DEVELOPMENT OF TEA-WASTE IMPREGNATED WITH IRON OXIDE NANOPARTICLES FOR MAGNETIC MICRO-SOLID PHASE EXTRACTION OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN WATER SAMPLES

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DEVELOPMENT OF TEA-WASTE IMPREGNATED WITH IRON OXIDE NANOPARTICLES FOR MAGNETIC MICRO-SOLID PHASE EXTRACTION OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN WATER SAMPLES

ABSTRACT

The presence of pharmaceutical compounds as well as their degradation products in the aquatic environment is of great concern. Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the major pharmaceutical products that may be present in environmental water samples. In this study, a simple method based on the magnetic micro-solid phase extraction (MMSPE) technique was developed for the determination of NSAIDs in water samples prior to the UV-Vis spectrophotometer analysis. A new tea waste-impregnated with magnetic nanoparticles (MNP-TW) was successfully synthesized by the chemical co-precipitation technique. The characterization studies were carried out by Brunauer–Emmett–Teller (BET), Fourier Transform Infrared Spectroscopy (FT-IR), X-Ray Diffraction (XRD), transmission electron microscope (TEM), field emission scanning electron microscopy with energy dispersive X-ray spectroscopy (FESEM-EDX), vibrating-sample magnetometry (VSM) and thermogravimetric analysis (TGA). MNP-TW was utilized as an MSPE sorbent for the extraction and determination of ibuprofen (IBP), diclofenac (DCF) and naproxen (NAP) separately. Experimental variables affecting the extraction efficiency of NSAIDs such as sample pH, sorbent dosage, extraction time, ionic strength, the volume of sample, type of desorption solvent, desorption time and desorption volume were studied and optimized in detail. Under the optimal conditions, the calibration curves were linear for the concentration ranging between 30 and 700 µg L^{-1} with the coefficient of determination (R^2) between 0.9964 to 0.9981. The limit of detection (LOD) was in the range from 10.30 to 11.70 µg L^{-1}, the limit of quantification (LOQ) was in the range from 31.20 to 35.40 µg L^{-1} and the method exhibited excellent precision (RSD ≤ 4.83%), repeatability (RSD ≤ 4.66%) and relative recovery (86% - 115%). The green assessment was conducted, and the Analytical eco scale score obtained from this method would be 77 which shows this method is neatly a green analysis. The method presented the advantages of the study which show that the integration of MNP-TW and MMSPE with UV-Vis spectrophotometer provides a simple, sensitive, and rapid method for the extraction and determination of NSAIDs in water samples. The usage of tea waste in the extraction process presents many advantages, as it is biodegradable and versatile, and it contributes to an intelligent and sustainable economic strategy projected toward a circular economy approach.

Keywords: Magnetic tea waste; Ibuprofen; Magnetic micro-solid phase extraction;
UV-Vis spectrophotometer; Green assessment

PEMBANGUNAN SISA TEH YANG DIRESAPKAN DENGAN PARTIKEL NANO FERUM OKSIDA UNTUK PENGEKSTRAKAN MIKRO FASA PEPEJAL MAGNETIK UBAT ANTI-RADANG BUKAN STEROID DI DALAM SAMPEL AIR

ABSTRAK

Kehadiran sebatian farmaseutikal serta produk degradasinya di dalam persekitaran akuatik amat membimbangkan. Ubat anti-radang bukan steroid (NSAID) ini adalah satu produk farmaseutikal utama yang mungkin terdapat dalam sampel air persekitaran. Oleh itu, dalam kajian ini, satu kaedah mudah berdasarkan teknik pengekstrakan mikro fasa pepejal magnetik (MNP-TW-MMSPE) telah dibangunkan untuk penentuan sebatian NSAID dalam sampel air sebelum analisis menggunakan spektrofotometer UV-Vis. Nanopartikel magnetik novel yang diresapi dengan sisa teh (MNP-TW) telah berjaya disintesis dengan menggunakan teknik pemendakan bersama kimia. Kajian pencirian telah dijalankan oleh analisis Brunauer–Emmett–Teller (BET), Spektroskopi Inframerah Transformasi Fourier (FT-IR), Pembelauan Sinar-X (XRD), Mikroskopi Elektron Transmisi (TEM), Mikroskopi Elektron Imbasan Dengan Penyebaran Tenaga Sinar-X (FESEM-EDX), Magnetometer Sampel Bergetar (VSM) dan Analisi Termogravimetrik (TGA). MNP-TW digunakan sebagai bahan penyerap bagi teknik MMSPE untuk pengekstrakan dan penentuan ibuprofen (IBP), diklofenak (DCF), dan naproxen (NAP) secara individu. Pembolehubah ekeperimen yang mempengaruhi kecekapan pengekstrakan NSAID seperti pH sampel, dos penyerap, masa pengekstrakan, kekuatan ion, isipadu sampel, jenis eluen, masa nyahjerapan dan isipadu nyahjerapan telah dikaji dan dioptimumkan secara terperinci. Di bawah keadaan optimum, lengkung penentukuran adalah linear untuk kepekatan antara 30 dan 700 µg L^{-1} dengan pekali penentuan (R^2) antara 0.9964 hingga 0.9981. Had pengesanan (LOD) berada dalam julat dari 10.30 hingga 11.70 µg L^{-1}, had kuantifikasi (LOQ) berada dalam julat dari 31.20

hingga 35.40 µg L^{-1} dan kaedah ini menunjukkan ketepatan yang sangat baik dengan (RSD ≤ 4.83%), kebolehulangan (RSD ≤ 4.66%) dan kebolehdapatan semula (86% - 115%). Penilaian hijau telah dijalankan, dan skor skala eko analitik yang diperoleh daripada kaedah ini ialah 77 yang menunjukkan kaedah ini adalah analisis hijau. Kaedah ini membentangkan kelebihan kajian yang menunjukkan bahawa gabungan MNP-TW-MMSPE dengan spektrofotometer UV-Vis menyediakan kaedah yang mudah, sensitif, dan pantas untuk pengekstrakan dan penentuan NSAID dalam sampel air. Penggunaan sisa teh dalam proses pengekstrakan memberikan banyak faedah dan kelebihan, kerana ia boleh terbiodegradasi dan ia menyumbangkan kepada strategi pintar dan mampan yang diunjurkan ke arah pendekatan ekonomi kitaran.

Kata kunci: Sisa teh magnetik; NSAID; Pengekstrakan mikro fasa pepejal magnetik; Spektrofotometer UV-Vis; Penilaian hijau

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LIST OF ABBREVIATIONS

λ	: Lambda (wavelength)
AA-EQS	: Annual average ecological quality standards
AASHVG-1	: Atomic absorption spectrophotometer hydride vapor generator
ACN	: Acetonitrile
BaA	: Benzo[a]anthracene
BaP	: Benzo[a]pyrene
BbF	: Benzo[b]fluoranthene
C	: Carbon
CapLC-DAD	: Capillary Liquid Chromatograph (caplc) with Diode Array Detection
CAR	: Carbaryl
Chr	: Chrysene
Cl	: Chlorine
COX-1	: Cyclooxygenases-1
COX-2	: Cyclooxygenases-2
CTAB	: Cetyltrimethylammonium bromide
DCF	: Diclofenac
DF	: Dilution factor
DI	: Deionized water
d-MSPE	: Dispersive magnetic solid phase microextraction
DNA	: Deoxyribonucleic acid
DTA	: Differential thermal analysis
EDX	: Energy-dispersive X-ray

EF	:	Enrichment factor
ERY	:	Erythrosine
FAAS	:	Flame atomic absorption spectroscopy
FESEM	:	Field emission scanning electron microscopy
FT-IR	:	Fourier transform infrared spectroscopy
GC-FID	:	Gas chromatography-flame ionization detection
GC-MS	:	Gas chromatography-mass spectrometry
GHS	:	Globally Harmonized System of Classification and Labelling of Chemicals
H	:	Hydrogen
HF-SLPME	:	Hollow Fibre Solid-Liquid phase Microextraction
HPLC	:	High-performance liquid chromatography
HPLC/UV	:	High-performance liquid chromatography-ultraviolet
HPLC-DAD	:	High-Performance Liquid Chromatography with photodiode-array detection
IBP	:	Ibuprofen
ICP-AES	:	Inductively coupled plasma atomic emission spectroscopy
ICP-MS	:	Inductively coupled plasma mass spectrometry
JCPDS	:	Joint Committee on Powder Diffraction Standards
LC-MS	:	Liquid chromatography-mass spectrometry
LC-TOF	:	Liquid chromatography time-of-flight mass spectrometry
LLE	:	Liquid-liquid extraction
LOD	:	Limit of detection
LOQ	:	Limit of Quantification
LPME	:	Liquid-phase microextraction

m-d-µ-SPE	:	Magnetic-based dispersive micro-solid phase extraction
ME	:	Microextraction
MeOH	:	Methanol
Mins	:	Minutes
MMSPE	:	Magnetic micro-solid phase extraction
MNP	:	Magnetic nanoparticles
MNP-TW	:	Magnetic nanoparticles modified with tea waste
MSPE	:	Magnetic Solid Phase extraction
MSPE-Bio-DLLME	:	Magnetic Solid Phase extraction-biosorption based dispersive liquid-liquid Microextraction
N	:	Nitrogen
NAP	:	Naproxen
NM	:	Nano material
NP	:	Nano particles
NSAIDs	:	Non-steroidal anti-inflammatory drugs
O	:	Oxygen
PAH	:	Polycyclic aromatic hydrocarbons
PF	:	Preconcentration factor
PGHS	:	Prostaglandin-endoperoxide synthase
PNEC	:	Predicted effect concentrations
RSD	:	Relative standard deviations
SD	:	Standard deviations
FESEM	:	Field emission scanning electron microscopy
SPE	:	Solid phase extraction
SPME	:	Solid phase microextraction

TEM	:	Transmission electron microscopy
TGA	:	Thermogravimetric analysis
TW	:	Tea waste
UADSPME	:	Ultrasound-assisted dispersive Solid Phase Microextraction
UAMDSPME	:	Ultrasound-assisted magnetic dispersive solid-phase Microextraction
UHPLC-DAD	:	Ultra-high-performance liquid chromatographic-diode array
UPLC-MS	:	Ultra-performance liquid chromatography - tandem mass spectrometer
USEPA	:	United states environmental protection agency
UV-Vis	:	Ultraviolet–visible
VSM	:	Vibrating-sample magnetometry
w/w	:	Weight per weight
WFD	:	Water framework directive
XRD	:	X-Ray diffraction analysis

CHAPTER 1: INTRODUCTION

1.1 Background of study

A class of medications known as non-steroidal anti-inflammatory drugs (NSAIDs) is one of the most popularly used (over-the-counter) drugs, to treat pain, fever, and inflammation in both animals and humans due to their analgesic, antipyretic, anti-inflammatory, and other effects (Bindu et al., 2020). NSAIDs work by inhibiting specific enzymes; namely cyclooxygenases (COX-1 and COX-2), which participate in the release of prostaglandins by injured cells (Omran, 2013). Acute overdose or long-term usage can result in significant adverse effects including ulcers, gastrointestinal bleeding, renal failure, and aplastic anaemia (Eslami et al., 2015).

NSAIDs which are the “emerging” or “new” unregulated pollutants have become an environmental concern. NSAIDs are easily introduced into water systems due to their strong hydrophilicity, low adsorption coefficients and high stability and persistence (Wang et al., 2017). Even in very low quantities, these pollutants might endanger aquatic ecosystem and human health since they can enter the environment through diverse paths, including the disposal of excess medications, patient excretion, effluent from pharmaceutical manufacturing industries, and hospital waste (Sebok et al., 2008).

Unfortunately, there are still high concentration (ng L^{-1} to µg L^{-1} level) of NSAIDs found in the effluent in wastewater treatment plants (WWTP) due to incomplete removal of drugs from the effluent water (Hunter et al., 2011; Mohd Hanafiah et al., 2022). Continuous exposure to these bio-accumulative compounds would harm aquatic life and pose a risk to human health and fish-eating animals (Shahhosseini et al., 2021; Wang et al., 2017). In recent years, previous studies (Abd Rahman et al., 2016; Larsson et al., 2014; Li et al., 2013; Matongo et al., 2015; Mohd Hanafiah et al., 2023; Mohd Hanafiah et al., 2022) Nosek et al., 2014) have reported the timeline series of NSAIDs concentrations found in Malaysian influent wastewater which were greater compared to other countries such as South Africa, Sweden, China, Algeria and Poland.

These compounds are exempt from the regulations. On a variety of criteria, different countries have different approaches to policy creation, regulatory enforcement, and implementation (Abd Rahman et al., 2016). The United States Environmental Protection Agency (USEPA) is instrumental in establishing and enforcing drinking water regulations to guarantee the provision of safe, clean drinking water for the American population. Their efforts contribute to the prevention of waterborne diseases and the protection of public health. USEPA is considering some medications as prospective candidates to be added to the list of prioritized organic pollutants in drinking water, such as diclofenac (Manzo et al., 2014; Mi et al., 2020; Wang et al., 2017).

A recent study revealed the presence of NSAIDs in river water and treated water at Selangor at µg L^{-1} level (Mohd Hanafiah et al., 2023; Mohd Hanafiah et al., 2022; Praveena et al., 2018). This has proved that these drugs exist in the current urban water cycle, which could induce adverse effects on humans and the environment (risk quotient in high and low-risk categories). These pollutants should be considered as a priority to be monitored, in the environment to protect human health, aquatic diversity, and the environment's water health. However, direct NSAIDs determination is typically unachievable due to the trace level concentration and severe matrix effects of the samples. Therefore, sample pretreatment techniques are very much crucial before measurement (Liu et al., 2019). Several extraction techniques were applied to NSAIDs, including liquid-liquid extraction (LLE), solid-phase extraction (SPE), etc. SPE is the sample pre-treatment technique that is employed most among these approaches. However, the conventional SPE method typically consumes a high volume of toxic samples, sorbents and organic solvents, suffers from a significant matrix effect, and has a limited rate of diffusion (Wang et al., 2017). Besides, SPE requires expensive sorbents, a time-consuming, multi-step experimental process and the generation of a high amount of waste (Emiroğlu et al., 2021; Liu et al., 2019; Ravi & Sundararaman, 2020; Wang et al., 2017).

Magnetic solid-phase extraction (MSPE) seems to be the mostly preferred analytical approach in sample preparation based on the use of magnetic sorbent. The development of the MSPE is based on the employment of adsorbents that can be magnetized. Applying an external magnetic field would make it simpler to separate and retrieve the magnetic components without the use of filtration or centrifugation. This method simplifies and expedites the separation process. On the other hand, this swift separation reduces the contact time between the sample matrix and the sorbent, minimizing the risk of particle aggregation and subsequent back pressure. As of now, pre-concentration and separation are two areas where MSPE shows a great deal of promise (Emiroğlu et al., 2021; Liu et al., 2019; Wang et al., 2017). In this technique, the increased efficiency allows for the extraction of a higher proportion of the target analytes, reducing the need for extensive sample processing and minimizing potential sources of back pressure (Han et al., 2019).

Many efforts have been made to develop micro-extraction (ME) techniques as an alternative to conventional extraction procedures. This technique offers advantages such as minimal sample requirements, reduced solvent consumption, enhanced sensitivity, fast extraction processes, compatibility with small-scale systems, versatility, high selectivity, cost-effectiveness, ease of automation, and adherence to green chemistry principles. These benefits make microextraction valuable tools in modern analytical chemistry (Armenta et al., 2015; Gałuszka et al., 2012; Racamonde et al., 2015). In addition, small sample volumes, making them suitable for situations where sample availability is limited. This can be crucial when dealing with precious or rare samples. In this context, the use of natural sorbents represents an additional and convenient option for green method sample preparation. The advantages of using natural sorbents for extraction include their wide availability from renewable sources, low toxicity, and biodegradability. The use of surpluses of natural products as raw materials for the preparation of new sorbents is an interesting contribution of analytical chemistry to change the production model. Therefore, in this study, a simple and fast magnetic micro-solid phase extraction (MMSPE) method was employed using tea waste impregnated with magnetic nanoparticles as a sorbent to extract NSAIDs from water samples.

Black tea is the most consumed beverage worldwide. In 2008, the annual production of dried tea was 3.75 million tonnes. Average tea consumption per person per year worldwide stands at 0.5 kg, which amounts to consumption of an estimated 150 litres per year or 500 mL per person per day. Black tea is particularly rich in polyphenol compounds. In this study, tea waste has been largely used due to some factors such as low cost, easily obtained, greater surface area, reduced disposal cost, and high sorption affinity (L. Liu et al., 2018; Mondal, 2009). Furthermore, tea waste was focused in this study because it contains low molecular mass polyphenols known as “theaflavins” that have lots of aromatic rings which could facilitate the adsorption of analytes (Amarasinghe & Williams, 2007; Drynan et al., 2010; Kabir et al., 2021; Weng et al., 2014).

Carboxylate, aromatic carboxylate, phenolic hydroxyl, and oxyl groups are the major responsible functional groups. The exploration of magnetic nanoparticles, specifically those modified with tea waste, as adsorbents for extracting and detecting pharmaceutical drug pollutants is an area that has not received extensive attention. While existing research has predominantly concentrated on their application in environmental remediation for pollutant removal, the investigation into their potential use in the extraction and determination of pharmaceutical drug pollutants remains relatively limited

(Inbaraj et al., 2021; Lunge et al., 2014; Panneerselvam et al., 2011; Wen et al., 2017). Thus, this study dealt with the application of tea waste impregnated with magnetic nanoparticles (MNP-TW) from kitchen waste as the adsorbent for magnetic micro-solid phase extraction technique (MNP-TW-MMSPE) which was developed for the extraction of NSAIDs species including ibuprofen (IBP), diclofenac (DCF) and naproxen (NAP) in water samples prior to Ultraviolet-Visible spectrophotometer analysis. MNP-TW was found to be eco-friendly in nature, cost-effectiveness, waste valorization, renewability, tailored surface chemistry, high surface area, magnetic responsiveness, reduced environmental impact, enhanced analyte recovery, and versatility. These advantages make them attractive for sustainable and efficient sample preparation in analytical chemistry (Drynan et al., 2010; Lunge et al., 2014). Furthermore, the magnetic properties of the adsorbents allow for efficient recovery of analytes during the separation step, reducing the likelihood of analyte loss and improving the overall sensitivity, thus omitting the sample clean-up procedure, and lessens sample preparation time. The extraction parameters such as the amount of adsorbent, extraction time, ionic strength, type of eluent, desorption time, the volume of desorption solvent, sample volume and sample pH were optimized comprehensively. At optimum conditions, the developed method (MNP-TW-MMSPE) collectively contributes to the extraction analysis, making a valuable technique in analytical chemistry and was successfully applied to water samples for the extraction of NSAIDs.

1.2 Problem statement

According to Malaysian Statistics on Medicine (MSOM), NSAIDs were considered the top 50 most utilized drugs from 2015 to 2016. The increment in statistics was attributed to large drug consumption by the household community for chronic diseases such as hypertension, diabetes, cardiovascular disease, and cancer. Studies have found that 90% of Ibuprofen would be metabolized in the human body after 24 hours of oral administration. Approximately, 1-12% of the drug is expected to be excreted in the form of the parent compound and other significant metabolites. These compounds have the potential to accumulate in sewage treatment plants, given the elevated usage within the community. (Mohd Hanafiah et al., 2022).

The sources of NSAIDs in the water body cycle can be originated from pharmaceutical industries, hospitals, direct disposal from remaining medicines, aquaculture, and agriculture. However, wastewater from sewage treatment plants (STP) is considered the primary source as they are the centre of water collection from the nearby household community.

By narrowing the scope of NSAIDs investigation in Malaysia, surprisingly NSAIDs are detected in Malaysian influent wastewater treatment plants, 10 folds higher compared to other countries like China, Sweden, Poland, and Algeria. At Johor, ibuprofen was detected in influent water at the concentration of (1.03×10^2 to 7.69×10^2 ng L^{-1}) (Mohd Hanafiah et al., 2023). This reveals the inadequate attention has been paid, likely lack of comprehensive monitoring programs specifically targeting NSAIDs in water systems. Limited data on the occurrence and concentrations of these pharmaceuticals in Malaysian waters can contribute to the perception that they are not a significant environmental concern. Surface water such as river water is widely used as a primary resource for drinking (Mohd Hanafiah et al., 2022). Since NSAIDs can accumulate in the human body through consumption, their analysis is essential to ensure optimizing therapeutic outcomes, ensuring patient safety, preventing overdoses, individualizing treatment plans, managing drug interactions, monitoring renal function, promoting treatment compliance, and advancing pharmacokinetic research.

Hence, accurate quantitative analysis is crucial, leading to the development of methods like gas chromatography, liquid chromatography, capillary electrophoresis, voltammetry, and mass spectroscopy. Combinations of these techniques are also viable, but challenges may arise with increased equipment costs and the need for specialized expertise. Conversely, UV-Vis spectrophotometers, being widely accessible, offer rapid and cost-effective results with ease of use. However, their lower sensitivity necessitates the incorporation of pre-concentration-separation techniques for precise and accurate measurements (Duman et al., 2020).

Different sample preparation techniques and separation methods have been developed and reported for NSAID determination. Among the sample preparation techniques, the magnetic solid phase extraction (MSPE) technique stands out as the most preferred. Recent advances in magnetic nanoparticles (MNPs) have been widely developed for NSAID extraction. However, pristine MNPs usually suffer from non-specific adsorption, aggregation issues leading to decreased efficiency, magnetic interference affecting signal clarity, limited loading capacity for certain analytes, variability in magnetic properties impacting reproducibility, and the influence of sample matrix effects on extraction efficiency. Despite these drawbacks, ongoing research aims to address these issues, enhancing performance and broadening the applicability of pristine MNPs in MSPE analysis. To overcome these issues, various types of functionalized carbon materials have been designed and incorporated into magnetic particles to satisfy the applications (Hsen & Latrous, 2023). However, most of these adsorbents are tuned with a focus on their affinity towards target analytes (Hsen & Latrous, 2023). Herein, to maximize the extraction process, the efficiency and selectivity, a low-cost adsorbent were studied.

Based on the literature review, in the year 2011, Malaysia was ranked the 18th largest tea producer in Asia with 0.45% of the world's total tea production by the Food and Agriculture Organization of the United Nations. On average, for every 22 kg of tea production, 4 kg (18%) of tea will contribute to waste generation. This tea waste contains a high value of nitrogen and carbon chemicals, and they are oxygen-demanding pollutants, that take a longer time for biodegradation. On the other hand, tea leaves are made up of components that are rich in functional groups such as carboxylate, aromatic carboxylate, phenolic hydroxyl and oxyl groups. The polymer framework of cellulose-based materials exhibits a robust chemical adsorption affinity for acidic or anionic compounds. This characteristic makes them a prime candidate as a potential adsorbent, specifically chosen for their ability to attract NSAIDs (Atirah Mohd Nazir et al., 2020; Panneerselvam et al., 2011; Pua et al., 2020).

Time-consuming traditional extraction techniques have been replaced with microextraction techniques (ME). ME is more effective in separation and enrichment, which requires less solvent, is well suited for automation, and has shorter extraction steps. ME supports green chemistry, allows simultaneous separation and enrichment, and is simple to use on small and complex materials. Additionally, it has improved the preconcentration factor, recovery value, speed, accuracy, and precision (Duman et al., 2020).

To comprehensively address the issues, this study is systematically conducted. We hope the findings in this study can be a preliminary benchmark or added value of a new method for the analysis of NSAIDs in water samples. In addition, we anticipate that the study outcomes provide insight and awareness of monitoring NSAIDs in environmental water samples considering public health.

1.3 Scope of research

This study involves the application of tea waste impregnated with magnetic nanoparticles, namely magnetic nanoparticles tea waste (MNP-TW) which combines the merits of tea waste, and magnetic nanoparticles. It is important to highlight the rationality for such a design and impregnation of the nanoparticles since different moieties possess properties that contribute to extraction efficacy. For this, tea waste is chosen instead of other low-cost adsorbents due to its low cost, active, abundant, accessible, and environmentally friendly nature. In addition, the insoluble cell walls with fibrous content are largely made up of cellulose-based structural proteins. A high response surface of the functional groups and active sites is also present. Meanwhile, tea waste impregnated with magnetic nanoparticles makes the nanoparticles separate easily by employing an external magnetic field, improving the adsorption capacity by its large specific surface area. The synthesized nanoparticles are expected to exhibit unique properties such as high surface area and superparamagnetism.

The successful synthesis of these nanoparticles was confirmed by various characterization techniques such as Brunauer–Emmett–Teller (BET), Fourier transform infrared (FTIR), elemental analysis, vibrating sample magnetometer (VSM), scanning electron microscopy (SEM), transmission electron microscopy (TEM), x-ray powder diffraction (XRD) and thermogravimetric analysis (TGA). Thereafter, it was applied in magnetic micro-solid phase extraction technique for the determination of NSAIDs in water samples using a UV-Vis spectrophotometer.

1.4 Objectives of research

The objectives of this study are as follows:

1. To synthesize the tea waste impregnated with magnetic nanoparticles (MNP-TW) and compare the physicochemical properties of MNP-TW with pristine MNP.
2. To develop, optimize, evaluate, and validate the MNP-TW-MMSPE method for the determination of selected NSAIDs using UV-Vis Spectrophotometer.
3. To access the validated MNP-TW-MMSPE method for the determination of selected NSAIDs in water samples using a UV-Vis Spectrophotometer.

1.5 Organization of the thesis

This thesis is constructed into five chapters. Chapter 1 contains the background of the study, the problem statement, the scope of research, the objectives of the research, and the organization of the whole thesis. The literature review is summarized in Chapter 2. Chapter 3 discusses the experimental procedures done throughout this project. It is subdivided into five parts. In part one, details encompassing the chemicals, materials, reagents, and instruments employed are presented. Subsequently, part two delves into the preparation, applications, method validation, real sample applications, and the green assessment analysis of the proposed method, MNP-TW-MMSPE. Chapter 4 consists of the results and discussions. Characterizations of MNP-TW, optimizations of eight parameters and analytical performances are discussed in Chapter 4. Chapter 5 is about the conclusions and future recommendations.

CHAPTER 2: LITERATURE REVIEW

2.1 Non-steroidal anti-inflammatory drugs (NSAIDs)

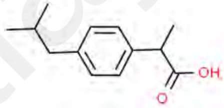
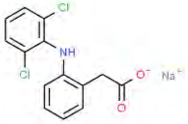
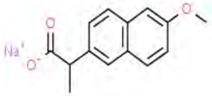
Non-steroidal anti-inflammatory drugs (NSAIDs) are substances that are other than steroids that can inhibit the inflammatory cascade components (Moses & Bertone, 2002). They are commonly used to treat inflammation, fever and pain (Asirvatham et al., 2019). The first NSAID that was introduced in 1899, aspirin (acetylsalicylic acid) was not called as anti-inflammatory agent because anti-inflammatory treatment in rheumatology practice was not clinically demonstrated at that time. In 1949, cortisone emerged and showed its anti-inflammatory properties which result in the term "non-steroidal anti-inflammatory drug" being used for the first time when phenylbutazone was introduced in 1952 (Bindu et al., 2020). At present, NSAIDs are grouped as the major derivatives of salicylic acid, acetic acid, enolic acid, anthranilic acid or propionic acid. Concurrent with the development of scientific knowledge, the classification has also been revised based on their selectivity for inhibiting cyclooxygenase/prostaglandin-endoperoxide synthase (PGHS) enzymes for which these medications are mostly intended (Bindu et al., 2020). NSAIDs possess similarities in their structure, which are the acidic moiety, either enols or carboxylic acid and the planar aromatic ring. The acidic group in NSAIDs plays an important role in exerting their therapeutic effect by cyclooxygenase inhibition. The presence of acidic moiety causes them to be generally stronger acids. The lipophilicity differences of NSAIDs are affected by the lipophilic character of the aryl group and substituents present in the structure of NSAIDs (Asirvatham et al., 2019; El-Sheikh et al., 2019; Manrique-Moreno et al., 2009; Neuvonen, 1991). **Table 2.1** shows the NSAIDs chosen for this study, their properties, and their molecular structure. These NSAIDs were primarily chosen as many studies reported the detection of these major compounds at high concentration and as their prescription for medication is quite popular among society.

NSAIDs have been known as “contaminants of emerging concern” (CEC) that causes pollution in aquatic systems (Choina et al., 2013; Tyumina et al., 2020). The concentration of NSAIDs detected in wastewater typically has higher concentration than that of surface water and groundwater. Due to the natural processes of photolysis, biotransformation, dispersion, volatilization, and sorption, the concentration of NSAIDs in surface water and groundwater is typically lower (Izadi et al., 2020). However, the presence of NSAIDs in water has exerted acute and chronic toxic effects on the organisms. It had been reported that organisms experienced problems such as reproduction disorder, endocrine disruption, locomotive disorder, body deformations, genotoxicity and teratogenic effects due to bioaccumulation (Hejna et al., 2022; Lonappan et al., 2016; Parolini, 2020; Wang et al., 2021; Wojcieszyńska & Guzik, 2020). The reported Annual Average Ecological Quality Standards (AA-EQS) and Predicted Effect Concentrations (PNEC) in freshwater for ibuprofen are both 10 ng L^{-1}. AA-EQS are concentrations where substances must be kept below for a given year to minimize environmental impact and for the water to be considered “good” at the Water Framework Directive classification point. Meanwhile, PNECs are concentrations where the substance is unlikely to cause short or long-term effects. These guidelines are based on half maximal effective concentration (EC50s) and lethal concentration (LC50s), which assume that most invertebrates will experience negligible lethal effects when pharmaceutical concentrations in the environment are below these levels. However, sub-lethal effects on organisms can still happen even at low concentrations (Hunter et al., 2011).

NSAIDs are notorious for causing oxidative stress, which manifests as changes in the enzymatic activity of compounds known to be antioxidants and/or in the transcription of genes linked to antioxidant/detoxifying pathways. Induction of irreversible DNA damage and cytological alterations that raise the likelihood of cancer development and even affect the genomic stability of entire populations are both thought to be primarily caused by oxidative stress (Wang et al., 2017). According to the studies addressed in this review, NSAID concentrations found in the environment may seriously harm aquatic habitats, which could affect socioeconomic concerns related to the aquatic industry, fisheries industry and sustainability (Świacka et al., 2021). Some NSAIDs, such as diclofenac are being classified by the United States Environmental Protection Agency (USEPA) as potential threats to be included in the list of prioritized organic pollutants in drinking water (Manzo et al., 2014). However, most Asian countries especially Malaysia have not established any standards or regulations on the safe levels of NSAIDs concentration that can be present in environmental water bodies, despite numerous studies have been conducted on the detection and occurrences.

The environmental ubiquity of pharmaceuticals has stimulated a lot of societal and global concerns which differ from country to country depending on the extent of consumption and monitoring.

Table 2.1: List of NSAIDs chosen for this study, their properties, and their molecular structure.

Order	NSAIDs	Chemical Formula	Molecular weight (g mol^{-1})	pKa	Log kOw	Molecular structure
1	Ibuprofen	$C_{13}H_{18}O_2$	206.3	4.52	3.50	
2	Diclofenac	$C_{14}H_{11}Cl_2NO_2$	296.1	4.00	1.90	
3	Naproxen	$C_{14}H_{14}O$	230.2	4.15	3.18	

2.1.1 Occurrences of NSAIDs in environmental water samples

There are two types of sources for NSAIDs in water: point sources and non-point sources. Some point sources of water pollution caused by the presence of NSAIDs are wastewater from industrial, hospital, and wastewater treatment plants and septic systems. However, runoff water is one of the non-point sources of NSAID-related water pollution. As the wastewater treatment plant is designed to remove mainly the degradable organic compound, it was found ineffective to remove the NSAIDs completely (Patel et al., 2019). Water contamination is caused by human excretion, flushing unwanted NSAIDs down the sinks and toilets, and dumping raw and treated waste containing NSAIDs from factories and hospitals. Water pollution can also be caused by the leachate from a septic tank that contains residential waste. The seepage of NSAIDs into soil and water can occur when household or other waste is deposited in a landfill. Moreover, NSAIDs may leak or flow into water from the livestock waste and the use of sewage sludge as fertilizer in agriculture (Li, 2014; Rzymski et al., 2017). Additionally, because of their strong polarity and solubility, they can bypass conventional wastewater treatment facilities and be released as effluents into environmental water bodies.

In recent years, the monitoring of intact pharmaceuticals in river water and wastewater treatment plants (WWTPs) received most of the attention. In 2020, diclofenac, naproxen, and ibuprofen were the three NSAIDs that were most frequently prescribed in Malaysia's primary healthcare sectors (Hwong et al., 2020). However, studies have shown that these most prescribed NSAIDs in 2020 were also the most detected in Asian environmental water samples in previous years (2014 - 2021). **Table 2.2** shows some key studies and ecological assessments conducted on the determination of NSAIDs in environmental water samples at Asian countries. As shown in **Table 2.2**, the concentrations of NSAIDs found in water samples in large population countries like Pakistan and India were in the range of 10 – 140 µg L^{-1}. In that list, a recent study published by (Mohd Hanafiah et al.,

2023) has recorded an alarming scenario where NSAIDs were detected in the range of 14.70 – 27.60 µg L^{-1} in the urban water cycle and commercial areas near Selangor, Malaysia. Therefore, based on the concern about the NSAID concentration in Malaysia and its potentially toxic effects on the organisms, these three NSAIDs are chosen as analytes for this study. Hence, it is essential to establish an analytical approach that is suitable for onsite monitoring, sensitive, less laborious, selective, and reliable for NSAIDs residue detection and quantification in water samples for both environmental monitoring and risk assessment.

Table 2.2: Maximum concentrations (µg L^{-1}) of NSAIDs found in Asian environmental water samples.

NSAIDs	Country	Location	Sampling year	Concentration (µg L^{-1})	Reference
Acetaminophen	India	Brahmaputra River	2017	1.50	(Kumar et al., 2019; Subedi et al., 2017)
	Pakistan	WWTP, Lahore City	2019	12.80	(Ashfaq et al., 2019)
	Singapore	WRP	2015	0.73 – 1.38	(Tran & Gin, 2017)
	Pakistan	Lahore Canal WWTP, Lahore	2015	23.81 – 27.90	(Ashfaq et al., 2017; Khan et al., 2018)
Naproxen	India	Lahore Canal	2015	140.00	(Ashfaq et al., 2019)
	Singapore	WRP	2015	2.10 – 2.50	(Tran & Gin, 2017)
Diclofenac	Pakistan	WWTP, Lahore	2014	0.91 – 72.00	(Ashfaq et al., 2017)
	Malaysia	Commercial area in Selangor	2020	27.60	(Mohd Hanafiah et al., 2022)
	Malaysia	Urban water cycle in Selangor	2021	24.90	(Mohd Hanafiah et al., 2023)
Ketoprofen	Pakistan	Lahore Canal	2015	0.068	(Ashfaq et al., 2019)
Ibuprofen	Singapore	WRP	2015	0.87 – 1.07	(Tran & Gin, 2017)
	Malaysia	WWTP in Selangor	2020	15.10	(Mohd Hanafiah et al., 2022)
	Malaysia	Urban water cycle in Selangor	2021	14.70	(Mohd Hanafiah et al., 2023)

2.2 Sample Preparation technique

Since the direct determination of trace-level analytes in complex matrices is challenging due to the inadequate sensitivity of the analytical instruments, sample preparation step is necessary before any analytical procedure. This phase involved the isolation and/or enrichment of target analytes to ensure that the samples were suitable for the instrument analysis. Prior to analysis, sample preparation was intended to enrich the concentration of the analytes for better detection and quantification. It was also aimed to separate the target analyte from the sample matrix, enrich and eliminate any interference or components that could have been present.

2.2.1 Magnetic micro-solid phase extraction

Numerous researchers have applied the magnetic micro-solid phase extraction (MMSPE) technique with various adsorbents mainly known for its easy separations, greater preconcentration and recovery properties. MMSPE involves minimal solvent usage, and the sorbents can be reused, aligning with environmentally friendly practices by generating less waste, reducing labor intensity, and maintaining low operating costs. Moreover, the use of an external magnetic field can facilitate the extraction processes without the requirement for centrifugation or filtration (Khan et al., 2014; Panhwar et al., 2015). As a result, many abbreviations and terminology were used including magnetic solid phase microextraction (magnetic μ-SPE) (Boon et al., 2019), magnetic-based dispersive micro-solid phase extraction (M-d-μ-SPE) (Rocio-Bautista et al., 2016), and dispersive magnetic solid phase microextraction (d-MSPE)(Farahmandi et al., 2021; F. Liu et al., 2018), which have been observed from the reported researches. **Table 2.3** shows some of the previous works applying MMSPE as a versatile sample preparation technique using various magnetic adsorbents modified for the detection of various analytes in various sample matrices.

Table 2.3: Some previous works on the application of MMSPE as a sample preparation technique in various samples.

Core/Shell	Functional groups or final coatings	Analyte	Matrices	Detection	Limit of detection	References
Fe_3O_4	Polyaniline	Paraben	Fruit juice, sunscreen, urine	HPLC/UV	3.0 – 25.0 µg L^{-1}	(Farahmandi et al., 2021)
Fe_3O_4	Carbon nanodots	Erythrosine	Pharmaceutical tablets and syrup	UV-Vis spectrophotometer	60 ng L^{-1}	(Emiroğlu et al., 2021)
Fe_3O_4	Poly (β-cyclodextrin-ionic liquid)	PAH	Rice	GC-FID	0.01-0.18 µg kg^{-1}	(Boon et al., 2019)
Cyclodextrin-functionalized Fe_3O_4 dendrimer nanocomposites	Ionic liquid	Pyrethroids	Juice	HPLC	0.36–1.3 µg L^{-1}	(F. Liu et al., 2018)
Fe_3O_4	Multiwalled carbon nanotube	Patent blue V	Syrup, waters, artificial sweat	UV-Vis spectrophotometer	3.5 µg L^{-1}	(Duman et al., 2020)
Fe_3O_4	Silica	Organophosphorous	Wastewater	CapLC-DAD	50 – 100 ng L^{-1}	(Moliner-Martinez et al., 2014)
Fe_3O_4 graphene oxide	Pyrocatechol violet	copper	Water, black tea, diet supplements	FAAS	4.0 µg L^{-1}	(Ozkantar et al., 2020)
Fe_3O_4	Chip-based array	Copper, Zinc, Cadmium, Mercury, Lead	Cells	ICP-MS	4.2 – 49 ng L^{-1}	(Wang et al., 2015)
Fe_3O_4	-	Lead	Aqueous	FAAS	5.44 µg L^{-1}	(A. S. Silva et al., 2020)
Fe_3O_4	Sodium dodecyl sulfate	Fluoroquinolones	Water, urine	HPLC/UV	0.01 - 0.05 µg L^{-1}	(Manbohi & Ahmadi, 2015)

Fe_3O_4 = Magnetic Nanoparticles; **PAH** = Polycyclic Aromatic Hydrocarbon; **HPLC/UV** = High Performance Liquid Chromatography-Ultraviolet; **GC-FID** = Gas Chromatography Flame Ionization Detection; **HPLC** = High Performance Liquid Chromatography; **CapLC-DAD** = Capillary Liquid Chromatograph (CapLC) with Diode Array Detection; **FAAS** = Flame Atomic Absorption Spectrometry; **ICP-MS** = Inductively Coupled Plasma Mass Spectrometry

2.2.2 Magnetic micro-solid phase extraction for determination of NSAIDs

In this section, we can find more studies that employed MMSPE as the primary separation technique for the extraction of NSAIDs in various samples. **Table 2.4** shows previous works on this application and based on the review, the application of the MMSPE technique was found to be very famous and common among researchers. Various magnetic adsorbents with numerous functionalities have been employed. The enhanced adsorbent material has a higher selectivity and can be able to extract multiparameter of NSAIDs. Adsorbents with functional groups that can form strong interactions, such as hydrogen bonding or van der Waals forces, with the functional groups present in NSAIDs enhance selectivity. Some adsorbents can be tailored or modified to have specific binding sites that match the molecular structure of NSAIDs. This customization enhances the selectivity of the adsorbent (Alvarez-Torrellas et al., 2016). Certain adsorbents may possess inherent chemical properties that make them particularly effective in selectively attracting NSAIDs. Electrostatic interactions based on the surface charge of the adsorbent and NSAIDs can lead to selective adsorption, especially if there are specific charge interactions involved (Yıldırım et al., 2024; Zandian et al., 2024). This adds merit and confidence to apply the MMSPE technique for the extraction of NSAIDs in this study.

On the contrary, most of the studies focused on the modifications using organic compounds on the surface of the sorbents to improve the adsorption capability, binding capacity, solubility, and ease of separation of NSAIDs from the overall sample matrices. The modifications were found to involve very laborious synthesis like coating, functionalization, fabrication, grafting, etc., with complex compounds like ionic liquid, metal organic framework, beta-cyclodextrin, methyl methacrylate, etc., to enhance the properties of the adsorbents. The laborious synthesis will always contribute to high solvent usage, longer time and energy needed, and high waste generation (Liu et al., 2019). Therefore, a simple modification step can be applied to synthesize the sorbent using magnetic nanoparticles which have greater properties.

Table 2.4: Some previous works on the application of MMSPE techniques as sample preparation in NSAIDs detection in various samples.

Core/Shell	Functional groups or final coatings	Analyte	Matrices	Detection	Limit of detection (µg L^{-1})	References
Fe_3O_4	Silica, CTAB	Acetyl-salicylic acid Acetaminophen Diclofenac Ibuprofen	Effluent water	Capillary LC-MS	0.04 – 0.15	(Moliner-Martinez et al., 2011)
Fe_3O_4	*p-tert*-butylcalix[4]arene	Indoprofen Ketoprofen Ibuprofen Fenoprofen	Tap water, drinking water, river water	HPLC-DAD	0.061 – 0.267	(Syed Yaacob, Mohd Jamil, et al., 2018)
Fe_3O_4	Graphene oxide	Naproxen Ibuprofen	milk, urine, well and river water	HPLC-DAD	0.03 – 0.10	(Ghorbani et al., 2016)
Fe_3O_4	Filter paper	Ketoprofen Naproxen Diclofenac	River water, urine, human serum	HPLC	0.2 – 0.4	(Han et al., 2019)
Fe_3O_4	TiO_2 nanoparticles and C-Nanofibers	Ibuprofen	Surface water, lake water, sea water	HPLC-DAD	0.95	(Yilmaz et al., 2020)
Fe_3O_4	βCD-functionalized TDI-modified Sporopollenin	Indoprofen Ketoprofen Ibuprofen Fenoprofen	Tap water, drinking water, river water	HPLC	0.16 – 0.37	(Syed Yaacob, Kamboh, et al., 2018)

Table 2.4, (continued).

Fe_3O_4	Metal-organic framework with core-shell structure	Meloxicam Carprofen Indomethacin Tolfenamic acid Diclofenac Naproxen Mefenamic acid	Wastewater, lake water, feed water,	UPLC-MS	0.02 – 0.09	(Liu et al., 2019)
Fe_3O_4	MIL-101(Cr)	Piroxicam Ketoprofen Meloxicam Naproxen Diclofenac Indomethacin Mefenamic acid Tolfenamic acid	Tap water, river water, pharmaceutical wastewater, hospital wastewater, influent, effluent	UPLC-MS	0.01 – 0.06	(Wang et al., 2017)

Fe_3O_4 = Magnetic nanoparticle; **CTAB** = Cetyltrimethylammonium bromide; **LC-MS** = Liquid Chromatography-mass spectrometry; **HPLC-DAD** = High Performance Liquid Chromatography with photodiode-array detection; **HPLC** = High Performance Liquid Chromatography; **UPLC-MS/MS** = Ultra-high performance liquid chromatography-tandem mass spectrometer

2.3 Magnetic nanoparticles

The research and development of nanotechnology-based materials has drawn a lot of interest among the scientific community (Haeri et al., 2017; Rezaeifar et al., 2016; Sarafraz-Yazdi et al., 2012; Yilmaz et al., 2020). Due to their tunable features and promising applications in terms of magnetization, reusability, and ease of recovery, MNPs have been widely utilized in the field of analytical chemistry.

MNPs can be controlled by applying external magnetic fields. It can be used for magnetic drug targets, nano-sorbents in environmental engineering, magnetic resonance imaging, biomedicine, sensors, and many other applications. MNPs large surface areas to volume ratio, high dispersibility, quantum size effects, superparamagnetic behaviour, and ease of surface modification, makes MNPs useful in a wide range of applications (Boon et al., 2019).

The most popular iron oxides used to synthesize MNPs are maghemite (Fe_2O_3) and magnetite (Fe_3O_4) due to their large magnetic moment, biocompatibility, and ease of preparation. For these reasons, numerous researches have concentrated on the synthesis of MNPs, which have a high surface area with nano-size dimension, superior sorption capability, and a strong response under an applied external magnetic field (Husin et al., 2021).

Several techniques, including laser ablation, mechanical grinding, chemical co-precipitation, high-temperature decomposition of organic precursors, and micro-emulsion, can be used to make magnetic nanoparticles (Boon et al., 2019). Chemical co-precipitation is a technique that is mostly employed because it is inexpensive and easy to prepare. This procedure required combining ferrous (II) and ferric (III) ions in an inert condition with the highly basic solution at a high temperature with rapid stirring in a 1:2 molar ratio (Sun et al., 2004).

Besides the advantages, MNPs still have a propensity to aggregate due to their high surface energies, which were caused by the huge surface area to volume ratio. In addition, unaltered MNPs are susceptible to oxidation, which can reduce their magnetic and dispersibility properties, making it more difficult to manage their stability, size, and form. Pristine MNPs are unstable in an acidic medium. They lack selectivity, easily oxidize, and agglomerate in an aqueous solution (Haeri et al., 2017). Thus, various approaches can be adopted to select the right material that is easily accessible and available abundantly in nature to be modified with MNP to overcome these limitations.

2.3.1 Magnetic nanoparticles modified with agricultural waste

Agricultural waste is among the most widely used adsorbents in recent years due to their easily accessible, abundantly available, great biocompatibility, low cost, highly degradable, and non-toxicity properties (Kabir et al., 2021). (Ravi & Sundararaman, 2020) address agricultural waste as “nourishment squander”, which means agricultural waste has high value and multiple functions that can be reused for a different intended purposes with better efficiency.

Table 2.5 shows the types of modifications done to magnetic nanoparticles using agricultural waste material. Based on the review, many researchers have studied the modifications of MNPs with various agricultural waste. In 2014, (Ebrahimian Pirbazari et al., 2014) used agricultural biomass, NaOH-treated wheat straw as a template impregnated with MNP on its surface to investigate the removal of methylene blue from an aqueous solution. In 2016, (Kaykioglu & Gunes, 2016) used magnetic nanoparticles modified with rice husk ash as a support material to investigate the removal of acid red 114 dye from an aqueous solution. The author indicated there has not been any previous study conducted on MNP with rice husk ash. In 2021, (Nordin et al., 2021) studied the modification of cellulose with polyethyleneimine (PEI) and MNP for the removal of anionic dye (RB5). These studies show that modified MNP with agricultural waste has always shown better properties compared to native conditions and it may work better for the intended purpose.

Despite many studies, the literature related to the extraction of pharmaceutical compounds by modified magnetic-agricultural waste is limited, and there are many interesting adsorbents, including magnetic nanoparticle tea waste are yet to be explored.

Table 2.5: Comparison of types of modifications in preparation of magnetic nanoparticles modified using agricultural waste material.

Agricultural waste	Analyte	Sample	Detection	Reference
Cellulose with polyethyleneimine	Anionic dye	Wastewater	UV-Vis Spectrophotometer	(Nordin et al., 2021)
Eggshell membrane	Lead	Wastewater	Inductively coupled plasma optical emission spectroscopy	(Peigneux et al., 2020)
Chicken eggshell powder	Chromium (VI)	Tested water, surface water, underground water, tannery wastewater	Atomic adsorption spectrometer	(Ravi & Sundararaman, 2020)
Eggshell membrane	Copper (II) and Titanium (I)	Tap water, well water, rainwater, human hair, rice, and tea leaves	Electro thermal Atomic Absorption Spectroscopy	(Naghizadeh et al., 2018)
Rice husk ash	Acid red 114 dye	Aqueous solution	Spectrophotometer	(Kaykioglu & Gunes, 2016)
Activated carbon and biochar	Zinc, Copper, Lead	Aqueous solution	High-Performance Liquid Chromatography	(Han et al., 2015)
Wheat straw	Methylene blue	Aqueous solution	UV-Vis Spectrophotometer	(Ebrahimian Pirbazari et al., 2014)
Almond shell-activated carbon	Trinitrophenol	Water	UV-Vis Spectrophotometer	(Mohan et al., 2011)

2.3.2 Magnetic nanoparticles modified with tea waste as adsorbent

In Malaysia, a large amount of tea waste is generated every year due to the great fan base for tea consumption. Based on the literature review, on average, Malaysia produces 0.45% of the world's total tea production. In general, the waste created from making tea is an oxygen-demanding contaminant that takes a very long time to degrade (Atirah Mohd Nazir et al., 2020). On the other hand, the tea template can function as a powerful adsorbent for the extraction of pollutants. The presence of many functional groups on the surface of the tea residue serves as potential pollutant-binding sites (Wong et al., 2018). Due to their high surface area, efficiency in separation, efficiency in mass transfer, and chemical stability, tea-waste impregnated with MNPs was synthesized successfully and has gained a lot of interest (Drynan et al., 2010).

(Malhotra et al., 2018) have demonstrated the usage of tea leaves wastes as an environment-friendly, cheap bio sorbent for the removal of NSAID from wastewater. This was a study on the removal of Diclofenac (NSAIDs) utilizing tea waste. Their investigation focused on a single analyte. However, to date, no research has been conducted on the extraction study using a multi-analyte approach for NSAIDs employing tea waste. This approach forms the basis of the current study.

(Wong et al., 2018) have studied the removal of acetaminophen (analgesics) from wastewater using activated carbon from spent tea leaves in wastewater. These studies are strong evidence that tea waste has the potential to bind and extract pharmaceutical compounds, specifically NSAIDs, from water samples. Therefore, an approach has been taken in the modification of MNP with one of the very common agricultural waste, tea waste as a potential robust adsorbent (Kabir et al., 2021).

Table 2.6 shows some studies that have performed modifications on tea waste with MNPs for several applications. (Lunge et al., 2014) have used ferric chloride as an iron source and tea as a template to synthesis magnetic nano iron oxide for the adsorption of arsenic ions in water samples. (Panneerselvam et al., 2011) have investigated the preparation of magnetic nanoparticles, impregnated onto tea waste from agricultural biomass for the adsorption of nickel ions in an aqueous solution. (Wen et al., 2017) have prepared a magnetic material by decorating pristine MNP on tea leaf waste to investigate the adsorption performance towards copper and zinc ions in wastewater. All the mentioned authors have used co-precipitation as a common method to synthesis these materials and on top of that, it was only applied for removal studies (remediation). Surprisingly, none has applied magnetic tea waste with any extraction studies, especially the MMSPE technique for chemical analysis application. Therefore, this is the first attempt to investigate the application of magnetic tea waste with the MMSPE technique for the extraction of NSAIDs in water samples using UV-Vis spectrophotometer.

The goal of the current study is to use and manage such valuable agricultural biomass for great purposes more effectively. The key idea of utilizing waste products generated from our daily routine use to synthesize new material that can solve alarming environmental issues is indirectly contributing to the sustainable development goals (SDGs) that were adopted by the United Nations in 2015. Goal no. 12: Responsible consumption and production explains the urge to manage our shared natural resources and the way we dispose of any type of waste and pollutants. This goal encourages industries, businesses, and consumers to recycle, reduce and reuse waste as it supports developing countries to move towards more sustainable patterns of consumption by 2030. On par with the SDGs, the nanocomposite of MNP with tea waste as agricultural waste in this study has permitted us to prepare a new class of material for the extraction of NSAIDs in water samples. This research dissertation employs unconventional methodologies, distinct from the commonly adopted approaches within this domain, to achieve a notable and innovative outcome.

Table 2.6: Some previous works using magnetic nanoparticles modified with tea waste coupled with various detectors in aqueous samples.

Analyte	Technique	Sample	Detectors	Reference
Arsenic	Removal	Aqueous solution	AASHVG-1	(Lunge et al., 2014)
Nickel	Removal	Aqueous solution	UV-Vis Spectrophotometer	(Panneerselvam et al., 2011)
Copper Zinc	Removal	Aqueous solution	ICP-AES	(Wen et al., 2017)
Acetaminophen	Removal	wastewater	UV-Vis Spectrophotometer	(Wong et al., 2018)
Diclofenac	Removal	wastewater	UV-Vis Spectrophotometer	(Malhotra et al., 2018)
Benzo[a]anthracene (BaA) Chrysene (Chr) Benzo[b]fluoranthene (BbF) Benzo[a]pyrene (BaP)	Removal	Aqueous solution	UHPLC-DAD	(Inbaraj et al., 2021)

AASHVG = Atomic absorption spectrophotometer hydride vapor generator; **ICP-AES** = inductively coupled plasma atomic emission spectroscopy; **UHPLC-DAD** = ultra-high-performance liquid chromatographic-diode array

CHAPTER 3: RESEARCH METHODOLOGY

3.1 Chemicals, materials, and reagents

Black tea leaves were purchased from a supermarket in Shah Alam, Selangor. Ibuprofen (IBP), diclofenac (DCF) and naproxen (NAP) (purity ≥ 99%) were selected NSAIDS as analytes, purchased from Aldrich (USA). **Figure 3.1** shows the UV-Vis spectra examined using UV-Vis spectrophotometer, when 500 µg L^{-1} of ibuprofen (λ : 222 nm), diclofenac (λ : 276 nm) and naproxen (λ : 230 nm) were wavelength screened. Solvents used like acetonitrile and methanol were HPLC grade, 99.7% were purchased from Merck (Darmstadt, Germany). Iron (II) chloride tetrahydrate ($FeCl_2.4H_2O$) and iron (III) chloride hexahydrate ($FeCl_3.6H_2O$) were obtained from R&M Chemicals (Essex, UK). Sodium chloride (NaCl) and sodium hydroxide (NaOH) were provided from Friedemann Schmidt (Parkwood, WA, Australia). The ultrapure water with a resistivity of > 18.2MΩ was prepared by the Merck Milli-Q system (Lane End, UK).

The standard stock solutions (1000 mg L^{-1} for each analyte) were prepared in methanol and preserved in a refrigerator at 4ºC to avoid the degradation process. The working standard solutions containing all analytes were freshly prepared by diluting the stock solutions with ultrapure water to the desired concentration.

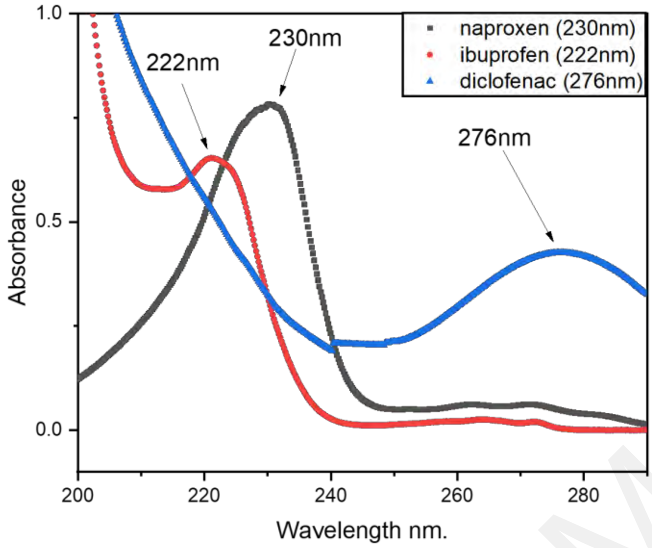


Figure 3.1: The UV-Vis spectra for individual NSAIDs species at the respective wavelength in the analyte-rich phase.

3.2 Instruments

A Shimadzu (Kyoto, Japan) Model UV-1650 Ultraviolet-Visible spectrophotometer was used for the measurement of the NSAIDs compounds to record their spectrophotometric measurements (absorbance) with matched 1 cm quartz cells. Absorption spectra were determined between 190 nm and 400 nm. A vortex was used to desorb the analyte from the sorbent to the solvent. An orbital shaker, model: SKU: 719, from TECH-LAB was used for the extraction of NSAIDs from the aqueous solution to the adsorbent. The pH values of the sample solutions were determined by a pH meter (Accumet AB150, Fisher Scientific).

3.3 Preparation of MNP-TW

The preparation of the MNP-TW method was inspired by (Panneerselvam et al., 2011) for its simple and less complex synthesis. The black tea purchased was used to mix tea beverages and the residue was collected, and soaked in boiled water several times, until decolorized. This resembles the multiple uses of the tea residue before disposing of it. The residue was thoroughly washed with water and dried at 85ºC overnight (Atirah Mohd Nazir et al., 2020; Panneerselvam et al., 2011). Once dried, the material was ground and sieved. Then, the chemical co-precipitation technique was implemented where 11.68 g of ferric chloride and 4.3 g of ferrous chloride were dissolved in distilled water. Under N_2 condition, the mixture was heated at 80ºC with vigorous stirring at 2000 rpm for 1 hour. N_2 gas was continuously bubbled to expel oxygen gas. After 1 hour, 10 mL of 30% of ammonia solution was added drop wise. The solution was then added with 5 g of the fine tea waste material. The reaction was carried out for 30 mins at the same temperature under constant stirring. To eliminate the unreacted chemicals, the suspension was cooled down to room temperature and repeatedly washed with distilled water. Lastly, the material was washed with ethanol to enhance the crystal formation. The washed residue was dried in the oven at 50ºC for 12 hours. **Equations 3.1** and **3.2** show MNP-TW material formation which was inspired from and tested with the magnet as shown in **Figure 3.2**. It was crystal clear that the MNP-TW was attached to the magnet, due to the magnetic behaviour. The reactions that occur in the synthesis of MNP-TW are shown in **Equations 3.1** and **3.2**.

$$FeSO_4.7H_2O + 2FeCl_3.6H_2O + 8NH_4OH \rightarrow Fe_3O_4 + 6NH_4Cl + (NH_4)2SO_4 + 17H_2O \quad \textbf{(3.1)}$$

$$Fe^3O^4 + TW + 17H^2O \rightarrow TW - Fe_3O_4 \quad \textbf{(3.2)}$$

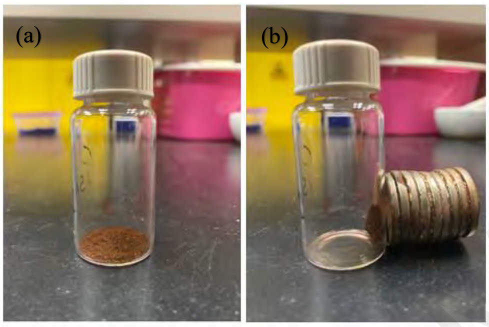
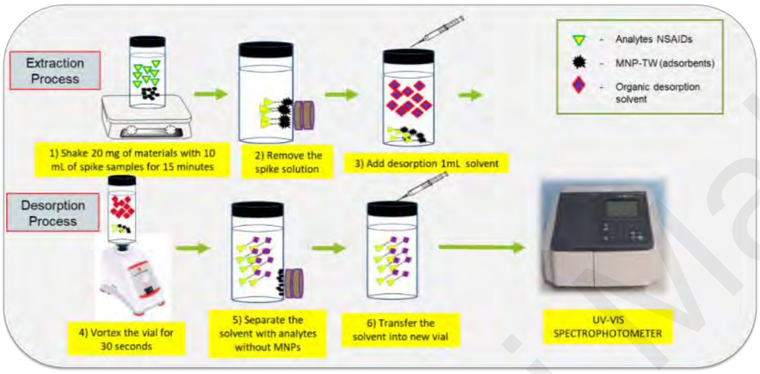


Figure 3.2: (a) The image of MNP-TW before attracted to external magnetic force by neodymium magnet. (b) The image of MNP-TW after attracted to external magnetic force by neodymium magnet.

3.3.1 The procedure of MNP-TW-MMSPE for the determination of NSAIDs

In the MNP-TW-MMSPE study, a 10 mL sample solution containing known concentrations of IBP, DIC, or NAP standard solution was placed in a vial. Then 20 mg of synthesized MNP-TW was added to the sample solution. The mixture was shaken on an orbital shaker at 1000 rpm for 15 mins. After the extraction process was completed, the particles residue was separated by a neodymium magnet and collected. Because the neodymium magnet could successfully separate the magnetic particles from the liquid phase, the time for centrifugation or filtration step were saved. The aqueous phase was discarded, and 1.0 mL of methanol was added into the vial and the suspension was kept on vortex for 30 s to desorb the analytes from the surface of MNP-TW. The eluent was then added in 3 mL of desorption solvent and analyzed by UV–Vis spectrophotometer at 222 nm, 276 nm, and 230 nm to determine the concentration of IBP, DIC and NAP, respectively. The same procedure was applied for the blank and standard solutions. All analytes were extracted and analyzed individually (single detection). **Figure 3.3** shows a schematic representation of MMSPE procedures.

Figure 3.3: Schematic representation of MMSPE procedures.



3.4 Optimization of the MNP-TW-MMSPE method

To comprehensively assess the performance of MNP-TW, some essential experimental parameters, including sorbent dosage, sample pH, extraction and desorption time, ionic strength, sample volume, type and volume of desorption solvent have been investigated. These parameters were analyzed in water samples spiked with 500 µg L^{-1} of IBP, DCF and NAP, separately in triplicate (n=3). The extraction efficiency was calculated as in **Equations 3.3** and **3.4**:

$$Extraction\ efficiency, (\%) = \frac{C_S \times V_S}{C_O \times V_O} \times DF \times 100\% \qquad \textbf{(3.3)}$$

$$DF = \frac{V_f}{V_i} \qquad \textbf{(3.4)}$$

where *Cs* represents the NSAIDs species concentration (µg L^{-1}) in the sample-aqueous mixture of volume *Vs* (mL); *Co* represents the NSAIDs species concentration (µg L^{-1}) in the standard solution of volume Vo (mL), DF is the dilution factor due to adding the eluent in 3 mL of solvent to make sure the sample volume is adequate for analysis. V_f and V_i represents the final volume and initial volume of the sample, respectively.

3.4.1 Optimization of sorbent dosage

The different amounts of sorbent were studied in the range of 5 – 30 mg. The extraction parameter conditions were like the MMSPE procedure in section **3.3.1**.

3.4.2 Optimization of pH

The effect of sample pH were studied from pH 3 to pH 11 at room temperature. The preferred pH was adjusted using 0.1 M HCl and 0.1M NaOH monitored using a pH meter (Accumet AB150, Fisher Scientific). The extraction parameter conditions were comparable to the MMSPE procedure in section **3.3.1**.

3.4.3 Optimization of extraction time

The prolonged extraction time was investigated from 10 mins to 60 mins to enhance the extraction efficiency towards the analytes. The extraction parameter conditions were like the MMSPE procedure in section **3.3.1**.

3.4.4 Optimization of ionic strength

The effect of ionic strength was studied with the addition of 0% to 5% (w/v) of NaCl in the sample solution. The extraction parameter conditions were like the MMSPE procedure in section **3.3.1**.

3.4.5 Optimization of sample volume

Several sample volumes were tested from 5 mL to 30 mL. The extraction parameter conditions were like the MMSPE procedure in section **3.3.1**.

3.4.6 Optimization of desorption conditions

Three types of solvents were used as desorption solvents in the MMSPE procedure, such as acetonitrile (ACN), methanol (MeOH) and acetone. The effect of desorption time was investigated in the range of 10 to 50 mins. Different volumes of desorption solvent were employed from the range of 200 µL to 1000 µL. The extraction parameter conditions were like the MMSPE procedure in section **3.3.1**.

3.5 Reusability and carryover study

After considering how important it is for the environment to reduce waste and save chemicals, the feasibility of reusing MNP-TW was investigated. The identical MNP-TW that had been fully washed three times with 1.5 mL of methanol each and dried at 65 °C for 30 mins was used again for this study. The reusability process begins after the adsorbent is washed and dried before the next MMSPE application.

3.6 Method Validation

A series of experiments were designed to attain linearity range, precision, limit of detection (LOD), limit of quantification (LOQ) and other characteristics of the developed method.

3.6.1 Linearity and precision

Linear range standardization curves was plotted in the range between 30 µg L^{-1} to 700 µg L^{-1}. The repeatability and precision of the advanced method were signified by 3 replicates of spiked DI water with 300 µg L^{-1} of each NSAIDs. The data collected in standard deviation (SD) and relative standard deviation (RSD, %) were designed using the following **Equations 3.5** and **3.6**:

$$SD = \sqrt{\frac{\sum(x-\bar{x})^2}{n-1}} \tag{3.5}$$

$$RSD(\%) = \frac{SD}{\bar{x}} \times 100\% \qquad \textbf{(3.6)}$$

where $\bar{x}$ indicates mean, x is the results of every run, and n is the number of measurements (repeatability).

3.6.2 Limits of detection (LOD) and limit of quantification (LOQ)

The limit of detection and quantification of MNP-TW-MMSPE towards the sensitivity of the studied analytes were determined by **Equations 3.7** and **3.8**

$$LOD = 3.3 * (\frac{SD}{M}) \qquad \textbf{(3.7)}$$

$$LOQ = 10 * (\frac{SD}{M}) \qquad \textbf{(3.8)}$$

where SD represents the standard deviation of the blank residuals, and M is the slope of the calibration curve.

3.6.3 Pre-concentration factor (PF)

The pre-concentration factor is the concentration ratio of the analyte in the final enriched extract to the initial sample solution (Naeemullah et al., 2012). A volume of 300 µg L^{-1} of NSAID was spiked in water sample and will run through the MNP-TW-MMSPE procedure and the PF value will be calculated as **Equation 3.9**.

$$PF = \frac{absorbance\ of\ final\ enriched\ extract}{absorbance\ of\ initial\ standard\ solution} \times \frac{extraction\ sample\ volume}{desorption\ eluent\ volume} \qquad \textbf{(3.9)}$$

3.6.4 Sorbent-to-sorbent reproducibility study

The MNP-TW repeatability was assessed in terms of batch-to-batch or lot-to-lot to evaluate the efficacy of MNP-TW reproducibility. NSAIDs spiked at 500 µg L^{-1} in water samples employing three batches of sorbents (n=3) that were synthesized under the same conditions but at different times. RSD (%) was used to express the result using **Equation 3.6**.

3.6.5 Relative recovery study

The percentage of relative recoveries (%R) for the real sample was calculated by using the following **Equation 3.10**.

$$\%R = \frac{Concentration\ of\ spiked\ sample - Concentration\ of\ unspike\ sample}{Concentration\ of\ spike\ value\ added} \times 100\% \qquad \textbf{(3.10)}$$

3.7 Real sample analysis

The calibration curves in the range of 30 – 700 µg L^{-1} were constructed by plotting the absorbance signal against the concentration of each NSAID species according to the general procedure under the optimized conditions. The developed method has been applied to evaluate its feasibility by spiking each NSAIDs into the water samples. Two different water samples were collected. Tap water was collected in Universiti Malaya laboratory and a wastewater sample was collected near a rubber factory in Meru, Selangor. The water samples collected were preserved and stored in polyethylene bottle, chilled, and filtered through a 0.45 µm membrane filter to remove solid particles before use. The presence of NSAID was not detected in any water samples later thus depicting that the water samples collected were safe from NSAIDs contamination.

3.8 Green assessment

The analytical Eco-Scale as a comprehensive approach has been chosen to evaluate the greenness of this method. It is evaluated based on the penalty points assigned to parameters of an analytical process that are not in agreement with the idea of green method analysis. This approach compares the differences in parameters and steps of the analytical process. The penalty points were contributed for the amounts of chemicals/reagents, the consumed energy by electrical devices, the possible occupational hazards as well as the waste product generated from this method. The allocated penalty points for the reagents are based on the level of risks which include their hazards such as physical, health and environment based on the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (Armenta et al., 2015; Gałuszka et al., 2012; Zain et al., 2014).

CHAPTER 4: RESULT AND DISCUSSION

4.1 Characterization of MNP-TW as adsorbent

4.1.1 FT-IR analysis

FT-IR spectra of MNP-TW, MNP and TW between 4000 cm^{-1} and 400 cm^{-1} are presented in **Figure 4.1**. The spectra display several absorption peaks, reflecting the complex nature of tea waste. By comparison for MNP-TW, MNP and TW, the troughs, due to bonded OH groups are observed in the range of 3340 - 3380 cm^{-1}. A broad band at 3409 cm^{-1}, 3406 cm^{-1} and 3384 cm^{-1} from TW spectra is attributed to the presence of bonded (-OH) groups whereas, at (2930 - 2842 cm^{-1}) and (2931 - 2850 cm^{-1}) is attributed to the aliphatic (C-H) groups which might probably from the tea waste. The peaks between 1630 cm^{-1} and 1057 cm^{-1} represent C=O stretching mode conjugated with the NH2 (Amide 1 band) in MNP-TW representing the carboxylic group and stretching of polysaccharides indicating the presence of a great amount of carboxylic acid. The skeletal vibrations of C=C stretching (aromatic rings) at 1630 cm^{-1} with the hydroxyl group in MNP-TW and TW are the representation of the large content of polyphenols in MNP-TW. The stretching vibration of the Fe-O bond was responsible for the transmittance band at 634 cm^{-1}. Additionally, the reduced intensity of Fe-O suggested that MNP-TW composites had a significant TW loading. The peaks in the spectra of MNP and TW coincided with those of MNP-TW, proving that MNP-TW nanoparticles were successfully formed (L. Liu et al., 2018; Panneerselvam et al., 2011; Wen et al., 2017; Wong et al., 2018).

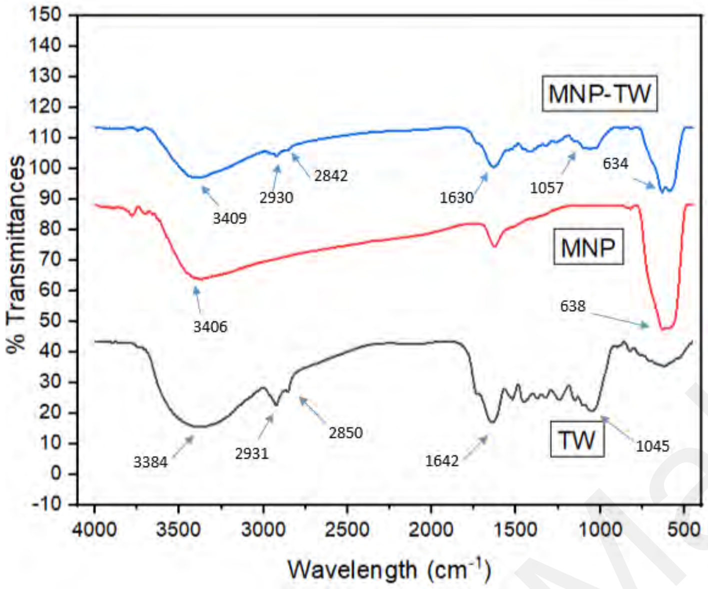


Figure 4.1: The FT-IR spectra of MNP-TW, MNP and parent TW.

4.1.2 Magnetization studies

The predominant characteristic of a magnetic material lies in its magnetic properties, which are essential for the rapid separation of materials from an aqueous medium, especially in magnetic micro-solid phase extraction (Mμ-SPE) applications. The magnetic behaviour of MNP-TW and MNP was assessed using VSM (Vibrating Sample Magnetometry), as displayed in **Figure 4.2**. It was discovered that MNP and MNP-TW had saturation magnetizations (Ms) of 62.51 and 40.47 emu g^{-1}, respectively. The difference in the magnetization values of both MNP-TW and MNP yielded 22.04 emu g^{-1} which is 35.3% (w/w), which was close to that of weight loss calculated from thermogravimetric (TG) analysis (~31.6% in w/w). Thus, this further proved that the synthesis was successful [10,27]. **Figure 4.2** shows the saturation magnetization (Ms) of MNP and MNP-TW (Liu et al., 2019; Wen et al., 2017).

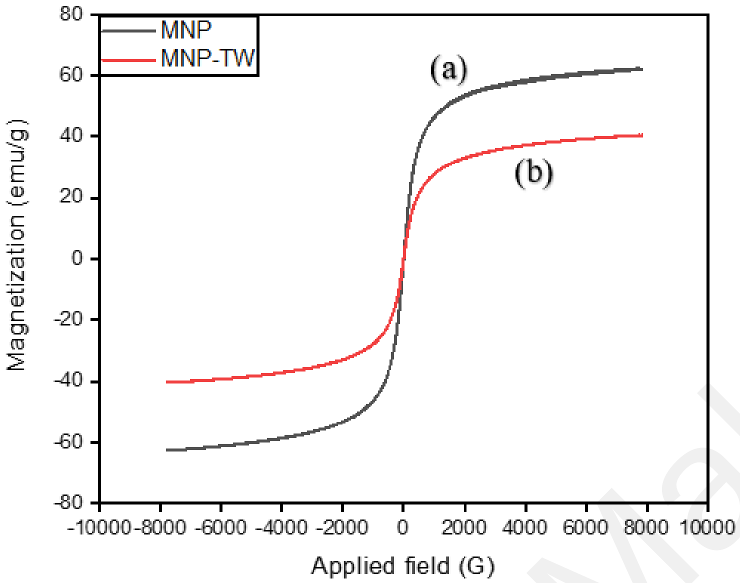


Figure 4.2: VSM analysis of (a) MNP and (b) MNP-TW

4.1.3 FESEM analysis

In **Figure 4.3(a)**, The parent TW has smooth, heterogeneous, irregular bumpy structure surfaces. It indicates TW is primarily composed of structural proteins derived from cellulose and has insoluble cell walls with fibrous composition. As there are more adsorption sites, this feature would help to increase the extraction efficiency. In **Figure 4.3(b),** the MNP surface has more pores and compact particles with rough morphology. It adhered closely together, which causes the nanoparticles to aggregate. In MNP-TW, MNP has completely covered the parent TW as shown in **Figure 4.3(c)**, and all the MNP particles have aggregated to create a spherical, cage-like structure. Since the iron oxide occupied the active sites, **Figure 4.3(c)** depicts a single TW fibrous material with more holes and active sites available at 1.00 µm (Panneerselvam et al., 2011). In addition, the corresponding photographs of TW, MNP and MNP-TW were provided inset of **Figure 4.3(a), (b)** and **(c)**.

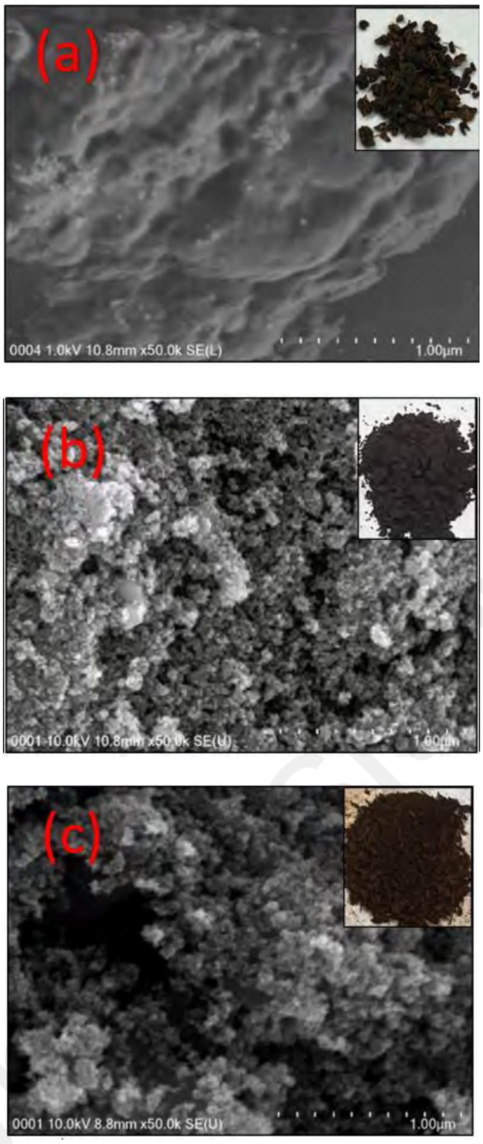
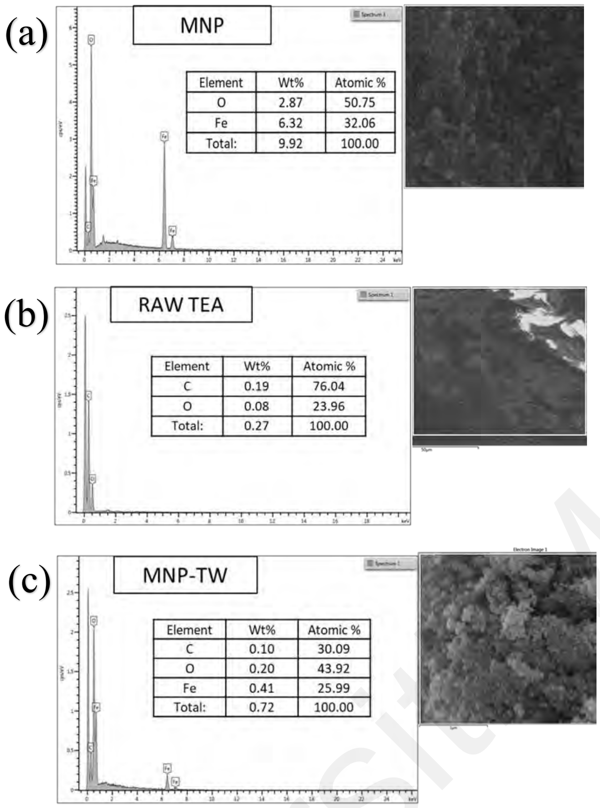


Figure 4.3: FESEM analysis of 50k× magnification: (a) TW, (b) MNP, (c) MNP-TW, inset: photographs of TW, MNP and MNP-TW

4.1.4 EDX analysis

Figures 4.4 a), b) and **c)** show the results of the EDX analysis. By comparison, the weight percentage of iron (Fe=0.41%) and carbon (C=0.10%) in MNP-TW has confirmed the impregnation of the tea waste with MNP and further proves the successful formation of MNP-TW.

It was observed that carbon weight percentage has reduced from (b) Raw Tea (0.19%) to (c) MNP-TW (0.10%). The reduction in carbon content observed is likely due to high temperature steps or chemical reactions during impregnation may lead to the breakdown of organic carbon compounds. The impregnation of magnetic nanoparticles may involve chemical interactions modifying or breaking down carbon-containing compounds. Besides, the impregnation process may induce structural changes in the tea waste, altering the arrangement of carbon-containing molecules (Siddiqui et al., 2023).



Element	Wt%	Atomic %
O	2.87	50.75
Fe	6.32	32.06
Total:	9.92	100.00

Element	Wt%	Atomic %
C	0.19	76.04
O	0.08	23.96
Total:	0.27	100.00

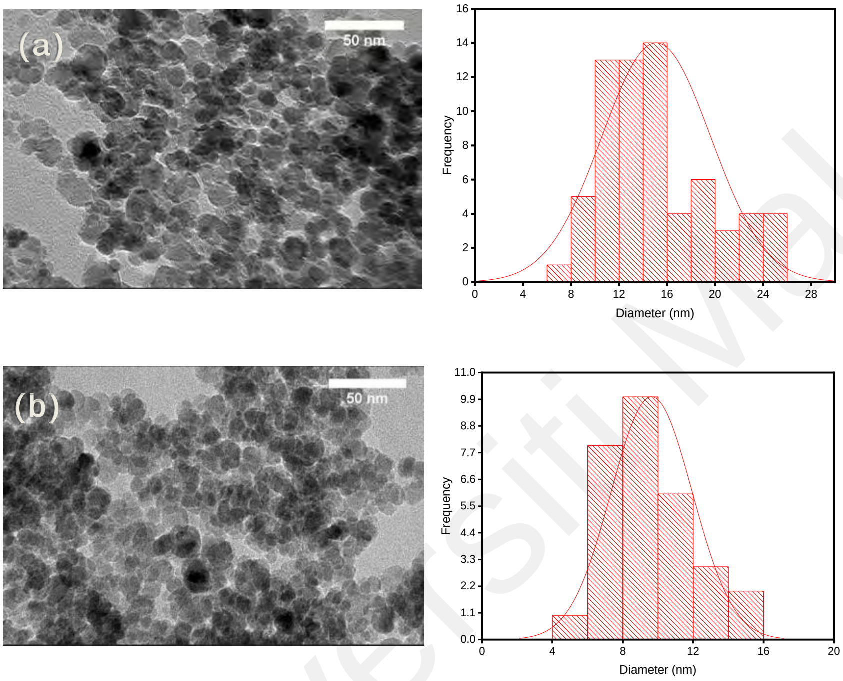
Element	Wt%	Atomic %
C	0.10	30.09
O	0.20	43.92
Fe	0.41	25.99
Total:	0.72	100.00

Figure 4.4: (a) EDX spectrum of MNP, (b) EDX spectrum of parent TW and (c) EDX spectrum of MNP-TW.

4.1.5 TEM analysis

In TEM analysis, the particles of individual MNP and MNP-TW were difficult to visualize. Therefore, their mean particle size was determined by randomly choosing the observed particle grains in the TEM image and plotting the particle size distribution histogram with the aid of J image software. From **Figure 4.5(a)** and **Figure 4.5(b)**, the average diameter obtained from the plot for MNP (15.1 nm) is higher compared to MNP-TW (9.6 nm). The reduction in the average diameter of nanoparticles from MNP to MNP-TW is due to the infusion of MNP into the surfaces and pores of the tea waste during the synthesis, which was essential for an effective magnetic separation to occur. A similar observation was reported by Wen and co-workers (Wen et al., 2017). Further impregnation on the surface of tea waste produced nanoparticles with tiny, spherical morphology (Bakhshaei et al., 2016; Panneerselvam et al., 2011).

Figure 4.5: TEM images of 50 nm scale image and corresponding particle diameter distributions of (a) MNP and (b) MNP-TW



4.1.6 BET analysis

In Brunauer-Emmett-Teller (BET) analysis, the porous structure of MNP and MNP-TW were studied by using nitrogen adsorption-desorption isotherms. The unmodified MNP (67.14 m^2 g^{-1}) yielded a BET surface higher than MNP-TW (48.38 m^2 g^{-1}). The decline in values could be attributed to the increment in particle diameter due to the presence of an impregnation layer from magnetic nanoparticles on the surface of tea waste (Altaf et al., 2021; Inbaraj et al., 2021).

Barret-Joyner-Halenda model (BJH) was used to calculate the pore size distribution that gave pore diameters of 13.1 nm and 17.8 nm for MNP and MNP-TW, respectively. These findings align with the IUPAC classification, which categorizes mesoporous materials within a diameter range of 2 - 50 nm. The increase in pore size could potentially be attributed to the presence of an impregnation layer derived from magnetic nanoparticles. This layer might have contributed to the dimensional enlargement of particles, thereby confirming the successful synthesis of the investigated materials.

Figure 4.6(a) and **(b)** show the hysteresis loop of MNP and MNP-TW respectively. In **Figure 4.6(a)** the MNP displayed type IV isotherm with H1-type hysteresis loop indicative of its mesoporosity. The outcomes are in line with the SEM analysis, whereby porous material that exhibited type H1 contained uniform sphere aggregates. However, in **Figure 4.6(b)**, MNP-TW demonstrated type II with H3-type hysteresis loop which indicates the formation of a monolayer on the material's surface. This behaviour is said to be common for materials with relatively low surface area, where multilayer adsorption occurs after monolayer adsorption. The H3-type hysteresis loop observed in Type II isotherms signifies the presence of a macroporous surface with relatively uniform cylindrical mesopores or ink-bottle-shaped pores in MNP-TW. While mesoporous and macroporous materials differ in their pore size ranges, they can sometimes be related to certain materials. For example, a material could exhibit a hierarchical porous structure containing both mesopores and macropores. This combination of different pore sizes might be advantageous, providing multiple levels of adsorption capabilities for different-sized molecules or particles (Boon et al., 2019; Panneerselvam et al., 2011; Raoov et al., 2014). **Table 4.1** presents the BET analysis of MNP and MNP-TW.

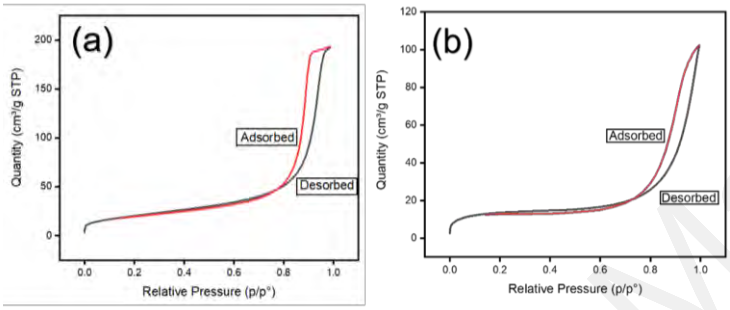


Figure 4.6: BET Hysteresis loop of (a) MNP and (b) MNP-TW

Table 4.1: BET analysis of MNP and MNP-TW

Characteristics	MNP	MNP-TW
Surface area (m^2/g)	67.14	48.38
Pore volume (cm^3/g)	0.30	0.16
N^2 adsorption/desorption isotherm	Type IV	Type II
Hysteresis type loop	H1	H3
BJH pore diameter (nm)	13.09	17.83

4.1.7 TGA analysis

The thermal stability of a molecule is measured by thermo-gravimetric analysis (TGA), which is also employed to analyze MNP and MNP-TW. According to **Figure 4.7 (a)**, the weight-loss curve for MNP and MNP-TW required a multi-step approach. In general, the first step can be understood because of the loss of water, while the second step may be responsible for other compounds. Upon increasing the temperature to 200 ºC, the weight of MNPs was reduced by 3.69%, apparently caused by the loss of moisture content. However, only a minor loss in weight (2.50%) occurred in the temperature ranging from 200 ºC to 400 ºC due to minor volatile fractions with the remaining MNPs purity obtained at 93.81%. For MNP-TW, a three-step degradation pattern was obtained. The first step involved a loss of 5.96% moisture content at temperature < 200 ºC, followed by a 13.22% reduction in weight between 200 ºC to 400 ºC in the second step which is attributed to the loss of cellulose and hemicellulose residues as well as volatile fractions. In the third step, a loss in weight by 12.45% was observed at 400 ºC to 800 ºC, accounting for the devolatilization of thermally stable volatile compounds, oxidation of carbon and degradation of lignin. A final residue mass of 68.37% was obtained (Inbaraj et al., 2021). **Figure 4.7 (b)** provides additional evidence of that MNP and MNP-TW. The findings are summarized and displayed in **Table 4.2**.

Table 4.2: TGA analysis of MNP and MNP-TW.

Adsorbents	Region	Temperature (ºC)	Weight loss (%)	Assignment	Total weight loss (%)
MNP	A1	36.38 – 108.29	3.69	Water/ moisture loss	6.19
	B1	226.12 – 369.95	2.50	Volatile fractions	
MNP-TW	A2	30.75 – 98.98	5.96	Water/ moisture loss	31.63
	B2	229.81 – 380.99	13.22	Cellulose, hemicellulose, volatile fractions.	
	C	463.95 – 898.66	12.45	Devolatilization of thermally stable volatile compounds, oxidation of carbon, degradation of lignin	

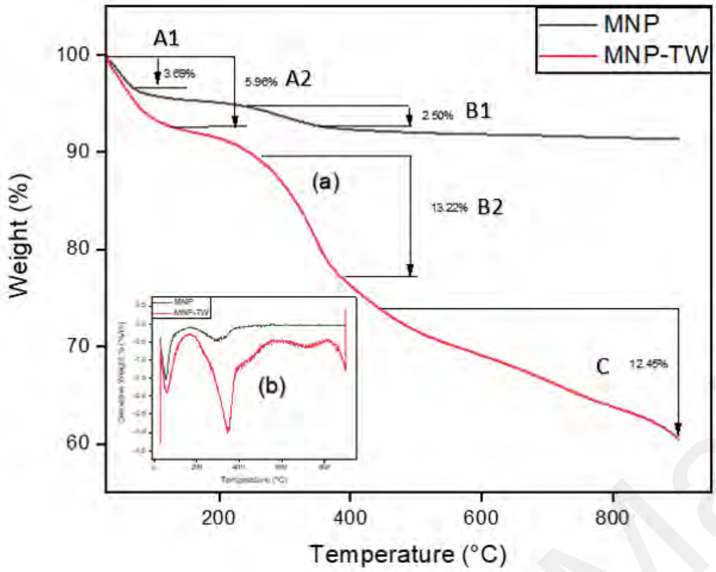


Figure 4.7: (a) TGA analysis of MNP and MNP-TW. (b) DTA diagram of MNP and MNP-TW.

4.1.8 XRD analysis

As shown in **Figure 4.8**, the analysis of crystallinity was carried out using X-ray powder diffraction XRD spectroscopy. The typical peaks of MNP-TW were found to correspond to the Miller index values of (220), (311), (400), (422), (511), and (440) planes of MNP with a face-centred cubic structure at 2Θ = 30.3°, 35.7°, 43.3°, 53.8°, 57.4°, and 63.1°, respectively which indicates the cubic phase of the full faces centers of magnetic metal oxide (JCPDS No. 75-0033). The two patterns showed a broad and relatively weak diffraction peak at 23°, which indicates the amorphous carbon, consists of aromatic carbon sheets oriented in a relatively random manner (Wen et al., 2017). It should be observed that the impregnation process of MNP on tea waste did not alter the cubic phase of the magnetic metal oxide, as shown by the identical XRD pattern of MNP-TW. The results obtained from **Figure 4.8**, can be used to determine the crystallite sizes of MNP and MNP-TW with the Scherer equation in **Equation 4.1**.

$$D = k\lambda/\beta cos\Theta \qquad \textbf{(4.1)}$$

Where **D** is crystalline sizes (nm), **k** is grain shape factor constant, **λ** is the wavelength of the XRD beam, **β** is the full width at half maximum for the diffraction peak (radian), and **Θ** is the diffraction angle.

The quantitative analysis based on the Scherer equation showed that the average crystallite size of MNP and MNP-TW are 14.1 nm and 11.4 nm, respectively. As can be realized, the crystallite size of MNP-TW is lower than the size of MNPs achieved by BET and TEM techniques.

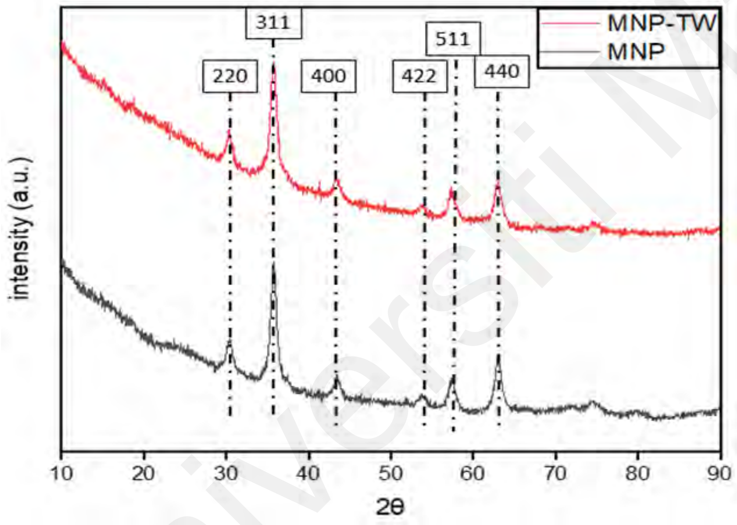


Figure 4.8: XRD patterns of MNP and MNP-TW.

4.2 Optimization of the MNP-TW-MMSPE technique

4.2.1 Preliminary comparison between MNP and MNP-TW

The extraction performance of MNP-TW and native MNP was examined in the extraction of NSAIDs using similar extraction conditions (n=3), which included 20 mg of sorbent, 10 mL of sample solution, 30 min for extraction time, 30 s for desorption time, and 1.0 mL of acetonitrile as the desorption solvent. This experiment was conducted to ascertain the impact of tea-waste impregnation on the sorbents' ability to extract materials. **Figure 4.9** displayed the measured (absorbance) of NSAIDs applying MNP and MNP-TW. According to the bar chart, MNP-TW demonstrated a higher extraction efficiency, which can be attributed to the tea waste impregnated with magnetic nanoparticles, which increased the porosity of the adsorbent and drew more analyte particles towards it (Panneerselvam et al., 2011). Additionally, the polyphenol compound in tea waste which contains functional groups such as hydroxyl groups, carboxyl groups and benzene rings in its structure, enhances the selectivity for NSAIDs and adds another outstanding characteristic to the interaction system. Furthermore, the greater extraction capability of MNP-TW towards the studied NSAIDs could be due to strong π–π interaction and electrostatic interaction (Li et al., 2018).

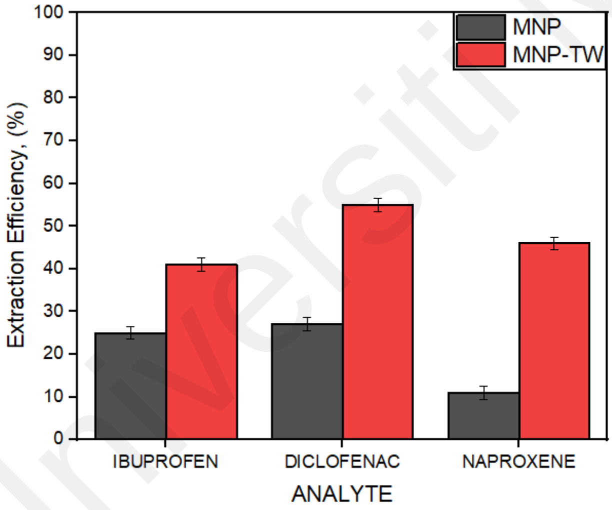


Figure 4.9: The performance capacity in terms of extraction efficiency of MNP and MNP-TW.

4.2.2 Effect of sorbent dosage

The amount of MNP-TW in the range of 5-30 mg was evaluated with other conditions kept unchanged. From **Figure 4.10**, the optimum amount for ibuprofen and diclofenac was 25 mg, whereas for naproxen was 15 mg. When the amount of MNP-TW increases, the extraction efficiency increases too. MNP-TW provides a large surface area which facilitates strong adsorption for their π-π electrostatic interactions with the aromatic rings of the targets, which explains the adsorption capacity variation and thus the limited number of active sites (Hsen & Latrous, 2023). However, the extraction efficiency decreases after 25 mg for ibuprofen and diclofenac and 15 mg for naproxen with the increase of adsorbent dosage due to particle aggregation that happens when the high mass of adsorbent is present which reduces the surface area of MNP-TW exposed to NSAIDs for the adsorption to occur (Han et al., 2019; Liu et al., 2019; Malhotra et al., 2018).

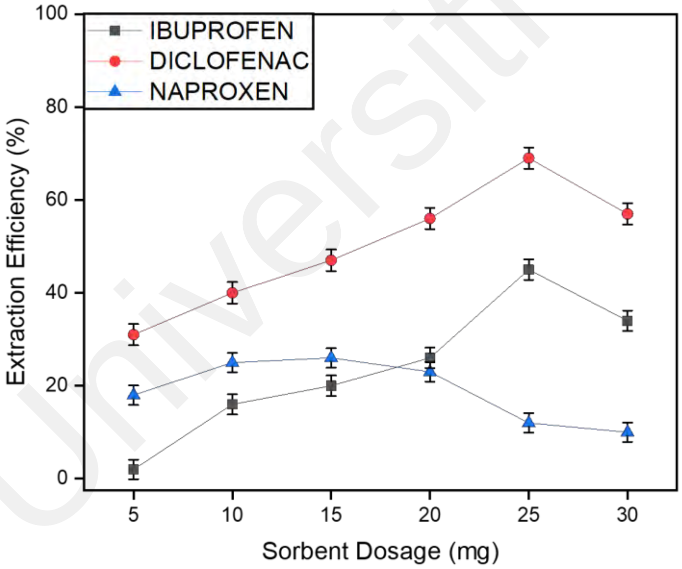


Figure 4.10: Effect of the sorbent dosage of MNP-TW on the MNP-TW-MMSPE efficiency of NSAIDs (n=3).

4.2.3 Effect of pH

From FT-IR characterization **(Figure 4.1)**, the spectrum demonstrates the presence of carbonyl, hydroxyl, and carboxyl groups on the surface of MNP-TW which are likely to participate in analytes binding (Panneerselvam et al., 2011). The oxygen-bonded functional groups enhance the affinity of the MNP-TW with the analyte, making the magnetic materials suitable for extraction. It also acts as a hydrogen bond donor and acceptor. The target analytes and the adsorbent's present forms, as well as the charged NSAIDs species and the associated density on the adsorbent surface, are all significantly influenced by the pH values of water samples (El-Sheikh et al., 2019). The impact of pH values in the range of 3 to 11 was investigated and presented in **Figure 4.11**. At pH 4, the maximum extraction efficiencies were discovered for all target analytes. It might be explained by the significant hydrogen bonding and hydrophobic interactions between the adsorbent and the target analytes. ibuprofen (IBP), diclofenac (DCF), and naproxen (NAP) have dissociation constants (pKa) in the range of 4.00 - 5.20. These drugs are weak acids, and the pH will affect the ionization of NSAIDs and surface of MNP-TW.

At pH < 4, where the pH < pKa, the solution is rich in hydrogen, H^+ and hydronium, and H_3O^+ ions making the polar analytes prone to protonation which makes the NSAIDs in a neutral state. The protonation effect impeded the hydrogen bonding interaction and thus weakens the adsorption.

At optimum pH 4, near or equal to the pKa value, most of the target analytes existed in molecular form. There was an equal amount of neutral and deprotonated NSAIDs species. The hydrogen bonding interaction was the strongest, leading to optimal adsorption (El-Sheikh et al., 2019).

When pH > 4, where the pH > pKa most analytes were deprotonated, changed to anionic forms and the MNP-TW became electroneutral or even negatively charged, thus resulting in reduced interaction or repulsion (Manzo et al., 2014; Sarafraz-Yazdi et al., 2012). Since all analytes would be ionized and present in their conjugated forms at sample pH greater than their pKa values, an increase in the sample pH bigger than 4 led to a gradual fall in the extraction recovery (Sarafraz-Yazdi et al., 2012). To prepare the sample solution for further analysis, the pH was adjusted to 4 for subsequent analysis (Li et al., 2018; Liu et al., 2019).

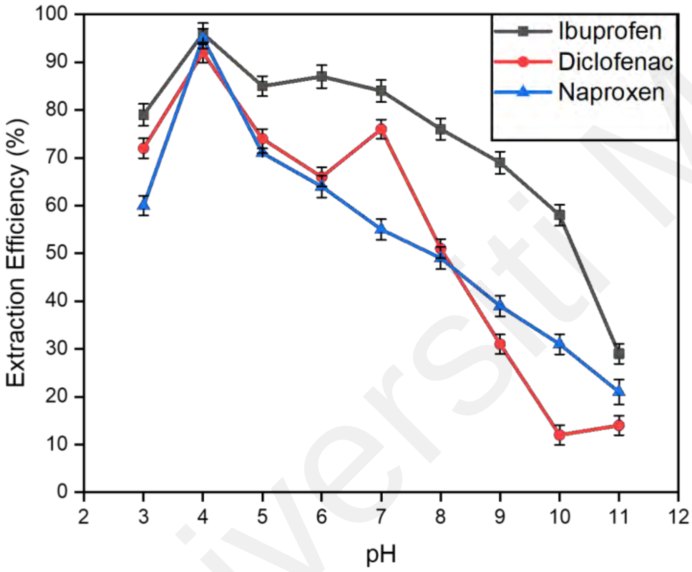


Figure 4.11: Effect of pH of MNP-TW on the MNP-TW-MMSPE efficiency of NSAIDs (n=3).

4.2.4 Effect of extraction time

The length of the extraction process has a significant impact on how the analytes are distributed between the aqueous phase and the sorbent adsorption sites, which helps to increase extraction efficiency. Equilibrium is reached when the sorbent can extract the most analyte possible. To get the best microextraction efficiency, the extraction time was investigated. The time required for analyte diffusion into a thicker sorbent was greater than for thinner materials. The effect of different extraction times (10-60 mins) was studied at room temperature as shown in **Figure 4.12**. The extraction efficiency was greater for IBP at 10 mins whereas for DCF and NAP at 20 mins, then decreased. IBP achieved lower extraction time compared to DCF and NAP probably due to upon examine the structures of IBP, DCF and NAP, the size and shape of the drug molecules can affect their binding kinetics with MNP-TW. IBP (molecular weight: 206.29 g mol^{-1}) being smaller in size compared to DCF (molecular weight: 296.15 g mol^{-1}) and NAP (molecular weight: 230.26 g mol^{-1}), might have fewer steric hindrances, allowing for faster binding with polyphenols (Syed Yaacob, Kamboh, et al., 2018). Therefore, the optimum extraction time for ibuprofen was 10 mins and for diclofenac and naproxen at 20 mins which were selected for further experiments (Rezaeifar et al., 2016).

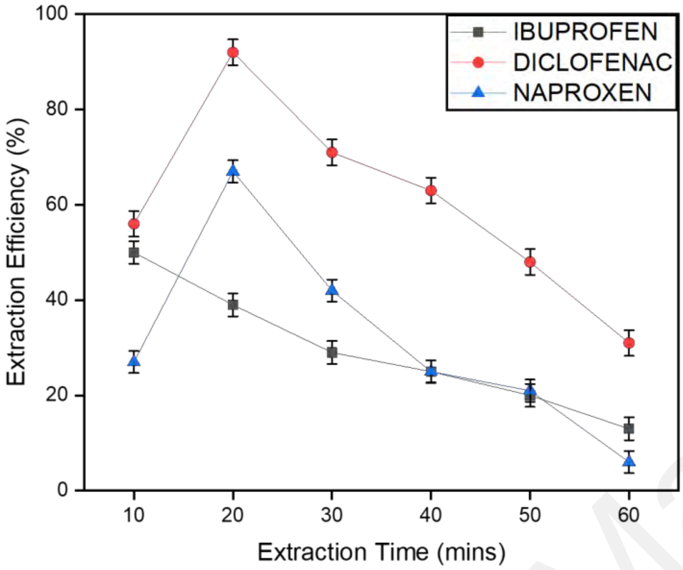


Figure 4.12: Effect of extraction time of MNP-TW on the MNP-TW-MMSPE efficiency of NSAIDs (n=3).

4.2.5 Effect of ionic strength

Ionic strength was varied from 0 - 5% of NaCl salt content in the sample solution. In **Figure 4.13**, the optimum ionic strength was 0% of NaCl salt content in the sample solution which was selected for further experiments. The purpose to addition of NaCl salt is to make the NSAIDs becomes less soluble in the solution and tends to partition preferentially adsorb onto MNP-TW. In this study, ionic strength was examined to see its contribution to the extraction efficiency of NSAIDs with MNP-TW. However, the high viscosity and density of the solution may hamper the molecular mass transfer of the analytes to the sorbents. Therefore, no salts were added to the sample solution in the latter experiments. In addition, at a high concentration of the salt solution, Na^+ and Cl^- ions reversed the metathesis reaction to make MNP-TW more polar, and slower the diffusion rate of the analyte from aqueous to sorbents since the solvation cage of the analyte was disrupted (Han et al., 2019; Wang et al., 2017). As such, the extraction performance declined. Therefore, further studies continued with 0% (w/v) of NaCl which means without the addition of NaCl salt content in the sample solution.

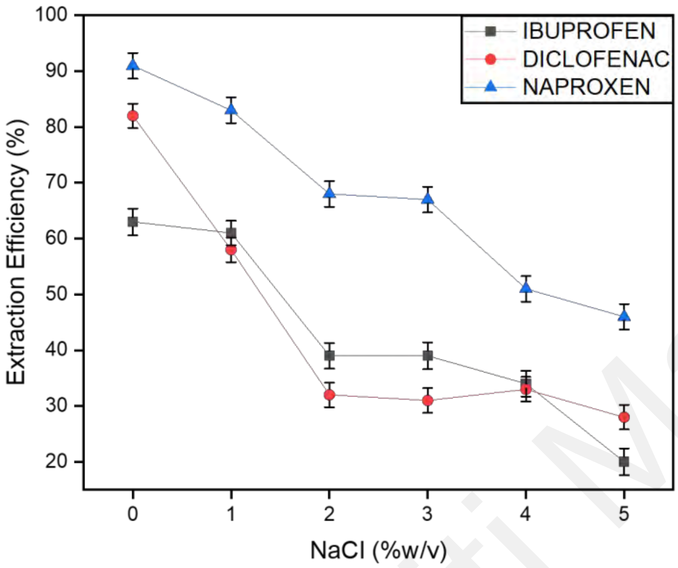


Figure 4.13: Effect of ionic strength of MNP-TW on the MNP-TW-MMSPE efficiency of NSAIDs (n=3).

4.2.6 Effect of sample volume

The sample volume is directly related to the enrichment factor (EF) and loading capacity of the adsorbent. Hence, the sample volume was examined in the range of 5 to 30 mL to attain a high enrichment factor. In **Figure 4.14**, results indicate that all the NSAIDs prefer lower sample volumes. From 10 to 30 mL, the trend seemed to decrease. Higher volumes cause the adsorption sites to completely saturate with analytes and it could not be processed as the amount of sorbent in the volume unit of the sample decreased due to high dispersion of the sorbent in aqueous media. This makes the adsorption of analytes more difficult (Boon et al., 2019). Based on the results, ibuprofen with 10 mL whereas diclofenac and naproxen with 5 mL were selected as the optimum sample volume for the proposed method (Manzo et al., 2014).

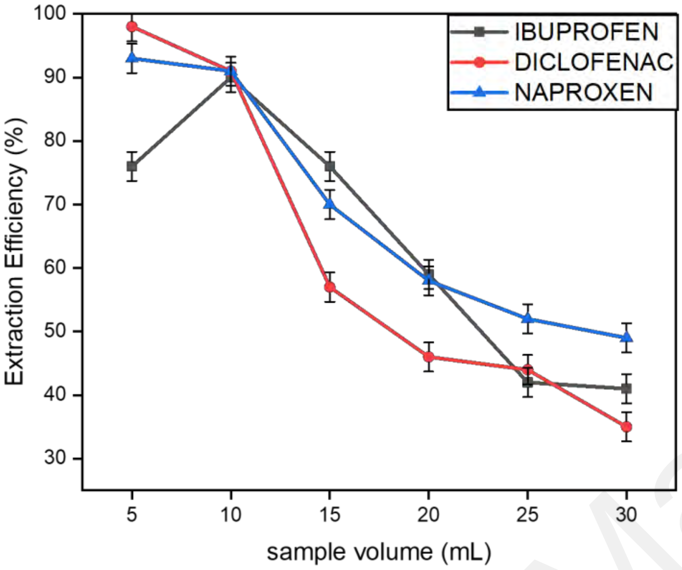


Figure 4.14: Effect of sample volume of MNP-TW on the MNP-TW-MMSPE efficiency of NSAIDs (n=3).

4.2.7 Effect of type of desorption solvent

In the case of MNP-TW-MMSPE, the analytes were desorbed by a polar, organic solvent from the surface of MNP-TW, after extraction. Different desorption solvents were evaluated (methanol, acetonitrile, acetone). In **Figure 4.15**, the best desorption solvent for IBP and DCF were acetonitrile, whereas for NAP was methanol. IBP and DCF are both NSAIDs with similar chemical structures, belonging to the propionic acid derivative and acetic acid derivative classes, respectively. These compounds typically exhibit moderate polarity due to the presence of polar functional groups (such as carboxylic acids) in their structures. While they are not highly polar like some other NSAIDs, they are not considered nonpolar either. In the context of solvent polarity, both IBP and DCF may have varying affinities for solvents based on their moderate polarity. NAP is generally considered to be more polar than IBP and DCF. This is due to its chemical structure, which contains a napthyl and carboxylic acid group, making it more hydrophilic and polar compared to the other two compounds. In the context of solvent polarity, NAP might exhibit higher solubility and extraction efficiency in relatively more polar solvents like methanol, which can better interact with its polar functional groups and facilitate its desorption. The affinity of the desorption solvent towards NSAIDs depends on the solvent polarity and the solubility of the analyte in the solvent. The selected polar solvents have higher solvent strength (Madikizela & Chimuka, 2016; Sarafraz-Yazdi et al., 2012; Yıldırım et al., 2024; Zandian et al., 2024).

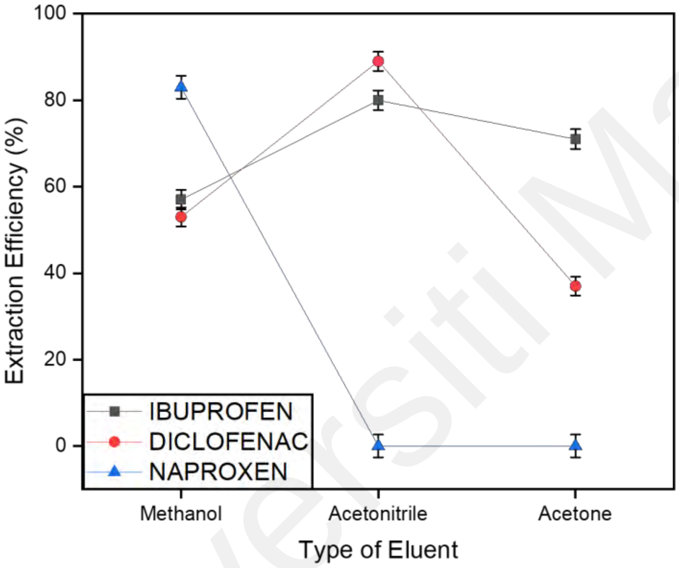


Figure 4.15: Effect of type of desorption solvent of MNP-TW on the MNP-TW-MMSPE efficiency of NSAIDs (n=3).

4.2.8 Effect of desorption time

The vortex method was employed in the desorption process. To ensure complete desorption, the time was tested in the range from 10 to 50 s. In **Figure 4.16**, for IBP, DCF and NAP the analytical signals achieved optimum when desorption time was fixed at 20 s, 40 s, and 30 s for IBP, DCF and NAP, respectively. The optimum desorption time allowed the complete desorption of the analytes from the adsorbent material. The decrease trend observed in **Figure 4.16** after the optimum desorption time could be due to the re-adsorption of the target analytes onto the sorbent upon increased duration leading to incomplete desorption.

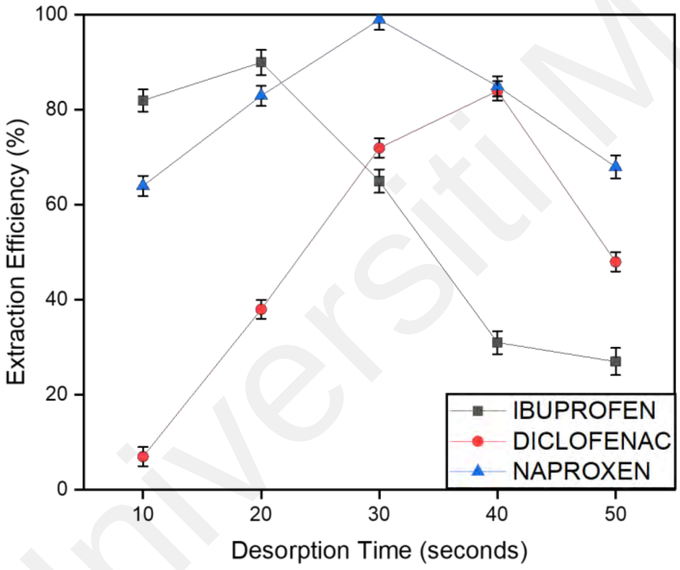


Figure 4.16: Effect of desorption time of MNP-TW on the MNP-TW-MMSPE efficiency of NSAIDs (n=3).

4.2.9 Effect of desorption volume

The effect of desorption volume on the elution of analytes was examined. Desorption volume was investigated from 200 µL to 1000 µL. Based on **Figure 4.17**, all 3 analytes prefer 800 µL as the optimal volume of eluent and sufficient to elute the analyte from the adsorbent to accommodate the maximum extraction from the sorbent, which portrays that the smaller the volume used, the higher the extraction performance.

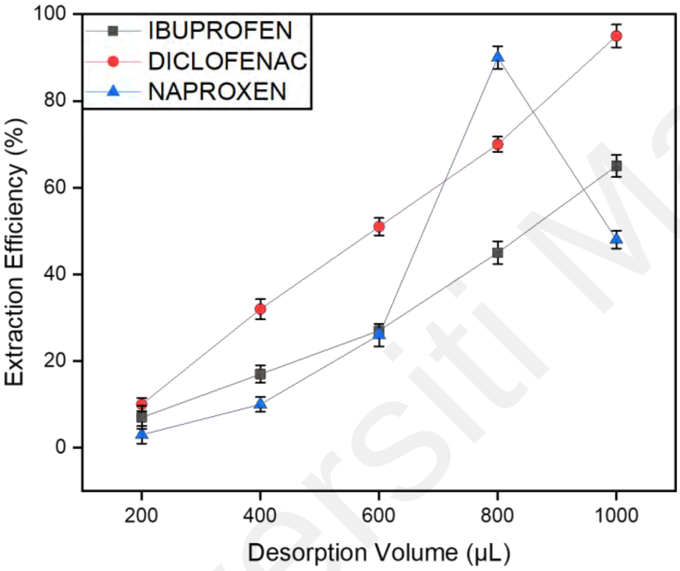


Figure 4.17: Effect of desorption volume of MNP-TW on the MNP-TW-MMSPE efficiency of NSAIDs (n=3).

To sum up, based on the overall outcomes, the optimum extraction parameters were finally selected as presented in **Table 4.3** below.

Table 4.3: Optimum conditions for the extraction of NSAIDs by MNP-TW-MMSPE.

Parameter	Ibuprofen	Diclofenac	Naproxen
Dosage of sorbent	25 mg	25 mg	15 mg
pH	4.0	4.0	4.0
Extraction time	10.0 mins	20.0 mins	20.0 mins
Ionic Strength, % (w/v)	without addition of NaCl salt	without addition of NaCl salt	without addition of NaCl salt
Type of eluent	ACN	ACN	MeOH
Desorption time	20.0 seconds	40.0 seconds	30.0 seconds
Desorption volume	800 μL	800 μL	800 μL
Volume of sample	10 mL	5 mL	5 mL

4.3 Reusability and carryover study

After considering how important it is for the environment to reduce waste and save chemicals, the feasibility of reusing MNP-TW was investigated. The same MNP-TW material that had been fully washed with 1.5 mL of methanol and dried at 65 °C for 30 mins was used for this reusability study. Based on **Figure 4.18**, there was no carryover of analytes during the MSPE method, and the sorbents could be reused up to 2 times with a percentage recovery of >70% *(as per ICH guidelines for analytical method validation)*. This demonstrates MNP-TW and its potential for reuse in the actual MMSPE application.

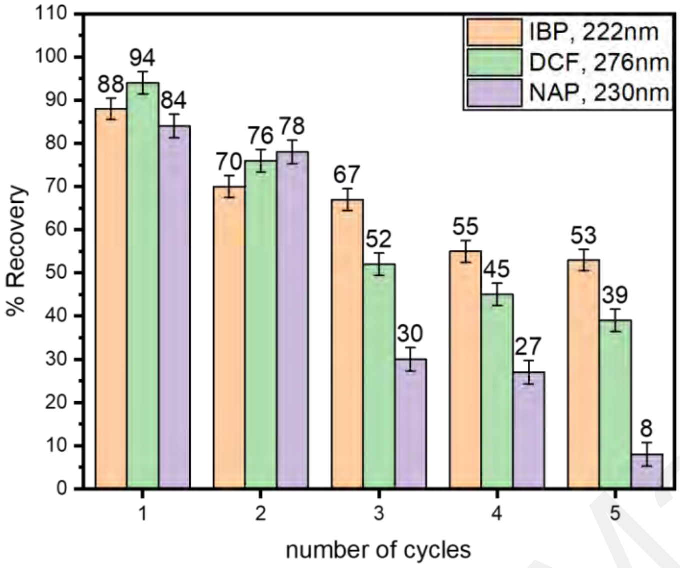


Figure 4.18: The reusability analysis of MNP-TW-MMSPE.

4.4 Method validation

Under the optimized conditions, linearity, the limit of detection (LOD), the limit of quantification (LOQ), precision, pre-concentration factor (PF), matrix effect, and sorbent-to-sorbent reproducibility study were carried out as shown in **Table 4.4** to validate the performance of the proposed MMSPE with UV-Vis spectrophotometric method. The calibration graphs were obtained by plotting the absorbance signal against the concentrations of each target analyte following the standard MMSPE technique. The calibration ranges were between 30 – 700 µg L^{-1} for water samples with three replicates.

Each analyte exhibited a remarkable linearity and a positive coefficient R^2 of determination ranging from 0.9964 – 0.9981 during the analytical performances. The LOD shows between 10.30 – 11.70 µg L^{-1} and LOQ of 31.20 – 35.40 µg L^{-1}. The relative standard deviations (RSD) ranged from 1.48% to 4.83%. This demonstrates higher reproducibility of the MNP-TW preparation method

Table 4.4: Analytical performance values of the developed MNP-TW-MMSPE procedure in water matrices.

Water	Ibuprofen (222 nm)	Diclofenac (276 nm)	Naproxen (230 nm)
linearity (μg L^{1})	30 - 700	30 - 700	30 - 700
(R^2)	0.9980	0.9964	0.9981
LOD (μg L^{-1})	10.30	11.70	11.10
LOQ (μg L^{-1})	31.20	35.40	33.70
Intra-day, (n=30) RSD (%) at 300 μg L^{-1}	1.48	3.98	4.66
Inter-day, (n=10) RSD (%) at 300 μg L^{-1}	1.53	4.12	4.83
Pre-concentration factor at 800 μg L^{-1}	116	174	153

4.5 Sorbent-to-sorbent reproducibility study

The MNP-TW synthesis repeatability was assessed in terms of batch-to-batch or lot-to-lot reproducibility. The extraction efficiency of each batch was studied by spiking 500 μg L^{-1} in water samples employing three batches of sorbents (n=3) that were manufactured under the same conditions but at different times. From **Figure 4.19**, 0.4% to 15.6%, the RSD values appeared to be improved and acceptable. This suggests that the MNP-TW preparation used in this investigation has good reproducibility.

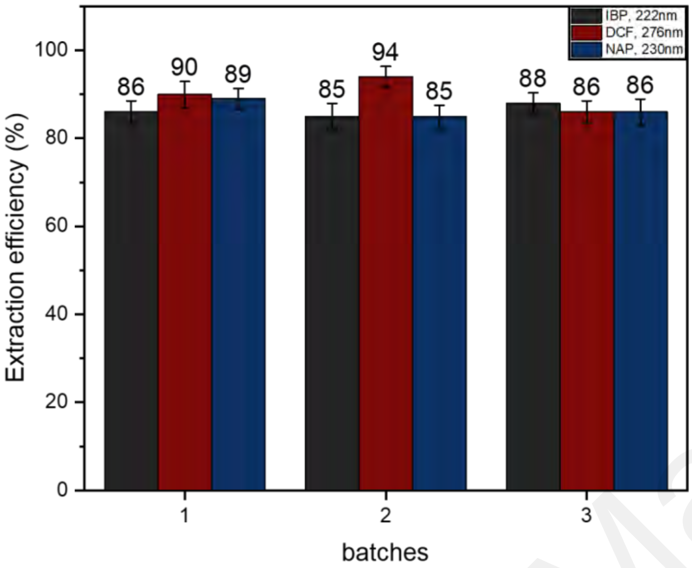


Figure 4.19: The reproducibility analysis of MNP-TW

4.6 Real sample analysis

To study the effectiveness of the suggested method for application on real water samples, tap water and effluent water were tested. The samples were screened for detection of NSAIDs, and the results shows negative and hence the water samples were spiked simultaneously with 100, 400 and 700 µg L^{-1} of all target analytes. All experiments were repeated three times *(n = 3)*. Plotting the absorbance signal against the concentration of NSAIDs species exposed to the usual process under optimal conditions resulted in a calibration graph for the concentration range 30 – 700 µg L^{-1}. The findings were compiled in **Table 4.5**, where the full recoveries for all NSAIDs species fell between the ranges of 82 to 114%. As a result, the technique can be regarded as extracting NSAIDs from samples. **Figure 4.20** shows a typical UV-Vis spectrum obtained from a water sample spiked with NSAIDs at 50 µg L^{-1} and 100 µg L^{-1} evaluated with and without the MNP-TW-µ-SPE technique and compared with an unspiked sample. This indicates that the matrix effect did not have any significant effect on the recovery of the spiked analyte. In addition, it shows the effectiveness of the MNP-TW-µ-SPE to enrich the NSAIDs in water samples.

Table 4.5: Addition-recovery experiments results of NSAIDs in water samples (n= 3).

Analyte	Samples	Correlation of determination, R^2	Spiking (µg L^{-1})	Recovery (% mean ± RSD) n=3
Ibuprofen (222nm)	1	0.9980	100	94
			400	98
			700	113
	2		100	84
			400	86
			700	110
Diclofenac (276nm)	1	0.9964	100	96
			400	105
			700	114
	2		100	84
			400	95
			700	94
Naproxen (230nm)	1	0.9981	100	91
			400	100
			700	103
	2		100	82
			400	83
			700	94

Sample 1 = Tap water
Sample 2 = Effluent water

Figure 4.20 (a), (b), (c) shows the typical UV-Vis spectra obtained from spiked wastewater samples at concentration levels of 50 µg L^{-1} and 100 µg L^{-1}. It was compared with an unspiked sample and spiked wastewater sample at a concentration of 50 µg L^{-1} without MNP-TW-MMSPE. This indicates that the matrix effect did not have any significant effect (negligible) in the extraction efficiency. In addition, it shows the effectiveness of the MNP-TW- MMSPE method in extraction of the NSAIDs in the water sample matrices.

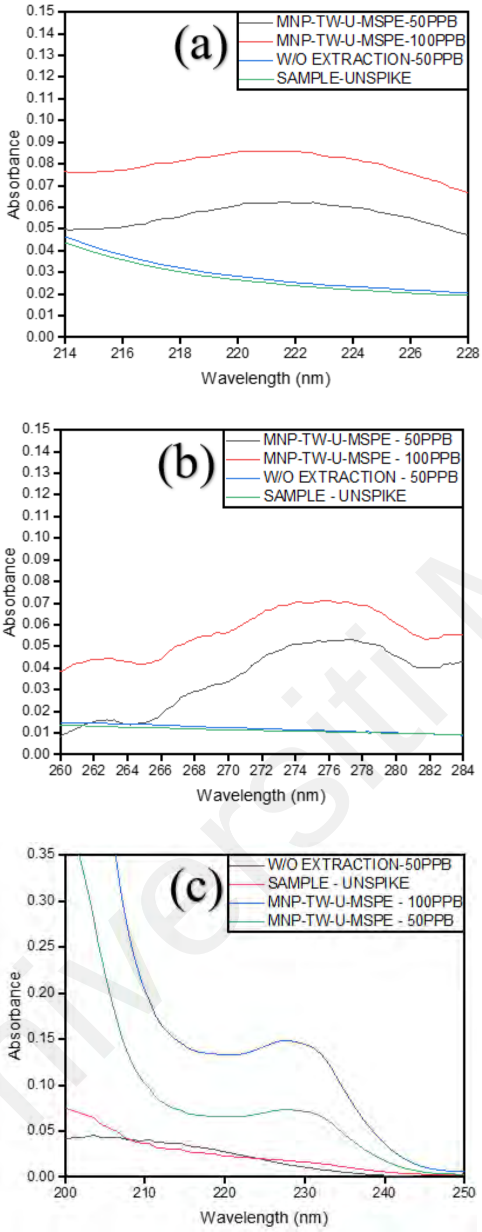


Figure 4.20: Typical UV-Vis spectra of NSAIDs in wastewater sample using MNP-TW-MMSPE. The spectrum corresponds to (a) IBP, (b) DCF and (c) NAP.

4.7 Green assessment analysis

The analytical eco-scale (AES) as a novel comprehensive approach has been chosen to evaluate the level of green analytical methodology. It is evaluated based on the penalty points assigned to parameters of an analytical process that are not in agreement with the idea of green method analysis. This approach compares differences in parameters and steps of the analytical process. The penalty points were contributed for the amounts of chemicals/reagents, the consumed energy by electrical devices, the possible occupational hazards as well and the waste product generated from this method as shown in **Table 4.6**. The allocated penalty points for the reagents are based on the level of risks which include their hazards based on the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (Armenta et al., 2015; Gałuszka et al., 2012; Zain et al., 2014).

If the amount of chemical is < 10 mL (g), 1 penalty point is assigned while 2 penalty points are given for reagent amounts between 10 to 100 mL (g). In addition, the signal word ‘warning’ or ‘danger’ of a reagent is also considered in the hazard penalty. Based on the GHS information, ammonia (25%), acetonitrile, methanol and acetone have been labelled with the signal word ‘warning’, thus assigning 1 penalty point each.

The total energy consumption contributed to 4 penalty points. 0 penalty point was contributed by UV-Vis due to 0.1 kWh of energy per sample being consumed and the other 2 penalty points for each stirrer and orbital shaker during material synthesis that consumed an average of 1.5 hours. 4 penalty points were recommended for waste generation where >10mL of waste was produced during the material synthesis and extraction process. The occupational hazards hold 3 penalty points. Altogether, 23 penalty points were accumulated, and the net value was deducted from 100 points which were the total ideal scores. Therefore, the total AES score was 77 which shows the MNP-TW-

MMSPE method for the determination of NSAIDs in water samples is neatly a green analysis (acceptable green method analysis > 50 points).

Table 4.6: AES scores of the MNP-TW-MMSPE method.

Reagents	**Penalty points**
Ammonia (30%) 10 mL	3
Ethanol 10 mL	3
Acetonitrile 4 mL	2
Methanol 4 mL	2
	∑ 10
Instruments	**Penalty points**
UV-Vis Spectrophotometer	0
Stirrer	2
Oven (> 1.5 kWh per sample)	2
Orbital shaker	2
Occupational Hazard	3
Waste	4
	∑ 13
Total penalty points: 23	
AES Total score: (100-23) = 77	

4.8 Comparison of the MNP-TW-MMSPE method with others

The developed MNP-TW-MMSPE was compared with previous literature for the extraction methods of NSAIDs which are summarized in **Table 4.7**. By comparison, MNP-TW-MMSPE has obtained the lowest LOD among the other methods that have chosen UV-Vis spectrophotometer as the detection instrument. The newly developed MNP-TW-MMSPE method is nothing less, as it has achieved a significantly lower limit of detection even by using tea waste as an adsorbent and UV-Vis spectrophotometer. As discussed in **Table 2.2**, the concentration of NSAIDs detected in Asian countries specifically in urban water cycle and commercial areas near Selangor were recorded in the range of 14.70 – 27.60 µg L$^{-1.}$ MNP-TW-MMSPE has achieved lower LOD (10.3 to 11.7 µg L^{-1}) than the detected concentration (Mohd Hanafiah et al., 2023; Mohd Hanafiah et al., 2022).

It was also observed that MNP-TW-MMSPE has achieved a good pre-concentration factor for microextraction compared to other methods. This clearly shows that MNP modified with agricultural waste such as tea waste has great potential to achieve a lower detection limit, with lower RSD values and great recoveries.

Therefore, the MNP-TW-MMSPE method represents a noteworthy advancement in analytical procedures, offering rapid, reproducible, and straightforward technique with lower LOD and RSD values, alongside satisfactory extraction recoveries of NSAIDs from water samples. This method is reliable for NSAIDs residue detection and quantification in water samples for both environmental monitoring and risk assessment.

Table 4.7: Comparison of the analytical performance of the method developed with other extraction methods in the literature.

Extraction method	Analyte	Linear Range (µg L^{-1})	LOD (µg L^{-1})	Instrument	Pre-concentration factor	Recovery %	Reference
MMSPE (modified with arginine amino acid.)	DCF	50–10000	39	UV-Vis	-	92.0 – 100.8	(Shahhosseini et al., 2021)
MSPE (modified carbon nanodots)	ERY	100–500	60	UV-Vis	6.7	94.8 – 97.6	(Emiroğlu et al., 2021)
UADSPME (molecularly imprinted polymer)	CAR	100–1200	33	UV-Vis	25	97 - 112	(Bazrafshan et al., 2017)
MNP-TW-MMSPE	IBP	30 – 700	10.3	UV-Vis	116	84.0 – 113.0	**This Work**
	DCF	30 – 700	11.7		174	84.0 – 114.0	
	NAP	30 – 700	11.1		153	82.0 – 103.0	

MSPE = Magnetic Solid Phase Extraction; **MMSPE**= Magnetic Solid Phase Microextraction; **UADSPME** = Ultrasound-assisted dispersive Solid Phase Microextraction; **IBP** = Ibuprofen; **NAP** = Naproxene; **DCF** = Diclofenac; **ERY** = Erythrosine; **CAR** = Carbaryl; **LOD** = Limit of Detection; **UV-Vis** = Ultraviolet-visible spectrophotometer

CHAPTER 5: CONCLUSION AND RECOMMENDATION

5.1 Summary

In this study, we have successfully synthesized and characterized tea waste impregnated with magnetic nanoparticles by simple chemical co-precipitation method and investigated their applications in MMSPE techniques for the determination of selected NSAIDs in water samples with UV-Vis spectrophotometry detection analysis.

MNP-TW could be easily separated by magnetic separation technique and showed excellent NSAIDs sorption properties. The morphology studies indicated that iron oxide has completely impregnated the parent tea waste and has aggregated to create a spherical, cage-like structure. In TEM analysis, the MNP-TW retained their initial structures but exhibited a rougher surface with an average particle size of **9.6 nm** compared to MNP with an average particle size of **15.1 nm**. The thinner structures were observed in the MNP-TW as the nanoparticles were well dispersed onto the surface of the tea waste and tended to cluster as they are magnetic, which is essential for the magnetic separation of the target analyte from aqueous solutions. The maximum saturation (*Ms*) of MNP and MNP-TW were 62.51 and 40.47 emu g^{-1}, respectively. Furthermore, the organic component in MNP-TW was roughly 35.3% (w/w), and the difference value of 22.04 emu g^{-1} was calculated. The reduced magnetization indicates the impregnation of MNP on the surface of parent TW which proved the synthesis was successful. All the characterization results confirmed the successful synthesis of MNP-TW.

The newly synthesized MNP-TW exhibits great performance compared to native MNP towards the extraction of NSAIDs in water samples. The analytical features of developed microextraction techniques such as method development, validation and real sample analysis were described in detail. The negligible matrix effect on the studied water samples revealed that MNP-TW enhanced the sample purification and enrichment. This technique attained a good preconcentration factor owing to the outstanding characteristics of tea waste and magnetic nanoparticles.

It is interesting to point out that MMSPE generally achieved better or comparable results than the other techniques because of its extraction process taking a shorter time and it shows higher efficiency.

Under optimized MMSPE conditions, the calibration curves were linear for the NSAIDs concentration ranging between 30 and 700 µg L^{-1} with the correlation of determinations (R^2) from 0.9964 to 0.9981 for all analytes. Besides, the detection limits ranged from 10.30 to 11.70 µg L^{-1} in real matrix with acceptable recovery values from 82 to 114%.

Apart from that, a comparison with previous works also had been presented along with the developed techniques in this study, and surprisingly who exhibited a fair, better, and comparable performance than those reported in the literature.

To sum up, MMSPE technique and MNP-TW adsorbent applied are not new. However, they have been integrated and applied for the sensitive extraction of NSAIDs in water samples. A new application of the combined sorbent and technique has been successfully employed in the study. All the objectives of this study have been achieved accordingly. The findings have successfully addressed the research gaps and the needs as stated in **Chapter 1**.

5.2 Future directions

We have discovered interesting directions for future work, as mentioned below.

(a) Further investigation on the properties and applications of MNP-TW with other NSAID compounds or probably with different pharmaceutical compounds (E.g.: antibiotics) is required since this combination displays great performance with better findings.

(b) To incorporate MNP-TW in the extraction of NSAIDs with advanced instruments like HPLC, GC-FID or LC-MS to acquire lower detection limit with better recovery.

(c) The developed technique can be applied to other types of sample matrices due to the availability of active sites on MNP-TW. Different interactions could be studied for the extraction behaviour including but not limited to ionic bonding, hydrogen bonding, van der Waals forces, π-π interaction, and host guest interaction.

Therefore, future studies on the topics discussed are highly recommended.

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