**), which is attributed to symmetric bond stretching vibrations originating from Fe-Cl of FeCl_4^- as reported elsewhere [96], [158]–[160].

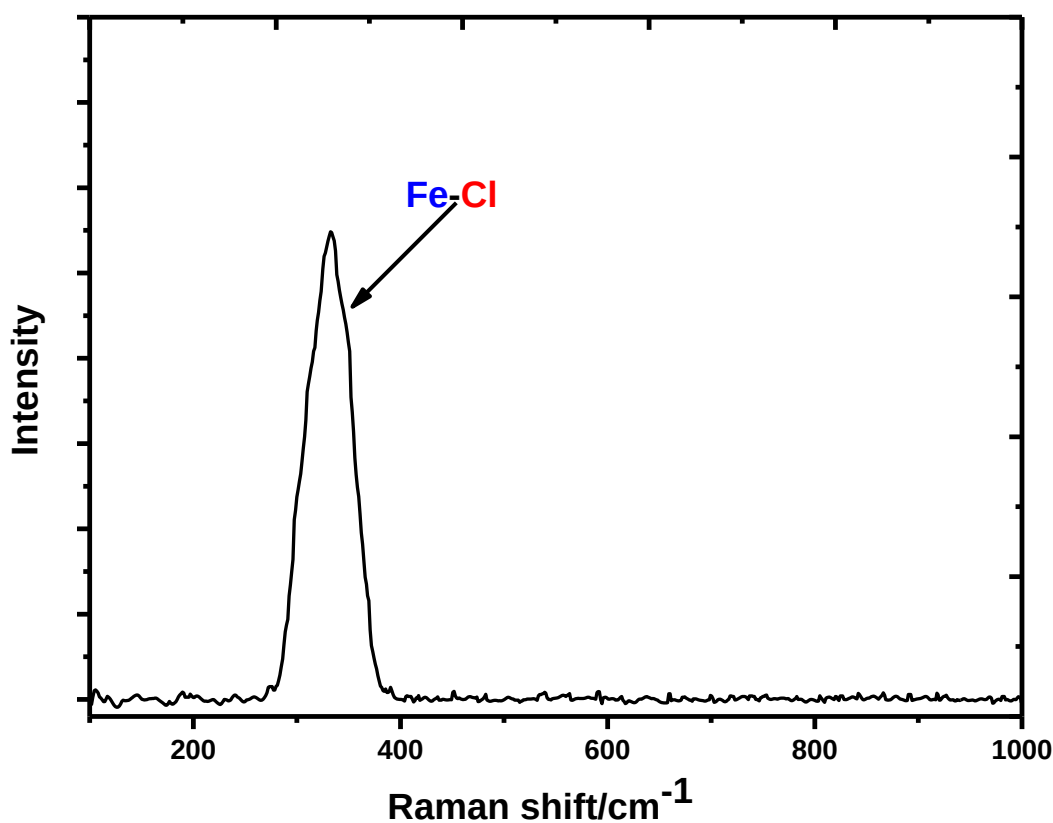


Figure 53: Raman spectra of $[\text{OA}]\text{FeCl}_4$

6.3.1.4 Scanning electron microscopy (SEM)

The morphology of the material was also studied and imaged using the JEOL JSM-6610LV model. Images acquired at the microlevel (**Fig. 54 a and b**) showed bright images due to the presence of highly conductive FeCl_4^- , most of which appears on the surface of the MIL. Moreover, EDX elemental analysis confirmed the formation of the compound in the complex. No agglomeration was observed in the micrograph; however, the particles appear to have irregular shapes and sizes.

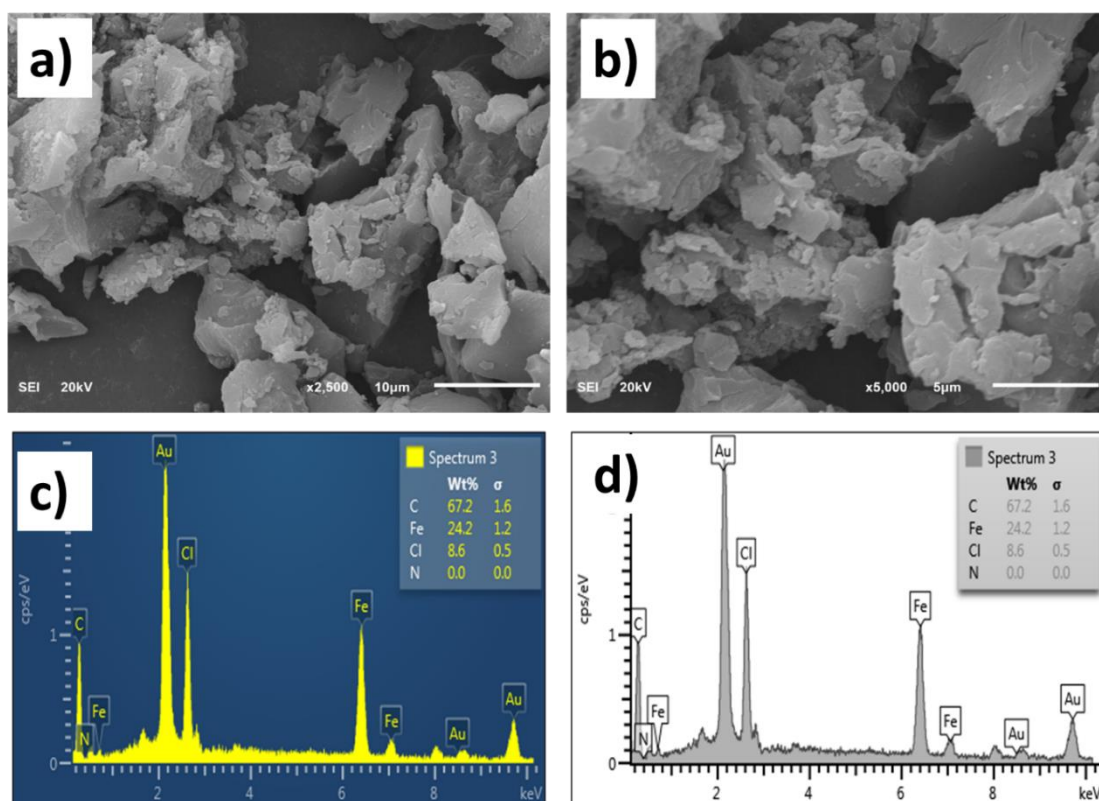


Figure 54: SEM image of a) 10 μm b) 5 μm, c) and d) respective elemental analysis in EDX images of $[\text{OA}]\text{FeCl}_4$

6.3.1.5 Thermogravimetric (TGA) analysis

Thermogravimetric (TGA) analysis of MIL was performed using thermogravimetric analyzer model SDT Q600. First, approximately 8.5 mg of the MIL in alumina pan is heated at high temperatures up to 900 °C at a rate of 10 °C per min under nitrogen flow and the decomposition pattern is recorded. As can be seen in **(Fig. 55a)**, there was no significant weight loss up to about 243.3 °C, and at 500 °C the weight loss was about 40%. The peak observed at about 58 °C results from the endothermic behavior of MIL due to its melting point. In general, the decomposition of the material starts by a nucleophilic attack from the anion part of the MIL to the cation part [162]. This finding confirms that the material has excellent thermal stability even at high temperatures.

6.3.1.6 Zeta potential

Zeta potential was evaluated using the model device Zeta Potential Analyzer Zeta PALS. Six pH values 2, 4, 6, 8, 10 and 12 were investigated by dispersing 10 mg of the MIL in 10 mL of double distilled water by sonication for 1 hour. The zeta potential is an important parameter to explain the stability of the particles. It is observed that the material has a larger zeta potential value of 15.9 mV, which indicates that the material is stabilized by electrostatic repulsion [195]. The MIL shows a positive charge at low pH and a negative charge at higher pH with an isoelectric point at about 3.5 **(Fig. 55b)**. The positive charge

may be attributed to the cationic part of the MIL, while the negative charge may be due to the presence of the anionic part FeCl_4^- .

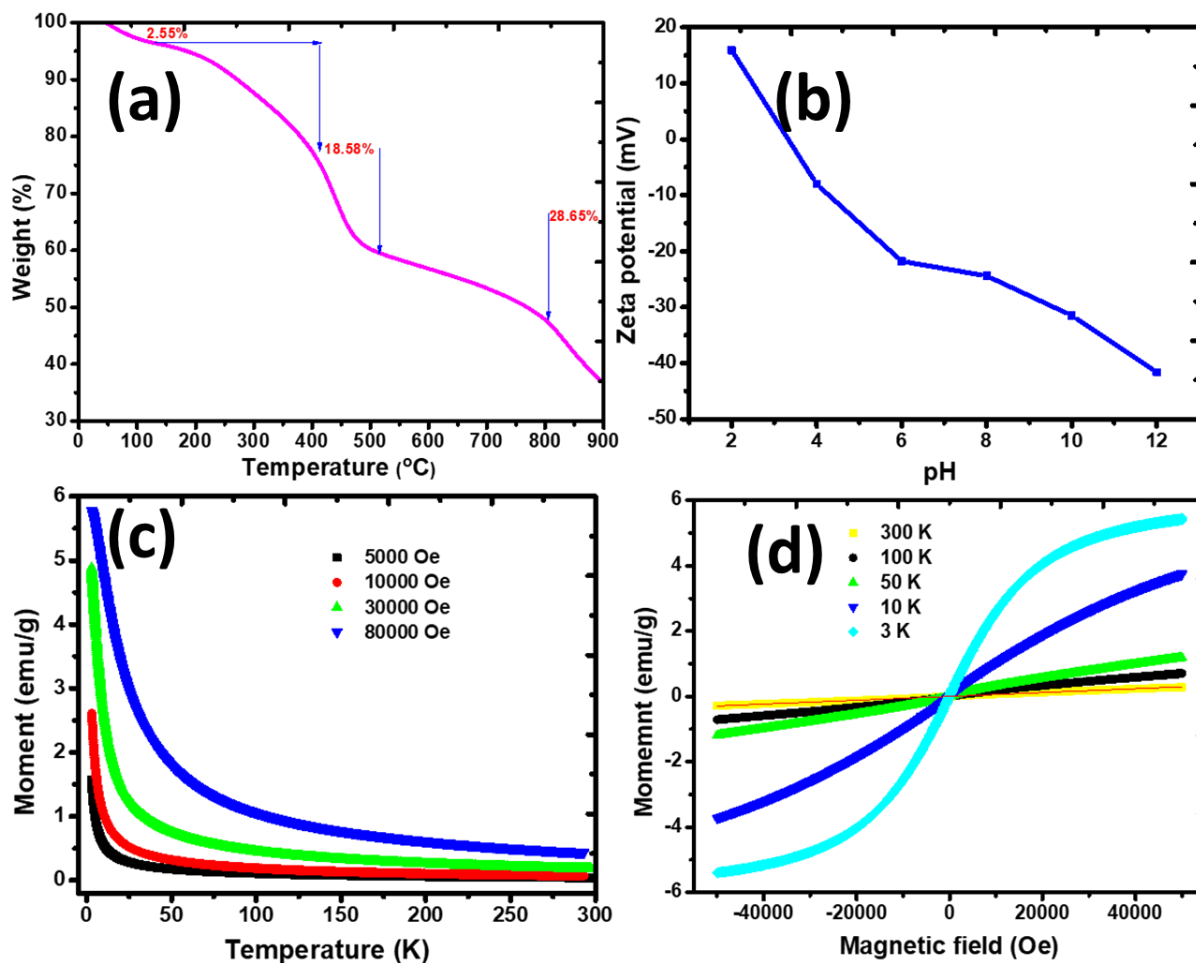


Figure 55: (a) TGA analysis curve of $[\text{OA}]\text{FeCl}_4$; (b) Zeta potential vs. pH of the $[\text{OA}]\text{FeCl}_4$; (c) Magnetization of $[\text{OA}]\text{FeCl}_4$ as a function of temperature under applied magnetic field at 5000 – 80,000 Oe and (d) Magnetization as a function of the applied magnetic field at 3–300 K temperature.

6.3.1.7 Magnetic property analysis

Magnetic property measurements were made using the instrument Physical Property Measurement System (PPMS), DaynaCool (Quantum Design, US). About 24.1 mg of the sample MIL was loaded to measure the magnetic susceptibility over a temperature range (0-300 K). Similarly, the magnetic field was varied from 5000-80000 Oe. It was found that the magnetic susceptibility decreases with increasing temperature from 0-300 K over all the magnetic fields studied (**Fig. 55c**). Moreover, the temperature dependence of magnetization was evaluated from 3-300 K and the relationship between temperature and magnetic moment is in perfect agreement with the law of Curie-Weiss (**Fig. 55d**). The result shows a similar trend and properties reported in the published literature for ferrous magnetic ionic liquids for all tested temperatures [96], [164]. Moreover, a linear relationship between the magnetization of MIL and the applied magnetic field at 300 K (room temperature) was obtained (**Fig. 55c**). The slope of the fitted line (red) shows that the magnetic susceptibility is 5.89, which is much higher than the reported MILs as shown in **Table 11**. This direct relationship between the magnetic moment and the magnetic field implies that the synthesized MIL is paramagnetic and that there is no strong coupling arising from the spin angular momentum of the cations.

Table 11: Comparison of Magnetic susceptibility of [OA]FeCl₄ with other reported MILs containing FeCl₄.

MIL	Temperature (K)	Magnetic susceptibility (emu/g)	Ref.
[P ₆₆₆₁₄]	300	4.29	[45]
[Bmim]	300	4.11	[196]
[C ₁₀ mim]	300	4.01	[197]
[Nbmim]	300	4.34	[196]
[PR ₄]	300	4.34	[197]
[OA]FeCl ₄	300	5.98	(This work)

6.3.2 Optimization of the extraction conditions

Various factors affecting extraction such as eluent, pH, eluent volume, desorption time, sorbent dosage, extraction time and salt concentration were optimized to study the reliability of the developed method. In all experiments, triplets were performed at ambient conditions.

6.3.2.1 Effect of sorbent amount

The effect of sorbent dosage was studied by varying the amount of sorbent from 10-50 mg. The sorbents were dispersed in the sample solution and all other parameters were kept constant. It was found that with increasing dosage the extraction efficiency was increased up to 40 mg. Further addition of sorbents did not significantly improve the extraction efficiency. This is generally expected as the addition of more sorbents results in more available active sites for adsorption of the analyte. However, addition of MIL beyond 40 mg of sorbent appears to saturate the system, resulting in maximum extraction. Therefore, 40 mg was considered to be the best dosage for the extraction of the three analytes where equilibrium was achieved showing excellent extraction efficiency.

6.3.2.2 Effect of sample pH

The pH is one of the most important parameters in extraction because it affects the shape of the analytes, changes the charge type, and influences the density of the sorbent surface [198]. To evaluate the effect of pH, the sample solution was adjusted from 2 to 9 and it was observed that the neutral pH was optimum for all analytes in this study (**Fig. 56a**). Moreover, the pKa values of CLOM, LOP and KETO were 9.4, 8.5 and 4.4, respectively, which is still above the isoelectric point [199]–[201]. The drugs are effectively extracted at neutral pH 7 by hydrophobic interaction due to the long carbon chains of the sorbent and the presence of benzene rings of the analytes. Generally, at lower pH, electrostatic

repulsion occurs between the positive charge of the analyte and the cationic part of the MIL, and when the pH is increased above 7, the efficiency decreases due to the lower cationic interaction of the π -bond. However, mainly the hydrophobic interaction between the MIL and the analytes is responsible for the successful extraction of the compounds. Therefore, a neutral pH of 7 is best for the effective extraction of the analytes. It was found that the performance for all analytes decreases when the pH increases to 9. This is due to reduced molecular interaction as most of the analytes are in their ionic form in the aqueous medium.

6.3.2.3 Effect of salt concentration

The salt concentration of the sample solution was evaluated using sodium chloride salt and the recovery was observed at different salt concentrations such as 0%, 5%, 10%, 20% and 30% w/v (**Fig. 56b**). Introduction of salt in the sample solution leads to increase in ionic strength and hence lower solubility of the drugs which improves their extraction. In this study, it is observed that as the salt concentration increases, the recovery is improved but the highest peak area was obtained at 20% w/v and further studies were carried out at 20% w/v.

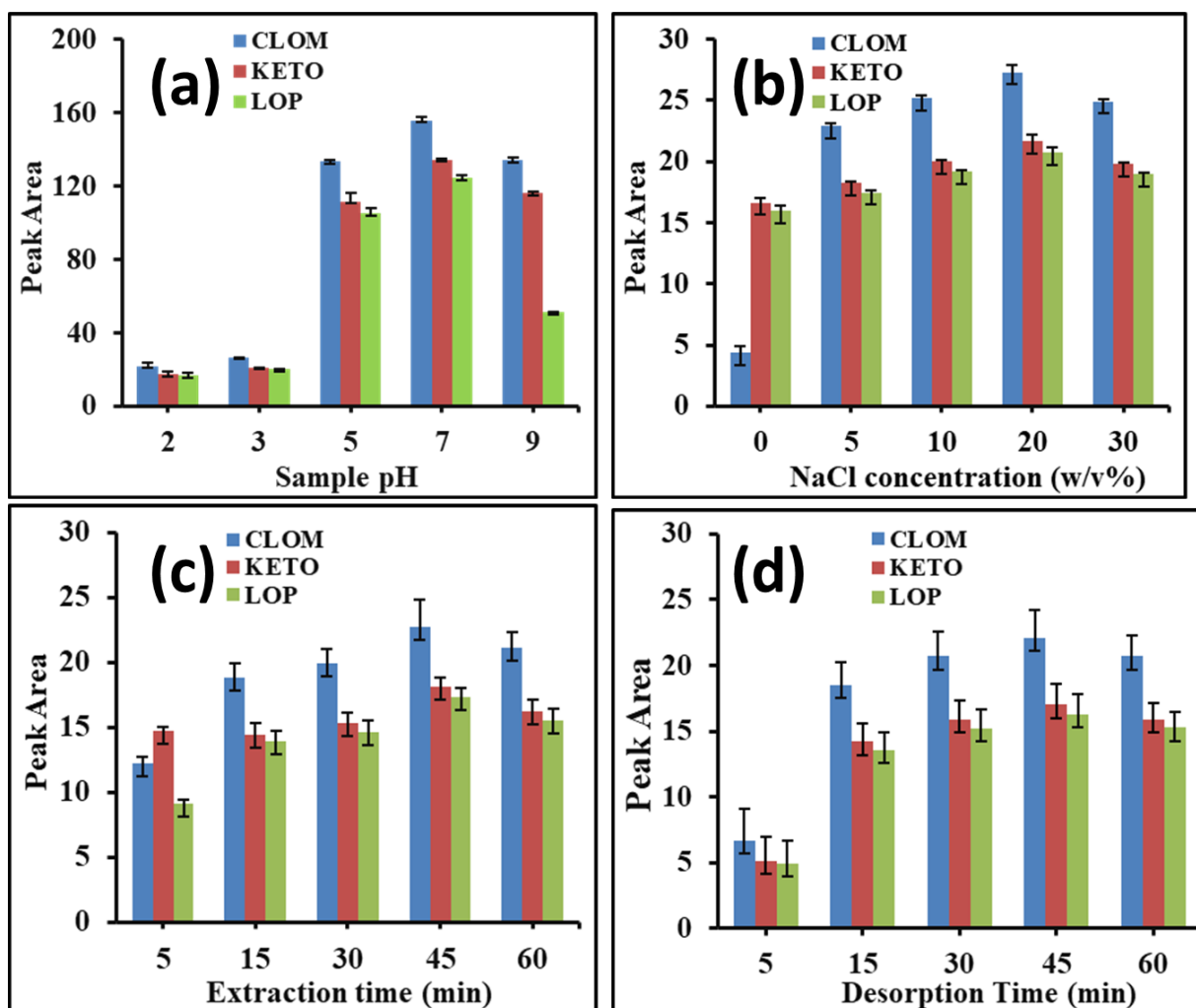


Figure 56: Effect of a) sample pH, b) NaCl concentration, c) extraction time and d) desorption time on the extraction performance of the drugs on [OA]FeCl₄ sorbent. All optimizations were performed in a 10 mL deionized water sample solution, spiked with 300 µg/L of the analyte.

6.3.2.4 Effect of extraction and desorption time

Extraction time affects both analysis speed and extraction performance. To achieve better sensitivity, high speed, and precision, it is important to determine the best extraction time that establishes the right balance between the sorbent and the sample solution. Therefore, the time required for the sorbent to fully adsorb the analytes is critical to the extraction process. To understand the efficient contact time, different extraction times ranging from 5 to 60 min were performed (**Fig. 56c**). It can be observed that the maximum analytical signal was obtained in 45 min, which can be related to the large surface area of the sorbent and the efficient contact between the sorbent and the analytes in the solution. In addition, the time for the elution of the analytes from the sorbent in the same time range was investigated in the ultrasonic treatment and it was found that 45 min was also sufficient to completely desorb the analytes from the sorbent (**Fig. 56d**). The negligible decrease observed when the extraction time was increased to 60 min may be attributed to the evaporation of the solvent and re-extraction of the compounds. A similar trend was reported when ketoprofen and other NSAIDS were extracted in water samples [202].

6.3.2.5 Desorption solvent and its volume

It has been reported that micelle-structured sorbents are easily disturbed by organic solvents, leading to the desorption of analytes after extraction. Therefore, in this study, we investigated the desorption of analytes in different water miscible solvents such as ethanol,

methanol, acetone, and acetonitrile. It was found that acetonitrile showed maximum recovery for almost all analytes. However, LOP showed slightly better recovery in ethanol and methanol but with negligible difference as compared to acetonitrile (**Fig. 57a**). Based on these results, acetonitrile was chosen as the best desorption solvent and a similar result was reported in the literature [203]–[205]. Then, the optimal acetonitrile desorption volume was investigated by varying it from 100 μL to 500 μL . The result showed that 400 μL was sufficient to completely recover the analytes from the sorbent and elute (**Fig. 57b**). Therefore, 400 μL of acetonitrile was used as the eluent for the rest of the study.

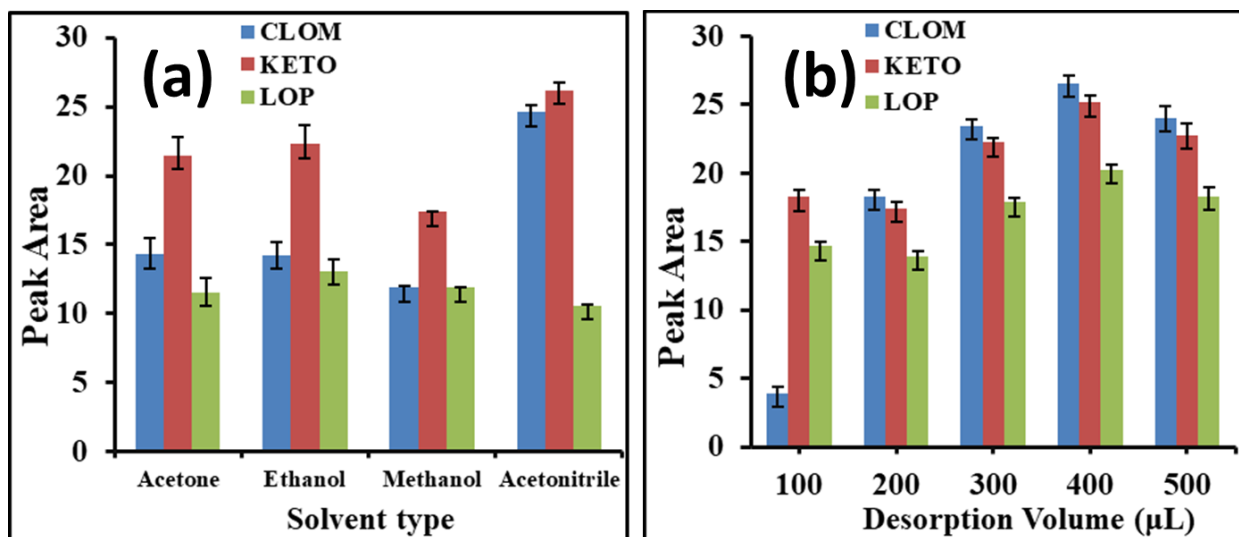


Figure 57: Effect of a) solvent type, and b) desorption volume. Optimization was performed in a 10 mL deionized water sample solution, spiked with 300 $\mu\text{g/L}$ of the analyte.

6.3.3 Figures of merit of MIL-D- μ -SPE method

The analytical performance of the developed extraction method was tested using standard solutions of the three analytes under the optimized conditions of **Table 12**. The calibration curve of the analytes was constructed in a concentration range from 1 to 750 $\mu\text{g/L}$ in 10 mL sample solution in double distilled water. The regression coefficient (R^2) was determined to be 0.9974, 0.9967, and 0.9931 for CLOM, KETO, and LOP, respectively. The detection limit (LOD) was calculated as three times the ratio of the standard deviation of the signal from the blank divided by the slope of the calibration curve and was 2.3 $\mu\text{g/L}$, 2.4 $\mu\text{g/L}$, and 2.9 $\mu\text{g/L}$ for CLOM, KETO, and LOP, respectively. The relative standard deviation (RSD%) was calculated as 3.1, 2.6, and 3.0 ($n=3$) for interday and 2.7, 3.0, and 3.7 ($n=3$) for intraday for CLOM, KETO, and LOP, respectively. The enrichment factor (EF) was defined as the ratio of the sample volume (10 mL) to the final desorption volume (400 μL), which is 25 for all analytes. The lowest in the linear dynamic range was selected as the LOQ value (1 $\mu\text{g/L}$) for all.

6.3.4 Real samples analysis

To investigate the applicability and accuracy of the proposed method, a complex matrix of human urine and wastewater samples was performed. The samples were first spiked with analyte concentrations of 1, 250 and 750 $\mu\text{g/L}$ under the optimized conditions. The results are shown in **Table 13**, where 3 replicate analysis of the complex samples showed perfect

agreement with the spiked amount. Furthermore, a comparison of the chromatogram of 250 µg/L spiked and unspiked wastewater and human urine samples is shown in **(Fig. 58)**. The results obtained show similar values to those obtained with double distilled water. The samples were also not contaminated as no new peaks were detected in the analyte range of the non-spiked samples.

Table 12: Analytical figures of merit of the proposed D-µSPE-HPLC

Analytical parameters	Obtained values		
	CLOM	KETO	LOP
Correlation coefficients (r^2)	0.9974	0.9967	0.9931
Limit of detection (LOD) µg/L	2.3	2.4	2.9
Intra-day RSD, %	2.7	3.0	3.7
Inter-day RSD, %	3.1	2.6	3.0
Average recovery, %	96.0	93.9	89.7
LDR, µg/L	1-750	1-750	1-750

Table 13: Determination of CLOM, KETO, and LOP in wastewater and human urine samples.

Analyte	Sample type	Added, µg/L	Found, µg/L	Recovery %	RSD, %
Clomipramine	Wastewater	1	0.874	87.4	4.1
		250	248.1	99.2	2.7
		750	727.3	99.6	2.7
	Human urine	1	0.855	85.5	2.4
		250	246.6	98.6	2.1
		750	726.9	96.7	2.4
Ketoprofen	Wastewater	1	0.930	93.0	6.0
		250	231.0	92.4	2.6
		750	753.0	100.4	4.9
	Human urine	1	0.910	91.0	2.6
		250	231.8	92.7	2.1
		750	644.4	85.9	2.4
Loperamide	Wastewater	1	0.960	96.0	3.9
		250	245.0	98.0	2.9
		750	758.0	101	2.8
	Human urine	1	0.880	88.0	3.6
		250	254.0	101.6	2.1
		750	757.0	100.9	2.4

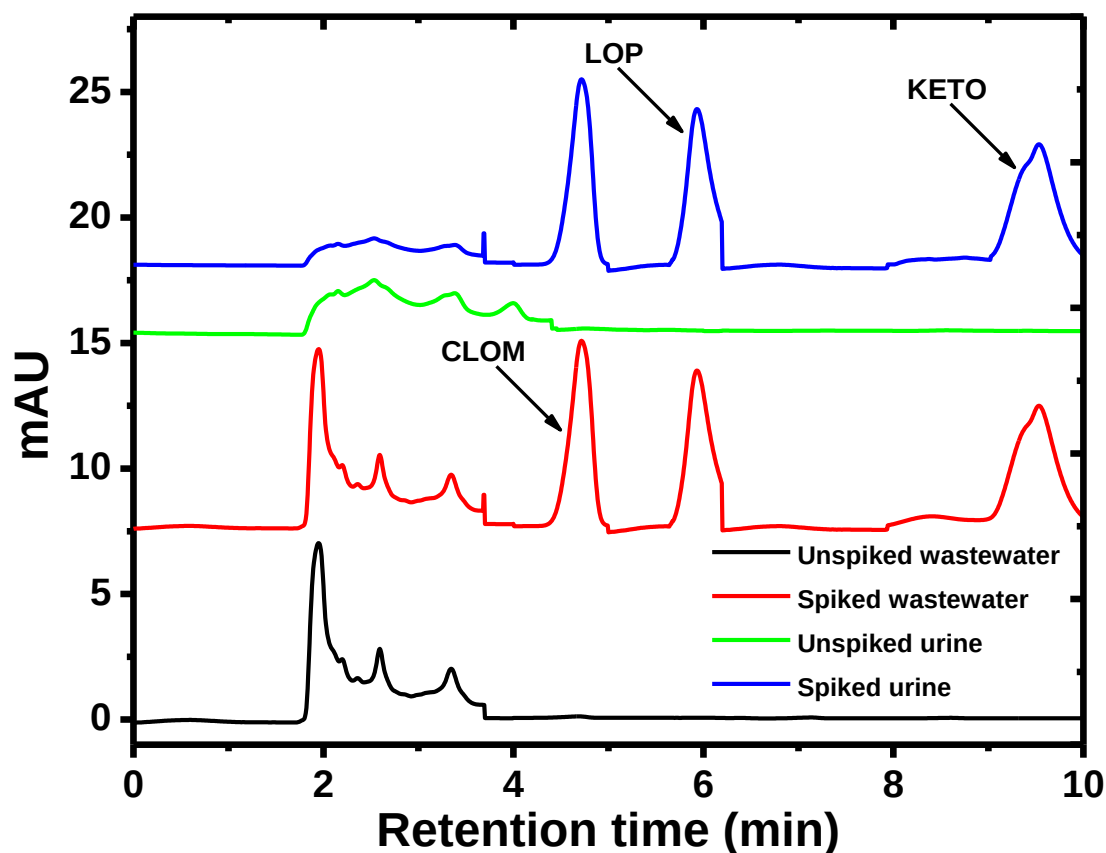


Figure 58: HPLC-DAD chromatograms 250 $\mu\text{g/L}$ of urine and wastewater samples after optimization. Peaks at 4.7 min, 5.9 min, and 9.5 min are corresponding to CLOM, LOP, and KETO, respectively.

6.3.5 Comparison of the method with published literature

The analytical method is compared with other published work on the quantification and determination of CLOM, LOP and KETO, as shown in **Table 14**. The method exhibits low detection for simultaneous preconcentration of the analytes and shows high sensitivity comparable to or better than the reported chromatographic methods. Moreover, the method

is cost effective as three different categories of drugs are determined simultaneously in less than 10 min retention time. In addition, the method has a much better RSD % than almost all reported work with comparable LODs and linearity.

6.3.6 Recycling and reuse of the sorbent.

The reusability of MIL was also investigated. Neither physical destruction nor significant loss of the sorbent was observed, but a negligible amount was lost during centrifugation and washing. Before reuse, the sorbent is first washed thoroughly with double distilled water and checked for residual analytes. Prior to the next extraction application, the sorbent is oven dried overnight at approximately 45 °C. The material was tested for at least three consecutive cycles, and it was found that the extraction efficiency did not change significantly, with performance still above 93%. The reusability of the MIL makes the extraction method more attractive and environmentally friendly.

Table 14: Comparison of present method with other methods for CLOM, LOP, and KETO preconcentration and extraction.

Analyte	Method	Sample matrix	Linearity	LOD	Extraction time (min)	RSD (%)	Ref
CLOM	UA-DM- μ -SPE on amino-functionalized Fe_3O_4	Human plasma	0.017–0.70 mg/L	0.005 mg/L	15	3.5	[206]
CLOM	Surfactant-coated Fe_3O_4 @decanoic acid nanoparticles	Human urine	5–5000 $\mu\text{g/L}$	2.0–4.0 $\mu\text{g/L}$	20	5.5	[207]
KETO	D- μ -SPE-HLLME- HPLC-UV	Water	0.1–50 $\mu\text{g/L}$	0.05 $\mu\text{g/L}$	5	9.3	[208]
KETO	Fe_3O_4 -sporopollenin-cyanopropyltriethoxysilane D- μ -SPE HPLC	Water	1.0–1000 $\mu\text{g/L}$	0.21–0.51 $\mu\text{g/L}$	5	-	[202]
LOP	Supported liquid membrane (SLM)-CE	Urine	5–40 $\mu\text{g/mL}$	1000 $\mu\text{g/L}$	30	13.4	[209]
	MIL (Z)-octadec-9-en-1-aminium tetrachloroferrate (III)	Wastewater & Human urine	1–750 $\mu\text{g/L}$	2.3 $\mu\text{g/L}$ (CLOM) 2.4 $\mu\text{g/L}$ (KETO) 2.9 $\mu\text{g/L}$ (LOP)	45	2.7 (CLOM) 3.0 (KETO) 3.7 (LOP)	This work

6.4 Conclusion

In this study, magnetic ionic liquid (Z)-octadec-9-en-1-aminium tetrachloroferrate (III) was successfully synthesized and characterized as a sorbent for dispersive micro solid phase extraction and quantification of three different categories of drugs clomipramine (CLOM), ketoprofen (KETO) and loperamide (LOP) in wastewater and human urine samples as a model for an analytical problem. The proposed method has the advantage of simple sorbent preparation, simultaneous extraction, and quantification of three different drug classes, cost effective, and reliable recovery with lower organic solvent consumption. The performance can be attributed to the hydrophobicity and electrostatic interaction of analytes and sorbent, which facilitate extraction in sample solution and desorption in organic solvent. The proposed method showed better and comparable results with the existing methods such as linearity of 1-750 $\mu\text{g/L}$, LOD values of 2.3 - 2.9 $\mu\text{g/L}$ and RSD of 2.7 - 3.7%. The proposed method shows a new direction in research where simple MILs can be used as efficient sorbents in $\mu\text{-SPE}$ without any modification for simultaneous pre-concentration of different types of drugs. Moreover, the method is environmentally friendly as the sorbent can be reused several times.

CHAPTER 7

Removal of methylene blue and rose bengal dyes from aqueous solutions using 1-naphthylammonium tetrachloroferrate (III)³

7.1 Introduction

Dyes are environmental pollutants in an aqueous medium, and recently over 9000 different types of dyes have been included in the Dye Index. Many industries use dyes; however, textile processing industry is the major user as the market demands attractive fabric dyes [3]. If not handled properly, dyes can have adverse health effects on flora and fauna in the aquatic environment. Various techniques have been used for the removal of dyes from aqueous media. The biological treatment process is widely used, but it is time consuming and some of the microorganisms can be hazardous if not handled properly. Due to the complex chemical structure of dyes which is chromogenic-chromatographic makes them difficult in water treatment plants [210], [211], besides most of the dyes undergo a slow biodegradation process and remain in the environment for a longer time.

Some of the other techniques include adsorption [69], [70], electrocoagulation [71], reverse osmosis [72], electrochemical oxidation [73], ion exchange [74], Fenton oxidation [75] and ozonation [76]. Among these techniques, adsorption is considered as an effective method for dye removal, especially considering the cost and availability of adsorbents. For

³ This chapter has been published in journal of molecular liquids.

example, activated carbon is commercially available and used as adsorbent. However, the high cost associated with it is a major drawback [77]. Also, the commonly used modified materials have shown to be efficient but can be toxic, especially when epichlorohydrin and glutaraldehyde are used as crosslinkers [212]. In addition, metal organic frameworks (MOFs) are emerging adsorbents [213]. Several research works have been devoted to improve the design of MOFs for such applications in recent years. However, MOFs cannot accommodate large molecules due to their small pores, and they also have a slow diffusion process. Biosorption and biomass are similarly attractive, but sluggish adsorption rates, pH dependence, and clogging problems are major challenges [214].

Nevertheless, researchers are focusing on developing efficient, cost-effective, and environmentally friendly adsorbents for water treatment. Ionic liquids (ILs) have recently gained interest in chemical and biological analysis and contaminant removal applications [25]. ILs are stable, less volatile and can be easily modified. Several research works have shown ILs as potential adsorbents for the removal of dyes [20]–[25].

Therefore, in this work, a IL (1-naphthylammonium tetrachloroferrate (III) ($[1\text{-NA}]^+[\text{FeCl}_4]^-$) was used for the adsorptive removal of MB and RB dyes in an aqueous medium. RB is a xanthene dye and is widely used in the photochemical industry and in the manufacture of textiles. This dye is also used in some treatments such as psoriasis. In high concentrations, it can be dangerous and cause skin irritation, blisters, and pain [215]. MB has many applications in pesticides, paints, and textiles and is highly toxic and difficult to biodegrade due to the aromatic rings in its structure [216]. Therefore, the benzene rings in the structure of 1-naphthylammonium tetrachloroferrate (III) can promote π - π bonding and

hydrophobic interactions with dyes. The ionic nature of the adsorbent may also promote electrostatic interactions with the selected ionic dyes. These interactions were also confirmed by DFT calculations, which were in agreement with the experimental data.

7.2 Materials and methods

7.2.1 Materials

All chemicals and reagents were used as received. Starting material 1-naphthylamine was obtained from Fluka AG, MB, and RB dyes of 99% purity were purchased from Merck and Sigma Aldrich, respectively. Dichloromethane (DCM) and HPLC grade methanol, hydrochloric acid (HCl), sodium hydroxide (NaOH) pellets, iron (III) chloride (FeCl_3) and deuterated chloroform (CDCl_3) were also obtained from Sigma Aldrich.

7.2.2 Preparation of the ionic liquid

For the synthesis of IL a previously known method was adopted with some modifications [153]. Essentially, the synthesis procedure involved several main steps (**Fig. 59**). In the first step, 1 g of 1-naphthylamine was completely dissolved in DCM and water (1:1 v/v, 5mL each) with an equimolar amount of HCl and stirred constantly at room temperature for about 4 hours to form an intermediate naphthalene-1-aminium chloride ($[\text{1-NA}]^+[\text{Cl}]^-$). The mixture was then allowed to stand for 1 hour to separate into two layers, with the water layer removed by decantation and DCM over a temperature-controlled water bath,

followed by washing to remove excess acid. The ionic liquid 1-naphthylammonium tetrachloroferrate (III) was prepared by mixing equimolar amounts of naphthalene-1-aminium chloride and FeCl_3 in methanol with vigorous stirring overnight. The methanol was then removed using temperature-controlled water bath and the resulting product was washed several times with deionized water and centrifuged to remove all unreacted FeCl_3 . Finally, the product was air dried to give a sticky dark brown solid. **(Fig. 59 and 61)** show detailed steps and plausible mechanisms involved in the synthesis. The lone pairs of 1-naphthylamine were protonated by HCl due to an acid-base reaction, forming a quaternary naphthalene-1-aminium chloride intermediate, which was followed by the uptake of the chloride ion by FeCl_3 , resulting in the product 1-naphthylammonium tetrachloroferrate (III) (IL). **(Fig. 60a)**, 1-Naphthylammonium tetrachloroferrate (III) (IL) **(Fig. 60b)**, Rose bengal (RB) and **(Fig. 60c)**, Methylene blue (MB) structures are shown.

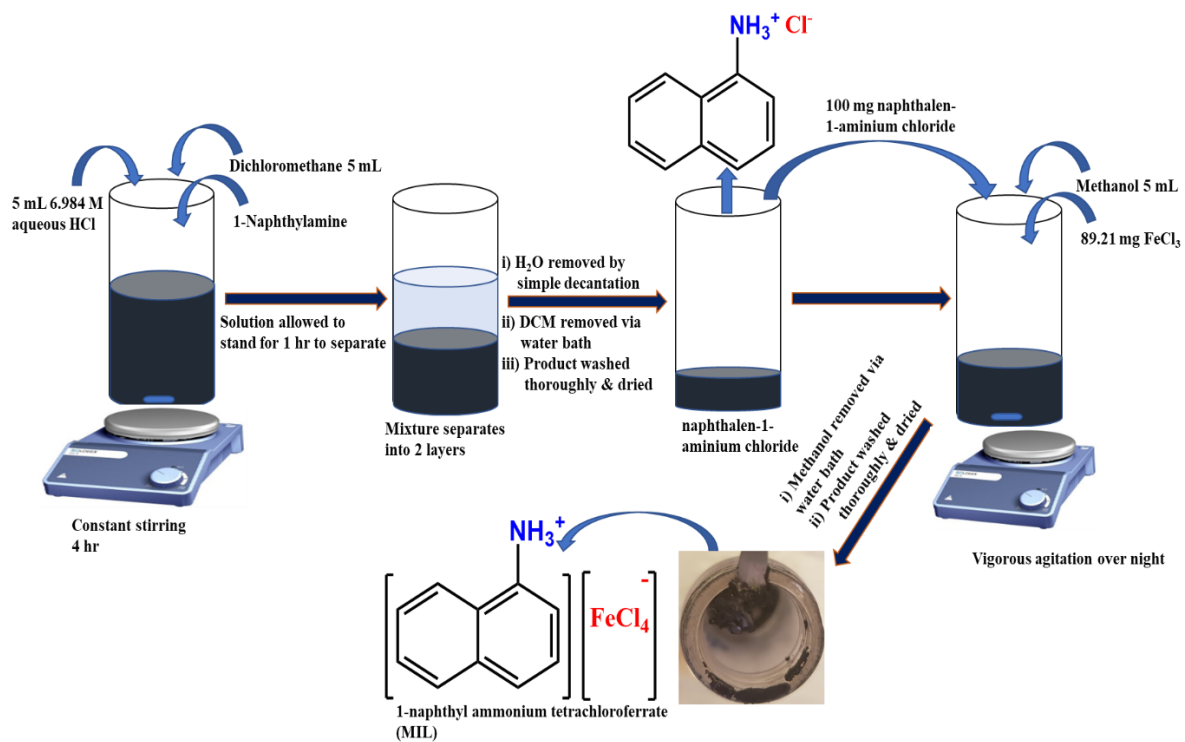


Figure 59: Synthetic scheme of 1-naphthylammonium tetrachloroferrate (III) (IL).

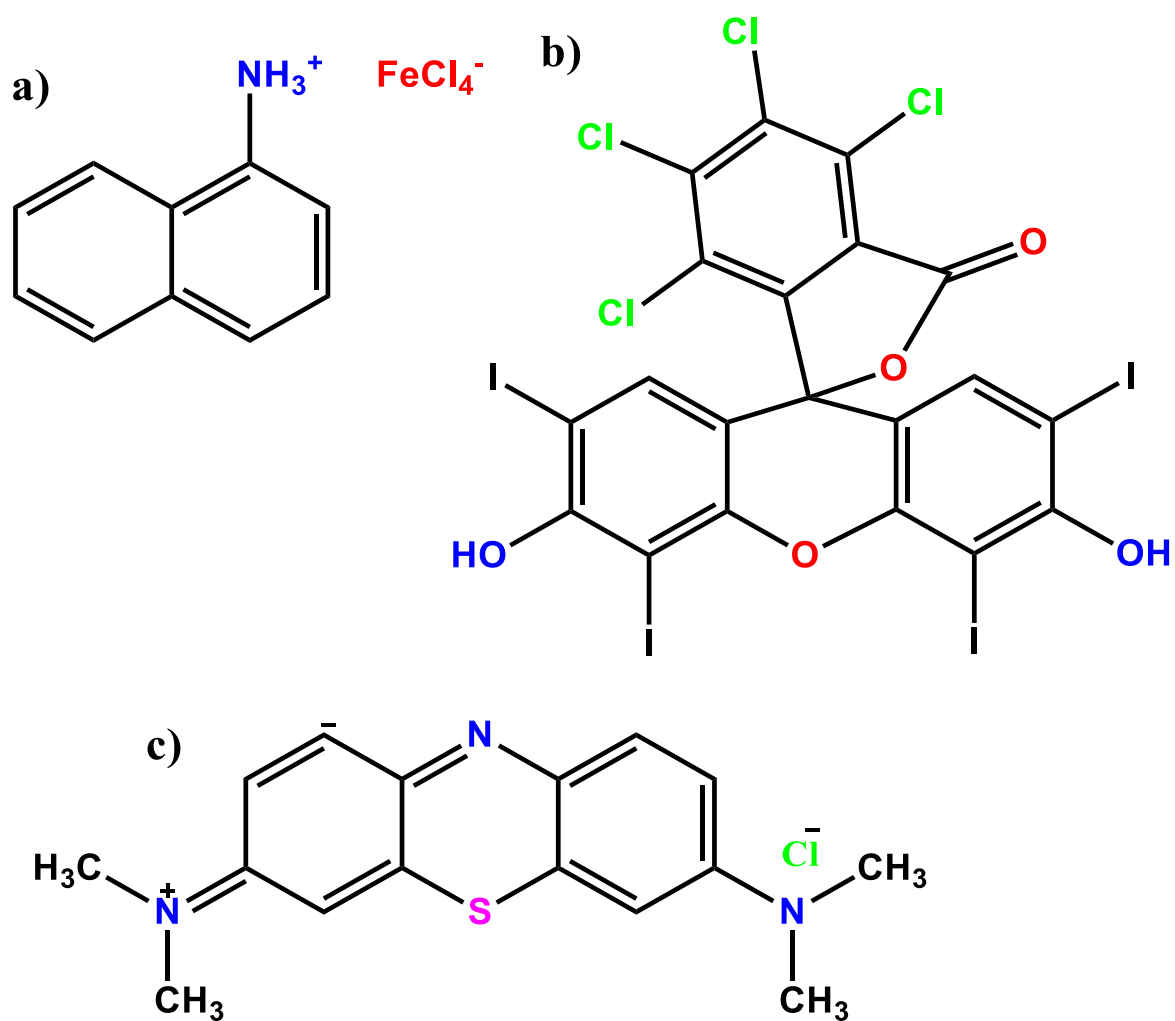


Figure 60: Structures of important and target compounds a) 1-naphthyl ammonium tetrachloroferrate (III) (IL) b) Rose Bengal (RB) c) Methylene Blue (MB)

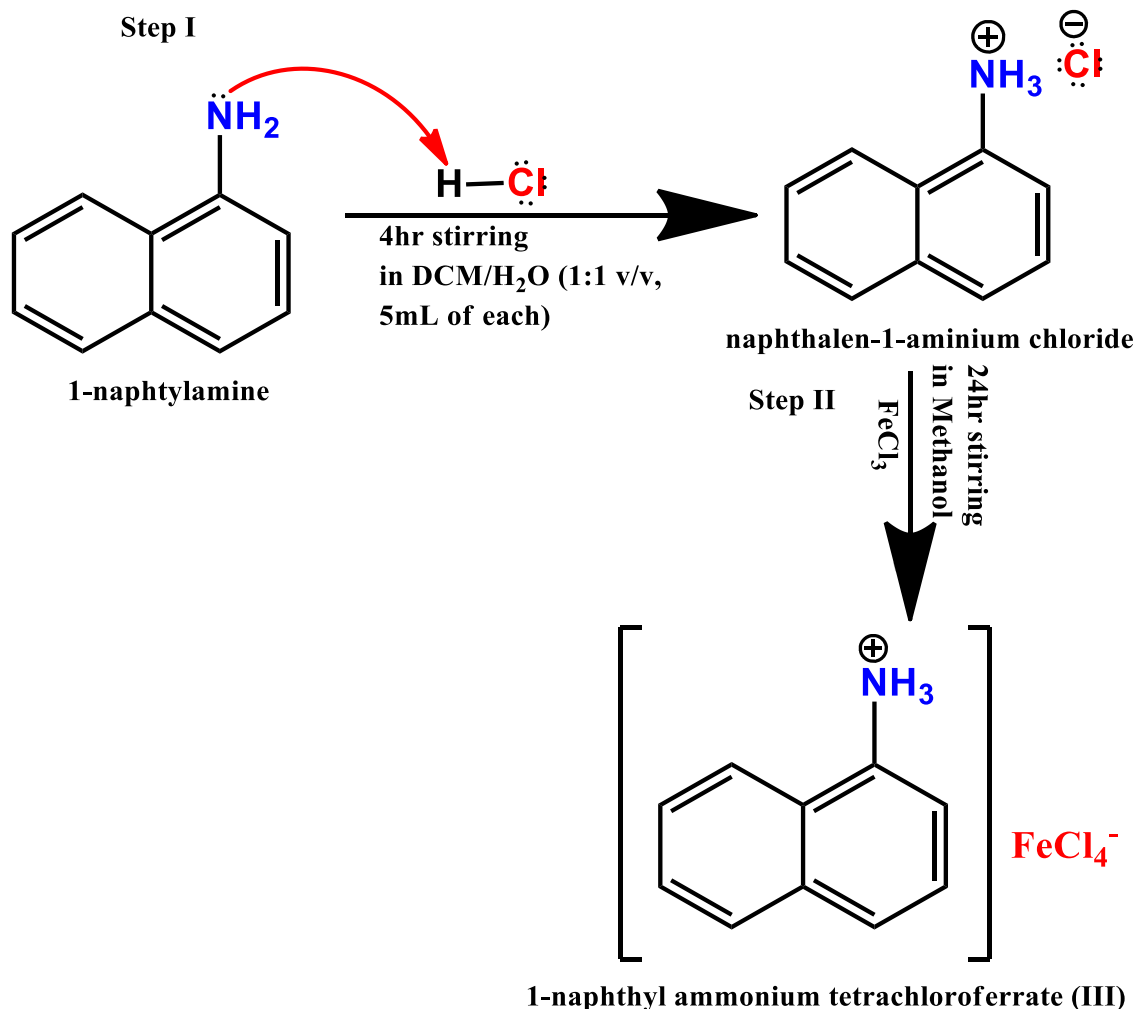


Figure 61: Mechanism of 1-naphthyl ammonium tetrachloroferrate (III) (IL) synthesis.

7.2.3 Adsorption experiments

All adsorption experiments were performed at room temperature in the laboratory with Lab Companion SK-600 Benchtop Shaker using 125 mL Erlenmeyer glass flasks containing 10 to 50 mL of sample solution with the desired concentrations of dyes, adjusted pH, IL dosage and contact time. The pH of the solution was adjusted from 3 to 11 using 0.1 M

HCl and 0.1 M NaOH solutions. The experiments were carried out in duplicates in low light environment and the adsorbent was recovered from the solution by centrifugation at 7500 rpm for 5 min.

Dye concentrations were measured using a UV-Vis spectrophotometer (Genesys 10S Thermo Fisher Scientific, USA) at a wavelength of 665 nm for MB and 550 nm for RB. The adsorption experiment was performed by adding known amounts of 1-naphthylammonium tetrachloroferrate (III) (IL) to the 10 mL solution of the dyes with concentrations ranging from 5 to 400 mg/L. To understand the effect of pH on the adsorption of the dyes, the pH of the solution was varied from 3 to 11 with an initial concentration of 40 mg/L and an IL dosage range of 5 to 60 mg.

Equation 3 was used to calculate the adsorption capacity. Q_e denotes the adsorption capacity, V is the volume of dye solution in liters, C_i is the initial concentration, while C_e is the equilibrium concentration of dyes in mg/L and m is the amount of adsorbent used in grams.

$$Q_e = \frac{V(C_i - C_e)}{m} \quad (3)$$

7.2.4 DFT procedure

Structural units of the IL and the isolated dye molecules, MB, and RB, as well as the IL-dye complexes were optimized using density functional theory (DFT) on the [217], [218] hybrid functional, B3LYP. The 6-31G* basis set was used for C, H, N, O, S and Cl atoms, while the lanl2dz basis set was chosen for Fe and I atoms. The 6-31G* basis set was chosen for the nonmetals because it provides the best estimate of solvation energies when using an implicit solvent model compared to higher basis sets and often provides data in good agreement with experimental results at a reasonable cost [219], [220]. Full geometry optimizations have been performed up to the minima without imposing symmetry constraints on the potential energy surface. Tomasi's polarized continuum model-self-consistent reaction field (PCM-SCRF) was used for simulations in aqueous media and water was chosen as the solvent [221]. Using the DFT-Koopman theorem, which relates the ionization energy, I.E, and electron affinity, E.A, to the energies of the highest occupied molecular orbital, EHOMO, and the lowest unoccupied molecular orbital, ELUMO [222], quantum chemical reactivity descriptors were estimated, as shown in **Table 15**.

Table 15: Quantum chemical reactivity descriptors and their definitions

Descriptor	Symbol	Definition
Ionization energy	I.E	- EHOMO
Electron affinity	E.A	- ELUMO
Global hardness	H	$\frac{1}{2}(I.E - E.A)$
Electronegativity	X	$\frac{1}{2}(I.E + E.A)$
Electrophilicity index	Ω	$\frac{\mu^2}{2\eta}$; where $\mu = -\chi$

The adsorption of the dye molecules by the ionic liquid in both acidic and basic media was simulated at the molecular level according to the model reported elsewhere [219]. According to the model, the interaction of the dye molecules and the IL can be considered local at the molecular level. Therefore, the quantum chemical studies can be limited to the calculation of the adsorption energies between the IL and the dye molecules. The adsorption energies were calculated according to **Equation 4**:

$$E_{ads} = E_{IL/dye} - (E_{IL} + E_{dye}) \quad (4)$$

Where, $E_{IL/dye}$, E_{IL} and E_{dye} represent the free energies of the IL-dyes complexes, the isolated IL, and the isolated dye molecules, respectively. All calculations were accomplished on the Gaussian 09 software suite [223].

7.3 Results and discussion

7.3.1 Characterization of 1-naphthyl ammonium tetrachloroferrate (III) IL

Various characterization techniques were performed on the material IL to understand the surface morphology, structural bonding, thermal stability, and other physical properties as shown below. The mass spectra of negative and positive ion electrospray ionization were studied and compared to verify the structure and purity of the synthesized IL (**Fig. 62 and 63**). An ion trap model LCQ fleet Mass Spectrometer from Thermo scientific with mass range between 50 and 2000 m/z and ESI source with HESI I probe was used. Characteristic peaks were observed at electrospray MS^+ m/z 145.05 (**Fig. 50**), consistent with the molecular weight of the cationic part of IL ($[1-NA]^+$). This confirms the information about the structure of the cationic moiety naphthalen-1-aminium. The anionic part of IL $[FeCl_4]^-$ appears in the electrospray MS^- m/z 197.94 (**Fig. 51**), which is characteristic of the molecular weight. These observed peaks are a clear indication that the IL, 1-naphthylammonium tetrachloroferrate (III) ($[1-NA]^+[FeCl_4]^-$), was synthesized with no or low impurities. The total molecular weight of IL is shown in (**Fig. 64**).

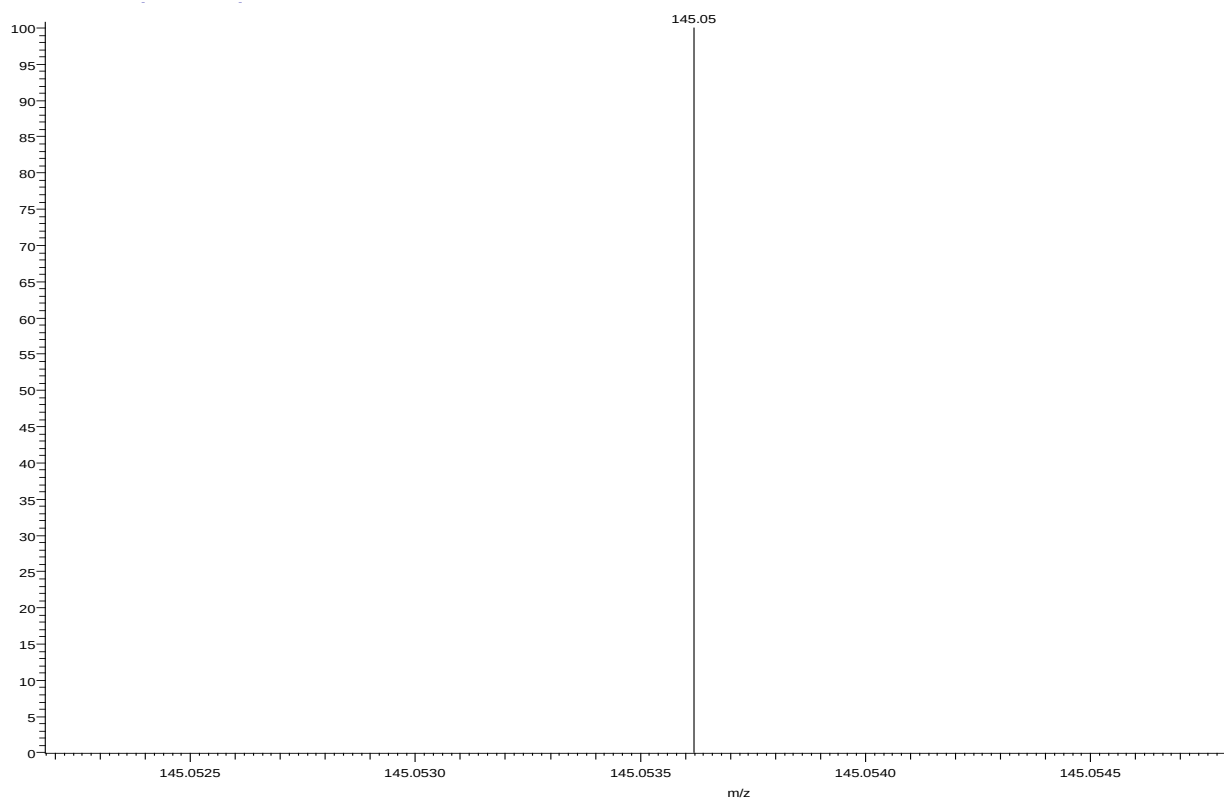


Figure 62: ESI-MS spectra of cationic part naphthalen-1-aminium ([1-NA]⁺)

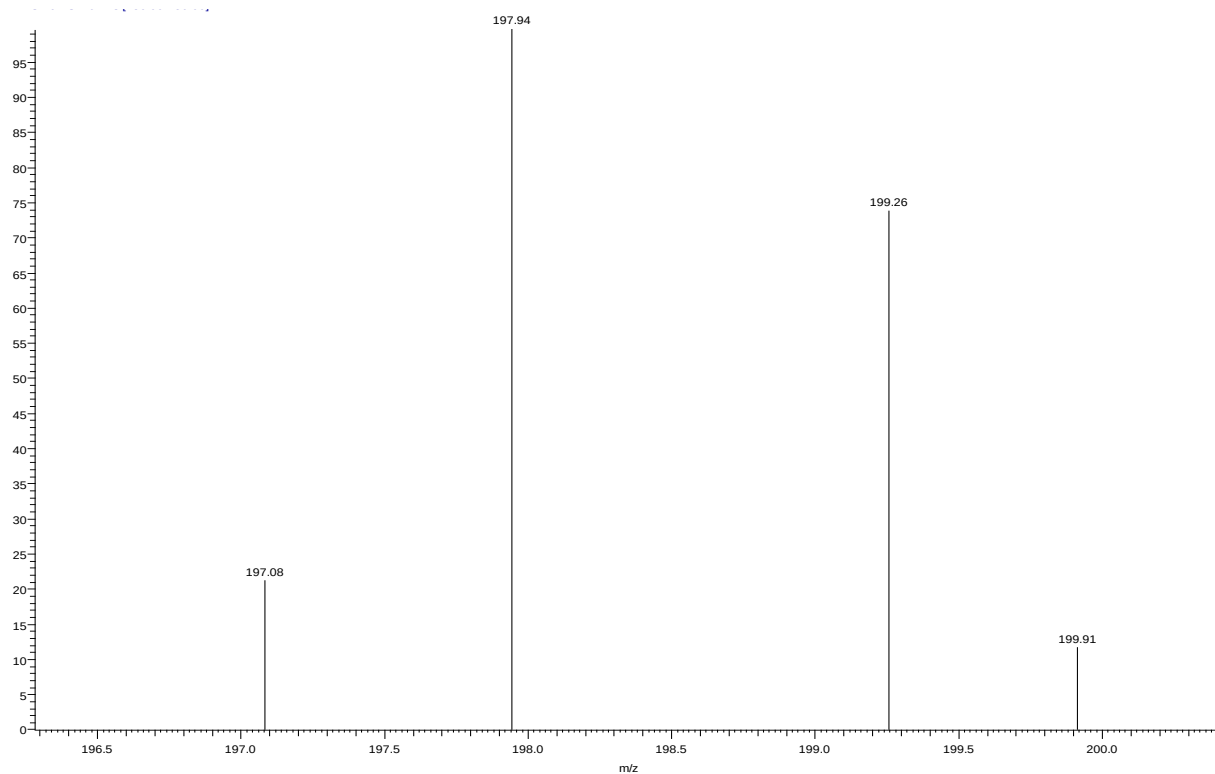


Figure 63: ESI-MS spectra of anionic part tetrachloroferrate (FeCl_4^-)

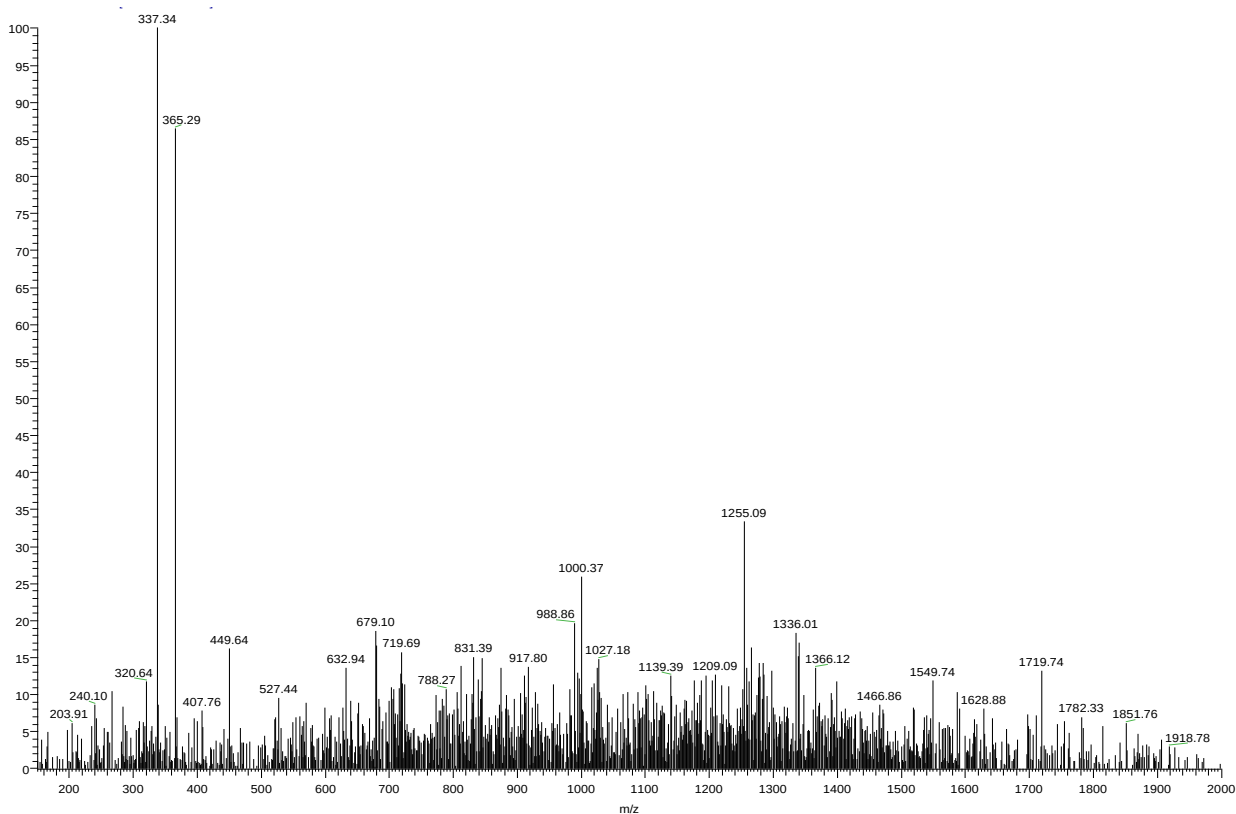


Figure 64: MS spectra total molecular weight of the MIL

The FT-IR spectra of 1-naphylamine, naphthalene-1-aminium chloride ($[1\text{-NA}]^+[\text{Cl}]^-$) and 1-naphthylammonium tetrachloroferrate (III) ($[1\text{-NA}]^+[\text{FeCl}_4]^-$) are shown in **(Fig. 65a, 65b and 65c)**, respectively. Measurements were performed using the IR system Smart iTR NICOLET iS10 Thermo Fisher Scientific USA. Samples were finely ground with a clean mortar and pestle and analyzed directly with the instrument, with wavenumbers ranging from 500 to 4000 cm^{-1} . The observed peak at 3342 cm^{-1} is due to asymmetric and symmetric stretching of N-H, while the band at about 2957 cm^{-1} is associated with

stretching vibrations of C-H and the band at 1623 cm^{-1} is associated with stretching vibrations of C=N. The peaks observed at 1508 cm^{-1} and 1174 cm^{-1} are attributed to C-N and C-H bending vibrations, respectively. The band at about 3400 cm^{-1} (**Fig. 65c**) is attributed to the presence of OH group stretching vibrations. The bands detected at about 671 to 760 cm^{-1} are attributed to aromatic hydrogen bending vibrations of C-N. Therefore, the naphthalene-1-aminium chloride intermediate and the starting material 1-naphthylamine can be considered to have a similar pattern, indicating high purity of the compound, and no change in compositions is observed.

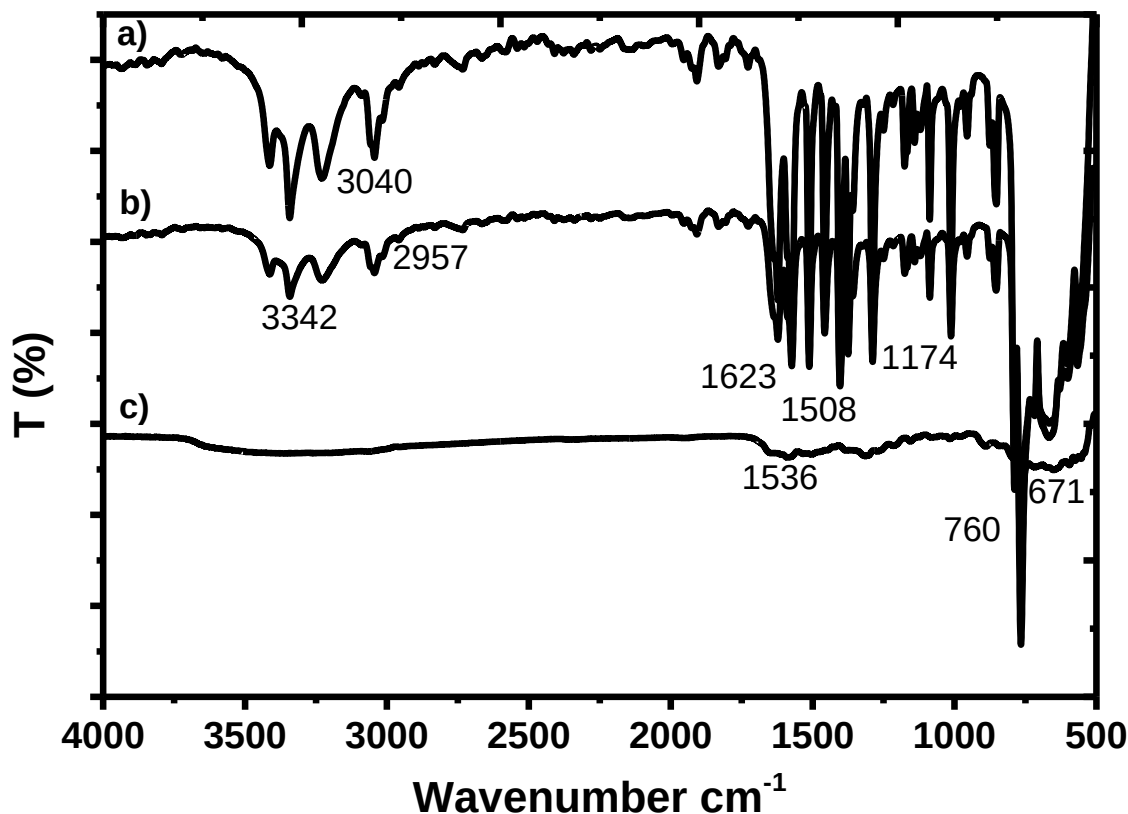


Figure 65: The FTIR spectra of a) 1-naphthylamine, b) $[1\text{-NA}]^+[\text{Cl}]^-$ and c) $[1\text{-NA}]^+[\text{FeCl}_4]^-$

The UV-Vis absorption spectrum was measured in ethanol at a concentration of 1×10^{-3} M for all samples using a UV-Vis spectrophotometer (Genesys 10S Thermo Fisher Scientific, USA). Broad spectra ranging from 280 nm to 380 nm were observed for both 1-naphthylamine and naphthalene-1-aminium chloride (**Fig. 66**). The lower wavelength around 280 nm could be due to a π - π^* transition depending on the length and degree of conjugation. In the case of 1-naphthylammonium tetrachloroferrate (III) (II), a hypsochromic shift is registered from the broad band at 380 nm to a sharp peak at 300 nm caused by steric hindrance between the NH^{3+} and FeCl_4^- , making the benzene ring stiffer and therefore shifting to lower wavelengths [153]. The other observed absorption band extends from 500 nm to about 680 nm and could be related to charge transfer excitation, which could occur within the chain or between chains connected to $[\text{FeCl}_4]^-$.

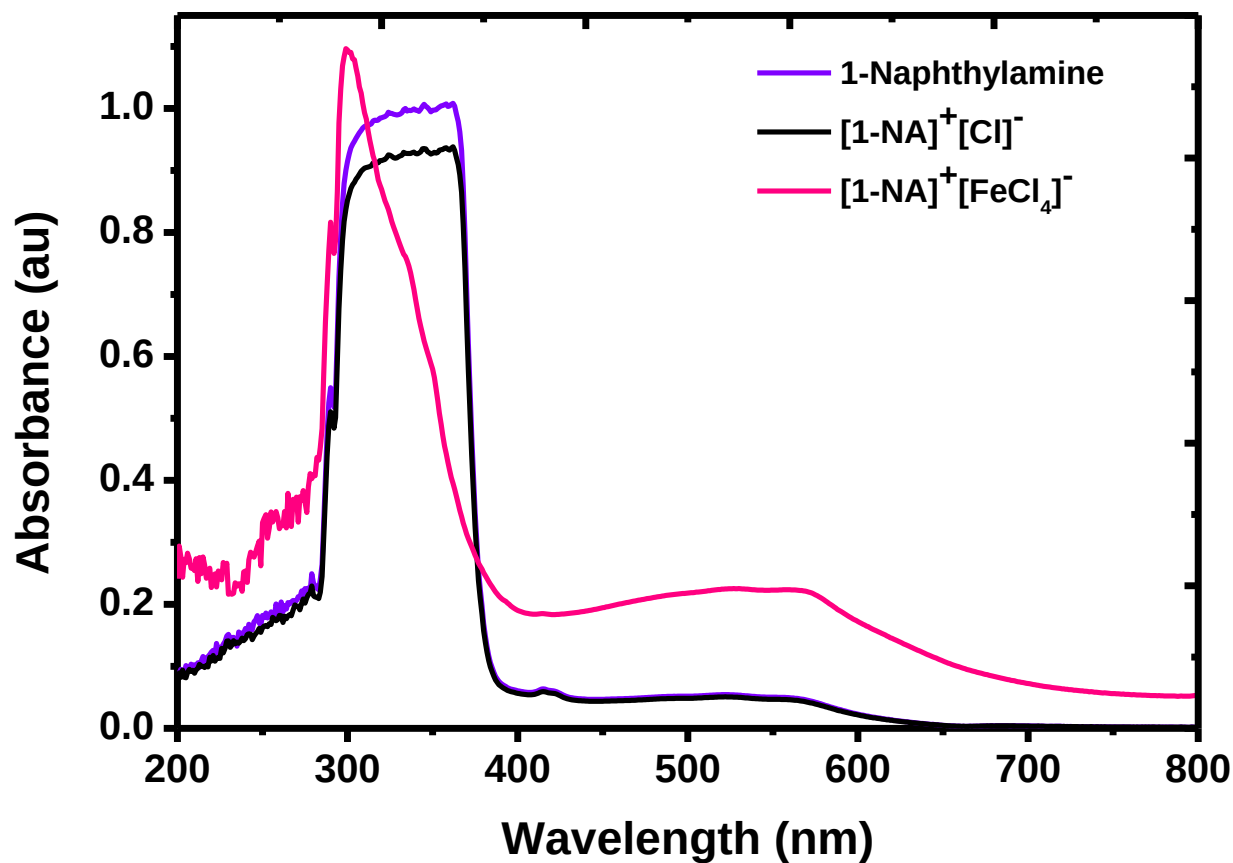


Figure 66: The absorption spectra of [1-NA]⁺[FeCl₄]⁻ in ethanol (1×10^{-3} M)

¹H NMR spectra of the starting material 1-naphthylamine (**Fig. 67**) and the intermediate ([1-NA]⁺[Cl]⁻) (**Fig. 68**) in deuterated chloroform (CDCl₃) showed peaks between 6.7 and 7.8 ppm for protons associated with the aromatic backbone of IL and the 1-naphthylamine, confirming the purity and structure of the compounds. In general, the proton NMR shows direct proportionality with the number of hydrogens present, but with a very slight shift to a higher delta due to protonation. In general, no additional peak is observed, further confirming the high purity of the intermediate structure.

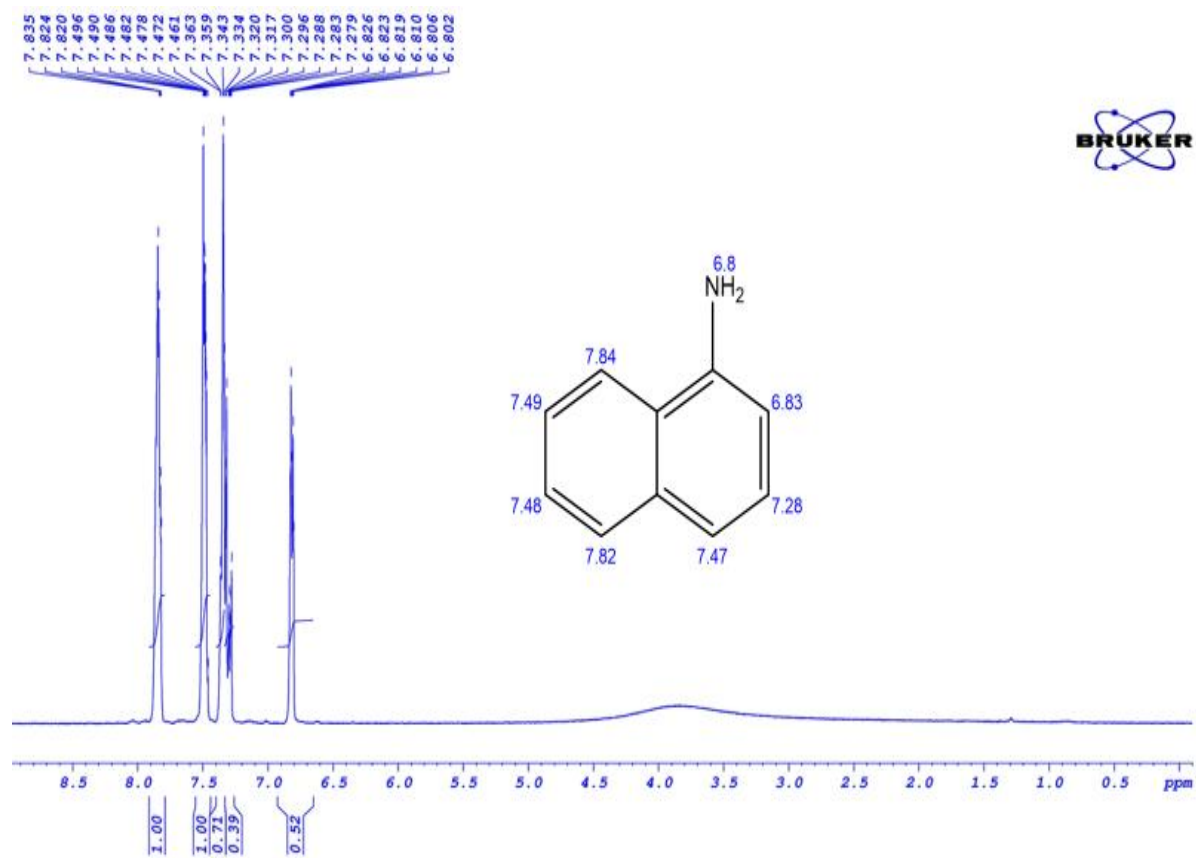


Figure 67: ¹H NMR spectra of 1-naphthylamine

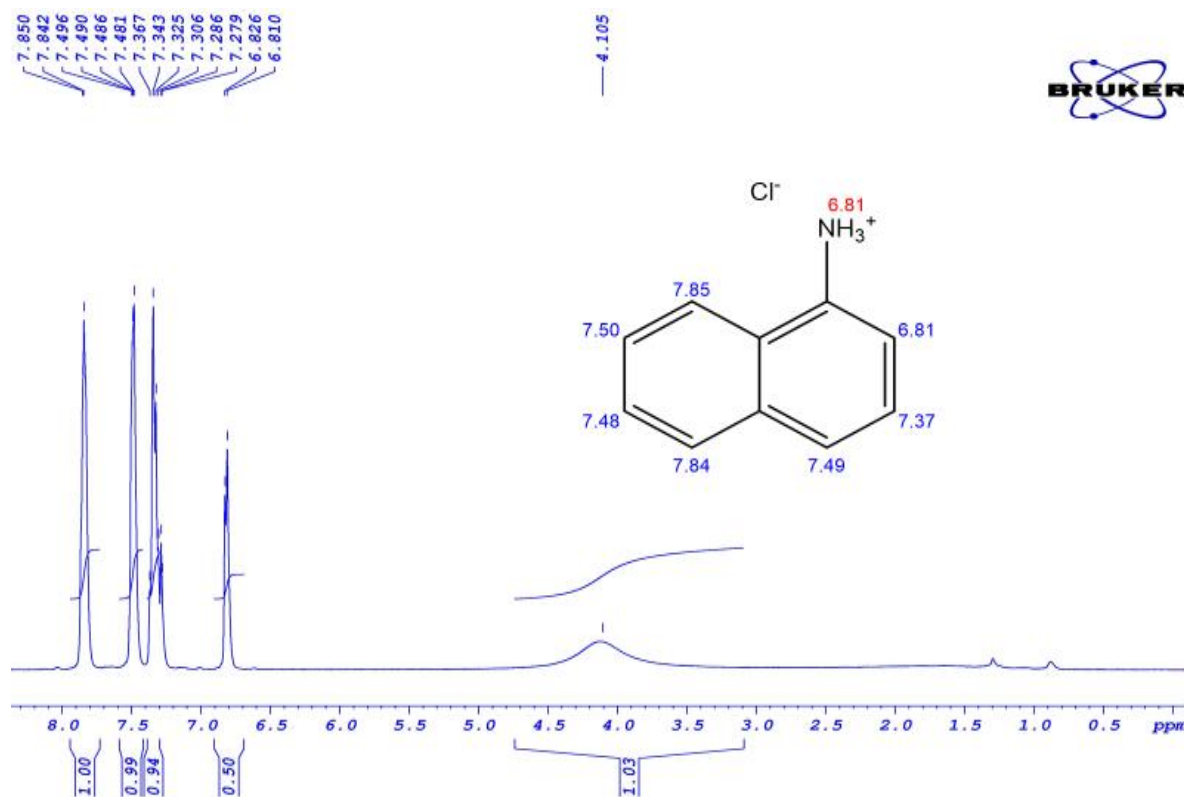


Figure 68: ^1H NMR spectra of naphthalen-1-aminium chloride

Moreover, the purity of the IL was further confirmed by dissolving it in acetonitrile at a concentration of 10 mg/L and performing chromatographic analysis on High-Performance Liquid Chromatography (HPLC) using a diode array detector (DAD), where only one sharp peak was observed at about 8.8 min retention time (**Fig. 69**) confirms the high purity of the complex.

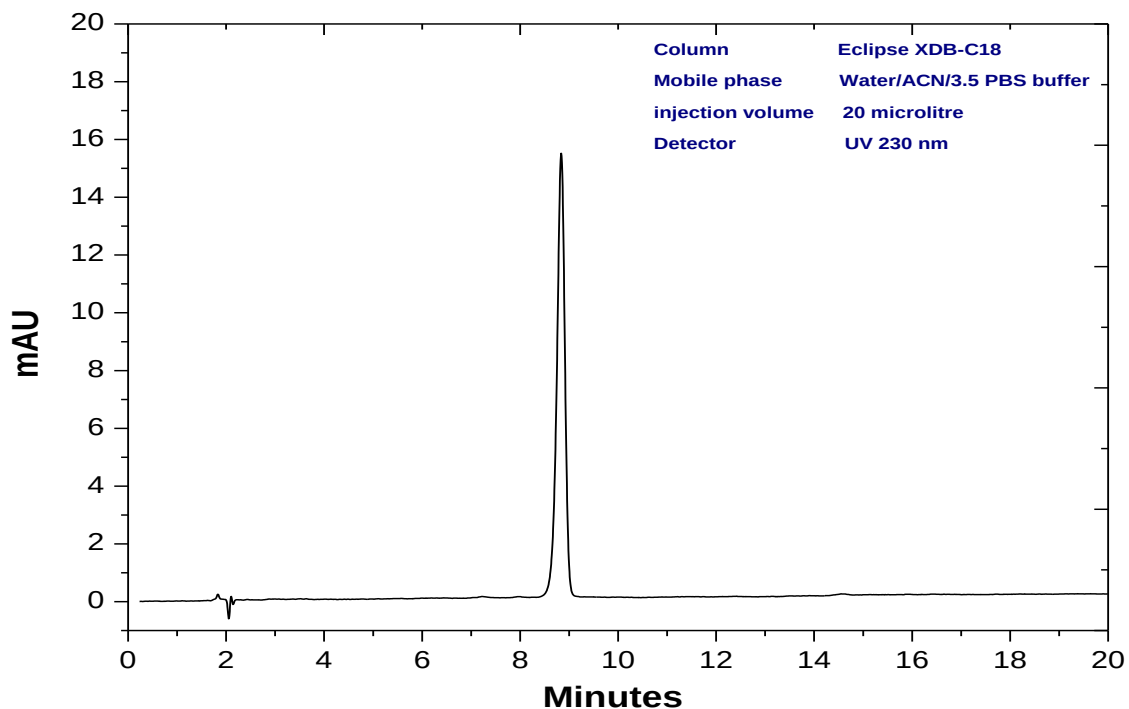


Figure 69: HPLC Chromatogram of $[1\text{-NA}]^+[\text{FeCl}_4]^-$ to confirm the purity

The thermal properties of the synthesized IL were investigated using the SDT Q600 V20.9 thermogravimetric analyzer, scanning from room temperature to 900 °C in a nitrogen flow of 50 mL/min at a heating rate of 10 K/min in a sealed aluminum crucible, and the results are shown in **(Fig. 70)**. From the TGA curve, it is evident that the synthesized IL is thermally stable even at temperatures higher than 655 K and 623 K. An endothermic broad peak was observed at 340 K which could be associated with the melting point of the material, which was also confirmed by the melting point reading falling in this range. It can be concluded that the material exhibits excellent thermal stability and minimal material loss even at high temperatures.

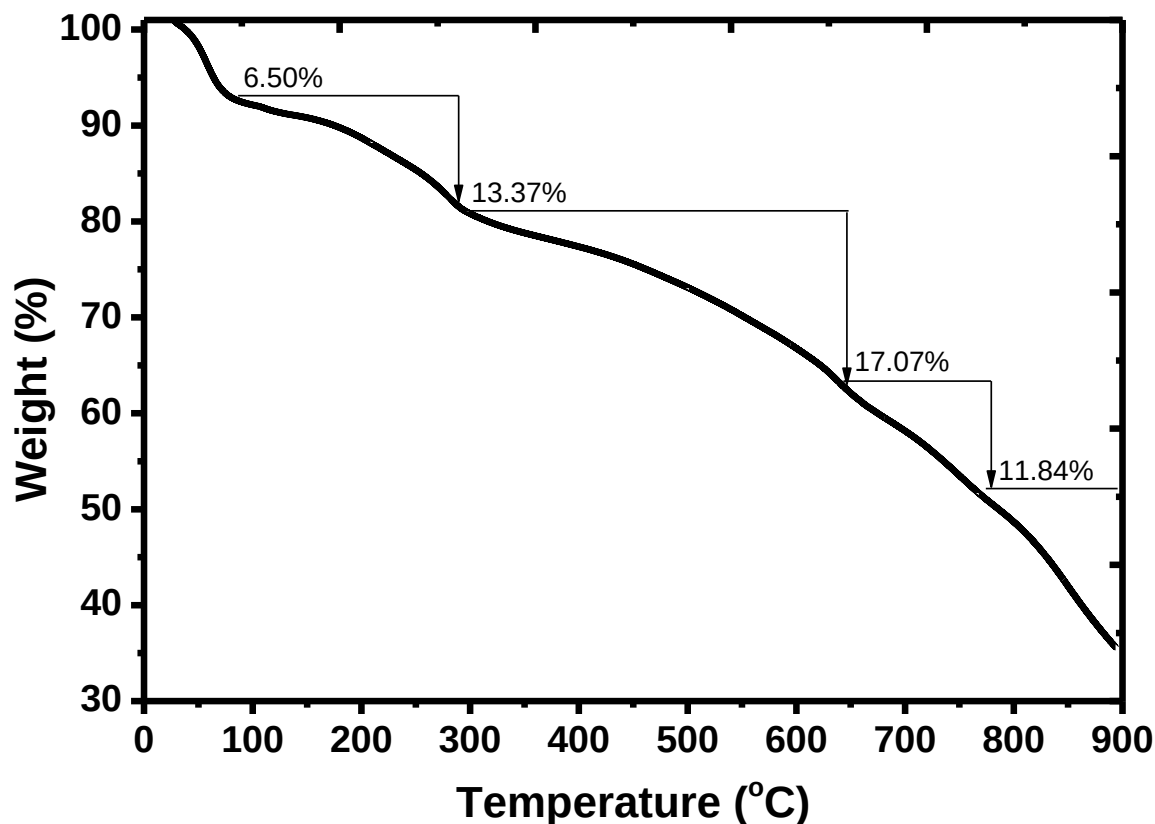


Figure 70: TGA curve showing thermal stability of $[1\text{-NA}]^+[\text{FeCl}_4]^-$ in terms of weight loss.

The surface morphology of IL before and after adsorption was studied under the field emission scanning electron microscope (FESEM) model Quarto S. Images (**Figs. 72a and 72c**) show a bright fibrous morphology, which can be associated with the high conductivity of $[\text{FeCl}_4]^-$. In contrast, the FESEM images (**Fig. 72b and d**) show a slightly darker surface, possibly due to adsorption. The EDX spectra of IL (**Fig. 72e and f**) show the presence of peaks corresponding to C, O, Fe, N, and Cl and the absence of additional peaks. EDX

elemental mapping supports this finding, which is represented by the good distribution of elements over all surfaces of the material.

XRD was performed to observe the crystallinity of the material, and the Rigaku instrument model UltimaIV X-ray diffractometer was used to scan from 5 to 90 $2\theta(^{\circ})$ at $\lambda=1.5418 \text{ \AA}$. In **(Fig. 71)**, it can be seen that the starting material 1-naphthylamine and the intermediate $[1\text{-NA}]^+[\text{Cl}]^-$ showed similar peaks with high intensity, indicating a crystalline lattice structure, but in contrast, $[1\text{-NA}]^+[\text{FeCl}_4]^-$ showed an amorphous structure, indicating freedom of movement and random distribution with the paramagnetic property of the material, which is also confirmed in **(Fig. 74)** EPR spectrum.

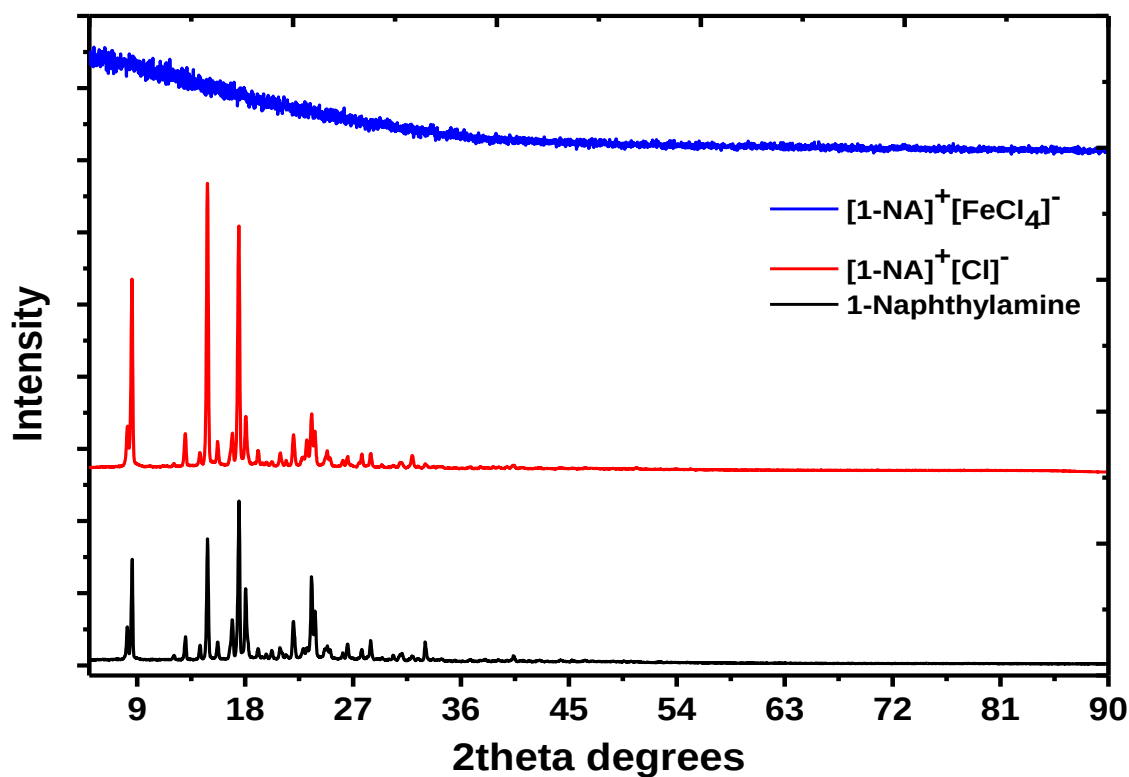


Figure 71: XRD spectra of $[1\text{-NA}]^+[\text{FeCl}_4]^-$

The zeta potential of the material was studied with six variables of basic and acidic pH in water using the Zeta Potential Analyzer Zeta model PALS. The material showed a pattern that had a negative charge above pH 3. As shown in **(Fig. 73)**, the zeta potential was plotted from pH 2 to pH 12, with triplet readings for each pH, with standard deviations ranging from 0.36 to 1.51.

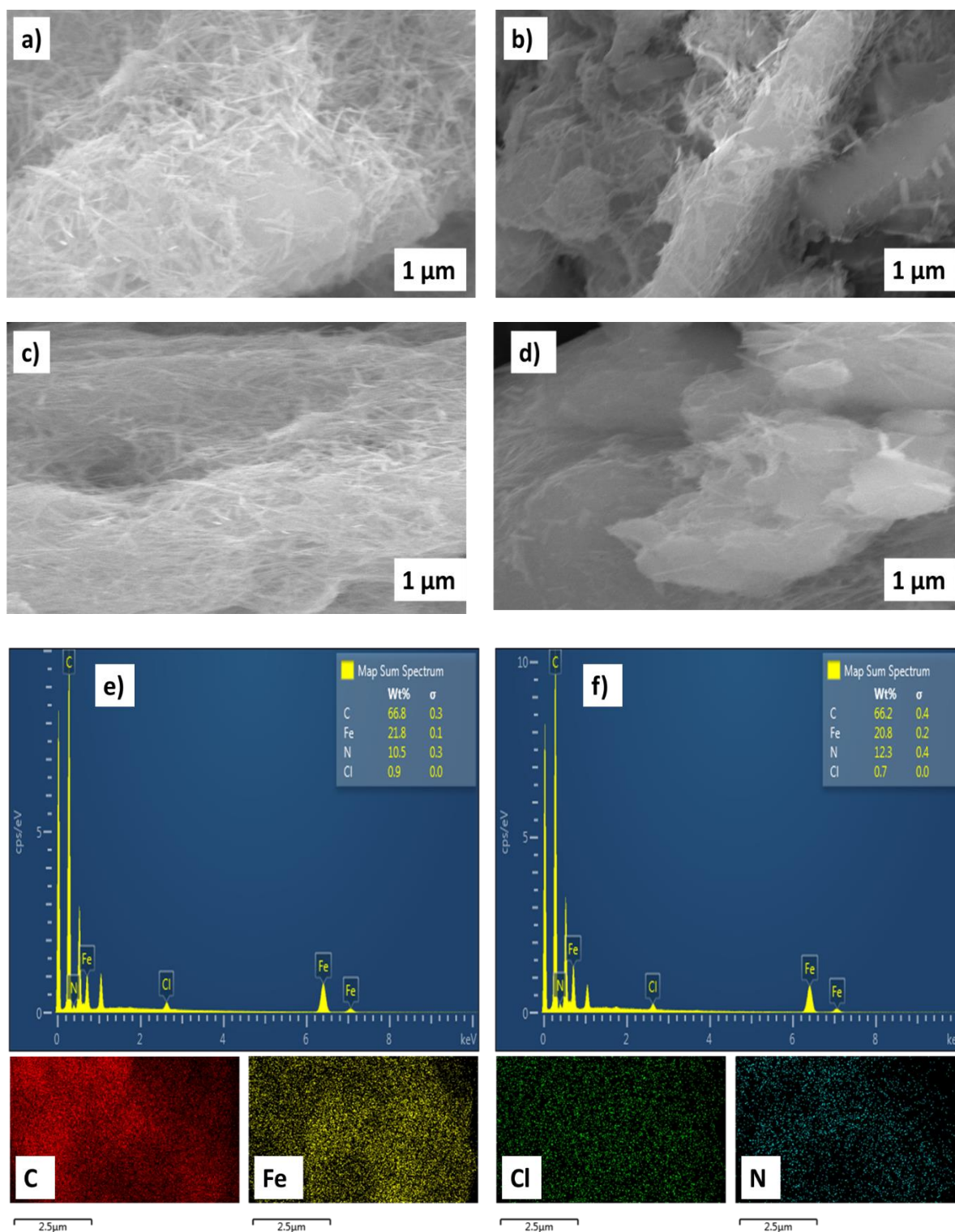


Figure 72: SEM images of $[1-NA][FeCl_4]$ a) before b) after c) before and d) after adsorption of methylene blue and rose Bengal dyes respectively; Energy dispersive X-ray (EDX) images e) and f) and C, Fe, Cl & N showing mapping of elements

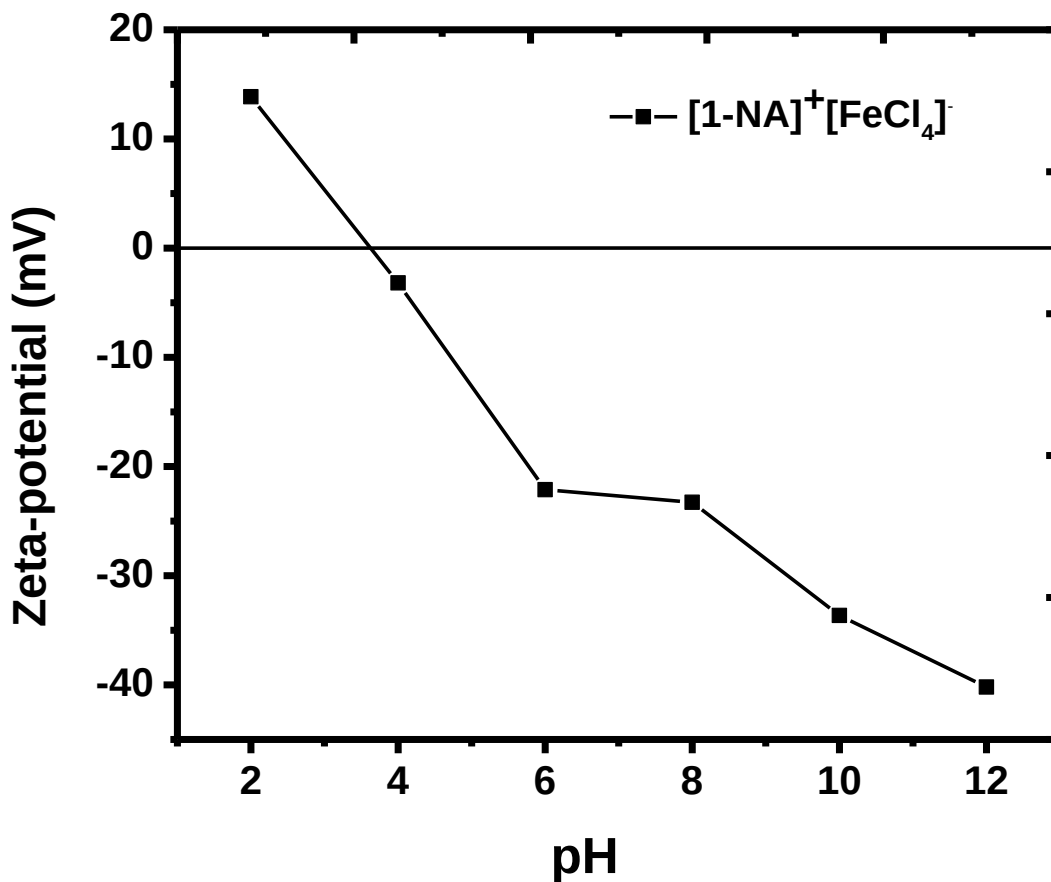


Figure 73: Zeta-potential of $[1\text{-NA}]^+[\text{FeCl}_4]^-$ as a function of pH

Electron paramagnetic resonance (EPR) was performed using a miniscope model of a benchtop EPR spectrometer in the X-band from 9.3 to 9.55 GHz. A very sharp singlet peak was observed at $g = 2.06386$ with a derivative property that can be attributed to the unpaired free electron of the iron present in the material (**Fig. 74**). **Equation 5** below was used to calculate the g value at $\nu = 9.3750$ GHz. However, when ethyl ether was used as solvent instead of methanol in the second part of the synthesis procedure, loss of paramagnetic property was observed as shown in (**Fig. 75**). Therefore, based on the above observation, the second part of the synthesis was carried out in methanol.

$$g = 71.4484 \nu \text{ (GHz)} / B \text{ (mT)} \quad (5)$$

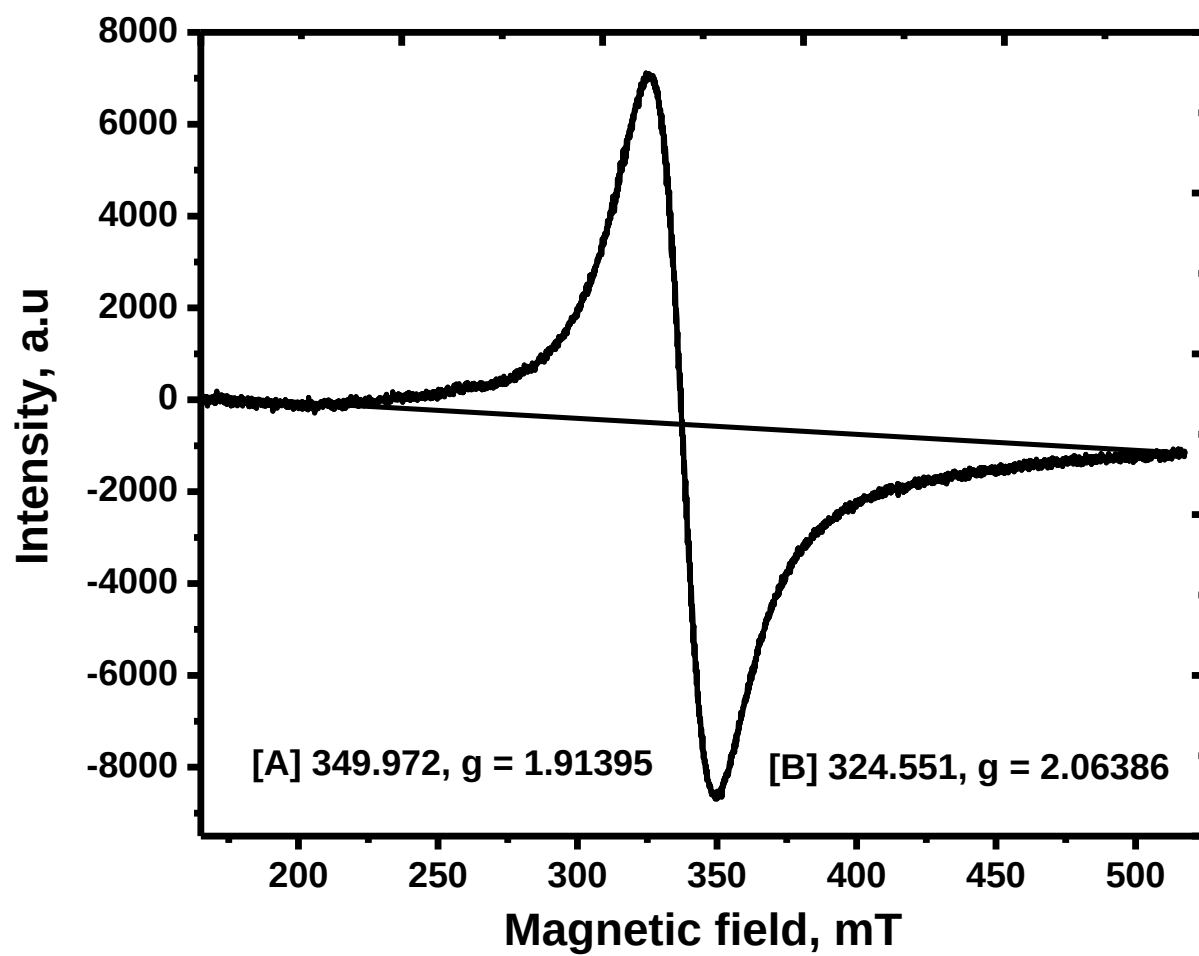


Figure 74: EPR spectrum of $[1\text{-NA}]^+[\text{FeCl}_4]^-$ synthesized in methanol solvent

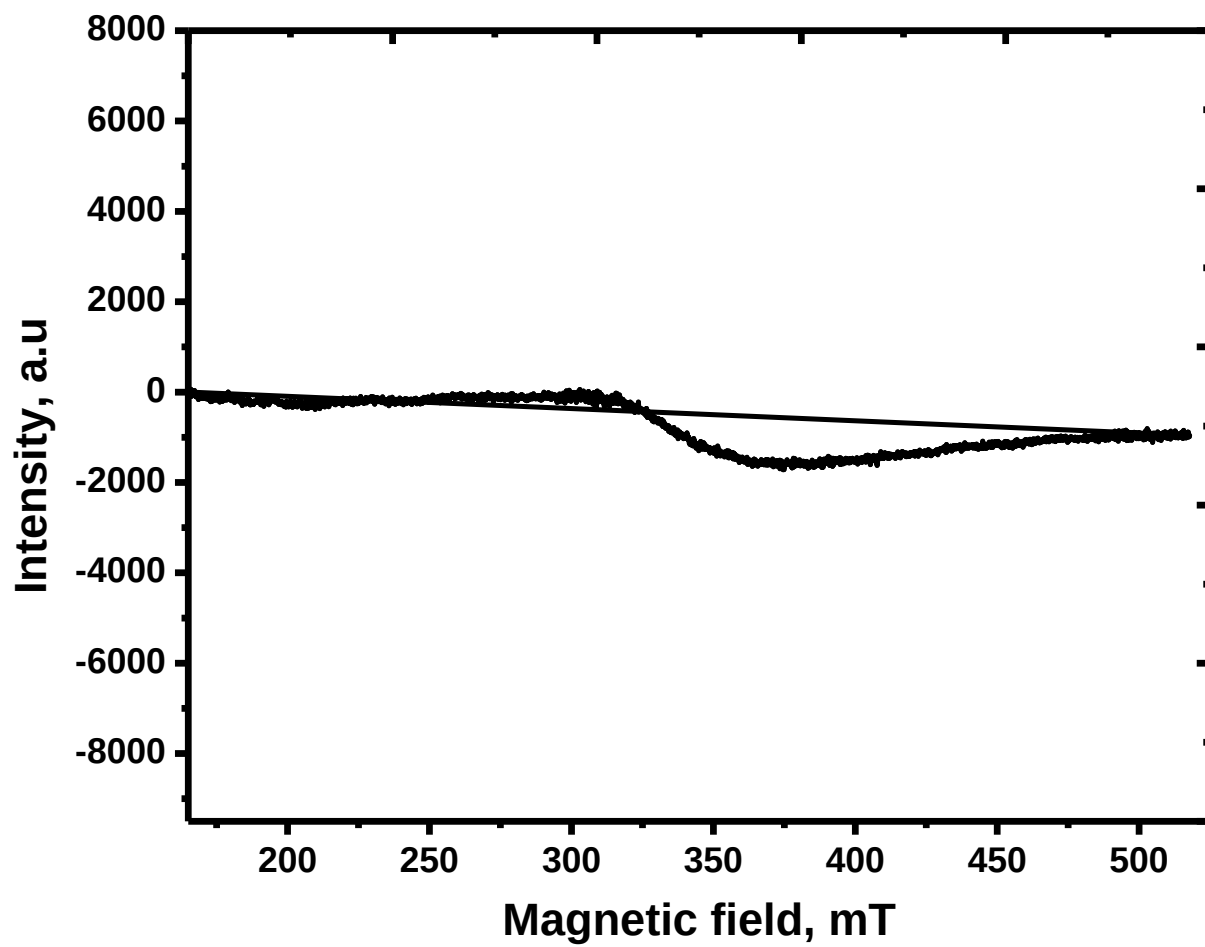


Figure 75: EPR spectrum of $[1\text{-NA}]^+[\text{FeCl}_4]^-$ synthesized in an ethyl ether solvent

Raman spectra were recorded in a range from 100 cm^{-1} to 1000 cm^{-1} using the surface-enhanced Raman scattering spectroscopy (SERS), model LabRam. The excitation laser source used was 633 nm. Sharp dominant peak was observed at about 457.4 cm^{-1} , which were assigned to the symmetric bond stretching vibrations originating from Fe-Cl of FeCl_4^- for $[1\text{-NA}]\text{FeCl}_4$ (**Fig. 76**). Similar observations have also been reported for FeCl_4^- containing ionic liquids [96], [158]–[160].

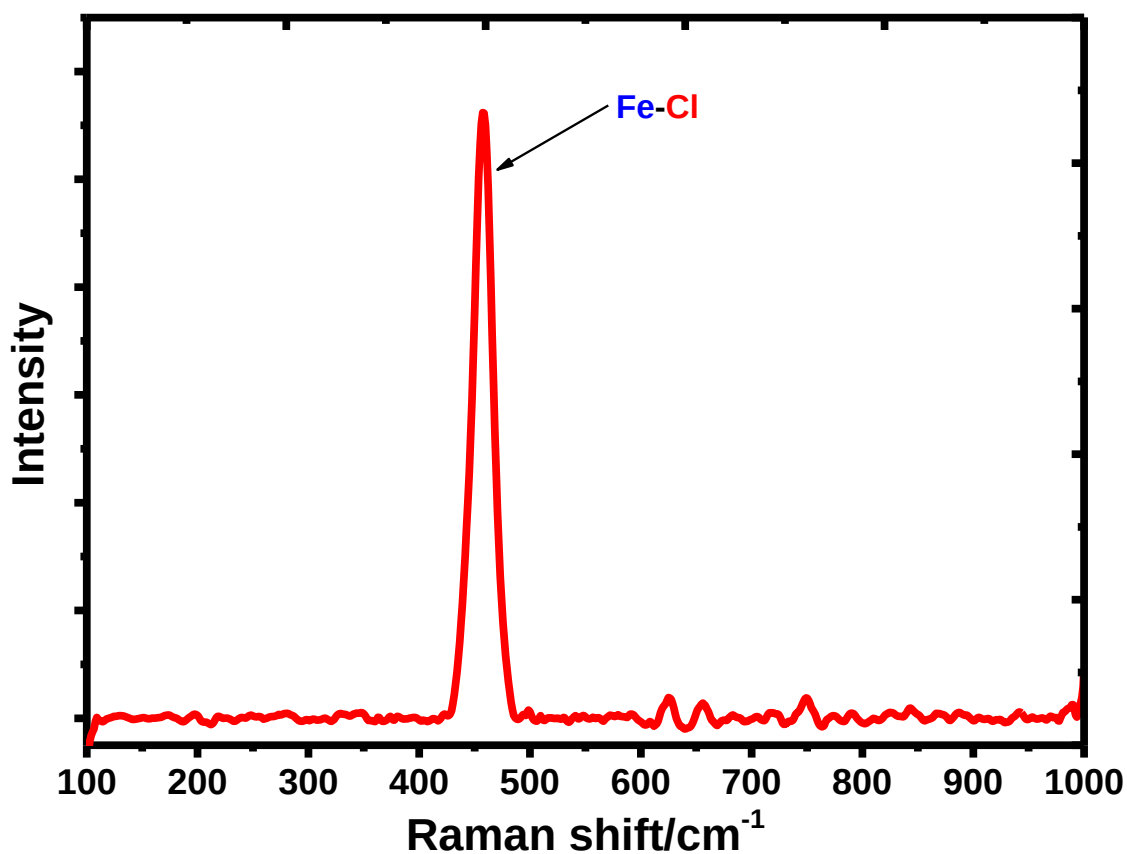


Figure 76: Raman spectrum of $[1\text{-NA}]^+[\text{FeCl}_4]^-$

The melting point of IL-based salt is very important since they melt either at 100 °C or below. In this study, we have used the Stuart MPS10 Series melting point apparatus to measure the melting point at an ambient temperature of 295K and recorded approximately 63.1°C (336.25K). The melting point of ILs is dependent on asymmetry or symmetry and charge densities of the constituent ions hence, monoanionic and monocationic species are stoichiometrically paired as the molar ratio is 1:1. This results in a low melting point of the IL that allows easy tunability as well as interesting physiochemical properties, as observed in $[1\text{-NA}]^+[\text{FeCl}_4]^-$ IL.

7.3.2 Effect of different parameters on adsorptive removal of dyes

To achieve efficient adsorption, the parameters affecting the dye removal process must be optimized. In this work, we investigated the efficiency of IL, 1-naphthylammonium tetrachloroferrate (III), in the adsorptive removal of MB and RB dyes from aqueous media. Then, the parameters affecting the adsorption efficiency, such as dye concentrations, contact time, the volume of the sample, pH, adsorbent dosage and shaking speed were optimized.

7.3.2.1 Effect of adsorbent dosage

The first parameter in an absorption study is the selection of the correct dosage of adsorbent to determine the appropriate and efficient amount. Therefore, the effect of dosage was studied for both methylene blue and rose bengal in the range of 5 to 60 mg (**Fig. 77a**). It was found that increasing the dosage improved the percentage removal, which can be attributed to a larger surface area available for adsorption [224], [225]. However, a slight decrease in RB was observed when the dosage exceeded 20 mg. This aspect can be further investigated and could be due to the equilibrium that occurs between the dye ion and the adsorbent, as the molecular size of RB is three times larger than that of methylene blue. It could also be due to the agglomeration of the material blocking the adsorption sites. In the case of MB, a uniform increase in adsorption efficiency was observed up to a dosage of 60 mg of sorbent with 92% removal. Therefore, dosages of 20 and 60 mg were chosen for RB and MB, respectively.

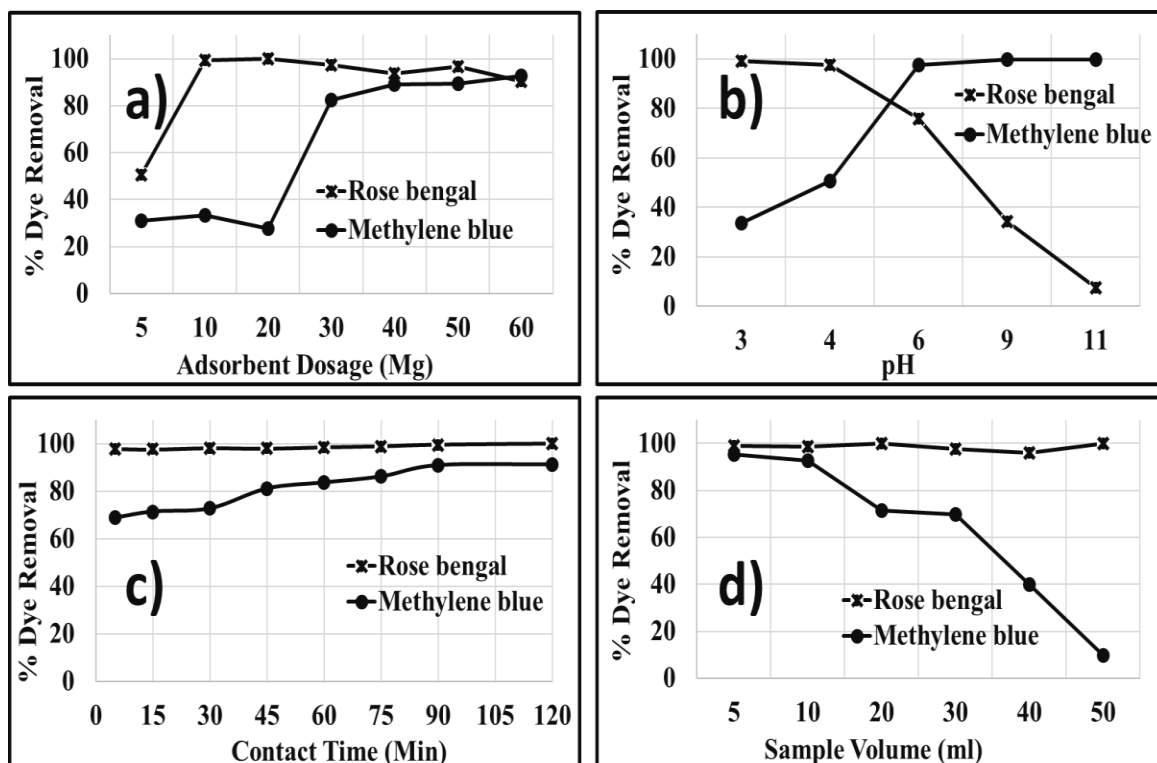


Figure 77: Effects of various factors a) adsorbent dosage (mg) b) pH c) contact time (min) d) Sample Volume (mL)

7.3.2.2 Effect of pH

The most significant parameter in an aqueous solution that affects the adsorption of dyes and alters the charge on the surface of the adsorbent and the ionization performance of the dye, and the adsorbent is basically the pH [226]. The effect of pH on the removal of MB and RB is shown in **(Fig. 77b)**. The removal of MB increases with an increase in pH from 3 to 11. However, 6 was chosen as the optimum pH at which 92% removal of MB occurred. At pH 9, MB decomposes irreversibly and hence the highest removal was recorded at pH

9 and 11 [227]. The RB removal was much higher compared to MB but in reverse order where the removal efficiency decreased with increasing pH, mainly due to electrostatic repulsion, with an efficiency of 99% at pH 3. Again, pH 4 was chosen for RB as it also decomposes at lower pH values but is reversible with pH adjustment. Therefore, the results obtained show that the RB dye is better removed in acidic media, which is in agreement with the literature [228], [229], in contrast to MB, which showed better removal in a basic medium, which is also in agreement with the literature [230]. The measurement of zeta potential is also in agreement with the finding indicating greater negative potential at pH above 3 in water (**Fig. 73**), therefore, the cationic MB was better removed in basic media. The anionic RB showed excellent adsorption in acidic media as the surface of the material exhibited a positive charge at lower pH, confirming that the adsorption is due to electrostatic attractive forces between the dye and IL [231], [232].

7.3.2.3 Effect of dyes concentration and shaker speed

Adsorption of dyes increased when the shaking speed was increased from 50 to 300 rpm. The contact probability between dye and adsorbent increased with increase in shaking speed. Equilibrium was reached at 150 rpm. The dye concentration was varied from 5 to 400 mg/L and it was recorded that with increasing concentration, the adsorption capacity of the material decreased in the case of MB, showing excellent removal at 5 mg/L with 98%. In contrast, in the case of RB, a continuous increase in removal was observed with an increase in dye concentration up to 250 ppm, after which a sharp decrease was observed,

indicating the saturation of the adsorbent. For both dyes, 40 mg/L was chosen as the optimum concentration. The dye removal depends on the concentration.

7.3.2.4 Effect of sample volume and contact time

The contact time was varied from 5 to 120 min to evaluate the effect of exposure time of the two dyes on the adsorbent 1-naphthylammonium tetrachloroferrate (III). The results in **(Fig. 77c)** show that the removal efficiency improves with increasing time. Equilibrium was reached at 30 min and 120 min for RB and MB, respectively. The effect of sample volume was also investigated, and it was found that adsorption decreased with increasing sample volume in the case of MB, which could be due to a decrease in contact. No great difference was observed in the case of RB **(Fig. 77d)**.

7.3.2.5 Adsorption kinetics

The dye adsorption processes can be described using the kinetic parameters [233]. Typically, the kinetic parameters of adsorption are determined from the pseudo-first order [234] and pseudo-second order [235] kinetic models expressed by the Lagergren rate **Equation 6** and Ho and McKay rate **Equation 7**, respectively.

$$\ln(q_e - q_t) = \ln q_e - k_1 t \quad (6)$$

$$\frac{t}{q_t} = \frac{1}{k_2 q_e^2} + \frac{t}{q_e} \quad (7)$$

The q_e and q_t parameters (in mg/g unit) represent the equilibrium amount of dye adsorbed and the amount of dye adsorbed at the contact time, t (min) respectively. The k_1 (min^{-1}) and k_2 ($\text{g/mg} \cdot \text{min}$) represents the pseudo-first-order and pseudo-second-order rate constants, respectively. The adsorption kinetics plots presented in **(Fig. 78)** show pseudo-first-order and pseudo-second-order plots for MB and RB. The plot of $\ln(q_e - q_t)$ against t gives slope and intercept equal to $-k_1$ and $\ln q_e$ respectively, whereas the plot of $\frac{t}{q_t}$ against t gives slope and intercept equal to $\frac{1}{q_e}$ and $\frac{1}{k_2 q_e^2}$ respectively. The kinetic parameters (k_1 , k_2 , $q_e(\text{expt})$ and $q_e(\text{cal})$) for both MB and RB dyes are summarized in **Table 16**. The high R^2 value for the pseudo-second-order plots for both MB and RB implies that the adsorption process for both MB and RB on the surface of IL most probably occurs via the second-order rate equation and therefore, controlled by the physisorption mechanism [235]. This is further corroborated by the well-fitting of experimental adsorption capacity ($Q_e(\text{exp})$) with the calculated adsorption capacity ($Q_e(\text{cal})$).

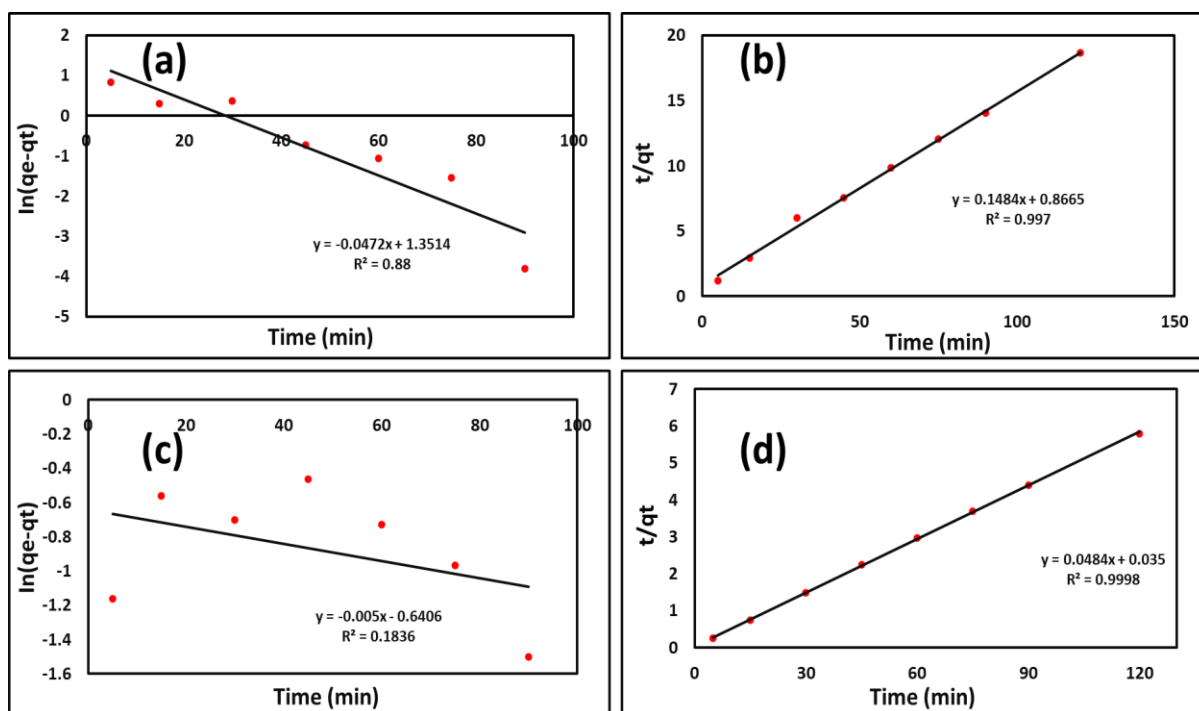


Figure 78: Adsorption kinetics plots: (a) First-order and (b) Second-order for MB; (c) First-order and (d) Second-order for RB.

Table 16: Kinetic parameters for adsorption of MB and RB by IL.

Dye	Pseudo-first order				Pseudo-second order		
	$Q_e(\text{exp})$ (mg/g)	$k_1(10^3)$ (min^{-1})	$Q_e(\text{cal})$ (mg/g)	R^2	$k_2(10^2)$ (g/mg.min)	$Q_e(\text{cal})$ (mg/g)	R^2
MB	6.443	47.2	3.863	0.8800	2.54	6.739	0.9973
RB	20.70	5.0	0.527	0.1836	6.69	20.661	0.9998

7.3.2.6 Adsorption isotherms

Adsorption isotherms are commonly used to obtain a reasonable understanding of the interaction between adsorbent and adsorbate. Langmuir and Freundlich isotherms are the commonly used models for this study and are expressed by **Equation 8** and **Equation 9**, respectively.

$$\frac{C_e}{q_e} = \frac{1}{K_L q_m} + \frac{C_e}{q_m} \quad (8)$$

$$\ln q_e = \ln K_F + \frac{1}{n} \ln C_e \quad (9)$$

The Langmuir model assumes that the adsorption process of the adsorbate occurs homogeneously at the surface of the adsorbent due to the specific adsorption sites and energies as well as the steric hindrances, and lateral interactions between the adsorbate molecules do not play a role [236]. The Freundlich isotherm, on the other hand, assumes a heterogeneous course of the adsorption process, which leads to a non-uniform distribution of the adsorption energies over the adsorption surface [237]. The Langmuir model is tested by plotting $\frac{C_e}{q_e}$ against C_e , to give slope equal to $\frac{1}{q_m}$ and intercept of $\frac{1}{K_L q_m}$. The $C_e \left(\frac{mg}{L} \right)$ and

$q_e(\frac{mg}{g})$ correspond to the equilibrium concentration of adsorbate and adsorption capacity of the adsorbent, respectively. The K_L (Langmuir equilibrium constant) which relates directly with adsorption energy and q_m that signifies the monolayer adsorption capacity are both extracted from the slope and intercept of **Equation 8**. Similarly, the plot of $\ln q_e$ against $\ln C_e$ (using Freundlich equation) gives a slope equal to $\frac{1}{n}$ and intercept of $\ln K_F$, and the constants n and K_F for the adsorbates are determined accordingly [238]. The summary of the Langmuir and Freundlich adsorption isotherms is shown in **Table 17**, and the degree of fit of the models is assessed by comparing their correlation coefficient (R^2) values, with a larger R^2 value indicating a better fit. From the R^2 values, it can be seen that the adsorption isotherm MB is best described by the Langmuir model, while the adsorption isotherm of RB is best described by the Freundlich model (**Fig. 79**). Interestingly, however, the RB dye shows a much higher adsorption capacity (almost 20-fold) and a much lower adsorption energy (by a factor of 0.3) than the dye MB.

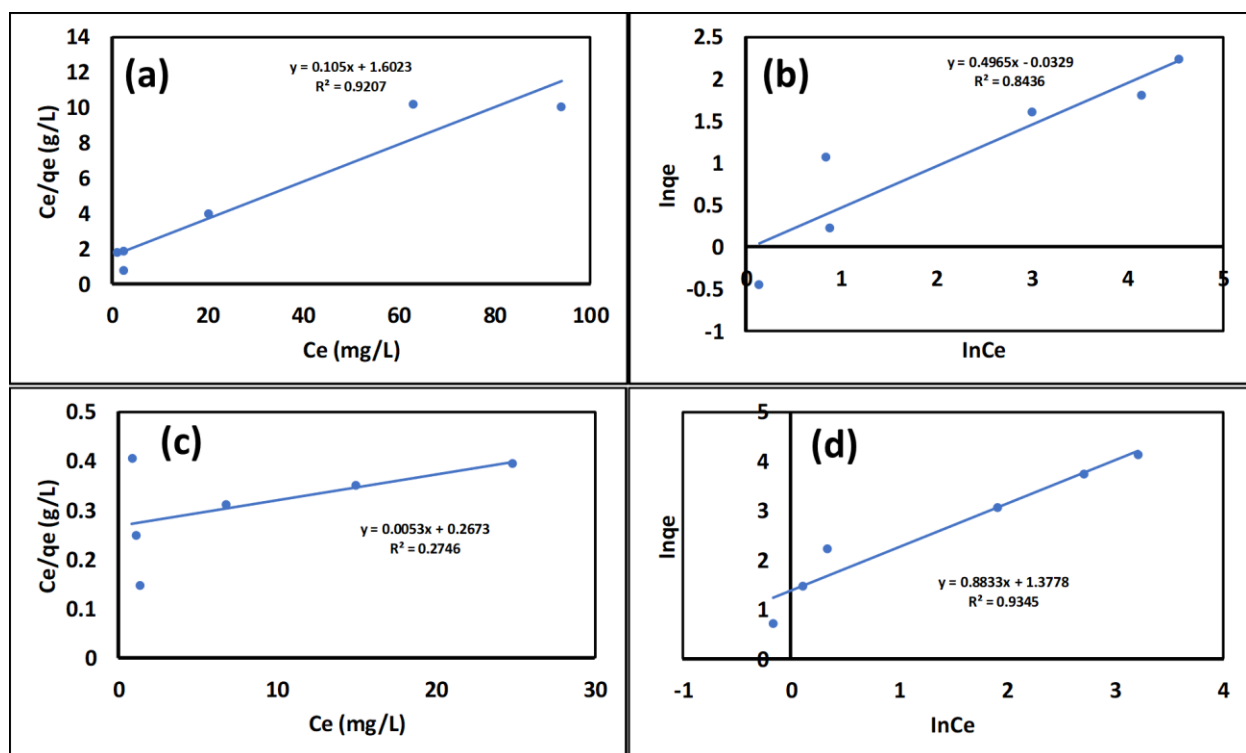


Figure 79: Adsorption isotherms plots: (a) Langmuir and (b) Freundlich for MB; (c) Langmuir and (d) Freundlich for RB.

Table 17: Isotherm parameters for adsorption of MB and RB on the IL adsorbent

Langmuir isotherm				Freundlich isotherm		
Dye	q_m (mg/g)	$K_L(10^2)$ (L/mg)	R^2	N	K_F	R^2
MB	9.524	6.55	0.9207	0.589	1.51	0.8436
RB	188.7	1.98	0.2746	1.13	3.97	0.9345

7.3.2.7 DFT results

The ground state geometries representing the lowest energy conformers and the electrostatic potential maps (ESP) of IL, MB and RB are shown in **(Fig. 80)**. ESP The maps of the molecules represent the charge distribution on their surface and are shown in different colors. Regions of low potential are represented by red color and are characterized by an abundance of electrons, while regions of high potential are represented in blue, and these regions are characterized by a relative absence of electrons. Light blue regions represent slightly electron deficient regions, yellow indicates slightly electron rich regions and green represents neutral regions on the surface of the molecule. The ESP map of IL shows high electron density around the naphthalene fragment of the molecule as well as around the halogen atoms, and this represents the regions where charge transfer reactions with the dye molecules are likely to occur. Similarly, the ESP maps of the dye molecules show regions of low density around the aromatic fragments and the heteroatoms, indicating a high tendency for the molecules to accept charge donations from IL to these regions. ESP of the molecules therefore indicates the relative distribution of charges on the molecules and suggests the possibility of adsorption of the dyes by IL.

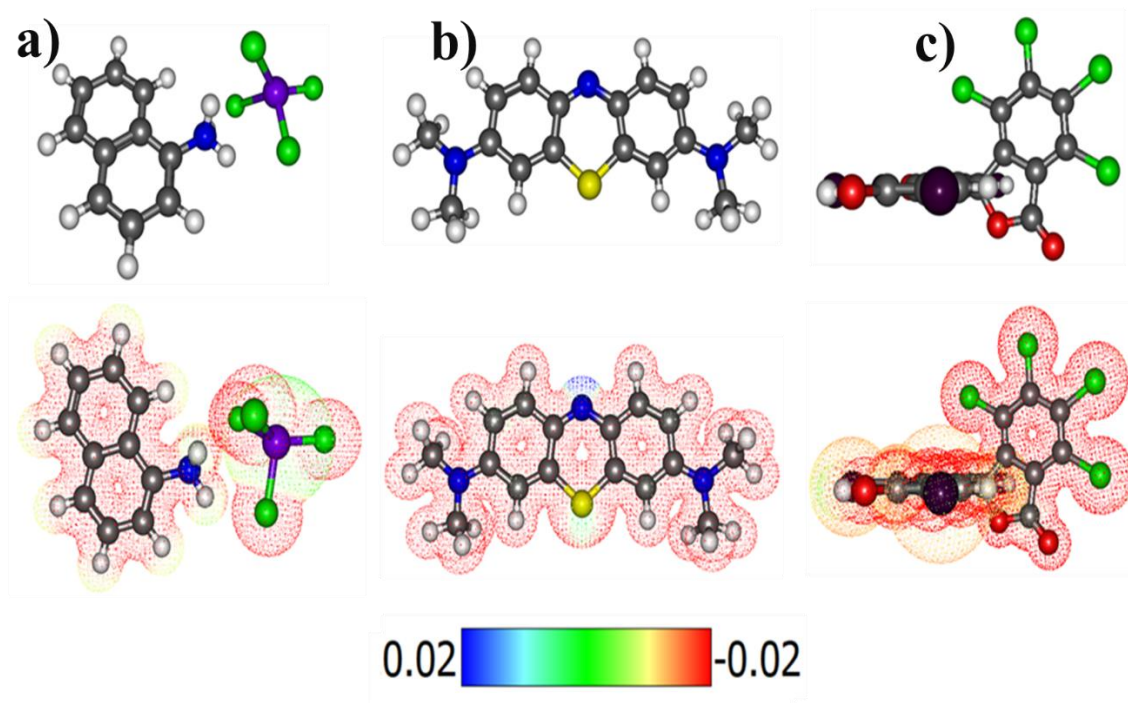


Figure 80: Optimized geometries (top) and ESP potential distribution (bottom) of (a) IL, (b) MB and (c) RB

The frontier orbital distribution of the dye molecules (MB and RB) was calculated and shown in **(Fig. 81)**. According to the frontier orbital theory, the electron transfer in a molecule is reflected by the energy gap (ΔE) between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). Consequently, a molecule that has a lower value of ΔE is more susceptible to charge transfer processes and more reactive. Inspection of the frontier orbital distributions on the dye molecules shows that the HOMO and the LUMO orbitals were distributed over the aromatic components and the heteroatoms (O, S, N, Cl, I), indicating centers that are likely to interact with the

adsorbent. The corresponding energy gap ΔE shows that MB with a value of 3.572 eV has a higher tendency to be adsorbed under neutral conditions than RB with a ΔE value of 4.084 eV. After complexation with the dye molecules, a corresponding shift in the ΔE of IL was observed, indicating the stabilization of the adsorbent by the dye molecules (**Fig. 82**). However, a more positive shift of 1.261 eV was observed in the complex with MB compared to 0.484 eV in the RB complex, indicating the selectivity of IL over MB under neutral conditions. Also, the distribution of the frontier orbitals in MB showed no significant change upon interaction with IL in contrast to those of RB. This is consistent with the predictions of frontier orbital theory and suggests that the symmetry of the orbitals in RB does not favor proper overlap with the orbitals of IL, leading to poor interactions, as shown by the energy gap ΔE [239].

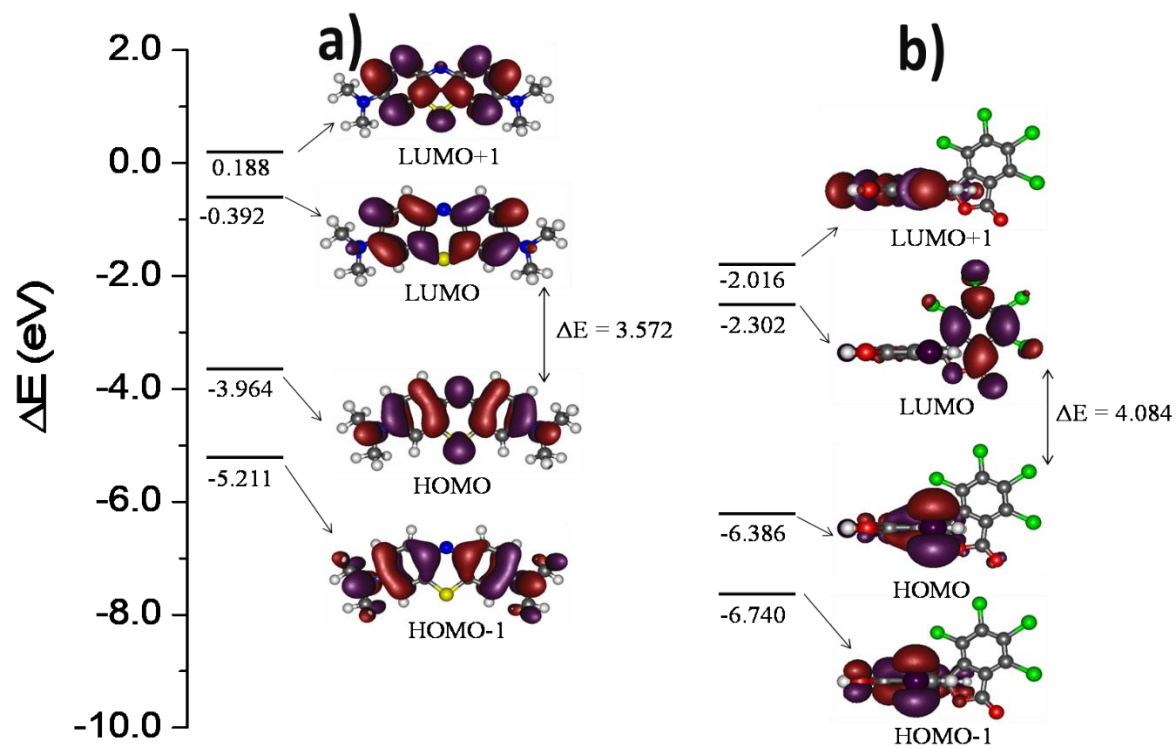


Figure 81: Frontier orbital distributions of (a) MB and (b) RB dye molecules

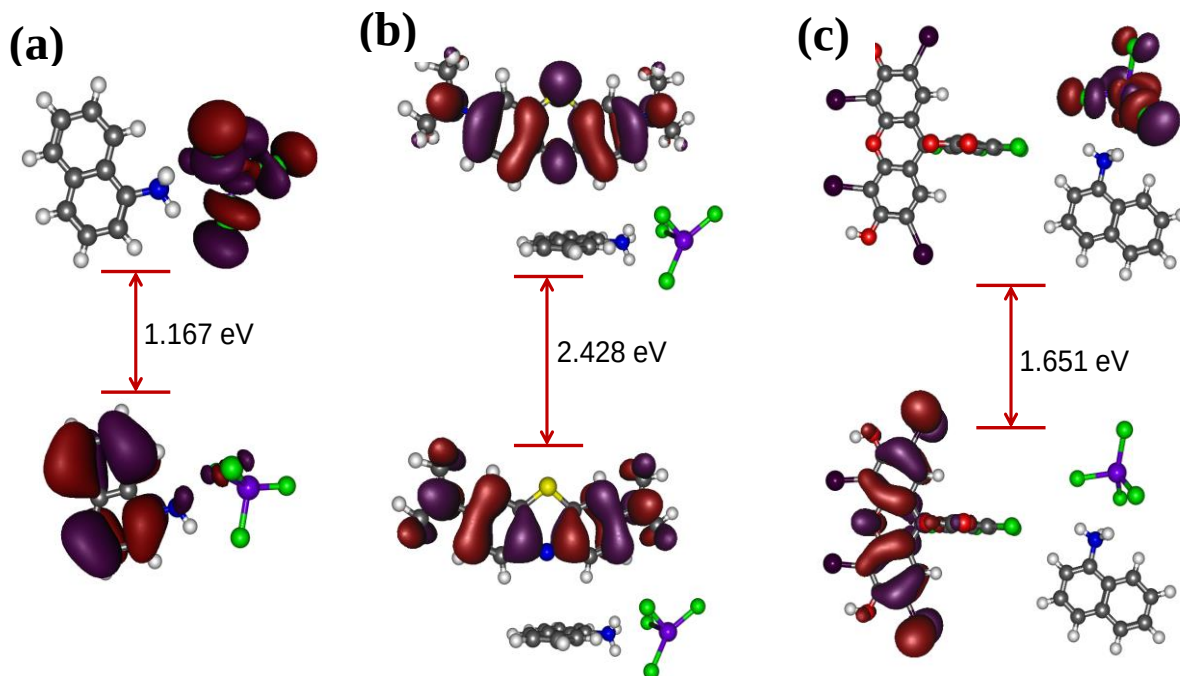


Figure 82: Calculated frontier orbital of IL (a) before complexation, (b-c) after complexation with MB and RB dye molecules

Other quantum chemical reactivity descriptors, which include global hardness (η), electronegativity (χ), and electrophilicity index (ω), were calculated and presented in **Table 18**. The resistance of a molecule to the distortion caused by electron density overlap is measured by its global hardness. According to the hard-soft acid-base (HSAB) theory, hard molecules exhibit lower reactivities due to their lower tendency to charge donation [240]. Electronegativity (χ), on the other hand, expresses the electron attraction capacity of a molecule. It indicates the possibility that a molecule retains its free electrons when interacting with other molecules. The electrophilicity index (ω) measures the stabilization energy of a molecule when it accepts electrons. Molecules that have a higher ω are

considered to be strongly electrophilic and do not form strong interactions with other molecules [241]. The results of quantum chemical reactivity calculations **Table 18** show that MB with lower values of 1.786 eV, 2.178 eV and 1.328 eV for η , χ and ω , respectively, has a higher adsorption tendency in the presence of the IL at neutral conditions, compared to RB with values of 2.042 eV, 4.344 eV and 4.621 eV, in good agreement with the experimental results.

Table 18: Quantum chemical reactivity descriptors of IL, MB, and RB molecules

Molecule	E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE (eV)	η (eV)	χ (eV)	ω (eV)
IL	-6.319	-5.152	1.167	0.583	5.735	28.19
MB	-3.964	-0.392	3.572	1.786	2.178	1.328
RB	-6.386	-2.303	4.084	2.042	4.344	4.621

The interaction of the IL and the dye molecules were simulated at the molecular level in the neutral, acidic, and basic media. The results are shown in **(Fig. 83)**. The simulations in the acidic medium were performed with the protonated forms of the molecules, while the calculations in the basic medium were performed with the deprotonated forms of the molecules. The corresponding adsorption energies are shown in **Table 19**. Interestingly, the IL in neutral medium showed higher affinity for MB with an adsorption energy of 13.2 kcal/mol, while the affinity for RB in acidic medium increased significantly with an

adsorption energy of 20.2 kcal/mol. The bond distances of the nearest atoms of the IL and the RB molecule in the acidic medium further showed a Lewis acid-base interaction as the bond distance, 2.806 Å, is smaller than the Van der Waals radii, 2.990 Å [242]. Therefore, the DFT simulation results showed a higher adsorption capacity of MB in neutral and basic media, while RB in acidic medium showed a higher adsorption capacity at IL, in good agreement with experimental data.

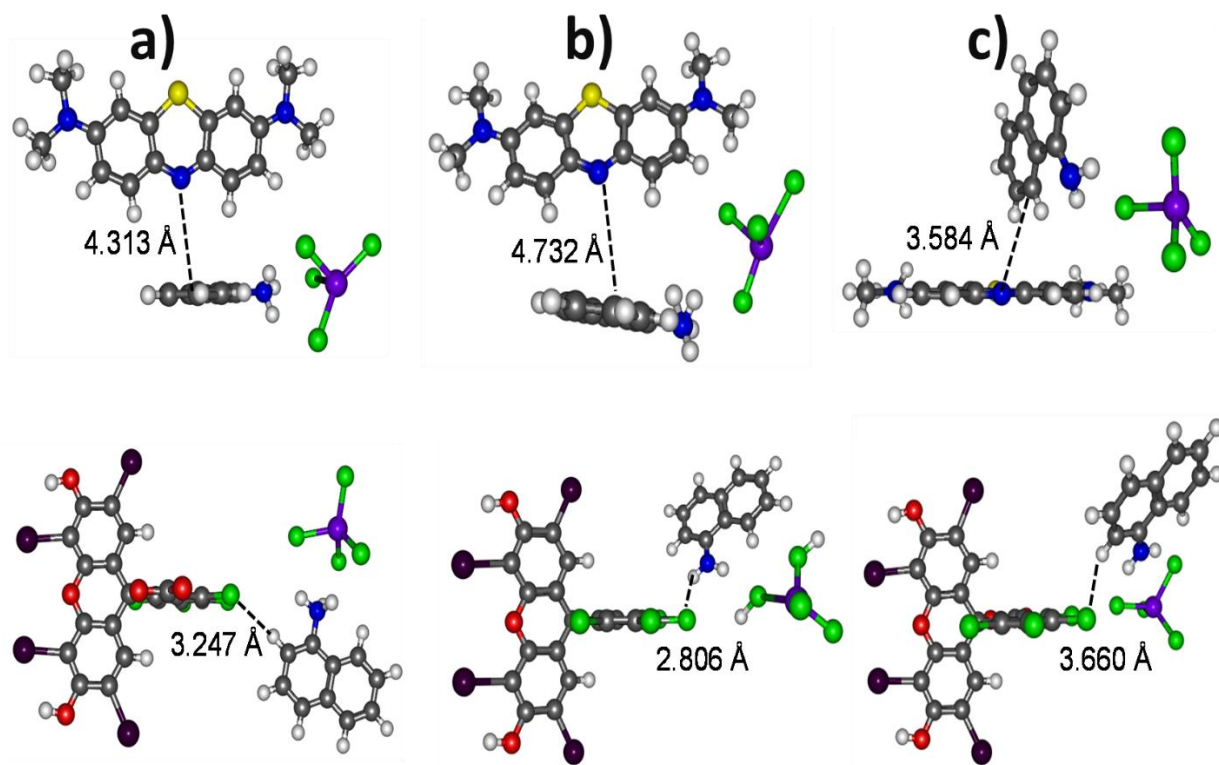


Figure 83: Molecular-level interactions of MB (top) and RB (bottom) in (a) neutral medium, (b) acidic medium and (c) basic medium

Table 19: Adsorption energies and binding distances of MB and RB on IL

Medium	Dye molecule	Adsorption energy (kcal/mol)	Binding distance (Å)
Neutral	MB	13.2	4.313
	RB	10.1	3.247
Acidic	MB	7.97	4.732
	RB	20.2	2.806
Basic	MB	15.6	3.584
	RB	15.1	3.660

7.3.2.8 Wastewater samples

The applicability and performance of the material IL was also tested in real wastewater samples. **(Fig. 84a and b)** show both dyes before and after treatment to compare the removal results with the batch equilibrium method. The two dyes were spiked into the wastewater and a remarkable removal percentage of 98% for RB and 87% for MB was obtained. The results of this study confirm that IL 1-naphthylammonium tetrachloroferrate (III) is a suitable material for the removal of MB and RB from wastewater and aqueous solutions.

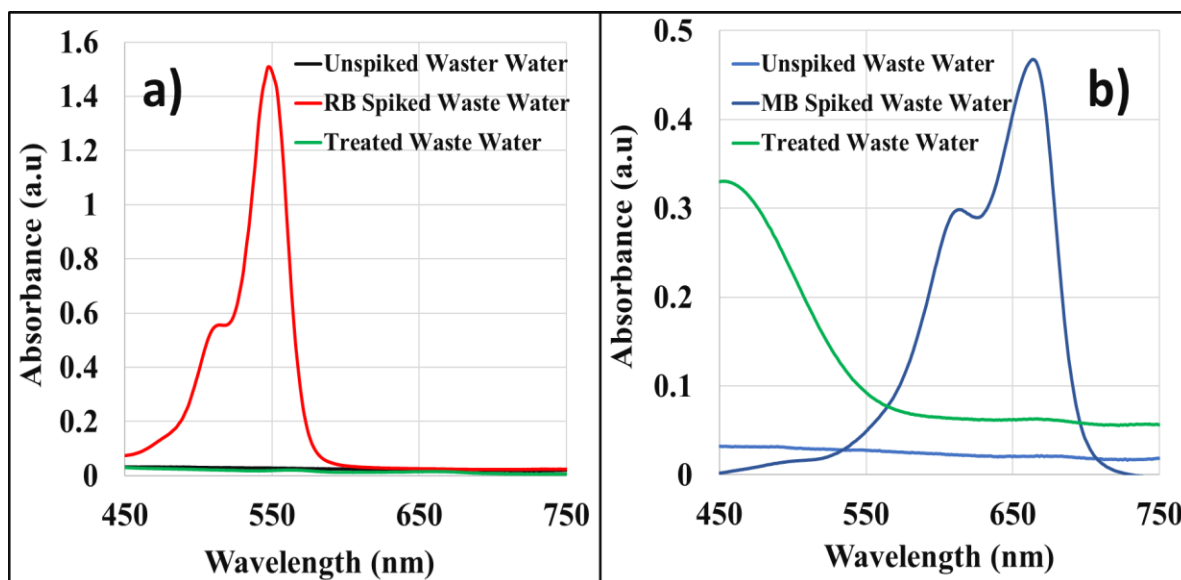


Figure 84: Real wastewater samples showing before and after treatment a) rose bengal b) methylene blue dyes.

7.3.2.9 Recycling and reuse of adsorbent

Recycling and reuse of adsorbents are important from a sustainability point of view. Furthermore, contaminated adsorbents can pose serious health hazards if not disposed of properly. Therefore, recycling of adsorbents is an industrially feasible, economically viable and environmentally friendly process. The recycling process used here consists of changing the pH of the medium, which was achieved by using 0.1 M NaOH and 0.1 M HCl. This pH-treated adsorbent could be recycled and reused up to 3 times without any significant decrease in adsorption capacity. However, a small loss of adsorbent was inevitable during the regeneration process. Atta *et al.* reported the fivefold use of crosslinked poly (ionic liquid) cryogels as adsorbents for the removal of MB [20]. Dang *et al.* also recently

demonstrated an efficient adsorbent of ionic liquids@TpBd-(SO₃)₂ for the removal of cationic dyes, which could be reused five times [243], and talc-coated ionic liquid-decorated Fe₃O₄@SiO₂ were reused four times as an efficient adsorbent for the removal of MB dye [244]. The mechanism of adsorption is detailed in the DFT simulations in **(Fig. 83)**. The electrostatic attraction between the negatively charged adsorbent particles and the positively charged MB enhances the interfacial diffusion of the dye to the surface of the active site of IL 1-naphthylammonium tetrachloroferrate (III) and vice versa in the case of RB. The desorption pathways of MB are attributed to the protonation of the particles, which reduces the attractive forces between the active sites of IL and the cationic MB, while deprotonation occurs in the case of the anionic RB.

After adsorption of the dyes, the solution was centrifuged again at 7500 rpm for 5 min and then carefully decanted. The adsorbent was desorbed with 10 mL of pH adjusted deionized water under sonication for 10 min. The pH was adjusted to 11 for RB and 2 for MB. The adsorbent was then separated by centrifugation for 5 min at 7500 rpm and the solution decanted. Finally, to confirm whether the desorption was complete and effective, a sample was taken from the solution and measured in a UV-Vis spectrophotometer. Most experiments showed excellent desorption of more than 95% in the case of RB. However, 85% was obtained in the case of MB. After desorption, the adsorbent can be rinsed several times with deionized water, dried in an oven at 40 °C overnight and used again.

7.3.2.10 Comparison of the material with other adsorbents

The adsorption efficiency of the adsorbent 1-naphthylammonium tetrachloroferrate (III) IL was compared with other adsorbents using Langmuir $Q_{\max}$ as it is the measure of the maximum adsorption capacity of the adsorbent. **Table 20** summarizes the comparison of the removal of the two dyes with the previous studies.

Table 20: Comparison of adsorption capacities $Q_{\max}$ in mg/g with other existing literatures

Methylene blue dye			Rose bengal dye		
Adsorbent	$Q_{\max}$ (mg/g)	Ref.	Adsorbent	$Q_{\max}$ (mg/g)	Ref.
Fe-BDC MOF	8.65	[245]	Amberlite Ira-938 resin	142.86	[246]
E. strobilacea char modified phosphoric acid (ESP)	21.93	[247]	Molecular imprinted chitosan-TiO ₂	79.37	[215]
Tea waste biochar and municipal sludge	12.58	[248]	Folic Acid-Polyaniline Hybrid Hydrogel	206.0	[228]
Graphene oxide hydrogel	7.85	[249]	Zinc chloride activated carbon	90.91	[250]
Neem leaf powder	8.76	[251]	<i>Myristica fragrans</i> Shells	5.31	[252]
Activated Carbon loaded with CuO	10.54	[253]	Modified Montmorillonite Clay	296.13	[254]
Talc sheets coated Ionic liquid decorated Fe ₃ O ₄ @SiO ₂	6.23	[244]	IL, 1-naphthyl ammonium tetrachloroferrate (III)	188.7	This work
IL, 1-naphthyl ammonium tetrachloroferrate (III)	9.52	This work			

7.4 Conclusion

In this work, an IL, 1-naphthylammonium tetrachloroferrate (III) was synthesized and used for the adsorption of MB and RB from aqueous solutions. The synthesis of 1-naphthylammonium tetrachloroferrate (III) was confirmed by the appearance of both cationic and anionic mass spectrometric fragments of the IL in electrospray ionization mass spectrometry analysis. Further characterization of the IL was carried out by FTIR, UV-Vis spectrometry, ^1H NMR analysis, TGA analysis, SEM /EDX, XRD and EPR analysis. The adsorbent IL showed equilibrium adsorption capacity (Q_e) of 6.443 mg/g and 20.70 mg/g and maximum adsorption capacity ($Q_{\max}$) of 9.52 mg/g and 188.7 mg/g for MB and RB, respectively. The kinetic studies showed that both dyes followed a pseudo-second order kinetic model with an R^2 value of 0.99. The theoretical DFT calculations performed using Gaussian 09 software showed a relatively high interaction and strong reactivity between the IL adsorbent and the anionic dye RB in acidic medium, while the cationic MB in neutral or near basic medium, which is in agreement with the experimental results. Based on the above findings, the 1-naphthylammonium tetrachloroferrate (III) IL has shown great potential as an adsorbent for the removal of RB and MB from water resources. Due to the degree of aromaticity in these dyes, it will be interesting if future studies consider incorporating more aromaticity into the IL structure. This will lead to strong π - π interactions in addition to the electrostatic interactions between the dyes and the adsorbent, which will most likely lead to fast adsorption kinetics and higher adsorption capacities.

CHAPTER 8

CONCLUSIONS

In this work, several ionic liquids containing cobalt and iron have been successfully synthesized, characterized, and used for various applications. The ionic liquid 4-methylbenzenaminium tetrachloroferrate (III) was prepared and used in stir bar assisted membrane protected micro solid phase extraction techniques coupled with GC-MS (SB- μ -SPE-GC-MS) for organochlorine pesticides (OCPs) from environmental water samples. The sorbent used was IL as it exists in solid phase below 65 °C. The porous polypropylene membrane reduces any interference and eliminates the need for additional sample cleanup steps. The technique is also environmentally friendly and cost effective as it reduces the consumption of organic solvents. Another advantage is the ease of preparation of the μ -SPE device. The extraction properties of IL 4-methylbenzenaminium tetrachloroferrate (III) are related to the formation of hydrophobic as well as electrostatic interactions with the target OCPs. SB- μ -SPE showed excellent performance in terms of analytical figures of merit. Our study suggests that this method has great potential for application in the analysis of OCPs in real samples.

The second part involved the development of a dispersive micro solid phase extraction coupled with high performance liquid chromatography (D- μ -SPE-HPLC-DAD) for the quantification and pre-concentration of the anticonvulsant carbamazepine in human urine and wastewater samples by comparing two ILs, one with cobalt ((Z)-octadec-9-en-1-

aminium trichlorocobaltate (II)) and one with iron ((Z)-octadec-9-en-1-aminium tetrachloroferrate (III)) as sorbent at room temperature. It was observed that (Z)-Octadec-9-en-1-aminium tetrachloroferrate (III) showed better extraction performance of CBZ from wastewater and urine samples, which may be related to both hydrophobicity and the advantage arising from the stable Fe complex with (d^6) compared to the unstable $D(z^2)$ orbital of Co(II) (d^7) in a low-spin. The method enabled simple, sensitive, efficient, and selective determination and quantification of the drug carbamazepine, with easy preparation of the sorbent and reduced consumption of organic solvents. This work creates a new direction for the application of tunable ILs as sorbents at ambient conditions for the extraction and quantification of complex trace contaminants and pharmaceutical products in the environment. The method was also found to be efficient in real sample application.

In another similar study in this work, the magnetic ionic liquids, (Z)-octadec-9-en-1-aminium tetrachloroferrate (III) sorbent is extended for the simultaneous preconcentration and determination of three different categories of pharmaceutical compounds such as clomipramine (antidepressants), ketoprofen (nonsteroidal anti-inflammatory drugs) and loperamide (antidiarrheal drugs) from wastewater and human urine samples. The method is economically favorable as three different drug classes are simultaneously pre-concentrated and quantified in 10 minutes retention time. Moreover, the developed method has a remarkable RSD % for all analytes and with reasonable LODs and linearity compared to relevant similar published works.

In the last part of this work, an ionic liquid (IL), 1-naphthylammonium tetrachloroferrate (III), was synthesized and used as an adsorbent for the removal of the dyes methylene blue (MB) and rose bengal (RB) from aqueous solutions, showing excellent adsorption capacity. The results showed that the two dyes were homogeneously adsorbed on the surface of the material and the adsorption kinetics followed the pseudo-second order kinetic model. The density functional theory calculation (DFT) also confirmed the experimental results and showed a high affinity and electrostatic interaction between the dyes and the adsorbent. The IL, 1-Naphthylammonium tetrachloroferrate (III) has shown great potential as an adsorbent for the removal of both anionic RB and cationic MB from real wastewater.

Finally, in the last part of this work, the applicability of the synthesized IL particles for D- μ -SPE-HPLC-DAD and SB- μ -SPE-GCMS as well as the adsorption of the cationic dye methylene blue and the anionic dye rose bengal from environmental and biological samples is investigated. The results of these studies show that cobalt- or iron-containing ionic liquids derived from simple amines can be successfully used as sorbents for various applications at room temperature and show excellent results. However, no OCPs were detected in wastewater, but when spiked, a low detection limit of 0.25 to 3.4 $\mu\text{g/L}$ was observed for the simultaneous determination of nineteen priority OCPs in SB- μ -SPE-GCMS. Similarly, a detection limit of 0.51 $\mu\text{g/L}$ was obtained for the drug carbamazepine in D- μ -SPE-HPLC-DAD. When a similar approach was extended to simultaneous extraction of the pharmaceutical compounds' clomipramine, ketoprofen and loperamide, the detection limit was 2.3 $\mu\text{g/L}$, 2.4 $\mu\text{g/L}$ and 2.9 $\mu\text{g/L}$, respectively. A removal capacity of 99% and 92% was also observed for rose bengal and methylene blue, respectively for the dye's adsorption study.

The exceptional performance recorded for most of the ILs synthesized in this work can be attributed to the hydrophobicity and polarity of the ionic liquids. Moreover, the ILs can be efficiently used for chromophore analytes as most of the synthesized particles show low adsorption range in UV-Vis, indicating a potential material for UV-Vis analysis, which is illustrated by the use of both cationic and anionic dyes as analytes. Chromatographic techniques such as LC and GC have also shown promising results. This work aims to extend the novelty in adsorption of heavy metals from real industrial wastewater and raw groundwater applications in the future and to investigate the efficiency of other amines.

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